#medbear
SURGERY NOTES

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TRAUMA (MULTI-SPECIALITY) APPROACH

ADVANCED TRAUMA LIFE SUPPORT ALGORITHM

TRAUMA DEATHS (TRIMODAL DISTRIBUTION):

- Immediate death occurring at time of injury – i.e. due to devastating wounds/lacerations
- Early death occurring within the 1st few hours of injury – i.e. tension pneumothorax, blood loss, IC bleed
- Late death occurring days / weeks after initial injury – i.e. 2° complications – sepsis, ARDS, SIRS, MOF

MAIN PRINCIPLES:

- Treat greatest threat to life first
- Definitive diagnosis is less important
- Time is important – the "golden hour" after trauma is when 30% of trauma deaths occur, and are preventable by ATLS

APPROACH (INITIAL ASSESSMENT)

1. Preparation and Triage
2. Primary survey (ABCDE) and Resuscitation of Vital Functions
3. Re-evaluation of the patient and taking a History of the event
4. Secondary survey (head-to-toe evaluation)
5. Post-resuscitation monitoring and re-evaluation
6. Optimise for transfer and definitive care

PRIMARY SURVEY (ABCDE) AND RESUSCITATION

1. **AIRWAY ASSESSMENT WITH CERVICAL SPINE CONTROL**
   - Ascertain pathway
     - (1) Foreign Bodies, (2) Facial/Mandibular #, (3) Laryngeal/Tracheal #
   - Assess for airway obstruction
     - Engage the patient in conversation – a patient who cannot respond verbally is assumed to have an obstructed airway till proven otherwise
     - (1) stridor, (2) retractions, (3) cyanosis
   - Establish a patient airway
     - Jaw Thrust – displace tongue anteriorly from the pharyngeal inlet relieving obstruction
     - Simple Suctioning / Clear Airway of Foreign Bodies
     - Nasopharyngeal airway / Oropharyngeal Airway
     - Establish a definitive airway
       a. Tracheal Intubation (refer anaesthesia notes for more details)
          - Orotracheal route using rapid-sequence induction (RSI)
          - Pre-oxygenate patient with 100% Oxygen
          - In-line cervical spine stabilisation wither anterior portion of cervical collar removed
          - Sellick Manoeuvre to prevent aspiration (there is increasing controversy as to the utility of cricoid pressure due to concerns about its efficacy and potential for obscuring the view of the vocal chords)
          - Drugs – short acting sedative or hypnotic agent (i.e. etomidate 0.3mg/kg IV or midazolam 1-2.5mg IV) and paralytic agent administered immediately after the sedative (succinylcholine 1-1.25mg/kg IV or rocuronium 0.6-0.85mg/kg IV)
          - ETT tube inserted through vocal chords and adequacy of ventilation is assessed
       b. Needle Cricothyroidectomy with jet insufflation of the airway
       c. Surgical Cricothyroidectomy

- In a multi-system trauma patient assume cervical spine injury till proven otherwise
  - NEXUS C-Spine Clearance (NSAID)
    a. No focal **N**eurological deficit
    b. No **S**pinal (posterior midline cervical) tenderness
    c. Patient is **A**lert and orientated to time / place / person
    d. No evidence of **I**ntoxication
    e. No painful **D**istracting injuries (i.e. long bone fracture)

2. BREATHING (OXYGENATION AND VENTILATION OF THE LUNGS)

- Assessment of breathing
  - Expose the neck and chest: ensure immobilization of the head and neck
  - Determine rate and depth of respiration
  - Inspect and palpate the neck and chest for tracheal deviation, unilateral and bilateral chest movements, use of accessory muscles and any signs of injury (i.e. flail chest)
  - Auscultate chest bilaterally: bases and apices
  - If unequal breath sounds – percuss the chest for presence of dullness or hyper-resonance to determine hemothorax or pneumothorax

- Life-threatening conditions that require immediate attention and treatment [**ATOM FC**]
  - Airway Obstruction – i.e. Tracheobronchial Disruption
  - Tension Pneumothorax (TP)
    - Immediate insertion of a large bore 14G IV catheter into the 2nd IC space, midclavicular line, followed by tube thoracostomy (triangle of safety – mid-axillary line, lateral border of pectoralis major, upper border of the 5th rib)
  - Open pneumothorax
    - Occlusive dressing, taped securely on 3 sides to create a flutter valve effect (if taped all 4 sides can result in TP)
  - Massive Hemothorax (>1500ml)
    - Tube thoracostomy (32Fr or larger) connected to an underwater seal-suction device
  - Flail chest with pulmonary contusion
    - 2 or more ribs that are fractured at 2 segments – no bony continuity with rest of thoracic cage → paradoxical movement (see below)
    - Adequate pain control with aggressive pulmonary toilet and respiratory support (hypoxia 2° to underling pulmonary contusion)
  - Cardiac Tamponade
    - Pericardiocentesis & Direct operative repair

- Management of Breathing
  - Attach pulse oximeter and administer high concentration of oxygen (non-rebreather mask with a reservoir is required to achieve a theoretical FiO_2 of 100%)
  - KIV – ventilate with bag-valve mask if patient requires assistance with breathing
  - Attach an end-tidal CO_2 ($ETCO_2$) monitoring device to the ETT.

- Classes of haemorrhagic shock! (see below 'shock')

3. CIRCULATION WITH HAEMORRHAGE CONTROL

- Hypotension following injury must be considered to be hypovolemic in origin until proven otherwise
- Physiologic response to blood loss vary between individuals (i.e. elderly may not show a normal tachycardia response, worse if patient is on beta-blockers, children have abundant physiological reverse and may demonstrate few signs even to severe hypovolemia)

- Assessment of organ perfusion
  - **Level of consciousness** (secondary to reduced cerebral perfusion)
  - **Skin Colour** (ashen and grey skin of face and white skin of extremities suggest blood loss of at least 30%)
  - **Pulse Rate and Character** (full vs. thread vs. rapid)
  - **Blood Pressure** (if radial pulse present – BP>80mmHg, if only carotid pulse present – BP>60mmHg)

- Management
  1. Apply direct pressure to external site of bleeding
  2. Insert 2 large bore (14G / 16 G) IV catheters (antecubital veins)
  3. Labs: GXM (4-6units), FBC[1], U/E/Cr, PT/PTT, ABG (if no O-negative blood is available use type specific blood)
  4. Initiate vigorous IV fluid therapy with warmed crystalloids (i.e. Ringer's Lactate, 1-2L), KIV blood replacement
  5. Apply ECG monitor / Pulse Oximeter / Automated BP cuff
     - Dysrhythmia: consider cardiac tamponade
     - PEA: consider treatable causes (5Hs and 5Ts)
       - 5Hs – hypovolemia., hypoxia, H+ (acidosis), Hyper/Hypokalaemia, Hypothermia
       - 5Ts – toxicity (drug overdose), tamponade (cardiac), pneumothorax, thrombosis (AMI), thromboembolic (PE)
     - Bradycardia, aberrant conduction, ventricular ectopic: ?hypoxia / hypo-perfusion
  6. Insert indwelling urinary and nasogastric catheters unless contraindicated
     - Urinary Cather insertion is contraindicated when
       - Blood at urethral meatus
       - Scrotal hematoma
       - High-riding prostate
       - Perineal ecchymosis / hematoma
     - NG tube is indicated to reduce stomach distension and decrease risk of aspiration – contraindications include:
       - CXF rhinorrhoea / otorrhea – suggestive of cribriform plate (base of skull) fracture insert NG tube orally instead of nasally
       - Periorbital ecchymosis,
       - Mid-face instability,
       - Hemotympanum
  7. Prevent hypothermia
  8. Reassess frequently

[1] The haematocrit value is not immediately altered with acute haemorrhage – it should not be an indicator of circulating blood volume in trauma patients. Serial haematocrit values, however, may give an indication of on-going blood loss.

4. **DISABILITY / INTRACRANIAL MASS LESION**
   - AVPUP score:
     - Alert
     - Verbal stimuli (responds to),
     - Pain stimuli,
     - Unresponsive,
     - Pupillary size and reaction

   - Glasgow coma scale

Eye		Verbal		Motor	
Spontaneous opening	4	Oriented speech	5	Obeys Command	6
Opens to voice	3	Confused	4	Localizes	5
Opens to painful stimuli	2	Inappropriate	3	Withdraws	4
No response	1	Incomprehensible	2	Decorticate (flex)	3
		No verbal response	1	Decerebrate (extend)	2
				No Movement	1

   GCS: 14-15 (minor); 8-13 (moderate); 3-7 (severe)
   - Any patient with GCS ≤ 8 should be intubated to protect the airway
   - Call for neurosurgical consult as indicated

5. **EXPOSURE / ENVIRONMENT / BODY TEMPERATURE**
   - Completely undress patient by cutting off clothing
   - Look for visible / palpable injuries
   - Prevent hypothermia – "hot air" heating blankets, infusion of warmed IV fluids
   - Inspection back / DRE – log-rolling with in-line cervical spine immobilization
   - Continue monitoring vitals (HR, BP, SpO_2) + ECG + urine o/p (aim: >0.5ml/kg/hr)
   - Trauma-X-ray Series
     - (1) Lateral C-Spine, (2) AP CXR, (3) AP Pelvis
   - Other Investigations
     - Focused abdominal sonography in trauma (FAST)
     - Diagnostic Peritoneal Lavage
     - Computed Tomography

SECONDARY SURVEY
- A complete head-to-toe examination to inventory all injuries sustained in the trauma after primary survey is completed.

1. **AMPLE HISTORY**
- **A**llergies, **M**edications, **P**ast Med Hx, **L**ast meal, **E**vents/environment related to the injury

2. **COMPLETE HEAD-TO-TOE EXAMINATION**
- Head
  - Complete neurological examination – cranial nerves
  - GCS or AVPU assessment (GCS ≤ 8 – KIV intubation)
  - Comprehensive examination of eyes and ears for base of skull fractures (periorbital hematomas – raccoon eyes, mastoid hematomas – battle's sign, hemotympanum, CSF rhinorrhoea and otorrhea)

- Maxillofacial ***frequently missed injuries***
  - Bony tenderness, crepitus or discontinuity
    - Mid-facial fractures – check by grasping maxilla and attempting to move it
  - Palpable deformity
  - Inspect for septal hematoma
  - Comprehensive oral/dental examination
    - Mandibular fracture – check for mucosal violation and abnormal dental occlusion
  - **Caution**: potential airway obstruction in maxillofacial injury; cribriform plate # with CSF rhinorrhoea → do not insert NG tube, use orogastric tube to decompress stomach

- Neck (r/o cervical spine, vascular or aero digestive tract injuries)
  - Nexus C-Spine Clearance
  - Inspect – blunt and penetrating injuries, tracheal deviation, use of accessory breathing muscles (any hoarseness of voice, stridor suggesting airway obstruction)
  - Palpate – tenderness, deformity, swelling, crepitus (subcutaneous emphysema) and tracheal deviation
  - Auscultate – carotid arteries bruit

- Chest
  - Inspect – blunt and penetrating injuries, use of accessory breathing muscles, bilateral symmetrical respiratory excursion
  - Palpate – fractures and subcutaneous emphysema
  - Auscultate – quality / location of breath sounds (and also heart sounds)
    - Also check $EtCO_2$, O_2 saturations, and ABG to ensure adequate ventilation and oxygenation
  - CXR rule out any thoracic extra-anatomic air (subcutaneous air, pneumomediastinum or pneumopericardium)
    - Pulmonary parenchymal injury with occult pneumothorax
    - Tracheobronchial injury
    - Oesophageal perforation
    - Cervicofacial trauma (self-limiting)

- Abdomen (r/o intra-abdominal injury rather than characterise its exact nature)
  - Inspect – blunt and penetrating injuries ("seat-belt sign")
  - Palpate – any lower rib fractures (liver / spleen injuries)
  - Percuss – rebound tenderness
  - Auscultate – bowel sounds
  - Assess Pelvis stability (palpate iliac wings)
  - **Diagnostic Evaluations: FAST, DPL, CT scan**

- Perineal, Rectal & Vaginal Examination
  - **Perineum**: contusion, hematomas, laceration, urethral blood, scrotal hematoma
  - **DRE**: Sphincter tone, high-riding prostate, pelvic fracture (may feel fragments of bone); rectal wall integrity, rectal blood
  - **Vaginal examination**: blood, lacerations

- Musculoskeletal – extremities
  - Back – log-roll patient
    - Inspect – wounds and hematomas
    - Palpate – vertebral step-off or tenderness
  - Upper and Lower Limbs – r/o presence of soft-tissue, vascular, orthopaedic or neurological injuries
    - Inspect – gross deformity, active bleeding, open wounds, expanding hematoma, ischemia
    - Palpate – subcutaneous air, hematomas, presence and character of peripheral pulses
  - Occult compartment syndrome
  - Neurological Examination
  - X-rays as appropriate
  - Ankle-Brachial Indices (ABIs) should be measured if suspicious of possible vascular injury
  - **Caution**: potential blood loss is high in certain injuries (e.g. pelvic #, femoral shaft #) – aim to volume resuscitation, reduce pelvic volume, put external fixator on, KIV angiography / embolization

- Central Nervous System
  - Frequent re-evaluation
  - Prevent secondary brain injury
  - Imaging as indicated
  - Early neurosurgical consultation

GENERAL

- Have a high index of suspicion for injuries to avoid missing them (frequent re-evaluation)
- Rapidly recognise when patient is deteriorating (continuous monitoring)
- Any rapid decompensating by the patient should initiate a return to the primary survey
- In penetrating trauma, all entry and exiting wounds must be accounted for
- IV analgesia as appropriate for pain management

BURNS INJURY MANAGEMENT

Minor: ≤15% TBSA, Moderate: 15-25% TBSA, Severe: ≥25% TBSA
Rule of 9: (adult) – head 9%, back 18%, chest 18%, R arm 9%, L arm 9%, perineum 1%, R leg 18%, L leg 18%
(child) – head 18%, back 18%, chest 18%, R arm 9%, L arm 9%, perineum 1%, R leg 13.5%, L leg 13.5%

Management

- Inhalation injury: intubate and administer 100% oxygen
- Administer 2-4ml / kg / %BSA burn in 24 hours (+maintenance in children) – ½ in 1st 8hr and ½ in next 16hrs (hartmann's solution)
- Monitor urinary output
- Expose and prevent hypothermia
- Chemical burns: brush and irrigate

DISSEMINATED INTRAVASCULAR COAGULATION (DIC) – ACUTE

Systemic processing producing both thrombosis and haemorrhage – 2° to trauma, shock, infection, malignancy (esp. APML), obstetric complications

Pathogenesis

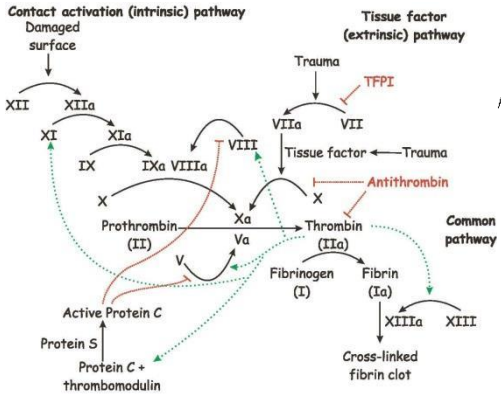
- Massive intravascular activation of coagulation (i.e. thrombin) that overwhelms control mechanisms thrombosis in microvasculature
  - Fibrin deposition in microcirculation
    - Secondary fibrinolysis (due to release of tPA)→ ↑ **FDP → bleeding**
    - Intravascular fibrin strands cause mechanical shearing of RBC → **MAHA**
    - Ischemic organ damage (due to thrombotic manifestations)
  - Acute **consumption of coagulation factors and platelets → bleeding**

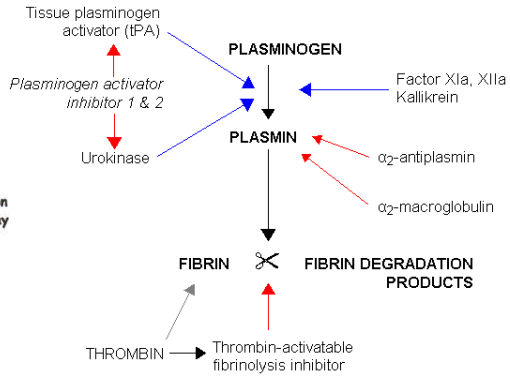
Diagnosis

- ↑ PT/ ↑ PTT, ↓ fibrinogen, ↑ FDP/D-dimer, ↓ platelets, +ve schistocytes, ↑ LDH, ↓ haptoglobin

Management

- Treat underlying process
- Support with FFP, cryoprecipitate & platelet (aim: fibrinogen > 100mg/dL)





ABDOMINAL TRAUMA

- All penetrating injuries below the nipple line should be suspected of entering the abdominal cavity
- All multiple trauma patients with hypotension are assumed to have intra-abdominal injuries till proven otherwise

TYPES OF INTRA-ABDOMINAL INJURY IN BLUNT TRAUMA

- Solid organ injury: spleen, liver – bleeding (may be quite massive)
- Hollow viscus injury with rupture
- Vascular injury with bleeding

INDICATIONS FOR IMMEDIATE LAPAROTOMY

1. Evisceration, stab wounds with implement in-situ, gunshot wounds traversing abdominal cavity
2. Any penetrating injury to the abdomen with haemodynamic instability or peritoneal irritation
3. Obvious or strongly suspected intra-abdominal injury with shock or difficulty in stabilising haemodynamics
4. Obvious signs of peritoneal irritation
5. Rectal exam reveals fresh blood
6. Persistent fresh blood aspirated from nasogastric tube (oropharyngeal injuries excluded as source of bleeding)
7. X-ray evidence of pneumoperitoneum or diaphragmatic rupture

INVESTIGATIONS (IN THE ABSENCE OF THE ABOVE INDICATIONS)

- If patient is stable: FAST and/or CT scan
- If patient is unstable: FAST and/or DPL

FOCUSED ASSESSMENT WITH SONOGRAPHY IN TRAUMA (FAST)

- Rapid, reproducible, portable and non-invasive bedside test to detect fluid in the abdomen or pericardium (≥ 100ml and more typically 500ml of peritoneal fluid, sensitivity: 60-95%)
- Fails to identify injury to hollow viscus and to reliably exclude injury in penetrating trauma

- <u>Ultrasonography evaluation of four windows:</u>
    1. Subxiphoid: Pericardium
    2. RUQ: Perihepatic Space (aka. Morrison's Pouch or hepatorenal recess)
    3. LUQ: Perisplenic Region (splenorenal recess)
    4. Pelvis: Pouch of Douglas (suprapubic window)
    5. (eFAST) – add b/l anterior thoracic sonography – detect pneumothorax

- **Disadvantages**
    - Does not image solid parenchymal damage, retroperitoneum, diaphragmatic defects or bowel injury
    - Compromised in uncooperative, agitated patient, obesity, substantial bowel gas, subcutaneous air
    - Less sensitive, more operator-dependent than DPL and cannot distinguish blood from ascites
    - Intermediate results require follow-up attempts or alternative diagnostic tests

CT SCAN

- Only suitable for stable patient as quite long time involved in imaging with only patient in the room → risk of rapid decompensation

- **Advantages**
    - Able to precisely locate intra-abdominal lesions preoperatively
    - Able to evaluate retroperitoneal injuries
    - Able to identify injuries that can be managed non-operatively
    - Not invasive

- **Disadvantages**
    - Expensive, time required to transport patient, use of contrast

DIAGNOSTIC PERITONEAL LAVAGE (DPL) – RARELY DONE

- Sensitivity of 97-98% with a 1% complication rate
- Useful in hypotensive, unstable patient with multiple injuries as a mean of excluding intra-abdominal bleeding
- Involves an incision in the midline, below umbilicus, dissection down to peritoneum → a catheter is placed and a litre of N/S is run into the peritoneal cavity → bag is then planed on floor and allowed to fill
- All patients undergoing DPL require prior evacuation of the stomach via NG tube as well as drainage of bladder by indwelling catheter
- **Absolute Contraindication**: indication for laparotomy already exists
- Involves making a cut in the infraumbilical region and inserting a catheter into the peritoneal cavity, aspirate, then instillation of saline (1000ml) and re-aspiration

- <u>Positive DPL in setting of blunt abdominal trauma and (penetrating trauma)</u>
    - Frank blood (>10ml) or any enteric contents
    - RBC >100,000 per mm^3 (penetrating: > 10,000 RBC)
    - WBC >500 per mm^3 (penetrating: > 50 WBC)

CARDIOTHORACIC TRAUMA

There are 5 clinical scenarios in chest trauma where bedside procedures are lifesaving: cardiac tamponade, airway obstruction, flail chest, hemothorax, and pneumothorax.

CARDIAC TAMPONADE

High index of suspicion required

Clinical features

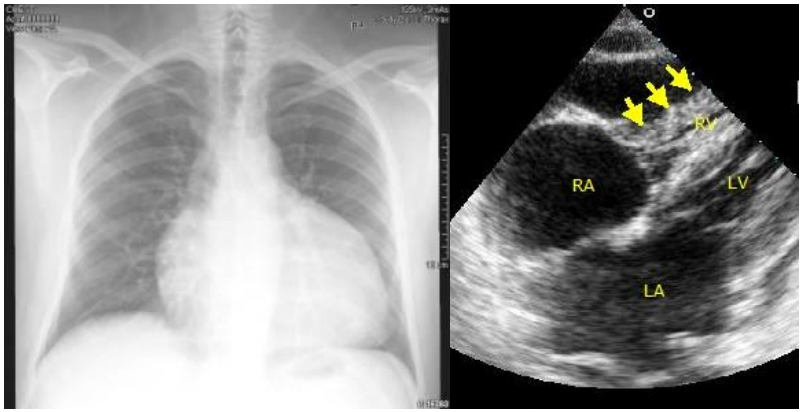
- Chest trauma and hypotension
- Beck's triad (hypotension, muffled heart sounds, distended neck veins) – only in 50% of cases as hypo-vol. may prevent neck vein distension; muffled heart sounds least reliable
- Pulseless electrical activity
- Kussmaul's signs (increased neck distension during inspiration, pulsus paradoxus)

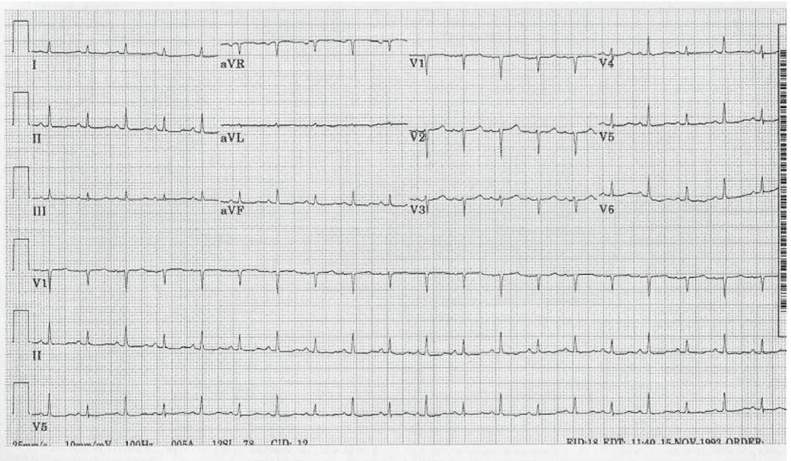
Diagnostic clues

- Enlarged cardiac shadow in CXR (globular heart – very rarely seen)
- Small ECG voltages, electrical alternans = alternation of QRS complex amplitude or axis between beats.
- 2DE – separation of pericardial layers detected (fluid exceeds 15-35ml); early diastolic collapse of RV wall (tamponade)

Management

- Aggressive fluid resuscitation – helps maintain cardiac output and buys time.
- Pericardiocentesis: 2D-echo guided or ECG lead-guided (Stop inserting needle when an abrupt change in the ECG waveform is noted. If the ECG waveform shows an injury pattern (ST segment elevation), slowly withdraw the needle until the pattern returns to normal, as this change in waveform suggests that the spinal needle is in direct contact with the myocardium)





*ACC/AHA definition for low QRS voltage is amplitude <5mm in standard limb leads or <10mm in precordial leads

AIRWAY OBSTRUCTION

Due to laryngeal injury or posterior/fracture dislocation of SCJ

Diagnostic Clues (for laryngeal trauma)

- Hoarseness
- Subcutaneous Emphysema
- Palpable Fracture

Management:

- Definitive airway – ETT, tracheostomy, cricothyroidotomy

FLAIL CHEST

2 or more ribs are fractured at 2 points

Diagnostic Clues

- Paradoxical movement of the chest wall
- Respiratory distress (hypoxemia due to underlying pulmonary contusion, contributed to by pain with restricted chest wall movement)
- External evidence of chest trauma
- Pain on respiratory effort.

Management:

- Ensure adequate oxygenation and ventilation; judicious fluid therapy (avoid fluid overload); adequate intravenous analgesia
- Consider mechanical ventilation in high risk patients: shock, severe head injury, previous pulmonary disease, fracture of ≥8 ribs, age > 65, ≥3 associated injuries

MASSIVE HAEMOTHORAX

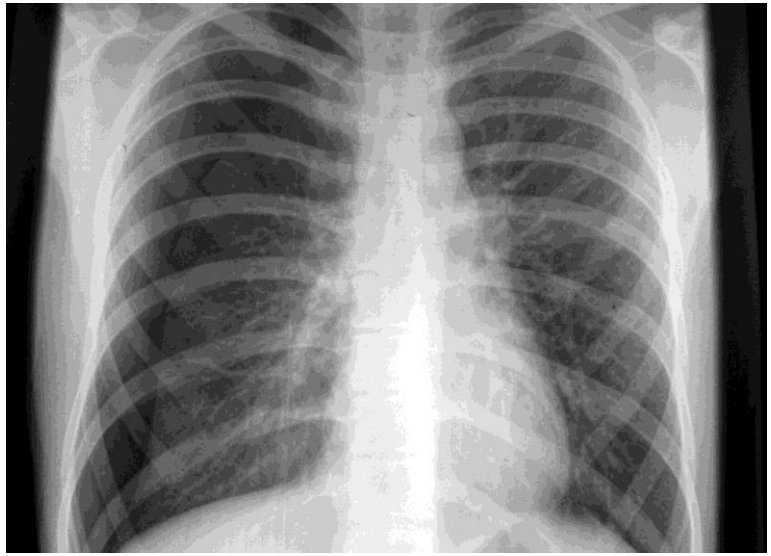
blood >1500mls or on-going haemorrhage of more than 200ml / hr over 3-4 hours

Management:

- Ensure adequate oxygenation, establish 2 large bore IV access and fluid resuscitation (KIV blood transfusion and correction of coagulopathy)
- Chest tube insertion in the triangle of safety (bound by the lateral border of the pectoralis major medially, a line just anterior to the mid-axillary line laterally, and the upper border of the fifth rib inferiorly)
- Be wary of sudden cessation of chest tube drainage as tube can get blocked by clot
- massive hemothorax, call urgent cardiothoracic consult

note: think of possible damage to great vessels, hilar structures and heart in penetrating anterior chest wounds medial to nipple line and posterior chest wounds medial to scapula

PNEUMOTHORAX (TENSION/ OPEN)



Tension pneumothorax = develops when air is trapped in the pleural cavity under positive pressure, displacing mediastinal structures and compromising cardiopulmonary function

- It is a clinical diagnosis (CXR will only delay treatment, and may cause death) – signs of pneumothorax, hypotension, neck vein distension, severe respiratory distress
- Decreased venous return caused by compression of the relatively thin walls of the atria impairs cardiac function. The inferior vena cava is thought to be the first to kink and restrict blood flow back to the heart. It is most evident in trauma patients who may be hypovolemic with reduced venous blood return to the heart.

Management

- Needle thoracotomy: 14G needle, 2nd IC space in the midclavicular line
- Followed by tube thoracotomy at the 5th IC space between anterior and mid-axillary line. (triangle of safety: lateral border of the pectoralis major medially, a line just anterior to the mid-axillary line laterally, and the upper border of the fifth rib inferiorly)*

Open pneumothorax occurs in a large chest wall defect with equilibration between intrathoracic and atmospheric pressure, producing a "sucking chest wound".

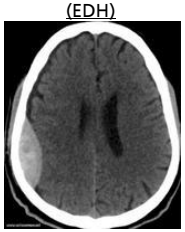
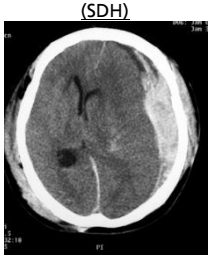
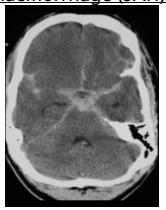
- Cover defect with a sterile dressing, taping it down on 3 sides to produce a flutter-valve effect, letting air out of the pleural cavity but not back in
- Insert chest tube (not through the wound)

* If possible (provided no cervical spine injury is suspected) the patient is sat up at 45deg and the hand is placed behind their neck on the affected side to expose the field and open up the intercostal space. The area is prepared with antiseptic and draped. LA is infiltrated into the skin, sub-cut tissues and down to the pleura. A 2 cm transverse incision is made in 5th IC space (aiming above the rib as the IC NVB sits in the groove just below the rib). Blunt dissection is then performed down to the pleura with a pair of forceps which then are pushed through the pleura into the pleural space. A finger is placed in the hole and swept around to free any adhesions and create the space for the tube. A chest drain is inserted using a pair of forceps; usually French gauge 24–28 (if a hemopneumothorax exists, a larger tube size, Fr. 38, is usually used). The drain is fixed with a stitch and a purse-string or mattress suture is placed in the wound (to allow it to be closed when the drain is removed). The chest drain is connected to an underwater seal (this allows air to escape during expiration, but no air to enter on inspiration). Ensure that the underwater seal is below the level of the patient, otherwise the water will enter the chest. Re-X-ray the patient after the procedure to ensure correct positioning of the tube.

NEUROSURGICAL TRAUMA

AIM: prevention of secondary brain injury (from hypotension, hypoxemia, increased ICP etc.) since neuronal death is irreversible.

PATHOLOGIES

Concussion	• Physiological dysfunction without anatomical or radiological abnormality (physiological dysfunction is the first step towards cell death, but is reversible if no further insult occurs) • Usually recovers in 2-3 hours	
Contusion	• Small haematoma <1cm	
Intracranial haemorrhage	Extradural haemorrhage (EDH) 	Lens-shaped haematoma: between skull & dura • Pathology: result from laceration of middle meningeal artery due to temporal bone # – can cause rapid neurological deterioration – if > 1cm in width or have positive clinical symptoms → urgent surgical evacuation • Classically presents with 'lucid interval' which precedes rapid deterioration • 20% of patients with EDH are alert and well; brain is minimally damaged, thus drainage gives good results
	Subdural haemorrhage (SDH) 	Crescent shaped haematoma: between dura & arachnoid **Acute SDH**: high-speed acceleration / deceleration trauma which shears small bridging (emissary) veins • More severe than EDH (usually due to nature of injury that causes SDH to occur – associated with higher impact, thus brain has other injuries) – (i.e. shaken baby syndrome, in which similar shearing forces classically cause intra- and pre-retinal haemorrhages) • Pathology: underlying brain damage in addition to expanding SOL • Removal of blood does not solve brain damage → poorer results **Chronic SDH:** present in elderly and alcoholics days to weeks after initial HI – can cause focal neurological deficits, AMS, metabolic abnormalities and/or seizures • If symptomatic = stop anticoagulants / antiplatelets, reverse effect by FPP, PT complex, factor Vii, platelet transfusion, observe and monitor, once resolve = burr-hole drainage + subdural drain placement
	Traumatic subarachnoid haemorrhage (SAH) 	Star shaped appearance (cisterns) • Usually only small amount of blood → conservative tx sufficient
	Intraparenchymal haemorrhage (IPH)	Any shape, size, location • If large haematoma, will require evacuation

Diffuse axonal injury	• A major causes of unconsciousness and persistent vegetative state after head trauma • If severe, will see punctate haemorrhages at the grey-white border • Arises from injury that causes rotational and shearing forces (high impact injury) – rapid acceleration and deceleration of brain in the intracranial cavity against relatively fixed points of attachment at the falx and tentorium (e.g. RTA, falls, assaults, shaken baby syndrome) • Maximal effects at corpus callosum and brainstem
Cerebral oedema (3 types)	Hypoxic / Cytotoxic (cellular) • Decreased blood supply (oxygenation) → loss of function of Na-K pump as ATP decreases → increased intracellular sodium → cellular swelling • Conventionally thought to be resistant to any known medical treatment
	Interstitial • Impaired absorption of CSF → increases in transependymal CSF flow → acute hydrocephalus • Also not responsive to steroid administration, and its response to osmotherapy is debatable
	Vasogenic • Breakdown of blood-brain barrier → proteins enter interstitial space → oedema • Seen in TBI, neoplasms, and inflammatory conditions • This oedema subtype is responsive to both steroid administration and osmotherapy

PATHOPHYSIOLOGY

Monroe-Kellie doctrine	The CNS & its contents (brain, CSF, blood) are enclosed in a rigid space whose total volume tends to remain constant → increase in the volume of one component will elevate pressure and decrease the volume of one of the other elements **Cerebral perfusion pressure = Mean arterial pressure – Intracranial pressure** **'When an intracranial mass is introduced, compensation must occur by a reciprocal decrease in the volume of venous blood and CSF'** Compensatory mechanisms: • Hyperventilation → vasoconstriction of cerebral vessels due to ↓ pCO_2 → ↓ blood volume • CSF pushed into spinal canal (but limited volume available) → Removal of any reversible cause of raised ICP will improve cerebral perfusion
Fixed dilated pupil	• Early → gradual dilation, sluggish response to light ipsilateral to the lesion • Late → dilatation of ipsilateral pupil and non-reactive to light • Final → bilateral pupil dilatation and fixation • Constrictor fibres to the pupil run in the oculomotor nerve, which exits the brainstem at the upper midbrain – nerve fibres lie just under the tentorium • Uncus of the temporal lobe sits on the tentorium • In raised ICP, the **uncus herniates over the edge of the tentorium**, compressing the fibres of the oculomotor nerve just below • Thus a fixed dilated pupil occurs on the side of the compression due to **unopposed sympathetic supply** (dilates the pupil)
Cushing's reflex **(very late px of brain stem dysfunction)**	A triad of: Widened pulse pressure (HTN) Irregular breathing (Cheyne-Stokes breathing) Bradycardia From Monroe-Kellie, ↑ MAP maintains cerebral perfusion pressure when ICP is raised. Increase in mean arterial pressure achieved by sympathetic overdrive: a) Increased heart rate b) Increased contractility c) Increased vasoconstriction – increased total peripheral resistance (a) and (b) increase cardiac output → increased BP; (c) increases BP • Baroreceptors detect abnormally raised BP and try to decrease it by triggering a parasympathetic response via vagus nerve + Direct distortion of vagus nerve due to raised ICP → heart rate ↓↓ • Distortion and/or increased pressure of brainstem (controls involuntary breathing) → irregular breathing and/or apnoea

RELATIVE INDICATIONS FOR SURGICAL EVACUATION

- Neurologic symptoms 2° mass lesion, midline shift > 5-10mm
- Elevated ICP refractory to medical management

MANAGEMENT

Assessment

3 important parameters: ABCs, GCS, pupil size

Minor head injury (GCS >13)	• Most common • Indications for admission: Persistent headache and/or vomiting CSF leak Neurological deficit Skull fracture History of loss of consciousness Amnesia • In ward: NBM, IV drip (no dextrose saline!), no sedation, monitor GCS • If pt deteriorates → CT scan Exclude metabolic causes (e.g. hypoglycaemia) Do septic workup (exclude sepsis)
Mod. head injury (GCS 8 - 13)	• All will be CT-scanned at ED → NES will operate if any indication to do so • In ward: as per mild head injury
Severe head injury	Must scan to look for reversible causes of raised ICP but stabilise patient first Screen for other life-threatening injuries (likely to be multi-trauma patient) Management of ICP – to maintain CPP and prevent cerebral edema • **Medical** – osmosis diuresis, loop diuretics NOT steroids • **Surgical** – CSF diversion, decompression, removal of mass effect • **Raise head of bed** (improves venous drainage but could ↓ BP to the head) • **Intubate and hyperventilate** (the induced constriction of blood vessels limits blood flow to the brain at a time when the brain may already be ischemic -- hence it is no longer widely used. Furthermore, the brain adjusts to the new level of carbon dioxide after 48 to 72 hours of hyperventilation, which could cause the vessels to rapidly dilate if carbon-dioxide levels were returned to normal too quickly) • **IV mannitol**: create a hypertonic solution within the blood to draw water out of the neurons. This helps to reduce the fluid within intracranial space, however prolonged administration may lead to increase in ICP (must catheterise patient also; do not give if patient is unstable) Achieve haemodynamic stability • Check for long bone fractures • FAST for bleeding into abdominal cavity • ABG to detect acidosis • Keep monitoring patient and re-investigate where appropriate Operate if reversible cause found • **Craniectomy** (i.e. bone flap not replaced) or **craniotomy** (bone flap replaced after blood evacuated) [Burr hole usually not big enough to drain an acute bleed] • Evacuate clot • Insert endo-ventricular drain (EVD) if there is hydrocephalus Total sedation after operation, ward in ICU • Prevents patient from struggling which will raise ICP
Depressed skull #	• Can leave alone unless depression is greater than the thickness of the skull bone
Compound depressed fracture	• There is through-and-through skin laceration over the fracture • Always explore to ensure underlying dura is intact, and repair if dura is torn (since meningitis can occur with a torn dura)

MUSCULOSKELETAL TRAUMA

GENERAL POINTS

- Extremity trauma tends not to be life-threatening
- But occult blood loss can occur in large volume – i.e. pelvic # (up to 3L), femoral shaft # (2L)
- Need to have high level of suspicion and treat with urgency
- Look out for any tachycardia, early signs of shock
- Prepare to resuscitate patient

ASSESSMENT OF THE EXTREMITY

- Perfusion: colour, pulses, skin temperature, capillary refill
- Viability of the limb
- Neurological assessment
- Wounds – open or closed injury; abrasion over a fracture is considered open fracture
- Soft tissue assessment
- Deformity
- Abnormal joint mobility – ligamentous injury around joint; in knee, highly likely that popliteal artery is injured as well

THE PULSELESS EXTREMITY	**Things to consider** • Is pulselessness due to shock? • Arterial or venous compromise? • Is there compartment syndrome (pulselessness is a very late sign) • Any pre-existing vascular disease? **Physical examination** • Any limb deformity (can result in kinking of vessels)? • Any joint instability (dislocation of a joint can result in intimal tear in the major vessel running across it, with thrombosis and occlusion)? • Skin colour/temperature • Post-reduction tibial pulse in knee dislocation – if still absent, do an urgent angiogram!
SOFT TISSUE INJURIES	**Types** • Open: laceration, abrasion • Crushing • De-gloving: open or closed • Closed **Wound care** • Swabs of the wounds for culture and sensitivity • IV antibiotic prophylaxis • Tetanus toxoid cover • Photograph wound • Betadine (povidone-iodine) dressing • In OT: generous debridement, irrigation (within 4-8 hours, especially in open fractures), fracture stabilisation (internal or external fixation depending on Gustilo classification) • Leave wound OPEN

MANAGEMENT OF FRACTURES	• Recognise fracture and/or dislocation • Complete neurovascular examination of the limb involved before reduction • Appropriate X-rays (at least 2 planes) • Analgesia • Correction of deformity • Temporary immobilisation – backslab, malleable splint • Neurovascular examination; examine for compartment syndrome • Circulation chart

	OPEN FRACTURES
	Definition: a fracture with direct communication to the external environment
	
	Gustilo-Andersen classification
	Type I: <1cm AND clean
	Type II: >1cm AND no extensive soft tissue injury, moderate contamination, no periosteal stripping
	Type IIIA: Extensive soft tissue injury, contamination & periosteal stripping but adequate soft tissue coverage of bone OR > 10cm, high energy trauma
	Type IIIB: Extensive soft tissue loss, contamination with periosteal stripping and exposure of bone which requires replacement of exposed bone with a free flap for coverage
	Type IIIC: Extensive soft tissue loss, contamination with periosteal stripping and Arterial injury requiring repair
	
	Management of open fractures
	• Stabilise patient – trauma survey and resuscitation
	• IV broad spectrum antibiotics & updated tetanus prophylaxis
	  ○ Type I & II: 1st gen cephalosporin
	  ○ Type III: 1st gen cephalosporin + aminoglycoside
	  ○ ± penicillin for anaerobic coverage (if indicated –i.e. bowel contamination)
	• Pain relief and analgesia
	• Photograph Wound
	• Cover the wound with sterile saline soaked dressing/gauze
	• Temporary immobilisation and splinting
	• Appropriate X-rays
	• NBM
	• Pre-op investigations: FBC, U/E/Cr, PT/PTT, GXM, ECG, CXR
	• Arrange for emergency operation
	• Angiogram if needed
	
	Surgery involves
	• Aggressive debridement and irrigation with low pressure saline lavage
	  ○ Bony fragments without soft-tissue attachment can be removed
	  ○ Type I: 3L, Type II: 6L, Type III: 9L
	• Fracture Stabilization – internal or external fixation
	• Staged debridement and irrigation – Q24-48hrs as indicated
	• Early soft tissue coverage or wound closure

SHOCK

- Definition: inadequate tissue and organ perfusion to meet metabolic demands leading to eventual global cellular hypoxia
- Hypotension: **SBP < 90mmH or MAP <60mmHg or reduction in SBP >30mmHg from baseline**

- Pathophysiology of Shock
  i. MAP ∝ CO x SVR
  ii. CO = SV x HR
  iii. SV ∝ preload, afterload and myocardial contractility
  iv. → **MAP ∝ HR, preload, afterload, contractility**
- With systemic hypotension = release of catecholamines, aldosterone, renin and cortisol which act together to increase HR, preload, afterload and contractility.

RECOGNITION OF SHOCK

- Inadequate tissue perfusion
  i. Skin – cold, pale, decreased capillary refill
  ii. Renal – decreased urine output (<0.5ml/kg/hr)
  iii. CNS – anxiety, confusion, lethargy
- Increased sympathetic tone
  i. Narrowed Pulse Pressure
  ii. Tachycardia

Class	1	2	3	4
Blood Loss (%)	< 15	15-30	30-40	>40
Blood Loss (ml)	< 750	750–1500	1500–2000	> 2000
Heart Rate (bpm)	Normal (<100)	>100	>120	>140
Blood Pressure	Normal	SBP – N DBP – ↑	SBP – ↓ DBP – ↓	SBP – ↓ ↓ DBP – ↓ ↓
Pulse Pressure	Normal or Increased	Decreased	Decreased	Decreased
Respiratory Rate	Normal (14-20)	↑ (20-30)	↑ ↑ (30-40)	↑ ↑ ↑ (>35)
Urine Output (ml/hr)	Normal (>30)	↓ (20-30)	Oliguria (5-15)	Anuria (<5)
Mental State	Minimal Anxiety	Mild Anxiety	Confusion	Lethargy
Fluid Replacement (3:1 rule)	Crystalloid	Crystalloid	Crystalloid + Blood	Crystalloid + Blood

*The first noticeable change in systemic BP is a drop in pulse pressure, increased SVR in response to decrease preload predominantly increases the diastolic BP resulting in an overall decrease in pulse pressure
** Narrowed pulse pressure = less than 25% of systolic value

- Stage 1: Normal BP as compensated by increased systemic vascular resistance
- Stage 2: ↑ HR, postural hypotension, ± sweating / anxiety – partially compensated by increased SVR
- Stage 3: Systolic BP <100 mmHg, ↑ HR, ↑ RR, altered mental state (confusion)
- Stage 4: Very low BP, ↓ HR, weak pulse pressure, depressed mental state, urine output negligible

ENDPOINT OF RESUSCITATIONS[2]

- Normalization of BP, HR, Urine Output → most patient (50-85%) still in "compensated" shock
- Serum markers – **lactate** (<2 mmol/L), **base deficit** (between -2 and +2) & **gastric mucosa pH** (7.30 – 7.35) are more appropriate end-points → aim for normalization within 24hours

[2] J Trauma. 1998 May;44(5):908-14.

TYPES OF SHOCK

Shock Classification	Causes	Sign & Symptoms	Investigations
Hypovolemic Loss of circulating blood volume	Acute Hemorrhage (usually at least 20%) Dehydration – burns Severe GE, Others: acute pancreatitis, ruptured AAA, ruptured ectopic pregnancy	Pallor Cold Clammy Skin ↑ HR ↑ peri vas Ω ↓ JVP	FBC U/E/Cr Cardiac Enzymes PT/PTT GXM ABG UPT
Cardiogenic Intrinsic cardiac failure	Blunt Cardiac Injury AMI Others: Valvular Stenosis, Regurgitation or Rupture, Ischemia, Arrhythmias, Cardiomyopathy, AVSD	Pallor Cold clammy skin ↑ HR ↑ peri vas Ω ↑ **JVP** **Pulmonary Edema**	Cardiac enzymes ECG
Obstructive impaired venous return	Tension Pneumothorax^ Cardiac Tamponade Pulmonary Embolism ^ Tension pneumothorax = air enters pleura space → flap valve mechanism prevents escapes → increased intra-pleural pressure → long collapse → mediastinal shift → impaired in venous return → decreased cardiac output	↑ JVP	D-dimer
Neurogenic (distributive) Loss of symp. tone*	Spinal injury * lack of sympathetic tone → decreased SVR → pooling of blood in extremities → hypotension	Warm peripheries N/↓ heart rate Neuro deficit ↓ JVP	Normal
Septic (distributive)	Infections – sepsis (SIRS)	Fever, Rigor Warm peripheries ↑ HR ↓ peri vas Ω (hyper-dynamic state) ↑ CO ↓ JVP	FBC Bld C/S CRP
Anaphylactic (distributive)	Bites / Stings Allergens – Drugs / Food	Fever, rigors Warm peripheries a/w angioedema, bronchospasm	

MANAGEMENT

- **Aim:** ensure adequate delivery of oxygen to the peripheral tissues by optimizing Sao_2, Hb concentration and Cardiac Output
  - i. Sao_2 – maximized in acute setting, check with pulse oximetry
  - ii. [Hb] – transfusion trigger of 7g/dL
  - iii. CO – HR and SV (estimated indirectly from ECG tracing)

General Management	
Recognize early features of shock	▪ Narrowed Pulse Pressure, Postural Hypotension ▪ Tachycardia ▪ Hypotension → SBP <90mmH or MAP <60mmHg or ↓ in SBP >30mmHg from baseline ▪ Assess hypotensive patients early
Airway	▪ Maintain airway – 100% oxygen with non-rebreather mask ▪ Consider intubation if necessary
Breathing	▪ 100% O_2 via non-rebreather mask
Circulation	▪ 2 large bore (14-16G) IV catheter (start fluid resuscitation) ▪ ± Inotropic support ○ IV dopamine 5-10μg/kg/min ○ IV dobutamine 5-10μg/kg/min (esp. for cardiogenic shock) ○ IV norepinephrine 5-20μg/kg/min (esp. for septic shock)
Monitoring	▪ Vitals – HR, BP, SpO_2, RR, Temperature ▪ ECG ▪ Urine output – Indwelling Urinary Catheter
Evaluate Life-Threatening Causes	▪ Tension Pneumothorax – decompress with 14G cannula over the 2nd inter-costal space midclavicular line ▪ Cardiac Tamponade – Start IV fluid bolus with 500ml N/S and/or IV dopamine infusion 5 ug/kg/min and prepare for pericardiocentesis
Identify Underlying Causes	▪ History – current symptoms (trauma, infective), past medical hx (IHD, medications) ▪ Examination – vitals, urine output, systemic review, PR exam ▪ Investigations (as indicated) – FBC, GXM, PT/PTT, U/E/Cr, Cardiac Screen (enzymes + ECG), ABG, CXR, Septic Work-up (Blood Culture, Inflammatory Markers – i.e. CRP)
Inform Senior Early	

Hypovolemic Shock	
Investigations	▪ FBC (hct – unreliable, may be falsely elevated in acute alcohol abusers (diuretic effect of alcohol), (absolute neutrophil count is neither sensitive nor specific in septic shock) ▪ U/E/Cr ▪ Troponin T (cardiac enzyme) ▪ PT/PTT, D-dimer (coagulation profile with DIVC screen) ▪ GXM 6 units ▪ ABG – metabolic acidosis + elevated lactate + base deficit = poor prognosis ▪ UPT – r/o ectopic pregnancy (Ask for LMP) ▪ ECG & CXR – any associated chest pain and breathlessness ▪ Urine Dipstick (with placing of an indwelling urinary catheter) ▪ Examine abdomen for any pulsatile AAA ▪ CVP line insertion to guide fluid resuscitation
Fluid Rx	▪ 1 L crystalloid fast infusion within 1 hr ▪ Assess response ▪ Subsequent colloid or whole blood infusion

Cardiogenic Shock	
ECG Trop T & cardiac enzymes	Manage accordingly – refer acute coronary syndrome & ACLS notes

Obstructive Shock	
Tension Pneumothorax	Refer to Emergency Medicine Black Book
Cardiac Tamponade	**Clinical Likelihood of PE (Well's Score)**
Pulmonary Embolism	Clinical Symptoms of DVT – dyspnea of sudden onset, tachypnea (> 20), chest pain (pleuritic / sub-sternal) – 3 Other Diagnosis less likely than PE – 3 HR > 100bpm – 1.5 Immobilization or Surgery in previous 1/12 – 1.5 Previous DVT / PE – 1.5 Hemoptysis – 1 Malignancy (with treatment within 6/12) – 1 0-2 Low (15%) 3-6 Mod (29%) > 6 High (59%) > 4 consider dx imaging ≤ 4 – KIV D-dimer

Neurogenic Shock	
Hx/PE	▪ Trauma – site, mechanism, force ▪ Neuro exam, DRE – document initial neurological deficits ▪ Triad of hypotension, relative bradycardia and hypothermia
Immobilize	▪ Immobilize spine in neutral position
Investigations (50% in C-spine)	▪ C-spine X-ray (AP & lat) – ensure visualization up to C7/T1 junction ▪ ± Swimmer's view (visualize C7/T1 joint) & open mouth view (visualize C1/2 injury) ▪ Thoracic & lumbar spine X-ray (AP & lat) ▪ ± CT / MRI scan
Fluid Rx	▪ Titrate fluid resuscitate with urine output ▪ ± vasopressors if BP does not respond to fluid challenge
IV high dose methylprednisolone	▪ **30 mg/kg over 1st hour, followed by 5.4mg/kg/h for next 23 hrs** ▪ Indications – non-penetrating spinal cord injury & w/in 8 hrs of injury ▪ Contraindications ○ <13YO ○ Pregnancy ○ > 8 hours after injury ○ Brachial Plexus Injury
Differential	Differentiate from spinal shock (a state of transient physiological reflex depression of cord function below level of injury a/w loss of all sensorimotor functions) – spinal shock has increase in BP due to release of catecholamines followed by hypotension, flaccid paralysis and bladder/bowel paralysis noted. These symptoms last several hours to days until the reflex arcs below level of injury begin to function again – bulbocavernous reflex – spinal shock is not true shock
Disposition	▪ Refer Ortho / NeuroSx

Septic Shock (severe sepsis + refractory hypotension)

SIRS = ≥ 2 of the following present:
- Temp >38 or <36°C
- HR > 90bpm
- RR > 20 breaths/min OR $PaCO_2$<32mmHg
- WCC>12000/mm^3, <4000/mm^3,or >10% immature forms

Note: immunocompromised patients can be septic without eliciting an inflammatory response

Clinical Definition of Sepsis Syndrome	▪ **Sepsis** = SIRS + documented infection ▪ **Severe Sepsis** = sepsis + evidence of end-organ dysfunction → as evidenced by hypotension (SBP < 90mmHg), hypo-perfusion (oliguria, elevated lactate) ▪ **Septic Shock** = severe sepsis + refractory hypotension	
Clinical Effects	▪ Flushed, warm peripheries ▪ Hypotension, Tachycardia, Tachypnea, ▪ Hypoxia ▪ Metabolic Acidosis ▪ Deranged Clotting Function	
Hx / PE	▪ Identify site of infxn – UTI (indwelling catheter), gallbladder dz, peritonitis, pneumonia, appendicitis, immunocompromised state	
Investigations	▪ **FBC:** ↑ TW ▪ U/E/Cr ▪ DIVC screen – PT/PTT, platelet, fibrinogen, D-dimer ▪ **Blood C/S** (2 different sites) ▪ **Capillary blood glucose** ▪ ABG ▪ **CXR:** pneumonia, ARDS ▪ ECG ▪ Urine dipstick – UTI ▪ **Urine C/S**	
Fluid Rx	▪ Rapid infusion 1-2L crystalloids ▪ ± CVP line insertion	
± Inotropic support	▪ if no response to fluid Rx ▪ Noradrenaline (drug of choice) – 1μg/kg/min OR ▪ Dopamine 5-20μg/kg/min	
Empirical Abx	Immunocompetent w/o obvious source	▪ 3rd gen cephalosporin (**IV ceftriaxone 1g**) OR ▪ Quinolones (**ciprofloxacin 200mg**)
	Immunocompromised w/o obvious source	▪ Anti-pseudomonal Abx (**IV ceftazidime 1g**) OR ▪ **Quinolone** ▪ PLUS aminoglycoside (**Gentamicin 80mg**)
	Gram-positive (burns, FB / lines present)	▪ **IV cefazolin 2g** ▪ **IV vancomycin 1g** if hx of IVDA, indwelling cath. Or penicillin allergy
	Anaerobic source (intra-abdo, biliary, female genital tract, aspiration pneumonia)	▪ **IV metronidazole 500mg + ceftriaxone 1g + IV gentamicin 80mg**
Prognosis	▪ 1 organ – 70% survival ▪ 2 organs – 50% survival ▪ 4 organs – mortality approaches 100%	

Anaphylactic Shock

Definitions
- Urticaria – edematous & pruritic plaques w pale center & raised edges
- Angioedema – edema of deeper layers of the skin. Non-pruritic. May be a/w numbness & pain
- Anaphylaxis – severe systemic allergic rxn to an Ag. Ppt by abrupt release of chemical mediators in a previously sensitized patient
- Anaphylactoid rxn – resembles anaphylactic rxn, but due to direct histamine release from mast cells w/o need for prior sensitization

Common causes
- Drugs – penicillin & NSAIDS commonest, aspirin, TCM, sulpha drugs
- Food – shellfish, egg white, peanuts
- Venoms – bees, wasps, hornets
- Environment – dust, pollen
- Infections – EBV, HBV, coxsackie virus, parasites

Stop Pptant	▪ Stop administration of suspected agent / flick out insect stinger with tongue blade ▪ Gastric lavage & activated charcoal if drug was ingested	
Airway	▪ Prepare for intubation or cricothyroidotomy – ENT/Anesthesia consult	
Fluid Rx	▪ 2L Hartman's or N/S bolus	
Drug Rx	**Adrenaline**	▪ Normotensive – **0.01ml/kg (max 0.5ml) 1:1000 dilution SC/IM** ▪ Hypotensive – **0.1ml/kg (max 5ml) 1:10,000 dilution IV** over 5 mins
	Glucagon	▪ Indications: failure of adrenaline Rx OR if adrenaline is contraindicated e.g. IHD, severe HPT, pregnancy, β-blocker use ▪ **0.5-1.0mg IV/IM**. Can be repeated once after 30mins
	Antihistamines	▪ Diphenhydramine 25mg IM/IV ▪ **Chlorpheniramine 10mg IM/IV** ▪ Promethazine 25mg IM/IV
	Cimetidine	▪ For persistent symptoms unresponsive to above Rx ▪ **200-400mg IV bolus**
	Nebulized bronchodilator	▪ for persistent bronchospasm ▪ **Salbutamol 2:2 q20-30mins**
	Corticosteroids	▪ **Hydrocortisone 200-300mg IV bolus, q 6hr**

PERIOPERATIVE CARE

INPUT / OUTPUT

Normal daily intake	Normal daily output	
Water		
Diet: 2300 ml **Metabolism: 200ml**	Urine Skin loss* Lung loss Faecal loss * Sweating in pyrexia / heat can cause several litres extra loss per day	1400ml (min obligatory volume = 400ml) 500ml (obligatory diffusion & vaporisation) 500ml (obligatory) 100ml
Sodium		
Diet: 150 mmol/day (range 50 – 300 mmol)	Stool Skin transpiration Urine	5 mmol/day 5 mmol/day (in absence of sweating) 140 mmol/day (can fall to 15 mmol/day)
Potassium		
Diet: 100 mmol/day (range 50 – 200 mmol)	Stool Skin Urine	10 mmol/day (obligatory) < 5 mmol/day 85 mmol/day (rarely falls below 60 mmol/day)

DAILY GASTROINTESTINAL ABSORBTION AND SECRETIONS[3]

	Absorbed	Secreted / Ingested
Mouth	Nothing	2-3L fluid ingested 1.5L saliva secreted
Stomach	Lipid-soluble compounds, i.e. alcohol	2-3L gastric juice secreted
Gallbladder	Absorbs water and concentrate bile	500ml bile secreted
Pancreas	Nothing	1.5 pancreatic juices secreted
Small Bowel	8-9L fluid absorbed	1.5L intestinal fluid secreted
Large Bowel	1L of fluid absorbed	100ml excreted in faeces

DAILY CALORIC REQUIREMENTS
2000 – 2500 kcal/day

CALORIC CONTENTS
- Glucose: 4 kcal/g
- Protein 4 kcal/g
- Fats: 9 kcal/g
- Alcohol: 7 kcal/g

HCT
From loss of pure plasma (burns/pancreatitis/peritonitis): 1 point ↑ = 100ml loss of fluid
From loss of isotonic extracellular fluid (GIT): 1 point ↑ = 500 ml loss of fluid
From loss of pure water (evaporation from lungs): no change

Parenteral Solutions

Crystalloids	Normal Saline	- Defined as solutions of electrolytes and water → hence, ions such as K^+, Mg^{2+} or Ca^{2+} when necessary can be added to suit patient's requirements - 0.9% N/S → infusion of large volumes can lead to total body sodium overload and hyperchloremia → can result in **hyperchloremic metabolic acidosis** i. Good for initial fluid resuscitation* ii. Following correction of deficit, less concentrated saline are more appropriate to replace on-going fluid losses - 0.45%/0.33%/0.2% N/S → Fluids are hypoosmotic and hypotonic → rapid infusion can result in **RBC lysis** → for this reason 5% dextrose is added to increase tonicity - 3% N/S – hypertonic saline solution → for replacing sodium deficit in patients with symptomatic hyponatremia or for urgent operation
	Lactated Ringer (Hartmann's solution)	- Used to replace fluid with the ionic composition of plasma (i.e. blood loss, oedema fluid, small bowel losses) - Ideal for replacement of existing fluid deficit when serum electrolyte concentration are normal - Risk of **hyponatremia** with extended use and in patients with impaired renal function
	5% Dextrose (D5W)	- Function – (1) volume expander and (2) means of parenteral nutrition - Glucose is rapidly metabolized by liver and remaining water will distribute itself across all components with little fluid remaining within blood space → not for fluid resuscitation!! - Excess 5% dextrose water → risk of hyponatremia
Colloids	Hetastarch Dextran	- Benefit of promoting retention of fluids in the intravascular space and of reducing excess interstitial fluid (oedema)
	Albumin (5%/10%/20%)	- Increase plasma oncotic pressure → retarding movement of water into interstitial space (oedema) – DON'T USE IN ALL PATIENTS PX WITH EDEMA i. 5% comes in 200ml → contains 10g of albumin ii. 10% comes in 100ml → contains 10g of albumin iii. 20% comes in 50ml → contains 10g of albumin - Caution in patients whose condition (i.e. ARDS, burns, sepsis) is secondary to **micro-vascular abnormalities** → exogenously administered proteins in colloid solution can extravasate into the interstitial space and intensify interstitial oedema
	Gelatin	- Gelofusin (urea-linked) - Haemaccel (succinate-linked) - Risks – allergic reactions, renal impairment

*0.9% N/S (isotonic) – does not remain within the intravascular space but will diffuse into the interstitial space (throughout ECF) but the sodium it carriers will not enter the ICF due to active sodium extrusion from the cells → immediate expansion of intravascular volume | In contrast, D5W, once glucose metabolized, remaining water would initial dilute ECF relative to ICF and water would be equally distributed throughout the body → don't use for fluid resuscitation!

[3] from "revision guide for surgical trainees" (2nd Edition)

FLUIDS / MAINTENANCE

The aim of fluid management is the avoidance of shock or inadequate end-organ perfusion as poor perfusion may lead to hypoxia and irreversible end-organ damage

Body composition[4]

- Total body water = 60% body weight in adult males*
  - Intracellular Fluid = 2/3 of TBW
  - Extracellular Fluid = 1/3 of TBW (or about 20% of body weight)
    - Interstitial Space = 3/4 of ECF
    - **Intravascular Volume = 1/4 of ECF** (of TBW or 5% of body weight)
- 3rd Space (potential space) = pathological expansion of the interstitial space via capillary leak in response to injury and illness. The shift of fluid between the intravascular space and the 3rd space is important in the evaluation of surgical patients

*approx. 50% in adult females, 80% in infants which decrease to 65% by 1 year of age

Principles of Fluid Management

Maintenance Fluid Requirement	Prior Fluid Deficit	On-going/ anticipated losses
Holliday-Segar normogram: 1st 10 kg – 100 ml/kg/day (**4ml/kg/hr**) 2nd 10 kg – 50 ml/kg/day (**2ml/kg/hr**) > 20 kg – 20 ml/kg/day (**1ml/kg/hr**) ↑ 10% fluids for every 1°C above 37°C ↑ **fluids:** burns, sweating, tachypnoea ↓ **fluids:** oliguric RF , oedematous states, hypothyroidism, SIADH	Estimated Deficits Based on history and PE (weight x % dehydration = __/L) Mild (thirsty) – 1.5L Mod (tachycardia) – 3L Severe (hypotensive) – 6L * when patient is >3-5% dehydrated always check U/E/Cr stat	Blood: trauma / surgery Gastrointestinal: NG aspirates, vomiting, fistula, stoma, surgical drains*, diarrhoea, intraluminal (i.e. IO, paralytic ileus) 3rd space loss: inflammation (i.e. acute pancreatitis, peritonitis, septicaemia)

Daily Electrolytes Requirements

		For a 70kg Individual / day	Primary Location	Normal Serum Values
Na^+	1-2 mmol/kg/day	~ 140 mmol / day	Extracellular Fluid (ECF)	135-145mmol/L
K^+	0.5-1mmol/kg/day	~ 70 mmol/day	Intracellular Fluid (ICF)	3.5-5.0mmol/L

(for ions with a ±1 charge: 1 mEq = 1 mmol | for ions with a ±2 charge: 1 mEq = ½ mmol)

*MCQ: hyperK^+ paralyses the heart in diastole | hyperCa^{2+} paralyses the heart in systole

Important Equations (patients with hyponatremia)

1. TBW = weight (kg) x correction factor (i.e. women = 0.5, males = 0.6, children = 0.6)
2. Sodium deficit = TBW x (desired serum Na – actual serum Na)
3. Δ serum Na per L infusate = [(infusate Na – serum Na) / (TBW + 1)]

* DO NOT correct more than **12mmol**/day → risk of osmotic demyelinating syndrome (lock-in syndrome)

Important Equation (patients with hypernatremia)

1. Water deficit (in L) = TBW x [(actual serum Na / 140) – 1]

Rate of Fluid Administration

- Fluid bolus (if patient in hypovolemic shock) → 1L 0.9 N/S fast
  i. Use Lactated Ringers / 0.45% N/S for large volume resuscitation
- Fluid replacement → ½ in first 8 hours followed by ½ over the next 16 hours

Components of regularly used IV fluids

	0.9% N/S	D/S (D_5 NS)	½ D/S	Lactated Ringers	Pre-Mix (KCL in 5% dextrose and 0.33 NaCL)	3% N/S	Gelatin
Na^+	154mEq/L	154mEq/L	77mEq/L	130mEq/L	56mEq/L	513mEq/L	154mEq/L
Cl^-	154mEq/L	154mEq/L	77mEq/L	109mEq/L	76mEq/L	513mEq/L	120mEq/L
K^+				4mEq/L	20mEq/L		
Ca^{2+}				2.7mEq/L			
Others		50g/L dextrose	25g/L dextrose	Lactate 28meq/L	50g/L dextrose		40g/L gelatin

Sterile Water = do not administer without dextrose IV as can cause haemolysis
* For patients with renal impairment / diabetes insipidus (hypernatremia state), use of fluid with Na^+ (i.e.0.9% N/S) will lead to retention of Na^+ with retention of water predisposing the patient to a fluid overloaded state. Instead, free water can be replaced with using 5% D/W (5% dextrose in water) or 0.45% N/S

Lactated Ringer → physiological fluids – (use with care in patients with renal problems)

3% N/S → used when want to quickly correct hyponatremia (i.e. symptomatic hyponatremia, urgent operation)

If concentration of KCl > 40 mmol in 500ml is required → give via infusion in the ICU with cardiac monitoring
Added K is not usually required in the 1st 24-48h after surgery because K is released from damaged cells

Case Scenario

60yr man, 70kg, presenting c/o vomiting and abdominal pain, Noted to have vomited about 2L. In the ED, Temp: 37.2 BP: 90/60, HR: 120.

Amount of fluids to replace:
- Maintenance / day → **2.5L** [(100 x 10) + (50 x 10) + (20 x 50)]
- Prior Losses → estimated **3.5L** (assume 5% dehydration)
- On-going Losses → **2L**

Rate of fluid administration:
- Run 1-2L fast and then reassess response – can use lactated ringers
- Give ½ (4L) over first 8 hours and ½ (4L) over next 16 hours

Choice of IV fluids:
- Check electrolytes stat and replace accordingly
  i. 1L 0.9% N/S = daily sodium requirement met (~150mmol/L)
  ii. Divided doses of K = K requirements are met (~ 70mmol/L)
  iii. **D_5 (Dextrose 5%) = 50g of dextrose in 1L (isotonic, 200kcal; 1g glucose = 4kcal)**
- Can use a mixture of 0.9% N/S & D_5 + potassium in divided doses
- Now more common to use Pre-Mix (i.e. 3.5L) which would add up to ~ 196 mmol of Na^+ and ~ 70 mmol of K^+

[4] Greenfield's Surgery Scientific Principles and Practice 5th Edition (pg190)

CALCULATING PERIOPERATIVE FLUID REQUIREMENTS[5]

Table 14.3 Calculating perioperative fluid requirements sections 1 + 2 + 3 + 4 = Total fluid needed; *give as directed in italics.*

1. **Basal fluid requirement** based on weight of the patient in kg. 10 kg infant 40 ml/h;80 kg adult 120 kg/h. *Give continuously.*										
Wt (kg)	10	20	30	40	50	60	70	80	90	100
Hourly maintenance ml/h	40	60	70	80	90	100	110	120	130	140
2. The **"NPO" deficit**: basal requirement times hours since fasting started: (8 h × 1.) *Replace in the first hour or two.*										
NPO deficit after 8 h (ml)	40×8=320	60×8=480	70×8=560	80×8=640	90×8=720	100×8=800	110×8=880	120×8=960	130×8=1,040	140×8=1,120
3. The **replacement for surgical blood loss**[a] is three (3) times the estimated blood loss: *Give as the loss occurs.*										
Blood loss (ml)	25	50	75	100	150	200	300	400	500	750
Replacement for blood loss (ml crystalloid)	75	150	225	300	450	600	900	1,200	1,500	2,250
4. The **replacement**[b] **for "third-space losses"** is related to the type of surgery: *Give as needed to support blood pressure, CVP, and urine output.*										
Type of surgery	Minor or peripheral surgery such as ankle fracture, ENT surgery.			Intermediate such as hip surgery, healthy laparoscopy.			Heavy losses such as intraabdominal sepsis, radical neck dissection, large flaps.			
Replacement for third space loss (ml/kg/h)	1–3 ml/kg/h			3–6 ml/kg/h			6–10 ml/kg/h or more			

How to use Table 14.3: There are four (4) separate components to be calculated to replace losses with intravenous fluids: (1) Maintenance fluid requirement (in ml/h); (2) NPO deficit from fasting before surgery (in ml); (3) Blood loss to be replaced (in ml); and (4) The so-called "third-space losses" which occur by expansion of the interstitial space after trauma or illness (in ml/h). This table's four sections show how to calculate each component. Add them up and then administer fluid *as indicated by the italics.*

[a]**Notes: (a) Using crystalloid the rule is: administer roughly three times the EBL. (b) If colloid is used to replace EBL, the ratio is about 1 to 1.**

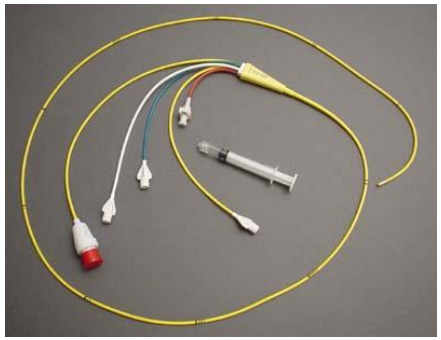
[b]**Notes: (a) Use crystalloid to replace third space losses. (b) If colloid is used, less is needed.**

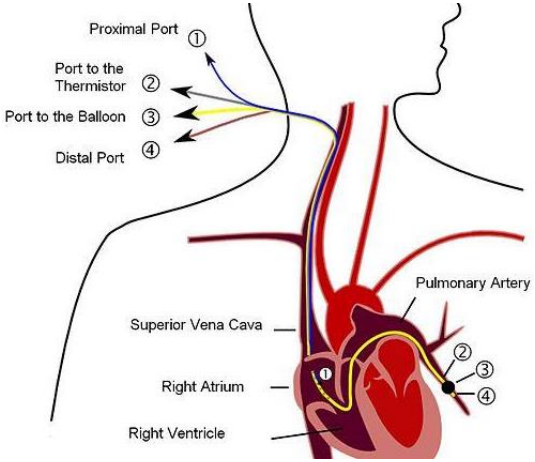
Table 14.4 Example fluid replacement calculation.

Patient and procedure:
An 80 kg male patient undergoes a 1-h tonsillectomy at 8:00 am after being made NPO at midnight.
Blood Loss:
Estimated blood loss is ultimately 250 ml
Crystalloid vs. colloid choice:
Crystalloid is adequate, no colloid needed for this small volume blood loss. Lactated Ringers is optimal though saline could be used.
Replacement:
(Calculated from the four parts of Table 14.3.)
Total crystalloid administered is:
120 ml (maintenance for the 1 h duration)
+960 ml (for the NPO deficit)
+750 ml (for the blood loss)
±250 ml (for the third space loss, estimated at 2 ml/kg/h)
=2080 of NS or LR over the 2 h perioperative period.
Postoperative maintenance:
May be 120 ml per hour with adjustments made based on vital signs and urine output.

CVP MONITORING

Swan-Ganz/ pulmonary artery catheter





- Pressure in RA
- Pressure in PA
- Pulmonary capillary wedge pressure (indirect estimate of LA pressure)

Normal CVP = 5 – 10 mmHg

- Useful in evaluating blood volume status when fluids are administered during hypotensive shock
- Administer fluids at a rate that maintains CVP at 12 – 15 mmHg (cardiac output optimal)

Ohm's Law:

$$CO = \frac{MAP - CVP}{SVR} \times 80$$

VENTILATION

Ventilator settings

- Tidal Volume = vol of air in each breath (8-12 cm^3 /kg)
- Rate = no of breaths delivered per min
- FiO_2 = amt of O_2 delivered (N = 40%; the higher it is , the more O_2 damage to the lungs)
- PEEP = positive end expiratory pressure (opens alveoli that would otherwise collapse in expiration)
  - Normal: 3 – 5 cmH_2O (physiologic PEEP)
  - Therapeutic PEEP can go up to 10 – 35 cmH_2O (but too high impedes venous return to the heart)

Atelectasis = V/Q mismatch (shunt)

[5] Anesthesia Student Survival Guide (chapter 14)

ACID BASE & ELECTROLYTES

The carbonic acid-bicarbonate system [Dissolved CO_2 + H_2O ↔ H_2CO_3 ↔ HCO_3- + H+] is catalysed by carbonic anhydrase

Henderson-Hesselbach's Equation: pH = 6.1 + log [(HCO_3^-) / (0.03 x PCO_2)]
(This also implies: pH = constant + (kidney function / lung function)

Normal ABG results

- pH: 7.38-7.42 (7.40)
- $PaCO_2$: 35-44 mmHg (40mmHg)
- PaO_2: 75-100mmHg
- HCO_3^-: 22-26 mmol/L (24mmHg)
- Base Excess: -2 to +2 mmol/L

Approach to ABG interpretations

1. What is the pH?
2. Is the primary disorder respiratory or metabolic
3. Calculate the Serum Anion gap
4. Identify the compensatory process (if one is present)
5. Identify if this is a mixed picture
   - in assessment of HAGMA use delta ratio to determine if mixed picture is present

pH & Primary Disorder

- Expected change occurs in the same direction in 1° metabolic disorder and in the opposite direction in 1° respiratory disorders

- Academia (pH <7.35)
  - if PCO_2 elevated (> 44) = respiratory acidosis
  - if HCO_3^- is low (< 22) = metabolic acidosis
- Alkalemia (pH > 7.45)
  - if PCO_2 is low (< 36) = respiratory alkalosis
  - if HCO_3^- is high (> 26) = metabolic alkalosis

If pH is normal, check for balanced acid base disorder:

[HCO_3] < 20	PCO_2 < 35	Metabolic acidosis + Respiratory alkalosis
[HCO_3] > 24	PCO_2 > 45	Metabolic alkalosis + Respiratory acidosis
[HCO_3] & PCO_2 normal	AG > 11	HAGMA + metabolic alkalosis
[HCO_3] & PCO_2 normal	AG normal	Normal *(unlikely NAGMA + metabolic alkalosis)*

Serum Anion gap = (Na^+) – (Cl^- + HCO_3^-)

- Normal = 3-11 mmol/L
- Hypoalbuminemia: anion gap ↓ in 2.5 mmol/L for every ↓ 10g/L of serum [albumin]
- Elevated anion gap = HAGMA even in the presence of a normal pH / [HCO_3]

Compensatory Process

- The body does not fully compensate the primary acid-base disorder
- Pace of compensation varies depending on whether it is respiratory or metabolic compensation

Metabolic Acidosis	↓ [HCO_3] 1 mmol/L = ↓ PCO_2 **1.2** mmHg Expected PCO_2 = (**1.5** x [HCO_3]) + **8 ±2** mmHg ▪ PCO_2 < expected → concurrent respiratory alkalosis ▪ PCO_2 > expected → concurrent respiratory acidosis Delta ratio = $\frac{\Delta AG}{\Delta HCO3^-} = \frac{AG-12}{24-HCO3^-}$: < 0.4 → hyperchloremic NAGMA 0.4-0.8 → combined HAGMA and NAGMA 1.0-2.0 → pure HAGMA (lactic acidosis ~1.6, DKA ratio ~1.0 due to urine ketone loss) > 2.0 → concurrent metabolic alkalosis
Metabolic Alkalosis	↑ [HCO_3] 1 mmol/L = ↑ PCO_2 **0.7** mmHg Expected PCO_2 = (**0.6** x [HCO_3 – 24]) + **40** mmHg ▪ PCO_2 < expected → concurrent respiratory alkalosis ▪ PCO_2 > expected → concurrent respiratory acidosis
Respiratory Acidosis	Acute: ↑ PCO_2 10 mmHg = ↑ [HCO_3] **1 mmol/L** Chronic: ↑ PCO_2 10 mmHg = ↑ [HCO_3] **4 mmol/L**
Respiratory Alkalosis	Acute: ↓ PCO_2 10 mmHg = ↓ [HCO_3] **2 mmol/L** Chronic: ↓ PCO_2 10mmHg = ↓ [HCO_3] **5 mmol/L**

Underlying Aetiology

Respiratory Acidosis (respiratory depression)	Respiratory Alkalosis (hyperventilation)
- **CNS depression** – head injury, drugs (i.e. opiates), coma, CVA, encephalitis - **NM disorders** – MG, GBS - **Skeletal Disease** – AS, flail chest, kyphoscoliosis - **Artificial Ventilation** - **Impaired Gaseous Exchange** – pneumonia, ARDS, obstructive airway disease, pulmonary contusions	- **Stimulation of respiratory centre** – high altitude, pneumonia, pulmonary embolism, pulmonary edema, fever, head injury - **Increased alveolar gas exchange** – hyperventilation (i.e. hysteria, pain, anxiety), artificial ventilation

Metabolic Acidosis	Metabolic Alkalosis
- **Excessive production of H+** – DKA, lactic acidosis, ingestion of toxins, septicaemia, starvation - Impaired excretion of H+ – acute / chronic RF - **Excess loss of base** – diarrhoea, intestinal, biliary, pancreatic fistula, renal tubular acidosis,	- **Excess loss of H+** – vomiting, NG aspirate, gastric fistula, diuretic therapy (thiazide / loop), Cushing's syndrome, Conn's syndrome - **Excess Intake of base** – antacids (i.e. milk-alkali syndrome)

NUTRITION

Nutritional support may supplement normal feeding, or completely replace normal feeding

Benefits of nutritional support

- Preservation of nutritional status
- Prevention of complications of protein malnutrition
- Decrease post-operative complications – i.e. delayed wound healing, risk of infections

Nutritional support should be considered for:

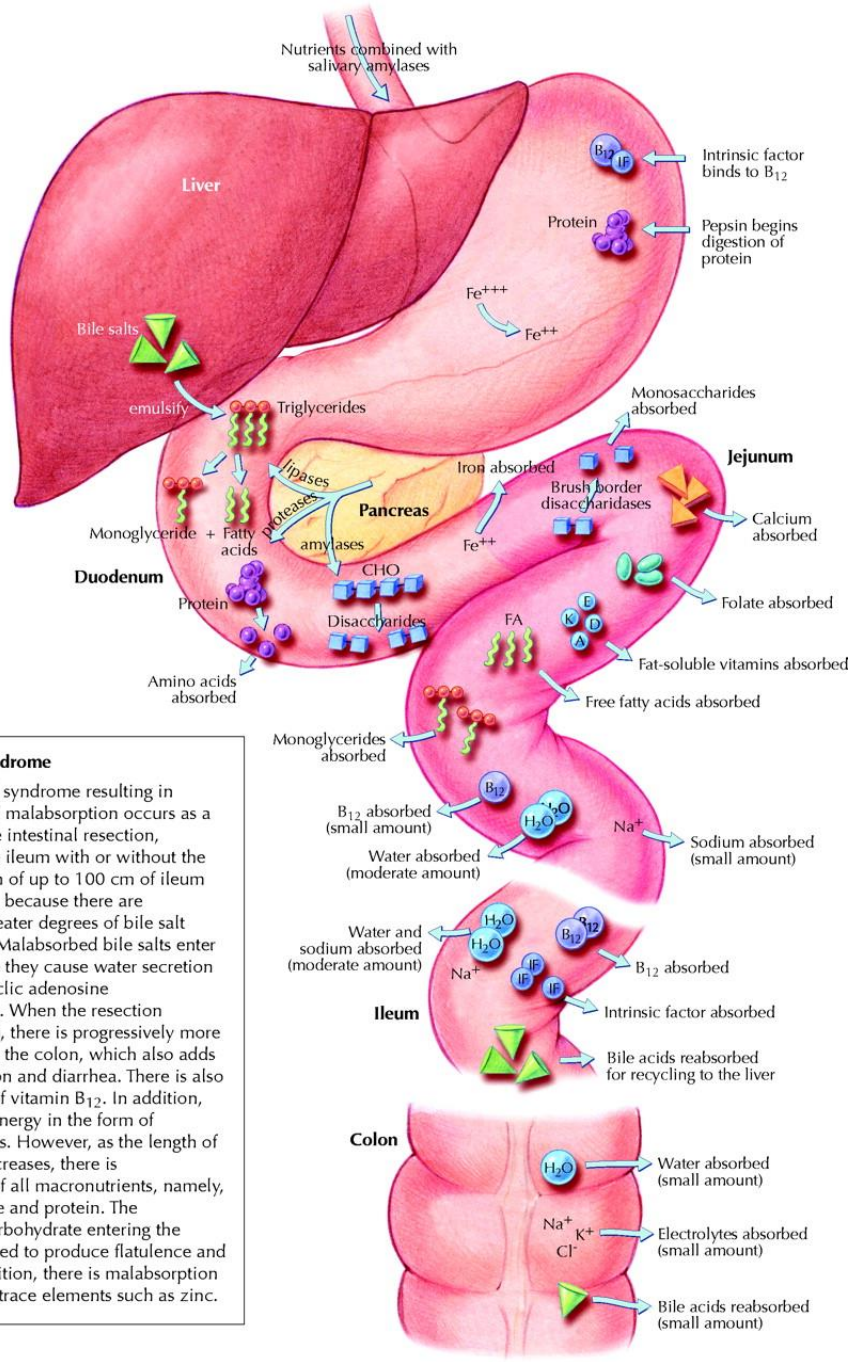
- Patients already with malnutrition → surgery / trauma / sepsis
- Patients at risk of malnutrition
  - Depleted reserves
  - Poor oral intake for > 5 days
  - Impaired bowel function
  - Critical illness
  - Need for prolonged bowel rest

Nutritional support should be considered for:

- BMI < 18.5
- Unintentional weight loss > 10% BW within last 3 – 6 months
- BMI < 20 and unintentional weight loss > 5% within last 3 – 6 months
- Poor absorptive capacity, high nutrient losses, increased catabolic rate

CLINICAL ASSESSMENT

History	- Dietary History - Significant LOW (5% in the last month or 10% over 6 months) or current body weight 80-85% (or less) of ideal body weight - Beware of patients who presents with ascites / oedema
Physical Examination	- Evidence of muscle wasting → thenar and temporal muscles - Depletion of subcutaneous fat → loose or flabby skin - Peripheral oedema and/or ascites → due to hypo-proteinemia - Features of vitamin deficiency → nail and mucosal changes - Ecchymosis and easy bruising - Easy to detect >15% loss
Anthropometric Measurements	- Weight for Height comparison - BMI < 19 or > 10% decrease - Triceps-skinfold - Mid arm muscle circumference - Urinary Creatinine height index - Others : bioelectric impedance / hand grip dynamometry
Laboratory Investigations	- Serum albumin: < 35g/L (half-life: 14-20days) - Serum pre-albumin: mild (10-17mg/dl), moderate (5-10mg/dL) and severe (<5mg/dL) – half-life 2-3 days - Serum transferrin: <200mg/dL (half-life: 10days) - Others: total lymphocyte count <1800/mm3, Skin anergy testing, test reflecting specific nutritional deficit – i.e. prothrombin time, U/E/Cr, LFT



Short bowel syndrome

The short bowel syndrome resulting in dehydration and malabsorption occurs as a result of massive intestinal resection, especially of the ileum with or without the colon. Resection of up to 100 cm of ileum causes diarrhea, because there are progressively greater degrees of bile salt malabsorption. Malabsorbed bile salts enter the colon where they cause water secretion by activating cyclic adenosine monophosphate. When the resection exceeds 100 cm, there is progressively more fatty acid loss in the colon, which also adds to water secretion and diarrhea. There is also malabsorption of vitamin B_{12}. In addition, there is loss of energy in the form of increased fat loss. However, as the length of the resection increases, there is malabsorption of all macronutrients, namely, fat, carbohydrate and protein. The malabsorbed carbohydrate entering the colon is fermented to produce flatulence and diarrhea. In addition, there is malabsorption of vitamins and trace elements such as zinc.

REFEEDING SYNDROME[6]

A potentially fatal medical condition which occurs as a result of fluid and electrolyte shifts during nutritional rehabilitation of malnourished patients

- Pathophysiology
  - Glucose cause rapid rise in insulin → trigger cellular uptake of PO^{4+} (,K^{+} & Mg^{2+})
  - Starvation → thiamine & mineral deficiency → exacerbated by onset of anabolic processes
  - Renal re-absorption of sodium increases (secondary to insulin) → fluid retention

- Clinical Manifestation
  - Electrolyte Deficiencies → hypoPO^{4+}, hypoK^{+}, hypoMg^{2+}
  - Thiamine Deficiencies
  - Volume Overload

- Medical Complications
  - Cardiovascular → heart failure, arrhythmias, peripheral edema
  - Respiratory → impaired respiratory function leading to dyspnoea, respiratory failure
  - Gastrointestinal → constipation / diarrhoea, elevated LFTs
  - Muscular → impaired contractility, myalgia, tetany, rhabdomyolysis
  - Neurological → tremor, paraesthesia, delirium, seizures

- Risk factors
  - **Reduced Intake – i.e. prolonged fasting or low energy diet / Marasmus**
    - Dysphagia (stroke patients, oesophageal cancer patients etc.)
    - High stress patient unfed for >7 days
    - Anorexia nervosa, Depression, Chronic Alcoholism
  - **Reduced absorption – i.e. malabsorptive syndromes**
    - Inflammatory Bowel Disease
    - Chronic Pancreatitis
    - Short Gut Syndrome
  - **Increased Metabolic Demands**
    - Post-operative patients
    - Oncology Patients
  - **Others – lowered physiological reserves**
    - Elderly patients (multiple co-morbid, decreased physiological reserve)
    - Uncontrolled DM (electrolyte depletion, diuresis)
    - LT user of antacids (Mg^{2+} & Al salts bind PO^{4+}) or diuretics (loss of electrolytes)

- Prevention and Management
  - Identification of high risk individuals: ≥2 of the following:
    - BMI < 18.5
    - Unintentional weight loss >10% in past 3-6 months
    - Little or no nutritional intake for > 5 days
    - History of alcohol misuse, drugs (i.e. insulin, chemotherapy, antacids, diuretics)
  - Nutritional replenishment commence after correction of electrolyte abnormalities
  - Vitamin supplementation started with re-feeding and continued for at least 10 days
  - NICE guidelines – re-feeding is started at no more than 50% of estimated energy requirements – rate can be increased if no refeeding problems detected clinically or biochemically

[6] BMJ. 2008 Jun 28;336(7659):1495-8

INSULIN

- Small peptide consisting of 91 amino acids, derived from pro-insulin.
- It is stored within granules in the B cells and is secreted into the circulation via exocytosis
- It has a short ½ life (5-10-min) and is rapidly broken down by the liver and kidneys
- **Glucose is the most potent stimulus that affection secretion of insulin**
- It is an anabolic hormone with a variety of actions:

Metabolic Functions	**Carbohydrate**	- Promote glucose uptake into muscles and fats (mediated by **GLUT-4**) - Promote glycogen storage – ↑ glycogenesis and ↓ glycogenolysis ▪ LIVER → glycogen can be converted to glucose to maintain plasma glucose level ▪ MUSCLE → glycogen only used in muscle cells for glycolysis (muscle lacks **glucose-6-phosphatase** to release free glycogen) - Stimulate use of glucose (glycolysis)
	Protein	- Stimulate Amino Acid uptake into hepatocytes, skeletal muscle - Stimulate Protein synthesis (↑ number and efficiency of ribosomes) - Inhibit protein degradation - Inhibit amino acid conversion to glucose
	Lipid	- Inhibit lipolysis by inhibiting **hormone-sensitive lipase** - Stimulate lipogenesis
Renal Function	- Insulin increases sodium reabsorption in the renal tubules	
Paracrine Effects	- Insulin decreases alpha cell secretion of glucagon	
Vascular Fx	- Insulin stimulates endothelial nitric oxide vasodilatation – lack of insulin (impaired in T1DM and T2DM can contribute to atherosclerosis in these patients)	
Growth & Cancer	- Higher fasting serum insulin concentration linked with increased risk of cancer	

PHOSPHATE

- Hypophosphatemia (intra-cellular processes and structural integrity of cell membrane)
  - Confusion
  - Convulsion
  - Muscle Weakness – can lead to diaphragmatic weakness
  - Left shift of oxyhaemoglobin curve – decrease oxygen delivery to tissue (↓ in 2,3 DPG)
- Hyperphosphatemia
  - Usually asymptomatic and no treatment is required

MAGNESIUM

- Necessary for muscle and nerve function also needed for normal PTH secretion

POTASSIUM

- Hypokalaemia
  - Fatigue and lethargy with eventual muscle weakness
  - ECG: flattened T wave → appearance of U wave depressed ST segment
- Hyperkalaemia
  - Sudden cardiac arrhythmias with cardiac arrest
  - ECG: peaked T waves → prolonged PR interval → loss of P waves → widened QRS → sine wave pattern

ENTERAL FEEDING

Provision of nutritional requirements via non-invasive or invasive methods with standard formulation or disease specific formulations

Choice of feeding regimen

Continuous	- Allow lowest possible hourly feeding rate → better GI tolerance - Better control of blood glucose due to continuous CBH input - When post-pyloric feeding is required, continuous feeding is often better tolerated than intermittent
Intermittent	- Daytime feeds may reduce aspiration risk if it is difficult to maintain 30deg elevation overnight - More physiological (daytime feeding)
Bolus	- Patient must have competent oesophageal sphincter – minimize aspiration risk - Physiological similar to typical eating pattern

Advantages:

- Maintains the GIT cyto-architecture and mucosal integrity, absorptive function and normal microbial flora → reduce risk of bacterial translocation
- More physiological, ↓complications, gut mucosa preserved, no bacterial translocation,
- Cheaper

Indications:

- Nutritional support is needed
- Problem with swallowing – i.e. stroke or oesophageal obstruction
- Proximal small intestine intact & functional (functional GIT but unable to sustain an adequate oral diet)
- Stimulation of secretory function does not worsen the condition being treated (e.g. small bowel fistula)

Contraindications:

- Complete small bowel obstruction
- Ileus
- Inadequately treated shock states (risk of intestinal ischemia)
- Severe diarrhoea (slow rate of feeding)
- Proximal small intestinal fistula, high o/p enterocutaneous fistula
- Severe pancreatitis

Types of Feeding Tubes:

Non-Invasive → tubes inserted down upper GIT, following normal anatomy	- Nasogastric Tubes - Orogastric Tubes - Naso-duodenal Tubes → when gastric emptying is a problem - Naso-jejunal Tubes
Invasive → require invasive procedure for insertion	- Gastrostomy Tubes i. Percutaneous endoscopic gastrostomy (PEG) → used for <u>feeding</u>, <u>drainage</u> and/or <u>prevention of volvulus</u> (rare, fix stomach to abdominal wall) ii. Open Gastrostomy - Jejunostomy Tubes

Types of Oral Feeds:

- Ensure (protein 9 gm /serving)
- Ensure Plus (highly concentrated in calories 1.5 cal/ml & protein 13 g/serving)
- Glucerna (for DM patients → ↓ carbohydrates, modified fat)
- Pulmocare (for COPD patients → high calorie, low carb to help ↓ CO_2 production)
- Novasource Renal (for renal patients → low protein & nitrogen content)

Complications of enteral feeding (12% overall complication rates):

Gastrointestinal	- Distention - Nausea & Vomiting - Diarrhoea / Constipation - Intestinal Ischemia
Mechanical	- Malposition of feeding tube – displacement and catheter migration - Sinusitis - Ulcerations / Erosions - Tube Blockage
Metabolic	- Hypernatremia - Hyperglycaemia
Infectious	- Aspiration Pneumonia - Bacterial Contamination - Infection at the PEG site - Peritonitis

PARENTERAL NUTRITION

Provision of all nutritional requirements by the intravenous route alone – **insert a small cannula into a large vein with a high rate of blood flow**

Advantages / Disadvantages:

- Allow greater caloric intake BUT
  - More expensive
  - More complications, needing more technical expertise

Types of Parenteral Nutrition:

Peripheral Parental Nutrition	- Given through peripheral vein - Short term use - Low caloric requirements - Needs large amount of fluids - Mildly stressed patients
Central (Total) Parental Nutrition	- Need venous access to a large central line → risk of thrombophlebitis due to concentrated dextrose content if given through peripheral veins i. Long peripheral line, subclavian approach, internal jugular approach, external jugular approach (all → superior vena cava)

Steps to Ordering TPN

Determine Total Fluid Volume	- Maintenance requirements → by body weight - Add on-going losses → based on I/O charts - Add insensible fluid losses → add 10% for every 1deg rise in temperature
Determine Non-N Caloric Needs → determine how much **fat and CBH** to give	- Based on total energy expenditure (TEE) - Resting Energy Expenditure (REE) → 25 to 30kcal/kg/day (schofield equation) - **TEE = REE + Stress Factor + Activity Factor** - Fats (25-30% of calories) and Carbohydrates (70-75% of calories)
Determine **Protein** Requirements	- based on calorie: nitrogen ratio → normal 150cal : 1g nitrogen - based on degree of stress and body weight **i. non-stress → 0.8g/kg/day** ii. mild stress 1.0-1.2g / kg / day iii. moderate stress → 1.3-1.75g/kg/day **iv. severe stress 2-2.5g/kg/day** - based on nitrogen balance → aim for positive balance of 1.5-2g/kg/day
Determine Electrolyte and Trace element requirements	Electrolyte Requirements - **Na^+ → 1-2mmol/kg/day** (or 60-120 meq/day) - **K^+ → 0.5-1 mmol/kg/day** (or 30-60meq/day) - **Mg^{2+} → 0.35-0.45 meq/kg/day** (or 10-20meq/day) - **Ca^{2+} → 0.2-0.3 meq/kg/day** (or 10-15meq/day) - **PO_4^{2-} → 20-30mmol/day** Trace Elements - Commercial preparations exist to provide RDA - Zn → 2-4mg/day - Cr → 10-15ug/day - Cu → 0.3-0.5mg/day - Mn → 0.4-0.8 mg/day
Determine need for additives	- Vitamins → give 2-3x that of oral intake - 1 ampoule MultiVit per bag of TPN - MultiVit does not include Vitamin K (can give 1mg/day or 5-10mg/week) - Mediations needed → Insulin

Stopping TPN:

- Aim to stop when enteral feeding can restart, wean slowly to avoid hypoglycaemia

Indication for TPN

Abnormal gut function	- Obstruction of GIT: proximal small bowel obstruction not immediately relieved - **Short bowel syndrome**: i. Temporary (before adaptation) in < 3m of functional small intestine ii. Permanent in < 1m of functional small intestine - Proximal intestinal fistula (i.e. in patients with small bowel obstruction – i.e. secondary to carcinomatosis peritonei) : facilitate fistula closure - Refractory inflammatory bowel disease of the GIT (e.g. Crohn's, UC)
Others	- Cannot consume adequate amounts of nutrients via enteral feeding – Inability to use the GIT: pancreatitis with pseudocysts/abscess (enteral nutrition not tolerated) - Anticipated not to be able to eat orally by 5 days – secondary to critical illness - Prognosis warrants aggressive nutritional support

Indication for TPN: ☐ Bowel Obstruction ☐ Fistula/Abscess ☐ Ileus ☐ Inflammatory Bowel Disease
(Check one) ☐ Malabsorption/Maldigestion ☐ Pancreatitis ☐ Short Bowel
☐ Other:_____

Please check one below or fill in the Custom Column – Quantities are a 24 hour supply.

	☐ Standard	☐ Renal	☐ Liver	Custom
Amino Acids	1.5 GM/Kg	1 GM/Kg	1 GM/Kg	GM/Kg
Dextrose	4 GM/Kg	4 GM/Kg	4 GM/Kg	GM/Kg
Calcium	12 mEq	12 mEq	12 mEq	mEq
Magnesium	16 mEq	0 mEq	16 mEq	mEq
Sodium	80 mEq	20 mEq	40 mEq	mEq
Potassium	80 mEq	0 mmol	70 mEq	mEq
Phosphate	20 mmol	0 Meq	20 mmol	mmol
Acetate	50 mEq	10 mEq	40 mEq	Min max balance
Chloride	80 mEq	10 mEq	40 mEq	Pharmacy to Adjust
Multivitamins (Infuvite Adult	10mL (100% RDA)	10mL (100% RDA)	10mL (100% RDA)	mL
Trace Elements (MTE-5 Conc.)	1 ml (100% RDA)	1 ml (100% RDA)	1 ml (100% RDA)	mL
Lipids	1 GM/Kg	1 GM/Kg	1 GM/Kg	GM
Insulin	Units	Units	Units	Units

Routine TPN Orders: (See Next Page for Additional Information including Wt. Calc.) TPN Rate: _____ml/hr

- Nutrition consult and monitoring. Pharmacist to adjust TPN per dietician's recommendations
- Initial TPN rate at 30ml/hour for 12 hours. If no evidence of refeeding shifts after 12 hours, increase rate to goal.
  ** See next page for definition of refeeding syndrome
- Daily weights every AM
- 24 hour urine collection for UUN every Sunday (Starting at 0400)
- Prealbumin, CRP & Triglyceride prior to Initiation of TPN on day 1, then every Monday & Thursday
- CMP, Mag, Phos on day 1, day 2. and day 3, then twice weekly on Monday & Thursday
- Infuse 10% Dextrose at same rate for any delay in TPN
- Blood Glucose to be checked every 6 hours.

For non-critical care patients, if Blood Glucose greater than 180. call MD for insulin orders
For critical care patients (including PCU), if Blood Glucose greater than 120mg/dL.

☐ Start Insulin Infusion Orders (place signed copy in chart) ☐ Call MD for Insulin Orders

Complications:

Mechanical	- **Related to insertion** → pneumothorax, air embolism, arterial injury, bleeding, brachial plexus injury, catheter misplacement, catheter embolism, thoracic duct injury - **Related to catheter in situ** → venous thrombosis and catheter occlusion
Metabolic	- **Electrolyte abnormalities** → hyper/hypoglycaemia, electrolyte abnormalities – check U/E/Cr, acid-base abnormalities, hyperlipidaemia - **Hepatic complications** → biochemical abnormalities, cholestatic jaundice (too much calories, too much fat), acalculous cholecystitis – check LFTs
Infectious	- **Insertion site contamination** - **Catheter contamination** ← improper insertion technique, contaminated TPN solution, contaminated tubing, use of catheter for non-feeding purposes i. If suspect that feed is the source → stop the feed → fever should settle quickly (despite the fact that CVP line is still in-situ → KIV remove and replace line. - **Secondary contamination / risk of bacterial translocation** → septicaemia

PERIOPERATIVE CARE – AN ANAESTHETIST'S PERSPECTIVE

- Fasting: minimum 6 hours for milk and food, 2 hours for clear fluids
- < 50yr with nil PMHx = no investigation,
- > 50yr = do FBC, RP, ECG + indicated investigations, GXM if expected blood loss or low Hb,
- In the absence of new clinical changes, blood test are valid for 3/12, ECG 6/12 and CXR 1yr

PRE-ANAESTHETIC ASSESSMENT*

Organ System	Specific Pointers
General	- Height, Weight, BMI - Medication Hx (see below) - Drug Allergies - Previous anaesthetic experience and its complication, if any
Cardiovascular	- Blood Pressure and Heart Rate - Screen for HTN, IHD, Cardiac Murmurs, Arrhythmias → **ECG** - 2D ECHO if indicated
Respiratory	- Smoking Hx – smokers 6x increased risk of respiratory complications – advise to stop smoking 6 weeks prior to surgery - Assessment of chronic respiratory disease – i.e. asthma, COPD - Presence of active URTI – recommend postponement of elective surgery for 2-4wks - **CXR**
Endocrine	- Assessment of endocrine disease – i.e. DM, thyroid dysfunction - Screen for obesity and OSA (KIV sleep study to evaluate severity)
Renal	- **U/E/Cr** - UPT for female patients who may be pregnant
Haematological	- **FBC, PT/PTT & GXM** - Peri-operative management of patients on anticoagulants - Arrange for autologous blood transfusion if indicated
Others	- Recommend patient to maintain / improve fitness prior to surgery - Advise to cut down on alcohol intake

CRUCIAL MEDICATION HISTORY

Types of Drugs	Specific Pointers
Drug Allergy	- Document type of allergic reaction – rash, periorbital swelling
Anti-platelets	- Indication for antiplatelet - Anti-platelet agents needs to be discontinued for 1-2weeks before surgery for full restoration of platelet function (i.e. aspirin / clopidogrel = stop 7 days, dipyridamole = stop 10 days, ticlopidine = stop 14 days)
Anti-coagulants (recommendation varies from hospital)	- Indication for anticoagulation - **Low Risk of thromboembolisation** (i.e. non-valvular AF w/o hx of stroke/TIA, stroke >3/12 without AF) → stop warfarin 6 days prior to surgery - **High Risk TE** → stop warfarin and bridge with clexane 1mg/kg/BD 5 days before surgery, last dose on morning of surgery - Recheck INR day before surgery – if > 1.5 surgeon will decide next step
Medication for chronic disease	- Taken up to the day of surgery (i.e. anti-HTN, statins, thyroid meds, antibiotics) – serve with sips of water
Supplements (i.e. herbal and TCMs)	- Awareness of interaction with anaesthesia - Supplements needs to be discontinued for 1-2weeks before surgery – in cases of interaction with coagulation and anaesthesia

MANAGEMENT OF MEDICAL PROBLEMS IN SURGICAL PATIENTS

Diabetes	Peri-operative Management
T2DM on Diet	- No special measures – check blood glucose prior and soon after surgery
T2DM on OHGA	- Continue OHGA till morning of surgery then hold off - If can eat post-op → give OHGA^ & Meal - If can't (NBM post-op) → start on insulin sliding scale ^hold off metformin in patient with suspected renal insufficiency, hepatic impairment or CCF ^patients on high dose sulfonylureas – start on low dose and up-titrate
Insulin-dependent DM	- Adjust basal insulin dosage and stop prandial insulin (see below)** - Start on dextrose drip (i.e. D5W or ½ D/S) at 50-75ml / hour as maintenance – avoid metabolic changes of starvation - Start on supplemental **insulin sliding scale,** monitor capillary blood glucose regularly - If can eat post-op → titrate back to usual insulin regimen
Others	
Long-Term Steroids	- IV hydrocortisone before and after operation till patient can resume oral intake
COPD	- Pre-op: arrange for CXR and Lung Function Test ± baseline ABG - Chest Physiotherapy – breathing exercise – pre-op and post-op - Smokers – encouraged to stop smoking 4-6weeks prior to surgery
DVT	- ± LMWH - Thromboembolic deterrent (TED) stockings - Intermittent pneumatic leg compression - Early Mobilization * for cancer patients (high risk of post-op thrombosis), there is benefit of perioperative anticoagulant prophylaxis[7]

**MANAGEMENT OF INSULIN THERAPY BEFORE SURGERY[8]

3 Steps: (1) ascertain type of DM, (2) adjusting basal insulin dosage, (3) stopping prandial insulin

- 1. Is this type 1 or type 2 DM → consequence of inappropriate insulin management differs
- 2a. Long-acting basal insulin (Glargine / Detemir) regimen:
  - If patient no hypoglycaemic episodes and total basal insulin = total daily mealtime (prandial) dose (i.e. 50% basal, 50% prandial ratio) → full dose of long-acting basal insulin to be given
  - If patient has hypoglycaemic episodes → reduce basal insulin by 25%
  - If patient no hypoglycaemic episodes but disproportionately more basal than meal-time insulin → add total daily dose and give half as basal long-acting insulin
- 2b. Intermediate-acting basal insulin (NPH) regimen:
  - Night before surgery → give full dose of NPH, decrease 25% if patient skipping night time meal
  - Morning of surgery → reduce dose by 50%
- 2c. Pre-mixed insulin (i.e. 70/30 NPH/Regular) regimen: (2 options)
  - Switch to long-acting insulin – i.e. add up total pre-mixed insulin requirement and give half as long-acting basal insulin morning or evening before surgery
  - 50% morning dose of pre-mixed insulin and put patient on dextrose drip and blood glucose checks
- 3. Stop all prandial insulin
  - Sliding scale (SSI) alone has no known benefit – it should be added to basal insulin and not as sole insulin therapy. For SSI, fast-acting insulin (i.e. aspart, glulisine, lispro) is preferred over regular insulin
  - Use the basal plus (SSI) approach (i.e. glargine once daily plus corrective doses with glulisine before meals) – effective glycaemic control achieved in T2DM surgical patients[9]

[7] Chest. 2004 Sep;126(3 Suppl):338S-400S.
[8] Cleveland Clinic Journal of Medicine, Volume 80, Number 11, November 2013
[9] Diabetes Care 36:2169–2174, 2013

POST-OPERATIVE COMPLICATIONS

IMMEDIATE (<1 hour post-op)	Local • Damage to surrounding structures • Primary haemorrhage (either starting during surgery or following post-op ↑ in BP) Replace blood loss and may require return to theatre to re-explore wound Systemic • Basal atelectasis (collapse of alveoli): ↑ bronchial secretions post-op & patient does not breathe deeply due to pain Tx: chest physiotherapy, incentive spirometry • Shock: due to blood loss, or inadequate fluid replacement peri-operatively • AMI, pulmonary embolism
EARLY (first 24-48 hours post-op)	Local • Pain, haemorrhage Systemic • Atelectasis (commonest cause of mild pyrexia in first 48hr) • Shock, AMI, PE • Nausea & vomiting (analgesia/anaesthesia induced) • Acute confusion: dehydration or sepsis (post-op confusion seen in 40%)
LATE (between 48 hours to 1 month post-op)	Local • Post-op paralytic ileus • Post-op wound infection (usually within 1st week post-op) RF: dirty operation, long operation (>2hrs), old age, immunosuppressed, DM Pain, redness, swelling, discharge, usually due to skin staphylococci • Wound or anastomotic dehiscence (POD 7 – 10) Serosanguinous exudate RF: infection, poor blood supply, malnutrition, steroids Tx: Analgesia, sterile wound dressing, fluid resus., re-suture under GA in OT Mortality up to 30% • Incisional hernia 10-15% of abdominal wounds Usually asymptomatic, but if painful, consider strangulation (uncommon due to wide neck) RF: Obesity, poor muscle tone (old age), (increased intra-abdominal pressure (chronic cough, straining from constipation), wound infection, multiple use of same incision site Tx: Surgical repair of hernia if strangulated or if enlarging • Bowel obstruction due to adhesions • Fistula formation • Secondary haemorrhage: often as a result of infection (usually 1-2wk post-op)

POST-OP HAEMORRHAGE

EARLY	• Damage to blood vessels/vascular organs (primary haemorrhage) • Consumptive coagulopathy – if large volumes of blood transfused • Pre-op anticoagulation • Unrecognized bleeding diathesis • Reactionary – due to increase CO and BP Management • FBC (plt), PT/PTT, GXM & order blood • Give protamine sulfate (1mg per 100units of heparin given over the past 4 hours) • Give FFP / platelet concentrates if clotting screen abnormal • Consider surgical re-exploration
LATE (several days)	• Usually due to infection leading to erosion of vessels at the operation site • Management: Treat infection and consider exploratory surgery

POST-OP FEVER

Day 0-2 (immediate to acute)	• Basal Atelectasis – occurs within 48hrs, needs chest physiotherapy • Tissue damage / necrosis – IL6, TNF-α release causing fever • Drug Fever – i.e. malignant hyperthermia • Blood Transfusion
Day 3-7 (acute)	• Wind – pneumonia • Water – Drip site (thrombophlebitis), UTI (esp. if catheterized), Drain Infection • Walk – DVT / PE • Wound Infection • Wonder Drug
> 7 days (subacute)	• Surgical Site Infection / Wound Infection – i.e. intra-abdominal abscess • DVT / PE • Drug – fever from antibiotics associated diarrhoea, febrile drug reaction
> 1 month (delayed)	• Surgical Site Infection • Infective Endocarditis

POST-OP POOR URINE OUPUT

Pre-Renal	• Renal Hypo-perfusion / Heart Failure
Renal	• Acute Tubular Necrosis
Post-Renal	• Obstruction (i.e. blocked catheter, BPH)
Others	• Anticholinergic Drugs / Opioids / Epidural Anaesthesia • Pain (i.e. after hernia repair)

POOR WOUND HEALING

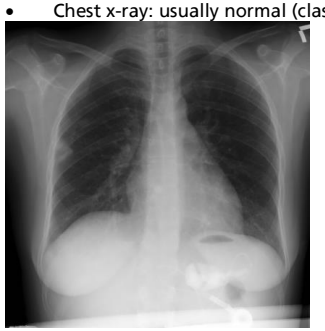
Patient factors	Wound factors	Surgeon factors
• Poor blood supply • Malnutrition • Vitamin deficiency • Immunosuppressive therapy • Long term steroids • Radiotherapy • Co-morbidities e.g. DM, HIV	• Wound infection • Poor wound care	• Suturing under tension • Did not observe aseptic technique

WOUND INFECTION

Wound Class	Examples	Expected Infection Rates[10]
Clean	Hernia Repair, Breast Surgery, Varicose Vein Surgery	< 2%
Clean Contaminated	Cholecystectomy, Hysterectomy	< 8%
Contaminated	Penetrating Abdominal Injury, Open #, Animal or Human Bites, Enterotomy during bowel obstruction	~ 15%
Dirty	Perforated Diverticulitis, Faecal Peritonitis	> 25%

[10] from "revision guide for surgical trainees" (2nd Edition)

DVT/PE
Affects 25-50% of surgical patients
DVT in deep calf veins: 5-10% risk of PE
DVT in iliofemoral veins: 50-60% risk of PE

Risk Factors [Virchow's Triad]	1. Stasis → bed rest, inactivity, CHF, CVA within 3/12, air travel >6hrs 2. Endothelial Injury → trauma, surgery, prior DVT, inflammation 3. Thrombophilia → anti-protein C resistance, protein C/S deficiency, APS, prothrombin gene mutation, hyperhomocysteinemia, OCP, HRT, Tamoxifen, 4. Others – malignancy (active), history of thrombosis
Presentation (DVT)	• Mild fever – Post-Op fever (day 5-7) • Calf warmth, tender, swelling, erythema, venous distention, pitting oedema • Phlegmasia Cerulea Dolens: stagnant blood → edema, cyanosis, pain • Homan's sign: calf pain on dorsiflexion, seen in <5% of patients • Others: seizures, syncope, new onset atrial fibrillation etc.
Presentation (PE)	• Dyspnoea (73%), pleuritic chest pain (66%), cough (37%), haemoptysis (13%) • ↑ RR (>70%), crackles (51%), ↑ HR (30%), fever, cyanosis • MASSIVE PE: syncope, hypotension, PEA, CCF (↑ JVP, S_3)
Investigations	DVT • Duplex ultrasound: 95% sensitivity and specificity for symptomatic DVT • D-Dimer: <500 helps r/o DVT (not indicated if pre-test probability is high) PE – diagnostic studies • Chest x-ray: usually normal (classical findings listed below are rarely seen)  Atelectasis, Pleural effusion, Raised hemi-diaphragm Westermark sign: dilatation of the pulmonary vessels proximal to the embolism, with collapse of the distal vessels (oligemia) Hampton hump: late sign, wedged shaped infiltrate with apex towards the hilum • ECG[11] - T wave inversion in V1-V4 (most common abnormality; quoted: 68%) - Sinus tachycardia - AF rhythm - Signs of RV strain → Right axis deviation, P pulmonale, RBBB - Rarely: $S_1Q_3T_3$ • ABG: hypoxemia, hypocapnia, respiratory alkalosis • D-Dimer: high sensitivity, poor specificity – used to r/o PE in patients with unlikely pre-test probability • **CT pulmonary angiogram (gold standard)** Look for filling defects in pulmonary artery

[11] CHEST 1997; 111:537-43

Prophylaxis/ Treatment	Non-pharmacological • Use of inflatable calf pumps intra-operatively • Early, aggressive ambulation post-surgery • Thromboembolic deterrent (TED) stockings • Intermittent pneumatic leg compression Pharmacological • **Unfractionated heparin or LMW heparin** Unfractionated heparin (onset: IV = immediate, SC = 30min, ½ life: 1-2hrs) - Potentiates effect of anti-thrombin III, inactivates thrombin (PTT ↑) - Efficacy monitored using aPTT - Antidote: protamine sulphate - Side effects: heparin induced thrombocytopenia (HIT) – predispose to thrombosis (STOP heparin! & start other anticoagulant – i.e. DTI) LMW heparin (Clexane/Enoxaparin) (onset: as above, ½ life: 4-5hrs) - Potentiates effect of anti-factor 10a (not reflected by PTT) - More predictable dose-effect relationship - Reversibility by protamine sulphate limited (60% reversal) • **Warfarin** – long term (onset: 2-4days, goal INR 2-3) - Vitamin K antagonist, inhibits synthesis of **factors II, VII, IX, X, Protein C / S** - Start with heparin for ≥ 5 days, stop heparin when target INR reached - Antidote: vitamin K, FFP - SE: bleed, hepatitis, skin necrosis (patients with protein C/S deficiency, and patients with HIT+ve) *Duration of Treatment • 1st DVT or PE 2° reversible/time-limited RF → 3 months • 1st unprovoked DVT or PE ≥ 3 months (reassess if low bleed risk) → lifelong • 2nd DVT / PE → lifelong Surgical • IVC filter (permanent or temp.: remove after 2 weeks of anti-coagulation) • Indications: ○ History of recurrent DVT/PE ○ Free floating thrombus seen on duplex scan ○ Anticoagulation contraindicated **Treatment of VTE** • Supplemental oxygen, intubation, mechanical ventilation • Anticoagulation – LMWH (i.e. enoxaparin 1.0 mg/kg SC) • Thrombolysis – TPA 100mg over 2 hours • Surgical/ catheter embolectomy • Thrombectomy (for large, proximal PE + hemodynamic compromise + CI to lysis)
Well's Criteria A set of criteria to determine the **pre-test probability** of DVT	**Clinical feature** / **Score** Active cancer (treatment on-going or within the previous 6 months or palliative) — 1 Paralysis, paresis, or recent plaster immobilization of the lower extremities — 1 Recently bedridden for more than 3 days or major surgery, within 4 weeks — 1 Localized tenderness along the distribution of the deep venous system — 1 Entire leg swollen — 1 Calf swelling > 3 cm compared to the asx leg (measured below tibial tuberosity) — 1 Pitting oedema (greater in the symptomatic leg) — 1 Collateral superficial veins (nonvaricose) — 1 Alternative diagnosis as likely or more likely than that of deep venous thrombosis — -2 High Probability: ≥ 3 – treat as susp DVT and perform compression U/S Moderate Probability 1 or 2 – treat as susp DVT and perform compression U/S Low Probability ≤0 – D-dimer test

SURVIVING SEPSIS[12]

Sepsis if a systemic, deleterious host response to infection leading to severe sepsis and septic shock

DIAGNOSTIC CRITERIA FOR SEPSIS

General Variables	- **Temperature** >38.3°C or <36.0°C - **HR** >90/min - **Tachypnea** - **Altered Mental Status** - **Significant Edema** of +ve Fluid Balance (>20ml/kg over 24hours) - **Hyperglycaemia** in the absence of DM (>7.7mmol/L)
Inflammatory Variables	- WBC >12,000uL^{-1} or <4000uL^{-1} or normal WBC with >10% (immature forms) - CRP and/or Procalcitonin > 2SD above normal value
Hemodynamic Variable	- Arterial hypotension (SBP <90mmHg or SBP decrease >40mmHg in adults)
Organ Dysfunction Variables	- Arterial Hypoxemia (P_aO_2 / F_{iO2} < 300) - Acute Oliguria (urine o/p <0.5ml/kg/hr for at least 2 hours despite adequate fluid resuscitation) - Creatinine Increase > 44.2umol/L - Coagulation abnormalities – INR >1.5 or aPTT >60sec - Ileus (absent bowel sounds) - Thrombocytopenia < 100,000uL^{-1} - Hyperbilirubinemia > 70umol/L
Tissue Perfusion Variables	- Hyperlactatemia >1mmol/L - Decreased capillary refill or mottling

DIAGNOSTIC CRITERIA FOR SEVERE SEPSIS

Sepsis induced tissue hypo-perfusion or organ dysfunction

1	Sepsis-induced hypo-perfusion
2	Lactate above upper limit of normal
3	Urine output < 0.5ml/kg/hr for more than 2 hours despite adequate fluid resuscitation
4	Acute Lung Injury with Pa02/Fi02 < 250 in absence of pneumonia as infectious source or ALI with Pa02 / Fi02 < 200 in presence of pneumonia as infectious source
5	Creatinine > 176.8umol/L (2.0mg/dL)
6	Bilirubin > 34.2umol/L (2mg/dL)
7	Platelet < 100,000uL
8	Coagulopathy – INR >1.5

SURVIVING SEPSIS CAMPAIGN BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:

1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥4mmol/L

TO BE COMPLETED WITHIN 6 HOURS:

5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation ($Scvo_2$)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, $Scvo_2$ of ≥70%, and normalization of lactate.

[12] Crit Care Med. 2013 Feb;41(2):580-637

MANAGEMENT OF SEVERE SEPSIS – AFTER ABC

Initial Resuscitation & Infection Issues		
	RECOMMENDATION	THINGS TO DO
Initial Resuscitation (golden 6 hours – early goal directed therapy)	- CVP 8-12mmHg - MAP ≥ 65mmHg - Urine output ≥ 0.5ml/kg/hr - Central Venous O2 Saturation 70% - Target resuscitation to normalize lactate (alternative to $Scvo_2$)	- Measure lactate level KIV re-measure if initial value is elevated - IV fluid replacement KIV dobutamine infusion & transfused RBC - Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L
Screening for sepsis	- Recommend routine screening of dangerously ill patients to allow earlier implementation of sepsis bundle	
Diagnosis	- Obtain cultures before anti-microbial initiated (max delay 45min) - if suspect invasive candidiasis – there are specific Ab assay to use	- 2 sets of blood c/s (both aerobic and anaerobic) - Imaging studies performed to confirm potential source of infection
Anti-microbial Therapy	- Administer within first hour of recognition of septic shock / severe sepsis - Choose broad-spectrum anti-infective therapy that have activity against ALL likely pathogens - If inflammatory markers (pro-cal) low and no evidence of infection can discontinue antibiotics - Ab not to be used in patients with severe inflammatory states determined to be of non-infectious cause	- Administer empirical broad-spectrum Ab (3-5 days max) - i.e. severe infection a/w respi failure and septic shock → Extended spectrum beta-lactams + aminoglycoside and/or fluroquinolone (for PAE bacteraemia) - beta-lactam + macrolide for patients with septic shock due to strep pneumonia - i.e. antiviral therapy in patients with severe sepsis / septic shock of viral origin - Deescalate once blood culture returns
Source Control	- Diagnosed infective source within first 12hours and emergent source control carried out – if patient is severely septic intervene with least physiological insult (percutaneous rather than surgery) - If infected peripancreatic necrosis is the source intervention delayed till demarcation of viable and non-viable tissue has occurred	- Check IV plugs – if they are potential source for sepsis, they should be promptly removed - List patient for procedure for emergent source control

Hemodynamic support and adjunctive therapy		
	RECOMMENDATION	THINGS TO DO
Fluid Therapy	- Crystalloid is the initial fluid of choice KIV albumin infusion if substantial amount of crystalloid used - DON'T USE hydroxyethyl starches (HES) – absence of clear benefit with colloids	- Fluid challenge in patients with sepsis induced tissue hypo-perfusion with 30ml/kg of crystalloid
Vasopressor	- Target MAP of 65mmHg - Dopamine is alternative vasopressor to norepinephrine - Phenylephrine is not recommended as initial therapy – used for salvage therapy - No benefit of using low dose dopamine for renal protection	- Norepinephrine is the 1st choice vasopressor - Epinephrine next in line with additional agent is needed - Vasopressin (up to 0.03u/min) can be used as well - Insert arterial catheter when using vasopressor
Inotropic Therapy	- Trial of dobutamine infusion up to 20ug/kg be administered or added to vasopressor	
Corticosteroids	- If adequate fluid resuscitation – no role for corticosteroids - If fluid resuscitation not adequate – KIV IV hydrocortisone 200mg / day - Corticosteroid not be administered for treatment of sepsis in absence of shock	- If steroids are used – give continuous flow
Supportive therapy*		
	RECOMMENDATION	THINGS TO DO
Blood Products	- Target Hb 7.0 – 9.0 g/dL in adults - Administer platelets if counts <10,000/mm^3 or if patient at risk of bleeding and counts <20,000mm^3 - Don't use FFP to correct clotting abnormalities in absence of bleeding	- Full blood count - RBC transfusion if Hb <7.0 - KIV platelet transfusion
Glucose Control	- Target upper blood glucose of ≤ 10mmol/L	- KIV start insulin when 2 consecutive blood glucose >10mmol/L
Nutrition	- Oral or enteral feeding as tolerated rather than complete fasting or only IV glucose within 1st 48 hours - Use IV glucose and enteral nutrition rather than TPN alone or parenteral nutrition with enteral feeding in first 7 days	- Low dose feeding – i.e. 500 calories diet

* there is a whole long list of other recommendations – for the full list read the journal article – surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock (PMID: 23353941)

ACUTE ABDOMINAL PAIN

APPROACH TO ACUTE ABDOMEN

- Definition: the presence of an abdominal pathology which if left untreated (<72 hours) will result in patient morbidity and mortality[13]
- Sudden onset of severe abdominal pain (new pain or an increase in chronic pain) is the hallmark of the acute abdomen
- Most common general surgical problem presenting to the emergency department
- Abdominal Pain arising from intra-abdominal pathology originates in the peritoneum (visceral and parietal layer)
- A transition from visceral to somatic pain indicates extension of the underlying process

	Visceral	Parietal	Referred Pain
Innervation	Bilaterally by the autonomic nervous system (sympathetic and parasympathetic)	Unilaterally via spinal somatic nerves that also supply abdominal wall	Results from central neural pathways that are common to the somatic nerves and visceral organs
Predisposing Factors	Stretch (distension, pressure, traction), Inflammation, Ischemia	Irritation of the parietal peritoneum (i.e. inflammatory process – bacterial peritonitis from acute appendicitis or mechanical stimulation – surgical incision)	(i.e. biliary tract pain referred to right inferior scapular area)
Site of Pain	Embryologic origin of the affected organ determines location of visceral pain in the abdominal midline	Well-localized pain	Well-localized pain though distant from the involved organ
Character of Pain	Dullness, poor localization, cramping or burning	Sharp, severe	Produces symptoms not signs

CLASSICAL SIGNS IN PATIENTS WITH ABDOMINAL PAIN

Sign	Findings	Association
Cullen's	Bluish Periumbilical Discoloration	Retroperitoneal Haemorrhage
Grey Turner's	Discolouration of the flanks	
Kehr's	Severe acute pain in the tip of the shoulder due to blood / irritants in peritoneal cavity when lying down with legs up	Splenic / Ectopic Preg. Rupture
Murphy's	Inspiratory Arrest with continuous palpation of gallbladder	Acute Cholecystitis
Chandelier	Cervical excitation cause patient to lift buttocks off table	PID, Ectopic Preg
Mc Burney's	Tenderness, 1/3 distance from ASIS to umbilicus on R. side	Appendicitis
Iliopsoas	Hyperextension of R hip causes abdominal pain	
Obturator's	Internal Rotation of flexed right hip cause abdominal pain	
Rovsing's	RLQ pain with palpation of the left lower quadrant	

[13] Acute Care Surgery (L.D. Britt, A.B. Peitzman, P.S. Barie, G.J. Jurkovich)

IMMEDIATE LIFE-THREATENING CONDITIONS OF ABDOMINAL PAIN IN ADULTS[14]

1. **Perforated Viscus (i.e. perforated peptic ulcer most common)**
   - Patient tends to be in the younger age group (20-30)
   - Can presents to A&E 2-3 days after onset of epigastric pain
     - Suspected in individuals with hx of PUD symptoms and who develop sudden onset of severe, diffuse abdominal pain
   - Others causes includes:
     - Perforated oesophagus (Boerhaave syndrome)
     - Perforated bowel (ischemic bowel, toxic megacolon, diverticulitis)
     - Perforated appendix
2. **Ruptured Abdominal aortic aneurysm (AAA)**
   - Risk Factors: advanced age (>60 years). COPD, pulmonary disease, PVD, HTN, smoking and family history
   - Hallmark: pulsatile epigastric mass, if ruptured → exsanguinating haemorrhage, unstable hypotension
3. **Mesenteric Ischemia**
   - Risk Factors: advanced age, ATH, low cardiac o/p state, cardiac arrhythmias (i.e. AF), severe cardiac valvular disease, recent AMI, intra-abdominal malignancy
   - Hallmark: acute onset of severe periumbilical abdominal pain out of proportion to findings on physical examination
4. **Acute Bowel Obstruction (i.e. small bowel obstruction most common)**
   - Hallmark: crampy abdominal pain, abdominal distention, obstipation, vomiting → progression of pain from crampy to constant and more severe can be a sign of impending strangulation
5. **Severe Pancreatitis**
   - Unless it is haemorrhagic pancreatitis (rare on 1st presentation)
6. **Ruptured HCC**
7. **Medical Conditions**
   - Diabetic Ketoacidosis
   - Acute MI
   - Addison's Disease (Addisonian crisis)
8. **Obstetric Conditions**
   - Ruptured Ectopic Pregnancy
   - Placental Abruption

[14] uptodate: Evaluation of the adult with abdominal pain in the emergency department

HISTORY TAKING

Patient's Bio-data
Presenting Complain
History of Presenting Complain
- Site of Pain (see below differential diagnosis of abdominal pain)
- Onset and Duration of Pain
  - Within Seconds
    (1) Infarction (MI / Mesenteric Occlusion),
    (2) Rupture (Ruptured AAA),
    (3) Perforation (Perforated Peptic ulcer)
  - Within Minutes
    (1) Inflammatory (Acute appendicitis, Pancreatitis, Diverticulitis)
    (2) Colic (Biliary colic, Ureteral colic, Small Bowel Obstruction)
    (3) Ischemia (Mesenteric Ischemia, Strangulated Intestinal Obstruction, Volvulus)
  - Over Several Hours
    (1) Inflammatory (Appendicitis, Cholecystitis)
    (2) Obstruction (Non-strangulated Bowel Obstruction, Urinary Retention)
    (3) Mechanical (Ectopic Pregnancy, Perforating Tumours)
- Character of Pain
  - Colicky Pain – waxing and waning pain which occur secondary to hyper-peristalsis of smooth muscle against a mechanical site of obstruction
    * Exception: biliary colic – constant, intense pain last for 30min to several hrs.
  - Sharp Persistent Severe Pain – infective or inflammatory process
- Radiation of Pain
  - Back – Pancreatitis, AAA, Aortic Dissection
  - Shoulder Tip or Angle of Scapula
    - Right – Cholecystitis, Liver Abscess, Subphrenic Abscess
    - Left – Splenic Abscess, Subphrenic Abscess
  - Loin to Groin – Renal Colic (begin in patient's back and radiate to the ipsilateral groin)
  - Flank – Pyelonephritis, Retroperitoneal Hematoma, AAA
- Associated Symptoms
  - Nausea and Vomiting – vomiting after onset of pain suggest appendicitis, vomiting before onset of pain suggest GE / food poisoning
  - Bilious Vomit – suggest process distal to the duodenum
  - Hematemesis – suggest peptic ulcer or gastritis
  - Fever or chills – suggest inflammatory or infectious process
  - Anorexia – very non-specific symptom
- Time Course of Pain (any pattern)
- Exacerbating and Reliving Factors
  - Diffuse Peritonitis – hallmark: pain worse with movement improved by lying still
  - Renal Colic – hallmark: writing in pain, unable to keep still
  - Intestinal Obstruction – visceral pain relieved after vomiting
- Severity of Pain (pain score)

Past Medical History
- Medical conditions may precipitate intra-abdominal pathology
- Risk Factors for Abdominal Vascular Disease (AAA / Mesenteric Ischemia)
  - Peripheral Vascular Disease
  - Coronary Artery Disease
- Risk Factor for Bowel Obstruction / Perforation
  - History of Cancer
  - History of Peptic Ulcer Disease
- Exclusion of extra-abdominal causes of abdominal pain
  - Myocardial Ischemia
  - Lower Lobe Pneumonia
- Exclusion of gynaecological causes of abdominal pain
  - Last Menstrual Period – if suspect ectopic pregnancy

Drug History
- Risk Factors for complications of Peptic Ulcer Disease
  - Any NSAIDs ingestion, aspirin, ibuprofen
- Other important medications of note
  - Corticosteroids – mask signs of inflammation
  - Antibiotics – mask pain caused by peritonitis, may lead to Ab induced pseudomembranous colitis (PMC) caused by clostridium difficile
  - Opioid Analgesia – even if administered prior to PE, it is not a/w decrease in diagnostic accuracy[15]

Social History
Family History
Systemic Review

[15] Ann Emerg Med. 2006;296:1764

PHYSICAL EXAMINATION

General Appearance
- Lying motionless (Acute Appendicitis, Diffuse Peritonitis)
- Restless, writhe in pain (Ureteric Colic, Intestinal Colic)
- Bending Forward (Pancreatitis)

Vital Signs + Peripheral Signs
- Hemodynamic Instability – r/o life threatening causes of epigastric pain
- High Grade Fever – suggests abscess, cholangitis or pneumonia
- Peripheral signs: jaundice, pallor, peripheral vasoconstriction, hydration status

Abdominal Examination
- Inspection (from the foot of the bed)
  - Distension, Surgical Scars, Bulging Masses, Area of erythema, Pulsations, Peristalsis
- Palpation (patient in supine position, eyes fixed on patient's eye)
  - Peritoneal Signs – rebound tenderness, guarding, board-like rigidity
  - Any palpable masses
  - Hernias – incisional, ventral, umbilical, inguinal, femoral
  - Pain out of proportion to PE findings – suggest mesenteric ischemia
- Percussion
  - Dullness over bladder – acute retention of urine
  - Tympanic sounds over distended bowel – intestinal obstruction
- Auscultation
  - Absence of bowel sounds – possibly ileus from diffuse peritonitis
  - High-pitched tinkling bowel sounds – suggestive of obstruction
- Rectal Examination
- Pelvic Examination – PV + bimanual examination
- Testicular and Scrotal Examination

Cardiorespiratory Examination
- Any signs of pleurisy, AMI, basal pneumonia

Others
- Peripheral vascular signs of embolization
- Evidence of coagulopathy

INVESTIGATIONS

Haematological Investigations
- Full Blood Count
  - Haemoglobin (Hb) – signs of anemia or occult bleeding, in acute bleeds due to hemoconcentration, Hb can be falsely elevated – correlate with other parameters
  - Mean Corpuscular Volume (MCV) – can be low if have iron deficiency secondary to GI blood loss
  - Haematocrit (Hct) – low haematocrit can be due to occult blood loss
  - White Blood Cell (WBC) – infectious source present
  - Left Shift on the differential – indicate presence of an inflammatory source
- Urea Electrolyte Creatinine (U/E/Cr)
  - Hypokalemic, Hypochloremic and Metabolic Alkalosis – prolonged vomiting and severe volume depletion (gastric outlet obstruction) – a/w high urea and creatinine if patient is dehydrated
  - Low Serum Bicarbonate or Metabolic Acidosis – ?general tissue hypo-perfusion (intestinal ischemia)
  - HypoK^+ / HypoCa^{2+} can cause ileus, third spacing can also cause electrolyte imbalance
  - Cr – for suitability of contrast scans
  - Glucose – to exclude DKA
- Liver Function Test (LFTs)
  - Hepatitis vs. obstructive vs. mixed picture
- Pancreatic Enzymes (amylase and lipase)
  - Serum amylase peaks at 6-24 hours (if > 3x normal limits) suggestive of acute pancreatitis.
  - Amylase can also be raised in perforated viscus, IO, ischemic bowel, ectopic pregnancy
- Cardiac Enzymes (CK/CKMB/Trop T), ECG – r/o ACS
- Lactic Acid Level (consideration of intestinal ischemia)
  - Serum lactate as an indicator of tissue hypoxia (suggestive of mesenteric ischemia or worsening sepsis)
- Urinalysis – Urine FEME / UC9
  - Assess urological causes of abdominal pain
- Urine Pregnancy Test (b-Human chorionic gonadotropin)
  - In woman with pain or bleeding and serum beta-hCG < 1500mIU/ml, the risk of ectopic pregnancy is substantially increased[16]
- GXM / PT/PTT – if surgery required

Radiological Investigations
- Plain Abdominal X-Ray Series
  - Erect Chest X-Ray – look for free air under the diaphragm (diff dx: Chilaiditi syndrome)
  - Supine Abdominal X-Ray or KUB
    - Free air distribution throughout SB (jejunum – valvulae conniventes) and LB (haustrations)
    - Coffee Bean Sign ('bent inner tube' – indicative of sigmoid volvulus)
    - Calcifications – most urinary stones are radio-opaque (90%), only 15% of gallstones are calcified
    - Sentinel Loop in acute pancreatitis
    - Calcification in the pancreas – chronic pancreatitis
    - Ground glass appearance – ascites
    - KUB – can look for rectal gas (beware of the presence of colonic gas following DRE)
  - Erect Abdominal X-Ray (not routine) – look for air-fluid level (5 or more is diagnostic for intestinal obstruction)
- Ultrasonography
  - Can detect up to 95% of gallstones
  - Acute Cholecystitis – diagnosed via (1) thickened gallbladder wall (>3mm), (2) pericholecystic fluid, (3) stone impacted at neck of gallbladder and (4) sonographic murphy's sign
- Computed Tomography (CT)
  - Evaluate acute mesenteric ischemia with CT angiography
  - Good for evaluating retroperitoneal structures – suspected leaking AAA or nephrolithiasis
- Magnetic Resonance Imaging (MRI)
  - Greatest application in pregnant women with acute abdominal and pelvic pain

INITIAL MANAGEMENT

1. NBM + IV hydration KIV IV PPI (i.e. pantoprazole)
2. NGT with low intermittent suction + I/O & stool charting
3. Monitor fluid balance: insert urinary catheter ± CVP line
4. Serial Abdominal Examination – evaluate need for laparotomy
5. Inform senior, OT, HD or ICU early if necessary and/or if in doubt
6. Treat underlying aetiology – IV broad spectrum antibiotics if septic + analgesia

[16] Acad Emerg Med. 2003 Feb;10(2):119-26

DIFFERENTIAL DIAGNOSIS OF ABDOMINAL PAIN

Right Hypochondriac

Thoracic
- Pneumonia
- Pleural effusion

Others
- Sub-phrenic abscess
- Pancreatitis
- PUD
- Appendicitis

Hepatic
- Hepatitis (viral, autoimm etc)
- Hepatomegaly
- Abscess

Biliary
- Cholangitis
- Cholecystitis
- Gallstone disease

Epigastric

Thoracic
- MI
- Pericarditis
- Aortic aneurysm

Others
- Pancreatitis

Gastrointestinal
- Oesophagitis
- GERD
- PUD
- Gastric outlet obstruction

CA stomach

Left Hypochondriac

Thoracic
- Pneumonia
- Pleural effusion
- MI

Gastrointestinal
- PUD
- Diverticulitis
- Mesenteric ischemia

Others
- Sub-phrenic abscess
- Splenomegaly
- Pancreatitis

Right Lumbar

Biliary (see RUQ)

Urological

Infection
- Pyelonephritis
- Abscess

Others
- PKD
- Renal cyst
- Angiomyolipoma
- Infarction

Obstruction
- Hydronephrosis
- Nephrolithiasis
- Ureteral obstruction

Cancer
- RCC
- TCC renal pelvis
- Bladder ca (ureteral obstructn)

Others
- Appendicitis

Umbilical

Gastrointestinal
- Appendicitis (early)
- I/O
- Mesenteric ischemia
- Colitis
- IBD

Others
- Aortic Aneurysm
- Pancreatitis

Left Lumbar

Splenic disease

Urological (see RL)

Right Iliac Fossa

Gastrointestinal
- Appendicitis
- Terminal ileitis
- Meckel's diverticulitis
- Mesenteric ischemia
- Mesenteric adenitis
- IBD
- Colitis
- Colorectal CA
- Hernia

O&G
- Ovarian cyst
- Ovarian torsion
- Ectopic pregnancy
- PID

Orthopaedics (See LIF)

Hypogastric

Gastrointestinal
- Colorectal CA

Urological
- ARU
- Bladder calculi
- Cystitis / UTI

O&G
- Ectopic pregnancy
- Abortion
- PID
- Uterine rupture
- Fibroid complications
- Adenomyosis
- Endometriosis

Left Iliac Fossa

Orthopaedics

Infection
- Septic hip arthritis
- TB hip

Degeneration
- OA hip

Inflammation
- RA hip
- Ankylosing spondylitis
- Reiter's syndrome

Infiltration
- 1° bone tumour (hip)
- Metastasis to hip

Destruction
- # - NOF, pubic rami

Radiation
- Back pathologies (referred pain)

Paediatric ortho conditions
- Transient synovitis
- Perthes' disease
- SCFE

Gastrointestinal
- Diverticulitis
- IBD
- Colitis
- Colorectal CA
- Hernia

O&G (see RLQ)

DIFFERENTIAL DIAGNOSIS OF PALPABLE ABDOMINAL MASS

Right Hypochondriac

Liver

Massive
- Cancer: HCC, Metastases, Myeloprolftve dz
- Alcoholic liver disease
- Rt ht failure/tricuspid regurg

Moderate
- Above causes
- Lymphoproliferative disease Haemochromatosis
- Amyloidosis

Mild
- Above causes
- Infxns: Viral – Hep, IMS; Bacterial – abscess; Parasitic – hydatid cyst, amoebic abscess
- Biliary obstruction
- Cirrhosis

Gallbladder
- Pancreatic/periampullary CA
- Acute cholecystitis
- Hydrops
- Empyema
- Mirizzi syndrome

Ascending colon
- Cancer
- Diverticular mass/abscess
- Faeces

Right adrenal gland

Right kidney (see RL)

Epigastrium

Liver (see RHC)

Pancreas
- Pseudo cyst
- Tumour

Transverse colon
- Cancer
- Diverticular mass/abscess
- Faeces

Stomach
- Cancer
- Distension (GOO)

Aorta
- Aortic aneurysm

Retroperitoneal lNpathy
- Lymphoma
- Teratoma
- Other malignancies

Left Hypochondriac

Spleen

Massive
- Infections
- CML
- Myelofibrosis

Moderate
- Above causes
- Portal hypertension
- Lymphoproliferative disease (lymphoma, CLL)
- Hemolytic Anemia (thal, HS)
- Storage disease (Gaucher's)

Mild
- Above causes
- Infxns: Viral hep, IMS, Endocarditis
- Autoimmune – SLE, RA, PAN
- Myeloprolftve dz – PRV, essential thrombocytopenia
- Infiltratn – sarcoid, amyloid

Stomach

Descending colon
- Cancer
- Diverticular mass/abscess
- Faeces

Left kidney (see RL)

Left adrenal gland

Right Lumbar

Right Kidney
- Hydro/pyonephrosis
- Cancer – RCC
- Polycystic dz
- Single cyst
- Amyloidosis
- Tuberous sclerosis, VHL

Right adrenal gland

Liver (see RHC)

Ascending colon mass
- Cancer
- Diverticular mass/abscess
- Faeces

Umbilical

Liver (see RHC)

Stomach(see Epigastrium)

Small intestine
- Obstruction

Mesenteric cyst

Pancreas (see Epigastrium)

Aorta
- Aortic Aneurysm

Retroperitoneal lNpathy
- Lymphoma
- Teratoma
- Other malignancies

Left Lumbar

Spleen (see LHC)

Left kidney (see right lumbar)

Descending colon
- Cancer
- Diverticular mass/abscess
- Faeces

RIF

Gastrointestinal
- Appendiceal mass/abscess
- TB gut
- CA caecum
- Distended caecum (due to distal obstruction)
- Crohn's dz (terminal ileitis)

Orthopedics
- Chondroma/sarcoma of ilium
- Bony metastasis

O&G
- Ovarian cyst/tumour
- Fibroids

Urogenital:
- Transplanted kidney
- Bladder diverticulum
- Ectopic or undesc testis

Vascular:
- Iliac artery aneurysm
- Iliac lymphadenitis

Skin & Msk:
- Psoas abscess

Hypogastrium

Bladder
- Acute retention of urine
- Chronic retention of urine

Anal/rectal mass
- Cancer

Uterus
- Gravid uterus
- Fibroids
- Tumour

Ovary
- Cyst
- Tumour

LIF

Gastrointestinal
- Diverticular mass/abscess
- colon/sigmoid cancer
- Crohn's disease (terminal ileitis)
- Faeces

Similar causes as RIF mass

INTESTINAL OBSTRUCTION

Intestinal obstruction occurs when normal flow of intestinal contents is interrupted. It can be classified pathologically into mechanical obstruction (dynamic) or function obstruction (adynamic)

Classification

A. Pathological → dynamic vs. adynamic
B. Anatomical → small bowel (high / low) vs. large bowel
C. Clinical → acute vs. chronic vs. acute on chronic vs. sub-acute
D. Pathological Changes → simple (blood supply intact) vs. strangulated

PATHOLOGICAL CLASSIFICATION

Mechanical – peristalsis working against a mechanical obstruction

Intra-luminal	- Impaction (stools) – i.e. bed-ridden patients (8%) - Gallstone 'ileus' - Foreign Body - Trichobezoars / Phytobezoars
Intra-mural	- Malignancy & Malignant Strictures (15%) - Inflammatory Strictures (TB / Crohn's, diverticulitis, radiation colitis) (15%) - Intestinal Atresia
Extra-mural	- Intraperitoneal bands and adhesions (40%) - Hernia (12%) - Volvulus – sigmoid / cecum (more commonly sigmoid) - Intussusception - Lymph Node Compression - Superior Mesenteric Artery Syndrome

Functional – absence of peristalsis without obstruction

Absent Peristalsis	- **Paralytic Ileus**: hypo-mobility w/o obstruction → accumulate gas & fluids with associated distention, vomiting, absence of bowel sounds and obstipation ▪ Failure of transmission of peristaltic waves secondary to NM failure (Myenteric (Auerbach's) and submucosa (Meissner's) plexuses ▪ DDx: mechanical/pseudo: hypo/absent BS as opposed to high-pitched tinkling ▪ Causes: 1. Post-operative (most common) 2. Infection – intra-abdominal sepsis 3. Reflex Ileus 4. Metabolic – uraemia & hypokalaemia most common
Pseudo-Obstruction	- Recurrent obstruction (usually colon) that occurs in the absence of a mechanical cause or acute intra-abdominal disease - Causes: ▪ Small Intestinal Pseudo-obstruction (idiopathic or a/w familial visceral myopathy) ▪ Acute Colonic Pseudo Obstruction 1. Toxic Megacolon* 2. Ogilvie Syndrome** ▪ Chronic Colonic Pseudo Obstruction 1. Hirschsprung Disease 2. Paraneoplastic immune mediated – small cell Lung CA 3. Infection – Chagas' Disease

ANATOMICAL CLASSIFICATION

Small Bowel Obstruction	High	- Vomiting occurs early and is profuse with rapid dehydration - Distention is minimal
	Low	- Pain is predominant with central distention - Multiple central fluid level seen on AXR
Large Bowel Obstruction	- Distention is early and pronounced - Pain is mild and vomiting and dehydration are late - Proximal colon & cecum distended (competent ileocecal valve)	

CLINICAL CLASSIFICATION

Acute	- Usually in small bowel with sudden onset of colicky central abdominal pain and distention and early vomiting and constipation
Chronic	- Usually seen in large bowel obstruction with lower abdominal colic and obstipation followed by distention
Acute on Chronic	- Short history of distention and vomiting against a backdrop of pain and constipation
Sub-acute	- Incomplete obstruction - Recurrent attacks of colic relieved by passing flatus or faeces

"Small bowel obstruction is more common than large bowel. The most common causes of small bowel obstruction are adhesions, hernia and cancers. The most common causes for large bowel obstruction are cancers, cancers, cancers, diverticular disease or volvulus"

CAUSES OF PARALYTIC ILEUS

Post-operative (most common)	- Physiologic ileus spontaneously resolves within 2-3 days, after sigmoid motility returns to normal, usually self-limiting - Normal resumption of bowel activity after abdominal surgery follows a predictable pattern: **SB - within hours; stomach - 1-2 days; colon - 3-5 days** - Clinically significant if: ▪ Ileus that persists for more than 72 hours following surgery ▪ No return of bowel sounds on auscultation ▪ No passage of flatus ▪ Abdominal distention becomes more marked and tympanic ▪ Pain is not a feature
Infection	- Sepsis (may give rise to localised or generalised ileus) ▪ Resultant adhesions may contribute a mechanical element to the initial neurologic aetiology
Infraction	- Ischemic Bowel
Reflex Ileus	- Retroperitoneal hematoma - Intra-abdominal inflammation/peritonitis, biliary/renal colic - Trauma: (#ribs/spine/HI) - Spinal Cord injury above T_5 level
Metabolic	- Metabolic: hypoK/ hypoMg/ hypoNa, uraemia - Metabolic Acidosis (i.e. DKA) - Hypothyroidism - Drugs: opiate-induced, antacids, TCA

*** TOXIC MEGACOLON – potentially** lethal complication of inflammatory bowel disease (IBD) or infectious colitis that is characterized by total or segmental non-obstructive colonic dilatation plus systemic toxicity

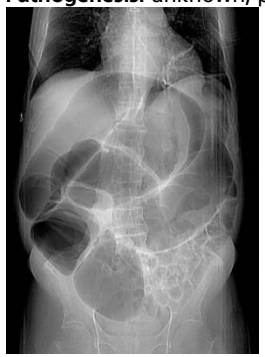
Clinical Features:
- Severe bloody diarrhoea
- Toxic patient – Altered sensorium, tachycardia, fever, postural hypotension, lower abdominal distention and tenderness ± localized or generalised peritonitis

Diagnostic Criteria[17]
- Radiological evidence of colonic distention PLUS (≥ 3 of the followings)
  - Fever > 38deg
  - HR > 120bpm
  - Neutrophil > 10,500 / micoL
  - Anemia
  - PLUS at least one of the following – 5a. Dehydration, 5b. Altered sensorium, 5c. Electrolyte disturbance, 5d. hypotension

[17] Gastroenterology. 1969;57(1):68.

**** OGILVIE SYNDROME** – acute gross dilatation of the cecum (> 10cm) and right hemi-colon (occasionally extending to the rectum) in the absence of an anatomic lesion that obstructs the flow of intestinal contents

Pathogenesis: unknown, probably due to impairment of the autonomic nervous system



Associated with an underlying disease in 95% of patients[18]

Trauma	Fractures
Infections	Pneumonia / Sepsis
Cardiac	MI / Heart Failure
Obstetric / Gynaecologic	C-section / Normal vaginal delivery, Spinal anaesthesia during childbirth
Retroperitoneal Pathology	Malignancy / Haemorrhage
Surgery	Pelvic, abdominal, orthopaedics
Neurological Conditions	
Drugs	Opiate, CCB, epidural analgesics, anti-cholinergic
Others	Metabolic, Cancer, Respiratory failure, Renal failure

Clinical Features:
- Nausea, vomiting, abdominal pain, constipation and paradoxically diarrhoea
- Abdominal Distention always present
- **Diagnosis of exclusion** – made after excluding toxic megacolon or mechanical obstruction

The risk of colonic perforation increases when caecal diameter **> 12 cm** and when the distention has been present for **greater than 6 days**.[19] Conservative therapy can be continued for 24-48 hours if no excessive pain or no excessive caecal dilatation (> 12cm)

Appropriate management includes supportive therapy (serial P/E and AXR Q12-24h) and selective use of **neostigmine** and **colonoscopy for decompression**

The Law of Laplace states: in a long pliable tube, the site of largest diameter requires the least pressure to distend. Hence, in a patient suffering a distal large bowel obstruction, in the setting of a competent ileocecal valve, the cecum is the most common site of perforation.

