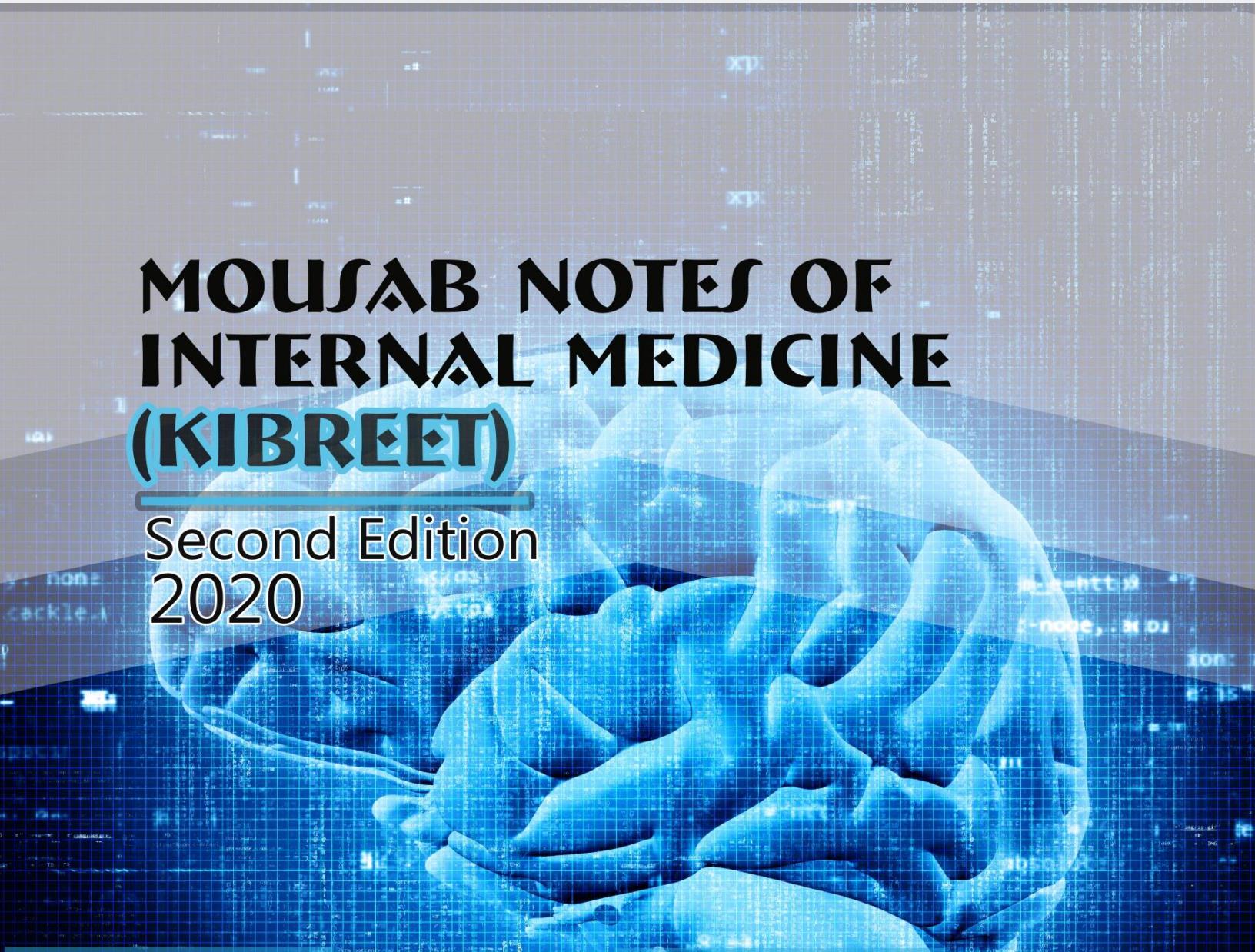
MOUSAB NOTES OF INTERNAL MEDICINE (KIBREET)

Second Edition
2020



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Faculty of Medicine

Awasif Batch (90)

Academic Secretary

- This is the 2ed Edition of **MOUSAB NOTES OF INTERNAL MEDICINE. (2020)**

- The content of this note is text transcription from audio recordings of **Dr Mousab Mohammed Ibrahim (Kibreet) _ Batch 88 Qasawir** Reviews of Internal Medicine for 6th year medical students (Batch 89, 90) at Faculty of Medicine, University of Khartoum.

- This edition is designed as a soft copy; a hard copy version is available in the Telegram channel https://t.me/Kibreet which also contains all Dr.Mousab Ibrahim (Kibreet) audio records.
- Hyperlinks are available in the "contents" page at the beginning of each system.

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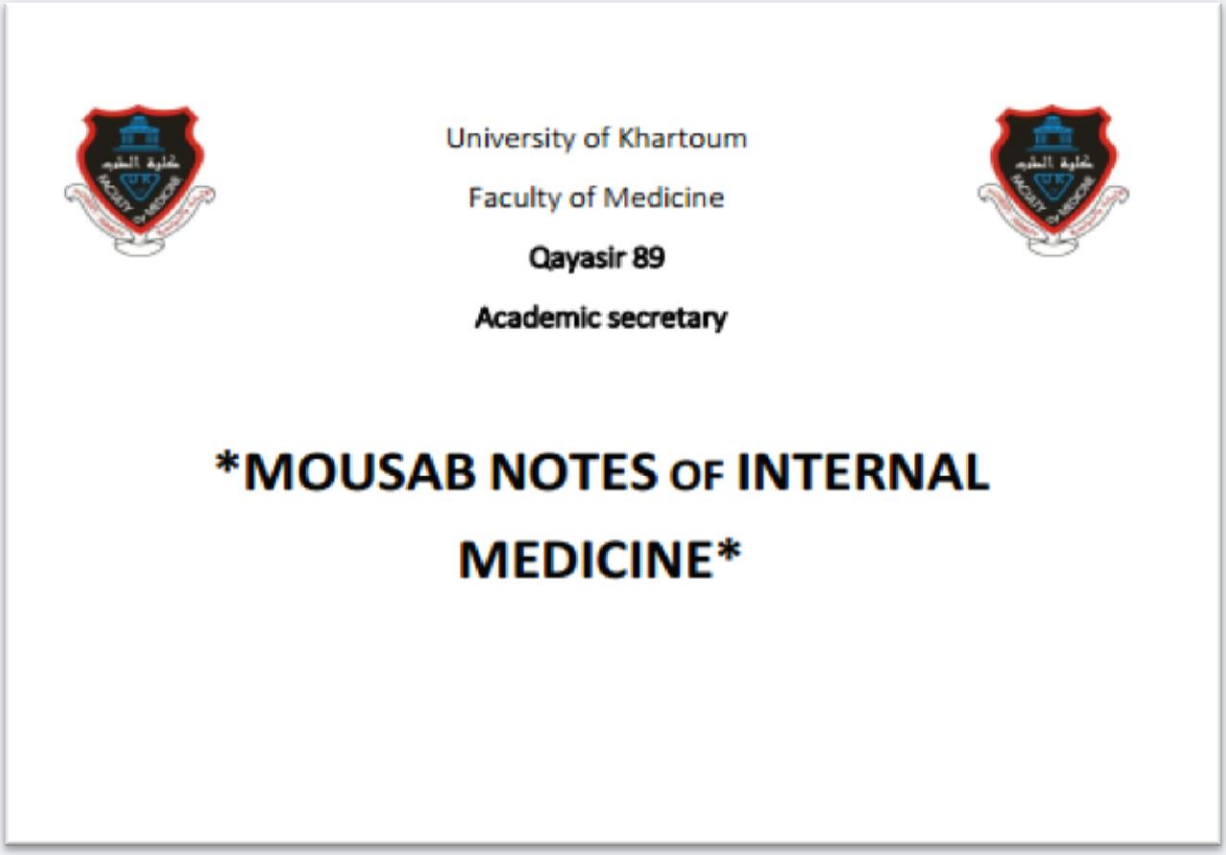
1est edition



***هذا الشيت هو تفريغ لمراجعات د.مصعب محمد للمستوى السادس قياصر، قامت الأمانة الأكاديمية للدفعة 89 قياصر تنسيق وكتابة هذا الشيت.**

- ***تنبيه مهم:** بأي حال من الأحوال، لا يعتبر هذا الشيت بديلا عن المراجع الأساسية للمادة والمحاضرات. **رجاء** ألا يستخدم كمرجع أساسي، بل كمادة للمراجعة بعد المذاكرة من المرجع أو المحاضرة

كتابة: المقداد حيدر – حازم الدرديري
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Endocrine System

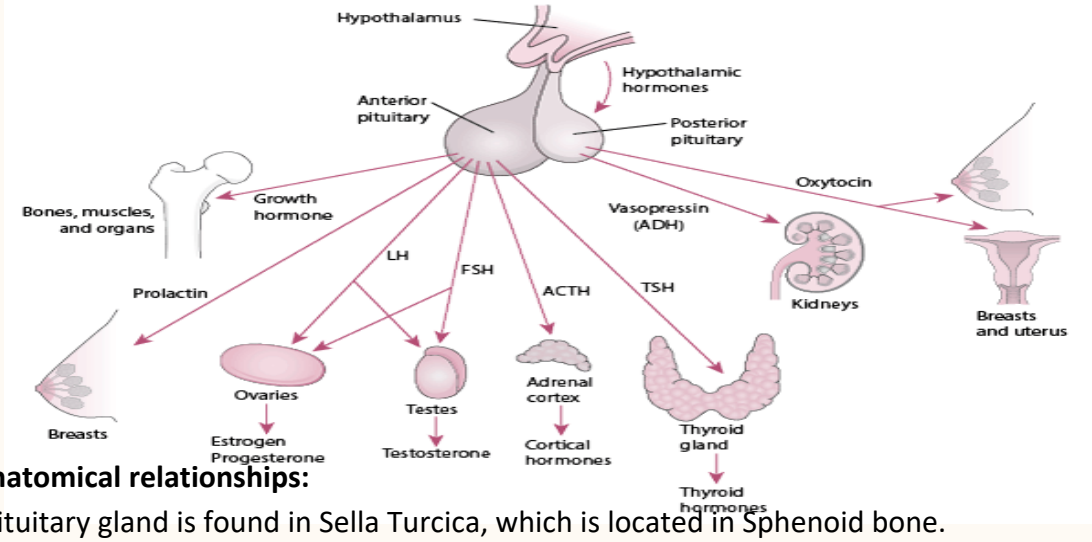
**Recorded on 21, 23 Aug .2017

Contents

Pituitary Gland:

- Pituitary gland is also called hypophysis, it consists of 2 lobes:

1. **Anterior pituitary (Adeno-hypophysis): it secrets:**	2. **Posterior Pituitary (Neuro-hypophysis): it releases:**
a. **Growth Hormone (GH).** b. **Prolactin (PRL).** c. **Adreno Cortico-Tropic Hormone (ACTH).** d. **Thyroid Stimulating Hormone (TSH).** e. **Follicle Stimulating Hormone (FSH).** f. **Luteinizing Hormone (LH).** **[FSH and LH are the gonadotropins].**	a. Oxytocin b. Anti-Diuretic Hormone (ADH). - In embryo, ectoderm has two parts, Surface ectoderm (which gives rise to skin, appendages, etc.), and Neuro Ectoderm (which gives rise to Nervous system). - Hypothalamus controls pituitary (Hypothalamic-Pituitary-Axis):
Anterior pituitary: There is NO direct connection, and connection is through *hormones* released by hypothalamus in the blood. These hormones are either: *stimulatory* (the releasing hormones, e.g.(TRH)), or *Inhibitory:* **o The most important releasing hormones are:** - **TRH** **o The most important inhibitory hormones are:** - **Somatostatin: it inhibits GH.** - **Dopamine: it inhibits PRL.**	**Posterior Pituitary:** is connected directly to hypothalamus by *pituitary stalk*, which is a group of nerves that regulates pituitary gland (both posterior pituitary and hypothalamus are nervous tissues).



✵ **Anatomical relationships:**

- Pituitary gland is found in Sella Turcica, which is located in Sphenoid bone.

Superiorly: Optic chiasm.

Laterally: Cavernous sinus; it is one of the dural venous sinuses close to 3^{rd}, 4^{th}, 6^{th} cranial nerves, and 1^{st} branch of the 5^{th} nerve.
Inferiorly: Sphenoid sinus; it is one of the paranasal sinuses.

- When there is pituitary adenoma pt may present with signs of increased intracranial pressure (ICP); headache, nausea, projectile vomiting, diplopia, papilledema, but more importantly and CHARACTERISTIC for pituitary enlargement is:
    - ❶ Bi-temporal hemianopia: due to compression of optic chiasm.
    - ❷ Cranial Nerve Palsy of 3^{rd}, 4^{th}, 6^{th}, and ophthalmic division of trigeminal due to compression of cavernous sinus and surroundings.
    - ❸ CSF rhinorrhea: due to obstruction of sphenoid sinus that drains to the nose.

- So, clinical features of pituitary adenoma are due to compression (pressure symptoms) and due to excessive release of hormones.
- BUT the most common pituitary adenoma is non-functioning pituitary adenoma, and pt present only with pressure symptoms:
    1. Signs and symptoms of increased ICP.
    2. Bi-temporal hemianopia.
    3. CN palsy of the nerves supplying the eye.
    4. Rhinorrhea.

❖ Disease Of Pituitary Gland:

1. Adenomas:

- Could be either macro-adenoma (>1cm) or micro-adenoma (<1cm).
- The most common pituitary adenoma is non-functioning pituitary adenoma (MCQs).
- The most common functioning pituitary adenoma is prolactinoma (an MCQs question)

a) Prolactinoma:

- **Causes of high PRL level:**
  1. Physiological hyperprolactinemia: pregnancy and lactation (note that milk production does not occur during pregnancy, because during pregnancy estrogen and progesterone levels are elevated, and they inhibit milk production).
  2. Prolactinoma: pituitary adenoma producing PRL.
  3. Hypothyroidism: Normally TRH stimulates production of TSH and PRL, pt with hypothyroidism has low T3 and low T4 → No negative feed-back inhibition on TRH → high TRH → high TSH and high PRL.
  4. Others: ما مهمة شديد
     I. Acromegaly: 30% of GH producing adenomas secretes PRL (in addition to GH), that is why acromegaly is sometimes associated high PRL.
     II. Dopamine antagonists: e.g. anti-psychotic, anti-depressants and anti-emetics.
     III. Liver and Kidney diseases: because PRL is metabolized by the liver and excreted by the kidneys.
- **Clinical features:**
  - **Female:** Galactorrhea and amenorrhea.
  - **Male:** Galactorrhea, loss of libido and impotence.
  - Pressure symptoms of adenoma are more obvious in macro-adenoma than in micro-adenoma (prolactinoma in males is usually macro because they develop galactorrhea late, so they seek medical care late, while in females prolactinoma is usually micro because they develop galactorrhea early, so they seek medical care early).
- **Investigations:**
  - Prolactin level.
  - Pregnancy test in females to exclude physiological causes.
  - TFT: to exclude hypothyroidism.
  - MRI pituitary (NOT CT because tissues are better seen by MRI).
- **Treatment:**
  - *First line* is Medical: by dopamine agonists (Bromocriptine or Cabergoline).
  - *Second line* is Surgical removal of the tumor: either trans-sphenoidal surgey or through the head.

NOTE: **Dopamine agonists are two types:**

1. **Ergot derived:** e.g. Bromocriptine and Cabergoline.