[18] Dis Colon Rectum. 1986;29(3):203.
[19] Gastrointest Endosc Clin N Am. 2007 Apr;17(2):341-60, vi-vii

PATHOPHYSIOLOGY

Changes in the Bowel

Distal Collapse	- Below level of obstruction, bowel exhibits normal peristalsis and absorption until it becomes empty → contract and become immobile
Proximal Dilation	- Initial proximal peristalsis increased to overcome obstruction - If obstruction not relieved → dilatation occurs with absent peristalsis ▪ Gas Accumulation → significant overgrowth of both aerobic and anaerobic organisms & from swallowed air (gas composition – O_2 , CO_2 , H_2S & N_2) ▪ Fluid Accumulation → impaired absorption from gut leading to sequestration of fluid in the bowel lumen (risk of dehydration and electrolyte imbalance)
Strangulation	- Compromised venous return due to dilated bowel → - Increased capillary pressure → - Local mural distention due to fluid and cellular exudation → - Compromised artery supply → - **HAEMORRHAGIC INFARCTION** - Risk of translocation of intestinal bacterial and toxins into peritoneal cavity → - **PERITONITIS AND SEPTICEMIA** - When long segments of bowel are strangulated, sequestration of blood occurs in the strangulated segment → - **HYPOVALEMIC SHOCK *** Clinical Fx: blood supply compromised, sharper and more constant localised pain, peritonism is the cardinal sign. May have fever, raised WCC and signs of mesenteric ischemia
Simple / Closed Loop Obstruction	- Simple: one obstructive point, no vascular compromise - Closed-loop: obstruct at 2 points forming a loop of grossly distended bowel – at risk for perforation, (tenderness and perforation usually at caecum) >10 cm requires urgent decompression ▪ Clinical Fx: Constant RIF pain, guarding, tenderness, absence of dilated small bowels ▪ **Pathophysiology:** strangulation lead to venous compromise lead to edema lead to arterial compromised causing gangrene and potential for perforation ▪ **Causes:** o Volvulus o Herniation of bowel o Tight carcinomatous stricture of colon with competent ileocecal valve

HISTORY

4 cardinal symptoms

Pain	- Visceral pain secondary to distention – colicky, 4-5 days duration - Centred on the umbilicus (small bowel) or lower abdomen (large bowel) - Complete obstruction: constant, sharp pain - Strangulation: pain is severe and constant - Volvulus: sudden, severe pain - Paralytic ileus: no pain involved
Vomiting	- Ask if projectile, bilious or faecal stained - Time and load of vomitus can determine if obstruction is proximal or distal ▪ High SB: greenish blue, bile stained ▪ Lower SB: brown and increasingly foul smelling (feculent = thick brown foul) ▪ LB: uncommon esp. if competent ileocecal valve, usually late symptom
Abdominal Distention	- Prominent feature in large intestinal (distal) obstruction - Usually not seen in high obstruction, esp. if patient is vomiting - Closed loop: RIF bulge that is hyper-resonant - SB: distension in centre of abdomen
Constipation / Obstipation	- Constipation (where flatus only is passed) - Obstipation (where neither faeces nor flatus is passed) – cardinal feature of complete intestinal obstruction - Ask patient about NORMAL BOWEL OUTPUT FREQEUNCY

Other pertinent history

- Symptoms of GIT bleed, infection
- Previous surgeries
- Underlying GIT disorders
- Risk factors for ischaemic bowel: atherosclerotic RH, heart disease, previous stroke
- Suspicion of malignancy: LOW, LOA, Previous Cancer, Family history of cancer

PHYSICAL EXAMINATION

- **Vitals**: Is patient stable? Any fever? (sepsis) Hypotension, tachycardia? (dehydration)
- **General inspection**: Abdominal distension? Cachexia? Confusion?
- **Peripheries**: Look for signs of dehydration e.g. capillary refill, dry tongue, palpate lymph nodes
- **Abdomen**:
  - Any distension?
  - Scars from previous abdominal surgery?
  - Visible peristalsis? – severe obstruction
  - Signs of peritonitis: guarding, rebound tenderness, or SNT
  - Any masses, hernia – inguinal + femoral (more likely strangulated)
  - Bowel sounds:
    - Initially hyperactive, later may be sluggish or absent
    - Tinkling BS: small bowel obstruction
  - Succussion splash + epigastric tenderness: gastric outlet obstruction
- **DRE**: any masses felt, any impacted stools?

Note: Range of clinical manifestation of small bowel obstruction – Intestinal obstruction to ischemia to gangrenous to perforation

INVESTIGATIONS

Diagnosticate

- AXR (erect AXR no longer routinely ordered, radiological dx based on a supine AXR)

1. Erect AXR: air fluid levels
   - In general ≥ 5 fluid levels are diagnostic of intestinal obstruction
   - In the small bowel – number of air fluid levels is directly proportional to the degree of obstruction and to its site (more number = distal lesion)

2. **Supine AXR:** look for small or large bowel dilatation on radiograph

Duodenum	- C-shaped
Jejunum	- Dilated small bowel >3cm is considered abnormal - Centrally located multiple dilated gas filled bowel - Stack of coins appearance (plicae circulares / valvulae conniventes) – completely pass across width of the bowel, regularly spaced - No gas is seen in the colon
Distal Ileum	- Featureless
Colon	- Dilatation of the caecum >9cm or the colon >6cm is abnormal - Peripherally located - Incomplete bands (haustrations due to presence of taenia coli) – spaced irregularly, do not cross whole diameter of the bowel

3. Special Considerations

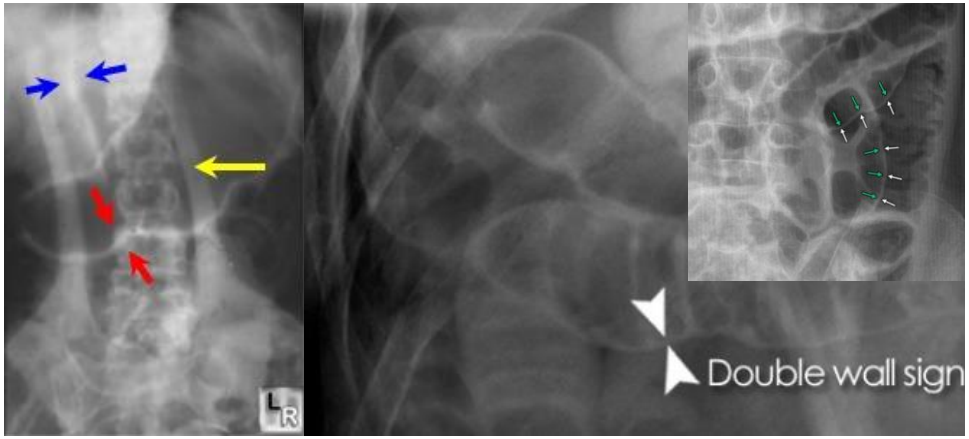
Volvulus	Sigmoid Volvulus → massive colonic distention with dilated loop of bowel running diagonally across the abdomen from right to left (COFFEE BEAN SIGN) Caecal Volvulus → gas filled ileum and ± distended caecum – no longer in RIF (barium enema shows BIRD BEAK DEFORMITY)
Intussusception	Ileocolic → evidence of small / large bowel obstruction with an absent caecal gas shadow (barium enema demonstrate CLAW SIGN)
Inflammatory Bowel	Ulcerative Colitis → signs of bowel inflammation such as mucosal thickening 'thumb-printing' or a featureless colon 'lead pipe' colon
Toxic Megacolon	Evidence of bowel wall oedema with 'thumb-printing', and pseudo-polyps or 'mucosal islands'
Gallstone Ileus	Look for aerobilia (occurs in cholecystoduodenal fistula) & opacity near the ileocecal valve

- KUB (extends to the pubic symphysis)
  - Able to look for rectal gas – r/o if it is a complete IO (note: if patient just got PR may have presence of rectal gas)
- Barium Enema
  - Gastrografin preferable if risk of perforation; risk of barium peritonitis (100% mortality!)
  - Upper GI barium studies contraindicated
- Colonoscopy done without bowel prep (not necessary, and also contraindicated, in IO)
- CT colonography

Assess Complications	- FBC: any infections, anemia
	- U/E/Cr: any dehydration due to (or acute renal failure from dehydration)
	  ▪ Intraluminal 3rd Space Loss (damaged enterocytes unable to reabsorb)
	  ▪ Vomiting (also assess K+ loss: can perpetuate paralytic ileus)
	- ABG
	  ▪ Acidosis from bowel ischemia
	  ▪ Alkalosis due to vomiting (more for pyloric stenosis in children)
	- Lactate (do trending)
	  ▪ Non-specific surrogate measurement for anaerobic respiration
	  ▪ Correlate with clinical signs (i.e. abdominal pain) if suspecting ischemic bowel
	- Amylase
	  ▪ ? acute pancreatitis (AXR may just show small bowel dilatation)
	- Erect CXR: free air under diaphragm, any aspiration pneumonia
	- AXR: **Rigler's Sign / double-wall sign** → indicates pneumoperitoneum. **Thumb-print sign / pneumatosis intestinalis** → ischemic bowel

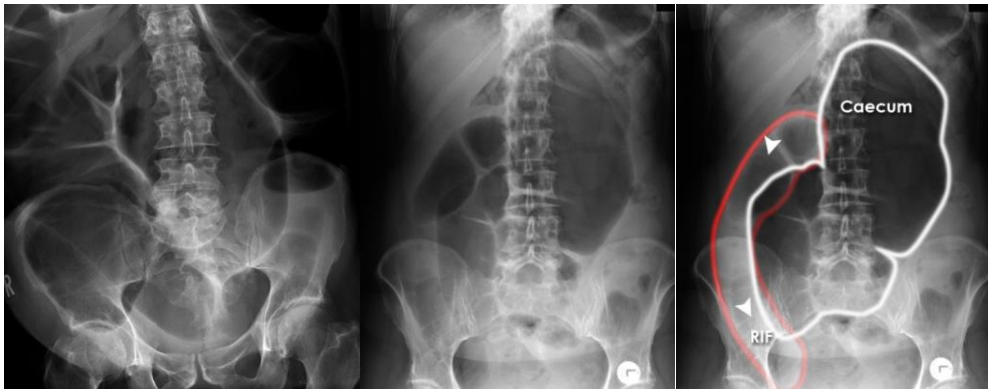
Pre-operative	- GXM 4 pints of blood - PT/PTT - ECG / Cardiac Enzymes

X-RAY FINDINGS

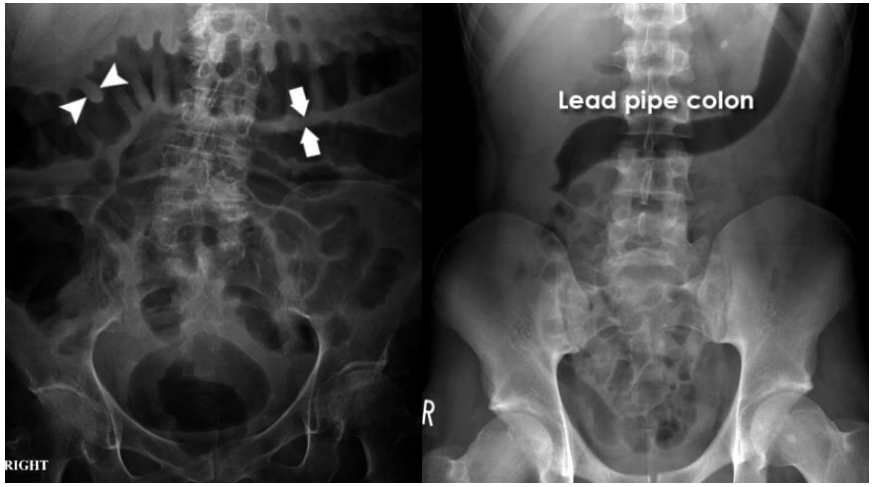


Rigler's Sign = double wall sign (obvious bowel wall due to extra-luminal air)

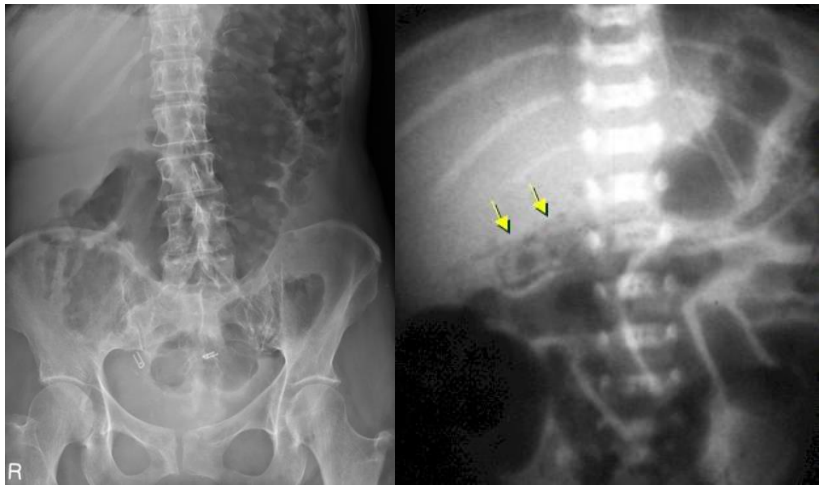
- Blue arrows = falciform ligament, made visible by a free air in the peritoneal cavity
- The red arrows = both sides of the wall of the stomach (Rigler's sign), a sign of free air
- The yellow arrow points to a skin fold



Right Side – Sigmoid Volvulus | Left Side – Caecal Volvulus



Right Side – Mucosal thickening - 'thumb-printing' | Left Side – Lead pipe colon a/w longstanding ulcerative colitis



Right Side – Toxic Megacolon | Left Side – Bowel ischemia with necrosis → Gas in bowel wall (pneumatosis intestinalis) due to gas gangrene

ACUTE MANAGEMENT

Rule out surgical emergencies → if suspected, immediate consult with GS Reg

1. **Ischaemic bowel with bowel necrosis – pneumatosis intestinalis**
2. Perforation/peritonitis
3. Obstructed and strangulated abdominal hernia
4. Volvulus (sigmoid, caecal, stomach)
5. Closed-loop obstruction (competent ileocecal valve)

"Fever, tachycardia, hypotension, increasingly progressive pain – do septic workup (visceral pain in paraumbilical region progressing to localising pain suggest impending perforation – consider surgical intervention)"

1. ABCs
   - Most important → breathing and Spo2 – may be affected due to splinting of the diaphragm – give supplemental oxygen

2. Keep NBM – 70% recover with bowel rest and decompression
3. NG tube suction
   - Large bore NG tube (small diameter easy to get blocked up)
   - Either passive connection or low-intermittent suction
     1. Passive – tubes placed on free drainage with 4-hourly aspiration
     2. Continuous / intermittent – suck intermittently till bowel wall collapse, useful for patients with estimated high NG tube o/p

4. IV fluid rehydration – since water and electrolytes (K^+ and Cl^-) are depleted

5. Urinary catheterization to monitor urine output
   - Assess the hydration status – patient may be hypotensive (resuscitate, monitor vitals)
     - Subjective Measure → skin turgor, mucous membrane, lethargy
     - Objective Measure → urinary output (>0.5ml/kg/hr), blood pressure, CVP line

6. Correct electrolyte abnormities
   - Tailor rehydration to patient's urine o/p (insert urinary catheter) – ensure end organ perfusion is good – treat with N/S
   - Correct acidosis, replace K^+ as guided by investigations
   - Do renal panel – look at urea and creatinine (>100:1 = pre-renal dehydration, < 40:1 suggest intrinsic renal damage)

7. ± Prophylactic broad-spectrum antibiotics
   - Pre-emptively prevents bacterial flora translocation (not usually given unless suspect ischemic bowel or bowel perforation)
   - 3rd generation cephalosporin and metronidazole (Rocephin and Flagyl)
     - IV Ceftriaxone 1g + Metronidazole 500mg
   - If have raised TW – r/o bacterial infections
     1. Look at neutrophils
     2. Look for left shift – increase % of less well differentiated neutrophils

8. ± CVP monitoring
   - Assess dynamically as a response to fluid challenge
   - CVP trending more impt than individual pressure measurements to assess volume status

9. Surgical decompression (if bowel ischemia, unresolved mechanical obstruction) – see below
   - Pre-operative investigations

"In IO there can be oedema of the small bowel due to 3rd space loss into bowel wall and abdominal cavity – this does not take part in intravascular space and this loss though massive can't be quantified. With depleted intravascular space it leads to hypotension whereby end organ perfusion worsens. Can give patient 4-5L of IV fluid and consider putting up CVP line to ensure patient is adequately perfused – if CVP is too low consider colloids (exception: sepsis) – with leaky capillaries vessels, infusion of large molecules can worsen intravascular loss as large molecules if drawn out into interstitial space draws more fluid out."

DEFINITIVE MANAGEMENT (Depends on cause)

1. **Post-op paralytic ileus** (>3 days post-op)
   - Supportive management: drip & suck, wait for peristalsis to restart
   - Oral gastrografin: hyperosmotic, causes intraluminal osmosis , can re-establish peristalsis
   - Prokinetics agents: erythromycin, metoclopramide, cisapride

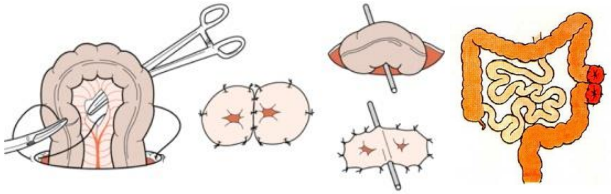
2. **Sigmoid volvulus**

Non-surgical/ conservative

6. Ryle's tube decompression:
   - Gown up
   - Put end of Ryle's tube in a bottle submerged in water
   - Insert lubricated Ryle's tube into anus
2. Flexible sigmoidoscopic decompression (recur in as much as 50%. Elective laparoscopic sigmoid resection and right hemi-colectomy following endoscopic decompression is increasingly being described and performed to treat patients with volvulus. The suggested interval between endoscopic decompression and definitive surgical intervention is 48-72 hours)

Surgical

a. Sigmoid colectomy with primary anastomosis: Primary anastomosis is performed if the divided bowel ends are viable, peritoneal contamination is not evident, and the patient is hemodynamically stable
b. Sigmoid colectomy with Hartman's procedure (may be reversed in 3-6/12 – depends on overall clinical condition and ability to withstand another major surgery)
c. Sigmoid colectomy & formation of double barrel colostomy (**Paul-Mikulicz procedure**) with future re-anastomosis



d. Sigmoidopexy: fix sigmoid to posterior abdominal wall (rarely done as high risk of recurrence)

Other volvulus

- Caecal volvulus: right hemi-colectomy with primary ileocolic anastomosis is the surgical procedure of choice (not endoscopic decompression as only successful in 15-20%. rare to create ileostomy)
- Gastric volvulus: gastropexy

3. **Closed loop obstruction** (if due to distal tumour)
   - Resect bowel, primary anastomosis with proximal defunctioning colostomy
   - Hartmann's/Paul-Mikulicz procedure if bowel is too inflamed/oedematous to anastomose (high risk of leakage)
   - Palliative: colonoscopy with stenting

4. **Ischaemic bowel**
   - Bowel ischemia alone can cause paralytic ileus, usually occurring in the splenic flexure (watershed area receiving blood from the most distal arterial branches)
   - Supportive management e.g. NBM, drip & suck, antibiotics while waiting for collaterals to re-supply bowel, re-establish peristalsis
   - Surgical intervention if bowel is non-viable e.g. gangrenous or necrotic

5. **Perforation** (usually in caecum as it is thin walled)
   - Occurs due to ischemia of stretched out bowel wall; >12cm dilated
   - Emergency laparotomy: resect lesion & perforated bowel with generous peritoneal lavage
   - If lesion e.g. tumour is proximal enough to the cecum, can do extended right hemi-colectomy
   - If lesion is distal, may require total-colectomy with ileo-rectal anastomosis
   - Continue antibiotics following surgery

6. **Obstructed abdominal hernia**
   - Herniorrhaphy

7. **Intussusception**
   - Children: usually due to hypertrophic Peyer's patches. Administer air or barium enema: watch intussusception reduce on fluoroscopy
   - Elderly: usually leading point present (polyp, Ca). Barium enema unlikely to work, or if works recurrence rate is high, therefore surgery is 1st line treatment

ISCHEMIC BOWEL (ISCHEMIC COLITIS)

- Ischemic colitis is the most common form (> 50%) of ischemic injury of the GIT
- It can present either as occlusive or a non-occlusive form → compromise in intestinal blood flow which is inadequate for meeting the metabolic demands of a region of the colon

EPIDEMIOLOGY

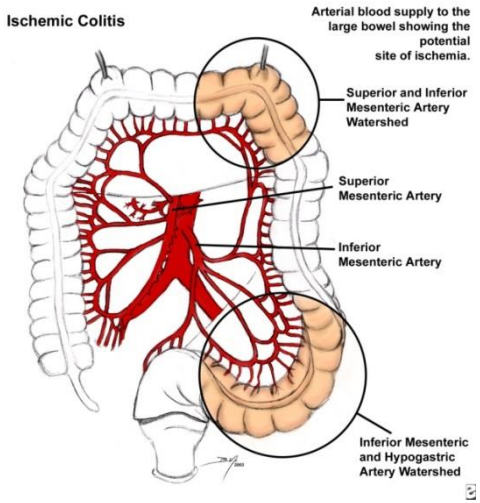
- Common in elderly patients (90% of cases occur in patients > 60yrs)

RISK FACTORS

	Examples	
Occlusive Vascular Disease	Mesenteric Artery Emboli Thrombosis Trauma	
Non-occlusive vascular disease	Hypo-perfusion State	Congestive Heart Failure Transient hypotension (pre-op period) Shock (i.e. hypovolemic, sepsis)
	Mechanical Factors	Colonic Obstruction due to tumours, adhesions, volvulus, hernia, diverticula or prolapse
	Medications (long list)	Chemotherapeutic agents Antibiotics, NSAIDs
	Iatrogenic	Post-AAA repair Complication of CABG surgery, colonic surgery
	Increased coagulability	Deficiency of Protein C/S or anti-thrombin III Factor V Leiden mutations Anti-phospholipid antibodies

2 Watershed areas:
a) Marginal artery of Drummond / Griffith's point: SMA and IMA
b) Sudeck's point: Left colic artery and Superior rectal artery

Three progressive phases of ischemic colitis have been described:



a) A hyperactive phase occurs first, in which the primary symptoms are severe abdominal pain and the passage of bloody stools. Many patients get better and do not progress beyond this phase.

b) A paralytic phase can follow if ischemia continues; in this phase, the abdominal pain becomes more widespread, the belly becomes more tender to the touch, and bowel motility decreases, resulting in abdominal bloating, no further bloody stools, and absent bowel sounds.

c) Finally, a shock phase can develop as fluids start to leak through the damaged colon lining. This can result in shock and metabolic acidosis with dehydration, hypotension, tachycardia and confusion. Patients who progress to this phase are often critically ill and require intensive care.

Acute mesenteric ischemia (classical triad)
1. Acute severe abdominal pain
2. No physical signs
3. Rapid hypovolemia → shock

PRESENTATION

- Sudden onset of crampy abdominal pain → followed by mild rectal bleeding within 24 hours (bright red)
- Diarrhoea with urge to defecate
- Abd Exam: tenderness over affected colon, PR: heme-positive stools
- Fever is unusual (although WCC is usually raised)
- (if severe ischemia) → marked tenderness with peritoneal signs a/w metabolic acidosis and septic shock

INVESTIGATIONS

- FBC: high Hb/ Hct (due to plasma loss/ hemoconcentration), high TW >15 in 75%
- ABG: Metabolic acidosis (persistent) – 50%
- U/E/Cr: renal failure, hypovolemia
- PT/PTT: hypercoagulable states (if present, can add Protein C/S, AT III)
- Raised amylase / LDH
- Markers for ischemia – lactate, LDH, amylase level, leucocytes, ALP

- AXR
  - Submucosal haemorrhage and edema in the colon produce a characteristic thumb-printing
  - Dilated bowel from ileus
  - Intramural air/ air in portal venous system (ischemia)
  - Free air in abdomen (perf)
- CTAP
  - Exclude other causes of abdominal pain
  - Ischemic colitis: SMA or superior mesenteric vein thrombosis, intestinal pneumatosis, portal venous gas, lack of bowel wall enhancement in contrast CT, thumb-printing and ischemia of other organs.
  - Nonspecific findings: distended bowel, an absence of intestinal gas, a thickened bowel wall, mesenteric vascular engagement, ascites and air-fluid levels

- Stool culture – salmonella, shingella, campylobacter, E.coli
- Colonoscopy – procedure of choice if diagnosis remains unclear

MANAGEMENT

- Conservative → NBM, IV fluids, NG tube on suction (if ileus is present), decompression of distended colon with rectal tube, broad spectrum antibiotics, KIV parenteral nutrition

- Surgical → emergency laparotomy (if there are signs of clinical worsening despite conservative therapy – i.e. sepsis, persistent fever, peritoneal irritations, protracted pain, free intra-abdominal air, endoscopically proved extensive gangrene)

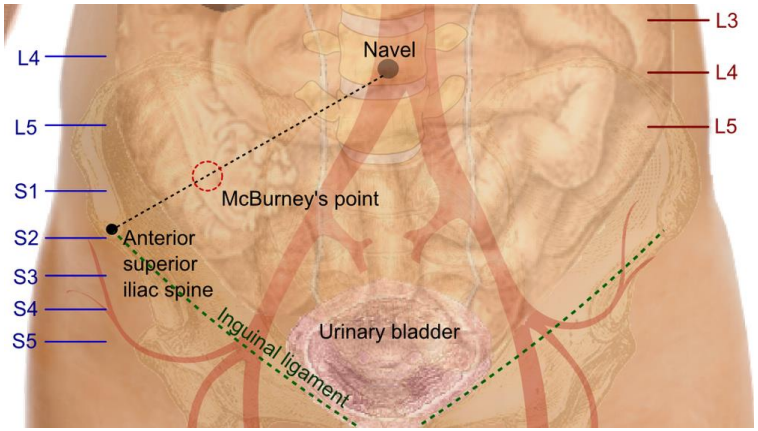
ACUTE APPENDICITIS

INTRODUCTION
- Classically 7.5cm to 10cm
- Vermiform appendix have high propensity for inflammation resulting in acute appendicitis
- Acute appendicitis is the most common cause of acute abdomen
- Early and accurate pre-operative diagnosis remains an enigmatic challenge and reminder of the art of surgical diagnosis

ANATOMY
- Blind muscular tube with mucosal, sub-mucosal, muscular and serosa layers
- Appendix location
  - **Retrocaecal position (75%)**
  - Pelvic (21%), Subcaecal (1.5%), Paracaecal (2%)
  - Constant base of appendix – at confluence of 3 taeniae coli, fuse to form outer longitudinal muscle coat of the appendix
- Meso-appendix contents
  - Appendicular artery (branch of the ileocolic artery branch of SMA) – end artery
    - Thrombosis leads to gangrenous appendicitis
  - Lymphatic channels (empty to ileocaecal lymph nodes)
  - Adults – laden with fats, children – transparent

AETIOLOGY
- Decreased dietary fibre and increased refined carbohydrates
- Obstruction of appendiceal lumen
  - Fecaliths: calcium salts & faecal debris collect around nidus of faecal material within appendix
  - Lymphoid hyperplasia: a/w inflammatory (Crohn's) & infective dz (GE, URTI, IMS, measles)
  - Less common causes: parasites, TB, tumour, FB

PATHOPHYSIOLOGY
"Lymphoid hyperplasia → luminal obstruction → continuous mucous secretion and inflammatory exudates → increase intraluminal pressure → obstruct lymph drainage → edema and bacterial translocation to submucosal → mucosal ulceration → progression → further distension of the appendix → venous obstruction and ischemia of appendix wall → bacteria invades through muscularis propria and submucosal → acute appendicitis"



HISTORY – characterized by 4 classical features
1. Migratory Pain (umbilicus to RIF)
   a. Visceral discomfort (poorly localised, mid-gut) in response to appendiceal inflammation and obstruction
   b. Somatic pain (intense, constant, localised) in response to progressive inflammation and irritation of parietal peritoneum in RIF
2. Nausea and Vomiting
   a. Almost always occur after pain
   b. If it precedes pain (? Intestinal obstruction)
3. Fever
   a. First 6 hours – rarely any alteration
   b. After 6 hours – slight pyrexia (37.2-37.7°C) and increase in pulse rate (80-90bpm)
   c. In children if temperature > 38.5°C (? mesenteric adenitis)
4. Anorexia (~75%)
   a. Useful and constant clinical feature especially in children
5. Others
   a. Diarrhoea / Constipation – 18%

PHYSICAL EXAMINATION
Cardinal Features:
- Unwell patient with low grade pyrexia
- Localised abdominal tenderness
- Muscle guarding and rebound tenderness

Inspection
- Limitation of respiratory movements in the lower abdomen

Palpation
- **Mc Burney's Point** = 1/3 of distance from right ASIS to umbilicus
- Detect muscle guarding over the point of maximum tenderness (Mc Burney's point)
- RIF tenderness (Mc Burney's point) – present in 96% of patients
- Tenderness on percussion, rebound tenderness, rigidity & guarding

Signs to elicit
- Cough sign: RIF pain on coughing (localized peritonitis)
- **Rovsing sign**: RIF pain with deep palpation of the LIF
- **Obturator sign**: RIF pain with int. rotation of a flexed right hip (spasm of obturator internus)
- **Psoas sign**: RIF pain with right hip flexed (inflamed appendix lying on psoas muscle)
- Infants/children may present with inflamed hemiscrotum due to migration of pus through patent processus vaginalis – often mistaken for acute testicular torsion

DIFFERENTIAL DIAGNOSES

Children	Adults	Female Adults	Elderly
Gastroenteritis	Terminal Ileitis	Ovarian Torsion	Diverticulitis
Mesenteric Adenitis	Perforated Peptic Ulcer Disease	Ectopic Pregnancy	Intestinal Obstruction
Meckel's Diverticulum	Testicular Torsion	Pelvic Inflammatory Disease	Colonic Carcinoma
Lobar Pneumonia	Epididymitis Orchitis	Ruptured Ovarian Cyst	
Intussusception			

INVESTIGATIONS

I would like to do investigations to (1) assist my clinical suspicion of acute appendicitis. This is crucial as negative appendectomy rate is 15-30% if based solely on clinical suspicion. I would then do (2) pre-operative investigation to rule out differential causes and look for complications of the disease. Finally, I would perform other (3) pre-operative investigations.

(1) Diagnosis

- **Alvarado Score – [MANTRELS]**

Symptoms	**M**igratory RIF pain	1 point	- Alvarado ≤ 3 = no imaging, unlikely appendicitis - Alvarado 4-6 = recommend CT scan - Alvarado ≥ 7 = surgical consultation *The sensitivity of Alvarado scores 7 or higher for appendicitis was 77% (28/36), and the specificity 100% (8/8)[20]
	Anorexia	1 point	
	Nausea and/or Vomiting	1 point	
Signs	**T**enderness (RIF)	2 points	
	Rebound Tenderness	1 point	
	↑ Temperature (> 37.3°C)	1 point	
Laboratory	**L**eucocytosis > 10,000	2 points	
	Left **Shift** of Neutrophils	1 point	

- Do FBC (assess WBC) – normal WBC does not r/o appendicitis
- Abdominal u/s or contrast-enhance CT (high diagnostic accuracy)
  - Able to r/o other differing pathologies
- CRP – raised inflammatory markers

(2) Rule out differential causes and assess complications

- Pregnancy Test – r/o ectopic pregnancy
- Erect CXR – r/o perforation (free air under diaphragm), r/o lobar pneumonia at right lung base
- UFEME (may have pyuria & haematuria)
- U/E/Cr – identify any electrolyte imbalance

(3) Other Pre-operative investigations

- **Blood:** FBC, U/E/Cr, CRP, Blood culture*, PT/PTT, GXM
- **Urine**: UFEME (may have pyuria & haematuria)
- **Imaging**: Erect CXR, CTAP, abdominal U/S**, MRI

* The most common organism involved in gangrenous and perforated appendicitis are Escherichia Coli, Peptostreptococcus, Bacillus Fragilis and Pseudomonas[21]

**diagnostic modality of choice in pregnancy (graded compression ultrasonography) – if inconclusive KIV MRI

MANAGEMENT

- NBM, IV drip, IV antibiotics (cephalosporin and metronidazole)
  - Non-perforated → single pre-op antibiotic dose 30-60 min before skin incision for surgical wound prophylaxis. Post-op antibiotics are not necessary – can use unasyn or cefazolin with metronidazole
  - Perforated → start broad spectrum antibiotics for 5-7 days (till infection resolves)
- Correct electrolyte imbalance
- Symptomatic relief: anti-emetics & analgesia
- Definitive treatment: appendectomy (open or laparoscopic)
- Conservative treatment for appendix mass: **Ochsner Sherren regime**
  - Omentum wraps around inflamed appendix resulting in localised inflammatory process (phlegmon)
  - Inadvertent surgery is difficult and dangerous (hard to find appendix)
  - Careful recording of the patient's condition noting (1) pulse rate, (2) extent of the mass and (3) spread of abdominal pain
  - Symptomatic treatment as well as antibiotics, do contrast enhanced CT
  - When mass has reduced in size, patient is stable, do surgery (less inflammation: easier)
  - Exceptions: very young or very old patients, or patients with suspected appendicular abscess (drained radiologically), clinical deterioration (evidence of peritonitis)

Delayed diagnosis and treatment account for much of the mortality and morbidity associated with appendicitis.

The rate of perforation varies from 16% to 40%, with a higher frequency occurring in younger age groups (40-57%) and in patients older than 50 years (55-70%), in whom misdiagnosis and delayed diagnosis are common.

Complications occur in 1-5% of patients with appendicitis, and postoperative wound infections account for almost one third of the associated morbidity.

Complications from appendectomy

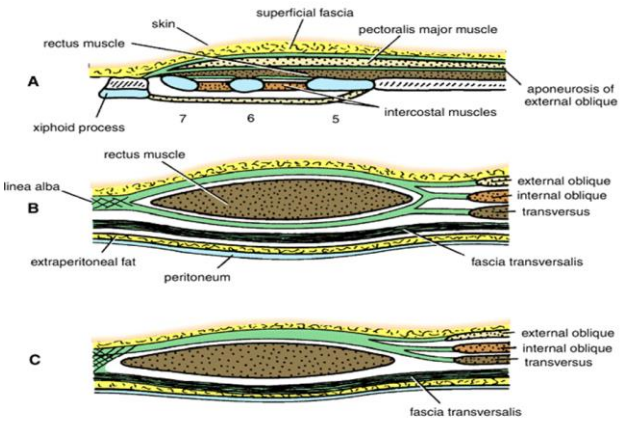
- Local (stump) → retained fecalith, stump appendicitis, leak, fistula
- Haemorrhage → intra-abdominal, abdominal wall hematoma, scrotal hematoma
- Infection / Sepsis → wound infection, abscess (intra-abd, appendiceal stump, pelvic, scrotal)
- Paralytic Ileus

[20] Am J Emerg Med. 2007 Jun;25(5):489-93.
[21] Can J Surg. 2008 June; 51(3): E54–E55.

SURGICAL ANATOMY

ANATOMY OF ABDOMEN

LAYERS OF THE ANTERIOR ABDOMINAL WALL



Formation of the Rectus Sheath:

A: above the costal margins
B: above the arcuate line
C: below the arcuate line

The **linea alba** is a fibrous sheath composed of the aponeuroses of the 3 flat muscles. It extends from the xiphoid process to the pubic symphysis. It separates the left and right rectus abdominis muscle. It doesn't contain any primary nerves or blood vessels → excellent for routine and rapid access

The **linea semilunaris** marks the lateral border of the rectus abdominis.

The **arcuate line** can be marked on the posterior layer of the rectus sheath at the level of the ASIS. It is also where the inferior epigastric vessels perforate the rectus abdominis

Layers of the anterior abdominal wall	Layers at the midline abdominal wall

- Skin
- Subcutaneous Tissue
- Fascia
  ▪ Camper's fascia* – superficial fatty layer
  ▪ Scarpa's fascia** – deep fibrous layer
- Muscle
  ▪ Rectus Abdominis
  ▪ External Oblique Muscle
  ▪ Internal Oblique Muscle
  ▪ Transverse Abdominal Muscle
- Transversalis Fascia
- Extra-peritoneal Fat
- Parietal Peritoneum
	- Skin
	- Subcutaneous Tissue
	- Fascia
	  ▪ Camper's fascia – superficial fatty layer
	  ▪ Scarpa's fascia – deep fibrous layer
	- Linea Alba – aponeuroses of the 3 flat muscle
	- Transversalis Fascia
	- Extra-peritoneal Fat
	- Parietal Peritoneum

* Camper's fascia extends onto penis and scrotum → in rupture of the bulbous urethra, urine tracks into scrotum, perineum and penis and into abdominal wall deep to Scarpa's fascia. It does not track into the thigh because the attachment of the Scarpa's fascia to the deep fascia of the thigh

** Scarpa's fascia attach to the deep fascia of the thigh → an ectopic testis in the groin cannot descend any lower into the thigh

DIASTASIS RECTI

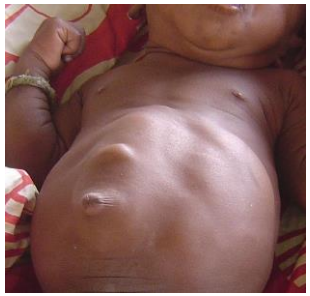
- Defined as a separation of the rectus abdominis muscle into right and left halves
- A cosmetic condition with no associated morbidity or mortality
- Diastasis of this muscle principally occur in → new-borns (esp. premature new-borns) and pregnant women (esp. multiparous women)

Presentation

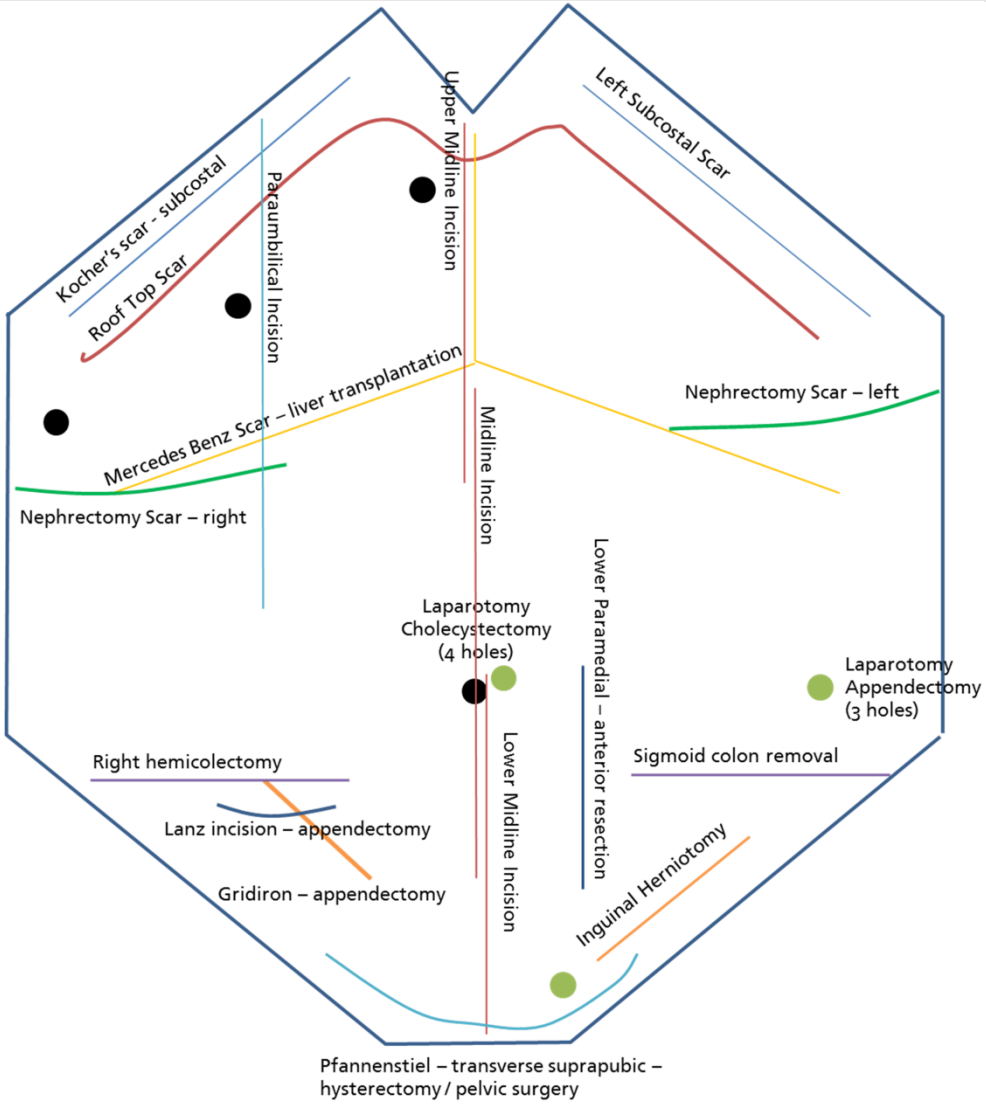
- Appear as a ridge down the midline of the abdomen, (i.e. xiphoid process to umbilicus)
- Prominent with straining and may disappear when abdominal muscles are relaxed

Treatment

- No treatment needed – physiotherapy can help correct or mitigate some cases



ABDOMINAL SCARS



Incisions are made based on:

- Shortest Distance
- Cosmetic Reasons
- Surgeon's Preference
- Avoidance of Nerves / Muscles

With presence of scars → look for incisional hernia → from the end of the bed, ask the patient to raise their head off the bed and cough to demonstrate this.

CLINICAL EFFECTS OF TUMOUR

Classification		
Local	Bleeding	due to ulceration: Haematemesis / Haematuria
	Pain	
	Obstruction	Large bowel obstruction with carcinoma
	Irritation	Cough due to bronchial tumour
	Pressure	Nerves, blood vessels, bile ducts (i.e. cancer of head of pancreas and obstructive jaundice)
Systemic	Lymph Nodes	May be discrete / hard / irregular / meted
	Hepatic	Hepatomegaly – primary in stomach, colon, bronchus or breast Jaundice – nodes in porta hepatis with 1° in stomach, pancreas or colon
	Lungs	Pleural Effusion – from bronchus or breast cancer
	Bone	Pathological Fracture – bony mets from breast, bronchus, thyroid, prostate or kidney
	Brain	Fits, confusion, personality change from cerebral metastases – i.e. from breast, bronchus, malignant melanoma
	Anemia	Pancytopenia / Bone Marrow deposits
	Ascites	Ovarian or GI malignancy
Paraneoplastic	Humoral (mediated by tumour secreted pdt)	- Bronchial CA and Cushing's syndrome due to inappropriate secretion of ACTH - Bronchial CA and inappropriate secretion of ADH - Hypercalcaemia of malignancy caused by secretion of PTH related peptide - Carcinoid syndrome with liver metastases from a carcinoid tumour due to 5HT
	Immunological (autoimmune)	- Dermatomyositis due to underlying malignancy - Membranous Glomerulonephritis initiated by underlying malignancy
Metabolic	Thyroid	Thyrotoxicosis from thyroid adenoma
	Adrenal	Cushing's syndrome from adrenal cortical adenoma
	Parathyroid	Hyperparathyroidism from parathyroid adenoma
	Pancreas	Insulin from an insulinoma
Constitutional	Cachexia	All tumours – LOW/LOA
	PUO	i.e. lymphoma, hypernephroma
Others	Hypertrophic Pulmonary Osteoarthropathy a/w Bronchial Cancer	
	Thrombophlebitis migrans associated with visceral cancer usually carcinoma of the head of pancreas (Trousseau sign of malignancy)	
	Acanthosis Nigricans a/w carcinoma of the pancreas	

TUMOUR MARKERS

A substance secreted into the blood or other body fluid or expressed on the cell surface of malignant cells in larger quantity than in normal counterparts

Tumour	Marker
Prostate	PSA
HCC	Alpha-fetoprotein
Testicular	B-HCG, A-FP, placental Alkaline phosphatase
Choriocarcinoma	B-HCG
Ovarian	CA 125
Colorectal	Carcinoembryonic antigen (CEA)

* The value of tumour markers is in following the course of a malignant disease and monitoring the response to treatment and hence prognosis – can also be used for tumour localization and antibody directed therapy

OESOPHAGEAL DISEASES

ANATOMY OF THE OESOPHAGUS

- Oesophagus is a muscular tube that is 25cm long
- Starts at the cricoid cartilage (C6 vertebra) from the oropharynx and continues into the stomach at the level of T10
- Upper oesophageal sphincter is formed by cricopharyngeus muscle
- Lower sphincter is not an anatomical sphincter, but physiological:
  - Increased tone of the muscularis propria at the lower oesophageal sphincter
  - Fibres of the right diaphragmatic crus loop around the cardio-oesophageal junction and contract during coughing, sneezing etc. when intra-abdominal pressure increases, thus preventing reflux
  - Angle of His where the oesophagus joins the stomach – acts as a valve
  - Intra-abdominal pressure being higher than intra-thoracic pressure

- 3 narrow points along the course of the oesophagus
  1. Cricopharyngeus sphincter (15cm from incisor teeth)
  2. Aortic Arch and left main bronchus crosses the oesophagus (25cm from incisors)
  3. Where the oesophagus pierces through the diaphragm, the lower oesophageal sphincter (LES) is situated at this level (40cm from incisors)

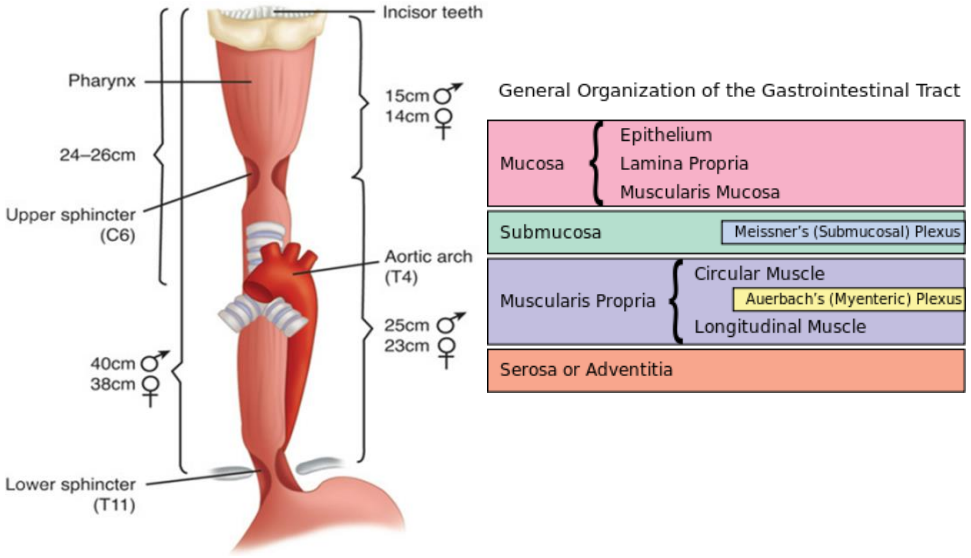
<u>Structure/Histology (from outside to inside)</u>

- **Adventitia** – Most of oesophagus lined by adventitia, only short segment of intra-abdominal oesophagus lined by serosa
- **Outer Longitudinal Layer of Muscularis Propria**
- **Inner Circular layer of Muscularis Propria**
  - Between the layers contains the myenteric plexus (Auerbach's plexus)
- **Muscularis Propria** – upper 1/3 is skeletal, lower 1/3 is smooth, middle 1/3 is mixed
- **Submucosa** – contains submucosal plexus (Meissner's Plexus)
- **Mucosa** – stratified squamous non-keratinising epithelium

	Upper 1/3	Middle 1/3	Lower 1/3
Muscularis Propria	striated muscle	striated and smooth muscle	smooth muscle
Blood Supply	Inferior thyroid artery	Oesophageal branches of the aorta	Oesophageal branches of left gastric artery
Venous Return	Brachiocephalic veins	Azygos veins	Left gastric vein* (tributary of portal vein)
Lymph Drainage	Deep Cervical Nodes	Superior and Posterior Mediastinal Nodes	Nodes along L. Gastric Blood Vessels; Celiac Nodes

* a porto-systemic anastomosis exists at the lower oesophagus thus leading to formation of varices in portal HTN

- Parasympathetic via the vagus nerves that has synaptic connections to the myenteric (Auerbach's) plexus. Meissner's submucosal plexus is sparse in the oesophagus.



PHYSIOLOGY OF THE OESOPHAGUS

Oral (voluntary) Phase	- Process of mastication forms a food bolus on the dorsum of the tongue - The tongue then contracts upwards and backwards pushing the food bolus against the hard palate - Soft palate elevates (contraction of palatoglossus) to close off nasopharynx - Further elevation of tongue pushes food bolus into oropharynx
Oropharyngeal Phase	- As the base of the tongue is elevated posterior, the epiglottis falls back; at the same time, the pharyngeal muscles contract to bring the posterior surface of the larynx upwards to make the laryngeal inlet smaller → closed off by the epiglottis - Pharyngeal muscles contract to propel food bolus past the relaxed cricopharyngeus into the oesophagus
Oesophageal Stage	- Once in the oesophagus, involuntary contractions of the muscularis propria form peristaltic waves to propel food bolus into stomach

APPROACH TO DYSPHAGIA

CAUSES OF DYSPHAGIA

- Dysphagia can be divided into *oropharyngeal* and *oesophageal* dysphagia
- In each anatomic region the dysphagia can be caused by neuromuscular dysfunction (impaired physiology of swallowing) or mechanical obstruction to the lumen

Oropharyngeal Dysphagia	Oesophageal Dysphagia
Neuromuscular diseases: Central Causes Stroke / CVA accidents Brain stem tumours Parkinson's disease Peripheral Causes Motor Neuron Disease (i.e. ALS) Peripheral neuropathy Myasthenia gravis Skeletal Muscle Disease (myopathies) – I.e. Muscular Dystrophy (myotonic dystrophy), Polymyositis, Dermatomyositis Post infectious Poliomyelitis Syphilis	**Neuromuscular diseases:** Primary Motility Disorder Achalasia / Vigorous Achalasia Spastic Motility Disorders - Diffuse oesophageal spasm - Nutcracker oesophagus - Hypertensive lower oesophageal sphincter Secondary Motility Disorder Scleroderma (Systemic Sclerosis) Multiple Sclerosis Sjogren's Syndrome Diabetic Neuropathy
Obstructive lesions: Intra-luminal Causes Oesophageal webs Intra-mural Causes Oropharyngeal Tumour Inflammatory masses e.g. abscess Extra-luminal Causes Anterior Mediastinal masses – 4Ts: thyroid, thymus, teratoma, terrible lymphoma) **Others:** Pharyngeal pouch (Zenker's divert)	**Obstructive lesions:** Intra-luminal Causes Lower oesophageal rings (Schatzki's ring) Oesophageal webs (Plummer-Vinson) Foreign bodies (i.e. fish bone) Intra-mural Causes Tumour Strictures: - Peptic (reflux oesophagitis) - Radiation - Chemical (caustic ingestion) - Medication - Malignant Extra-luminal Causes Anterior Mediastinal masses – 4Ts: thyroid, thymus, teratoma, terrible lymphoma Bronchogenic Carcinoma Very rare causes: CVS abnormalities - Thoracic aorta aneurysm (dysphagia aortica) - Aberrant R subclavian artery (dysphagia lusoria) - Left atrial dilataion (dysphagia megalatriensis)

HISTORY:

1. Establish if there is odynophagia (pain with swallowing)[22]
   (i) Caustic Ingestion – acid / alkali
   (ii) Drug-Induced Esophagitis
      - Antibiotics (i.e. doxycycline), KCl (slow release), Quinidine, Iron Sulfate, Zidovudin, NSAIDs
   (iii) Radiation Esophagitis
   (iv) Infectious Esophagitis
      - **Healthy –** Candida Albicans, HSV
      - **HIV patients –** Fungal (candida, histoplamosis), Viral (HSV, CMV, HIV, EBV), Mycobacteria (TB, avium-complex), Protozoan (cryptosporidium, pneumocystis carinii), Ulcers (aphthous ulcers)
   (v) Severe ulcerative Esophagitis secondary to GERD
   (vi) Oesophageal Carcinoma (pain occurs late)

2. Which phase of swallowing is affected (oropharyngeal vs. oesophageal dysphagia)
   (i) Oropharyngeal
      - Presenting complaint is usually of difficulty in initiating swallowing
      - May be associated with choking, coughing, nasal regurgitation
      - Voice may sound nasal (bulbar palsy)
      - Cause of oropharyngeal dysphagia is usually neuromuscular rather than mechanical; stroke is the most common cause
   (ii) Oesophageal
      - Presenting complaint is that of food "getting stuck" in the throat or chest
      - Localisation of the symptom often does not correspond to actual site of pathology
      - Can be due to either neuromuscular dysfunction or mechanical obstruction

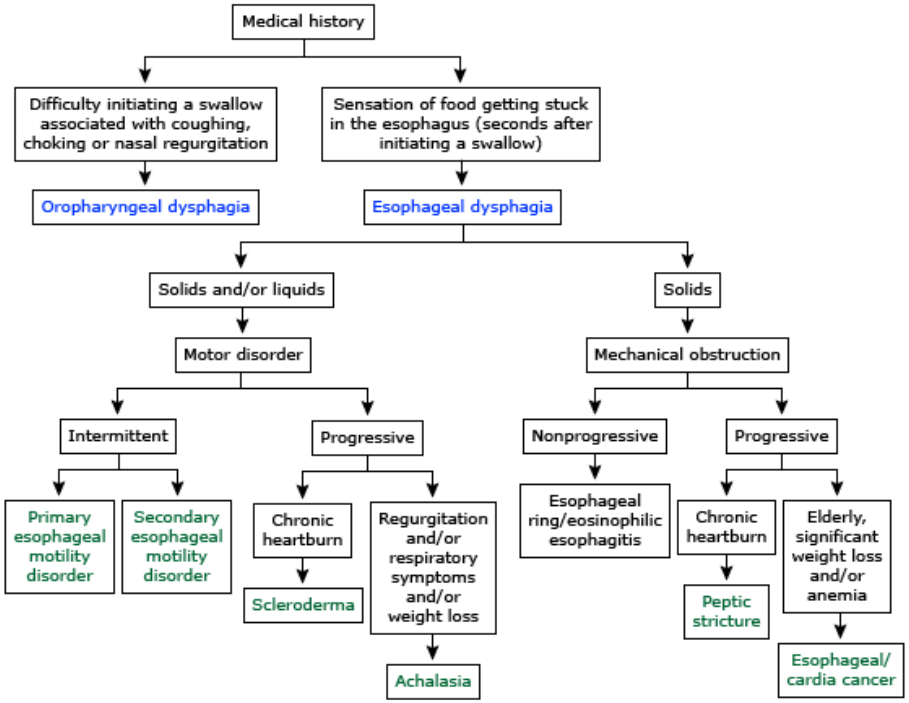
3. **Differentiating obstructive from function (neuromuscular dysfunction) causes**
   (i) Mechanical
      - Patient complains of more difficulty swallowing solids than fluids
      - May have regurgitation of undigested food
      - Recent onset dysphagia that is progressively worsening, with loss of weight → high suspicion of oesophageal cancer
      - Intermittent symptoms suggestive of webs, rings

   (ii) Neuromuscular
      - Patient complains of more trouble swallowing fluids than solids
      - Dysphagia more long-standing, slowly progressive
      - Intermittent symptoms suggestive of diffuse oesophageal spasm, nutcracker oesophagus
      - May have history of stroke, neuromuscular disease

[22] Chapter 6: Dysphagia, odynophagia, heartburn, and other esophageal symptoms (Joel E. Richter)

4. **History of predisposing conditions (RF)**
   - Reflux symptoms e.g. retrosternal burning pain (heartburn), sour fluid reflux into mouth (acid brash), excessive salivation (water brash), postural aggravation on lying down
   - Caustic chemical ingestion in the past
   - Smoking, chronic alcohol intake
   - Symptoms of systemic disease e.g. stroke (focal neurological deficits), myopathies, limited cutaneous systemic sclerosis (CREST – calcinosis, raynaud's, esophageal dysmotility, sclerodactyly, and telangiectasia),
   - Medication history: Antibiotics (e.g., doxycycline, tetracycline, clindamycin, trimethoprim-sulfamethoxazole), potassium chloride, non-steroidal anti-inflammatory drugs (NSAIDs), quinidine, emperonium bromide, and alendronate (Fosamax)

5. **Complications**
   - Symptoms of anemia (bleeding from tumour, or as part of Plummer-Vinson syndrome*)
   - Symptoms of aspiration pneumonia – fever, cough, shortness of breath esp. at night
   - Malnutrition
   - Locally Advanced Tumour
     - Hoarseness (recurrent laryngeal nerve)
     - Thoracic Spine Pain (spread posterior to thoracic spine)
     - Fever, cough and haemoptysis (tracheo-oesophageal fistula)
     - Haematemesis (invasion into aorta) – rare
   - Mets: Neck lump (lymph node), jaundice, bone pain
   - LOW / LOA (cancer or achalasia)



PHYSICAL EXAMINATION

1. **General condition**
   - Patient's level of alertness and cognitive status (impact safety of swallowing)
   - Vitals: the patient may be hypovolemic from vomiting/decreased intake
   - Nutrition: presence of cachexia
   - Dehydration (mucous membranes, skin turgor, etc.)
   - Conjunctival pallor: bleeding from tumour, oesophagitis ulcerations, or associated with P-V syndrome
   - Scleral icterus: metastases to liver

2. **Disease / Causes**
   - Neuro Examination (esp. CN V, VII-XII, PD features, myopathy)
   - Inspect for any neck masses
   - Bedside Swallowing Test (direct observation of the act of swallowing)
   - Scars/marks over the chest and abdomen suggesting previous surgery, radiation
   - Palpable mass in abdomen (not likely)
   - PR examination for melaena

3. **Complications of disease**
   - Signs of pneumonia: patient febrile, may be toxic, lung crepitations, decreased air entry usually over right lower lobe
   - Signs of Mets: Cervical lymphadenopathy (i.e. Virchow's), Hepatomegaly, Ascites

4. **Treatment**
   - Tube feeding through NG tube, gastrostomy/jejunostomy – if aspirates seen, what is the colour?
   - Total Parenteral Nutrition (TPN)

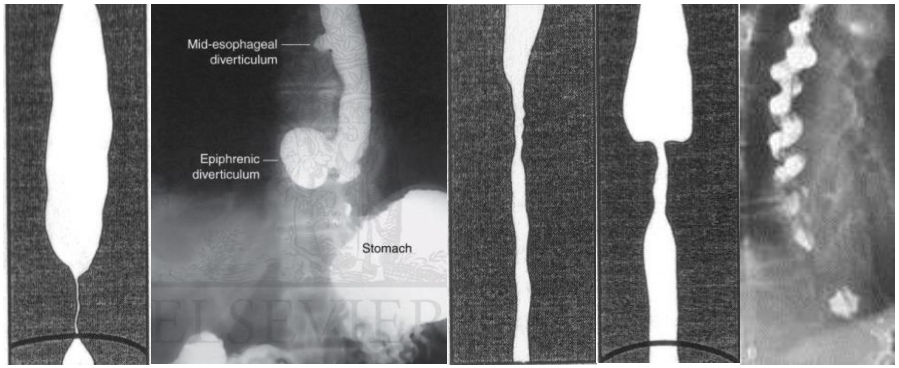
* Plummer-Vinson Syndrome / Paterson Brown-Kelly Syndrome
- Triad of post-cricoid dysphagia, Fe deficiency anemia and cervical oesophageal webs
- also a/w glossitis + angular cheilitis, koilonychia, splenomegaly, enlarged thyroid
- Pathophysiology: unknown -?iron/nutritional deficiency, genetics, autoimmune
- Complication: oesophageal or pharyngeal squamous cell carcinoma (SCC)

INVESTIGATIONS

Diagnostic

1. Oesophagogastroduodenoscopy (OGD)
   - Advantage is **direct visualisation** of the lesion, ability to take **tissue biopsy** (esp. useful in malignancy), and **therapeutic** (stopping bleeding from a tumour, stenting the lumen, etc.)

2. Barium swallow
   - Advantage of barium swallow is that it is less invasive than OGD, especially when suspecting webs, diverticula in the oesophagus where OGD may cause perforation; however if patient is at high risk of aspiration, barium swallow is dangerous.
   - Visualisation of obstructive lesions:
     - Shouldering of a stricture (benign strictures form a smoother contour whereas malignant strictures form a more right-angled contour)
     - Bird's beak / Rat's Tail sign of achalasia
   - Visualisation of pharyngeal pouch or oesophageal diverticulum
   - Diffuse oesophageal spasm gives a corkscrew appearance



Achalasia | Oesophageal Diverticulum | Stricture | Carcinoma | Spasm

3. Oesophageal Manometry*
   - Assess motor function of the UES, oesophageal body and LES
   - Gold standard for diagnosing achalasia

4. Video-fluoroscopic examination of swallowing (VFES) – using barium or flexible-endoscopic examination of swallowing (FEES)
   - Used to assess oropharyngeal dysphagia (neuromuscular causes) by looking for penetration and aspiration of various consistencies of food during swallowing
   - VFES limited to cervical oesophagus (unable to r/o distal oesophageal lesions)

Supportive

1. Blood investigations:
   - Full blood count – Low Hb (anemia from chronic blood loss)
     High TW (aspiration pneumonia)
   - U/E/Cr – electrolyte disturbances from vomiting, poor oral intake; raised creatinine and urea in dehydration (creatinine will be raised more than urea if patient has pre-renal failure from dehydration)
   - LFTs – low albumin with nutritional deprivation

2. CXR
   - Consolidation (aspiration pneumonia)
   - Any tracheal deviation / masses compressing on oesophagus

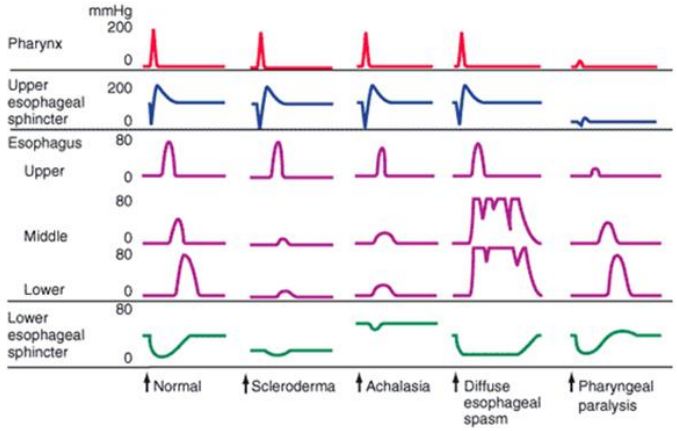
3. 24-hour pH probe monitoring
   - If patient complains of reflux symptoms and no signs are seen on OGD (see later section on Gastro-oesophageal reflux disease)

INITIAL MANAGEMENT

1. **Stabilise patient**
   - Resuscitate if patient is hemodynamically unstable
   - IV fluids (correct fluid deficits and also any electrolyte derangements)
   - Consider feeding with fluids if patient can tolerate it (only having problems with solid food) otherwise consider tube feeding or TPN → need to correct patient's nutritionally debilitated state
   - Keep NBM if patient cannot tolerate even fluids
   - Treat any aspiration pneumonia – NBM, IV antibiotics

2. **Investigate for underlying cause and treat it**

*Oesophageal Manometry



ACHALASIA

EPIDEMIOLOGY
- Rare (1 in 100,000) but most common primary oesophageal dysmotility
- Typically presents in the ages 35-45.

PATHOPHYSIOLOGY – CHARACTERIZED BY TRIAD OF
- Aperistalsis of the oesophagus (alteration in the ganglia of Auerbach's plexus)
- Increased LES tone/pressure (hypertensive LES)
- Failure of LES to relax with swallowing

CAUSES
- Primary Achalasia: idiopathic (failure of distal oesophageal inhibitory neurons)
- Secondary Achalasia: Chagas Disease, diabetic autonomic neuropathy, lesions of dorsal motor nuclei (polio or surgical ablation)
- Pseudo-achalasia: Malignancy (i.e. gastric adenocarcinoma)

CLINICAL FEATURES
- Patient's Age
- Progressive dysphagia (99%), immediate regurgitation after meals (>70%), odynophagia (30%), aspiration with resultant bronchitis and pneumonia (10%), nocturnal cough, weight loss and retrosternal chest pain (due to oesophageal spasm)
- Patients may also develop an oesophageal diverticulum – experiences regurgitation of food several hours after eating and/or halitosis
- In pseudo-achalasia: advanced age at symptoms onset (>60yr), short duration of symptoms (<6mth), rapid weight loss, difficulty advancing endoscope through the GEJ of a non-dilated oesophagus[23]

COMPLICATIONS[24]
- Stasis of food can lead to friability , erosions and/or candida esophagitis
- Increased risk of developing oesophageal squamous cell carcinoma (0-140x normal population) – usually occurs >10years after diagnosis
- Predisposition to Barrett's metaplasia and oesophageal adenocarcinoma (see below)

[23] Am J Gastroenterol. 1994;89(11):2014.
[24] Scand J Gastroenterol Suppl. 2006;(243):7-10

INVESTIGATIONS
- Oesophageal Manometry → (for definitive diagnosis) – characterized by:
  1. Lack of progressive peristalsis (aperistalsis)
  2. Abnormally high pressures at the LES
  3. Incomplete LES relaxation on swallowing
- CXR → a widened mediastinum with an air-fluid level and large amounts of retained food and fluid in the dilated oesophagus with absence of gastric air bubble
- Barium swallow →
  - "Bird's beak" tapering of distal oesophagus with proximal dilatation (not specific)
  - Later = severely dilated oesophagus that takes on the contortion of a "sigmoid" shape
- OGD → to rule out mechanical stricture and malignancy (at esophagogastric junction)
- EUS → useful for characterizing tumours of the distal oesophagus and cardia (differentiate with pseudo-achalasia)
- CT Thorax/Abdomen → to rule out malignancies

MANAGEMENT / TREATMENT
- Lifestyle & Medical (aim: decrease LES tone)
  - CCB (nifedipine) and nitrates (nitroglycerine)
  - Endoscopic injection of botulinum toxin (block Ach release from nerve terminals)
- Endoscopic
  - Per-oral Endoscopic Myotomy (POEM)
  - Pneumatic balloon dilatation (65% of patients improve, 40% response rate at 5 years)
    - Risks: perforation with dilatation, recurrence of symptoms
- Surgical treatment
  - Laparoscopic Heller esophagomyotomy (myotomy of the lower oesophagus) with anterior 180-degree partial (Dor) fundoplication (reduce post-operative reflux)*
    - Excellent results in 90-98% of patients
    - Risks: bleeding, infection, oesophageal perforation

*Patients with achalasia can be treated successfully by a minimally invasive surgical technique called laparoscopic esophagomyotomy (Heller myotomy) with partial fundoplication. This involves 5 small incisions for placement of trocars (one for a camera port and 4 for the surgical instruments – i.e. graspers, electro cautery and suturing instruments). Gastroesophageal fat pad is mobilized with the dissection carried down to the oesophagus. The layers (outer longitudinal and inner circular muscle fibres) are dissected / cauterized to expose the oesophagus. Care is taken not to tear / burn the submucosal (i.e. heel of the hook cautery is kept away from the submucosal). After dissection, patient undergoes endoscopic gastroscopy (OGD) to ensure that no oesophageal perforation has occurred and to ensure adequate dissection has been performed. Anterior partial fundoplication is then performed to reduce post-operative gastric reflux.
Intraoperative oesophageal perforation has been reported to occur in at least 10% to 14% of laparoscopic myotomy cases[25], but is likely underreported and may not even be considered a complication by some.

Post-op, contrast study can be done to show widened outflow tract to the stomach. This procedure will help relieve symptomatic achalasia (i.e. dysphagia). Gastrografin study can also be performed to confirm that no oesophageal perforation is present.

[25] J Gastrointest Surg 2007;11:309-313

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

EPIDEMIOLOGY[26]
- 10-30% of the Western population affected by weekly symptoms
- Prevalence of GERD and its related complications in Asia is reported to be increasing though still lower than that in the Western countries
- Indians more commonly report reflux symptoms and are more commonly diagnosed with endoscopic esophagitis as compared to Chinese or Malays

PATHOPHYSIOLOGY
- Defective LES and/or increased abdominal pressure leads to reflux of acidic gastric contents into the lower oesophagus resulting in acid-induced mucosal damage
- Other etiology of GERD
  - Inefficient oesophageal clearance of refluxed material
  - Fixed gastric outlet obstruction / Functional delayed gastric emptying
  - Increased gastric acid secretion
  - Inappropriate relaxation of LES
  - Increased intra-abdominal pressure – obesity, tight garments, large meal
- Acid incites inflammation in the lower oesophagus – extent of inflammation increases with increasing duration of contact with acid
- Chronic inflammation results in complications of GORD: oesophagitis, stricture, Barrett's oesophagus, adenocarcinoma

CATEGORIES
- Patients with non-erosive reflux disease (NERD)
- Patients with erosive esophagitis
- Patients with Barrett's oesophagus

CAUSES/RISK FACTORS
- Hiatal hernia (functional decrease in LES tone)
- Decrease LES tone – Alcohol, caffeine, smoking
- Increased intra-abdominal pressure – pregnancy, chronic cough, obesity, constipation
- Delayed gastric emptying – Eating habits (lying down after a heavy meal)
- Motility disorder of oesophagus e.g. scleroderma (systemic sclerosis)
- Drugs that cause smooth muscle relaxation e.g. NSAIDs, CCB, BB, nitrates, alpha-blocker, theophylline, anticholinergic

DIAGNOSTIC CLUES
- Posturally aggravated (lying flat) sub-sternal or epigastric burning pain / discomfort that is readily relieved by antacid
- Heartburn and Acid Regurgitation (>90% specificity but low sensitivity)
- Atypical Symptoms → Chest Pain (non-cardiac), Chronic Cough, Dysphagia, Dyspepsia, Epigastric Pain, Effortless Emesis, Hoarseness, Recurrent Otitis Media

COMPLICATIONS
- 20% of patients with GERD get esophagitis, strictures or Barrett oesophagus. Other loss common complications include acute or chronic bleeding and aspiration
- Malignancy (adenocarcinoma arising from Barrett's oesophagus) – see below

DIAGNOSIS
1. History is important as most patients with reflux are seen in the primary setting with no facilities for detailed investigation
   - Exclude cardiac cause of chest pain, and exclude malignant cause of dysphagia

2. Oesophagogastroduodenoscopy (OGD)
   - Cannot actually diagnose reflux
   - Good for evaluation of esophagitis (see below) and presence of Barrett changes (take biopsy specimens)
   - Indications for OGD in patients with GERD (see below)
   - May see a hiatal hernia which is associated with reflux (though not all patients with hiatus hernia will have reflux)

3. 24 hour oesophageal pH probe
   - Gold standard in diagnosis of GERD (ambulatory 24hr oesophageal pH probe) especially if oesophagitis is not seen on OGD
   - Diagnosis based on the percentage of time in 24hrs the pH reading is below 4
   - A **DeMeester score** is derived based on frequency of reflux episodes and time required for oesophagus to clear the acid

   Measurement technique
   - Antimony probe most commonly used; alternative is the Bravo capsule (a wireless capsule that is temporarily attached to the oesophageal wall)
   - The probe is placed 5cm above the manometrically-determined upper limit of the LES (for the wired probe), or 6cm above the endoscopically-determined squamocolumnar junction (for the wireless capsule)

4. Barium swallow and follow-through
   - Not of much value in diagnosing reflux (low sensitivity and specificity)
   - Can document the presence or absence of hiatus hernia, presence of oesophageal stricture and ulcers

5. Manometry
   - Appropriate in patients with reflux symptoms once surgery is being considered
   - Defines the location and function of the LES and helps to exclude achalasia, scleroderma (systemic sclerosis) and diffuse oesophageal spasm
   - Manometrically abnormal LES: (1) pressure < 6mmHg, (2) overall length < 2cm and (3) an abdominal length of < 1cm → patients with one or more of these abnormal values have 90% chance of having reflux

[26] J Gastroenterol. 2010 Aug;45(8):808-15.

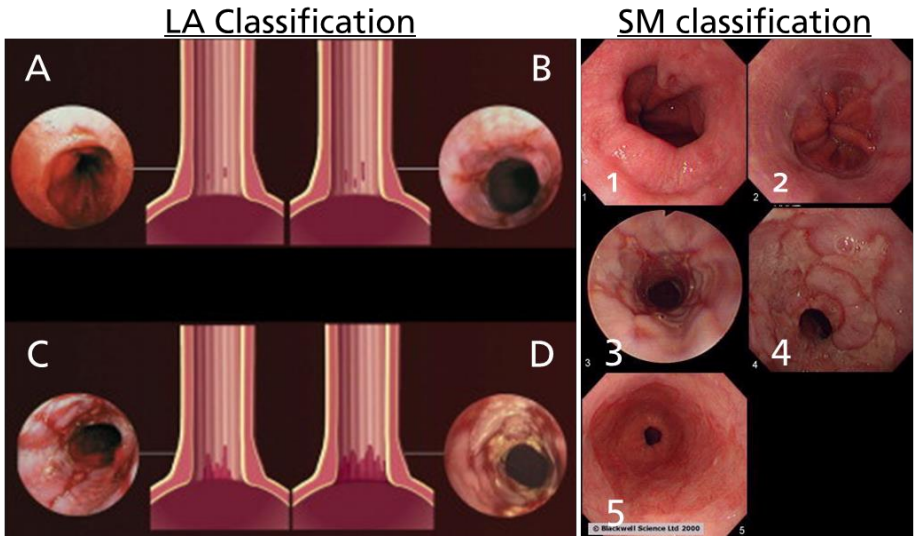
INDICATIONS FOR OGD IN PATIENTS WITH GERD

1. Persistent of progressive GERD symptoms despite appropriate medical therapy
2. Dysphagia or Odynophagia
3. Involuntary weight loss > 5% with upper GI symptoms
4. Evidence of upper GI bleed or anemia
5. Persistent vomiting
6. Evaluation of a mass, stricture or ulcer detected on imaging studies
7. Evaluation of patient with recurrent symptoms after endoscopic or surgical anti-reflux procedures
8. Screening for Barrett's oesophagus in selected patients

GRADING OF OESOPHAGITIS

1. Los Angeles classification
   - Grade A: ≥1 isolated mucosal breaks ≤ 5mm long
   - Grade B: ≥ 1 isolated mucosal breaks > 5mm long
   - Grade C: ≥ 1 mucosal breaks bridging the tops of folds but involving <75% of the circumference
   - Grade D: ≥ 1 mucosal breaks bridging the tops of folds and involving > 75% of the circumference

2. Savary-Miller classification
   - Grade I: Single erosion above gastro-oesophageal mucosal junction
   - Grade II: Multiple confluent but not circumferential erosion
   - Grade III: Circumferential erosive and exudative lesions
   - Grade IV: Chronic change with oesophageal ulceration and associated stricture
   - Grade V: Barrett's oesophagus (histologically confirmed intestinal differentiation within columnar epithelium)



MANAGEMENT / TREATMENT

Lifestyle

1. Dietary Alterations
   - Avoid fatty foods, alcohol, caffeine, chocolate or anything that worsens symptoms
   - Remain upright after meals or walk after eating
   - Avoid excessive eating; eat smaller, more frequent meals
2. Obese Patients
   - Encourage weight loss – regular exercise program
   - Avoid tight-fitting garments
3. Sleeping Alterations
   - Elevate head (6-8 inches) when sleeping
   - Encourage not to lie down to sleep within an hour of eating
4. Smoking and alcohol intake cessation
5. Drugs – change or reduce dose of drugs that exacerbate reflux

Medication (aim: lower gastric acidity or enhance oesophageal/gastric clearance)

1. Acid suppression therapy
   - Antacids, Proton Pump Inhibitors or H2-receptor antagonists
   - PPI are standard therapy for erosive and non-erosive esophagitis[27]
2. Prokinetics to increase LES pressure
   - Metoclopramide (dopaminergic antagonist)

[27] J Clin Gastroenterol. 2007;41:131

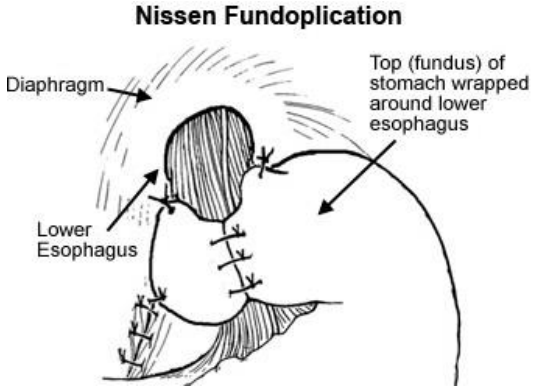
Surgical

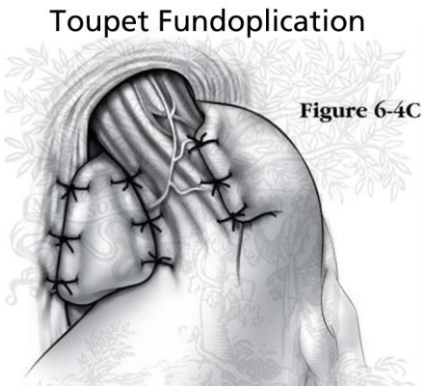
- Indications
  - Failure of relief with maximal medical therapy (persistent symptomatic reflux)
  - Manometric evidence of a defective LES
  - Compliance problems – patient does not want to be on medication for life
  - Severe symptoms or progressive disease (i.e. oesophagitis with frank ulceration or stricture)
  - Complications of reflux oesophagitis – respiratory complications, Barrett's oesophagus

- Goal of surgery:
  - Increase pressure at the gastro-oesophageal junction but not so much that it prevents food from entering the stomach (too tight → dysphagia)

- Surgery versus conservative treatment
  - Surgery has higher rates of cure and better long-term results
  - No need to adhere to strict lifestyle and diet change as well as long-term medication
  - Disadvantage of surgery is the associated morbidity and mortality

- Fundoplication is the mainstay of surgical therapy
  - Can be done via open (trans-abdominal) or laparoscopic surgery (most laparoscopic now)
  - **Nissen fundoplication** (most commonly done) – a 360 degree (total) wrap of the fundus around the gastro-oesophageal junction (10-year freedom from recurrence of > 90%)
  - **Partial fundoplication** can also be done in patients where oesophageal motility is poor or the oesophagus is foreshortened; anterior 90 degrees, anterior 180 deg, and posterior 270 deg (**Toupet)** fundoplication are various options available





- Complications of Nissen fundoplication
  - Mortality Rate (< 1%)
  - Bleeding, Infection, Oesophageal perforation
  - **"Gas bloat syndrome"** – patient experiences difficulty burping gas that is swallowed (self-limiting within 2-4weeks)
  - **Dumping Syndrome** (rapid gastric emptying) – food enters SI largely undigested
  - Excessively tight wrap resulting in dysphagia
  - Excessively loose or short wrap – reflux recurs (failure of treatment)
  - **Perforation of the oesophagus** – most feared complication, may result in mediastinitis if not promptly detected and repaired intra-operatively
  - **"Slipped-Nissen"** occurs when the wrap slides down, the GE junction retracts into the chest, and the stomach is partitioned; usually due to a foreshortened oesophagus unrecognised in the first operation

- Post-operatively
  - Arrange for gastrografin swallow to ensure that there is no perforation in the oesophagus

- Management of stricture
  - Rule out malignant cause of stricture by taking biopsy
  - Dilatation (variety of means available – balloon, dilators, etc.)
  - Treatment of underlying reflux
  - If resistant to dilatation → resection and reconstruction

BARRETT'S OESOPHAGUS

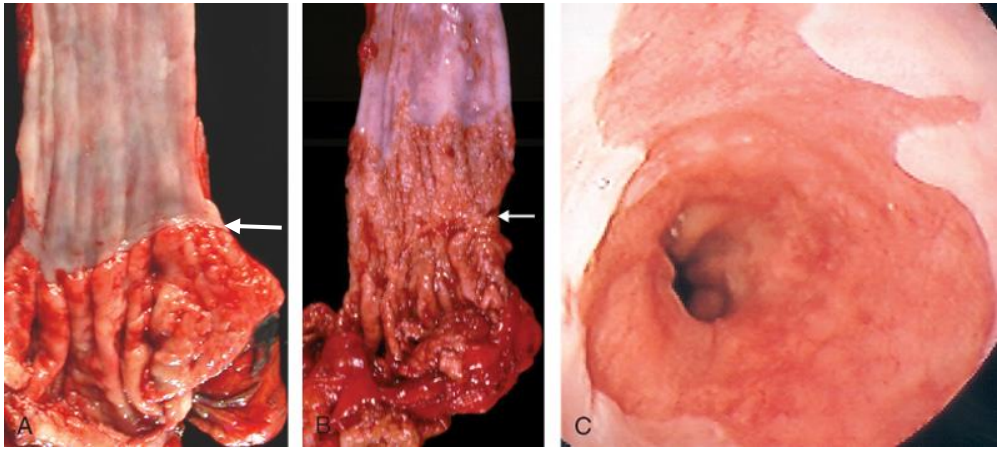
EPIDEMIOLOGY
- Diagnosed in 10-15% of patients with esophagitis, persistent symptomatic reflux disease
- Highest prevalence in middle-aged white males (males / females ratio 4:1)

CAUSES / RISK FACTORS
- Associated with long-term acid reflux → adaptation mechanism where intestinal epithelium withstands exposure to acidic reflux better than oesophageal epithelium
- Presence of hiatal hernia associated with 80% of cases of Barrett oesophagus

PATHOPHYSIOLOGY
- Characterized by intestinal metaplasia within the oesophageal squamous mucosa (stratified squamous epithelium (SSE) converted to mucus-secreting columnar epithelium with goblet cells)

DIAGNOSTIC CLUES[28]
- In patients with long standing gastric reflux and endoscopically proven Barrett → Dysphagia (75%), Heartburn (50%), Bleeding (25%)

- Diagnosed on endoscopy and histology:
  - Normal SSE (A) → pale-pink and smooth (note: squamocolumnar junction or "Z-line" represents the normal esophagogastric junction where the squamous mucosa of the oesophagus and columnar mucosa of the stomach meets.)
  - Barrett Oesophagus (B and C) → salmon-pink, velvety mucosa



[28] Ann Surg. 1983;198:554

COMPLICATIONS
- Oesophageal ulcers and it's resultant complications (4Bs: bleed, burrow, burst, block)
  - Ulcers penetrate the metaplastic columnar epithelium in a manner similar to that seen in gastric ulcers
- Oesophageal scarring and strictures
- Increased risk of development of dysplasia and adenocarcinoma (30-100 folds)
  - Persistent of high grade dysplasia require therapeutic intervention

MANAGEMENT / TREATMENT
1. Treatment of underlying reflux
   - Lifestyle changes, acid suppression (H_2 receptor antagonist or PPI), surgery (similar principle to treatment of GERD)
   - Elimination of reflux may halt progression of disease, heal ulceration and prevent stricture formation, however, it is not shown to decrease risk of cancer → still requires endoscopic surveillance

2. Endoscopic surveillance[29]
   - Patients with chronic, longstanding GERD → screening endoscopy recommended
   - Patients with established Barrett's Oesophagus with no dysplasia → 2 scopes in a year and if negative repeat, once every 3 years
   - Patients with low grade dysplasia → follow up OGD at 6 months and if negative repeat yearly
   - Patients with high grade dysplasia, should be treated otherwise → intensive surveillance (q3mths for at least one year) with multiple large capacity biopsy specimen to detect cancer development
   - Patient with indeterminate dysplasia with evidence of acute inflammation due to GERD → repeat OGD and biopsy after 8 weeks of effective acid suppression therapy

3. Treatment of high-grade dysplasia
   - Esophagectomy → definitive treatment to remove all dysplasia with cure rates ~100%, but is associated with high morbidity and mortality
   - Endoscopic radiofrequency ablation → complete eradication success rates for low-grade dysplasia (90.5%) and high grade dysplasia (81.0%)[30] and associated risk reduction in disease progression

[29] Gastrointestinal Endoscopy Volume 63, No. 4 : 2006
[30] N Engl J Med. 2009 May 28;360(22):2277-88

CANCER OF THE OESOPHAGUS

EPIDEMIOLOGY[31]

- Male predominance → age standardized incidence rates for SCC: 3.85 per 100,000 in males and 0.81 per 100,000 in females
- Incidence of SCC is greater than adenocarcinoma (incidence of adenocarcinoma → 0.5 per 100,000 in males)
- Frequency of oesophageal adenocarcinoma is increasing owing to increased prevalence of GERD and obesity (especially in western countries)
- In contrast, the incidence of squamous cell carcinoma (SCC) of the oesophagus has declined in the United States, and this has been attributed to a drop in the prevalence of cigarette smoking

RISK FACTORS

RF for Squamous Cell Carcinoma (SCC)	RF for Adenocarcinoma
Race: African / American	Race: whites
Alcohol and Smoking	**Chronic GERD**
Nutritional Deficiencies: lack of fresh vegetables and fruits	**Barrett Oesophagus (40x)**
Caustic oesophageal injuries	**Obesity**
Ingestion of nitrosamines	Smoking
Achalasia	
Others: Plummer-Vinson Syndrome, Tylosis (AD disorder), Oesophageal Diverticula and webs,	

- Age (> 60), Gender (male), Family History are also risk factors
- No significance difference between betel nut chewers and non-chewers for developing oesophageal SCC

PATHOLOGY

- SCC can arise anywhere in the oesophagus (typically found in the middle third of oesophagus) while adenocarcinoma typically occurs in distal third oesophagus
- Adenocarcinoma → background of chronic GERD and Barrett oesophagus → intestinal metaplasia → dysplasia → invasive adenocarcinoma
- SCC → carcinoma in situ → invasive SCC progression (plentiful submucosal lymphatics present in oesophageal wall which permits tumour cell infiltration above and below level of apparent tumour → surgical resection may not clear all tumour cells)

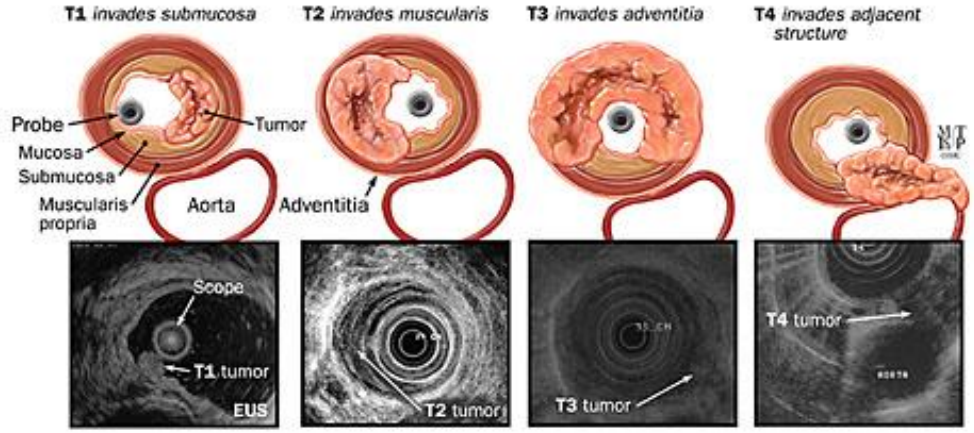
- Tumour spread: direct extension into surrounding structures (pericardium, trachea → risk of tracheoesophageal fistula), vascular invasion, lymphatic spread
- Common sites of metastases: liver, lung, bone

STAGING (TNM)

T	Tis	Carcinoma in situ / High Grade Dysplasia
	T1	Tumour invades submucosal (a) lamina propria or muscularis mucosae (b) submucosa
	T2	Tumour invades muscularis propria
	T3	Tumour invades adventia
	T4	Tumour invades adjacent structures (a) resectable – invading pleura, pericardium or diaphragm (b) unresectable – invading aorta, vertebral body, trachea
N	No	No regional node mets
	N1-3	N1 = 1-2 regional LN N2 = 3-6 regional LN N3 = seven or more regional LN
M	Mo	No distant metastasis
	M1	Distant metastasis

Adenocarcinoma Stage				SCC Stage			
Stage	**T**	**N**	**M**	**Stage**	**T**	**N**	**M**
0	Tis	0	0	**0**	Tis	0	0
1A	1	0	0	**1A**	1	0	0
1B	1-2	0	0	**1B**	1	0	0
2A	2	0	0	**2A**	2-3	0	0
2B	3	0	0	**2B**	2-3	0	0
	1-2	1	0				
3A	1-2	2	0	**3A**	2-3	0	0
	3	1					
	4a	0					
3B	3	2	0	**3B**	2-3	0	0
3C	4a	1-2	0	**3C**	1-2	1	0
	4b	Any					
	Any	3					
4	Any	Any	1	**4**	1-2	2	0
					3	1-2	0
					4a	0-2	0
					4b	Any	0
					Any	3	0
					Any	Any	1

* Histological grade of tumour is also part of the scoring but is not included here



[31] Am J Gastroenterol. 2006 Jul;101(7):1430-6.

PRESENTATION

Most patients with early-stage disease are asymptomatic or may have symptoms of reflux, non-specific e.g. retrosternal discomfort, "indigestion". However, approximately 50% of patients have unresectable lesions or distant metastasis on presentation.

1. Progressive dysphagia (first and most common presentation)
   - Fluid and soft food better tolerated than hard/bulky food
2. Odynophagia → pain develops late, usually due to extra-oesophageal involvement
3. Weight loss → secondary to reduced appetite, malnutrition and active cancer
4. Regurgitation → secondary to tumour disrupting normal peristalsis and causing oesophageal obstruction (risk of aspiration pneumonia)
5. Anemia (with or without melaena/frank haematemesis – bleeding is usually occult) → tumour surface may be fragile and bleed

Features suggestive of complicated oesophageal cancer

6. Locally Advanced
   - Bleeding (hematemesis, melena, Fe-deficiency anemia)
   - Obstructive (malnutrition, aspiration pneumonia)
   - Hoarseness → vocal cord paralysis (RLN: left > right)
   - Respiratory (cough, fever or aspiration pneumonia) → tracheo-oesophageal fistula
7. Systemic
   - Nodal → Check for supraclavicular LN
   - Bone → Persistent back / bone pain, pathological #, hypercalcemia
   - Liver → RHC pain, LOW, Jaundice, Ascites
   - Lung → Haemoptysis, cough, SOB, pleura effusion
   - Brain → Increased ICP, seizure, meningeal involvement

"I would like to do investigations to (1) establish the diagnosis. My second set of investigation is to (2) stage the disease to identify if it is locally or systemically invasive as this stratifies treatment into curative or palliative. This is crucial as surgical oncology is for local control. In addition, staging provides prognostic information useful for physicians, patients and families to aid in management-related decisions in cases of advanced disease. I would then do pre-operative investigations to look for (3) complications of the disease. Finally if the patient is suitable for tumour resection, I would perform other (4) pre-operative investigations. "

INVESTIGATIONS

Diagnosis

1. Barium swallow (non-invasive)
   - Can assess for tumour complications (i.e. tracheo-oesophageal fistula) and can show proximal dilatation, mucosal irregularity and annular constrictions
   - Diagnostic accuracy rate of roughly 70%
2. Oesophagogastroduodenoscopy (OGD) and biopsy or brush cytology
   - Allows biopsy of the lesion → confirmatory histological diagnosis
   - Brush cytology → evaluate malignant appearing strictures that are non-traversable by standard endoscope
   - Combination of endoscopic biopsy and brush cytology has accuracy rate ~100%

Staging (divide to local and systemic staging)

1. Endoscopic ultrasound (EUS)
   - EUS combines endoscopy with high frequency ultrasound within the oesophageal lumen and provides high resolution image of the tumour, the oesophageal wall and adjacent structures
   - EUS is good for T staging (determine depth of wall invasion), and N staging (identify malignant (hypoechoic, sharply demarcated, homogenous) lymph nodes) – replaced CT as the loco-regional tumour staging of choice
2. Chest X-ray
   - Presence of any lung metastases
   - Aspiration pneumonia – pleura effusion, collapse, consolidation
   - Pleural and/or pericardial effusion
   - Tracheal deviation or extrinsic compression of tracheobronchial system
   - Widened superior mediastinum in an upper oesophagus tumour
   - Raised hemidiaphragm with phrenic nerve involvement
   - Any chronic respiratory conditions
3. CT scan or MRI of the thorax with extension to include liver and adrenals
   - Modality of choice for staging distant metastasis
   - Can be used for T, N, and M staging
     - Nodes > 10mm are considered to be metastatic
4. Positron Emission Tomography with integrated CT Scan (PET/CT)
   - FDG-PET is the most useful test to r/o distant metastatic disease[32] (identified in ~20% if patients who are free of metastases on CT / EUS)
   - Usually indicated for assessing recurrence more so than diagnosis
5. Rigid Bronchoscopy with biopsy and brush cytology
   - For patients with supracarinal primary tumours and suspicion of airway involvement
6. Surgical Laparoscopic Staging (most beneficial for patients with adenocarcinoma)
   - For patients who appear free of distant metastases
   - Laparoscopic ultrasound and peritoneal lavage also performed at time of laparoscopy
   - Can r/o occult liver metastasis and peritoneal carcinomatosis not evident on CT scan

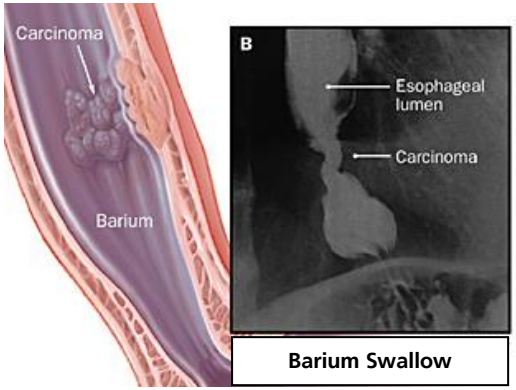
[32] uptodate: Management of locally advanced unresectable esophageal cancer

Complications

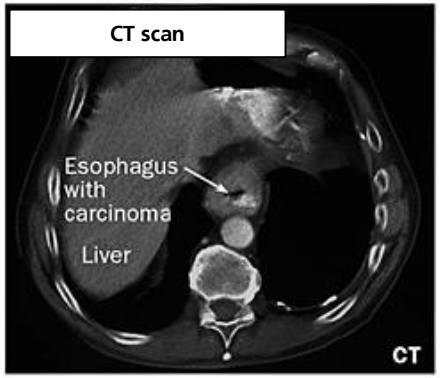
1. Full blood count → Low Hb (anemia from chronic blood loss)
   High TW (aspiration pneumonia)
2. Urea, electrolytes, creatinine → electrolyte disturbances from vomiting, poor intake (urea: creatinine ratio of > 100:1 would suggest pre-renal cause of dehydration)
3. Liver function tests → low albumin with nutritional deprivation
4. Laryngoscopy → assess vocal cord paralysis

Pre-operative Investigations

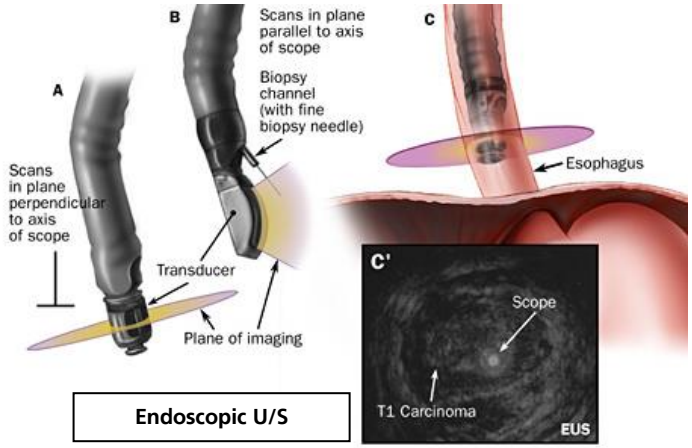
1. GXM
2. PT/PTT - in view of patient going for invasive procedures (i.e. OGD)
3. CXR / ECG / Lung Function Test / 2D Echogram



Barium Swallow



CT scan



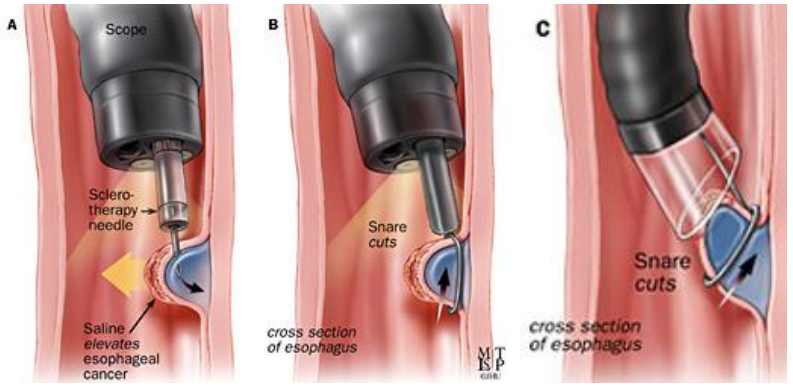
Endoscopic U/S

TREATMENT

- Three modalities available – surgery, chemotherapy, radiotherapy – used singly or in combination → multimodality therapies gives best possible outcomes
- Choice of treatment depends on several patient factors: age, co-morbidities, nutritional state, life expectancy, and prognosis of cancer
- RT with concurrent chemotherapy w/o surgery results in survival outcomes that are similar to surgery (5 yr survival ~20%) though local recurrence rates are higher (~50%)
- Aims of treatment: Curative or palliative (50% have unresectable cancer on presentation)
  - Curative intent for localised CA → **Stage 0, 1, 2A** (Tis, T_1, T_2, T_3 with no regional LN mets)
  - Prolongation of survival → treatment goal for **Stage 2B and 3**
  - Palliative treatment (endoscopic methods to treat malignant dysphagia or fistulous disease) for metastatic disease → **Stage 4**

Endoscopic Therapy for Localized Disease

- Endoscopic Mucosal Resection
  - Advocated for early cancers → Stage 0 and 1
  - Less invasive, safe and highly effective non-surgical therapy



Neoadjuvant Therapy

- Long-term survival advantage with the use of trimodal therapy with CT/RT followed by surgery in the treatment of oesophageal cancer as compared to surgery alone → small RCT showed Five-year survival was 39% (95% CI, 21% to 57%) v 16% (95% CI, 5% to 33%) in favour of trimodality therapy for tumours that are surgically resectable (T1-3, NX).[33]

[33] J Clin Oncol. 2008 Mar 1;26(7):1086-92.

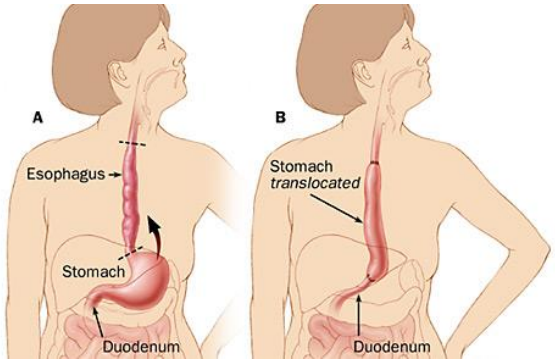
Surgical Resection = Open / Minimally Invasive Esophagectomy

(i) Transthoracic Esophagectomy (TTE) → Ivor Lewis TTE or McKeown Esophagectomy

- Ivor Lewis → Two-stage procedure involving gastric mobilisation (first stage, done through upper midline abdominal incision), oesophagectomy, extended lymphadenectomy and intra-thoracic esophagogastric anastomosis (second stage, through right thoracotomy incision)
- McKeown → Three stage procedure – start with right posterolateral thoracotomy then abdominal and then cervical portion (for cervical esophagogastric anastomosis)

(ii) Trans-hiatal Esophagectomy (THE) – see below

- Two incisions – one in the abdomen (laparotomy) and one in the neck (left neck incision)
- Avoids thoracotomy and involves a cervical esophagogastric anastomosis
- Blunt oesophagectomy (removal of oesophagus), gastric mobilisation, and esophagogastric anastomosis in the neck (translocation of the stomach)
- Less morbidity than Ivor-Lewis as the chest is not opened
- The colon or jejunum can also be used if the stomach is not a suitable conduit



Overall 5-year survival rate is 19-32%. The 30-day mortality rate s/p surgery is 3%.

Management Post-esophagectomy[34]

- Analgesia – IV or epidural (i.e. morphine or bupivacaine)
- Gastrointestinal
  - NBM – 5 to 7 days
  - Jejunostomy feeding tube – placed during surgery and start feeding on POD 2-3
  - NG tube on low level intermittent / continuous suction
  - Gastrografin swallow – day 5 to 7 to check for anastomotic leak before initiating oral intake
  - Escalation of feeds as tolerated – aim for 6 to 8 small frequent meals each day
- Prevention of complications
  - Early mobilization (SOOB from POD 1)
  - Aggressive Pulmonary Rehabilitation (i.e. incentive spirometry, deep breathing exercise etc.)

Complications Post-esophagectomy

- Cardiovascular Complications
  - Post-esophagectomy atrial fibrillation – 17%
  - AMI / VTE
- Pulmonary Complications
  - Atelectasis, Pneumonia, ARDS
- Oesophageal anastomosis complications
  - Anastomotic leak and resultant mediastinitis (chest anastomosis) most feared
  - Anastomotic strictures – usually 2° to healed anastomotic leaks
  - Conduit Ischemia
- Gastric Outlet Obstruction
- Other local traumatic complications
  - Chylothorax
  - Recurrent Laryngeal Nerve

[34] Crit Care Nurse 2004;24:16-29

Palliative treatment (aim: relief obstruction and dysphagia) – median survival of 4 months

- Radiotherapy
  - Used for attempted cure and palliation of patients with SCC (radio-sensitive) deemed unsuitable for resection
  - Usually given in combination with chemotherapy → 5-FU with mitomycin C / cisplatin
  - Modalities: External beam radiation or brachytherapy
  - Palliation of dysphagia is successful temporarily in 80% of patients but rarely provide relief for longer than several months
- Chemotherapy
  - Current regimen: 5-Fluorouracil and Cisplatin
  - Addition of chemotherapy to external beam radiation for unresectable cancers shown to have improved survival compared to EBRT alone

- Nutritional support with percutaneous endoscopic gastrostomy (PEG) or jejunostomy tube (PEJ)
- Endoscopic Intraluminal Prosthesis
  - Mostly only pureed diet tolerated
  - Self-expanding wire-mesh stent with silicon coating (risk of perforation, erosion, migration of stent, obstruction of tube by food / proximal tumour growth)
  - Preferred for patients with malignant stricture and/or fistula
  - Once stent is in place, patient can't go for RT (risk of stent dropping)
- Endoscopic Laser Techniques
- Photodynamic Therapy (relatively new)
  - Injection of photosensitizing agent activated by low-power laser lights resulting in selective tumour necrosis
  - Used to open oesophageal lumen in patients with complete oesophageal obstruction
  - Useful for patient with prior RT / chemo and as salvage therapy in patients whom stents have failed due to migration or tumour ingrowth / overgrowth

Feeding in oesophageal obstruction

- Feeding via oropharyngeal route is preferred unless the passage is obstructed or it is unsafe for the patient to feed via that route (i.e. risk of aspiration)
- If still able to pass **NG tube** around tumour → feed via NG (but also consider complications with long-term NG placement e.g. erosions around nasal area, sinusitis); consider **PEG placement*** for long-term feeding if able to get scope around tumour
- If unable to pass tube or scope around tumour, consider **open gastrostomy**
- Total parenteral nutrition is another option but has more complications, more costly
- Relief of obstruction via various techniques as listed above help to enable oral feeding, but most techniques are not long-lasting and dysphagia will return with tumour growth

***PEG placement** 1st person put a scope down to the stomach, point it to the anterior abdominal wall, shine light, 2nd person see light coming through from anterior abdominal, will poke a big bore needle through skin into stomach – inserted vertically. 1st person will look for needle coming through, if air aspirated but 1st person don't see needle worry about perforation into bowel wall. A loop is passed into stomach for 1st patient to catch on – who then pull it out of the stomach and out of mouth, - loop is used as a guide to guide a tube down back thru the anterior abdominal wall. 2nd person pulls tube out but the end of the tube which has a stopper is stuck to the inside of the abdomen. 2nd person anchors down tube to the skin.

UPPER BLEEDING GIT AND ITS CAUSES

APPROACH TO BLEEDING UPPER GIT

CAUSES

Variceal Bleed

1. Gastro-oesophageal varices (30%)

Non-variceal Bleed

2. Peptic ulcer disease (bleeding peptic ulcer) (50%)
3. Gastritis, gastric erosions, duodenitis
4. Mallory-Weiss tear (10%)
5. Gastric malignancy (10%)
6. Dieulafoy lesion – large tortuous arteriole (aneurysm) in the upper part of the stomach
7. Aorto-enteric fistula (5%)

Others

8. Bleeding from other sources: Haemoptysis, nasopharyngeal bleeding

HISTORY (if patient is stable)

1. **Nature of bleeding (confirm hematemesis and rule out haemoptysis)**

Haemoptysis

- Bloody expectoration from the larynx, trachea, bronchi and the lungs
- Patient will describe a feeling of something in their throat followed with the abrupt expectoration of blood (**frothy and bright red**)

Hematemesis (red blood or coffee-ground emesis)

- Vomiting of blood from upper GIT (proximal to the ligament of Treitz, at D-J junction)
- The vomited blood might be mixed with food particles
- The colour of the vomitus depends on the contact time with the HCl acid of the stomach (red → brown)
- **Coffee grounds vomitus** is altered blood (due to gastric acid) and can come from gastric ulcer, gastritis/erosions, or variceal blood that has entered the stomach (suggest limited bleeding)
- Can be **fresh red blood** as in variceal bleeding, Mallory-Weiss tear, AV malformation (suggest moderate to severe bleeding)

Hematemesis	Haemoptysis
Not associated with cough	Associated with Cough
Not Frothy	Frothy
Darker Red (altered by gastric acid)	Bright Red (aerated)
Melena Present	Melena Absent

Factors predictive of UBGIT[35]

- Patient-reported history of melena (LR: 5.1-5.9)
- Melenic stool on examination (LR: 25)
- Blood or coffee grounds detected during NG lavage (LR: 9.6)
- Ratio of BUN to Serum Cr > 30 (LR: 7.5)

*Note: the presence of blood clots in the stool made an UBGIT less likely (LR: 0.05)

Melena

- Passage of altered blood (black tarry stool) that originate proximal to the ligament of Treitz (90%) – types of melena:
  (a) **Fresh melena** – jet black with sheen, tarry, non-particulate, almost liquid in consistency (suggest fairly acute bleeding)
  (b) **Stale melena** – black-grey, dull, mixed with normal stool, occasionally particulate (suggest bleed which stopped followed with melena)
- **Ddx: Iron stool** – greenish hue on rubbing between gloved fingers, particulate
- If gloved finger is stirred in a cup of water, melena will "dissolve" completely with no sedimentation and turn the water black, but iron stool will sedimentate and turn the water green

Frank PR bleeding

- Very brisk upper GI bleed can present as frank PR bleeding as blood passes down so fast it doesn't get altered (severe bleeding)

Note: spectrum from coffee-ground vomitus → melena (stale / fresh) → hematemesis → UBGIT masquerading as PR bleed

2. **Determine Etiology (variceal vs. non-variceal bleed)**

- Any previous variceal bleed → ask patient whether he/she goes for regular banding or OGD screening and banding
- Any history of chronic liver disease → ask for risk factors (i.e. alcohol ingestion, hepatitis B/C, any regular follow-up for liver disease – AFP, U/S HBS)

[35] JAMA. 2012 Mar;307(10):1072-9.

3. **Aetiological clues (differentiating causes of non-variceal bleed)**

Peptic Ulcer Disease (most common cause)
- History of dyspepsia, previous H. pylori infections, previous OGD done
- Drug History – NSAIDs, antiplatelets, steroids, anticoagulants, TCM
- Secondary to cirrhosis-induced hypergastrinemia from decreased hepatic metabolism of GI hormones

Stress Ulcer
- Curling ulcer – large acute ulcer in the duodenum (cx from burns)
- Cushing's ulcer – gastric ulcer produced by elevated ICP

Mallory-Weiss tear
- It is a diagnosis of exclusion
- Secondary to violent retching following alcoholic binge → lead to longitudinal tear below the GE junction leading to haematemesis

Dieulafoy's Disease – AVM of the gastric fundus
- Presents with massive or recurrent bleeding coming from an area of apparently normal gastric mucosa → characterized by a large tortuous arteriole in the submucosal that bleeds
- More common in males, with multiple co-morbids (i.e. HTN, IHD, CRF, DM)
- Suspect in bleeding with no history of alcohol abuse or NSAIDs use

Malignancy (gastric carcinoma)
- Early → asymptomatic, epigastric pain, dyspepsia
- Intermediate → anemia, melena, hematemesis, early satiety, dysphagia, nausea/vomiting, bloatedness
- Late → loss of appetite, loss of weight, obstructive jaundice (mets to liver)

4. **Amount of blood**
- If patient is having haematemesis, ask how much blood → Cup? Bowl?
- Hematemesis: easily 1.5L of blood in stomach before vomiting out (bleeding more than pylorus can empty)

5. **Complications**
- Symptomatic anemia → SOB on exertion, dizziness, syncope, chest pain, palpitation, lethargy/fatigue
- Gauge percentage of blood loss
  - 15-30% → class 2 – Narrowed Pulse Pressure, Resting Tachycardia, Postural Hypotension
  - 30-40% → class 3 – Supine Hypotension, marked tachypnoea, confused, anxious
  - > 40% → class 4 – Minimal urine output, markedly depressed or lethargic
- AMI → esp. if it's an old patient with previous history of IHD

6. **Comorbidities**
- Makes patient more susceptible to hypoxemia → Elderly patient (>60), IHD, COPD
- Predispose to fluid overload during resuscitation → IHD/CCF, CRF

PHYSICAL EXAMINATION

1. Vital Signs (most important)
   - Assess hemodynamic stability and postural BP
   - Any resting tachycardia

2. Confirm UBGIT
   - DRE for melenic stool (differentiate from Fe-laden stools)

3. Determine Etiology
   - Variceal Bleed → stigmata of chronic liver disease, jaundice
   - Non-variceal bleed
     - H&N: Bleeding source in nose or mouth, cervical lymph nodes,
     - Abd: Tenderness, guarding, rebound, epigastric mass, arterial bruit of AAA
     - Rectal: PR bleed, anal, perianal or rectal pathology

4. Look for complications
   - Signs of Anemia
     - Face – (i) conjunctival pallor (ii) pallor of mucus membrane
     - Cardiac Auscultation – short systolic flow murmur at aortic area
     - Pulse – (i) tachycardia (ii) bounding (iii) collapsing pulse
     - Hands – pallor of palmar creases
   - Lungs → examine for aspiration pneumonia
   - Exclude Peritonism

IMMEDIATE MANAGEMENT

Whatever the cause, the patient should first be resuscitated and then investigated urgently to determine the cause of bleeding → inform GS registrar on call of the patient's admission

1. Resuscitation

- ABC
  - Assess if patient can respond logically → good cerebral perfusion, otherwise aim to protect airway
  - Patient may still be in early stage (class 1) hypovolemic shock → manage pre-emptively
    1. Nasal Prongs (supplemental O_2 to increase O_2 carrying capacity which is determined by Hb concentration and O_2 saturation)
    2. IV cannula → 2 large bore 18G catheter inserted into the veins at the antecubital fossa

Note other structures present: (from medial to lateral) → median nerve, brachial artery, bicep brachii tendon, radial nerve) – Mother Buys 10 Rabbits

IV Cannula Sizes: 14G – orange, 16G – grey, 18G, green, 20G, pink, 22G, Blue, 24G – yellow

  - Bloods for investigation
    1. GXM: order in active bleed 4 pints PCT
    2. FBC (Hb will not drop in first 24hrs, thrombocytopenia → secondary to hypersplenism in portal hypertension – can exacerbate bleeding, MCV and MCHC → determine cause of anemia)
    3. U/E/Cr (dehydration → raised Ur more than Cr (isolated uraemia suggestive of bleeding GIT), Metabolic Disturbances → hypokalemic, hypochloremic, metabolic alkalosis with paradoxical aciduria*
    4. PT/PTT (r/o coagulopathy which can exacerbate bleeding)
    5. LFT (Child's score - ind etiology and outcome) – do in alcoholic hx or liver disease
    6. ABG, Lactate

  - Other Investigations
    7. ECG and cardiac enzymes to detect any AMI (STEMI)
    8. CXR: r/o perforation, aspiration

*With vomiting → K^+, Cl^-, Na^+ and H_2O is loss from the body → Intravascular hypovolemia sensed by JGA and leads to the activation of the RAAS → body reabsorb Na^+ and H_2O via kidney (Na^+/K^+ ATPase) and excrete K^+ → But since K^+ is critical in maintaining cardiac membrane stabilization → body attempts to conserve K^+ by paradoxically increasing excretion of H^+ (alkalosis also leads to a lowering of the circulating ionized calcium, and tetany can occur)

- If patient is in Class II shock – do monitoring
  - I/O charting – insert an IDC to measure urine o/p (aim: 0.5ml/kg/hr)
  - CVP monitoring
  - For massive UBGIT where patient presents with hypotension, can insert NG tube and aspirate to confirm suspicious (do not insert in suspect varices)

- IV resuscitation
  - 1L N/S run fast (i.e. over 15min) – caution in patients with renal & heart failure
  - Reassess patient response:
    - (1) Responder → sustained improvement clinically & biochemically
    - (2) Transient responder
    - (3) Non-responder
  - Transient Responder → KIV colloids (gelofusine / haemaccel) + wait for GXM
  - Non-responder Management → KIV colloids, E-bloods and adjunct monitoring (CVP line) → aim to stabilise patient for transfer to scope room for emergency scope in the setting of acute bleed
    - Restrictive transfusion strategy to keep Hb > 7g/dL (showed improved outcomes as compared to liberal transfusion strategy [transfusion when Hb < 9] in patients with acute UBGIT) [36]
    - May consider platelets if patient is on antiplatelet meds (qualitative defect in platelets - even if plt is normal, they are dysfunctional)
    - FFP if patient is on anticoagulants or PT/PTT prolonged (± vitamin K)

2. Adjuncts

- NG tube if patient is having haematemesis – prevents aspiration, allows gastric lavage prior to OGD (DO NOT insert if suspect varices)
- Catheterisation – monitor I/O balance esp. in elderly or when large amount of fluid resuscitation required, or anticipating surgery
- Intubate if: 1) massive uncontrolled active hematemesis
  2) signs of decompensation e.g. obtunded

3. **Early medications**

- IV omeprazole 80mg bolus → 8mg/hr infusion X 3/7
  - ↑ stomach pH and stabilises clot formation
  - regimen to prevent re-bleed (normal Tx dose 40mg bd)
- If suspecting varices – IV somatostatin/octreotide, IV antibiotics
- Withhold all antiplatelets, anticoagulants, NSAIDS

4. Close monitoring

- Monitor for: SHOCK (↑ HR, ↓ BP, ↓ urine output, ↑ confusion & lethargy)
- Keep NBM and patient's parameter monitored hourly

[36] N Engl J Med 2013; 368:2341

5. Emergency oesophagogastroduodenoscopy(OGD)
Alternatively, scope the next available OGD (usually following day)

- 3 Indications:
  1. Shock / hemodynamic instability (ensure BP is stable before OGD – requires sedation)
  2. Active BGIT (esp. hematemesis, also fresh melena)
  3. Suspected variceal bleed

- Not just low Hb as emergency scope causes more stress
- GXM bloods and transfused as clinically indicated

- Role of endoscopy → (i) diagnosticate, (ii) therapeutic, (iii) prognosticate

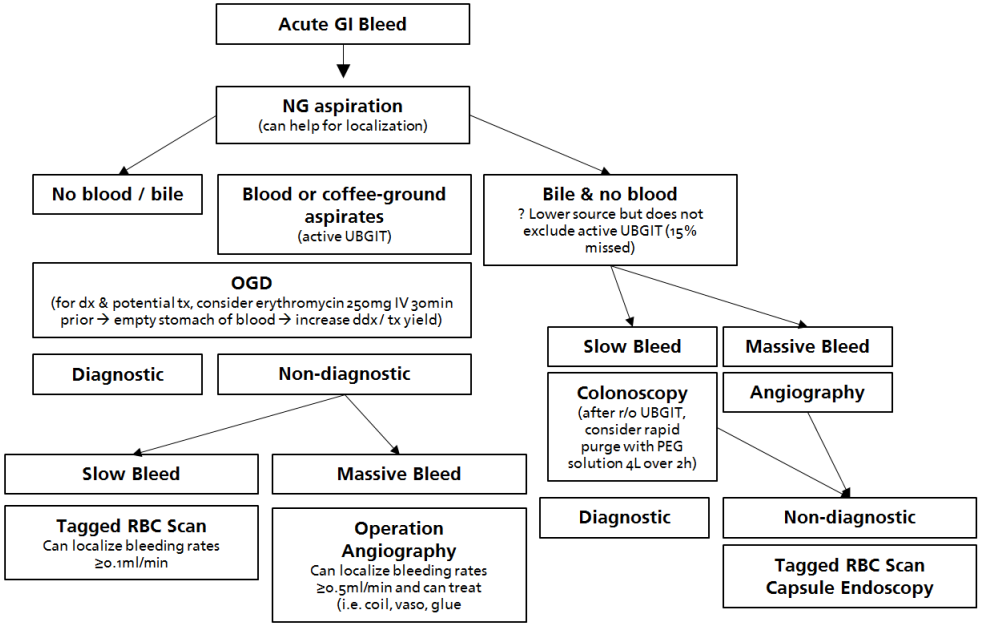
Diagnostic	- Confirm UBGIT & identify source of bleeding, - Biopsy of gastric mucosa (+ CLO test* if ulcer) – All gastric ulcers should be biopsied (6 bites) – risk of underlying malignancy & would require f/u scope in 6 weeks to document ulcer healing *Biopsy rapid urease testing (CLOtest = Campylobacter-Like Organism) → test ability of H. pylori to secrete urease enzyme which cleaves urea to liberate ammonia and bicarbonate (↑ pH) → colour change from Yellow (-ve) to Red (+ve)
Therapeutic	- Varices: (i) **Band ligation**/sclerotherapy, (ii) glue - Non-variceal: (i) **HaemoClip**, (ii)Injection of adrenaline (1:10,000), (iii) Argon Plasma Coagulation (heater probe)
Prognostic	- Endoscopic stigmata of recent haemorrhage – forest classification (see PUD)

- After endoscopic treatment → patient is to receive **80mg bolus IV PPI followed by continuous infusion of 8mg / hr of IV PPI for 72 hours** (thereafter revert to oral PPI) → reduce rate of recurrent bleeding, shortened length of hospitalization, decreased need for endoscopic retreatment and blood transfusion[37]

- Contraindications: Perforation – air insufflation during OGD will cause
  - abdominal compartment syndrome → decrease venous return → patient may DIE
  - splinting of the diaphragm

- Risk of OGD
  - Anaesthetic Risk
    1. Risk of Sedation – respiratory depression secondary to airway compromise
    2. CVS risk – AMI, CVA
  - Procedural-Related Risk
    1. Bleeding and Perforation (1 in 10,000)
    2. Failure of endoscopic haemostasis
    3. Failure of complete scope – standard OGD scope to D2 (ligament of Treitz)

DIAGNOSTIC STUDIES[38]



[37] N Engl J Med 2000; 343:310-316

[38] Pocket Medicine 4th Edition: Gastrointestinal Bleeding – Section 3-3

SUBSEQEUNT MANAGEMENT

1. Risk Stratification → Rockall Score (see below) or Blatchford Scoring System

History	1. Age of Patient 2. Major Co-Morbid → IHD, CCF, Renal / Liver Failure
Physical Examination	1. Shock – Tachycardia or Hypotension
OGD findings	1. Stigmata of recent haemorrhage 2. Diagnosis → Mallory-Weiss or Malignancy or Others

2. Correct Risk Factors

- H. Pylori Infection → PPI (Omeprazole) 20mg + Clarithromycin 500mg + Amoxicillin 1000mg / Metronidazole 400mg BD x 1/52 then Omeprazole 20mg BD x6/52 → followed by test of cure
- H. Pylori Negative → PO PPI
- NSAIDs induced gastric bleed → choose alternatives (i.e. COX-2 inhibitors or add PPI cover)

3. Management of Re-bleeding

- Repeat OGD and re-attempt endoscopic haemostasis
- If failure of endoscopic haemostasis
  - Surgery → normally have 2 goals: curative and decrease acid component, but mortality and morbidity risk is high so better to keep surgery short thus rather than decreasing acid component, patient is placed on life-long PPI
  - Radiological Intervention → CT mesenteric angiogram OR mesenteric angiogram KIV embolization
    1. CT: non-invasive, require contrast (risk of nephropathy)
    2. Mesenteric Angiogram: catheterize through femoral vein (risk of puncture), require contrast, if negative can be due to low blood flow rate → KIV prop up BP but risk of further bleed (clinical judgment call)

Rockall score for the prognostication of upper gastrointestinal bleeding [3]

	Score 0	1	2	3
Pre-upper gastrointestinal endoscopy				
Age	<60 years	60–79 years	≥80 years	
Shock	*No shock* BP >100 mmHg and pulse <100	*Tachycardia* BP >100 mmHg and pulse >100	*Hypotension* BP <100 mmHg	
Comorbidity	No major comorbidity		Ischaemic heart disease, cardiac failure, any major comorbidity	Renal or liver failure Disseminated malignancy
Post-upper gastrointestinal endoscopy				
Diagnosis	Mallory-Weiss or no lesion found, and no major stigmata of recent haemorrhage	All other diagnoses	Gastrointestinal malignancy	
Major stigmata of recent haemorrhage	None or dark spot only		Blood in upper gastrointestinal tract, non-bleeding visible vessel, spurting vessel or adherent clot	

BP systolic blood pressure

Patients with a score of 0, 1 or 2 have a lower risk of haemorrhage, whereas approximately 50% of patients with a post-endoscopy score of 8 or more will re-bleed.

Blatchford Scoring System: only clinical and laboratory factors, no endoscopic component

Admission risk marker	Score	Admission risk marker	Score
Blood Urea		**Systolic BP**	
i) 6.5 - 8.0	2	i) 100 - 110 mm Hg	1
ii) 8.0 - 10	3	ii) 90 - 100 mm Hg	2
iii) 10 - 25	4	iii) < 90 mm Hg	3
iv) > 25	6		
Haemoglobin (males)		**Other markers**	
i) 13 - 12 gm %	1		
ii)10 - 12 gm %	3	i) Pulse >/= 100 / min	1
iii) < 10 gm %	6	ii) Presentation with melaena	1
		iii)Presentation with syncope	2
Haemoglobin (females)		iv)Hepatic Disease	2
		v) Cardiac Failure	2
i) 10 - 12 gm %	1		
ii) < 10 gm %	6		

AIMS 65 Scoring System: prognosticate inpatient mortality rates

Albumin <30g/L	1 point = 1% mortality 2 points = 3% mortality 3 points = 9% mortality 4 points = 15% mortality 5 points = 25% mortality
INR > 1.5	
Altered Mental States (GCS < 14)	
Systolic BP <90mmHg	
Age > 65	

PORTAL HYPERTENSION

Hepatic venous pressure gradient (HVPG) ≥ 6mmHg (normal = 1-5mmHg)

- Portal HTN ≥ 10mmHg – high risk of gastroesophageal varices developing
- Portal HTN ≥ 12mmHg – high risk of variceal bleed and development of ascites

Normal portal flow rate is about 1-1.5L/min

ANATOMY

- Portal veins drain blood for the small intestines, large intestines, stomach, spleen, pancreas and gallbladder.
- The SMV and the splenic vein unite behind the neck of the pancreas to form the portal vein
- The portal trunk divides into 2 lobar veins
  - Right branch drains the cystic vein
  - Left branch drains the umbilical and paraumbilical vein (caput medusa in portal HTN)
- The left gastric (coronary) vein with runs along the lesser curvature of the stomach receives distal oesophageal veins (oesophageal varices in portal HTN)

PATHOPHYSIOLOGY

Portal Hypertension: chronic increase in portal pressure due to mechanical obstruction of the portal venous system. It is almost an unavoidable consequence of cirrhosis and responsible for many complications of CLD (see below)

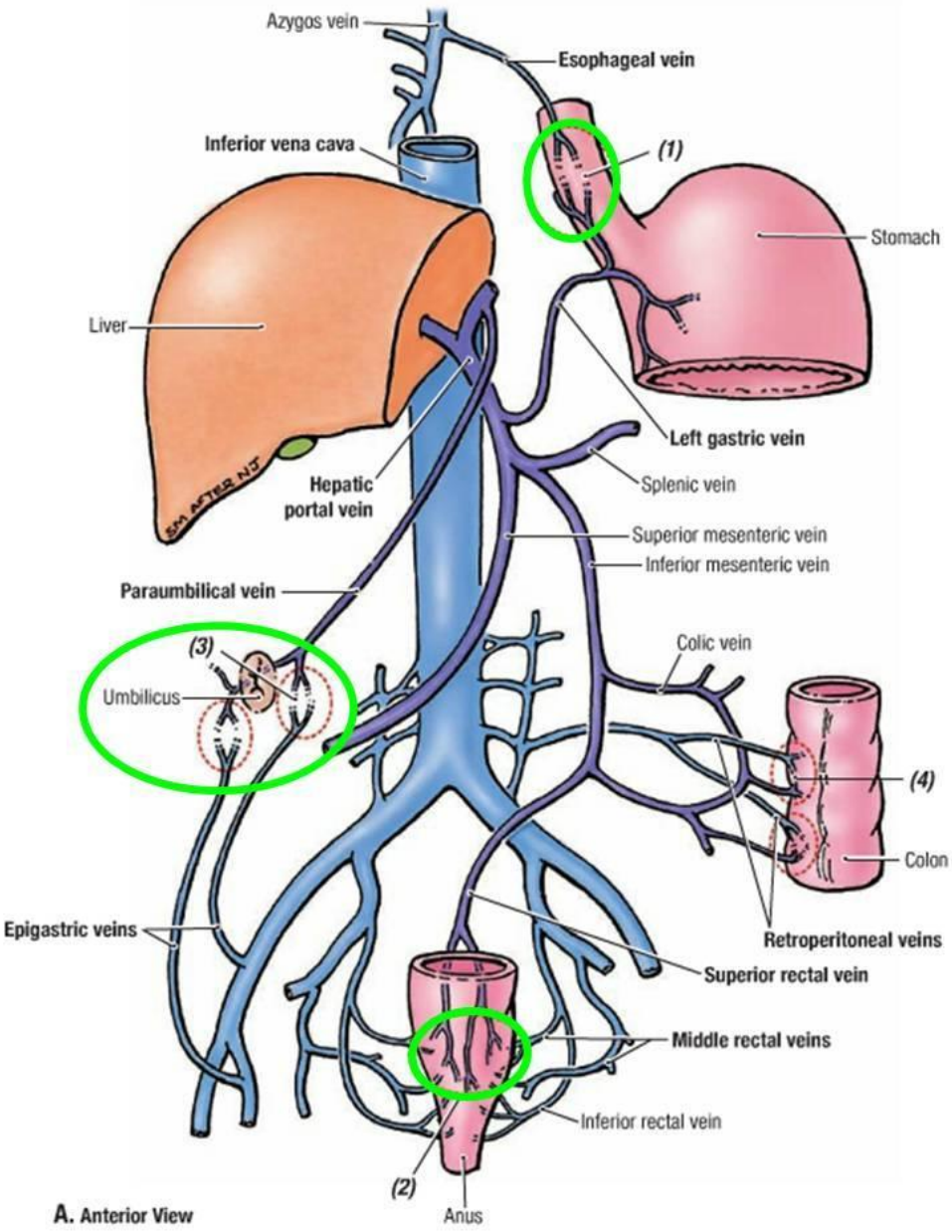
Cirrhosis (1) architecture distortion (nodules compression sinusoids & active intra-hepatic vasoconstriction [↓ NO]) → increase in resistance to portal blood flow → formation of porto-systemic collaterals (2) high arterial pressure (splanchnic arteriolar vasodilatation) on low pressure venous system & insufficient portal decompression through collaterals (higher resistance)→ increased portal blood flow (hyperdynamic circulation)

Ohm's Law is V = IR | Poiseuille's Law $R=8hL/pr^4$

→ this can be applied to vascular flow where P = FR or **$P = F8hl/pr^4$**

→ decrease portal vascular radius produce a dramatic increase in portal vascular resistance

↑ portal pressure gradient (P) = ↑ in resistance to portal flow (R) (intrahepatic & collateral) and ↑ in portal blood inflow (F)



CAUSES OF PORTAL HYPERTENSION

Pre-hepatic	Heptaic	Post-hepatic
Massive Splenomegaly with consequent ↑ in splenic vein blood flow	**CIRRHOSIS** (most commonly due to alcohol and/or hepatitis B/C)	Severe right-sided HF
		Constrictive Pericarditis
Portal vein thrombosis	Massive Fatty Change	Hepatic vein thrombosis (Budd Chiari Syndrome*)
	Hemochromatosis	
	Wilson's Disease	
	Schistosomiasis	IVC thrombosis
Congenital Atresia	Caroli Disease	Congenital IVC malformation
	Congenital Hepatic Fibrosis	

* Gives rise to ascites, hepatomegaly and pain, commonly caused by thrombophilic disorder – treatment: shunting or liver transplantation & long term anticoagulation

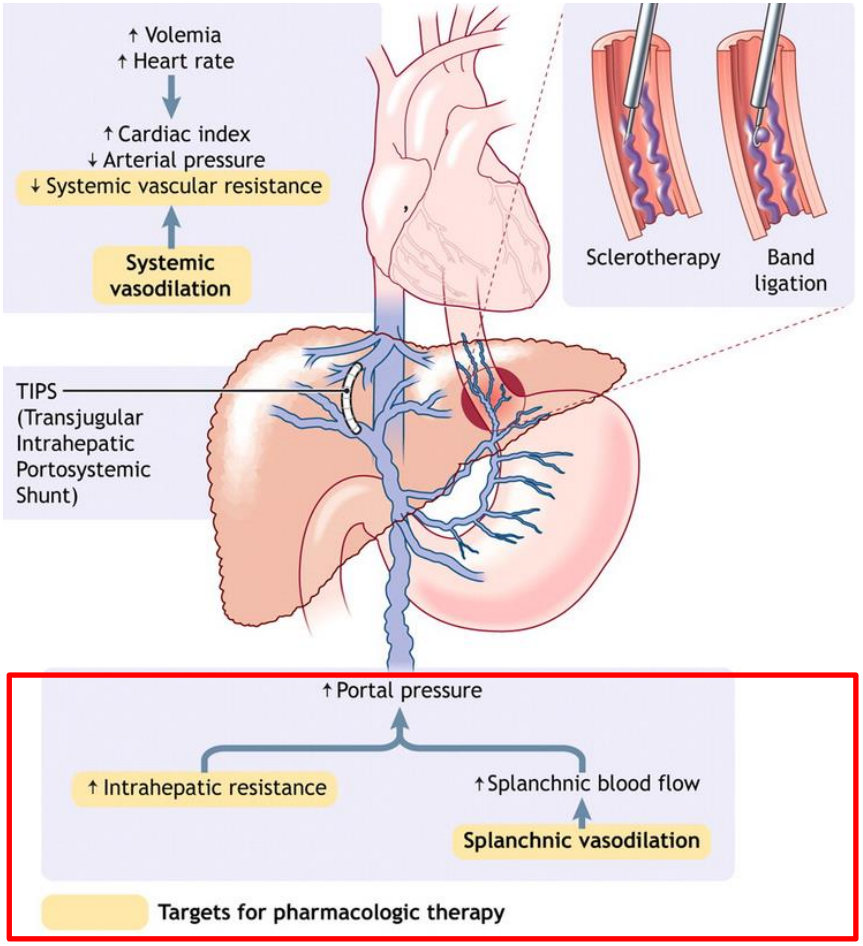
INVESTIGATIONS

- Ultrasound (Liver & Spleen) – radiological findings:
  - Dilated splenic and superior mesenteric veins ≥ 11mm
  - Splenomegaly > 12cm
  - Reduction in portal flow mean velocity <12 cm/second
  - Dilated portal vein ≥ 13mm
  - Porto-systemic collaterals – recanalization of the umbilical vein
  - Other findings: ascites, nodular liver, portal/splenic/SMV thrombosis

COMPLICATIONS (PORTAL HYPERTENSION)

1. Ascites
   - Increased fluid shift (sterling's law) lead to increased lymphatic drainage from liver which overwhelms thoracic duct capacity → percolation of hepatic lymph into peritoneal cavity
   - Life threatening complications → spontaneous bacterial peritonitis (SBP)
2. Formation of porto-systemic shunts (see below)
3. Portal Hypertensive Gastropathy → gastric mucosa friability & dilated blood vessels → UBGIT
4. Congestive Splenomegaly
5. Hepatic Encephalopathy
   - Secondary to hyperammonemia (neuro-toxin) exacerbated by porto-systemic shunting

Region	Name of clinical condition	Portal circulation	Systemic circulation
Oesophageal	Oesophageal Varies	Oesophageal Branch Of Left Gastric Vein	Oesophageal Branch Of Azygos Vein
Rectal	Rectal Varices (Haemorrhoids)	Superior Rectal Vein	Middle Rectal & Inferior Rectal Vein
Paraumbilical	Caput Medusae	Paraumbilical Veins	Superficial Epigastric Veins
Retroperitoneal	(No Clinical Name)	Right, Middle & Left Colic Veins	Renal Vein, Suprarenal Vein, Paravertebral Vein & Gonadal Vein
Intra-Hepatic	Patent Ductus Venosus	Left Branch Of Portal Vein	Inferior Vena Cava



ASCITES

PATHOGENESIS (IN CIRRHOTIC PATIENTS)

- Progressive liver cirrhosis → obstruction of intra-hepatic vasculature →
- Portal HTN develops → ↑ splanchnic NO released → splanchnic vasodilatation →
- ↓ effective intra-abdominal blood volume – "tank is bigger but less full" →
- Renal hypoperfusion → stimulate RAAS → ↑ vasoconstriction & renal hypoperfusion* →
- ↑ aldosterone** → ↑ retention of salt and water

* At risk of hepatorenal syndrome (HRS) 2° to altering blood flow and blood vessel tone in the kidneys
** Hence diuretic of choice in treatment of ascites in patients with liver disease is spironolactone (aldosterone antagonist) – which decrease reabsorption of salt and water

CLINICAL PRESENTATION

- Progressive abdominal distension ± painless or abdominal discomfort
- a/w weight gain, SOB, early satiety, and dyspnoea
- Fever, abdominal tenderness, and AMS ← suspect SBP

PHYSICAL EXAMINATION

- Examine to confirm diagnosis
  - Abdominal distension
  - Flank dullness → shifting dullness (pathognomonic) → fluid thrill
  - Eversion of the umbilicus – also check for hernias
- Examine for likely causes
  - Peripheral stigmata of chronic liver disease and portal HPT ← CLD
    - Look for signs of hepatic decompensation – confusion or GI bleed
  - Raised JVP + Peripheral edema ← Right Ventricular Failure (RVF)
  - Cachexia, cervical lymphadenopathy ← ?gastric, ovarian, liver mets
  - Anasarca ← nephrotic syndrome
    - Tell examiner you would like to check urinalysis

CLASSIFICATION

SAAG ≥ 1.1g/dL	SAAG <1.1g/dL
Liver Cirrhosis (81%)	Malignancy: peritoneal carcinomatosis
Liver: Alcoholic Hepatitis, Massive Liver Metastases	Infective: peritoneal tuberculosis
Heart: congestive cardiac failure, constrictive pericarditis	Inflammation: Pancreatitis, Pancreatic Ascites
Budd-Chiari Syndrome	Chylous Ascites^
Portal Vein Thrombosis	Serositis
Idiopathic Portal Fibrosis	Nephrotic Syndrome

SAAG = serum-ascites albumin gradient – the gradient correlates directly with portal pressure; those whose **gradient is ≥ 1.1g/dL have portal HTN** and those with gradient of <1.1g/dL do not (accuracy 97%)

^ milky-appearing peritoneal fluid that is rich in triglycerides, develops when there is a disruption of the lymphatic system, which occurs due to traumatic injury or obstruction (from benign or malignant causes)

INVESTIGATIONS

- Chest X-Ray
  - ± right pleural effusion – diaphragmatic channel open up and transmit fluid
- Liver & Spleen Ultrasound / CT scan
- Peritoneal tap
  - **Therapeutic**
    - Relieve of discomfort & diaphragm splinting from distension
  - **Diagnostic**
    - colour / appearance – clear, bloody, cloudy, milky
      - clear / translucent yellow → cirrhosis
      - bloody → malignancy or traumatic paracentesis
      - turbid / cloudy → infection
      - milky → chylous ascites
      - brown & if ascetic [Br] > serum [Br] → ruptured GB or perforated DU
    - cell count and differential (FEME)
    - albumin – to determine SAAG
    - total protein concentration
    - amylase concentration (pancreatic ascites or bowel perforation)
    - Microbiology – gram stain smear, culture (aerobic / anaerobic), cytology
    - Others – LDH / TG / Glucose / TB culture / Br / proBNP

TREATMENT

- Conservative
  - Low salt diet – 2000mg / day or 88mol/day
  - Fluid restriction – only if serum sodium <125mmol/L
  - Monitor weight and urine sodium regularly
- Pharmacological
  - Diuresis – spironolactone ± furosemide
    - Typical dose: 100mg spironolactone and 40mg furosemide OM (ratio 10:4) – max 400mg:160mg
    - Solely ascites → use spironolactone, if concomitant pedal edema → add furosemide
    - ± Amiloride (if painful gynecomastia due to spironolactone)
  - Antibiotics – if suspect spontaneous bacterial peritonitis (SBP)
    - +ve ascitic fluid bacterial c/s
    - ↑ ascitic fluid PMN ≥ 250cells/mm^3 (or ascitic fluid WBC > 500cells/mm^3)
    - IV ceftriaxone or oral quinolones (i.e. ciprofloxacin)
  - Avoid or use with caution in patients with cirrhosis – propranolol / ACEi / ARBs / NSAIDs
- Therapeutic Paracentesis (i.e. coop-loop for tense ascites) + IV albumin 20% infusion
  - Site: 2FB above and 2FB lateral to ASIS – perform under aseptic technique, LA, US guided
  - Insert a pigtail catheter via seldinger technique → drain – (i.e. 500ml Q6H into stoma bag)
  - Approximately 8g IV albumin for every 1L of ascitic fluid drained
  - Albumin infusion → prevents **paracentesis induced circulatory dysfunction**[39] with risk of hypotension, recurrent ascites, HRS and death – with albumin, large volume of ascites can be drained (i.e. 6-8L)
- Surgical – Liver transplantation and shunts (patients with liver disease)
  - Transjugular Intrahepatic Porto-Systemic Shunts (TIPSS)
  - Peritoneovenous shunt (Le Veen or Denver)
- Treatment of underlying cause if possible
  - Liver transplant for cirrhotic liver

[39] Hepatology. 2012 Apr;55(4):1172-81.

VARICEAL BLEEDING[40]

- Gastroesophageal varies are the most clinically important collaterals because their rupture results in potentially fatal hematemesis
- Prevalence of gastroesophageal varies increases in Child's Score (A: 40%, C: 85%)
- Strongest predictor for development of varices in patients with cirrhosis is the hepatic venous pressure gradient of > 10mmHg
- Most important predictor of haemorrhage is the size of varices, other predictors includes decompensated cirrhosis and endoscopic stigmata of recent haemorrhage (see below)
- Variceal bleeding associated with mortality of at least 20% at 6 weeks

WHEN TO SUSPECT VARICEAL SOURCE IN UBGIT

- Any previous variceal bleed → ask patient whether he/she goes for regular banding or OGD screening and banding
- Any history of chronic liver disease → ask for risk factors (i.e. alcohol ingestion, hepatitis B/C)
- Any stigmata of chronic liver disease

MANAGEMENT OF VARICES can be divided into three categories:

1. Active Variceal Bleed
2. Prophylaxis
3. Chronic management

I. ACTIVE VARICEAL BLEED – MANAGEMENT

Hemodynamically Unstable Patient

1. **Resuscitate (manage in critical care area)**
   - Maintain airway – KIV intubation If patient has altered mental state (encephalopathy) or hematemesis is copious
   - Breathing → supplemental high flow oxygen, maintain Spo2 >94%
   - Establish 2 or more large bore peripheral IV lines
   - Monitoring → Vitals, ECG, pulse oximeter, urine output (IDC)
   - Labs → GXM (4units), FBC, U/E/Cr, PT/PTT, ±LFT, ±Cardiac Enzymes
   - Infuse fluids → 1 litre N/S fast and reassess parameters
   - ICU bed and facilities should be made available

Note: DO NOT insert NG tube if oesophageal varies is suspected → worsen variceal bleed
Note: Under-resuscitate in variceal bleed as blood volume expansion increases portal venous pressure in patients with cirrhosis which may sustain active bleed or precipitate further bleeding → initiate blood transfusion if Hb <7g/dL with goal of maintaining level ≥ 7 g/dL (for patients likely to suffer from adverse events in setting of significant anemia – i.e. unstable CAD can keep Hb ≥ 9 g/dL)
Note: alcohol withdrawal should be anticipated

2. **Pharmacological Management**
   - IV broad-spectrum Ab 7 days → (ciprofloxacin 500mg bd or ceftriaxone 1g / day)
   - IV somatostatin (250ug bolus followed by 250ug/h infusion for 3-5days) or IV octreotide (50mcg bolus followed by 50mcg/hour for 3-5days)
   - IV omeprazole 80mg bolus
   - IV Vitamin K (10mg) – should be given routinely to cirrhotic with coagulopathy

   - ± IV Terlipressin (2mg Q6H) (synthetic vasopressin) is the vasoactive drug of choice with a 34% mortality relative risk reduction (CI in patients with IHD)
   - ± Recombinant activated factor VII (rFVIIa) – for correcting PT in cirrhotic

Note: Infection is a strong prognostic indicator in acute bleed → use of Ab reduce risk of spontaneous bacterial peritonitis (SBP), re-bleeding and mortality

Note: IV somatostatin/octreotide → Not given in ulcer bleed; mode of action is as a splanchnic vasoconstrictor which decreases portal blood flow and hence portal pressures. Also, it acts indirectly to inhibit secretion of gut hormones that increase portal blood flow

3. **Management of severe variceal bleeding (balloon tamponade)**
   - Protect airway before inserting tube.
   - Sengstaken-Blakemore tube / Minnesota tube (maximum 24 hours – temporary deflate after 12 hours to prevent pressure necrosis) in patients with uncontrollable bleeding for whom a more definitive therapy is planned (i.e. TIPS or endoscopic therapy)
   - Consists of (1) gastric balloon (2) oesophageal balloon (3) gastric opening (4) oesophageal opening – (3/4) → for aspiration

   - Others: Linton-Nachlas tube (only gastric balloon, no oesophageal balloon)

[40] HEPATOLOGY, Vol. 46, No. 3, 2007

4. **Definitive Management (endoscopy and TIPS)**

Endoscopy

- Confirms diagnosis and institute definitive management
- (1) Sclerotherapy (into bleeding varies or overlying mucosa)
    - Induce inflammation and fibrosis
    - Controls bleeding in 70% after 1st injection and 85%after a second
- (2) Variceal band ligation → ligation is superior to sclerotherapy in initial control of bleeding and associated with fewer adverse effects[41]

TIPSS (Transjugular Intrahepatic Porto-Systemic Shunt)

- Involves radiologically guided intra-hepatic placement of a stent between branches of the hepatic and portal venous circulation → acute decompression of portal pressure thus controlling refractory variceal bleed
- Considered in patients whose bleeding is refractory to pharmacological and endoscopic therapy
- TIPSS is not a good long-term preventive strategy

Emergency Shunt surgery

- Risk of more frequent encephalopathy and higher mortality (can be extrapolated to TIPS because its physiology is the same as that of surgical shunts (i.e. divert blood away from liver)
- **Selective**
    - Proximal splenorenal shunt (splenectomy with end-to-side anastomosis of portal side of splenic vein to left renal vein)
    - Distal splenorenal shunt (Warren-Zeppa shunt – splenic vein divided and splenic side anastomosed end-to-side to left renal vein)
- **Non-selective**
    - Portacaval shunts (joining portal vein to IVC) – side-to-side, end-to-side
    - Mesocaval shunts (joining superior mesenteric vein to IVC)

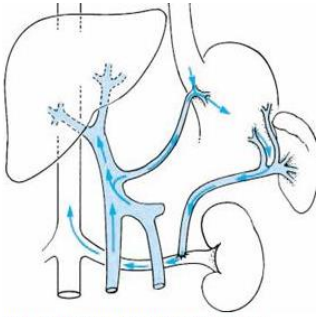


Fig 1. Splenorenal shunt (google images)

Salvage Haemostatic Surgery (esophagogastric devascularisation) – rarely done

- Sugiura Surgery / Modified Sugiura

Complications of Splenectomy[42]

Intra-operatively	- Bleeding – may necessitate conversion to hand-assisted or open procedure - Injury to surrounding organs (i.e. pancreas, splenic flexure of the transverse colon, greater curve of the stomach, diaphragmatic injury)
Early	- Pulmonary Complications – atelectasis, pneumonia and pleura effusion - Sub-phrenic Abscess - Wound Problems (hematoma formation, seromas, wound infection) - Vascular Cx → arteriothrombosis & venous thrombosis (acute portal vein thrombosis) - Thrombocytosis → plt count usually peaks after 7-10days (KIV prophylactic aspirin) - Stomach → gastro-paresis, ileus - Rare: post-splenectomy necrotizing pancreatitis, pulmonary hypertension
Late	- Overwhelming Post-splenectomy Infection (OPSI) → encapsulated bacteria (i.e. strep pneumonia, H. Influenza & N. meningitides), risk of mortality highest in first 2 years* ▪ Polyvalent Pneumococcal Vaccine (Pneumovax) – repeat every 5-7yrs ▪ Meningococcal Vaccine – once ▪ Haemophilus Influenza Type B conjugate vaccine ▪ Seasonal Influenza Vaccine

* Patients present with nonspecific flu like symptoms rapidly progressing to fulminant sepsis, consumptive coagulopathy, bacteraemia and death within 12-48hrs – estimated mortality = 0.73 per 1000 patient years – hence need for early physician consultation in event of fever or other prodromal symptoms

[41] Semin Liver Dis, 1999;19:439

[42] Hematol J 2001;**2**(3):210-211

II. PROPHYLAXIS OF VARICEAL BLEEDING[43]

1. **Secondary prophylaxis of variceal bleeding**
   - Patients with cirrhosis who survive an episode of active variceal bleed should receive therapy to prevent recurrent of variceal haemorrhage
   - Best option is combination of:
     - Band ligation (3 weekly ligation until completely obliterated) &
     - Non-selective beta-blockers (Propranolol unless CI)

2. **Primary prophylaxis of variceal bleeding**
   - Prevention of variceal haemorrhage in patients who have never bled (reduce bleeding risk by 30-45%, number to treat = 11)
   - Patients with large varices (grade 3) or medium varices (grade 2) with endoscopic red signs or Child's C cirrhosis should be treated
   - Best option is:
     - Non-selective beta-blockers (Propranolol & Nadolol) → reduce risk of bleeding and slow progression of small varices into larger ones
       1. block ß1 receptor → decrease cardiac o/p
       2. block ß2 receptor → produce splanchnic vasoconstriction and reduce portal flow and portal pressure
   - If contraindicated to BB → long acting nitrates (isosorbide mononitrate)
   - Insufficient evidence to support treatment of patients with small varices
   - No evidence for prophylaxis with BB in patients with cirrhosis without varices

Predictors of variceal haemorrhage:

1 Site:
   - Varices at the gastro-oesophageal junction have the thinnest coat of supporting tissue and are at highest risk of rupture and bleeding

2 Size:
   - Grade 1: Small straight varices not disappearing with insufflation
   - Grade 2: Enlarged tortuous varices that occupy less than one-third of the lumen
   - Grade 3: Large varices that occupy more than one-third of the lumen

3 Child's score – patients with higher Child's score have higher risk

4 Red signs: Endoscopic Stigmata of Recent Haemorrhage (ESRH)
   - Red wale marks (longitudinal red streaks)
   - Cherry red spots (flat discrete spots)
   - Hematocystic spots (raised discrete spots – resemble "blood blisters")
   - Diffuse erythema

5 Previous variceal haemorrhage:
   - 70% of patients will have further variceal bleeds after an index bleed (risk highest in first 48hours after first bleed)
   - 30% re-bleed within 6 weeks, 30% re-bleed after 6 weeks

[43] Clinical Practice Guidelines (May 2007) - Management Of Acute Variceal Bleeding

III. CHRONIC MANAGEMENT

- Start patient on an ablation regimen (endoscopy with initial ligation/sclerotherapy and subsequent endoscopic monitoring and repeated ligation/sclerotherapy as required to completely ablate varices)
- If patient bleeds again → failed ablation → consider surgery (as above – shunts, or Sugiura)
- LT propranolol + PPI → Acid suppressive therapy is theorized to improve the stability of clot, and infusion of omeprazole has been shown to reduce risk of recurrent bleeding and need for emergent surgery in all cases of UBGIT[44]

[44] Br Med Bull. 2007;83:307-24.