- Are used in treatment of prolactinoma.
- The most important side-effect is fibrosis of serosal membranes (e.g. pleura, pericardium, and peritoneum).
- Pts with Parkinson need the drug for life, so they are not given ergot derived dopamine agonists because they may develop fibrosis.

2. **Non-ergot derived:** e.g. Ropinirole, and Rotigotine

- Side-Effect is binge behavior (e.g. excessive eating or gambling).
- Non-ergot derived dopamine agonists are used in treatment of Parkinson's disease].

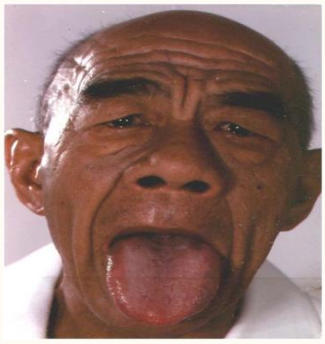
b) Acromegaly:

➢ **Causes:**

- Almost always due to pituitary adenoma, and usually it is macro-adenoma.
- Pressure symptoms of adenoma are more obvious in macro-adenoma than in micro-adenoma. That is why they are usually seen in Acromegaly.
- In addition to GH, 30% of theses adenomas secrete PRL.

➢ **Clinical features:**

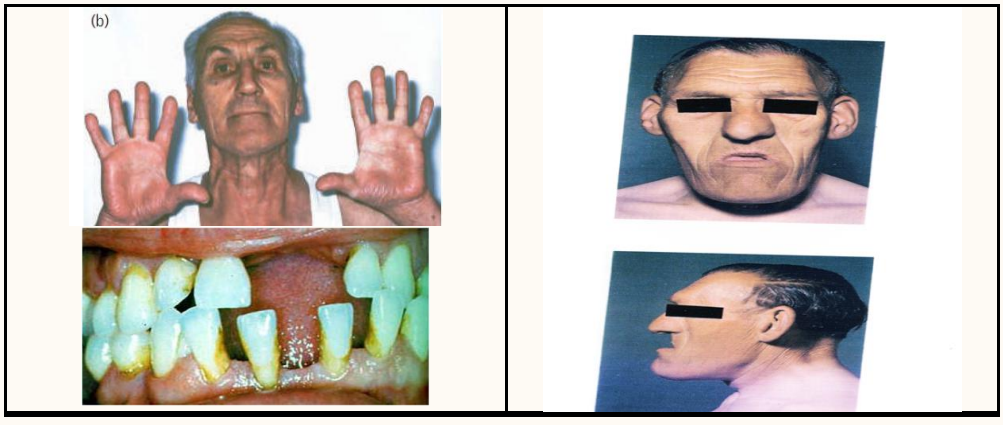
- First sign of acromegaly is enlargement of hands and feet.
- Then Prognathism (enlargement of the jaw).
- Enlargement of the tongue.



[**NOTE:** D.D. of **large tongue {Macroglossia}:** (An OSPE question)

1. Acromegaly.
2. Amyloidosis.
3. Hypothyroidism (myxedema and cretinism).
4. Down syndrome: NOT truly large tongue, but the jaw is small (micrognathia), that is why pt looks like he has large tongue.

- Enlargement and hypertrophy of sweat glands (pt has oily skin).
- Carpal tunnel syndrome.



➢ **Investigations:**

- We do not measure GH level (because the level is not constant through the day), we measure Insulin Like Growth Factor I or II (ILGF I, II), (ILGF is also called somatomedin).

📄 **NOTE:**
- The inhibitor of GH is called somatostatin.
- Somatomedin (ILGF) is the metabolite of GH.
- GH has many actions in the body, but most of the actions are mediated by somatomedins.

- ILGF level is the best screening test for acromegaly.
- High levels of ILGF does not confirm the diagnosis.
- Oral GTT (Glucose Tolerance Test) is the confirmatory test.

📄 **NOTE**:
- GH is a counter regulatory hormone.
- Counter regulatory hormones are hormones that increase the level of glucose in the blood, when you give oral glucose they should be suppressed or inhibited.
- E.g. of counter regulatory hormones; GH, thyroid hormone, cortisol, adrenalin.

- In acromegaly when you do oral GTT → failure of suppression of GH.

➢ **Treatment:**

- Always first line is surgical.
- But before surgery give somatostatin analogue to decrease the size of adenoma.
- Octreotide is the somatostatin used.
- You can give GH receptor antagonist called Bigvisomant.

➢ **Complications:**

- CVS complications; 1. Cardiomyopathies (mainly hypertrophic). 2. Heart failure: it is the most common cause of death in pt with acromegaly. 3. Hypertension.
- Diabetes or impaired GTT.
- Colorectal polyps: due to enlargement of epithelial cells in the colon, these polyps may develop into colorectal cancer.
- Colorectal cancer.

2. Pituitary insufficiency:

- There are many causes of pituitary insufficiency, e.g. non-functioning tumors, surgery, radiations, trauma, encephalitis, meningitis, ….etc. But most importantly and more common in exams are:
    a. Sheehan syndrome.
    b. Pituitary apoplexy.

A. Sheehan syndrome:

- Enlargement of pituitary gland during pregnancy is normal. If pt develops postpartum hemorrhage, blood supply to pituitary decreases, but this pt has large pituitary that needs high amount of blood, this results in pituitary ischemia and pituitary insufficiency.

📄**NOTE:** The uterus also enlarges during pregnancy, but it does not develop ischemia in post-partum hemorrhage, because there is high number of blood vessels in the uterus. The number of blood vessels supplying pituitary gland does not increase, that is why pituitary gland is susceptible to ischemia.

- So, post-partum hemorrhage causes damage to pituitary.
- **Case scenario:** pregnant lady, developed post-partum hemorrhage after delivery, then she was not able to lactate her child.

B. Pituitary Apoplexy:

- Is a pituitary adenoma that suddenly develops hemorrhage, and its size increases suddenly.

➢ **Clinically:**

- Pressure signs and symptoms of adenoma.
- **Meningism:** i.e. 1. Neck stiffness. 2. Photo-phobia. 3. Phono-phobia. 4. Positive Kernig sing. 5. Positive brudzinski sign.

> 🗎 **NOTEs**: D.D. of meningism:
> 1. Meningitis and Encephalitis.
> 2. Sub-arachnoid hemorrhage (SAH).
> 3. Pituitary apoplexy.
>
> **N.B. ☺:** if there is a pt with signs and symptoms of meningitis, with elements of decrease level of consciousness or behavioral changes → this is meningo-encephalitis because in meningitis level of consciousness does not change.

- To differentiate meningo-encephalitis and SAH from pituitary apoplexy: measure blood pressure:
  - ✓ In meningo-encephalitis and SAH blood pressure is very high, due to vasoconstriction that occurs due to hemorrhage.
  - ✓ While in pituitary apoplexy blood pressure is very low, because there is NO aldosterone → sodium and water reabsorption decreases → blood pressure decreases.
  - So in clinical presentation of pituitary apoplexy there is **<u>meningism with low blood pressure</u>** +/- pressure symptoms.

> 🗎 **NOTE:** MCQs question:
> - In pituitary insufficiency the first hormones to decrease are Gonadotropins.
> - The last hormone to decrease is ACTH, because cortisol is mandatory for life.
> - The hormone that must be corrected firstly is cortisol because it is mandatory for life.

3. Posterior pituitary: secretes:

a) Oxytocin:

- it induces uterine contractions. It is NOT associated with any clinical disease.

b) Vasopressin (ADH):

- Vasopressin has two receptors:
  1. V1 receptors: found in blood vessels, causes vasoconstriction, hence the name vasopressin.
  2. V2 receptors: found in collecting ducts and distal convoluted tubules of kidney, it causes reabsorption of water through Aquaporin II channels (does NOT cause reabsorption of sodium).