PEPTIC ULCER DISEASE

EPIDEMIOLOGY[45] (UK AUDIT)

- Remitting and relapsing lesions most often diagnosed in middle-aged to older adults
- Incidence = 100 per 100,000 per year
- M:F ratio for duodenal ulcers = 3:1
- Lifetime risk for developing PUD = 10%
- Overall mortality = 7-10%, unchanged for last 2 decades – mostly due to ulcer bleeding especially in elderly with significant comorbidities

MAIN AETIOLOGICAL FACTORS

Helicobacter Pylori Infection	- 60% of population are positive for H. pylori by age 21 - About 10-20% of infected patients develop an ulcer - Gastric ulcer 2° to H. pylori infection tend to occur on lesser curvature[46] - a/w 85% of duodenal ulcers & 68% of gastric ulcers[47]
NSAID	- 8-fold increase in risk of duodenal ulcers - 40-fold increase in risk of gastric ulcer (more often on greater curvature) - Ulcers in NSAID user were more likely to be a/w UBGIT - Dose-dependent relationships → ulcers do not recur when NSAIDs discontinued
Smoking	- 2 times increased risk compared to non-smokers (impairs mucosal blood flow and healing, or provide favourable milieu for H. pylori)
Others	- Alcohol → alcoholic cirrhosis a/w with higher incidence of PUD - Acid hypersecretion → commonly a/w duodenal ulcers - Previous Peptic Ulcer - Psychological Stress - Other Drugs → corticosteroids (high dose + frequent use delay healing of lesion rather than causing de novo ulceration), anticoagulant (increased risk of bleed)

LOCATION OF PEPTIC ULCER

- Duodenum – 1st portion (75%)
- Stomach – lesser curvature, antrum (20%)
- Stomal ulcer – at the stoma of a gastroenterostomy
- Meckel's Diverticulum – specifically when it possess ectopic gastric mucosa
- Distal duodenum and Jejunum – in addition to stomach and 1st part of duodenum → Zollinger-Ellison Syndrome*

*Zollinger-Ellison Syndrome is the hypersecretion of gastric acid due to a gastrinoma → rare cause PUD in 0.1-1% of patients → suspect if patient present with recurrent ulcers despite adequate treatment, multiple ulcers, ulcers in unusual locations, complicated PUD (haemorrhage, perforation, obstruction) with no history of NSIAD use and are H. Pylori negative.
→ Confirm with high fasting serum gastrin levels in the presence of high acid secretion
→ triad of
(1) PUD in unusual locations – i.e. jejunal, whole duodenal, gastric
(2) Massive gastric acid hypersecretion,
(3) Gastrin-producing tumour (gastrinoma) – most in pancreas, can also be in duodenum, stomach, ovary
→ Management: PPI + Surgery (to remove tumour and carry out anti-ulceration operation i.e. wedge resection)

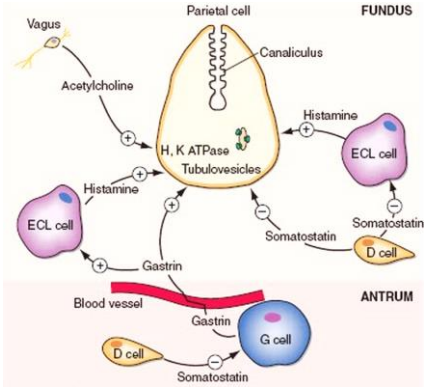
PATHOGENESIS

- Ulcer development depends on imbalance btw acid secretion and the mucosal protective factors
  - **Aggressive factors**: gastric acid activity, pepsin activity, H. Pylori & NSAIDs
    - HCl secreted by parietal cells (see below)
    - Pepsinogen secreted by chief cells – pepsinogen converted to pepsin by HCl
    - Major production site = gastric fundus and body
  - **Protective mechanisms**:
    - Mucus secretion
    - Bicarbonate secretion into mucus
    - Robust mucosal blood flow to remove protons
    - Epithelial regenerative capacity (i.e. cell renewal)
    - Prostaglandin secretion by mucosa to maintain blood flow

- Duodenal ulcers due to **excessive acid & pepsin secretion** that overwhelms (impaired) mucosal defences (hence epigastric pain experienced when hungry, which is relieved by food)

- NSAIDs → impair mucosal prostaglandin synthesis (through non-selective COX inhibition)
  - PGs are important for (1) mucin production, (2) mucosal bicarbonate secretion, (3) maintaining mucosal blood flow and (4) inhibiting gastric acid secretion

- Gastric acid secretion by the parietal cell is stimulated by **histamine** (ECL cells), **gastrin** (G cells) or **ACH** (vagal nerve stimulation) which in turn activates **H^+K^+ATPase** which leads to secretion of Hydrochloric Acid (HCL)
  - Major site of gastrin production is in the pyloric antrum
  - Smaller division of the vagus nerve (**nerves of Latarjet**) supply the pyloric region and are responsible for relaxation of the pylorus to allow emptying
  - H^+K^+ATPase is inhibited by PPI



[45] Am J Gastroenterol 90: 206-210 & Robbins
[46] Endoscopy. 1996 Feb;28(2):229-33.
[47] Singapore Med J. 2000 Oct;41(10):478-81.

PRESENTATION

1. **Incidentally detected on OGD**
2. **Symptoms of dyspepsia**
   (a) Ulcer-like dyspepsia: burning, gnawing, intermittent epigastric pain
      - Duodenal ulcer → relieved by food and ingestion of antacids
      - Gastric ulcer → pain exacerbated with food intake → patient avoid food and presents with weight loss (unlike duodenal ulcers)

   (b) Dysmotility-like dyspepsia: non-painful discomfort (upper abdomen), a/w upper abdominal fullness, nausea, vomiting early satiety, bloating, belching

   (c) Unspecified dyspepsia

3. **Bleed**
   - Mild and chronic: iron deficiency anemia
   - Severe and acute: haematemesis (coffee-grounds vomitus) or melena
4. **Perforation**
   - With consequent acute peritonitis
   - Sudden onset of epigastric pain – patient able to recall exact timing
   - No relieving factors
   - O/E:
      - Toxic (fever)
      - Shock (SBP <100mmHg / Tachycardia)
      - Board-like rigidity, guarding (signs of peritonism)
   - Erect CXR will show free air under diaphragm
      - 70% of PPU has free gas under diaphragm
      - 70% of free gas under diaphragm is caused by PPU
      - 100% failure if you cannot identify this in exams
   - When diagnosis in doubt – severe peritoneal signs with no free air
      - Repeat CXR or decubitus AXR
      - Urgent CT abdomen with contrast
      - Urgent Barium contrast meal with follow through (if no CT)

INVESTIGATIONS: [OESOPHAGOGASTRODUODENOSCOPY] (OGD) – 3 INDICATIONS

(a) Diagnosis

- Confirmation of Peptic Ulcer Disease (PUD) – note location of ulcer
- Biopsy to rule out malignancy (usually 6 bites) – especially if s/s (weight loss, anemia, obstruction) or appearance of ulcer (associated mass, folds around ulcer) are present
- Biopsy rapid urease testing (CLOtest) – antral biopsy for H. pylori → biopsy tissue placed into a medium containing urea and an indicator such as phenol red. The urease produced by H. pylori hydrolyses urea to ammonia, which raises the pH of the medium, and changes the colour of the specimen from **yellow (NEGATIVE)** to **red (POSITIVE).**

→ Endoscopic biopsy = most accurate diagnostic method for H. pylori

(b) Therapeutic

- Ligation of bleeding vessels
   i. Injection with adrenaline (1:10,000 dilute to 10ml - continue with N/S if need more) or absolute alcohol – tamponade effect is the most effective. Also vasoconstrictive effect for adrenaline
      → Inject around ulcer (4 quadrants)
      → Complications: perforation, bleeding, necrosis, arrhythmia)
   ii. Coagulation (Heater probe = thermal / Argon plasma)
   iii. Haemostatic clipping (endo-clip)

Principle: Dual modality better than single (as less risk of recurrent bleed and mortality) → usually **Injection + Clip/Heater probe**

- No study proves superiority of either therapy

Post-endotherapy:

- Monitor for re-bleed = drop in Hb (not melena / vomit blood clots as these are expected. Changes in vitals may be too late.)
- Diet individualised: usually NBM 1-2/7, 3/7 if worrisome, <1/7 if straight forward ulcer
- Re-scope the following day if you're worried about outcome from the first scope (not routine)
- Oralise PPI after 3/7 infusion (if worrisome, can give IV bolus PPI BD)
- TCU 3-4/52 at clinic

(c) Prognostication of bleeding risk (in UBGIT)

- Forrest classification[48] (or endoscopic stigmata of recent haemorrhage – ESRH)
- For patients (Forrest Ia, Ib, IIa and IIb) after successful endoscopic treatment[49]:
   i. High risk of re-bleeding = initial Hb ≤ 9g / dL, endoscopist with < 2 years of therapeutic experience, need for > 15cc of epinephrine, chronic renal disease, liver cirrhosis
   ii. High risk of mortality = initial active spurting bleeding, re-bleeding

[48] Lancet. 1974 Aug 17;2(7877):394-7.
[49] Clin Endosc. 2011 December; 44(2): 93–100.

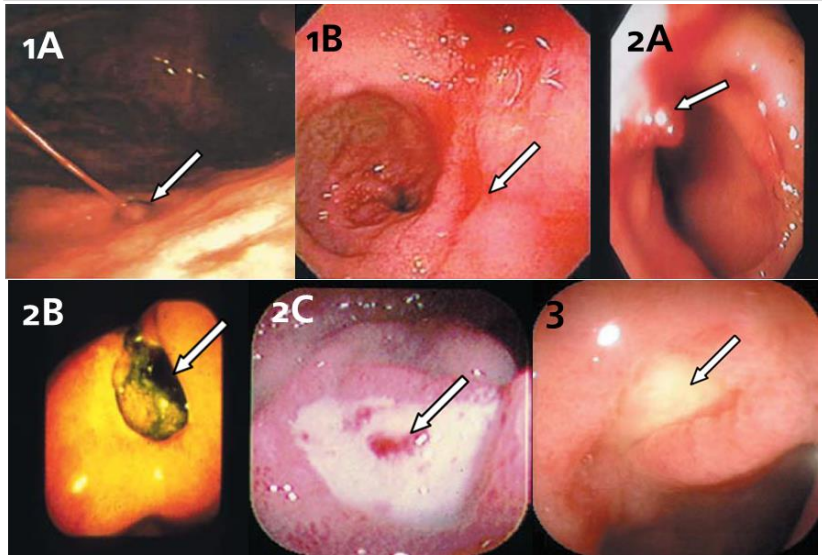
OTHER INVESTIGATIONS

- Barium Meal & Follow-Through: though less invasive, it is less accurate at defining mucosal disease or distinguishing benign from malignant ulcer disease. (see below)
- Fasting Serum Gastrin: screen for gastrinoma (Zollinger-Ellison Syndrome)
- Serum Calcium: screen for multiple endocrine neoplasia (MEN)
- Urea Breath Test: screen for H. Pylori Infection (see below)
- Stool Antigen Test: screen for H. Pylori Infection
- Serologic Testing (IgG and IgA ELISA tests): screen for H. Pylori Infection (not recommended)

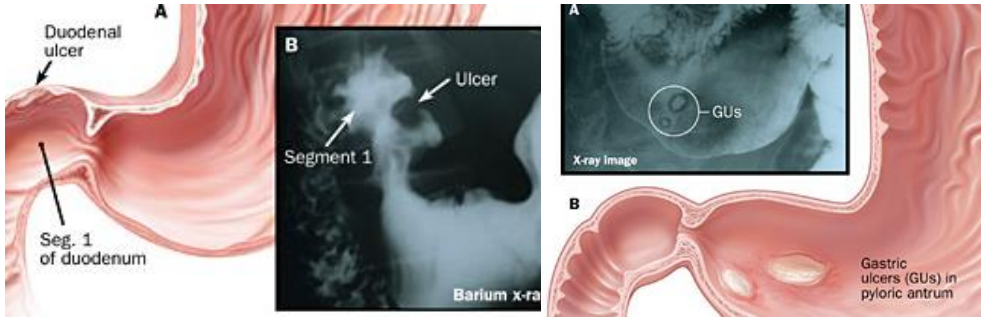
Forrest Classification

	Forrest grade (endoscopic stigmata)	Prevalence	Bleeding risk
1A	Spurting (arterial)	18%	100%
1B	Non-spurting, ooze (venous)		55% (17-100%)
2A	Non-bleeding ulcer with visible vessel	17%	43% (8-81%)
2B	Non-bleeding ulcer with adherent clot	17%	22% (14-36%)
2C	Ulcer with haematin-covered base (flat base)	20%	10% (0-13%)
3	Ulcer with clean base	42%	5% (0-10%)

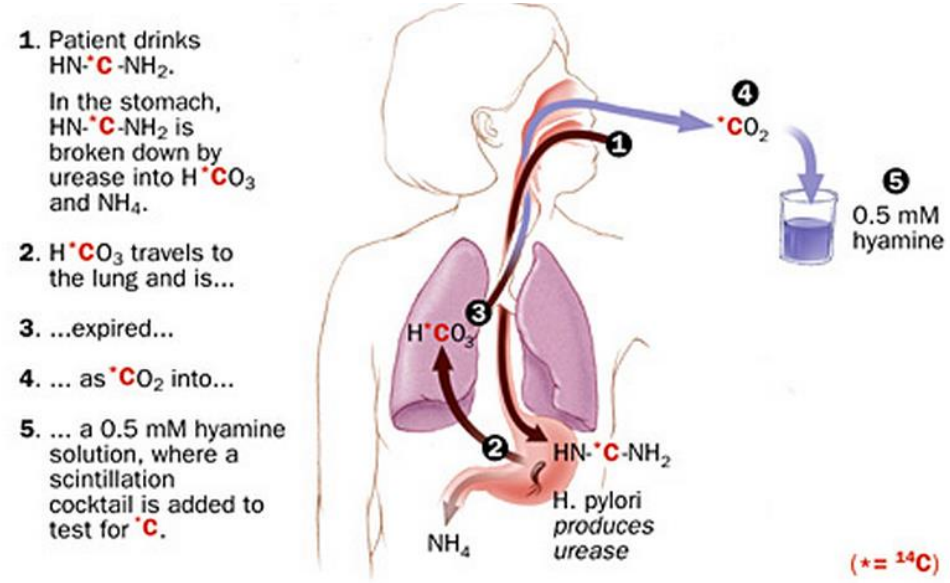
Forrest Classification	Rebleeding Incidence	Surgical Requirement	Incidence of Death
Type I: Active Bleed	55-100%	35%	11%
Ia: Spurting Bleed			
Ib: Oozing Bleed			
Type II: Recent Bleed	40-50%	34%	11%
IIa: Non-Bleeding Visible Vessel (NBVV)	20-30%	10%	7%
IIb: Adherent Clot			
Type III: Lesion without Bleeding	10%	6%	3%
Flat Spot	5%	0.5%	2%
Clean Base			



Barium Meal



Urea Breath Test



TREATMENT (PUD)

1. **Medical Therapy & Lifestyle Modifications**
   a. Smoking & Alcohol Cessation
   b. Proton Pump Inhibitor – 20mg BD
      - Increase Intra-gastric pH (less acidic environment) ↓ risk of platelet disaggregation and helps maintain clotting thus preventing re-bleeding – i.e. pH = 6.0 disaggregation = 77%, pH = 7.3 disaggregation = 0%
      - PPI are effective for facilitating ulcer healing (Omeprazole 20mg OM) – superior to double dose famotidine (40mg BD) – achieve healing only if offending meds is stopped
      - SE: diarrhoea, ↑ risk of C. diff (esp. in elderly), decreased efficacy of clopidogrel
   c. NSAID-associated PUD
      - Discontinue offending medication and initiate anti-secretory therapy (see above)
   d. H. Pylori Eradication
      - First line triple therapy: **omeprazole 20mg BD (for 6 weeks), amoxicillin 1g BD, clarithromycin 500mg BD for 10-14 days**
      - In penicillin-allergic patients, substitute amoxicillin with metronidazole 400mg BD
      - Document eradication by endoscopy + CLO test, urea breath test or stool serology testing
      - Treatment failure occurs in up to 20% → treat with quadruple therapy: **colloidal bismuth sub-citrate 120mg QDS, tetracycline 500mg QDS, metronidazole 400mg BD, omeprazole 20mg BD for 7-14 day**

2. **Endoscopic Therapy ± follow up Endoscopic Therapy**
   a. Therapeutic Endoscopy (see above / below)
   b. Follow-up Endoscopy
      - Re-scope in 6 weeks to document gastric ulcer healing → If ulcer still present, biopsy ulcer again (exclude malignancy for GU) and also do antral biopsy for rapid urease test – CLOtest (to confirm eradication of H. pylori)
      - Non-healing gastric ulcers should be resected surgically

3. **Transcatheter Arterial Embolization (see below)**

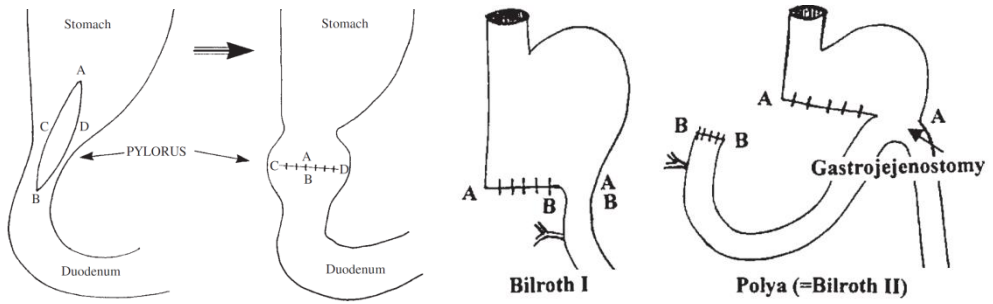
4. **Surgical Therapy**
   - Need for surgical intervention is declining with widespread use of H2 receptor antagonist (famotidine) and **proton pump inhibitors (omeprazole)**
   - Complications such as refractory haemorrhage, perforation or gastric outlet obstruction remain the major indication for surgical indications
   - Indication for surgical management (see below)

Duodenal Surgery	Gastric Surgery
1. Persistent Bleeding (erosion of posterior duodenal ulcer into gastroduodenal artery) 2. Peroration (anterior duodenal ulcer tend to perforate) 3. Gastric Outlet Obstruction 4. Failure of Medical Management or Non-compliance	1. Failure to heal after 3 months of medical mx 2. Dysplasia or Carcinoma 3. Recurrence 4. Perforation, Persistent Bleeding

Duodenal Ulcers

- Usually benign ulcers → monitor patient's response to medical intervention

Procedure	Remarks
Truncal vagotomy with pyloroplasty	**Truncal vagotomy*** → eliminate direct cholinergic stimulation to gastric section; parietal cells become less responsive to histamine and gastrin and vagal stimulation for gastrin release is abolished ***Truncal vagotomy** results in reduced acid secretion and a stomach which fails to empty adequately (transected nerve of Latarjet) therefore must combine with pyloroplasty → incise pylorus longitudinally through mucosal later then suture the incision transversely (see below)[50] – prevent stenosis / GOO
Truncal vagotomy with antrectomy and Billroth 1 /2	**Truncal vagotomy with antrectomy** yields maximal acid suppression with lowest ulcer recurrence rate (1-2%) but carries highest post-operative morbidity (5-15%) and mortality rates (1-2%)
Highly selective vagotomy (HSV)	**HSV** has lowest post-operative morbidity and mortality but is technically challenging to perform with high recurrence rate (5 to 15%) → selecting only branches that supply peptic cell. Does not require drainage as *nerves of latarjet* that supply pyloric sphincter are not affected



Gastric Ulcer

- Have higher risk of malignancy → non-healing gastric ulcers should be resected surgically
  a. Wedge Excision
  b. Antrectomy with inclusion of ulcer, depending on ulcer location
  c. Total Gastrectomy

- Concurrent acid-reducing operation is reserved for acid hyper-secreting patients or patient who are known to have refractory PUD despite maximal medical management (rare)
- Proximal ½ ulcers may require Total Gastrectomy

[50] Surgical Talk Revision in Surgery (2nd Edition) p118

TREATMENT (COMPLICATED PUD)

<table>
<tr><th>Complications</th><th>Duodenal Ulcers</th><th>Gastric Ulcers</th></tr>
<tr><td rowspan="3">Haemorrhage (BLEED)</td><td colspan="2">- Leading cause of death due to PUD a/w 5-15% mortality
- Endoscopic treatment → preferred therapy for treatment of bleeding ulcer
▪ Endoscopic Injection of epinephrine – tamponade & vasoconstrictive effect
▪ Thermal → Heater Probe – coaptive effect – compress till sealing of vessels
▪ Mechanical → Hemo-clip / Hemo-spray
* combined therapy is the standard of care
- Pharmacological → IV omeprazole 80mg bolus dose + 8mg / hour for 3 days – for prevention of PU re-bleeding[51]
- Worldwide DBRCT trial[52]: endoscopic haemostasis (single / combo) + IV esomeprazole 80mg bolus + 8mg/h (72 hours) OR placebo + esomeprazole 40mg per day (27days)
▪ At 72 hours: risk reduction of 43%
▪ Difference in re-bleeding recurrence remained significant at 7 and 30 days
▪ Reduce need for endoscopic re-treatment and surgical intervention
- If PPI infusion not available → recommend second endoscopy
- Transcatheter Arterial Embolization (TAE) – alternative to salvage surgery
▪ Celiac and superior mesenteric angiogram performed – in case of contrast extravasation → super selective cannulation of the bleeding vessel followed by angiographic coiling from a distal to proximal manner would be done till extravasation ceased
▪ TAE vs. Salvage Surgery[53] – In patients with ulcer bleeding after failed endoscopic haemostasis, TAE reduces the need for surgery without increasing the overall mortality and is associated with fewer complications.</td></tr>
<tr><td colspan="2">- Indications for surgical interventions (see above as well)
▪ Hemodynamically unstable despite vigorous resuscitation > 6units transfusion
▪ Failure of endoscopic haemostasis
▪ Repeated episodes of bleeding after initial stabilization (up to 2 attempts at obtaining endoscopic haemostasis)
▪ Shock a/w recurrent haemorrhage
▪ Continued slow bleed with transfusion requirement ≥ 3 units / day</td></tr>
<tr><td>⇨ Duodenotomy and 3 point ligation (oversewing/under-running)
⇨ Post-operative H. Pylori eradication

* Bleeding DU usually located at posterior duodenal wall within 2cm of the pylorus typically erode into gastroduodenal artery</td><td>⇨ Biopsy followed by oversewing the bleeding vessels or wedge excision of the ulcer</td></tr>
</table>

<table>
<tr><th>Complications</th><th>Duodenal Ulcers</th><th>Gastric Ulcers</th></tr>
<tr><td rowspan="3">Perforation (BURST)</td><td colspan="2">- Px: sudden acute onset of severe abdominal pain → generalized peritonitis (contents spill into abdominal cavity) or localized (perforation walled off by omentum or adjacent structures preventing peritoneal contamination)
- More common in elderly patients on chronic NSAID therapy and in GU than DU
- Finding of free air under the diaphragm present in most cases
- Initial Management:
▪ NBM + IV hydration KIV IV PPI (i.e. pantoprazole)
▪ NGT with low intermittent suction + I/O & stool charting
▪ IV broad spectrum antibiotics if septic + analgesia
▪ Monitor fluid balance: insert urinary catheter ± CVP line
▪ Serial Abdominal Examination – evaluate need for laparotomy
▪ Inform senior, OT, HD or ICU early if necessary and/or if in doubt</td></tr>
<tr><td>⇨ Lap omental (Graham) patch repair
⇨ Peritoneal debridement / washout
⇨ H. Pylori eradication

* perf DU usually located at anterior wall of D1</td><td>⇨ Simple wedge resection (ulcerectomy) →eliminate perforation and exclude malignancy (trace histology)
⇨ If perforation too large for 1° repair (> 1.5cm) or suspected malignancy → Gastrectomy (Billroth II) or Serosal Patch
⇨ (if location not ideal of resection) → multiple biopsies and omental patching</td></tr>
<tr><td rowspan="2">Gastric Outlet Obstruction (BLOCK)</td><td colspan="2">- Due to fibrosis and scarring of the pylorus from chronic PUD
- (rare) – patient presents with recurrent vomiting of poorly digested food, dehydration, hypochloremic, hypokalemic metabolic alkalosis
- Correction of volume and electrolytes → NG suction → IV antisecretory agents → OGD (evaluate nature of obstruction) → endoscopic hydrostatic balloon dilation → surgical therapy (indications)
▪ Persistent obstruction after 7 days of non-operative management
▪ Recurrent obstruction</td></tr>
<tr><td colspan="2">⇨ Antrectomy (include ulcer) with Billroth 1 or 2 reconstruction</td></tr>
<tr><td>Penetration (BURROW)</td><td colspan="2">- PUD may erode through entire thickness of gastric / duodenal wall into adjacent abdominal organs (i.e. pancreas, bile ducts, liver, small / large intestines)
- Px: acute onset of pancreatitis, cholangitis, diarrhoea of undigested food
- Surgery not recommended</td></tr>
</table>

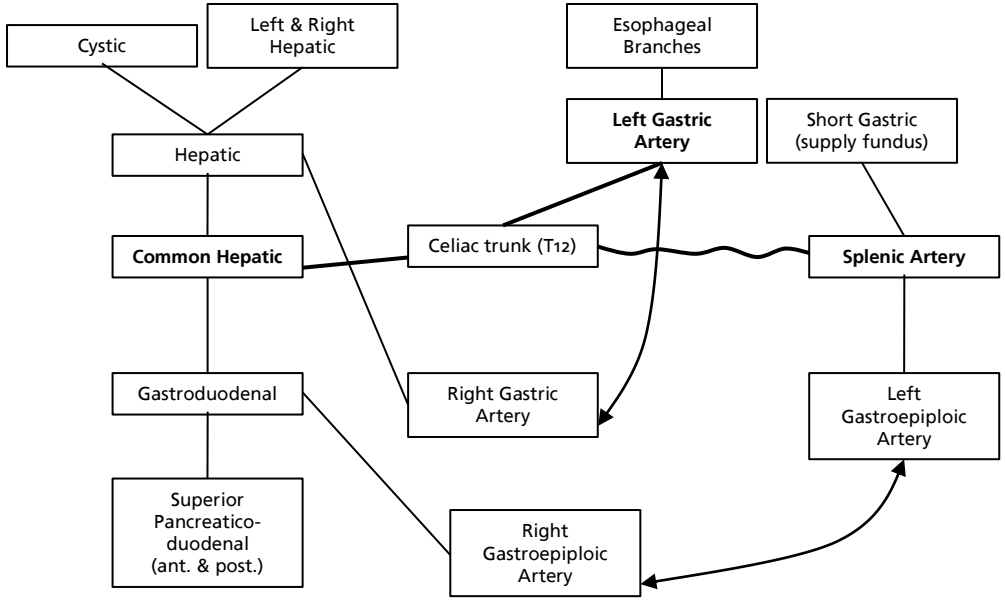
Complications of Massive Blood Transfusion

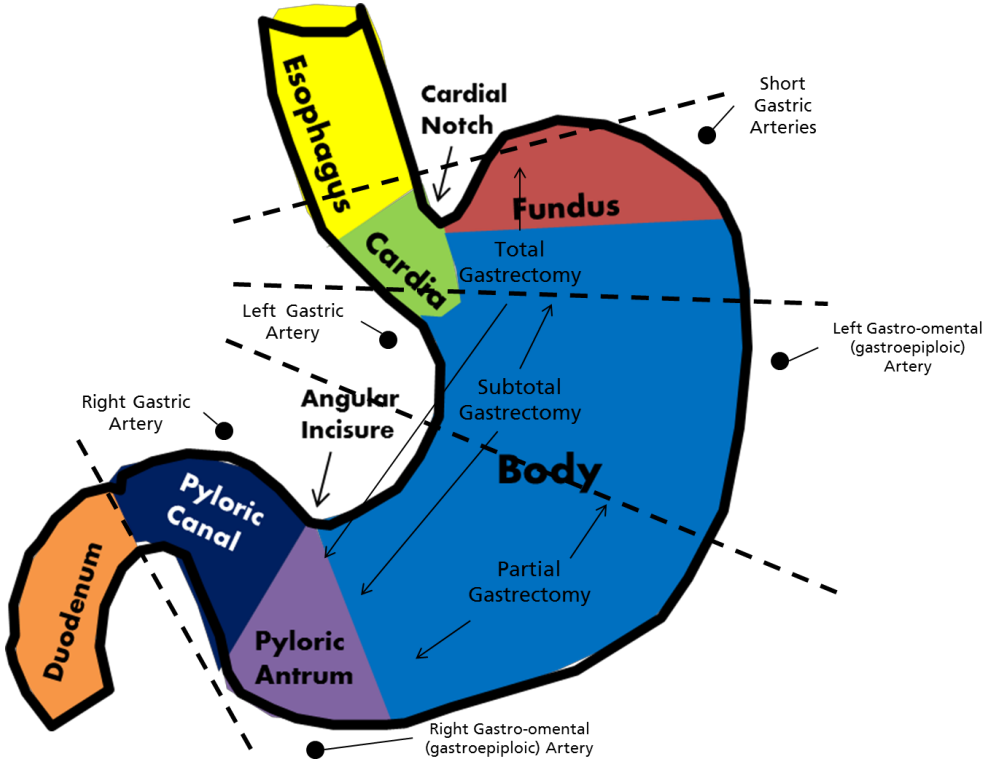
<table>
<tr><td>1</td><td colspan="2">Fluid overload and acute pulmonary edema</td></tr>
<tr><td>2</td><td>Immune related complications</td><td>Transfusion Related Acute Lung Injury (TRALI)
Acute Febrile Haemolytic Reaction
Non-haemolytic febrile transfusion risk
Allergic Reaction / Anaphylaxis</td></tr>
<tr><td>3</td><td>Infection related complications</td><td>Bacterial Infection
Viral Infection – Hep B (1 in 205,000), Hep C (1 in 1.8 million), HIV (1 in 1.9 million)</td></tr>
<tr><td>4</td><td>Metabolic Complications</td><td>Hyperkalaemia
Citrate Toxicity
Dilution of clotting factors → bleeding problems
Thrombocytopenia
Hypocalcaemia</td></tr>
<tr><td>5</td><td colspan="2">Hypothermia</td></tr>
</table>

* most common cause of febrile reaction post-transfusion = febrile non-hemolytic transfusion reaction (FNHTR) – caused by antibodies directed against donor leukocytes and HLA antigens

[51] N Engl J Med 2000; 343:310-316
[52] Ann Intern Med. 2009 Apr 7;150(7):455-64
[53] Gastrointest Endosc. 2011 May;73(5):900-8

Anatomy of the Stomach (Blood Supply and Lymphatic Drainage)



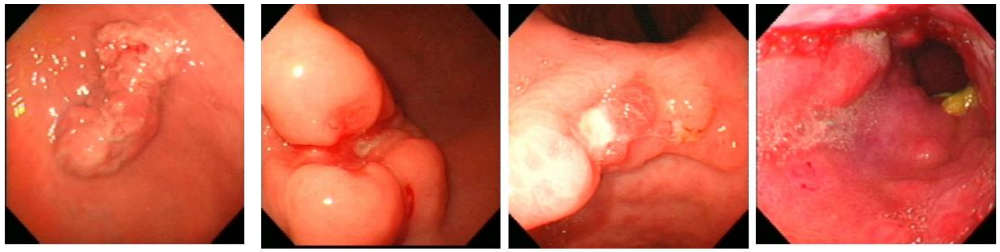


GASTRIC CANCER

EPIDEMIOLOGY[54]

- 7th most common cancer in males and 8th most common in females in Singapore
- 4th leading cause of cancer related mortality in males and 5th in females in Singapore
- Ethnic: Gastric Cancer more common among Chinese > Indian > Malays
- Gender: Gastric Cancer more common in Males > Females
- ASR of Gastric Cancer: 11.8 / 100,000 in Males and 7.0/ 100,000 in Females
- Lifetime risk for stomach cancer in Chinese Males: 1 in 50
- Large geographical variation – increase prevalence across Asia (Korea → Japan → China) and Eastern Europe
- Overall incidence slowly decreasing but sharp increase in cancer of the gastric cardia / GE junction in western countries (related to increased incidence of GERD)

BORRMANN'S CLASSIFICATION



Type 1	Type 2	Type 3	Type 4
Polypoid	Excavating	Ulcerative	Diffuse thickening

How to describe OGD findings of GOO

- Fungating/excavating/ulcerative tumour with contact bleeding in antrum and occluding it
- (i) Presence of food debris and (ii) absence of duodenal visualization implicates inability to intubate past the pylorus
- Consonant with GOO secondary to distal gastric carcinoma (likely Borrmann type X)
- Proceed with a bx for histo confirmation and prognostication by Lauren's Classification

Type 4 – Linitis Plastica

- Poorly differentiated
- Diffuse involvement ± signet ring cells
- Usually in younger, female patients, late presentation (malignant ascites) with poor prognosis

RISK FACTORS – MULTIFACTORIAL (INFECTION, ENVIRONMENT, GENETICS)
(Divide RF into Major and Minor Risk Factors – major includes: H. pylori and Diet)

1. **Infection – Helicobacter Pylori**
   - Ask patient about past infection, whether he has been on triple therapy before, about previous endoscopic procedures and its results
   - Lead to chronic gastritis (intestinal metaplasia as a precursor lesion)
   - 2x increased risk of developing gastric cancer

2. **Environmental**
   - **Diet:** preserved foods (nitrosamines – canned food), smoked foods (high salt),
   - **Smoking:** 2x increased risk of gastric cancer (intestinal cancer of distal stomach)
   - **Low socioeconomic status:** poor refrigeration of food and diet a/w increased risk
   - **Aspirin, Fresh Fruits & Vegetables, Selenium & Vitamin C → protective factors**

3. **Genetic**
   - **Family History**: 1.5x increased risk in siblings / offspring of patients with gastric CA
   - **Blood Group A**
   - **Hereditary (familial) diffuse gastric cancer:** linked to germline mutation of e-cadherin (CDH 1) → early onset, highly penetrant, diffuse gastric carcinoma
     - Prophylactic Gastrectomy has been performed on carriers of truncating germline CDH_1 mutations
     - Common among New Zealanders, Autosomal Dominance syndrome

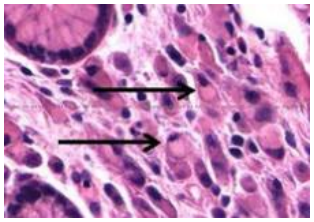
4. **Significant Past Medical History**
   - Previous Gastric Resection (i.e. Partial Gastrectomy) – allow reflux of bile induces chronic gastritis – significant if surgery > 7 years ago
   - Barrett Oesophagus – increased risk of gastroesophageal junctional tumour
   - Previous diagnosis of gastric polyps (adenomatous / inflammatory)
   - Chronic Atrophic Gastritis
     - Menetrier's Disease (hyperplastic hypersecretory gastropathy)
     - Pernicious Anemia – risk of gastric cancer in the long term

[54] Trends in Cancer Incidence in Singapore 2008-2012 (data report are as of 7th June 2013)

HISTOLOGICAL TYPES

Adenocarcinomas (95%)

- From mucous producing cells in the gastric mucosa
- **Lauren classification (divide into 2 main sub-types or mixed):**
  - (a) Intestinal (expanding) type – papillary, tubular, mucinous
    - Occur in elderly males and in the distal stomach (more likely to cause GOO)
    - Precursor lesion of intestinal metaplasia and dysplasia (as in chronic gastritis)
    - Haematogenous spread to distal organs
  - (b) Diffuse (infiltrative) type – signet ring cell, undifferentiated
    - a/w invasive growth pattern and rapid submucosal spread → linitis plastica
    - Occur in younger patients, females and in the proximal stomach
    - Transmural and Lymphatic spread with early metastases are more common
    - Worse overall prognosis



Signet Ring Cells: large cytoplasmic mucin vacuoles and peripherally displaced crescent shaped nuclei

Involves CDH1 mutation (encodes E-cadherin) which is also seen in lobular carcinomas of the breast (some of which have signet ring cells too)

Non-adenocarcinoma (5%)

Types	**Gastric Neuroendocrine Tumours (carcinoids)**	**Gastric Lymphoma** (B-cell lymphomas – extra-nodal MALT type)	**Gastrointestinal Stromal Tumour (GIST)****
Derived From	Enterochromaffin-like (ECL) cells in gastric mucosa	Lymphocytes in gastric mucosa	Interstitial cells of Cajal
Etiology	Hypergastrinemia (i.e. Zollinger-Ellison syndrome, MEN type 1)	H. Pylori chronic gastritis, Trisomy 3 and t(11;18) translocation	c-KIT (gain of function mutation), PDGFRA (platelet derived growth factor receptor α gene mutation)
Remarks	Carcinoid Syndrome – a/w metastatic disease*	MALT = mucosal associated lymphoid tissue	c-KIT positive tumours treat with imatinib (TKI)

*"Carcinoid syndrome: due to release of vasoactive substances into systemic circulation; characterized by cutaneous flushing, sweating, bronchospasm, colicky abdominal pain, diarrhoea, right-sided cardiac valvular fibrosis (note: carcinoids confined to the GIT typically do not cause carcinoid syndrome as vasoactive substances produce undergo 'first-pass' effect in liver, hence carcinoid syndrome is strongly associated with metastatic disease)"

** Mesenchymal Tumours of the GIT → **leiomyomas / leiomyosarcoma, neurofibroma & GIST**. GIST – ¾ are benign with indicators of malignancy including **(1) size > 10cm, (2) mitotic index >5/10hpf & (3) site (extra-gastric position)** – many are found incidentally but may present as vague abdominal pain (mass effect), GI bleed (necrosis of overlying mucosa), early satiety, LOW (obstructive symptoms)

PRESENTATION

	Early to Intermediate	Intermediate to Late	Late
History	- **Asymptomatic** - **Non-specific Epigastric Pain / Dyspepsia** (require high index of suspicious, early presentation and intervention = better prognosis) Any previous OGD? (in Japan – OGD is a screening tool) Gastric anti-secretory agents will improve symptoms and may mask Gastric CA– disease should first be excluded (new onset dyspepsia at age > 35 should cause concern)	- **Anemia^, Melena, Hematemesis** - **Early Satiety and dysphagia** (cardia tumour) - **Nausea, Vomiting** (obstruction → dysphagia, epigastric fullness, bloatedness) If present with pyloric tumour, presentation is like **GOO** ^Fe Deficiency Anemia 2° to tumour bleed – low ferritin, low serum Fe, high transferrin, high TIBC	- **Loss of appetite** - **Loss of weight** - (see above – spread) * non-metastatic effects (1) thrombophlebitis / migratory phlebitis (Trousseau Syndrome) and (2) DVT are due to effects of the tumour on thrombotic and haemostatic mechanisms (3) Seborrheic keratosis and freckles (Leser-Trelat sign)
PE	- **Asymptomatic** - **Slight Epigastric Tenderness**	- **Melena** - **Palpable Epigastric Mass** - **Succussion Splash**	- **Cachexia** - **Non-metastatic effects*** - **Metastatic Effects**

SPREAD

- Local Spread (direct extension to neighbouring organs) – i.e. gastric antrum cancer spread
  - (a) Pancreas
  - (b) Transverse colon
  - (c) Duodenum
- Lymphatic Spread
  - (a) Local lymphatic spread to peri-gastric lymph nodes → further spread follow the arterial supply (i.e. nodes along the branches of the celiac artery: left gastric artery, common hepatic artery and splenic artery) → further spread to para-aortic nodes
  - (b) Enlarged Left Supraclavicular nodes (Virchow's node)
- Haematogenous Spread (via venous circulation)
  - (a) Hepatosplenomegaly with ascites and jaundice (liver)
  - (b) Rarely: Bony Tenderness (bone), Neurological Deficits (brain), Lungs (usually these organs are not worked up for metastasis)
- Trans-coelomic Spread (Peritoneal Seeding)
  - (a) Seeding to the omentum, parietal peritoneum → Peritoneal Carcinomatosis (can lead to small bowel obstruction which is hard to treat owing to multiple sites of involvement)
  - (b) Infiltration of the umbilicus (Sister Mary Joseph's node)
  - (c) Enlarged ovaries on PE (Krukenberg's tumour)
  - (d) Fullness in pelvic cul-de-sac (Blumer's shelf = shelf-like tumour of ant rectal wall, rectal mass ddx tuberculous peritonitis

COMPLICATIONS

- **Bleeding** → Fe deficiency anemia, melena, hematemesis
- **Gastric outlet obstruction** → vomiting, dehydration, biochemical abnormalities (hypokalemic, hypochloremic metabolic alkalosis), aspiration ± pneumonia) → risk of aspiration pneumonia
- **Malnutrition** → cachexia
- **Perforation**

INVESTIGATIONS

Establish the Diagnosis	OGD + Biopsy	- Allow direct visualization and multiple biopsies of suspicious lesions (biopsy the edges of the ulcers) - Screening examination (routinely done in Japan) – in US population, warranted for high risk individuals: >20 years post-partial gastrectomy, patients with pernicious anemia or atrophic gastritis, positive familial history
	Double contrast upper GI barium contrast (limited diagnostic value) – except for linitis plastica (↓ distensibility, "leather-flask" appearance more obvious)	
Staging Investigations (divide to local & systemic staging) (1st test to do is to exclude mets)	- Most significant prognostic factor is depth of tumour invasion - **3 classifications** (Boorman – based on macroscopic appearance of tumour, Lauren – divides tumour to intestinal or diffuse types and TMN – reflects depth of tumour infiltration, nodal involvement and present of distant mets)	
	Endoscopic Ultrasound	- Superior to CT in delineating depth of tumour invasion (gold standard for T staging) and identifying perigastric lymphadenopathy (N staging accuracy = 70%) - Addition of FNA for suspicious node increases accuracy to ~100%
	Computer Tomography (CT)	- Abdominal/Pelvis: Assess for haematogenous spread to distant organ (i.e. most commonly liver mets), detect metastatic disease in the form of malignant ascites - CT Thorax (for gastric cardia tumour) - Limited accuracy in determining nodal involvement
	Positron emission tomography (PET)	- Combines spatial resolution of CT with contrast resolution of PET - Superior to CT scan alone
	Laparoscopic Staging	- Routine use of laparoscopy has been shown to detect small volume peritoneal and liver mets in 20-30% of patients believed to have local-regional disease (upstage)
Supportive Investigation to assess for complications	FBC	- Assess Hb levels
	U/E/Cr	- Biochemical abnormalities a/w gastric outlet obstruction
	LFT	- Albumin as a marker of nutritional status (< 35 is poor, <28 contraindicated for surgery) - Liver Mets (rarely, unless widespread liver mets, more for HCC)
Preoperative Investigations	ECG / CXR	- Investigations done on top of history and physical examination
	GXM / PT/PTT	

After investigations, a decision on treatment should be made on whether patient should go for curative or palliative treatment options.

STAGING (TMN)[55]

- Tumour arising at the esophagogastric (EG) junction, or arising in the stomach 5cm or less from the EG junction and cross the EG junction → staged as **oesophageal carcinoma (TNM system)**
- **Gastric cancer TNM staging** → for distal stomach tumours and for tumours arising in the proximal 5cm but not crossing the EG junction

T	To	No evidence of primary tumour
	Tis	Carcinoma in situ: intraepithelial tumour w/o invasion of the lamina propria
	T1	Tumour invades (a) lamina propria, muscularis mucosae, or (b) submucosa
	T2	Tumour invades muscularis propria
	T3	Tumour penetrates subserosa connective tissue – include those extending into gastrocolic or gastrohepatic ligaments, or into greater or lesser omentum
	T4	Tumour invades (a) serosa (visceral peritoneum) or (b) adjacent structures (i.e. spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, SI and retroperitoneum)
N	No	No regional LN metastasis
	N1	Metastasis in 1-2 regional LN
	N2	Metastasis in 3-6 regional LN
	N3	Metastasis in 7 or more regional LN
M	Mo	No Metastatic spread to distant organs
	M1	Distant Metastasis or Positive Peritoneal Cytology

	T	N	M
Stage 0	Tis	0	0
Stage 1A	1	0	0
Stage 1B	2	0	0
	1	1	0
Stage 2A	3	0	0
	2	1	0
	1	2	0
Stage 2B	4a	0	0
	3	1	0
	2	2	0
	1	3	0
Stage 3A	4a	1	0
	3	2	0
	2	3	0
Stage 3B	4b	0/1	0
	4a	2	0
	3	3	0
Stage 3C	4b	2/3	0
	4a	3	0
Stage 4	Any T	Any N	M1

[55] Ann Surg Oncol (2010) 17:3077–3079

TREATMENT

CURATIVE INTENTION

- Patient's case would be discussed at multidisciplinary tumour board

Endoscopic Therapy

- Therapeutic endoscopy may be curative for early gastric cancer (gastric cancer superficial to muscularis propria regardless of LN status)
- Endoscopic mucosal resection (EMR) or Endoscopic submucosal dissection (ESD)
- Excellent Prognosis

Pre-operative

- Nutritional Support
  - Assess – history (significant weight loss = 10% drop in last 12 months), physical examination (BMI < 18.5kg/m^2), labs (serum albumin <35g/L)
  - Pre-operative nutritional support significantly improves morbidity and mortality in the malnourished surgical patient → at least 7 days to have clinical benefit, route: enteral or parenteral, estimated nutritional requirements = 20-35kcal/kg/day
- Neoadjuvant Chemotherapy (see below)

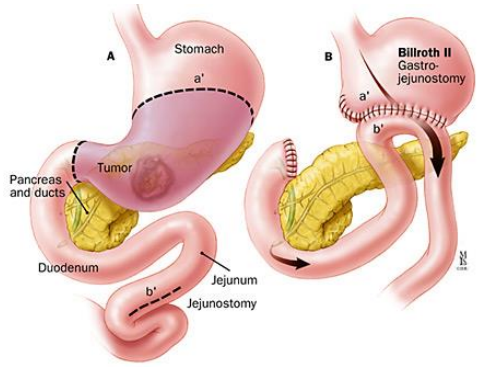
Surgical Principle:

- Wide resection to achieve negative margins (≥6cm confirmed with intra-op frozen section)
- En-bloc resection of lymph nodes and any structures involved by local invasion
- Re-establish GI continuity with a gastroenterostomy – 3 options
- Adjuvant Chemotherapy (see below)

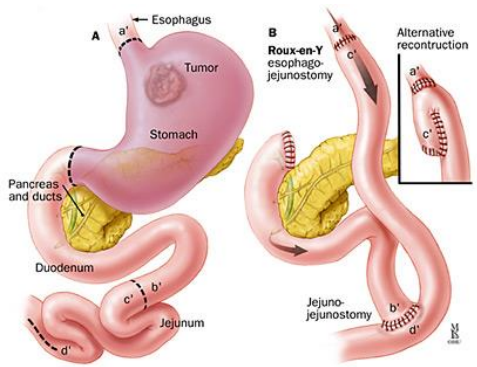
- Choice among total gastrectomy, subtotal gastrectomy and partial gastrectomy
  - **Partial Gastrectomy** → involves excision of the stomach with the right gastric artery (RGA) and right gastroepiploic artery (RGeA) transected
  - **Subtotal Gastrectomy** → involves excision of the stomach with the RGA, LGA, RGeA and LGeA transected
  - **Total Gastrectomy** → involves excision of the whole stomach with the RGA, LGA, RGeA, LGeA and short gastric arteries transected

  - Subtotal gastrectomy leaves a small portion of proximal stomach – easier to anastomose to jejunum than oesophagus since oesophagus does not have serosa (higher risk of leak)
  - Subtotal gastrectomy is associated with less morbidity, better functional outcome (some residual reservoir function preserved) – preferred option for distal tumours
  - Total gastrectomy is the resection of choice for proximal tumours (fundus, cardia, body) as well as diffuse-type tumours and cardio-oesophageal junction tumours

- Reconstruction
  - Billroth I (end-to-end gastroduodenostomy) – still commonly performed in Korea & Japan
  - Billroth II/Polya (gastrojejunostomy) – no protection against biliary reflux into stomach
  - Roux-En-Y oesophagojejunostomy – preferred option after total gastrectomy



Subtotal gastrectomy with Billroth II anastomosis



Total gastrectomy with Roux-en-Y

- Extent of Lymphadenectomy
  - Early retrospective study (from Japan) showed improved survival with radical LN dissection
  - General consensus – D2 lymphadenectomy → removal of perigastric nodes (D1) and nodes along left gastric artery, common hepatic artery, celiac trunk and splenic hilus and splenic artery (D2 resection – i.e. clearance of major arterial trunks)

- Chemotherapy / Radiotherapy
  - **Neo-adjuvant Therapy** – significant improvements in 5 year survival rates in patient with gastric cancer who were treated with 6 cycles of chemotherapy (3 pre-operatively an 3 post-operatively)[56] → chemotherapy regimen: 5FU, epirubicin, cisplatin (potential for increasing resectability rates – down-staging)
  - **Adjuvant Therapy** – improvement in overall disease free survival rates with resected gastric cancer treated post-operatively with 5-FU chemotherapy coupled with radiation therapy

Post-operative

- Feeding
  - NBM till POD 3-5 followed by escalation of feeds to diet of choice (DOC)
  - Advise small, frequent meals with nutritional supplementation (high calories and protein)
  - Vitamin B12 injection to circumvent loss of IF and Fe-tablets for Fe deficiency anemia
- Identify Complications (see below)
- Adjuvant Chemotherapy (see above)
- Follow-up: no established guidelines on post-operative endoscopic surveillance

[56] N Engl J Med. 2006;3565:11 (MAGIC Trial)

Complications of gastrectomy:

Early

1. Bleeding / Infection
2. Injury to surrounding organs
3. Anastomotic leak (day 5-7)
4. Duodenal Stump Blowout → due to progressive afferent limb dilation from kink/volvulus (day5-7)

Late

- Early satiety
  - Advise patient to have small frequent meals
- Dumping syndromes*
  - **Early dumping syndrome**: food enters small bowel too rapidly, drawing fluid into the bowel by osmosis (i.e. rapid fluid shift) → treat by eating small frequent meals with low carbohydrates and high protein/fat
  - **Late dumping syndrome**: occur 1-2hr after a meal due to reactive hyperinsulinaemia with hypoglycaemia in response to rapid delivery of food into small intestine → treat by eating more carbohydrates
- Nutritional deficiency
  - Iron deficiency – mixed picture
    1. Loss of intrinsic factor → B12 deficiency
    2. Decreased conversion of iron from Fe^{3+} to Fe^{2+} by gastric acid → decreased iron absorption in terminal ileum
  - Need to supplement with **B12 injections** and **Fe supplements**
- Loop Syndromes (Afferent Loop Syndrome)
  - Occurs in Billroth II reconstruction
  - Mechanical obstruction of the afferent jejunal loop due to kinking, anastomotic narrowing, or adhesions → postprandial epigastric pain with nausea, non-bilious vomiting
  - one of the main causes of duodenal stump blowout in the early postoperative period and is also an etiology for postoperative obstructive jaundice, ascending cholangitis, and pancreatitis due to transmission of high pressures back to the biliopancreatic ductal system
  - Can be decreased by doing Roux-en-Y surgery (but may still occur)
- Retained antrum syndrome
  - Not enough antrum removed leads to increased acidity in residual stomach, with formation of marginal ulcers on the jejunal side of the anastomosis
- Intestinal hurry
  - Inadequate reservoir function leads to poor digestion → may have phytobezoar formation
- Biliary/intestinal reflux into stomach (bile reflux gastritis)
  - Leads to symptoms of dyspepsia
  - More common in patients who underwent Billroth 2 procedure as compared to patients who underwent Roux-En-Y
- Recurrence of gastric cancer

* **Pathophysiology of dumping:** With meal → rapid gastric emptying leading to:

1. Hyperosmolar jejunal chyme → intraluminal fluid sequestration leading to:
   - Decreased blood volume → **hypotension, tachycardia, palpitations, dizziness**
   - Abdominal bloating → **diarrhoea**
2. Inappropriate gut hormone release → **vasomotor and GI symptoms**
3. Rapid glucose absorption → inappropriate insulin release → **late hypoglycaemia**

PALLIATIVE INTENTION

- For patients with unequivocal evidence of incurability – i.e. haematogenous metastases, involvement of the distant peritoneum, N4 level nodal disease (para-aortic and paracolic region) and disease beyond N4 level nodes and fixation to structures that cannot be removed
  - **Painful Bony Mets** – External Beam Radiotherapy (EBRT)
  - **Bleeding** – transcatheter embolization (catheter up femoral artery), external beam radiation (delayed effect – 2-3 weeks before radiation kills enough cancer cell for bleeding to stop) or palliative gastrectomy
  - **Obstruction** – gastrectomy, endoscopic laser ablation, surgical options: subtotal gastrectomy (6-15% mortality), total gastrectomy (20-40%), gastrojejunostomy for obstruction, self-expanding metallic stent (SEMS)
  - **Perforation** – require surgery

LONG TERM MANAGEMENT

- **CEA** and **CA-125** → cancer markers used to monitor for recurrence
- 5 year survival rates for curative surgery is higher in Japan (50-75%) compared to the West (25%)
- **Iron supplementation** and **Vitamin B12** (prevention of nutritional deficiency)

PROGNOSIS[57]

0	At Dx	1	2	3	4	5
IA	100.0	90.2	84.8	79.8	74.8	70.8
IB	100.0	87.4	77.9	69.9	62.7	57.4
IIA	100.0	82.1	67.4	57.2	50.2	45.5
IIB	100.0	76.8	58.3	46.0	38.4	32.8
IIIA	100.0	66.5	42.4	29.9	23.5	19.8
IIIB	100.0	61.6	35.4	22.9	17.8	14.0
IIIC	100.0	47.4	21.8	14.2	11.0	9.2
IV	100.0	27.0	10.0	5.6	4.5	4.0

[57] AJCC Cancer Staging Manual, Seventh Edition (2010)

COLORECTAL DISEASES

APPROACH TO BLEEDING LOWER GIT

DEFINITION
- Bleeding that emanates from a source distal to the Ligaments of Treitz
- Massive LBGIT – require ≥ 3 units of blood over 24 hours
- Males, advanced age, presence of diverticulosis and angiodysplasia are significant RF for LBGIT

CAUSES
Large Bowel
1) Colon
   - Diverticular Disease (bleeding diverticulosis)
   - Angiodysplasia (capillary, cavernous haemangioma)
   - Colitis
     - Infective (bacteria – pseudomembranous colitis, virus – CMV colitis, parasites – amoebic colitis)
     - Inflammatory (i.e. UC, CD, Indeterminate IBD)
     - Chemical (i.e. NSAIDs use, Anti-angina drug (nicorandil))
     - Ischaemic: bleed occur at water-shed area (splenic flexure)
     - Radiation (rare)
   - Colonic Carcinoma / Post-polypectomy bleeding
   - Dieulafoy's Lesion (most common in stomach – 75%, duodenum – 14%, colon 5%)
   - Others: Colonic varices, Aortocolonic fistula, Vasculitis
2) Benign Anorectal disease: haemorrhoids, rectal varices, rectal ulcer
3) Anus: anal fissure

Small Bowel
4) Angiodysplasia
5) Ileum: Meckel's diverticulum – usually dark red blood
6) Others: enteritis/CD, Aortoduodenal fistula (patients with synthetic vascular graft), Jejunoileal diverticula, Neoplasms/Lymphoma

Upper GIT (proximal to ligament of Treitz)
7) Massive Upper GIT bleeding, e.g. bleeding D1 ulcer

HISTORY

1. Nature of bleeding

Bloody Diarrhoea (ddx)
- IBD
- Infective – i.e. amoeba TB, hookworm, Antibiotic Associated Colitis (C. difficile)

Haematochezia
- Definition: gross/fresh blood seen either on toilet paper after defecation or mixed with stools
- ddx: diverticulitis, angiodysplasia (AVM, common in old), haemorrhoids, massive upper GI bleed

Melena
- Definition: black tarry stools resulting from oxidation of hematin (altered blood) in the GIT (usually above ligament of Treitz)
- As for history as per UBGIT

It takes about 14 hours for blood to be broken down within the intestinal lumen; therefore if transit time is less than 14 hours the patient will have haematochezia, and if greater than 14 hours the patient will exhibit melena. One often-stated rule of thumb is that melena only occurs if the source of bleeding is above ligament of Treitz.

2. Aetiological Clues

Exclude Upper GIT caused	- Any melena, hematemesis, coffee ground vomitus - (see history for UBGIT)	
Diverticular Disease (diverticulosis)	- Painless Hematochezia (maroon or bright red) - Perforating artery adjacent to the colonic diverticulum may become attenuated and eventually erode → arterial bleed (bright red) – torrential bleeding that stops spontaneously - Not a/w melena or chronic blood loss	
Angiodysplasia	- Small AVM composed of clusters of dilated vessels in the mucosa and submucosal - Bleeding more commonly affect the right colon	
Colonic Neoplasm	- Rarely presents with massive blood loss but rather with chronic microcytic anemia and possible syncope - Rule out **red flags** → alternating constipation and diarrhoea, change in stool calibre (pencil-thin), tenesmus, constitutional symptoms (LOA, LOW) - Assess **risk factors** (see below) - Assess for any **metastatic complications** (see below)	
Colitis	Inflammatory	- (IBD) – more commonly due to ulcerative colitis (usually a/w diarrhoea mixed with blood and mucus) → ask about history of UC or Crohn's, joint, liver, eye & skin manifestations
	Radiation	
	Ischemic	- ask about CVS risk factors, previous AMI, stroke
	Infective	- any fever/chills/rigors, night sweats, N/V, diarrhoea, pain, - recent travel/contact history, eating seafood, - previous TB exposure or infection, BCG vaccination status
	Chemical	- NSAIDS, anti-angina drugs (nicorandil)
Haemorrhoids	- Blood coating stool (bleeding when passing motion) - Patient may note perianal mass ± painful (external haemorrhoids) or painless (internal haemorrhoids) - a/w constipation, recent pregnancy, low fibre diet, chronic straining	
Anal Fissure	- Patient with hx of constipation - a/w severe sharp pain occurring with staring on defecation - DRE a/w sharp pain	
Coagulopathy	- Known bleeding disorders (easy bleeding, petechial)	

3. **Complications**
   - Symptoms of dehydration & shock: extreme thirst, confusion, pallor, ↓ urine output
   - Symptomatic anemia → SOB on exertion, postural dizziness, syncope, chest pain, palpitation, lethargy/fatigue
   - Gauge percentage of blood loss
     - 15-30% → class 2 – Narrowed Pulse Pressure, Resting Tachycardia, Postural Hypotension
     - 30-40% → class 3 – Supine Hypotension, marked tachypnoea, confused, anxious
     - > 40% → class 4 – Minimal urine output, markedly depressed or lethargic
   - Patients with symptomatic anemia may have concomitant AMI → esp. if it's an old patient with previous history of IHD

4. **Comorbidities**
   - Makes patient more susceptible to hypoxemia → Elderly patient (>60), IHD, COPD
   - Predispose to fluid overload during resuscitation → IHD/CCF, CRF

PHYSICAL EXAMINATION

1. Vitals
   - Assess hemodynamic stability and postural BP
   - Urine output
   - Any Fever

2. Confirm LBGIT
   - DRE for fresh blood (haematochezia)

3. Determine Etiology
   - Any skin manifestation of IBD
   - DRE – any anal fissure, prolapsed haemorrhoids, any masses felt
   - Offer proctoscopy to look for internal haemorrhoids / any active bleed

4. Look for complications
   - Signs of Anemia
     - Face – (i) conjunctival pallor (ii) pallor of mucus membrane
     - Cardiac Auscultation – short systolic flow murmur at aortic area
     - Pulse – (i) tachycardia (ii) bounding (iii) collapsing pulse
     - Hands – pallor of palmar creases
   - Signs of dehydration – capillary refill time, dry tongue,

ACUTE MANAGEMENT (MASSIVE LOWER GIT BLEED)

- Defined: haemorrhage distal to the ligament of Treitz that requires ≥ 3 units of blood in 24 hrs
- Principle → resuscitation, identify site of bleed, treat accordingly

Resuscitation

- ABC – supplemental oxygen, insert 2 large-bore IV cannula with fast infusion of crystalloids (i.e. 1L N/S over 15min)
- Infuse colloids if on-going blood loss while waiting for whole blood (GXM)
- Catheterise and monitor urine output, insert NGT on suction to detect UBGIT
- Continuous vital signs monitoring & I/O charting ± CVP & stool chart
- ECG + cardiac enzymes to detect possible AMI
- Take blood for investigations
  - **FBC:** low Hb level (repeat FBC 2-3 hours later or when necessary) – packed cell transfusion → **4 pint PCT**: give FFP to prevent over-dilution of clotting factors
  - **U/E/Cr**: hydration status, any ARF from shock, electrolyte imbalance – replace
  - **PT/PTT:** must correct coagulopathy before trying to stop bleeding – fresh frozen plasma
  - **ABG:** ?metabolic acidosis in shock 2° organ ischemia – IV bicarb, dialysis if severe
  - **Lactate**
  - **GXM:** 4 pints

Identify source & stop bleeding

- Gastric Lavage via NG tube
  - Rule out upper GI source of bleeding
- Nuclear Scan (technetium-99m sulphur colloid)
  - Can identify bleeding sources with rates as low as 0.1-0.5ml/min
- Mesenteric Angiography or CT mesenteric angiogram

CT mesenteric angiogram	Mesenteric angiogram
Requires minimal bleeding rate (0.5ml/min) angiography optimally sensitive when bleed at 1ml/min → may consider raising BP before scan but be aware of risk of further bleed	
Diagnose: blush in active bleeding and ↓ perfusion in ischaemic bowel	
Non-invasive but have radiation	Invasive procedure (more precise, can cannulate all 3 main trunks and their branches), no radiation but have procedure related risks
require IV contrast (assess renal function)	require IV contrast (assess renal function)
No therapeutic indications	Allows either therapeutic vasopressin infusion or embolization → stop bleed in 85% of cases

- Colonoscopy
  - Frequently fails to identify source of massive lower GI bleeds
  - More useful in the setting of a stable patient, with slower bleeding and after administration of an adequate bowel preparation
  - Therapeutic advantage → inject vasoconstrictive agents (epinephrine) or applying thermal therapy (laser photocoagulation) to control bleeding
  - Diagnostic – able to identify cancer, diverticulosis, angiodysplasia, areas of inflammation and bleeding
- Laparotomy with saline lavage
  - For patients who continue to bleed with no source identified
  - On table angiogram
  - Oversewing of bleeding vessel, partial/total colectomy as last resort

COLORECTAL CARCINOMA

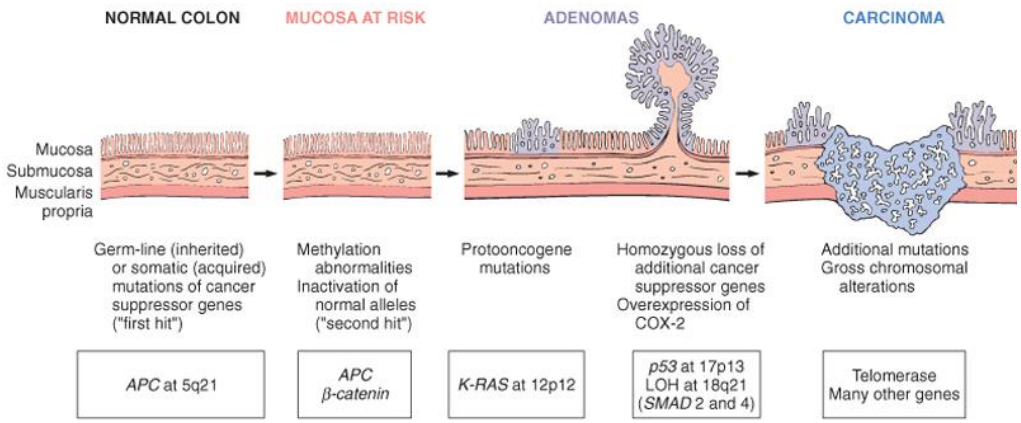
EPIDEMIOLOGY[58]

- Commonest cancer in Singapore men, number 2 cancer in Singapore women
- Ethnic: Colorectal Cancer more common among Chinese
- Gender: Colorectal Cancer more common in Males > Females
- ASR of Gastric Cancer: 42.7 / 100,000 in Chinese ♂ and 28.7 / 100,000 in Chinese ♀
- Peak incidence is between 60 to 70 (if found in a young patient, suspect familial syndrome (FAP, HNPCC) or pre-existing inflammatory bowel disease (UC, CD))
- Sporadic Cancer → 85% of colorectal neoplasia, Familial cancer syndromes → 15%

MOLECULAR PATHOGENESIS (2 PATHWAYS)

Hereditary Colorectal Carcinoma			
Molecular Pathway	Clinical Phenotype	Histopathology	Genetics
Chromosomal Instability	FAP	Innumerable Adenomatous Polyps, Moderately differentiated adenocarcinoma	Germline APC inactivation
Microsatellite Instability	HNPCC	Mucinous, Poorly Differentiated with Lymphocytic Infiltrates	Germline inactivation of MLH_1 or MSH_2 DNA repair genes

Sporadic Colorectal Carcinoma			
Molecular Pathway	Clinical Phenotype	Histopathology	Genetics
Chromosomal Instability	Left-sided predominant cancer	Tubular, tubulo-villous, and villous adenomas, Moderately differentiated adenocarcinomas	Somatic inactivation or mutation of multiple genes (APC/β-catenin, K-RAS, SMADS, p53)
Microsatellite Instability	Right-sided predominant cancer	No precursor lesions, Sessile serrated adenomas, Large hyperplastic polyps, Mucinous carcinomas	Somatic inactivation of MLH_1 or MSH_2 DNA repair genes



(1) APC pathway (adenoma-carcinoma sequence) or chromosomal instability pathway

- Accounts for **85%** of sporadic colorectal carcinomas
- Stepwise accumulation of mutations in a series of oncogenes and tumour suppressor genes:
  1. Loss of the **APC suppressor gene on 5q21** (congenitally absent in patients with familial adenomatous polyposis – APC) is the earliest event in adenoma formation
  2. With the loss of APC, **Beta-catenin accumulates** and activates the transcription of genes (**MYC and cyclin D1**) which promote cell proliferation (APC is required to break down beta-catenin)
  3. **K-RAS (12p12) mutation** follows the loss of APC – an activating mutation that causes the RAS to keep delivering mitotic signals and prevent apoptosis
  4. **Loss of tumour suppressor gene at 18q21 ($SMAD_2$ and $SMAD_4$)** → unrestrained cell growth
  5. **Loss of p53 (17p13)** (tumour suppressor gene) occurs late in carcinogenesis

- The molecular evolution of colon cancer through this pathway occurs through a series of morphologically identifiable stages: localised epithelial proliferation → small adenoma → large, more dysplastic adenoma → carcinoma in-situ → invasive cancer

(2) Defects in DNA mismatch repair or microsatellite instability

- Accounts for **15%** of sporadic colorectal carcinomas
- Like the APC pathway, there is accumulation of mutations, but due to a different mechanism, and without clearly identifiable morphologic correlates i.e. no adenomas
- Due to mutations in one of the five DNA repair genes (MSH_2, MSH6, MLH_1, PMS_1, PMS_2) – inherited mutations give rise to HNPCC
- MLH_1 are the most commonly involved in sporadic colorectal carcinomas
- Loss of DNA mismatch repair genes results in **microsatellite instability** which affects coding or promoter regions of genes involved in cell growth such as the **BAX gene** (promote apoptosis) and the **type II TGF-β receptor** (inhibits growth of colonic epithelial cells)
- Accumulated mutation in these growth regulating genes → emergence of colorectal carcinomas
- Tumours that arise from this pathway have a **better prognosis** than tumours that arise from the APC pathway

Feature	Chromosomal Instability	Microsatellite Instability
Genes Mutated	APC, K-RAS, $SMAD_2$, $SMAD_4$, p53, telomerase	MSH_2, MSH6, MLH_1, TGFβRII, BAX, BRAF
Associated Familial Syndrome	Familial Polyposis Coli	HNPCC
% of Sporadic Colorectal Cancer	85%	15%
Precursor Lesion	Tubular/villous adenoma	Sessile serrated adenoma
Colorectal Cancer Type	Typical adenocarcinoma	Mucinous adenocarcinoma (may have signet-ring cells)
Amount of DNA	Aneuploid or polyploid	Diploid
Typical Location	Left-sided	Right-sided
Degree of Differentiation	Highly Differentiated	Poorly Differentiated
Presence of Lymphocytic Infiltration	Little	Marked
Mucinous	Rarely Mucinous	Often Mucinous
Relative Prognosis	Worse Prognosis	Better Prognosis

[58] Trends in Cancer Incidence in Singapore 2008-2012 (data report are as of 7th June 2013)

DISTRIBUTION OF CRC

- Most common site of CRC: sigmoid colon (25%), rectum (21%), cecum (20%), recto-sigmoid junction (20%), transverse colon (15%), and ascending colon (10%)

SCREENING

- For everyone aged 50 years and above (screening improves survival)
- Why CRC is suitable for screening?
  - Prevalent and Lethal Disease
  - Precursor can be detected early (long asymptomatic period)
  - Early detection makes a difference (can institute treatment – i.e. polypectomy)
  - Safe, effective, cheap test available
- Screening Recommendation of colon and rectal cancers[59]
  - Start at 50yr and stop at 85yr

RISK GROUP	SCREENING TOOL	ONSET (Age)	FREQUENCY
A. Average risk Asymptomatic or family history limited to non-first degree relatives (screening tool alternatives in order of supporting evidence)	Faecal occult blood testing	50 years	Annually
	Colonoscopy	50 years	Every 10 years
	CT Colonography	50 years	Every 5 years
B. Increased risk			
1. Colorectal cancer in first degree relative age 60 years or younger or two or more first degree relatives	Colonoscopy	10 years prior to youngest case in the family or age 40 years, whichever is earlier	Every 5 years
2. Colorectal cancer in first degree relative over the age of 60 years	Colonoscopy	10 years prior to youngest case in the family or age 50 years, whichever is earlier	Every 10 years
3. Personal history of colorectal polyps	Colonoscopy	3 years after polypectomy in the presence of high risk features (>1 cm, multiple, villous architecture); otherwise, 5 years after polypectomy for low risk polyps	-
4. Personal history of colorectal malignancy	Colonoscopy	One year after resection	Every 3 years
5. Personal history of ovarian or endometrial cancer	Colonoscopy	One year after resection	-
C. High risk			
1. Family history of familial adenomatous polyposis	Flexible sigmoidoscopy (switch to colonoscopy if adenomas identified); consider genetic counselling and testing	10 to 12 years (from puberty)	Annually
2. Family history of hereditary non-polyposis colorectal cancer	Colonoscopy; consicer genetic counselling and testing	20-25 years	Every 1-2 years
3. Inflammatory bowel disease a. left-sided colitis b. pan-colitis	 Colonoscopy Colonoscopy	 From 15th year of diagnosis onwards From 8th year of diagnosis onwards	 Every 1-2 years Every 1-2 years

History of Polyps on prior colonoscopy

- If have small hyperplastic polyps: continue screening as average risk
- 1-2 tubular adenoma, low grade dysplasia: colonoscopy 5-10yr after polyp removal
- 3-10 adenoma OR large (1cm adenoma), high grade, villous: 3yr colonoscopy after polyp removal
- >10 adenoma: repeat colonoscopy within 3 years
- Sessile adenoma that are removed in pieces: colonoscopy 2-6 months after adenoma removal

[59] http://www.colorectalclinic.com/?id=28

RISK FACTORS[60]

		Increased Risk	Protective
Modifiable	Diet	- Red / Processed Meat (cooked at high temp) - Animal Fat - Alcohol	- Fruits and Vegetables - High Fibre Grain - Vitamin Supplements (i.e. folate)
	Lifestyle	- Smoking - Obesity	- Physical Activity
	Drugs		- HRT - Aspirin (? mechanism) - NSAIDs (? mechanism)

Non-modifiable	Age	- Males and females > 50 years old
	Ethnicity	- Chinese has a higher risk among the races in Singapore
	Family History[61]	- 1 first-degree relative with CRC → RR 2.3x - > 1 first-degree relative with CRC → RR 4.3x - 1 first-degree relative diagnosed with CRC before age 45 years → RR 3.9x - 1 first-degree relative with colorectal adenoma → RR 2.0x *important to ask for: age at diagnosis!
	Hereditary CRC Syndromes[62]	- FAP (90% by age 45), attenuated FAP (69% by age 80) - Lynch Syndrome (40-80% by age 75) - PJS (39% by age 70), JPS (17-68% by age 60) - Other: Cowden Syndrome, Cronkhite-Canada have a small increased malignant potential
	Familial Cancer Syndromes (HNPCC)	- Diagnosed with **Amsterdam Criteria** aka. 3-2-1 rule a. At least 3 relatives with histologically confirmed colorectal cancer* (1 of whom is a first degree relative of the other 2) – FAP excluded b. At least 2 successive generation involved c. At least 1 of the cancer diagnosed before age of 50 *These criteria were found to be too strict and were expanded to include the associated non-colorectal cancers (cancer of the endometrium, small intestine, ureter or renal pelvis); in 1998. These were called the Amsterdam II clinical criteria for families with Lynch syndrome (wiki)
	Personal History	- Inflammatory Bowel Syndrome (i.e. Ulcerative Colitis (UC) of more than 10 years duration, or Crohn's Disease) - Past history of colorectal polyp or colorectal cancer (potential for metachronous colorectal cancer / adenomas) - Increased risk if have history of large (> 1cm) adenomatous polyps, and polyps with tubulovillous or villous histology, particularly if multiple

[60] http://www.singaporecancersociety.org.sg/lac-fcco-risk-factors.shtml
[61] Am J Gastroenterol 96 (10): 2992-3003, 2001.
[62] http://www.cancer.gov/cancertopics/pdq/genetics/colorectal/HealthProfessional/Page3#Section_120

HISTORY

(Assuming patient comes in for LBGIT and diagnosis is unknown)

1. Note down Patient's Biodata – Age, Ethnicity, Gender
2. Ask about symptomatology (clinical manifestation)
   - Any **abdominal pain** (most common ~44%)
   - Any **bleed (haematochezia / melena)** – quantify bleeding
   - Any **symptomatic anemia** (especially chest pain in the elderly patients)
   - Any **changes in bowel habits** – in particular rule out these **red flags**
     - Alternating constipation and diarrhoea
     - Spurious diarrhoea* (secondary to obstruction and bacterial degradation)
     - Diminished stool calibre (pencil thin stool)
     - Tenesmus (feeling of incomplete defecation, frequently painful)
3. Ask about risk factors (modifiable and non-modifiable)
   - Significant past medical, surgical, hospitalization History
   - Past colonoscopy and/or FOBT
   - Drug history & drug allergies
   - Significant family history
   - Social history
4. Ask about complications suggestive of invasive / metastatic disease
   - Complications
     - **Perforation** → symptoms of peritonism (rigid guarding, rebound)
     - **Intestinal Obstruction** → abdominal distension, abdominal pain, vomiting, obstipation
     - **Fistula Formation** → fecaluria, pneumaturia, recurrent UTI (recto-bladder fistula), recto-vagina fistula
     - **Local Invasion** → Invasion of sacral nerves (intractable pain), invasion of trigone of bladder (LUTS), invasion of ureter (hydroureter/hydronephrosis), peritoneal involvement (p/w ascites)
     - **Symptoms of infection** → abscesses, peritonitis
   - Metastatic Symptoms
     - Liver – RHC discomfort, jaundice
     - Bone – bone pain, fractures
     - Lungs – SOB (pleura effusion most common), decrease ET, orthopnoea
     - Brain – LL weakness, morning headache, AMS
   - Constitutional Symptoms – LOW, LOA, malaise
5. Systemic Review – consider other differential diagnosis!

*due to obstruction leading to increased peristalsis and intestinal secretion above the level of the obstruction and secondly due to stasis, faecal material above obstruction undergoes degradation by bacterial and liquefaction → passage of this liquefied stools periodically

SPREAD

1. Intramural – along bowel wall or Intraluminal
2. Direct extension into surrounding tissues – small bowel, ovary
3. Lymphatic – follow arterial supply
4. Haematogenous – to liver, lungs
5. Transcoelomic – i.e. peritoneal carcinomatosis

(assuming patient is a known colorectal cancer patient)

1. How was **cancer detected** (asymptomatic vs. symptomatic)

- Was tumour detected on routine screening colonoscopy
- For symptomatic patients – primary symptoms at diagnosis – which anatomical side is more likely
  - Abdominal pain can occur at any anatomical site – caused by partial obstruction, peritoneal dissemination or perforation leading to generalized peritonitis

Right Sided (colonic tumour)	- Anemia symptoms (iron deficiency anemia) – usually occult bleeding (4x higher mean daily blood loss than tumour on the left side) - May present with right sided abdominal mass - Not as common to have change in bowel habits or obstructive symptoms (stools more liquid and colon more spacious on the right)
Left sided (colonic tumour)	- Change in bowel habits - Hematochezia - Symptoms of Intestinal Obstruction (partial vs. complete)
Left Sided (rectal tumour)	- Tenesmus = constant intense desire to defecate, feeling of incomplete defecation may be painful (i.e. rectal pain) – when defecating, nothing/ small amount of mucus and loose faeces due to SOL in lumen/wall of rectum - Mucoid stools (suggests polypoidal masses) - Hematochezia - Diminished stool calibre (pencil-thin stools) - Change in bowel habits - Symptoms of Intestinal Obstruction (partial vs. complete)

2. **Severity / Complications** – determine stage of the cancer
   - Complications – mainly bleed, burrow (fistula, local invasion), burst (perforation – localized or generalised), block (IO, compression on ureter), bacterial (infection – abscess, peritonitis)
   - Metastatic Symptoms
   - Constitutional Symptoms
3. **Treatment** – i.e. surgery (for cancer and/or for complications), CT, RT, stoma creation
4. **Treatment complications** – i.e. complications of CT, **recurrence of disease**

5. Recognition of an individual with **inherited colon cancer syndrome** (see FAP and HNPCC)
   - Diagnosed under the age of 45
   - Adenomas >2cm diagnosed under the age of 40
   - Multiple colonic malignancies – either synchronous* or metachronous*
   - Multiple primary cancers – either colonic or extracolonic
   - ≥ 10 adenomas present over a lifetime in addition to a family history of colon cancer
   - Multiple closely related family members who have been diagnosed with colon cancer
   - Colon cancer in more than 1 generation
   - Clustering of extracolonic cancers in family members (i.e. gastric, breast, thyroid, uterine)

*Synchronous: tumours are detected simultaneously (within 6 months of initial CRC) – 3 to 5% of patients
*Metachronous: non-anastomotic new tumours (after 6 months of initial CRC) – 1.5 to 3% of patients in 1st 3-5yrs

PHYSICAL EXAM

1. Vital Signs – Temperature, Blood Pressure, Pulse Rate, RR, Pain Score
2. General Appearance
   a. any signs of altered mental state – alert, orientated to TPP
   b. any signs of poor nutritional status – cachexia
   c. any signs of anemia – nail bed pallor, palmar crease pallor, conjunctival pallor
   d. any signs of jaundice – sclera icterus, jaundice
3. Abdominal Examination (remember to check hernia orifice)
   a. any previous scars – check for incisional hernia
   b. any organomegaly (enlarged liver, irregular surface)
   c. any tenderness, any masses, abdominal distension
   d. any signs suggestive of IO – tinkling bowel sounds
   e. any supraclavicular LN enlargement (virchow's node)
   f. any inguinal LN enlargement (very low rectal tumours, near dentate line have risk of spread to inguinal LN)
4. AE → Digital Rectal Examination
   a. hard, non-tender, polypoidal, irregular, mobile, fixed
   b. contact bleeding
   c. distance from anal verge >7cm (internal anal sphincter)
   d. location – more worrying if tumour is located anteriorly
   e. muscle tone – guides management
   f. mucoid stools (polypoidal mass)
5. Lung Examination – any pleura effusion, consolidation
6. Cardiac Examination – any signs of anemia
7. Any bony tenderness

**Carcinoembryonic antigen level (CEA) – (normal range: 0-2.5mcg/L, in smokers: 0-5mcg/L)

- A oncofetal protein, lacks both sensitivity and specificity
- CEA is a useful prognostic and surveillance tumour marker in colorectal cancer (in patients with established disease absolute level of serum CEA correlates with disease burden)
- Measured pre-operatively as a baseline level – if the CEA is raised pre-op and falls to within normal range post-op, it is likely tumour has been totally removed.
- Usually, normal values 6wks post-op
- Follow-up after surgery with CEA testing (high = likely recurrence, normal = does not r/o disease recurrence) – 30-40% of all CRC recurrence not a/w elevated CEA

- False positive raised CEA: **smoking**, adjuvant therapy with 5-FU, **inflammatory** states (i.e. pancreatitis, diverticulitis, cholecystitis etc.) and **cancers** (i.e. stomach, lung, breast, pancreas, cervix, bladder, kidney etc.)

INVESTIGATIONS

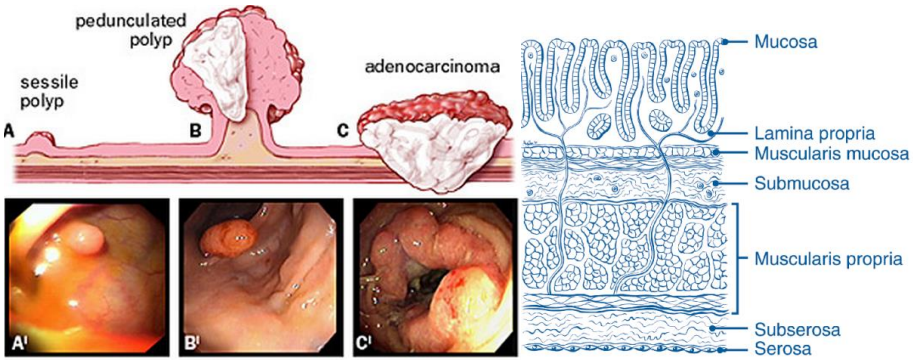
- Once the diagnosis is suspected based on history, PE or screening test, every attempts should be made to obtain biopsy of the primary lesion and rule out synchronous cancer (3% to 5%)
- In the acute setting (where patient may be symptomatic) → Resuscitate + do FBC first to assess Hb level

Establish the Diagnosis	Colonoscopy (diagnosticate and therapeutic)	- Ensure good bowel preparation - Allow direct visualization (site, size, location) - Enables biopsies of suspicious lesions for histological diagnosis - Enables detection of synchronous lesions (synchronous polyps in 30%, synchronous cancer in 3 to 5%) - Allow for therapeutic procedures (i.e. polypectomy, stenting of obstructed colon)
	Other investigative tools: - Double contrast barium & air enema (need to insert rigid sigmoidoscopy 10-15cm to instil air and contrast, limited diagnostic value, may miss small lesions and distal lesions) → classically see apple core lesion with barium enema (see below) - CT colonography aka. virtual colonoscopy → next best to colonoscopy, needs IV contrast, air and contrast enema, detect tumour that are ≥ 1cm	
Staging Investigations (for local and systemic staging)	EUS (trans-rectal u/s for rectal tumour)	- Superior to CT in delineating depth of tumour invasion – locally advanced rectal CA (≥T3) requires neoadjuvant chemoRT - Can also assess local lymph node status
	MRI Rectum (for rectal cancer)	- Superior to CT for delineating fat planes in T staging - Circumferential resection margin (CRM) refers to the fascia propria - High risk tumours for recurrence: CRM < 2mm, T3/4 (+/- bulky T2) → Neoadjuvant ChemoRT
	Computer Tomography (Thorax, Abdominal, Pelvis, Brain)	- Local T Staging and invasion into bladder, ureter, uterus, duodenum (esp. for right sided colonic tumours) - Staging of regional lymph node mets - Lungs: lung mets (alternatively can do CXR) - Abdominal/Pelvis: Assess for haematogenous spread to distant organ (i.e. most commonly liver mets) ▪ detect metastatic disease in the form of peritoneal seeding, omental kinking, malignant ascites, hydroureter, hydronephrosis, IO (i.e. carcinomatosis peritonei) - CT Brain if symptomatic
	Bone Scan	- If symptomatic (more for breast, lung, prostate, thyroid cancers)
	Positron emission tomography with CT (PET-CT)	- Combines spatial resolution of CT with contrast resolution of PET - Superior to CT scan alone
Supportive Investigation to assess for complications	FBC (± Fe study)	- Assess Hb levels (assess for iron-deficiency anemia)
	U/E/Cr	- Biochemical abnormalities a/w 3rd space losses (intraluminal) or vomiting (i.e. in IO) - Cr may be ↑ (pre-renal failure) → risk of contrast nephropathy - Hypokalemia – ?villous adenoma (hypersecretory syndrome)
	LFT	- Albumin as a marker of nutritional status (< 35 is poor) - Liver Mets (ALP first to be raised)
	Erect and Supine AXR	- look for intestinal obstruction (usually large bowel closed loop obstruction) and caecal distension; near perforation
	Erect CXR	- in perforated tumour to detect air under diaphragm
Preoperative Investigations	CEA**	
	ECG / CXR	
	GXM / PT/PTT	

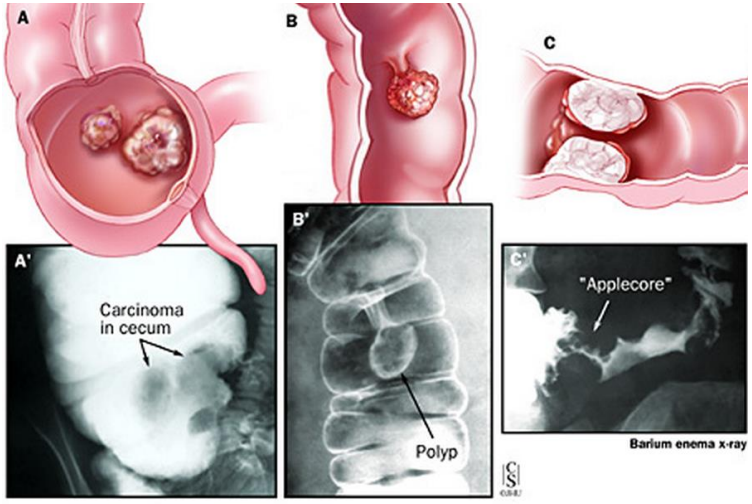
Colonoscopy: Bowel Preparation for Colonoscopy[63]

Medication	- Stop Fe-tablets (≥ 5 day prior) - ± stop anticoagulants (depends on indication and VTE risk) - adjust metformin / insulin as indicated - NSAIDs & Aspirin can be continued safety
Diet	- Low residual diet 2-5 days prior → then clear liquids 1 day prior → then NBM 6-8hr prior
Preparation*	- Full-volume (4L) PEG or Low-volume (2L) PEG + Bisacodyl - Split-dose preparation (preferred to full-evening dose) ▪ 6PM → 250ml PEG Q15min to finish 2L PEG (bowel o/p start by 1st hour post-PEG) ▪ 6AM → 250ml PEG Q15min to finish 2L PEG (bowel o/p should be clear and watery)
Adjunct	- Metoclopramide (given with PEG)

* Other preparations: magnesium citrate (2.5L – hyper-osmotic) – avoid in heart failure, renal impairment, decompensated cirrhosis



Double Contrast Barium & Air Enema



[63] uptodate: Bowel preparation for colonoscopy and flexible sigmoidoscopy in adults

American Joint Committee on Cancer

Colon and Rectum Cancer Staging

7th EDITION

ANATOMIC STAGE/PROGNOSTIC GROUPS

Stage	T	N	M	Dukes*	MAC*
0	Tis	N0	M0	–	–
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1–T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3–T4a	N1/N1c	M0	C	C2
	T2–T3	N2a	M0	C	C1/C2
	T1–T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3–T4a	N2b	M0	C	C2
	T4b	N1–N2	M0	C	C3
IVA	Any T	Any N	M1a	–	–
IVB	Any T	Any N	M1b	–	–

NOTE: cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pretreatment (for example, ypTNM). Patients who have a complete pathologic response are ypT0N0cM0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).
* Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (any TN1 M0 and Any T N2 M0). MAC is the modified Astler-Coller classification.

Primary Tumor (T)

- **TX** Primary tumor cannot be assessed
- **T0** No evidence of primary tumor
- **Tis** Carcinoma in situ: intraepithelial or invasion of lamina propria[1]
- **T1** Tumor invades submucosa
- **T2** Tumor invades muscularis propria
- **T3** Tumor invades through the muscularis propria into pericolorectal tissues
- **T4a** Tumor penetrates to the surface of the visceral peritoneum[2]
- **T4b** Tumor directly invades or is adherent to other organs or structures[2,3]

Regional Lymph Nodes (N)[4]

- **NX** Regional lymph nodes cannot be assessed
- **N0** No regional lymph node metastasis
- **N1** Metastasis in 1–3 regional lymph nodes
- **N1a** Metastasis in one regional lymph node
- **N1b** Metastasis in 2–3 regional lymph nodes
- **N1c** Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
- **N2** Metastasis in 4 or more regional lymph nodes
- **N2a** Metastasis in 4–6 regional lymph nodes
- **N2b** Metastasis in 7 or more regional lymph nodes

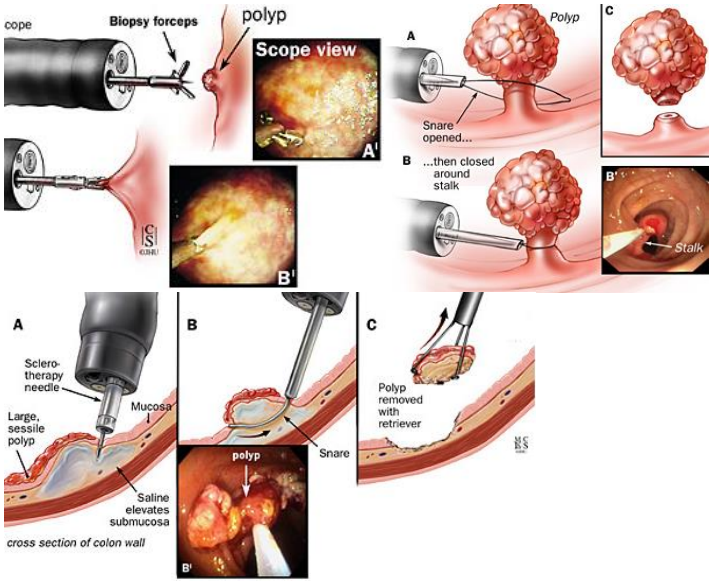
Distant Metastasis (M)

- **M0** No distant metastasis
- **M1** Distant metastasis
- **M1a** Metastasis confined to one organ or site (for example, liver, lung, ovary, nonregional node)
- **M1b** Metastases in more than one organ/site or the peritoneum

TREATMENT (CURATIVE)

Pre-operative measures
- Decision for surgery discussed and confirmed during multi-disciplinary tumour board meeting – (involves medical oncologist, pathologist, radiologist and surgeon)
- Pre-operative investigations (i.e. CEA, CXR, ECG, PT/PTT, GXM) + anaesthesia referral
- Bowel preparation
  - Modification of diet – 3 days low residue diet (reduce frequency and volume of stools – low fibre, reduce food that increase bowel activity), and one day clear feeds
  - NBM from 12mn (on day of op)
  - Bowel prep (polyethylene glycol – 2L PEG) – contraindicated in GI obstruction, perforation
- Stoma site discussion with stoma care nursing specialist
- Prophylactic intravenous antibiotics (max at first incision)
  - IV ceftriaxone and metronidazole within 1 hour of skin incision
- DVT Prophylaxis
  - Prophylactic Subcutaneous Heparin
  - Anti-embolus stockings are fitted

Endoscopic Therapy (colonoscopy)
- Polyps → removed with biopsy forceps, snare resection (pedunculated polyps) or saline injection to submucosal to elevate polyp then removal by snare resection (sessile polyps)
- Post-polypectomy → (for polyps larger than 1cm or for multiple polyps) → f/u colonoscopies should be performed every year, patient with small (<1 cm) tubular adenoma do not have an appreciable increased risk of colorectal cancer
-



Principles of surgery for <u>colonic</u> carcinomas

1. Remove the cancer completely with clear margins
2. Resect adjacent draining lymph nodes
3. Avoid excessive disruption or spillage of tumour cells
4. Reconstruct the bowel, if possible, in order to achieve intestinal continuity and normal or near normal bowel function post-operatively.

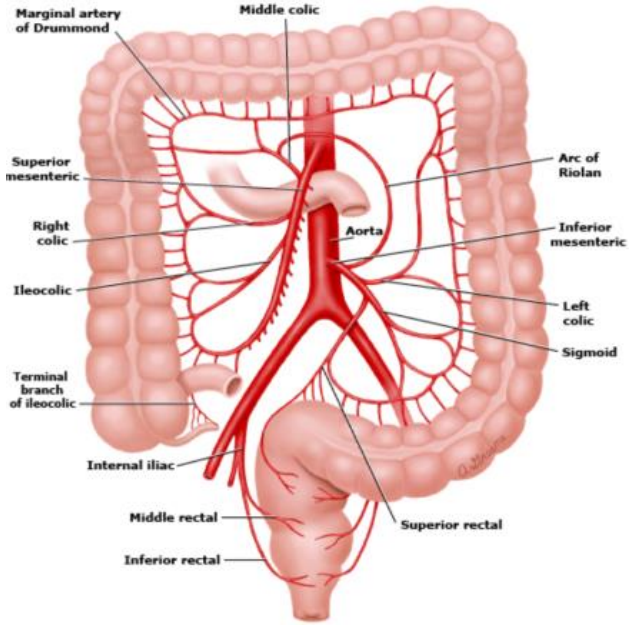
- <u>Exploration with palpation of the liver and inspection of pelvic peritoneum</u>
- <u>Mobilization of the involved segment (i.e. splenic flexure)</u>
- <u>Main segmental vessels are ligated & divided (i.e. high tie at the IMA for oncological clearance)</u>
- <u>En-bloc resection of tumour with adequate margins</u>
  - For colonic tumours, a margin of <u>5 cm proximally and distally is adequate</u>
  - While segmental resection is sufficient for primary tumour removal, a wider resection is often required to achieve sufficient lymphadenectomy
  - Adequate clearance of the draining lymphatics involves excision of the vascular arcades supplying the segment of involved colon back to their origin (from the SMA or IMA) as <u>lymphatics follow the arteries</u> generally

- <u>Obstructed left sided carcinoma</u>
  - No difference shown for doing a staged procedure (i.e. tumour removed with proximal end of colon brought out as a colostomy) as compared to creating a primary anastomosis
  - On-table bowel decompression (irrigation) for clearance of faecal material
  - Segmental colectomy for the tumour with intraoperative decompression is comparable to subtotal/total colectomy without decompression with regard to bowel function and rates of complication

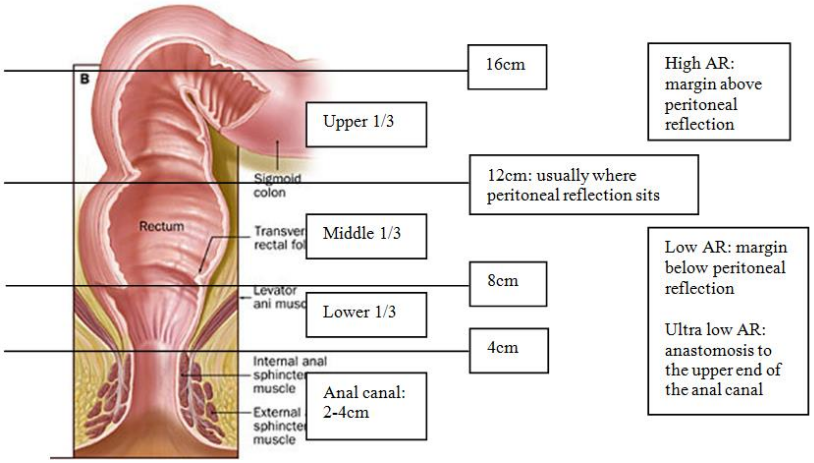
<u>Arterial supply (Colon & Rectum)</u>
- **Superior Mesenteric Artery** (L_1): Ileo-colic, Right colic and Middle colic
- **Inferior Mesenteric Artery** (L_3): Left colic, Sigmoid, Superior rectal
- **Internal Iliac Artery** (L_4): Middle and Inferior rectal

- **Marginal Artery of Drummond**: a continuous vessel running along the inner perimeter of the large intestine in the mesentery as part of the vascular arcade that connects the SMA and IMA, from the ileocolic junction to the rectum.

- **Arc of Riolan:** connects middle colic of SMA with left colic of IMA, runs close to the root of the mesentery (can be absent as an anatomical variant)



Principles of surgery for <u>rectal</u> carcinomas



Differences between rectal cancer and colon cancer

1. Confinement of pelvis and sphincter making wide excision impossible
2. Proximity to urogenital structures and nerves → cx: impotency in males
3. Dual blood supply (superior rectal artery – from IMA, middle and inferior rectal artery from internal iliac artery) and lymphatic drainage
4. Trans anal accessibility → rectum is defined as within 12cm from anal verge

<u>Rectum</u>

- Measures 12cm long, commencing anterior to the 3rd segment of the sacrum and ending 2.5cm in-front of the coccyx where it bends sharply backwards to become the anal canal
  - Upper 1/3 = covered by peritoneum on its front and side
  - Middle 1/3 = covered by peritoneum only on its anterior aspect
  - Lower 1/3 = completely extra-peritoneal, lying below pelvic peritoneum
- Contains 3 lateral inflexions projected to the left, right and left again from above downwards (each inflexion capped by a valve of Houston)

<u>Anal Canal</u>

- Measures 4cm long and passes downwards and backwards
- Surrounded by complex arrangement of sphincter (both smooth and striated muscle)
- The **<u>dentate line</u>** (pectinate line) divides the upper 2/3 and lower 1/3 of the anal canal

Distinction	Above Dentate Line	Below Dentate Line
Embryology	Endoderm	Ectoderm
Epithelium	Columnar Epithelium (adenocarcinoma)	Stratified Squamous Epithelium (SCC)
Nerves	Autonomic NS (inferior hypogastric plexus)	Somatic Innervation (inferior rectal nerve)
Venous Drainage	Portal Venous System (via superior rectal vein)	Systemic Venous System (via middle and inferior rectal vein)
Lymph Node Drainage	Abdominal Nodes (i.e. internal iliac, inferior mesenteric LN)	Superficial Inguinal Lymph Node

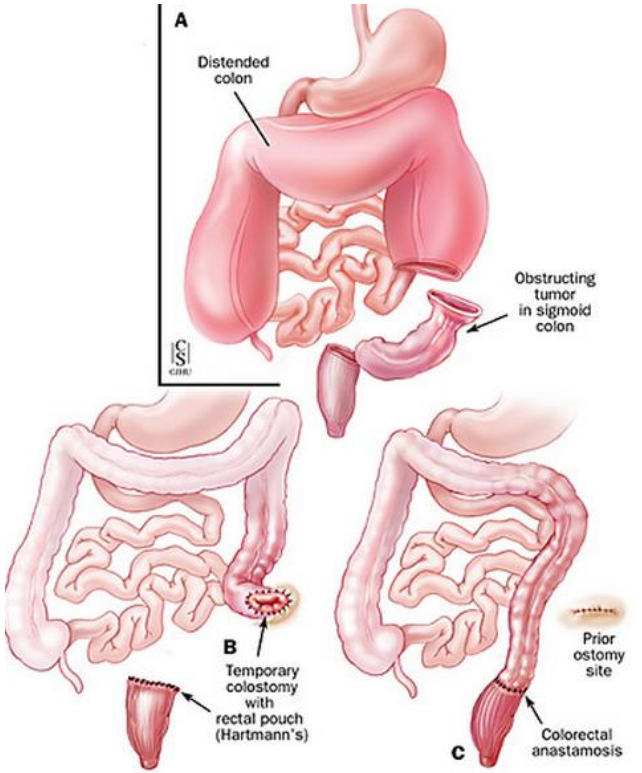
<u>Type of Surgery</u>

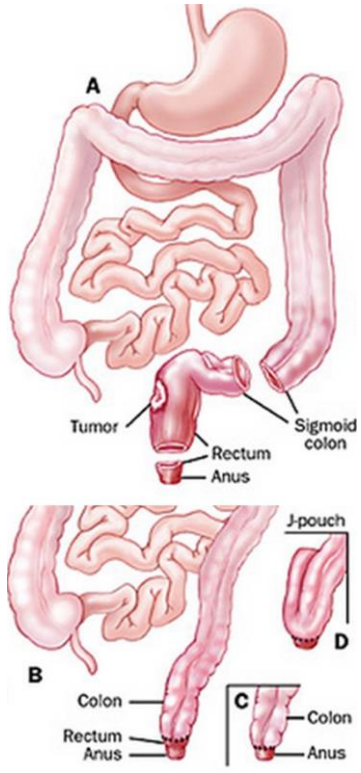
1. Local excision (only for small tumours)
2. Restorative anterior or low/ultra-low anterior resection (AR) ± temporary colostomy (Hartmann's) / diverting ileostomy
3. Abdominoperineal Resection (APR) with permanent colostomy

<u>Low Anterior Resection ± Hartmann's</u>

- Suitable for lesions located in the upper 2/3 of the rectum
- Anterior Resection → anterior approach to surgically resect the recto-sigmoid colon with a primary anastomosis between descending colon and rectum
- Hartmann's operation → surgical resection of the (i.e. recto-sigmoid colon) with closure of the rectal stump and formation of a temporary end colostomy (it is used when immediate anastomosis is not possible) – see below

- Colorectal anastomosis or coloanal reconstructions are alternatives to permanent colostomy. Construction of a colon J-pouch creates a neo-rectal reservoir that can reduce frequency and urgency of bowel movements and nocturnal bowel movements in selected cases – see below

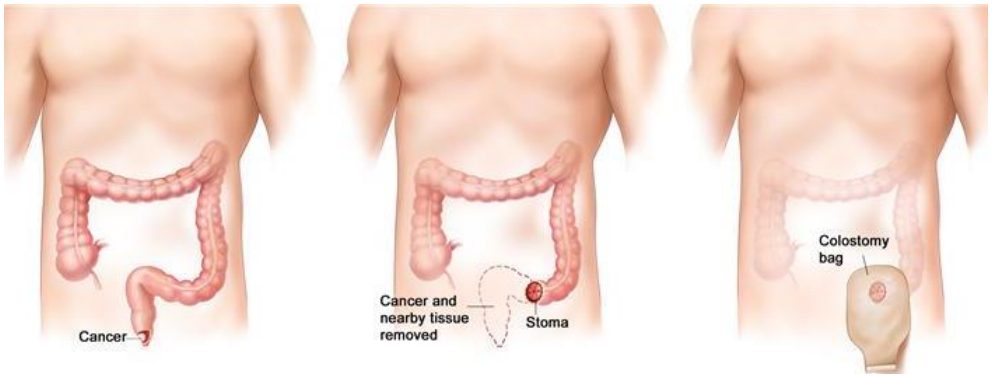




Abdominoperineal Resection (APR) with permanent end colostomy

- Operation where a diseased rectum and anus are removed leaving the patient with a scar where the anus used to be and a permanent end colostomy on the tummy with a bag for collection of faecal material → operation involves 2 steps (1) abdomen incision and (2) perineum incision

- **Indication** → rectal tumour sited in the distal 1/3 of the rectum – within 5cm of anal verge
- Involves removal of the anus, the rectum and part of the sigmoid colon along with associated regional lymph nodes through incision made in the abdomen and perineum
- APR generally results in a worse quality of life as compared to lower anterior resections (LAR)



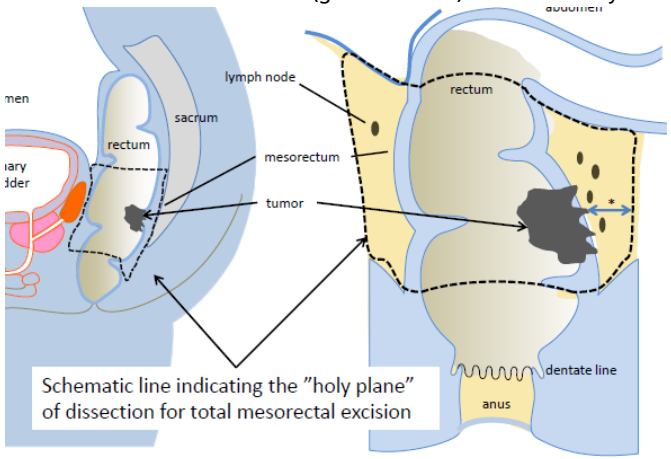
Operative Technique

- High ligation of the IMA at the aorta (careful attention to preserve gonadal vessels and ureter)
- Transection of colon at the descending / sigmoid junction

- En-bloc resection with adequate margins
  - For rectal tumours a margin of 5 cm proximally and 2 cm distally is adequate (as it has been found that lymphatic spread of rectal tumours is predominantly in the proximal direction)
  - Radial margins are also important as there is a zone of downward spread within the meso-rectum (peritoneal investment of the upper rectum; just anterior to the sacrum)
- Type of Surgery (sphincter-sparing versus loss of sphincter)
  - The anal sphincter can be spared if the distal margin is >1-2cm above the level of the sphincter complex, usually taken to be at the level of the dentate line (which is 5cm above the anal verge) i.e. distal margin of the tumour must be >7cm from the anal verge
  - Sphincter-sparing → low anterior resection (below the peritoneal reflection); ultra-low AR if just above the anal sphincter*
  - Sphincter-sacrificing surgery → abdominoperineal resection (APR) (entire anus and sphincter complex is dissected, with creation of a permanent end colostomy)
  - **Before consideration of either surgery – ask patient of any history of faecal incontinence**

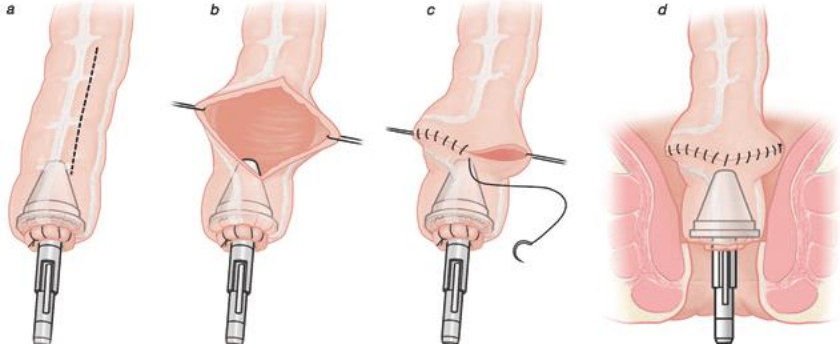
* for ultra-low AR, surgery tends to be performed with a diverting ileostomy as risk of coloanal anastomotic breakdown is high

- Total Mesorectal Excision (TME)
  - Presence of radial spread is an important prognostic indicator
  - TME is indicated as part of low anterior resection for patients with adenocarcinoma of the middle and lower rectum (gold standard) → dramatically reduce local recurrence rates[64]



[64] Recent Results Cancer Res. 2005;165:112-9.

- Reconstruction (anastomosis)
  - Perform an anastomosis only if there is good blood supply (note: dilated LB proximal to obstruction may be oedematous and hence not suitable for anastomosis)
  - Formation of a straight coloanal anastomosis in anterior resections is associated with poor function due to the lack of reservoir function
  - Creation of a colonic J-pouch using the proximal end of colon (the end of the colon is folded back on itself to form a J, and the two limbs opened and stitched together to form a pouch, the apex of the J being anastomosed to the anus) is associated with improved post-operative function (see above)
  - Coloplasty is another alternative that is equivalent to colonic J-pouch (the distal colon is cut longitudinally but sewn transversely, widening the diameter at that segment to form a small pouch), done when there is difficulty creating the colonic J-pouch (see below)



- Extended resections
  - For locally advanced, adherent tumours (T4), multivisceral resection of organs involved (pelvic exenteration) is associated with improved local control and overall survival compared with standard resection, though high morbidity of 25-50% is associated
  - Consider neoadjuvant chemoradiotherapy prior to surgery to downstage disease

- Stoma creation
  - A de-functioning loop ileostomy (or loop colostomy) is usually created during a low / ultra-low AR as the manipulation of the colon deep within the pelvic cavity causes increased risk of an anastomotic leak & also poorer blood supply to anastomosis
  - A de-functioning stoma does not protect against anastomotic leak, but mitigates against disastrous complications of faecal peritonitis should a leak occur
  - Closed in 2-6/12 after check with gastrografin (medical imaging) reveals no leak

- Neoadjuvant chemo-radiotherapy for rectal tumours
  - Neoadjuvant RT with 5-fluorouracil can downstage tumour significantly → ability to preserve sphincter, field sterilisation, facilitate surgical resection of tumour, reduce local recurrence (compared to RT alone), don't require post-op RT on normal healthy tissue
  - Reserved for patients with large, bulky tumours (**i.e. tumour where circumferential resection margin (CRM) reaches the fascia propria**) or evidence of nodal metastases (stage 2/3, especially T4 lesions) in mid and low rectal surgery
  - Not possible for colon carcinomas due to risk of small bowel radiation if given above peritoneal reflection

- Surgical treatment according to stage

	Stage of disease	Treatment
T1	Involvement of submucosa, but no penetration through muscularis propria	Local excision (AR or APR)
T2	Invasion into, but not penetration through, muscularis propria	a) Local excision + adjuvant Chemo/RT OR b) radical resection
T3	Penetration through muscularis propria into subserosa (if present), or pericolic fat, but not into peritoneal cavity or other organs	Neoadjuvant chemo / RT before radical resection
T4	Invasion of other organs or involvement of free peritoneal cavity	

Operative complications[65]

Immediate (<24h)	Damage to other organs e.g. ureters, spleen Ureter can occur during: 1) High ligation of the IMA 2) Mobilization of the upper meso-rectum at the level of the sacral promontory 3) During deepest portion of the pelvic phase of proctectomy 4) During the deepest portion of the perineal phase of an APR
Early (<30 days)	**Anastomosis Leakage*** → between post-op D4-7 → if free leaks → risk of diffuse faecal peritonitis and septic shock or if contained leaks → may present later as an abscess or enterocutaneous fistula **Wound infection**** → occur in 5-15% of patients **Bleeding** → pelvic bleeding **Early stoma complications** *small bowel and ileocolic anastomosis have lowest reported leak rates (1-3%) and highest rate are for coloanal anastomoses (10-20%) **Risk Factors: malnutrition, DM, immunosuppression, >60 years, ASA >2, faecal contamination, extensive surgery, length of pre-operative hospitalization
Late (>30 days)	Impotence (damage of pelvic nerves) → occur in 15-50% of males (discussed pre-operatively) Adhesions (I/O) Anastomotic stricture Diarrhoea Late stoma complications Anterior Resection Syndrome → urgency, faecal incontinence, increased bowel frequency, evacuation dysfunction (worsen patient's QOL) Tumour Recurrence

[65] http://www.fascrs.org/physicians/education/core_subjects/2011/Complications/

Surgery of liver metastases from colorectal cancer: new promises[66]

- Benefits of surgical resection and systemic chemotherapy have been established with a 5 year survival approaching 40%
- Shrinkage of tumours after administration of pre-operative chemotherapy and the availability of ablative techniques now allow the treatment, with curative intent, of metastases initially considered as non-resectable
- Selection of patient (with liver mets) for surgery → (1) able to perform surgery leaving no macroscopic residual liver disease and (2) patient able to tolerate hepatic resection
  - ♦ Ideal Candidates: < 4 lesions each < 5cm in size, without extrahepatic disease
- Goals of surgery → remove all metastatic sites with a margin of 1cm

Palliative therapy

- 5-FU in combination with folinic acid is first-line therapy
- Alternatives for first-line therapy: Raltitrexed when 5-FU is not tolerated; capecitabine or UFT (uracil combined with tegafur) plus folinic acid

Surgery for palliation

- Resection of 1° for palliation of symptoms such as bleeding, perforation, obstruction or pain
- Resection of asymptomatic primary is controversial, but may confer survival benefit in a select group of patients where metastatic tumour burden is restricted to one side? and liver involvement is not extensive

Surgery for recurrence / metachronous lesions

- Anastomotic recurrence occur in 2 to 4% of patients with colon cancer, higher for rectal cancer (80% of anastomotic recurrence detected within 2.5yr from primary resection)[67]
- Loco-regional recurrence, if detected early with adequate resection, can confer survival benefit

[66] Br Med Bull (2002) 64 (1): 127-140.
[67] uptodate: Surveillance after colorectal cancer resection

Radiotherapy

- Role as neoadjuvant therapy in rectal cancer to downstage tumour – benefits: see above
  - Pre-op RT with TME = reduced local recurrence rates (compared to TME alone)[68]
- Post-op adjuvant therapy in stg II or III rectal CA – not needed if RT used as neoadjuvant therapy

Chemotherapy

Adjuvant therapy (to eradicate micrometastases, reduce likelihood of recurrence)

- Colon cancer:
  - Stage II = controversial
  - Stage III (node positive) = initiate chemotherapy within 6-8 weeks of surgery,
    - 6 month course of oxaliplatin based regimen – FOLFOX[69] (oxaliplatin + leucovorin (LV) and short-term infusion 5-FU)
    - 30% risk reduction in recurrence and 22-32% reduction in mortality
    - For patients CI to oxaliplain (i.e. pre-existing neuropathy) 5-FU/LV is acceptable option
    - Alternative is 6 months of oral capecitabine

- Rectal cancer:
  - Stage 1 = no adjuvant therapy needed
  - Stage 2 & 3 (even with TME performed) = combined chemo and radiotherapy[70]
    - fluoropyrimidine as a radiation sensitizer during postoperative RT
    - Infusional 5-FU
    - 2 months of chemotherapy followed by 6 weeks of concomitant fluoropyrimidine based chemoradiotherapy followed by 2 months of chemotherapy

FOLLOW UP[71]

- Follow-up visits (history and physical exam) 3-monthly for the first 2 years, then 6-monthly for the next three years, and subsequently yearly, measure CEA at each visit
- Yearly colonoscopy ← identify metachronous CRC
- CXR and liver ultrasound to detect metastases (recommended frequency not known)

PROGNOSIS – FROM 7TH EDITION AJCC STAGING MANUAL

Stage	5 year observed survival rates – colonic cancer	
I	74%	82% (2008 – 2012 – Singapore's Data)
II	A – 67%, B – 59%, C – 37%	70%
III	A – 73%*, B – 46%, C – 28%	52%
IV	6%	9%

* survival was better for some stage III cancers than some stage II cancers, the reasons for this is not clear

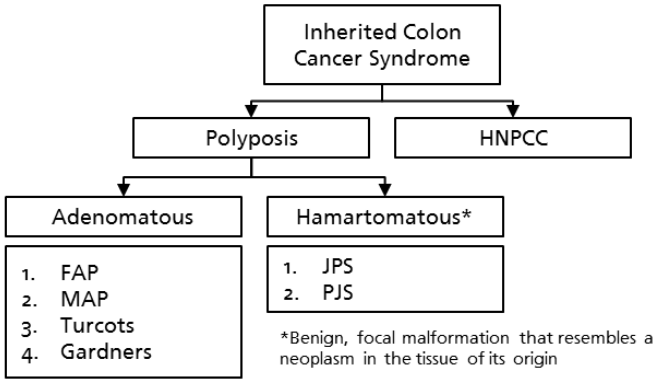
Stage	5 year observed survival rates – rectal cancer
I	74%
II	A – 65%, B – 52%, C – 32%
III	A – 74%*, B – 45%, C – 33%
IV	6%

* survival was better for some stage III cancers than some stage II cancers, the reasons for this is not clear

[68] N Engl J Med. 2001 Aug 30;345(9):638-46.
[69] J Clin Oncol. 2009;27(19):3109. MOSAIC trial
[70] Cochrane Database Syst Rev. 2012;3:CD004078.
[71] Practice NCCN Guidelines in Oncology-v2. Colon Cancer; 2005.

Associated Conditions

- Up to 30% of colon cancers exhibits familial clustering
- 3-5% a/w high risk inherited colon cancer syndromes
- Genetic testing is feasible in FAP, MAP, HNPCC, JPS and PJS
- If Amsterdam and Bethesda guidelines are followed about 15% of cases of colon cancer will up being genetically tested
- Individuals with a lifetime of 10 polyps should be tested



^ also have inflammatory and hyperplastic polyps – no malignant potential
^^ histological diagnosis: (1) tubular – 75-85% (2) tubulovillous – 10-15% (3) villous – 5-10%

- The **size** and **degree of villous feature** is predictive of malignancy risk – i.e. villous adenoma > 4cm = 90% risk
- Villous adenoma → px with secretory diarrhoea resulting in hypokalaemia

Familial adenomatous polyposis (FAP)

- Accounts for **<1% of total CRC burden**
- 1 in 20,000 live births, autosomal dominant inheritance
- Germline mutation of tumour suppressor gene APC (5q21-q22) – 10 – 30% of patients with classical FAP do not have APC mutations
- By age 35, 95% have > 100 adenomatous polyps, near 100% with colorectal carcinoma by age 40
- Variants: Turcot's / Gardner's / attenuated FAP

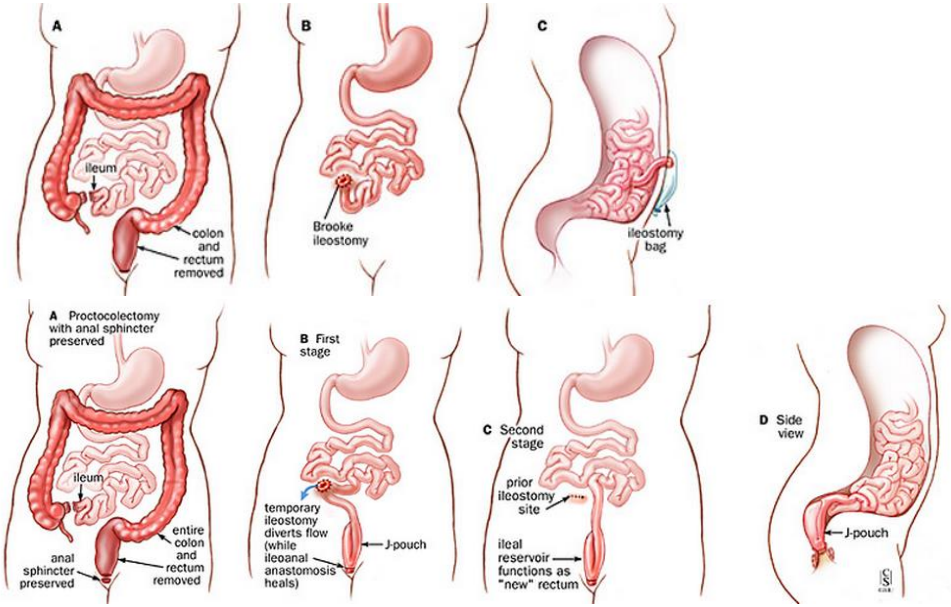
- Other sites for polyps: **Duodenum**, stomach
- Extra-intestinal manifestations

Benign Extracolonic Manifestations	Malignant Extracolonic Manifestations
- Bone: Osteoma of skull/ mandible, Dental abnormalities - Skin: Epidermoid cysts, Fibroma (nasopharynx) - Eye: Congenital hypertrophy of retinal pigment epithelium (CHRPE) - **Desmoid tumours** (benign tumours in the abdomen or in the fascia) - Adrenal Glands (adenoma)	- **Hepatoblastoma** most common tumour in childhood, from infancy to 4 years) - Thyroid cancer (follicular or papillary type) – more common in females (17:1) - Brain Tumour (80% medulloblastoma of the CP angle of the brain, 70% occur before age 16) - Pancreatic Tumours

- Diagnosis
  - Colonoscopy showing >100 polyps – disease characterized by the appearance of hundreds or thousands of adenomatous polyps in the colon in addition to extra-colonic tumours of the **duodenum** and **pancreas (periampullary carcinoma**)
  - Genetic testing of at-risk family members (screen index case 1st)

- Surveillance
  - Yearly colonoscopy for at-risk family members from 12y onwards till 35-40yrs if negative
  - 5 yearly OGD for surveillance of Periampullary Cancer (start around 25-30yrs)
  - Subtotal colectomy is an option if the rectum is relatively spared of polyps

- Treatment
  - Prophylactic Surgery (before the age of 25) → Panproctocolectomy with end ileostomy (see below) or ileal-pouch anal anastomosis (IPAA)
    - IPAA – involves folding loops of ileum back on themselves and stitching or stapling them together to form a reservoir pouch which is them anastomosed to the anus (see below)
  - OR Total Abdominal Colectomy with ileorectal anastomosis (TAC + IRA) with lifelong surveillance



Hereditary Non-Polyposis Colorectal CA (HNPCC)[72]

- Most common hereditary CRC syndrome
- Characterized by early onset, colorectal, endometrial, gastric and genitourinary cancers in individuals with a strong family history of cancer
- Autosomal Dominant → Accounts **for 1-3% of total CRC burden** due to defective mismatch repair genes (MMR): MSH2 and MLH1 (90%), MSH6 (10%) → defects in one of those genes confers 80% lifetime risk of developing HNPCC
- Pathology
  - Tumours usually proximal to splenic flexure – predominantly right sided tumour
  - Tumours tend to arise from polyps which are commonly flat, with villous histology → resultant tumour is often poorly differentiated
- Divided into Lynch syndrome I or Lynch syndrome II based on clinical features
  - Lynch Syndrome type I: familial colon cancer
  - Lynch Syndrome type II: HNPCC associated with increased risk of cancer of the GI tract and reproductive system (i.e. endometrial cancer, and also ovarian, gastric, small bowel, hepatobiliary, and renal pelvis/ureter cancers)

- Diagnosis (based on the Amsterdam criteria)
  - **Amsterdam II (incorporates extra colonic malignancies)**
    - 3 or more relatives with HNPCC-associated cancer (i.e. colorectal, endometrial, renal pelvis, small bowel, ureteral cancers), one of whom is a first degree relative of the other two (FAP excluded)
    - 2 generations of the same family affected by cancer
    - 1 (at least) cancer case diagnosed before age of 50
  - **Immunohistochemistry of the MMR proteins or DNA MSI**
    - For all patients (<70 yrs) with CRC or endometrial cancer (EC)
    - Revised Bethesda guidelines for DNA MSI testing of colorectal cancer[73]

- Risk Factors – for development of adenoma or CRC in LS
  - Smoking and high BMI increases the risk
  - Regular aspirin reduces incidence of cancer in LS

- Surveillance
  - 1-3yrly colonoscopy starting at 20 years old (impt not to miss out right sided lesions)
  - Gynaecological Examination, trans-vaginal u/s, aspiration biopsy from age 35-40 → may lead to detection of premalignant disease and early EC
  - Benefits of extra-colonic CA surveillance is unknown – performed in research setting

- Offer a THBSO with total colectomy if CRC surgery is scheduled
- THBSO largely prevents endometrial and ovarian cancer – discuss with patients who have completed their families esp. after the age of 40

Ulcerative colitis

- Screening – yearly colonoscopy starting after 10 years of UC (risk increase 1% per year after 10 years of disease)
- Treatment: restorative proctocolectomy with IPAA or TPC with end-ileostomy

Juvenile Polyposis Syndrome (JPS)

- Uncommon, AD
- Characterized by hamartomatous polyposis with an increased risk of cancer
- Polyps = abundant lamina propria, absence of smooth muscle and mucous filled cysts
- Diagnosis of JPS is made when 3-10 juvenile polyps are found in the colon or any juvenile polyps are found anywhere else in the GIT
- Lifetime colorectal cancer risk = 60%
- Extra colonic tumours in the stomach, small intestines and pancreas

Peutz-Jeghers Syndrome (PJS)

- Rare, AD
- Presents with hamartomatous polyps in the colon, small intestines and stomach
- Characteristic pigmentation of the perioral and buccal mucosa
- Mostly presents with bowel obstruction from intussusception or from GI bleeding
- Lifetime colorectal cancer risk = 40%
- Increased risk of breast, pancreatic, lung, uterine and gastric cancers

Common Familial Colon Cancer

- Colon cancer can also cluster in families who do not have any of these previously mentioned syndrome – colorectal cancer type X → families who meet Amsterdam criteria but lack MSI and evidence of germline mutations in DNA mismatch repair genes
- Background lifetime risk – 5%
- 1 affected first degree relatives – risk increases 2-3 fold over the background risk
- 2 affected first degree relatives – risk increases 3-4 folds
- 1 affected first degree relative with colon cancer before age 50 – risk increase 3-4 folds
- Proposed that moderate risk heritable colon cancers stem from interaction between several genes and environmental triggers

[72] Gut. 2013 Jun;62(6):812-23.
[73] http://jnci.oxfordjournals.org/content/96/4/261.full

STOMA PRINCIPLES

Stoma: artificial opening of a luminal organ into the external environment

Indications

1. For input: feeding (Percutaneous endoscopic gastrostomy)
2. For output: decompression/ lavage, defunctioning/ diversion, draining/ exteriorization (urine, faeces)

Nursing intervention

- Stoma care nurse to perform counselling & discuss best site for stoma placement preoperatively

Stoma siting

- Over the rectus sheath → reduces risk of prolapse,
- Away from the surgical incision → reduces risk of wound contamination and infection
- Away from skin creases or bony prominences → stoma wafer can be flushed with the skin (gaps between skin and wafer → leakage of fluid → skin excoriation & infection)
- Away from old surgical scars → reduces risk of hernia
- Sited for easy accessibility i.e. not under a large fold of abdominal fat
- Intra-operatively, avoid tension over the stoma to marked site →causes decreased vascularity of the stoma → risk of stoma necrosis

Types of stomas

Colostomy

- Artificial opening (large bowel) to divert faeces and flatus to the exterior where it can be collected by an external appliance → can be temporary or permanent

Permanent (end colostomy)

- When patient or surgeon factors are against reversal of stoma (relative)
- When no distal bowel remaining (absolute)
  - After Abdominoperineal Resection for low rectal/ anal tumour
  - After Panproctocolectomy without ileal pouch anal anastomosis

Temporary

- Decompression – relief of bowel obstruction causing proximal dilatation
- Defunctioning – to reduce effects of anastomotic leak
  - Esp. after low anterior resection, where risk of anastomotic leakage is high 2° to poor blood supply to anastomotic site
  - Usually loop ileostomies or colostomies with 2 openings (ileostomies usually on the right side, colostomies in the epigastric/hypochondriac [transverse colostomy] or left side)
- To rest an inflamed distal portion e.g. acute Crohn's

Stoma bags – single vs. two piece system

Single piece systems stick on to patient's skin.	Two piece systems have a separate base (a flange) that sticks to the skin, and the bag attaches to this. Bag can be changed without removing the flange.
	

Some bags have a second opening at the bottom to allow emptying. These are most useful in the period immediately after operation and in patients who have had ileostomy, who need to drain their bag regularly. Closed bags are used when the faeces are well formed and are usually only changed once or twice a day. Most patients with a stoma will use an opaque bag, but in the period immediately after operation a transparent bag is used to observe the new stoma for complications such as persistent oedema or necrosis. Modern stoma bags are fitted with a carbon or charcoal flatus filter that allows gas to escape to prevent the bag from ballooning or detaching and neutralises odour.

Physical Examination

		Ileostomy	Colostomy
Key Findings	Location	Right Iliac fossa	Left Iliac Fossa
	Calibre	Small	Large
	Flushed / Spouted	Protrudes ~3cm 'spout' – prevent ileal content (corrosive) to contact the skin	Flushed to the Skin
	Contents	Watery greenish ileal output	Firm brown faecal output
	Abdominal Scars	- Midline laparotomy scar / APR scar - Previous stoma scar	
Complications		- Mucosa (pink and healthy or dusky) - Overlying skin changes (stoma cx – erythema and excoriations) - Ask patient to cough to check for parastomal herniation	
Complete Examination		- *DRE* for patency of anal orifice (determine if temporary or permanent stoma) - Request to remove face plate to examine the number and patency of lumen - Obtain a psychosexual history - Request for I/O chart (especially if ileostomy): exclude high output stoma	

Stoma Complications

Early

- Bleeding & Infection
- Necrosis of terminal bowel (stoma appears dusky (grey → black); check by intubating with a glass tube into the stoma to look at colour of mucosa) → refashion stoma
- Obstruction (faecal impaction → explore with finger, enema / secondary to adhesion – more in ileostomy)
- Leakage → skin erosion, parastomal infection → re-site
- Stoma diarrhoea (high output) → r/o intra-abdominal sepsis, correct water & electrolyte imbalance (hypoNa^+, hypoMg^{2+}, hypoK^+), add anti-motility agent to thicken output (loperamide ± codeine) – see below

Intermediate

- Prolapse of bowel → refashion/refresh
- Retraction → refashion

Late

- Parastomal hernia (+ve cough impulse) → refashion
- Stenosis (unable to pass finger through) → refashion
- Fistulae
- Skin excoriation
- Psychological problems

High Stoma Output (Jejunostomy)[74]

- Defined as one producing an effluent volume >1000/ml/day
- Clinically significant when effluent volume > 2000ml/day → cause water, Na^+ & Mg^{2+} depletion
- Primary cause: loss of normal daily secretions (1.5L saliva, 2-3L gastric juice, 1.5L pancreatico-biliary) produced in response to food and drink.
- Other causes of high output (exclude first): intra-abdominal sepsis, infective enteritis (i.e. clostridium difficile), partial / intermittent bowel obstruction, recurrent disease in the remaining bowel (i.e. Crohn's disease or irradiation bowel disease), sudden stopping of drugs (i.e. steroids or opiates), administration of prokinetic drugs (i.e. metoclopramide)

Complication – Hypokalaemia pathophysiology

1. Sodium depletion (each L of jejustomy fluid contains 100mmol/l of Na^+) leading to secondary hyperaldosteronism (increase Na+ re-absorption and concomitantly greater than normal urinary loss of K^+ and Mg^{2+})
2. Hypomagnesaemia leading to increase renal potassium excretion

Management[75]

STAGE 1: Exclude Potential Causes

- Rule out intra-abdominal sepsis and intermittent bowel obstruction.
- Could medication be contributing to the HOS? Consider pro-kinetics, withdrawal of steroids.
- Does the patient have an enteric infection? Exclude *Clostridium difficile* by stool toxin analysis

STAGE 2: Initial management – Reduce fluid and electrolyte losses

- Restrict ORAL FLUIDS to 500 ml daily (Rehydrate patient with intravenous saline).
- Commence loperamide 4 mg QDS to reduce stoma losses. This should be given 30–60 min before meals and at bedtime.
- Monitor strict fluid balance, daily weights, and serum biochemistry, including magnesium levels.
- Screen for under nutrition (including BMI, % weight loss and current or expected oral intake) and refer to dietician as appropriate.

Review stoma output after 48–72 h – if settles increase oral fluid intake.

STAGE 2: Ongoing HOS – optimise treatment with anti-secretory / diarrhoeal medication

- Continue oral fluid restriction. (If stoma output is >3000 ml/day consider placing the patient NBM for 24 h to assess gastrointestinal secretion).
- Commence St.Marks or WHO glucose-electrolyte replacement solution 1000 ml daily, orally, in addition to oral fluid restriction. Once IV fluids stopped check random urine sodium (aim >20 mmol/l).
- Increase loperamide dose to 8 mg QDS.
- Review proton-pump inhibitors. Initiate or change to omeprazole 40 mg OD-BD to reduce volume of gastric secretions.
- Continue strict monitoring (fluid balance charts, twice weekly weights, weekly magnesium levels). If serum magnesium <0.5 mmol/l give 12–16 mmol of Magnesium sulphate IV in 0.9% NaCl. Begin oral supplements (Magnesium oxide capsules 3 x 4 mmol,nocte).

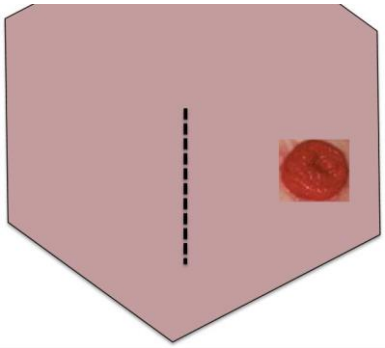
STAGE 3: Evaluate efficacy of additional treatment if HOS continues

REFER TO NUTRITION SUPPORT TEAM FOR FURTHER ADVICE

- Add in codeine phosphate 15 mg – 60 mg QDS, 30–60 min before meals (use cautiously in patients with renal impairment and contraindicated if GFR<15).
- Increase loperamide dose by 2–4 mg QDS.
- If stoma output remains >2000 ml daily after 2 weeks of therapy octreotide 200 mcg TDS for 3–5 days can be trialled. If no significant improvement in stoma output discontinue.
- Review compliance to oral fluids and increase St.Marks/WHO solution if required.

[74] World J Gastroenterol 2001; December 7(6):741-751

[75] Colorectal Dis. 2011 Feb;13(2):191-7

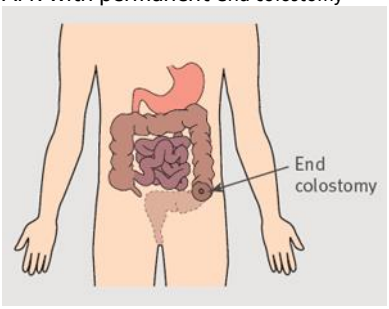


2 possibilities → permanent end colostomy or temporary end colostomy (to differentiate do a DRE to check anal canal patency)

Anal Canal Absent → permanent end colostomy, patient most probably has undergone an APR for low rectal tumour

Anal Canal Present → temporary end colostomy, patient has undergone a Hartmann's resection for an obstructing rectal tumour

APR with permanent end colostomy

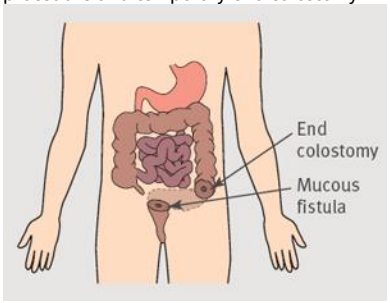


This procedure is most commonly performed to manage carcinoma of the lower rectum or anus, diverticular disease, and rare cases of faecal incontinence that do not respond to medical mx.

For example, a very low rectal cancer (distal 1/3) will require resection of the rectum and anus (APR). The remaining descending and sigmoid colon is mobilised and the cut end brought to the abdominal surface at an opening about 2 cm across.

This is usually sited in the left iliac fossa. The best site is usually through the lateral edge of the rectus sheath, 6cm above and medial to the ASIS. (i.e. midway between ASIS and umbilicus)

Anterior Resection with Hartmann's procedure and temporary end colostomy

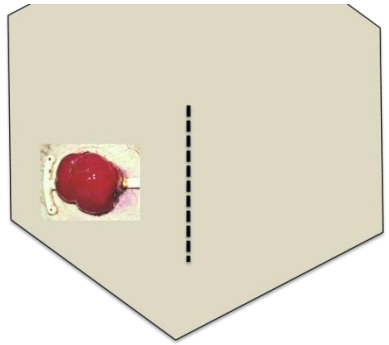


If the colostomy is temporary, a second operation is needed to reconnect the two ends.

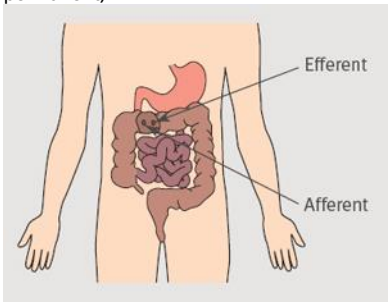
If the anus, rectum, and a portion of the lower colon have not been removed, as in Hartmann's procedure, two outcomes are possible.

In the first, the distal, non-functioning part of the colon and the rectum can be stapled or sewn closed and left inside the abdomen as a rectal stump. The proximal colon is then taken out as an end colostomy. Because the rectum has not been removed, the urge to have a bowel movement may occur. Mucus and some old stool, if present, will be passed.

Less commonly, two separate stomas may be created. One stoma is the exit of the functioning part of the colon through which stool and gas pass. The second stoma opens into the non-functioning portion of the colon and rectum and is called a mucous fistula. The second stoma is usually small, flat, pink-red in colour, and moist, and it produces only mucus.



Loop colostomy (can be temporary or permanent)

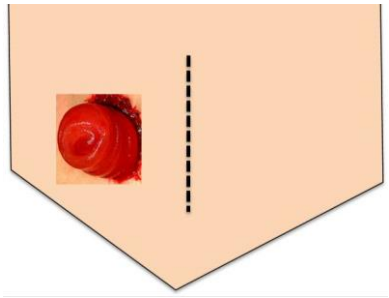


Suspect if colostomy but in the RIF (can be in LIF), 2 adjacent lumens, bag contains semi-solid brown stools.

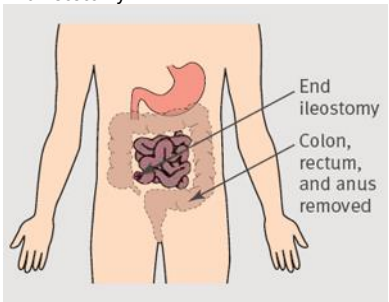
A loop colostomy was traditionally created to defunction an inflamed sigmoid in diverticular disease or to defunction a distal anastomosis. Also, can be indicated for prophylactic decompression before RT in an obstructing rectal tumour.

A loop of colon is brought to the surface of the body and may be supported on a rod, which is removed after 5-7 days. The bowel wall is partially cut to produce two openings—of an afferent limb and an efferent limb. The opening of the afferent limb leads to the functioning part of the colon, through which stool and gas pass out. The opening of the efferent limb leads into the non-functioning part of the colon.

The stoma site was usually high on the abdomen above the waistline because the transverse colon was commonly used. However, currently, loop colostomies are more often fashioned from the sigmoid colon to defunction the rectum (i.e. in cancer) or anus (i.e. in incontinence). Then again, loop colostomy has largely been replaced by loop ileostomy.



End ileostomy

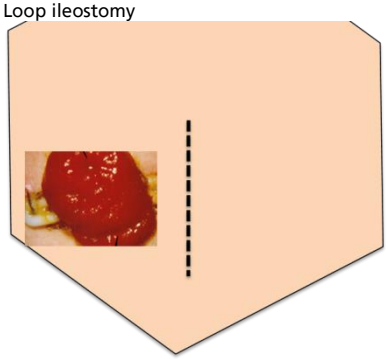


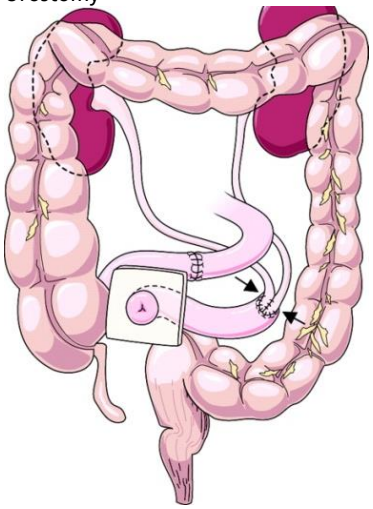
2 possibilities → temporary end ileostomy or permanent end ileostomy (to differentiate do a DRE to check for anal canal patency)

No anal canal → permanent end ileostomy, patient has undergone panproctocolectomy. This occurs most commonly in severe ulcerative colitis but also in familial polyposis and some cases of colorectal cancer (i.e. HNPCC).After a panproctocolectomy the ileostomy is permanent.

The ileum is resected just short of its junction with the caecum, and 6-7 cm of the small bowel is brought through the abdominal wall, usually in the right iliac fossa. It is everted to form a spout and then sutured to the bowel wall to protect the skin from the irritating content of the ileal fluid.

Anal Canal Present → Temporary end ileostomy. Patient has undergone an emergency subtotal colectomy, which leaves part of the sigmoid colon and rectum left in place; for acute ulcerative colitis; acute ischaemic bowel; or neoplastic obstruction of the sigmoid.

Loop ileostomy 	Suspect if ileostomy with 2 adjacent lumens and bag contains greenish liquid contents. This type of stoma allows for defunctioning of an obstructed colon (in cancer), defunctioning of a distal anastomosis (after resection and primary anastomosis either as an emergency or after radiotherapy), or defunctioning of the anus (in incontinence or perineal involvement in Crohn's disease). Loop ileostomy has largely replaced loop colostomy because it is easier to site, less bulky, absence of odour and easier to surgically close. A loop ileostomy has two openings, and most are temporary.
End-loop ileostomy	This less commonly performed procedure is used when an end ileostomy cannot be fashioned safely because the patient is obese or because of unfavourable mesenteric anatomy. The formation of this stoma is similar to a loop ileostomy, but the efferent limb is short and blind ended. On inspection at the bedside this type of stoma is indistinguishable from a loop ileostomy.
Double barrel stoma	When the caecum is removed, the surgeon might create a double barrel stoma. In essence, this is an end ileostomy (small bowel) and a mucous fistula (the remaining colon) sited beside each other. On examination this will look almost identical to a loop ileostomy; however, closer inspection will show two separate stomas.

Urostomy 	This is a general term for the surgical diversion of the urinary tract. The main reasons for a urostomy are cancer of the bladder, neuropathic bladder, and resistant urinary incontinence. The bladder is usually removed, but this may depend on the underlying condition. Formation of an ileal conduit is the most common procedure, which constitutes isolation of a segment of ileum. One end of the ileum is closed and the two ureters are anastomosed to it. Finally, the open end of ileum is brought out onto the skin as an everted spout and will look similar to an end ileostomy. Urine drains almost constantly from the kidneys through the ureters and ileal conduit into a bag. Patient may present with hyperchloremic metabolic acidosis and/or less frequently hypokalemia, hypocalcemia and hypomagnesemia*

Question	Answer	Stoma
Where is the stoma?	Left iliac fossa	Most likely a colostomy
	Right iliac fossa	Most likely an ileostomy
How does the bowel lie in relation to the external skin?	Flush with skin	Most likely a colostomy
	Raised spout	Ileostomy; less commonly a urostomy
How many lumens are present?	One	End colostomy; end ileostomy; urostomy
	Two (adjacent)—efferent limb may be difficult to see	Loop colostomy; loop ileostomy; end-loop ileostomy
	Two (separate stomas)	Most likely end colostomy with a mucous fistula; double barrel stoma; rarely bowel stoma and urostomy
What are the contents of the stoma bag (don't be afraid to feel it)?	Fully formed stool	Colostomy
	Semisolid or liquid stool	Most likely ileostomy; colostomy
	Urine	Urostomy
	Mucus	Mucous fistula

DIVERTICULAR DISEASE

PATHOLOGY – acquired pseudo-diverticular out pouching of colonic mucosa and submucosal (not complete 4 layers, hence not true diverticular)

TERMS
- Diverticulosis coli – presence of acquired pseudo-diverticular within the colon
- Diverticular disease – symptomatic diverticulosis coli
  - Simple (75%) with no complications
  - Complicated (25%) with abscess, fistula, obstruction, peritonitis, sepsis
- Diverticulitis – inflammation of a diverticula

EPIDEMIOLOGY[76]
- Prevalence increases with age → 5% at age 40, 30% at age 60, 65% at age 80
- Diverticulosis is symptomatic in 70% of cases, leads to diverticulitis in 15-25% and is associated with bleeding in 5-15%
- Distribution (in Caucasians): sigmoid involvement (95%), involvement of the sigmoid alone (65%), involvement of the entire colon (7%), not in rectum as taenia coli has fused
  - LDD (i.e. sigmoid colon) is most commonly affected owing to decrease luminal diameter and increased luminal pressure – onset usually in 7th & 8th decade of life
- Risk factors
  - Diet = lack of dietary fibre or high in red meat / fat
  - Genetics = in Caucasian almost always LDD, in Asians / Africans predominant RDD
  - Others = ADPKD patients on dialysis
- In Singapore – right sided diverticular disease was more common in all age groups – older patients were more likely to have LDD as compared to younger patients. Among ethnic groups, Chinese were more likely to have RDD (RDD: peaks in 6th decade of life) [77]

PATHOGENESIS

1. **Increased intraluminal pressure**
   - Forces mucosa and submucosal through areas of weakness in gut wall – occurs in the colon as the muscularis propria layer is aggregated into 3 bands (taeniae coli)
   - Associated with lack of dietary fibre
2. **Degenerative changes in colonic wall**
   - Usually at point of entry of terminal arterial branches where serosa is weakest
   - Associated with weakening of collagen structure with age

PRESENTATIONS

1. **Acute diverticulitis (due to obstruction of diverticula)**
   - Due to underlying micro/macro perforation of a diverticulum 2° inflammation and focal necrosis (small perforation is walled off by pericolic fat and mesentery)
   - Symptoms: LLQ pain, N/V, Constipation / diarrhoea, Urinary urgency
   - Signs: Low grade fever, Localised LLQ tenderness, ±mass (i.e. abscess / phlegmon)
   - Investigation:
     - FBC: ↑ WBC
     - CT AP: (helps identify patient's respond to conservative therapy)
       - Localized bowel wall thickening (>4mm)
       - Fat standing: ↑ soft tissue density within pericolonic fat 2° to inflammation
       - Colonic diverticula
       - Complicated Diverticulitis – **Pericolonic abscess** (fluid collection surrounded by inflammatory changes), **Fistula** (extra-luminal air collection within other organs), **Peritonitis** (free air)

2. **Chronic diverticulitis**
   - Recurrent LIF pain
   - Irregular bowel habit
   - Passage of mucus PR

3. **Complicated diverticulitis**
   a. LGIT haemorrhage – vessel disruption occur on the mucosal side of the artery → bleeding occur into the lumen instead of into the peritoneal cavity
      - Diverticular bleeding usually occur in the absence of diverticulitis
      - Usually stop spontaneously in ~75% of patients – risk of re-bleeding is ~25% and risk of bleeding a 3rd time is ~50%[78]
   b. Fistula formation (commonest: colovesical fistula formation) – 2° to pericolic abscess discharging, operation or drainage of pericolic abscess. May present with urinary symptoms (i.e. UTI). Others – colo-cutaneous, colo-uterine, colo-enteric, colo-vaginal
   c. Perforation – limited spread → phlegmon, further spread but still localized → diverticular abscess, free perforation (rare) → generalized peritonitis
   d. Bowel obstruction – due to combination of oedema or compression from an abscess or recurrent progressive fibrosis and/or strictures

Elderly and patients on steroids may have no sign even in severe diverticulitis.
There is an increased rate of free perforation (43% vs. 14% in Immunocompetent patients), increased need for surgery (58% vs. 33%), and increased postoperative mortality (39% vs. 2%).[79]

[76] WGO Practice Guidelines Diverticular disease 1 (2007)
[77] Colorectal Dis. 2011 Mar;13(3):312-6.
[78] Aliment Pharmacol Ther 2010; 32: 466–471
[79] WGO Practice Guidelines Diverticular disease 1

STAGING

- Hinchey classification of acute diverticulitis

Stage 1	Pericolonic / Mesenteric abscess	- Antibiotics, NBM, IV fluids - KIV percutaneous drainage of acute pericolonic abscess
Stage 2	Pelvic / retroperitoneal abscess	- Percutaneous drainage under radiological guidance - KIV elective 1 stage surgery – resection of segmental colectomy** with primary anastomosis
Stage 3*	Purulent peritonitis	- 2 stage operation – Hartmann's procedure (segmental colectomy** + diverting end colostomy & rectal stump formation) + secondary re-anastomosis 3 months later
Stage 4	Faecal peritonitis	

*Current controversy of management for stage 3: Hartmann's vs. segmental resection with primary anastomosis with or without defunctioning ileostomy

**Proximal margins through un-inflamed, non-thickened bowel & distal resection margins extend to normal, pliable rectum. Recurrent diverticulitis after resection is frequently related to inadequate distal

MANAGEMENT (COLONIC DIVERTICULAR BLEEDING)[80]

- ABC – resuscitate and stabilize patient
- Colonoscopy – to localize and treat bleeding
- Angiography / Embolization – alternative to colonoscopy when bleeding site cannot be identified (to localize and treat bleeding)
  - Can detect bleeding rates > 0.5ml/min
- Surgical Intervention (see below)
  - Segmental colectomy (after source of bleeding identified) with restoration of continuity by end-to-end anastomosis (last resort: sub-total colectomy)
  - Blind segmental resection is contraindicated

TREATMENT[81]

- Uncomplicated Diverticulitis (w/o inflammatory related complications) = CONSERVATIVE
  - CT scan proven – uncomplicated diverticulitis
  - NBM → clear liquid diet → high fibre low residual diet
  - Analgesia
  - Antibiotics (10-14days) → IV ceftriaxone & metronidazole KIV oralize to augmentin
  - If no scopes done before – offer colonoscopy 4-6weeks later to evaluate extent of disease and r/o colonic neoplasia, IBD, colitis
  - Risk of recurrence → 20-40% (similar severity to 1st episode)
- Complicated Diverticulitis (i.e. perforation, obstruction, abscess or fistula) = SURGICAL
  - ABC + NBM + Analgesia + IV Antibiotics (as above) + Colonoscopy in 6/52
  - Peritonitis → ABC + Antibiotics + Emergency Exploratory Laparotomy
    - Perforation → 2 stage surgery
    - Obstruction → 1 or 2 stage surgery
    - Abscess → CT guided drainage ± 1 stage surgery
    - Fistula (usually sigmoid colon involved) → Elective 1 stage surgery

[80] uptodate: Colonic diverticular bleeding
[81] uptodate: Treatment of acute diverticulitis

Indications for emergency operation	1. Sepsis from abscess or faecal peritonitis 2. Perforation 3. Diverticulitis not responding to conservative management 4. Obstruction with impending perforation – need to rule out cancer at the same time 5. Emergency bleed (controversial → clamping both side & look for active bleed into segment→ segmental resection) a. Hemodynamically unstable with failure of embolization b. Need > 4 units of PCT c. Previous bleed
Indications for elective operation (i.e. subtotal colectomy)	1. Stricture 2. Fistula 3. Recurrent attacks (≥2) – occurs in 30% of patients after 1st episode. a/w higher mortality & complication rates 4. Young patients <40YO – high recurrence rates 5. Immunocompromised patients (e.g. renal transplant) – may not show S/S of acute attack or complications

Recurrent diverticulitis after surgical treatment

- Incidence ranging from 1% to 10%
- In general, the progression of diverticular disease in the remaining colon is approximately 15%.
- Important factors to be considered in terms of surgery are the adequacy of resection, meaning the degree of proximal resection and level of distal anastomosis. The use of the rectum as the distal margin decreases the rate of recurrence.
- Care also must be taken to exclude other components of differential diagnosis, especially irritable bowel syndrome, inflammatory bowel disease, and ischemic colitis.

Advice to patients

- Likelihood of re-bleeding = 10% in 1st year and 25% at 4 years[82]
- 70% of patients will not have recurrence after first attack
- After first attack, 1/3 will have second. out of whom 1/3 will have 3rd
- Advise high fibre diet (prevents recurrence in >70%) & to drink lots of fluid, weight reduction and exercise

[82] Ann Surg. 1994 Nov; 220(5):653-6.

Presentation	Clinical features	Investigations	Differentials	Management
Acute Diverticulitis	- LIF pain – colicky, progressing to constant, relieved by defecation - LIF tenderness - Palpable LIF mass - Nausea - Urinary symptoms - Pyrexia - Increase pulse rate	- **FBC** – leucocytosis, ↑ **ESR** - **Erect CXR** to rule out perforation - **AXR** – ileus, air-fluid level w/in an abscess - **CT scan w triple contrast** (choice) ▪ Severity, complication, clinical staging ▪ Water soluble contrast: IV for vascular lesions, oral for small bowels, enema for large bowels ▪ Features – diverticula elsewhere, confirm colitis (mesenteric fat infiltration, concentric bowel thickening) but only suggest diverticulitis, pelvic abscess, free gas, extravasated contrast ▪ Cannot tell if inflm is due to diverticula ▪ Better than intraluminal examinations as bulk of inflm is extraluminal - **Laparoscopy** – if diagnosis is in doubt - **Avoid Barium enema** – CI as barium may leak out into abdo cavity - **Avoid colonoscopy** as risk of perforation is high (by air insufflations or instruments) + worsens diverticulitis	Can dev anywhere in GIT. See Ddx to RIF/LIF pain - GI: colitis, GE, IBS, IBD, mesenteric ischemia/ adenitis, Ca colorectal - Right colon/redundant (extra bend in descending colon) sigmoid colon: appendicitis - Transverse colon: PUD, pancreatitis, cholecystitis - Inflm adj to UT: UTI, stones, cancer, cyst/ Angiomyolipoma, hydronephrosis - Lower quad pain in F (Obgyn): PID, torsion of cyst/ ovary, endometriosis, ectopic pregnancy - Retroperitoneal perf (leg pain): thigh abscess, leg emphysema - #, infx, inflm,	**Conservative** - Bed rest - NBM, IV fluid - Broad-spectrum antibiotics – augmentin or metronidazole or ciprofloxacin - Antispasmodics After acute phase settled (4-6 wks) - Colonoscopy – confirm dx & exclude CA colon and/ or - Barium enema is inferior to colonoscopy in terms of image quality and is usually only performed if the patient has strictures or an excessively tortuous sigmoid colon where colonoscopy is difficult or dangerous Role of surgery: see below
Chronic Diverticulitis Not a common clinical entity	- Recurrent LIF pain - Irregular bowel habits – constipation & bouts of diarrhoea - Passage of mucus PR - Ruled out cancer, IBD, ureteric colic, Msk pain etc.	- **Rigid sigmoidoscopy** – oedematous mucosa & rigidity of rectosigmoid jx - **Flexible sigmoidoscopy** – diverticular orifices - **Barium enema** – 'saw-tooth' appearance, diverticula, strictures - **Colonoscopy** – exclude differentials (i.e. Ca colon)	- **CA colon – may coexist**. Hard to differentiate – therefore, ALWAYS exclude CA colon e.g. histology after bowel resection - Ischaemic colitis - Radiation colitis - Colonic endometriosis	**Conservative** – see above **Surgical** Indications: - Severe / recurrent attacks - Possible CA colon Stage: Segmental resection of affected colon + anastomosis
Generalised peritonitis / perforation	- Acute onset abdominal pain – severe & continuous - Abdominal guarding & rigidity - Vomiting - Tachycardia - Pyrexia	- **FBC** – ↑ TW, ↑ Hb (dehydration) - **U/E/Cr** – dehydration & ARF - **CXR** – free gas under diaphragm	- Other causes of peritonitis – perforated PUD/ appendicitis/ bowel/ ectopic pregnancy, ischaemic bowel, acute pancreatitis, ruptured AA/ hepatoma, torsion of testis/ ovary, pyonephrosis	Mx as for acute abdomen - **Resuscitate** - **Surgical** ▪ Peritoneal toilet ▪ Hartmann's procedure (Resection of affected segment + End sigmoid colostomy)
Pericolic abscess	- May follow acute diverticulitis - LIF tenderness & guarding - LIF mass – may be detected on DRE - Swinging fever	- **FBC** – ↑ TW - **CT** – differentiate between inflammatory phlegmon (spreading diffuse inflammation with pus/purulent exudates) & pericolic abscess		- **CT/ US guided percutaneous aspiration** - **Surgery** – evacuation of pus ± resection of affected segment
Persistent inflammatory mass	- LIF tenderness & palpable mass - Fever - Malaise			
Small bowel I/O				- Usually temporary, due to attachment of enteric loop against area of acute diverticulitis - Surgery if does not resolve
Large bowel I/O	- PHx of recurrent acute diverticulitis or irregular bowel habit - Colicky abdominal pain, constipation & abdo distension	- **AXR** – dilated bowels prox to stenosis - **Water soluble contrast enema**	- CA colon	- **NBM, Drip & suck** - **Surgery** – Resection ± primary anastomosis
Haemorrhage	- Usually in the elderly who have higher density of sigmoid diverticula - Massive bleed (altered blood ± clots; not melena) usually right-sided - Colicky pain as blood is irritative & causes spasm	- **Invx as for LGIT bleed** – resus, investigations + colonoscopy & angiography (both diagnostic AND therapeutic value) - ± on-table enteroscopy if required - ± tagged RBC scan (not as sensitive compared to angiogram): RBC tagged with radioisotope	- Anorectal bleed - Angiodysplasia - Ischaemic colitis - Colorectal CA - Colitis (inflm or infx) - UBGIT - Coagulopathy	- **Resuscitate** & correct coagulopathy - Colonoscopic management: adrenaline injection, endoclips on bleeding vessel, heat coagulation - **Radiologic embolisation** of site of bleeding with temp foam material via angiography - **Surgery** – segmental resection; total colectomy if unable to localise bleed
Vesicocolic fistula	- PHx of chronic diverticulitis & UTI - Hx of dysuria, freq, haematuria, pneumaturia, fecaluria	- **UFEME & urine c/s**: confirm UTI and organisms (polymicrobial as opposed to sterile pyuria in 'UTI from adj diverticulitis') - **Cystoscopy** – cystitis - **KUB** – air in bladder - **Barium enema** – ↓ diverticular bowel segment - **Sigmoidoscopy** – usually normal	- Other causes of fistula – CA colon, CA bladder, Crohn's disease, post-irradiation necrosis	- **Surgery** – Resection of affected colon + anastomosis + closure of bladder fistula opening

MECKEL'S DIVERTICULUM

Blind out-pouching of the anti-mesenteric aspect of the small intestine (i.e. ileum) that has all four layers of the small bowel wall (i.e. true congenital diverticulum), covered with serosa

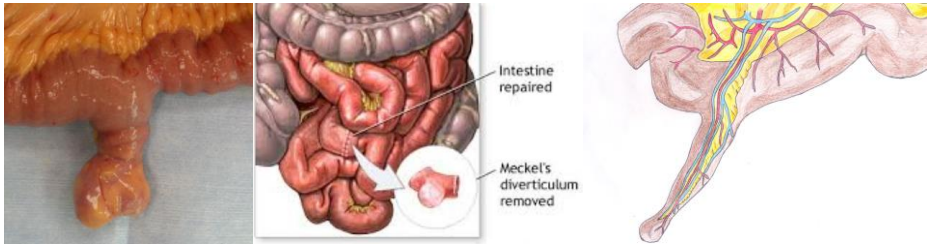
EMBRYOLOGY

- It results from incomplete obliteration of the vitelline duct / persistent remnant of the omphalomesenteric duct (connects mid-gut to yolk sac in the fetus)
- Vitelline duct abnormalities:

Vitelline Fistula | Vitelline Cyst | Vitelline Cord | Meckel's Diverticulum | Meckel's Diverticulum & vitelline cord

RULE OF 2s

- 2 inches in length, 2cm wide,
- 2 feet (60cm) from ileocaecal valve
- 2% of the population
  - No familial predisposition
  - Increased prevalence in children with malformation of umbilicus, alimentary tract, nervous system, CVS system
- 2:1 ratio ♂>♀
- 2-4% becomes symptomatic
  - Increased risk in (1) presence of ectopic tissue, (2) age <50yrs, (3) diverticulum length >2cm, (4) males, (5) broad based diverticulum, (6) presence of fibrous bands
- 2 types of ectopic tissue
  - Gastric (60%) – gastric acid secretion can produce inflammation, peptic ulceration & bleeding, strictures with subsequent IO
  - Pancreatic (6%)
  - May have both types of tissue or other types (i.e. jejunal, colonic, rectal, hepatobiliary)



* The artery feeding the Meckel's diverticulum is long, non-branching, originating from the SMA, transverse the mesentery towards the RLQ where it terminates

PRESENTATION

- Asymptomatic: incidental finding during abdominal exploration or imaging (i.e. barium)
- Symptomatic:
  1. **Haematochezia** (most common in children): usually massive & painless, due to peptic ulceration
  2. **Intestinal Obstruction** (most common presentation):
     - Recurrent Intussusception – Meckel's diverticulum act as the lead point
     - Volvulus
     - Abdominal Wall Hernia – Littre's Hernia (at inguinal (50%), femoral (20%))
     - Meckel's Diverticulitis – inflammation results in reduced luminal diameter
  3. **Meckel's Diverticulitis**: may present exactly like acute appendicitis i.e. periumbilical pain radiating to RIF. Less prone to inflammation as most Meckel's have wide base, little lymphoid tissue & are self-emptying – if perforate, symptoms simulate those of a perforated duodenal ulcer.
  4. **Chronic Peptic Ulceration**: as diverticulum is related to the mid-gut, the pain, although related to food, is felt around the umbilicus
  5. Others: **umbilical fistula, tumour, perforation etc.**

INVESTIGATIONS

Blood: As per IO or lower BGIT
Imaging:

- Meckel's Scan: **Technetium-99m pertechnetate scan** (detects gastric mucosa)
- Barium studies: small bowel enteroclysis
- CT angiography – help detect signs of bleed (0.3ml/min)
- CT NOT helpful as hard to distinguish Meckel's diverticulum from small bowel loops

MANAGEMENT

- Asymptomatic[83]
  - Detected on imaging: do not perform elective resection
  - Detected during surgery:
    - resect in children up to young adulthood
    - resect in adult (<50yrs) – esp. if palpable, length >2cm and broad base >2cm
    - do not resect in patients (> 50yrs)

- Symptomatic
  - NBM, IV drip, correct electrolyte imbalance
  - IO: NG tube on constant suction, supine AXR
  - PR bleed: start PPI, ± PCT, gastric lavage to r/o UBGIT, OGD & colonoscopy
  - Definitive treatment: surgery (open or laparoscopic)
    - Broad base: wedge ileal resection with anastomosis
    - Narrow base: resection of the diverticulum

[83] uptodate: Meckel's diverticulum

Inflammatory Bowel Disease[84]

IBD is chronic, relapsing often debilitating diseases that have profound psychological as well as physical effects

	Crohn's Disease (CD)	Ulcerative colitis (UC)
Age	Bimodal peaks at 15-30 and 60-80 years	Bimodal peaks at 20-40 and 60-80 years
Gender	Female Predominance	Male Predominance
Genetics	Mutation in CARD15 (NOD2) gene on chr 16 (in 1/3 of patients) – associated with ileal disease (disease due to T-helper mediated pro-inflammatory response)	
Risk Factors	- Family hx – 10x ↑ risk in 1st deg relatives - Smoking - Infections - Drugs – NSAIDs, OCP, Antibiotics - Diet – refined sugars, low-fibre diet	- Diet – sugar, cola drinks - Smoking (protective – induce remission) - Appendectomy (protective) - Drugs – NSAIDs
Bowel involvement	- Entire GIT anywhere from mouth to anus - Terminal Ileum (35%) - Ileocecal region (40%) - Confined to colon (20%) - Anus, Perineum - **Rectum characteristically spared**	- Initial episode of UC[85] ▪ 30-50% limited to recto-sigmoid ▪ 20-30% left sided colitis ▪ 20% pancolitis - **Always affect the rectum** - Occasional terminal Ileum involvement (backwash ileitis) – diffuse involvement
Distribution	Skip lesions with normal mucosa between	Diffused, non-sparing
Extent of Inflammation	Transmural – with deep ulceration, fissuring and abscess formation	Superficial ulceration (limited to mucosa)
Nature of inflammation	Chronic (granulomatous 35% – non-caseating)	Acute-on-Chronic (non-granulomatous)
Fistula & Sinuses	Present	Absent
Fibrosis	Marked, Strictures	Mild to None
Gut Wall	Thickened with narrowed lumen (produce string sign in barium x-ray)	Thin with normal lumen diameter
Histo-pathology	Macroscopic: cobblestone appearance (diseased tissue is depressed below level of interspersed spared mucosa), **deep ulcers** and fissures Microscopic: transmural inflammation (lymphocytes, plasma cells and macrophages), **non-caseating granulomas**, glands are preserved	Macroscopic: **shallow ulcers**, pseudo-polyps and mucosal bridges (regenerating islands of mucosa amidst shallow ulceration) Microscopic: inflammatory pseudopolyps, inflammation limited to mucosal layer (**neutrophils, plasma cells, eosinophils**), glands destroyed with crypt abscesses, mucosal atrophy (chronic) **Granulomata are not a feature**
Carcinoma Risk	Slight increased risk of CRC Increased risk of small bowel lymphoma	Substantially ↑ risk of CRC – risk increases 1% per year after 10 years of the disease
Associated Ab	ASCA: anti-saccharomyces cerevisiae antibodies	p-ANCA: perinuclear antineutrophil cytoplastic Ab
Severity	Harvey Bradshaw severity index	Modified Truelove & Witts severity index (Mild, moderate, severe, fulminant)

Systemic Manifestations	Unrelated to disease activity	Joints	- Sacroilitis (18% but usually asymptomatic) - Ankylosing spondylitis (rare)
		Hands	- Clubbing
	Related to disease activity	Eyes	- Uveitis (up to 10%) - Episcleritis
		Perioral	- Aphthous Ulceration (20% with CD)
		Joints	- Acute Arthritis
		Liver & biliary tract	- Primary Sclerosing Cholangitis (UC) - Gallstones - Fatty Change - Amyloidosis - Granuloma - Cholangiocarcinoma
		Kidneys	- Ureteric calculi (oxalate in CD, urate in UC)
		Skin	- Erythema Nodosum (5-10%) – non-ulcerative - Pyoderma gangrenosum (more common in UC) – ulcerative
Complications	Nutritional Deficiencies Malignancy Risk Perforation and Peritonitis		Nutritional Deficiencies Malignancy Risk Toxic megacolon*

* triggered by administration of narcotic, anti-diarrheal, anti-cholinergic and anti-depressant, NSAID. In severe cases → Involvement of the muscularis propria lead to damage to the nerve plexus, resulting in colonic dysmotility, dilation, and eventual infarction and gangrene

Treatment				
	Active	Maintenance	Active	Maintenance
Mild-Mod	Oral prednisolone Controlled ileal release budesonide KIV antibiotics	Smoking cessation	5-ASA – high dose mesalazine Steroids – oral prednisolone	5-ASA ? continue smoking ? appendectomy
Mod-Severe	IV hydrocortisone Immunotherapy – azathioprine / MTX	Immunotherapy – azathioprine / MTX	KIV Antibiotics IV with rectal hydrocortisone Surgery	Immunotherapy – azathioprine, cyclosporine

Modified Truelove and Witts Severity Index[86]

Activity	Mild	Moderate	Severe
Number of bloody stools per day (*n*)	<4	4–6	>6
Temperature (°C)	Afebrile	Intermediate	>37.8
Heart rate (beats per minute)	Normal	Intermediate	>90
Haemoglobin (g/dl)	>11	10.5–11	<10.5
Erythrocyte sedimentation rate (mm/h)	<20	20–30	>30

[84] PACES for the MRCP 3rd Edition (Tim Hall)
[85] uptodate: Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults

[86] Br Med J 1955;ii:1041–8.

CROHN'S DISEASE

EPIDEMIOLOGY
- Bimodal distribution: affects young in the 2nd & 3rd decades of life, with second onset in the 5th & 6th decades of life
- Genetic association – Higher prevalence amongst Ashkenazi Jews & in cooler climates e.g. Scandinavia, UK, Germany, northern USA

CLINICAL PRESENTATION
- Diarrhoea, abdominal pain, anal lesions, rectal bleeding, fatigue, LOW, fever
- Crohn's fistula
  - colo-vesical fistula – faeces in urine/ pneumaturia,
  - colo-ovarian fistula – faeces per vaginal/ PID
- Non-specific systemic: LOW, LOA, fever, fatigue, symptoms of anemia, chronic malnutrition

Clinical Subtypes
1. Active ileal and ileocecal disease
   - RIF inflammatory mass or abscess formation ← **constant pain**
   - Small bowel obstruction (strictures) ← **colicky pain + abdominal distention**
   - ± diarrhoea and/or LOW
2. Active Crohn's Colitis
   - Symptoms are similar to UC but frank bleeding is less common
3. Perianal Crohn's Disease
   - Fissuring, fistulae or abscess
4. Others
   - CD confined to mouth, stomach, duodenum or rectum only

PHYSICAL EXAMINTION – usually normal +/- extra-intestinal manifestations
- Acute severe: fever, tachycardia, tender/distended abdomen
- Complications of Disease
  - Nutritional Deficiency
  - RIF mass,
  - Midline laparotomy scar – suggest previous surgery
  - Perianal enlarged skin tags/ fistula/ abscesses, anal stricture
  - Extra-intestinal Manifestation → clubbing, perioral aphthous ulceration, erythema nodosum, joint pain, fatty liver
- Complications of treatment (i.e. cushingoid features)

DIAGNOSIS → Histological Diagnosis
- Ultrasound: for diagnosing ileal CD
- Contrast radiographic studies: assess location & extent of disease, look for strictures & fistulae
  - Barium studies/follow through: small bowel series & enema (cobblestone)
  - CT scan with oral & IV contrast
  - MRI
- Endoscopy: look for typical features
  - Colonoscopy with tissue biopsy (non-caseating granulomas)
  - OGD: upper GIT involvement
  - Endoanal U/S (EUS): identify fistula tracts

MANAGEMENT
Non-Pharmacological
- Trigger Avoidance
  - NSAIDs and antibiotics
  - Smoking Cessation – improves maintenance of remission
- Nutrition e.g. TPN (may also aid closure of fistulae)
  - Elemental Diet (amino acid and glucose)
  - Polymeric Diets
  - Vitamin Supplementation (in cases of malabsorption)

Pharmacological

Class	Drug	Action	Remarks
ANTI-MICROBIAL	Metronidazole	Sepsis or bacterial overgrowth	
	Ciprofloxacin	Fistulating disease (peri-anal)	
CORTICOSTEROIDS to induce remission, not to use long-term	Budesonide* 9mg/day	Mild to moderately active CD	Budesonide as effective as pred. with fewer s/e & superior to mesalazine and placebo
	Prednisolone 40-60mg/day		
	IV hydrocortisone	Severe disease	
SALICYLATES 5-Aminosalicylic Acid (5-ASA) less beneficial for active CD than for active UC	Sulfasalazine 1g BD	Active colonic disease but not maintenance	
	Mesalazine 4g OD	Maintenance after surgical intervention not after medically induced remission	Not useful in active disease
Immunotherapy (IMMUNOMODULATOR)	Azathioprine	Maintaining remission	administered via IV have lasting effects
	Methotrexate		
Immunotherapy (BIOLOGICAL THERAPY) For CD non-responsive to steroids and/or immunomodulators	Infliximab**	Induction of response, remission and maintenance therapy for patients with mod-severe CD	Contraindications → **STOIC** (sepsis, TB, optic neuritis, infusion reaction, cancer)
	Adalimumab		

* budesonide – have extensive first-pass metabolism in the liver and is a reasonable alternative to patients with active iletits or right sided crohn's disease (less systemic side effects)

**Remicade (infliximab) = TNFα blocker
- The ACCENT II Study → among patients whose fistulas closed after infliximab induction therapy, continued infusion at fixed intervals (5mg / kg every 8 weeks) maintained closure for a longer period as compared to placebo.[87] Also, effective in short-term closure of recto-vaginal fistulas and maintenance treatment was more effective than placebo in prolonging recto-vaginal fistula closure.[88]

Pre-treatment → rule out TB, hepatitis first (as tx can cause reactivation)
Treatment → require close surveillance for SE (blood disorders, infections, lymphoma & solid tissue cancers, hepatotoxicity, drug-induced lupus, demyelinating disorders)

[87] N Engl J Med. 2004 Feb 26;350(9):876-85.
[88] Clin Gastroenterol Hepatol. 2004 Oct;2(10):912-20

Surgical
- Principles
  - **Avoid surgery until absolutely necessary** (80% require surgery within 20 years of onset) & when indicated perform bowel preserving surgery as repeated bowel resections can lead to short gut syndrome
  - Indications :
    - Disease refractory to medical therapy (common)
    - Serious complications of medical therapy
    - Severe bleeding, perforation
    - Intestinal obstruction due to strictures
    - Fistulae
    - Abscesses
    - Toxic megacolon (failed to response to medical therapy within 24hours)
    - Malignancy

- Procedure (laparoscopic or open)
  - CT abdomen for pre-operative **percutaneous drainage of abscesses** (decrease inflammation & risk of sepsis)
  - **Small bowel*** (bowel preservation is key)
    - Short segment disease: strictureplasty
    - Long strictures (>12cm): surgical resection with primary anastomosis
    - Fistula: resect diseased bowel & repair involved organ
  - **Large bowel**
    - Right hemicolectomy (most commonly performed)
    - Total colectomy + ileorectal anastomosis (if rectum spared) or panproctocolectomy + end ileostomy (if rectum affected)
    - Toxic Megacolon → Total colectomy with Hartmann pouch with ileorectal anastomosis in future
  - **Perianal disease**
    - Setons, fistulotomy, proctectomy in severe disease

* Obstruction secondary to intestinal strictures due to repeated bouts of inflammation and subsequent fibrosis, transmural inflammation leading to fistulas (Enteroenteric, enterocutaneous, enterovesical, and rectovaginal fistulas)

Screening for colorectal cancers
- Recommendations for ulcerative colitis also applies to crohn's disease (see below)

ULCERATIVE COLITIS

CLINICAL PRESENTATION
- Diarrhoea, abdominal pain and bleeding
- Bloody diarrhoea is the central feature of UC

DIFFERENTIAL DIAGNOSIS
- Infection
  - Yersinnia spp.
  - Mycobacterial (TB)
- Colitis
  - Ischemic colitis
  - Microscopic colitis* (watery rather than bloody diarrhoea)
  - Radiation colitis
  - Drug-induced colitis – usually due to NSAIDs
- Neoplasm
  - Small Bowel Cancer / Lymphoma
  - Colorectal Cancer
- Diverticulitis
- Irritable Bowel Syndrome
- Chronic Pancreatitis and malabsorption
- Others → Celiac Disease, Sarcoidosis, Rectal Mucosal Prolapse

* Microscopic Colitis
- Triad of chronic water diarrhoea, normal colonoscopy and characteristic microscopic inflammation of the lamina propria
- More common in older people
- Loperamide is useful for mild disease
- Budesonide ± immunomodulators (azathioprine) needed for more severe disease

INVESTIGATIONS

Supportive (looking for complications & assessing severity of disease)
- Blood tests
  - FBC: anemia, leucocytosis & thrombocytosis indicate more severe disease
  - U/E/Cr: hypokalaemia & dehydration in prolonged diarrhoea
  - LFT: hypoalbuminemia due to poor nutritional intake
  - CRP, ESR: markers of severity
  - Autoantibody assay: p-ANCA ↑ in UC, ASCA ↑ in CD
- Radiological
  - AXR to evaluate colonic calibre (>5.5 cm is abnormal)
  - CXR to rule out perforation (risk of perforation in acute disease)

Diagnostic (mainly at rectum)
- Endoscopy: look for typical features
  - Flexible sigmoidoscopy with tissue biopsy: bleeding may occur with contact with scope.

MANAGEMENT

Medical

Class	Drug	Action	Remarks
CORTICOSTEROIDS **to induce remission, not to use long-term**	Steroid suppositories or foam enemas	distal colitis (topical tx)	
	Oral Prednisolone	mild-mod disease	
	IV & rectal hydrocortisone 400mg OD	severe disease	
SALICYLATES 5-Aminosalicylic Acid (5-ASA) **Relapse rate is reduced from 80% to 20% at 1 year**	Sulfasalazine* 2g OD	Induction and maintenance of remission	Reduce risk of developing colorectal cancer
	Mesalazine** (suppository or enema)		
	Olsalazine***	Useful if have proximal constipation and distal disease	
Immunotherapy (IMMUNOMODULATOR)	Azathioprine^	Maintenance after severe disease	MTX is ineffective in UC unlike CD
	Cyclosporine		
Immunotherapy (BIOLOGICAL THERAPY) **For UC non-responsive to steroids and/or immunomodulators**	Infliximab^^	Induction of response, remission and maintenance therapy for patients with severe UC	
ANTI-MICROBIAL		Infection – clostridium difficile, shigella, salmonella, campylobacter, amoebiasis	

*** s/e of sulfasalazine** → headache, nausea, agranulocytosis, SJS
**** s/e mesalazine** → nephrotoxicity | refractory distal disease might respond to mesalazine suppositories thrice weekly
***** s/e olsalazine** → watery diarrhoea

^ azathioprine – standard practice to measure thiopurine methyltransferase (TMPT) before initiating azathioprine – identify people at risk of bone marrow suppression
^^ Infliximab – although the etiology of UC differs from that of CD, RCTs have demonstrated that infliximab is also beneficial for the tx of mod-severe UC in patients who are either intolerant of or refractory to immunosuppressant agents or steroids, or those who are steroid-dependent. ACT 1 and ACT 2 (Acute ulcerative Colitis Treatment) trials showed that 44-45% of patients treated with infliximab for a year maintained a response to the medication, cf 21% on placebo

Acute Severe Colitis
- Natural mortality of 25% that is markedly reduced by surgery and corticosteroid treatment
- Assess severity – Truelove and Witt criteria
- Initial Investigation & Management
  - Stool microscopy, culture and sensitivity for bacterial (C. difficile), ova, cysts, parasites, virus (CMV)
  - AXR – to exclude toxic megacolon (>5.5cm in diameter) and mucosal islands – 75% would require surgery
  - IV Fluids + Electrolyte Monitoring + Thromboembolic Prophylaxis
  - Avoid – anti-diarrhoea drugs (i.e. loperamide, opioids), antispasmodic (i.e. buscopan), anticholinergic and NSAIDs
  - Antibiotics + Corticosteroids
  - KIV surgical intervention

Surgical
- Indications (emergent)
  1. Acute fulminant colitis with acute abdomen → Toxic megacolon (colon > 5.5cm)
  2. Impending Perforation (i.e. dilatation with thumb-printing or pneumatosis) or free/walled off perforation
  3. Acute fulminant colitis without acute abdomen → unremitting bloody diarrhoea

- Indications (elective)
  4. Disease refractory to medical therapy with severe & extensive colitis (most common)
  5. Serious complications of medical therapy
  6. Malignancy – precancerous lesions or prophylactic risk reduction
  7. Debilitating extra-intestinal manifestation – i.e. thromboembolic complications,

- Procedure (laparoscopic or open)
  - Emergent Procedure → total colectomy + end ileostomy: diseased rectum left in-situ with resection (proctectomy) & IPAA at later date when patient has regained health & steroids have been withdrawn (as rectum is extraperitoneal organ and dissection/resection takes a long time). Foley catheter used to decompress rectum for 3-4 days
  - Elective Procedure →Proctocolectomy with IPAA (ileo-pouch anal anastomosis): standard of care for patients with UC who ultimately require colectomy. Avoid necessity for long term stoma.
  - Alternative: Panproctocolectomy + end ileostomy

- Complications:
  - Mortality 2-7%, 30% if perforation
  - Pouchitis: Tx with Abx (metronidazole + ciprofloxacin X 2/52) + immunosuppression

Screening for colorectal cancers[89]
- American Gastroenterological Association
  - Colonoscopy after **8 years in patients with pan-colitis**
  - Colonoscopy after **15 years in patients with colitis involving only left colon**
  - Repeat colonoscopy every one – two years
- British Society of Gastroenterology
  - Surveillance colonoscopy 10 years after onset of symptoms (done when disease in remission)
  - Interval depends of severity and additional risk factors
    - **5 yearly** – no active endoscopic / histological inflammation, left sided colitis, crohn's colitis involving less than 50% of colon
    - **3 yearly** – mildly active inflammation, post inflammatory polyps, family history of CRC in 1st degree relative ≥ 50years old
    - **1 yearly** – moderately active inflammation, stricture in preceding 5 years, primary sclerosing cholangitis, family history of CRC in 1st degree relatives ≤ 50 years old
  - 2-4 random biopsy of specimen every 10cm from entire colon should be sampled
  - Post-colectomy surveillance colonoscopy – interval as above

[89] uptodate: Colorectal cancer surveillance in inflammatory bowel disease

ANAL & PERIANAL DISORDERS

HAEMORRHOIDS

- They are clusters of vascular tissue (i.e. arterioles, venules, arteriolar-venular connections), smooth muscle (i.e. Treitz muscle), and connective tissue lined by the normal epithelium of the anal canal.
- Internal haemorrhoids are symptomatic anal cushions and characteristically lie in the **3,7 and 11 o'clock position** (patient in lithotomy position)

	External Haemorrhoids	Internal Haemorrhoids
Origin	**Ectoderm →** stratified squamous epithelium	**Endoderm →** columnar epithelium of anal mucosa
Location	**Below the dentate line**	**Above the dentate line**
Innervation	**Somatic innervation** (inferior rectal nerve)	**Autonomic nervous system →** not sensitive to pin-prick sensation
Pain	- May thrombose causing pain and itching, - Secondary scarring may lead to skin tag formation	- Can produce perianal pain by prolapsing and causing spasm of the sphincter complex around the haemorrhoids, - Can also cause acute pain when incarcerated and strangulated
Venous Drainage	Inferior rectal vein → Inferior vena cava	Superior rectal vein → Portal venous system
	Rich anastomoses exist between these 2 and middle rectal vein (porto-systemic anastomosis)	

CAUSES

1. Decreased venous return / increase intra-abdominal pressure: pregnancy, constipation (low fibre diet) → straining
2. Portal hypertension and anorectal varices
3. Increase rectal vein pressure: obesity, prolonged sitting

CLASSIFICATION

Banov grading for internal haemorrhoids (see below)

Grade	Description	Treatment
I	Palpable, non-prolapsing + bleeding	Lifestyle, Daflon
II	Prolapse with straining and defecation, spontaneously reduce ± bleeding	Lifestyle, Daflon, Elastic ligation
III	Protrude spontaneously or with straining, require manual reduction ± bleeding	Lifestyle, Daflon, Elastic ligation, Haemorrhoidectomy (excision / stapled)
IV	Chronically prolapsed, cannot reduce, often with dentate line released from internal position ± bleeding	Lifestyle, Daflon, Haemorrhoidectomy (excision / stapled)

CLINICAL PRESENTATION

- The most common presentation of haemorrhoids is **rectal bleeding, pain, mucus discharge, pruritus, or prolapse.**
- Painless fresh PR bleeding after defecation: coating / dripping, not mixed with stools

Most symptoms arise from enlarged internal haemorrhoids.

- Abnormal swelling of the anal cushions causes dilatation and engorgement of the arteriovenous plexuses. This leads to stretching of the suspensory muscles and eventual prolapse of rectal tissue through the anal canal. The engorged anal mucosa is easily traumatized; leading to rectal bleeding that is typically bright red due to high blood oxygen content within the arteriovenous anastomoses.
- Prolapse leads to soiling and mucus discharge (triggering pruritus) and predisposes to incarceration and strangulation.

External haemorrhoids cause symptoms in 2 ways.

- Acute thrombosis: usually related to a specific event, such as physical exertion, straining with constipation, a bout of diarrhoea, or a change in diet. Pain results from rapid distention of innervated skin by the clot and surrounding oedema. The pain lasts 7-14 days and resolves with resolution of the thrombosis
- Occasionally erode the overlying skin and cause bleeding

COMPLICATIONS

- Strangulation and Thrombosis
- Ulceration
- Gangrene
- Portal Pyaemia (septicaemia)
- Fibrosis

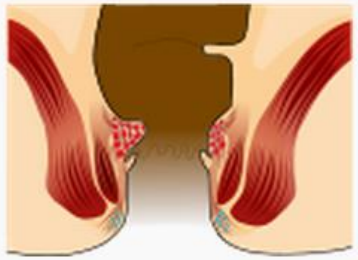
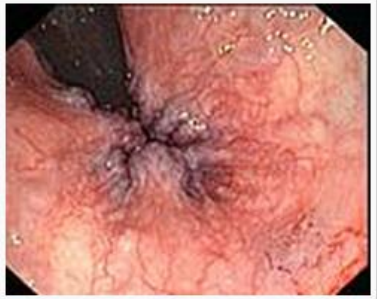
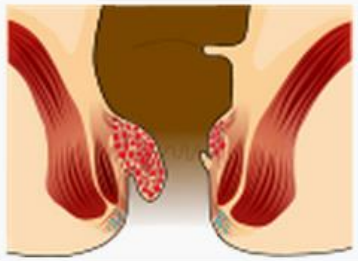
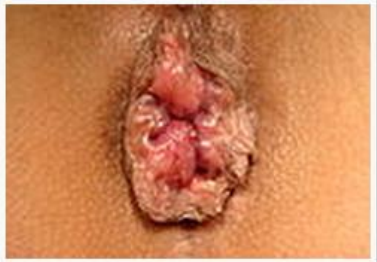
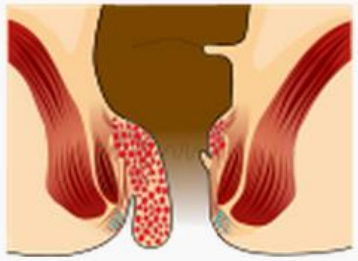
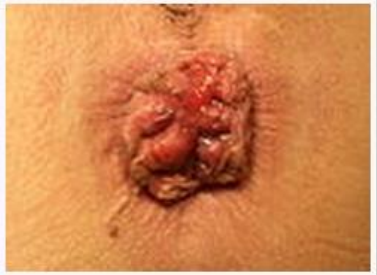
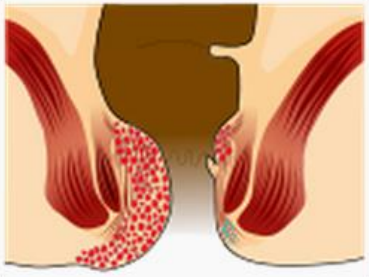
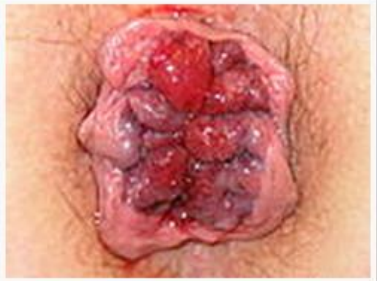
MANAGEMENT OF ACUTELY THROMBOSED EXTERNAL HAEMORRHOIDS

- <24 hours – treat by surgical excision of the thrombosed vein outside the mucocutaneous junction with the wound left open
- > 48 hours – treat with non-surgical management, symptomatic

MANAGEMENT INTERNAL HAEMORRHOIDS

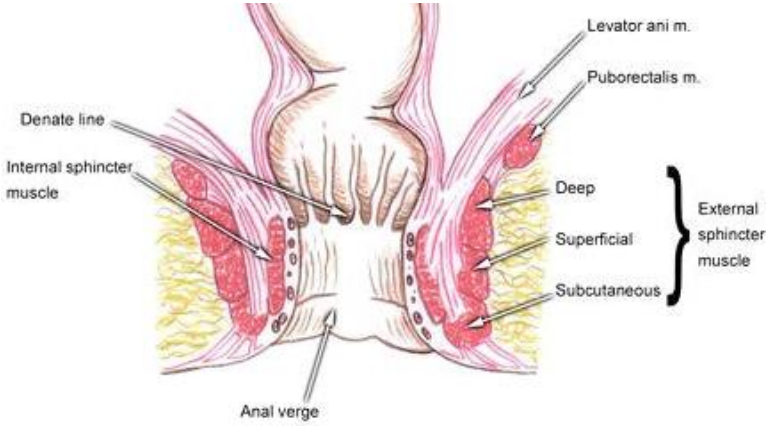
- Exclude other causes of rectal bleeding – i.e. colorectal carcinoma

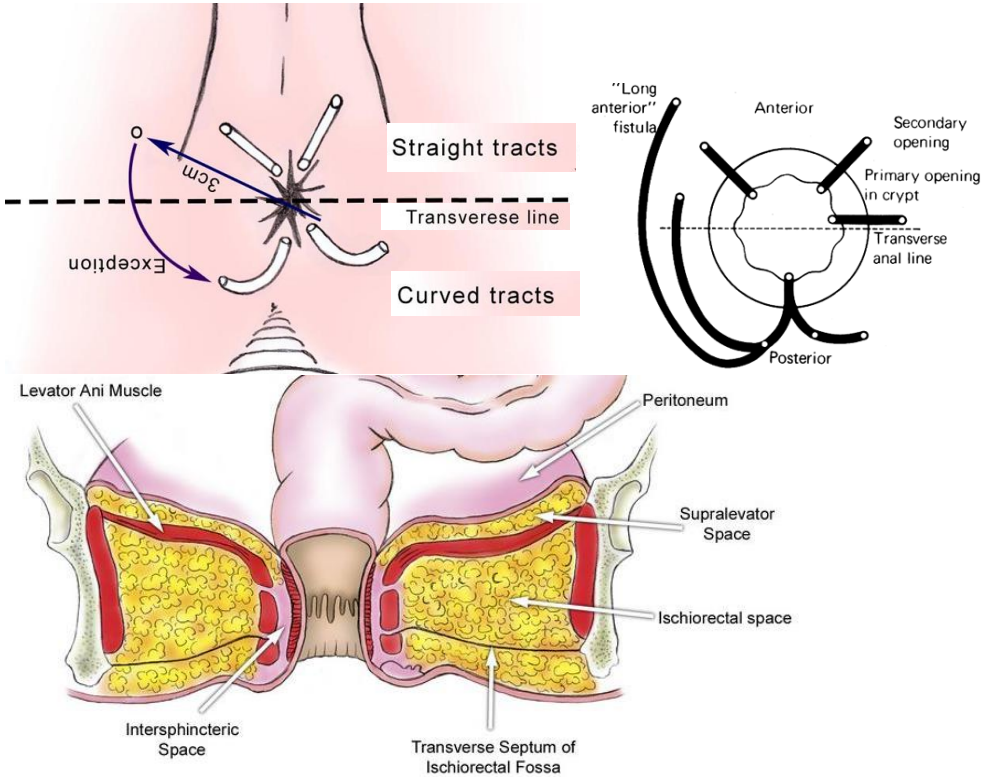
Grade 1 No prolapse, just prominent blood vessels	Conservative: • Lifestyle modifications → dietary fibre, oral fluids (water), stool softener, avoidance of straining during defecation • Meds → NSAIDs, Daflon (orange colour tablet, improves venous tone → 3tabs bd for 3/7 then 2tabs bd for 2/52)
Grade 2 Prolapse upon bearing down but spontaneously reduce	Surgery: • <u>Rubber band (elastic) ligation</u> → outpatient treatment, a small rubber-band is applied to the base of the haemorrhoids, made 1-2cm above the dentate line to avoid pain and infection → cut off blood supply to haemorrhoids causing them to shrink and then fall off Most patient should be able to return to work the day following the ligation procedure Note: warn patient that necrotic haemorrhoid would slough off in 3-5 days with bleeding occurring at that time (also, stop anticoagulant for 7 days after banding) Complications: failure of procedure (rubber band can't go in, rubber band slips out), new occurrence, recurrence, → because it is only possible to 'pinch off' a small portion of the pile at any one time, a large prolapsing haemorrhoid may require 2-3 repeat ligation 6 weeks apart to achieve the desired effects. • Injection sclerotherapy (phenol emollient oil) → involves injecting a chemical that scars the enlarged piles, reducing the blood-flow and thereby shrinking the haemorrhoids and alleviating symptoms
Grade 3 Prolapse upon bearing down and requires manual reduction	Acute Management of Grade 4 symptomatic haemorrhoids: • <u>Reduce size of haemorrhoids and arrange for prompt surgical consult</u> → use a hyperosmolar solution to reduce haemorrhoids size (i.e. **gauze with lignocaine gel + cold water + sugar** [or dextrose solution] and give patient daflon), aim to be able to manually reduce haemorrhoids back into anal canal first before further surgical intervention. Surgery: Haemorrhoidectomy • <u>Staple</u> → procedure performed by a circumferential excision of redundant rectal mucosa approx. 5cm superior to the dentate line using a specially designed circular stapler Most patient will be fairly comfortable within 1-2 weeks as opposed to 4-6 weeks healing time in conventional methods • <u>Excision</u> → procedure is performed with patient in prone flexed position, and the resulting elliptical defects are completely closed with chromic suture (Ferguson haemorrhoidectomy) Complications: 10-50% risk of urinary retention, bleeding, infection, sphincter injury, anal stenosis <u>Trans-anal Haemorrhoidal Dearterialization</u> → blood vessels supplying the haemorrhoids are located with a Doppler u/s and then tied off using surgical stiches
Grade 4 Prolapsed and cannot be manually reduced	

Grade	Diagram	Picture
1		
2		
3		
4		

ANAL FISTULA

Anal fistulae are abnormal communications, hollow tracts lined with granulation tissue connecting the primary opening inside the anal canal to a secondary opening in the perineal skin. They are usually associated with anorectal abscesses (obstruction of ducts → infection).





Conditions associated with multiple anal fistulas:

1. Crohn's disease
2. TB
3. Actinomycosis
4. Hidradenitis suppurativa

EPIDEMIOLOGY

- 9 per 100,000/yr (Western Europe)
- Commonly affect those in the 3rd – 5th decade of life

CLINICAL PRESENTATION

- Intermittent purulent discharge ± bleeding
- Pain – which increases till temporary relief occurs with pus discharge

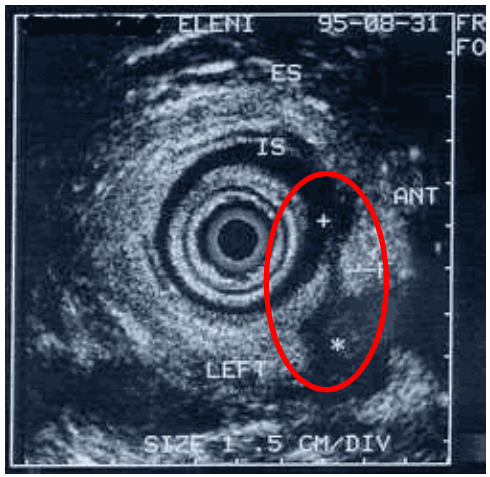
GOODSALL'S RULE

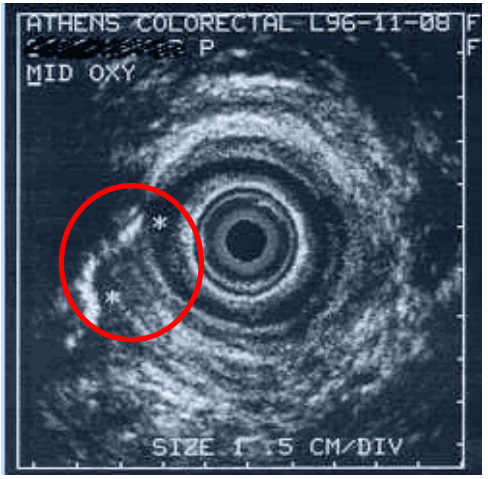
- For fistula within 3cm of the anal verge and posterior to line drawn through ischial spines if
  - Anterior to transverse anal line: straight radially directed tract into anal canal
  - Posterior to transverse anal line: curve tract open into anal canal midline posteriorly (at level of dentate line)

Tracts closer to anal verge = simpler, shorter
Tracts further away = transsphincteric, long, high tracts

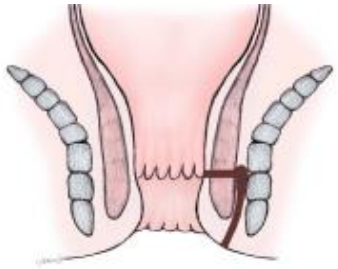
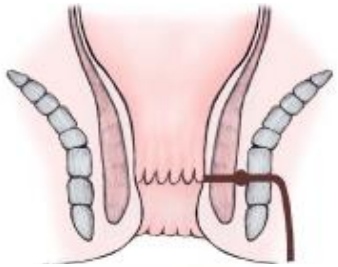
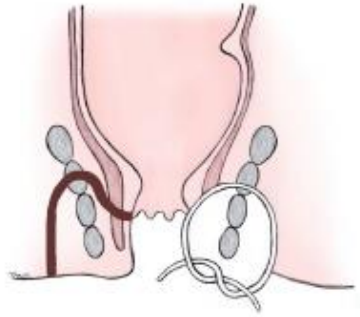
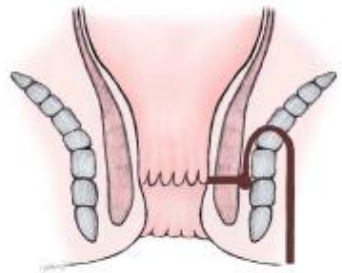
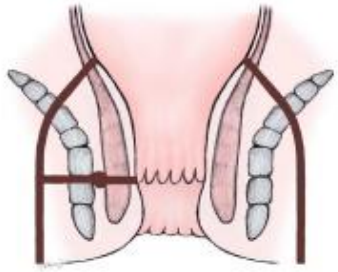
INVESTIGATIONS

- Endoanal U/S (H_2O_2 aided for hyperechoic effect) – to view course of fistula tract
- MRI – able to visualise entire pelvis, beyond the sphincter complex (gold standard)
- CT/fistulography (in emergency situation) – for complex fistulas / unusual anatomy





CRYPTOGLANDULAR THEORY OF PARKS / PARKS CLASSIFICATION

Type	Diagram	Management
Inter-sphincteric • The common course is via internal sphincter to the intersphincteric space and then to the perineum. • 70% of all anal fistulae • Other possible tracts include no perineal opening, high blind tract, and high tract to lower rectum or pelvis.		Fistulotomy • Division of the internal sphincter alone usually does not compromise faecal continence • Base of the wound is curetted and left open to heal by secondary intention
Trans-sphincteric • The common course is low via internal & external sphincters into the ischiorectal fossa and then to the perineum. • 25% of all anal fistulae • Other possible tracts include high tract with perineal opening and high blind tract	 	**Low:** Fistulotomy • On pts who have good pre-op anal sphincter function **High / anterior fistulae in women:** (Higher risk for post-fistulotomy incontinence) Conservative approach 1. Cutting seton • Reactive suture / elastic placed through the fistula tract • Tightening of seton tie sequentially until it cuts through the fistula tract 2. Partial fistulectomy & endoanal flap 3. Injection of fibrin glue
Supra-sphincteric • The common course is via inter-sphincteric space superiorly to above puborectalis muscle into ischiorectal fossa and then to perineum. • 5% of all anal fistulae • Other possible tracts include high blind tract (i.e. palpable through rectal wall above dentate line). • a/w drainage of ischiorectal abscess		Cutting seton Endorectal advancement flap Sphincter reconstruction
Extra-sphincteric • The common course is from perianal skin through levator ani muscles to the rectal wall completely outside the sphincter mechanism. • 1% of all anal fistulae • Not related to sphincter complex • a/w Crohn's, CA, recurrent fistulas		Endorectal advancement flap Laparotomy & resection of involved intestinal segment and curettage of fistula tract (for those fistulae from more proximal sections of the colon)

TREATMENT

- Puborectalis is the key to future continence
- Low fistula = lay open with fistulotomy or fistulectomy
- High fistula = require 2 stage surgery
- Seton – loose vs. tight
- Endorectal advancement flap can be considered

<u>Fistulotomy (for simple, short tracts) – cut & lay open tract to heal</u>

- A grooved probe is passed from the external to the internal opening and the track laid open over the probe
- Track is curetted to remove granulation tissue, the edges of the wounds are trimmed
- Wound may then be marsupialized

<u>Fistulectomy – core along tract & remove tract entirely</u>

- Coring out of the fistula with a diathermy cautery

<u>Seton – for complex, long, high tracts</u>

- Involves running a surgical-grade cord through the fistula tract so that the cord creates a loop that joins up outside the fistula → allow fistula to drain continuously while it is healing, rather than allowing the exterior of the wound to close over
- Setons can <u>be tied loosely</u> (long term palliation, temporary measure before surgical treatment as in Fistulotomy or Fistulectomy) <u>or tightly</u> (cut through tissue inside the loop while scarring behind the loop – i.e. pull out the fistula without surgery)

Anal Fissures

- Anal Fissures → a split in the anoderm (that is distal to the dentate line)
- Most common etiology of a primary anal fissure → Trauma
- 90% occurs in the posterior anal midline and 10% occur anteriorly

CLINICAL PRESENTATION

- Tearing pain with defecation
- Severe anal spasm that last for hours afterward
- Bright PR Bleed (usually noted on toilet paper or on surface of stool)
- Perianal pruritus and/or skin irritation

PHYSCIAL EXAMINATION

- Acute: superficial tear (usually posteriorly) – if lateral (consider secondary causes)
  - Patients often unable to tolerate DRE / Anal Speculum
- Chronic: hypertrophied with skin tags and/or papillae
  - Boat shaped
  - Punched out
  - Exposing internal sphincter
  - Sentinel skin tag
  - Hypertrophic anal papilla

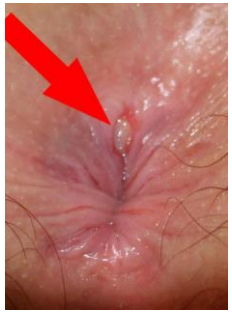
SECONDARY ANAL FISSURE

- Crohn's Disease (fissure in lateral position)
- Extra-pulmonary TB
- Anal Squamous Cell Cancer
- Anorectal Fistula
- Infections – CMV, HSV, chlamydia and syphilis

MANAGEMENT

- If a/w rectal bleeding → offer colonoscopy
- Most will heal because of good blood supply (within 1 day / 2 days)
- 90% of patients heal with medical treatment →
  - Lifestyle modifications (increased fibre)
  - Sitz baths
  - Topical nifedipine ointment
  - GTN paste
  - Botulinum toxoid injections

- If they don't heal, usually due to spasm of internal sphincter muscle → surgical management → lateral internal sphincterotomy (LIS) (90% successful)
- Recurrence and minor incontinence occur in < 10% of patients



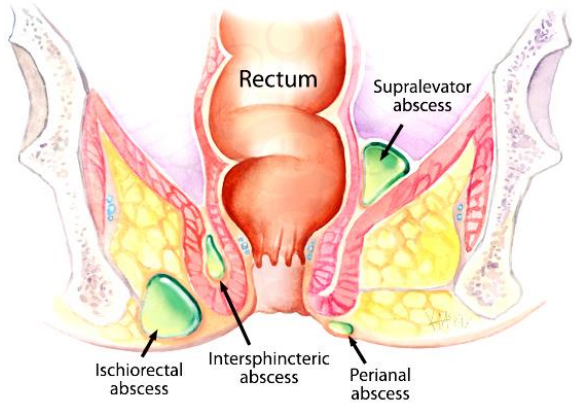
Anorectal Abscess

- Infection of the anal glands in the anal crypts at the denate line
- Initial abscess occurs in the inter-sphincteric space and can then spread:
  - Superficial to the external sphincter → Perianal space
  - Through the external sphincter → Ischiorectal space
  - Deep to the external sphincter → Supra-levator space

CLINICAL PRESENTATION

- Pain in the perianal area – classically dull, aching or throbbing, worse on sitting down and right before a bowel movement
- O/E → small, erythematous, well-defined, fluctuant, subcutaneous mass near the anal orifice

ANATOMICAL CLASSIFICATION



Perianal (60%)
Ischiorectal (20%)
Inter-sphincteric (5%)
Supra-levator (4%)

* common bacterial = E.coli, staphylococcus

TREATMENT

- Surgical drainage (with skin incision kept close to anal verge)
- ± Antibiotics – indicated only if patient is (1) immunocompromised, (2) diabetic, (3) have extensive cellulitis, (4) valvular heart disease
- Post-operatively: analgesics, stool bulking agents and stool softeners

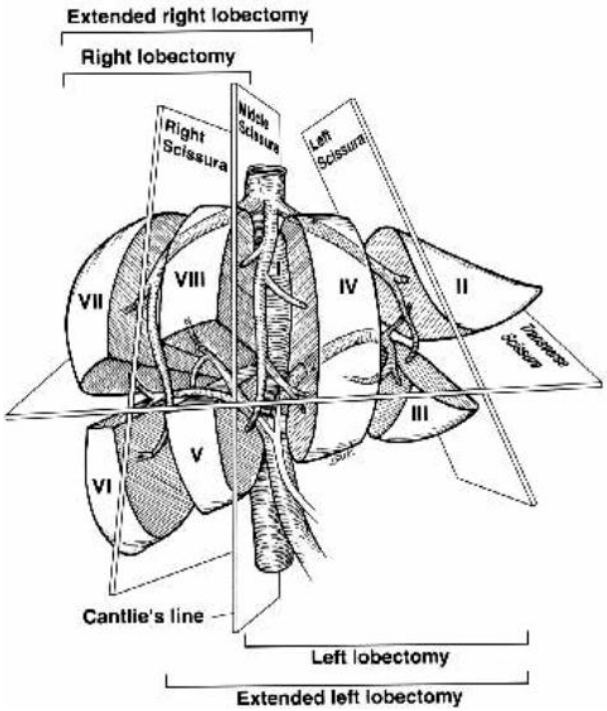
COMPLICATIONS

- Sepsis
- Anal Fistula – 40% of patients develop a chronic fistula

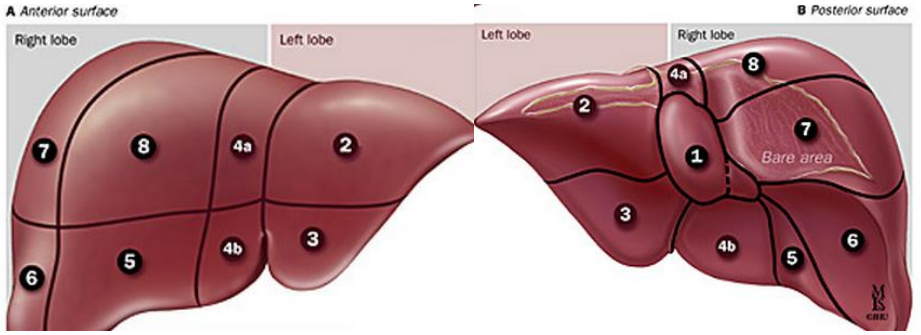
SURGICAL DISEASES OF THE LIVER

SURGICAL ANATOMY OF THE LIVER

- The liver is divided into two almost equally sized hemilivers, right and left → resection of a hemilivers is termed a *hepatectomy*
- The **anatomical division** of the liver lobes is demarcated by the falciform ligament → separate liver into right and left lobes (left: consists of segments II and III)
- The **functional division** (more practical in surgery) is demarcated by the plane of the gallbladder and inferior vena cava (**Cantlie's Line**, also by the plane in which the middle hepatic vein runs) →important for reading CT scans and in surgery



- The liver can be further divided into 8 functional segments (**Couinaud segments**) that each have their own vascular inflow, outflow, and biliary drainage, independent of the other segments → resection of a segment is termed a *segmentectomy*
- The segments are divided by one transverse plane and three sagittal planes
- The **transverse plane** is at the level of the main branches of the **portal vein**, and divides the liver into an upper half and a lower half
- The **sagittal planes** are formed by the three main **hepatic veins** (right, middle and left)



- **Segment I is the caudate lobe**
- **Segments II to VIII are named clockwise**, starting from the upper right corner (i.e. the upper left segment of liver)
- Segment IV can be further divided into IVa and IVb, where IVa is the superior sub-segment and IVb is the inferior sub-segment
- The liver has two blood supplies – **portal vein** (formed from the joining of the splenic vein and superior mesenteric vein) and **hepatic artery** (a branch of the coeliac trunk)
- Drainage is via the three hepatic veins into the inferior vena cava

OPERATIVE CONDUCT

Open Liver Resection	Achieved with bilateral subcostal incision with a midline extension to the xiphoid process (**Mercedes Benz Incision**) Vascular control can be augmented by intermittent occlusion of all hepatic inflow (**Pringle Manoeuvre**) or total vascular exclusion Post-operatively monitor - Frequent blood sugar measurement - Phosphorous level (support liver regeneration) - LFTs (hyperbilirubinemia is unusual but may occur) - INR (prolongation may develop ➔ give FFP to keep INR < 2.0 - Dosage of pain medication (adjusted as ↓ clearance of hepatically metabolized drugs) Complications - Intra-abdominal abscess - Bile leakage leading to bile fistula or localized collection (biloma) - Liver failure (insufficient residual functional hepatic parenchyma)
Laparoscopic Liver Resection	Multiple case series have demonstrated similar mortality (0.3%) and morbidity (10.5%) for laparoscopic when compared to open though no RCT has compared both surgical approaches.

Causes of Hepatomegaly

Physiological		Riedel's Lobe, Hyperextended Chest
Infective	Bacterial	Pyogenic Liver Abscess, Tuberculosis
	Viral	Hepatitis, EBV, CMV, HIV
	Protozoa	Malaria, Histoplasmosis, Amoebiasis, Hydatid , Schistosomiasis
Alcoholic		Fatty Liver, Cirrhosis
Metabolic		Wilson's Disease, Haemochromatosis, Infiltration – amyloidosis
Malignant		Primary / Secondary Solid Tumours, Lymphoma, Leukaemia
Vascular / Cardiac		Right Heart Failure (RHF), Tricuspid Regurgitation (pulsatile liver), Budd-Chiari Syndrome

Physiology of the Liver (functions)

Bile Production	- Bile is diverted from liver into the gallbladder due to high tone in the sphincter of oddi - CCK stimulates contraction of gallbladder and release of bile into the duodenum - Bile secretion is governed by 2 factors → enterohepatic circulation and another mechanism independent of this	
Metabolic Functions	**Carbohydrate**	- Glucose (delivered via portal vein) → glycogen (glycogenesis) - In time of need, glycogen → glucose (glycogenolysis)
	Protein	- In time of depleted glycogen: amino acids → glucose (gluconeogenesis) - Synthesis plasma proteins → albumin + clotting factors - Handles degradation of amino acid metabolism: (amino acids → ammonia → urea)
	Lipid	- Glucose → FFAs → transported to adipose tissue → combined with glycerol → stored as TG - In times of starvation → provide fatty acid glycerol for gluconeogenesis - Synthesis of lipoproteins and cholesterol
Clotting Factors / Protein Synthesis	- Synthesises all the plasma proteins (other than immunoglobulin)	
Vitamin D activation	- Activation of Vitamin D is a 2-stage hydroxylation process - Liver (first stage) → hydroxylation to give 25-hydroxycholecalciferol → - Kidney (second stage) → 1,25-hydroxycholecalciferol	
Detoxification	- Detoxify peptide hormones, steroid hormones, catecholamines, drugs, toxins	
Vitamin and Mineral Storage	- Stores → iron, copper - Stores → vitamin A,D,E,K,B12	
Phagocytosis	- Kupffer cells in the hepatic sinusoids remove bacteria, debris and old RBCs	
Haemopoiesis	- In disease states (i.e. chronic haemolysis) → extramedullary haemopoiesis	

* all soluble coagulation factors are manufactured in the liver with the exception of factor VIII (endothelium), calcium, platelet factors and thromboplastin

Disease of the Liver

Hepatic Neoplasm		
Benign	Haemangioma	
	Focal nodular Hyperplasia (FNH)	
	Hepatic Adenoma	
	Bile Duct Hamartomas	
	Cyst – if multiple: familial (polycystic) or non-familial	
Malignant	Primary	Hepatocellular Carcinoma (or hepatoma)
		Cholangiocarcinoma (only 10% intrahepatic) – presents like HCC except no background of cirrhosis
	Secondary	Colorectal, stomach, pancreas, breast, urogenital tract, lung
Hepatic Abscess		
	Pyogenic Abscess	
	Amoebic Abscess	
Hepatic Cyst		
Nonparasitic Cyst	Asymptomatic Cysts	
	Symptomatic Cysts	
	Polycystic Liver Disease	
Echinococcal Cysts	Hydatid Cysts	
Portal Hypertension		
Intrahepatic Obstruction	Cirrhosis	
	Hepatic Fibrosis	
	Hemochromatosis	
	Wilson's Disease	
Peri-hepatic Obstruction	Congenital Atresia	
	Portal Vein Thrombosis	
Post-hepatic obstruction	Thrombosis of hepatic Veins (Budd-Chiari Syndrome)	
	Congenital IVC malformation	
	IVC thrombosis	
	Constrictive Pericarditis	

LIVER HAEMANGIOMA

Hamartomatous outgrowths of endothelium made of widened (dilated) blood vessels rather than true neoplasms. Some of these tumours express oestrogen receptors.

EPIDEMIOLOGY[90]
- Prevalence 3% to 20%
- Female to male ratio 5-6:1 (middle-aged women)
- Most common benign liver tumour

PATHOGENESIS
- Vascular malformation that enlarges by ectasia, congenital in origin (poorly understood)

PRESENTATION
1. Usually asymptomatic, found incidentally
2. Pain from liver capsule stretch – nonspecific upper abdominal fullness or vague abdominal pain (larger lesions, > 5cm)
3. Mass effects compressing on surrounding organs
4. Life Threatening Haemorrhage – ppt. by needle biopsy (extremely uncommon)
5. Heart failure from large arteriovenous shunt
6. **Kasabach-Merritt syndrome** for large haemangioma – rare consumptive coagulopathy, thrombocytopenia (sequestration of platelets and clotting factors in a giant haemangioma) → treat with urgent resection (rare disease, usually of infants)

DIAGNOSIS
- DO NOT BIOPSY (risk of severe haemorrhage)
- Imaging Investigations
- **Ultrasound (accuracy 70-80%)**
  - well defined, lobulated, homogenous, hypoechoic masses
  - **compressibility of the lesion** is pathognomonic
- **Computed tomography (CT) – triphasic CT**
  - low density area with characteristic peripheral enhancement in early phase
  - contrast enhancement progress towards the centre
  - **tumours appears brightest and uniformly enhanced in delayed phases**
- **Gadolinium enhanced magnetic resonance imaging (MRI)**
  - bright on T2-weighted images

TREATMENT
- Majority treated safety with **observation**
- For symptomatic or complicated lesions → surgical removal
  - Enucleation under vascular control (intermittent Pringle manoeuvre)
  - Formal anatomical resection (i.e. right hepatectomy)
- Large, unresectable lesions → low dose radiation therapy or embolization

[90] The Washington Manual of Surgery (p346)

HEPATIC ADENOMA[91]

Benign proliferation of hepatocytes – not to be confused with 'hepatoma' which refers to HCC

EPIDEMIOLOGY / RISK FACTORS
- Female to male ratio 10:1 (found in young women)
- a/w: anabolic steroids, oestrogen & progesterone preparation (i.e. OCP)

PRESENTATION
- Asymptomatic
- Symptomatic → **spontaneous rupture and intra-peritoneal haemorrhage**
  - Between 25-35% will rupture with nearly 100% of ruptures occurring in lesions >5cm[92]
  - Require close observation during pregnancy
  - Others symptoms: abdominal pain, vague symptoms of fullness / discomfort in the RUQ
- Increased risk of malignant transformation

DIAGNOSIS
- **Computed tomography (CT) – triphasic CT**
  - Early enhancement starting from peripheries with centripetal progression

TREATMENT
- **Surgical Resection – indications**
  - Lesion > 5cm in diameter
  - Lesion that fail to shrink after discontinuation of OCPs
  - Patient who cannot stop OCP (for medical reasons) with HA >5cm

[91] The Washington Manual of Surgery (p346)
[92] Ann Surg Oncology 2009;16(3):640-648

HEPATOCELLULAR CARCINOMA[93]

EPIDEMIOLOGY
- Annual incidence in Singapore is 18 / 100,000 in males & 4.6 / 100,000 in females
  - 4th most frequent cancer among males, not in top 10 among females (M:F = 2-3:1)
  - 3rd most frequent cancer death among males and 4th among females
- Worldwide: 6th most prevalent cancer and 3rd most frequent cause of cancer-related death
- HCC diagnosed mainly in the fifth and sixth decade
- 1° liver cancers are mainly HCCs (85%), with a small proportion of intrahepatic cholangiocarcinoma (6%)

AETIOLOGY AND RISK FACTORS
- HCC develops within an established b/g of CLD in 70-90% of all patients
- HBV infection a/w increased risk of FCC because of DNA damage induced by HBV integration → this can be prevented with HBV vaccination

1. Alcoholic Cirrhosis

2. Non-Alcoholic Cirrhosis
- Non-alcoholic Steatohepatitis (NASH) or non-alcoholic fatty liver disease
- Infection / Hepatitis
  - Chronic Hepatitis B – high HBV DNA load, HBeAg positivity increase the risk
  - Chronic Hepatitis C – accounts for 1/3 of HCC in USA
- Autoimmune
  - Primary Biliary Cirrhosis
  - Secondary Biliary Cirrhosis
    - ⇨ Chronic obstruction of the biliary tree (secondary to PSC) – usually cause cholangiocarcinoma but can also cause HCC
    - ⇨ Recurrent infection in the biliary tree – recurrent pyogenic cholangitis
    - ⇨ Recurrent stricture formation (iatrogenic injury) – lead to secondary BC
- Metabolic
  - Hemochromatosis – increased risk of between 20 to 219x[94] (HH patients with HFE gene)
  - Wilson's Disease
  - Alpha 1 Antitrypsin Deficiency
- Others
  - Diet – red meat & saturated fats
  - Aflatoxins B1 (mouldy peanuts / corn / soybeans) – linked with p53 mutation
  - Diabetes – independent RF for HCC[95]
  - Smoking
  - Alcohol – synergistic effect in individuals with chronic HBV/HCV

PATHOLOGY
- Pathogenesis involves a chronic inflammatory process or on-going hepatocellular damage with high cellular regeneration, which leads to increased rates of genetic mutation in the cells and accumulation of these mutations leading to carcinoma formation
- Two histological subtypes:
  - **Non-Fibrolamellar** – associated with HBV and cirrhosis
  - **Fibrolamellar (FLC)** – associated with younger patients (20-40 years old), equal gender distribution, no association with hep B or cirrhosis, 70% resectable, good prognosis (5 yr. survival rate >70%)
- Metastasises to **lymph nodes, bones, lungs and adrenals**

Liver Cirrhosis
- End stage of chronic liver disease characterized by 3 main morphological characteristic (1) bridging fibrosis (2) regenerative parenchyma nodule and (3) disruption of liver architecture
- Patients with cirrhosis are at high risk of developing HCC → recommended ultrasonography 6/12 and measurement of serum AFP

- A model to predict prognosis in patients with cirrhosis is the Model for End Stage Liver Disease (MELD) score
  - 3.8 x $\log_e$ **serum Br** (mg/dL)
  - 11.2 x $\log_e$ **INR**
  - 9.6 x $\log_e$ **serum Cr*** (mg/dL)
  - 6.4 (constant for **liver disease etiology**)

* If patient has been dialysed twice within the last 7 days, then the value for serum Cr should be 4.0

- MELD score → adopted for use in prioritizing patients awaiting liver transplantation and has an expanding role in predicting outcomes in patients with liver disease in the non-transplantation setting
  - MELD score between 6-40 are considered for transplantation allocation in USA
  - With TIPSS best outcomes with score <14 and poor outcomes with score >24

[93] Lancet 2012; 379:1245-55
[94] Genetics in Medicine (2009) 11, 307–313
[95] N Engl J Med 2011; 365:1118-27

PRESENTATION

1. Asymptomatic

- During screening (ultrasound) for chronic hepatitis B carrier
- Investigations for liver cirrhosis
- HCC need not present with decompensated chronic liver disease
- Incidentally found on imaging of the abdomen

2. Local signs & symptoms

- Upper abdominal pain – dull and persistent (2° to capsular distension)
- Hepatomegaly
- Early satiety/ vomiting (likely 2° to compression)
- Constitutional: LOW, LOA, malaise (80% of patients)
- Pyrexia (central tumour necrosis)
- Budd-Chiari syndrome: occlusion of the hepatic, intrahepatic or portal vein causing portal hypertension & congestive hepatopathy
- Jaundice (5-10%)
  - Cholestatic: invasion/compression of intrahepatic ducts or extrahepatic compression by metastatic LN
  - Hepatic: a/w pre-existing cirrhosis or acute flare of chronic hepatitis

3. Tumour rupture (<3%)

- Severe abdominal pain (peritonism), pallor with shock [ddx: ruptured AAA]
  - 50% mortality; Rx with TAE; reports of peritoneal seeding in survivors
- US +ve for peritoneal fluid, FAST +ve for blood

4. Features of decompensated chronic liver disease

- Worsening liver function (hepatic encephalopathy (see below), jaundice – yellow sclera and skin, coagulopathy – purpura, ascites – shifting dullness and fluid thrill) → suspect HCC when there is decompensation of liver cirrhosis
- Hepatorenal syndrome in late stages of liver failure
  - Functional form of ARF in a patient with advanced liver disease due to cirrhosis (or acute liver failure, alcoholic hepatitis, metastatic liver disease) in the absence of identifiable renal pathology
  - Caused by intense vasoconstriction of renal circulation → renal hypoperfusion
  - Leads to ↓ GFR, ↓ urine o/p and ↓ urinary sodium excretion

5. Features of Portal Hypertension

- Ascites, LL oedema, haematemesis & melena 2° to bleeding varices
- Congestive splenomegaly, secondary hyper-splenism (can cause peripheral blood cytopenias), caput medusa, venous hum, hepatic encephalopathy

6. Metastases (low incidence in HCC, mortality rarely from mets)

- Bone pain, Dyspnoea

7. Paraneoplastic syndromes

- Hypoglycaemia (high metabolic demands of tumour)
- Erythrocytosis (tumour produces erythropoietin)
- Hypercalcaemia, watery diarrhoea etc.

Stages of Hepatic Encephalopathy (West Haven Classification)[96]

0	Lack of detectable changes in personality or behaviour
1	Shortened attention span, impaired addition or subtraction, hypersomnia, insomnia or inversion of sleep pattern, euphoria or depression, asterixis can be detected
2	Lethargy, inappropriate behaviours, slurred speech, obvious asterixis
3	Gross disorientation, semi-stupor to stupor, bizarre behaviours
4	Coma

CAUSES OF HEPATIC ENCEPHALOPATHY

1.	Bleeding GIT	Blood-meal = high protein = high nitrogenous waste product for liver to handle = can precipitate hepatic encephalopathy
2.	Infections	- Spontaneous Bacterial Peritonitis (SBP) - Sepsis → Pneumonia, UTI
3.	Drugs	- Benzodiazepam (especially if patient have noted liver dysfunction) - Opioids - Diuretics – can case electrolyte imbalances
4.	Electrolyte Imbalances	- Na/K abnormalities (sudden changes) – i.e. vomiting (hypoK+) - Large volume paracentesis (>3-5L will result in hypokalaemia)
5.	Others	- High Protein Diet - Constipation - Transjugular intrahepatic portosystemic shunting (TIPSS) - Catabolic States → surgery, trauma

[96] Am J Gastroenterol. Jul 2001;96(7):1968-76.

INVESTIGATIONS

"I would like to do investigations to obtain (1) diagnosis. My (2) second set of investigation is to stage the disease to identify if it is locally or systemically invasive and to evaluate the severity of the underlying liver disease. This is crucial as surgical oncology is for local control. I would then (3) do investigations to look for complications of the disease and other pre-operative investigations. "

Diagnostic Approach[97] [EASL guidelines – 2012]

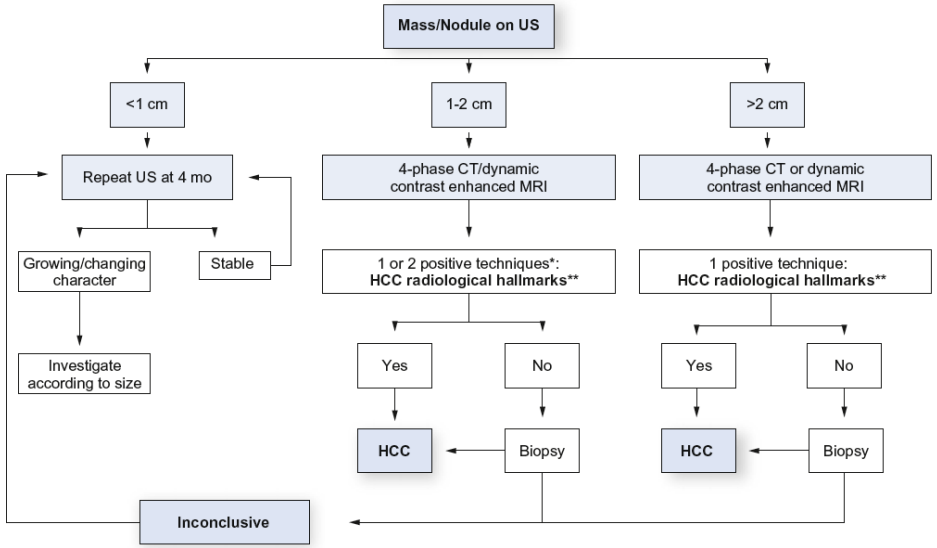


Fig. 2. Diagnostic algorithm and recall policy. *One imaging technique only recommended in centers of excellence with high-end radiological equipment. **HCC radiological hallmark: arterial hypervascularity and venous/late phase washout.

A. Triphasic CT scan (with arterial and portal venous phase contrast imaging) – GOLD STANDARD
   a) **Arterial Phase** – early enhancement, lesions are hyper-dense relative to hypo-dense hepatic parenchyma (aorta [& HCC, bleeds] lights up, IVC and portal vein are dark)
   b) **Portal Venous Phase** – most CT scans taken at this phase, majority of contrast flow into portal vein and liver (liver is bright), tumour will look dull (wash out) – tumour washout defined as hypo-intensity of a nodule in the delayed phase as compared with surrounding hepatic parenchyma
   c) **Delayed Phase** – progressive decrease in contrast intensity of the lesion, scan may show a tumour capsule which is a specific sign indicating HCC

- Radiological hallmark (HCC): arterial hypervascularity and venous/late phase washout
  - Haemangioma: capsular enhancement in delayed phase
  - Metastasis: enhancement in portal venous phase
- In a patient with hepatitis B/C and raised AFP, a liver lesion on imaging should be considered HCC until proven otherwise
- CT can also look for nodal involvement, and metastases to the adrenals

B. Alpha-Feto Protein (AFP) and Hepatitis Markers
- AFP has been dropped from the diagnostic scheme
- AFP has important prognostic implications – i.e. AFP > 1000 have high risk of recurrent disease following transplant regardless of tumour size
- When used as a diagnostic test, AFP levels (20 ng/ml) show good sensitivity but low specificity
- A rise in serum AFP in a patient with cirrhosis should raise concern that HCC has developed
- **False +ve:** pregnancy, infants, cirrhosis, hepatitis, teratoma, gastric cancer
- Hepatitis Markers to look for carrier status

C. MRI Scan (dynamic, contrast-enhanced)
- Most accurate imaging modality for distinguishing HCC from dysplastic or regenerative nodules in **cirrhotic** patients
- HCC appears highly intense on T_2 images and low intensity pattern on T_1 weighted images
- Used if patient has contrast allergy (contraindication to CT scan)
- Adjunct investigation done when CT findings are equivocal

D. Ultrasonography
- Accurate in detection of HCC especially when coupled with concomitant AFP elevation

E. Histology
- If required, laparoscopic or image guided percutaneous biopsies can be used to obtain tissue diagnosis – pathological hallmark (HCC): stromal invasion
- Tissue diagnosis is not required before therapeutic intervention if other modalities favour HCC as the diagnosis

F. Hepatic angiogram with lipiodol and post-lipiodol CT scan
- Lipiodol will be retained in HCC even after many days as the HCC does not contain Kupffer cells to ingest lipiodol
- Hepatic angiogram may reveal abnormal blood vessels within the HCC
- CT scan of the liver weeks after lipiodol ingestion will pick up the areas of tumour (where the pre-lipiodol CT may not have demonstrated the tumour clearly) – to evaluate effectiveness of treatment

[97] Journal of Hepatology 2012 vol. 56 j 908–943

Staging Studies

A. Liver Function Test (LFTs)

- For staging and prognosticating (CHILD'S scoring classification)
- (A)lbumin (B)ilirubin (C)oagulation (D)istension (E)ncephalopathy
    a) Class A = 5-6 points (better survival function)
    b) Class B = 7-9 (still amenable for resection)
    c) Class C = 10-15 (not for resection – offer local ablative treatment)

Child-Pugh classification of CLD/cirrhosis

1) Prognosis – as it helps to quantitate residual liver function
2) Strength of medical treatment
3) Necessity of liver transplant

Points	1	2	3
Albumin (g/L)	>35	28-35	<28
Bilirubin (μmoles/L)	< 34	35-50	>51
(mg/dL)	<2.0	2.0-3.0	>3.0
Coagulopathy (INR)	<1.7	1.70- 2.3	>2.3
(PT – sec prolongation)	<4.0	4.0-6.0	>6.0
Distension (ascites)	None	Slight - mod	Severe/refractory
Encephalopathy	None	Grade I – II	Grade III-IV

Child's	A(5-6)	B(7-9)	C(10-15)
1 year survival %	100	80	45
2 year survival %	85	60	35
Disease status	Well compensated disease	Significant functional compromise	Decompensated liver disease, consider transplant
Treatment in concomitant HCC	Resection of up to 4 segments	Maximum resection of 2 segments	Consider transplant

B. CT TAP

- CT thorax – identify any lung metastasis
- CT abdomen / pelvis – identify locally recurrent / synchronous colonic cancer
    - can also do colonoscopy if suspect primary colon cancer
    - Look also for mets to **liver, adrenals, peritoneum and LNs.**

C. Bone Scan – identify any bone mets

Complications and Pre-operative Investigations

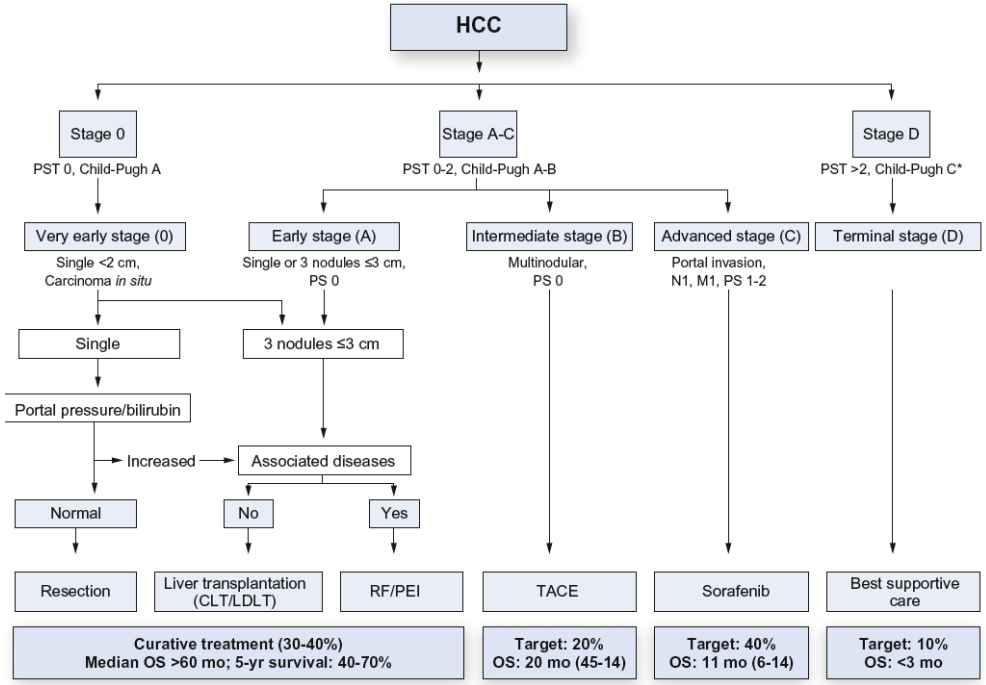
A. Basic Laboratory Investigations

- **FBC** (low Hb from BGIT, raised TW in SBP)
- **U/E/Cr** (dehydration, 3rd spacing of fluids, use of diuretics for ascites, r/o nephropathy for contrast imaging)
- **PT/PTT** (also part of CHILD's scoring)
- **GXM**
- (if indicated – looking for GI primary) – CEA, CA19-9, colonoscopy

B. Fitness for Surgery

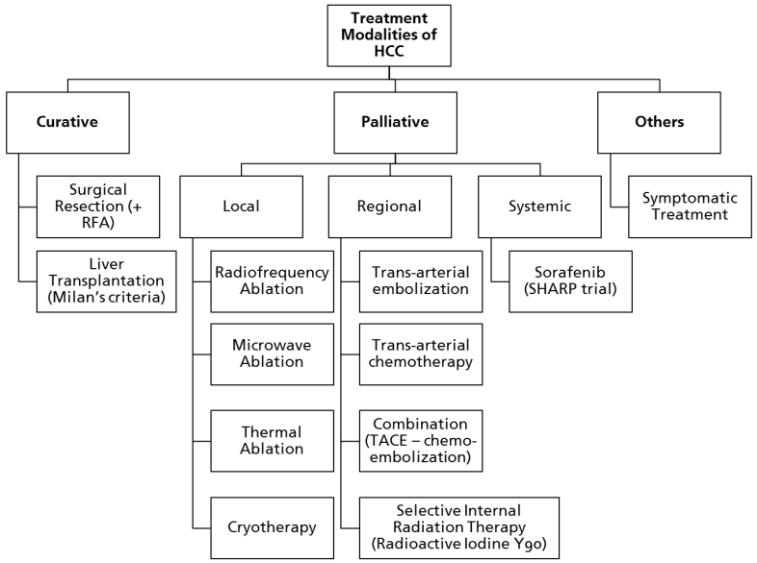
- **ECG**
- **CXR** (if CT thorax not done)

TREATMENT



[98] *PST = performance status test = ECOG score

Fig. 3. Updated BCLC staging system and treatment strategy, 2011.



[98] Journal of Hepatology 2012 vol. 56 j 908–943

1. CURATIVE SURGERY (achieve tumour removal with good liver function)

- **2 surgical possibilities:**
  - **Resection** of tumour (partial hepatectomy) + RFA
  - Liver **transplantation**
- Surgical Resection is the treatment of choice for non-cirrhotic patients with HCC
- Only about 10-20% of patients with HCC will have disease amenable to surgery
- The **only curative treatment** for HCC is surgical removal of the tumour
- 5 year survival rates for patients with HCC treated with resection is 40-50% with recurrence rate 40-50%
  - Poor prognostic factors: micro vascular invasion, multi-nodular tumours

1A. Hepatectomy

- Problem in patients with cirrhosis is that there is already a **"field-change"** effect in the liver, thus a new tumour can still develop in the remnant liver
- Requires a fine balance between **adequate resection margins (1cm is adequate)** and **preservation of sufficient functional liver** to prevent liver failure
- Good immediate and short-term results, but not long term due to occurrence of new primaries in the cirrhotic liver

1B. Liver Transplantation

- **Milan criteria** for transplantation (>75% 5-year survival if followed)
  (a) Single tumour ≤ 5cm, max 3 total tumours with none > 3cm
  (b) No evidence of gross vascular invasion
  (c) No regional nodal or distant metastasis
- **University of California, San Francisco (UCSF) criteria**:
  (a) Single tumour <6.5cm, max 3 tumours with none >4.5cm & cumulative tumour size <8cm
- **Barcelona Clinic Liver Cancer Group criteria**:
  (a) Single tumour <7cm, 3 tumours <5cm, 5 tumours <3cm OR:
  (b) Down-staging to conventional Milan criteria with pre-transplant adjuvant therapies (controversial)
- **MELD score** (see above)
- Problems with availability of donor organ – the disease might have progressed past being suitable for transplant by the time donor organ is available
  - Possibility of **"bridging therapy"** such as RFA, TACE, Yttrium-90 to shrink disease and prevent progression until donor liver is available
- In hepatitis B carriers, there is a risk for reinfection of the donor liver (high risk factors are HBeAg positivity, high HBV DNA levels) – can be aggressively treated with **anti-viral drugs** 2 months before transplant and **anti-HBV immunoglobulin** long-term after transplant

Factors affecting resectability:

1. Stage of Disease

- Metastatic disease is not suitable for resection
- Multi-centric disease affecting both lobes is a contraindication to hepatectomy

2. General fitness for operation

3. Liver function pre-operatively

- Cirrhotic patients have increased risk of post-operative mortality (4-14%) compared to non-cirrhotic patients (0-4%) due to complications such as liver failure, bleeding and infection
- Use of **indocyanine green** (ICG) – the percentage of ICG remaining in the liver after 15 minutes indicates the level of liver function. If **>15% remains after 15 minutes,** the patient cannot tolerate major liver resection (>3 segments removed)
- CT volumetry: residual liver function calculated with a CT liver scan via a computer programme
- If patient has cirrhosis, assess Child's status → **Child's A** and **good Child's B** = KIV resection

4. Residual liver function post-operatively (at least 20%)

- Dependent on tumour size and how much of the liver it takes up, as tumour is non-functional
- A large tumour taking up most of the liver segments being resected translates to smaller amount of functional liver tissue being resected, while a small tumour means that more functional tissue is removed with the same resection margins

5. Degree of portal hypertension

- Resection of the liver results in worsened portal hypertension since the effective portal venous capillary bed has decreased → increased resistance to flow

6. Location of tumour

- Has to be located in a suitable location for resection

2. PALLIATIVE THERAPY

2A. Local

- Radiofrequency ablation (RFA) – best results for loco-regional strategies
    - Option for patients with early stage HCC not suitable for resection or transplant
    - Can also be for down staging tumours with subsequent liver transplant
    - A needle electrode is placed in the tumour, destroying tissue by heating it to temp of 60 to 100 deg.
- Percutaneous ethanol injection (PEI)
- Microwave / Thermal Ablation
- Cryotherapy / Cryoablation

2B. Regional

- Trans-arterial chemoembolization (TACE)
    - Selective intra-arterial administration of chemotherapeutic agents followed by embolization of major tumour artery
    - Enter from groin (femoral artery) with guide-wire going up to the aorta (look for celiac axis) and then enter hepatic artery
    - Inject contrast will light up tumour (neovascularization which appears as corkscrew organised vessels)
    - Contraindications – portal thrombosis, both blood supply decrease leading to worsening liver function
    - Complications
        1. Fever (secondary to cytokine release as a result of tumour lysis – TNF alpha, IL-1), abdominal pain, nausea, vomiting
        2. LFTs – deranged raised ALT and AST (reflection of ischemic hepatitis) – hepatic failure due to infarction of adjacent normal liver (TACE should not be used for Child's class C cirrhosis)
    - Requires a repeat CT (triphasic) 1/12 later to evaluate effectiveness of treatment
- Trans-arterial embolization (TAE)
- Selective Intrahepatic Radiation – Yttrium-90 radioactive beads injected into hepatic artery, irradiating the tumour

2C. Systemic

- Limited results; Sorafenib, 200mg BD, (multi-kinase inhibitor) improves median survival and time to radiologic progression by 3 months compared to placebo – SHARP trial[99]
    - Have anti-angiogenic and anti-proliferative properties
- Sorafenib used in combination with TACE in advanced primary HCC – superior to Sorafenib monotherapy – ?impact on overall survival

Without treatment, HCC have a very poor prognosis with median length of survival of 3 to 6 months after diagnosis

[99] N Engl J Med. 2008 Jul 24;359(4):378-90.

Liver Metastases

- Still more common than primary liver tumour for malignancy occurring in the liver
- Primaries: **Colorectal, gastric, pancreatic, urogenital, breast, lung**

COLORECTAL CANCER METS TO LIVER

- Approx. 50% of all patients with colorectal cancer develop metastases, 1/3 have isolated colorectal liver metastases
- Without treatment (i.e. partial hepatectomy) median survival is 6 – 12 months.
- In contrast, resection of hepatic mets a/w 25-45% 5-yr survival rate and a 20% 10-yr survival rate (must exclude the presence of extra-hepatic disease)
- For unresectable hepatic colorectal mets → multi-drug systemic chemotherapy or local ablation with radiofrequency ablation
- Post-operative follow-up: serial PE, serum CEA level, CT AP every 3-4/12 for first 2 years, then every 6 months for subsequent 3 years
    - Recurrence of liver mets → repeat hepatic resection

OTHER LIVER METASTASES

- GI neuroendocrine hepatic mets → hepatic resection
- Presence of hepatic mets from melanoma or cancer of the breast or stomach → disseminated disease → hepatic resection is not recommended

PRESENTATION DEPENDS ON SITE OF METASTASIS

	Mets to liver parenchyma	Mets to porta hepatis LN
Hx	- Incidentally found on follow up (for cancer) - Hard mass - Heaviness - Pain from rupture	- Symptoms of obstructive jaundice ▪ Yellow sclera ▪ Tea-coloured urine ▪ Pale stools
P/E	- Hard, irregular nodular hepatomegaly - Jaundice is a late sign	- Jaundice early, progressive - Hepatomegaly may not be present
Invx	- Both obstructive and transaminitis picture	- Obstructive picture in early stages

* Isolated porta hepatis metastasis without liver involvement is extremely rare

INVESTIGATIONS

MRI

- Low intensity lesion on T1 weighted images
- Intermediate intensity on T2 weighted images

Triphasic CT

- **Hypodense on arterial phase** (as metastases are usually hypo-vascular compared to hypervascular HCC; spread via portal vein)
- **Increasing contrast uptake on portal venous and delayed phases**

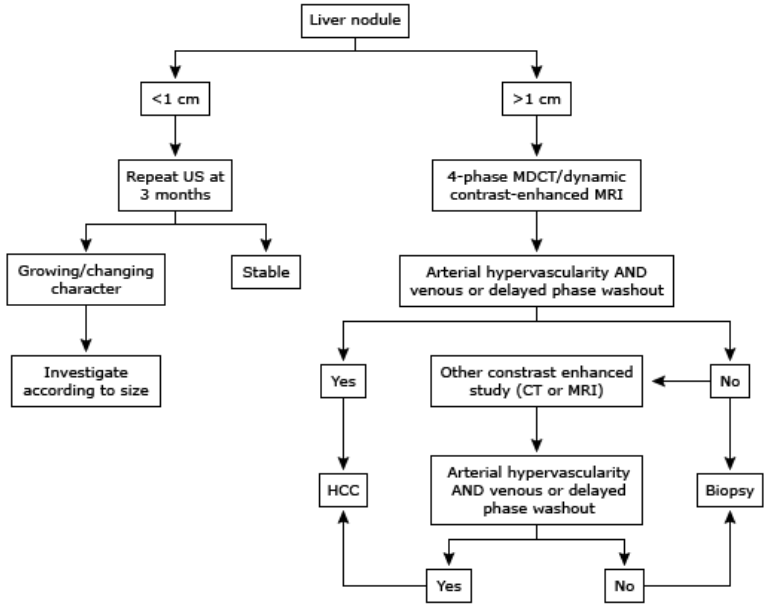
ROLE OF SURGERY

- Promising results with colorectal and neuroendocrine metastases if isolated resectable metastatic disease
- Increasing role in urogenital, breast mets
- Poor results for stomach, oesophageal mets
- Palliation for symptoms in neuroendocrine metastases

Screening for Chronic Hepatitis Carriers

"Early detection and treatment of HCC is the sole option to achieve long-term disease free survival"

- Combination of **6/12 to yearly ultrasound with AFP levels**
- US is operator dependent & may miss certain areas of the liver where imaging is difficult, but it is not associated with radiation exposure – sensitivity of 60-80% and specificity >90%
- AFP is also not a perfect screening test as 20% of HCC will not have raised AFP – even with the most efficient cut-off (10-20 ug/L), diagnostic accuracy is around 60%[100]
- Combination of ultrasound and AFP can increase the sensitivity and specificity of screening
- Frequency of screening is controversial, but should be increased in patients at increased risk – HbeAg positivity, high HBV DNA levels
- Important as it detects smaller and resectable HCCs → increasing survival from 26 to 88/52
- **Screen family** for chronic hepatitis B carrier status especially if there is a family history! – e.g. mother had hep B/HCC, sibling has hep B, etc.



[100] Gastroenterology 2010; 138:493-502

HEPATIC ABSCESS (PYOGENIC)

Pus-filled area in the liver (usually in the right lobe, 2:1)[101] occurring secondary to other sources of bacterial sepsis – possible organisms includes: klebsiella, E. coli, proteus vulgaris, streptococcus milleri/fecalis, staphylococcus epidermidis, bacteroides fragilis,

ROUTES OF INFECTION

- **Direct spread of bacterial** from biliary system infections (ascending cholangitis, empyema of gallbladder) – 60% of cases
- **Intra-abdominal source** through portal vein – acute appendicitis, diverticulitis, IBD – Crohn's disease, pancreatitis, pelvic abscess
- **External inoculation** – iatrogenic (radiofrequency ablation), traumatic
- **Haematogenous** spread in sepsis e.g. infective endocarditis

PRESENTATION

- **Spiking Fever** with chills (90% of patients)
- **Abdominal Pain** (RHC pain due to capsular stretch) – 50-75% of patients
- Jaundice, and Hepatomegaly – 50% of patients
- Nonspecific symptoms – anorexia, anemia, weight loss (possible malignancy), pain radiation to shoulder, cough/hiccups (diaphragmatic irritation), malaise, diaphoresis
- RF: elderly, diabetics, immunocompromised patients, liver transplant, underling hepatobiliary pancreatic disease

INVESTIGATIONS

- Haematological
  - FBC (leucocytosis – marker of inflammation)
  - CRP / ESR / ± Pro-Calcitonin
    - ⇨ Trend the values to monitor for treatment response
  - LFTs – deranged (marker of severity)
    - ⇨ ALP – 5 sources (liver – heat stable, bone – heat liable, placenta, kidney and intestines)
  - Renal Panel (urea and Cr – assess hydration status and fitness for contrast CT scan)
  - UFEME – check for pyuria
  - Blood / Pus Culture
  - Tumour Markers (AFP, CA19-9, CEA – may resemble infected tumour on imaging)
- Imaging
  - Chest X-Ray (erect, anterior-posterior) – practical for anyone > 40
    - ⇨ Elevation of right hemi-diaphragm
    - ⇨ Infiltration at right lung base
    - ⇨ Right sided pleura effusion
  - Ultrasound Hepato-biliary System (HBS) – exclude liver tumour
    - ⇨ Septations, hypoechoic rim
  - CT scanning (definitive diagnosis) – exclude liver tumour
    - ⇨ Findings: Irregular lesion with central area of necrosis, air-fluid levels, may be multiloculated.
    - ⇨ Rim-enhancing appearance on triphasic CT scan.
- Diagnostic
  - Aspiration (for culture and sensitivity) – reflects origin of infectious process
    - ⇨ **Mixed species** (most common)
    - ⇨ Gram –ve bacilli (i.e. klebsiella) and enterococci suggests biliary tree source
    - ⇨ Staphylococcus or Streptococcus milleri suggest haematogenous seeding
  - Amoebic serology, PCR **Stool** ova, cysts and parasites – suspicious for amoebic abscess if patient recovering from chemotherapy or have recently travelled to an endemic area in the preceding 6 months.
  - ± Melioidosis Serology
  - **Patients >60yrs** with **DM** & **K Pneumoniae PLA** (w/o apparent underlying hepatobiliary disease) → colonoscopy to r/o colonic malignant lesions[102]
  - Incidence of GI cancers (i.e. colonic, small intestine, biliary tract & pancreatic) was increased 4.3 fold among patients with PLA compared with controls[103]

TREATMENT

1. Resuscitate if necessary
2. Close monitoring of vitals with strict IO charting
3. Watch for complications – i.e. klebsiella endophthalmitis
   - Especially in patients with diabetes along with K. pneumoniae induced pyogenic liver abscess complaining of ocular symptoms
   - If patient c/o BOV = requires prompt eye referral
4. Antibiotics via PICC (for abscess < 3cm)
   - Empirical antibiotics – IV **ceftriaxone** 1gm 12 hourly + **metronidazol**e 500mg 8 hourly
   - Change to definitive antibiotics when blood c/s results return
   - Total duration of 4-**6 /52**
5. Drainage
   Drainage if >3cm – open, laparoscopic or percutaneous

Percutaneous Drainage	Open drainage (OD)
- Radiologically guided - Can be done under LA - May require multiple attempts if unable to completely drain pus (either tube blocked by necrotic tissues or presence of septations) - Drains are left in place until drainage becomes minimal (roughly 7 days) Contraindications: ▪ Ascites (pus can leak into peritoneal cavity) ▪ Uncorrected coagulopathy ▪ Proximity to vital structures	- Gold standard of care - Invasive procedure, done under GA - Single procedure - Not dependent on location Indications: ▪ Concomitant pathology requiring surgery e.g. gall stones ▪ Multiple abscesses or multiloculated abscess ▪ Immunocompromised patient ▪ Failed percutaneous drainage (tube blocked, or patient not getting better) ▪ Ascites ▪ Ruptured abscess
Laparoscopic Drainage (LD)	
Laparoscopic drainage of liver abscesses may be an alternative to open surgical drainage minimizing the adverse effects of open surgery and yet maximizing the efficacy of surgical drainage. It is associated with shorter surgery duration, less blood loss, faster recovery and hence shorter hospital stay compared to OD.	

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[101] Bilateral involvement in 5%, more often on the right due to anatomical consideration – right receive blood from both the superior mesenteric and portal veins and right have greater hepatic mass.

[102] Colorectal Dis. 2012 Dec;14(12):e794-801

[103] Gastroenterology. 2014 Jan;146(1):129-37.e1

HEPATIC ABSCESS (AMOEBIC)

Amoebic abscess should be considered in **every case of solitary** hepatic abscess

EPIDEMIOLOGY

- 7- 10 times more frequent in adult men
- Amoebiasis caused by protozoan **entamoeba histolytica** (exist as infective cyst stage and a trophozoite stage (cause invasive disease)) – haematogenous spread from gut (form colonic ulcers) via portal vein (**travel hx is IMPT**)
- Transmission is faecal-oral

PRESENTATION

- Travellers returning from an endemic area (present within 8-20 weeks)
- **Persistent Fever**
- Right Upper Quadrant Pain – may be referred to epigastrium, right shoulder
- ± Diarrhoea (suggestive of intestinal amoebiasis) – in <1/3 of patients
- Hepatomegaly and point tenderness over liver – in 50% of patients
- Jaundice – occurs in <10% of patients
- **Complications**: rupture of abscess causing **peritonitis**

TREATMENT

- Metronidazole (very responsive) – 750mg oral TDS or IV 500mg QDS, 7-10 days
  - Contraindicated in pregnant patients
- Needle Aspiration (to confirm diagnosis)
  - Aspirated material – proteinaceous debris and an anchovy paste (fluid of necrotic hepatocytes)
- Intraluminal agents – paromomycin, iodoquinol, diloxanide furoate

COMPLICATIONS

- Bacterial Super-infection
- Erosion into surrounding structures
- Free Rupture into peritoneal cavity
- Complicated case – mortality as high as 20%

HEPATIC CYSTS

CLASSIFICATION

- Nonparasitic Cysts (asymptomatic or symptomatic)
  - Simple Liver Cysts
  - Polycystic Liver Disease
  - Neoplastic Cysts (rare)
- Echinococcal Cysts (most common Hydatid cyst)

CLINICAL PRESENTATION

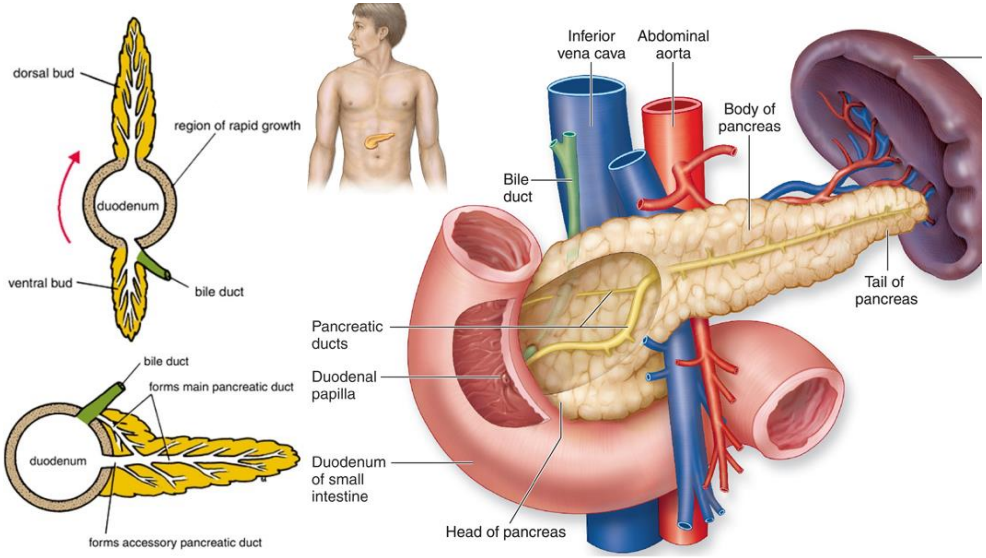
- Asymptomatic → identified on imaging for other symptoms
- Symptomatic
  - RUQ tenderness
  - Palpable Hepatomegaly
  - Bleeding, Infection, Torsion, Rupture
  - Mass Effect → compression of IVC, cholestasis due to compression of CBD, portal HTN
  - Fistulation into duodenum

	Pathogenesis	Treatment
Simple Liver Cyst	congenital malformation when an aberrant bile duct loses communication with the rest of the biliary tree and becomes progressively dilated (fluid within the cyst is not bilious, fluid is secreted by epithelial lining of the cyst → needle aspiration is not curative)	Aspiration combined with ethanol sclerotherapy (high failure and recurrence rates) OR Laparoscopic 'un-roofing' of the cyst
Polycystic Liver Disease	congenital a/w with AD-PKD (mutation in PKD1 andPKD2 gene), kidney cysts usually precedes liver cyst (rarely a/w hepatic fibrosis and liver failure)	Drainage of superficial cyst into abdominal cavity (un-roofing of cysts) and Fenestration of deeper cyst OR Liver resection (with retention of least cystic area of hepatic parenchyma)
Neoplastic Cysts	mixed cysts with solid components and septations – i.e. cystadenoma or cystadenocarcinoma)	Formal Resection or Enucleation to completely remove cyst epithelium
Hydatid (Echinococcal) Cysts	caused by infestation with the parasite echinococcus granulosus, 80% are single cyst located in the right liver	Anti-hydatid agents (i.e. albendazole) and Percutaneous treatment (PAIReD – puncture, aspiration, injection of ethanol, re-aspiration, drainage)
	The CYST SHOULD NOT BE ASPIRATED as an initial test cause aspiration can cause spillage of the organism and spread of the disease throughout the abdominal compartment	
Choledochal Cysts	cysts that contains bile is assumed to be in communication with the biliary system	

PANCREATIC DISEASES

EMBRYOLOGY AND ANATOMY (PANCREAS)

- The pancreas is a retroperitoneal structure, located behind the stomach, between the duodenum and spleen
- **Embryology**: developed from the dorsal and ventral buds (with the bile duct) → ventral bud rotates around the 2nd part of the duodenum (bringing the bile duct over to the left side of the 2nd part of the duodenum) → majority of main pancreatic duct (duct of Wirsung) from ventral bud and accessory duct (duct of Santorini) from dorsal bud.
- Duct of Wirsung → arise in the tail → traverses length of pancreas → terminate at papilla of Vater (surrounded by sphincter of Oddi)
- Duct of Santorini → arise from lower part of the head → terminate separately at lesser papilla
- **Anatomy (4parts):**
  - Head: lie within c-shaped concavity of duodenum, uncinate process extends to the left behind the superior mesenteric vessels (SMV)
  - Neck: lie in-front of the portal vein and overlie origin of SMV
  - Body: runs upwards and to the left across the midline
  - Tail: passes forward in the splenorenal ligament (vulnerable to damage in splenectomy), anterior to left adrenal gland contacting hilum of spleen
- **Blood supply:**
  - Celiac artery → splenic artery (tail) & superior pancreaticoduodenal artery (head)
  - Superior Mesenteric Artery → inferior pancreaticoduodenal artery (head)
  - Venous drainage via the pancreaticoduodenal veins → portal vein



ACUTE PANCREATITIS[104]

DEFINITION

- Reversible pancreatic parenchymal damage of varying severity owing to an acute inflammatory disease of the pancreas

The diagnosis of acute pancreatitis requires 2 of the following 3 features:

1. Abdominal pain consistent with epigastric pain (acute onset of a persistent, severe, epigastric pain often radiating to the back)
2. Serum lipase / amylase activity of at least 3x greater than the upper limit of normal
3. Characteristic findings of acute pancreatitis on CECT or MRI or trans-abdominal ultrasound

EPIDEMIOLOGY

- In 80% of patients, acute pancreatitis is mild and resolves without serious morbidity
- The remaining 20% of patients develops a severe form of acute pancreatitis with local and systemic complications associated with mortality rates as high as 40%[105]
  - Most late death due to multi-organ dysfunction secondary to infected pancreatic necrosis

CAUSES (I GET SMASHED)

1. **Idiopathic** (15-25%)
2. Gallstones (38%)
3. Ethanol (36%)*
4. **Trauma**
5. **Steroids**
6. Mumps and other **infections** (i.e. VZV, CMV, mycoplasma, parasitic infections)
7. **Autoimmune** – SLE, Sjogren's Syndrome
8. Scorpion toxin and other **toxins** (i.e. organophosphates poisoning)
9. Hypercalcaemia, hypertriglyceridemia (**metabolic causes**)
10. **ERCP** (2-5%)**
11. **Drugs** (1-2%) – i.e. SAND: sulfamethoxazole-trimethoprim (co-trimoxazole), azathioprine (immunosuppressant), NSAIDs (valproic acid), Diuretics (Furosemide)
12. Rare causes: **Neoplasm** (i.e. pancreatic or ampullary tumour), **Congenital** (i.e. pancreas divisum), **Genetics**

* The disease develops in pts whose alcohol ingestion is habitual over 5-15 years. Alcoholics are usually admitted with an acute exacerbation of chronic pancreatitis. Occasionally, however, pancreatitis can develop in a patient with a weekend binging habit.

** Post-ERCP pancreatitis in high risk patients might be prevented by a temporary pancreatic stent placement

[104] Lancet. 2008 Jan 12;371(9607):143-52
[105] Nat Clin Pract Gastroenterol Hepatol. 2005;2:473

PATHOPHYSIOLOGY

- Acute pancreatitis is caused by unregulated activation of trypsin within pancreatic acinar cells, activating pro-enzymes leading to auto-digestion and an inflammatory cascade that both amplifies the local inflammatory response and can result in a progression to SIRS

- Gallstones are thought to cause acute pancreatitis due to **obstruction** of the pancreatic duct causing interstitial **oedema** which **impairs blood flow** to the pancreatic cells → ischaemic cellular **injury → activation of pro-enzymes → destruction of pancreatic acinar cells**

- Alcohol is postulated to cause acute pancreatitis via its direct toxic effects and/or its metabolites (acetaldehyde, fatty acid ethyl esters (FAEEs), generation of oxidant stress) on acinar cells which predisposes the gland to autodigestive injury. [106] (i.e. FAEEs which are generated when O_2 levels in the pancreas is low trigger an excessive increase in calcium ion concentration in the cell water inside the pancreatic cell which in turn activates the digestive enzymes[107])

CLINICAL PRESENTATION[108]

- History of Presenting Complain (symptoms)
  - Acute and constant pain the epigastric area (or RUQ/LUQ) classically described as a boring sensation that radiates to the back
  - Patient is unable to get comfortable when lying supine with pain alleviated by sitting up and leaning forward
  - Pain might last for several days
  - Nausea, vomiting

- Other Significant History
  - Rule out other differential diagnosis – i.e. **gastric causes** (PUD), **hepatobiliary causes** (hepatitis, GB / CBD disease) **medical causes** (AMI, DKA, lower lobe pneumonia), **important to rule out** (perforated viscus)

- If pancreatitis is suspected, aim to ascertain etiology (risk factors)
  - Gall stone disease: biliary colic, cholecystitis, CBD stone, cholangitis
  - Recent alcohol abuse or chronic alcohol abuse
  - Recent blunt trauma or ERCP done
  - PMHx: metabolic disease, autoimmune disease
  - Recent symptoms of mumps (viral fever + bilateral jaw pain/swelling)
  - Recent drug history: steroids, NSAIDs, diuretics

[106] Dig Dis 2005;23:232–240
[107] MRC/33/09, http://www.mrc.ac.uk/Newspublications/News/MRC006138
[108] Med Clin North Am. 2006 May;90(3):481-503.

PHYSICAL EXAMINATION[109]

General Appearance
- Lying motionless (Diffuse Peritonitis)
- Sitting Up, Leaning Forward (Pancreatitis)
- Small red tender nodules on skin and legs – subcutaneous fat necrosis (rare)

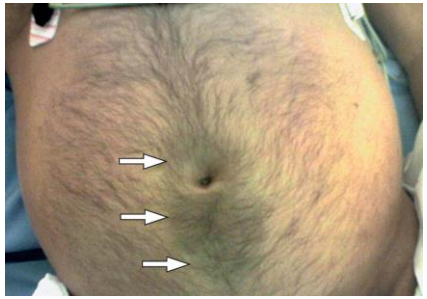
Vital Signs
- Tachycardia and Hypotension (due to fluid shifts with IV volume becoming markedly depleted)
- Low Grade Fever
- Tachypnoea → herald development of ARDS (auscultate lungs – crepitations, reduced air-entry)

Abdominal Examination
- Inspection (from the foot of the bed)
  - Abdominal Distension
- Palpation (patient in supine position, eyes fixed on patient's eye)
  - Focal Epigastric Tenderness
  - Palpable Mass (i.e. pseudocysts, pancreatic phlegmon)
  - **Signs of Peritonism** – rebound tenderness, guarding, board-like rigidity
  - **Signs of Haemorrhagic Pancreatitis** (severe pancreatitis a/w 40% mortality rate, is usually seen in 1-3% of patients and usually develops within 48 hours after onset of symptoms)
    1. Grey-Turner Sign (flank ecchymosis)
    2. Cullen's Sign (periumbilical ecchymosis) – see below
    3. Fox's Sign (inguinal ecchymosis)
- Auscultation
  - Diminished / Absent bowel sounds → paralytic ileus from diffuse peritonitis

Request for input/output charts

Respiratory Examination
- r/o pleura effusion, ARDS

Cullen Sign: exudates from pancreatic necrotic areas tracking along the falciform ligament and into the retroperitoneal and seen in the periumbilical region



[109] Med Clin North Am. 2006 May;90(3):481-503.

INVESTIGATIONS

DIAGNOSTIC[110]

1. Serum amylase (normal = 30-100U/L)
   - Levels ≥ 3 times the normal upper limit – sensitivity 50% and spec. 99%
   - Levels rise within a 6-24hours and normalizes in 3-7days
   - Elevation for > 10 days indicate complications (i.e. pseudocysts formation)
   - Magnitude of elevation not a/w disease severity or prognosis of disease
2. Serum lipase (normal =10-140 U/L)
   - Levels ≥ 3 times the normal upper limit – **sensitivity 64%** & spec. 97%
   - Levels rise within 4-8hours and stays elevated for 8-14days
   - Useful for patients with delayed presentation of acute pancreatitis
3. Urinary diastase
   - Similar function to serum lipase, used when serum amylase is equivocally raised or normal

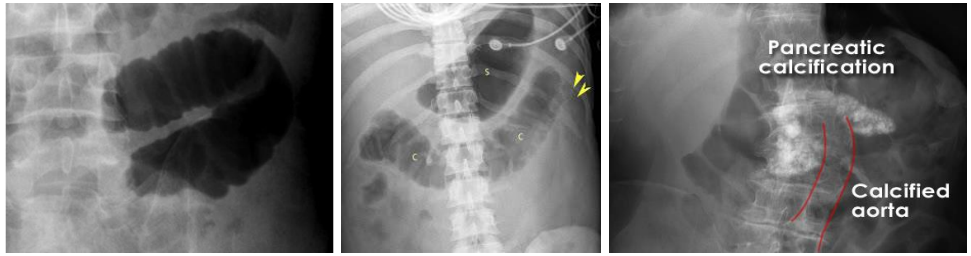
Other causes of elevated serum amylase

GI sources	- PUD, Intestinal Obstruction, Perforated bowel, Ischaemic bowel (amylase > 1000), Cholecystitis, Cholangitis, Appendicitis - Complication of pancreatitis (pseudocyst, abscess, ascites), pancreatic cancer,
Non-GI sources	- Renal Failure - ARDS - Ruptured ectopic pregnancy / Ovarian Cysts / PID - Salivary gland injury or inflammation - Macroamylasemia - Diabetic Ketoacidosis (DKA) or any acidosis (ketotic and non-ketotic) - Neoplasms (prostate, lung, oesophagus, breast, multiple myeloma, pheochromocytoma)

ASSESS SEVERITY AND PROGNOSTICATE DISEASE (BASED ON VARIOUS SCORING CRITERIA)

Ranson / Glasgow Criteria

1. Lactate Dehydrogenase (serum LDH)
2. Liver Function Test
   - Enzymes (serum AST) – aspartate
   - Albumin
3. Glucose
4. Full Blood Count
   - Elevated white cell count (WCC) → associated with worse prognosis
   - Haematocrit levels higher than 44% a/w worse prognosis (patients with inadequate fluid resuscitation as evidence by persistence of hemoconcentration at 24 hours are at increased risk of developing necrotizing pancreatitis[111])
5. Renal Panel + Ca^{2+}
   - Urea, any electrolyte imbalance, dehydration, degree of renal impairment
   - Hypocalcaemia
6. ABG – calculate base deficit (negative base excess)
7. C-Reactive Protein (CRP) → Marker of severity
8. ECG / Cardiac Enzymes → AMI
9. Erect CXR & Supine AXR
   - **Erect CXR** may show air under the diaphragm (perforated viscus), pleural effusion, elevated hemidiaphragm, pulmonary infiltrates; complete whiteout (ARDS)
   - **Supine AXR** may show the "sentinel loop sign" (dilated proximal jejunal loop near the pancreas –) or "colon cut-off sign" (distended colon from ascending to mid-transverse with no air distally) due to localized ileus 2^{o} to inflammation around the pancreas
   - Presence of calcifications within the pancreas may indicate chronic pancreatitis



10. Contrast-Enhanced CT Abdomen (CECT)
    - Useful in confirming diagnosis of pancreatitis if haematological results are inconclusive
    - Useful in severely ill patients with suspicion of necrotizing pancreatitis (only after aggressive volume resuscitation to diminish risk of contrast-associated nephrotoxicity)
    - Patients with persisting organ failure, signs of sepsis or deterioration in clinical status 6-10 days after admission – CT assess local complications such as fluid collections and necrosis
11. MRI / MR cholangiopancreatography (MRCP)
    - Substitute for CT scan in patients allergic to iodinated contrast or in acute renal failure
    - MRCP good for visualizing cholelithiasis, choledocholithiasis, anomalies of the pancreatic and common bile ducts

INVESTIGATING UNDERLYING ETIOLOGY

1. Liver Function Test (LFTs)
   - Elevation of ALT > 150mg/dl → gallstone pancreatitis
   - Elevation of Br > 5mg/dl that does not fall after 6-12 hours → impacted stone in ampulla of Vater
   - Elevation of AST → for Ranson and Glasgow scoring system
2. Ultrasound Abdomen
   - Pancreas is not visualized in up to 40% of patients due to overlying bowel gas and body habitus
   - Good for visualising biliary tree and picking up gallstones (can intervene!)
     - Dilated CBD → ERCP to remove gallstones/Bx tumour
     - Not dilated → MRCP (susp parenchymal disease)
3. Ca/Mg/PO_4 with albumin → hypercalcaemia
4. Fasting Lipids → hyperlipidaemia

[110] Ann R Coll Surg Engl. 2009 July; 91(5): 381–384.
[111] Pancreatology. 2002;2(2):104-7.

SEVERITY STRATIFICATION (RANSON, GLASGOW, APACHE II)

ATLANTA CLASSIFICATION[112] (FOR SEVERITY)

Mild	Moderate	Severe
No organ failure	Transient organ failure (resolves within 48 hours)	Persistent organ failure (>48 hours), single or multiple organ failure
No local or systemic complications	Local complications or exacerbation of co-morbid disease	Local complications are peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst and walled-off necrosis (sterile or infected)
usually resolves in the first week		
Mortality is rare		Mortality range from 36-50%

- Onset of acute pancreatitis is defined as the onset of abdominal pain (not the time of admission to the hospital) – time interval between onset of abdominal pain and first admission should be noted.

Danger signs in the first few hours
- Encephalopathy
- Hypoxemia, Tachypnoea
- Tachycardia >130/min, Hypotension <90mmHg, Haematocrit >44%
- Presence of Grey Turner's/Cullen's sign
- Oliguria <50mls/hr, Azotaemia

I. Glasgow (Imrie's criteria) – PANCREAS

The Glasgow system uses age and 7 laboratory values collected during the first 48 hours following admission for pancreatitis to predict for severe pancreatitis. It is used for both alcoholic and gallstone pancreatitis.

1.	**Pa**O_2	<60mmHg
2.	**A**ge	>55yrs
3.	**N**eutrophil/WBC	>15x10^9/dL
4.	**C**alcium	<2mmol/L
5.	**R**enal (urea)	>16mmol/L
6.	**E**nzymes LDH	>600IU/L
	or AST/ALT	> 200IU/L
7.	**A**lbumin	<32g/L
8.	**S**ugar (Glucose)	>10mmol/L

≥ 3 criteria → severe

- Preferred over Ranson's scoring in certain centres

II. Ranson's criteria[113] [LEGAL and CAlvin & HOBBES]

In 1974 Ranson et al. identified 11 objective clinical and laboratory measurements available within 48 hours of admission each of which had value in predicting severity and could be used as a basis for a predictive scoring system

On admission – LEGAL		Initial 48 hour – Calvin & HOBBES	
Serum LDH	> 350IU/L	Serum Calcium	< 2.0mmol/L or 8.0mg/dL
Serum AST	> 250 IU/L	Haematocrit Fall	> 10%
Blood Glucose	> 10mmol/L	Oxygen (PaO_2)	< 60mmHg
Age	> 55 years	BUN (after IV fluid hydration)	≥ 1.8 mmol/L or ≥ 5.0mg/dL
WBC	> 16,000 cells / mm^3	Base Deficit (-ve base excess)	> 4mEq/L
		Sequestration of Fluids	>6L

- Ranson's criteria prognosticates mortality according to score
- Any patient with a score of 3 and above is considered to have severe pancreatitis
- Mortality: 0-2 0-2%
  3-4 15%
  5-6 50%
  ≥7 70-90%

- Shortfalls of Ranson's:
  - validated for alcoholic pancreatitis only → revised Ranson's score was created for gallstone pancreatitis (same parameters but different cut-off values)
  - difficult to tell aetiology in acute setting & cumbersome to wait for 48 hours, and difficult to assess for negative fluid balance

III. C-reactive peptide
- **Combination of Glasgow score and CRP** improves overall prognostic value
- As a single prognostic marker; <100 is unlikely severe
- If CRP is **>150mg/dL at 48 hours**, the pancreatitis is more likely to be severe – possibly an early indicator of progression of acute pancreatitis into a serious state
- No relevance >3/7 of onset as other confounding factors come into the picture

IV. Acute Physiology and Chronic Health Evaluation II Score (APACHE II)

APACHE II takes into account 12 continuous variables, age of the patient, pre-morbid conditions and the GCS. The major advantage is that it can be used to monitor a patient's response to therapy while the Ranson and the Glasgow scales are meant for assessment at presentation.

V. Balthazar's CT severity index (consider a CT AP @ ~ 3-4/7 from onset)
- Grades severity of disease according to CT findings
- Rarely used

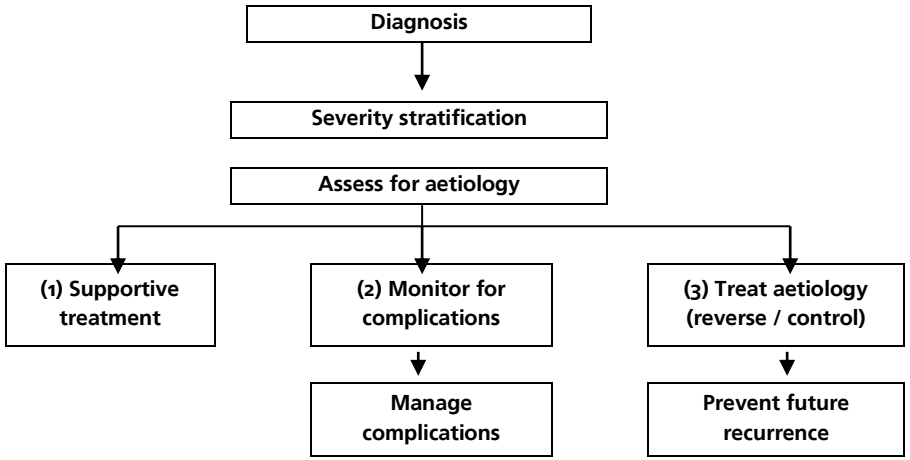
[112] Gut. 2013 Jan;62(1):102-11

[113] Surg Gynecol Obstet. 1974 Jul;139(1):69-81.

COURSE OF DISEASE

- Most episodes (75%) are mild and self-limiting, needing only brief hospitalization
- 20-25% patients develop a severe disease with local and extra-pancreatic complications characterized by early development and persistence of hypovolemia and multiple organ dysfunction
- Death is bi-modally distributed:
  (a) Early
    - Within 1/52; due to severe organ failure, SIRS
    - Very little can be done in terms of treatment
  (b) Late
    - Most common cause is infection with resultant sepsis
    - Multi-organ failure can be the course of death

MANAGEMENT / TREATMENT STRATEGY



(1) SUPPORTIVE TREATMENT

- The cornerstone of therapy in acute pancreatitis is the prevention of pancreatic stimulation (keep patient NBM)
- **Aggressive IV fluid resuscitation** to maintain IV volume and allow adequate perfusion of the pancreas and extra-pancreatic organs (i.e. kidneys) & close monitoring of vitals
- Pain Management – adequate analgesia
- Prevent Vomiting secondary to Ileus – NG tube insertion, Anti-emetics
- Antibiotic Management – prophylactic or therapeutic
- **± Definitive treatment** – i.e. ERCP if have evidence on on-going biliary obstruction (90% of patients with acute pancreatitis will respond to medical therapy)

1. **Resuscitate if needed**

2. **Monitoring (after resuscitating)**
   - In general ward if mild pancreatitis; HD/ICU monitoring if severe (≥3)
   - Fluid resuscitate with crystalloids – to correct fluid losses in the 3rd space
   - Monitor vitals [SpO2, BP, HR, Temp.], urine output (aim: >0.5ml/kg/hr) & ± CVP
   - Frequent monitoring of electrolyte including calcium (every 6-8 hours initially)
   - Monitoring of ABG – assess oxygenation and acid-base status

3. **NBM (gastric rest) with nutritional support**
   - May include **gastric decompression with NGT** if there is persistent vomiting, significant gastroparesis, or intestinal obstruction (ileus)
   - **Acid suppression** does not change course of disease, but protects against stress ulcer formation; octetride has no benefit (thought to reduce pancreatic secretions)
   - Fast patients for at least 2/7 until more stable
   - May start **oral feeding early** with fluids in mild pancreatitis if tolerated
   - Prolonged NBM results in poorer recovery due to nutritional debilitation – think about NJ feeding, or open jejunostomy creation early in patients with severe pancreatitis; if not tolerable, then consider TPN

4. **Analgesia**
   - **Do not give NSAIDs** as they can worsen pancreatitis & cause renal failure (since there is already decreased renal perfusion in acute pancreatitis)
   - Use **opioid analgesics (tramadol, pethidine)** other than morphine (causes increased tone of sphincter of Oddi)

5. **Treatment of fluid and electrolyte abnormalities → hypocalcaemia, hypoglycaemia**

6. **Antibiotics**
   - Either **prophylactic** or **therapeutic**
     - Not shown to have any benefit in mild pancreatitis
   - **Prophylactic in severe acute pancreatitis** to prevent infection of necrosis (infection will occur in 40-70% of patients with necrosis and increases the mortality rate from 12 to 33%)
     - Carbapenem (only **imipenem** has been shown to prevent sepsis)
   - **Therapeutic in cholangitis** (coexisting with gallstone disease or as a complication of pancreatitis) **& infection of pancreatic necrosis/ pseudocyst**
   - Duration: **14 days**

7. **Support for organ failure – with presence of organ failure, manage patient in surgical HD**
   - Ventilate with PEEP if hypoxemic (e.g. ARDS)
   - Dialysis & CVP monitoring if in ARF
   - Fluid resuscitation & inotropes if Hypotensive

(2) MONITORING AND TREATING COMPLICATIONS

Local complications[114]

- Acute fluid collections (30-50%)
  - Due to increased vascular permeability; 70-80% resolve spontaneously
- Pseudocyst (10-20%)
  - Persistent fluid collection (enzymes, blood, necrotic tissue) walled off by fibrosis and not an epithelium-lined surface (after 4 weeks)
  - Presents as persistent pain, mass on examination, persistently ↑ amylase or lipase
  - 50% resolve spontaneously if not surgical intervention* (see below)
  - Can be further complicated by GOO, infx, peritonitis, h'ge (erosion of splenic vessels)
- Sterile Pancreatic necrosis (20%)
  - Areas of no contrast uptake on CT with intravenous contrast
  - ? prophylactic antibiotics with imipenem (see above)
  - Supportive measures, KIV surgery if patient unstable
- Infection (5%) – usually 2° enteric GNR
  - **Pancreatic Abscess**
    - Circumscribed collection of pus (w/o pancreatic tissue)
    - Treat with antibiotics + drainage (CT guided if possible)
  - **Infected pancreatic necrosis**
    - Gas bubbles on CT scan, FNA in deteriorating patient with necrosis
    - If gram stain & culture positive → treat with antibiotics + evacuation (percutaneous followed by surgical debridement after 4 weeks)
- Chronic pancreatitis, exocrine insufficiency & endocrine insufficiency

Systemic complications

- Peritoneal sepsis
- Pancreatic ascites (massive accumulation of pancreatic fluid in peritoneum) – lead to abdominal compartment syndrome
- Pleura Effusion
- Intra-abdominal haemorrhage (erosion of splenic vessels) – shock
- Multiple organ failure (ARDS, acute renal failure, hypovolemic shock, DIVC)
- Hypocalcaemia, hyper/ hypoglycaemia

*Pseudocyst

- Operate if **> 6cm** and persisting for **> 6 weeks + pain** as the chance of spontaneous resolution is low and risk of complications (infection, haemorrhage, rupture) is high
- Surgery can be **open**, **laparoscopic**, **endoscopic or percutaneous** (radiologically guided)
  - Endoscopic – internal drainage via a **cystogastrostomy**, cystoduodenostomy or cystojejunostomy

[114] Pocket Medicine 4th Edition: Pancreatitis – section 3-13

Intervention for local complications

- ERCP
  - No benefit in mild biliary pancreatitis
  - Indications:
    - **Severe** pancreatitis
    - Evidence of **ductal stones**
    - **Cholangitis**
    - **No response to treatment within 48 hours**
  - ERCP should be done within first 48-72 hours for maximum benefit

- CT-guided aspiration of pancreatic necrosis
  - Can help differentiate between sterile and infected necrosis
  - Consider surgery if patient doing poorly

- Wide debridement (Necrosectomy) for infected necrosis
  - Lavage and drainage procedure is done after necrosectomy to decrease infective load

- Role of surgery
  - Infected necrotic pancreas (mortality 100% without operation)
  - Sterile necrotic pancreas (necrosectomy)
    - Delay surgery till as late as possible for demarcation/organization of necrotic areas (repeated surgeries required)
  - Diagnostic uncertainty
  - Complications e.g. intra-abdominal haemorrhage / pseudocyst

(3) MANAGEMENT OF AETIOLOGY & PREVENTION OF RECURRENCE

- **Avoid alcohol, stop all offending medication & control hyperlipidaemia**

- **ERCP + endoscopic sphincterotomy**
  - Done in acute setting (within 72hours) for patients with severe biliary pancreatitis

- **Cholecystectomy for biliary pancreatitis**
  - Patients with biliary pancreatitis who do not undergo cholecystectomy have a 40% 6 week recurrence risk
  - Cholecystectomy can be done in the same admission for patients with mild biliary pancreatitis – await PONCHO trial results[115]
  - In patients with severe pancreatitis, there is reluctance to do the surgery early, as the patient may develop complications that require surgical intervention – better to do all surgery in the same operation instead of opening the patient twice

[115] Trials. 2012 Nov 26;13:225.

CHRONIC PANCREATITIS

Long-standing inflammation of the pancreas with diffuse scarring and structuring in the pancreatic duct leading to irreversible destruction of the exocrine and in the late stage the endocrine parenchyma

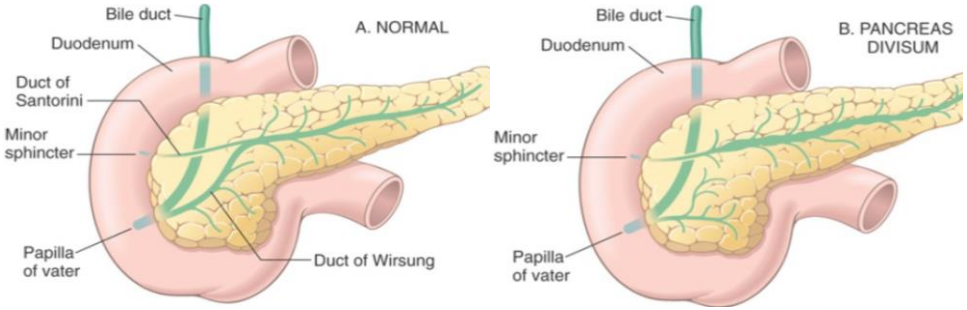
CAUSES (NOT GALLSTONES)

- Alcohol abuse (70%) & Smoking
- Autoimmune
- Idiopathic
- Metabolic (hypercalcaemia, hypertriglyceridemia, hyperparathyroidism)
- Drugs – i.e. steroids, azathioprine
- Trauma
- Genetic (cystic fibrosis)
- Congenital (sphincter of Oddi dysfunction, pancreas divisum – see below)

* Not all patients diagnosed with chronic pancreatitis have a history of recurrent acute pancreatitis

Pancreas Divisum

- Most common congenital anomaly of the pancreas (3-10%)
- Absence of fusion between the dorsal and ventral duct system during 6th week of development
  - Normally, distal dorsal duct joints to proximal ventral duct to form the main pancreatic duct (duct of Wirsung) → terminate at the papilla of Vater
  - In pancreas divisum → lack of fusion leads to a short duct of Wirsung and majority of pancreatic secretion having to drain through the minor pancreatic duct (duct of Santorini) → terminate at minor duodenal papilla
- This lead to a stenosed or inadequately patent minor papilla preventing normal drainage of pancreatic secretions → lead to increased intra-ductal pressure.



PATHOGENESIS

- Progressive destruction of the pancreas by repeated flare-ups of mild and subclinical types of acute pancreatitis
- Characterized by diffuse scarring and strictures In the pancreatic duct
- The Islet of Langerhans (endocrine function*) have a greater resistance to injury than do the exocrine tissues

*Endocrine Function (5 different cell types): Alpha (glucagon), Beta (insulin and amylin), Delta (somatostatin), PP/Gamma (pancreatic polypeptide), Epsilon (ghrelin)

CLINICAL PRESENTATION

- Pain (upper mid epigastric pain radiating to the back, getting progressive worse)
  - Can last from hours to days
  - Mostly episodic, some have persistent relentless pain
  - Cardinal symptom and is present in 85-90% of patients
- Change in bowel habits (diarrhoea) followed later by steatorrhoea
- Newly diagnosed DM (30%) – late
- LOW (secondary to anorexia and malabsorption)

PHYSICAL EXAMINATION

- LOW (secondary to anorexia and malabsorption)
- Tenderness of upper abdomen
- Enlarged pancreas is occasionally palpable, especially in thin patients (differential: presence of pseudocyst)
- ± jaundice (secondary to stricture of the common bile duct)
- ± splenomegaly (secondary to thrombosis of the splenic vein)
- ± ascites (secondary to a pancreatic peritoneal fistula)

COMPLICATIONS

1	Local Complications	- Persistent Pseudocyst, splenic vein thrombosis (splenomegaly), fistula (pancreatico-enteric, pancreaticopleural fistula)
2	Common Bile Duct Obstruction	- Result from transient obstruction from pancreatic inflammation and oedema or from strictures on the intrapancreatic common bile duct
3	Duodenal Obstruction	- Occur due to acute pancreatic inflammation, chronic fibrotic reaction, pancreatic pseudocyst or neoplasm
4	Pancreatic Cancer	- Chronic pancreatitis suggested to increase risk by 2-3 x
5	Pancreatic Insufficiency	- Type 1 DM - Steatorrhoea, Vitamin deficiency, Malnutrition

INVESTIGATIONS

DIAGNOSTIC (RADIOLOGICAL)

- ERCP (gold standard imaging test for diagnosis of chronic pancreatitis)[116]
  - Characteristic → "chain of lakes" appearance of ductal anatomy
  - Can also evaluate pancreatic mass lesions, cytology, delineation of ductal anatomy and can be therapeutic
  - 3-7% risk of causing acute pancreatitis
- Endoscopic Ultrasound (EUS)
  - Diagnosis for chronic pancreatitis based on Rosemont Criteria

DIAGNOSTIC (LABORATORY) – ASSESSING PANCREATIC FUNCTION

- Pancreatic Secretin Stimulation Test (gold standard but invasive)
  - Patient is given IV secretin and the pancreatic secretions (released into the duodenum) are aspirated (removed with suction) and analysed over a period of about 2 hours
- Pancreatic Endocrine Function – i.e. fasting blood glucose, 2hr post-prandial blood glucose or glucose tolerance test
  - Abnormal test results in 14-65% with early chronic pancreatitis
  - Abnormal results in 90% of patients when calcifications are present
- 72hr faecal collection for estimation of daily faecal fat
  - Simple and cheap test for assessing pancreatic function → determine if patient has significant steatorrhoea
  - Limited role in definitive diagnosis of chronic pancreatitis (require high degree of pancreatic insufficiency to have a positive test)

Note: serum amylase and lipase levels are elevated in acute pancreatitis but rarely useful in chronic pancreatitis and are commonly normal due to 'burn out' of the pancreas

ASSESS FOR COMPLICATIONS

- Abdominal X-Ray
  - Identify diffuse calcification of the pancreas
- CT / MRI
  - CT → good for diagnosing pancreatic parenchyma or ductal disease
  - Useful to evaluate mass lesions and sequelae of chronic pancreatitis
  - MRCP → good for evaluating dilated duct and strictures

MANAGEMENT PRINCIPLES

- Treatment aimed at underlying aetiology, symptoms and complications
- Patient can be managed via (1) lifestyle modifications (2) medical therapy (3) surgical

- Treat underlying cause → abstain from alcohol consumption
- Supportive Treatment
  - Malabsorption / steatorrhoea → pancreatic enzyme supplements
  - Diabetes → lifestyle choices, OHGA, Insulin
  - Pain Relief → narcotics / TCAs, abstinence from alcohol
- Treating Complications
  - Pancreatic Pleural Effusions → tube thoracostomy
  - Pancreatic Ascites → paracentesis
  - Ductal Cx → Endoscopic Therapy (sphincterotomy, stenting, stone retrieval, lithotripsy)
  - Pseudocyst, aneurysm, fistula, local obstruction → surgical management

SURGICAL PRINICIPLES (MANAGEMENT)

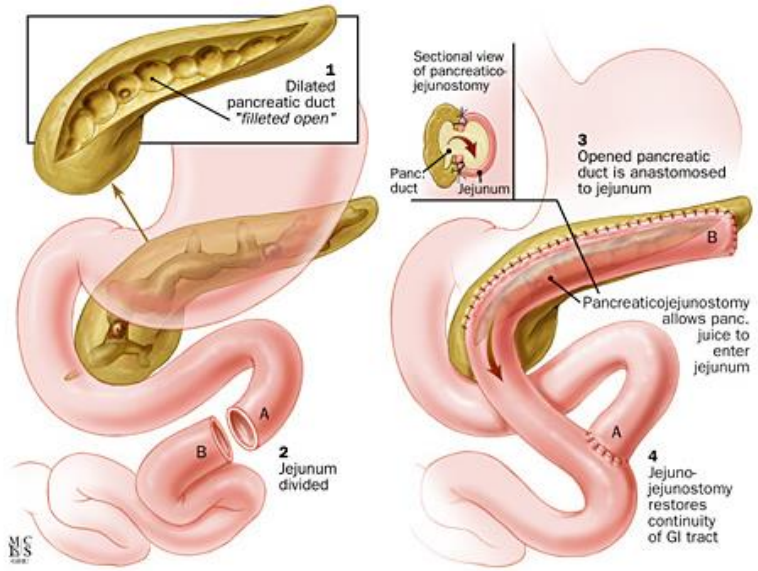
- Indications
  - Unremitting Pain
  - Inability to rule out neoplasm
  - Treatment of complications (pseudocyst, aneurysm and fistula, local obstruction secondary to fibrosis (CBD, duodenum)

- Choice of Procedure

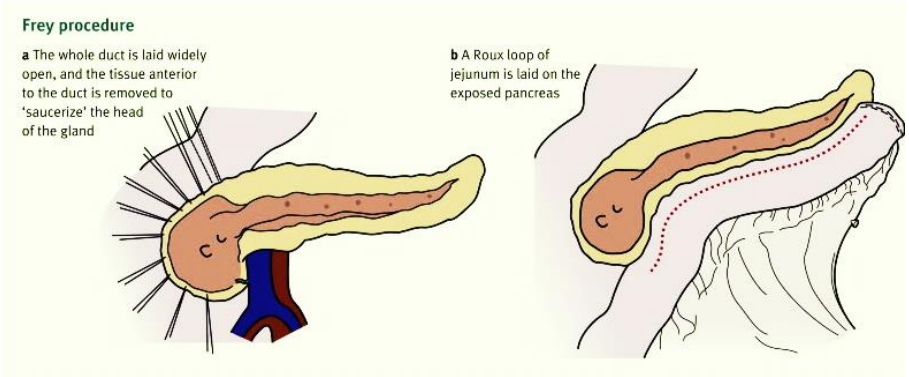
Principle	Procedure	Remarks
Drainage Preferable for patients with dilated ducts	Puestow Procedure (see below)	Distal pancreatectomy with a distal pancreaticojejunostomy anastomosis
	Partington-Rochelle	Modification of Puestow – eliminate distal pancreatectomy
Combined Duct Drainage and Resections	Beger Procedure	Duodenum-preserving resection of a portion of the pancreatic head, pancreas transected at pancreatic neck
	Frey Procedure (see below)	Modification of Beger – pancreatic neck not transected, parenchyma is extensively cored out from head to extent of diseased segment distally, lateral pancreaticojejunostomy
Resection (pancreatectomy)	Whipple Procedure (see below)	Indicated in cases where pancreatitis mainly affects head of the pancreas
	Subtotal / Total Pancreatectomy	
Nerve Block	Celiac Plexus Block	Ganglionectomy or direct injection of sclerosing agents

[116] Gut. 1984;25:1107-1112

Puestow Procedure

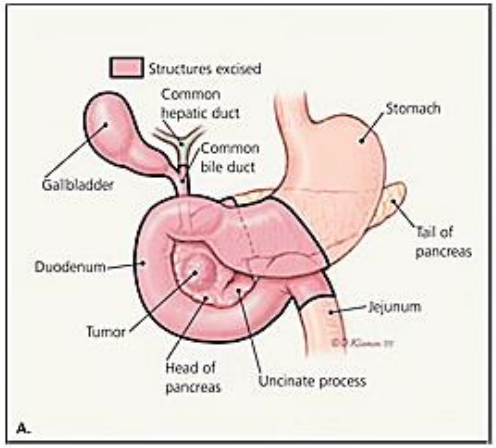


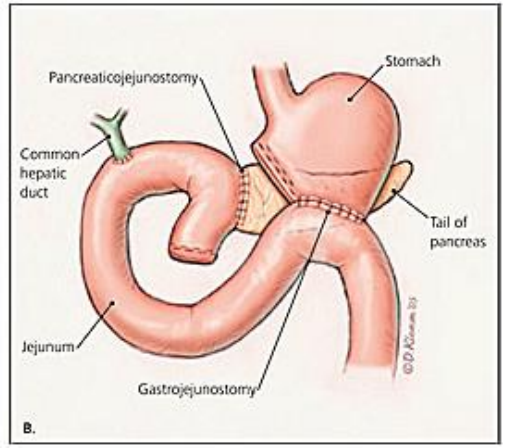
Frey Procedure



Whipple Procedure (pancreaticoduodenectomy)

- En-bloc removal of distal segment of the stomach, duodenum, proximal 15cm of jejunum, head of pancreas, common bile duct, gallbladder
- Pancreatic and biliary anastomosis placed 45-60 cm proximal to gastrojejunostomy
- Principle: pancreas and duodenum share the same arterial blood supply (gastroduodenal artery) – so both must be removed





PANCREATIC CANCER[117]

EPIDEMIOLOGY

- 5th in males and 6th in females leading cause of cancer mortality in Singapore
- Leads to estimate 227,000 deaths per years worldwide[118]
- Very poor prognosis – most patient have incurable disease at time of diagnosis
- Overall 5-year survival is about 5%, median age at diagnosis is 65 years[119]

RISK FACTORS

Modifiable	Lifestyle	- Smoking* - Obesity
	Diet	- High Fat Diet - High Meat Diet - Diet low in Vegetable and Folate
	Occupational Exposure	- Chlorinated hydrocarbon solvents (industrial carcinogens) - Nickel

Non-modifiable	Family History	- Family History of Chronic Pancreatitis * - First-degree relatives with pancreatic tumour (familial pancreatic cancer)** – especially so with young onset (< 50 years) pancreatic cancer
	Age / Gender	- Advancing Age - Male Sex
	Personal History	- **Diabetes Mellitus** (preliminary findings suggests metformin could protect against pancreatic cancer[120])
	Familial Pancreatic Cancer	- Inherited susceptibility to pancreatic cancer a/w certain genes [i.e. BRACA 2, STK11 (Peutz-Jeghers), (HNPCC, Lynch syndrome, CDKN2A (familial atypical multiple mole melanoma)]
	Others	- Helicobacter Pylori Infection - Periodontal Disease - Ethnicity: African American - Blood Group (Non-O blood group)

* Dominant risk factors – 20% of pancreatic tumours attributed to smoking, 7-10% of affected individuals have a positive family hx of chronic pancreatitis

** First degree relatives of individual with familial pancreatic cancer → **9X increased risk** of pancreatic cancer over the general population, risk increase to **32x with ≥3 first degree relatives** have pancreatic cancer

PATHOLOGY

- Pancreatic intra-epithelial neoplasm (most commonly) to invasive pancreatic carcinoma sequence
- Involves progressive genetic mutations
  - Telomere shortening → contribute to chromosomal instability (early)
  - Mutational activation of KRAS oncogene (early)
  - Inactivation of tumour suppressor genes → SMAD4, BRAC2, P53, CDKN2A (advanced)
- Most common histology is ductal adenocarcinoma (90%), other histological subtypes includes squamous cell carcinoma, acinar cell carcinoma (production of exocrine enzymes, may cause metastatic fat necrosis due to lipases released into circulation), undifferentiated carcinoma, pancreatoblastoma (rare, found in children 1-15years)
- Common sites involved:
  - Head of Pancreas (60%) – can lead to earlier detection secondary to obstruction of bile duct → better prognosis
  - Body of Pancreas (15%)
  - Tail of Pancreas (5%)
  - Entire Pancreas (20%)

CLINICAL PRESENTATION

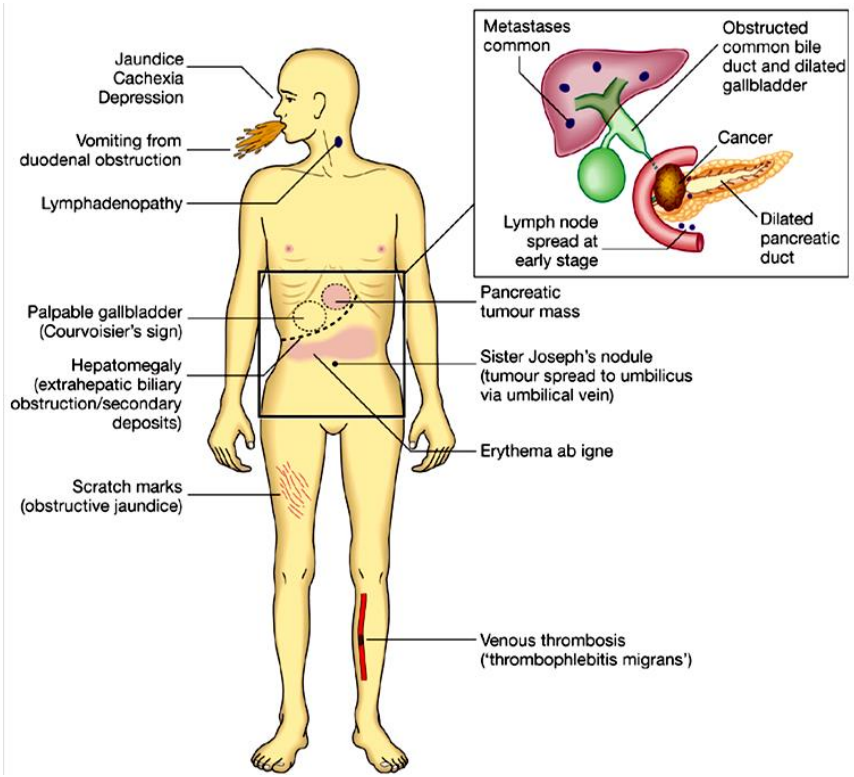
- Early stage pancreatic cancer is usually clinically silent and disease only become apparent after the tumour invades the surrounding tissues or metastasis to distant organs (majority present with advanced disease)

Pancreatic Head or Periampullary	Pancreatic Body / Tail
- OBSTRUCTIVE JAUNDICE → Painless obstructive jaundice with palpable GB (Courvoisier's sign) ± Cholangitis (due to biliary obstruction) - Gastric Outlet Obstruction → nausea and vomiting - LOW (secondary to anorexia / maldigestion) - Pancreatic duct obstruction → maldigestion / recurrent pancreatitis - Endocrine: Diabetes mellitus (25% of patients with pancreatic cancer have DM on dx) – note that new onset DM within the year prior to dx is found in 15% of patients but the correlation is still unclear - Bleeding upper GIT (haematemesis and/or melena)	**Late presentation** - Coeliac and mesenteric plexus invasion – dull constant (incessant and boring) PAIN in the epigastrium radiating to the back, relieves with bending forward - Malaise, weight loss, anorexia, nausea - Exocrine insufficiency with duct obstruction → steatorrhoea, malabsorption - Metastatic symptoms: ascites, bone pain, CNS symptoms, dyspnoea - Paraneoplastic syndromes – migratory thrombophlebitis (Trousseau's Sign) in 6% (due to tumour-elaborated procoagulants and plt aggregating factors)
Also: - Deep and superficial venous thrombosis - Panniculitis (inflammation of subcutaneous adipose tissue) - Depression	

IMMEDIATE MANAGEMENT

- Treat any **life-threatening complications** such as cholangitis, pancreatitis, bleeding

[117] Lancet. 2011 Aug 13;378(9791):607-20
[118] Nat Rev Gastroenterol Hepatol 2009;6: 699–708.
[119] Cancer Statistics. 2010;60(5):277-300
[120] Gastroenterology 2009; 137: 482–88.