- **Diseases related to ADH:**

1. SIADH:

- Discussed in Renal system chapter.

NOTE about hyponatremia: SIADH causes hyponatremia.

- **Hyponatremia** has 3 types:

1. Hypo-volemic hyponatremia: there is features of dehydration; dry membranes, sunken eyes, … etc.
2. Eu-volemic hyponatremia.
3. Hyper-volemic hyponatremia: there is edema; e.g. heart failure, nephrotic syndrome.

- SIADH causes eu-volemic hyponatremia.

- SIADH is caused by lung or brain pathologies, e.g. meningitis, encephalitis, SAH, radiation, trauma, lung cancer secreting ADH, pneumonia, pulmonary embolism, … etc.

2. Diabetes insipidus (DI): Deficiency of ADH

Types: Has two types:

1. **Cranial DI:** there is problem in the brain (hypothalamus):
   - Wolfram syndrome (in pediatrics): DM + DI + optic atrophy + deafness.
   - Trauma.
   - Surgery.
   - Radiation.
2. **Nephrogenic DI:** Kidney receptors do not respond to ADH.
   - Causes:
     I. Genetic: X-linked (there is family history).
     II. Electrolytes disturbance: hypokalemia or hypercalcemia.
     III. Drugs: e.g. lithium, demeclocycline (ADH antagonist).
     IV. Interstitial kidney diseases and sickle cell anemia.

Clinical features:

- Clinical features are caused by absence of water reabsorption.
- Pt presents with polyuria and polydipsia.

> 🗎 **NOTE:** D.D. of polyuria and polydipsia:
> 1. DM.
> 2. DI.
> 3. Psychogenic polydipsia: pt drinks high amount of water → high amount of urine.

Investigations:

- Confirm polyuria by measuring urine output.
- Serum osmolarity and serum sodium: both are high.
- Urine osmolarity or specific gravity: Low.

> 🗎 **NOTE:** in psychogenic polydipsia serum osmolarity and serum sodium are low, so psychogenic polydipsia is excluded by measuring serum osmolarity.
> DM Is excluded by history and by oral GTT.

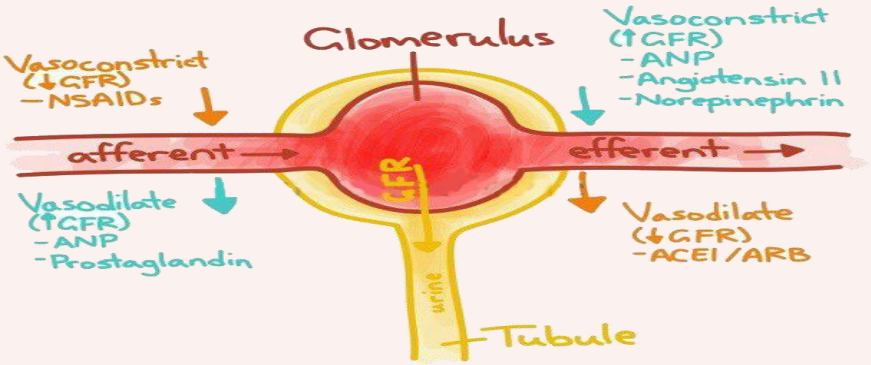
- Water deprivation test: in DI there is failure to concentrate urine. Then give synthetic ADH (Desmopressin) to differentiate cranial DI from nephrogenic DI:
  - ✓ If urine gets concentrated: this means that pt is not producing ADH, and the cause is central (cranial).
  - ✓ No response: this is nephrogenic DI (because the problem is in kidney receptors).

Treatment:

- For cranial DI: give desmopressin (oral, subcutaneous, or intra-nasal).
- For nephrogenic DI:
  - This pt has two problems: 1. Fluid loss. 2. High level of sodium.
    - ✓ Fluid loss is corrected by *NSAID (indomethacin).*
    - ✓ High level of sodium is corrected by *thiazide diuretics*

And you should treat the underlying cause if possible (e.g. hypokalemia or hypercalcemia).

Important notes:



◊ If we want to increase filtration (GFR), we should increase hydrostatic pressure by either dilation of afferent arterioles, or by constriction of efferent arterioles.

- ✓ Dilation of afferent arterioles is mediated by prostaglandins.
- ✓ Constriction of efferent arterioles is mediated by Angiotensin II.

◊ And if we want to decrease filtration (GFR), we decrease the hydrostatic pressure by either constriction of afferent arterioles, or by dilation of efferent arterioles.

- ✓ Constriction of afferent arterioles is by NSAID.
- ✓ Dilation of efferent arterioles is by ACEI.

◊ So, GFR is decreased by ↓:

- NSAID.
- ACEI.

◊ And is increased by ↑:

- PG.
- Angiotensin II.

[PG ≠ NSAID] [Angiotensin ≠ ACEI]

Important note about NSAID:

- NSAID has 3 actions:

① Anti-inflammatory. ② Analgesic. ③ Anti-platelet.

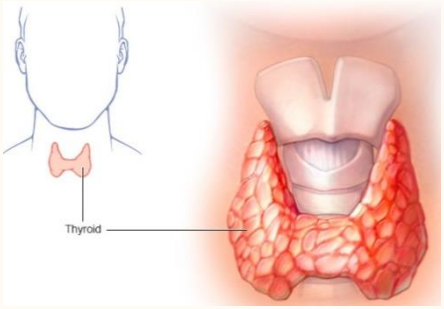
- If you want the analgesic action; give paracetamol (paracetamol has NO anti-inflammatory action).
- If you want anti-inflammatory action; give ibuprofen.
- If you want anti-platelet action; give aspirin.

❖ **Cranio-pharyngoma:** A child, with growth deficiency, X-ray or CT of the brain shows supra-sellar calcified mass or tumor.

Thyroid Gland:

In Medicine focus on Hypo + Hyperthyroidism
In Surgery → Goiter
In Pediatrics → Cretinism

Diseases of thyroid gland:



1. **Diseases with high level of thyroid hormone ↑:**
   - **a.** Thyrotoxicosis and Gravis disease.
   - **b.** De Quervain thyroiditis.
   - **c.** Sub-clinical hyperthyroidism.
2. **Diseases with low level of thyroid hormone ↓:**
   - **a.** Hypothyroidism and Hashimoto thyroiditis.
   - **b.** Sub-clinical hypothyroidism.
3. **Goiter.**

❖ Hyperthyroidism (thyrotoxicosis):

➢ **Causes:**

1. Gravis diseases (toxic diffuse goiter): the most common cause of hyperthyroidism.
2. Toxic Multi-Nodular Goiter (TMNG): also called Plummer's disease.
3. Toxic adenoma.
4. Transient hyperthyroidism (thyroiditis): De Quervain Thyroiditis and post-partum thyroiditis.
5. Drugs: e.g. Amiodarone (it causes both hypo and hyperthyroidism).
6. Iatrogenic: exogenous cause of thyrotoxicosis, i.e. by thyroxin intake (also called Thyrotoxicosis Factitia).

- Thyrotoxicosis is usually primary, secondary thyrotoxicosis is rare (Secondary thyrotoxicosis means pituitary adenoma producing TSH).
- The most important component of thyroid function test (TFT) is TSH **(MCQs سؤال).**
- In hyperthyroidism TSH is low, T3 and T4 are high.
- The amount of T4 produced is larger than the amount of T3, But the active form is T3.
- There is peripheral de-iodination of T4 to T3.

- In all causes of hyperthyroidism thyroglobulin level is elevated, because it is a precursor in synthesis of thyroid hormone, the only EXCEPTION is Exogenous thyrotoxicosis.
- **In Radioactive iodine test (diagnostic):**
  1. Diffuse increase in iodine uptake → Gravis disease.
  2. Patchy increase in iodine uptake → TMNG.
  3. Solitary increase in iodine uptake → Toxic adenoma.
  4. Decreased iodine uptake → either Thyrotoxicosis Factitia or thyroiditis.

❖ De Quervain thyroiditis (Sub-acute thyroiditis):

- It is viral infection followed by **PAINFUL** enlargement of thyroid gland, pt has fever, and inflammatory markers are elevated (high ESR).
- Usually following upper respiratory tract infection.
- **Treatment:** do not give anti-thyroid drugs, just give simple analgesia (if needed), to decrease pain and inflammation. Anti-thyroid drugs have no role because the disease is caused by destruction of cells of the thyroid gland, and thyroid hormones get released in the blood causing thyrotoxicosis. (i.e. anti-thyroid drugs decrease production of thyroid hormone, but in De Quervain thyroiditis hormone production is not elevated, so there is no role for anti-thyroid drugs).

❖ Gravis disease: مهم جداً

- Gravis disease is: Thyrotoxicosis + diffuse goiter (ما بجي في السيرجري☺)
- + eye signs (exophthalmos, lid lag, led retraction, chemosis) + dermopathy (peri-tibial myxedema and acropachy).
- Peri-tibial myxedema is non-pitting edema around tibia.
- Thyroid acropachy is finger clubbing associated with bone formation.

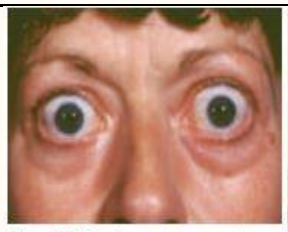


Fig 5.14 Thyroid eye disease: lid retraction causing a 'staring' appearance.

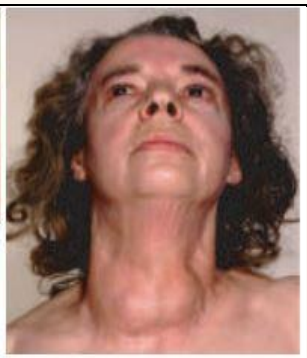


Fig 5.15 Goitre.

OSPE: Bilateral lid retraction in Graves' disease + exophthalmos

Complications → dryness ,, corneal ulcer

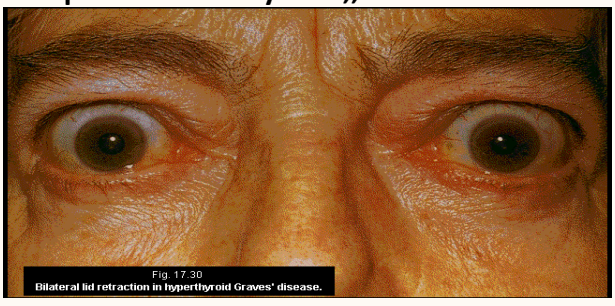


Fig. 17.30
Bilateral lid retraction in hyperthyroid Graves' disease.

- **Clinical features:**
  - Hyperthyroidism:
    1. Heat intolerance.
    2. Weight loss.
    3. High pulse.
    4. Myopathy (due to protein destruction).
    5. Increase glucose (because thyroid hormone is one of the counter regulatory hormones, and pt may develop DM).
    6. Irritability.
    7. Diarrhea (increased GI motility).
    8. Increased affinity of β receptors to noradrenaline.
  - Diffuse goiter.
- **Investigations:**
  - TFT: TSH → Low.
    T3 and T4 → High.
  - Antibodies: (they bind to TSH receptors in thyroid gland to stimulate it)
    I. Thyroid stimulating immunoglobulin (TSI).
    II. TSH receptor Antibody (TRAB).
    III. Long Acting Thyroid Stimulating Antibodies (LATS).
    ➔ I, II, and III are 3 names of one antibody.

- **Management:**
  - Main treatment is anti-thyroid drugs, but they need one week to start functioning, that is why we start treatment by β blockers (An MCQs question):
    1. B-blockers: to control symptoms only.
    2. Anti-thyroid drugs: Carbimazole, but it is contra-indicated in pregnancy, so if pt Is pregnant give her propylthiouracil (blocks conversion of T4 to T3).

> 🗎 **NOTE:** Anti-thyroid drugs are given by one of two methods:
> ① Titration method: give the drug and then decrease the dose according to TSH level, it needs long time (up to 2 years).
> ② Block and replace method: give the highest dose of anti-thyroid to block thyroid gland, then give thyroxin as replacement, needs about 9 months, so it is relatively shorter than titration method.
> **Side Effect of anti-thyroid drugs:** agranulocytosis
> Scenario; pt taking anti-thyroid drugs, then he develops throat pain or any infection, CBC shows low WBCs. This is agranulocytosis, it is treated by stopping the drug.

3. Radio-active iodine: Contra-indicated in pregnancy, and in pt younger than 16 years, and active eye disease (because it makes eye disease worse).
4. Surgery.

- **Treatment of thyroid eye disease:**
  1. Stop smoking: the most important step.
  2. High dose steroids.
  3. If 1 and 2 fail, go to surgery.

❖ Thyrotoxic crisis (thyroid storm): Is an emergency.

- **Risk factors:**
  1. Surgery in unprepared pt, or radio-active iodine therapy in unprepared pt (pt must be in euthyroid state before these procedures, if he was in hyperthyroid state he will develop thyroid storm).
  2. Stress: infection, MI, surgery.
- **Clinical features:**

1. Hyperpyrexia (high temperature).
2. Cardiovascular disturbances: start as tachycardia, then it becomes arrhythmia, then heart failure.
3. If he is conscious and awake he will develop CNS symptoms: confusion, convulsions (but these symptoms are usually not seen, because pt usually develop thyroid storm on table).

- **Management:**

1. ICU admission.

2. Symptomatic treatment:

I. Fever: give IV fluids, and cooling.

II. Cardiovascular disturbances should be treated.

When symptoms are treated, and pt is stabilized give:

3. β Blockers, IV anti-thyroid drugs, and Lugol's iodine (Lugol's iodine decreases vascularity of thyroid gland).

4. IV steroids: prevent peripheral de-iodination of T4 to T3.

❖ **Sub-clinical hyperthyroidism**: بتجي في الام سي كيوز كتير

- Low TSH, normal T3 and T4.
- Next step: confirm persistency of this sub-clinical hyperthyroidism by repeating the test after 2 to 4 months.
- When persistency is confirmed: treatment is indicated only if TSH is very low (<0.1).
- Sub-clinical hyperthyroidism may cause:
  1. Atrial fibrillation.
  2. Osteoporosis.

📄 **NOTE:** Thyroid hormone increases protein catabolism, and stimulates osteoclasts.
- Osteoclast is responsible for bone resorption.
- Bone consist of calcium and proteins, and thyroid hormone decreases both calcium and protein.
- So thyrotoxicosis is one of the causes of hypercalcemia.

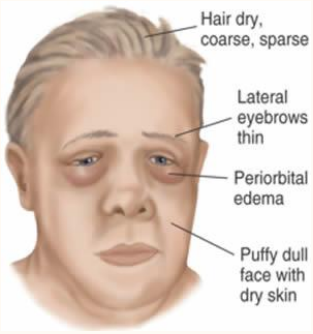
❖ Hypothyroidism:

Causes:

1. The most common cause of hypothyroidism world-wide and in Sudan is iodine deficiency.
2. The most common cause of hypothyroidism in developed countries is Hashimoto thyroiditis (an autoimmune disease).
3. Drugs: Amiodarone. مراقة
4. Surgery or radio-active iodine.
5. Secondary causes. ما مهمة

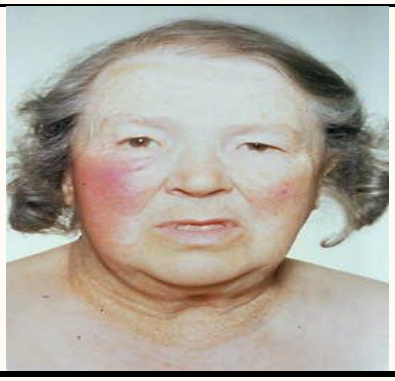
❖ Hashimoto thyroiditis:

- Is an autoimmune disease. More common in females.
- Associated with other autoimmune diseases, e.g. vitiligo, DM type I, Adison disease, pernicious anemia, etc.