INVESTIGATIONS

DIAGNOSTICATE

1. **Tri-phasic "pancreatic protocol CT Scan" (3-phases – arterial, venous and portal venous) and (thin slices – ≤ 3mm)**
   - Better sensitivity (85-90%) and specificity (90-95%) in diagnosing pancreatic cancer
   - Fine cut CT imaging – allow assessment of relationship of mass to vascular structure as this is crucial in determining resectability
     - Tumour appears as hypo attenuating indistinct mass – distorts normal architecture
     - Simultaneous dilatation of the common bile duct (intra-pancreatic segment) and the pancreatic duct (double-duct sign) → secondary to pancreatic head tumour or periampullary tumours

2. **Endoscopic ultrasound + FNA biopsy**
   - Tissue diagnosis is crucial to rule out benign disorders that present with pancreatic enlargement and obstructive jaundice (i.e. autoimmune pancreatitis)
   - A biopsy specimen is not needed when the suspicious of cancer is high as the resection will provide therapeutic benefits and substantially delaying surgery could set back commencement of effective treatment.
   - FNA with EUS guidance is preferred to radiologically guided percutaneous needle biopsies as there is less risk of tumour seeding

3. **ERCP (KIV stenting)**
   - ERCP can be used for diagnosis when a mass is not seen on CT and can be used to obtain tissue diagnosis if necessary
   - ERCP stenting increases risk of post-operative complications in patients with resectable disease (though can be performed for drainage of biliary obstruction)

4. **MRI pancreas with MRCP** – MRI pancreas is not superior to CT scan; MRCP is useful in delineating biliary system anatomy especially if the system is not obstructed and there are no therapeutic indications for ERCP (since there are considerable risks with ERCP)

5. **Laboratory Test**
   a. **CA 19-9**
      - Not a screening test for pancreatic cancer as it can be false positive
      - Can act as a prognostic marker[121] →
        - Preoperative amounts of CA19-9 > 100-200U/ml predicts unresectability and survival[122]
        - Normal perioperative CA19-9 associated with a 5 year survival of 42%
        - Lower post-operative CA19-9 at 3 months and before adjuvant chemotherapy were independent favourable prognostic factors.
      - Can be used as a marker for tumour recurrence during post-op follow-up
   b. **Elevated Serum Bilirubin**
   c. **Elevated Alkaline phosphatase**
   d. **Mild increase in AST and ALT (after prolonged obstruction)**

The most difficult clinical situation in which to diagnose pancreatic carcinoma is in the patient with underlying chronic pancreatitis. All of the above imaging studies may show abnormalities that may not help to differentiate between pancreatic carcinoma and chronic pancreatitis. Even tumour markers can be elevated in patients with chronic pancreatitis. → Often combine multiple imaging modalities, close clinical follow-up, serial imaging studies, and, occasionally, empiric resection, to diagnose an underlying pancreatic carcinoma

STAGING

Clinical staging classifies patients into (1) Local Resectable, (2) Borderline Resectable, (3) Locally Advanced or Unresectable and (4) Unresectable – metastatic disease

	Local Resectable	Borderline	Locally Advanced	Metastatic
Incidence	About 10%	10%	30%	About 60%
Median Survival[123]	17-23 months	Up to 20 months	8-14 months	4-6 months
Stage	Stage 0 to IIB	Stage III with tumour abutment	Stage III (T4, any N, M0)	Stage IV (any T, any N, M1)

1. **CT thorax or CXR** – assess for pulmonary metastases
2. **CT abdomen** – assess for T, N stage and liver metastases
3. **Endoscopic ultrasound** – assess for T, N stage
4. **Bones** – bone scan when suspicion is high
5. **Staging laparoscopy** – for peritoneal metastases, just before definitive operation for a resectable tumour (since CT/MRI may miss small peritoneal deposits in around 25%) → if no peritoneal disease found, continue with surgery, otherwise, close up and abort surgery

[121] Cancer. 2009;115(12):2630-2639
[122] Ann Surg Oncol 2008;15: 3512–20.
[123] Lancet. 2011 Aug 13;378(9791):607-20

Assessing Complications

1. FBC – assess any infections (i.e. cholangitis) – if high KIV
    a. CRP/ESR – assess if inflammation is present
    b. Blood Cultures
2. LFTs – consistent with the picture of obstructive jaundice?, assess nutritional status (albumin)
3. U/E/Cr – assess electrolyte abnormalities a/w GOO (vomiting)
4. Random Glucose Test – assess for any DM

Preoperative Investigations

1. GXM
2. PT/PTT
3. ECG / CXR
4. CA19-9

PRINCIPLES OF MANAGEMENT

"Patients with pancreatic cancers are best managed by a multi-disciplinary team including oncologists, surgeons, radiologists, gastroenterologists, radiation oncologists, pathologists, pain management experts, social workers, dieticians and when appropriate palliative care experts."

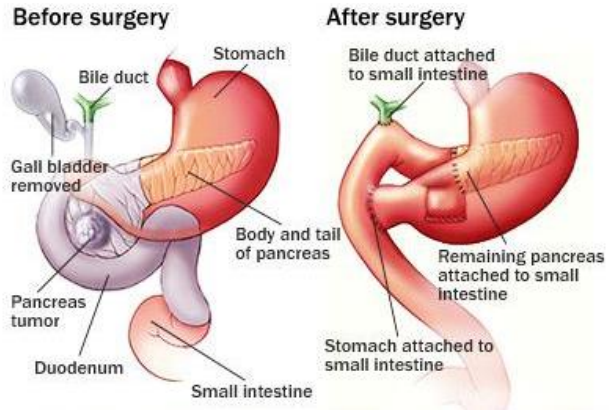
Radiotherapy and Chemotherapy

Neoadjuvant chemotherapy

- Possibly associated with improvement in survival → can downstage patients with borderline resectable disease (usually used only in this setting)
- Chemoradiation can downstage about 30% of patients with locally advanced disease to resectable pancreatic cancer

Adjuvant chemotherapy (5-FU, gemcitabine)

- Strong evidence exists that adjuvant therapy increases survival
- Overall survival (OS) was longer among recipients of CRT versus surgery alone [median survival 21.1 vs. 15.5 months, (P < .001)][124]



[124] Ann Surg Oncol. 2010 April; 17(4): 981–990.

Surgery – Curative Resection (local resectable disease)

Pre-operative Biliary Drainage

- For patients with cholangitis or symptomatic liver dysfx → otherwise no proven benefit
- Should be done before initiation of chemotherapy and radiotherapy
- Will lower non-specific CA19-9 → more reliable estimate of disease burden

Local Resectable disease

- No distant metastases (lung, liver, bone, peritoneum)
- Patent superior mesenteric vein and portal vein (i.e. no tumour thrombus)
- Definable tissue plane between tumour and celiac axis, hepatic artery and SMA

Whipple's operation (Pancreaticoduodenectomy)

- Head of pancreas and duodenum share the same arterial supply (gastroduodenal artery) → both organs must be removed if the single blood supply is severed
- Octreotide → given for 1 week to reduce pancreatic secretion → reduce likelihood of a leak
- Exploration and Assessment:
    1. Staging laparoscopy to confirm absence of peritoneal metastases
- En-bloc resection:
    1. Head of the pancreas
    2. Duodenum, proximal 15cm of jejunum,
    3. Common bile duct
    4. Gallbladder and its cystic duct
    5. Distal part of the stomach (gastric antrum)
    6. Regional lymph nodes
- Reconstruction:
    1. Distal pancreas to jejunum (pancreaticojejunostomy)
    2. Hepatic duct to jejunum (hepaticojejunostomy) → 45-60 cm proximal to the gastrojejunostomy
    3. Stomach to jejunum (gastrojejunostomy)
- Consensus panels recommends that PD be done at specialized centres doing at least 15-20 of these operations a year → however, in general, recurrence rate is still high with overall 5 year survival at about 20% for patients after resection
- Operative mortality in experienced centres < 5%

Distal Pancreatectomy + splenectomy

- Done for resectable lesions of the body and tail of the pancreas
- When removing the spleen → vaccination against pneumococci, meningococcal and HiB

Pylorus-preserving proximal pancreaticoduodenectomy

- Preserve gastric antrum and pylorus
- Compared to Whipple's Procedure
    - reduced morbidity, fewer post-gastrectomy symptoms, less entero-gastric reflux, improved post-operative nutrition
    - No difference in long-term survival / mortality

PALLIATIVE OF PANCREATIC CANCER

- About 80-85% of patients are not suitable for curative resection
- Median survival for patients with locally advanced, non-metastatic pancreatic cancer is 8-14 months and for patients with metastatic pancreatic cancer is 4-6 months
- Palliation of symptoms can be achieved either surgically or endoscopically

SURGICAL MEASURES

Surgical bypass of obstruction → Triple bypass involving anastomosis between

(a) Stomach and jejunum (gastrojejunostomy)
(b) Biliary system and jejunum (choledocho-/hepatico-/cholecysto-jejunostomy)
(c) Jejunum and jejunum, to prevent reflux of food into biliary tree – essentially a Roux-en-Y loop (entero-enterostomy)

→ Removes risk of duodenal obstruction and avoid recurrent jaundice

NON-SURGICAL PALLIATIVE MEASURES

- Palliative chemotherapy (i.e. gemcitabine) /radiotherapy/chemoradiotherapy

Complications	Treatment
Pain from coeliac plexus infiltration	• Treat with endoscopic ultrasound or CT guided ablation of the plexus • Ganglionectomy or direct injection of sclerosing agents • Slow-release morphine (step-wise escalation)
Obstructive Jaundice (most often with pancreatic head cancers)	• Benefit from endoscopic stenting – stent obstructed biliary duct • Percutaneous Transhepatic Cholangiography (PTC) Biliary Drainage
Gastric outlet obstruction (in about 20% of patients)	• Benefit from duodenal wall stents (wall stent) → results in an earlier discharge from hospital and possibly improved survival compared to gastrojejunostomy (median survival 110.5 days vs. 64 days)[125] • PEG (percutaneous endoscopic gastrostomy) placement for decompression
Venous thromboembolism	• Prophylaxis is recommended – low molecular weight heparin
Others (i.e. steatorrhoea / DM) – to improve quality of life	• Encourage normal activities • Enzyme replacement for steatorrhoea • Treat DM

Complications of Whipple's operation

- Mortality rate is **2-7%**, with a morbidity rate of up to 20-30% (mostly mild complications)
- Distal pancreatectomy has a higher morbidity and leak rates than PD though mortality rates remains the same
- **Intraoperative/early complications**
  (a) Delayed gastric emptying → subsides with conservative treatment
  (b) Pancreatic fistula
  (c) Wound Infection

→ Above-listed are the 3 most common complications of PD

  (d) Injury to other organs – liver, kidney, bowel
  (e) Bleeding – GI haemorrhage, operative site haemorrhage
  (f) Infection → intra-abdominal abscess, peritonitis, sepsis
  (g) Pancreatitis
  (h) Pancreatic anastomotic leak (5-20%)
  (i) Biliary anastomotic breakdown
  (j) Pseudocyst formation may occur due to anastomotic leaks

- **Late**
  (a) Long-term exocrine insufficiency resulting in malabsorption and steatorrhoea
  (b) Gastric stasis with pylorus-preserving Whipple's
  (c) Diarrhoea resulting from autonomic nerve injury during lymph node dissection
  (d) Endocrine insufficiency → DM

[125] Surg Endosc. 2002 Feb;16(2):310-2. Epub 2001 Nov 12.

DISEASES OF THE BILIARY SYSTEM

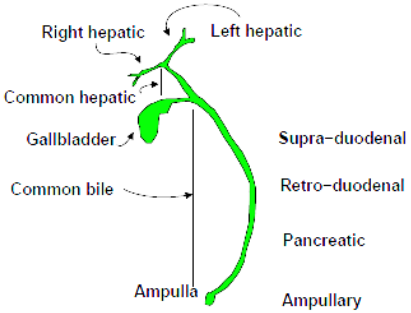
	Pre-hepatic Jaundice	Hepatic Jaundice	Post-hepatic Jaundice
Jaundice / Skin Colour	Unconjugated hyperbilirubinemia / Lemon Yellow	Conjugated hyperbilirubinemia / Orange Tint	Conjugated hyperbilirubinemia / Greenish Tinge
Stool Colour	Dark in colour (increased stercobilin)	Normal Colour	Pale (no bile pigments)
Urine Colour	Normal colour (unconjugated Br cannot be filtered into urine)	Tea Colour	Tea Colour (bilirubinuria, no urobilinogen)
Pruritus	NO pruritus (no bile accumulation)	-	Intense Pruritus, presence of scratch marks (bile accumulation)
Spleen	Splenomegaly	Normal to Mildly Enlarged	-
Liver Function Test* (ALP)**	ALT & AST: Normal ALP & GGT: Normal Liver Proteins: Normal ↑ LDH, ↓ haptoglobin	ALT & AST: Raised disproportionate to ALP and GGT ▪ AST>ALT → toxins (AST in mitochondria) ▪ ALT>AST → viral (ALT in cytoplasm) ALP & GGT: Raised (in cholestatic phase) Liver Proteins: Reduced serum albumin in chronic liver failure	AST & ALT: Mildly Elevated ALP & GGT: Raised, disproportionate to AST & ALT Liver Proteins: Normal
Full Blood Count	Anemia with Reticulocytosis	Low Platelets	-
Others		Anorexia Hepatic Tenderness ± Prolonged PT/PTT, Prolonged INR (cirrhosis)	Enlarged Gallbladder
Other Investigations	PBF Direct Coomb's test for autoimmune haemolytic anemia Stool OCP (ova, cysts, parasites) malaria	AFP: exclude complication of malignancy Viral hepatitis serology: ▪ Acute: Anti-HBc IgM, Anti-HAV IgM ▪ Chronic: HBsAg, anti-HCV, HCV RNA Autoimmune screen: ANA, anti-dsDNA, AMA Metabolic screen: Ceruloplasmin, 24 hour urine copper Do abdominal U/S: ▪ Surface nodularity, ↑ echogenicity in cirrhosis ▪ Signs of portal HTN (splenomegaly & ascites)	Do abdominal U/S ▪ If ducts dilated (>8mm), do ERCP/MRCP/PTC ▪ If ducts not dilated, further serologic testing: AMA (M2-IgG most specific for PBC), p-ANCA (PSC), ANA & anti-SMA. Consider ERCP, liver biopsy
Causes	<u>Unconjugated Hyperbilirubinemia</u> ▪ Gilbert's Syndrome <u>Haemolytic Anemia</u> 1) Inherited ▪ Thalassemia ▪ G6DP ▪ Spherocytosis ▪ Sickle-cell anemia 2) Acquired ▪ Infective: malaria ▪ Autoimmune: SLE, Evan's syndrome ▪ Haemolytic uremic syndrome (thrombocytopenia, ARF, haemolytic anemia)	<u>Infective</u> ▪ Acute Viral Hepatitis (HAV, HBV) ▪ EBV, CMV, Herpes Simplex, TB <u>Autoimmune Hepatitis</u> ▪ SLE <u>Drug Induced Hepatitis</u> 1) Direct action (metabolite-related) ▪ Phenytoin, carbamazepine, Isoniazid, statins, MTX, Paracetamol (Transaminases can be > 1000IU/L) 2) Immunological Reaction ▪ Methyldopa, Halothane <u>Liver cirrhosis/chronic liver disease</u> ▪ Alcoholic liver disease ▪ Chronic viral hepatitis (HBV, HCV) ▪ Metabolic (Wilson's, hemochromatosis) ▪ Infiltrative (Sarcoidosis, amyloidosis) <u>Inherited ↓ /absent activity of UGT (unconjugated hyperBr)</u> ▪ Gilbert's syndrome ▪ Crigler Najjar 1 & 2 <u>Inherited impaired biliary excretion (conjugated hyperBr)</u> ▪ Dubin-Johnson syndrome ▪ Rotor syndrome	<u>Intraluminal</u> ▪ Gallstones (painful, biliary colic) ▪ Parasites: Ascaris lumbricoides, schistosomiasis <u>Mural</u> ▪ Biliary strictures post ERCP ▪ Biliary strictures from gallstones, chronic pancreatitis ▪ PBC (intrahepatic bile ducts): middle aged ♀ ▪ PSC (intra & extrahepatic): ♂ with IBD esp. UC ▪ Cholangitis (Charcot's triad) ▪ Choledochal cyst (type I-V) ▪ Distal cholangiocarcinoma <u>Extraluminal</u> ▪ Ca head of pancreas (painless, w distended GB) ▪ Peri-ampullary Cancers (cholangio, dudeno, ampullary) ▪ Mirizzi's syndrome (chronic cholecystitis) ▪ Malignant Lymph nodes at the porta hepatitis <u>Others</u> ▪ Intrahepatic causes → hepatitis, drugs, cirrhosis, PBC ▪ Biliary atresia ▪ Drug-induced: Paracetamol, penicillin, corticosteroids

* Note: liver function test indicates the 'health' of various components of the liver; transaminases (AST & ALT) indicate hepatocyte health, alkaline phosphatase & γ-glutamyltransferase (ALP & GGT) indicate bile duct epithelium health, liver proteins such as albumin & clotting factors (measured in proxy by PT/PTT) serve as a severity index to indicate residual liver function

** ALP: consist of a group of iso-enzymes found in <u>(1) liver, (2) bile duct, (3) kidney, (4) bone, (5) placenta, (6) malignant tumour (i.e. bronchial carcinoma)</u> → heat inactivation can separate it into heat liable (bone) and heat stable (liver) [bone burns, liver lasts], ALP can also vary with age being elevated in pregnancy and children

APPROACH TO OBSTRUCTIVE JAUNDICE[1]

- Obstructive Jaundice results from biliary obstruction which is blockage of any duct that carries bile from liver to gall-bladder and then to the small intestines
- Jaundice is defined as yellow pigmentation of the skin and eyes as a result of excess bilirubin in the circulation, clinically detectable when levels are >40umol/L (normal: <22umol/L)



PHYSIOLOGY (BILIRUBIN METABOLISM)

- RBCs are broken down in the spleen → biliverdin (heme oxygenase)
- unconjugated bilirubin (biliverdin reductase) which is water insoluble and tightly bound to albumin, does not pass into urine but instead → transported to liver
- In the liver → it gets conjugated with glucuronic acid (uridine diphosphate glucoronyl transferase – UDPGT) to conjugated bilirubin (water soluble)
- Bilirubin is stored in the gallbladder and excreted in the bile → enters small intestines
- Intestinal bacteria converts conjugated bilirubin to urobilinogen
    1. Recirculate back to bile via enterohepatic circulation
    2. Excreted in the urine
    3. Excreted in the faeces as stercobilinogen (gives faeces their brown colour)

Liver can usually cope with increase in unconjugated bilirubin → patient with haemolysis may therefore be slightly jaundiced with a normal colour urine and stools.

Under normal circumstances, tiny amount of urobilinogen is excreted in the urine, in complete biliary obstruction or severe intrahepatic cholestasis → conjugated bilirubin leaks out and appears in urine giving it a tea-coloured appearance and feces take appearance of china clay.

PHYSIOLOGY (FUNCTIONS OF THE GALLBLADDER)

1. Reservoir for bile
2. Concentration of bile → active absorption of water, NaCl and HCO_{3-} by mucous membrane of the gallbladder → bile gets concentrated 5-10x
3. Secretion of Mucus → with obstruction of the cystic duct → risk of mucocele formation

* Rate of bile secretion controlled by cholecystokinin (CCK)
GB lined by **simple columnar epithelium with microvilli (for absorption to concentrate bile), no goblet cells

HISTORY

1. Is it jaundice?

Clinical Assessment	- Inspect mucous membrane of the sclera, mouth, palms and soles in natural light (these areas are protected from the sun, photo degradation of bile is minimized)
For Exclusion	A skin discoloration can be mimicked by: - (DIET) Consumption of large qty of food containing lycopene or carotene - (DRUG) Ingestion of drugs such as rifampicin, quinacrine or TCMs

2. Is it direct or indirect hyperbilirubinemia?

Direct HyperBr (conjugated)	Tea coloured urine, pale stools, pruritus
Indirect HyperBr (unconjugated)	Normal coloured urine and stools

3. Is it hepatic (parenchymal) or post-hepatic (cholestatic)?

Hepatic Jaundice	Any acute hepatitis, history of alcohol abuse, any stigmata of chronic liver disease – (i.e. palmar erythema, caput medusa, ascites, dupuytren's contracture) Symptoms suggestive of viral hepatitis: prodromal of fever, malaise, arthralgia, myalgia, nausea/vomiting, etc. Risk factors for viral hepatitis: travel history, ingestion of seafood, family history of hepatitis (esp. mother, siblings), blood transfusions, drug abuse/needle sharing, needle stick injuries, sexual contact Hepatitis Panel: Anti-Hbs, HbsAg, Anti-Hbc (Total), Anti-HCV
Post-hepatic jaundice	Abdominal pain, pruritus (as a result of bile salt retention), palpable liver (>2cm below costal margins)

Cholestasis: decreased delivery of Br into the intestine (subsequent accumulation in the hepatocytes and in blood) → can be due to defect in hepatocellular fx (medical jaundice) or obstruction in biliary tree (surgical jaundice). Using history, physical examination and haematological investigations (LFTs → total Br, ALP, GGT) can help differentiate hepatic vs. post-hepatic jaundice

[1] Approach to the Jaundiced Patient. ACS Surgery: Principles and practice.2006.

4. What are the differential diagnoses?

Cholangitis	Charcot's Triad → Jaundice, Fever (a/w chills and rigor) & RHC Pain Reynold's Pentad → above 3 + hypotension and mental obtundation - Choledocholithiasis is the most likely diagnosis → Mx: ABC, IV Antibiotics, ERCP (to establish adequate biliary drainage), If ERCP cannot be done – KIV percutaneous transhepatic biliary drainage or surgery
Choledocholithiasis	- Ask patient about past history of gallstone disease / biliary colic symptoms / previous history of surgery / ERCP - Suspect choledocholithiasis if jaundice is episodic (recurrent spikes), painful or if u/s shows presence of gallstones – usually if patient is young and have painful jaundice more likely to be benign causes → Mx: ERCP (high diagnostic yield, therapeutic function in clearing CBD stone in 95% of patients) or MRCP KIV laparoscopic cholecystectomy → Alternative Mx: laparoscopic cholecystectomy with intraoperative cholangiography
Lesions other than choledocholithiasis	- Malignancy is suspected when patient is old, jaundice is new onset, painless and progressively worsening - Ask about constitutional symptoms (i.e. LOA/LOW/malaise) and metastatic symptoms (i.e. bone pain, dyspnoea, neck lump) – impt to r/o pancreatic CA or other malignancies - Pain is a late symptom of pancreatic cancer and tend to be constant and relentless compared to biliary colic which subsides after a few hours - Perform spiral CT or MRI with MRCP to diagnosticate& assess resectability → Mx: depends if tumour is resectable (no involvement of the SMV, portal vein, SMA and porta hepatis, no local adenopathy, no extra-pancreatic extension of tumour) – see pancreatic tumour management
Post-operative Jaundice	- Affects 1% of all surgical patients undergoing hepatobiliary procedures - Differential (biliary): (1) retained CBD stones, (2) post-op biliary leak, (3) injury to CBD resulting in stricture formation - Differential (non-biliary): based on time after operation (1) within 48 hours – breakdown of RBC, (2) 5-10days – secondary to intraoperative hypotension / hypoxemia, (3) 7-10 days – medication induced hepatitis, (4) >7 days – a/w manifestation of septic response, (5) 5-12 weeks – non-A/B/C viral hepatitis after transfusion of blood products

5. What are the possible complications?

Liver Decompensation	- Encephalopathy, hepatic fetor, worsening ascites
Acute Pancreatitis (gallstone as cause)	- Abdominal pain radiating to the back with N/V
Fat malabsorption	- Steatorrhoea, fat-soluble vitamin deficiency (A, D, E, K) – especially coagulopathy (very unlikely in acute setting)

6. Where is the level of obstruction? What is the cause of the obstruction?

Imaging Goals	(1) Confirm presence of extra-hepatic obstruction (2) Determine level of obstruction (3) Identify specific cause of obstruction (4) Staging in cases of malignancy
Imaging Modalities	(1) Direct cholangiography (gold standard) → endoscopic retrograde cholangiopancreatography (ERCP) or perc. transhepatic cholangiography (PTC)) a. ERCP risks: bleeding perforation, pancreatitis, cholangitis (4-7%) b. PTC risks: bleeding, bile leakage, cholangitis (4%) (2) Ultrasound HBS – Determines level of obstruction and confirms presence of intrahepatic or extra hepatic ductal dilatation of biliary system in 95% of patients, if absent a. Unlikely that obstructing lesion is present – does US point to a specific hepatic cause of jaundice b. It may be too early in the course of the disease, biliary dilation has yet to occur – KIV hepatoiminodiacetic (HIDA) scan c. Intermittent dilatation – consider possibility of a passed stone (choledocholithiasis) (3) Computed Tomography (CT) or spiral CT (4) Magnetic Resonance Cholangiopancreatography (MRCP) or endoscopic u/s (EUS) a. For visualizing the biliary and pancreatic ducts b. MRCP limitation in diagnosing small CBD stones c. Spiral CT, EUS and MRCP in combination with MRI useful in diagnosing and staging biliopancreatic tumours → EUS good for peri-ampullary tumours and MRI with MRCP for more proximal disease of the biliary tree

CAUSES OF CHOLESTATIC JAUNDICE

- Commonest causes – Gallstones, Tumour, Hepatitis
- Painless Cholestatic Jaundice → r/o Periampullary cancer (i.e. HOP cancer, Cholangiocarcinoma)
- Painful → stones, strictures, hepatic causes

Intrahepatic		- Hepatitis - Drugs - Cirrhosis - Primary Biliary Cirrhosis
Extra-Hepatic	Intraluminal	Benign - Gallstones - Parasitic Infections (recurrent pyogenic cholangitis)
	Mural	Benign - Post-instrumentation strictures (ERCP, operation) - Strictures from other causes (gallstones, chronic pancreatitis) - Primary sclerosing cholangitis - Choledochal cyst Malignant - Cholangiocarcinoma (distal)
	Extramural	Benign - Mirizzi syndrome - Pancreatitis Malignant - Head of pancreas cancer - Metastases to the porta hepatis (malignant lymph nodes)

PHYSICAL EXAMINATION

- Vitals: is patient hemodynamically stable? Any fever?
- General Inspection: jaundice? Any abdominal distention? Any leg swelling?
- Abdomen:
  - Any scars of abdominal surgery?
  - Stigmata of chronic liver disease? – gynaecomastia, spider nevi, caput medusae,
  - Generalized distention? (ascites could be due to malnutrition, peritoneal malignancy, or obstruction of portal vein by cancer)
  - Hepatomegaly? (Could be due to metastatic disease, or primary liver pathology)
  - Enlarged palpable gallbladder? (Recall Courvoisier's law – if the gallbladder is palpable in a person with painless obstructive jaundice, the cause is unlikely to be stones)
  - Splenomegaly? (Portal hypertension – think pre-hepatic, hepatic, post hepatic)
- DRE: Pale stools?
- Cervical and supraclavicular lymph nodes
- Bony tenderness
- Respiratory examination

INVESTIGATIONS

Bloods

Firstly to confirm obstructive jaundice:

1. LFT – classical obstructive picture
   a. Bilirubin raised (± direct>indirect; Normal 3:7)
   b. Raised ALP (and GGT – only ordered if dx is ambiguous, not routine) more than AST and ALT **classical picture more often seen in CA than gallstone disease
   c. Mildly raised liver enzymes (ALT/AST) – biliary backpressure leads to hepatocyte damage

Secondly to confirm inflammation/infection:

2. FBC – ↑ TW to suggest bacterial infection (impt as some pts haven't mounted febrile response), anemia (correct before ERCP), thrombocytopenia (chronic liver disease, viral infection)

Thirdly to assess for potential complications

3. U/E/Cr – assess dehydration, HRS, Cr level for suitability of CT imaging!
4. Amylase – any concomitant pancreatitis
5. PT/PTT – any prolonged PT from vitamin K malabsorption, coagulopathy secondary to liver dysfunction (to be CORRECTED before procedures like ERCP can be done), sepsis causing DIVC/coagulopathy
6. Tumour markers – CA 19-9, CEA (cholangiocarcinoma and pancreatic cancer)
7. Blood c/s if febrile and jaundiced (TRO HBS sepsis)
8. GXM – in case of op (i.e. cholecystectomy)

Imaging

1. U/S HBS: best for imaging stones
   a. US findings:
      i. Choledocholithiasis: Duct dilation≥6mm (impt to identify dilated INTRAhepatic ducts as it indicates that (a) obstruction is more severe (b) PTC is a possible option if ERCP fails)
      ii. Gallstone disease / Cholecystitis: GB stones or sludge, thickened GB wall, pericholecystic fluid, fat stranding
      iii. Complications of gallstones:
      iv. Liver consistency (fatty or cirrhotic)
   b. Disadvantages:
      i. Unable to detect malignancy well
      ii. Unable to detect distal CBD stones well
      iii. Sensitivity reduced with fat patient habitus
      iv. Operator dependent
2. CTAP:
   a. Indications
      i. Suspected perforated GB (view air around GB in lung window)
      ii. Rule out malignant aetiology
   b. Advantages
      i. Preferred if there is a suspicion of malignancy (Ca pancreas or other periampullary cancer) → define the tumour (T) better & stage at the same time (N & M)
      ii. Logistics (can be done earlier esp. cholangitic patient to plan for early intervention)
3. CXR
   a. ARDS in cholangitis
   b. Pleural effusion

MANAGEMENT

The patient is managed as for the causative aetiology (see relevant sections)

Endoscopic Retrograde Cholangiopancreatography (ERCP)[2]

- Evolved from a diagnostic procedure to an almost exclusive therapeutic procedure with introduction of endoscopic sphincterotomy
- Performed at o/p setting with IV sedation and analgesia, and local anaesthetic spray in throat
  - Correct coagulopathy & stop anticoagulants (5 days) if sphincterotomy anticipated
  - Ab prophylaxis – suspected biliary obstruction, known pancreatic pseudocyst or ductal leak

Biliary Disease	- Choledocholithiasis (mainly therapeutic) ▪ Therapeutic: **sphincterotomy** and **stone extraction** (balloon / wire basket KIV stent) ▪ Pre-operative: emergent ERCP if worsening cholangitis ▪ Post-operative: elective ERCP to remove retained CBD stones - Malignant and Benign Biliary Strictures ▪ Diagnostic: **brushing, biopsies & FNAC** (combined sensitivity 62%) ▪ Therapeutic: **stricture dilatation** (hydrostatic balloon / graduated catheter) KIV stenting - Post-operative Biliary Leaks ▪ Therapeutic: **endoscopic stenting** to decompress bile ducts - Sphincter of Oddi Dysfunction ▪ Therapeutic: endoscopic sphincterotomy
Pancreatic Disease	- Recurrent Acute Pancreatitis ▪ Diagnostic: obtain definitive imaging of ductal anatomy ▪ Therapeutic: endoscopic sphincterotomy - Chronic Pancreatitis (and its associated complications – i.e. strictures) - Pancreatic Duct Leaks ▪ Therapeutic: pancreatic-duct stent - Pancreatic Fluid Collection – i.e. pseudocysts, pancreatic necrosis ▪ Therapeutic: pancreatic stent & sphincterotomy – drain pseudocyst that communications with pancreatic duct - Pancreatic Malignancies ▪ Diagnostic: ERCP directed brush biopsy / FNAC (combined sensitivity 65%)
Ampullary Disease	- Ampullary Adenoma ▪ Therapeutic: **snare ampullectomy** with combined biliary and pancreatic sphincterotomy

Complications[3] = overall rates (6.85%) – mild-mod: 5.2% | severe: 1.7%

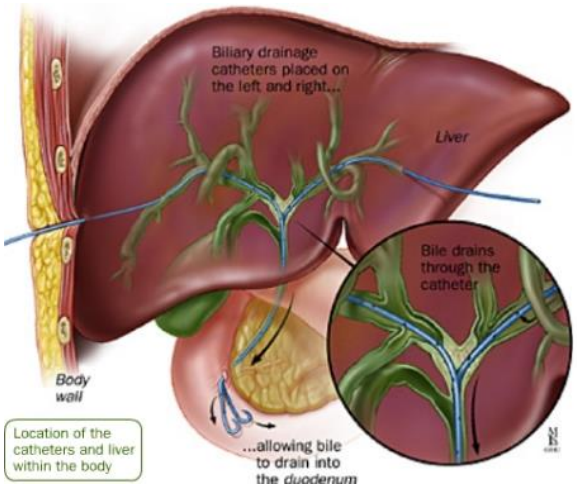
1. Pancreatitis – 3-4% (usually settles by itself)
   - Irritation of the pancreas duct by the injection of contrast
   - Edema when removing stone
2. Infections (i.e. cholecystitis / cholangitis) – 1-2%
3. Haemorrhage – 1-2%
   - Result from cutting the opening of the duct (sphincterotomy)
4. Perforation (i.e. duodenal or biliary) – 0.5%
5. CVS and/or analgesia-related – 1-2%
   - Risk of sedation: ↓ BP, ↓ O2 levels and respiratory depression
6. Fatality – 0.33%

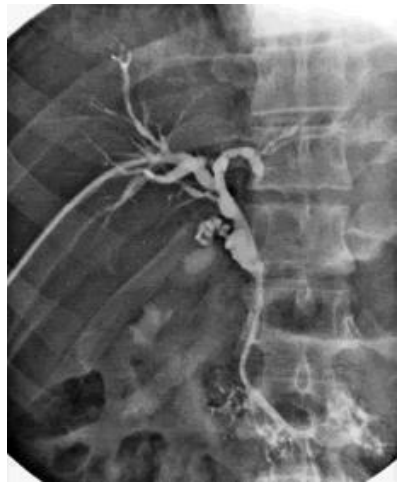
[2] Gastrointest Endosc. 2005 Jul;62(1):1-8

[3] Am J Gastroenterol. 2007 Aug;102(8):1781-8.

Percutaneous Transhepatic Cholangiography (PTC)[4]

- Also known as Percutaneous Transhepatic Biliary Drainage (PTBD)
- Involves transhepatic needle insertion into a bile duct followed by injection of contrast to opacify the bile ducts
- Indications
  - Patients who have biliary duct dilatation on ultrasound or other imaging modalities and are not candidates for ERCP
- Diagnostic
  - Assess intrahepatic ductal disease (i.e. sclerosing cholangitis & cholangiocarcinoma)
  - Obtain brushing, biopsies to evaluate for malignancy
- Therapeutic interventions
  - Drainage of infected bile in cholangitis
  - Extraction of biliary tract stones
  - Dilatation of benign biliary strictures
  - Placement of stent across a malignant strictures





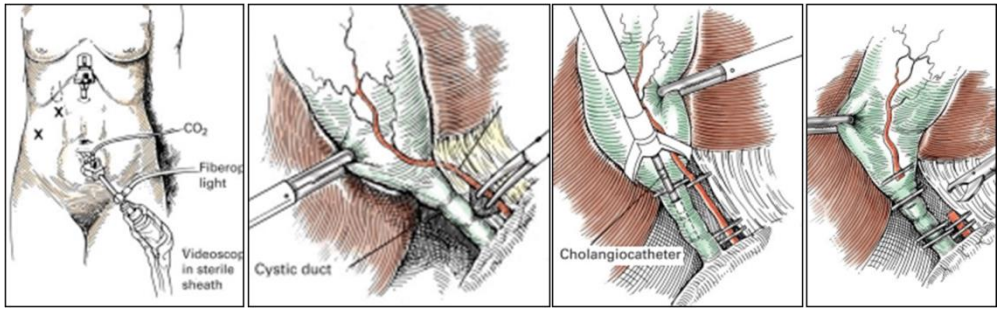
Complication (for most transhepatic procedure)

1. Cholangitis ~2%
2. Hemobilia – communication between biliary duct and vascular structure
   - Hepatic artery pseudoaneurysm
   - Hepatic artery-bile duct / portal vein fistula

[4] uptodate: Percutaneous transhepatic cholangiography

Laparoscopic Cholecystectomy (operative procedure)

- Hasson Open Technique – pneumoperitoneum established
  - Insertion of 10mm blunt trocar at central umbilical site – port for video-scope
  - Insufflation of the intraperitoneal space with CO_2 gas – intra-abd. pressure ~ 15mmHg
- 3 more 5mm ports inserted under direct visualization –
  1. subxiphoid – 5cm below xiphoid (on the right of the falciform ligament)
  2. right subcostal area – midclavicular line several cm below costal margin
  3. right flank – laterally almost at level of umbilicus
- To minimize bile duct injury – "critical view of safety"
  - Neck of GB dissected off liver bed – i.e. unfolding of Calot's triangle
  - Calot's Δ = cystic artery superiorly, cystic duct laterally and the common hepatic duct medially
  - The centre of calot's Δ contains a lymph node (Lund's node)
  - Cystic artery clipped & cystic duct singly clipped only proximally first
- ± intra-operative cholangiogram
  - Cannula inserted into cystic duct and dye is injected under an image intensifier (II)
  - If cholangiogram is satisfactory → distal cystic duct doubly clipped distally and divided
- GB dissected from GB bed and removed via umbilicus with the use of an applied medical bag
- GB bed is irrigated and haemostasis checked
- Recovery – 80% of patients discharged within 24 hours, most discharged by POD2



Conversion to open surgery

- RF: obesity, previous cholecystitis, prior upper abdominal surgery (adhesions ++)
- Based on patient safety (i.e. safe dissection can't be performed laparoscopically) and not considered a complication of surgery

Complications[5]

- Specific to Procedure
  - Injury to the bile duct – 0.25%
  - Injury to neighbouring structures (i.e. hepatic artery and bowel)
  - Un-retrieved gallstone spillage – LT risk of abscess and fistula formation
  - Retained stones in the CBD – requires subsequent management – <5%
  - Hernia at incision site – esp. in obese patients
  - ? post-cholecystectomy syndrome
- Specific to General Anaesthesia
  - Allergic reaction to anaesthetic
  - Lung infection, Stroke, heart attack, death
- Related to laparoscopic surgery
- Related to any surgery
  - Bleeding, wound infection, DVT, PE

[5] The Washington Manual of Surgery (6th edition) – pg 369

CHOLELITHIASIS

Cholelithiasis refers to the presence of gallstones in the gallbladder

EPIDEMIOLOGY

- Exact incidence in Singapore not known
- In the West: 25% in women and 12% in men (by age 60)
- Consistent 2:1 female to male ratio, 1:1 in elderly

STONE COMPOSITION AND PATHOPHYSIOLOGY

<table>
<tr><td colspan="2">Cholesterol Gallstones (85%)</td><td>- Radiolucent,
- Composed of cholesterol, yellow, finely granular, hard and faceted
- a/w – fat (metabolic syndrome), female, forty (age), fertile (estrogenic influence – pregnancy and OCP use lead to increase uptake and biosynthesis of cholesterol in the liver leading to increase biliary cholesterol excretion)

<u>Formation is due to disruption in the solubility equilibrium of bile</u>
1. Increased cholesterol secretion in bile
▪ Old
▪ Obesity, rapid weight loss
▪ Hyperlipidaemia
▪ Oestrogens ↑ : female, pregnancy, exogenous administration

2. Decreased emptying of the gallbladder
▪ Gallbladder malignancy (important cause to exclude)
▪ Gallbladder hypo-motility: truncal vagotomy, spinal cord injury
▪ Pregnancy
▪ Fasting, TPN</td></tr>
<tr><td rowspan="3">Pigment Stones (15%)</td><td>Black (sterile) Gallstones</td><td>- Radiopaque,
- Composed of calcium salts (calcium bilirubinate, calcium phosphate and calcium carbonate) hard, speculated and brittle

Formation is due to
1. Increased secretion of <u>bilirubin</u> into bile (e.g. chronic HAEMOLYSIS, most commonly G6PD-def, CIRRHOSIS, chronic liver disease, TPN),
2. Decreased bilirubin solubilizes, and gallbladder stasis</td></tr>
<tr><td>Brown (infected) Gallstones</td><td>- Radiopaque,
- Composed of calcium salts (calcium bilirubinate and calcium palmitate) and bacterial cell bodies, soft stones
- Increasing in incidence due to influx of foreign workers
- Related to recurrent pyogenic cholangitis

Formation is due to
1. Infection (especially klebsiella) with <u>bacterial degradation</u> of biliary lipids (hydrolyse conjugate bilirubin to free form), the degradation products of which then precipitate as calcium bilirubinate.
2. Biliary Stasis</td></tr>
<tr><td colspan="2">Mixed</td><td>- Majority</td></tr>
<tr><td colspan="2">Biliary Sludge</td><td>- Defined as microlithiasis suspended in bile; predisposes to stone formation
- Can be visualised on the ultrasound scan as layering in the biliary tree
- Sludge is a pre-stone condition, but not all sludge becomes stones
- 20% of biliary sludge will disappear, 60% recur, and 10% form stones</td></tr>
</table>

CLINICAL COURSE

Patients can be divided into 3 clinical stages → <u>asymptomatic</u>, <u>symptomatic</u> cholelithiasis and <u>complicated</u> cholelithiasis

Asymptomatic Gallstones

- Detected on routine imaging studies or incidentally at laparotomy
- 80-95% of patients will have asymptomatic gallstones
- Risk of symptom occurrence is 1 to 2% per year, of which the greatest risk is within the first 5 years of diagnosis – 10% at 5 yrs, 15% at 10 yrs, 18% at 15-20 yrs
- Of those who develop symptoms, 7-10% will have moderate symptoms, and 3-5% severe; the rest will have minor symptoms
- Thus the majority of patients do not require prophylactic cholecystectomy → expectant management

<u>Role of surgery in the asymptomatic patient:</u>

- Predisposing cause for gallbladder stasis that should be surgically treated e.g. gallbladder mass suspicious of malignancy,
- Patients with high risk of malignancy (gallbladder polyp, porcelain gallbladder) → prophylactic surgery
- Patients with chronic haemolytic disease (e.g. sickle cell anemia, thalassemia) – as high as 50-60% will develop symptomatic disease in their lifetime
- Immunocompromised → presentation is abnormal & difficult to detect

Symptomatic Gallstones

1. <u>Biliary colic</u>
   - Initiated by impaction of a gallstone in the outlet of the gallbladder
   - **Differential Diagnosis:** acute cholecystitis, liver disease, peptic ulcer disease, renal colic, GERD, IBS, inferior AMI, right lower lobe pneumonia
   - Symptoms – characterized by
     1. **Periodicity** → pain comes in distinct attacks lasting 30mins to several hours, often resolves spontaneously (if >6hrs, suspect complication i.e. cholecystitis)
     2. **Location** → epigastric (70%) or RHC pain
     3. **Radiation** → inferior angle of the right scapula, or tip of right shoulder
     4. **Character** → Not a true colic – Waxing-waning in character but rarely have any pain-free intervals between waves of pain (unlike ureteric colic where pain resolves completely in between) – basal pain is due to inflammation of ductal epithelium & proximal distension
     5. **Severity** → Pain is steady and intense
     6. **Timing** → Pain occurs within hours of eating a meal often awakening the patient from sleep
     7. **Other Symptoms** → back pain, LUQ pain, nausea and vomiting (patient gets better after vomiting) bloating, abdominal distension
   - CBD is not muscular, so absence of biliary colic, but a constant pain with OJ 2° to obstruction
   - Biliary colic is a "herald" symptom that indicates risk of further sequelae

Complications from cholelithiasis

1. **In the Gallbladder**
   a. Acute Calculous Cholecystitis – leading to
      i. Empyema of the gallbladder
      ii. Hydrops of the gallbladder
   b. Porcelain gallbladder / Chronic Cholecystitis – leading to
      i. Increased risk of gallbladder cancer (chronic inflammation can lead to scarring of the wall, combined with dystrophic calcification which leads to 'limey' bile and transform the gallbladder into a porcelain-like vessel – associated with GB cancer)
   c. Gallbladder Cancer
   d. Mirizzi's Syndrome – leading to
      i. Obstructive jaundice → (rare, gallstone impacted in cystic duct of neck of gallbladder causing compression of the CBD or common hepatic duct)

2. **In the Common Bile Duct**
   a. Choledocholithiasis – leading to
      i. Obstructive jaundice
      ii. Ascending cholangitis
      iii. Secondary biliary cirrhosis
      iv. Gallstone Pancreatitis

3. **In the Gut**
   a. Cholecystoenteric Fistula Formation – leading to
      i. Intestinal Obstruction → (Inflammation of gallbladder can lead to adhesions with the small bowel which is converted to a fistula over time whereby large stones can directly enter the small bowl)
   b. Bouveret Syndrome – leading to
      i. Gastric outlet obstruction → (rare, direct erosion of a large gallstone through the GB into the GIT)
   c. Gallstone dyspepsia
      i. non-ulcer dyspepsia – fatty food intolerance, dyspepsia and flatulence not due to other causes

***5 criteria for a normal cholangiopancreatogram**
(a) Normal intrahepatic ducts
(b) No filling defects
(c) Smooth common bile duct
(d) No stricture/narrowing of the common bile duct
(e) Good and free flow of contrast into duodenum

INVESTIGATIONS FOR GALLSTONE DISEASE

1. **Plain abdominal X-ray**
   - Pickup rate for gallstones is less than 10% since most stones are radiolucent

2. **Ultrasound of the hepatobiliary system**
   - Investigation of choice for gallstones
     - >92% sensitivity, 99% specificity
   - Even more sensitive than CT scan for stones since CT may miss small stones due to the spacing of the cuts taken
   - Features of stone on ultrasound: strong echogenic rim around the stone, with posterior acoustic shadowing
   - Bile should appear as black patch in gallbladder; if not homogeneous → sludge

3. **CT scan**
   - Usually not done to diagnose stones
     - Usually done in symptomatic patient where it is uncertain what is the cause of symptoms → looking for other possible causes as well (liver/pancreatic)
     - Cx: detect complications of gallstones

4. **Magnetic resonance cholangiopancreatography (MRCP)***
   - MRCP is not the same as MRI liver/pancreas – only selected cuts taken in order to reconstruct the biliary tree & is without contrast → only T2 images, so the resolution is not as good as MRI
   - Comparable to ERCP, and also minimally invasive → preferred to ERCP if patient does not require any therapeutic intervention that ERCP provides

5. **Endoscopic retrograde cholangiopancreatography (ERCP)***
   - The largest value of ERCP lies in its **therapeutic potential (success rates > 90%)**
     - Stone removal (using Fogarty-balloon catheter, or Dormia wire basket)
     - Sphincterotomy (in order to relieve obstruction or facilitate removal of stone)
     - Stenting (plastic vs. metal)
   - Complications (see above)
     - Specific to procedure = pancreatitis, infection, haemorrhage, perforation
     - Specific to sedation = hypotension, respiratory depression, nausea, vomiting

6. **Percutaneous transhepatic cholangiography (PTC) /biliary drainage (PTBD)**
   - PTC involves a tube being inserted under radiologic guidance into one of the biliary ducts (must be dilated duct)
   - Rarely done now; main indications
     - Diagnostic: high obstruction not well visualised in ERCP or previous surgery with altered anatomy (e.g. gastrectomy)
     - Therapeutic: obstructed system that cannot be drained from below
   - Mostly for therapeutic rather than diagnostic purposes
   - Complications: bleeding (esp. in biliary obs pts due to coagulopathy sec to decreased Vit K abs); leakage of bile when tube is removed

7. **HIDA scan**
   - No longer used commonly, except in biliary atresia

TREATMENT

Asymptomatic
- No surgery required unless patient has indications for surgery (see above)
- Expectant management and close follow-up
- Counsel patient about symptoms – biliary colic, acute cholecystitis, obstructive jaundice, etc.

Symptomatic
- Cholecystectomy is the only way to treat gallbladder stones that are symptomatic
- Can be open or laparoscopic – laparoscopic is preferred as it is associated with shorter hospital stay, less pain, less complications post-operatively

- Risks of laparoscopic cholecystectomy
  a) Conversion to open operation up to 5% (due to abnormal anatomy; difficult or complicated dissection; iatrogenic injury); conversion rate is higher if there is on-going infection e.g. cholecystitis – up to 1 in 3 to 1 in 4
  b) Injury to surroundings: bowel & biliary structures e.g. CBD
  c) Spilled bile → peritonitis, sepsis
  d) Haemorrhage
  e) Infection

- Non- surgical means of stone treatment
  - Shockwave lithotripsy – more morbidity cf renal lithotripsy as less fluid around to dampen waves; good results only for cholesterol stones. Expensive. Bile salt therapy necessary following lithotripsy to dissolve gallstone fragments.
    - CI: more than 3 stones, large/calcified stones, non-functioning GB, Cx of gallstones
  - Medical Tx in radiolucent gallstones, <15mm, mod obesity, no/mild symptoms. (success in 75% who fulfil this criteria)
    - Chemodissolution: LT oral bile acid ursodeoxycholic/ chenodeoxycholic acid (thought to reduce hepatic synthesis of cholesterol and reduce cholesterol secretion)
      9 mths intensive followed by lifelong maintenance. Toxicity and S/E, high cost.
    - Liver diet: mod carbohydrates, low fat and cholesterol, high fibre

All therapeutic regimens retaining the GB have 50% recurrence of stones aft 5yrs (no LT benefit)

ACUTE CALCULOUS CHOLECYSTITIS

- Initiated by obstruction of the cystic duct by an impacted gallstone
- Persistence of stone impaction leads to inflammation of the gallbladder which may be acute, chronic or acute on chronic

PATHOPHYSIOLOGY
- Gallstone gets stuck in the cystic duct causing obstruction of biliary flow
- Gallbladder becomes distended and inflamed
- 50% of cultures are sterile (infection occurs eventually. In elderly, DM → severe with gas-forming organisms causing emphysematous cholecystitis)

PRESENTATION
- Constant, unremitting severe RHC pain – due to inflammation spreading to the parietal peritoneum (less commonly epigastric)
- Radiates to the inferior angle of the scapula, interscapular
- Associated with anorexia, nausea, vomiting
- Tachycardia, Low grade fever (chills uncommon), Dehydration

- RHC tenderness with guarding found on clinical examination
- Murphy's sign positive (inspiratory arrest during deep palpation of the RUQ)
- Boas's sign – hyperaesthesia below the right scapula
- Palpable GB (30%) – omentum wrapping around GB; worst case scenario is empyema
- Mild Jaundice may be present, if severe consider other differentials

INVESTIGATIONS
1. Ultrasound HBS – features of acute cholecystitis includes
   a) Thickened Gallbladder Wall
   b) Sonographic Murphy's positive
   c) Pericholecystic fluid (oedema of gallbladder wall)
   d) Presence of gallstones in biliary system
   e) Contracted gallbladder (from chronic gallstone disease)

2. CT Abdomen
   a) Fat stranding around gallbladder not seen on ultrasound but on CT
   b) Exclude complications (empyema, perforation)

3. FBC: leukocytosis – if severely elevated (>20) – consider complications (i.e. gangrene, perforation, cholangitis)
4. Amylase (can be raised mildly, if >1000, pancreatitis!),
5. LFT (mild transaminitis)
6. U/E/Cr (dehydration)
7. CXR, KUB
   a) Radiopaque gallstones, aerobilia (due to fistula).
   b) Exclude lower lobe pneumonia, perf viscus, abnormal right hemidiaph/thorax
8. Pre-Op: PT/PTT, ECG

MANAGEMENT

- Assess the patient's vitals and resuscitate the patient if needed – IV fluid resuscitation
- Empirical intravenous antibiotics – IV ceftriaxone and metronidazole
- NBM – bowel rest
- Careful monitoring for signs of failure (peritonism, non-resolving fever/pain)
- Septic workup
- Analgesia
- Definitive treatment – open or laparoscopic cholecystectomy
- Alternative Treatment – percutaneous cholecystostomy
    - Involves percutaneous catheter placement in the gallbladder lumen under imaging guidance (alternative to surgical cholecystectomy)
    - Indications: moribund patients who are not fit for surgery or when early surgery is difficult due to extensive inflammation
    - Drains the gallbladder and alleviates the inflammation (resolves acute episode)
    - Followed by elective cholecystectomy 4-6 weeks later

Physiological Effects of Cholecystectomy

- Reflux disease & biliary gastritis (2° to the loss of concentrating action of the GB leading to increased flow of bile)
- Abdominal pain & diarrhoea (2° to disturbed micelles formation leading to fat intolerance and malabsorption)

Timing of cholecystectomy

- Dependent on several factors:
    - Severity of illness
    - Response to resuscitation and antibiotic therapy
    - Logistical considerations (availability of OT, surgeon etc.)

- Possibilities available:
    - **Emergency** (immediate; in sick patients who are not responding to treatment)
    - **Early** (within few days of onset)
    - **Delayed/Interval** (after 6-8 weeks)

Early	Delayed
Meta-analysis[6] of existing literature shows no significant differences in early versus delayed procedures with regards to mortality, conversion rates, bile duct injury and peri-operative complications	
Advantages ▪ Easier to operate as the gallbladder is oedematous ▪ Reduced hospital length of stay Disadvantages ▪ Possibly higher risk of operative complications (controversial) – 3x higher risk than for elective surgery[7]	Disadvantages ▪ Chance of interval complications requiring re-admission

COMPLICATIONS (ACUTE CHOLECYSTITIS)

1. **Hydrops**
    - Cystic duct obstruction leads to a tense gallbladder filled with mucus
    - May lead to gallbladder wall necrosis if pressure exceeds capillary blood pressure

2. **Empyema**
    - Gallbladder is filled with pus due to bacterial infection of the stagnant bile (cystic duct being obstructed by a stone)
    - Patient is usually toxic, requiring urgent surgery

3. **Gangrene and perforation**
    - Localised perforation → abscess that is confined by the omentum
    - Free perforation → generalised peritonitis and sepsis, requiring emergency laparotomy

4. **Cholecystoenteric fistula**
    - Commonly in duodenum, then colon, and stomach; after repeated attacks of cholecystitis
    - Usually asymptomatic
    - On AXR, aerobilia is seen in 40% of cases
    - Symptomatic fistulas should be treated with cholecystectomy and fistula closure

5. **Gallstone ileus**
    - Stones causing Cholecystoenteric fistula pass into the enteric lumen
    - Patient presents with symptoms of small bowel obstruction an air in the biliary tree
    - Accounts for 1-2% of IO overall
    - Most common site of obstruction is terminal ileum (2 feet proximal to ileocecal valve)
        - Ppt: unexplained gradual onset of SB obstruction
        - Ix: AXR, Barium follow through
        - Small stones (<2-3cm) usually pass spontaneously without problems
        - If >2.5cm and migrated into gut → impact at terminal ileum (commonest), duodenum, sigmoid colon
    - Mortality is 10-15%, mostly in elderly patients in whom gallstone ileus is more common
    - Treatment:
        - Exploratory laparotomy, with enterolithotomy (removal of obstructing gallstone via small bowel enterotomy proximal to point of obstruction)
        - Entire bowel searched thoroughly for other stones
        - Cholecystectomy – can be performed in the same operation if patient is stable (low risk) and inflammation is not too severe
        - ? fistula repair

PROGNOSIS

- 5% mortality
- Nearly all >6oyears, with DM
- Causes: 2° cardiovascular pulmonary complications (older), uncontrolled sepsis with peritonitis and intra-abdominal abscess

[6] Br J Surg. 2010;97:141
[7] Arch Surg. 1996;131:382

CHOLEDOCHOLITHIASIS

- Presence of gallstones in the common bile duct (originated from the gallbladder and pass through the cystic duct into the common bile duct)

PRESENTATION

- RUQ or epigastric pain (pain often more prolonged than seen with biliary colic)
- Nausea and/or Vomiting
- Obstructive Jaundice – tea-coloured urine, pale stools
- Complications: acute cholangitis & acute pancreatitis

INVESTIGATIONS

BLOODS

- LFTs:
  - Early biliary obstruction: ALT/AST elevated
  - Later: ALP/Serum Br (direct)/GGT more elevated than AST/ALT (cholestatic pattern)
- FBC: leukocytosis (may suggest cholangitis)
- Serum Amylase: (CBD stone may cause pancreatitis)

IMAGING

Ultrasound HBS

- Gallstones in gallbladder
- Gallstone in CBD – ductal stones visible ~50% owing to obscuring gas in the duodenum
- Dilated CBD
  - 5mm is normal in the 50s and 6mm in the 60s and so on[8]
  - In older patients, post-cholecystectomy, or patients on LT opiates, the CBD may be larger

Other Modalities: MRCP, EUS

MANAGEMENT[9]

- **Surgery** → Laparoscopic Cholecystectomy (LC) and intra-operative cholangiography (IOC) followed by Lap. CBD exploration (if stones are seen)
  - ± open CBD exploration or post-op ERCP (if Lap. CBD exploration fails to clear stone)
- **Endoscopic** → ERCP with sphincterotomy and stone removal → Interval LC with IOC

When to do operative removal of stones (i.e. not suitable for ERCP)

- Stone >25mm
- Intrahepatic stone
- Large number of stones
- Impacted stone
- Dual pathology
- Tortuous duct
- Previous Billroth II (unsuitable anatomy for ERCP)

When to do ERCP removal of stones

- Not surgical candidates
- Had prior cholecystectomy
- Patients with acute cholangitis

[8] Ultrasound Quarterly 2010;26:67Y74
[9] The Washington Manual of Surgery (6th edition) – pg368

CHOLANGITIS

- A life-threatening bacterial infection of the biliary tree associated with partial or complete obstruction of the ductal system
- A delay in treatment can result in multi-organ failure secondary to septicaemia

PRESENTATION

- **Charcot's triad**: Right Upper Quadrant (RUQ) pain, intermittent fever with chills and jaundice (only 50-70% of patients have the classic triad)
- **Reynold's pentad**: Charcot's triad + mental obtundation + hemodynamic instability – seen in less than 10% of patients, more prevalent in the elderly
- A surgical emergency!

PATHOLOGY

- Usually results from obstruction to the biliary system with infection of stagnant bile
- Most common cause is choledocholithiasis (60%);
- Consider benign strictures (instrumentation), malignancy (pancreatic, biliary), foreign body (previous instrumentation), PSC, Choledochal cysts, Mirizzi's, haemophilia, biliary enteric anastomosis
- Common causative organisms are gram negative bacteria and anaerobes – Klebsiella, E. coli, Enterobacter, Enterococcus
- Small proportion (elderly, prev biliary surgery) – anaerobes (bacteriodes, clostridium), developing world – parasites (Clonorchis sinensis, Ascaris lumbricoides)

COMPLICATIONS

- Sepsis
- Electrolyte abnormality (dehydration)
- Infection
- Coagulopathy (Vit K)

INVESTIGATIONS

1. **Establish the Diagnosis**
   a. Ultrasound → dilated bile ducts
   b. LFTs → cholestatic picture
   c. Blood / Bile Culture → isolation of causative organism

MANAGEMENT

The main goals of treatment is directed towards treating the biliary infection and obstruction

1. **Resuscitation** – "In view of cholangitis being a surgical emergency, I will like to resuscitate the patient who may be in septic shock". Anticipate rapid deterioration.
   - Inform seniors
   - Obtain good intravenous access and fluid resuscitate as appropriate
   - Take bloods for investigations – cultures especially
   - Close monitoring of vitals in HD/ICU
     - Hrly para + SpO_2 → Keep MAP ≥ 65mmHg (or to inform doctors if SBP<100mmHg)
     - Catheterise and watch urine output (hrly urine output) – hepatorenal! (keep ≥0.5mg/kg/hr)
     - CVP line insertion if patient has shock unresponsive to fluid resuscitation (keep 10-12mmHg)

2. **IV Antibiotics**
   - IV ceftriaxone and metronidazole; imipenem if the patient is in shock

3. **Emergent biliary decompression**
   - Timing
     - usually deferred until 24-48h after admission when patient is stable and/or has improved with systemic antibiotics
     - Emergency if deteriorating / Abx not improving infection (15%)
   - Biliary decompression
     a) Decompression commonly performed using ERCP
        - endoscopic sphincterotomy + stenting or external drainage (nasobiliary drain: bile duct to nose for continuous drainage)
        - Success rate 90%
        - If cause of obstruction can be treated in the same setting (e.g. stones to be removed) then treat the cause also
   - Other methods to decompress:
     - percutaneous transhepatic drainage (esp. if neoplastic obstruction)
     - operative decompression

4. **Definitive Therapy**
   - Choices for definitive treatment:
     (a) Open cholecystectomy with CBD exploration
     (b) Laparoscopic cholecystectomy
     (c) Laparoscopic cholecystectomy with CBD exploration

CBD EXPLORATION

- **Cholangiogram or choledochoscopy is performed**
  - Cholangiogram involves injection of dye – can image higher ducts
  - Choledochoscopy involves using a scope to visualise the large biliary ducts – cannot image higher ducts, thus not as sensitive, but can be used to remove stones visualised in the duct
  - Choice of imaging depends on site of obstruction and the cause

- **Removal of stones**
  - Manual removal with stone-grasping forceps
  - Flushing out stones
  - Dredging stones out using balloon catheter or Dormia basket
  - Lithotripsy

- **Consider use of biliary stent or T-tube after removal of stone(s)**

If there is a lot of instrumentation of the biliary system during the operation, one should anticipate swelling and oedema of the biliary system resulting in post-operative obstruction and build-up of bile → higher risk of biliary leakage

(a) **Stent** – removed later by endoscopy
(b) **T-tube (usually inserted after CBD-E)**
  - A T-shaped tube with its horizontal limb placed in the CBD and the vertical limb leading out to drain bile
  - Functions as a "pressure release valve" as most of the bile will flow through the horizontal limb of the tube into the distal part of the CBD; only when there is obstruction to flow will bile be diverted out through the vertical limb
  - Allows for post-op cholangiogram to check for remaining stones (at POD 9-10) before removal – free flow of contrast into duodenum, no residual stones, and no free leak of contrast into peritoneum
  - If all normal → release anchoring stitch and exert gentle traction on the tube; the tube should slip out easily, if not, call for help
  - If stones are present → leave tube in for 4-6 weeks to form a fibrous tract → allows for instrumentation of tract with a scope to remove the stones

BILIARY BYPASS (UNCOMMON)

- Consider biliary bypass if there are
  i. Multiple stones,
  ii. The CBD is more than 2cm in diameter, or
  iii. There are strictures

- Since the CBD has been chronically dilated, quite unlikely that it will function normally even after removal of the obstruction
- Mostly replaced by endoscopic stenting
- Cholecystojejunostomy preferred over Roux-en-Y choledochojejunostomy

Acute Acalculous Cholecystitis

- No gallstones involved in the pathogenesis
- Risk factors:
  - Very ill patients (i.e. prolonged ICU stay)
  - Sepsis with hypotension – hypotension → formation of viscous bile and GB ischemia → bile may get infected → cholecystitis
  - Immunosuppression
  - Major trauma & burns
  - DM
  - Salmonella typhi infection
  - Prolonged NBM and dependence on parenteral nutrition – lead to biliary stasis
- Mortality rate is high – about 30% (with treatment), up to 70% (untreated)
- Insidious onset – GB necrosis, gangrene and perforation are frequent at time of diagnosis
- Treatment involves broad spectrum antibiotics & emergent cholecystectomy. If patient is unstable → percutaneous cholecystostomy followed by interval cholecystectomy

Mirizzi's Syndrome

- Originally described in 1948 as a partial or spastic obstruction of the common hepatic duct secondary to an impacted gallstone in the cystic duct or infundibulum of the gallbladder
- Definition[10]:
  - Cystic duct is anatomically parallel to common hepatic duct
  - Impaction of a stone in the cystic duct or neck of the gallbladder
  - Mechanical obstruction of the CHD by the stone itself or by secondary inflammation
  - Intermittent or constant jaundice causing possible recurrent cholangitis and if longstanding secondary biliary cirrhosis

PATHOLOGY

- Gallstone in the Hartmann's pouch compressing the CHD resulting in obstructive jaundice
- Impacted gallstone may erode into the CHD or CBD → cholecystohepatic or cholecystocholedochal fistula
- Compression effect is not just mechanical (the stone) but also by the surrounding inflammation
- One of the caveats to Courvoisier's law

GRADING

- Grade I: No fistula; extrinsic compression on CHD
- Grade II: Fistulation into common bile duct with the fistula <1/3 diameter of the CHD
- Grade III: Fistula 1/3 to 2/3 diameter of CHD
- Grade IV: Fistula >2/3 diameter of CHD

MANAGEMENT

- Grade 1: attempt laparoscopic cholecystectomy
- Grades 2-4: open cholecystectomy with CBD exploration

[10] Am Surg. 2001 Jan;67(1):11-4.

Carcinoma of the Gallbladder

- This is a rare disease but extremely variable by geographical regions and racial groups
  - Highest incidence in Chileans, American Indians, northern Indians
- Risk Factors
  - Patient's Age – 60s to 70s
  - Chronic Cholecystitis / Cholelithiasis / Calcification of the gallbladder → porcelain gallbladder
  - Mirizzi's Syndrome[11]
- Pathology
  - Majority Adenocarcinoma (90%)
  - Tumour spread → direct extension to the liver, bile ducts, duodenum, stomach, transcoelomic spread with seeding in the peritoneal cavity, lymphatic spread to perihilar lymphatics, haematogenous to lungs
- Signs and Symptoms
  - Early → mimic gallstone inflammation – biliary colic, cholecystitis (RHC pain)
  - Late → biliary & stomach obstruction (jaundice, vomiting, LOA, LOW, palpable mass)
- Treatment
  - Mostly incidental histological finding after cholecystectomy
  - Early Stage → cholecystectomy
  - Late (Transmural) → cholecystectomy + liver resection + regional LN dissection +/- adjuvant chemoRT
  - Palliative: Endoscopic stent to biliary tree and stomach
- Prognosis: poor – median survival <6/12, 5 year survival = 5%

[11] J Hepatobiliary Pancreat Surg. 2006;13(4):323-6.

CHOLANGIOCARCINOMA[12]

- Cancer that arises from the ductular epithelium of the biliary tree either within the liver or more commonly from the extra-hepatic bile ducts

EPIDEMIOLOGY

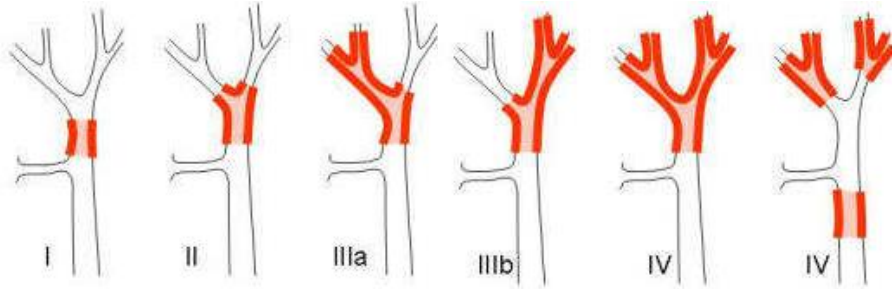
- Uncommon Malignancy – 3% of all GI cancers
- Highest incidence of cholangiocarcinoma – in THAILAND – related to widespread parasitic (opisthorchiasis) infestation
- Median age of onset is 65 years, Male preponderance
- Incidence and mortality rates of intrahepatic cholangiocarcinoma are rising and those of extrahepatic cholangiocarcinoma are declining internationally

CLASSIFICATION

- Intrahepatic – within the liver parenchymal (5-10%)
- Extrahepatic – upper duct – (60-70%) – location of klatskin tumours*
- Extrahepatic – distal CBD – (20-30%)

Bismuth classification

i. Type I: below confluence of hepatic ducts
ii. Type II: tumour reaching confluence
iii. Type IIIA/B: involving common hepatic duct and either right or left hepatic duct
iv. Type IV: multicentric or involving confluence and both hepatic ducts



*klatskin tumour – tumour that arise at the bifurcation of the hepatic ducts

ASSOCIATIONS

- Chronic cholestasis – leading to prolonged inflammation of the biliary epithelium:
  - Primary sclerosing cholangitis (side note: 2/3 of patients with PSC have IBD – UC)
  - Parasitic infection – *Opisthorchis viverrini, Clonorchis sinensis*
  - Hepatolithiasis → biliary stasis → recurrent bacterial infections → LT inflammation
  - Viral Hepatitis
- Fibro-polycystic liver disease
  - Caroli's Syndrome – multifocal segmental dilatation of large intrahepatic bile ducts
  - Congenital hepatic fibrosis
  - Choledochal cysts – cystic dilatations of the bile ducts
- Thorotrast (thorium dioxide) exposure

[12] Lancet. 2005 Oct 8;366(9493):1303-14.

PRESENTATION

Lesion at bifurcation of the hepatic ducts or in distal CBD	- Present with sequelae of biliary obstruction → painless progressive jaundice, pale stools, dark urine and pruritus - Presentation with cholangitis is unusual
Lesion arising within intra-hepatic ducts of the liver parenchyma	- Present with non-specific symptoms → malaise, weight loss and abdominal pain

DIFFERENTIAL DIAGNOSIS

- Benign Strictures (iatrogenic bile duct injuries, PSC, choledocholithiasis)
- Other carcinomas – GB cancer or metastatic hilar nodal metastases

INVESTIGATIONS

- LFTs → non-specific rise in serum Br, rise in ALP and GGT
- CA 19-9 >100µl/ml (sensitivity – 53%) → can also be increased in pancreatic cancer, colorectal cancer, gastric cancer, gynaecological cancers and cholangitis
- CEA – primarily a tumour marker for colorectal cancer, can be used in cholangioCA workup

- Trans-abdominal Ultrasound
  - Identify biliary duct dilatation
  - Can localise site of obstruction
    a. hilar lesions = intrahepatic duct dilatation with normal extrahepatic ducts
    b. distal lesions = intra and extrahepatic ducts dilated
- Contrast enhanced triple phase, helical CT → detect intrahepatic cholangiocarcinoma
- Cholangiography (non-invasive & invasive)
  - Non-invasive = MRCP → superior to ERCP for assessing tumour anatomy and resectability
  - Invasive = PTC / ERCP (benefit of cytologic analysis via ductal brushing or FNA)
- Endoscopic ultrasound with FNA → cytologic diagnosis + assess nodal involvement
- PET-CT
- CT TAP → assess metastatic spread

CURATIVE TREATMENT

- A complete surgical resection with histologically negative margins is the only cure
- Only 25% of tumours are resectable
- **Extra-hepatic cholangioCA affecting CBD** → resection of biliary tree and hilar lymphatics
- **Hilar (klatskin's) tumour** → above + partial hepatectomy (caudate lobe – segment 1)
- **Distal cholangioCA** → pancreatoduodenectomy (whipple's procedure)

Contraindications to surgery

- Bilateral or multifocal intrahepatic disease
- Involvement of portal vein trunk or hepatic artery
- Bilateral involvement of hepatic arterial or portal venous branches
- Unilateral hepatic vascular invasion with contralateral ductal spread
- Distant metastases

PALLIATION

- The aims of palliative endoscopic biliary drainage are to
  - Relieve jaundice and pruritus
  - Prevention of cholangitis
  - Avoid liver failure due to progressive biliary obstruction
  - Enhance quality of life
- Endoscopic/percutaneous transhepatic biliary stenting with self-expanding metal stents
- Stricture of the main bile duct (Bismuth I lesions) → unilateral stents
- Hilar or Bismuth II-IV strictures → unilateral or bilateral stents
  - Only 25% of the liver needs to be drained for adequate palliation
  - Controversial between the use of single or double stents for hilar lesions – no difference showed between either procedure in terms of procedure related mortality, late complications and survival[13]

- Other palliative techniques
  - Percutaneous Transhepatic Cholangiography and biliary drainage
  - Palliative radiotherapy & chemotherapy
  - Photodynamic therapy

PROGNOSIS

- Most patients have unresectable disease at presentation and die within 12 months from the effects of cancer cachexia
- 5 year survival rates post-surgery
  - Intra-hepatic cholangiocarcinoma → 8-47%
  - Distal cholangiocarcinoma → 20-54%

[13] Gastrointest Endosc 2001; 53: 547–53.

PERIAMPULLARY TUMOURS

- Tumours that arise within 2cm of the ampulla of vater in the duodenum
- Require high index of suspicious

Tumours	Important History
Pancreatic Head / Uncinate Process Carcinoma	- New onset diabetes + recalcitrant diabetes – ask about diabetic control (is it well managed with medications!) - Dull aching pain radiating to the back - Pseudo GOO (gastric outlet obstruction) – duodenal obstruction (10-15% present like that) - Worsening steatorrhoea
Cholangiocarcinoma (lower CBD tumours)	- Present with jaundice, abdominal pain and LOW - Age of patient = elderly (require high index of suspicion)
Periampullary Duodenum Carcinoma	- Patient usually in the 6th to 8th decade of life - Present with abdominal pain, iron deficiency anemia*, LOW, nausea & vomiting and obstructive jaundice *UBGIT symptoms = obstructive jaundice + anemia (chronic GI bleed) → silver stools (Thomas's sign) – can occur in any periampullary carcinoma
Ampulla of Vater Carcinoma**	- Present with early obstructive jaundice, biliary colic, bleeding or pancreatitis - Intermittent Jaundice – as tumour grow they outgrow blood and food supply, as a result they die, get passed out of the ampulla of vater and the lumen re-expands and jaundice is alleviated

**some consider ampullary carcinoma a distinct entity from periampullary carcinoma

BENIGN STRICTURES AND BILE DUCT INJURIES

Iatrogenic Injury after Instrumentation or Surgery		- Laparoscopic Cholecystectomy is the leading cause of iatrogenic bile duct injuries and subsequent benign strictures - Other surgeries includes → gastrectomy, hepatic resection, hepatic transplantation

Inflammatory	Oriental Cholangiohepatitis aka. Recurrent Pyogenic Cholangitis	- Infection with (1) ascaris lumbricoides (2) trematodes (i.e. clonorchis sinensis & opisthorchis viverrini)
		- Characterized by:
		  - Recurrent bacterial cholangitis
		  - a/w intra-hepatic pigment stones and
		  - intra-hepatic biliary obstruction
		- Mx → treat current infection, achieve biliary drainage, manage cx

	Primary Sclerosing Cholangitis (PSC)	- Autoimmune cholestatic disorder characterized by progressive fibrous obliteration of the intra-hepatic and extra-hepatic bile ducts - Liver biopsy – fibrous obliteration of small bile ducts / onion skin pattern - a/w p-ANCA - PSC affects ~5% of UC patients, and 60-80% of PSC patients suffer from IBD (ulcerative colitis)[14] - PSC is a risk factor for cholangiocarcinoma – affect 10-20% of patients
	Other Causes	- Choledocholithiasis, Pancreatitis, Radiotherapy - Parasitic Infestation → ascaris lumbricoides, Asiatic cholangiohepatitis
	Trauma Congenital	 - Biliary Atresia

[14] Inflamm Bowel Dis. 2002 Jul;8(4):287-90

DISEASES OF THE BREAST

ANATOMY

- The breast is a modified sweat gland that is located between the subcutaneous fat and the fascia of the **pectoralis muscle** and **serratus anterior** muscle
  - Consists of: fat, fibrous tissue & glandular tissue (fat predominant in a non-lactating breast)
- Posterior to the breast and anterior the pectoralis fascia is the retro-mammary space
- Extends from the lateral sternal border to the mid-axillary line, from the 2nd to the 6th rib
- The axillary tail (axillary tail of Spence) pierces the deep fascia and enters the axilla
- Consists of 15-20 lobules of glandular tissue that drains into a lactiferous duct which converges towards the nipple (and each becomes dilated to form a lactiferous sinus beneath the areola)
- Lobules are separated by fibrous septa running from the subcutaneous tissues to the fascia of the chest wall (suspensory ligaments of Astley Cooper)
  - Dimpling of the skin over a breast carcinoma is due to malignant infiltration and contraction of the Cooper's Ligament
- The areola is lubricated by the glands of Montgomery (large modified sebaceous glands)

Vasculature

- Arterial supply – (1) internal thoracic artery (via perforating branches), (2) axillary artery [(2nd division) long thoracic, thracoacromial branches and (3rd division) subcapsular (thoracodorsal branch)] and (3) the 2nd to 5th intercostals
- Venous drainage – (1) internal thoracic, (2) axillary vein, (3) lateral thoracic, (4) intercostals veins

Lymphatic drainage:

- Axillary nodes – 75% of ipsilateral breast drains to the axillary nodes
  - 40-50 nodes in 5 groups: anterior, posterior, medial, lateral, apical
  - Drains into supraclavicular and jugular nodes
- Internal mammary nodes -- 20% of drainage from the ipsilateral breast
  - Account for about – upper and lower inner quadrants
  - About 4 nodes per side, with one node in each of the first three interspaces and one in the fifth or sixth interspace
- Inter-pectoral (Rotter's nodes) – between pectoralis major and pectoralis minor muscles

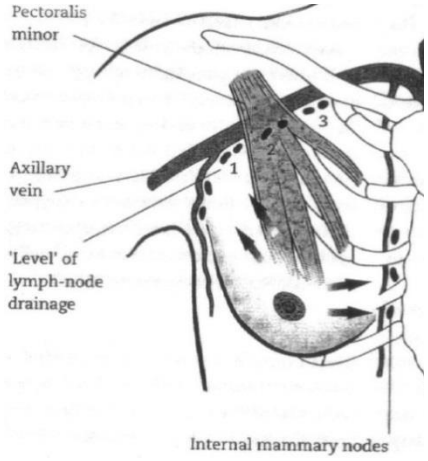
Anatomic/ Surgical division of axillary nodes into levels I, II and III (relative to pectoralis minor)
Level I: lateral to pectoralis minor
Level II: posterior to pectoralis minor
Level III: medial to pectoralis minor, extending up to apex of axilla

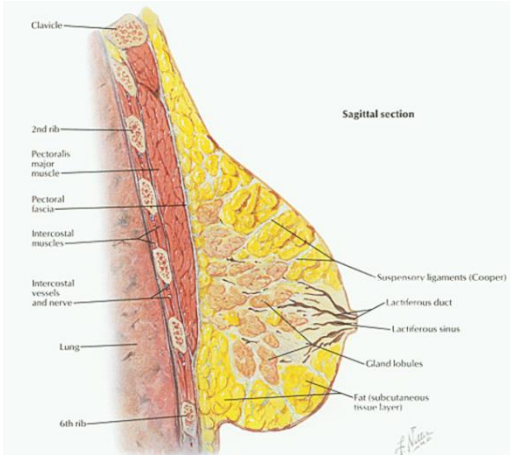
APPROACH TO BREAST LUMP

Painless lump	**Painful** lump
Elderly: 1. **Carcinoma** Younger: 2. Cyst 3. Fibroadenoma – can get cyclical pain (swell with the rest of the breast cos it's breast tissue) 4. Phyllodes Tumour (usually btw age 40-50) 5. Area of fibroadenosis (nodularity)	1. **Area of Fibroadenosis** 2. **Cyst** 3. **Abscess** (usually in lactating women) 4. **Fat necrosis** (minor trauma) 5. Periductal mastitis 6. Galactocoele (lactating women) 7. Carcinoma (rare; ~10% & advanced) May not be painful if pt has received tx / some infx.

Cyst, fibroadenosis and carcinoma can be painful/ painless.

Type of lump	Age	Pain	Surface / Margins	Consistency	Mobility
Breast Cyst	30-55	Occ	Smooth Well defined edges	Soft Firm (fluid) Fluctuant	Not fixed, Mobile
	Asymptomatic cyst: watch & wait, observe Symptomatic cyst: should be aspirated, if not palpable after aspiration TCU 1/12 - If cyst (1) recurs (2) does not resolve completely with aspiration (3) yields bloody aspiration then send patient for mammogram + ultrasound to r/o intra-cystic tumours				
Fibroadenoma	< 30	No	Smooth, bosselated	Firm, Rubbery	Very mobile
	- They may enlarge during pregnancy and involute after menopause - They have well-circumscribed border on mammogram and u/s - If < 2cm – can be managed conservatively, if mass is symptomatic, greater than 2 cm, or enlarges it should be excised				
Fibrocystic Breast Change (FBC)	20-55	Occ	Smooth Well defined edges	Lumpy, Cobblestone	Not fixed, Mobile
	- Patient suspected of FBC should be re-examined again (preferable on day 10 of the menstrual cycle) –hormonal influence is lowest, mass would have diminished in size - A persistent dominant mass must undergo further inv to r/o cancer				
Cancer	35+	No	Irregular	Stony hard	Tethered or fixed





APPROACH TO NIPPLE DISCHARGE

Discharge Colour	Cause	Management
Grossly bloody (red)	Intraductal papilloma	- Commonest cause of bloody nipple discharge in ♀ (20-40) - Mammogram: no mass detected due to their small size, clinically difficult to palpate - Investigate with ductogram - Treatment: microdochectomy with pre-op ductogram, major duct excision
	Mammary ductal carcinoma	- 2 forms: invasive ductal carcinoma or DCIS - Unilateral spontaneous discharge = suspicious - Mammogram: DCIS – clustered pleomorphic calcifications IDC – spiculated mass - Treatment: surgery (see below)
	Fibrocystic change	- A persistent dominant mass a/w nipple discharge must undergo further radiological evaluation, biopsy or both to exclude cancer - Closer follow up indicated
Clear (serous) or straw-coloured (yellow)	Ductal papilloma	As above
	Ductal carcinoma	As above
	Mammary ductal ectasia (non-puerperal mastitis)	- Benign Cond: lactiferous ducts gets swollen and blocked - Treatment: none, usually self-limiting - Predisposed to non-puerperal abscess which would require antibiotics ± surgical drainage
Green, brown, black (cell debris)	Mammary ductal ectasia	
Purulent, foul-smelling	Lactational Mastitis or Breast Abscess	- Lactational Mastitis (swollen, red and tender breast) – usually caused by staphylococcus aureus (purulent discharge is uncommon) - Breast abscess is the most common complication - Treatment: antibiotics & continue breastfeeding, if fail to improve or abscess cavity seen on u/s treat with surgical drainage
White milky discharge	Drug related galactorrhoea	- Any meds that might affect hypothalamic- pituitary axis - (1) deplete dopamine (i.e. tri-cyclic antidepressant, methyldopa, benzodiazepines) - (2) dopamine receptor blocker (i.e. haloperidol) - (3) estrogenic effect (i.e. digitalis) - Treatment: medication can be tapered / changed
	Spontaneous galactorrhoea	- r/o pituitary prolactinoma - Measure serum prolactin level & neuroimaging (CT / MRI) - Treatment: bromocriptine or resection of prolactinoma
	Lactation	No treatment
Blood stained (spot on bra)	Paget Disease	See below
	Dermatitis / Eczema	- Treatment: short-term course with steroid cream

Pathological Nipple Discharge
- Discharge: Serous (yellow / clear), sanguineous (bloody), serosanguinous (blood-tinged)
- Unilateral, uniductal, persistent and spontaneous grossly bloody discharge suggest pathological process in the breast
- Patients with bloody nipple discharge has higher risk of breast cancer (52%) than patients with non-bloody discharge (19%)[15]

Physiological Nipple Discharge
- Discharge: white or clear, yellow (straw-coloured), green, brown or grey
- Discharge is usually bilateral, involving multiple ducts

HISTORY (NIPPLE DISCHARGE):

1. **Is the discharge truly from the nipple?**
   - Exclude eczema, dermatitis or Paget's disease (common complaint: staining of the bra without obvious nipple discharge)
2. **Is the discharge more likely to be pathological?**
   - Nature of discharge – grossly bloody more significant
   - Unilateral or bilateral discharge – unilateral more significant
   - Uniductal or multi-ductal discharge – uniductal more significant
   - Spontaneous or only on pressing – spontaneous more significant
   - Persistent or intermittent – persistent more significant
3. **Is there any recent pregnancy**
   - Relation to breastfeeding – if discharge present after > 1 yr after stopping breastfeeding more worrisome
4. **Is it troubling the patient?**
   - Have the patient sought treatment elsewhere?

INVESTIGATION

1. Mammography (≥ 35yrs), U/S or MRI of both breasts to detect any underlying malignancy
2. Histology of biopsied lesion (core biopsy with clip placement) if found on imaging – clip is placed to allow subsequent localization if surgery is required
3. Ductography – duct is cannulated and radiopaque contrast is injected
4. Ductoscopy – 1mm rigid video-scope to perform internal exploration of duct

* Discharge for cytology to detect malignant cells (rarely helpful, not recommended)

MANAGEMENT (SUMMARY)
- If Intraductal papilloma – microdochectomy with pre-op ductogram, major duct excision (all retro-areolar ducts transacted and excised)
- If Intraductal carcinoma – appropriate cancer surgery should be planned
- If mastitis or abscess – antibiotics ± incision and drainage for abscess
- If drug induced galactorrhoea – medication can be tapered or changed
- If pituitary prolactinoma – bromocriptine or surgical resection
- Conservative management for most other pathologies unless discharge persists and is troubling patient → microdochectomy of offending duct

[15] Breast Cancer Res Treat. 2012;132(1):9

HISTORY

1. History of Lump (apply for any lumps) – Key Questions

- <u>When and how did you first notice the lump?</u>
  - Site of the lump?
  - Incidental / self-examination?
  - Previous Trauma
- <u>How has the lump changed since you first noticed it?</u>
  - Duration since first noticed
    - Any increase in size from first noticed to now?
    - Any changes in the nipple e.g. retraction
  - Overlying skin changes noted:
    - Erythema, warmth,
    - Dimpling (more prominent hair follicles 2° to dermal oedema from blocked lymphatics)
    - Swelling?
    - Any general asymmetry of the breasts noticed?
- <u>What symptoms does it cause you?</u>
  - Painful or painless?
  - Nipple discharge? If present, what is the colour and consistency
- <u>Have you got any more or have you had this before?</u>
  - Single or multiple?
  - Any other lumps elsewhere – other breast? Axilla? Neck?
  - Does it come periodically – (i.e. in relation to menstrual cycle / previous pregnancy)
- <u>What do you think it is?</u>
  - To assess patient's anxiety

2. Assessment of Cancer Risk

<u>Increased risk: (1.5 to 4 folds increase)</u>

- Early menarche (<12yr) – increased oestrogen exposure
- Late menopause (>55yr) – increased oestrogen exposure
- Late age at first full term pregnancy (first birth after 30 a/w doubling of risk as compared to first birth before the age of 18)
- How many children? (nulliparity → increased risk)
- Hormone Replacement Therapy (0.2% at 5yrs, 0.6% at 10yr & 1.2% at 15yr of continuous HRT) – risk disappear within 5 years of ceasing HRT[16]
- Oestrogen based OCP

<u>Protective factors:</u>

- Whether patient breastfed her children, and if so, for how long
- Physical activity (healthy lifestyle)

3. Other risk factors for cancer

- Age
- Family history (at least 2 generation) of breast cancer or gynaecological cancer
  - Age at diagnosis
  - First degree relative with breast cancer = risk doubles
  - Risk increased if relative had either early onset cancer (<40yr) or bilateral disease
  - Any associated cancers – ovary, colon, prostate, gastric, pancreatic
- Previous breast disease:
  - Previously treated breast cancer
  - Previous breast biopsy
    - No increased risk – adenosis, cysts, apocrine metaplasia
    - Atypical ductal hyperplasia (ADH) or atypical lobular hyperplasia (ALH) carries a 4-5 fold ↑ risk (risk ↑ to 10-fold if there is positive family history)
  - Previous mammogram results
- Exposure to ionising radiation (i.e. RT for previous breast disease or hodgkin lymphoma)
- Daily Alcohol intake, especially before age of 30 (link has been shown)

4. Systemic review

- LOA, LOW (constitutional)
- Fever (infective cause)
- Bone pain, SOB (metastasis)

<u>BRCA1 AND BRCA2</u>

- Breast CA susceptibility gene a/w 80% of hereditary breast CA but accounts for only 5% of all breast CA
- Autosomal Dominant inheritance
- BRAC 1 mutation[17] – lifetime risk (by age 70) of 57% for breast CA & 40% for ovarian CA
- BRCA 2 mutation – lifetime risk (by age 70) of 49% for breast CA & 18% for ovarian CA
- Criteria for referral for genetic counselling
  - a) Family History
    - ≥ 2 relatives with breast cancer, one under 50
    - ≥ 3 relatives with breast cancer, any age
    - Previously identified BRAC 1 / 2 mutation in the family
    - Pancreatic cancer with breast and/or ovarian in same side of family
    - Ashkenazi Jewish ancestry
  - b) Personal History
    - Breast cancer dx at age 50 or younger
    - Ovarian cancer
    - Male breast cancer
    - Triple negative breast cancer

* Besides **breast CA,** BRCA1 gene mutation → ↑ risk of **ovarian, fallopian tube and prostate cancers**

[16] Lancet. 1997 Oct 11;350(9084):1047-59.

[17] J Clin Oncol. Apr 10, 2007; 25(11): 1329–1333.

PHYSICAL EXAMINATION

Preliminaries (HELP)

- **Hi:** Introduce yourself & ask for **permission** to examine the breast (always have a **chaperone** to accompany you if you are male)
- **Expose** patient adequately from the waist up with exposure of axillae
- **Lighting:** good
- **Position** the patient at 45° or sitting position if a bed is not available

Inspection

- General appearance – cachexic, jaundiced, pallor, breathlessness
- Patient's hands relaxed at her sides – look for:
    - any **asymmetry** in the breast contours, any lumps
    - any scars of previous operation or procedure e.g. punch biopsy
- Look for overlying skin changes (F + PURE)
    - Fixation of skin to the lump
    - Peau d'orange
    - Ulcerating, fungating cancerous lump
    - Retraction of skin – underlying cancerous lump
    - Erythema
- Look for **nipple changes** (7 D's):
    - Discharge (blood-stained)
    - Deviation – underlying hard lump
    - Depression (retraction) – underlying hard lump
    - Destruction (a/w puckering of nipple) – underlying cancer
    - Discolouration
    - Displacement
    - Dermatitis (eczema like rash with crusting) – Paget's Disease
- Ask patient to raise her arms (to accentuate any tethering to the skin → dimpling)
- Ask the patient to contract the pectoralis major (push her hands against her hips) → may reveal a previously unnoticeable lump (not tethered to pectoralis)

Palpation

- Patient should be lying down at 45 degrees to the horizontal with her ipsilateral hand tucked behind her head – this splays the breast out so it can be palpated properly
- Start with the normal side first!
- Ask for any pain before starting to palpate
- Use one hand to retract and stabilise the breast and palpate with the other
- Palpate in a systematic manner e.g. quadrant by quadrant from centre outwards
- Examine the entire breast including the axillary tail
- When the lump is located, check with the patient whether this is the same lump
- Continue to examine carefully for other lumps (multiple lumps are unlikely malignant, usually fibroadenoma or fibroadenosis)
- Ask patient if she can show you the discharge by expressing it herself (NEVER squeeze the nipple yourself!); if patient cannot do it, then ask the chaperone to help
- **Characterise the lump:**
    - Shape – hemispherical or oval
    - Size – measure __cm by __ cm
    - Site – which breast, which quadrant, length (cm) from nipple
    - Warmth of overlying skin
    - Tender or non-tender to touch
    - Surface – smooth or nodular/irregular
    - Margins – regular and smooth, or irregular and ill-defined edge
    - Consistency – soft, firm, or hard
    - Fluctuance
    - **Tethered to the skin** – try to pick up the skin above the lump
    - **Fixation to underlying pectoralis muscle** – ask patient to press her hands against her hips to contract the pectoralis major muscle, then try to move the lump in 2 perpendicular directions, then ask patient to relax and try to move the lump again
    - Mobility of lump (mobile in all direction, not mobile)

Axillary lymph nodes

- Palpate the normal side first
- Rest the patient's right forearm on your right forearm and use your left hand to palpate the right axilla (vice versa for the left side)
- Palpate gently, slowly, and systematically, covering the five major groups of nodes: anterior, posterior, medial, lateral, and apical
- If any lymph nodes are found to be enlarged, note the number of lymph nodes, their site, size, tenderness, consistency (firm, hard, matted), mobility

To complete the examination

- Examine the supraclavicular LNs & cervical LNs
- Examine the lungs for any pleural effusion
- Percuss the spine for bony tenderness
- Examine the abdomen looking for hepatomegaly
- **Thank patient and cover up**

INVESTIGATIONS

"The evaluation of a breast lump is via the **TRIPLE ASSESSMENT**"

(1) Clinical Examination
(2) A Radiological Assessment – mammogram or ultrasound
(3) A Histopathological Assessment – cytology or biopsy

All 3 must be concordant for benign to have >99% specificity to r/o malignancy

(2) Breast Imaging – mammogram, ultrasound or MRI

1. Mammography

- Most sensitive of the proven breast imaging modalities
- Usually performed in asymptomatic older women (>40YO) [breast tissue in younger women is denser; more difficult to pick up abnormalities], but >35YO in symptomatic women
- Normally, 2 views are done:
  - **craniocaudal (CC)**
    - Right /Left
    - 70% tumours in lateral quadrant (upper)
  - **mediolateral oblique (MLO)**
    - Captures the tail
    - Right /Left
    - 80% tumours in oblique milky way
- Additional specialised views: magnification and coned compression; done on request to help magnify areas of abnormality to further characterize any lesion.
- Look at the axilla on the MLO view for any **enlarged lymph nodes**
- Malignant Mammographic Findings
  - New or spiculated masses
  - Clustered micro-calcifications in linear or branching array
  - Architecture Distortion
- Benign Mammographic Findings
  - Radial Scar
  - Fat Necrosis – characteristic oil cyst
  - Milk of Calcium – characteristic microcalcifications appear discoid on CC view and sickle shaped on MLO view

BI-RADS (Breast Imaging Reporting and Data System) classification

- Category 0: Need additional imaging evaluation
- Category 1: Negative (nothing to comment on, 0.05%, 1 in 2000 risk still present)
- Category 2: Benign – **routine screening recommended**
- Category 3: Probably benign (> 98%) , 6/12 follow-up suggested
- Category 4: Suspicious, **biopsy should be considered** (25-74% risk)
- Category 5: Highly suggestive of malignancy (≥ 95% risk)
- Category 6: Known malignancy

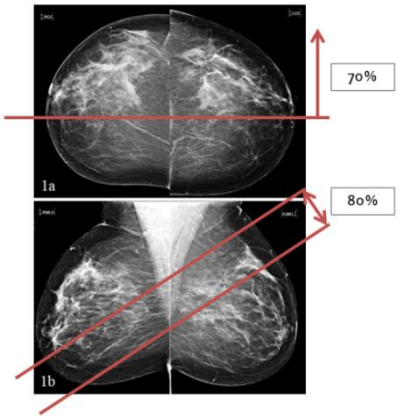
Abnormal features:

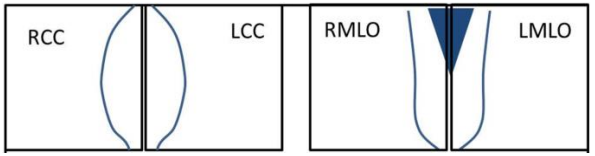
(a) Microcalcifications (<0.5mm in size)
- If calcifications >0.5mm → macrocalcifications; >5/mm² → cluster
- Sole feature of 33% of cancers detected on mammography
- Causes: DCIS (microcals in a straight line), invasive cancer, fibrocystic disease (microcals scattered), papilloma

(b) Spiculated mass or stellate lesion with poor outline or comet sign
- **95%** of spiculated masses on mammography are due to malignancy
- Stellate lesion is a localised distortion of the breast parenchyma without perceptible mass lesion – high chance of it being malignant
- Causes: Invasive cancer, radial scar (benign), fat necrosis, abscess, etc.

(c) Architectural distortion (of the contour), tent sign , nipple changes

(d) Neo-density or asymmetric density (look for bilateral synchronous ca; satellite lesion)

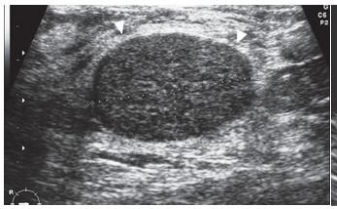




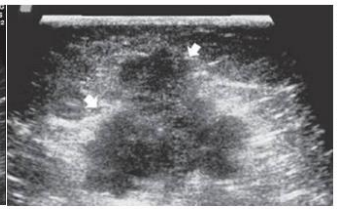
2. **Ultrasound**[18] (Stavros Study)
   - Usually 1st investigation in young patients (<35 years old) or pregnant, lactating patients;
   - Not the gold standard for screening
   - Sensitivity = 98.4%, Negative Predictive Value = 99.5% → permits imaging rather than biopsy for benign lesions on u/s
   - Uses:
     - Differentiates both palpable and mammographic lesions as either cystic or solid
     - Subsequent characterization and classification of solid nodules (see below)
     - Guide procedures e.g. Biopsy, drainage of abscess, aspiration of cyst
     - Evaluation of a palpable mass with a negative mammogram
     - Evaluation in mammographically-difficult areas e.g. chest wall, axilla
   - Pitfalls:
     - Operator dependent, non-standardised techniques, poor resolution,
     - Unable to detect most micro calcifications

   - Features of malignancy [**BITCH**]
     - Borders = spiculation, microlobulation, angular margins
     - Internal Calcification
     - Taller than wide (fir-tree appearance; invasion of fascia)
     - Central Vascularity / Compressibility (malignant lesions displace breast tissue w/o change in height)
     - Hypoechoic nodule / Posterior acoustic shadowing

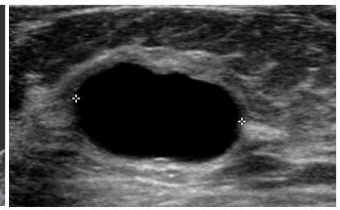
   - Benign Features
     - Smooth Margins, well circumscribed
     - Thin Echogenic Capsule
     - Ellipsoid Shape (wider than deep)
     - Macrolobulations
     - Hyperechogenicity



Fibroadenoma



Malignant Lesion



Breast Cyst

3. **MRI of the breast**
   - Expensive, but good soft tissue definition without radiation (>90% sensitivity)
   - Indications:
     - Occult lesions: Axillary LAD but Mammogram & US –ve
     - Determine extent of the disease (i.e. chest wall involvement)
     - Suspicion of multicentric or bilateral malignancy (esp. ILC)
     - Assessment of response to neoadjuvant chemotherapy
     - When planning for breast conservation surgery
     - Screening in high risk patient

(3) Breast Biopsy – cytology or histology
- Options available:
  (a) Fine needle aspiration cytology (FNAC)
  (b) Core biopsy (Trucut/ mammotome)
  (c) Incisional or Excisional biopsy

Mostly a choice between FNAC and core biopsy
- FNAC is less invasive, less painful, smaller wound, does not require any local anaesthetic, but only cells are obtained with no histology
  - Cannot differentiate between in-situ cancer and invasive cancer
  - Requires skilled cytopathologist
- Core biopsy is more invasive, requires LA, will result in a larger wound, more painful
  - Risk of complications higher (biopsy needle is a spring-loaded firing mechanism, improper angling may result in puncture of the lung or heart)
  - Can obtain tissue specimen (differentiate between invasive and non-invasive disease)
  - Can stain for ER/PR status → better diagnostic value
- Both procedures can be guided via clinical palpation or radiological guided (if the mass is small or difficult to palpate)
  - Ultrasound guidance
  - Stereotactic guidance (stereotactic mammotome)

[18] Radiology. 1995 Jul;196(1):123-34.

BREAST CANCER

EPIDEMIOLOGY[19]

- Most common cancer in females (37.2% of all female cancer in Singapore)
- It has increased about 3 folds from 22.0 / 100,000 in 1973-77 to 62.4 / 100,000 in 2008-12
- Age-standardised incidence 62.4 per 100,000
- Age-specific incidence increases sharply from age 30 and peak at 60-69 then gradually declined in the 70 and above age group
- Lifetime risk in Singapore is 6.45% (1 out of 16 develop breast cancer by age 75)
- Breast Cancer is the leading cause of death among females (2nd is lung cancer, 3rd is colorectal cancer, 4th is liver cancer)

RISK FACTORS (SEE ABOVE)

HISTOPATHOLOGY

- Top 3 most common types (1) IDC, (2) DCIS, (3) ILC

	Ductal	Lobular
Non-invasive (precursor lesion)	<u>Ductal Carcinoma in Situ</u> - Malignant cells arising from terminal duct-lobular unit, confined by BM - **Distort lobular architecture** - Main presentation = abnormal mammogram (clustered pleomorphic calcification), otherwise physical exam usually normal - Can be **multifocal** (2 or more lesion within same quadrant) or **multicentric** (in different quadrants) - **Positive for E-cadherin** - Excellent prognosis if treated - Treatment: **Surgical excision** [partial mastectomy (unicentric lesion) or total mastectomy (multicentric lesions) with margins > 10mm] together with **adjuvant radiation** - ± adjuvant tamoxifen (ER +ve DCIS) and aromatase inhibitors (Post-M women) - low recurrence rate – 2.5% at 12yr - Choice of treatment for DCIS can be guided by **<u>Van Nuys Scoring System</u>** – 13 point scoring system - Low score – partial mastectomy - Intermediate score – partial mastectomy + adjuvant radiation - High score – total mastectomy - 33% risk of untreated DCIS will progress to IDC (affect same breast and quadrant)	<u>Lobular Carcinoma in Situ</u> - Malignant cells arising from terminal duct-lobular unit, confined by BM - **Do not distort lobular architecture** - Main presentation = incidental finding - LCIS not considered a pre-invasive lesion but rather an indicator of increased cancer risk ~ 1% per year (20-30 % at 15 years) - Usually multicentric and bilateral - **Negative for E-Cadherin (involved in cell-cell adhesion)** - Treatment: (1) lifelong close surveillance (2) bilateral total mastectomies (3) prophylaxis with tamoxifen - Progression to cancer – can be IDC, ILC and may occur in any breast

[19] Trends in Cancer Incidence in Singapore 2008-2012 (data report are as of 7th June 2013)

	Ductal	Lobular
Invasive[20]	<u>Invasive Ductal Carcinoma (75-80%)</u> - 71% ER+, 47% PR+, 18% HER2 +	<u>Invasive Lobular Carcinoma (5-10%)</u> - 93% ER+, 60% PR+, 0.8% HER2+

Others	<u>Other histological subtypes</u> - Medullary (5-7%), Mucinous (3%), Tubular (1-2%) - Better prognosis than IDC <u>Inflammatory breast carcinoma (IBC: aggressive cancer)</u> - Typical presentation: rapid swelling, ± skin changes (Peau d'orange) and nipple depression (retraction), erythematous swollen breast w/o palpable mass - under lying cancer is poor differentiated and diffusely invades breast parenchyma - Often resembles mastitis (in IBC, true inflammation is absent or minimal) - Diagnosis: only reliable method is biopsy - Treatment: Multi-modal therapy – radio-chemo-hormonal therapy ± surgery

PRESENTATION

- Asymptomatic: detected on mammographic screening
- Symptomatic:
  - Self-detected painless lump in the breast (>1/3 of patients)
  - Self-detected painless lumps in the axilla
  - Nipple changes & overlying skin changes (see above)
  - Nipple discharge
  - Constitutional: LOW, LOA
  - Metastatic:
    - Bone pain / fractures
    - Shortness of breath
    - Jaundiced

FEATURES SUGGESTIVE OF BREAST CANCER

- Surface: irregular or nodular
- Edge: poorly defined, (areas more like normal breast tissue in between abnormal areas)
- Consistency: firm / hard
- Nil tenderness, nil fluctuant
- ± tethered to overlying skin or fixed to underlying muscle
- ± nipple involvement / discharge (see above)
- Lymphadenopathy

DIAGNOSIS – BY TRIPLE ASSESSMENT (see above)

- Non-invasive (in-situ) Breast Cancer (DCIS / LCIS)
- Invasive Breast Cancer
  - Early Breast Cancer (stage 1 & 2)
  - Locally Advanced Breast Cancer (stage 3 & T3No)
    - Non-inflammatory
    - Inflammatory – inflammatory LABC (T4d)
  - Metastatic Breast Cancer (stage 4)

[20] Am J Clin Pathol 2005;123:541-546

STAGING – 7TH EDITION AJCC

T stage	N stage	M stage
TX: not assessable To: no evidence of primary tumour Tis: Carcinoma in Situ T1: Tumour <2cm - T1a: 0.1-0.5cm - T1b: 0.5-1.0cm - T1c: 1.0-2.0cm **T2: Tumour >2cm but <5cm** T3: Tumour >5cm T4: Tumour with direct extension to - **T4a: chest wall (ribs, IC, serratus)*** - **T4b: skin (Peau d'orange, ulceration, satellite skin nodule)** - T4c: T4a + T4b - T4d: inflammatory breast cancer	NX: regional LN not assessable No: no lymph node involvement N1: mets to **movable** ipsilateral level I, II axillary LN N2: mets to ipsilateral level I,II axillary LN – **clinically fixed or matted or mets** to ipsilateral mammary LN in absence of axillary LN N3: mets to **ipsilateral infraclavicular** (level III) lymph nodes, ipsilateral mammary LN, **ipsilateral supraclavicular LN** (with or w/o level I & II axillary LN)	MX: presence of distant mets not assessable Mo: no distant mets M1: **distant detectable metastasis (histologically proven > 0.2mm)**

Stage 0	Stage I	Stage II	Stage III	Stage IV
Tis **DCIS**	**T1**No **Early BC**	T2**No**, T3**No^** To**N1**, T1**N1**, T2**N1** **Early Breast Cancer**	T3 N1 To**N2**, T1**N2**, T2**N2**, T3**N2** Any T, **N3** **T4**, any N **Locally advanced BC**	Any T, any N, M1 **Adv. BC**

*involvement of pectoralis major muscle alone not considered T4!
^ T3No (tumour > 5cm) considered as a locally advanced breast cancer

SPREAD

- Local: skin & subcutaneous tissues, underlying ribs and muscle (chest wall)
- Lymphatics: axillary, internal mammary LNs, supraclavicular LNs
- Haematogenous: lungs, liver, brain, bone (i.e. spine), adrenals, ovaries

Staging Investigations for distant metastasis:

(i) CXR or CT thorax (for lung metastases; look for isolated hyperdensity)
(ii) LFT (raised ALP) or US HBS or CT abdomen (for liver / adrenal or ovarian metastasis*)
(iii) Bone scan
(iv) PET scan
(v) CT or MRI brain (not routinely done)

* Krukenberg tumour can occur with breast cancer particularly invasive lobular breast carcinoma

PROGNOSIS

- Nottingham Prognostic Index = [0.2 * S] + N + G
  - Size of Tumour
  - Number of lymph nodes involved
  - Grade of tumour

- Hormone Receptor
  - Intense ER and PR staining is a good prognostic factor
  - Tumour responsive to tamoxifen
- Her 2 / Neu (epidermal growth factor)
  - Overexpression of Her2/Neu is a poor prognostic factor (increased rates of mets, decreased time to recurrence and decreased overall survival)
  - Patients are treated with trastuzumab (Herceptin) or lapatinib (Tykerb) containing adjuvant regimen for one year
    - Tumours that are Her2 +ve by IHC stain of 3+
- Triple Negative Breast Cancer (poor prognosis)
- Presence of lymphovascular Invasion (poor prognosis)

- Breast cancer is 2nd most common cause of brain metastases after lung cancer[21]
- Occurrence of brain metastases a/w median survival 2-16 months & impaired QOL

SURVIVAL – Singapore's data from 2008 – 2012 (5 year survival)

Stage I: 88.64%
Stage II: 82.62%
Stage III: 59.77%
Stage IV: 19.14%

[21] Breast. 2013 Oct;22(5):993-8

THERAPEUTIC OPTIONS

(a) Loco-regional control:
Surgery (WEAC vs. SMAC)
Radiotherapy

(b) Systemic Treatment:
Chemotherapy
Hormonal therapy
Targeted therapy

Aim of adjuvant therapy:
1. Prevent local recurrence
   a. RT
   b. ± CT, HT, TT
2. Eradicate micrometastases
   a. CT, HT, TT
   b. ± RT

→ Reduces recurrence by 1/3; but if recurs have poor prognosis

Surgery

1. Preparing for operation:
   - Anaesthesia workup and necessary imaging. Mark out the site
   - Psychological counselling, consent taking, discuss breast reconstruction

2. Wide excision (breast-conserving surgery; standard of care)
   - Removal of tumour with clear margins, while achieving good cosmetic result
   - **Criteria: [Nodal status does not influence decision for WE or SM]**
     - ≤T2: Tumour <5cm in size, no skin or chest wall involvement
     - Only 1 tumour, not multicentric/ multiple DCIS/ LCIS unless same quadrant
     - No metastatic disease
     - Appropriate tumour size-to-breast ratio (to achieve good cosmetic result)
     - Patient **must** agree to **post-operative radiotherapy**
   - Results: overall survival at 25 years for WEAC comparable to SMAC, with slightly higher local recurrence rates (for WEAC: 1% per year, 4% in 5 years)
   - Higher risk in younger patients as cancer tends to be more aggressive

3. Simple mastectomy (if any CI to wide excision)
   - Removal of breast tissue, nipple-areolar complex, and overlying skin
   - Lower rates of local recurrence; similar long term prognosis as WE (Italian trial)

4. Axillary clearance (see below)
   - **Sentinel lymph node (SLN) biopsy is the standard of care**
   - Performed for all invasive carcinoma (WE or SM)
   - Surgeon dependent for DCIS (theoretically cancer cells are confined to the breast)
   - A positive sentinel lymph node is a/w further axillary disease, earlier disease recurrence and a poorer overall survival rate[22]
   - If the SLN is positive for metastasis (**micro-metastasis ≥ 0.2mm**) a standard completion axillary clearance is the current recommendation[23]
     - Removal of level I and level II nodes and if grossly involved then level III nodes (motor and sensory nerves are preserved)
     - Should remove ≥10 nodes (identified by pathologist)
     - Patients with ≥4 positive axillary LN should undergo adjuvant radiation to the regional LN (i.e. internal mammary and medial supraclavicular nodes)[24][25]

5. Palliative surgery
   - Palliative mastectomy for symptoms (bleeding, fungating, infected tumour)
   - Surgery at other sites:
     - Fixation of pathological fractures,
     - decompression of spinal cord compression,
     - surgical excision of brain metastases

6. Breast reconstruction
   - Safe, can be done during breast surgery or at a later time
   - No delay in subsequent treatment and no increase in rates of relapse
   - Cx: abnormal sensation of breast
   - Options:
     (i) Prosthesis / Implant
     (ii) Muscle flap from rectus abdominis (TRAM) or latissimus dorsi (LDMF)

Principles of Axillary Clearance & how it is performed:

- The sentinel lymph node, being the first lymph node draining the breast, is representative of the rest of the axilla; if the SLN is negative for tumour cells, then the rest of the axillary nodes should be negative as well
- Solitary internal mammary LAD is rare – Use of blue dye (methylene blue) or radioactive isotope (technetium-99m sulphur colloid or colloidal albumin) injected in the vicinity of the tumour or sub-areolar area just before surgery → concentrates in the sentinel node – the axillary nodal basin (medial)
- During the op, look for the SLN by its blue colour, or using a Geiger-Muller counter (gamma probe) to detect the node with highest radioactivity
- Send node for frozen section (FS) – common for more than one LN to be identified
- Classification of nodal metastatic disease: (1) macro-metastases (deposit >2mm), (2) micro-metastases (0.2-2mm) and (3) isolated tumour cells (<0.2mm)

Complications of mastectomy ± axillary clearance:

Immediate	- Injury to axillary vessels - Neuropathy 2° to injury to motor nerves of the axilla (i.e. long thoracic, thoracodorsal and medial pectoral nerves)
Early	- Haemorrhage / Hematoma (POD1) - Wound Infection (POD3) – tx promptly with Ab (infection can damage lymphatics further) - Seromas (pocket of clear serous fluid) – tx with repeated aspiration / reinsertion of drain - Flap ischemia - Pain and numbness in the upper arm and axilla - Restricted shoulder mobility * Inform patient that blue dye on breast may be there for up to 4 weeks and that 1st few days post-op urine colour may be green = NORMAL
Late	- Cosmetic deformity - Lymphedema (incidence 10-40%) – radiation to axilla increases this risk, lymphedema increase risk of lymphangiosarcoma (Stewart-Treves syndrome) • Lymphedema tx: arm PT, pneumatic compression devices and fitted compression sleeves • Lymphangiosarcoma tx: large resection / amputation of affected limb + neoadjuvant / adjuvant RT ± CT

[22] Ann Surg Oncol 2010;27(Suppl. 3):S303-11
[23] The Surgeon 10 (2012) 326-329
[24] Washington Manual 6th edition (pg. 635)
[25] Radiation Oncology 2013, 8:267 [review of 3 trials – French, MA.20 & EORTC randomized controlled trials]

Radiotherapy*

1. Adjuvant
   - External beam whole breast radiotherapy (WBRT) to be done for most patients treated with breast conserving therapy (BCT)
   - WBRT for patients who undergo a mastectomy for locally advanced breast cancer (i.e. T4 tumour, T3 with positive margins and/or ≥4 pathologically involved nodes)
   - Patients with ≥4 pathologically involved nodes should undergo RT to the regional LN
   - Regimen consists of 25 to 30 cycles in total, 1 cycle per day from Monday to Friday over 5-6/52 until maximum dose (no repeat RT for recurrences) – (to check)
2. Palliative

* No role of neo-adjuvant radiotherapy for curative breast cancer

Side effects of radiotherapy:

Short Term	Long Term	Radiation to Axilla
1. Skin Irritation	1. Skin Pigmentation	1. Lymphedema
2. Tiredness	2. Rib Fracture (1%)	2. Axillary Fibrosis
3. Breast Swelling	3. Angiosarcoma	
4. Cough (<5%)	4. RT induced Cancer (1 in 1000)	
	5. No risk of heart or lung disease?	

Chemotherapy

1. Neoadjuvant
   - Given in LABC (stage III) to shrink the tumour before surgical resection
   - 20% achieve complete clinical response (cCR) i.e. tumour is no longer palpable
     - Further 20% will achieve complete pathological response (cPR) i.e. no more tumour cells = good prognosis
   - Need to place a clip into the tumour before starting neoadjuvant therapy to guide surgery in case the tumour "disappears"; operate according pre-op staging
   - Cx: as for CT drug, e.g. mouth ulcers, N/V, hair loss, immunosuppression

2. Adjuvant (check)
   - Typical Regime: 6-8 cycles of FEC (F = 5-flurouracil, E = epirubicin, C = cyclophosphamide) – i.e. all 3 drugs injected on first day of each 3 week cycle
   - Start 3/52 after surgery; given in stage III / LABC (LN+ve) & in some early breast cancers depending on stage (see below)
   - Premenopausal patients tend to have better response to chemotherapy than hormonal therapy (and vice versa for postmenopausal patients)

3. Palliative
   - Anthracyclines and taxanes are the mainstay
   - Helps to reduce load of disease to alleviate symptoms, increase survival

Hormonal therapy

- Used in adjuvant setting to eradicate micrometastases (likewise with CT & TT)
- For ER/PR +ve → will have 90% response
- Preferred for postmenopausal women as response to hormonal therapy is better
- May render patient postmenopausal for better response to HT via medical ablation with LHRH-a or surgical oophorectomy
- Mostly used as adjuvant therapy but can also be used as palliative treatment & preventive treatment in high risk patients
- Also reduces risk in contralateral breast

Classes

(a) Selective oestrogen receptor modulators (SERMs): Tamoxifen

- Daily for 5 years then stop – known to have carryover benefits for next 10years
- 25% reduction in risk of recurrence and 15% reduction in mortality from breast cancer (5yr)
- Side effects:
  1. Tamoxifen flare – menopausal symptoms (i.e. hot flushes, ↑ HR, sweating, fatigue etc.)
  2. **endometrial cancer** (0.1% per year)
  3. deep vein thrombosis

* For women with ER+ early breast cancer 10 years of treatment expected to have greater protective effect than 5 years of treatment – (10yr RR risk 21.4% vs. 25.1% and 10yr breast cancer mortality was 12.2% vs. 15.0% for controls) → ATLAS trial[26]

(b) Aromatase inhibitors: Lanastrazole, letrozole, exemestane

- Inhibit peripheral conversion of testosterone and androstenedione to oestradiol
- Only suitable for post-menopausal patients as use of these agents will cause over-activity of the HPA axis in premenopausal women
- Side effects:
  1. musculoskeletal pain
  2. **osteoporosis**

Post-menopausal = AI x 5yrs or Tamoxifen x 5yrs (cost issue)
Pre-menopausal = Tamoxifen x5yrs KIV ovarian ablation for high risk patients

Targeted therapy = Herceptin (trastuzumab)

- Administered IV monthly for 12 months
- Targets Her-2-neu a.k.a. C-erbB2 receptor (a type of epidermal growth factor receptor [EGFR] that is overexpressed in 18-20% of IDC)
- Used in C-erbB2 positive tumours, early or late stage
- Side effects of Herceptin:
  1. **cardiomyopathy** & CCF
  2. pulmonary toxicity
  3. infusion reactions
  4. febrile neutropaenia
- Avastin (or bevacizumab, targets VEGF receptors, used in advanced cancer)
- Lapatinib (targets Her-1 and Her-2, used in advanced cancers)

[26] Lancet. 2013 March 9; 381(9869): 805–816. (ATLAS: adjuvant tamoxifen, longer against shorter)

TREATMENT BY TUMOUR STAGE

Options can be divided into aims of control (curative or palliative intent):

- Non-invasive (in-situ) Breast Cancer – i.e. DCIS / LCIS
- Invasive Breast Cancer – undergo staging
    - Early Breast Cancer (stage 1 & 2)
    - Locally Advanced Breast Cancer (stage 3 & T3No)
        - Non-inflammatory
        - Inflammatory – inflammatory LABC (T4d)
    - Metastatic Breast Cancer (stage 4)

Ductal Carcinoma in Situ (non-invasive)

- Surgical excision – margins > 10mm a/w local recurrence rate 14% at 12 years[27]
    - partial mastectomy (i.e. wide excision) – needle localization to identify area to be excised (for unicenteric lesions)
    - total (simple) mastectomy (multicentric lesions) ± immediate reconstruction
- Assessment of axillary LN: axillary dissection not performed in pure DCIS
    - SLNB considered if likely to find invasive cancer on final pathological staging
    - Some surgeons prefers to do SLNB in all patients with DCIS undergoing mastectomy (SLNB cannot be performed post-mastectomy if an occult invasive cancer is found)
    - +ve SLNB necessitates complete axillary dissection
- Adjuvant therapy
    - ± adjuvant tamoxifen or aromatase inhibitors (for post-M women)
        - Indication: benefit found for ER positive DCIS
        - Tamoxifen – ↓RR by 37% over 5 years and ↓risk of developing contralateral breast cancer (NSABP B-24 trial)
        - No survival benefits
    - ± Adjuvant radiation
        - Indications: patients with DCIS treated with partial mastectomy – more benefit for younger women with close margins / large tumours
        - Decrease local recurrence rates
        - No survival benefits
- Choice of Treatment depends on scoring of Van Nuys Prognostic Index
    - Low Score: Wide Excision Alone
    - Intermediate Score: Wide Excision with Adjuvant Radiotherapy
    - High Score: Simple Mastectomy

Lobular Carcinoma in Situ (not a pre-invasive lesion) – ↑ risk 1% / year

- Life-long surveillance
- Bilateral Total Mastectomies with immediate reconstruction (for selected high risk patients)
- Prophylaxis with tamoxifen / raloxifene (for post-M women)

[27] Am J Surg. 2006;192:420

Stage 1 and Stage 2 Early Invasive Breast Cancer

- Curative Intent – clear surgically with adequate margins (negative margins >2mm)[28]
- Breast Conservation Therapy (BCT)
    - Neoadjuvant chemotherapy or hormonal therapy – aim to reduce size of tumour
    - Partial Mastectomy with Sentinel Lymph Node Biopsy (SLNB) KIV Wide Excision Axillary Clearance (WEAC)
- Non-Conservative Therapy – Mastectomy
    - Halsted Radical Mastectomy*
    - Modified Radical Mastectomy
    - Total (simple) Mastectomy with SLNB KIV Simple Mastectomy with Axillary Clearance (SMAC) aka 'modified radical mastectomy (MRM)'
        - ± skin-sparing mastectomy with immediate reconstruction → improved cosmesis
        - ± nipple-sparing mastectomy

*radical = total mastectomy + complete ALND (level I, II & III) + **removal of pectoralis major and minor** + removal of overlying skin
** modified = total mastectomy + complete ALND (level I, II) + removal of overlying skin

- Immediate Reconstruction
    - Latissimus dorsi myocutaneous flaps (LDMF) ± silicone implants
    - Transverse rectus abdominis myocutaneous flaps (TRAM) ± silicone implants
        - Immediate reconstruction not shown to affect patient outcome adversely – detection of recurrence not delayed, onset of chemotherapy not changed

- Adjuvant Therapy (node positive patients)
    - Adjuvant radiation – required component after BCT
        - Decreases RR from 30% to <7% at 5 years
        - If patient unwilling to go for adjuvant radiation = contraindication for BCT
    - Adjuvant Chemotherapy (for all node-positive patients)
    - Adjuvant Hormonal Therapy for 5 years (for ER/±PR positive tumours)
    - Adjuvant Trastuzumab – IV monthly for 1 year (for Her2/neu positive tumours)

- Adjuvant Therapy (node negative patients)
    - Individualized approach

[28] Ann Surg Oncol. 2013 Mar;20(3):811-8

Stage 3 Locally Advanced Breast Cancer (non-inflammatory)

- Neoadjuvant Chemotherapy (cyclophosphamide, anthracycline and taxane) – downstage tumour, improves survival & predicts tumour response to adjuvant therapy
- Neoadjuvant Herceptin (i.e. trastuzumab) for HER2 positive breast cancer

- Surgical Excision (no role for SLNB – axillary nodes already positive) – WEAC / SMAC
  - Surgical resection dependent on size of tumour and resectability (if tumour is too large, the skin defect will be very large → inoperable)
  - Patients who received neoadjuvant CT and can be converted to BCT candidates with no difference in overall outcome survival
  - Patients with T4 breast lesion recommended to undergo mastectomy
  - If nodes left unattended may lead to compression of axillary vein – worsens lymphedema or infiltration into brachial plexus (neuropathic pain)

- Adjuvant Radiation + Systemic Therapy (CT, HT, TT) – individualized

Locally Advanced Breast Cancer (inflammatory) – T4d

- Investigate with skin punch biopsy (differentiate with mastitis)
- Approximately 30% have distant mets at time of diagnosis
- Aggressive multimodal therapy – medial survival 2 yrs with a 5yr survival of only 5%
  - Early 4 cycles of FAC (doxorubicin in combination with fluorouracil and cyclophosphamide), then surgery followed by additional 4 cycles of FAC then adjuvant radiation therapy

Stage 4 Invasive Advanced Breast Cancer

- Intention: Palliative, aim for disease control, maintain QoL
- Role of Surgery:
  - Loco-regional Therapy – minimal / palliative (i.e. remove fungating, smelly primary tumour) – toilet mastectomy
  - Treatment of complications – i.e. if have pleura effusion → drain it
  - For pain control / bleeding
  - For metastatic lesions – i.e. mets to spine
- Systemic Therapy is the mainstay of treatment – CT, HT or TT
- Occurrence of brain metastases (BM) a/w poor prognosis with 1yr survival of 20% and impaired quality of life (breast cancer is 2nd most common cause of BM after lung cancer)[29]

[29] Breast. 2013 Oct;22(5):993-8

FOLLOW-UP[30]

- 3 to 6 months for first 3 years
- Every 6 to 12 months for next 2 years
- Annually thereafter
- Post-treatment mammogram should be obtained 1 year after initial mammogram and at least 6 months after completion of radiation therapy
- Annual mammogram for contralateral breast (risk of 2nd breast CA is 0.5 to 1% per yr)
- Patient at high risk for familial breast cancer → referred for genetic counseling
- **Regular gynecological f/u is recommended** (tamoxifen ↑ risk of endometrial cancer)

BREAST SCREENING[31]

- BSE in the absence of mammography does not reduce mortality from breast cancer[32] → however; it helps improve women's awareness of their own breast and about breast cancer
- Mammogram a/w with a 20% breast cancer mortality reduction for women aged 40 to 74
- Screening is most effective in detecting early breast cancer in women aged 50-69

Normal risk, asymptomatic **Patients on HRT therapy**	< 40	▪ Monthly breast self-examination (perfrom 7-10 days after start of menstruation) ▪ Should not undergo breast screening with any imaging modality
	40-49	▪ Annual mammogram* ▪ Ultrasound and Clinical Breast Exam (CBE) not routinely required
	50-69	▪ Bi-annual mammogram ▪ Ultrasound and CBE not routinely required
	> 70	▪ Optional bi-annual mammogram
Increased genetic risk	5-10 yrs before onset of breast disease in youngest family member or at age 25-30 yrs for BRCA mutation carrier	▪ Monthly BSE ▪ 6 mthly CBE ± U/S breast ± MRI ▪ Annual mammography

* Relative high incidence of breast cancer for Singaporean women in this age group (40% dx before 50 years)

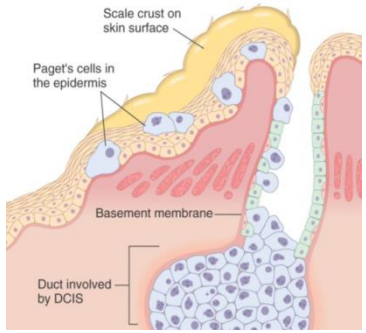
[30] J Clin Oncol. 2006; 24:5091-5097
[31] MOH CPG Feb 2010 – Cancer Screening
[32] J Natl Cancer Inst 2002;94:1445-57.

Paget's Disease of the Nipple

- Presents as erythema and eczematous change of the nipple (not the areola) with crusting exudates, may develop into erosions and ulcerations, clinically resembles eczema
- Often associated with underlying ductal carcinoma in situ (DCIS) or invasive carcinoma in 85-88% of cases often w/o associated breast mass or mammographic abnormality

	Paget's Disease	Eczema
Breast Affected	Unilateral	Bilateral
Long Term Effect	Destroys the Nipple	Does not destroy the nipple
Associated with	Associated with underlying DCIS or invasive carcinoma (85-88%)	Not associated with underlying lump
Steroids		a/w dramatic improvement

- Pathogenesis
  - Malignant cells invade across the epithelial-epidermal junction and enter the epidermis of the nipple, breaking the normal epidermal barrier thus allowing fluid to be extruded onto the nipple
  - Pathological Hallmark: malignant, intraepithelial adenocarcinoma cells (Paget cells) occurring singly or in small groups within the epidermis of the nipple



Extension of DCIS along ducts within the epithelial layer to the area under the skin over the nipple

- Investigations
  - Mammography (bilateral)
  - Breast MRI (if have –ve PE & mammography) → if MRI +ve, require confirmatory biopsy
  - Punch biopsy or full-thickness wedge biopsy of the nipple
- Prognosis of the underlying cancer is not altered by the presence of Paget's disease of the nipple
  - Palpable mass → most have IDC & axillary nodal involvement = 5yr survival 37-43%
  - No palpable mass → most have DCIS = 5yr survival 90-100%
- Treatment should be planned according to the underlying cancer if found
  - Simple Mastectomy
  - Breast Conserving Therapy & RT
    - Complete resection of the nipple areola complex followed by whole breast RT

Gynaecomastia

- Benign enlargement of male breast tissue
- Occur most commonly in adolescent and older age groups

Causes – (**DOPING-NO**)

Drugs	- Oestrogens - Spironolactone - Cimetidine - Digitalis - Tricyclic Antidepressants - Cannabis - Anabolic Steroid Abuse - Amphetamines - Cyproterone - Griseofulvin - Bicalutamide (Casodex) – for prostate cancer treatment
Organ Failure	- Liver Failure - Renal Failure - Hyperthyroidism
Physiological	- Neonates - Puberty - Old Age
Idiopathic	
Nutrition	- Malnutrition
G – hypoGonadism	- Klinefelter's Syndrome → increased risk of male breast cancer (16-30X) - Agenesis
Neoplasm	- Carcinoma of the male breast - Testicular Tumours - Bronchial Carcinoma (inappropriate secretion of hormones) - Prolactinoma
Others	- Pseudo-gynaecomastia

Investigation:

- Testicular u/s (if PE shows testicular mass)
- Mammography and breast u/s with biopsy (if suspicious for malignancy)
- LFT, Renal Panel, TFT (to r/o chronic diseases)
- Testosterone, LH/FSH, Oestradiol, prolactin
- α-FP, ß-HCG

Treatment (for physiological gynaecomastia)

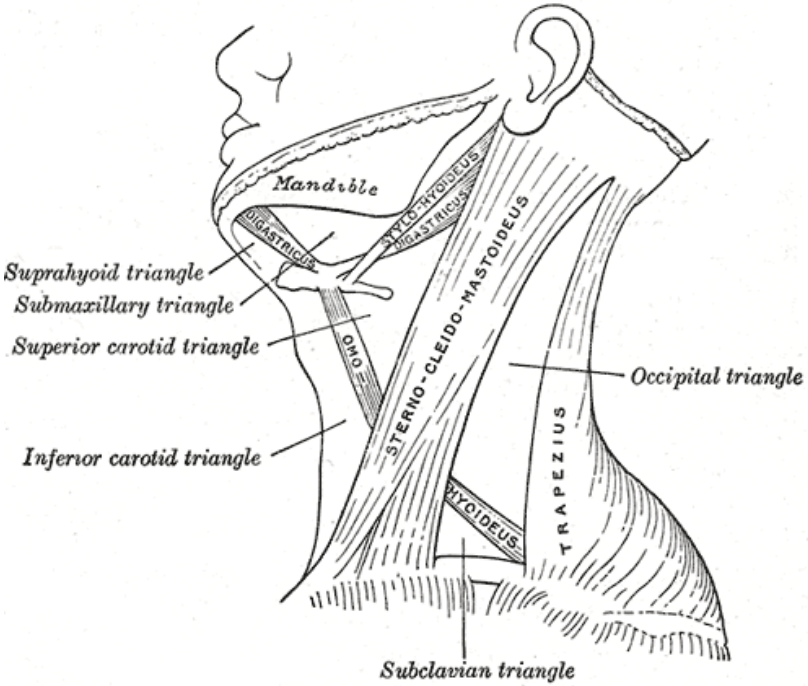
- Conservative management
  - Tamoxifen (10mg for 3/12) – reduction of pain and breast enlargement
- Surgical excision

APPROACH TO NECK MASSES

NECK MASSES

ANATOMY

- The neck is composed of two triangles on each side – anterior and posterior triangles
- The anterior triangle is bounded by the lower border of the mandible superiorly, the midline anteriorly, and the anterior border of the sternocleidomastoid posteriorly
- The posterior triangle is bounded by the posterior border of the sternocleidomastoid anteriorly, the anterior border of the trapezius posteriorly, and the clavicle inferiorly



- Masses in the neck region can be subdivided according to the triangle they occur in as there are pathologies peculiar to each triangle
- Locations: (i) Midline
  (ii) Anterior triangle
  (iii) Posterior triangle
- In general, enlarged lymph nodes are the most common cause of a lump in the neck, regardless of location (see section on Lymph node enlargement)

MASSES BY LOCATION

Midline

1. Submental lymph node
2. Thyroglossal cyst
3. Thyroid nodule in the isthmus
4. Sublingual dermoid cyst
5. Plunging ranula (retention cyst of the sublingual)
6. Rarely, hyoid pathology e.g. bursa

Anterior triangle

1. Lymph node – along anterior border of sternocleidomastoid (levels II, III, IV)
2. Thyroid nodule
3. Submandibular gland mass (see later section on Salivary gland swellings)
4. Branchial cyst ± fistula
5. Chemodectoma (carotid body tumour)
6. Carotid aneurysm
7. Pharyngeal pouch
8. Laryngocoele (rare; an air-filled, compressible structure seen in glass-blowers)

Posterior triangle

1. Lymph node – level V and supraclavicular lymph node groups
2. Cystic hygroma
3. Cervical rib
4. Brachial plexus neuroma/schwannoma

CAUSES OF MIDLINE MASS

Approach:
- Move with swallowing? – divides thyroglossal cyst and thyroid nodule from other causes
- If it moves with swallowing, does it move with tongue protrusion – thyroglossal cyst moves with protrusion but a thyroid nodule does not

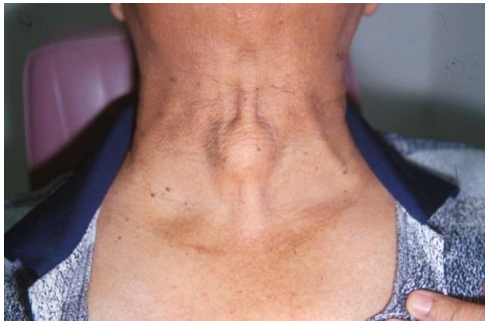
Thyroglossal cyst
Epidemiology:
- Equal in males and females.
- Occurs mostly in children and adolescents but up to one-third occur in patients > 20 years.

Pathology:
- A cystic expansion of the remnant thyroglossal tract – failure of the thyroglossal duct to obliterate after embryologic descent of the thyroid from the foramen cecum at the base of the tongue to low anterior neck

Features:
- Smooth, rounded, cystic lump. 75% are in the midline while 25% are slightly to the left or right. Usually asymptomatic but may become infected with sinus formation and seropurulent discharge (occurs with incision or rupture of cyst)

Histology:
- Cyst with columnar or squamous epithelial lining which may be ciliated. The cyst may also contain thyroid and lymphoid tissue.
- If malignancy occurs (CA of the thyroglossal duct), it is usually a papillary carcinoma (~90%).

Treatment:
- Sistrunk procedure – resection of the cyst, its tract and central portion of the hyoid bone



Dermoid cyst
Pathology:
- Can be congenital or acquired.
  (i) Congenital – developmental inclusion of epidermis along lines of fusion of skin dermatomes (seen in younger patients, present since birth). Locations include:
    - medial & lateral ends of the eyebrows (internal & external angular dermoid cysts)
    - midline of the nose (nasal dermoid cysts)
    - midline of the neck and trunk
  (ii) Acquired – due to forced inclusion of skin into subcutaneous tissue following an injury, usually on fingers. Seen in older patients, no previous history of mass, history of trauma to area (may have associated scar).

Histology:
- Cyst lined by epidermis, with evidence of adnexal structures such as hair follicles, sebaceous glands and sweat glands – cystic teratoma

Features:
- Small non-tender mobile subcutaneous lump, may be fluctuant, skin-coloured or bluish.

Management:
- Imaging investigations (e.g. XR, U/S, CT) are important especially for cysts on the skull as they can communicate with cerebrospinal fluid.
- Complete surgical excision of the cyst, preferably in one piece w/o spillage of cyst contents

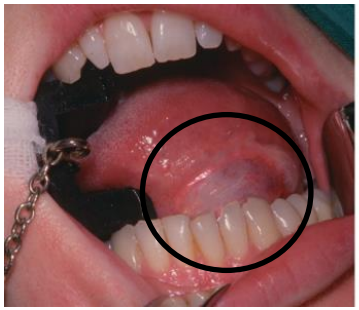
Plunging ranula

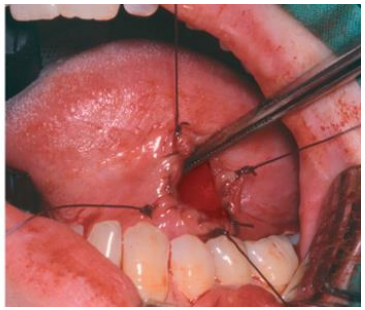
Pathology:

- A pseudocyst associated with the sublingual glands and submandibular ducts.
- Ranulas can be congenital or acquired after oral trauma
    - Congenital → secondary to an imperforate salivary duct or ostial adhesions
    - Acquired → trauma to sublingual gland leading to mucus extravasation and formation of a pseudocyst (mucus escape reaction)
- Simple Ranula → confined to floor of the mouth
- Plunging Ranula → a large ranula can present as a neck mass if it extends through the mylohyoid musculature of the floor of the mouth

Treatment:

- Complete resection if possible, often in continuity with the associated sublingual gland (but often difficult due to close association with the lingual nerve and submandibular duct).
- If complete resection not possible, marsupialisation and suturing of the pseudocyst wall to the oral mucosa may be effective.





CAUSES OF ANTERIOR TRIANGLE MASS

Branchial cyst and/or fistula

Epidemiology:

- Affects both sexes equally, usually in young adults in their 20s

Pathology:

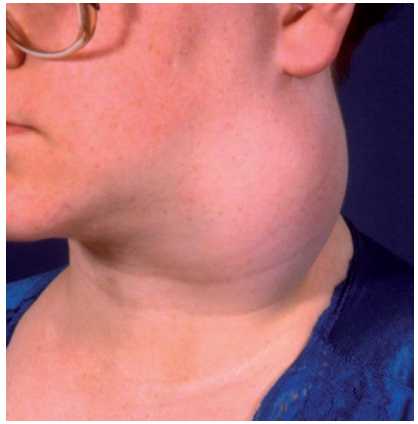
- Develop because of failure of fusion of the embryonic second and/or third branchial arches (failure of obliteration of the second branchial cleft)
- It is lined by squamous epithelium

Features:

- Occurs anterior to the upper or middle third of the sternocleidomastoid muscle
- Smooth firm swelling, ovoid in shape, with its long axis running downwards and forwards
- May be fluctuant, usually not transilluminable (due to desquamated epithelial cell contents)
- Look for fistula in this area – a branchial fistula will run between tonsillar fossa and the anterior neck, passing between the external and internal carotid arteries
- FNA of the cyst will yield opalescent fluid with cholesterol crystals under microscopy
- May be complicated by recurrent infections – purulent discharge, fixation to surrounding structures

Management:

- If fistula present, perform fistulogram to delineate course.
- Surgical excision of the cyst where possible.
- If fistula/sinus present, inject Bonney's blue dye into tract prior to surgery to allow accurate surgical excision.
- Treatment of infection with antibiotics.
- Complications: cyst recurrence; chronic discharging sinus.



Chemodectoma

Pathology:

- Defined as a tumour of the paraganglion cells (paraganglionoma) of the carotid body
- Located at the bifurcation of the common carotid artery (into the internal and external carotids)
- They are usually benign, but locally invasive
- Risk of malignancy is 10%, with metastasis to local lymph nodes, no histopathological features for malignancy, thus malignant nature can only be diagnosed by presence of metastasis

Features:

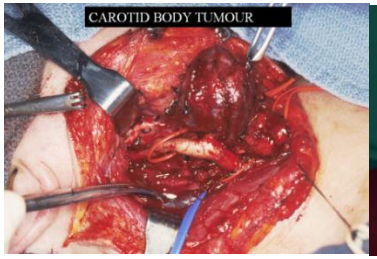
- Solid, firm mass at the level of the hyoid bone (where the bifurcation is – level II of the neck) – be gentle during palpation as pressure on the carotid body can cause vasovagal syncope.
- Mass is pulsatile but not expansile, due to transmitted pulsation from carotids.
- Due to close a/w carotid arteries, lump can be moved side to side but not up and down.
- May be bilateral.
- If suspecting aneurysm, listen for bruit, look for signs of Horner's syndrome, and examine the rest of the peripheral vascular system.

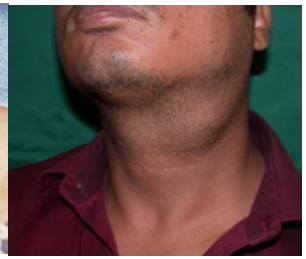
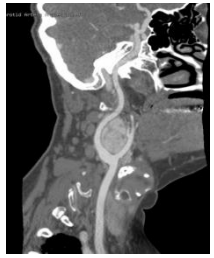
Differentials and investigation:

- Main differential is carotid artery aneurysm; aneurysm can occur at any level but carotid body tumour occurs at the level of the hyoid bone.
- DO NOT PERFORM FNAC
- CT and/or MRI can be used to delineate tumour anatomy in relation to surrounding structures; CT reveals homogenous mass with intense enhancement following IV contrast administration.
- Angiography is the gold standard investigation – shows a hypervascular mass displacing the bifurcation. May also show vessel compromise by tumour invasion, and undetected synchronous tumours.

Treatment:

- Rule out associated syndromes (i.e. pheochromocytoma) in the pre-op preparation!
- Surgical excision with pre-operative embolisation (reduces bleeding and complications, and facilitates resection); any enlarged ipsilateral lymph nodes are also removed due to the small possibility of malignancy
- Radiotherapy is an effective alternative for patients who are unfit for surgery or whose tumours are too large.

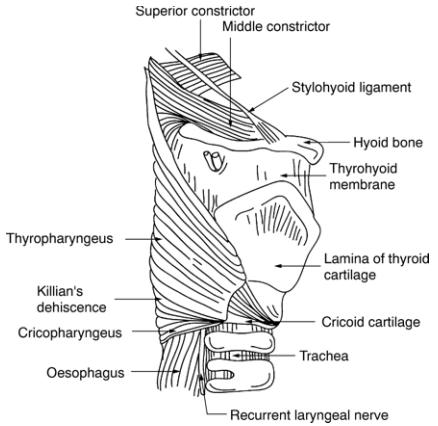


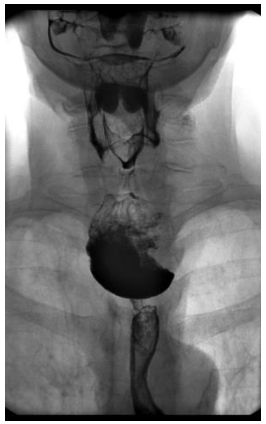



Pharyngeal pouch (also called Zenker's diverticulum)

Pathology:

- A herniation of the pharyngeal mucosa (pulsion diverticulum) between 2 parts of the inferior pharyngeal constrictor – thyropharyngeus & cricopharyngeus – weak area situated posteriorly (**Killian's Dehiscence**)





Features

- Occurs in older patients
- A cystic swelling low down in the anterior triangle, usually on the left
- Squelching sound on deep palpation
- Patient complains of halitosis, regurgitation of undigested food with coughing and dysphagia in the neck, hoarseness, weight loss
- Complications: chest infection (due to aspiration); diverticular neoplasm (<1%)

Diagnosis: barium swallow

Treatment

- Leave it alone if small and asymptomatic
- Minimally invasive treatment: endoscopic cricothyroid myotomy
- Surgical approaches (several available)
    - Diverticulectomy + cricothyroidotomy (diverticulectomy associated with risk of mediastinitis, dangerous)
    - Diverticulopexy (done in high risk patients, involves suspending the lumen of the pouch in the caudal direction so that food and secretions cannot enter the pouch; as the diverticulum is still present, the risk for malignancy still remains)

CAUSES OF POSTERIOR TRIANGLE MASS

Cystic hygroma

Pathology:

A cystic hygroma is a congenital cystic lymphatic malformation found in the posterior triangle of the neck, probably formed during coalescence of primitive lymph elements. It consists of thin-walled, single or multiple interconnecting or separate cysts which insinuate themselves widely into the tissues at the root of the neck.

Features:

- 50-65% present at birth, but occasionally may present later in childhood or adulthood
- Lobulated cystic swelling that is soft, fluctuant, and compressible (usually into another part of the cyst), located in the posterior triangle at the root of the neck
- Classically "brilliantly transilluminable"
- A large cyst may extend deeply into the retropharyngeal space

Complications:

- Cystic hygroma seen on prenatal ultrasound in the first trimester suggests chromosomal abnormality (50% of foetuses, usually trisomy 21) or other structural abnormalities (33% of foetuses with no chromosomal abnormality, usually congenital heart anomalies)
- May obstruct delivery
- Compressive problems after delivery – respiratory, swallowing

Management:

- Radiological investigations e.g. CXR, CT to delineate extent of cyst
- Non-surgical treatment – aspiration and injection of sclerosant (usually unsuccessful)
- Surgical excision – partial (to alleviate symptoms) or complete

Cervical rib

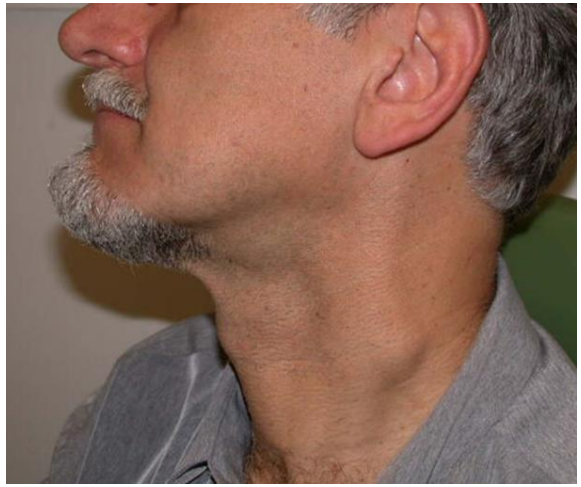
Features:

- Usually more symptoms than signs as it causes thoracic outlet syndrome
- A hard mass in the posterior triangle at the root of the neck
- Symptoms/signs:
  - Arterial: pallor, gangrene or necrosis of the tips of the fingers
  - Venous: oedema, cyanosis
  - Neurological: complaints of radicular symptoms (pain, paraesthesia), wasting of the small muscles of the hand
- Adson's test can be done – ask patient to extend neck and rotate it towards side of symptoms → radial pulse will be diminished, occasionally with reproduction of radicular symptoms in the limb
- Diagnosis by CXR

Neuroma/Schwannoma

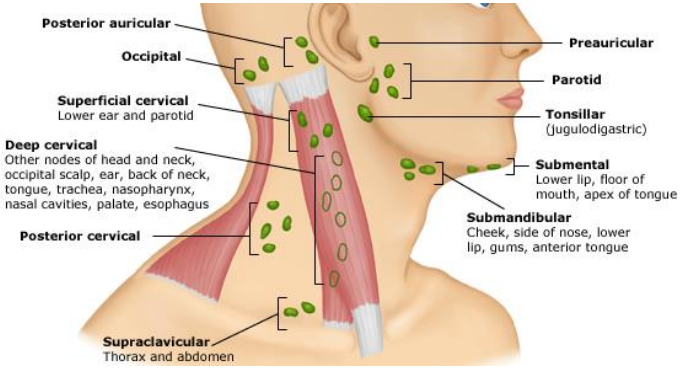
Features:

- Slow growing tumour arising from peripheral neural structures of the neck e.g. brachial plexus, cervical plexus, vagus nerve, phrenic nerve, etc.
- Fusiform, is mobile in plane perpendicular to axis of nerve but not parallel (mobile in 1 plane)
- Usually benign
- May be Tinnel's positive – tap on the mass for any paraesthesia occurring in distribution of the nerve
- DO NOT PERFORM FNA – excruciatingly painful



CERVICAL LYMPHADENOPATHY

ANATOMY



Levels:

There are six levels of LN in the neck, and different structures drain to different groups of nodes:

Lymph Node Level	Anatomical Boundaries[33]
IA (submental)	- Bordered by anterior belly of digastric muscle and hyoid bone
IB (submandibular)	- Bordered by anterior belly of digastric muscle, stylohyoid muscle and body of mandible
II (upper jugular)	- **Skull base superiorly, hyoid bone inferiorly**, stylohyoid muscle medially, posterior aspect of SCM laterally
III (mid jugular)	- **Hyoid bone superiorly, cricoid cartilage inferiorly,** lateral aspect of sternohyoid muscle medially and posterior aspect of SCM laterally
IV (lower jugular)	- **Cricoid cartilage superiorly, clavicle inferiorly**, lateral aspect of sternohyoid muscle medially and posterior aspect of SCM laterally
Va (post. triangle) Vb (supraclavicular)	- Convergence of SCM and trapezius muscle superiorly, clavicle inferiorly, posterior border of SCM medially, anterior border to trapezius muscle laterally
VI (ant. compt. grp)	- Central compartment (trachea-esophageal groove → non-palpable) – hyoid bone superiorly, suprasternal notch inferiorly, common carotid arteries laterally
VII	- Superior mediastinum

Drainage:

- **Oral cavity and oropharynx → levels I – III**
- **Thyroid & larynx → levels II – VI (thyroid malignancy first spread to level VI ndoes)**
- **Nasopharynx (NPC) → II – V (usually upper neck – level II and high level V)**

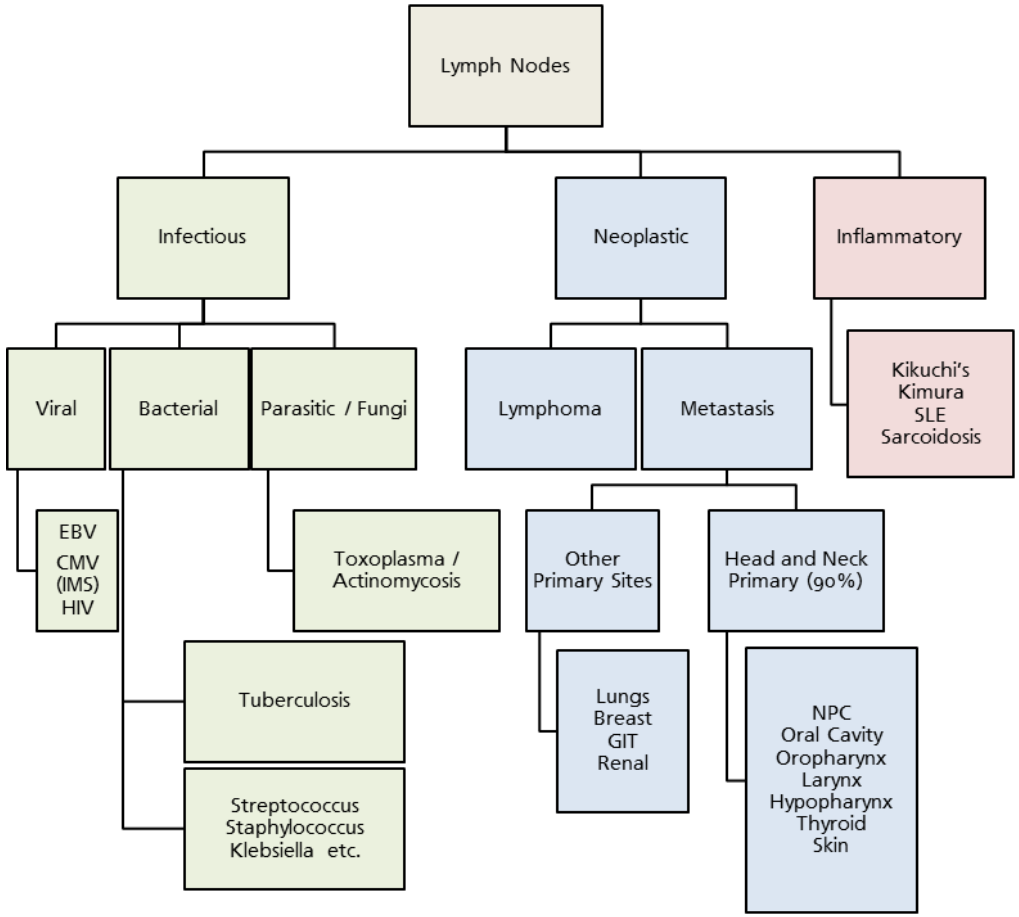
Course of the Thoracic Duct

- Commence at the **cisterna chyli** between AA and right crus of diaphragm
- Passes upwards through aortic opening
- Ascends behind oesophagus inclining to the left at the level of T_5
- At the root of the neck, it arches laterally lying between carotid sheath and vertebral artery to enter junction between left internal jugular veins and left subclavian veins
- **Virchow's node therefore lies between the 2 heads of the SCM**

[33] Head and Neck Cancer: A Multidisciplinary Approach – pg 183 Table 10.1

CAUSES

Can be divided into three main groups: infective, inflammatory, and neoplastic



*** Bacteria**

Streptococcus, Staphylococcus, Klebsiella (from intraoral pathology e.g. dental abscess, tonsillitis)

**** Inflammatory**

Kikuchi's (necrotising lymphadenitis occurring in young females, presenting as painful cervical lymphadenopathy)

HISTORY
- Age
- RF for CA: smoking, alcohol. Betel nut
- The lump itself
    - onset, duration, associated symptoms, lumps elsewhere
    - Pain: inflammatory > CA
    - Growth pattern / rate of growth:
        - last few days = infx / inflammatory / haemorrhage into cyst
        - last few months = CA
- Constitutional symptoms
    - Fever, malaise, arthralgia, myalgia (viral prodrome);
    - Night sweats, low-grade fever (TB, B symptoms of lymphoma);
    - Loss of appetite, loss of weight (chronic infection, malignancy)
- Local symptoms – intra-oral diseases e.g. tooth decay, oral/tongue ulcer, tonsillitis.
- Use of dentures.
- Past medical history – cancer, TB (contact? diagnosed? treated or untreated?)
- Social history: travel and contact history, sexual history for HIV, ORAL SEX

PHYSICAL EXAMINATION

Inspection
- **SITE**
- Size, shape, surface: erythema, discharging sinus (multiple lymph node enlargement with discharging sinuses can be TB or actinomycosis; sulphur granules seen in actinomycosis)

"Is there any pain? I am going to feel the lump, if any pain, let me know"

Palpate from behind, one side at a time – start at submental, then submandibular, preauricular, postauricular, along anterior border of sternocleidomastoid, supraclavicular, posterior triangle, lastly occipital. Use pulps of the fingers in a gentle rolling movement.
- Tenderness to palpation
- Consistency – hard, matted nodes are more suspicious for malignancy
- Fixation to overlying skin or underlying structures

Potential drainage sites:
- Upper LN (5) : MOUTH!!, face, scalp, thyroid, salivary glands
- Lateral LN: thyroid
- Lower LN: UL, Breast, Lungs, Abdomen (if Virchows), Oesophagus
- Suspect lymphoma (3): axilla, parotid, inguinal + liver/spleen

To complete the examination:
- Examine skin, face, neck, scalp and external auditory canal
- Formal ENT clearance of upper aero-digestive tract (UADT) especially looking at the post-nasal space for nasopharyngeal carcinoma (NPC being the most common cancer causing enlarged cervical lymph nodes)
- Examination of the thyroid gland & major salivary glands
- Examination of lymphoreticular system – other lymph node groups, liver, spleen
- Full respiratory and abdominal examination especially if supraclavicular lymph node found
- Breast examination in female patient

INVESTIGATIONS
- **Fine needle aspiration**
    - Able to accurately diagnose CA and TB
    - Only lymphoma requires excision Bx to diagnose (to be done after FNAC)
    - Do not do excision Bx first as it can compromise resection later if LN mets is from H&N CA, because LN mets counted as locally advanced dz (still resectable).

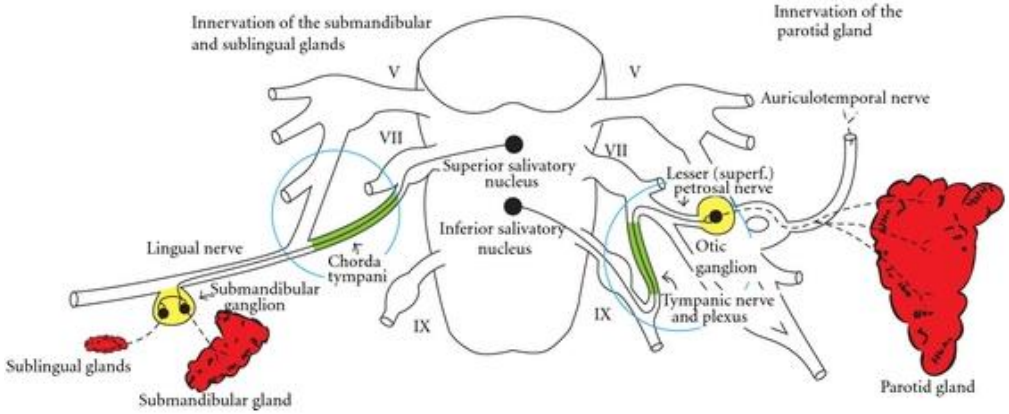
- Imaging: **CT**, ultrasound (esp. thyroid), MRI (mainly CA as pre-op w/u)
  → To assess nature of lump, extent, other enlarged nodes that are not clinically palpable, and can be used to visualise primary tumour if present

- Panendoscopy: to look for synchronous tumours as smoking / alcohol affect squamous cells
    - Nose – airway: nasolaryngoscopy, bronchoscopy
    - Mouth – CE junction: OGD

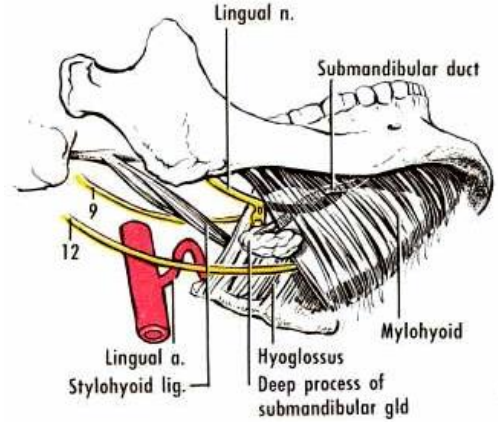
MANAGEMENT
- According to FNAC results
- Malignant – work up for primary if present (e.g. squamous cell carcinoma – look for oral cavity, skin, ENT, lung malignancy; adenocarcinoma – look for breast, GI tract malignancy) and treat as appropriate
- Infective/Inflammatory – treat underlying condition

SALIVARY GLAND SWELLINGS

ANATOMY



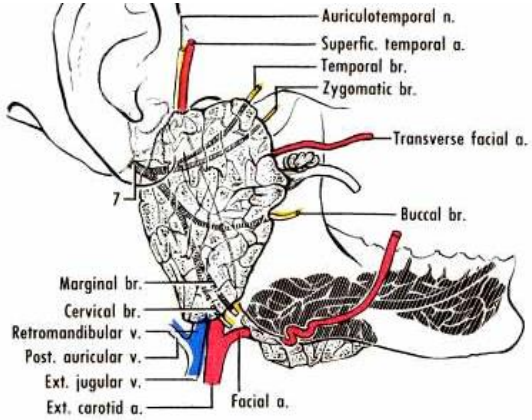
SUBMANDIBULAR GLAND



- Consists of a large superficial part and a small deep part that are continuous with one another around the free posterior border of the mylohyoid
- The deep part of the gland is closely associated with the lingual nerve (with the attached submandibular ganglion) above it, and the hypoglossal nerve and submandibular duct below it – surgery may injure these nerves

- **Nerve supply:** parasympathetic secretomotor supply from lingual nerve carrying postganglionic fibres (facial nerve (chorda tympani) – CNVII) from the submandibular ganglion (preganglionic fibres in superior salivary nucleus)
- **Submandibular duct** (of Wharton) arises from supf. part of the gland, runs forwards deep to mylohyoid and drains into the oral cavity at the sublingual papilla just adjacent to the frenulum
- **Histology:** mixed serous and mucous acini, few ducts

PARTOID GLAND



- Surrounded by tough fibrous capsule – the parotid sheath (thus mumps is painful as the gland swells within a tight envelope)
- Located between the posterior border of the ramus of the mandible and the mastoid process

- **Important structures** that pass through the gland in order from lateral to medial:
  - (i) Facial nerve and its branches
  - (ii) Retromandibular vein (maxillary veins drain into the superficial temporal vein)
  - (iii) External carotid artery (2 terminal branches: superficial temporal & maxillary artery)

- **Nerve supply:**
  - (i) Parasympathetic secretomotor supply from auriculotemporal nerve carrying postganglionic fibres (glossopharyngeal nerve – CN IX) from the otic ganglion (preganglionic fibres from inferior salivary nucleus);
  - (ii) Somatic sensory supply of the gland from auriculotemporal nerve; sensory supply of the capsule from the great auricular nerve.
- **Parotid duct** (of Stensen) runs 5cm across the masseter (surface marking: line from intertragic notch to midpoint of philtrum), drains into the mouth opposite the upper second molar tooth
- **Histology:** predominantly serous acini, many ducts (other glands have few ducts)

SUBLINGUAL GLAND

- A small almond-shaped gland located under the mucosa of the floor of the oral cavity
- Each gland has 15 or so ducts, half of which drain into the submandibular duct, the rest draining directly into the oral cavity
- **Nerve supply:** similar to the submandibular gland
- **Histology:** almost solely mucous acini, few ducts

HISTORY & PHYSICAL EXAMINATION

- About the lump: onset, duration, progress, associated symptoms e.g. pain
- If pain is present, is it precipitated by food ingestion? (suggestive of sialolithiasis)
- Symptoms of infection e.g. fever, malaise; if considering mumps, ask about testicular pain and swelling (orchitis), abdominal pain (pancreatitis)
- Any noticed facial asymmetry – incomplete closure of the eye on one side, drooping corner of the mouth, drooling
- Any symptoms of xerostomia (e.g. cannot eat biscuit or bread without water), xerophthalmia
- History of connective tissue disease e.g. rheumatoid arthritis, SLE

Inspect

- Put yourself at the level of the patient's face and look from front for any asymmetry with an obvious mass on one side – parotid mass is located between the angle of the jaw and the ear, and lifts the earlobe if large; submandibular mass is located just under the mandible
- Look for scars – parotidectomy scar runs anteriorly to the ear, below the earlobe and around posteriorly before looping forward again under the jaw
- Look for fistula/sinus
- Look at the patient's face for asymmetry (facial nerve palsy)

Palpate from behind

- Ask patient about any pain before starting to palpate
- Palpate the obviously enlarged gland, and always remember to also palpate the contralateral gland for any swelling
- Check for warmth of overlying skin, tenderness, consistency, surface, margins
- Fixation to underlying structures – for parotid, ask patient to clench the teeth to contract the masseter, then try to move the gland
- Fixation to overlying skin
- Palpate for cervical lymphadenopathy

Other tests

- Facial nerve examination
- Examination of the duct openings:
    - Using a torch and a tongue depressor, examine opposite the second upper molar tooth for the opening of the parotid duct, and under the tongue for the opening of the submandibular duct.
    - Look for red inflamed duct opening, discharge (purulent), or any visible stone.
    - For the parotid duct, can palpate the duct along the masseter for stone, and look for discharge inside the mouth while palpating.
- Palpate the gland openings for stones.
- Bimanual palpation of the submandibular gland

Suspicious features of malignancy:

- Hyperaemic hot skin over lump
- Pain
- Fixation to underlying structures or skin
- Hard consistency
- Irregular surface or ill-defined border
- Facial nerve involvement

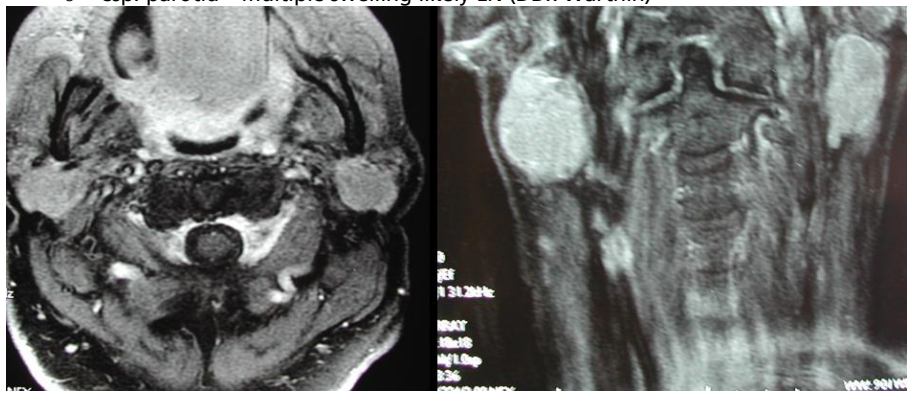
CAUSES OF SWELLING OF THE PAROTID

Parenchymal swelling	**Neoplasia**	- Benign (i.e. Pleomorphic adenoma, Warthin's, Monomorphic adenoma, Oncocytoma) - Malignant (i.e. mucoepidermoid, adenoid cystic carcinoma, carcinoma ex-pleomorphic, acinic cell adenocarcinoma) - Lymphoma and leukaemia*
	Stones	- Sialolithasis
	Infection/ Inflammation	- Mumps* - Acute sialadenitis - Chronic recurrent sialadenitis - HIV*
	Autoimmune	- Sjogren's syndrome*
	Infiltration	- Sarcoidosis*
	Systemic disease*	- Alcoholic liver disease - Diabetes mellitus - Pancreatitis - Acromegaly - Malnutrition
Non-parenchymal swelling	**Nodes**	- Metastatic (i.e. NPC, peri-auricular lesions)
	Blood Vessels	- AVM, haemangioma
	Lymphatics	- Lymphangiomas
	Nerves	- Facial schwannoma
	Fats	- Lipoma

* are conditions in which parotid swelling is bilateral

INVESTIGATION

- FNAC: malign vs. benign
- CT: confirm salivary gland (vs LN)
    - esp. parotid – multiple swelling likely LN (DDx Warthin)



SALIVARY GLAND TUMOURS

Epidemiology:
- 80% occur in the parotid, of which 80% are benign (80% of the benign tumours are pleomorphic adenomas)
- 10% occur in the submandibular, of which 60% are benign (95% pleomorphic adenoma)
- 15% occur in minor salivary glands, of which 50% are benign (all benign tumours are pleomorphic adenomas)
- 0.3% occur in sublingual glands, of which all are malignant

Pathology

Epithelial		Non-epithelial
Adenomas (benign)	**Carcinomas (malignant)**	
Pleomorphic adenoma Warthin's tumour Monomorphic Adenoma Oncocytoma	Mucoepidermoid Carcinoma Adenoid cystic carcinoma Carcinoma ex-Pleomorphic Acinic cell Adenocarcinoma Squamous cell ca Undifferentiated	Haemangioma Lymphangioma Neurofibroma Neurilemmoma (schwannoma) Lipoma Sarcoma Malignant lymphoma

Pleomorphic adenoma

Epidemiology:
- Most common benign tumour
- 85% occur in the parotid gland
- Equal sex ratio, occurs in younger patients less than 50 years old

Histology:
Very heterogeneous appearance, containing epithelial cells surrounded by loose stroma with islands of chondromyxoid (mesenchymal components), and interspersed islands of myoepithelial cells. The tumour appears to be encapsulated, but histology shows multiple sites of capsular penetration by tumour cells.

Features:
- Slow-growing, painless swelling occurring in the lower pole of the parotid
- Irregular and lobulated surface, texture of cartilage (slightly harder than Warthin's)
- Does not invade or metastasise
- Chance of malignant transformation if left for 10-15 years (1-6% risk)
- If not completely excised, can recur (recurrence rate of 2%)

Diagnosis by clinical, FNAC, ± MRI

Treatment – surgical excision
- Parotid: Superficial parotidectomy for superficial tumour; if tumour is deep or large, total parotidectomy with preservation of the facial nerve
- Submandibular: Total gland excision together with adjacent connective tissue, sparing lingual and hypoglossal nerves

Warthin's tumour

Epidemiology:
- 2nd most common tumour of the salivary gland
- Only occurs in the parotid gland (10% of parotid tumours) – almost exclusively in the superficial lobe of the parotid gland
- More common in males than females (4:1)
- Occurs in older patients (50 – 70 years)
- Related to cigarette smoking

Histology:
- Benign neoplasm (aka papillary cystadenoma lymphomatosum or just adenolymphoma)
- Grossly → bilateral (10%), multifocal (10%), oval/round encapsulated mass containing cystic spaces filled with milky secretion (mucin)
- Consists cystic spaces lined by two-tiered epithelium, surrounded by dense lymphoid stroma with germinal centres.

Features:
- Slowly enlarging, soft to firm cystic fluctuant swelling in parotid tail
- Invariably benign with no risk of malignant change
- Check for contralateral enlargement

Diagnosis by clinical, FNAC ± MRI

Treatment
- Can be left alone if absolutely certain that the entire mass is composed of only Warthin's tumour cells, since there is no malignant potential
- Superficial parotidectomy if causing trouble to patient

Malignant tumours

Most common malignancies are mucoepidermoid (34%) and adenoid cystic carcinomas (22%) – equal sex ratio, can occur in any salivary gland, in older patients (usually >60 yrs)

Mucoepidermoid ca is the most common malignant tumour in the parotid, while adenoid cystic ca is the most common in the submandibular, sublingual and minor salivary glands

Malignant pleomorphic adenoma

- Usually occurs in pre-existing pleomorphic adenoma, rarely de novo
- Worst prognosis of any salivary gland tumour
- 30-70% recurrence and metastasis rate

Treatment of salivary gland cancers

Parotid:

- Total parotidectomy with sacrifice of facial nerve if tumour has infiltrated it (may be grafted with great auricular nerve)
- Radical neck dissection if neck nodes positive
- Postoperative radiotherapy

Submandibular:

- Radical excision of gland with lymphatic clearance of submandibular triangle
- Radical neck dissection if neck nodes positive
- Postoperative radiotherapy

COMPLICATIONS OF PAROTIDECTOMY[34]

Immediate (intra-operative)

1. Intraoperative facial nerve transection – LMN palsy
   - Facial Nerve Branches (motor branches) = Temporal, Zygomatic, Buccal, Mandibular, Cervical
   - Zygomatic: lead to incomplete closure of eye → use ophthalmic drops and eye protection at night
   - *in contrast, **submandibular gland surgery** can damage the hypoglossal and/or lingual nerves
2. Rupture of capsule of parotid tumour
3. Incomplete surgical resection of parotid tumour

Early (1 to 30 days)

1. Temporary facial weakness (neuropraxia of facial nerve – 90% resolves in 1 month)
2. Division of great auricular nerve → loss of sensation over pinna
3. Parotid fistula → treat conservatively, ± anticholinergic ± botulinum toxin
4. Trismus (inflammation and fibrosis of masseter muscle – usually mild and transient)
5. Wound infection / Wound seroma
6. Haemorrhage / Hematoma
7. Skin flap necrosis (rare)

Late (more than 30 days)

1. Facial synkinesis after facial palsy
2. Hypoesthesia of greater auricular nerve
3. Recurrent Tumour
4. Cosmetic problems – soft tissue deficit, hypertrophic scar / keloid
5. Frey's syndrome – **gustatory sweating** (aberrant regeneration of the severed parasympathetic secretomotor fibres onto the sympathetic receptors innervating the blood vessels and sweat glands following injury to the auriculotemporal nerve)

[34] Acta Otorhinolaryngol Ital. Jun 2005; 25(3): 174–178.

SIALOLITHIASIS

Epidemiology
- Stones of the salivary gland that may be impacted within the gland itself or in the duct.
- Usually occurs in males more than females, and between the ages of 30 and 60.
- 80% of salivary stones occur in the submandibular gland (due to its higher mucus and calcium content with a long duct, and slow flow of the saliva against gravity); 10% occur in the parotid, 7% sublingual.
- Most submandibular gland stones occur in the duct, while 50% of parotid stones occur in the gland itself.
- 80-95% of submandibular stones are radio-opaque and can be seen on an X-ray of the floor of the mouth, and 60% of parotid stones are radio-opaque.

Presentation
- **Complete obstruction**
  Acute pain and swelling of the gland involved at meal times, rapid onset within minutes of starting to eat, resolves about an hour after the meal.
- **Partial obstruction**
  Occasional symptomatic episodes interspersed by asymptomatic periods of days to weeks, chronically enlarged mass in the submandibular region
- Can result in **sialadenitis**, and even abscess formation → worsening of symptoms of pain and redness; systemic symptoms such as fever, chills; purulent discharge from duct opening
- Stone may be palpable along the duct or at the opening of the duct

Investigations
- Non-contrast CT scan – can pick up almost all stones when fine cuts are requested
- Plain X-rays can pick up radio-opaque stones
- Sialogram (rarely done today as it is invasive and technically demanding, and CT is better. Contraindicated in acute sialadenitis and contrast allergy.)

Management
- **General measures:**
  - Good hydration, soft diet, good oral hygiene
  - Massage of the gland, milking the duct, application of moist hot towel
  - Analgesia – NSAIDs such as ibuprofen
  - Antibiotics if patient has sialadenitis – usually antibiotics to cover Staph and Strep e.g. Augmentin
  - Refer specialist treatment if symptoms persist for several days, or sialadenitis persists despite antibiotic therapy

- **Surgical removal**
  - Trans oral removal of stones for submandibular duct stones (50% can be removed thus), less for parotid duct stones
  - If stones cannot be removed via trans oral surgery or is intraglandular, partial gland resection can be performed
- Other options: Lithotripsy, wire basket removal, sialoendoscopy

THE THYROID GLAND

APPROACH TO THYROID PROBLEMS – 2 MAIN TYPES

1. **Problem with configuration/anatomy**
   (i) Solitary thyroid nodule (most common in exam)
      - Dominant Nodule of a MNG / Follicular Adenoma / Cysts / Carcinoma

   (ii) Multinodular goitre
      - Toxic MNG / Hashimoto's thyroiditis

   (iii) Diffuse enlargement
      - Graves' Disease
      - Simple, non-toxic goitre / Hashimoto's thyroiditis / Sub-acute thyroiditis / Lymphoma
2. **Problem with function (see below)**

HISTORY TAKING

About the LUMP (benign or malignant)
- **Onset** (gradual or sudden), **duration** (rate of growth of neck mass)
- **Size** (Diffuse or one side predominant? **Any sudden increase in size?** – malignant growth; ddx includes haemorrhage into necrotic nodule or cyst, sub-acute thyroiditis)
- **Red Flags** – dysphonia, dysphagia, or dyspnoea (see below)

About SYMPTOMATOLOGY
- Most patients with thyroid nodules have few or no symptoms!

History	Hyperthyroid	Hypothyroid
General Mood	Hyperactive Easily Irritable Insomnia or Anxiety Depression (elderly)	Tiredness / Lethargy Mood change including depression
Other Symptoms	Weight loss despite increased appetite	Weight gain despite decreased appetite
	Heat intolerance (preference for cold) Increased sweating	Cold intolerance (preference for warmth)
	Diarrhoea	Constipation
	Palpitations, Tremors	Bradycardia
	Oligomenorrhoea and loss of libido	Menorrhagia

About COMPLICATIONS OF DISEASE

Local	- **Pain** – bleeding into cyst can result in sudden increase in size and pain; rarely pain can occur in anaplastic carcinoma and thyroiditis - **Compressive Symptoms** – difficulty swallowing, difficulty breathing, hoarseness of voice (benign pathologies almost never compress the recurrent laryngeal nerve) - **Fixed Gaze** – risk of optic nerve compression (surgical emergency)
Systemic	- **High Output Cardiac Failure** – ask about dyspnoea, effort tolerance - **Thyroid Storm** or **Thyrotoxicosis Crisis** (metabolic and hemodynamic instability)

About RISK FACTORS
- History of **autoimmune disease** e.g. type I DM, SLE, RA, pernicious anemia (associations with Graves and Hashimoto's)
- History of **cancer** elsewhere – metastatic disease to thyroid; lymphoma; papillary cancer is associated with familial polyposis syndromes → ask about GI polyps/cancers
- History of **thyroid disease** – long-standing MNG can progress to lymphoma
- Occupational history – any exposure to **ionizing radiation** (papillary cancer risk ↑ 3x)
- **Family history** of thyroid cancer – ~20% of medullary cancers are familial (MEN2, AD inheritance), ~ 5% of papillary cancers
- **Smoking**

About previous TREATMENT for any thyroid disease
- **Medications** e.g. propylthiouracil, carbimazole, propranolol – length, efficacy, side effects
- **Radioactive iodine** treatment – what was the result? Is the patient receiving replacement?
- **Surgery** – what kind of surgery, any complications?
- **Follow-up** – what investigations done?

PHYSICAL EXAMINATION

AIM: thyroid ± lymphadenopathy ± features of malignancy ± compressive symptoms ± current thyroid status (hyper / hypo / euthyroid)

A. THYROID GLAND

PRELIMINARIES

1. Greet Patient and ask for permission to examine (any voice hoarseness – RLN invaded)
2. Position patient and expose adequately – entire neck, sternum and clavicles
3. Inspection from the front
   a. Any swelling?
   b. Any scars? (any transverse incision in a skin crease, 2FB above suprasternal notch)
   c. Any skin changes over the mass?
   d. Any stigmata of hyperthyroidism (i.e. agitation) or hypothyroidism (i.e. bradykinesia)
   e. Check for plethora of face, distended neck veins – may be due to compressive nature of mass (but rarely seen).

CONSIDER DIFFERENTIAL DIAGNOSIS FOR THYROID LUMP

1. Check if mass moves on swallowing by asking patient to take a sip of water – "Please take a sip of water and hold it in your mouth, do not swallow until I tell you to."
2. Check if mass moves on protruding the tongue – "Please open your jaw slightly. Now, without moving your jaw, please stick your tongue out and back in again."
3. Check if mass moves on swallowing or tongue protrusion again with hands palpating thyroid

***** A thyroid swelling moves only on swallowing; a thyroglossal cyst will move on ***both*** swallowing and protrusion of the tongue

PALPATE THYROID FROM BEHIND – one side at a time with the opposite hand stabilizing the gland. Gently tilt head forward to relax anterior neck muscles, rest fingers on lateral lobe of thyroid (Ask for pain before palpating!)

1. **Characteristics of lump and surrounding skin:**
   a. site (anterior triangle),
   b. size (discrete nodule or multinodular enlargement or diffuse enlargement?),
   c. consistency (soft, cystic, hard, multinodular?),
   d. mobility (fixed to skin? Fixed to underlying structures?),
   e. tenderness.
2. Palpate lymph nodes – submental, submandibular, pre/post auricular, down SCM (II, III, IV), supraclavicular, occipital
   a. Separate & tender (reactive hyperplasia)
   b. Hard & clustered (carcinoma)
   c. Soft and rubbery (lymphoma)
3. Feel the carotid pulsation on both side – are they well felt?

AROUND THE THYROID

1. Palpate for tracheal deviation
2. Percuss manubrium for signs of any retrosternal extension
3. Auscultate of any neck bruit (using the bell) – specific for Graves'

B. THYROID STATUS

FACE

1. Expression – staring, unblinking (hyperthyroid); lethargic, apathetic (hypothyroid)
2. Complexion – dry, 'peaches-and-cream' complexion, loss of outer third of eyebrows (hypothyroid)
3. Eyes*
   a. Lid lag (eyelid lags behind eye when patient follows your finger downwards)
   b. Lid retraction (sclera visible between upper limbus of iris and upper eyelid)
   c. **Exophthalmos** (sclera visible between lower limbus and lower eyelid)
   d. **Chemosis** (oedema and erythema of conjunctiva) – if present consider using fluorescein to look for corneal ulceration
   e. **Ophthalmoplegia** (restriction of eye movements; ask about diplopia!)
   f. **Proptosis** (look from above patient's head – eye visible over supraorbital ridge)

* Lid lag and lid retraction are result of excess sympathetic activity and not specific to Graces' disease. The rest (c-f) are specific for Graves' disease – affects up to 60% clinically (smoking, age, male and RAI increase risk of ophthalmopathy in GD)

UPPER LIMB

1. Examine for Proximal myopathy
2. Fine postural tremor – accentuate by placing a sheet of paper on the hands
3. Reflexes (elbow reflex)

* Offer Pemberton's Sign flushing of face with both hand raised – (1min)

PALM

1. Palms – ↑ sweating, palmar erythema (hyperthyroidism), areas of vitiligo (a/w AI disorders, i.e. Graves' disease)
2. Feel pulse – tachycardia, AF (more in toxic MNG than Graves'), bradycardia (hypothyroidism)
3. Nails – thyroid acropachy (clubbing), onycholysis – plummer's nail

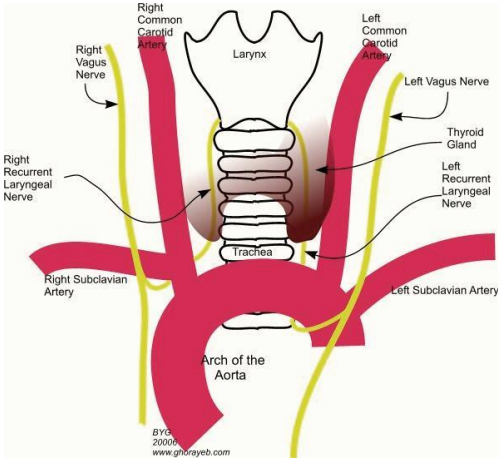
OTHERS

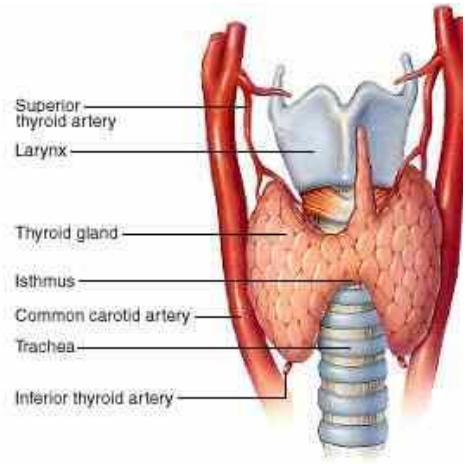
1. Legs for pretibial myxoedema* (specific for Graves' (3%) or hypothyroid)
2. Reflexes (ankle jerk) – slow to relax in hypothyroidism
3. Offer to check **thyroid status** and ask patient about **compressive symptoms**.

* Elevated shin lesions with well-defined edges (infiltrative dermopathy) – lesions may be nodular or plaque like, purplish red or brown and the skin is shiny with a thickened orange peel appearance

Examination	Hyperthyroid	Hypothyroid
General Inspection	Weight Loss	Obesity
	Alopecia	Dry Thin Hair
	Face appears flushed	'Peaches & cream' complexion
Eyes	lid retraction, lid retraction, exophthalmos, oculomotor palsies	Loss of outer 1/3 of eye-brows
Upper Limb + Hands	Proximal Myopathy	Muscle Weakness
	Warm & Sweaty palms Tremors Thyroid Acropachy (clubbing) Hyperreflexia Tachycardia at rest ± AF	Cold peripheries Carpal Tunnel Syndrome Hyporeflexia Bradycardia
Lower Limb	Pre-tibial Myxoedema	Oedema

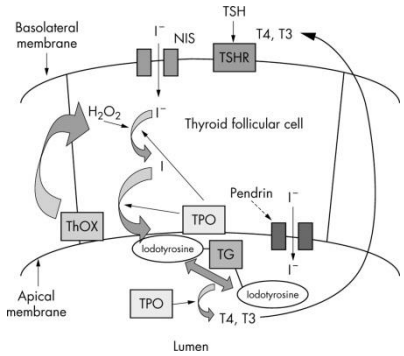
PART 1: RELEVANT ANATOMY (EMBRYOLOGY, ANATOMY AND PHYSIOLOGY)





Synthesis of thyroid hormone

- **IODIDE TRAPPING** → TSH receptor (TSHR) bound to TSH stimulates iodide transport into the thyroid gland by the sodium iodide symporter (NIS)
- **IODIDE OXIDATION + ORGANIFICATION** → Iodide is oxidised and bound to tyrosine residues in thyroglobulin (TG) to form iodotyrosine (MIT / DIT)
- **COUPLING** → MIT and DIT couple to form the hormonally active iodothyronines, T_4 and T_3.
- **Thyroid peroxidase (TPO) catalyses the oxidation, organification, and coupling reactions**



Anti-thyroid drugs

Class	Drug	Actions	Remarks
Thioamides	Carbimazole Propylthiouracil Methimazole	Inhibits TPO – thyroid peroxidase PTU also inhibits peripheral deiodination of T_4	PTU – not the 1st line drug, only used in pregnancy (1st trimester) – not used for 2nd & 3rd trimester due to risk of hepatotoxicity – switch to MMI at start of 2nd trimester[35] CMZ – s/e: agranulocytosis, rash (hypersensitivity reaction), cholestatic hepatitis, arthralgia
Iodides	Lugol's Solution	Interferes with organification and inhibit hormone release	Advantage – helps to decrease size and vascularity of gland

[35] uptodate: Hyperthyroidism during pregnancy: Treatment

EMBRYONIC ORIGINS

Thyroid gland: develop from the endoderm of the primitive foregut → site of the initial development at the foramen caecum (midline, junction between anterior two-thirds and posterior one-third of the tongue → descents down thyroglossal tract into the neck anterior to the hyoid bone and laryngeal cartilage (thyroid completes its descent in the 7th gestational wk)

Parathyroid glands: 2 superior and 2 inferior glands. The inferior parathyroid glands arise from the 3rd pharyngeal pouch (dorsal wing) – ventral wing becomes the thymus which migrates caudally and medially pulling the parathyroid with it. The superior parathyroid glands arise from the 4th pharyngeal pouch (dorsal wing)

ANATOMY

Structure: 2 lateral lobes joined by an isthmus that lies in front of the 2nd, 3rd and 4th tracheal rings, anterior to larynx and trachea. Strap muscles of the neck lie superficial to the thyroid gland.

Nerves and vessels:

- Superior Thyroid Artery (from external carotid*)
  - Divide the superior thyroid artery close to the gland, to avoid damage to the external branch of the superior laryngeal nerve
- Inferior Thyroid Artery (from thyrocervical trunk, branch of 1st part of subclavian artery)
  - Divide the inferior thyroid artery far away from the gland to avoid damage to the recurrent laryngeal nerve
- External Branch of Superior Laryngeal Nerve – supplies the **cricothyroid** (tense vocal cord) and runs immediately deep to the superior thyroid artery
  - If injured = inability to produce high pitch sounds along with easy voice fatigability (usually monotoned voice – range and power of voice affected) – permanent paralysis is rare if nerve has been identified during op.
  - For most patients, the changes are subtle
- Recurrently laryngeal nerve – supplies all **intrinsic muscles of the larynx** (except for the cricothyroid) and runs close to the inferior thyroid artery. The nerve runs behind the pre-tracheal fascia, hence will not be damaged if the fascia is not breached
  - If unilateral damage = affected cord lies in the paramedical position (inadequate glottis closure) presents with weak breathy voice, hoarseness
  - If bilateral damage = acute dyspnoea as a result of the paramedical position of both vocal folds which reduce airway to 2-3mm and which tend to get sucked together on inspiration
  - The right recurrent laryngeal nerve is more susceptible to damage during thyroidectomy (relative medial location) though a left vocal cord palsy is the most common (long intra-thoracic course, commonly involved in inflammatory and neoplastic conditions involving the left hilum)

Parathyroid: Superior parathyroid glands usually located on the posterior part of the upper lobe of the thyroid. Inferior parathyroid glands are subject to variations (i.e. posterior part of the lower pole of the thyroid, carotid sheath, superior mediastinum in a/w (or even within) the thymus, rarely behind the oesophagus)

* Branches of the external carotid artery → "Some Attending's Like Freaking Out Potential Medical Students "
- superior thyroid artery – ascending pharyngeal artery – lingual artery – facial artery – occipital artery – posterior auricular artery – maxillary artery – superficial temporal artery

CLINICAL PHYSIOLOGY

Causes of thyrotoxicosis

	Disease	Remarks
Primary Hyperthyroidism	**Graves' Disease**	Thyroid-stimulating IgG antibodies (TSI) are TSH receptor antibody (TRAb) that bind to and stimulate the TSH receptors >80% positive
	Toxic Adenoma^	Solitary secreting adenoma
	Toxic MNG	Most common cause in older patients
Secondary Hyperthyroidism	TSH-secreting pituitary adenoma	TSH detectable despite high FT_4 and FT_3
	Gestational thyrotoxicosis	Hyperemesis gravidum due to high levels of HCG in 1st trimester which stimulates TSH receptors
	Neoplasms	Ovarian Teratoma – struma ovarii Choriocarcinoma – tumour can produce both HCG and TSH Metastatic Thyroid Carcinoma
Thyrotoxicosis without Hyperthyroidism	Destructive thyroiditis	**Sub-acute (de Quervain's) –** due to release of large amount of steroid hormones **Drugs – Amiodarone / Lithium**
	Excess thyroid hormones	

^ Plummer's Disease – single toxic nodule (adenoma) present with the b/g of a suppressed multinodular goitre (MNG)

Causes of hypothyroidism

	Disease	Remarks
Primary Hypothyroidism	**Hashimoto's thyroiditis***	- Autoimmune inflammation (dense lymphocytic infiltrate) - Microsomal auto-Ab >90% (anti-thyroglobulin – anti-TG and/or anti-thyroid peroxidase – anti-TPO) - Typically affects middle-age and older women, presenting with hypothyroidism, a goitre or both
	Autoimmune (atrophic)	Microsomal autoantibodies are present
	Iodine Deficiency	Most common cause of goitre
	Others	**Genetic Defects** – Pendred's Syndrome** **Drugs –** Lithium, Amiodarone, Sulphonylureas **Neoplasms –** infiltration and destruction of the gland secondary to a malignant neoplasms **Iatrogenic –** post-thyroidectomy & irradiation
Secondary Hypothyroidism	Hypopituitarism	
	Isolated TSH deficiency	

* a/w vitiligo, pernicious anemia, T1DM, Addison's disease & premature ovarian failure

** AR condition leading to bilateral sensorineural hearing loss and goitre with occasional hypothyroidism

Thyrotoxicosis → biochemical and physiological manifestation of excess excessive circulating free T_4 (can occur with or w/o hyperthyroidism)

Hyperthyroidism → thyroid gland over-activity resulting in thyrotoxicosis

- **TRH** from hypothalamus → stimulate **TSH** from anterior pituitary → **T_3 / T_4**
- Thyroid Follicular cells → synthesize T_3 & T_4

Function of Thyroid Hormones (T_3 & T_4)

System	Action
Cardiac	- ↑ HR and cardiac output - ↑ B-receptor production – ↑ sensitivity to catecholamines (I.e. adrenaline) - Promotes erythropoiesis - ↓ peripheral vascular resistance
Metabolic	- ↑ basal metabolic rate (thermogenic) - ↓ cholesterol production + ↑ catabolism of fatty acids - ↑ absorption of glucose, gluconeogenesis and glycolysis - ↑ synthesis and catabolism of proteins
Respiratory	- ↑ ventilation rate
Gastrointestinal	- ↑ motility and secretion
CNS	- ↑ CNS activity and alertness - Normal neuronal function
Growth and Development	- Normal myelination and axonal development - Stimulate skeletal growth - Promote bone mineralization

- **Parathyroid Hormone → involves in calcium homeostasis**
  - Increase osteoclastic activity → Ca^{2+} release from bone
  - Increase rate of Ca^{2+} re-absorption from the renal tubules
  - Stimulates urinary phosphate excretion
  - Increase absorption of Vitamin D
  - Stimulates rate at which Vitamin D is converted to active 1,25 form in the kidneys

- **Calcitonin (produced by the para-follicular C cells) → oppose effects of PTH on calcium**
  - Inhibits osteoclastic activity
  - Inhibits Ca^{2+} re-absorption from the renal tubules
  - Inhibits calcium absorption by the intestines
  - **Inhibits phosphate reabsorption by renal tubules (mirrors PTH)**

Calcium Physiology (FUNCTIONS)

- Intracellular Calcium → mediator of intra-cellular signals (second messengers in signal transduction)
- Extracellular Calcium
  - Excitability of nerve and muscles → calcium level fall, Na^+ permeability will increase, and the threshold will fall thus increasing nerve and muscle activity
  - Muscle contraction → excitation-contraction coupling
  - Secretion Process
  - Clotting – calcium is essential blood clotting factor
  - Bone Formation

PART 2: APPROACH TO THE SOLITARY THYROID NODULE[36]

Prevalence:

- Estimated prevalence on the basis of palpation ranges from 3-7%
- Prevalence of cancer from palpable lesion is 5-6.5% → similar even if nodule is non-palpable and detected incidentally (5.4-7.7%)
- 20-48% of patients with one palpable thyroid nodule (discrete lesions distinct from surrounding thyroid parenchyma) are found to have additional nodules on u/s investigation
- More common in elderly, women, iodine deficiency and previous radiation exposure

Differential diagnoses:

1. Dominant nodule of a multinodular goitre
2. Cyst (simple, colloid, or haemorrhagic)
3. Follicular adenoma
4. Cancer (need to exclude!)

History and physical examination – as above

- Sudden pain – commonly due to haemorrhage in cystic nodule
- Progressive and painful enlargement → consider anaplastic carcinoma or primary lymphoma

Clinical features suggesting increased risk of malignant potential

1. **Male** – thyroid nodules less common in male but more likely to be malignant
2. Age **<14yrs** or **>70yrs** (majority of nodules which occurs in 3rd to 6th decades – likely benign)
3. History of head and neck ionizing **radiation**
4. **Family history** of medullary / papillary thyroid cancer or MEN type 2
5. **Slow but progressive growth of the nodule (**during weeks or months)
6. **Firm or hard, solitary or dominant** thyroid nodule (which is different from rest of gland)
7. **Fixed** nodule
8. Cervical **lymphadenopathy** (esp. lateral nodal compartments)
    a. **Level VI lymph nodes**: first nodes that a thyroid malignancy spreads to; they lie in the tracheo-oesophageal groove and are not palpable.
9. Compressive symptoms – i.e. tracheal compression (cough and dysphonia)
10. **Hoarseness** (i.e. recurrent laryngeal nerve invasion)
11. Other **symptoms of invasion** e.g. haemoptysis, stridor, dysphagia, dyspnoea, dysphonia*

* differentiated thyroid carcinoma rarely cause airway obstruction, vocal cord paralysis or oesophageal symptoms at their clinical presentation → absence of local symptoms does not r/o malignant tumour

Management of benign nodule:

- Soft, small, round nodule with benign FNAC results, non-functional, not causing any symptoms → can follow-up and monitor any increase in size

Key Recommendations:

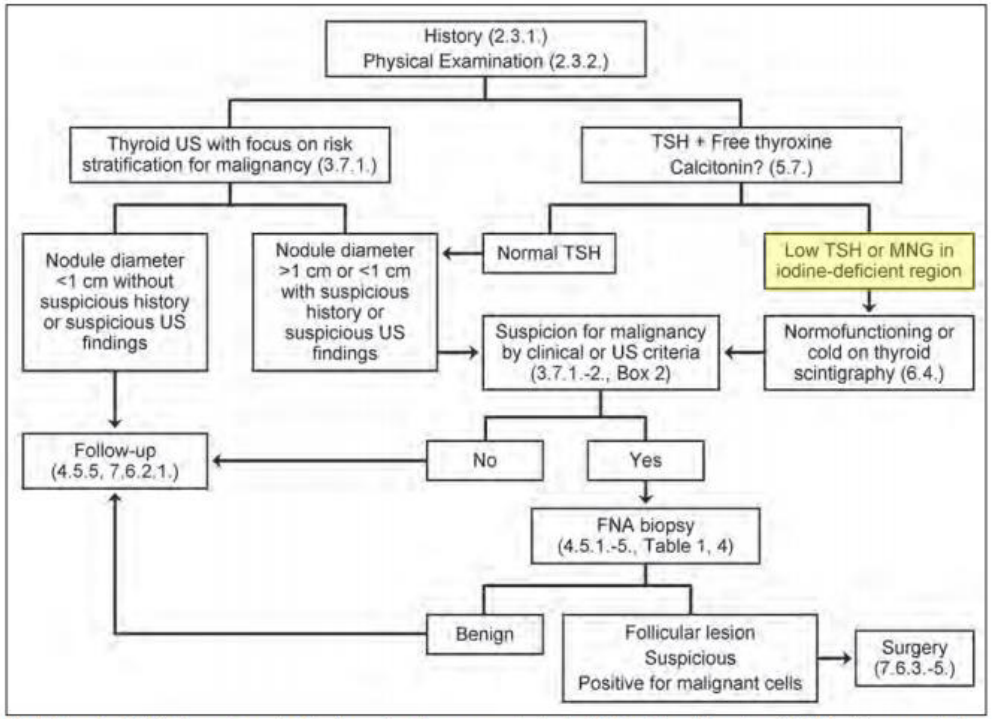


Fig 1. Flowchart indicating a scheme for the diagnosis and management of palpable thyroid nodules. Associated Key Recommendations shown in parentheses. FNA, fine-needle aspiration; MNG, multinodular goiter; TSH, thyrotropin; US, ultrasonography.

* In practice, even if thyroid nodule <1cm can still consider u/s guided FNA rather than just regular clinical f/u

[36] AACE/AME/ETA Thyroid Nodule guidelines, Endocr Pract. 2010;16

Investigations:

1. FINE NEEDLE ASPIRATION CYTOLOGY (SENSITIVITY – 83%, SPECIFICITY – 92%)
   - The single most important investigation modality for management of thyroid nodule!
   - Best performed under **u/s guidance** to increase diagnostic accuracy
   - Can be both therapeutic and diagnostic for cyst – chocolate-brown fluid aspirated; feel lump after aspiration to check for resolution
   - Cannot differentiate follicular adenoma from follicular carcinoma as the mark of malignant disease is capsular invasion (FNAC provides limited assessment of architecture)
     - **Need to assess the WHOLE capsule for invasion (hence FNAC, Incisional biopsy or frozen section cannot be used for diagnosis)**
   - Procedure: inject local anaesthetic in area, insert 22G needle and apply suction while fanning needle in region of nodule, release suction before pulling out needle, expel contents onto slide, then fix
   - Cytologic smears should be interpreted by an experienced on-site cytopathologist and reported based on the BETHESDA CLASSIFICATION (see below)

2. ULTRASOUND OF THYROID
   - For all patients with a palpable thyroid nodule or with clinical risk factors
   - Advantages:
     (i) Objective **measurement** of nodule size and characteristics (see below)
     (ii) Detection of **subclinical nodule/screening** – of value in papillary carcinoma since multi-centric disease occurs in 15%
     (iii) Detection of **lymph node** enlargement (especially level VI nodes)
     (iv) Can define **consistency** of nodule – solid, cystic, or complex
     (v) Can be used to guide FNA biopsy and/or cyst aspiration
   - Suspicious sonographic features (***a/w thyroid cancers**)
     (i) **Calcifications – micro*,** dense/macro, rim (psammoma bodies → papillary cancer)
     (ii) **Vascularity – intra-nodular*,** peripheral, absent
     (iii) **Margins – infiltrative*,** spiculated*, well-defined regular
     (iv) **Echogenicity – hypo*,** hyper, iso-…
     (v) Shape – taller than wide*
     (vi) **Halo – absent*,** thin, regular
   - No u/s feature is independently fully predictive of a malignancy
   - Standardized reporting indicating – position, shape, size, margins, contents, echogenicity and vascular pattern of the nodule

3. THYROID FUNCTION TEST
   - Measurement of serum TSH is the best initial laboratory test of thyroid function (**MCQ**) – followed by free T_4 and T_3
   - Easy to perform, establish baseline, detect any abnormal function

   - ± anti-thyroid peroxidase antibodies (TPOAb) – if TSH value is above reference
   - ± anti-thyroglobulin – if suggestive of chronic lymphocytic thyroiditis (Hashimoto) in conjunction with normal serum TPOAb levels
   - ± anti-TSH antibody (TRAb) – if TSH value is below reference

4. CALCITONIN ASSAY
   - Mandatory for patients with history or clinical suspicion of familial MTC or MEN2
   - Calcitonin levels can be increased in → pulmonary / pancreatic endocrine tumours, kidney failure, AI thyroid disease, hypergastrinemia (fr PPI therapy), alcohol, smoking and sepsis

5. RADIO-ISOTOPE SCAN (^{123}I OR $^{99M}TcO_4$ (SODIUM PERTECHNETATE)
   - For patients with low serum TSH value or a MNG to detect functional autonomy (i.e. identify cold or indeterminate areas for FNA biopsy and hot area that do not need cytologic evaluation)
   - **Hot** nodule: only 1% malignant; but **cold** or **indeterminate** nodule: 3-15% malignant
   - ^{131}I is not recommended for routine diagnostic use

6. BASELINE TUMOUR MARKERS (IF SUSPECTED OR CONFIRMED MALIGNANCY)
   - For differentiated thyroid cancer: thyroglobulin
   - For medullary thyroid cancer: calcitonin, carcinoembryonic antigen (CEA)

7. CT SCAN OR MRI
   - Not routine in thyroid nodular study as they are rarely diagnostic for malignant lesions
   - Uses:
     (i) Sub-sternal and / or Retrosternal extension
     (ii) Staging known malignancy
       a. Evaluating invasion of surrounding structures
       b. Lymph node involvement
   - Care to be taken with CT as contrast contains iodine and will affect post-op radioactive iodine body scan once given
   - MRI has same functions as CT but higher cost

8. ENT EXAMINATION OF VOCAL CORDS
   - In the rare occasion that there is pre-existing vocal cord palsy on one side → take extra care not to injure opposite recurrent laryngeal nerve as that can cause bilateral vocal cord palsy

Bethesda Classification[37]

	Diagnostic Category	Examples	Malignancy (%)	Management
I	**Non-diagnostic / Unsatisfactory**	Cyst fluid, blood, clotting artefact	1-4	Repeat FNA with u/s guidance
II	Benign	Colloid, adenomatous nodule, thyroiditis	0-3	Clinical Follow-up
III	Atypia / Follicular lesion of undetermined significance		5-15	Repeat FNA
IV	Follicular neoplasm or suspicious for a follicular neoplasm	Includes hurtle cell neoplasm	15-30	Surgical Lobectomy
V	Suspicious for Malignancy		60-75	Near-total thyroidectomy or surgical lobectomy*
VI	Malignant	Papillary, medullary, anaplastic, NHL, SCC, metastatic	97-99	Near-total thyroidectomy*

* If metastatic tumour rather than a primary thyroid malignancy, surgery may not be indicated

[37] Am J Clin Pathol 2009;132:658-665

PART 3: THYROID CANCERS[38]

	Differentiated thyroid carcinoma		Medullary carcinoma	Anaplastic carcinoma	Lymphoma
	Papillary carcinoma	Follicular carcinoma			
Proportion	75%	10%	7%	3%	5%
Age	30-50 years	40-60 years	>50 years for sporadic type; 20-30 years for familial	60-70 years	>50 years
F:M ratio	2.5:1	3:1	1:1	3:2	2:1
Risk factors	- **Childhood radiation** exposure - **Polyposis syndromes** (FAP, Gardner's, etc.) - **Werner syndrome, Carney complex** - Positive family history in 5%	- Follicular adenoma is NOT a risk factor - Iodine deficiency may be associated - Hx of MNG	- Significant family history in the familial type – **MEN2** (AD, complete penetrance, associated with parathyroid adenoma and pheochromocytoma – *see notes below*)	- **Longstanding goitre** - History of **previous** differentiated thyroid **ca** (30% of anaplastic ca)	- History of lymphoma or MALT elsewhere - **Hashimoto's thyroiditis** (60X ↑ risk)
Pathological features	- Characteristic (1) Orphan Annie nuclei, (2) nuclear pseudoinclusions - Papillary architecture with (3) psammoma bodies - **Tall cell variant** (nuclear features of papillary ca within follicular lesion) behaves like papillary ca, has worse prognosis	- Follicular structures similar to normal thyroid - Diagnosis of cancer made on evidence of capsular or vascular invasion by tumour cells (vs. follicular adenoma) - **Hurthle cell variant** – worse prognosis	- Arise from thyroid parafollicular C cells (**which produce calcitonin**) - Distinctive deposits of acellular amyloid material – altered calcitonin collections (shown with congo red stain) - Multicentric C-cell hyperplasia may be seen in familial cases	- Small blue round cells that are highly anaplastic – may resemble lymphoma	- FNAC may suggest lymphoma but definitive diagnosis requires trucut or excision biopsy - Almost always **non-Hodgkin's** of B-cell type
Clinical features	- Slow-growing tumour - Spread by **lymphatics (cervical)** - 70% multicentric - LN involvement in 80% of disease at diagnosis (level VI first)	- Solitary - **Haematologic** spread to liver, lung, bone, brain - LN involvement in 10% (rare)	- Sporadic cases (80%), firm, palpable, unilateral nodule (worse prognosis) - Familial cases (20%, bilateral, multicentric tumour (better prognosis) - Aggressive growth; spread via local, lymphatic (cervical), haematological (liver, lung, bone) routes - 95% produce **calcitonin**, 80% produce **CEA** - Always exclude MEN2 – genetic testing (DNA mutation in TK receptor RET proto-oncogene), elevated basal serum calcitonin (>20-100pg/mL) - Screen for pheochromocytoma – serum or urine metanephrines/normetanephrines	- Large bulky mass involving neck structures – **locally advanced** - Aggressive growth - **Multiple metastases** probably present at presentation - **Invasion of local structures (dysphagia, respiratory compromise, hoarseness)**	- Usually presents as rapidly enlarging goitre with compressive symptoms - 60-80% aggressive and 30% more indolent
	- Very good prognosis - Poor prognostic factors (**AMES**): **A**ge>40, presence of **m**etastases, **e**xtra-thyroid invasion, **s**ize>4cm (*more details on risk stratification below*)				
Treatment	**Surgical resection** - Hemithyroidectomy for selected low-risk patients (see below) - **Total thyroidectomy** for the majority - LN clearance: tracheo-oesophageal nodes cleared (central compartment clearance – level VI), and lateral neck dissection (levels II, III, IV) performed for all patients with biopsy proven lymph node metastasis - For suspicious lesion – hemithyroidectomy with histology, KIV completion TT **Adjuvant therapy** - Radioablation (RAI) of metastatic or residual cancer and residual thyroid tissue (75-100mCi of ^{131}I at 4 weeks after TT while patient is hypothyroid (no replacement of T_4 yet – keep patient in hypothyroid state so any remnant thyroid tissue present would crave for iodine and take up the RAI) **TSH suppression** - Lifelong long-term suppression of TSH (levels to <0.005U/L) with L-thyroxine to decrease recurrence and improve survival **Follow-up** - Check TSH levels - Thyroglobulin as a tumour marker of recurrence - Radioactive iodine scan to detect recurrence, followed by ablation		Surgical resection - Aggressive resection – **total thyroidectomy** with **level VI nodes (central compartment) clearance** - **Selective Neck Dissection** indicated for conically involved ipsilateral cervical lymph nodes - Sampling of cervical and mediastinal nodes and modified dissection where positive No good adjuvant therapy Use of external beam radiation is controversial Follow-up - Thyroxine replacement (not for TSH suppression but to maintain euthyroid state) - Serum **calcitonin** and **CEA** six mths after surgery (if normal, considered cured – 5% 5yr recurrence) - High calcitonin – screen for residual or metastatic disease, treat surgically, with RT or chemo as appropriate	Palliative therapy for compressive effects - Chemotherapy to shrink tumour (i.e. doxorubicin + cisplatin) - Surgical debulking - Tracheostomy - External Beam RT – for patients who are not surgical candidates * not responsive to I^{131} therapy ** combination of CT + RT following complete resection may prolong survival	Chemotherapy and/or radiotherapy depending on type of lymphoma
5yr survival	95% in low-risk, 88% in intermediate-risk, 50% in high-risk patients Slightly worse for follicular cancer		60-70%	Median survival <6mths	Dependent on histo, stage, treatment, etc.

[38] NUHS Lecture Slides – common thyroid disorder in surgery

RISK STRATIFICATION:

- Patient factors:
  - **Age:** – >45 years old is high risk
  - **Gender** – male is high risk
- Tumour factors:
  - **Size** – nodule >4cm has higher risk
  - **Histology** – Tall cell variant (Papillary CA) & Hurthle cell variant (Follicular CA) have worse prognosis
  - **Extra-thyroidal extension** into surrounding structures
  - **Lymph node or distant metastases**
- Various score systems have been formulated to stratify risk:
  - **MACIS – M**etastasis, **A**ge, **C**ompleteness of resection, **I**nvasion, **S**ize
  - For patients with follicular thyroid cancer – the proportion of variation in survival time explained (PVE) associated with each system was (from highest to lowest) 0.48 for MACIS, 0.46 for AGES, 0.44 for EORTC, 0.40 for AMES, and 0.33 for TNM. [39]
- Patients can be divided into three groups:
  - **Low risk** – low risk patient and low risk disease (i.e. no high risk features)
  - **Intermediate risk** – low risk patient with high risk disease, or high risk patient with low risk disease
  - **High ris**k – high risk patient and high risk disease

- Risk guides treatment – **low risk patients can undergo hemi-thyroidectomy** without ablative radioiodine therapy post-op, while **high risk patients undergo total thyroidectomy** with post-op ablative RAI treatment; treatment in intermediate risk patients is tailored to the disease, but usually it is similar to that in high risk patients
- 5 year survival is also prognosticated by the risk: low risk patients have a survival of 95-98%, intermediate risk patients 88%, and high risk patients 50%

- Thus, risk stratification helps to guide the extent of surgical resection in differentiated thyroid cancer according to the patient's disease.

TOTAL THYROIDECTOMY VERSUS HEMI THYROIDECTOMY

Advantages of TT:

- Evidence for micro-foci of disease and multicentricity of cancer – removal of the entire thyroid decreases risk of recurrence
- Ability to use adjuvant radioiodine to ablate any residual cancer tissue after surgery
- Ability to use radioiodine to detect recurrent disease (normal thyroid picks up iodine better than cancer cells, thus the presence of the thyroid gland will decrease the ability of RAI to pick up recurrent cancer) and as treatment for recurrence
- Ability to use serum thyroglobulin as a cancer marker for recurrence

Disadvantages of TT:

- Risk of bilateral recurrent laryngeal nerve injury and permanent hypoparathyroidism
- Very low incidence of cancer recurrence in residual thyroid – micro-foci probably not clinically significant
- Limited thyroidectomy may spare patient from having to be on lifelong thyroid hormone replacement

[39] Thyroid. 2004 Jun;14(6):453-8.

Lymph node clearance

- Tracheo-oesophageal groove (level VI) node clearance usually done
- Radical neck dissection or modified radical neck if:
  (i) Tracheo-oesophageal groove nodes histologically positive for cancer
  (ii) Clinically positive nodes in the neck – palpable or enlarged on ultrasound

Radical Neck Dissection (RND)

- The removal, en-bloc, of the entire ipsilateral lymphatic structures of the neck, from the mandible superiorly to the clavicle inferiorly, from the infrahyoid muscles medially to the anterior border of the trapezius laterally
- **Classic radical neck dissection (Crile's)** – (1) internal jugular vein, (2) sternocleidomastoid muscle, and (3) spinal accessory nerve are resected. Structures not resected: carotid arteries, vagus nerve, hypoglossal nerve, brachial plexus, phrenic nerve

Modified Radical neck Dissection (MRND)

I. Type I: one of the three structures not removed, usually SAN
II. Type II: two of the structures not removed – SAN and IJV
III. Type III: all of the three structures not removed – SCM, SAN, IJV
    a. Known as Functional Neck Dissection

Extended Neck Dissection

- Resection of lymph nodes and/or structures not included in the classic neck dissection

Complications of radical neck dissection (CHIIPS)

(i) Carotid blowout – risk factors: infection, irradiation → resuscitate, apply constant pressure all the way to the OT!
(ii) Haematoma → bring back to OT to find source of bleeding and stop it
(iii) Injury to nerves – vagus (vocal cord paralysis), cervical sympathetic chain (Horner's), mandibular branch of facial (lower lip weakness)
(iv) Infection (wound) – risk factors: previous irradiation, if upper aero digestive tract is opened during surgery with salivary contamination, salivary fistula
(v) Poor healing – usually in irradiated skin; weakest point is the junction of the trifurcate incision
(vi) Salivary fistula (usually when patient has received RT to the neck, and if the upper GI tract was opened during the surgery) – infection can result

Multiple Endocrine Neoplasia (MEN)

A group of inherited diseases resulting in proliferative lesions (hyperplasia, adenomas, carcinomas) of multiple endocrine organs

Features:

- Autosomal dominant inheritance – screen family members
- Tumours occur at younger age than sporadic cancers
- Multiple endocrine organs involved, either synchronously or metachronous
- Multifocal tumours in each organ involved
- Tumour usually preceded by asymptomatic stage of endocrine hyperplasia
- More aggressive and higher chance of recurrence compared to sporadic type of tumours in the same organs

MEN 1

- Gene involved is the tumour suppressor gene MEN1 located on *chromosome 11q13* where mutations cause loss of function of the gene
- 3 P's:
    - **Parathyroid** (95%) – hyperparathyroidism from hyperplasia of parathyroid glands
    - **Pancreas** (>40%) – aggressive metastatic tumours (e.g. gastrinoma, insulinoma), leading cause of death in MEN 1 patients
    - **Pituitary** (>30%) – most commonly prolactin-producing adenoma; some have growth hormone-secreting tumours

MEN 2

- Gene involved is *RET proto-oncogene at chromosome 10q11.2* where activating mutations occur
- Two distinct groups of disorders
    - MEN 2a (Sipple syndrome)
        - **Medullary thyroid carcinoma** (all patients) – offer prophylactic TT
        - **Pheochromocytoma** (50%)
        - **Parathyroid hyperplasia, Hyperparathyroidism** (30%)
        - Other features: abdominal pain, Hirschsprung disease
    - MEN 2b (William syndrome)
        - Medullary carcinoma and Pheochromocytoma involvement like MEN 2a, but **no hyperparathyroidism**
        - **Neurocutaneous manifestations**: ganglioneuromatosis
        - Characteristic features: **Gnathism of the mid-face, Marfanoid habitus, multiple mucosal neuromas**

Part 4: Surgery in Benign Thyroid Disease

Indications for surgery: (6Cs)

1. Cannot be treated medically - failed medical therapy or unsuitable for medical tx
2. Cancer
3. Compression on neighbouring structures
4. Cosmesis
5. Compliance/cost problems – with long-term medical therapy (but patient may still require long-term therapy after op if he/she becomes hypothyroid or is still hyperthyroid)
6. Child-bearing – if thionamides are not tolerated because of allergy or agranulocytosis

Types of surgery available:

1. Hemithyroidectomy – removal of one lobe of the gland, including the isthmus and the pyramidal lobe; usually for suspicious thyroid nodules
2. Total thyroidectomy – entire gland removed completely; usually done in MNG
3. Subtotal thyroidectomy (rarely done)
    - Conventional subtotal thyroidectomy – leave a thumb-sized amount (about 4-6g) of remaining thyroid tissue on both sides
    - Harley-Dunhill subtotal thyroidectomy – leave a thumb-sized amount only on one side with removal of the rest of the gland

Total versus subtotal thyroidectomy (for hyper functioning thyroid disease)

- Result of total thyroidectomy is always hypothyroidism, thus the patient will require life-long thyroid replacement and follow-up → problems with compliance, cost, inconvenience
- Results of subtotal thyroidectomy (at 5 years):
    - 60-70% euthyroid (do not require medication but still have to be followed up closely)
    - 16-20% hypothyroid (usually becomes evident within 1 year of surgery)
    - 8-10% hyperthyroid (% increases proportionately with time → failure of surgical therapy)

→ Difficulty in managing post-operatively and in the long term as patients need close monitoring (better off to just replace everyone after TT), but weigh this against the benefits of not requiring any medication (for which there is a good chance)

Complications of thyroid surgery: (Mostly H's, one I and one T)

IMMEDIATE (<24HRS)

1. **Haemorrhage with haematoma formation**
   - Haematoma forms in the paratracheal region, mostly below the strap muscles → can result in compression of airway if not released (patient can die!)
   - Cut the subcuticular stitches and also the stitches holding the strap muscles opposed to let the blood drain out
2. **Hoarseness or airway compromise from recurrent laryngeal nerve injury**
   - Risk of nerve injury is <1%
   - Unilateral nerve injury for hemithyroidectomy, bilateral nerve injury for total or subtotal thyroidectomy
   - If bilateral nerve palsy resulting in compromised airway, will require tracheostomy
3. **Hyperthyroidism**
   - Resection of gland can release large amounts of stored thyroid hormone into bloodstream
   - May result in thyroid storm (see Management of thyroid storm)
4. **Tracheomalacia**
   - Floppiness of trachea resulting from chronic compression e.g. by large goitre
   - Requires intubation to secure airway

INTERMEDIATE (1 DAY TO 1 MTH)

1. **Infection**
2. **Hypoparathyroidism leading to hypocalcaemia**
   - Risk of permanent hypoparathyroidism is 1-4% (only in total or subtotal thyroidectomies); 10-20% of patients may have temporary hypocalcaemia
   - Important to check the serum calcium levels post-operatively
     - Adjusted calcium should be > 1.90mmol/L
     - Some centres suggest checking serum PTH levels at skin closure to reliably predict clinically relevant hypocalcaemia[40]
   - Ask patient for any symptoms and look for signs of hypocalcaemia
     - Mnemonic: "CATS go numb" – Convulsion, Arrhythmias, Tetany, Spasm (laryngospasm) and numbness/paraesthesia (earliest symptom) in oral, perioral and extremities (hands and feet)
     - Tetany – Carpopedal spasm, Chvostek's Sign (spasm of the facial muscles on tapping the facial nerve) and Trousseau Sign of Latent Tetany (carpal spasm on inflating BP cuff over arm)
     - Life threatening complications – laryngospasm and cardiac arrhythmias
   - Check serum calcium together with albumin to get corrected calcium!
   - ECG – QT prolongation → risk of arrhythmias and going to torsades de pointes
   - **Corrected Calcium = Measured serum calcium + 0.02 (40 – Albumin)**
   - **Fast Replacement: IV 10ml of 10% calcium gluconate over 10min (slow bolus)**
     - Don't give bolus → patient will get cardiac arrest (heart stops in systolic state)
   - Replacement: 1.25g calcium carbonate BD ± calcitriol 0.5mcg OM (vary between institution)
   - Hypocalcaemia may also occur due to "hungry bone syndrome" after thyroidectomy in LT thyrotoxicosis

[40] World J Surg (2012) 36:1300–1306

LATE (MORE THAN 30 DAYS)

1. **Hypothyroidism**
2. **Hyperthyroidism (failed treatment)**
3. **Permanent hypoparathyroidism**
4. **Hypertrophic scarring or keloid formation** – ask patient if he/she has keloids

THYROID STORM

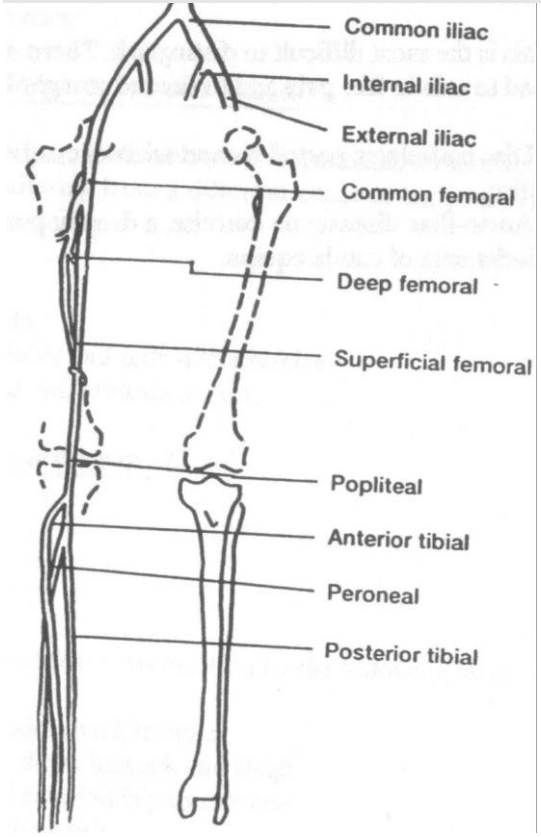
- Diagnostic Criteria – see below
- Physical Exam → may reveal goitre, ophthalmopathy, lid lag, hand tremor, warm moist skin
- Precipitating Causes
  - Thyroid Surgery (esp. if patient was hyperthyroid prior to surgery)
  - Radioiodine
  - Withdrawal of drugs
  - Acute Illness
- Treatment Principles – acute management
  - Intravenous (IV) Fluids
  - Glucocorticoids to reduce T_4-T_3 conversion → **IV hydrocortisone 100mg Q8H**
  - Beta-Blocker to control symptoms and signs → **Propranolol 60-80mg orally Q4H**
  - Thionamide to block new hormone synthesis → **Propylthiouracil (PTU) – 600mg then 200mg Q4-6H**
  - Iodine solution to block release of thyroid hormones → **Lugol's Solution 10 drops (20 drops/mL, 8mg iodine/drop) (oral)** – administer at least one hour after PTU administration to prevent iodine from being used as substrate for new hormone synthesis
- For definitive therapy → radioiodine therapy or surgery

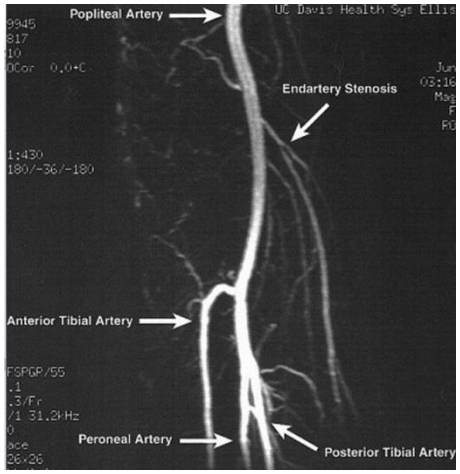
Burch and Wartofsky Scoring System (≥ 45 = highly suggestive, 25-44 = supports dx, <25 = unlikely)

Diagnostic Parameters	Scoring	Points
Temperature	37.2-37.7	5
	37.8-38.2	10
	38.3-38.8	15
	38.9-39.4	20
	39.4-39.9	25
	>40.0	30
Tachycardia	99-109	5
	110-119	10
	120-129	15
	130-139	20
	>140	25
CNS Effects	Mild (Agitation)	10
	Moderate (Delirium / Psychosis)	20
	Severe (Seizure / Coma)	30
Gastrointestinal & Hepatic Dysfunction	Moderate (Diarrhoea)	10
	Severe (Jaundice)	20
Congestive Heart Failure	Mild	5
	Moderate	10
	Severe	15
Atrial Fibrillation	Absent	0
	Present	10
Precipitant History	Absent	0
	Present	10

PERIPHERAL ARTERIAL DISEASE

ARTERIES OF THE LOWER LIMB

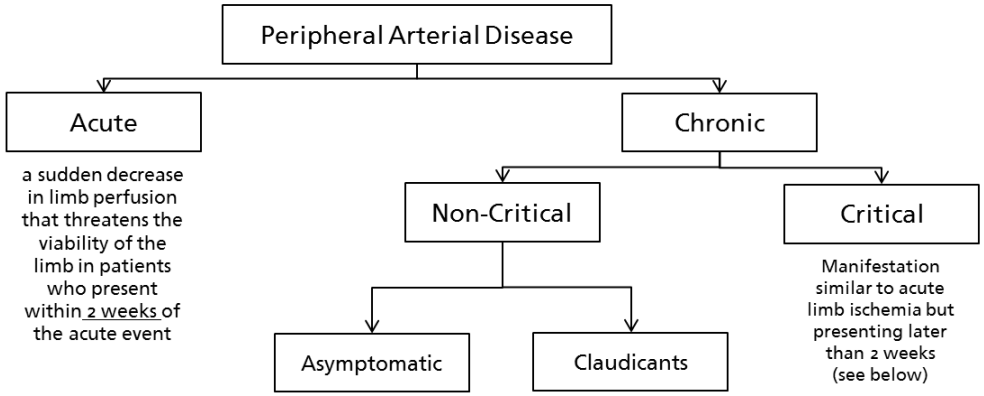




Clinical Significance

- Femoral artery may be palpated at the mid-inguinal point → site for ABG and arteriography
- A venous sample may be obtained from the femoral vein which lies immediately medial to the femoral artery
- The femoral artery is quite superficial in the femoral triangle → easily injured
- Popliteal artery can only be palpated in the lower part of the popliteal fossa (compressed against the upper end of the tibia) – in the upper part of the fossa it will be pushed into the inter-condylar notch
- Popliteal artery aneurysm can increase risk of → DVT (pressure on vein), pain and nerve palsies (pressure on tibial and common peroneal nerve)
- There is a rich anastomosis between femoral artery and its branches which is important in the development of collaterals in arteriosclerotic disease
- **External iliac artery** continues as the **femoral artery** after crossing the inguinal ligament (surface landmark: the *mid-inguinal point* i.e. midway between the pubic symphysis and the anterior superior iliac spine)
- The **femoral artery** then divide into (5) branches: **superficial epigastric artery, superficial circumflex artery, superficial external pudendal artery, deep external pudendal artery** and the **profunda femoris** (or deep femoral)
    - The **profunda femoris** arises postero-laterally from femoral artery, 5cm distal to the inguinal ligament – supplies the muscle of the thigh via (3) branches: **medial and lateral circumflex femoral arteries** and four **perforating branches**
    - The **superficial femoral** runs distally, entering the adductor canal and passes through the hiatus in the adductor magnus to reach the popliteal fossa, where it changes its name to become the popliteal artery
- The **popliteal artery** passes to lower border of popliteus and divides into (2) branches: **anterior tibial artery** and the **posterior tibial artery** (also called tibioperoneal trunk by some)
    - The **anterior tibial** gives off **small branches which form collaterals** with the vessel around the knee and then crosses into the anterior compartment of the leg and supplies the muscles there, and then extends in front of the ankle joint where it continues as the **dorsalis pedis** in the foot (surface landmark: one third of the way down a line joining the midpoint of the two malleoli to the cleft between the first and second toe located between the extensor halluces longus and extensor digitorium longus)
    - The **posterior tibial** gives off the **peroneal artery** (supplies lateral compartment) and itself supplies the posterior compartment of the leg and passes posterior to the medial malleolus (surface landmark: one third of the way down a line joining the medial malleolus to the heel) before dividing into **medial and lateral plantar arteries** to supply the sole of the foot
- Refer to diagram – important to know the arrangement of the anterior tibial, posterior tibial and peroneal vessels at the trifurcation as you may be asked to read an angiogram of these vessels.
- From lateral to medial: Anterior tibial, Peroneal, Posterior tibial

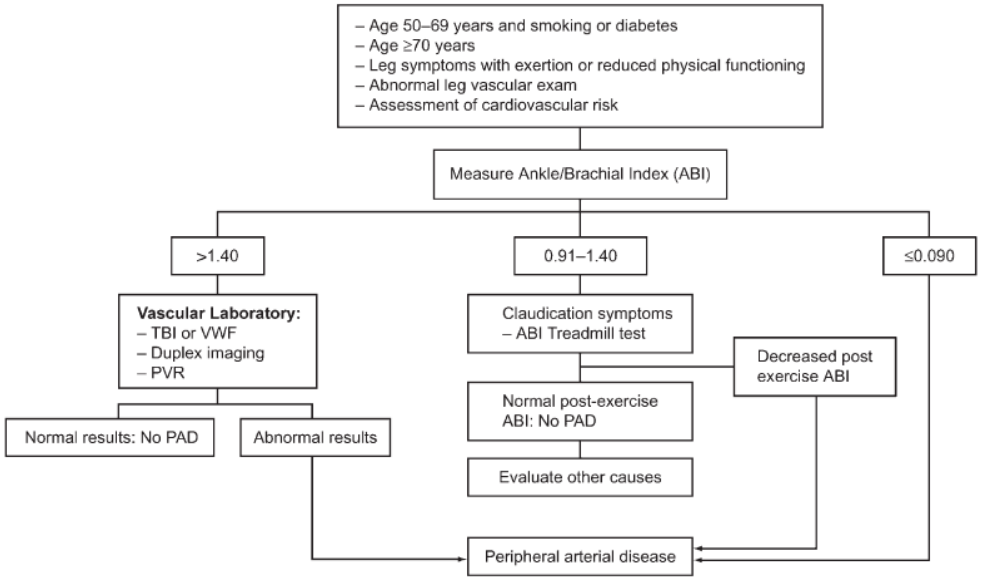
Forms of Peripheral Arterial Disorders[41][42]



1. Ischemic rest pain > 2 weeks
2. Ulcers or gangrene
3. Objective indicators* – ABI ≤0.5, systolic ankle pressure ≤60mmHg and/or toe pressure ≤30mmHg

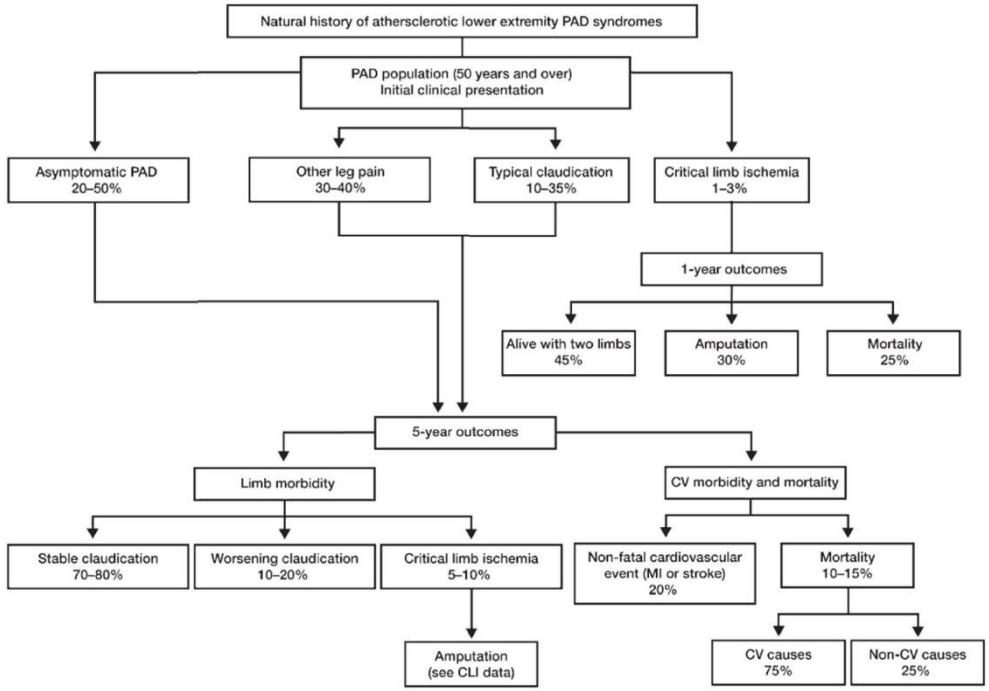
* Without objective indicator = not critical limb ischemia

Diagnosis of Peripheral Arterial Disease[43]



[41] J Intern Med. 2007 Mar;261(3):276-84.
[42] J Vasc Surg. 2007 Jan;45 Suppl S:S5-67.
[43] N Engl J Med 2001;344:1608–1621.

Natural Hx of ATH LL PAD Syndromes (50 Years & Older)[44]



- For patients with IC, only a quarter of patient will ever significantly deteriorate
  - Symptomatic stabilization due to →
    1. Development of collaterals
    2. Metabolic adaptation of ischemic muscle
    3. Patient alters gait to favour non-ischemic muscle groups
- For patients with IC the best predictor of deterioration of PAD (i.e. need for arterial surgery / major amputation) is an ABI of < 0.5
- Patients with low ankle pressure (i.e. 40-60mmHg) – risk of progression to severe ischemia or actual limb loss is 8.5% per year

[44] J Am Coll Cardiol 2006;47:1239–1312.

PERIPHERAL ARTERIAL SYSTEM (HISTORY / PHYSICAL EXAMINATION / INVESTIGATIONS / MANAGEMENT)

HISTORY

1. **Age of the patient & occupation**
2. **Pain of Intermittent Claudication**
   - **Which part** of the lower limb does the pain occur in
     1. Stenosis of lower aorta and common iliac → buttock claudication ± impotence
     2. Stenosis of external iliac → thigh claudication
     3. Stenosis of superficial femoral → calf claudication
   - Nature of the pain
   - Radiation
   - Severity
   - **Aggravating** factors – recurs predictably with exercise?
   - **Relieving** factors – rest (just standing is sufficient) – quick relief?
   - **Associated symptoms –** i.e. impotence in LeRiche's
   - **Duration:** When did pain first start – more than 2 weeks ago
   - **Progress** since first noticed until currently (worsening pain, increasing areas of lower limb affected, pain on less exertion, development of rest pain)
   - **Current claudication distance – fixed or variable**
   - **How has symptoms affected lifestyle** e.g. impaired mobility

3. **Rest Pain**
   - **Site – usually in least well perfused area (i.e. over toes and forefoot)**
     1. Calf pain at night in the absence of foot pain is unlikely ischemic in origin
   - Nature – i.e. aching
   - **Severity – i.e. wakes patient from sleep**
   - **Aggravating** factors – raising the limb, lying flat in bed
   - **Relieving** factors – putting limb in a dependent position
     1. i.e. getting up and walking, hanging foot over edge of the bed
   - Able to **relieve with normal analgesics**? Or require opioid analgesia?
   - **How long** has rest pain lasted for requiring opioid analgesia (if more than 2 weeks, considered a feature of critical limb ischemia)

4. **Any ulcer or gangrene in the lower limb? → worried about critical ischemia**
   - Ask about **onset** of ulcer/gangrene
   - **Progress** (stable, or increasing in size, getting worse)
   - If ulcer, any preceding trauma? Ill-fitting shoes? Altered sensation in the foot? Does patient take care to protect foot? Pain? Redness/swelling/warmth in surrounding skin? Purulent/foul-smelling discharge from the ulcer?
   - If gangrene, is it wet or dry? Redness/swelling/warmth in surrounding skin? Any feeling in the toe involved? Any sensory changes in the other normal toes, foot, limb?
   - Any **systemic signs of infection** – fever, chills, rigors, malaise

5. **Risk factors / Past Medical History**
   - Current smoker / Ex-smoker (strongest RF; 3-6x risk of IC, higher than the risk for IHD)
   - Diabetes mellitus – 2x increase risk, every 1% increase in HbA1c = 26% increase risk of PAD
     1. When was the last ABI? – recommend to do <u>every five years</u>
   - Hypertension
   - Hyperlipidaemia
   - Hyperhomocysteinemia – stronger RF for PAD than CAD
   - Coronary Artery Disease
   - Stroke / TIA (? carotid disease)
   - Family history – i.e. family hx of a first degree relative with a AAA

6. **Drug history**
   - Aspirin intake
   - Any allergies to contrast (for angiography)

7. **Social history**
   - **Impact on patient's quality of life – i.e. work and sleep**
   - **Premorbid function and current function**
   - Social support and home condition (need to climb stairs?)
   - Occupation

EXAMINATION – PERIPHERAL ARTERIAL SYSTEM[45]

Examine the patient's lower limbs in a warm room, with the patient exposed optimally (from the groin to the toes, wearing underwear). Patient is supine with the bed flat.

Look (Inspect) – most of the pathology will be around the feet and toes!

1. Colour of the lower limb
   - Red – vasodilatation of the microcirculation due to tissue ischemia
   - White – advanced ischemia
   - Purple/blue – excess deoxygenated blood in the tissue

2. Trophic changes
   - Loss of hair
   - Thickening of the nails
   - Dry, shiny skin – autonomic neuropathy
   - Small non-healing sores/ulcers – esp. between toes / soles / heels (look at pressure points)

3. Loss of digits / foot – due to previous gangrene / amputation – see below

4. Presence of ulcer (see below)
   - Look carefully at the entire lower limb, including the heels and between the toes
   - **Site** of the ulcer
     - Venous ulcers form at the medial malleolus
     - Arterial ulcers are more distal (in the least well perfused areas and over the pressure points) – lateral aspect of foot and lateral malleoli
     - Neuropathic ulcers form at areas such as the heel and at the metatarsal heads
   - **Size, shape**
   - **Edges** (punched out & well circumscribed – arterial; sloping – venous)
   - **Base**
     - Depth of the ulcer (can see underlying tendon? Down to bone?)
     - Appearance of the base – Necrotic? Granulating (beefy-red)? Sloughy?
     - Any discharge – pus, blood?
   - **Surrounding skin**
     - Erythema (cellulitis) – there may be an underlying abscess (confirm on palpation)
     - Blistering, purplish colour (possibility of necrotising fasciitis)

5. Presence of gangrene
   - Look between and at the tip of the toes
     1. **Wet** – complicated by infection → have ill-defined spreading edge
     2. **Dry** – not infected → well-defined edge → dead tissue may fall off (auto-amputation)
   - Extent of gangrene – line of demarcation
   - Skin blistering may occur
   - Differential diagnosis: acral lentiginous melanoma

6. (If the patient has diabetes, may see skin changes – diabetic dermopathy & joint deformities – Charcot's joint)
   - Diabetic Dermopathy → atrophic hyper-pigmented skin lesions usually on the shin
   - Charcot Joint → Chronic progressive destructive neuropathic joint arthropathy secondary to disturbance of sensory innervation of the affected joint

Feel (palpate)

1. Temperature – Warmth of the skin
   - Use the dorsum of the fingers of both hands to simultaneously run up the patient's feet to the shins and thighs bilaterally
   - Compare the temperature on both sides (note if one side is cooler)
   - If one limb feels cool, feel for the level where the skin becomes warm

2. Capillary Refill Time
   - Press hard on a toe for a few seconds, then release
   - Normal capillary refill is < 2 sec
   - If a toe is blue, check for blanchability (fixed staining = dead toe)

3. Palpating the ulcer if present – any swelling
   - Any surrounding tenderness (infection)
   - Bogginess of surrounding tissue (may have abscess formation)
   - See if any discharge from the ulcer when palpating

4. Inguinal Lymph Nodes
   - Especially so if the ulcer looks infected or if considering diff dx of melanoma

5. Sensation / Paraesthesia
6. Pulses
   - Feel the distal pulses and work your way proximally
   - **Grading** of pulses: 2+ is normal, 1+ is diminished
   - Report as (1) present; (2) reduced or (3) absent if not felt

Dorsalis pedis pulse	- 1/3 way down a line joining the midpoint of the two malleoli to the 1st webspace - Ask patient to point big toe to the sky (demonstrating EHL) – artery lies immediately lateral - Examine both dorsalis pedis pulse simultaneously
Posterior tibial pulse	- 1/3 way down a line joining the medial malleolus to the heel - Examine both posterior tibial pulse simultaneously
Popliteal pulse	- Ask patient to bend the knee ~60-90 degrees - Pulse is best felt by compressing it against the posterior aspect of the tibial - If the pulse is very well felt → ?popliteal aneurysm 1. Pulsating mass that does not alter with change in position of the knee 2. 50% are bilateral check contralateral side & 50% have an AAA 3. If distal pulses not felt → ?thrombosed aneurysm
Femoral pulse	- Mid-inguinal point (midpoint of the line joining the pubic symphysis to the anterior superior iliac spine), just below the inguinal ligament

[45] Clinical Cases and OSCEs in Surgery (2nd edition) – Case 111 / 118 / 120

Move

1. Weakness / Paralysis
2. Buerger's test → Buerger's angle
   - Get patient to lie as close to the side of the bed as possible
   - Do one side at a time
   - Holding the heel of the foot, with the patient's lower limb straightened, slowly **lift the entire lower limb**, looking at the colour of the toes
   - Stop when the toes become **pale** (white)
   - Estimate the angle the lower limb makes with the horizontal – this is the **Buerger's angle**
     - Normal lower limb can be raised to 90 degrees without turning white; if the Buerger's angle is less than 20 degrees, this indicates severe ischemia
   - There may be **venous guttering** of the lower limb at this angle as well
   - If the patient is lying near the side of the bed, tell the patient that you're going to put his leg over the edge of the bed before gently abducting the hip and then letting the **leg drop over the edge of the bed**
   - Look at the leg for **reactive hyperaemia** (foot turns purple-red)

Complete the exam

- Examine the rest of the peripheral pulse
- Offer to auscultate over the femoral and popliteal arteries for bruits
- Examine the abdomen for any abdominal aortic aneurysm
- Examine the neck for any carotid artery stenosis
- Measure the ankle-brachial pressure index (ABPI) on each side
- If suspect neuropathy → proprioception, vibration, pin-prick, monofilament, ankle jerk

AIM TO (1) INDICATE LIMB (2) SEGMENT OF VESSEL DISEASE (3) PRESENTING SYMPTOMS

Patient has **right lower limb** peripheral arterial disease involving the (**aorto-iliac / femoral-popliteal or tibial-peroneal**) segment with **tissue loss**

	Venous Ulcers	Ischemic Ulcers	Neuropathic Ulcers
Pain		Painful	Painless
Site	Gaiter region over medial malleolus of ankle	Tip of toes and pressure area	Heel, metatarsal heads (pressure bearing areas)
Size	Can be very large	Varying size, few mm to cm	Several cm
Shape	Variable, usually irregular	Regular outline	Regular outline, follows skin contour – 'punched-out'
Edges	Sloping pale purple / brown	Punched out clean	Clean
Base	Pink granulation tissue, white fibrous tissue	No granulation tissue, Bone may be exposed	Often exposing bone
Surrounding Skin	Chronic venous signs (i.e. lipodermatosclerosis)	Pale / Cyanotic	Normal / Red Appearance
Temperature	May be warmer	Cold Foot	Dry Warm Foot
Pulses	Present	Absent	Present
Sensation, Reflexes, Vibration		Variable	Loss
Bone		No Bony Deformity	Bony Deformity
Others		Calluses absent / infrequent Collapsed Vein	Local Sensory Loss Presence of callus Dilated Veins

* Aetiology of DM foot ulcers: (1) neuropathic – 45-60%; (2) ischemic – 10%; (3) mixed neuro-ischemic – 25-45% (correlate clinically)

Type of Amputations

- Disarticulation at joint (PIP, DIP)
- Ray amputation (amputate digit through metatarsal removing large part of 1 ray)
- Forefoot
- Lisfranc (tarsometatarsal)
- Chopard's (Midtarsal)
- Syme's (through ankle)
- BKA
- Through Knee (Stokes-Gritti)
- AKA
- Hip disarticulation
- Hindquarter amputation (hemipelvectomy)

INVESTIGATIONS

1. **Ankle-brachial pressure index**
   - How the ankle-brachial pressure index is done
     - **Brachial pressure** is measured with a BP cuff around the arm and a doppler probe at the brachial artery – cuff is inflated until the arterial signal is obliterated, then slowly deflated until the signal just starts being detected, at which the pressure is recorded
     - **Ankle pressures** measured with the cuff around the calf and the doppler at the dorsalis pedis and posterior tibial arteries – one reading for each artery

$$\textbf{Left ABI} = \frac{\text{Higher of the left ankle systolic pressure (posterior tibial or dorsalis pedis)}}{\text{Higher arm systolic pressure (left or right arm)}}$$

$$\textbf{Right ABI} = \frac{\text{Higher of the right ankle systolic pressure (posterior tibial or dorsalis pedis)}}{\text{Higher arm systolic pressure (left or right arm)}}$$

   - Interpreting the values
     - Normal ABI is > 0.9 (can be > 1.0 as ankle pressures tend to be higher than brachial)
     - ABI between 0.5 - 0.9 – occlusion, often associated with claudication
     - ABI <0.5: Critical Ischemia Rest pain
     - if >1.40, suggests non-compressible calcified vessel esp. seen in DM patients
       → Do **Toe pressures index (TPI)** instead (an abnormal TBI is <0.70)

   - Accuracy of the index
     - ABPI ≤0.9 strongly correlated with all-cause mortality independent of Framingham risk score
     - ABPI ≤0.9 – 95% sens & 99% spec. in detecting angiogram positive disease PAD and is a/w >50% stenosis in one or more major vessels
     - ABI ↓ by 0.10 associated with ↑ 10% of major vascular event

   - Exercise treadmill testing
     - For patients with normal ABI at rest in combination with classic symptoms
     - Measure ABPI before and after patient exercises on a treadmill
     - If the ABPI falls by >0.2 → claudication

2. **Arterial Duplex ultrasound**
   - 1st line imaging to all people with PAD
   - Operator dependent, non-invasive test, limited by difficulty to visualize iliac arteries and extensive calcification may compromise examination
   - Duplex (means two modalities) = 2D ultrasound (like the normal kind) plus Doppler ultrasound (measures flow and waveforms)
   - Normal arterial flow waveform should be triphasic; biphasic and monophasic waves are abnormal
   - Can define anatomy of occlusions and also look for relatively good arteries distally for "landing zone" of bypass graft

3. **MR Angiogram with contrast (gadolinium)**
   - Fast, non-invasive outpatient procedure (<15min) with no exposure to ionizing radiation and little risk of contrast nephropathy – 2nd line after duplex u/s
   - Not affected by arterial calcifications
   - Tendency to overestimate degree of stenosis, can be inaccurate in stented arteries

4. **CT Angiogram with iodinated contrast**
   - No significant difference in accuracy between CTA and MRA
   - Diffuse calcification may make interpretation difficult

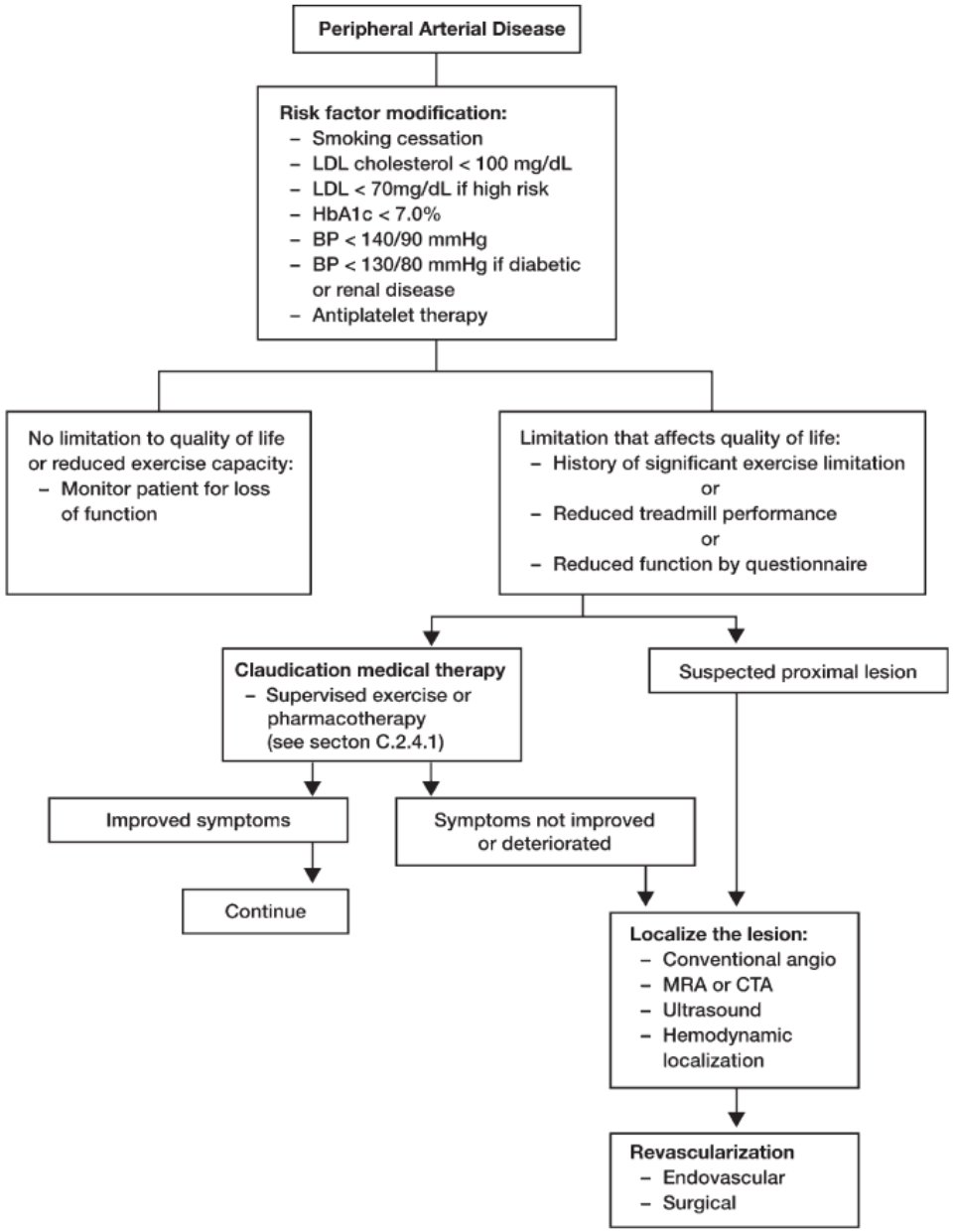
5. **Conventional Angiogram (arteriogram)**
   - Invasive and associated with risks of bleeding from arterial puncture, dissection/damage to artery with worsening ischemia, hematoma, false aneurysm, local infection
   - Also have risk of contrast media or drug allergic reaction
   - Usually only done if planning intervention e.g. angioplasty, stenting
   - Preparing for angiogram:
     - Take informed consent from patient
     - Ask about contrast allergy, asthma, renal disease, metformin
     - Investigations: FBC (platelets impt), PT/PTT, U/E/Cr

Angiogram with digital subtraction – the images of the underlying bone are removed so as to better visualise the arteries → gold standard for evaluating arterial tree before planned revascularization

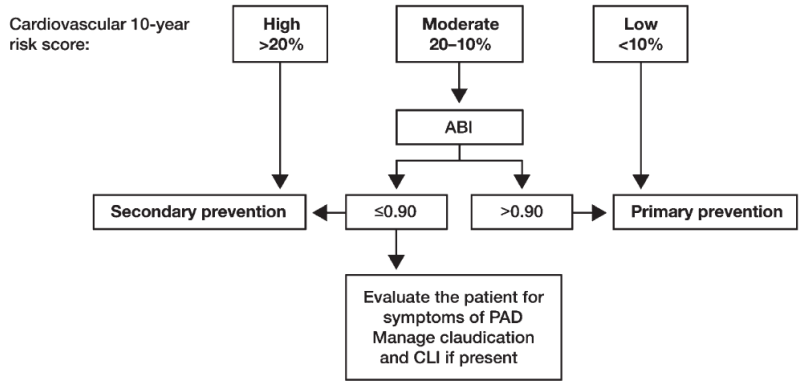
6. **Basic laboratory investigation**
   - C-Reactive Protein – if ↑ in asymptomatic patients → higher risk of developing PAD in subsequent 5 years[46]
   - FBC, U/E/Cr, PT/PTT, septic workup: blood c/s, wound c/s (as indicated)

[46] Eur J Vasc Endovasc Surg. 2007;33

MANAGEMENT – Overview of Treatment Approach[47]



[47] N Engl J Med 2001;344:1608–1621



* Secondary prevention = addition of antiplatelet

Cardiovascular Risk Factor Modification[48]

- Smoking Cessation* → ↓ progression of disease
  - Doctor's advice alone = **5% cessation at 5 years**
  - Doctor's advice + formal cessation program + nicotine replacement = **22% cessation rate at 5 years**
  - (above) + bupropion (anti-depressant) = best cessation rates!
  - Ask patient about status of smoking at every visit!

* smoking cessation not proven to symptomatically improve symptoms of claudication

- Assessment and treatment to optimise control of CVS risk factors – cardiologist
  - Weight Reduction
  - Lipid Control – **LDL < 2.6mmol/L**, if high risk LDL <1.8 mmol/L – i.e. statins
  - HTN control – **BP < 140/90mmHg**, if DM / CRF BP target **< 130/80mmHg** – i.e. ACEi
- Diabetes Control
  - Advise to "take care of foot as good as his/her face!" – podiatrist
  - **HbA1c <7.0%**

- Lifelong Antiplatelet and Antithrombotic Drugs
  - **Aspirin 100mg** or **Clopidogrel 75mg** – reduce risk of MI, stroke or vascular death in individuals with symptomatic atherosclerotic lower limb PAD
  - Patients with multiple atherosclerotic risk factors or established CVD and not at increased risk of bleeding – **KIV dual antiplatelet** (CHARISMA trial)[49]
  - No benefit of adding warfarin!

Claudication

- Supervised **exercise training**
  - for at least 30-45min at least 3x/week for at least 12 weeks
  - walk till pain comes, rest 2-3mins, walk again
  - keep a walking diary, record daily claudication distance in paces
- Pharmacological agents
  - Cilostazol – type III PDE inhibitor – inhibits platelet aggregation and cause vasodilatation
    - Contraindicated in patients with class III or IV Heart Failure
  - Pentoxifylline (not well established)

[48] Circulation. 2013 Apr 2;127(13):1425-43.
[49] N Engl J Med 2006; 354:1706-1717

Intervention (endovascular or surgical) – for Chronic Limb Ischemia

Indications

1. Limb salvage ← critical limb ischemia
2. Prevention of further peripheral atheroembolization
3. Incapacitating claudication – at least 6 months of conservative treatment first
   - Monitor claudication distance & ABI – intervene if deteriorating
   - If parameters improve but then plateau, discuss with patient about acceptance of symptoms, and the risks of intervention → weigh risks against benefits

- Complete arterial evaluation with CTA/MRA or conventional angiogram with digital subtraction
- Angioplasty preferred as it is less invasive, though not as effective in treating the symptoms
- Follow-up patients with regular ABI monitoring

1. Balloon angioplasty KIV intravascular stenting

- Aorto-iliac occlusive disease
  i. Indicated for symptomatic stenosis or occlusive lesions
  ii. Better results for common iliac artery then external iliac artery, better for short focal stenosis segments
  iii. Complications → bleeding, arterial dissection, vessel occlusion, arterial rupture, distal embolization, re-stenosis
- Infra-inguinal occlusive disease
  i. Short, focal stenosis (TASC A) are felt to be amenable to endovascular therapy whereas TASC D are best addressed by surgical bypass[50]

- New method: **subintimal angioplasty** – if lumen is so occluded that guide wire cannot pass through, the guide wire is threaded into the subintimal space to create a dissection around the occluded segment, and this space is then angioplastied to create a channel parallel to the actual lumen for blood to flow through (see below)

2. Bypass grafting

Consider bypass when lesions cannot be treated by angioplasty i.e. lesion extends for long distance through the vessel and/or no lumen for guide wire to pass through (complete occlusion)

- Aorto-iliac occlusive disease (see below)
  i. Aorto-bifemoral grafting – reported patency up to 95% at 5 years (tx of choice!)
  ii. Iliac angioplasty and femoral-femoral crossover bypass
  iii. Axillo-bifemoral bypass – alternative for high risk patients

- Infra-inguinal occlusive disease
  i. Above knee occlusion → femoral-popliteal bypass
  ii. Below knee occlusion → femoral to below knee popliteal / posterior tibial / anterior tibial / fibular arteries
  iii. Needs a good "landing zone" for graft distally – if vessel is diffusely diseased, difficult to perform bypass

[50] The Washington Manual of Surgery (2nd Edition) – pg. 446

3. Endarterectomy

- To address severe stenosis or occlusion of common femoral and profunda femoris arteries

4. Amputation[51]

- Level of amputation depends on vascularity of the limb and the indication (e.g. if infected, need to amputate above level of infection)
- As far as possible try to preserve function of the lower limb
- May require revascularisation interventions before amputation to ensure good healing, or to enable lower amputation
- Do not simply amputate without ensuring good vascular supply to the surgical site, otherwise the wound will not heal

Indications (4 D's)

- Dead (ischemic): peripheral vascular disease (80-90% of all cases)
- Damaged (trauma): unsalvageable limb, burns
- Dangerous: Gangrene, ascending sepsis, malignancy (soft tissue / bone)
- Damn nuisance (infection/neuropathy): osteomyelitis, necrotizing fasciitis

Complications s/p amputation:

These patients often have other medical problems (i.e. cardiovascular disease) – hence high risk of mortality – operative mortality as high as 20% and one year survival is 50%

Specific Early Complications	- Medical ▪ Hematoma and wound infection (rare: gas gangrene) ▪ Deep vein thrombosis and pulmonary embolism ▪ Phantom limb pain ▪ Skin necrosis – 2° to poor perfusion of stump – require re-fashioning - Psychological & Social
Specific Late Complications	- Osteomyelitis - Stump ulceration – 2° to pressure from prosthesis - Stump neuroma - Fixed Flexion deformity - Difficulty mobilizing - Spurs and osteophytes in underlying bone

Outcome after amputation:

Below Knee Amputation: 90% of patient will eventually be able to walk again

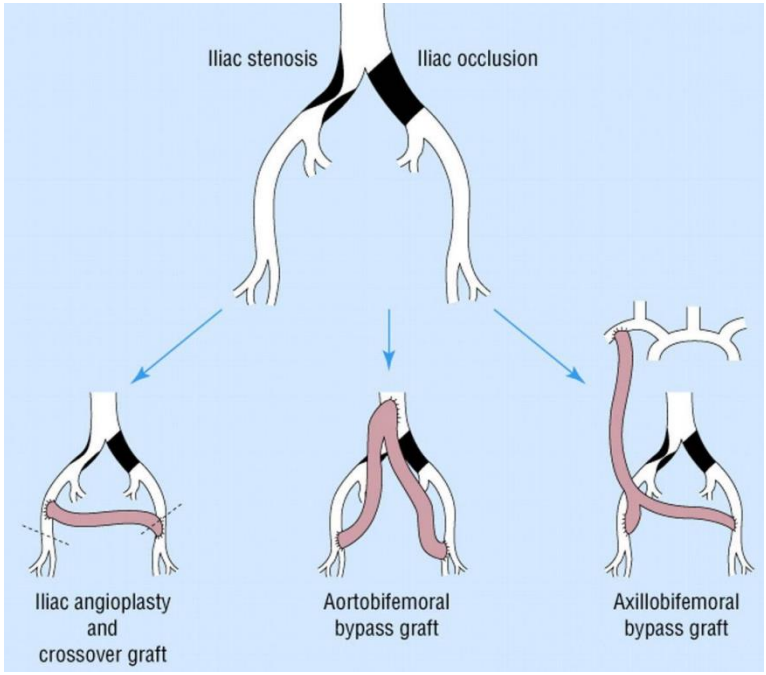
- Unilateral BKA → increase energy expenditure by **40%**
- Bilateral BKA → increase energy expenditure by **60-70%**

Above Knee Amputation: 50% of patients will eventually be able to walk again

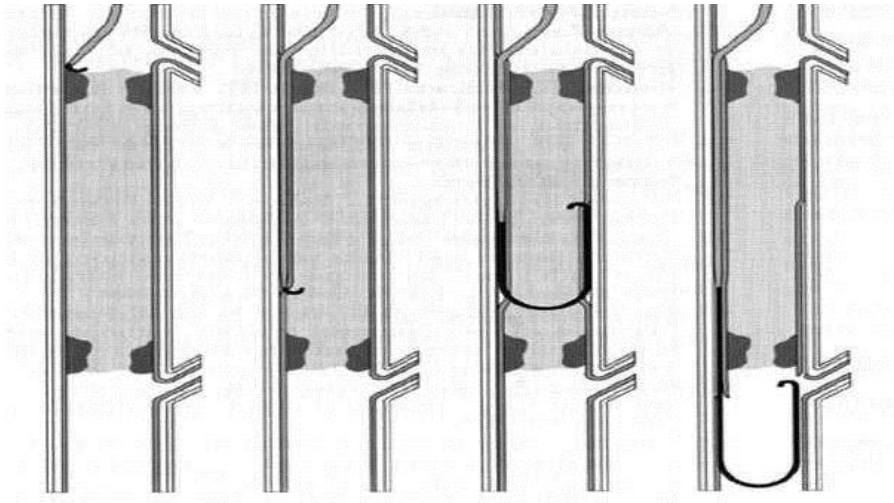
- Unilateral AKA → increase energy expenditure by **100%**

[51] Clinical Cases and OSCEs in Surgery (2nd Edition) – case 113

Bypass Grafting



Sub-intimal angioplasty



ACUTE LIMB ISCHEMIA[52]

Acute limb ischemia is defined as a **sudden decrease in limb perfusion that threatens the viability of the limb** (manifested by ischemic rest pain, ischemic ulcers, and/or gangrene) in patients who present **within 2/52** of the acute event (if >2/52, considered chronic ischemia).

The decrease in perfusion is usually due to sudden cessation of blood supply and nutrients to metabolically active tissues of the limb. This may be in a setting of already narrowed vessel lumen (acute on chronic ischemia) or in a normal lumen.

If adequate collateral circulation is absent, irreversible changes may appear 4-6hours after onset → emergent evaluation that defines anatomical level of obstruction and prompt revascularization (endovascular or surgical)

DDx:
- Acute DVT: Phlegmasia cerulean dolens = painful blue edema
- Blue toe syndrome: atheroembolism from AAA or more proximal
- Purple toe syndrome: Cx of warfarin therapy
- Venous insufficiency
- Venous occlusion
- Acrocyanosis

[52] N Engl J Med 2012;366:2198-206.

CAUSES:

1. **Arterial embolism**
   - **Most common cause** of acute limb ischemia (60-80% of the time)
   - The most likely source of embolus is the **heart** (80%), of which 70% is due to atrial fibrillation, 20% to AMI with left ventricular mural thrombus, and a small proportion to prosthetic heart valves (who are not receiving anticoagulant therapy)

   - Non-cardiac emboli arise from other arteries where there are atherosclerotic plaques or an aneurysm (the embolic material may be thrombus or part of a plaque, but atheroemboli are less likely to cause complete arterial occlusion)

   - Most common sites where emboli lodge:
     - Bifurcation of the femoral artery (most common site)
     - Trifurcation of the popliteal artery (next most common site in the lower limb)
     - Aortic bifurcation
     - External and internal iliacs
     - Arm (about 20% of emboli)

   - Emboli usually cause lower limb ischemia mostly
   - After emboli obstructs the vessel, thrombus can propagate distally (due to stasis of blood) and proximally (due to turbulence of incoming blood hitting embolus) by derangements in the Virchow's triad

2. **Acute thrombosis**
   - Thrombosis of a previously stenotic but patent artery (**atherosclerotic vessel**)
   - Less common cause of acute limb ischemia
   - When thrombotic occlusion of a vessel does occur, the resulting ischemia is usually less severe than in an embolic occlusion, because collaterals have had time to form around the chronically stenosed vessel
   - Other less common causes of acute thrombosis include the arteritides (usually affecting medium-sized arteries), ergotism, and hypercoagulable states (notably anti-phospholipid syndrome, heparin induced thrombocytopenia)

3. **Arterial trauma**
   - Increasing incidence of acute arterial occlusion due to endovascular diagnostic or interventional procedures
   - Trauma can cause development of an arteriovenous fistula that shunts blood away from the limb

   - Fracture or dislocations can stretch an artery and cause an intimal tear while the media and adventitia layers are intact (because they contain elastin and can stretch) → a thrombus forms at the site of the tear where underlying thrombogenic collagen is exposed
   - Compartment syndrome can result from trauma as well

4. **Dissecting aortic aneurysm**
   - As the blood dissects between the intima and media of the aorta, it can cause occlusion of the aortic branches at their origins

PATHOPHYSIOLOGY

In order of sensitivity to ischemia, the tissues affected are nerves (most sensitive), muscle, skin, and bone (least sensitive); thus early signs of ischemia involve pain and numbness, and muscle paralysis as well as skin changes occur later. The lower limb can survive about **6 to 8 hours** in an ischaemic state before injury becomes irreversible.

PRESENTATION

The classic **6 P's** of acute limb ischemia: Pain, Paraesthesia, Pallor, Pulselessness, Paralysis and Perishingly cold / Poikilothermia – impaired regulation of body temperature

1. **Pain Pain Pain Pain Pain Pain**
   - Develops acutely
   - Starts off in a distal part of the extremity and then progresses proximally, increasing in severity with time
   - Further progress leads to decrease in pain as the nerves die off from ischemia
   - Important to ask for any previous claudication pain (10% of claudicants can develop acute ischemia due to thrombosis of the stenosed vessel)

2. **Paraesthesia**
   - Starts off with paraesthesia (develops relatively early in the course of ischemia) and develops to complete loss of sensation
   - Progression: Light touch → Vibration → Proprioception → (late) Deep pain → Pressure sense

3. **Pallor**
   - Assess skin colour, temperature, and capillary refill time
   - The limb may still be slightly pink though pale, but in severe ischemia it can be marble-white (especially in embolus where there are no collaterals)
   - Other colours:
     - Mottling/Marbling (patches of blue on white): deoxygenation of stagnated blood; surrounding areas of pallor are due to vasoconstriction
     - Duskiness: due to deoxygenation of stagnated blood; if there is fixed staining (i.e. does not blanch on pressure) then the limb is non-viable
     - Black: gangrene
   - The discoloration usually affects a large part of the distal limb e.g. the toes, foot; rarely does it only affect one toe (more in chronic ischemia)
   - The site of arterial occlusion is usually one joint above the line of demarcation between normal and ischaemic tissue

4. **Pulselessness**
   - If able to feel one good pulse (PT or DP), quite unlikely that the limb is ischaemic, but still possible
   - If unable to feel, assess with a handheld Doppler the arterial and venous flow in the limb – there can still be flow without a palpable pulse
   - Also feel the pulses on the other limbs – gives a clue as to whether the cause is embolic or thrombotic (see below)

5. **Paralysis – poor prognostic sign**
   - Initial: heavy limb, Late irreversible ischemia: muscle turgidity
   - Total paralysis occurs late and usually indicates that the limb is non-viable
   - Intrinsic foot muscles > Leg muscles (toe mvmts produced by leg muscles → detect late)
   - Can assess viability of muscle by making a cut – viable muscle will be shiny and twitches in response to flicking, while dead muscle will be dull and will not twitch
   - Dangerous to save dead muscle as reperfusion can cause circulation of toxic metabolites in the muscle

Assess severity of acute limb ischemia

- Three categories: viable, threatened and non-viable
  (i) Viable: No immediate threat of tissue loss
  (ii) Threatened: Salvageable if re-vascularised promptly
  (iii) Non-viable: Limb cannot be salvaged and has to be amputated, no emergency to operate. Patient may require revascularisation to allow lower amputation or help amputation to heal

* threatened extremities a/w presence of **(1) rest pain, (2) sensory loss (3) muscle weakness**

Stage	Description and Prognosis	Findings		Doppler Signal		Recommendations
		Sensory Loss	Muscle Weakness	Arterial	Venous	
I	Limb viable	None	None	Audible	Audible	Imaging (i.e. u/s duplex, CTA/MRA) to determine nature and extent of occlusion
II	Limb threatened	None	None	Audible	Audible	
IIa	Marginally threatened, salvageable if promptly treated	Minimal (toes)	None	Often Inaudible	Audible	
IIb	Immediately threatened, salvageable with immediate revascularisation	> toes, a/w pain at rest	Mild / Moderate	Usually Inaudible	Audible	Imaging & emergency Revascularization
III	Non-viable	Profound, aesthetic	Profound, Paralysis (rigor)	Inaudible	Inaudible	Amputation after demarcation

DIFFERENTIATING BETWEEN EMBOLIC AND THROMBOTIC CAUSE

	Embolic	Thrombotic
Identifiable source	Present – AF, recent AMI	Less common
Claudication hx	Negative	Positive
Physical findings	Contralateral pulses present White limb (no blood)	Contralateral pulses diminished Dusky limb (collaterals still supplying limb)
Angiography	Minimal atherosclerosis, sharp cut-off, few collaterals	Diffuse atherosclerosis, irregular cut-off, well-developed collaterals

MANAGEMENT FOR ACUTE LIMB ISCHEMIA

1. Doppler u/s: viable vs. threatened vs. non-viable + level of obstruction
2. Pre-operative investigations (see below)
3. Early anticoagulation
    - Give IV heparin bolus 3000-5000 units
    - Follow with IV heparin infusion at 1000 units/hour
    - Ideal PTT is 2 to 2.5 times normal
    - Avoid clot propagation
4. Measures to improve existing perfusion
    - Keep foot dependent
    - Avoid pressure to heel, extremes of temperature
    - Max tissue oxygenation (O_2 supp) – give 100% oxygen
    - Correct hypotension
5. Surgical emergency requiring active intervention
    - Emergency thrombectomy / embolectomy
    - Intra-arterial thrombolysis ± angioplasty
    - Bypass graft
6. Postoperative anticoagulation with heparin ± vasodilators (i.e. NG) if have vasospasm
7. KIV fasciotomy to prevent compartment syndrome
8. Treat other associated conditions (CHF, AF)

PREOPERATIVE INVESTIGATIONS

- **FBC, U/E/Cr, PT/PTT, GXM**
- **CXR and ECG** if patient is older than 40 yrs old
- If suspecting an AMI with mural thrombus, do **cardiac enzymes**

- **Angiogram** can be done in patients with viable limb, but in patients with threatened limb there is no time for angiogram → may do on-table angiography
- High clinical probability of embolism does not need angiography

[Angiography is useful in **confirming** an occlusion, the **cause** – thrombotic or embolic – and also pinpointing the **level** of occlusion and the **anatomy]**

TREATMENT OPTIONS FOR ACUTE LIMB ISCHEMIA

"Aim to restore blood flow as rapidly as possible to a viable or threatened limb"

Open Surgical Revascularization	Endovascular Revascularization
- Embolectomy / Thrombectomy - Endarterectomy - Bypass grafting - Fasciotomy - Primary amputation	- Thrombolysis - Angioplasty - Stenting

Once dx of acute arterial ischemia 2° to emboli / thrombus → administer IV HEPARIN → IV bolus 80 units/kg (~5000U) followed by infusion of 18 units/kg/hr (~1000U/hr) – maintain PTT btw 60-80 sec (2-2.5x normal)

Intra-arterial catheter directed thrombolysis ± Angioplasty

- Diagnostic angiogram done before thrombolysis to locate occlusion
- Thrombolysis catheter inserted into the clot, and the thrombolytic agent (i.e. alteplase – recombinant tissue plasminogen activator – TPA) is infused
    - Functions: convert plasminogen to plasmin which then degrades fibrin
- Patient will be in HD with thrombolytic infusion for 6 hours (~1000-4000 units per minute)
- Clinical and angiographic examinations are performed during infusion to determine progress
- After 6 hours, redo angiogram to check for residual clot; if some clot remains, adjust catheter into the clot and infuse for 6 more hours
- **After complete lysis of the clot, can do balloon angioplasty/stent**
- Takes much longer than embolectomy
- Thrombolysis may be preferred for embolism in a diseased artery, since it may be difficult to trawl out the clot in a diffusely stenosed vessel – the clot may get caught on a proximal stenosed segment

- Contraindications:
    - Absolute
        - CVA within past 2 months
        - Active bleeding / recent BGIT past 10 days
        - Intracranial haemorrhage/ vascular brain neoplasm/ neuroSx past 3 months
    - Relative
        - CPR past 10 days
        - Major Sx / trauma past 10 days
        - Uncontrolled HTN

Emergent Embolectomy

- Can be done under LA but still require anaesthetist to monitor patient as he may be quite sick (e.g. AMI), and hyperkalaemia with cardiac arrhythmia can occur after reperfusion
- Involves clamping of the involved artery and making an arterotomy
- A **Fogarty balloon catheter** is inserted into the artery until distal to the clot, then the balloon is inflated to trawl the clot out of the artery
- Check for forward-bleeding and back-bleeding of the vessel (i.e. free spontaneous flow from proximal and distal ends of the artery when unclamped)
- Flush with heparinised saline
- Check foot – warm foot with good pulse indicates reperfusion
- Important to monitor ECG for any arrhythmias!
- Closure of arterotomy with meticulous haemostasis as patient is on heparin

- Post-operatively – look out for complications! (see below)
- Need to convert to full warfarin anticoagulation, up-titrating dose until INR 2-2.5 before stopping heparin (patient at risk of further embolic events)
- Novel oral anticoagulants that inhibits thrombin or factor Xa such as **diabigatran** or **rivaroxaban** considered for patients with AF – efficacy in prevention of peripheral artery thrombosis is not known
- Discharge patient to anticoagulation clinic for follow-up with warfarin advice

Results (endovascular vs. surgical revascularization)[53]

- Both have similar rates of limb salvage but thrombolysis have higher risk of stroke and major haemorrhage within 30days – also shown in the TOPAS trial (thrombolysis or peripheral arterial surgery) that complication rates were higher in the thrombolysis group
- Endovascular: best suited → patients with viable or marginally threatened limb, recent occlusion (< 2 wks), thrombosis of a synthetic graft or an occluded stent and at least having 1 identifiable runoff vessel*
- Surgical: best suited → patients with immediately threatened limb or with symptoms of occlusion for > 2 wks

* Run off = delayed part of the angiographic examination of a vascular bed to show small artery patency

Complications

- Reperfusion Injury – with re-establishment of arterial flow to ischemic tissue bed
  - Formation of oxygen free radicals that damage the tissue and cause WCC accumulation
  - With reperfusion → ↑ capillary permeability → local edema → compartmental HTN
  - No proven therapy that limits reperfusion injury

- Rhabdomyolysis
  - Reperfusion release K^+, lactic acid, myoglobin, creatinine phosphokinase
    - CK > 5000u/L and/or urine myloglobin >1142nmol/L (>20mg/dL) → risk of ARF
  - Can trigger of dangerous arrhythmias
  - Treatment: aggressive hydration ± IV bicarbonate to alkalinize urine

- Compartment Syndrome – pressure ≥ 30mmHg or within 30mmHg of diastolic pressure
  - Results when prolonged ischemia (≥6hr) and delayed reperfusion cause cell membrane damage and leakage of fluid into the interstitium
  - Pain out of proportion to clinical situation (earliest symptom)
  - Pain with passive stretch (most sensitive sign)
  - Anterior compartment most commonly involved but deep posterior compartment (where tibial nerve is located) is most functionally devastating
    - motor: dorsiflexion of foot and ankle
    - sensory: sensation on dorsum of foot and first web space
  - Treatment: emergent four-compartment fasciotomy

[53] Cochrane Database Syst Rev 2002;3:CD002784

CHRONIC LIMB ISCHEMIA

Chronic limb ischemia can be divided into **critical** and **non-critical** limb ischemia, and non-critical ischemia further subdivided into that which causes symptoms (usually claudication) and that which is asymptomatic.

Most common cause is **atherosclerosis** with gradually developing diffuse stenosis of the peripheral arteries resulting in diminished blood supply to the lower limb (imbalance between supply and demand). Pain is due to acidosis and the build-up of metabolites. Multiple collaterals form to bypass the obstructed vessels as a compensatory mechanism

Less common causes includes: buerger's disease (aka. thromboangitis obliterans), vasculitis (i.e. takayasu arteritis, bechet's disease), ergot toxicity, vasospasm

Clinical Presentation

Aorto-iliac Disease	- Claudication involving hip, thigh or buttock - Symptoms develop gradually, if sudden worsening → acute thrombosis of diseased vessel - Patient don't usually get rest pain → unless distal disease is present - **LeRiche's syndrome** → occlusion at the bifurcation of the terminal aorta, ▪ Classical tetrad of buttock claudication, impotence in men, absent femoral pulses (and distal pulses), and ± aortoiliac bruits.
Femoral-popliteal Disease	- Claudication involving the calves - With severe impairment of arterial flow → REST PAIN ▪ Burning pain in distal foot – worse at night or with elevation of leg ▪ Relieved by placing foot in dependent position - Classical examination findings ▪ Decreased / absent distal pulses ▪ Dependent rubor ▪ Trophic changes (see above)
Tibial-Peroneal Disease	

ASSESSMENT OF SEVERITY

The three L's of peripheral arterial disease:

(i) **Life** – does disease threaten life (e.g. sepsis; other complications of atherosclerosis e.g. stroke, AMI;) or will intervention cause risks
(ii) **Limb** – will patient lose the limb
(iii) **Lifestyle** – is the lifestyle of the patient severely handicapped, does it require intervention

Fontaine's Stages
Stage I: Asymptomatic
Stage IIa: Mild claudication
Stage IIb: Moderate to severe claudication
Stage III: Ischaemic rest pain
Stage IV: Ulceration or gangrene

NON-CRITICAL LIMB ISCHEMIA WITH INTERMITTENT CLAUDICATION

VASCULAR CLAUDICATION
Intermittent claudication is defined as a **reproducible discomfort** of a **defined group of muscles** that is **induced by exercise** and **relieved with rest**. Usually described as the patient as a cramping, aching pain in the muscle group on exertion such as walking, and alleviated on stopping (patient does not have to sit down for pain to go away) – **"shop window to shop window".**

- Calf claudication ← affects superficial femoral near to the adductor hiatus, or popliteal artery
- Foot claudication ← tibial and peroneal arterial disease, but rarely do patients with claudication due to atherosclerosis get foot pain alone (more common in Buerger's)
- Thigh claudication ← affects common femoral artery or aortoiliac disease

- Important to determine the "**claudication distance**" – within a short period of time the distance is usually fairly constant, but can shorten as the disease progresses
- Need to differentiate the various causes: vascular vs. neurogenic vs. musculoskeletal

NEUROGENIC CLAUDICATION – 2° SPINAL STENOSIS
- Vascular intermittent claudication needs to be differentiated from neurogenic claudication which can also present as pain in the lower limb on exertion
- The characteristic of neurogenic claudication is **"park bench to park bench"** where the patient has to sit down and **flex the spine to relieve the pain** (pain results from compression of the cord and spinal nerves in spinal stenosis; extension of the spine further narrows the spinal canal while flexion widens it)
- "Claudication distance" of neurogenic claudication is more variable
- Pain even on standing – patient prefers to stand in slight flexion
- Pulses will be absent/diminished in vascular but not in neurogenic claudication
- No pain at night – patient sleeps on lateral decubitus position
- Paraesthesia is common in neurogenic claudication

MANAGMENET FOR INTERMITTENT CLAUDICATION
- Most patient never require surgery
- Cardiovascular RF control (see above)
- Walking exercise program + pharmacological therapy (see above)
- Smoking Cessation and strict DM control (see above)

CRITICAL LIMB ISCHEMIA[54]

Critical limb ischemia (CLI) = patients with chronic ischemic rest pain >2 weeks, ulcers or gangrene attributable to objectively proven arterial occlusive disease
CLI is a clinical diagnosis and should be supported by objective testing

FEATURES:

1. **Rest pain** requiring regular **opioid analgesia** (e.g. codeine) lasting **>2 weeks**
   AND/OR
2. **Gangrene** or **ulcers** over the toes or feet
   AND
3. **Objective indication** of poor vascular supply to the lower limbs
   (b) Ankle brachial pressure index ≤0.5
   (c) Toe pressure index < 0.3
   (d) Toe pressure <30 mmHg, Ankle pressure <50mmHg

* in patients with ischemic ulcers the ankle pressure is typically 50-70mmHg and in patients with ischemic rest pain it is typically 30-50mmHg. Toe Pressure should include pressures in diabetic patients (critical level <50mmHg)

I. Rest pain

- Severe pain in the distal portion of the lower limb (usually toes, foot but may involve more proximal areas if disease is severe) occurring **at rest**
- In most cases, walking capacity is severely limited or impossible
- Rest pain typically occurs at night – ↓ blood supply as patient is not in dependent position and decrease BP during sleep → wakes patient from sleep (gets better after a short walk around the room)
- Pain is aggravated or precipitated by lifting the limb, relieved by dependency of the limb – many patients sleep with the leg hanging over the side of the bed to relieve the pain
- Not easily controllable with analgesia – requires opioids to control pain

II. Ischaemic ulcers (most are neuroarteropathic ulcers)

- Usually arise from minor traumatic wounds with poor healing
- Often painful
- Most often occur on the tips of the toes, bunion area, over the metatarsal heads (ball of the foot), lateral malleolus (as opposed to venous ulcers that occur over the medial malleolus)
- Usually deep, dry, punctate (unlike venous ulcers that tend to be superficial, moist, diffuse)
- May become infected resulting in cellulitis, even abscess formation, and spread to involve the underlying bone and joints → osteomyelitis, septic arthritis

III. Gangrene

- Cyanotic, anaesthetic tissue associated with or progressing to necrosis
- Occurs when arterial blood supply falls below that which is necessary to meet minimal metabolic requirements
- Either dry or wet:

DRY – hard, dry texture. Often has a clear demarcation between viable and necrotic tissue, occurs in patients with atherosclerotic disease. **Safe** and can be allowed to auto amputate after demarcation with precautions against infection.

WET – moist, swollen, frequently blistered, bacterial infection and putrefaction occurs, gangrene spreads proximally, often occurs in diabetics with decreased sensation and unrecognised trauma, requiring an **emergency** surgical debridement or amputation – proximal amputation is required where blood supply is better

Risk Factors for development of Critical Limb Ischemia

- Diabetic – 4x
- Smoker – 3x
- ABPI < 0.7 – 2x ABPI < 0.5 – 2.5x
- Age > 65yr – 2x
- Lipid abnormalities – 2x

Differential Diagnosis of ischemic rest pain

- Diabetic Neuropathy
- Complex Regional Pain Syndrome
- Nerve Root Compression
- Peripheral Sensory Neuropathy (other than diabetic neuropathy)
- Night Cramps
- Buerger's Disease (thromboangitis obliterans)

MANAGMENET FOR CRITICAL LIMB ISCHEMIA

- Multidisciplinary approach to optimize (1) pain control (2) CVS risk factors (3) other co-morbids
- Early surgical referral for active intervention & vascular reconstruction
- Candidate for revascularization → angiographic evaluation → open / endovascular therapy
- Non candidate for revascularization
  - Stable pain and lesion → medical treatment
  - Not-tolerable pain, spreading infection → amputation

[54] J Vasc Surg. 2007 Jan;45 Suppl S:S5-67.