➢ **Clinical features:**

1. Cold intolerance.
2. Weight gain.
3. Loss of hair (characteristically the outer third of eyebrows)
4. Bradycardia.
5. Slow relaxation phase in deep tendon reflexes (NOT hyperreflexia).
6. High cholesterol levels (thyroid hormone decreases the level of cholesterol).
7. Edema (also called myxedema): in hands (causing carpal tunnel syndrome), and in tongue (remember D.D. of large tongue).

OSPE: Hypothyroidism (loss of lateral outer eyebrows ,, loss of hair lines)	

- **Investigations:**
  - TFT: High TSH + Low T3 and T4.
  - Antibodies:
    I. Anti-thyroid Peroxidase Antibody (anti-TPO), also called anti-microsomal antibody (peroxidase is an enzyme used in production of thyroid hormones, it oxidizes iodide into iodine).
    II. Anti-thyroglobulin Antibody (Anti-TG Ab).
- **Treatment:**
  - Thyroxin replacement.
  - But you have to be aware in two groups of pts (start by low dose of thyroxin, then increase it slowly):
    1. Old pts.
    2. Pts with CVS diseases e.g. IHD, [thyroxin increases the heart rate, this increases the work load on the heart, and may cause ischemia and angina].

❖ Myxedema Coma:

- Is an emergency.
- Pt is classically old, with hypothyroidism but not compliant to his medications.

- **Clinical features:**
  1. Pt is very cold.
  2. Pulse is very weak.
  3. CNS symptoms (coma).
- **Treatment:**
  - Admission to ICU.
  - Symptomatic management (warming).
  - Give thyroxin.
  - Give steroids (because the cause of hypothyroidism may be pan-hypopituitarism, in pts with hypopituitarism cortisol level is low, and cortisol is mandatory for life that is why it is important to give steroids).

📄 **NOTE:** ما مهمة

- Hashimoto encephalopathy is a differential diagnosis of myxedema coma:
- Clinically pt with Hashimoto present with coma.
- Difference between Hashimoto encephalopathy and myxedema coma is that in myxedema coma features of hypothyroidism are present, but they are not present in pt with Hashimoto encephalopathy (just only coma).

❖ Sub-clinical hypothyroidism:

- TSH is high, T3 and T4 are normal.
- First step: confirm persistency after 2-4 months.
- If it was persistent we are afraid that pt may develop overt hypothyroidism.
- Indications of treatment:
    1. TSH is very high (>10).
    2. If the pt has positive antibody tests.
    3. If there is another autoimmune disease.
    4. If there is history of Gravis disease (gravis is an autoimmune disease).
- Treatment is by thyroxin

❖ Sick euthyroidism:

- One of the differential diagnoses of low TSH.
- TSH, T3, and T4 are all Low.
- Occurs usually in hospitalized pts.
- Does NOT present with clinical hypothyroidism.
- Treatment: just treat the underlying cause (cause of hospitalization).

📄 **NOTE:** Thyroid hormone may be free or bound to protein.

- We can measure the total hormone and the free hormone:

→ Causes of high total hormone with normal free hormone (high protein levels in the body):

i. Pregnancy.
ii. Oral contraceptive pills.

→ Causes of Low total hormone with normal free hormone (Low protein levels in the body):

i. Malnutrition.
ii. Malabsorption.
iii. Liver cirrhosis.
iv. Nephrotic syndrome.
v. Androgen intake (proteins get accumulated in muscles).

❖ Goiter:

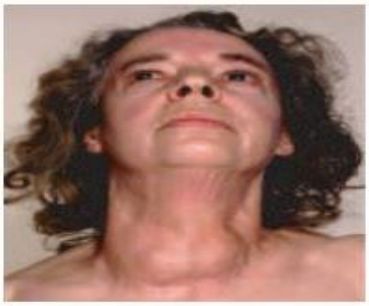


Fig 5.15 Goitre.

- Anatomical classification:

1. Diffuse. 2. Multinodular. 3.Solitary (adenoma).

- Physiological classification:
    1. Simple: tumor produces hormone.
    2. Toxic: tumor does not produce hormone.

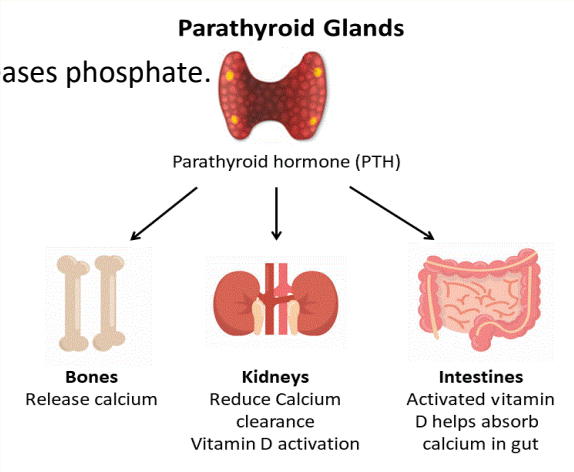
- So, goiter may be:
    1. Simple diffuse goiter: is physiological (pregnancy, and early iodine deficiency).
    2. Simple multi-nodular: common in surgery OSCE exams.
    3. Simple adenoma.
    4. Toxic diffuse: Gravis disease.
    5. Toxic Multi-nodular: Plummer syndrome.
    6. Toxic adenoma.

Parathyroid Gland:

Question: What are the hormones that control calcium level in the body?

Answer:

1. Parathyroid hormone (PTH): increases calcium and decreases phosphate.
2. Vitamin D: Increases both calcium and phosphate.
3. Calcitonin: Decreases both calcium and phosphate.



❖ Hypercalcemia:

➢ **Causes:**

1. Primary hyperparathyroidism.

2. Malignancies: squamous cell lung cancer (produces Para-Thyroid Hormone Related Peptide (PTHRP) ''see below''), Multiple myeloma, metastasis to vertebra (causes cellular destruction and calcium release in the blood).

3. Others:

I. Vitamin D intoxication.
II. Granuloma: e.g. TB, leprosy, Sarcoidosis. Because granuloma produces vitamin D.
III. Thyrotoxicosis: thyroid hormone stimulates osteoclasts (release Ca in blood).
IV. Familial hypocalciuric hypercalcemia: is an autosomal dominant disease in which calcium receptors in parathyroid gland and kidneys are not functioning. Parathyroid gland secrets PTH causing hypercalcemia, and because calcium receptors of the kidneys are not functioning calcium is not secreted in the urine causing hypocalciuria.
V. Tertiary hyperparathyroidism ''see below''.

➢ **Investigations:**

- Calcium level to confirm hypercalcemia.
- ECG: Short QT interval.
- Measure PTH level:
  - ➔ High or normal PTH: this is either:
    1. Primary hyperparathyroidism.
    2. Tertiary hyperparathyroidism ''see below''.
    3. Familial hypocalciuric hypercalcemia.

[You differentiate between primary hyperparathyroidism and Familial hypocalciuric hypercalcemia by measuring **urine calcium (24 hours urine calcium)**: it is NORMAL in primary hyperparathyroidism, and LOW in and Familial hypocalciuric hypercalcemia].

➔ Low PTH:

1. Malignancy: do serum protein electrophoresis for multiple myeloma, and do serum PTHRP level, and chest imaging for lung cancer, do bone scan for metastasis.
2. Granuloma and vitamin D intoxication: measure vitamin D level.
3. Thyrotoxicosis: do TFT.

- ECG features of hypercalcemia: Short QT interval.

📄 **NOTE:** Small cell lung cancer produces ACTH causing Cushing syndrome. Squamous cell lung cancer produces Para-Thyroid Hormone Related Peptide (PTHRP) (**Not PTH**), PTHRP causes hypercalcemia. ''see respiratory system, paraneoplastic syndromes associated with each type of lung cancer''.

➢ **Clinical features:**

[Use this phrase to remember symptoms of hypercalcemia**: Bones, stones, abdominal moans, and psychic groans]**

- Bone pain.
- Calcium stones in kidneys.
- Acute pancreatitis: pt present with abdominal pain, nausea, and vomiting.
  - **[**Pancreatic enzymes are normally produced in the pancreas as zymogens (not active), and get activated in the intestine.
  - If they get activated in the pancreas they will cause acute pancreatitis, So, **Acute pancreatitis is caused by:**
    1. Stones: close pancreatic duct leading to activation of the enzyme.
    2. Alcohol: causes cellular destruction leading to release of the enzyme.
    3. High level of calcium: leads to activation of pancreatic enzymes].

- Also it may cause peptic ulcer.
- CNS symptoms: e.g. seizures, psychosis.
- Polyuria and polydipsia: due to nephrogenic DI (remember that electrolyte disturbances cause DI ''see above'').
- Tachycardia: rapid contraction of cardiac muscles (calcium is important for muscle contraction). That is why in ECG there is Short QT interval (duration of contraction is short).

- **Treatment:**
  - First line: IV fluids + bisphosphonate (it inhibits osteoclasts, causing decrease in calcium level).
  - Bisphosphonate need long time to produce its desired effects, so if you need acute (rapid) correction you may need to give Calcitonin ± loop diuretics (e.g. furosemide. Loop diuretics causes Loss of calcium).
  - It there is no response → dialysis.

✵ Types of hyperparathyroidism:

1. **Primary:** high levels of PTH is caused by either adenoma or hyperplasia (as part of Multiple Endocrine Neoplasia (MEN) ''see below''), and rarely by carcinoma.

2. **Secondary:** pt already has low calcium or high phosphate leading to activation of PTH. There is high levels of PTH, and also high levels of Alkaline Phosphatase (ALP), ALP is an indicator of bone function ''see the note below''.

❖ **Causes of secondary hyperparathyroidism:**

I. High phosphate: in Chronic kidney diseases (chronic renal failure), normally kidneys re-absorb calcium and secrete phosphate, when there is renal failure phosphate will accumulate ''see renal system chapter''.

II. Low calcium: e.g. Rickets (vitamin D deficiency).

3. **Tertiary:** caused by progression of secondary type of hyperparathyroidism. i.e. pt has had secondary hyperparathyroidism but it persists for long time, and secretion of PTH become unopposed and autonomous. Calcium level is **very** high.

» So, in primary and tertiary hyperparathyroidism there is **hypercalcemia**, and in secondary hyperparathyroidism there is **hypocalcemia**.

📄 **NOTE: Bone profile:**	
1. Calcium	2. Phosphate
3. PTH.	4. ALP

- ALP level indicates functioning of osteoclast and osteoblast. These cells are activated by PTH, so high PTH causes high ALP.
- bone profile is very important in pediatrics, e.g. pt wit Rickets will have low calcium, low phosphate, high PTH, and high ALP. جات في الاوسبي بتاع قساور

→ So, high PTH with low calcium: this is secondary hyperparathyroidism.

→ High PTH with high calcium: either primary or tertiary hyperparathyroidism, to differentiate between them do bone profile looking for phosphate level:

- In primary hyperparathyroidism: phosphate level is LOW due to excess PTH.
- In tertiary hyperparathyroidism: phosphate level is HIGH. (the pt has had secondary hyperparathyroidism and high PTH due to high phosphate level (renal failure)).
- Also PTH is **very** high in tertiary hyperparathyroidism.
- You can also differentiate between them by history: if the pt has renal failure this is tertiary hyperparathyroidism.

❖ Hypocalcemia:

- **Causes:**
  1. Chronic kidney diseases: kidney fails to re-absorb calcium (associated with secondary hyperparathyroidism).
  2. Vitamin D deficiency: e.g. in rickets and osteomalacia.
  3. Hypoparathyroidism.
  4. <u>Pseudo-hypoparathyroidism:</u> PTH receptors are not functioning.
     Clinically; in addition to features of hypocalcemia, pt has skeletal features (short stature, and short 4^{th} and 5^{th} metacarpal bones) (an OSPE question).

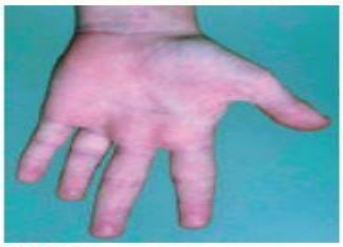
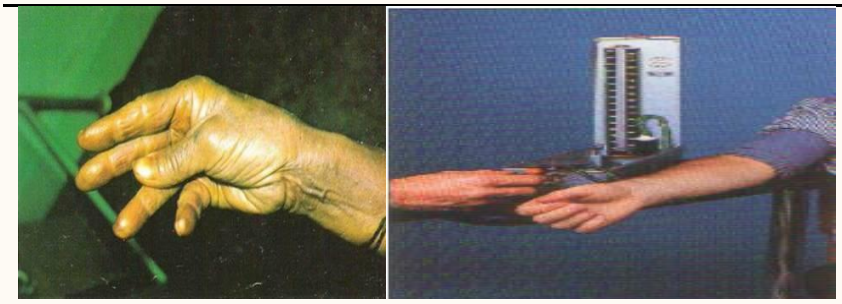


Fig 5.18 Pseudohypopara-thyroidism: short 4th and 5th metacarpals.

  5. Hypomagnesemia: magnesium is essential for function of PTH, low levels of magnesium lead to decrease activity of PTH, causing hypocalcemia.
  6. Alkalosis: in alkalosis hydrogen detaches from albumin, and calcium binds to this albumin leading to decrease in free ionized calcium (total level of calcium remains unchanged).

- **Clinical Features:**
  - Excitable tissues (nerves and muscles) are depolarized by Na^{+}. Ca^{++} ions prevent Na^{+} from depolarizing them.
  - When there is hypocalcemia Na^{+} causes excitation of these tissues.
  - Hyper-excitation of nerves presents as numbness, mainly perioral.
  - Hyper-excitation of muscles causes ***Trousseau and Chvostek signs.***



Trousseau sign

- **<u>So, clinical features of hypocalcemia are:</u>**

- Perioral numbness.
- Trousseau and Chvostek signs.
- Seizures.
- Muscle cramps and tetany.
- Carbo-pedal spasm.

- **Investigations:**
  ECG: Long QT interval.
- **Management:**
  IV calcium gluconate under ECG monitoring, because calcium can stop the heart in systole.

- **Relationship between calcium level and pH:**
  Acidosis: causes hypercalcemia**.** **&** **Alkalosis:** causes hypocalcemia.

Adrenal gland:

- Adrenal gland consists of cortex and medulla.

- **Cortex** consist of three zones:

1. Zona Glomerulosa: secrete mineralocorticoids (Aldosterone).
2. Zona Fasciculata: secretes glucocorticoids (cortisol).
3. Zona Reticulosa: secretes sex hormones.

- **Medulla** secretes Catecholamines (adrenaline, and nor-adrenaline).

Diseases of adrenal gland:

1. Diseases of adrenal cortex:

a. Cushing syndrome.

b. Hyperaldosteronism.

c. Hypoadrenalism and Addison's disease.

***2.* Diseases of Adrenal medulla:**

a. Pheochromocytoma

§ Diseases of adrenal cortex:-

❖ Cushing syndrome:

➢ **Causes:**

1. <u>ACTH dependent:</u>

a. Cushing Disease: ACTH is produced from pituitary adenoma.
b. Small cell lung cancer producing ACTH.