ARTERIOVENOUS (AV) ACCESS

- AV fistula: access created by connecting a native vein to an adjacent artery (autogenous)
- AV graft: uses grafts that are either synthetic or biologic (non-autogenous)

INDICATIONS – PRE-OPERATION EVALUATION

- Patients with renal insufficiency – referred for surgical evaluation 1 year before the anticipated need for dialysis
  - Indicated when creatinine clearance is < 25mL/min or when serum Cr >4mg/dL
- Patients (ESRD patients) should protect their forearm veins from venepuncture and intravenous catheters – avoid potential damage (i.e. stenosis) which could preclude future use
- Duplex Ultrasound – used for determining diameter of artery and adequacy of superficial and deep veins → if require further imaging
  - Contrast venography – evaluate patency and adequacy of venous system
  - Conventional arteriography – evaluate suspected arterial inflow stenosis or occlusion

ARTERIOVENOUS FISTULA

- Usually the radial or brachial artery is used – safest and longest lasting permanent means of vascular access – however – requires long maturation time (weeks to months) to provide a flow state adequate to sustain dialysis
  - Brescia-Cimino fistula (end-end anastomosis between cephalic vein and radial artery)
  - Gratz fistula (at elbow: anastomosing cephalic vein to brachial artery)
- Advantage of AV fistula (compared to AV graft)
  - Long term patency

ARTERIOVENOUS GRAFT

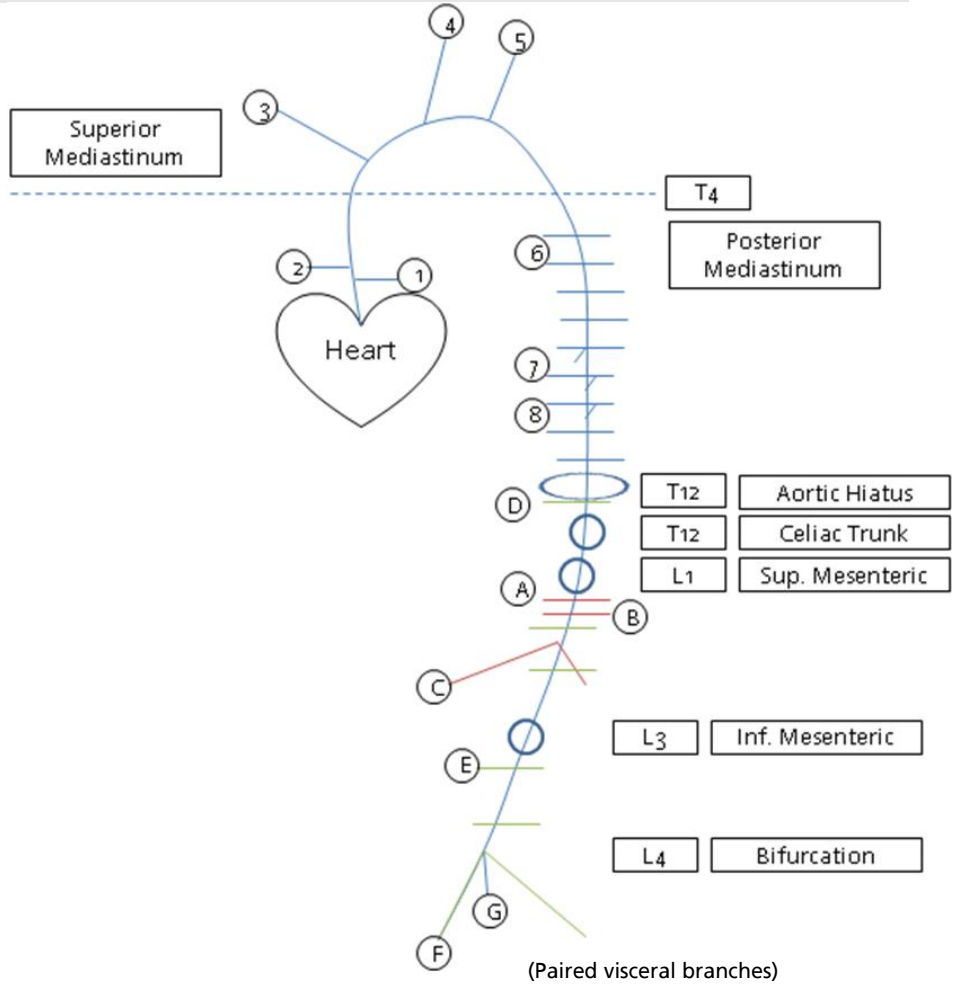
- AV grafts consists of biologic or synthetic conduit that connect an artery and a vein and are tunnelled under the skin and placed in a subcutaneous location
- Advantage of AV graft (compared to AV fistula):
  - Large surface area
  - Easy cannulation
  - Short maturation time – require 3-6 weeks (allows for material to incorporate into surrounding subcutaneous tissue and for inflammation and edema to subside)
  - Easy surgical handling

COMPLICATIONS

- Stenosis – which can lead to upstream pseudo-aneurysm formation
- Thrombosis
- Infection – usually with *staphylococcus aureus*
- Arterial Steal Syndrome – AV access diverts or steal blood from distal circulation → this syndrome occurs in about 1-4% of patients with distal AV access[55]
  - Present with: ischemic pain, neuropathy, ulceration and/or gangrene
- Venous Hypertension – secondary to outflow venous obstruction
  - Present with: skin discolouration and hyperpigmentation, (chronic cases → ulceration)
- Congestive Cardiac Failure – secondary to increased venous return leading to cardiomegaly and CCF (hyper-circulation)

[55] Ann Vasc Surg. 2000;14(2):138-144

BRANCHES OF THE AORTA



- 1 – Left coronary artery
- 2 – Right coronary artery
- 3 – Right brachiocephalic trunk
- 4 – Left internal carotid artery
- 5 – Left subclavian artery
- 6 – Posterior intercostals arteries (3^{rd} – 11^{th})
- 7 – Oesophageal arteries
- 8 – Posterior Mediastinum arteries
-
- 1^{st} & 2^{nd} posterior IC artery from subclavian arteries
- 1^{st} – 6^{th} anterior IC from internal thoracic artery
- 6^{th} – 12^{th} anterior IC musculophrenic artery (from internal thoracic artery)

(Paired visceral branches)
A – Middle Suprarenal artery (L1)
B – Renal artery (btw L1-L2)
C – Gonadal artery (L2)

(Paired parietal branches)
D – Inferior Phrenic Arteries (T12)
E – 4 Lumbar Arteries (L1 – L4)
F – Common Iliac Arteries (L4)

(Unpaired parietal artery)
G – Median Sacral Artery

ANEURYSM

A pathological, localized, permanent dilation of an artery to more than 1.5 times its original diameter involving all three layers of its parent wall

Aneurysm vs. Pseudo-aneurysm

- True → involves an intact attenuated vessel where the wall is formed totally by the 3 normal elements (i.e. intima, media and adventitia) → can be saccular or fusiform
- False / pseudo-aneurysm → a pulsating hematoma, the cavity of which is in direct continuity with the lumen of an artery, where the wall is formed by connective tissue which is not part of the vessel wall

Types of Aneurysm	Sub-types	Remarks
True Aneurysm	Saccular	- Focal outward bulge (only part of the circumference is involved)
	Fusiform	- Circumferential dilatation
Congenital Aneurysm	Berry	- Congenital defects in media at junction of vessels around the circle of Willis – 90% emerging from anterior circulation - Most common cause for subarachnoid haemorrhage - Increased incidence in patients with HTN and APKD
Acquired Aneurysm	Atheromatous	- Commonly affects abdominal aorta, popliteal and femoral artery - See below
	Mycotic	- a/w sub-acute infective endocarditis, any form of bacteraemia (i.e. salmonella)
	Syphilitic	- (rare nowadays) – tend to involve thoracic aorta (esp. arch)
	Dissecting (aortic dissection)	- Blood enters false lumen and then ruptures – either back into main lumen of artery distally or externally → sudden death - Most common in thoracic aorta (**Stanford B**) – treat medically - If involves ascending aorta (**Stanford A**) → may dissect across coronoy ostium leading to inferior MI or across aortic valve leading to AR → require primary surgical repair
	False	- Pulsating hematoma - a/w stab wounds, IA injections or IA radiological procedures
	Arteriovenous (aka. aneurysmal varices)	- Due to trauma or more commonly following formation of an AV fistula for dialysis

COMPLICATIONS OF ANEURYSMS

- Rupture
- Thrombosis with occlusion
- Distal emboli from mural thrombus
- Pressure on adjacent structures – i.e. AAA eroding vertebral bodies, femoral aneurysm pressing on femoral nerve

AORTIC DISSECTION

CLINICAL FEATURES

- Chest Pain a/w RF – i.e. HTN, Marfan's Syndrome, Pregnancy, Erles-Danlos Syndrome
- Sudden, severe tearing chest pain / upper abdominal pain, maximal at the onset
- Chest Pain a/w neurological symptoms (18-30%) – i.e. TIA, stroke, paraplegia
- Migratory pain from chest to abdomen to LL (ILEAD – ischemia of the lower extremity in AD)
- Myocardial Infarction (inferior) – lesion in the RCA affecting the coronary ostia (1-7%)
- Difference in pulse volume or SBP in both arms >20mmHg or BP in LL < UL
- Chest Pain a/w new onset aortic regurgitation (18-50%)

MANAGEMENT

- Resuscitate Patient (i.e. check airway, give supplemental O2, insert IV plugs)
  - Infuse N/S slowly unless patient is hypotensive
- Continuous Monitoring
  - ECG – to exclude concomitant AMI
  - BP – aim SBP btw 100-120 mmHg (give IV labetalol or IV nitroprusside infusion + IV propranolol titrated to HR 60-80min)
  - Strict I/O – urinary catheterization – aim urine o/p >30ml/hour
  - Strict neurological observation charting
- Bloods – i.e. FBC, RP, CE, PT/PTT, GXM 4-6U
- Radiograph – i.e. CT aortogram

ABDOMINAL AORTIC ANEURYSM[56]

DEFINITION
- Aortic diameter of >50% larger than normal (normal aorta → 2-2.5cm)
- A dilatation of < 50% of normal arterial diameter is termed aortic ectasia
- A diameter of 3-3.5cm is used to label for aortic aneurysm

EPIDEMIOLOGY
- 1.7% females and 5% males have aortic diameter of ≥ 3.0cm by age 65
- 95% have associated atheromatous degeneration and 95% occur below renal arteries
- Aneurysm disease may extend to the common iliac arteries in 20-25% of patients
- Patients with AAA have 15% risk of having concomitant femoral or popliteal aneurysm (should go for ultrasound screening)
- Patients are frequently asymptomatic often detected incidentally on abdominal imaging

RISK FACTORS
- Smoking → more than 90% of patients with aortic aneurysm have been smokers → with cessation of smoking risk of developing aneurysm declines years to about 1/13 of original risk
- Gender → Males to Females (4:1 ratio)
- Strong Family History → risk increase from 5% to 20-30% among male siblings of patients with aneurysm
- Monogenic disorders
  - Marfan's – caused by fibrillin-1-defect (weakening of elastic tissue)
  - Ehler-Danlos syndrome type IV – due to abnormal type III pro-collagen
- Other risk factors: HTN, COPD, atherosclerosis, advanced age, hyperhomocysteinemia

RISK OF RUPTURE[57]

Size of Aneurysm	Risk of rupture per year	Remarks
< 5cm	0.5-5%	▪ After an aneurysm ruptures 25% of patients reach the hospital alive and only 10% reach the OT alive ▪ OT mortality rate for ruptured AAA is >40%
5-6cm	3-15%	
6-7cm	20%	
8cm	50%	

PRESENTATION

Asymptomatic	- Most commonly found incidentally during physical examination or imaging	
Symptomatic (rAAA)	Classical Presentation	- Hypotension → going into shock (feared presentation) - Intense abdominal pain radiating to the back - Pulsatile abdominal mass
	Local compression (contained rAAA)	- Radicular symptoms in the thigh and groin (nerve root compression) - GI, urinary obstruction
	Rupture into IVC (aortocaval fistula)	- Audible abdominal bruit - Venous HTN → swollen cyanotic legs, lower GI bleed, haematuria
	Distal Embolization	- Intraluminal thrombus → emboli → acute ischemic limb or mottling of the lower trunk and extremity

[56] N Engl J Med. 2008 Jan 31;358(5):494-501
[57] J Vasc Surg. 2003;37(5):1106

PHYSICAL EXAMINATION
- Vital signs – is patient hemodynamically stable
- Visible pulsation over abdomen
- Pulsations and mass in epigastric region felt on deep palpation
- Mass is expansile – when fingers of both hands are placed at the edges on either side of the mass, the fingers are pushed upwards and outwards
- Auscultate for bruit over the mass
- Check the other arteries – femoral, popliteal – for any aneurysm, and listen for bruits
- Look at the lower limbs for any gangrene, infection, mottling

DIFFERENTIAL DIAGNOSIS OF UPPER ABDOMINAL PAIN WITH SHOCK
- Pale: rAAA, ruptured hepatoma, BGIT, ruptured spleen in trauma, mesenteric bleed
- Not pale: sepsis, pancreatitis, perforated viscus, AMI , pyonephrosis

INVESTIGATIONS
Diagnostic Imaging:
- Bedside ultrasound – to assess size and position
- Portable Chest X-Ray (look for dissection / mediastinal widening)
- CT Aortogram / Angiogram*

Pre-operative investigations: FBC, UECr, PT/PTT, GXM for 6-8 units of whole blood, ECG & CXR

*note that rAAA is a surgical emergency and patient may be transferred to the OT as soon as possible, there is no place for routine abdominal or CT films – CT aortogram / angiogram done only if patient is stable and a definitive diagnosis of AAA needs to be made

MANAGEMENT
Dependent upon clinical context: asymptomatic, symptomatic, or ruptured

Asymptomatic AAA
- Time available for investigation of size of AAA and related anatomy
- Indications for surgery:
  (a) Aneurysm ≥ **5.5 cm** in largest diameter (measured by ultrasonography)
  (b) Patient fit for surgery (expected mortality rate < 5%)
  (c) **Increase in diameter** of **more than 1cm per year**

- Patient's fitness for surgery needs to be properly assessed because it is a major operation – need to optimise cardiovascular function
- Operation is the same except that it is done under elective setting
- Mortality is <5% in the elective setting, serious morbidity ~10%
- The repair (i.e. endovascular or open) of asymptomatic AAA between 4.0 to 5.5cm in size confers no survival benefits = 'best care' favours surveillance[58]

Endovascular Aneurysm Repair (EVAR) trial 2 showed that statin therapy is a/w a halving of the rate of aneurysm rupture and 2 small retrospective studies[59,60] indicated that use of statins reduces aneurysm growth rates

[58] Cochrane Database Syst Rev. 2012 Mar 14 [4 trials: UKSAT, ADAM, CAESAR & PIVOTAL]
[59] Eur J Vasc Endovasc Surg 2006;32:21-6.
[60] Am J Cardiol 2006;97:279-80.

Symptomatic AAA

- Indications for surgery:
  (a) Aneurysm of any size that is painful or tender
  (b) Aneurysm of any size that is causing distal embolization

Ruptured AAA

- AAA can rupture anterior into the peritoneal cavity (20%) or posterolaterally into the retroperitoneal space (80%)
  - Anterior rupture → free bleeding into peritoneal cavity → few patients reach hospital alive
  - Posterolateral rupture → retroperitoneal hematoma (tamponade effect), < 50% reach hospital alive
- High suspicion in unstable hypotensive patient complaining of severe sharp pain radiating to the back; may feel a tender pulsatile mass in the abdomen → if there is doubt, an ultrasonogram may help

Acute Management (after early diagnosis)

1. Stabilise patient – resuscitation with fluid and blood products
   - Establish 2 large bore (14-16G) IV cannula with N/S → **permissive hypotension** is advocated for patients with clinical dx rAAA to maintain a clinically alert patient and systolic BP >70mmHg[61]
   - GXM 8U, FFP, Platelets, 100% O_2, continuous ECG and vitals monitoring
   - Transfuse with blood if possible once available, correct any coagulopathy
   - If possible, don't intubate as NMB agents will ↓ tamponade effect, worsening haemorrhage
2. Call for vascular surgeons or cardiothoracic surgeons, senior, OT, ICU/HD immediately
3. Keep NBM GI decompression with NG tube, catheterise ± CVP / IA line
4. Get informed consent for open AAA repair from patient / family emphasize the risk and high mortality rates 50-70%
5. Rapid Transfer to OT for open repair
6. **Clean and drape and be ready for midline laparotomy BEFORE induction of anaesthesia**
7. Start IV broad spectrum Ab + analgesia (to prevent exacerbation in BP / HR)

[61] Ann Surg 2009;249:510-5.

Open Surgical Procedure

Surgeons have to be gowned up with scalpel in hand, ready to operate before anaesthetist intubates patient!
A full length midline incision is made. The aorta is controlled proximally and distally with clamps. (can be clamped for about 30 minutes without significant visceral ischemia) Aneurysm sac is opened longitudinally; the surrounding haematoma and mural thrombus within the AAA are cleared out. Synthetic graft (Dacron – polytetrafluoroethylene) is placed within the aorta and the vessel wall closed up over the graft i.e. the graft forms the lumen of the aorta. Clamps are released slowly to prevent sudden hypotension.

Post-operative complications includes → **respiratory** (basal lobe consolidation, atelectasis), **cardiac** (ischemia, infarction), **colonic ischemia**, **neurological** (sexual dysfunction, spinal cord ischemia), **aortoenteric fistula** (px with hematemesis or melena) and **prosthetic infection**.

COMPLICATIONS OF SURGERY

Intra-operatively	Early	Late
- Haemorrhage - Distal limb embolization (trash foot) - Distal limb arterial thrombosis	- Acute Renal Failure - AMI (cause 50-60% of mortality) - CVA (2° to hypotension or embolism) - Spinal Cord Ischemia - Acute sigmoid colon ischemia (2-6%)	- Aortoenteric fistula – frank PR bleed, torrential - Prosthetic graft infection - False aneurysm formation - Sexual dysfunction (impotence)

Post-operative Investigations: FBC (blood loss and consumptive coagulopathy), U/E/Cr (renal insufficiency), KUB (check position of stent)

Endovascular stenting

Endograft is a Y-shaped graft with two branches for the iliac arteries and a main trunk for the proximal aorta. It is deployed within the aneurysm to form the lumen of the aorta and requires adequate "neck" proximally (10-15mm proximal neck) and good landing site distally (20mm iliac landing zone)

- Alternative to open repair – Endovascular aneurysm repair **(EVAR) trial 1**[62]
  - 30-day mortality rate was lower in the EVAR group as compared to open repair
  - 4-years: all-cause mortality was similar in the two groups BUT there was a reduction in aneurysm-related deaths in the EVAR group by half compared to the open repair group
  - 4-years: patients in the EVAR group have greater incidence of post-operative complications (41% vs. 9%) and re-intervention (20% vs. 6%) as compared to the open repair group
- In patients who are unfit for open repair of AAA – **EVAR trial 2**[63] → EVAR did not improve survival over no intervention and was a/w need for continued surveillance and re-intervention at substantial increase in cost
- Requires Long-Term follow up
  - CT angiogram is usually repeated 1 and 6 months after implantation and annually thereafter to check position of the stent (ensure that stent has not migrated)
  - If procedure is successful, follow-up studies will show thrombosis of the aneurysm sac with gradual decrease in diameter

[62] Lancet. 2005 Jun 25-Jul 1;365(9478):2179-86.
[63] Lancet. 2005 Jun 25-Jul 1;365(9478):2187-92.

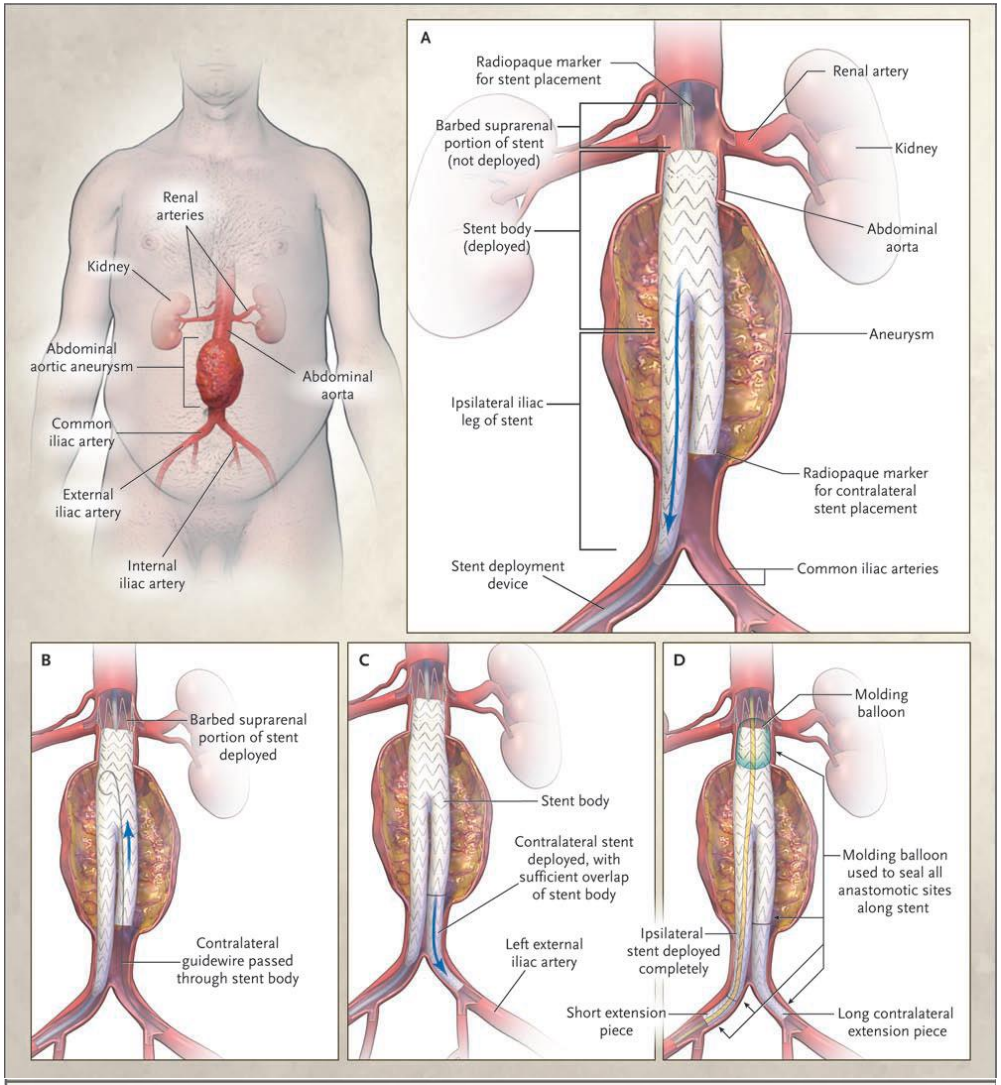
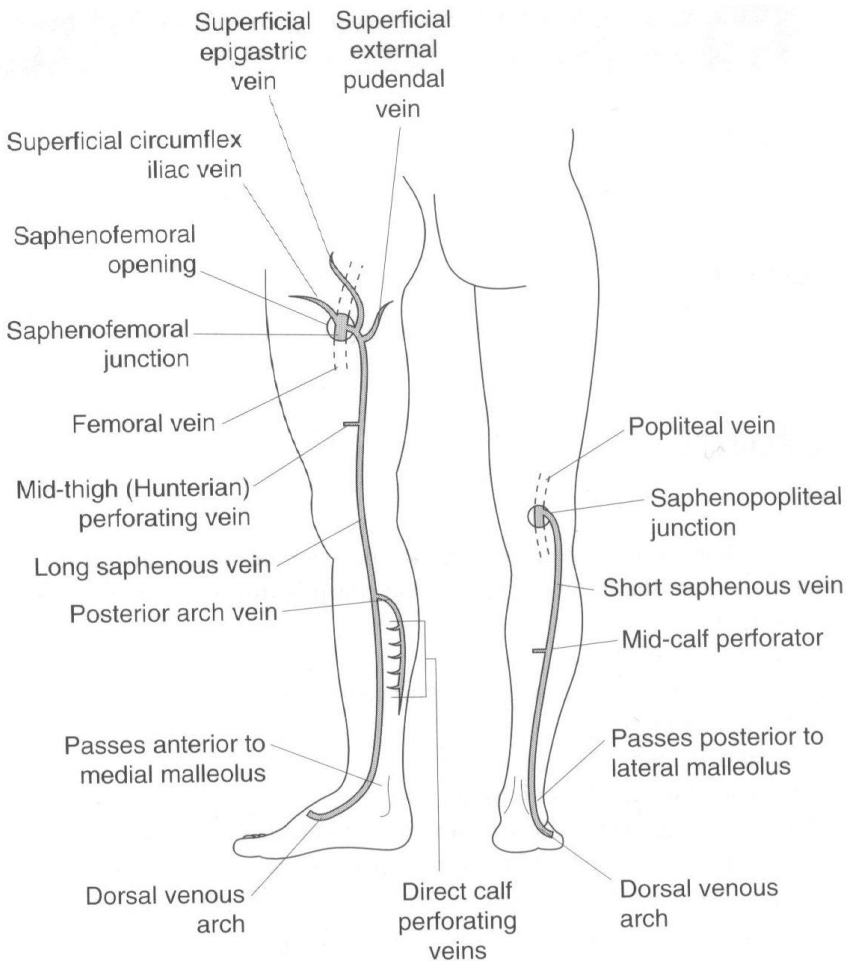


Figure 1. Endovascular Repair of an Abdominal Aortic Aneurysm, with the Use of an Endograft.

Panel A shows the initial insertion of the endograft. The proximal end of the endograft is then deployed proximally to the neck of the aneurysm, and barbs or hooks are used to help achieve adequate fixation of the device and prevent distal migration (Panel B). The contralateral access site is used to deploy the contralateral iliac artery limb of the graft (Panel C). The ipsilateral distal end of the graft is deployed in the ipsilateral iliac artery, and an endovascular balloon is inflated along the stent–graft to secure fixation of the anastomotic sites (Panel D). Blue arrows indicate movement of the guidewire.

PERIPHERAL VENOUS DISEASE

ANATOMY OF THE VENOUS SYSTEM OF THE LOWER LIMB



- The venous drainage of the lower limb is divided into a deep venous system and a superficial venous system separated by the deep fascia of the lower limb

- The deep venous system is composed of veins corresponding to the arterial supply e.g. anterior and posterior tibial veins, popliteal vein, femoral vein

- The superficial venous system is composed of two major veins, the great saphenous vein and the small saphenous vein

- **Course of the great saphenous vein (GSV):**
  - Arises from the medial side of the dorsal venous arch of the foot
  - Ascends immediately in front of the medial malleolus* (accompanied by saphenous nerve)
  - Runs up the leg posteriorly to pass a hand's breath behind the medial border of the patella
  - Ascends obliquely up the medial aspect of the thigh
  - Pierces the cribriform fascia at the saphenofemoral junction** (SFJ) to drain into the femoral vein at the saphenous opening (2.5cm inferolateral to the pubic tubercle)

* The relationship of the great saphenous vein to the medial malleolus is constant → KIV use for live-saving cannulation
** The SFJ is the confluence of the (1) GSV (2) superficial epigastric vein (3) superficial circumflex iliac vein and (4) superficial external pudendal vein

- **Course of the small saphenous vein (SSV):**
  - Arises from the lateral side of the dorsal venous arch of the foot
  - Passes posterior to the lateral malleolus
  - Ascends up the midline of the calf
  - Pierces the deep fascia over the popliteal fossa to drain into the popliteal vein
  - Accompanied in its course by the sural nerve

- The superficial system and the deep system communicate through **communicating veins** that contain valves which allow only one-way flow of blood from the superficial vein into the deep vein

- **Locations of the communicating veins:**
  - Saphenofemoral junction (GSV drains into femoral vein)
  - Hunterian perforator: mid-thigh
  - Dodd's perforator: distal thigh
  - Boyd's perforator: knee
  - Calf (posterior tibial) perforators: at 5, 10, and 15 cm above the medial malleolus

- **Physiology of venous drainage:**
  - Main mechanism is the calf muscle pump
  - Contraction of the calf muscles compresses large venous sinuses in the muscles, squeezing the blood into the popliteal vein and back to the heart
  - The deep veins have many bicuspid valves to prevent backflow → blood only flows towards the heart
  - During calf muscle relaxation, the intramuscular veins open and suck blood in from the superficial system through the communicating veins, thus draining the superficial veins

CHRONIC VENOUS INSUFFICIENCY

Chronic venous insufficiency develops when there is **venous hypertension**, which can result from:

1. **Obstruction to venous flow** e.g. tumour compression in the pelvis, pregnancy, deep vein thrombosis
2. **Dysfunction of venous valves** e.g. varicose veins
3. **Failure of the "venous pump"** – dependent on adequate muscle contraction (stroke, muscular weakness can cause failure) as well as competent venous valves

MANIFESTATIONS OF CHRONIC VENOUS INSUFFICIENCY (CVI):

1. **Venous dilatations**
   - **Telangiectasias** (spider veins or venous stars – intradermal veins) – **0.1-1mm**
   - **Reticular veins** (slightly larger intermediate veins) – **1-3mm**
   - **Varicosities** (visible, dilated tortuous superficial veins; formed by main tributaries of the saphenous veins because these do not have a strong coat of smooth muscle in their walls, unlike the saphenous veins; they are more superficial and not bound down to the deep fascia) – **≥3mm**
   - **Corona phlebectactica** (a network of small dilated venules beneath the lateral and/or medial malleolus with severe venous hypertension)

2. **Oedema – pitting**: The hallmark of CVI; present in all but the earliest stages
   - Unilateral oedema worsened by dependency (worse at end of the day) and better with recumbency

3. **Skin changes**
   - **Hyperpigmentation** of the skin over medial lower third of the leg (gaiter area) – due to extravasation with hemosiderin deposits
   - **Atrophie blanche** – avascular fibrotic scars (i.e. ivory white areas with hyper-pigmented borders and telangiectasia)
     - Prone to venous ulceration 2° to poor blood supply
   - **Venous stasis eczema** – pruritic, weeping, scaling, with erosions and crusting
   - **Lipodermatosclerosis** – a fibrosing panniculitis of the subcutaneous tissue that results in a firm area of tender, indurated, hyperpigmented skin that is fixed to subcutaneous tissue.
     - Results from severe venous hypertension
     - Starts in the gaiter area and extends circumferentially to surround the leg
     - If severe can result in an "inverted champagne bottle" appearance of the leg with brawny oedema above and below the area of lipodermatosclerosis
   - **Cellulitis**

4. **Venous ulcer formation**
   - Typical location is over the medial malleolus
   - Shallow, flat ulcer with sloping edges; base may be sloughy or granulating, usually quite moist-looking
   - Surrounding skin will show signs of CVI
   - In long-standing ulcer SCC can develop (Marjolin's ulcer) – If ulcer enlarges, becomes painful and malodorous, edge becomes thickened or raised, if inguinal lymph nodes are enlarged

These manifestations can be asymptomatic or associated with symptoms of leg fullness, aching discomfort, heaviness, nocturnal leg cramps, or bursting pain upon standing.

CEAP CLASSIFICATION OF CHRONIC VENOUS INSUFFICIENCY

TABLE 1. Basic CEAP Classification — Clinical, Etiologic, Anatomic, Pathophysiologic

C-Clinical Class	Characteristics*	
0	No clinical findings or symptoms	**E-Etiology****
1	Telangiectasia or reticular veins	C Congenital
2	Varicose veins	S Secondary
3	Edema, only due to a venous etiology	P Primary
4	(a) Pigmentation and/or eczema	**A-Anatomy****
	(b) Lipodermatosclerosis, atrophie blanché	S Superficial
5	Prior ulceration, now healed	P Perforator
6	Active ulceration.	D Deep
A,S	Subscript: Asymptomatic, Symptomatic	
		P-Pathophysiology**
Date	Date of investigation	R Reflux
Level	Level of investigation (I,II,III)	O Obstruction
		R-O Both
		N** No evident disease**

*Complaints are expected to be related to venous insufficiency and are not classified if another etiology is present (ie, edema secondary to heart failure).
**The N subscript indicates no evidence of disease. It is applicable to E, A, and/or P of CEAP.

VARICOSE VEIN

Varicose veins of the lower limbs: dilated, tortuous subcutaneous vein that are ≥3 mm in diameter measured in the upright position. Varicosity can involve the main axial superficial veins (i.e. GSV & SSV) or any other superficial vein tributaries of the LL.[64]

CAUSES

Primary	Secondary
- Idiopathic / multifactorial – may be related to posture and components and structure of the vein wall - Congenital	- Previous DVT - Deep Venous Obstruction - Superficial Thrombophlebitis - Destruction of valves by thrombosis - Increase in flow and pressure 2° AVF

PATHOPHYSIOLOGY

- Inherent weakness in the vein wall, leading to dilation and separation of valve cusps so they become incompetent
- This may be aggravated by obstruction to venous return (as above)

RISK FACTORS

- Age
- Parity
- Occupation – requiring long periods of standing
- Weight
- Posture – crossing legs all the time
- Increased abdominal pressure – constipation, chronic cough, etc.
- Pelvic tumour or other lesion compressing on the deep veins
- Family history: 1 parent (50% risk, both parents (up to 80% risk)

HISTORY

- Asymptomatic – varices of cosmetic concern
- Symptomatic:
  - local → nonspecific pain, tingling, aching, burning, muscle cramps, swelling, sensation of throbbing or heaviness, itching skin, restless leg, leg tiredness
    - Worsen with heat, worsen throughout course of day (esp. if stand for long periods)
    - Relieved by resting or elevating legs or wearing elastic stockings
- Complications : thrombophlebitis, bleeding, hyperpigmentation, eczema, ulceration
- Ask for past history of DVT & thrombophlebitis, obstetrics history, family history of varicosity or thrombotic disorders

EXAMINATION – Examine patient standing with adequate exposure of the lower limbs

Inspection – look all around the limb!

1. Presence of signs of chronic venous insufficiency* – see above 4 main features
   - Venous Dilatation
   - Pitting Oedema
   - Skin Changes
   - Venous Ulcer Formation – any suggestion of Marjolin ulcer
2. Scars – i.e. previous stab avulsions
3. Look at **course** of great saphenous vein and short saphenous vein for varicosities
4. Look at the **inguinal region** for any saphena Varix
5. Any signs of infection

* corona phlebectatica (ankle / malleolar flare) – fan-shaped pattern of small intra-dermal veins located around ankle / dorsum of foot → early sign of advanced venous disease

Palpate

1. Feel for any dilated **varicosities / venous aneurysm**
2. Palpate **along the course of the saphenous veins** and their tributaries to feel any varicosities and **for tenderness** (may be more palpable especially in fat legs)
3. Palpate the inguinal region for a **saphena varix** (compressible lump that refills when released)
4. Do the **cough test** to feel for reflux at the saphenofemoral junction (2.5 cm below and lateral to the pubic tubercle)
5. **Percussion (tap test**) – test for valvular incompetence (not a very valuable test) – positive if the distal hand can feel the wave of blood flowing retrograde after tapping the proximal varicosities
6. **Feel the peripheral pulses** of LL to exclude any ischemia as the management will involve compression of limbs (ABI >0.8)
7. **Feel the inguinal LN** – if have presence of venous ulcers

Move

1. Ankle Joint – patients with advanced venous disease have decreased mobility in ankle joints

[64] J Vasc Surg. 2011 May;53(5 Suppl):2S-48S.

Special tests

TOURNIQUET TEST

- Lie the patient down and empty the varicosities & tie a tourniquet just below the SFJ
- Ask the patient to stand up
- Look for filling up of the varicosities above and below the tourniquet
- If the veins dilate above but not below the tourniquet, this indicates that the perforators below the level of the tourniquet are not incompetent and that the SFJ is incompetent → confirm this by releasing the tourniquet and watching the veins dilate
- If the veins below the tourniquet are dilated when the patient stands up, then the incompetent perforator is below the level of the tourniquet
- Repeat the test, placing the tourniquet at different sites:
    1. Mid-thigh (just below the Hunterian perforator
    2. Below the knee
    3. Mid-calf

- The incompetent perforator is located just above the level where the tourniquet prevents dilation of the veins in the limb on standing
- The alternative is the triple tourniquet test, where three tourniquets are tied with the patient lying down and then released from the bottom up to locate the site of insufficiency

TRENDELENBURG TEST

- The SFJ is occluded (2.5 cm inferolateral to the pubic tubercle) with the patient lying down
- Get the patient to stand while holding the SFJ occluded
- If varicosities do not fill up, the SFJ is the site of incompetence; if they fill up, there are other sites of perforator valve incompetence (the SFJ may or may not be incompetent)

PERTHES' TEST

- Tie a tourniquet around the calf or thigh and ask patient repeatedly stand on tiptoe
- In a person with normal deep venous drainage and competent venous valves in the communicating veins the superficial veins should drain into the deep veins
- If the patient's varicosities remain enlarged then he or she has obstructed deep venous drainage or incompetent valves in the communicating veins

Completing the examination

- Auscultate over the varicosities for any bruit (indicate arteriovenous malformation)
- Examine the abdomen for any mass that may be causing the varicosities
- Examine the inguinal region for any lymphadenopathy – outflow obstruction

Use of a handheld Doppler probe to detect incompetence

- Doppler probe is placed in the popliteal fossa over small saphenous vein
- Squeeze the calf to empty the veins – should hear a whoosh as blood flows through the small saphenous vein
- When the calf is relaxed there should not be any sound – a second whoosh indicates reflux of blood i.e. there is valvular incompetence

INVESTIGATIONS

Venous duplex ultrasound

- Indications:
    - Recurrent varicose veins
    - History of superficial thromobophlebitis or DVT
    - Complications of CVI: Venous eczema, Hemosiderin staining, Venous ulceration, Lipodermatosclerosis

- Ask for SFJ and SPJ reflux, perforator, deep venous incompetency & DVT screen
- Can delineate deep and superficial venous systems and locate sites of incompetence
- **Valve closure time** should be assessed, usually within the GSV with times >0.5 sec abnormal
- Exclude presence of **deep vein thrombosis – stripping is contraindicated**

Others: continuous wave doppler

MANAGEMENT

Conservative

1. Lifestyle changes
    - Decrease amount of time spent standing
    - If due to job, change job or ask for change to position to stand & walking less
2. Graduated compression stockings, usually grade II → ensure good pulses
3. Medications e.g. Daflon

Surgical

Indications:

1. Cosmesis – large unsightly varicosities
2. Symptoms – pain, discomfort
3. Complications – signs of chronic venous insufficiency, venous ulceration

Available modalities:

1. High tie with great saphenous vein stripping, and stab avulsion of varicosities
    a. High tie (includes all venous tributaries)
    b. Complications: DVT , saphenous nerve injury (reduce risk by stripping on thigh portion of GSV)
2. Ultrasound-guided injection foam sclerotherapy
    a. Sclerosing agent: polidocanol, hypertonic saline, sodium tetradecyl sulfate
    b. Complications: cutaneous necrosis, hyperpigmentation, telangiectasic matting, thrombophlebitis, allergic reaction, venous thromboembolism
3. Endovenous laser/radio-frequency ablation of the saphenous vein
    a. Contraindications: saphenous vein thrombosis
    b. Complications: skin burns, DVT, PE, Vein perforation & hematoma, thrombophlebitis
    c. Outcomes are comparable with saphenectomy

VENOUS ULCERS

CAUSE – ANY CAUSE OF CHRONIC VENOUS INSUFFICIENCY

1. Obstruction to venous flow – thrombosis
2. Incompetent valves – varicose veins, deep vein reflux (post-DVT)
3. Muscle pump failure – stroke, neuromuscular disease

INVESTIGATIONS

1. Exclude infection of the ulcer and other complications
   - FBC for raised total white count
   - Swabs of the ulcer for Gram stain and culture
   - X-ray of the area to exclude underlying gas, bone involvement

2. Venous duplex to map out venous system
3. Check for peripheral arterial disease by doing ABPI
4. Biopsy if cannot exclude malignant transformation (Marjolin's ulcer)

MANAGEMENT:

Conservative

1. **4 layer compression stockings (change 2x/wk if ulcer, 1x/wk if no ulcer)**
   (a) Non-adherent wound dressing over ulcer (e.g. Menolin) followed by wool bandage
   (b) Crepe bandage
   (c) Blue-line bandage (Elset)
   (d) Adhesive bandage (Coban)

Aim: ankle pressure around 30mmHg (can vary according to needs)
Nowadays, 2 layer stockings are used too – can achieve the same ankle pressure but not as effective as it loses pressure more quickly so less consistent pressure.

2. Analgesia
3. Antibiotics if infected
4. Warn patient to avoid trauma to affected area
5. Encourage rest and elevate leg
6. Once healed, (cannot use with ulcer/wound) compression stockings should be fitted and continued for life

Surgical

- If ulcer fails to heal
- First, exclude malignancy or other causes of ulcer (biopsy)
- Split skin graft can be considered with excision of dead skin and graft attached to healthy granulation tissue
- Venous surgery for the underlying pathology

UROLOGICAL DISEASES

- The urinary system composed of kidneys, ureters, bladder, urethra and male external genitalia
- Functions of the urinary system **[SHEAF]**
  - **S**torage and excretion of urine
  - **H**ormone production → renin, erythropoietin, 1-25-dihydrocholecalciferol
  - **E**lectrolyte maintenance
  - **A**cid-Base maintenance
  - **F**luid maintenance
- History taking aims to answer:
  - What is the underlying aetiology?
  - What is the timeframe? – disease progression / symptomatology
  - Are there any complications from the disease – local / regional / systemic
  - Thus far, any treatment instituted for the patients?
  - Any complications from the treatment?
  - What are the outstanding issues?

CLASSIFICATION OF ANEMIA

MCV		
Microcytic	Normocytic	Macrocytic
Low Reticulocytes	**Normal WBC / Platelets**	**Low Reticulocytes**
Iron deficiency anemia	Anemia of Chronic Disease	Megaloblastic anemia – Vitamin B12 / Folate Deficiency
Sideroblastic anemia	Early Iron Deficiency Anemia	
	Renal Failure	Non-megaloblastic anemia – liver disease, alcohol, hypothyroidism
	Pure Red Cell Aplasia	
		Drugs – Zidovudine (anti-viral)
		Myelodysplastic Syndrome (MDS)
High Reticulocytes	**Pancytopenia**	**High Reticulocytes**
Thalassemia	Primary Failure – Aplastic Anemia	Reticulocytosis
	Secondary Failure – chemo/RT, myelodysplastic syndrome,	

Symptomatic anemia

- SOB on exertion, dizziness/syncope, chest pain, palpitation, lethargy/fatigue

Signs of Anemia

- Face – (i) conjunctival pallor (ii) pallor of mucus membrane
- Cardiac Auscultation – short systolic flow murmur at aortic area
- Pulse – (i) tachycardia (ii) bounding (iii) collapsing pulse
- Hands – pallor of palmar creases

APPROACH TO GROSS HAEMATURIA[65][66]

DEFINITION:

- Gross haematuria → visibly bloody or brown urine
  - Gross haematuria with passage of clots → lower urinary tract source
- Microscopic haematuria → ≥3 RBC per high-powered field (in 2 of 3 properly collected (freshly voided, clean-catch, midstream urine) urinalysis specimens)[67]

CAUSES FOR GROSS HEMATURIA – MAINLY POST-RENAL CAUSES

Trauma	▪ Urinary Catheterisation ▪ Flexible Cystoscopy ▪ Post-TURP
Infection	▪ Tuberculosis ▪ Cystitis (bladder) ▪ Prostatitis (prostate) ▪ Urinary Tract Infection
Tumour	▪ Transitional Cell Carcinoma (bladder, ureter) ▪ Prostate Cancer / Benign Prostate Hyperplasia (BPH)
Stones	▪ Nephrolithiasis (kidney stones) ▪ Ureterolithiasis (ureter stones) ▪ Cystolithiasis (bladder stones)

HISTORY

1. **Is the patient symptomatic or asymptomatic**

- Haematuria may be visible and reported by the patient (macroscopic haematuria) or invisible and detected on dipstick (microscopic haematuria)

2. **Is this truly pathological gross haematuria?**

If patient presents with red/brown urine but have negative dipstick

- Food dye – anthocyanins (beetroot) – red urine
- Drugs – levodopa, senna (orange), rifampicin (orange), phenolphthalein
- Others – porphyria, alkaptonuria, bilirubinuria

Rule out benign causes of haematuria

- Menstruation
- Exercise-induced myoglobinuria (vigorous exercise)
- Sexual Intercourse
- Trauma

* Urinalysis is best obtained when the other causes of bleeding has ceased

If patient present with red urine and have positive dipstick

- Can be true haematuria or false-positives (myoglobinuria or hemoglobinuria)

** Theoretically can centrifuge the urine to determine if the red/brown colour is in the urine sediment (haematuria) or the supernatant (not haematuria)

[65] Med Clin North Am. 2004 Mar;88(2):329-43
[66] uptodate: Etiology and evaluation of hematuria in adults
[67] Am Fam Physician.2001;63:1145-1154

3. **Are there any clues from history to suggest a particular aetiology?**

<u>When during urination does blood appear?</u>
- Initial – disease in the urethra, distal to the UG diaphragm
- Terminal – disease near bladder neck or prostatic urethra
- Throughout – disease in the bladder or upper urinary tract

<u>Lower Urinary Tract Symptoms [FUN DISH]</u>
- **Storage problem – irritative symptoms**: frequency, urgency / urge incontinence, nocturia
  - Possibly: UTI, stones, bladder tumour
- **Voiding problem – obstructive symptoms**: terminal dribbling, intermittency/incomplete emptying, poor stream, straining to pass urine, hesitancy
  - Possibly: BPH, prostate cancer, urethral stricture
- Others – polyuria, oliguria, urethral discharge

<u>Upper Urinary Tract Symptoms</u>
- Loin pain / tenderness: renal infection, infarction, rarely obstruction and glomerulonephritis
- Severe loin pain with radiation to iliac fossa, groin and genitalia: acute obstruction of the renal pelvis or ureter by calculus or blood clots

<u>Painful vs. painless haematuria</u>
- Classically, painless gross haematuria in a patient > 35 years-old is the hallmark of malignancy
- Dysuria suggest on-going infection / inflammation

Aetiology		Relevant Significant History
Post-renal	Trauma	- Hx of urinary catheterisation, flexible cystoscopy, TURP
	Infection	- Change in frequency, urgency, nocturia (irritative symptoms) - Dysuria, urethral discharge - Recent travel history – areas endemic for schistosomiasis or TB
	Tumours	- Red flags for malignancies - local-regional complications, metastatic & constitutional symptoms
	BPH	- Advanced age presenting with concurrent voiding problems (i.e. hesitancy, dribbling, poor stream)
	Stones	- Unilateral flank pain radiating to the groin
Renal	**Brief screen for glomerulonephritis – usually microscopic but can also be gross**	
	Anti-GBM	- Goodpasture → RPGN and lung haemorrhage – haemoptysis
	ANCA associated vasculitis	- Wegner's Granulomatosis - Microscopic Polyangitis - Eosinophilic Granulomatosis with Polyangitis (Chug Strauss)
	Immune Complex – renal limited	- Post-Strep GN → pharyngitis / impetigo 2-3wks prior to onset of haematuria - MPGN → - IgA Nephropathy → young male with episodic haematuria ppt by infection (synpharyngitic)
	Immune Complex – systemic related vasculitis	- SLE (esp. type III, IV) – read 2012 SLICC SLE Classification - HSP → painless palpable purpura, arthritis/arthralgia, abd pain, renal diz - IE → read Duke's Criteria
	Others (usually asymptomatic)	- Alport's → b/l SNHL + ocular abnormalities - APKD → family history, bilateral flank mass, insidious onset of HTN - Thin Basement Membrane Disease → family history

Common Causes of Haematuria
- Infection (UTI, prostatitis) or inflammation
- Stones – bladder, kidney, ureter
- Benign prostate hyperplasia (BPH)
- Malignancy (anywhere along the urinary system) – especially in older patients

4. **Does the haematuria represent extra-glomerular or glomerular bleeding?**
- Any frothy urine – suggest glomerular bleeding
- Any clots present – suggest extra-glomerular bleeding
- What is the colour of the bleeding?

	Extra-glomerular bleeding	Glomerular bleeding
Colour (if macroscopic)	Red or pink	Red, smoky brown, or "Coca-Cola"
Clots	May be present*	Absent
Proteinuria (time of onset is impt)	<500 mg/day	May be >500 mg/day > 2+ on urine dipstick
RBC morphology	Normal (isomorphic)	Some RBCs are dysmorphic
RBC casts	Absent	May be present**

* Gross haematuria with the passage of clots indicates a lower urinary tract source (extra-glomerular)
** The presence of red cell casts is diagnostic of glomerulonephritis or vasculitis

5. **Severity**
- Is the haematuria transient or persistent?
  - In a prospective cohort study, 1/3 of patients with initial positive urinalysis have transient haematuria[68]
- Symptoms of anemia – pallor, exertional chest pain, palpitations, SOP, giddiness, fatigue
- Any concomitant renal impairment – amount of urine, any fluid overload status

6. **Red Flags for malignancy**
- Male Gender
- Age (>35yr)
- Past or current smoker
- Occupational exposure – chemicals or dyes
- History of exposure to carcinogenic agents or chemotherapy
- History of analgesic abuse
- History of gross haematuria, urological disease, irritative urinary symptoms, pelvic radiation, chronic UTI, chronic indwelling FB

[68] Mayo Clin Proc. 2013 Feb;88(2):129-38. Epub 2013 Jan 9.

PHYSICAL EXAMINATION

1. Check patient's **vitals** – fever (pyelonephritis), HTN (glomerulonephritis)
2. Any Signs of Anemia – i.e. conjunctival **pallor**
3. **Heart – new murmur (endocarditis)**
4. **Lungs – crackles, rhonchi (Goodpasture's syndrome)**
5. **Abd – loin tenderness, renal mass**, bruit (renal ischemia), palpable bladder, suprapubic mass
    a. Are the kidneys ballotable, is the bladder percussible?
6. **Extremities – edema (glomerulonephritis), rashes (HSP, CTD, SLE)**
7. Scrotum – **varicocele** on the left (may have RCC of the left kidney with extension of tumour into renal vein, blocking the testicular vein where it drains into the left renal vein)
8. External genitalia – blood from urethra, any blood clots, shape of blood clot
9. Digital rectal exam – **prostate enlargement** (BPH versus cancer)

INVESTIGATIONS FLOWCHART

- Haematuria on repeated urine dipsticks
- Exclude menstruation, infection, trauma → RBC confirmed on urine microscopy, infection absent on culture
- **Renal imaging** to exclude anatomical bleeding lesions
- If anatomical lesion absent → full assessment and management by nephrologist (i.e. asking qns with regards to features of significant renal disease, consider possibility of doing renal biopsy)
- <u>if anatomical lesion present</u> → <u>full assessment and management by urologist (see below)</u>

INVESTIGATIONS

1. **Urine dipstick (UC9) – direct counting of RBC/ml of un-centrifuged urine**
    - Test for: leucocytes, RBC, pH, nitrates, ketones, urobilinogen, glucose, cast, crystals
    - Gold standard for the detection of microscopic haematuria
    - Positive dipstick dipsticks for blood should get microscopic confirmation
        - Sensitive but not specific test
        - Can be true haematuria or false-positives (myoglobinuria or hemoglobinuria)
    - If patient presents with red/brown urine but have negative dipstick
        - Food dye – anthocyanins (beetroot) – red urine
        - Drugs – levodopa, senna (orange), rifampicin (orange), phenolphthalein
        - Others – porphyria, alkaptonuria, bilirubinuria

2. **Urine Full Examination Microscopy Elements (UFEME)**
    - Test for: WBC/hpf, RBC/hpf, epithelial cell, casts, crystals, other formed elements
    - Confirm presence of red blood cells and casts
    - The absence of RBCs / RBC casts despite a +ve dipstick test suggest hemoglobinuria or myoglobinuria
    - Elevated WBC (pyuria is >5 WBC per hpf), organisms → infection

3. **Urine phase contrast – differentiates glomerular and non-glomerular bleed**
    - Glomerular → casts and dysmorphic RBCs
        - If associated with protein or renal failure → refer to nephrologist
    - Non-glomerular → isomorphic RBCs
        - CT urogram → urine cytology → cystoscopy

4. **Urine cytology for malignant cells**
    - Urine cytology has the greatest sensitivity for carcinoma of the bladder
    - If malignant or atypical cells are identified → recommend for cystoscopy

5. **Urine culture and sensitivity**
    - Recommend for exclusion of urinary tract infection prior to evaluation of haematuria

6. **Full blood count**
    - How low is the Hb?
    - Elevated TW – infection

7. **Urea, electrolytes and creatinine**
    - Any renal impairment and electrolyte abn (renal or pre-renal dz more likely)

8. **Plain KUB**
    - Stones, size of kidney
    - Margins: Superiorly needs to be above the upper pole of the right kidney (T_{12}), inferiorly needs to show the pubic symphysis

9. **Ultrasound of the kidneys**
    - Lower diagnostic yield as compared to CT urogram
    - Can characterize renal size, mass, presence of any hydronephrosis, renal stones

10. Multi-detector CT urogram (CTU) / MR urogram

- Recommended for patients with unexplained persistent gross haematuria
- Images of the kidney and genitourinary system are obtained in 3 phases
  - Non-contrast phase → detection of stones
  - Renal parenchymal phase → detection of tumours
  - Excretory / Delayed phase
- Advantages: Ability to see renal parenchyma tumours (IVU only sees outline)
- Disadvantages: Radiation ++ (3 CT scans), contrast allergy → can use MR urogram

11. Intravenous urogram (IVU) or intravenous pyelogram (IVP)

a. Distortion of renal **OUTLINE** and pelvic calyces by RCC, may have specks of calcification
b. Contrast UPTAKE: present or not (no contrast in obstruction / non-functioning), equal and symmetrical uptake
c. Configuration of the kidneys eg. Horseshoe kidneys
d. Stones (filling defect, proximal dilatation, decreased distal passage of contrast) + hydroureter and/or hydronephrosis
e. Filling defect in bladder due to TCC
f. Increased residual volume in bladder after micturition due to BPH

Intravenous contrast used to delineate anatomy of the kidneys and urinary system

- Various phases:
  1. **Control film** – plain KUB
     - Tomogram – zoom into kidneys before contrast
  2. **Nephrogram phase** (1 min after contrast) – contrast fills kidney parenchyma so kidneys become more visible → measure size, outline
  3. **Pyelogram phase** (3-5 min) – contrast fills calyces & pelvis, can detect dilated calyces/pelvis (hydronephrosis), any filling defects
  4. **Release film** (abdominal binder which was placed to slow the flow of contrast into the bladder is released) – shows ureters, any hydroureter, filling defects
     - Cystogram - any filling defects, abnormal appearance of the bladder (fir-tree appearance in neurogenic bladder)
  5. **Post-micturition** – any residual urine in bladder after voiding

- Contraindicated in:
  (a) Contrast allergy
  (b) Renal impairment (Cr >200)
  (c) Patients on metformin (can cause lactic acidosis; patients need to stop metformin 2 days before and after study)
  (d) Patients with asthma (given steroids for 3 days before study)
  (e) **Pregnancy**: ask LMP

12. Cystoscopy

- Recommended for patients with unexplained gross haematuria, passing of blood clots and persistent unexplained microscopic haematuria
- Gold standard for evaluating lower urinary tract
- Detection of bladder tumour (IVU may not pick up small tumours <1cm)
- Biopsy can be taken at the same time

13. Renal Biopsy

- Recommended for patients with glomerular haematuria in the presence of RF for progressive disease such as proteinuria, elevation in serum Cr concentration and new onset or worsening hypertension
  - Common findings are → (1) normal, (2) IgA nephropathy, (3) thin basement membrane disease, (4) mild nonspecific glomerular abnormalities and (5) hereditary nephritis (Alport's syndrome)
- NOT INDICATED in patients with persistent isolated non-glomerular haematuria (i.e. no dysmorphic RBC or red cell casts or proteinuria)

RENAL CELL CARCINOMA

EPIDEMIOLOGY

- 2-4% of human cancers – Incidence has risen over past 20 years
- Most frequent occurring solid lesion within kidney
- 2:1 male predominance
- Majority present in 5th to 7th decades of life
- Most cases are sporadic but seen in families with von Hippel-Lindau disease (VHL) and tuberous sclerosis complex (TSC)

PATHOLOGY

- Accounts for 85% of malignant renal tumours in adults
- Malignant tumour arising from the renal tubular epithelium
- Types of Renal Cell Carcinoma:

	Clear Cell Carcinoma	Papillary Carcinoma	Chromophobe Carcinoma
Accounts for	70-80%	10-15%	5%
Arise from	Proximal tubules	Distal tubules	Intercalated cells of collecting tubules
Pathogenesis	Sporadic or Familial (VHL)	MET oncogene	
Prognosis			Excellent

DIFFERENTIAL DIAGNOSIS

- Benign
  - Angiomyolipomas
  - Renal Adenoma / Cyst / Abscess
  - Pyelonephritis (acute / chronic)
  - Renal Oncocytoma
- Malignant
  - Renal Cell Carcinoma
  - Wilms' Tumour (nephroblastomas) – typically in children
  - Metastasis (lung, breast, GI, prostate, pancreas, melanoma)
  - Sarcoma

RISK FACTORS

- Smoking (2x increase in relative risk)
- Industrial exposure – coke oven workers (cadmium)
- Prior kidney irradiation
- Family history
  - Von-Hippel Lindau syndrome (AD) due to mutation of the VHL gene on short arm of chromosome 3p25-26. Associated with RCC (40%), renal cysts (75%), cysts of epididymis and pancreas, cerebellar hemangioblastomas, retinal angiomas and pheochromocytoma (14%)
  - Hereditary papillary RCC (HPRCC) due to mutation of the MET proto-oncogene on chromosome 7q31 → multifocal bilateral papillary carcinomas
- Acquired polycystic kidney disease (secondary to chronic dialysis) – needs yearly ultrasound

PRESENTATION

- Initially asymptomatic (may be detected incidentally on imaging studies)

- Symptomatic (**local symptoms**)
  - Painless gross haematuria is the most common presenting symptom → 50% of cases
  - Historical triad of flank pain, painless haematuria, palpable flank mass occurs in 11% of patients
- **Regional Symptoms**:
  - Left varicocele – left sided tumour may present with varicocele due to invasion of the left renal vein with tumour and obstruction of the left testicular vein
  - Extension into IVC can cause (a) lower limb oedema, (b) ascites, (c) liver dysfunction and (d) pulmonary embolism
- **Systemic (metaplastic) Symptoms**
  - Lungs (cannon-ball mets)
  - Liver
  - Bones
  - Brain
  - Lymph nodes (30% have tumour in para-aortic nodes at presentation)
- **Constitutional Symptoms:**
  - Weight loss, fever – due to tumour necrosis, anemia, and night sweats
- **Paraneoplastic syndromes** (10-40% of RCC)
  - Hypertension – due to renin overproduction
  - Non-metastatic liver dysfunction – Stauffer Syndrome (resolves after tumour removal)
    - Can have paraneoplastic elevation of serum ALP
  - Hypercalcaemia* – due to production of PTH-like protein / lytic bone mets
  - Polycythaemia – due to production of erythropoietin by the tumour

*Treatment for hypercalcaemia[69]

- Asymptomatic / mildly symptomatic → advised to avoid thiazide diuretics, lithium carbonate, volume depletion, prolonged bed rest or inactivity, and a high calcium diet (>1000 mg/day)
- Severe / symptomatic hypercalcaemia (> 3.5mmol/L) → patients usually dehydrated
  - Saline Hydration (initial therapy – onset hours) – **MCQ**
  - Calcitonin (onset: 4-6hrs)
  - Bisphosphonate – i.e. IV zoledronic acid or pampidronate (onset 24-72hours) – used if due to excessive bone resorption – i.e. malignancy related hypercalcemia, hypervitaminosis D etc.
  - Glucocorticoid (onset 2-5days) – used if due to lymphoma, sarcoidosis or other granulomatous disease
  - Dialysis (onset: hours)

[69] uptodate: treatment of hypercalcemia

INVESTIGATIONS

"Evaluation of renal mass requires radiological characterization and assessment for metastatic disease"

ESTABLISHING THE DIAGNOSIS

1. **Intravenous Urogram (IVU)**
   - Control film give information regarding position, size and outline of kidneys.
   - Carcinoma → Mottled central calcification (90% specificity), peripheral calcifications a/w RCC in 10-20% of cases.
   - Suggestive of renal mass – renal enlargement, displacement of renal pelvis or calyces, irregular renal borders or change in cortical density.

2. **Imaging – CT and/or ultrasound**
   - Presumptive diagnosis is made on imaging – a renal parenchymal mass with thickened irregular walls and enhancement after contrast injection suggests malignancy
   - Ultrasound – differentiate cystic from solid renal masses
   - Classical cyst will be smooth with definite border and absent of internal echogenicity with acoustic enhancement beyond posterior wall.
   - CT Kidneys (triphasic) – staging – LN involvement, perinephric extension, renal veins or IVU extension. (Bosniak classification of cystic masses (I – IV))

3. **MRI Kidneys**
   - Most effective in demonstrating presence and extent of renal vein or IVU tumour thrombi

4. **Pathological diagnosis**
   - Historically, percutaneous biopsy not done for resectable lesions due to fears of tumour seeding, however, now → diagnostic accuracy > 90% with low complication rates (<5%)[70]
   - In resectable lesions, a partial or total nephrectomy is often performed, and provides the tissue diagnosis post-operatively
   - In metastatic lesions, biopsy of the metastatic site is preferred

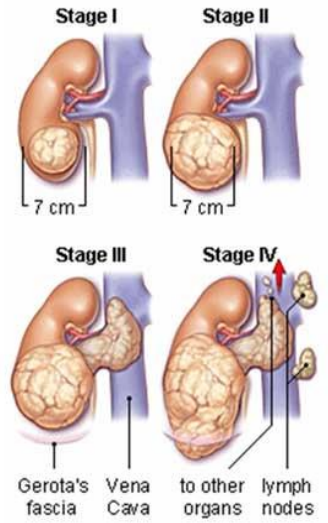
STAGING

1. **CT Abdomen**
   - Perinephric invasion, adjacent organ invasion
   - Extension into renal vein, IVC
   - Lymph node enlargement
   - Liver metastases

2. **CT Chest**
   - For lung metastases

3. **Bone scan**
   - Indicated in patients with abnormal ALP or bone related complaints with known renal mass

4. **MRI with gadaolinium of abdomen and heart**
   - Superior to CT for evaluation of IVC and right atrium involvement



[70] J Urol. 2007 Aug;178(2):379-86.

AJCC 2010 TNM Staging for Renal Cell Carcinoma

Primary Tumour (T Staging)	
Tx	Primary tumour cannot be assessed
To	No evidence of primary Tumour
T1a	Tumour **≤4cm**, limited to kidney
T1b	Tumour >4cm but **≤7cm**, limited to kidney
T2a	Tumour >7cm but **≤10cm**, limited to kidney
T2b	Tumour > 10cm, limited to kidney
T3a	Tumour extend into renal veins or perinephric tissues
T3b	Tumour extends into IVC below diaphragm
T3c	Tumour extends into IVC above diaphragm or wall of IVC
T4	Tumour invades beyond Gerota fascia

N Staging	
Nx	
No	No regional LN Mets
N1	Mets in regional LN

M Staging	
Mx	
Mo	No distant Mets
M1	Distant Mets

TREATMENT

RESECTABLE TUMOURS

- Surgery ± Adjuvant Therapy (i.e. IL-2) + Surveillance after resection to detect relapse early

Surgery[71]

- Laparoscopic versus open methods
- Retroperitoneal versus trans-peritoneal approach

1. **Partial nephrectomy (nephron saving – adrenal can be left alone)**
   - T1 – primary tumour of <7 cm
   - For tumours ≤5 cm (T1-T2, No, M1) both partial and radical nephrectomy provide excellent oncologic results[72] (prospective RCT)
2. **Total nephrectomy**
   - ≥T2 – primary tumour >7 cm
3. **Radical nephrectomy**
   - Done in T2 disease – entire kidney together with Gerota's fascia and nearby lymph nodes (i.e. around renal hilum)
     - Gold standard for localised RCC with a normal contralateral kidney.
     - As long as have clear margins = good
   - In T3/T4 disease, aim for radical nephrectomy and removal of structures affected e.g. adrenal gland + abdominal lymph nodes ± thrombectomy (involvement of IVC)

Adjuvant chemotherapy

- If patient underwent definitive surgery = no established role for adjuvant therapy
- Currently available cytostatics are ineffective for the treatment of metastasized RCC as response rates are low (5-15%) and most responses are short lived

Surveillance after resection to detect relapse early

[71] uptodate: Definitive surgical management of renal cell carcinoma
[72] Eur Urol. 2011;59(4):543.

Patients who cannot undergo resection
- Most small tumours grow slowly and do not become symptomatic or metastasise – reasonable to manage conservatively with periodic re-evaluation
- Alternatives: (heat) radiofrequency ablation, (freezing) cryotherapy of lesions

Complications of Nephrectomy
- Operative – operative mortality rate is approximately 2%.
  - General anaesthesia – atelectasis, AMI, pulmonary embolism, CVA, pneumonia and thrombophlebitis
  - Pleural injuries can result in pneumothorax
  - Injury neighbouring organs – gastrointestinal organs / major blood vessels
- Post-operative
  - Temporary or permanent renal failure
  - Ileus
  - Superficial and deep wound infections

ADVANCED TUMOURS

Immunotherapy
- High dose interleukin-2 – associated with good results in patients whose tumours respond to treatment, as treatment can induce long-term remissions without relapse. However, associated with high toxicity and often not tolerable
- Cytoreductive nephrectomy performed prior to starting immunotherapy can improve survival (primary tumour acts as an 'immunologic sink' of activated immune cells)

Molecular targeted therapy
- Sorafenib – an inhibitor of tyrosine kinase → blocks intracellular domain of the vascular endothelial growth factor (VEGF) receptor
- Bevacizumab – monoclonal antibody against VEGF

Prognosis

Stage I (T_1N_0):	>90% 5 year survival
Stage II (T_2N_0):	75-90%
Stage III (T_3N_0/N_1):	60-70%
Metastatic disease:	<10%

RENAL ANGIOMYOLIPOMAS

Most common benign tumour of the kidney and composed of blood vessels, smooth muscle and fat cells

RISK FACTORS
- Can be sporadic or
- a/w tuberous sclerosis complex (TSC) or pulmonary lymphangioleiomyomatosis (LAM)
  - TSC is present in about 10% of patients with clinically dx renal AML
  - TSC-associated AML are often multiple and affect both kidneys

CLINICAL FEATURES / COMPLICATIONS
- Most patients with sporadic AML are asymptomatic and usually are incidentally detected on renal imaging
- **Complications** → Retroperitoneal haemorrhage, Haematuria, Renal impairment

INVESTIGATION
- Imaging Studies – ultrasound, CT, MRI kidneys
  - Demonstration of fat in the tumour
    - Hypoechogenic on U/S
    - Low attenuation value on CT
    - Bright on T_1 images and dark on T_2 images on MRI
- Biopsy – image guided percutaneous needle biopsy as alternative to surgical exploration

TREATMENT
- Mostly conservative management
  - Repeat imaging studies – yearly to r/o rapid tumour growth
- AML ≤ 3cm and growing
  - Radiofrequency ablation
  - Cryoablation
- AML >4cm and with high vascularity – prophylactic surgery to prevent haemorrhage
  - Nephron-sparing surgery
  - Selective renal arterial embolization
  - Radical nephrectomy KIV tumour thrombectomy

BLADDER CANCER

EPIDEMIOLOGY
- 2nd most common urological CA – found in 1.9-10% of patients with microscopic haematuria
- Increasing incidence with age (80% diagnosed in patient ≥60 years old)
- 10th most frequent cancer in males in Singapore, 4:1 male predominance
- Most commonly transitional cell carcinoma (TCC)

PATHOLOGY
- TCC is the most common tumour of the bladder (>90%)
  - Exposure to carcinogenic substances in the urine → FIELD CHANGE EFFECT → thus urothelial tumours often occur multifocal
  - Divided into non-muscle-invasive / superficial (60-75%) or muscle-invasive

- Other types of bladder tumours: adenocarcinoma (1%, arises from remnant of the urachus in the dome of the bladder), squamous cell carcinoma (7-9%, due to chronic irritation e.g. long term indwelling catheter or untreated bladder stone)

RISK FACTORS

Occupational Risk Factors	- Exposure to aromatic amines (printing, textile, rubber, cable and plastic industries) - Industrial Chemicals – B-naphthylamine, aniline-containing dyes – synthetic rubber worker
Non-occupational Risk Factors	- Cigarette smoking – risk increased 2-3x - Chronic analgesia abuse (phenacetin) - Chronic parasitic infection (schistosoma haematobium – cause **squamous metaplasia not TCC**) – any travel to Egypt - Chemotherapy – i.e. cyclophosphamide (induce haemorrhagic cystitis) - Chronic cystitis – i.e. pelvic radiation - Others: males, age >50, personal hx of gross haematuria

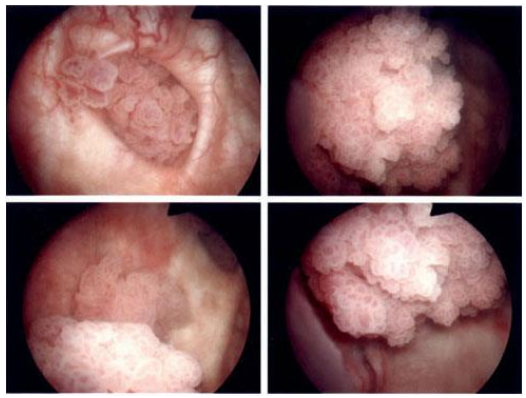
PRESENTATION
- **Persistent Painless Haematuria** is the most common presenting symptom (90%) – typically gross, painless, intermittent, occurring throughout the stream
- **Lower Urinary Tract Symptoms (LUTS)**
  - Irritative symptoms (frequency, dysuria, urgency) suggestive of carcinoma in-situ,
  - Obstructive symptoms (decreased stream, intermittent voiding, feeling of incomplete voiding, strangury) indicate tumour obstructing ureteric orifice
  - Dysuria – persistent pyuria
- **Pain** – in locally advanced or metastatic tumour → flank pain due to urinary obstruction, suprapubic pain due to local invasion, bone pain due to metastasis
- **Loco-Regional Complications** – extension to other organs: fistula formation
  - Vesico-colic fistula with pneumaturia
  - Vesico-vaginal fistula with incontinence
- **Metastatic Complications**
- **Constitutional symptoms** – LOW, LOA, fatigue

DIAGNOSIS
1. Baseline blood investigations
2. Urine cytology for malignant cells
3. Imaging – IVU / CT urogram or u/s to detect synchronous lesions (3% chance of prox. tumour)
4. Flexible cystoscopy or Rigid cystoscopy KIV TURBT (diagnostic, therapeutic & staging modality)
   a. Describe: exophytic papillary lesion that ± invade the muscular bladder wall
   b. Cystoscopy with cell brushings and biopsy
5. Chest X-Ray or CT chest (T2 disease)
6. Bone Scan

STAGING
1. CT abdo/pelvis for T, N and M staging
2. Transurethral resection of bladder tumour (TURBT) with histopathology

Ta	Superficial, does not involve lamina propria
Tis	Carcinoma in-situ: "flat tumour"
T1	Superficial, involves lamina propria (up to muscularis propria)
T2a	Superficial involvement of muscularis propria – up to inner half of muscle
T2b	Deep involvement of muscularis propria – up to outer half of muscle
T3a	Microscopic extension outside bladder (from TURBT specimen)
T3b	Macroscopic extension outside bladder
T4a	Invasion of prostate, vagina, uterus
T4b	Invasion of lateral pelvic walls, abdominal wall

Generally can be divided into 2 main groups:
(a) **Superficiel tumour** (70-80% of patients) – Ta, Tis, T1
(b) **Muscle-invasive tumour** (20-30%) – ≥T2



MANAGEMENT DEPENDENT ON STAGE

SUPERFICIAL TUMOUR (TA AND T1 LESIONS)

- Primary treatment is **TURBT** of the tumour
- **Intravesical therapy** indicated in patients with high risk of tumour recurrence or tumour progression (high grade, multi-focality, multiple recurrences, tumour size >3cm, primary or coexisting carcinoma in-situ, prostatic urethral involvement)
  - Bacillus Calmette-Guerin (BCG) – 1 instillation per week for 6 weeks
  - Mitomycin C – single instillation within 24hrs of TURBT – shown to decrease recurrence by 12%[73], or weekly/monthly treatments for up to 2 years

- **Follow-up:**
  - 3-monthly cystoscopy for 1 year
  - 6-monthly cystoscopy for next 4 years
  - Yearly cystoscopy thereafter
  - IVU every 2 years

  } Urine cytology with every cystoscopy

MUSCLE-INVASIVE (≥ T2 OR MORE)

- **Radical cystectomy with urinary diversion**
  - Radical cystoprostatectomy with pelvic lymphadenectomy in male – removal of bladder, prostate and possible urethra
  - Anterior exenteration with pelvic lymphadenectomy in female – removal of bladder, urethra, uterus, cervix and anterior vaginal wall
  - Note: about 50% of patients with invasive bladder cancer already have occult metastases at time of surgery

  - Ways of diverting urine output
    - Cutaneous ureterostomy (use ureters to create stoma, but easily stenosed due to small calibre; not continent)
    - Ileal conduit (a segment of ileum with ureters attached, as a stoma; not continent)
    - Neobladder construction using ileum (only if urethra not removed; continent, better quality of life)
    - Stoma with pouch construction under abdominal wall (not continent)

- Radiotherapy (not as good as surgery)
- Combined modality therapy ('bladder salvage' regime) – TUR, platinum-based chemotherapy and external beam radiotherapy

METASTATIC

Chemotherapy

- GC (gemcitabine + cisplatin)
- MVAC (MTX + vinblastine + doxyrubicin + cisplatin)

- Chemotherapy is the treatment of choice for locally advanced or metastatic bladder cancer – both neoadjuvant and adjuvant chemotherapy benefits patients with advanced bladder cancer who also undergo surgery[74]

PROGNOSIS

- Non-invasive TCC → 10-20% will progress
  - Cumulative 70% lifetime risk of tumour recurrence (non-invasive)
- Muscle-invasive – aggressive
  - >90% mortality within 2yrs in untreated patients,
  - Survival after cystectomy >50% after 5 yrs, mets usually to lung liver and bones

[73] Eur Urol. 2008;54:303-314
[74] Eur Urol. 2009;55,2:348-358

UROLITHIASIS

EPIDEMIOLOGY
- Urinary calculi occur in 1-5% of the population
- Stones may form in the kidney or the bladder – 90% of the calculi are radio-opaque
- 50% of patients with previous urinary calculi have a recurrence within 10 years

RISK FACTORS

Modifiable	- Diet - Dehydration – low urine volume - **Hyperparathyroidism** – primary hyperPTH will lead to hyperCa^{2+} - Hypervitaminosis D – massive ingestion of vitamin D - Milk-Alkali Syndrome – hyperCa^{2+} due to repeated ingestion of Ca^{2+} & absorbable alkali
Non-modifiable	- Age (majority occur during the 4^{th} – 6^{th} decade of life) - Gender (M:F – 3:1) - Cystinuria – inherited AR disease - Inborn error of purine metabolism - Chemotherapy – excess uric acid following treatment of leukaemia / polycythaemia - Idiopathic hypercalciuria - Gout

TYPES OF CALCULI

	Morphology	Pathogenesis	Clinical Features
Calcium Oxalate (75%)	'mulberry' stones covered with sharp projections	Alkaline urine	Tend to cause symptoms when comparatively small owing to their sharp surface
Struvite Stones (15%) – magnesium, ammonium, calcium phosphate	Smooth and dirty white	Strongly alkaline urine	May enlarge rapidly and fill the calyces taking on its shape – staghorn calculus
Urate Stones (5%)	Hard, smooth, faceted and light brown in colour	Acid urine	Radiolucent
Cystine Stones (2%)	Usually multiple stones	Acid urine and metabolic origins	Radio-opaque – cause of sulphur content
Xanthine (rare)		Due to inborn error of metabolism	RARE
Pyruvate Stones (rare)			

PATHOLOGY
- Cause of stone formation (1) super-saturation (2) infection (3) drugs
- Most important cause of stone formation is urine become supersaturated wrt. stone-forming salts, such that they exceed their solubility → precipitate out of solution and form crystals
  - Crystals may flow out with urine or become retained in the kidney at anchoring sites that promote growth and aggregation → stone formation
- Urinary tract infections can also cause infection stones – **struvite stones** (magnesium ammonium phosphate) form in Proteus vulgaris infections as this organism (urea splitting bacteria) splits urea into ammonium, generating alkaline urine
  - More common in women (more prone to UTI)
  - Proteus, Pseudomonas, Klebsiella (note: E. Coli is not capable of splitting urea therefore not a/w struvite stones)
- Drug-induced stone – medication or their metabolites can ppt in urine causing stone formation
- Bacteria can also form nidi for the formation of any kind of stone

ANATOMY OF THE URETER
- Each ureter is 25-30cm long and approximately 3mm in diameter
- The ureter is a hollow muscular tube which commence at the renal pelvis and terminates at its entry into the bladder → on plain radiograph:
  - Ureter exits from renal pelvis (L1 on left, L1/L2 junction on the right)
  - Runs along tips of the transverse process
  - Crosses in-front of the sacroiliac joint
  - Runs laterally on the pelvic wall towards the ischial spine
  - Curves anterior-medially to enter the bladder through the back at the vesicoureteric junction
- Points of constriction
  - Pelvic-ureteric junction (PUJ)
  - Pelvic brim (near bifurcation of the common iliac arteries)
  - Veisco-ureteric junction (VUJ) – entry to the bladder

PRESENTATION DEPENDS ON SITE

Pain
- Typically begins in the early morning and intensifies over 15-30min.
- Develops in paroxysms and related to movement of stones in the ureter

Clinical Presentation
- Obstruction – at pelvic-ureteric junction, in the ureter, at bladder neck (rarely at ext. urethral meatus)
- Ulceration – of calyces, pelvic mucosa or bladder → lead to haematuria
- Chronic Infection → lead to pyelonephritis, pyonephrosis, urosepsis, kidney failure

Renal stones
- Most often asymptomatic unless the stone gets lodged in the pelviureteric junction causing hydronephrosis and subsequent infection → pyonephrosis
- Vague flank pain may occur
- Small stones are commonest, but large-branched staghorn calculi may occur and completely fill the pelvis and calyces – if bilateral kidneys affected → chronic renal failure

Ureteric stones
- Even small stones can cause severe symptoms as the ureter is narrow
- Classic ureteric colic pain – severe, intermittent loin-to-groin pain (± to ipsilateral testis/labia)
- Haematuria – gross or microscopic (occur in 95% of patients)
- Can cause upper urinary tract infection → fever, pain
- Stone at VUJ – frequency, urgency, dysuria can result

Bladder stones
- May originate in the kidney with enlargement in the bladder – phosphate encrustation OR
- Formed primarily in the bladder
- May be asymptomatic
- Can cause irritative urinary symptoms – frequency, urgency
- Haematuria
- If infection is present – dysuria, fever, etc.
- In treating of bladder stones, also treat underlying cause – i.e. treating BPH if it is causing urinary retention and hence precipitating stone formation

HISTORY

Chronology of stone events
- Age of 1st stone presentation
- Number and size of stones
- Spontaneous passage vs. need for intervention
- Symptoms during the past episodes

Stone formation (systemic disease / underlying metabolic disorder)
- Crohn's
- Hyperparathyroidism, hyperthyroidism
- Gout, renal tubular acidosis
- Metastatic cancer, paraneoplastic syndrome

Stone formation (family, drug, social hx)
- Family hx of stones
- Intake of medications that increase risk of stone formation – antacids, salicylic acid, anti-viral (acyclovir, indinavir)
- Occupation hx
- Diet – high protein and sodium intake increase risk of stone formation

PHYSICAL EXAMINATION
- In ureteric colic, symptoms are often out of proportion to signs – no guarding, rebound
- If the patient has pyelonephritis, renal punch may be positive
- Otherwise unremarkable examination

INVESTIGATIONS

1. **Haematological**
   - Full Blood Count – mild leukocytosis (↑ WBC)
   - Serum Ca (if raised do PTH)
   - LFTs (albumin)
   - Serum Uric Acid
2. **Urine tests – dipstick, UFEME, urine culture/sensitivity, 24 hr urine collection**
   - 24 hr urine collection of metabolic profile → Ca^{2+}, Na^{+}, Oxylate, Uric Acid, PO_4^{-}, Mg^{2+}
   - Haematuria – microscopic or gross
   - Pyuria, micro-organisms (UTI)
   - pH of urine (acidic vs. alkaline stones)
3. **CT Scan**
   - CT KUB (non-contrast) – for first time presentation
   - Replaced IVU as the diagnostic test of choice in the acute setting to evaluate for stones
   - CT Urogram (tri-phasic)
     - No contrast – any stones, gross abnormalities
     - Medullary – any cysts, parenchyma abnormalities
     - Delayed phase – any filling defects
     - Evaluate anatomy and reflects renal function
4. **KUB X-Ray**
   - May be able to see radio-opaque stone (90% of renal stones are radio-opaque) – differentiate with radio-lucent stones (i.e. urate stones 2° gout)
   - Look at kidney size, any renal stones
   - Trace path of ureter along tips of transverse processes, across sacroiliac joint, and medially into bladder, looking for ureteric stones & bladder stones
   - Usually for follow-up and recurrence screening
5. **Intravenous urogram (IVU)**
   - Help visualise uric acid stone (detects radiolucent stones)
   - Shows dilated urinary system 2° to stone obstruction – hydroureter and/or hydronephrosis
   - Rough indication of renal function
6. **Ultrasound of kidney or bladder**
   - Any evidence of kidney stones or complication of stones – i.e. hydronephrosis
   - Choice for patients with contrast allergies and pregnant females
   - Features of stone: echogeneic rim, posterior acoustic shadowing
7. **MAG-3 renogram**
   - If pyelonephritis present due to stone obstruction, it is valuable to measure the renal function using the MAG-3 renogram
   - The renogram gives the differential function of each kidney – in normal individuals the function should be approximately 50% on each side (out of 100% for both kidneys combined)
   - If one kidney has less than 15% of total renal function, it is not worth salvaging the kidney

TREATMENT

PRINCIPLES

- Provision of effective pain control – i.e. IM pethidine, tramadol
- Treatment of any suspected UTI – antibiotics
- Allow for spontaneous passage of stones or decide on active stone removal
  - **Kidney Stones** – often asymptomatic – treatment pre-emptive in anticipation of potential complications (observe if <5mm and monitor for growth, treat if >7mm)
  - **Ureteric Stones** – symptomatic – trial of passage if <7mm, otherwise treat
- Treat underlying aetiology of stone formation – i.e. bladder stones sec to BPH tx with TURP, hypercalcaemia → treat disease if possible

CONSERVATIVE

- Stones < 5mm can be treated conservatively as 70% will be passed out; only treat if they do not pass out after 4 to 6 weeks, and/or cause symptoms
- Spontaneous stone passage aided with prescription of narcotic pain medications as well as daily alpha blocker therapy (tamsulosin) → improve stone passage by up to 20% → check for postural hypotension when patient is on tamsulosin
- High fluid intake
  - Drink about 2-3L of water/day or till urine clear
  - A glass of water before sleep is good practice
- Diet modifications
  - ↓ intake of protein-rich food red meat, animal internal organs – i.e. intestines, liver (for uric acid stones)
  - ↓ intake of oxalate rich food – i.e. peanut, spinach, beetroot, strawberries
  - Coffee and Tea in moderation (for calcium stones)
  - ↓ intake of sugars (fructose) – i.e. soft drinks, sweets, chocolate
  - ↑ intake of fibre – i.e. fruits, veg, high fibre diet (wholemeal bread, wheat & corn)
  - ↓ Salt Intake
  - **Normal Calcium Diet**
- Chemical dissolution – limited, slow process
  - Uric acid stones →alkalinising urine with baking soda or potassium citrate
  - Struvite stones → acidifying urine
- Urine should be strained with each void and radio-opaque stones tracked with KUB X-Ray

Summary of treatment modalities:

Location	Size	Treatment
Renal	< 5mm	Conservative management unless symptomatic/persistent
	5-10mm	ESWL
	10-20mm	Either ESWL or PCNL
	> 20mm	PCNL
Upper ureter	< 5mm	Conservative management unless symptomatic/persistent
	5-10mm	ESWL
	> 10mm	URS with lithotripsy
Middle ureter/ Distal ureter	< 5mm	Conservative management unless symptomatic/persistent
	> 5mm	URS with lithotripsy ESWL
Bladder	< 30mm	Cystolitholapaxy
	> 30mm	Open cystolithotomy (also if there are multiple stones)

SURGICAL INTERVENTION

Indications (7s):

- 7s → size, site, symptoms, stasis, stuck, sepsis, social
- S/S: Constant pain
- Stone complications
  - Obstructs urine flow
  - Causes urinary tract infection
  - Damages renal tissue or causes significant bleeding
  - Increase in size
- Unlikely to resolve with conservative treatment:
  - Does not pass after one month
  - Too large to pass spontaneously

Complications of treatment:

- Hematoma / Significant Bleeding
- Urinary tract infection
- Ureteric Injury – perforation / ureteric avulsion
- Failure of procedure –i.e. unable to assess stone with URS

Types of treatment available:

1. Extracorporeal shock wave lithotripsy (ESWL)
   - Calcium oxalate dihydrate, uric acid (may be difficult to target) and struvite stones fragment easily, but calcium oxalate monohydrate, calcium phosphate and cystine do not
   - Used for renal stones and upper ureter stones (size <2cm) – not so good for lower system due to difficulty in access
   - Contraindicated in pregnancy, untreated UTI, low platelets, untreated bleeding diathesis, distal obstruction (i.e. stricture)
   - Complications (1) procedure related (2) stone related
     1. skin bruising, perinephric / subcapsular haemorrhages, pancreatitis, urosepsis (if stone is infected)
     2. incomplete fragmentation

2. Percutaneous nephrolithotomy (PCNL)
   - Done for renal stones that are too large for ESWL to disintegrate
   - Contraindicated in uncorrected bleeding diathesis, patients unfit for GA
   - Complications (1) procedure related (2) stone related
     1. Hydrothorax, haemorrhage (early: puncture tract, delayed: from renal AVF), urosepsis, perforation of adjacent organs (rare), urinary fistula
     2. incomplete fragmentation

3. Ureterorenoscopy (URS) lithotripsy (Holmium:Yttrium Aluminium Garnet Laser lithotripsy, can also be done by pneumatic drill, electrohydraulic means)
   - For stones along the ureter
   - Risk of urosepsis, strictures, urethral injury, UTI

4. Cystolitholapaxy for bladder stone

5. Open surgery (pyelolithotomy or ureterolithotomy) – rarely done; only if failed other management strategies, altered anatomy, performing open surgery for another reason anyway, possible indications (1) large staghorn stone, (2) non-functioning kidneys with stone – to prevent infection and malignant transformation

Adjuncts:

- Double-J stent (or DJ stent) – inserted to stent the urinary system when worried that stone fragments after ESWL may cause obstruction e.g. when ESWL used for treatment of a large stone; or if system is obstructed to begin with, may want to stent to ensure good drainage after surgery

APPROACH TO ACUTE URINARY RETENTION[75]

- Acute Urinary Retention (AUR) is the most common urologic emergency – defined as a sudden and often painful inability to void despite having a full bladder
- Chronic Urinary Retention – painless retention a/w increased volume of residual urine

EPIDIMILOGY

- Incidence ↑ with age – 10% of men >70yrs and 30% of men >80yrs have an episode of AUR

PATHOPHYSIOLOGY[76]

1. Outflow Obstruction → flow of urine is impeded by mechanical (physical narrowing of urethral channel) and/or dynamic (tension within and around the urethra) factors
2. Neurological Impairment → 2° to disruption of sensory / motor nerve supply to detrusor muscle
3. Over-distention → precipitating event results in an acute distended bladder in the setting of an inefficient detrusor muscle
4. Medications → usually involving anticholinergic and sympathomimetic drugs

CAUSES

Mechanical Outflow Obstruction	Extraluminal	Benign Prostate Hyperplasia – 53% Prostate Cancer – 7.5% Faecal impaction / Constipation – 7% Pelvic / GI / Retroperitoneal masses – extrinsic bladder neck compression Pregnancy UV prolapse / Pelvic Organ Prolapse – cystocele / rectocele	
	Intramural	Tumour of the bladder neck (TCC) Urethritis (UTI) – 2% Urethral stricture from STD, prev instrumentation – 3.5%	
	Intraluminal	Stones – 2% Urethral strictures Blood clot – can be due to intra-vesicular bleeding from bladder tumour Foreign body	
Non-Mechanical (Functional)	Infection	Acute prostatitis – usually caused by E. coli / Proteus	
	Neurologic Impairment	Peripheral Nerves	**Diabetic neuropathy** **Radical Pelvic Surgery** Guillain-Barre Syndrome
		Spinal Cord	**Spinal Cord Trauma** Spinal Stenosis / Transverse myelitis / Spinal Cord hematoma or abscess
		Brain	**Cerebrovascular Disease** Parkinson's Disease / Multiple Sclerosis / Normal Pressure Hydrocephalus / Shy Drager Syndrome
	Drugs	**Sympathomimetic**	Alpha adrenergic agents – ephedrine, phenylephrine, pseudoephedrine Beta adrenergic agents – terbutaline
		Anticholinergic	
		Cardiac Meds	Antihypertensive – Hydralazine / Nifedipine Antiarrhythmic – Quinidine / Procainamide
		Pain Medications	NSAIDs – indomethacin Opioid analgesics (morphine, vincristine)
		Antihistamines	
		Antiparkinsonian	Levodopa / Bromocriptine
		Psychiatric Meds	Antidepressants / Antipsychotics Carbamazepine
		Others	Hormonal agents, Muscle relaxants, Dopamine,
	Others	Prolonged immobility Post-anaesthesia Post-operative complications – post rectal / gynaecological surgery Pain / Trauma	

[75] Am Fam Physician. 2008 Mar 1;77(5):643-650
[76] uptodate: acute urinary retention

HISTORY

Presenting Complain – confirmation of ARU:
- Inability to pass urine
- Suprapubic distension with pain (unlike chronic retention of urine which is painless) – severe!

History of Presenting Complain:
- Characterize current episode of ARU
- Previous history of urinary retention / urinary infection
- Precipitating events – recent surgery, new medications, pelvic trauma, immobilization, alcohol consumption, genitourinary instrumentations,

History suggestive of aetiology:
- BPH → previous hx of voiding / obstructive symptoms [DISH]
  - Terminal dribbling, intermittency/incomplete emptying, poor stream, straining to pass urine, hesitancy
- UTI / Acute Prostatitis → fever, dysuria, frequency, urgency, nocturia, haematuria
- Strictures → Previous urethral instrumentation or STD
- Detailed medication history
- Malignancy → constitutional symptoms / gross painless haematuria (i.e. TCC)
- Stones → Previous history of ureteric colic pain or stones
- Spinal Cord Compression → younger patients, history of cancer or IV drug abuser, presence of back pain or neurological symptoms
- Neurogenic Bladder → Lower limb weakness/paralysis, bowel incontinence, back trauma, history of spinal disease e.g. PID, spinal stenosis

Complications:
- **Infection** – symptoms of UTI
- **Stone** disease (if in the bladder, usually asymptomatic)
- **Renal failure** (more likely in chronic retention) – vomiting, lethargy, drowsiness
  - Since duration of obstruction in AUR is short, there is usually insufficient time for a significant elevation in serum creatinine

PHYSICAL EXAMINATION
- General condition – sallow appearance, scratch marks, pedal oedema, etc (uraemia)
- Abdomen
  - Palpable bladder – deep suprapubic palpation → tender
    - Bladder percussible when it contains at least 150ml of urine, palpable when > 200mls
  - Other pelvic masses – fibroid, gravid uterus, ovarian cyst
  - Faecal loading
  - Bilateral enlarged kidneys (hydronephrosis)
- Digital rectal examination
  - Any saddle anaesthesia
  - Anal tone
  - Prostate enlargement – firm and smooth or hard, craggy, irregular, rectal mucosa not mobile?
  - Faecal impaction
- Neurological examination
  - LMN paralysis of the lower limbs?
  - Any sensory level present?

INVESTIGATIONS (FOR CAUSES)
1. Bloods/Urine
   a. Urine dipstick, UFEME and culture/sensitivity (UTI, hematuria)
   b. U/E/Cr: raised creatinine (renal impairment secondary to obstructive nephropathy)
   c. FBC: raised TW (infection) – not usually done
2. Imaging
   1) KUB for stones, faecal loading
   2) U/S bladder: (1) stones, (2) tumour, (3) intravesical protrusion of prostate (4) residual urine volume
   3) U/S kidney, ureters: hydronephrosis, hydroureter (obstructive complication)

*** No role for the testing of prostate specific antigen (PSA)**
- to be done 4-6/52 later (as ARU can cause raised PSA)
- PSA velocity (rate of rise), free/total PSA, PSA density (= PSA/prostate volume)
- >/= 2 readings 2/52 apart
- Causes of raised PSA
  i. Cancer
  ii. BPH [usually <40]
  iii. Prostatitis
  iv. Instrumentation /catheterization >11days
  v. ARU
  vi. UTI

IMMEDIATE MANAGEMENT – CATHETERISATION

- 1st choice: U**rethral Catheterisation (14f) – rapid & complete decompression of bladder**

(Contraindication: S/S of urethral injury – (a) blood at urethral meatus, (b) high-riding prostate – more relevant in the trauma setting)

- If cannot pass into bladder:
  a) **enlarged prostate** → use thicker catheter (20-22f) (stiffer, easier to pass through)
  b) **urethral stricture** (clue: catheter is stuck quite proximally along the penile urethra / Past Hx of instrumentation – i.e. TURP /STD) → smaller gauge catheter (10-12F)
- Do not push too hard – may cause false passage creation if the obstruction is due to a stricture

- If urethral catheterisation fails, perform **suprapubic (SP) catheterisation**
  - Requires distended bladder which pushes the surrounding bowel loops away so that risk of bowel injury is lower
  - Local anaesthetic injected 2 FB above pubic symphysis
  - Small incision made in the skin and fascia, and trocar-type suprapubic tube is inserted – catheter advanced over the trocar and sutured in place
  - When a gush of urine is seen, the suprapubic catheter is inserted and secured
  - SP catheter good for patients expected to require long-term bladder drainage → prevents bladder neck and urethral dilation – prevents urinary incontinence, avoids risk of urethral strictures

TREATMENT

1. **Treat reversible causes**
   - Stop drugs that may have precipitated ARU – i.e. anticholinergic, anti-depressants, anti-histamines
   - Relieve constipation with fleet enema, lactulose, senna etc.
   - Treat any urinary tract infection if present

2. **Anticipate complications**
   (a) Post-obstructive diuresis = diuresis that persists after decompression of bladder
   - Urine output **>200ml/hr for 2 hours or more**
   - Due to tubular damage from chronic obstruction of drainage of the pelvicalyceal system, resulting in transient impairment of concentrating function. Usually seen in CRU, representing appropriate attempt to get rid of excess fluid in the body during period of obstruction.
   - Can result in hypotension and electrolyte abnormalities (hyponatraemia, hypokalaemia, hypovolaemia)
   - Close monitoring of urine output and fluid/electrolyte status with appropriate replacement and resuscitation

   (b) Haemorrhage ex-vacuo (transient haematuria)
   - Bladder mucosal disruption with sudden emptying of greatly distended bladder
   - Usually self-limiting, rarely clinically significant
   - Drain urine in 500-750ml aliquots, with 15-20min intervals between each

   (c) Hypotension
   - Secondary to vasovagal response or relief of pelvic venous congestion

3. **Trial-off catheter – to be attempted before considering surgical intervention**
   - Initial bladder decompression can be followed by a trial without catheter (i.e. catheter removal after 2-3 days) and determination if patient can void successfully
   - Take off catheter and watch patient's output, as well as perform bladder scan to measure bladder volume
   - If patient cannot pass urine and bladder volume >400ml → re-catheterise
   - When patient passes urine, can perform
     1) Urodynamic evaluation – is retention directly related to outlet obstruction with concomitant elevation in bladder presser or due to inefficient bladder muscle
     2) Bladder scan post-micturition to check residual volume

Failed Trial of void:

1. Long term catheterization
   a. Disadvantages: risk of UTI, urosepsis, trauma, stones, urethral strictures, erosion, prostatitis and potential development of squamous cell carcinoma
2. Clean intermittent self-catheterization:
   a. First-line treatment for UR caused by neurogenic bladder
   b. Advantages: improved rate of spontaneous voiding (pt can PU in btw), decrease complications such as renal failure, upper urinary tract deterioration and urosepsis
3. Transurethral resection of the prostate (TURP – if sec to BPH)
   a. Recommend for elective TURP after 4-6 weeks (> 30 days) following an episode of AUR – reduce intra-operative risk (i.e. bleeding and infection)

1 and 2 are done while waiting for medical therapy (i.e. alpha blockers and 5-alpha reductase inhibitors) to work

- Patients with BPH and have ARU treated with catheterization have a high likelihood of recurrent episode of urinary retention after successful trial off catheter – 56% within a week and 68% within a year
- Treatment with alfuzosin in patients who have had a successful voiding trial following ARU can delay recurrence of ARU and need for TURP

Urinary obstruction + Fever → Admit! (Uro emergency)

BENIGN PROSTATE HYPERPLASIA (BPH)

EPIDEMIOLOGY

- Affect most men over the age of 50 but only 10% present with symptoms
- Frequency rises with age after the age of 30, reaching 90% in men older than 80
- 25-50% of men with micro/macroscopic evidence of BPH will progress to clinical BPH
  - **Men > 55 yrs old with LUTS**
  - **Qmax < 15ml/s**
  - **Prostate size > 20g without cancer**

PATHOLOGY

- **Stromal – epithelial interaction theory**
  - Proliferation of both the epithelial and stromal components of the prostate with resultant enlargement of the gland (ratio of stroma: epithelial in normal = 2:1. In BPH = 5:1)
  - Commonly occurs in the central zone of the prostate
- **Hormones**
  - Major stimulus: **dihydrotestosterone** (produced from testosterone by **5-alpha reductase**)
  - stimulates prostate growth and maintenance of size (inducing growth factors and altering the extracellular matrix)
  - Age-related increases in oestrogen levels may also contribute to BPH by increasing the expression of dihydrotestosterone receptors on prostatic parenchymal cells
- **Stem cell theory**
  - Abnormal maturation and regulation of cell renewal process – increase in size of prostate due to decrease in cell death
  - Hormonal factors, growth factors and oncogenes all influence this balance
- **Static and dynamic components of prostatic obstruction**
  - STATIC – includes the stromal, epithelial cells and the extracellular matrix → androgen ablation, TURP targets this component
  - DYNAMIC – Obstruction to urine flow contributed by smooth muscles of the prostate. Mediated by alpha-1 receptors in the prostate stroma, bladder neck and prostatic capsule.

PRESENTATION

- Severity of symptoms depends on degree of encroachment on prostatic urethra
- **Lower urinary tract symptoms** (LUTS): **obstructive (**predominate) >> irritative symptoms (obstruction of the prostatic urethra)
  - Irritative symptoms significant for complications of urine retention: UTI, stones

Obstructive	Irritative
Terminal **d**ribbling / **D**ouble voiding (pis-en-deux) **I**ntermittency / **I**ncomplete voiding **S**training to pass urine (strangury) / Weak **s**tream **H**esitancy – difficult to start micturition Prolonged micturition **Obstructive S/S predominate**	Frequency Urgency Nocturia Dysuria* Urge incontinence Irritative S/S significant for Cx of urine retention: UTI, stones

*dysuria suggests on-going infection / inflammation – not grouped under either irritative or obstructive

- Cardinal Features
  - Obstructive S/S – hesitancy, poor stream, terminal dribbling, incomplete voiding
  - Irritative symptoms – frequency, nocturia
  - Acute retention of urine / Chronic retention of urine (CRU)
  - Haematuria – from ruptured dilated bladder neck veins
  - Occasionally, palpable bladder

- Complications of obstructive uropathy:
  - Hydroureter with reflux of urine
  - Hydronephrosis
  - Pyonephrosis
  - Pyelonephritis and impaired renal function

  - **Acute urinary retention** (previous admissions and IDC)
  - **UTI, Stones Formation**: irritative symptoms, haematuria, dysuria
  - **Hydronephrosis, pyelonephrosis, renal impairment**: loin pain, fever, polyuria/ anuria
  - **Overflow incontinence** 2° to CRU with high post-void residual volume in the bladder
  - **Hernia** – secondary to chronic straining
  - **Fever** (UTI – pyelonephritis from ascending infection)

- Try to Rule out other differentials:
  - **Stricture/ bladder neck contractures:** previous instrumentation or STDs causing urethritis / post-TURP
  - **Drug causes:** codeine (cough mixture), BB, anti-cholinergic, TCAs
  - **Chronic constipation**
  - **Ca bladder neck/ Ca Prostate:** LOW, LOA, bone pain, haematuria
  - **Neurogenic bladder**

- Other aspects of history: Social history (effect on lifestyle)

American Urological Association BPH Symptom Score Index Questionnaire

Having to urinate more frequently, as well as more urgently, can definitely interrupt the flow of your day. You should know that frequent urination is often a symptom of benign prostatic hyperplasia (BPH), a noncancerous enlargement of the prostate gland. BPH is a common condition among men over the age of 50. Waking up several times a night to urinate and having a weaker, slower, or delayed urine stream are other common symptoms.

_____ Circle the number that best applies to you

Patient Name **Date**

	not at all	less than 1 time in 5	less than _ the time	about _ the time	more than _ the time	almost always
1. Incomplete Emptying Over the last month how, often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5
2. Frequency During the last month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
3. Intermittency During the last month, how often have you stopped and started again several times when you urinate?	0	1	2	3	4	5
4. Urgency During the last month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Weak Stream During the last month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Straining During the last month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
	None	1 Time	2 Times	3 Times	4 Times	5 Or More Times
7. Nocturia During the last month, how many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5

Add the score for each number above, and write the total in the space to the right
SYMPTOM SCORE = 1-7 MILD 8-19 MODERATE 20-35 SEVERE TOTAL_____

0=Delighted 1=Pleased 2=Mostly Satisfied 3=Mixed 4=Mostly Not Satisfied 5=Unhappy

8. Quality of life How would you feel if you had to live with your urinary condition the way it is now, no better, no worse, for the rest of your life.	0	1	2	3	4	5

PHYSICAL EXAMINATION

Inspection

- Vitals: BP for HPT? (CRF) Fever? (UTI) Urine output? (CRF)
- Already on IDC? (ARU) Diapers? (incontinence) Hematuria? (UTI, stones)
- Sallow? Anemia? (of CRF/ underlying malignancy) Cachexia (CA)
- Hernia repair scar? (hernia)

Palpation

- Check for hernias
- Abdominoperineal masses (faecal loading, masses to compress)
- Any ballotable kidneys? (Hydronephrosis, Pyelonephritis)
- Renal punch? (Pyelonephritis)
- Palpable tender bladder in (ARU) non-tender (CRU)
- Pedal/ sacral oedema (CRF)
- Bony tenderness (tumour)

Confirm diagnosis and R/O DDx:

- DRE
  - impacted stools
  - prostate (benign):
    1. smooth, symmetrically enlarged (>3FB), no nodule
    2. median sulcus is intact
    3. Firm consistency
    4. Rectal mucosal is smooth, not attached to prostate

INVESTIGATIONS

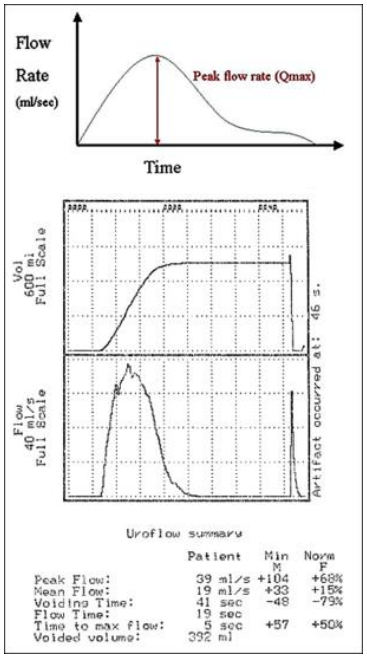
Blood

- FBC: anemia, raised WBC
- U/E/Cr: dehydration, raised creatinine → renal impairment due to chronic obstruction
- UFEME, cytology, urine c/s: for UTI and screen for cancer
- PSA (done 4-6/52 later to avoid false +ves): normal <4

Imaging

- **US kidney** – hydronephrosis, stones
- **US bladder** – PVRU >100ml, bladder stone, measure intravesical prostatic protrusion (IPP)
- **US prostate** – size, ?cancer
- KUB for bladder stone
- Cystoscopy to rule out stones, strictures/ bladder neck obstruction or cancer
- F-V charts for patients with frequency or nocturia as predominant symptoms
- Uroflowmetry (see below)

- **Uroflowmetry** to confirm obstruction to urinary outflow (IMPT!!)
  1. Normal bell shaped curve, saw tooth appearance
  2. Volume voided (>150ml to be valid): too low (falsely low peak flow rate), too high (falsely long duration, increase RU)
  3. Normal peak flow rate (Qmax) > 15ml/sec
  4. Total duration ~ 30sec (male), 20sec (female)
  5. Residual urine ~0ml in young adults, can accept up to 100-200ml in elderly



A) BOO with normal detrusor muscle: max flow rate 10ml/sec, prolonged flow.

B) BOO with abdominal straining: intermittent flow, peak flow rate may be normal or high, especially if outlet resistance is reduced

Uroflow
- Diagnosticate → Qmax <15ml/s with voided volume > 150ml and RU <150ml
- Prognosticate → Qmax < 10ml/s better outcomes after TURP than those with higher Qmax
- Does not differentiate BOO with detrusor dysfx →requires VUDS (video, urodynamic studies)
- ± urodynamic studies, TRUS with biopsy TRO prostate cancer if PSA >10

PROBLEMS
- Acute/chronic urinary retention, complicated by bladder stones & recurrent UTI
- Gross haematuria (after excluding other causes)
- Renal impairment secondary to outflow obstruction
- Co-existence of prostate cancer

MANAGEMENT
- Divided into watchful waiting, medical management, and surgical management
- Objectives of treatment: Rapid and sustained relief of symptoms, prevent long-term complications, improve patient's quality of life

I. Watchful waiting
- Suitable for patients with minimal symptoms, no complications and normal investigations
- Monitor patient's symptoms and clinical course annually

II. Medical treatment

1. Alpha blockers (Prazosin, Terazosin, Tamsulosin, **Alfuzosin**)
   - 3 days to be effective, 1st line therapy
   - Treatment of symptoms
     - Block α-1 adrenergic receptors in the bladder neck, prostate and urethra
     - Result in decreased outflow resistance and decreased bladder instability
   - **ALFAUR trial (alfuzosin in AUR – 10mg OD)** → increased successful trial off catheter (TOC) in men with 1st episode of spontaneous AUR and continued use reduced need for BPH surgery during a 6 month treatment period[77]
   - SEs: **postural hypo. (esp. if patient is on anti-HTN), dizziness, lethargy, light-headedness**

2. 5-alpha reductase inhibitors (Finasteride, **Dutasteride**)
   - Reduce prostate size (20%), decrease need for surgery (10-15%)
   - Takes 3-6 months to be effective and may require long term maintenance
   - Treats the disease (not just the symptoms) by inhibiting the conversion of testosterone to dihydrotestosterone by 5-alpha reductase → reduced prostate size
   - Proven to decrease need for surgery and acute retention rates
   - Only effective after 6 /12 (counsel the patient!), and in prostates >40g
   - **PCPT trial (prostate cancer prevention trial[78])** → finasteride ↓risk of prostate cancer (by 25%) but was associated with an increased risk of diagnosis of high-grade (6.4% vs. 5.1%) prostate cancer compared with placebo
   - Adverse Effects (Finasteride) → ↓libido (erectile dysfunction), ejaculatory dysfunction, impotence, gynaecomastia
   - Combination of Avodart and Tamsulosin (CombAT) study[79]
     - **Combodart – tamsulosin 0.4mg + dustasteride 0.5mg ($3/tab)**
     - Superior to monotherapy in reducing RR of BPH clinical progression in men with moderate-to-severe LUTS due to BPH and prostatic enlargement
     - Not superior to Dutasteride monotherapy at ↓ RR of AUR or BPH related surgery

[77] Urology. 2005 Jan;65(1):83-9
[78] N Engl J Med 2003; 349:215-224
[79] Eur Urol. 2010 Jan;57(1):123-31.

III. Surgery

Types

- **Transurethral resection of prostate (TURP) is the gold standard**
- Transurethral incision of the prostate (TUIP): decision made during TURP when the prostate does not appear to be enlarged → make small cuts around bladder neck area to open it up.
- Other techniques: laser prostatectomy, photo-selective vaporization of prostatic tissue (PVP), electro-vaporization (TVP), transurethral needle ablation of the prostate (TUNA), microwave thermotherapy, open prostatectomy

Indications:

1. Failed medical treatment – significant impact on patient's QOL
2. Significant Complications:
    - Upper Tract Injury – i.e. renal insufficiency, obstructive uropathy, hydronephrosis
    - Lower Tract injury – i.e. refractory urinary retention, recurrent UTI, bladder decompensation (i.e. high PVRU)
3. Recurrent/persistent gross haematuria
4. Bladder Calculi – since secondary to BPH

Caution: Must rule out neurogenic bladder / detrusor hypotonia before TURP!! → Do UDS

1. Insert narrow catheter with pressure gauge at the end into (detrusor pressure = a – b)
    a. Bladder: intravesical pressure
    b. Rectum: intra-abdominal pressure
2. Fill up bladder: look for detrusor contractions
3. Cough when erect: stress incontinence
4. Void: detrusor pressure should be sufficient, good flow (Qmax)

Aim: to widen bladder neck

Plan post-operation:

- Start continuous bladder washout with 22f, 3-way indwelling catheter – watch for colour of drain and presence of any clots

Complications of TURP: **bold** = must mention during consent taking

1. Risk of GA/ spinal analgesia
2. Bleeding, infection/ urosepsis
3. Local injury causing **incontinence** (1%), stricture / bladder neck stenosis
4. Perforation of the urethra or bladder dome → can form fistula
5. **Retrograde ejaculation (~40-60%) → ejaculate volume decrease**: (incompetent bladder neck)
    a. Check if patient is planning to have children (usually not an issue)
    b. **Penile Erection and Sexual Function not affected after surgery**
6. TUR syndrome (<1%) = hyponatremia
    - Symptoms: N/V, confusion, hypertension, visual disturbance, giddiness, seizure
    - Hyponatraemia due to constant irrigation during TURP (glycine used for irrigation – cannot use N/S, as ionic solutions make diathermy non-functional)
        i. water or 0.9% glycine is used for TURP
        ii. Water is hypo-osmotic compared to blood.
        iii. 0.9% glycine is iso-osmotic to blood
        iv. 0.9% glycine preferred because it does not "dilute" the blood
    - Venous channels opened up during TURP allows the irrigating fluid to enter the circulation – Fluid accumulate + Hemodilution + HypoNa$^+$ + Change in osmotic pressure
    - Risk ↑ with prolonged operation & ↑ pressure of irrigation, thus op is kept to < 1 hour, and irrigation pressures <60mmHg
    - Patient usually given spinal anaesthesia during TURP so the surgeon can assess the patient's mental status during the operation
    - Now uncommon as new technology allows isotonic irrigation
7. **Failure of procedure: S/S recur**

Delayed

1. Bladder neck stenosis
2. Urethral stricture
3. Incontinence
4. Regrowth of prostate
5. **Retrograde ejaculation** (~40-60%)
6. Impotence (5%) – rarely associated with ED

PROSTATIC CANCER

EPIDEMIOLOGY

- Prostate Cancer is the 3rd commonest cancer and the 6th most frequent cause of cancer death among males in Singapore
- Peak incidence between 60 and 85 years of age

PATHOLOGY

- Prostatic Intraepithelial Neoplasm (architecturally benign prostatic acini and ducts lined by atypical cells)
  - Low grade PIN (PIN 1): mild dysplasia – no ↑ risk of prostate CA – **NOT** commented / diagnosed upon
  - High grade PIN (PIN 2/3): moderate & severe dysplasia – 30-40% chance of concurrent / subsequent invasive cancer
- Adenocarcinoma (95%)
  - Arise in the outer parts (peripheral) of the prostate 70-80% of the time and are thus palpable on DRE and not resectable by TURP
  - Only 20% arise from transitional zone
- Others (histologic variants) – ductal adenoCA, mucinous adenoCA, signet cell CA, small cell CA

RISK FACTORS

- Advanced age
- Hormonal – growth of tumour can be inhibited by orchidectomy or administration of oestrogens
- Genetic – racial variations in onset and prevalence, family history
  - Long arm of chromosome 1q23
  - 1 first degree relative = 2x higher risk
  - 2 first degree relative = 4.5x higher risk
  - Familial Prostate Cancer = 5% of all prostate cancer
- Environmental – industrial chemical exposure, diet containing high animal fat consumption (western diet), Vitamin E, Soy
  - Low fat diets lowers testosterone levels (vice versa)

PRESENTATION

- Latent (incidental) carcinoma:
  - Microscopic focus of tumour detected incidentally at histological examination of prostatectomy specimens removed for BPH
  - Dormant lesions – mets in 30% after 10 years
- Clinical (symptomatic) carcinoma:
  - Can be incidentally picked up on DRE or due to elevated prostate-specific antigen (PSA) level (>100 is highly suggestive)
  - Urinary symptoms: dysuria, haematuria, hesitancy, dribbling, retention, incontinence
  - Asymmetrical, hard, irregular, craggy enlargement of prostate palpable PR
  - Mets especially to bone – pain, pathological fractures, anemia
  - Metastatic spread:
    - Direct – stromal invasion through the prostatic capsule, urethra, bladder base, seminal vesicles
    - Lymphatics – sacral, iliac and para-aortic nodes
    - Haematogenous to lung, liver and bones – pelvis, lumbosacral spine, femur

PHYSICAL EXAMINATION

- DRE: Asymmetric area of induration, or frank hard irregular nodule fixed to pelvic wall
- Percuss spine for any bone pain, pathological #
- Ballot Kidneys – any hydronephrosis
- Examine for lymphedema

DIAGNOSIS

1. **Serum PSA level***
   - > 10ng/ml: biopsy recommended as 67% of patients will have prostate cancer
   - 4-10ng/ml: biopsy advised, though only 20% will have prostate cancer
   - < 4ng/ml: majority will have negative biopsies, and yet there is a significant proportion of men with prostate cancer with PSA <4ng/ml
     - PSA density (serum PSA / prostate volume) → >0.15ng/ml/cc = ↑ risk prostate cancer
     - PSA velocity → Rate of rise >0.75ng/ml/yr = biopsy as ↑ risk prostate cancer
     - Free to Total PSA ratio (f/t PSA) → f/t PSA <10% = ↑ risk prostate cancer

*PSA can be falsely elevated in patient – organ specific but not disease specific
- LT catheter
- Recent UTI / Prostatitis
- Recent urethral instrumentation

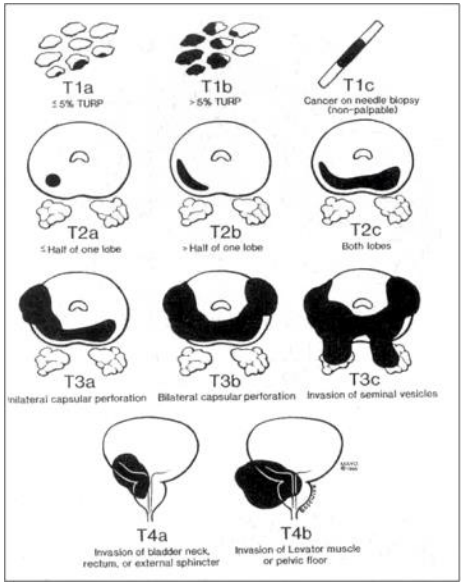
*PSA can be falsely decreased in patient – (i.e. drugs = 5-α reductase inhibitors, NSAIDs, Statins)

2. **Trans-rectal ultrasound (TRUS) with biopsy**
   - Histology of prostate carcinoma is graded by the Gleason score looking at glandular architecture at low magnification
   - Classically: hypoechoic lesion (30% chance of prostate cancer)

STAGING

1. **Clinical examination** (palpable tumour → T2)
2. **TRUS biopsy** for staging purpose
   a. Procedure-related complications – risk of sedation, bleeding (PR bleed, haematochezia, hematospermia), infection, urosepsis (1% chance of serious infection that require hospital stay – give prophylactic antibiotics (gentamicin))
3. **CT scan of the abdomen and pelvis** to assess extent of tumour invasion and nodal status (regional, non-regional)
4. **Bone scan** for metastasis – if PSA < 20 chance of Mets = 5%
   a. Patients with metastatic disease at presentation have a median 3-year survival
   b. Mets usually spread via the Batson venous plexus to the vertebral column

Staging (TNM staging)



T1: non-palpable lesions
- T1a: dx on TURP (Gleason score <7, <5% involvement)
- T1b: dx on TURP (Gleason score >7, >5% involvement)
- T1c: dx with PSA screening and TRUS biopsy

T2: confined to prostate
- T2a: confined to 1 lobe (≤ ½ of 1 lobe)
- T2b: confined to 1 lobe (> ½ of 1 lobe)
- T2c: both lobes

T3: extra-prostatic spread
- T3a: unilateral capsular penetration
- T3b: bilateral capsular invasion
- T3c: seminal vesicle invasion

T4: prostate stuck down to pelvic structures
- T4a: bladder neck, rectum, external sphincter invasion
- T4b: Levator muscle or pelvic floor invasion

15yrs mortality rates from Prostate Cancer*

Low Grade	Gleason 2-4	4-7%
Intermediate Grade	Gleason 5	6-11%
	Gleason 6	18-30%
	Gleason 7	40-60%
High Grade	Gleason 8-10	60-80%

*"The problem with prostate cancer is not with determining whether one has prostate CA but rather it is with evaluating the aggressiveness of the prostate CA. The only way so far is to evaluate clinically over time to assess how aggressive the prostate CA is and its impact on QoL. Surgical treatment of prostate CA will probably only bring real tangible benefits such as increase survival to 1 in 20 patients, however, for the other 20 patients undergoing surgery more than ½ may suffer the side effects of surgery such as incontinence, sexual dysfunction which severely impacts their QoL without any real survival benefits."

Gleason Grading System
- Based upon architectural features of prostate cancer cells (with low power field microscopy), closely correlates with clinical behaviour → higher score indicates a greater likelihood of having non-organ confined disease, as well as a worse outcome after treatment of localized disease[80]
- Tumours graded from 1 to 5, with grade 1 being the most, and grade 5 the least differentiated
- Derived by adding together the numerical values for the two most prevalent differentiation patterns (a primary grade and a secondary grade)

[80] Am J Surg Pathol. 1994;18(8):796.

TREATMENT
- Offer treatment if life expectancy is > 10 years (at 5yr, survival curve not affected between active surveillance or surgical intervention)
- Watchful waiting is possible in elderly (>75yo)

LOCALISED DISEASE (T1/2)

	Active Surveillance	Watchful Waiting
Aim	To Individualised Resection	To Avoid Resection
Patient Characteristics	Surgical Fitness Age 50-80	Age > 70 or Life expectancy < 15 years
Tumour Characteristics	T1-T2, Gleason Score 6/7 or less, initial PSA <10	Any T stage, Gleason Score 7 or less, Any PSA
Monitoring	Frequent PSA Repeat Biopsy	PSA testing not important No repeat biopsy
Indication for Treatment	Short PSA doubling time, high grade or more extensive cancer on biopsy	Symptomatic Progression
Treatment Timing	Early	Delayed
Treatment Intent	Radical	Palliative

1. Radical prostatectomy
   a. Treatment of choice for patients with life expectancy >10 years
   b. Open, laparoscopic or robot-assisted
   c. Open – retropubic or perineal approaches
   d. Cx: erectile dysfunction, urinary incontinence, bladder neck stenosis, risks of GA
2. Radiotherapy
   a. External beam radiotherapy (EBRT) – 33 treatments
   b. Interstitial Bradytherapy
   c. Cx: cystitis, prostatitis, bladder over-activity, erectile dysfunction

LOCALLY ADVANCED DISEASE (T3/4) → Radiotherapy with androgen ablation

METASTATIC DISEASE → Palliative RT + Androgen ablation
- Castration
  - Surgical orchidectomy
  - Medical – LHRH agonist –i.e. Goserelin (Zoladex®), Leuprolide (lupron®)
- Anti-androgen
  - Non-steroidal e.g. Flutamide
  - Steroidal – cyproterone acetate
- Combined androgen blockade
- Oestrogen therapy (diethylstilbestrol)

HORMONAL REFRACTORY PROSTATIC CANCER
- 2 consecutive PSA rises no less than 2 wks apart and/or documented dz progression based on clinical/radiological findings in pts with castrate levels of testosterone
- Management:
  1. Secondary hormonal manipulation
     - Glucocorticoids – prednisone, dexamethasone, hydrocortisone
     - Progesterone – megestrol acetate
     - Adrenal suppressive – ketoconazole, aminoglutethimide
  2. Chemotherapy
     - Docetaxel + Prednisone (gold standard)
     - Mitoxantrone + Prednisone

ADRENAL TUMOURS

Classified as either functional (hormone-secreting) or silent and as either benign or malignant

ANATOMY

- Located superior to the kidney and lateral to the IVC (right) and aorta (left)
- Arterial supply: **superior** (from inferior phrenic), **middle** (from aorta) and **inferior** (from renal artery) adrenal artery
- Right adrenal vein → drains to IVC
- Left adrenal vein → drains into left renal vein

PHYSIOLOGY (GFR → MGS/ACS)

- Adrenal Cortex
  - Zona **G**lomerulosa → **M**ineralocorticoid (i.e. **a**ldosterone) – stimulated by RAAS activity (elevated ANGII) → ↑ aldosterone leads to ↓ serum K^+
  - Zona **F**asciulata → **G**lucocorticoid (i.e. **c**ortisol*) – stimulated by ACTH from anterior pituitary
  - Zona **R**eticularis → **S**ex Hormones (i.e. androstenedione, DHEA)
- Adrenal Medulla
  - Produce epinephrine and norepinephrine
    - Alpha receptor → peripheral vasoconstriction
    - Beta 1 receptor → increase heart rate and contractility
    - Beta 2 receptor → relaxation of smooth muscles

* function of cortisol – regulate metabolism and response to stress

CLASSIFICATION

	Adrenal Cortex	Adrenal Medulla
Benign	**Adrenocortical Adenoma** Hypercortisolism (Cushing Syndrome) Hyperaldosteronism (Conn Syndrome)	**Pheochromocytoma**
Malignant	**Adrenocortical Carcinomas**	**Neuroblastoma**

MANAGEMENT PRINCIPLES[81]

- Non-functioning mass < 3cm should be f/u with appropriate CT scans (or MRI if a CT scan was the original test)
- If mass has not grown at 3-months or 1-year f/u = no further test is recommended
- If mass does grow within 1 year → adrenalectomy is required
- Immediate adrenalectomy is required for a hyper-functioning mass of any size and for non-functioning masses > 4cm

[81] Proc (Bayl Univ Med Cent). Jan 2003; 16(1): 7–12.

HYPERALDOSTERONISM

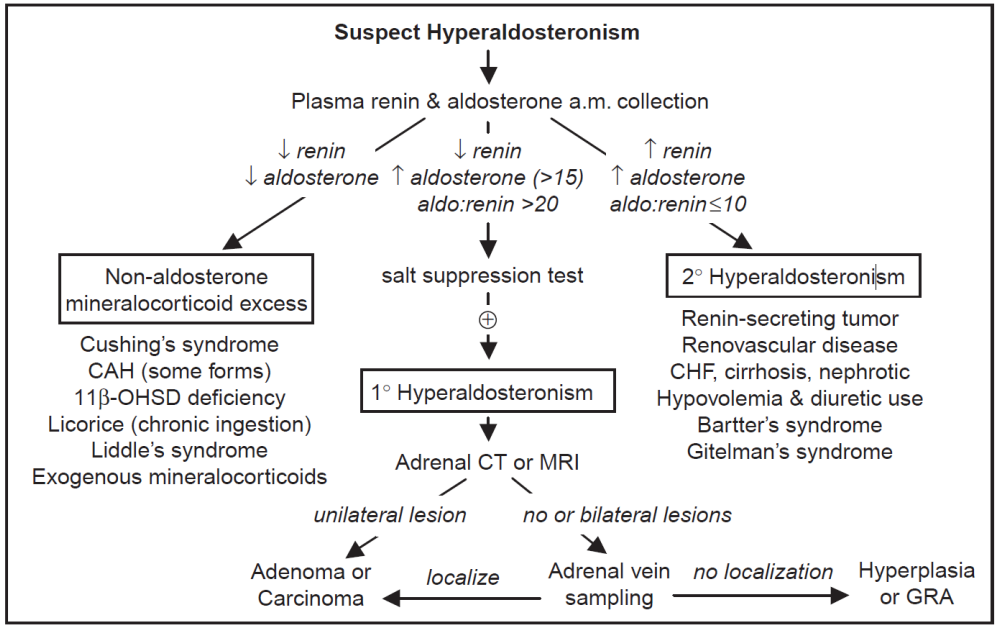
Aetiology:

- Primary – adrenal hyperplasia – 70%, adenoma (Conn's Syndrome – 25%), carcinoma – 5%
  - Renin independent increase in aldosterone
- Secondary – extra-renal disorders – i.e. RAS, CHF, Cirrhosis, Nephrotic Syndrome
  - Renin dependent increase in aldosterone

Clinical Features:

- Hypertension (11% of patients with HTN refractory to 3 drugs)[82]
- Hypokalemia (classically, often normal)
- Others – headache, muscle weakness, no peripheral edema, metabolic alkalosis, mild hyperNa^+

Investigations



Salt Suppression Test → Sodium Suppression Test / Saline Infusion Test

- Failure to supress aldosterone after sodium load
- Oral salt load (+ KCl) x3d with 24hr urine on 3rd day (+ve if urine aldo >12ug/d while Na >200 mEq/d)
- OR 2L NS over 4h, measure aldo at end of infusion (+ve if aldo >5ng/dL)

*if patient comes in with undetectable renin and aldosterone>30 ng/dL = primary aldosteronism, don't have to do confirmatory salt suppression testing

Treatment

- Unilateral Lesion → Adrenalectomy (posterior / laparoscopic approach)
- Spironolactone – to control HTN and correct hypoK+ (start pre-operatively for 2-3wks)
- ± K^+ replacement (oral or IV)
- Hyperplasia → spironolactone or eplerenone

[82] Lancet 2008;371:1921

HYPERCORTICOLISM (CUSHING SYNDROME)

Aetiology:
- Iatrogenic
- Cushing's Disease (60-70%) – pituitary adenoma or hyperplasia
- Adrenal Tumour (15-25%) – adenoma or carcinoma
- Ectopic ACTH (5-15%) – SCLC, medullary thyroid Ca, islet cell tumours, carcinoid, pheo

Clinical Manifestations:[83]
- Nonspecific: glucose intolerance, DM, HTN, obesity, oligomenorrhoea, osteoporosis
- More specific: central obesity w/ extremity wasting, dorsocervical fat pads, rounded facies
- Most specific: spontaneous bruising, proximal myopathy, wide striae, hyokalemia
- Others: depression, insomnia, psychosis. Impaired cognition, facial plethora, acne, hirsutism, hyperpigmentation (if ↑ ACTH), fungal skin infection, nephrolithiasis, polyuria

Investigations:
- Establish diagnosis of hypercortisolism where ≥2 first line tests abnormal
    1. 24hour urinary free cortisol (UFC)
    2. Low-dose dexamethasone suppression test* (2 options)
        - **O/N LD DST** = 1mg at 11pm with 8am serum cortisol level or
        - **48hr LD DST** = 0.5mg q6h x 2d with 24hr UFC)
    3. Late night (11pm) salivary cortisol**

- Localise the Lesion – ACTH dependent or ACTH independent
    1. Serum basal ACTH*** – measure on ≥2 days
        - Low (<5pg/ml) → do adrenal CT/MRI → likely **adrenal tumour / hyperplasia**
        - Normal / High (>20pg/ml) → do high-dose DST**** or CRH test
            - Suppressed 8am serum cortisol (<5mcg/dL) or supressed urinary cortisol → do gadolinium enhanced pituitary MRI
                - Positive → likely **Cushing disease**
                - Negative → do bilateral inferior petrosal sinus venous sampling (BIPSS)
            - Failure of suppression of serum or urinary cortisol
                - Likely **ectopic ACTH** (search for a source)

*not a good choice for patients in whom CBG levels may be abnormal
**not a good test for patients with erratic sleep schedule or shift work
***positive correlation between basal ACTH values and size of the pituitary adenoma
**** O/N **HD DST** = 8mg at 11pm with 8am serum cortisol or **O/N 48h HD DST** = 2mg q6h x2d with 24hr UFC

Treatment:
- Trans-sphenoidal resection of ACTH producing pituitary tumour – treat Cushing disease
- Identify source and resection of primary lesion – treat ectopic ACTH syndrome
- Adrenalectomy with pre and post-operative glucocorticoid replacement – treat adrenal tumour

PHEOCHROMOCYTOMA
Catecholamine-secreting tumour that arise from chromaffin cells (adrenal medulla) & the sympathetic ganglia (extra-adrenal)

Clinical Features: (5Ps)
- Pressure – HTN
- Pain – Headache, Chest Pain
- Palpitation – tachycardia, tremor, LOW, fever
- Perspiration (profuse)
- Pallor (vasoconstrictive spell)

Rule of 10
- 10% Malignant
- 10% Children
- 10% Bilateral or multiple
- 10% Recur
- 10% Incidentaloma
- 10% Extra-adrenal (known as paraganglioma)
- 10% Familial (MEN2, VHL, NF-1)

Investigations:
- 24hour urinary fractionated metanephrines and catecholamines
- Plasma free metanephrines
- Adrenal CT / MRI – KIV MIBG scintigraphy (^{131}I-meta-iodo-benzyl-guanidine)
- KIV genetic testing – a/w MEN2A/2B, VHL, NF1

Treatment:
- Alpha Blockade first (i.e. phenoxybenzamine – PO 10mg BD)
- ± Beta Blocker (propranolol) added if tachycardia / arrhythmias develop after complete alpha-adrenergic blockage
- Definitive → Adrenalectomy

[83] Pocket Medicine 4th Edition: Cushing's Syndrome (hypercortisolism) – section 7-7

HERNIA

Hernia: protrusion of an organ through an opening in the wall of the cavity in which it is normally contained

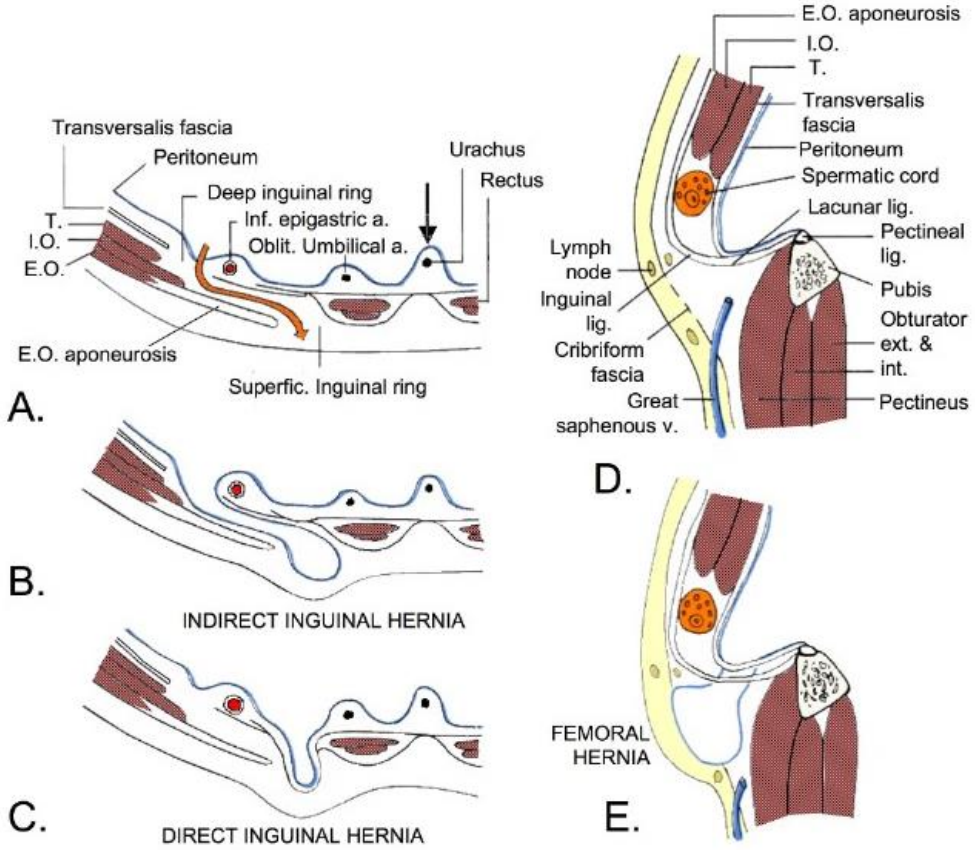
- Lifetime risk = 2-10%
- Causes of abdominal wall weakness
  - Congenital – normal (due to piercing structures), or patent processus vaginalis
  - Acquired – trauma, surgical incision or disease
- Consist of 3 parts:
  - Sac: pouch of peritoneum (neck & body)
  - Coverings of sac: layers of abdominal wall
  - Contents

Types:

A. Inguinal (96%) → indirect (2/3), direct or pantaloon (direct & indirect)
B. Femoral (4%)
C. Internal Hernia
   1. Sliding Hernia → herniation of posterior peritoneum with underlying retroperitoneal structures (i.e. caecum, sigmoid, bladder)
   2. Littre Hernia → hernia that contains a Meckel's diverticulum
   3. Amyand's Hernia → hernia that contain the appendix
D. Abdominal Wall Hernia
   1. Incisional Hernia → hernia through sites of previous incisions
   2. Umbilical / Paraumbilical Hernia **[see later section]**
   3. Epigastric Hernia → hernia through the linea alba above the umbilicus (i.e. extra-peritoneal fat)
      i. Frequently in athletically active young males
      ii. Presents as epigastric pain
   4. Richter Hernia → hernia involving only part of bowel (rather than entire circumference) – knuckle of bowel is strangulated but lumen is patent
   5. Spigelian Hernia → herniation of linea semilunaris: lat. border of rectus
   6. Lumbar Hernia – occur in Petit triangle (lower lumbar) or Grynfeltt triangle (upper lumbar)
   7. Obturator Hernia → herniation through the obturator canal a/w:
      i. Frequent in elderly lady who is thin (i.e. little old lady hernia)
      ii. Presents as intestinal obstruction
      iii. Howship-Romberg Sign – pain in medial thigh extending to knee caused by hernia compression of the obturator nerve
      iv. Loss of adductor reflex
E. Parastomal Hernia

PHYSICAL EXAMINTION (common signs)

- Location: all occur at congenital or acquitted weak spots in the abdominal wall
- Reducibility: on direct pressure or lying down
- Expansile cough impulse



INGUINAL HERNIA (DIRECT & INDIRECT)

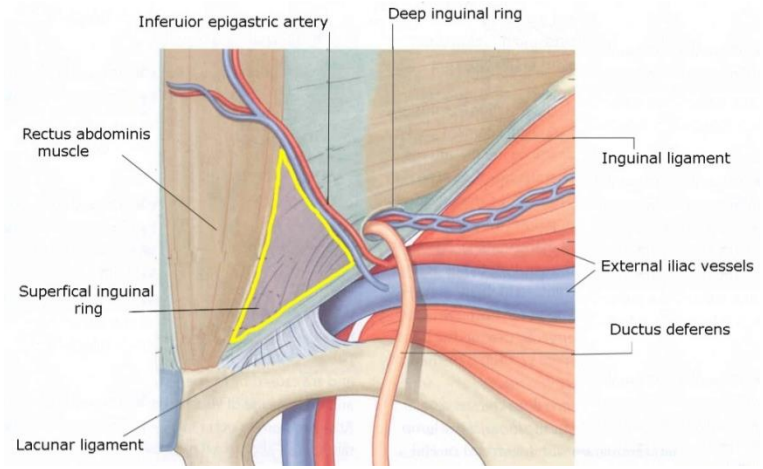
- The true incidence and prevalence of inguinal hernia worldwide is unknown
- Male : Female ratio is > 10:1
- Lifetime prevalence for males is 25% and 2% in females
- 2/3 of inguinal hernia are indirect
- 2/3 of recurrent hernia are direct
- 10% of inguinal hernia are at risk of incarceration – and a portion of these may become strangulated

Indirect inguinal hernia:

- Passes through the deep inguinal ring above the inguinal canal (lateral to the inferior epigastric artery) ± into the scrotum
- Hernia sac enters the inguinal canal with the spermatic cord via the deep ring, then emerges from the superficial ring & descends into the scrotum
- Congenital; patent processus vaginalis + weakened fascia at deep ring
- ♂>♀, R> L, 20% are bilateral, children>adults

Direct inguinal hernia:

- Bulges through the posterior wall of the canal medial to the inferior epigastric artery through the Hesselbach's triangle (weakness of the posterior wall)
  - Laterally → inferior epigastric artery,
  - Medially → lateral border of rectus abdominis,
  - Inferiorly → inguinal ligament
- Hernia sac is not with the spermatic cord
- Rare in ♀, usually occur bilaterally in ♂ with weak abdominal muscles and comorbid conditions causing ↑ intra-abdominal pressure



Clinical differences between indirect and direct inguinal hernia:

Indirect Hernia	Direct Hernia
Neck lies lateral to inferior epigastric artery, out of Hesselbach's triangle	Neck lies medial to inferior epigastric artery, within Hesselbach's triangle
Reduces upwards, laterally and backwards	Reduces upwards and straight backwards
Controlled after reduction by pressure over the deep ring	Controlled after reduction by pressure over the superficial ring
May descend down the scrotum	Does not descend down the scrotum
May cause strangulation at superficial ring (narrow)	Rarely causes strangulation due to wide hernia neck
Does not readily reduce on lying down	Readily reduces on lying down
More common in young adults and infants	More common in old men

* Clinically, inguinal hernia is location above and medial to the pubic tubercle while femoral hernia is located inferiorly and laterally.

Anatomy of inguinal canal

- 4-6cm long oblique passage passes through the lower part of the anterior abdominal wall, above the inguinal ligament from deep to superficial
- **Deep inguinal ring**: 2cm above midpoint of inguinal ligament* (defect in transversalis fascia)
- **Superficial ring**: above and medial to pubic tubercle (triangular defect in the aponeuroses of the external oblique)

*midpoint of inguinal ligament = midpoint between ASIS and Pubic Tubercle = deep inguinal ring
*mid-inguinal point = midpoint between ASIS and Pubic Symphysis = femoral pulse

Contents of the inguinal canal:

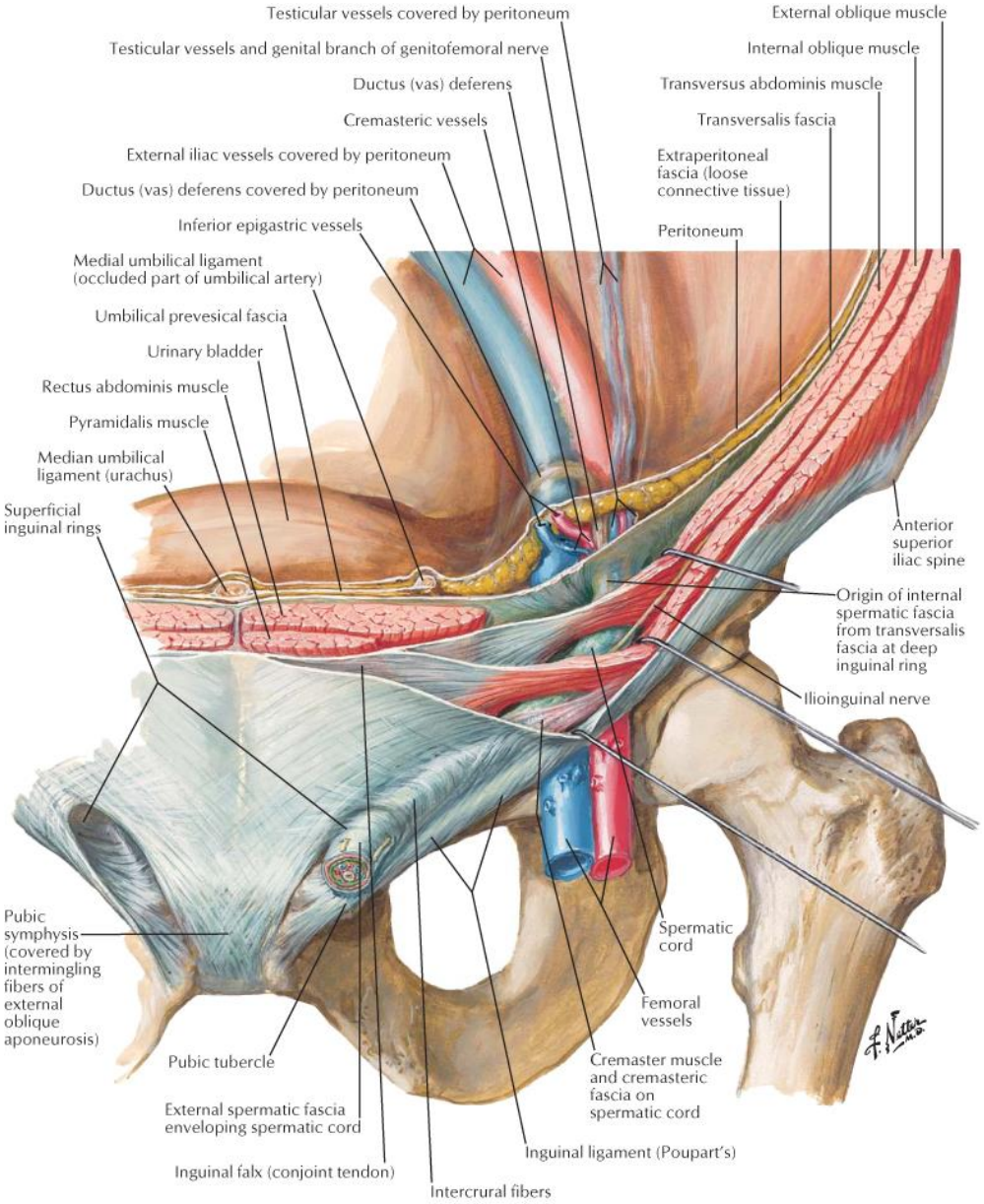
- Males: spermatic cord + ilioinguinal nerve (abdomen to testis)
- Females: round ligament of the uterus + ilioinguinal nerve (uterus to labium majus)

Boundaries:

- Anterior Wall: External Oblique Aponeurosis (reinforced in the lateral 1/3 by IO muscle)
- Posterior Wall: Transversalis Fascia (reinforced in the medial 1/3 by the conjoint tendon)
- Roof: Arching fibres of the IO and TA before they merge as the conjoint tendon
- Floor: Inguinal Ligament and Lacunar Ligament medially

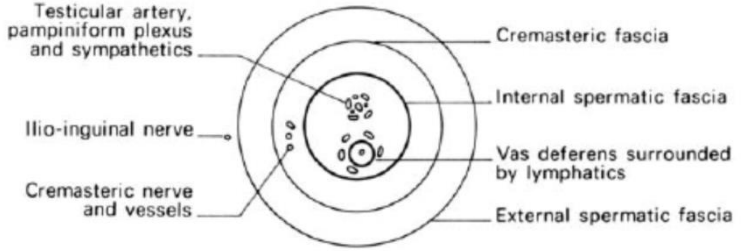
Layers of the Anterolateral Abdominal Wall:

- Skin
- Camper Fascia
- Scarpa Fascia
- External Oblique Aponeurosis
- Internal Oblique
- Transverses Abdominis
- Transversalis Fascia
- Pre-peritoneal Fat
- Peritoneum



Anatomy of the spermatic cord

Layers	External spermatic fascia: derived from external oblique
	Cremasteric fascia & muscle: derived from internal oblique
	Internal spermatic fascia: derived from transversalis fascia
Veins	Testicular Vein (Pampiniform Venous Plexus)
	Veins of the Vas Deferens
	Cremasteric Vein
Artery	Testicular artery (branch of abdominal aorta)
	Artery to the vas deferens (branch of inferior vesical artery from internal iliac artery)
	Cremasteric artery (branch of inferior epigastric artery)
Nerves	Ilioinguinal Nerve (strictly speaking, on and not in the cord)
	Sympathetic Fibres / Autonomic Nerves (T10)
	Nerve to Cremaster (genital branch of genitofemoral nerve)
Others	Remains of Processus Vaginalis
	Vas Deferens
	Lymphatics



Diagnosis

- Clinical Presentation:
  - Presents as an intermittent bulge in the groin related to exertion or long periods of standing
  - A purposeful Valsalva manoeuvre can reproduce the symptoms (i.e. unilateral discomfort) and/or the presence of a bulge
  - **Incarcerated Inguinal Hernia → pain + abdominal distention + nausea + vomiting**
- Radiological Evaluation:
  - Rarely indicated unless plain AXR to verify intestinal obstruction in cases of incarceration

Differential Diagnosis (for groin lump)

Hernia	Femoral Hernia
	Inguinal Hernia
Vascular	Femoral Artery Aneurysm
	Saphenous Varix
	Varicocele
Lymphatics	Inguinal Lymphadenopathy
	Lymphoma
Soft Tissue / Bone	Lipoma
	Groin Abscess – look for multiple puncture holes (r/o infected pseudoaneurysm)
	Muscle / Soft Tissue Tumour – Rhabdomyosarcoma
	Bone Tumour
Nerves	Neuroma
Others	Undescended Testes
	Hydrocele of the spermatic cord (young boys)

Complications

Reducible → Irreducible / Incarcerated → Obstructed → Strangulated

- Irreducible/ Incarcerated hernia: contents of hernia sac cannot be replaced into abdomen
- Obstructed: loop of bowel trapped in hernia sac such that its lumen, but not blood supply, is obstructed (no ischemia → not unduly tender, but with IO)
- Strangulated: blood supply to trapped bowel is cut off, bowel is dead or dying; **6hrs to gangrene**.
  - Acutely tender with s/s of IO; exception: (Richter's hernia: segment of bowel is trapped & ischaemic but lumen is patent → no IO)

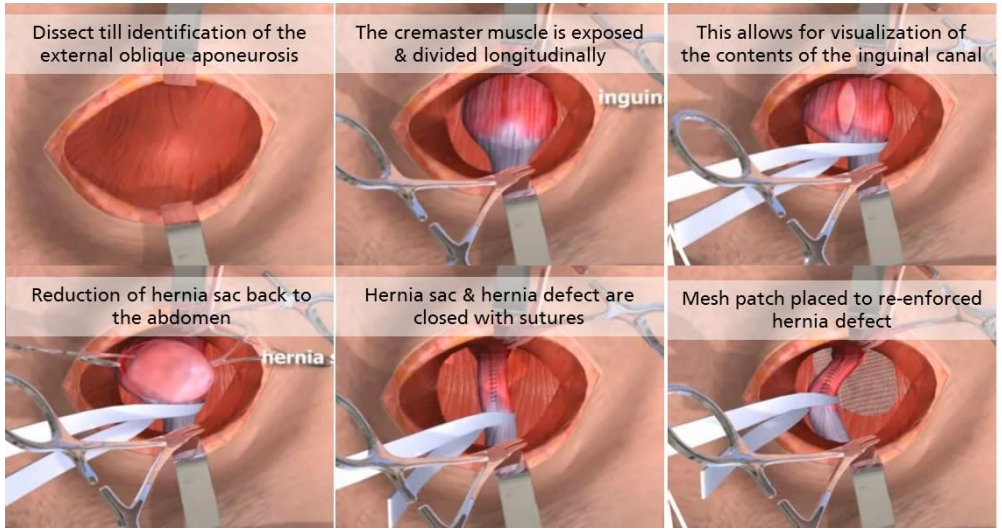
Management

Non-surgical:

- Raised intra-abdominal pressure
  - Weight loss, change jobs, avoid heavy lifting
  - Treat medical conditions causing chronic cough, chronic constipation
- Truss: for compression of reducible hernia at deep ring (poor pickup rate)
- If obstructed/strangulated: NBM, IV drip, NG tube on suction, IV ABx

Surgical:

- Principles: reduce bowel, ±excise hernia sac, reinforce posterior wall
  - Immediately if suspect incarceration to prevent any bowel perforation
- Open Inguinal Hernia Repair (with mesh / without mesh)
  - Herniotomy (removal of hernia sac only) – done in kids, rarely in adults
  - **Herniorrhaphy** (herniotomy + repair of posterior wall of inguinal canal)
    - I.e. – Shouldice repair → non-mesh technique: 2 continuous back & forth sutures with permanent suture material
  - **Hernioplasty** (reinforcement of the posterior inguinal canal wall with a synthetic mesh)
    - I.e. – Lichtenstein tension-free mesh repair → polypropylene mesh insertion & suture
- Laparoscopic Inguinal Hernia Repair (intraperitoneal or extraperitoneal)
  - Trans-abdominal pre-peritoneal (TAPP) repair
  - Totally extra-peritoneal repair (TEP)



Complications

- 2° to General Anaesthesia: AMI, CVA
- Immediate to early
  - **Acute Retention of Urine (ARU)**
  - Bruising , Bleeding / Scrotal Hematoma
  - **Iatrogenic Injury** to surrounding structures → paraesthesia, impotence
- Early
  - Infection of wound/ mesh
  - **Haematoma** (10%; no cough impulse, non-reducible, hard)
  - Wound dehiscence
  - Pain – discharge patient with adequate analgesia
- Late
  - Chronic post-operative groin pain (5%)
  - **Recurrence** (<0.5%) from inadequate ring and posterior wall closure
  - **Ischaemic orchitis** from thrombosis of pampiniform plexus draining testes
  - **Testicular atrophy** from testicular artery damage

Post- operation monitoring

- Monitor urine output and any bleeding / scrotal hematoma
- Early mobilization
- STO day 10
- Work leave for 6/52 if heavy lifting is involved
- Treat any medical conditions to avoid coughing, constipation
- Keep area clean and wash carefully, but able to bathe immediately

APPROACH TO INGUINAL HERNIA EXAMINATION

1. Groin vs. Inguinoscrotal	a) groin → cough impulse b) inguinoscrotal → **1. cough impulse (may not be present in a large one)** **2. cannot get above lump** **3. cannot separate from testis**
2. Risk factors:	Increased intra-abdo pressure: chronic cough, BPH, chronic constipation Also 4Cs: cirrhosis, cardiac failure, cancer, catheter (dialysis)
3. Complications	a) Obstructed/ Strangulated b) Spontaneous rupture c) Involved in peritoneal diseases
4. Patient profile	- Indirect: M, young, right, increase intraperitoneal fluid - Direct: M, old, raised intra-abdominal pressure
5. Treatment:	a) OPEN hernia repair!!! b) Lap only if 1. Recurrent, 2. Bilateral (2 types of lap: TEP, TAPP) c) Conservative only if: small, easily reducible, direct hernia
6. Post-op complications	a) Immediate: bruise, wound hematoma, scrotal hematoma, ARU, pain b) Later: mesh infection, recurrence (10% /10years), nerve injury, ischemic orchitis

5 Questions to Answer
1. Is this an inguinal-scrotal swelling or a groin lump?
2. Is this likely to be an inguinal hernia or a femoral hernia
3. Is the hernia reducible or irreducible
4. Is the hernia likely to be direct or an indirect hernia
5. Are there any pre-disposing factors

EXAMINATION OF AN INGUINAL HERNIA

- Don gloves, introduce and explain your intention, expose the patient adequately, use clothes peg to hold shirt up

STAND patient up, examine both sides
- Mr X is a ___ who appears comfortable at rest.
- I notice a groin / inguinoscrotal lump.

Squat down and examine!
- Inspect as per a lump: (if unable to see, ask the patient)
  1. Is lump above or below the inguinal ligament? Any scrotal lump?
  2. Estimate the dimensions of the lump
  3. Any skin changes? Previous scars? (look hard, don't miss a scar!)
  4. Any lump on the other side?
  5. Abdominal distension / visible abdominal mass?
- Sir, could you turn head to the left and cough? → Look for **visible cough impulse**
- Sir, is there any pain over the groin area? I am going to feel the lump.

Palpate:
1. Can **get above the lump**?
2. Can **feel testis**?
3. Lump: consistency, fluctuant, size, temperature, any tenderness?
4. Landmark for the pubic tubercle (show that hernia is above and medial to the PT)
5. Landmark for ASIS and note the midpoint of the inguinal ligament (midpoint btw ASIS & PT, 2cm above midpoint = deep inguinal ring)
6. Sir, could you turn head to the left and cough again? → Feel for **palpable cough impulse** (bilaterally?)

- Sir, could you reduce the lump for me?
  - Reducible: The point of reduction is "above and medial to the PT" (superficial ring)
  - Incarcerated (irreducible): The patient is unable to reduce the lump.

Lay the patient supine
- Reduce the hernia if patient has not done so
- Locate the Deep inguinal ring
  - Define pubic tubercle: umbilicus → pubic symphysis → 1st bony prominence laterally
  - Define anterior superior iliac spine (ASIS)
  - Define deep inguinal ring → midpoint of inguinal ligament → 2 cm above
- Keep pressure on deep ring (use right hand for right sided hernia and left hand for left sided hernia), ask patient to sit up & support his pelvis, then swing over the bed and stand

With patient **standing**:
- Sir, could you turn head to the left and cough?
  - If remains reduced – indirect hernia,
  - If not, direct hernia. (poor accuracy)
  - If hernia appears slightly and on removal of compression appear even more fully → pantaloon hernia
- Remove pressure & watch: hernia slide obliquely (indirect) or project forward (direct)
- Percuss & auscultate for bowel sounds

Examine other side

Offer:
1) Abdominal exam: scars, masses, ascites, ARU, constipation, IO
2) DRE for BPH, impacted stools
3) Respiratory exam for COPD
4) Ask patient for history
   - Smoking
   - Chronic cough
   - Heavy lifting (occupation)
   - Difficulty passing stools (constipation)
   - Difficulty passing urine (BPH)

APPROACH TO INGUINAL LYMPHADENOPATHY

Approach to Inguinal Lymphadenopathy

Loco-Regional	▪ Legs – any infection / malignancy (i.e. melanoma – located at nail beds) ▪ Examine Perineum – scrotal wall / penis / clitoris / vulva ▪ **Per Vagina Exam – lower third drain to superficial inguinal lymph nodes** ▪ **Per Rectum Exam – lower ½ of anal canal drain to superficial inguinal nodes** ▪ Urethra – external ½ drain to inguinal lymph nodes ▪ Abdominal wall (below umbilicus)
Systemic	▪ Check contralateral inguinal nodes ▪ Cervical Nodes ▪ Axillary Nodes ▪ Abdomen – for Hepatosplenomegaly

FEMORAL HERNIA

- Uncommon – 2-4% of all groin hernia
- 70% occur in women (pelvis is wider and the canal is therefore larger)
- 25% of femoral hernia → gets complicated by incarceration or strangulation
- **Rarely** put up for exams as it is operated quickly;

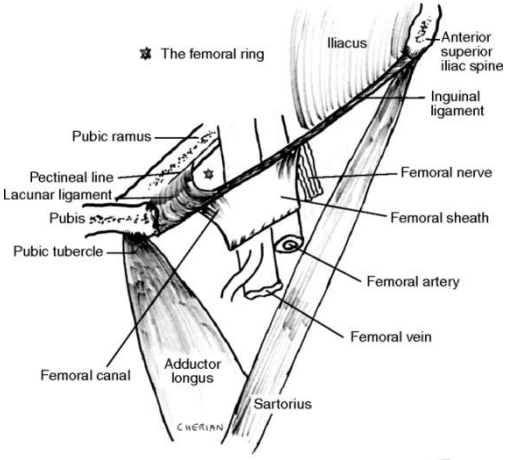
- Femoral hernia → marble- shaped lump in the upper thigh just below the inguinal ligament and medial to femoral pulse
  - usually irreducible; narrow neck → risk of strangulation is high
  - Usually does not have a cough impulse
- Incarcerated Femoral Hernia → firm tender mass

- Differential Diagnosis: (see above)
  - Skin/ soft tissue: cyst, lipoma
  - Vascular masses: saphena varix, femoral aneurysm, inguinal LAD
  - Hernia: inguinal hernia, obturator hernia
  - Other: psoas bursa, ectopic testis

Differences between an inguinal and a femoral hernia

Inguinal Hernia	Femoral Hernia
Appear through superficial ring	Appears through femoral canal
Superior and medial to pubic tubercle	Inferior and lateral to pubic tubercle
Usually reducible	**Usually not reducible**
Expansile cough impulse usually present	**Expansile cough impulse usually absent**
Low risk of strangulation	High risk of strangulation

Boundaries of the Femoral Canal



Medial Border = Lacunar Ligament
Lateral Border = Femoral Vein
Anteriorly = Iliopubic Tract
Posteriorly = Cooper Ligaments

Anatomy of the femoral canal

- Contents: Lymph Node of Cloquet, Adipose Tissue
- The femoral sheath is the downward protrusion of fascia containing the femoral vessels and lymphatics below the inguinal ligament.
- The medial compartment of the sheath constitutes the femoral canal, which carries the lymphatics.
- The superior opening of the femoral canal is known as the femoral ring.

Boundaries of the femoral ring:

- Anterior: inguinal ligament
- Posterior: iliopectineal ligament and superior ramus of pubis
- Medial: lacunar ligament
- Lateral: femoral vein

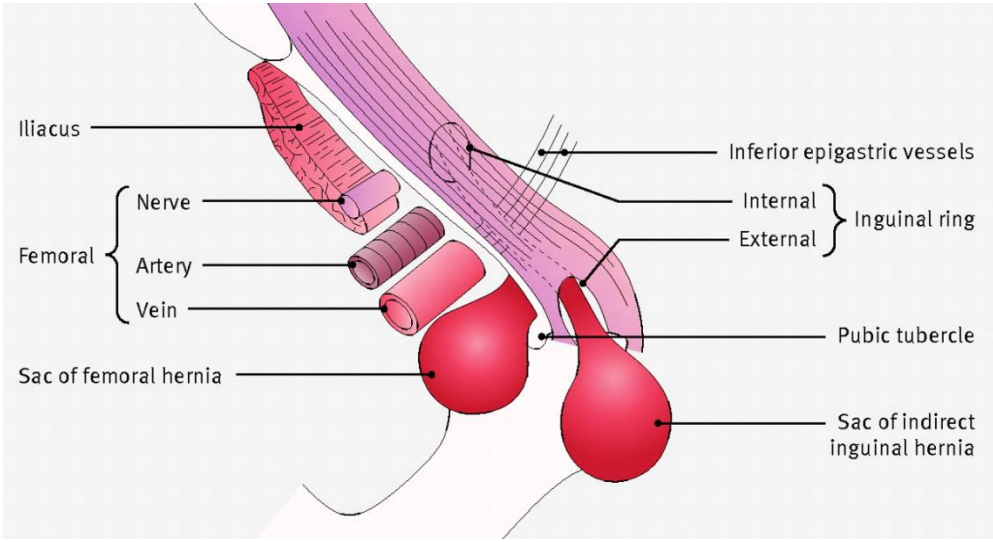
Management

Surgical:

- Preperitoneal Approach – transverse suprainguinal incision
- Inguinal Approach – cooper ligament repair (Mc Vay)
- Femoral Approach – horizontal incision made over the hernia, inferior and parallel to the inguinal ligament

Complications:

- Similar to Inguinal Hernia Repair (see above)
- Specific → femoral vein susceptible to injury (femoral vein forms the lateral border of the femoral canal



***NAVEL** = Nerve, Artery, Vein, Empty Space (where the femoral hernia sac is), Lymphatics

INCISIONAL HERNIA

Extrusion of the peritoneum & abdominal contents through a weak scar or accidental wound on the abd wall

- Physical examination similar, just add:
  - Inspect – body habitus, abdominal scars, prominence of bulge with neck flexion, peristalsis through the skin, visible cough impulse
  - Palpable – tenderness, size of defect, reducibility, cough impulse
  - Auscultate – bowel sounds
- Complications – i.e. intestinal obstruction, incarceration, strangulation, skin excoriation, persistent pain (similar to most hernia)
- Risk factors:
  - **PRE-OPERATION** → age, malnutrition, chronic disease (ESRF, CLD, Malignancy), steroids, DM (predispose to infections), morbid obesity, ↑ abdominal pressure 2° chronic bronchitis or ascites
  - **INTRA-OPEATION** → wrong suture material, wrong technique – i.e. too small bites, placing drains through wound
  - **POST-OPERATION** → wound breakdown / hematoma, ischemic wound due to excessive tension, complications – i.e. anastomotic leaks, infection, post-operative atelectasis and chest infection
- Treatment options:
  - Not every patient should undergo repair due to high risk of wound haematoma, infection, dehiscence and recurrent hernia – also many have concurrent medical problems increasing their anaesthetic risk
  - Conservative:
    - Offer corset or truss
    - Weight loss and control the risk factors
  - Surgical:
    - Offer if complications of hernia are present
    - Control CVS & resp. disease; encourage pre-op weight loss
    - Principles: **dissect the sac and close the defect using mesh overlapping**
    - Avoid placing plypropylene mesh in direct contact with the intestine because of risk of adhesion formation and fistulation

UMBILICAL / PARAUMBILICAL HERNIA[84]

Umbilical Paraumbilical Hernia = due to defects through the linea alba

	True Umbilical Hernia	Paraumbilical Hernia
Location	Occur through the umbilical scar	Occur around the umbilical scar
Epidemiology	Congenital – common in afro-Caribbean	Uncommon before 40 yrs old
Acquired Causes	Pregnancy, ascites, ovarian cyst, fibroids, bowel distention (stretching of linea alba fibres)	

- Physical Examination:
  - Inspect – body habitus, abdominal scars, prominence of bulge with neck flexion, associated ulceration, peristalsis through the skin, visible cough impulse
  - Palpate – size of defect, reducibility, cough impulse
- Issues of concern:
  - Narrow neck of hernia sac → higher risk of strangulation/ infarction – should repair
  - Fistula formation (i.e. enterocutaneous fistula) with discharge of contents may occur
- Management:
  - Conservative: treat medical co-morbidities – i.e. chronic cough
  - Surgical: **Mayo's 'vest over pants' operation**

[84] Clinical Cases and SOCEs in Surgery (2nd Edition) – pg 79-80

SCROTAL SWELLING

APPROACH TO SCROTAL SWELLINGS

ANSWER 4 QUESTIONS:

1. Can you get above the swelling?
2. Can you identify the testis and the epididymis?
3. Is the swelling transilluminable?
4. Is the swelling tender?

<table>
<tr><td rowspan="2">Cannot get above swelling</td><td>• Cough impulse
• Reducible
• Testis palpable
• Opaque</td><td colspan="3">Hernia</td></tr>
<tr><td>• No cough impulse
• Not reducible
• Testis not palpable
• Transilluminable</td><td colspan="3">Infantile hydrocoele</td></tr>
<tr><td rowspan="4">Can get above swelling</td><td rowspan="3">Testis not definable from epididymis</td><td rowspan="2">Opaque</td><td>Non tender</td><td>Chronic haematocoele
Gumma
Tumour</td></tr>
<tr><td>Tender</td><td>Torsion
Epididymo-orchitis
Acute haematocoele</td></tr>
<tr><td colspan="2">Transilluminable</td><td>Hydrocoele</td></tr>
<tr><td rowspan="4">Testis definable from epididymis</td><td rowspan="3">Opaque</td><td>Non-tender swelling of testis</td><td>Tumour</td></tr>
<tr><td>Non-tender swelling of epididymis</td><td>TB epididymis</td></tr>
<tr><td>Tender</td><td>Epididymoorchitis</td></tr>
<tr><td colspan="2">Transilluminable</td><td>Cyst of epididymis</td></tr>
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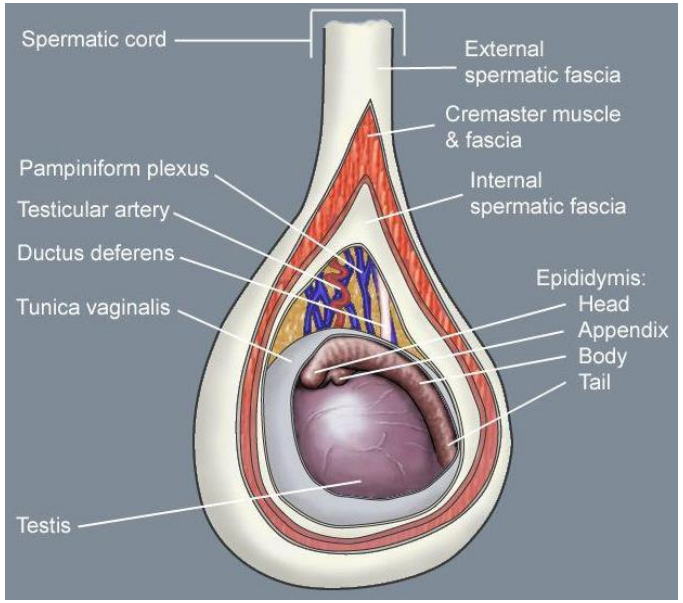
SCROTAL ANATOMY



- Tunica Vaginalis: potential space that encompasses the anterior two-thirds of the testicle → (fluid from a variety of sources may accumulate)
- Epididymis: positioned posterolaterally to the testicle → (must be differentiated from an abnormal mass)
- Spermatic Cord: consists of the testicular vessels and the vas deferens, is connected to the base of the epididymis

EXAMINATION OF THE SCROTUM

"Examine this gentleman's scrotum:"

Aim:
- Confirm swelling is confined to scrotum
- Establish whether testis and epididymis are identifiable
- Determine if the lump transilluminates

Inspect
- inspect the groin and scrotum: scars and swelling
  - Groin incisions are usually oblique
  - Scrotal incisions are usually in the median raphe (easy to miss)
  - Testicular lie

Palpate
- Ask for any pain; when palpate, look at patient for tenderness
- Palpate one testes at a time
- If palpated any swelling:
  - Is it tender?
  - Can you get above the swelling? → swelling confined to scrotum
  - Can you identify the epididymis and testis → lump is separate or part of them?
  - Palpate the normal contour of the testis identifying the epididymis and ductus deferens
  - If a lump is present – Is it transilluminable?

Offer to:
- Transilluminate the swelling if it is likely at hydrocele
- Continue the examine the groin if it is a inguinoscrotal hernia
- Examine the abdomen and groin
  - Lymph drainage of the testes are to the para-aortic nodes which are retroperitoneal and unless extremely large will not be palpable
  - Inguinal lymphadenopathy is not likely a response of testicular problems but rather from skin of scrotum and penis (i.e. SSC of penis)

TESTICULAR TUMOUR

Cancer that develops in the testicles which presents as a **painless testicular mass in young males** (15 – 35yr)

- Epidemiology & Risk Factors:
  - Life-time risk: 1 in 500
  - RF: cryptorchidism, HIV infection, gonadal dysgenesis
- Clinical Presentation:
  - Painless testicular mass / dull ache in one testis in a young man
  - ± hx of trauma accompanying discovery of mass
  - 10% presents with acutely painful testis (distinguish from torsion)
  - May present as back pain (if para-aortic nodes infiltrated with metastases)
- Points from examination:
  - Inseparable from the testis; can get above it
  - Hard, nodular, irregular, non-tender
  - Not transilluminable
  - Distinct from the superficial inguinal ring (can 'get above' mass)
- Differential Diagnosis
  - Chronic infection with scarring (i.e. orchitis / TB)
  - Long standing hydrocele with calcification

- Classification:

	Teratoma	Seminoma
Age of presentation	20-30yr	30-40yr
Tumour Markers	AFP and BhCG raised in 90%	Normal
Treatment of early disease	Chemotherapy (often only 2 cycles)	Adjuvant RT to para-aortic nodes ± Single dose of cisplatin
Treatment of advanced disease	Combination chemotherapy (platinum-based)	Adjuvant chemotherapy either single dose or combination (platinum-based)

  - Others:
    - Embryonal carcinoma, Choriocarcinoma, Yolk sac tumour
    - Leydig cell tumour – 10% malignant, a/w gynaecomastia
    - Sertoli cell tumour – a/w gynaecomastia)
    - Lymphoma (look for lymphoma elsewhere; poor prognosis)

- Investigations
  - US scrotum
    - Seminoma = hypoechoic lesions
    - Non-seminoma = inhomogeneous lesions
  - Tumour Markers (monitor effectiveness of therapy and screen for recurrence)
    - LDH, AFP, BhCG
  - Staging
    - CT AP – assess para-aortic lymph nodes involvement
    - CXR / US HBS – distant disease

- Management:
  - Staging, Radical orchidectomy via inguinal approach with combination chemotherapy
    - Stage 1 = testis lesion, no nodes involved, stage 2 = nodes below diaphragm, stage 3 = nodes above diaphragm, stage 4 = pulmonary and hepatic metastasis
    - op = early clumping of testicular artery & vein within the spermatic cord before testis is mobilized out of scrotum to prevent intra-operative seeding of tumour up testicular vein
- Prognosis
  - If no metastases: 5 year survival is 95% after orchidectomy and RT or CT

HYDROCELE

Asymptomatic fluid collection around the testicles (processus vaginalis) that transilluminates

- Points from examination:
  - Very **swollen scrotum**; uniformly enlarged
  - **Cannot define testis** well; not separable from testis
  - Maybe firm, tense or lax
  - **Maybe transilluminable** if acute (less in chronic hydrocele)
  - **Can get above the mass**; the superficial ring is distinct

- Pathology
  - During descent of the testis from the posterior abdominal wall, it carries a fold of peritoneum (processus vaginalis) – which normally forms the tunica vaginalis
  - Should this connection not get obliterated, fluid can accumulate in any part of this peritoneum derived covering and a hydrocele forms

- Anatomical Classification of Hydroceles
  - **Vaginal hydrocele:**
    - Only in tunica vaginalis & does not extend into the cord
  - **Hydrocele of the cord**
    - Mass around the cord; attached distally to the testis
    - Difficult to distinguish from irreducible inguino-scrotal hernia – may extend up and beyond
    - Traction of the testis causes a hydrocele of the cord to be pulled downwards
  - **Congenital hydrocele:**
    - Patent processus vaginalis filled with peritoneal fluid – sac communicates directly with the peritoneum
    - Patients give hx of intermittent scrotal swelling – usually resolves by 1yr of age
  - **Infantile hydrocele:**
    - Situation in between hydrocele of cord and congenital hydrocele
    - Processus vaginalis is obliterated at the deep ring and so the hydrocele does not communicate with the abdomen but remains patent in both cord and scrotum
- Secondary Hydrocele
  - From testicular tumour
  - From torsion
  - From trauma
  - From orchitis (any inflammation)
  - Following inguinal hernia repair

- Treatment options:
  - Conservative:
    - In congenital hydrocele – watch and wait, usually resolves by 1 year of age – if unresolved by 2.5 to 3 years → surgical closure
    - Watch & wait or Aspiration [tend to re-accumulate]
    - Must exclude a 2° cause – ultrasound scrotum
  - Surgical:
    - Lord's plication of the sac
    - Jaboulay's operation to evert the sac

EPIDIDYMAL CYST

- Points from examination:
  - Small mass separate from testis (within epididymis); can get above it
  - Firm; maybe loculated
  - Transilluminable if large cyst
- Often multiple in the head of epididymis
- May occur as a complication of vasectomy (spermatoceles)
  - Spermatocele do not transilluminate
- Treatment:
  - Conservative [mainstay]
  - Surgical: if painful, very large or frequent recurrences
    - Risk: operative damage and fibrosis of epididymis → subfertility

TESTICULAR TORSION (A SURGICAL EMERGENCY)

A true urologic emergency where the testis is rotated on its vascular pedicle resulting in ischemia – irreversible damage after 12hours of ischemia

- **Clinical features:**
  - Often in peri-pubertal (12-18 yr) age group
  - Clinical Diagnosis – **acute abdomen** (T10 innervation) **& acute onset of testicular pain and swelling** a/w nausea & vomiting
  - Previous attacks of self-limiting pain; ppt by trauma, cycling, straining, coitus
  - No history of voiding complains, dysuria, fever, exposure to STDs
- **Risk Factors**
  - Cryptorchidism (undescended testis)
  - Mal-descended testis hanging like a bell clapper within the tunica vaginalis
- **Physical Examination**
  - Swollen and tender scrotum,
  - High riding in scrotum with transverse lie
  - Absent cremasteric reflex (elicited by stroking inner thigh)
  - Negative Prehn Sign – no pain relief with lifting of affected testis (in contrast +ve prehn sign suggests epididymitis)
- **DDx:**
  - Epididymitis
  - Torsion of testicular appendage (pea coloured lump through scrotum)
  - Strangulated inguinoscrotal hernia
- **Investigation:**
  - Colour Doppler Ultrasound – help confirm or exclude diagnosis with 95% accuracy (useful when a low suspicion of testicular torsion exists)
- **Treatment**:
  - Emergency exploration if Doppler US –ve for flow or high index of clinical suspicion
    - Untwisting (lateral) of affected testis and bilateral orchidopexy
    - Warm up with warm pad to see reperfusion or check with doppler after untwisting [4 hours before ischemia]
    - If dead, excise and replace with prosthesis

VARICOCELE

Varicocele = dilatation of veins of the pampiniform plexus of the spermatic cord

Epidemiology:

- Present in 15-20% of post-pubertal males
- Predominantly occurs in left hemi-scrotum → pathophysiology (see below)
  - left spermatic vein enters the left renal vein at a perpendicular angle and the intravascular pressure in the left renal vein > right (compressed btw the aorta and SMA – "nutcracker effect")
  - Therefore → increased pressure in left spermatic vein which can dilate leading to incompetence of the valve leaflets → retrograde flow of blood toward testis in the erect position
- Bilateral varicocele occurs in 33% of patients, while unilateral right varicocele are very rare (search for underlying pathology)

History and Physical Examination:

- Can be asymptomatic or symptomatic (see below)
  - Dull aching, left scrotal pain – noticeable when standing and relieved by lying down
  - Testicular atrophy – compare both sides
  - Decreased fertility
- Best noticed on palpation with the patient standing up
  - Mass is separate from testis; can get above it
  - Feels like a bag or worms
  - Compressible mass above or surrounding the testis
  - Not transilluminable

Classification:

Subclinical (not palpable)	Vein larger than 3 mm on ultrasound; Doppler reflux on Valsalva maneuver
Grade I (small)	Palpable with Valsalva maneuver only
Grade II (medium)	Palpable at rest (without Valsalva maneuver), invisible
Grade III (large)	Easily visible

Causes:

- Idiopathic in younger males around puberty
- In older men with retroperitoneal disease: RCC

Treatment:

- Conservative: risk of infertility
  - Scrotal Support and NSAIDs
- Surgical:
  - Trans-femoral angiographic embolization with coil or sclerosant
  - Surgical Ligation: excise the surrounding dilated veins via high retroperitoneum, inguinal or laparoscopic approach

SCROTAL ABSCESS

History and Physical Examination

- History – poor hygiene
- Symptoms of UTI or STD – i.e. frequency, urgency, dysuria, penile discharge
- PE – erythematous and oedematous scrotum
- Scrotal fluctuant & may be palpable

Treatment:

- Analgesia PRN
- IV Antibiotics (Augmentin) → change to PO antibiotics on discharge
- Incision and Drainage with cavity left open and packed (allow wound to granulate from the base preventing a closed space from forming that becomes secondarily infected)

Complications:

- Incomplete drainage → persistence of abscess
- Failure to identify source of infection (i.e. urethral stricture) → recurrence
- Fournier gangrene (necrotizing fasciitis due to a synergistic poly-microbial infection)

FOURNIER GANGRENE

Necrotizing fasciitis of the perineum and genital region frequently due to a **synergistic polymicrobial infection**

Epidemiology:

- RF: diabetics, alcoholics, immunocompromised
- Source of infection:
  - Genitourinary (19%) – urethral stone / stricture / fistulae
  - Colorectal (21%) – ruptured appendicitis, colonic CA, diverticulitis, peri-rectal abscess
  - Dermatological (24%)
  - Idiopathic (36%)

History and Physical Examination:

- Abrupt onset with pruritus, rapidly progressing to edema, erythema and necrosis within hours
- Fever, chills and malaise
- Edema, erythema of skin of scrotum, phallus and perianal area – may progress to frank necrosis of skin and subcutaneous tissue
- Crepitus in tissue suggest presence of gas-forming organisms

Treatment:

- Broad spectrum antibiotics cover (against aerobic and anaerobic organisms)
- Wide debridement with aggressive post-operative support
  - Testes are often spared (have discrete blood supply)

1. LUMPS & BUMPS

1. APPROACH TO LUMPS & BUMPS

Permission: Introduce yourself
Position: Ensure patient (and you) are comfortable
Exposure: Expose area to be examined fully
(Remember: **Compare** with other side if applicable)

Inspection

1. **Number**: solitary / multiple
2. **Site**: take reference from bony points
3. **Shape** / **Symmetry**:
   - Hemispherical, Round, Exophytic
4. **Size**
5. **Scars**
6. **Colour & skin changes**?
   a. Sinuses, discharge
   b. Ulceration
   c. Erythema / cellulitis

Palpation (Ask patient: Is area **painful**?)

1. Overlying skin **temperature**
2. **Tenderness**
3. **Surface:**
   - Smooth/ Irregular/ Rough
4. **Margins** clearly defined?
5. **Consistency**
   - Hard > Firm > Tense > Soft
6. **Mobility**
   - Fully mobile in all directions?
   - Fixed and immobile?
   - Mobile only in certain directions?
7. **Relations to surrounding** tissues
   - Move lump in 2 perpendicular planes
     - Attached to **skin**? **muscle / tendon / bone**?
     - If appears to be attached to muscle:
       - Ask patient to tense muscle; Reassess mobility in the 2 planes
         - Intramuscular or below the muscle, it will disappear.
         - Above the muscle it will be more prominent.
         - Fixed to muscle, it will become less mobile.
8. **Fluctuant**? (for small / medium lumps)
   - Paget's sign: Rest 2 fingers on opposite sides of lump, press down on middle of lump➔ +ve: Feel fingers moving apart
9. **Special tests**
   - **Transillumination** [only for large lumps**;** Use pen torch on one side]
   - **Pulsatility** (only for some sites, e.g. Neck, abdomen)
     - Place finger on opposite sides of lump
       - Expansile: fingers pushed apart
       - Transmitted: Fingers pushed in same direction (usually upwards)
   - **Slip sign** – if lipoma is suspected
     - Tends to slip away from the examining finger on gentle pressure
   - **Compressibility / reducibility** [if AVM, haemangioma, hernia suspected]
     - Compressible: Disappears on pressure, reappears on release (AVM)
     - Reducible: Disappears on pressure, reappears with opposing force (hernia)
   - **Auscultation** – only for certain sites / lesions (e.g. neck, abdomen, etc.)

"Mr. X is a young Chinese gentleman…"
"On inspection, there is a (single) (hemispherical) lump on the (dorsum of the forearm)"
"It measures <take out ruler> (x by x cm)"
"There are (? scars, sinuses, ulceration, or discharge seen, nor overlying or surrounding skin changes)"

"Is the lump tender?"

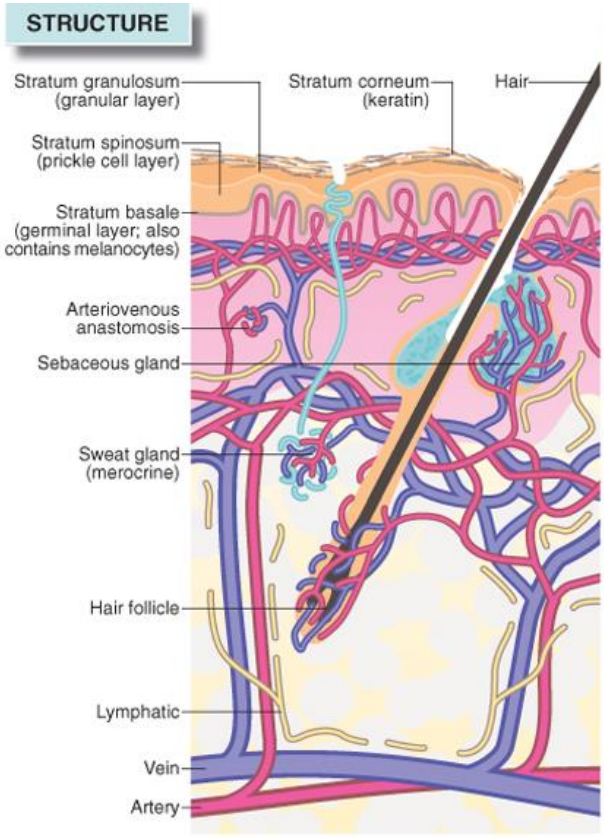
"On palpation, the overlying skin is (not) found to be warm. It is (non-tender)"
"The surface is (smooth), with clearly-defined margins"
"The consistency is firm, and it is (non-fluctuant)"
"The lump is (not) attached to the overlying skin, and it is non-pulsitile."
"It (appears to be attached to underlying muscle, as it is mobile horizontally but not longitudinally)"

S: site, size, shape, scars, skin changes, surface
E: edge, expansility/ pulsatility
C: colour, consistency, compressibility
T: tenderness, temperature, transillumability
O: others [fluctuance, fulid thrill]
R: reducability, relationship to each other

Ulcers:
Base: granulation tissue, slough, fascia, muscle, bone
Edge: sloping (healing), punched out, undermined, rolled (BCC), everted (SCC)
Discharge: serous, sanguinous, haemoserous, purulent

Request – *"I would like to complete my examination by…"*

- Examine the draining LNs
- If sebaceous cyst / lipoma → *"Looking for other lumps elsewhere"*
- Ganglion → *"Looking for other lumps elsewhere"* + *"Asking for hand dominance"* + *"Taking an occupational history"*

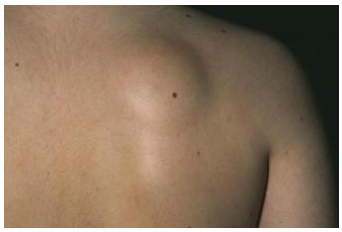


LESIONS	
Lesions derived from epidermis	Benign Skin tags (papillomas) Warts Seborrhoeic (senile) keratosis Keratoacanthoma Premalignant Solar keratosis Bowen's disease Erythroplasia of Queyrat Malignant Squamous cell carcinoma Basal cell carcinoma
Melanotic lesions	Benign pigmented naevi Malignant melanoma
Lesions derived from the dermis	Pyogenic granuloma Histiocytoma Keloid Secondary carcinomas Kaposi's sarcoma
Lesions derived from skin appendages	Epidermal (sebaceous) cyst Dermoid cysts (external angular and implantation) Pilonidal sinus Benign appendage tumours
Lesions derived from the hypodermis and deeper tissues	Lipoma and liposarcoma Neurofibroma and sarcoma Neurofibromatosis Schwannoma Deeper lesions, e.g. 'ganglion'
Lesions of vascular origin	Campbell de Morgan spots Spider naevi Angiomas Glomus tumours of the digits

Symptoms and signs	Diagnostic significance
1. Lump in or on the skin	
Size, shape and surface features Revealed by inspection-is the lesion smooth-surfaced, irregular, exophytic (i.e. projecting out of the surface)?	Epidermal lesions such as warts usually have a surface abnormality but deeper lesions are usually covered by normal epidermis. A **punctum** suggests the abnormality arises from an epidermal appendage, e.g. epidermal (sebaceous) cyst
Depth within the skin Superficial and deep attachments. Which tissue is the swellingderived from?	Tends to reflect the layer from which lesion is derived and therefore the range of differential diagnosis (i.e. epidermis, dermis, hypodermis or deeper)
Character of the margin Discreteness, tethering to surrounding tissues, three-dimensional shape	A regular shaped, discrete lesion is most likely cystic or encapsulated (e.g. benign tumour). Deep tethering implies origin from deeper structures (e.g. ganglion). Immobility of overlying epidermis suggests a lesion derived from skin appendage (e.g. epidermal cyst)
Consistency Soft, firm, hard, 'indurated', rubbery	Soft lesions are usually lipomas or fluid-filled cysts. Most cysts are fluctuant unless filled by semi-solid material (e.g.epidermal cysts), or the cyst is tense (e.g. small ganglion). Malignant lesions tend to be hard and irregular ('indurated') with an ill-defined margin due to invasion of surrounding tissue. Bony-hard lesions are either mineralised (e.g. gouty tophi) or consist of bone (e.g. exostoses)
Pulsatility	Pulsatility is usually transmitted from an underlying artery which may simply be tortuous or may be abnormal (e.g. aneurysm or arteriovenous fistula)
Emptying and refilling	Vascular lesions (e.g. venous malformations or haemangiomas) empty or blanch on pressure and then refill
Transilluminability	Lesions filled with clear fluid such as cysts 'light up' when transilluminated
Temperature	Excessive warmth implies acute inflammation, e.g. pilonidal abscess
2. Pain, tenderness and discomfort	These symptoms often indicate acute inflammation. Pain also develops if a non-inflammatory lesion becomes inflamed or infected (e.g. inflamed epidermal cyst). Malignant lesions are usually painless

3. Ulceration (i.e. loss of epidermal integrity with an inflamed base formed by dermis or deeper tissues)	Malignant lesions and keratoacanthomas tend to ulcerate as a result of central necrosis. Surface breakdown also occurs in arterial or venous insufficiency (e.g. ischaemic leg ulcers), chronic infection (e.g. TB or tropical ulcers) or trauma, particularly in an insensate foot
Character of the ulcer margin	Benign ulcers-the margin is only slightly raised by inflammatory oedema. The base lies below the level of normal skin Malignant ulcers-these begin as a solid mass of proliferating epidermal cells, the centre of which eventually becomes necrotic and breaks down. The margin is typically elevated 'rolled' and indurated by tumour growth and invasion
Behaviour of the ulcer	Malignant ulcers expand inexorably (though often slowly), but may go through cycles of breakdown and healing (often with bleeding)
4. Colour and pigmentation	
Normal colour	If a lesion is covered by normal-coloured skin then the lesion must lie deeply in the skin (e.g. epidermal cyst) or deep to the skin (e.g. ganglion)
Red or purple	Redness implies increased arterial vascularity, which is most common in inflammatory conditions like furuncles. Vascular abnormalities which contain a high proportion of arterial blood such as Campbell de Morgan spots or strawberry naevi are also red, whereas venous disorders such as port-wine stain are darker. Vascular lesions blanch on pressure and must be distinguished from purpura which does not
Deeply pigmented	Benign naevi (moles) and their malignant counterpart, malignant melanomas, are nearly always pigmented. Other lesions such as warts, papillomata or seborrhoeic keratoses may become pigmented secondarily. Hairy pigmented moles are almost never ~~malignant~~. Rarely, malignant melanomas may be non-pigmented (**amelanotic**). New darkening of a pigmented lesion should be viewed with suspicion as it may indicated malignant change
5. Rapidly developing lesion	Keratoacanthoma, warts and pyogenic granuloma may all develop rapidly and eventually regress spontaneously. When fully developed, these conditions may be difficult to distinguish from malignancy. Spontaneous regression marks the ~~lesion~~ as benign
6. Multiple, recurrent and spreading lesions	In certain rare syndromes, multiple similar lesions develop over a period. Examples include neurofibromatosis and recurrent lipomata in Dercum's disease. Prolonged or intense sun exposure predisposes a large area of skin to malignant change. Viral warts may appear in crops. Malignant melanoma may spread diffusely (**superficial spreading melanoma**) or produce satellite lesions via dermal lymphatics
7. Site of the lesion	Some skin lesions arise much more commonly in certain areas of the body. The reason may be anatomical (e.g. pilonidal sinus, external angular dermoid or multiple pilar cysts of the scalp) or because of exposure to sun (e.g. solar keratoses or basal cell carcinomas of hands and face)
8. Age when lesion noticed	Congenital vascular abnormalities such as strawberry naevus or port-wine stain may be present at birth. Benign pigmented naevi (moles) may be detectable at birth, but only begin to enlarge and darken after the age of 2

2. LIPOMA



Inspection

- Can be **single**, often multiple
- Usually at **neck, trunk**
- **Hemispherical** – may appear lobulated
- Scars ➔ Implies **recurrent** lipoma

Palpation

- **Smooth** or **lobulated on firm pressure** – bulging between strands of fibrous tissue)
- **Soft / firm** (depending on nature of fat)
- **Well defined** edges (may not be regular; series of curves corresponding to each lobule
- Pseudo-fluctuance if large – lipomas are not liquid; but fat maybe more liquid
- **Mobile** in all directions (if subcutaneous)
- Positive **slip sign;** No transilluminance / thrill
- Usually in the **subcutaneous tissue.** [check attachment skin & muscle]

"Mr. X is a young Chinese gentleman…"
*"On inspection, there is a **hemispherical lump** over the **right scapula**"*
*"It measures **10 by 8 cm**"*
*"There are **no scars**, **punctum**, **ulceration**, or **discharge** seen, nor any overlying or **surrounding skin changes**"*
*"On **palpation**, the overlying skin is **not warm**, it is **non-tender**"*
*"The surface is **lobulated**, and its **margins are not well-defined**"*
*"The consistency is **soft**, and it is **fluctuant**"*
*"The lump is **not attached** to the overlying skin"*
*"It is **mobile** in all directions with a **positive slip sign**"*
*"It is **not transilluminable**"*
*"I would like to complete my examination by looking for **other similar lumps**"*
"My provisional diagnosis is a lipoma"
"*My differential diagnosis is: large sebaceous cyst"*

Background Information

- Definition: Benign tumour consisting of mature fat cells (distended with fat from over-activity)
  - Malignant change **does not** occur
  - **Liposarcomas arise de novo**; occur in **older age** (**deeper tissues** – retroperitoneal, deep tissues of thigh, subscapular)
    - Liposarcoma classification
      1. Well-differentiated
      2. Myxoid, round cell (poorly differentiated myxoid)
      3. Pleomorphic liposarcoma
- Clinical features
  - Can occur at all ages (not common in children)
  - **Slow-growing**, never regress
  - May be **multiple**: **lipomatosis** (multiple continuous lipomata)
    - Occur in buttocks / neck
    - Can cause distortion of subcutaneous tissues.
- Treatment
  - Non-surgical – watch & wait
  - Surgical – If patient wants it removed (Pain / peripheral neuropathy – Dercum's disease, Cosmesis)
    - Can be removed under **LA**
    - Nuchal lipomas (back of the neck): extremely fibrous septae: difficult to excise
    - If close to joint: LA may not be possible (may communicate with joint)

- Variants of lipomas / syndromes associated with lipomas
  - **Adiposis dolorosa (Dercum's disease)**
    - Multiple painful lipomas in limbs, sometimes trunk
    - Associated with peripheral neuropathy
    - Angiolipomas: prominent vascular component
  - Hibernomas: brown fat cells
  - Cowden's disease – associated with:
    - *Thyroid cancers*
    - Lipomas
    - Palmoplantar keratoses
    - Multiple facial papules
    - Oral papillomatoses
  - Bannayan-Zonana syndrome – rare AD dz: lipomas with macrocephaly and haemangiomas, intestinal polyps

3. SEBACEOUS CYST

"Mr. X is a young Chinese gentleman…"
*"On **inspection**, there is a **single hemispherical** lump in the **middle of the forehead** just above the eyebrows"*
*"It measures **1 by 1 cm** in diameter"*
*"There is a **visible punctum** over the lump"*
*"There are no **scars**, **sinuses**, **ulceration**, or **discharge seen**, nor any overlying or **surrounding skin changes**"*

*"On **palpation**, the overlying skin is **not warm**. It is **non-tender**."*
*"The surface is **smooth**, with **clearly-defined** margins"*
*"The consistency is **firm**, and it is **non-fluctuant**"*
*"The lump is **attached to the overlying skin**"*
*"It is **mobile** in all directions"*
*"**Slip sign is negative**"*
"I would like to complete my examination by…"
*"Looking for **other lumps** elsewhere"*
*"My provisional diagnosis is a **sebaceous cyst**"*
My differentials are: Lipoma / Dermoid cyst

Inspection

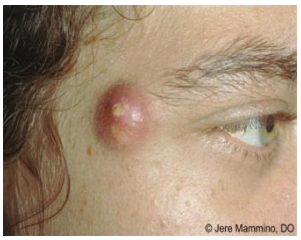
- Usually **solitary** (can be multiple)
- **Hemispherical**
- **Site:** face, trunk, back, neck, scalp, shoulders (none on palms / soles)
- Variable size ; few mm to 4-5 cm
- May have bluish discolouration
- Punctum in apex: in 50%
- May exhibit plastic deformation on palpation

Palpation

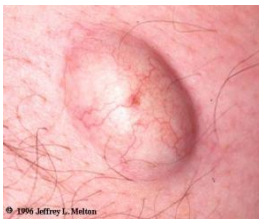
- Normal Temperature, non-tender (unless inflamed)
- **Smooth surface**
- **Well-defined margins** (lies in subcutaneous fat)
- **Tense** consistency, may stretch overlying skin (plastic deformation)
- **Non fluctuant**, not transilluminable
- **Attached to skin,** not attached to deeper structures, mobile in all directions

Background Information

- Sometimes considered to be similar to epidermoid cyst
  - More accurate terminology: pilar / trichilemmal cysts
- 2 histological types:
  - **Epidermal cyst:** from infundibular portions of hair follicles
  - **Trichilemmal cyst**: from hair follicle epithelium (most common on scalp), frequently multiple (AD inheritance)
- Arise from **infundibular** parts of hair follicles
- Definition: Distension of **sebaceous glands** with sebum from blockage of opening
- Clinical features
  - Occur in all age groups, rarely present before adolescence
  - Slow growing,– may appear suddenly at adolescence
  - May become **infected**: acutely painful, sudden increase in size
  - May **spontaneously discharge** contents through punctum, regress
    - Point of fixation & discharge along a hair follicle
    - Point gets pulled inwards on enlargement of the mass – creates punctum
    - **Sebaceous horn** may form from hardening of slow discharge from wide punctum
      - Sebum slowly exudes, dries and hardens into conical spike
      - Sebum usually washed away – horn results only if overlying skin not washed
      - Can be pulled out of skin
      - Treatment: excision / curettage along with base + histological assessment



Inflamed

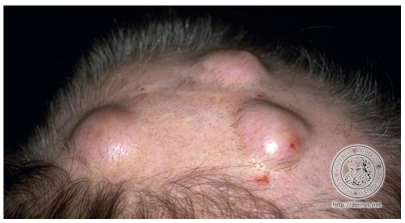


- Complications
  1. Infection (±discharge)
  2. Ulceration
  3. Calcification (trichilemmal cyst) (may lead to cyst hardening)
  4. Sebaceous horn formation, [hardening of a slow discharge of sebum from a large, central punctum.]
  5. Malignant change
- Treatment
  - Non-surgical: leave alone (if small, asymptomatic).
  - Surgical
    - Complete excision of cyst and contents under LA.
    - Prevention of recurrence: by removal of **elliptical portion** of skin containing punctum along the lines of Langers.
    - If at the angle of jaw, be careful of the facial nerve during operation. Damage to zygomatic branch can cause eye ulceration.

- **If lump is increasing in size, what to exclude?**
  - Malignancies: BCC, Malignant melanoma.

- **Cock's peculiar tumour (complication)**
  - Proliferating trichilemmal cysts that can grow to large size, ulcerate
    - may become infected, open, granulating & edematous
    - Boggy, painful, discharging swelling
    - solitary, 90% occur in scalp
  - often mistaken for SCC scalp; Angry, malignant-looking (malignant transformation rare)
    - Heaping up of granulation tissue from the lining of the cyst
    - burst through skin, giving everted appearance
    - regional lymphadenopathy may be present

- Gardner's syndrome (If multiple lumps found)
  - Genetic disorder associated with:
    - Multiple osteomata of skull & epidermal cysts
    - Adenomatous polyposis of large bowel & CRCs
    - Desmoid tumours
    - Thyroid cancers



4. GANGLION

Inspection

- Single; may have ovelying scar [recurrent mass]
- Hemispherical, flattened,
- **Near** joint **capsules, tendon sheaths** (**90% on wrist, hand** – ventral / dorsal)
- Variable (0.5 – 6 cm)

Palpation

- Normal temperature, non-tender
- **Smooth** surface with **Well-defined margins**
- May be multilocular
- Soft & fluctuant if large > firm consistency if small
- Weakly transilluminant. (gelatinous material)
- Mobility:
    - Should assess mobility in 2 perpendicular planes, then with underlying muscles tensed (less mobile when tensed)
    - **Not attached to overlying skin** (mobile over it)
    - **Attached to fibrous structures** of origin [to joint capsule, tendon sheath, intramuscular septum, fixed when tensed]
- Reducibility: may slip between deep structures when pressed (appears falsely reduce into joint)

Request

- Other similar lumps
- Ask which hand is dominant (may affect management)
- Occupation

"Mr. X is a young Chinese gentleman, who is alert and comfortable…"
*"On **inspection**, there is a single **hemispherical** lump on the **dorsum of the left wrist**"*
*"It measures **3 by 2 cm**"*
*"There are **no scars**, ulcerations, or discharge seen, nor any overlying or surrounding skin changes"*
*"On **palpation**, the overlying skin is **not warm**. It is **non-tender**"*
*"The surface is **smooth**, with **clearly-defined** margins"*
*"The consistency is **soft**, and it is **fluctuant**"*
*"The lump is **not attached** to the overlying skin"*
*"It appears to be **attached to underlying muscle**, as it is mobile horizontally but not longitudinally"*
*"It is **transilluminant**"*
"I would like to complete my examination by…"
"Looking for other similar lumps"
"Asking Mr. X for his hand dominance"
"Taking an occupational history"
"My provisional diagnosis is a ganglion"
My differential is a 1. Bursa
2. Cystic protrusions of synovial cavity of arthritic joints
3. Benign giant cell tumours of flexor shealth
(These 2 are normally soft in consistency. Ganglion is more tense.)

Background Information

- Definition: Cystic myxomatous degeneration related to synovial lined cavity [joint capsule or tendon sheath]
  Origin controversial: pockets of synovium communicating with joint, tendon sheath / degeneration of mucoid fibrous tissue
- Site:
    - Can occur anywhere in body
    - Common in areas of fibrous tissue (e.g. around joints, esp. Dorsal > Volar wrist @ scapholunate joint)
        - Most common soft-tissue mass in the hand
- Types:
  1. Simple
  2. Compound – chronic inflammation distends tendon sheath above and below the flexor retinaculum → r/o TB / RA
  3. Occult
  4. Interosseous

- Clinical features
  - Majority between 20 and 60 years (rare in children)
  - Grow slowly over months / years
  - Non painful

- Differentials
  - Bursae (soft)
  - Cystic protrusion of synovial cavity in OA (joint will be abnormal)
  - Benign giant cell tumours of flexor shealth (Pigmented VilloNodular Synovitis)
  - Lipoma
  - Sebaceous cyst

- Treatment
  - Non-surgical
    - Watch & wait, usually may disappear after a few months.
    - Aspiration + 3/52 of immobilisation (successful in 30-50%). High chance of recurrence 6-12/12 later.
  - Surgical
    - **Complete excision** to include **neck of ganglion** at site of origin. Along the lines of Langers.
    - Complications
      - Wound complications: Scar, haematoma, infection
      - Recurrence <10%
      - Damage to adjacent neurovascular structures.
      - Stiffness & Contractures

5. BASAL CELL CARCINOMA

– "Examine this gentleman's face"
(If the other side of the face, etc. needs to be inspected, ask the patient to turn his head – avoid moving around the patient)

"Mr. X is an elderly Chinese gentleman…"
*"On inspection, there is a **single hemispherical** lump just above alar of the nose"*
*"It measures **2 by 2 cm**"*
*"The **edges** of the lump are **well defined**, with a **pearly, rolled appearance**"*
*"There is a small area of **pigmentation on the periphery** of the lump, and **fine telangiectasia are seen** over the lump"*
"There are no visible scars, ulceration, or discharge seen, nor any other overlying or surrounding skin changes"
*"On palpation, the overlying skin is **not warm**. It is **non-tender**."*
*"The surface is **smooth**"*
*"The consistency is **firm**"*
*"The lump **arises from the skin**"*
*"It is **freely mobile over the underlying tissues**"*
"My provisional diagnosis is basal cell carcinoma"
"My differentials include SqCC, keratoacanthoma"
"I would like to complete my examination by…"
Examining for cervical lymphadenopathy (although very rare in BCC)

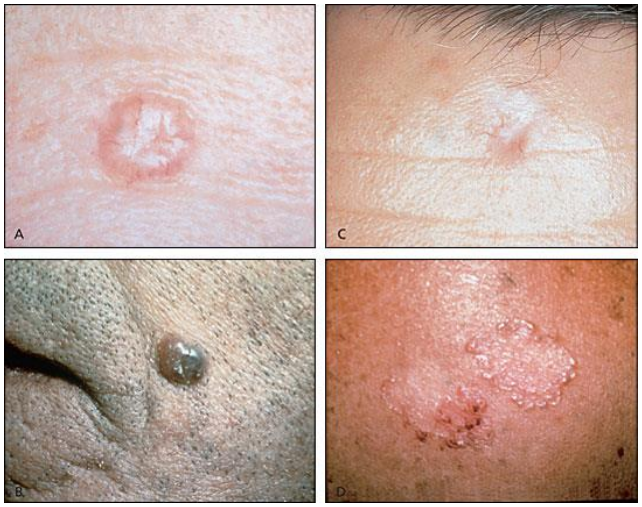
Inspection

- Single (often multiple)
- Commonly found on the **face,** (above line drawn from angle of mouth to earlobe)
- Hair-bearing, sun-exposed skin (especially around the eye)
- Lesions raised above the skin:
  - ***Nodular/ nodulo-ulcerated type*** (most common):
    - **Pearly, rolled edges** [smooth, glistening, slightly transparent]
    - May be pigmented, with telangiectasia over the lump
    - May have central ulceration; erode facial structures if advanced
  - *Cystic*: large cystic nodule
- Lesions not raised:
  - *Pigmented:* contains melanin; confused with malignant melanoma
  - *Sclerosing*: flat or depressed with ill defined edges; maybe ulcerated
  - *Bush-fire / Cicatricial*: multiple superficial erythematous lesions with pale atrophic areas
  - *Superficial*: erythematous scaly patches
- Base:
  - May be covered with coat of **dried serum & epithelial cells**
  - If deep: may expose deeper tissues (bone, muscle, etc.), covered with poor-quality granulation tissue
  - On face: may erode deep into facial structures

Palpation *(Important to palpate for **mobility**: fixation and deep local invasion)*

- Normal temperature, may be painful / itchy
- Firm / solid consistency
- should be mobile over underlying structures, confined to skin
  - If fixed, immobile ➔ deeper invasion
- Regional LAD (metastases are extremely rare, to rule out SCC)

+ Ask about pre-disposing factors

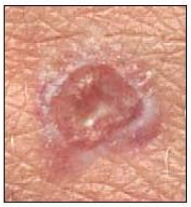


A = nodular
B = pigmented
C = sclerosing
D = superficial

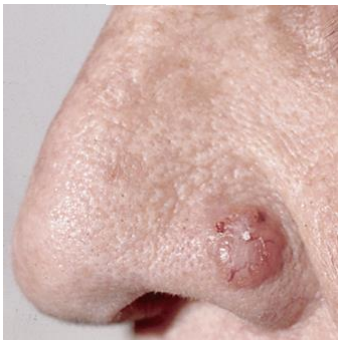
Background Information

- Locally invasive carcinoma of **basal layer of the epidermis**
- **Does not metastasize**, but can **infiltrate** adjacent tissues
- Common in **sun-exposed skin**
- Pre-disposing factors
  - Congenital (rare)
    - Xeroderma pigmentosum (familial, associated with failure of DNA transcription)
    - Gorlin's syndrome (rare autosomal dominant cancer)
  - Acquired
    - **Sunlight** (especially UV light; UV-B range)
    - Carcinogens (smoking, **arsenic)**
    - **Previous RT**
    - Malignant transformation in previous skin lesions (e.g. naevus sebaceous)

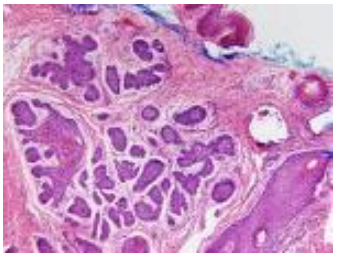
Basal cell carcinoma



- Clinical features
  - In **elderly** people (incidence increases with age)
  - Rare in dark-skinned races
  - Males > females
  - **Grow very slowly**; months / years typically
  - May **spread radially** – leaving central scar
  - Persistent nodule / ulcer with central scab (repeatedly falls off, reforms)
  - May have itch / pain
  - If neglected: deep infected ulcer



- Macroscopic appearances:
  - Above the skin:
    - Nodular
    - Nodulo-ulcerative / Deeply eroding ulcer ("rodent ulcer")
    - Cystic
  - Not raised above the skin:
    - Pigmented
    - Geographical / cicatricial / "bush-fire" (advancing edge, healing centre)
    - Sclerosing (flat / depressed tumour, ill-defined edge)
    - Superficial (erythematous scaly patches)



- Microscopic features
  - Most commonly islands and nests of basaloid cells in dermis
  - High mitotic rates, peripheral palisading
  - (islands arranged radially with long axes in // alignment)

- Origin of various appearances:
  - Tumour always starts as a **nodule**
  - When central epithelium dies, ulcer develops (**nodulo-ulcerative**)
    - **Edge rolled – raised up and rounded** (but not everted) (may be only clue to diagnosis)
  - If centre of tumour does not necrose / ulcerate: nodule enlarges → **cystic appearance**
    - Not really cystic: solid and non-fluctuant
  - If pigmented brown by excess melanin: **pigmented BCC**
  - **Geographical appearance**:
    - When nodule first ulcerates, rolled edge is circular
    - Shape becomes irregular as malignant cells spread
    - As ulcer heals: irregular, raised edge around flat white scar – "bush-fire" BCC

- **Differentials**
  - SqCC
    - Especially if ulcerated
    - But if rolled edge: more likely BCC
  - Keratoacanthoma (adenoma sebaceum, molluscum pseudo-carcinomatosum)
    - But scar will be deep (see below)
  - If pigmented: malignant melanoma (rare in Singapore)

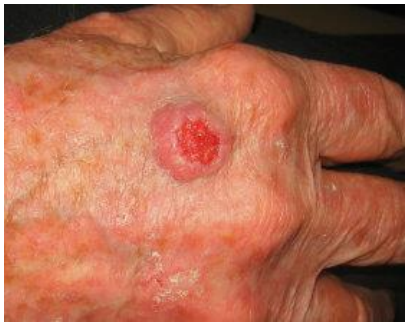
- Treatment
  - *Raised above skin:* **excision with 0.5 cm margin** (maximum)
  - *Not raised above skin:* **wider margin** of excision, especially if at inner acanthus of eye, nasolabial fold, nasal floor, ear
    - Frozen section may be needed to ensure adequate excision
  - Alternative:
    - **RT**
  - Eyes, ears, nasolabial fold lesions: **Moh's chemosurgery**
    - Staged chemosurgery, histological assessment of margins & electrodessication

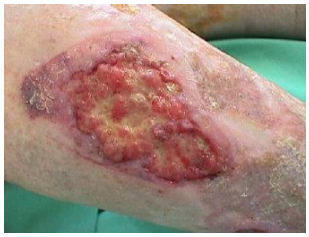
6. SQUAMOUS CELL CARCINOMA

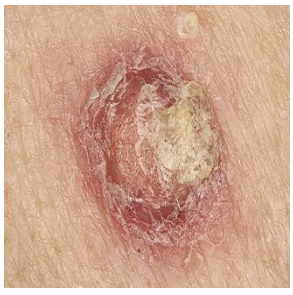
"Mr. X is an elderly Chinese gentleman…"
*"On **inspection**, there is a **single irregular ulcer** on the **dorsum of the right hand, proximal to the 1st & 2nd MCP joints**"*
*"It measures **1.5 by 1.5 cm**. The edge of the ulcer is **well-defined**, **red** and **heaped up**."*
*"The base of the ulcer is **shallow** and contains **red granulation tissue**."*
*"There are no scars, or **discharge** seen, nor any **surrounding skin changes**."*
*"On **palpation**, the surrounding skin is **not warm**. It is **non-tender**"*
*"The edges are **firm**"*
*"The lump **arises from the skin**"*
*"It is **fixed and immobile**"*
"My provisional diagnosis is squamous cell carcinoma"
"My differentials are…"
- *Benign: Keratoacanthoma, infected seborrhoeic wart, solar acanthosis, pyogenic granuloma*
- *Malignant: BCC, malignant melanoma, solar keratosis*

"I would like to complete my examination by…"
"Examining the local lymph nodes for lymphadenopathy"
"Taking a history looking for sites of metastases"
"Examining the abdomen and lungs for signs of metastases"

Inspection







- Single (may be multiple)
- More common on **sun-exposed skin** – head, neck, arms, hands, trunk
- may be of considerable size (> 1 cm)
- Round nodule or **Circular ulcer or Irregular/ exophytic/ fungating mass**
- **Well defined edges**:
  - everted (excessive growth raises it above skin)
  - dark, **red-brown** colour (very vascular)
- May have **central ulceration,** Base:
  - Necrotic tumour; may be covered with coagulated blood / serum
  - Granulation tissue: tends to be pale, unhealthy
  - Deep tissues may be exposed
  - Depth: variable (may be very deep; especially in soft tissue)
  - Can be copious, bloody, purulent, foul-smelling discharge
- Surrounding tissue may be oedematous, thickened

Palpation

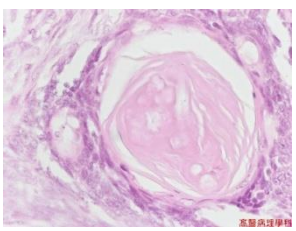
- normal temperature, not tender
- usually mobile
  - If immobile: invasion into deep structures

Request for:

- **Examination of local lymph nodes (5%** at time of presentation)
  - Often enlarged (but may not contain tumour even if enlarged – can be from infection)
- Examination for sites of metastases
  - Respiratory: lung (pleural effusion)
  - Abdominal: liver (hepatomegaly)
- Take a history looking for predisposing factors (see below)

Background Information

- Carcinoma of the cells of the epidermis forming superficial keratinous squamous layer
- Local invasion into epidermis, dermis, adjacent tissues, & lymphatic spread to LNs
- Microscopy:
  - Tongues of tumours cells spreading in all directions
  - "Epithelial pearls" – nest of squamous epithelium, cells are arranged in concentric circles surrounding a central focus of acellular keratin
- Clinical features
  - Incidence increases with **age** (usually elderly male)
  - **Predisposition:**
    - Congenital:
      - Xeroderma pigmentosum (AD, failure of DNA transcription)

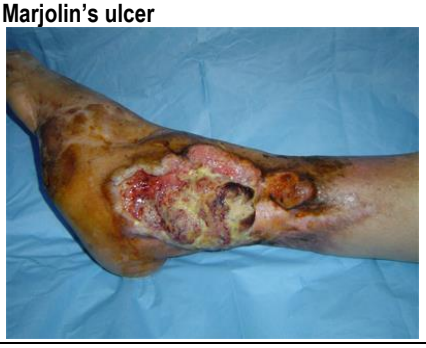
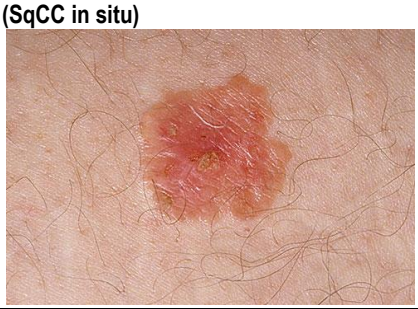
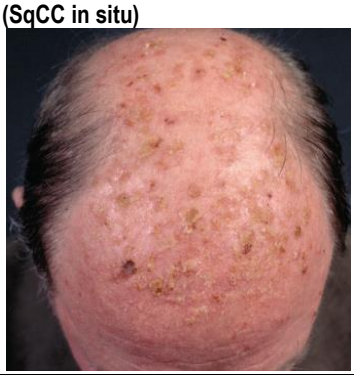


        - Acquired
            - Env^{n}: sunlight, Irradiation, Chemicals
            - Pre-existing lesions: Solar keratosis, Bowen's disease
            - Chronic ulcers: old burns, chronic venous ulcers
            - Immunosuppresion (post-transplant, HIV)
    - Usually has been **growing for 1 – 2 months** before being noticed
        - Begins as small nodules on skin
        - As enlargement occurs, centre necroses, sloughs
        - **Nodule turns into ulcer**
        - Ulcer initially circular with **prominent everted edges**
        - Subsequently enlarges & changes to any shape
            - Bleeding (more common with SCC than BCC)
            - Discharge
            - Pain (invasion of deep structures)
            - Lymphadenopathy

➢ Complications
    - Infection
    - Bleeding (massive / fatal if erosion into large vessel)

➢ Treatment (depending on site of lesion)
    - **Wide-excision with 1 cm margin**
    - **Radiotherapy** (if unresectable, nodal spread)
    - **+ Block dissection of regional lymph nodes** (if involved)
    - Eyes, ears, nasolabial fold lesions: Moh's chemosurgery
        - Staged chemosurgery, histological assessment of margins & electrodessication

Lesions Associated with SqCC

Marjolin's ulcer 	➢ SqCC arising in long-standing benign ulcer / scar o Commonest ulcer: venous ulcer o Commonest scar: burns ➢ Very similar in appearance to classic SqCC, but may not be so florid
Bowen's disease **(SqCC in situ)** 	➢ Very slowly growing, may progress to SqCC ➢ red, scaly irregular plaque **on the trunk** o if on the penis, vulva or oral cavity = **erythroplasia of Queyrat** ➢ **Intraepidermal carcinoma** o a/w visceral malignancies in 5-7 yrs time esp if area of skin has not been exposed to the sun ➢ HPV has been found in some lesions ➢ Microscopically o Epidermis (Atypical keratinocytes) o Basal layer is intact ➢ Treatment: **excision (SqCC will grow eventually)**
Solar (actinic) keratosis **(SqCC in situ)** 	o Multiple yellow-grey to brown scaly tumour ▪ Small, hard, ▪ Begin with thickening of skin o On sun-exposed skin of elderly patients o **25% may undergo change to SqCC** o Microscopically: hyperkeratosis, atypical dividing cells in prickle cell layer (irregular acanthosis), focal parakeratosis, basal layer atypical only (vs atypia in whole epidermis in SqCC) o Treatment: ▪ Non-surgical: **cryotherapy, topical chemotherapy** (5-FU) ▪ Surgical: **curettage** of affected skin

7. MALIGNANT MELANOMA

"Mr. X is a middle aged Chinese gentleman…"
*"On **inspection**, there is a **single flat-looking lesions** over the **right foot**"*
*"It measures **2 by 4 cm**"*
"It is variegated in appearance, and exhibits red, white, and black discolouration"
*"The margins are **clearly-defined** and **irregular**"*
"There are no scars, nor any surrounding pigmentation, erythema, or ulceration, bleeding, or discharge"
*"On **palpation**, the overlying lesion is **palpable**. It is **not warm**. It is **non-tender**"*
*"The surface is **smooth**, and its consistency is **firm**"*
*"The lump is **attached** to the skin, and moves with it over deeper structures"*
"My provisional diagnosis is malignant melanoma"
"My differential diagnoses are: BCC, pigmented naevus"
"I would like to complete my examination by…"
"Examining for regional lymphadenopathy"
"Take a history for: cardinal symptoms of malignant change, and any predisposing factors"

Inspection

- Usually single (may have satellite lesions around primary lesion)
- Site: Limbs, head & neck, trunk, subungual, mucocutaneous junction, mouth, anus
- Any colour: pale pink, brown, black, purple (rich blood supply)
- Clearly defined but irregular
- May ulcerate, discharge
- May have surrounding halo: brown (pigment), pink (inflammation)
- Types:
    - Superficial spreading melanoma (70%):
        - Legs of women and backs of men
        - Red, white, blue in colour
        - Irregular edge
    - Nodular type melanoma (15-30%):
        - On trunk
        - Polyploidal and raised
        - Smooth surface with irregular edge
        - Frequently ulcerated
    - Lentigo maligna melanoma:
        - On face or dorsum of hands & forearms
        - Underlying lesion is flat, brown-black with irregular outline
        - Malignant area is thicker and darker
    - Acral lentiginous melanoma:
        - More common in Asians and Blacks
        - On hairless skin: subungual area, palms, soles
        - Irregular area of brown/ balck pigmentation
    - Others: amelanotic melanoma, intra-cranial melanoma, retinal melanoma
        - *"Beware of the man with the glass eye and hepatomegaly"*

Palpation

- Normal Temperature, Non-tender
- Surface
    - If small: smooth epithelium
    - If ulcerates: covered with crust (blood + serum)
    - If bleeding, / infected: wet, soft, boggy
- Firm consistency (small satellite nodules feel hard)
- Mobile, moves with skin over deeper structures

Request

- Palpation for regional lymphadenopathy
- Palpation for other subcutaneous nodules (lying along course of draining lymphatics)

Background information

4 commonest types of malignant melanoma

- Superficial spreading melanoma (70%)
- Nodular melanoma (15 - 30%)
- Lentigo maligna melanoma
- Acral lentigous melanoma

Microscopic features

- Consists of loose nests of melanocytes in basal cell layer:
- Invade epidermis (leading to destruction, ulceration) & deeper into dermis, subcutaneous fat

Clinical Features

- Very rare before puberty (usually > 20 years old)
- Equally in both sexes (but distribution different – see below)
- > 25% arise de novo
    - **Change in surface, size, colour, Halo, satellite nodules**
    - **Ulceration, bleeding**
    - **Itch, No pain**
    - Lymphadenopathy
- Symptoms of distant metastases: LOW, SOB, jaundice
    - Lymphatogenouly to: regional LN
    - haematogenously to: Lungs [pleural effusion], Liver [hepatomegaly], Brain [focal neurological signs] & Skin and subcutaneous tissues

Predisposing Factors

- Congenital / non-modifiable
    - Light skinned race
    - **Xeroderma** pigmentosum
    - **Dysplastic naevus syndrome** (B-K mole, FAMM syndrome) – 100% risk if 2 family members affected
    - Large congenital naevi
    - **FHx in 1st degree relatives** (1.5X risk)
- Acquired / modifiable
    - **Sunlight exposure**
    - **Pre-existing skin lesions**
        - Lentigo
        - > 20 benign pigmented naevi (3 x risk)
    - **Previous melanoma** (3.5 x risk)

Features of pigmented skin lesion suspicious of malignancy

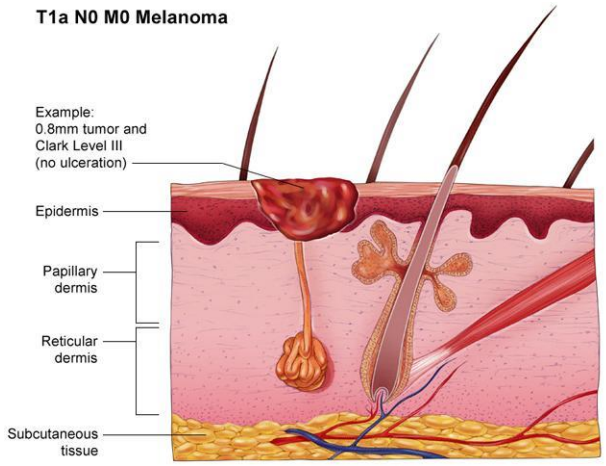
1. **A**symmetry
2. **B**leeding & ulceration (late)
3. **C**hange in: colour, size, shape, surface, number (early)
    a. Surface:
        i. Loss of normal surface markings (e.g. skin creases) around lesion
        ii. Skin may become rough / scaly
        iii. Itchy with pale-pink halo (inflammation)
    b. Size:
        i. Growth of newly-formed / long-standing mole
        ii. Increase in edge, width, thickness
    c. Colour:
        i. Becoming darker
        ii. Halo of brown discolouration in skin around the lesion
        iii. Patchy colour change (black, to blue-purple → ↑ vascularity)
        iv. Occasionally colourless: no melanin production
    d. Number:
        i. Satellite nodules of tumour around the lesion
        ii. Enlarged inguinal, axillary lymph nodes
4. **D**iameter >6mm
5. **E**levation (flat plaque → nodule)

Request

- **Examine draining lymph nodes**
- **Take a history for**:
  - **Cardinal symptoms of malignant change in a mole**
    - Rapid increase in size
    - Itching
    - Bleeding
    - Change in colour / shape / thickness
  - **Predisposing factors**

Differentials

- *Benign*
  - Moles (pigmented naevus – ↑ melanocytes, ↑ melanin)
  - Freckles (normal number of melanocytes, ↑ melanin from each)
  - Lentigo (↑ melanocytes, normal amount of melanin from each)
  - Pigmented seborrhoeic keratoses
  - Dermatofibroma
  - Thrombosed haemangioma
- *Malignant*
  - Pigmented BCC



Staging by depth of invasion

Clark's levels of invasion

Level	Extent of Tumour	5-Year Survival
I	Epidermis only	98%
II	Invades papillary dermis	96%
III	Fills papillary dermis	94%
IV	Invades reticular dermis	78%
V	Subcutaneous tissue invasion	44%

Breslow's thickness (different in absolute depth of invasion, LN involvement)

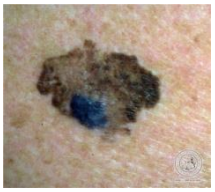
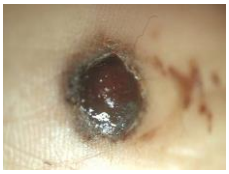
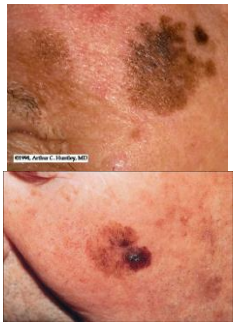
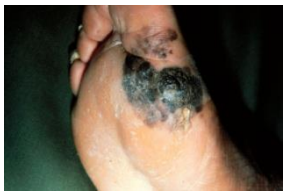
Breslow Thickness	10-Year Survival
< 0.76 mm	92%
< 3 mm	50%
< 4 mm	30%
LN Involvement	< 40% (8 yr)

- Also: **Beahrs and Myer's** system

- **Prognosis generally poor** – above 3 types of staging, or other indicators of poor prognosis:
  a. Elderly
  b. Male
  c. Lesions on trunk
  d. Ulceration
  e. Depigmentation, amelanotic
  f. Aneuploidy, high mitotic index

Treatment

- Prevention (**VERY IMPORTANT**):
  a. Avoidance of causative factors
- **Surgical excision with wide margins down to deep fascia**
  a. Main lesion:
     i. < 0.76 mm: excise with 1 cm margin
     ii. 0.76 – 1.0 mm: excise with 2 cm margin
     iii. > 1.0 mm: excise with 3 cm margin
  b. Nodal spread:
     i. If clinical suspicion, biopsy or FNAC of lymph nodes
     ii. If palpable: therapeutic block dissection
- **Palliation / adjuvant for distant metastases**
  a. Intralesional BCG therapy
  b. Immunotherapy: vaccines (raises anti-melanoma response), monoclonal antibody, cytokine interferon therapy

	Superficial Spreading	Nodular	Lentigo Maligna	Acral Lentiginous
%	**70%**	**15-30%**	–	Rare
Site	♂: Back ♀: Legs	Trunk	Face; Dorsum of hand / forearm	Hairless skin (palms, soles, subungual area)
Colour	Red, white, blue (varying pigmentation)	Most often black	Brown / black	Brown / black
Edge	Irregular	Regular outline	Irregular	Irregular
Shape	Palpable, but thin	Thick, polypoid, raised	Flat	Flat
Surface	-	Smooth	-	-
Remarks	-	• Frequently ulcerated, bleeding	• Arises from patch of Hutchinson's Lentigo • Malignant area usually thicker, darker • Area seldom ulcerates	• Rare type • Often misdiagnosed as haematoma, paronychia
Pictures				

8. NEUROFIBROMA

"Mr. X is a young Chinese gentleman…"
*"On **inspection**, there are two spherical, pedunculated masses on the back"*
*"One measures **2 cm**, and the other **0.5 cm in diameter**"*
They are pink in colour, with well-defined margins"
"There are no scars, sinuses, ulceration, or discharge seen, nor any surrounding skin changes"
*"On **palpation**, they are **not warm** and **non-tender**"*
*"Their surfaces are **smooth**, and are **firm**, and rubbery"*
"They are attached to the skin, and are mobile over the deeper tissue layers"
"My provisional diagnosis is neurofibromata"
"I would like to complete my examination by…"

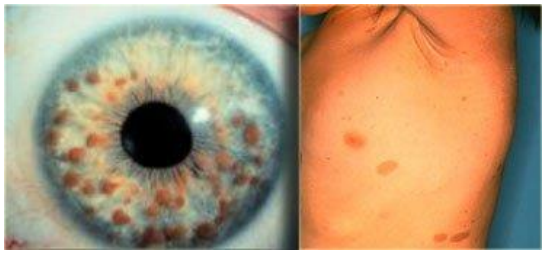
- *"Looking for other similar lesions"*
- *"Looking for manifestations of neurofibromatosis"*
- *"Examining the cranial nerves"*

Inspection

- Often multiple
- Anywhere in skin, subcutaneous tissues, e.g. forearm
- Spherical / Pedunculated / Fusiform (long axes lie along length of limb)
- Rarely more than few cm
- Comment on any café-au-lait spots

Palpation

- normal temp., Non-tender
- Smooth, Well-defined
- Soft/ fleshy, rubbery consistency
- Non-fluctuant
- If in subcutaneous tissue: mobile within it
- Move most freely perpendicular to course of nerve

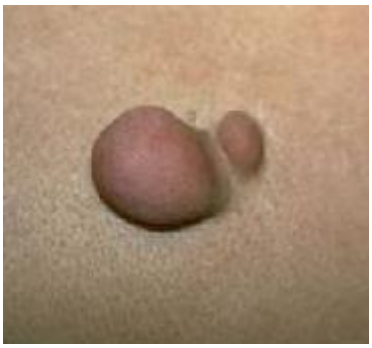


Request

- Look for other similar lesions & other manifestations of NF-1: café-au-lait spots, axillary freckling, lisch nodules, optic glioma
- Measure the BP (HPT 2^{o} to phaeochromocytoma, CoA, RAS)
- Examination of cranial nerve VII & VIII (acoustic neuroma)

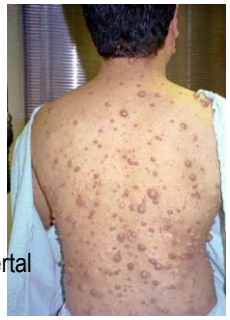
Background Information

Sporadic Neurofibroma



- Benign tumour containing mixture of elements from peripheral nerves:
  - Neural (ectodermal)
  - Fibrous (mesodermal)
- Often multiple
- History
  - Any age (but usually adult)
  - Symptoms: usually cause no discomfort, rarely disfiguring
  - If related to nerve trunk, may be tender
    - Patient may get tingling sensations in distribution of nerve
- Histology
  - Schwann cells: appear as bundles of elongated wavy spindle cells
  - Collagen fibrils, myxoid material
  - Often not encapsulated (unlike neurilemmomas)
- **Complications of Neurofibroma**
  - **Pressure effects**: spinal cord, nerve root compression
  - **Deafness**: involvement of VIII
  - Neurofibrosarcoma (only in NF-1): 5-13 %
  - **Intra-abdominal effects**: obstruction, chronic GI bleeding
  - **Skeletal** changes: kyphoscoliosis, cystic changes, pseudoarthrosis
- **Treatment** (single neurofibroma)
  - Non-surgical: leave alone if asymptomatic, patient agreeable
  - Surgical: indicated only if malignancy suspected
    - Local re-growth common (cannot be surgically detached from underlying nerve)

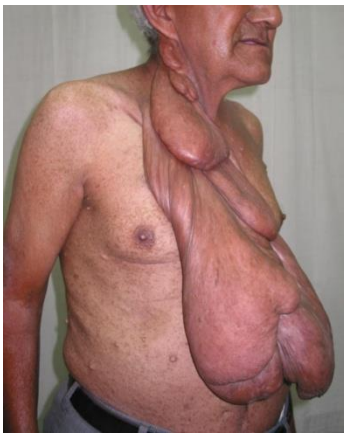
Neurofibromatosis I (Von Recklinhausen's disease)

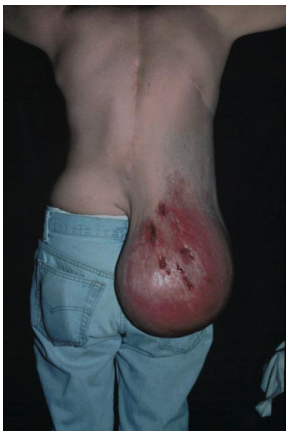


- AD, neurocutaneous syndrome; incidence 1 in 3000 births; chr 17q11.2
- NIH diagnostic criteria[1] for NF 1 (≥ 2 of the following clinical features)
    - Fibroma ≥2 NF or ≥1 plexiform NF
    - Iiris harmatomas ≥ 2 (Lisch Nodules)
    - Bone: sphenoid dysplasia, pseudoarthrosis
    - Relatives – 1st degree (parent, sibling or offspring)
    - Optic glioma
    - Macules ≥6 café au-lait macules of >5mm in prepubertal individuals & >15mm post-pubertal
    - Axillary freckling or Inguinal freckling
- Neurofibromata of all sizes (few mm to large subcutaneous nodules), related differently to skin
    - Within skin
    - Tethered to skin
    - Pedunculated
- Complications[2] of NF1
    - Learning Problems
    - Plexiform Neurofibroma
    - Epilepsy = CNS tumour, optic glioma, spinal NF
    - Aqueduct stenosis
    - Orthopedics = scoliosis, pseudoarthrosis of tibial and fibula, vertical scalloping, sphenoid wing dysplasia
    - Malignancy = MPNSTs, pelvic rhabdomyosarcomas
    - Other Cancers = GI neurofibromas, pheochromocytomas, duodenal carcinoid, glomus tumour of nail bed
    - Vascular = renal artery stenosis, cerebrovascular disease

Plexiform Neurofibroma (elephantiasis neurofibromatosis)

- Very rare
- Excessive overgrowth of neural tissue in subcutaneous layers, giving tissue swollen oedematous appearance
    - Often mistaken for lymphoedema, but lymphatic drainage is normal
- Can result in severe deformity: diffuse enlargement of peripheral nerve with skin involvement
- Risk of transformation to malignant peripheral nerve sheath tumours (MPNSTs) → present as painful expanding lesion

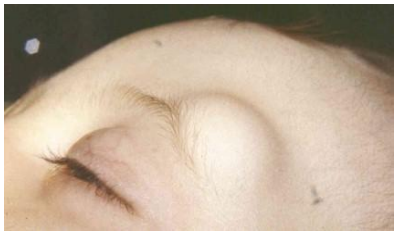


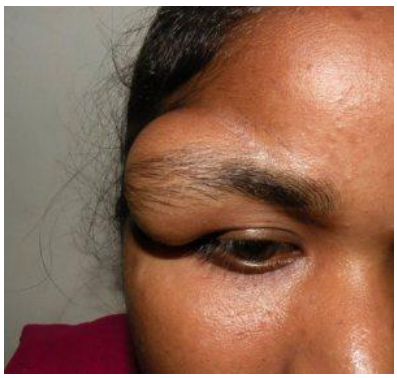


[1] uptodate: Neurofibromatosis type 1 (NF1): Pathogenesis, clinical features, and diagnosis
[2] PACES for the MRCP 3rd Edition (Tim Hall) – pg: 626

9. DERMOID CYST

"Ms. X is a young Chinese girl…"
*"On **inspection**, there is a **single ovoid** lump **just above the lateral edge of the left eyebrow**"*
*"It measures **3 by 2 cm**"*
*"There are no **scars**, ulceration, or discharge seen, nor any overlying or surrounding skin changes)"*
*"On **palpation**, the overlying skin is **not warm**. It is **non-tender.**"*
*"The surface is **smooth**, with **clearly-defined** margins"*
*"The consistency is **firm**, and it is **fluctuant**"*
*"The lump is not **attached** to the **overlying skin** nor **underlying tissue**s."*
*"It is **fully mobile** in all directions."*
*"My provisional diagnosis is a **congenital dermoid cyst**"*
"My differentials are: sebaceous cyst, lipoma"





Inspection

- Usually single
- Ovoid / spherical
- Site:
    - Congenital, 1-2 cm usually
        - Along lines of fusion of ophthalmic & maxillary facial processes
        - Inner & outer ends of upper eyebrow
    - Acquired, 0.5-1 cm usually
        - Beneath skin likely to be injured e.g. fingers
        - Scars often present

Palpation

- Not warm, maybe tender if infected
- Smooth surface, Well-defined margins
- Consistency
    - Congenital: Soft (not tense / hard)
    - Acquired: Hard & tense (sometimes stony hard)
- Fluctuant (if large)
- Mobile over deeper tissues
    - Deep to skin, in subcutaneous tissue
        i. Congenital: Not attached to skin or underlying structures
        ii. Acquired: may be tethered to scar

Background Information

- A dermoid cyst is a cyst deep to the skin, lined by skin
- 2 different methods of formation:
    - Congenital: Accident during antenatal development
    - Acquired: Implantation of skin into subcutaneous tissue by injury

Clinical features

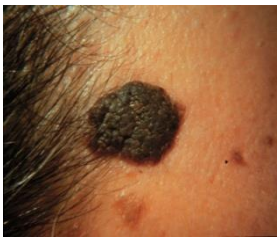
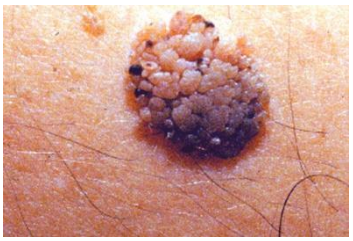
- Congenital (suspect if in child, young adult)
    - Formed intra-utero, when skin dermatomes fuse
    - Occur at any point in mid-line, common in neck / face / nose
        - Particularly along lines of fusion of ophthalmic & maxillary facial processes
        - Also: inner & outer ends of upper eyebrow
    - May be seen at birth
    - Distends a few years later, becomes obvious; few symptoms other than cosmetic problems
    - Rarely infected
- Acquired – Implantation dermoid (suspect if in adult – *Browse pg 60*)
    - Develop when piece of skin survives after being forcibly implanted into subcutaneous tissue
        - Often by injury: cut, stab, etc.
    - Symptoms
        - Small, tense lump
        - Painful and tender (in areas subjected to repeated trauma)
        - Local effects (e.g. problems with grip / touch if on finger)
        - Also rarely infected
    - Differentials
        - Sebaceous cyst (look for old injury, presence of scar near cyst: more likely dermoid)

Treatment

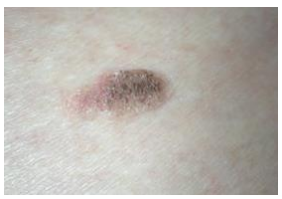
- Congenital
    - Surgical treatment; complete excision
    - Full extent should first be established with X-ray / CT
        - Midline cysts may communicate with CSF; must exclude bony defect
- Acquired
    - Complete excision of cyst

10. SEBORRHOEIC KERATOSIS *(Senile wart / seborrhoeic wart / verruca senilis / basal cell papilloma)*

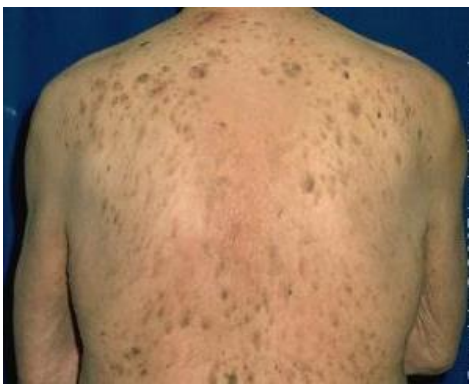
"Mr. X is an elderly Chinese gentleman…"
*"On **inspection**, there is a **single ovoid lesion** lump on the **back**"*
*"It measures **1 by 2 cm**"*
"The margins are well-defined, and it appears to be slightly raised above the skin"
"There are no scars, ulceration, or discharge seen, nor any surrounding skin changes"
*"On **palpation**, the overlying skin is **not warm**. It is **non-tender**"*
*"The surface is **rough and greasy**; the consistency is **firm**"*
*"The lump **arises from the skin**"*
"My provisional diagnosis is seborrhoeic keratosis"
"My differential diagnosis is: pigmented naevus, melanoma"
"I would like to complete my examination by…"
- *"Looking for similar lesions elsewhere"*

Inspection
- Often multiple
- Any part of skin; most found on back & face
- Round / oval
- Light brown → black
- "stuck on appearance"; appears warty
- Varying size; Few mm to 2-3 cm
- Distinct margins



Palpation
- No warmth, no tenderness
- Rough surface (sometimes papilliferous)
- More firm than surrounding skin
- Attached to skin
- Special tests
  - May be picked off gently – reveals patch of pale-pink skin, 1-2 surface capillaries (bleed slightly) (DON'T DO THIS IN EXAM)



Request to look for similar lesions elsewhere

Background Information
- Benign outgrowth of basal layer of epidermis
  - Raised above the level of normal epidermis
- Microscopy:
  - Hyperkeratosis (thickening of keratin layer)
  - Acanthosis (thickening of prickle cell layer)
  - Hyperplasia of variably pigmented basaloid cells

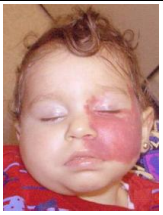
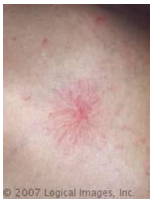
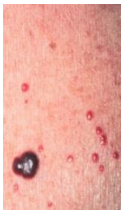
Clinical features
- Occur in both sexes
- More common in elderly people
- Begin as a patch,
  - increases in area, size over months / years
  - May not increase in thickeness
  - May suddenly fall off: leave pale-pink patch of skin
- Complications:
  - May become disfiguring, catch on clothes
  - May get infected (may imitate SCC, pyogenic granuloma)
  - Seldom bleeds (may cause it to change colour to brown)
- **Leser-Trelat sign**: Sudden onset of multiple seborrhoeic keratoses may imply visceral malignancy

Treatment
- Non-surgical
  - Can be left alone as it is benign
- Surgical – for cosmetic reasons, etc.
  - Superficial shaving (lies above level of normal epidermis)
  - Cautery

11. HAEMANGIOMA

Background Information

- Vascular malformations
  - Types
    - Capillary: ⅔ of cases, include the cutaneous haemangiomata, telangiectasias
    - Predominantly venous: venous angioma
      - Deeper levels of subcutaneous tissue, may extend into muscle / joint
      - May have distended veins over the surface of the mass
      - Empty with pressure, may have bruit
    - Predominantly lymphatic: lymphangioma circumscriptum
  - Features
    - Develop as abnormal proliferation of embryonic vascular network
    - Hamartomas
    - May ulcerate, induce hyperkeratosis in overlying stratum corneum
- Many forms of cutaneous haemangiomata: (see table)
  - Strawberry naevus (cavernous haemangioma)
  - Port-wine stain (naevus vinosus)
  - Spider naevus
  - Campbell de Morgan spot

	Strawberry Naevus	**Port-Wine Stain**	**Spider Naevi**	**Cambell de Morgan Spot**
Inspection				
Site	Head & Neck (can be anywhere)	Lips, face, mucous membranes of mouth, shoulders, neck, buttock	Upper torso, head and neck (drainage of SVC)	Trunk (bilat) – upper > lower Occasionally on limbs
Number	May be multiple	Usually single	Usually multiple	Usually multiple
Colour	Bright red / dark red	Purple-red	Bright red	Dark red / deep purple
Size	Variable; 1-10 cm	Variable	Variable; few mm	1-3 mm
Edge	Well-defined	Well-defined	–	Well-defined
Shape	Sessile → pedunculated as they grow larger	Variable	Variable	Circular, may be raised
Skin Changes	May have small areas of ulceration with scabs	May have dilated subcutaneous veins around lesion	–	–
Palpation				
Surface	Irregular, covered with smooth, pitted epithelium	Smooth	–	Smooth
Consistency	Soft	–	–	–
Mobility	Mobile	–	–	–
Relations	Confined to skin	–	–	–
Special Tests	Compressible: pressure squeezes mass, leaves it collapsed: slowly refills Not pulsatile	–	Compressible, fade completely	–
Background Information				
Age	Infants (congenital)	Infants (congenital)	–	Middle-age → elderly
Gender	♂ = ♀	–	–	–
Symptoms	• Cosmesis • May ulcerate, bleed on trauma	• Cosmesis • Bleeding may occur	–	• Cosmesis • Non-tender
Pressure	• Collapses on pressure	• Diminishes colour but doesn't revert to normal	• Branches fade when arteriole compressed	• Fade slightly
Remarks	Regress spontaneously (few months – 3 years)	• Extensive, intradermal • Present from birth, does not change in size • Sturge-Weber syndrome: facial PWS with corresponding haemangioma in brain – contralateral focal fits • Found in limbs when a/w Klippel-Tranaunay Syndrome	• Form of telangiectasia • Dilated skin arteriole feeding small branches (leaving radially) • Increase in number • Associated with pregnancy, chronic liver disease (> 5) – request for abdominal examination	• Formed by collection of dilated capillaries fed by single / small cluster of arterioles • Have appearance of drops of sealing wax • No clinical significance
Pictures				

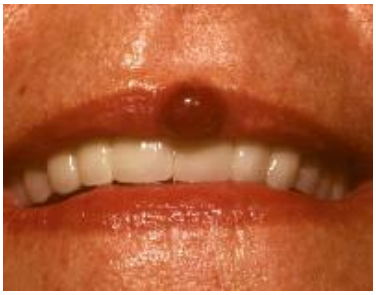
Also

- Telangiectasias
  - Dilatation of normal capillaries
  - Can be secondary to irradiation
  - Can be part of hereditary haemorrhagic telangiectasia (Osler-Rendu-Weber syndrome)
    - Autosomal dominant disease
    - Overt and occult haemorrhage can present as haematuria, haematemesis, melaena, epistaxis, iron-deficiency anaemia
- Vin rosé patch
  - Congenital intradermal vascular abnormality
  - Mild dilatation of vessels in sub-papillary dermal plexus
  - Can occur anywhere, gives skin pale-pink colour
  - Associated with other vascular abnormalities (e.g. haemangiomata, AV fistulae, lymphoedema)
  - Usually not disfiguring

12. PYOGENIC GRANULOMA

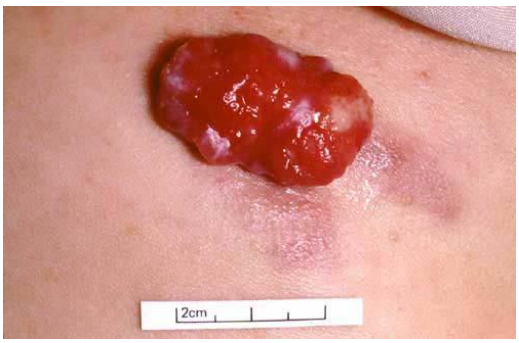
"Mr. X is a young Chinese gentleman…"
*"On **inspection**, there is a **single hemispherical** lump over the thenar eminence of the right hand"*
"It measures about 0.8 cm in diameter, with clearly-defined margins"
"It is bright red in colour, with surrouding erythema"
"There are no scars, sinuses, ulceration, active bleeding or discharge seen"
*"**I would like to proceed on to palpation**"*
*"On **palpation**, it is **not warm**. It is **slightly tender**"*
*"The surface is smooth. The consistency is **soft and fleshy**"*
*"The lump is **confined** to the skin"*
"My provisional diagnosis is pyogenic granuloma"
"My differential diagnoses are SCC, non-pigmented melanma"
"I would like to complete my examination by…"
- "Asking Mr. X for any previous injuries to the hand"
- "Asking him how rapidly the lump has been growing"

Inspection



- Single; usu < 1 cm, bright red
  - May be blood-encrusted or Ulceration
- Hemispherical; may be sessile / pedunculated
- Likely sites to be injured, e.g. hands, face
- Bright red; long-standing lesions may be skin-coloured
- May have sinuses, associated serous / purulent discharge, Erythema / cellulitis

Palpation – *request to palpate: may bleed easily*



- May be slightly tender
  - May bleed easily on palpation
- Well-defined edges
- Soft, fleshy consistency
- Confined to skin
- Slightly compressible (vascular origin)

Request
- Take history for previous injury
- Rate of growth of lump? (rapid growth in few days)

Background Information – *Neither pyogenic nor a granuloma!*
- **Rapidly-growing capillary haemangioma,** usually less then 1 cm
- Occur commonly after injury:
  - Small capillary loops develop in healing wound, form granulation tissue
  - When capillary loops grow too vigorously, form protruding mass, epithelisation
  - Mass form called pyogenic granuloma (surface often ulcerated, infected)

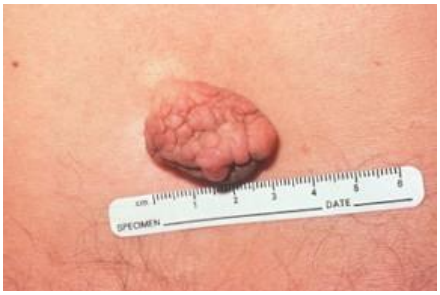
Clinical features
- Uncommon in children
- May have history of minor injury, chronic infection (e.g. paronychia)
- Rapidly-growing lump on skin,
- Bleeds easily, discharges serous / purulent fluid
  - Bleeding, pain stops once lump epithelises
- Once nodule is completely covered, begins to shrink (rarely disappears completely)

Treatment
- Surgical
  - Curettage with diathermy of the base
  - Complete excision biopsy
    - (if recurrent; malignancy e.g. amelanotic melanoma has to be excluded)
- Non-surgical
  - Regression is uncommon: surgical treatment best option
  - Silver nitrate cautery is possible

13. PAPILLOMA (skin tags / fibroepithelial polyps)

"Mr. X is a young Chinese gentleman…"
*"On **inspection**, there is a (**single**) (**hemispherical**) lump on the (dorsum of the forearm)"*
*"It measures **3 by 2 cm**."*
"The surface is papilliferous – there is no ulceration or discharge seen, nor any surrounding skin changes."
*"On **palpation**, the skin is **not warm**. It is **non-tender.** The consistency is soft."*
*"The lump is **attached** to the skin"*
"My provisional diagnosis is: papilloma"
"My differential diagnosis is: viral wart"
"I would like to complete my examination by…looking for similar lumps, asking for associated conditions"

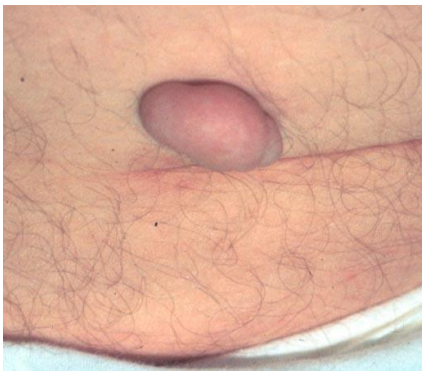
Inspection



- Single / multiple
- Variable: from raised plaque to pedunculated polyp
- Site: Neck, trunk, face, anus (anywhere on skin)
- Variable
- Flesh-coloured

Palpation

- Not warm, non-tender
- Variable: smooth to papilliferous
- Soft, not compressible
- Arises from skin



Request

- Similar lumps elsewhere
- Ask for associated conditions: pregnancy, diabetes, intestinal polyposis

Background Information

- An **overgrowth of all layers of the skin** with central **vascular core**
- Not a neoplasm, but a hamartoma (skin tag is a more accurate term)
- Increasingly common with age – may be congenital

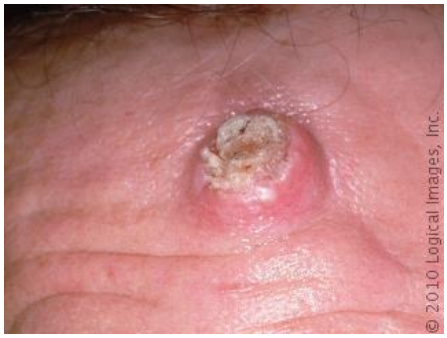
Clinical features

- Catches on cloths, rubs against other body parts
- May resemble carcinoma if granulation is excessive
- Complications:
    - May become red, swollen, and ulcerate
    - May become infarcted if injured
    - May be infected (contains all skin components – sebaceous glands, etc.)

Treatment

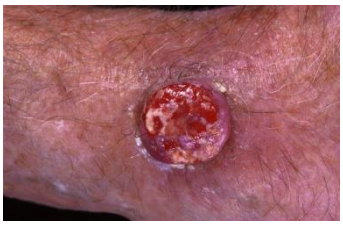
- Excision – diathermy, scissors
    - Bleeding from central vascular core controlled using single suture / diathermy

14. KERATOCANTHOMA (adenoma sebaceum, molluscum pseudo-carcinomatosum)



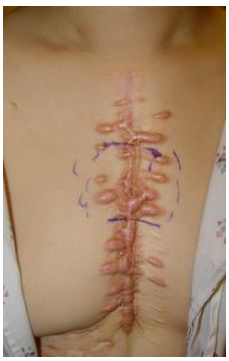
Inspection
- Often found on face
- Usually solitary;1 – 2 cm in diameter
- Hemispherical or conical, with central crater
- Normal skin colour

Palpation
- Firm and rubbery (central core is hard)
- Confined to skin, freely mobile over subcutaneous tissues



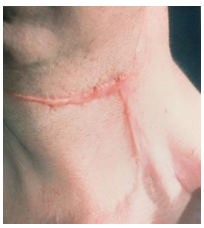
Background information
- Benign overgrowth of hair follicle cells with a central plug of keratin
- Occur in adults
- complain of rapidly-growing lump in skin
- Not painful, but can be unsightly
- Takes 2 – 4 weeks to grow, regresses in 2 – 3 months
  - Central slough appears,
  - surrounding skin retracts to form puckered scar
- Cause is unknown (may be self-limiting benign neoplasm or post-viral infection)
- Treatment:
  - Conservative if asymptomatic
  - Surgical excision of lesion with histology to r/o SqCC

15. KELOID (HYPERTROPHIC SCAR)

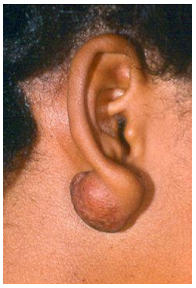


- **Healing by primary intention – 3 stages**:
  - Tissue defect filled by blood / fibrin
  - Replacement by collagen and fibrous tissue
  - Organisation of fibrous tissue to maximise wound strength
- Most surgical scars have thin lines, but tissue response may be excessive: hypertrophic / keloid scar

- **Wounds prone to hypertrophic / keloid scar**
  - Infection
  - Trauma
  - Burns
  - Tension
  - Susceptible areas: across flexion areas, earlobes, chest, neck, shoulder



- **Hypertrophic scar**
  - any age – common 8-20 years, ♂=♀, all races
  - Excessive amount of fibrous tissue, but **confined to scar** (between skin edges)
  - Located across flexor surfaces, skin creases
  - Common, especially if infection / excessive tension
  - Only enlarge for 2-3 months, then regress spontaneuosly
  - Do not recur if excised and causative factor eliminated



- **Keloid scar**
  - puberty to 30 years, ♀>♂, black, hispanic more likely
  - Hypertrophy and overgrowth **extend beyond original wound**
  - Located at earlobes, chin, neck, shoulder, chest
  - Due to local release of fibroblast growth factors
  - Continue to enlarge 6-12/12 after initial injury
  - May be tender, unsightly
  - Will recur unless special measures taken

- **Treatment (recurrence can be as high as 55%)**
  - Non-surgical: mechanical pressure therapy – topical silicone gel sheets (day and night for 1 year), Intralesional steroid, LA injections: e.g. triamcinolone with lignocaine
  - Surgical: revision of scar by direct suturing, skin grafting (avoid excessive tension)

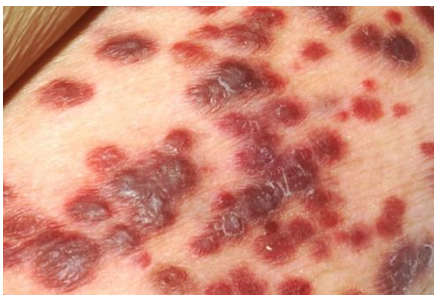
16. KAPOSI'S SARCOMA

Inspection

- Purple papules and plaques
- Solitary, but usually multiple
- Site: limbs, mouth, tip of nose/ palate or anywhere on the skin or mucosa

Request to take a history of previous transplantation or current underlying immunocompromise.

Background information



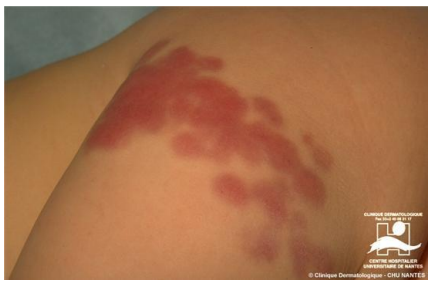
- Derived from capillary endothelial cells or from fibrous tisse
- Linked to HHV-8
- Types:
    - Classic Kaposi's Sarcoma
        - Confined to skin of lower limbs of elderly Jews
        - Not fatal
    - AIDS associated Kaposi's Sarcoma
        - AIDS defining; Found in 1/3 of AIDS patients
        - 1/3 develops a 2nd malignancy e.g. leukaemia/ lymphoma
    - Endemic (African) Kaposi's Sarcoma
        - Aggressive and invasive fatal tumour
        - Good response to chemotherapy
    - Transplation- associated Kaposi's Sarcoma
        - Following high dose immunosuppressive therapy
        - Often regress when treatment is ended

Treatment

- Conservative if asymptomatic. Start anti-retrovirals if HIV +ve
- Surgical: local radiotherapy amd chemotherapy (IFN- alpha, doxorubicin, intralesional vinblastine)

17. FIBROSARCOMA

Inspection



- Single; Usually limbs (but can be anywhere)
- Spherical or hemispherical
- If large, vascular: may make skin shiny & pink
- May have
    - Sinuses & Discharge
    - Ulceration
    - Erythema / cellulitis

Palpation

- Usually feel warmer (abnormal blood supply)
- May be tender
- Smooth surface (may be bosselated – covered with knobs)
- Well-defined margins (indistinct if fast-growing, invasive)
- Firm / hard consistency (rarely stony hard; do not ossify)
- Usually fixed
- May pulsate, have audible bruit, palpable thrill (may be very vascular)

Request to test for distal neurological status (for invasion of nerve)

Background Information

- Fibrosarcoma is one of the commonest mesodermal soft tissue malignant tumours
    - Pure benign fibroma is very rare
- History
    - More common in elderly (but can occur any age)
    - Common complaints
        - Growth: disfigurement, interference with ROM
        - Pain
        - Weakness (infiltration of other structures)
        - General debility
- Prognosis: generally good

18. PYODERMA GANGRENOSUM

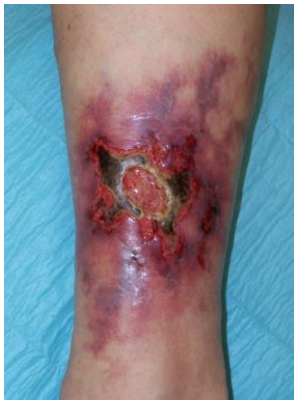
Inspect

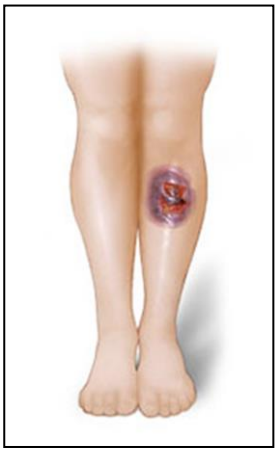
- Ulcer with a necrotis base
- Irregular bluish red overhanging edges
- a/w surrounding erythematous plaques with pustules

Request to examine for evidence of inflammatory bowel disease, RA

Backgound information

- more common in males
- pyoderma gangrenosum is associated with:
  - IBD
  - RA
  - Myeloproliferative disorders: PRV, myeloma
  - Autoimmune hepatitis
- **Differential diagnosis:**
  - Autoimmune: rheumatoid vasculitis
  - Infectious: tertiary syphilis, amoebiasis
  - Iatrogenic: warfarin necrosis
  - Others: Behcet's disease
- **Treatment:**
  - Non-surgical: treat underlying condition, saline cleansing, high dose oral or intralesional steroids. KIV cyclosporine & antibiotics
  - Surgical: serial allograft followed by autologous skin graft or muscle flap coverage when necessary





19. RADIOTHERAPY MARKS

Vital points on examination:

- Of the underlying disease:
  - Cachexia,
  - masectomy scar/ wide excision scar ➔ suggest breast cancer
  - obvious skin cancer,
  - clubbing & other signs of chest disease ➔ suggest lung cancer
  - suprapubic mass ➔ suggest pelvic tumour
  - neck swellings with cranial nerve palsies ➔ head and neck tumour
- of the radiotherapy:
  - site of radiation
  - shape: usually well defined borders
  - features of active RT:
    - Indian ink marks, skin markings
    - Erythema, desquamation
  - Features of previous RT:
    - Telangiectasia, hyperpigmentation
- Complications of radiotherapy:
  - Depends of site
  - Look for future cancers:
    - Haematogenous malignancy
    - Thyroid cancers
    - Breast cancers

Background information

- High energy X-rays interact with tissue to release electrons that cause local damage to DNA in adjacent cells via oxygen dependent mechanism.
  - Damage is usually irreparable, and normal cells have greater ability to repopulate than tumour cells in this setting
  - If reparable, manifests as chromosomal abnormalities

- Radiotherapy affects cells with:
  - Rapid turnover: Skin (epidermal layers), small intestine, bone marrow stem cells
  - Limited replicative ability: spinal cord, gonads

- Complications:
  - Early:
    - General: malaise, fatigue, LOA, N/V
    - Skin changes & temporary hair loss
    - Bone marrow suppresion, esp. if to long bone and pelvis
    - GI: diarrhea
  - Late:
    - Skin changes
    - Heart: IHD
    - Lung: pneumonitis, pulmonary fibrosis
    - Bld vssl: radiation arteritis, esp to carotids ➔ necrosis, distal ischaemia and vssl rupture
    - CNS: spinal cord myelopathy
    - Uro: bladder fibrosis, Renal impairment (depletion of tubular cells)
    - Abdo: IO 2^{o} to strictures & adhesions,
    - Genital: infertility
    - Endocrine: hypothyroidism
    - Eye: cataracts
    - Increase incidence of future cancers:
      - Haematogenous malignancy, e.g. leukemia
      - Solid tumours: Thyroid cancers
      - Breast cancers
- Minimalising of side effects of radiotherapy:
  - Lead shields to eyes, gonads and thyroid
  - Dose fractionation (to allow recovery of normal cells)
  - Prior chemotherapy (increase sensitivity of tumour cells)
  - Regional hypothermia
  - Radiolabelled antibody to deliver local radiation to tumour

2. SURGICAL INSTRUMENTS & PROCEDURES

1. DRAINS

FUNCTIONS OF DRAINS

Drains are inserted to:
Evacuate collections of pus, blood or fluids (e.g. lymph)
Drain potential collections

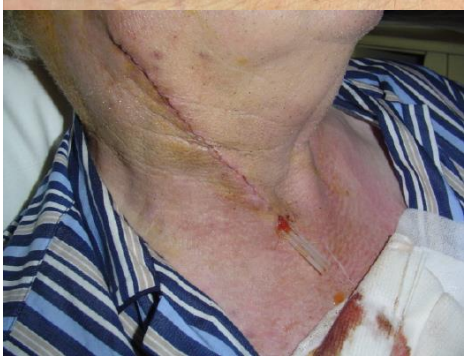
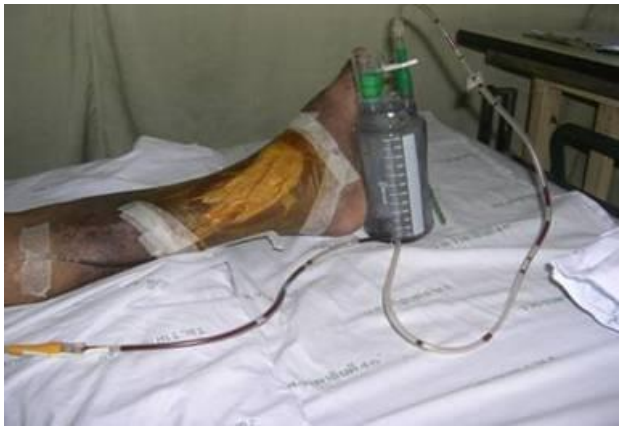
Rationale:
Drainage of fluid removes further fluid collections
Allow early detection of anastomotic leaks/ haemorrhage
Leave tract for potential collections to drain after removal

COMPLICATIONS

- Infection
- Bleeding
- Tissue damage- by mechanical pressure or suction
- Drain failure - blocked/slipped/kinked
- Incisional hernia - occurs when drain inserted through incision wound site- create a separate incision site for drain!

TYPES OF DRAINS

- Drains are often made from inert silastic material
- They induce minimal tissue reaction
- Red rubber drains induce an intense tissue reaction allowing a tract to form
- In some situations this may be useful (e.g. biliary t-tube)

Open	***Active***
  • Corrugated drain, Yeates drain, Penrose drain • Drain fluid collects in gauze pad or stoma bag • Easier to drain infected collections	 • Active drains require suction. • Jackson-Pratt Drain, Redivac Drain, T-tube • Have expandable chambers to create low-pressure suction • Used when small – mod amts of drainage are expected or when a passive drainage system won't provide adequate drainage • Tubing of the low-pressure active drainage system is placed through a separate puncture wound or the tube may exit the edge of the surgical wound • If the tubing isn't sutured in place, it could become dislodged • If a portion of the tube is pulled outside the skin, an air leak will cause the chamber to fill with air & it won't drain properly.
Closed	***Passive***
• Consist of tubes draining into a bag or bottle • They include chest and abdominal drains • The risk of infection is reduced	• Passive drains rely on gravity. • Passive drains have no suction, rely on gravity • Works by differential pressure betw body cavities and the exterior • Used when a mod – large amt of drainage is expected

CARE AND PREVENTION OF COMPLICATIONS OF TUBES:

- Prevent Infection- maintain meticulous skin care and aseptic technique around the insertion site
- Prevent blockage of the drain- do not allow bottles to fill up
- Prevent slippage by securing drain carefully to skin; refix as required
- Never hold a drainage collection device higher than the tube insertion site to prevent the drainage from flowing backward into the patient
- Note amount of drainage daily

REMOVAL OF DRAINS

- A drain is removed as soon as it is no longer required. The following are general guidelines:
- Drains put in to cover perioperative bleeding and haematoma formation, can come out after 24— 48 hours.
- Where a drain has been put in to drain an infection (abscess), remove it when fever settles or when there is evidence of complete drainage.

2. CENTRAL VENOUS PRESSURE LINE

INDICATIONS
1. Vascular access
2. Total parenteral nutrition
3. Infusion of irritant drugs
4. Measurement of CVP
5. Cardiac catheterization
6. Pulmonary artery catheterization
7. Transvenous cardiac pacing.

CONTRAINDICATIONS:
1. Do not insert into an infected area.
2. Avoid infraclavicular approach to subclavian vein if patient has apical emphysema or bullae.
3. Avoid internal jugular vein if carotid aneurysm present on the same side.
4. Bleeding diatheses
5. Septicaemia
6. Hypercoagulable states

ROUTES FOR CENTRAL VENOUS CANNULATION INCLUDE:

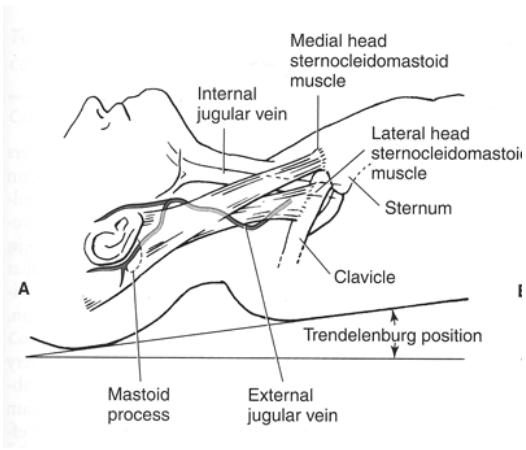
1. Internal jugular vein
2. Subclavian vein
3. Femoral vein
4. External jugular vein

CANNULATION OF THE INTERNAL JUGULAR VEIN

The internal jugular vein (IJV) is accessible, so cannulation of this vein is associated with a lower complication rate than with other approaches. Hence, it is the ***vessel of choice for central venous cannulation.***

Anatomy of the IJV

The vein originates at the jugular foramen and runs down the neck, to terminate behind the sternoclavicular joint, where it joins the subclavian vein. It lies alongside the carotid artery and vagus nerve within the carotid sheath. The vein is initially posterior to, then lateral and then anterolateral to the carotid artery during its descent in the neck. The vein lies most superficially in the upper part of the neck.



Relations of the IJV
- Anterior: Internal carotid artery and vagus nerve.
- Posterior: C1, sympathetic chain, dome of the pleura.
  On the left side, the IJV lies anterior to the thoracic duct.
- Medial: Carotid arteries, cranial nerves IX-XII

Technique of IJV cannulation

Place the patient in a supine position, at least 15 degrees head-down to distend the neck veins and to reduce the risk of air embolism. Turn the head away from the venepuncture site. Cleanse the skin and drape the area. Sterile gloves and a gown should be worn to avoid catheter-related sepsis.

Procedure
1. Use local anaesthetic to numb the venepuncture site.
2. Introduce the large calibre needle, attached to an empty 10 ml syringe.
3. Surface mark the internal jugular vein at the centre of the triangle formed by the two lower heads of the sternocleidomastoid muscle and the clavicle. Palpate the carotid artery and ensure that the needle enters the skin lateral to the artery.
4. Direct the needle caudally, parallel to the sagittal plane, aiming towards the ipsilateral nipple.
5. While needle is advanced, maintain gentle aspiration.
6. When vein is entered, flush of blood appears in the syringe. Now, cannulate the vein via the Seldinger technique (below).
7. Remove syringe, holding needle firmly in place. Occlude needle to prevent air embolism or bleeding.
8. Advance guide wire, J-shaped end first, into the vessel through the needle.
9. Hold guide wire in place and remove needle. Maintain a firm grip on the guide wire at all times.
10. Use a dilator to enlarge the hole in the vein. Remove the dilator.
11. Thread tip of catheter into the vein through the guidewire.
    Grasp the catheter near the skin and advance it into the vein with a slight twisting motion.
12. Advance catheter into final indwelling position. Hold catheter and REMOVE GUIDEWIRE.
13. Check lumen placement by aspirating through all the pigtails and flushing with saline next.
14. Suture the catheter to the skin to keep it in place.
15. Apply dressing according to hospital protocol.
16. The catheter tip should lie in the superior vena cava above the pericardial reflection.
17. Perform check chest X-ray to confirm position and exclude pneumothorax.

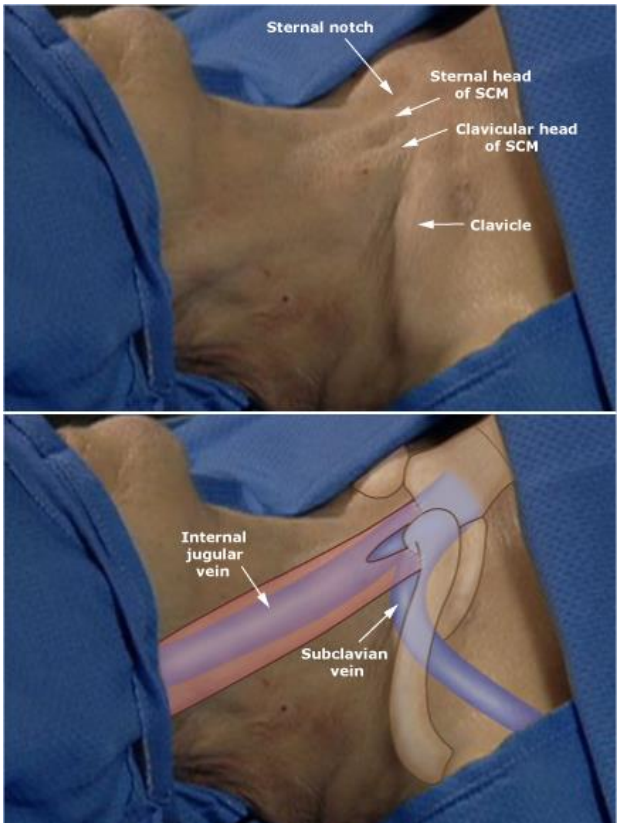
Complications
1. Pneumothorax/haemothorax
2. Air embolism - ensure head-down position.
3. Arrhythmias – This happens if cathether “irritates” the heart. Avoid passing guidewire too far, cardiac monitoring during insertion.
4. Carotid artery puncture/cannulation - palpate artery and ensure needle is lateral to it, or use ultrasound-guided placement, transduce needle before dilating and passing central line into vessel, or remove syringe from needle and ensure blood is venous.
5. Chylothorax- Avoid cannulating the vein on the left side as the thoracic duct lies there.
6. Catheter-related sepsis

CANNULATION OF THE SUBCLAVIAN VEIN

The subclavian vein (SVC) may be preferred for central venous access if
1. Patient has a cervical spine injury
2. Line is for long-term use e.g. dialysis, feeding. This site may be more comfortable for the patient.

Anatomy of the SCV

The SCV is the continuation of the axillary vein and originates at the lateral border of the first rib. The SCV passes over the first rib anterior to the subclavian artery, to join with the internal jugular vein at the medial end of the clavicle. The external jugular vein joins the SCV at the midpoint of the clavicle.



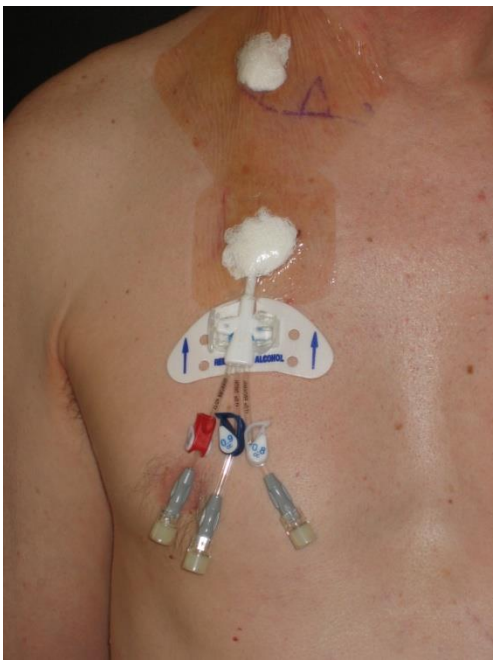
Technique

1. Place the patient in a supine position, head-down.
2. Turn the head to the contralateral side (if C-spine injury excluded).
3. Adopt full asepsis.
4. Introduce a needle attached to a 10 ml syringe.
5. Surface mark the subclavian vein 1 cm below the junction of the middle and medial thirds of the clavicle. Direct the needle medially, slightly cephalad, and posteriorly behind the clavicle toward the suprasternal notch.
6. Slowly advance needle while gently withdrawing plunger.
7. When a free flow of blood appears, follow the Seldinger approach, as detailed previously.
8. The catheter tip should lie in the superior vena cava above the pericardial reflection.
9. Perform check chest X-ray to confirm position and exclude pneumothorax.

Complications

As listed for internal jugular venous cannulation. The risk of pneumothorax is far greater with this technique. Damage to the subclavian artery may occur; direct pressure cannot be applied to prevent bleeding.

Ensure that a chest X-ray is ordered, to identify the position of the line and to exclude pneumothorax.



3. NASOGASTRIC TUBE

INDICATIONS [4]

1.	**Diagnostic**	a) bleeding from the upper gastrointestinal tract, haematemesis b) pentagastrin studies (rarely done now)	
2.	**Decompresssion**	Therapeutic	a) intestinal obstruction b) pyloric stenosis c) haematemesis, esp in pts at risk of hepatic encephalopathy
		Preventive: d) therapeutic and prophylactic decompression after major abdominal surgery e) prevention of further soilage after gastric perforation f) prevention of anastomotic rupture after gastric surgery g) prevention of obstruction of the operative field by air in the stomach	
3.	**Nutrition**	a) patients with dysphagia b) comatose or weak patients	
4.	**Lavage**	a) poisoning b) gastrointestinal bleeding	

CONTRAINDICATIONS
1. Base of skull #
2. Oesophageal tear
3. Severe facial injury

The cuffed endotracheal and tracheostomy tubes should be deflated prior to nasogastric tube insertion.

PRE-PROCEDURE
1. Gather equipment.
2. Don non-sterile gloves.
3. Explain the procedure to the patient and show equipment.
4. If possible, sit patient upright with head forward for optimal neck/stomach alignment. Otherwise, prop the patient up at 45 °.
5. Deflate the endotracheal tube or tracheostomy cuff
6. Determine the size of the nasogastric tube required (usually 14 – 16FG). If aspirating, use as large a tube as possible to reduce the risk of blocking during use or the formation of a false passage during introduction; if feeding, a smaller tube may be used (eg. 8FG) because it is more comfortable in the long term.

PROCEDURE
1. Estimate the length of the tube to be inserted: from the bridge of the nose to the tragus of the ear to the point halfway between the xiphisternum and the navel. Mark the measured length with a marker or note the distance.
2. Examine nostrils for deformity/obstructions (eg. choanal stenosis) to determine best side for insertion. Select the largest nostril for insertion.
3. Lubricate tube with water. The nose may be lubricated with lignocaine gel.
4. Introduce the tube through the nostril horizontally in, passing the tube along the floor of the nose. Resistance may be felt as tip reaches the nasopharynx, which is the most uncomfortable part of the procedure. In the operation theatre, when the patient is under general anaesthesia, the McGill's forceps may be used to guide the tube down.
5. Instruct the patient to swallow (you may offer ice chips/water if not contraindicated) and advance the tube as the patient swallows. Swallowing of small sips of water may enhance passage of tube into esophagus. If patient is uncooperative, bend his head to elicit a swallowing reflex.
6. Continue to advance the tube down the oesophagus. There should not be resistance. If resistance is met, rotate the tube slowly with downward advancement towards the closer ear. Do not force the tube down against resistance as this may form a false passage.
7. Withdraw the tube immediately if changes occur in the patient's respiratory status, if the tube coils in the mouth, or if the patient begins to cough or turns pretty colours.
8. Advance the tube until mark is reached (approximately 40cm). Stop.
9. Check for correct placement by attaching a syringe to the free end of the tube and aspirating a sample of gastric contents to test with litmus, auscultating the epigastrium while injecting air through the tube, or obtaining an x-ray to verify placement before instilling any feedings/medications or if you have concerns about the placement of the tube.
10. Secure the tube with adhesive tape.
11. Re-inflate the endotracheal tube or tracheostomy cuff if necessary.
12. If for suction, remove the syringe from the free end of the tube; connect to suction; set machine on type of suction and pressure as prescribed.
13. Document the reason for the tube insertion, type & size of tube, the nature and amount of aspirate, the type of suction and pressure setting if for suction, the nature and amount of drainage, and the effectiveness of the intervention.

PROBLEMS AND COMPLICATIONS [5]

1. Technical	**2. Gastrointestinal**	**3. Lung complications**	**4. Loss of fluids & electrolytes, especially sodium, potassium, chloride and hydrogen ions.**	**5. Dry mouth and parotitis due to fluid loss and mouth breathing.**
a) insertion into the trachea → choking. b) coiling & reentry into oesophagus (rare). c) trauma to the nose and the pharynx. d) dislodgement e) perforation of the pharynx and oesophagus	a) Gastric erosions b) Pressure necrosis of pharynx, oesophagus or the external nares. c) Varices: traumatic haemorrhage d) GERD e) Oesophageal erosions → strictures	a) decreased ventilation b) aspiration pneumonia		

4. TRACHEOSTOMY

INDICATIONS FOR TRACHEOSTOMY

1. Maintenance of airway patency.
2. Protection of the airway from aspiration.
3. Application of positive pressure to the airway.
4. Delivery of high oxygen concentrations.
5. Facilitation of secretion clearance.

RELATIVE CONTRAINDICATIONS

1. Evidence of infection in the soft tissues of the neck at the prospective surgical site.
2. Medically uncorrectable bleeding diatheses.
3. Gross distortion of the neck anatomy due to hematoma, tumour, thyromegaly, high innominate artery or scarring from previous neck surgery.
4. Documented or clinically suspected tracheomalacia.
5. Need for positive end-expiratory pressure (PEEP) of more than 15 cm of water.
6. Patient obesity with short neck that obscures neck landmarks.
7. Patient age younger than 15 years.

TYPES OF TRACHEOTOMY

1. Temporary: Portex (cuffed).
2. Permanent: Consist of inner and outer tubes made of stainless steel.

Tracheostomy is more useful in the elective setting compared to endotracheal intubation because:

1. Better tolerated.
2. Avoids risk of laryngeal stenosis
3. Avoids risk of endotracheal obstruction.

PROCEDURE

1. Position the patient. Place rolled towel under the patient's neck to hyperextend the neck for better exposure.

2. Clean and drape. Clean the skin of the neck from the chin to the suprasternal notch and laterally to the base of the neck and clavicles. Drape field.

3. Identify anatomical landmarks (thyroid cartilage, cricoid cartilage).

4. Administer local anaethesia.

5. Incise skin. In the emergency setting, make a vertical incision 3cm from cricoid cartilage downwards. In the elective setting, make a tranverse incision 4cm wide, 3cm above the suprasternal notch.

6. Dissect through the subcutaneous layers and platysma.

7. Identify the communicating branch of the anterior jugular vein, clamp and ligate the artery (ignore this in an emergency).

8. Visualise the thyroid isthmus and retract isthmus.

9. Retract cricoid cartilage upwards wth cricoid hook.

10. Incise the trachea between the 2nd and 3rd tracheal rings, making an inverted U-flap incision.

11. Insert tracheal dilator through the tracheostoma and remove the cricoid hooks.

12. Suction of blood and secretions in the lumen.

13. Insert the tracheostomy tube.

14. Remove the obturator and insert the inner cannula.

15. Dress wound and secure to the neck using sutures and adhesive tape.

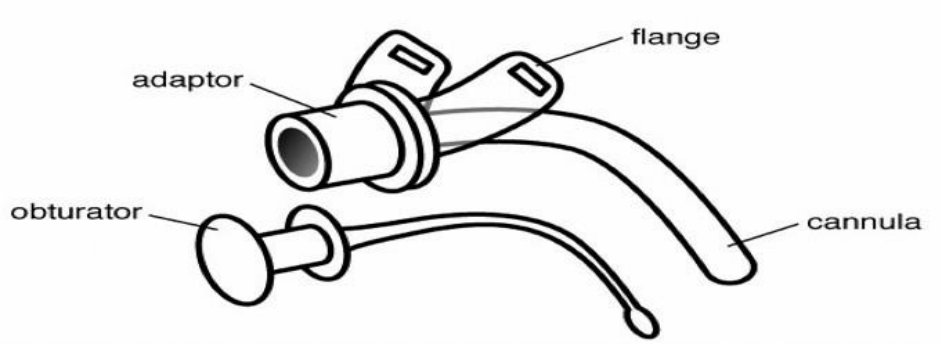
COMPLICATIONS

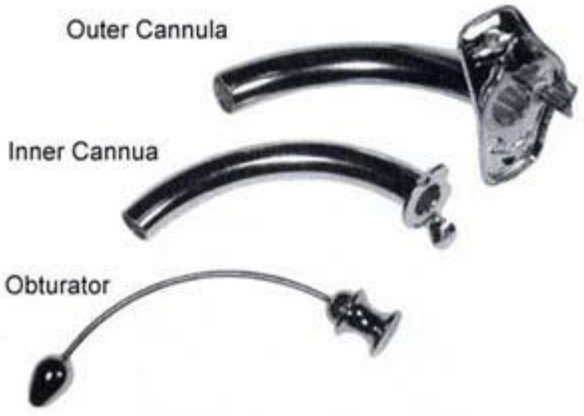
During Procedure
1. Bleeding if damage to the innominate or inferior thyroid artery.
2. Damage to surrounding structures, eg esophagus, recurrent laryngeal nerve, brachiocephalic vein.
3. Pneumothorax. Pneumomediastinum.

Immediate post-op
1. Surgical emphysema (refers to the condition that causes air to be trapped under the skin). Subcutaneous emphysema.
2. Obstruction, eg clot, mucus.
3. Bleeding.
4. Dislodgment.

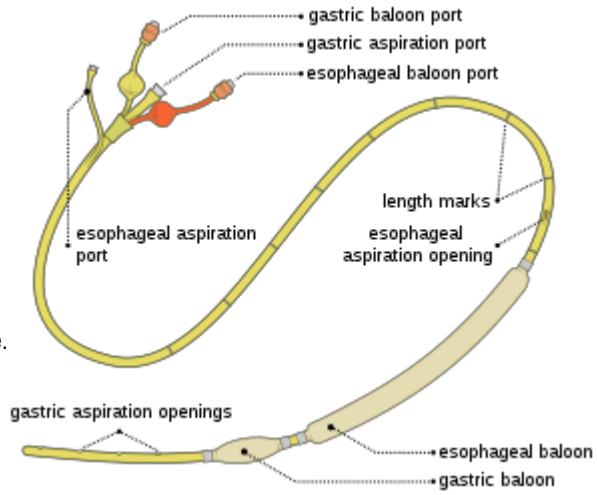
Late post-op
1. Infection .
2. Obstruction, eg dislodgment of tube, crust formation from secretions.
3. Tracheal stenosis.
4. Tracheomalacia.
5. Tracheo-esophageal fistula. Wound breakdown
6. Scarring.

POST-OP CARE
1. Position patient in a propped up position.
2. **Prevent obstruction** by suction, saline irrigation, mucolytic agents (mucomyst, guaifenesin) and humidified air.
3. Change Portex tube every 3rd day and remove the inner tube for cleaning everyday.
4. Unlock the metal tube every night so that the patient can cough it out if it becomes obstructed.





5. SENGSTAKEN-BLAKEMORE TUBE (MINNESOTA TUBE)

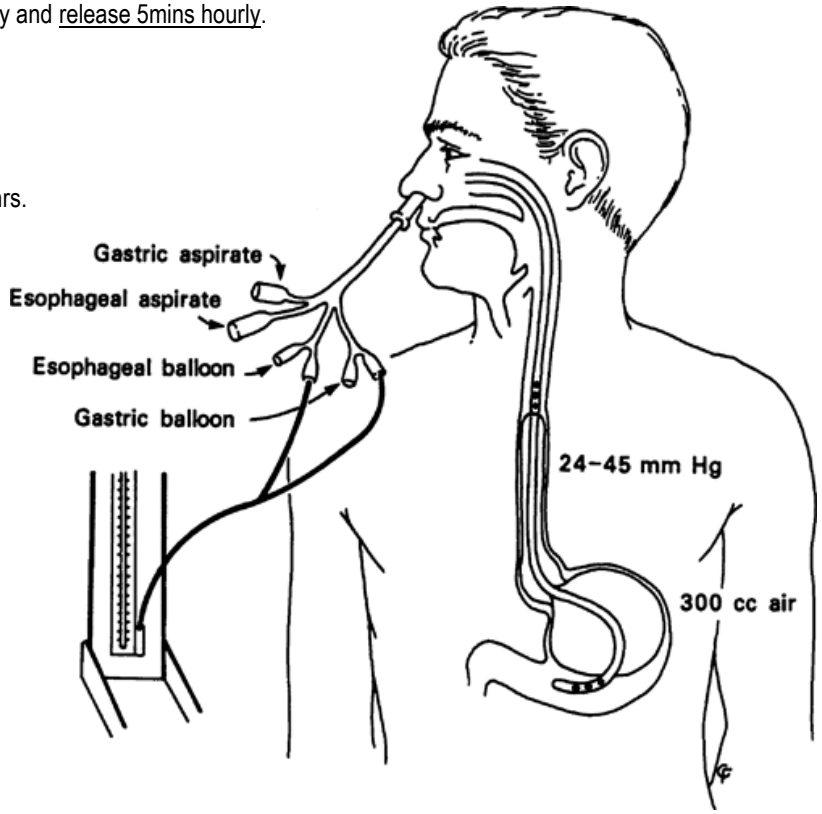


INDICATIONS
Oesophageal varices

CONTRAINDICATIONS
1. Base of skull fracture
2. Oesophageal tear
3. Severe facial injury

PROCEDURE - Keep SBT in fridge to make it stiff.

1. Measure the length of the tube. Test balloons. Test patency of the tube.
2. Sit the patient upright or at 45 degrees.
3. Apply local anaesthesia (lignocaine nasal spray).
4. Lubricate and insert the tube through the nose, asking the patient to swallow or drink water to aid in smoother passage of the tube through the pharynx and oesophagus.
5. Inflate the gastric balloon slowly with 100-150ml water.
6. Check that the tube is in the stomach by:
   (i) aspirating fluid and testing it with litmus,
   (ii) auscultating the epigastrium while injecting air, or
   (iii) doing an X-ray.
7. Traction.
8. Inflate the oesophageal balloon to 35 – 45mmHg (above portal HTN pressure): use the Y-connector piece with one arm to the BP set and the other to the syringe to pump in air.
9. Aspirate fluid from the oesophagus through the Ryle's tube, or if using the Minnesota tube, use the additional lumen provided (with the additional lumen for aspirating fluid in the oesophagus, the Minnesota tube decreases the likelihood of aspiration pneumonia occurring).
10. Check the oesophageal balloon pressure hourly and release 5mins hourly.
11. Release oeophageal balloon after 24hrs.
12. Release gastric balloon after 48hrs.
13. The tube should not be used for more than 72hrs.



COMPLICATIONS
1. Aspiration pneumonia
2. Respiratory obstruction
3. Oesophageal ulceration and rupture
4. Rebleeding
5. Gastric varices not controlled

6. URINARY CATHETERISATION

INDICATIONS FOR SHORT-TERM CATHETERISATION

1. Relief of **acute retention of urine**, e.g. benign prostatic hypertrophy, bladder outflow obstruction.
2. Bladder **washout**, e.g. blood clots causing acute retention of urine.
3. **Cystourethrogram**.
4. Administration of **intra-vesical drugs**.
5. As an **adjunctive** measure pre/post-operatively
   a) Pre-operatively:
      (i) To drain the bladder so as to improve access to the pelvis in urologic or pelvic surgery.
      (ii) To allow accurate measurement of urine output in major surgery.
   b) Post-operatively:
      (i) To relieve acute urinary retention because post –op pain results in failure of the sphincter to relax.
6. Urinary **output monitoring**, e.g. in patient with hypovolaemic shock or the critically ill.

INDICATIONS FOR LONG-TERM INDWELLING CATHETERIZATION

1. Refractory bladder outlet obstruction.
2. Chronic retention of urine, eg. neurogenic bladder.
3. Incontinence, e.g. in palliative care of terminally ill or patient's preference.

CONTRAINDICATIONS

1. Presence of urethral injury, as manifested by:
   a) blood from the meatus,
   b) scrotal haematoma,
   c) pelvic fracture, or
   d) high-riding prostate, elicited from a genital and digital rectal examination. (alternative: suprapubic drainage)
2. Urinary tract infection, as an indwelling catheter causes difficulty in treatment.

PROCEDURE[3]

1. Know indications, contraindications and complications associated with urinary catheterization
2. Prepare requisites, position procedure trolley appropriately
3. Check patient's identity using 2 identifiers
4. Obtain verbal consent and prepare patient for procedure. Have a chaperone if performing the procedure on a member of the opposite sex.
5. Respect patient's right to privacy and dignity throughout the process
6. Observe aseptic technique during procedure – perform hand wash
7. Open the sterile pack, catheter, urinary bag and lignocaine aseptically
8. Disinfect chlorhexidine sachet before opening and pour onto swabs
9. Perform hand rub before donning sterile gloves
10. Test the integrity of the catheter balloon with STERILE WATER
11. Place catheter into kidney dish and apply lignocaine gel on the catheter
12. Prepare cotton swabs
13. Clean in one direction away from glans along shaft
14. Drape the penis and retract foreskin and clean urethra meatus (in females: retract labia majora and swab perineum)
15. Inject lignocaine gel into the urethra (in females: apply lignocaine gel to catheter tip)
16. Wait for 3-4min (ideally) before inserting catheter.
17. Communicate, provide reassurance and monitor patient throughout procedure
18. Place the tray containing the catheter on the drape
19. Hold penile shaft in 60-90 degree position and insert catheter gently into meatus (in females: expose external urethral orifice)
20. If resistance is felt, increase traction on the penis slightly and apply steady gentle pressure on catheter
21. Advance catheter till the bifurcation point when urine flows out
22. Slowly inflate the balloon with STERILE WATER (usually 10ml) and check pain score of patient (should be painless)
23. Withdraw catheter gently till resistance is felt (snug against bladder neck)
24. Connect catheter to urine bag
25. Reposition foreskin and position penis upwards. Secure catheter on lower abdomen with tape.
26. Ensure the urine bag is below the level of bladder and urine flow is unobstructed
27. Clean up area and WASH HANDS BEFORE LEAVING
28. Document catheterization date, type of catheter used, amount of water in balloon, patient's response to procedure

"Urinary cathter __Fr inserted under aspetic technique. Balloon was filled with 10ml sterile water. Clear / light-yellow / dark-yellow / tea-coloured / bloody urine __ml drained. Atraumatic insertion, patient tolerated procedure well. SIGN."

COMPLICATIONS

1. Infection, which may lead to stone formation.
2. Stricture formation due either to faulty technique or an irritant material used in the catheter.
3. Creation of a false passage due to wrong technique of insertion.
4. Occasionally, irritation of the bladder may cause severe bladder spasms.

[3] TTSH Urinary Catheterization of Male Patient (Skills Performance Checklist)

7. CHEST TUBE

Chest tubes are inserted to drain blood, fluid, or air and allow full expansion of the lungs. The tube is placed between the ribs and into the space pleural space.

The area where the tube will be inserted is anesthetized locally. The patient may also be sedated. The chest tube is inserted through an incision between the ribs into the chest and is connected to a bottle or canister that contains sterile water (underwater seal). Suction is attached to the system to encourage drainage. A suture and adhesive tape is used to keep the tube in place.

The chest tube usually remains in place until the X-rays show that all the blood, fluid, or air has drained from the chest and the lung has fully re-expanded. When the chest tube is no longer needed, it can be easily removed, usually without the need for medications to sedate or numb the patient. Antibiotics may be used to prevent or treat infection.

INDICATIONS

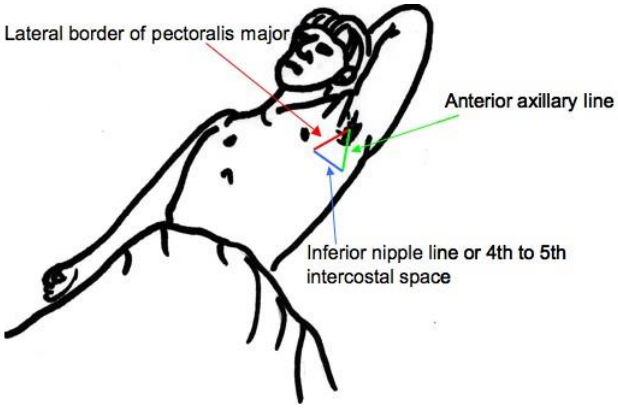
1. Pneumothorax.
2. Hemothorax.
3. Drainage of pleural effusion.
4. Chylothorax
5. Drainage of empyema/lung abcesses
6. Prophylactic placement of chest tubes in a patient with suspected chest trauma before transport to specialized trauma center

CONTRAINDICATIONS

1. Infection over insertion site
2. Uncontrolled bleeding diathesis/coagulopathy

MATERIALS

1. Iodine & alcohol swabs for skin prep
2. Sterile drapes & gloves
3. Scalpel blade & handle
4. Clamp
5. Silk suture
6. Needle holder
7. Petrolatum-impregnated gauze
8. Sterile gauze
9. Tape
10. Suction apparatus (Pleuravac)/underwater seal apparatus
11. Chest tube (size 32 to 40 Fr, depending on clinical setting)
12. 1% lignocaine with epinephrine, 10 cc syringe, 25- & 22-g needles



PRE-PROCEDURE PATIENT EDUCATION

1. Obtain informed consent
2. Inform the patient of the possibility of major complications and their treatment
3. Explain the major steps of the procedure, and necessity for repeated chest radiographs

PROCEDURE

1. Determine the site of insertion. Locate the triangle of safety; bounded by the lateral border of the pectoris major, 5th or 6th intercostal space, imaginary vertical line between the anterior and mid axillary lines.
2. Surgically prepare and drape the chest at the predetermined site of the tube insertion.
3. Locally anaesthetized the skin and rib periosteum.
4. Make a 2-3cm transverse incision at the predetermined site and bluntly dissect through the subcutaneous tissues, just over the top of the rib.
5. Puncture the parietal pleura with the tip of a clamp and put a gloved finger into the incision to avoid injury to other organs and to clear any adhesions, clots, etc.
6. Clamp the proximal end of the chest tube and advance the tube into the pleural space to the desired length.
7. Look for fogging of the chest tube with expiration or listen to air movement.
8. Connect the end of the chest tube to an underwater seal apparatus.
9. Suture the tube in place.
10. Apply a dressing and tape the tube to the chest.
11. Do a chest X ray
12. Obtain arterial blood gas values and/or institute pulse oximetry monitoring as necessary.

COMPLICATIONS

Damage to structures:

1. Laceration or puncture of the intrathoracic and/or abdominal organs, all of which can be prevented by using the finger technique before inserting the chest tube.
2. Damage to the intercostals nerve, artery or vein.
3. Subcutaneous emphysema, usually at tube site.

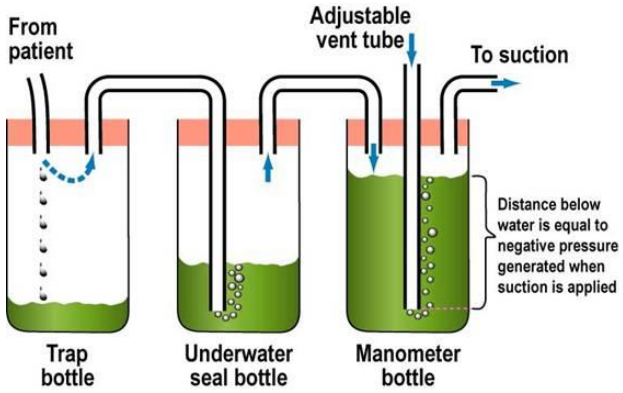
Equipment:

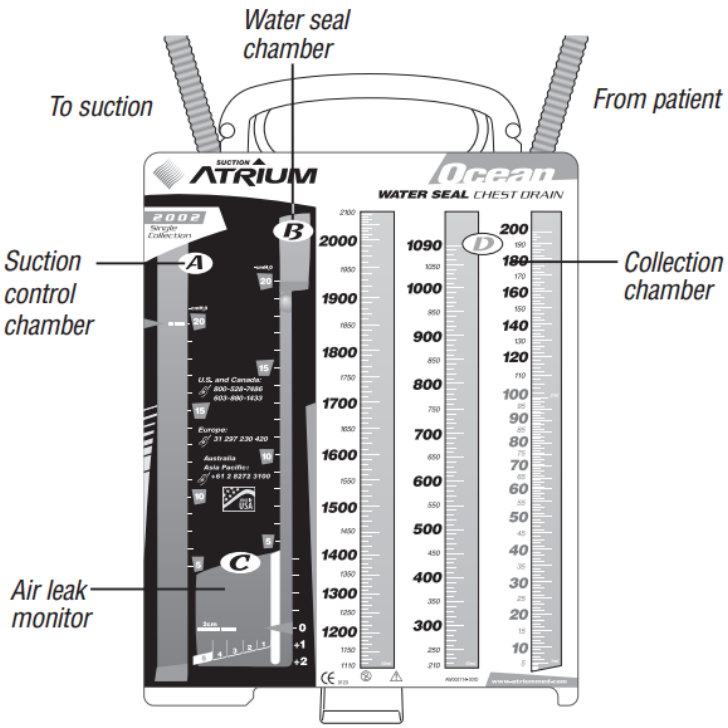
4. Incorrect intrathoracic or extrathoracic tube position.
5. Chest tube kinking, clogging or dislodging from the chest wall or disconnection from the underwater seal apparatus.
6. Anaphylactic or allergic reaction to surgical preparation or anaesthesia.

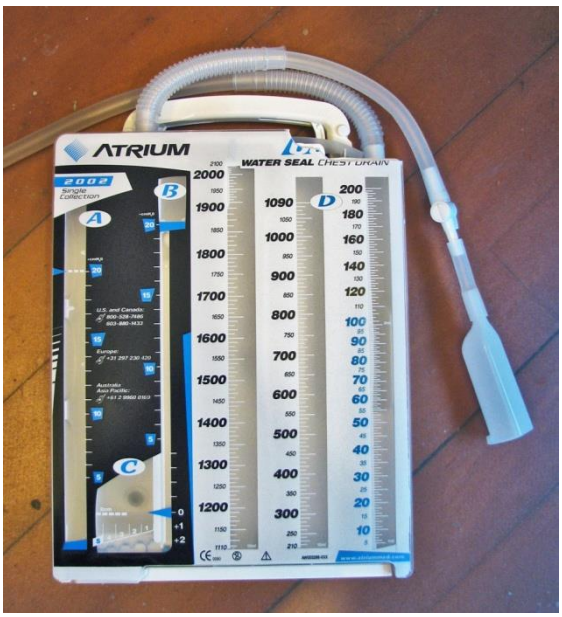
Failure:

7. Introduction of pleural infection.
8. Persistent pneumothorax
9. Recurrence of pneumothorax upon removal of the chest tube.
10. Lungs fail to expand due to plugged bronchus; bronchoscopy required.

Recovery from the chest tube insertion and removal is usually complete, with only a small scar. The patient will stay in the hospital until the chest tube is removed. While the chest tube is in place, the nursing staff will carefully check for possible air leaks, breathing difficulties, and need for additional oxygen. Frequent deep breathing and coughing is necessary to help re-expand the lung, assist with drainage, and prevent normal fluids from collecting in the lungs.







Matthew 5: 13-16 | Salt and Light

13 "You are the salt of the earth. But if the salt loses its saltiness, how can it be made salty again? It is no longer good for anything, except to be thrown out and trampled underfoot.

14 "You are the light of the world. A town built on a hill cannot be hidden. 15 Neither do people light a lamp and put it under a bowl. Instead they put it on its stand, and it gives light to everyone in the house. 16 In the same way, let your light shine before others, that they may see your good deeds and glorify your Father in heaven.

Philippians 4: 6-7

6 Do not be anxious about anything, but in every situation, by prayer and petition, with thanksgiving, present your requests to God. 7 And the peace of God, which transcends all understanding, will guard your hearts and your minds in Christ Jesus.

Hope this was useful
All the best for MBBS :D