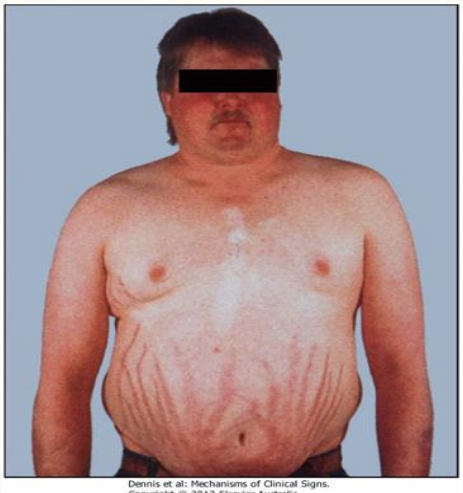
2. <u>Non-ACTH dependent:</u>

a. Exogenous cortisol: e.g. in pts with asthma.
b. Adrenal problems: a tumor (adenoma, hyperplasia, or carcinoma) secreting cortisol.

- In Non-ACTH dependent Cushing syndrome, the high level of cortisol exerts negative feed-back on ACTH, so, ACTH level is low.
- The most Common cause of Cushing syndrome is exogenous (iatrogenic) cortisol.
- The most common Non-iatrogenic cause of Cushing syndrome is Cushing disease (pituitary adenoma).

- **Actions of Cortisol:**

1. On carbohydrates: increase glucose level causing diabetes or impaired GTT (cortisol is a counter regulatory hormone).
2. On lipids: redistribution of lipids; Moon face, Buffalo hump, truncal obesity.
3. On proteins: cortisol is a catabolic hormone, it causes destruction of proteins, causing:
    1) Striae.
    2) Poor wound healing.
    3) Proximal myopathy: due to destruction of muscular proteins.
    4) Osteoporosis: due to destruction of bone proteins.
4. Retention of water and sodium causing hypertension (some aldosterone action).
5. Increases Androgen level: causing hirsutism, acne, and amenorrhea in females.
6. CNS actions: depression, psychosis, …etc.
7. Decreased immunity ''see the NOTE in Addison's disease below'': pt is susceptible to develop infections.



- **Clinical features:**

1. Diabetes.
2. Lipid redistribution.
3. Striae, poor wound healing, proximal myopathy, osteoporosis.
4. Hypertension.
5. Acne, hirsutism, and amenorrhea in females.
6. Depression, psychosis.
7. Increased susceptibility to infections.

- **Investigations:**

- Confirm presence of Cushing syndrome (i.e. high cortisol) by either:

1. **Low dose overnight dexamethasone suppression test:**

- If you give a normal person **low dose** of dexamethasone (an exogenous glucocorticoid) → it will exert negative feed-back on ACTH → low level of ACTH → low cortisol level.
- But in pt with Cushing syndrome there is Failure of suppression of cortisol.
- <u>False positive test</u> results occur in:
    1. Alcoholism: Alcohol is an enzyme inducer (it increases the activity of Cytochrome P450), so Dexamethasone is metabolized rapidly and suppression does not occur (so there is failure of suppression).
    2. Obesity: there is high level of cortisol.
    3. Depression: is a stressful condition in which there is high level of cortisol.

2. **24 hour urinary free cortisol:** there is a high level of cortisol in urine.

الاحسن ياتو واحد؟ اي دكتور بيقول كلام، ف الناس تشوف كلام المحاضرة

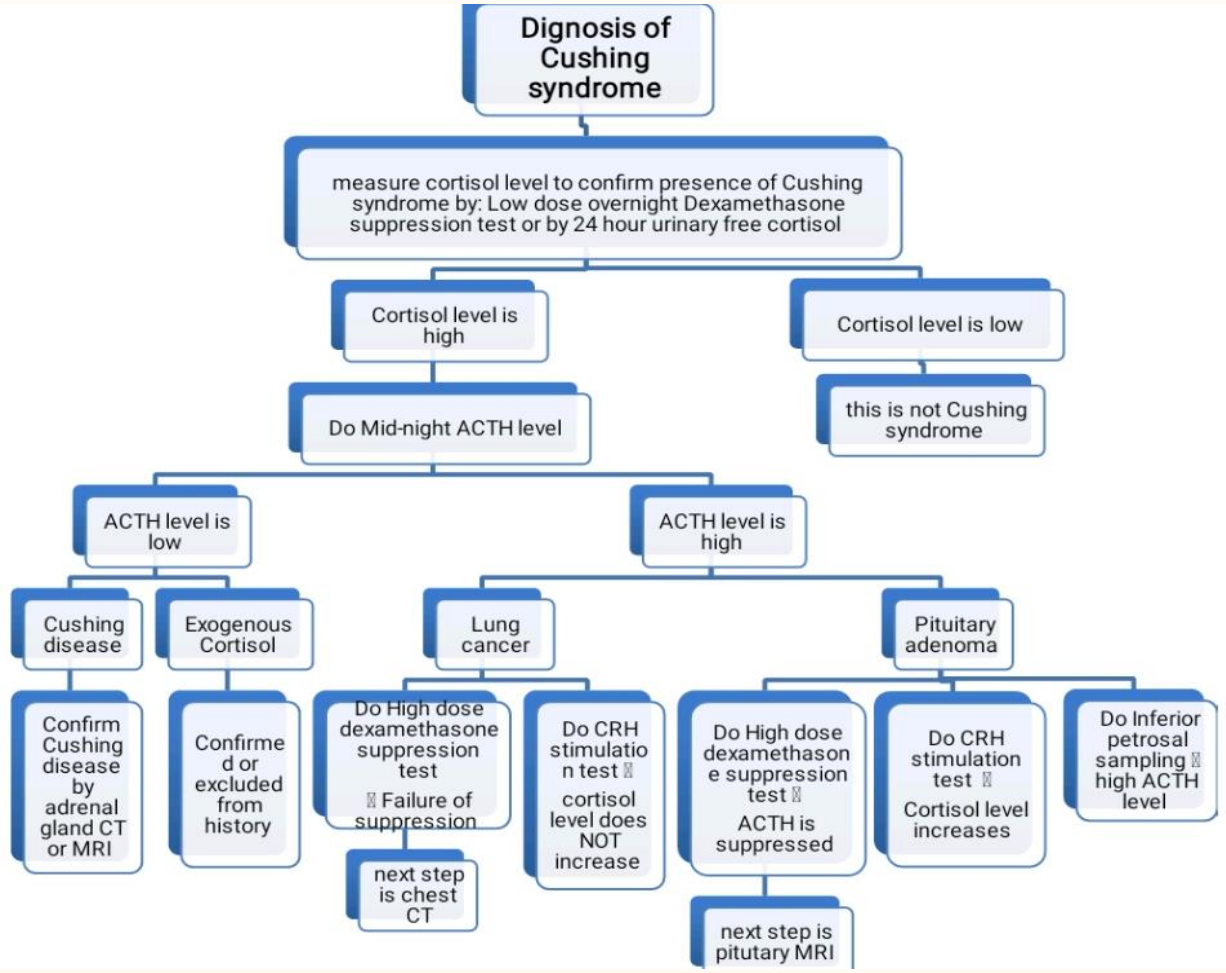
- **Med-night ACTH level:**

1. If it was **low↓**: the cause is adrenal (because high levels of cortisol exert negative feed-back on ACTH) → Next step: CT or MRI of adrenal gland.
   - This test result also occurs in exogenous cortisol, but you can exclude it from history.
2. If it was **high↑**: this is either lung cancer or pituitary adenoma, to differentiate between them:

   a. **<u>High dose</u> dexamethasone suppression test:** Lung produces high amount of ACTH that can't be suppressed even by **high dose** of dexamethasone:
      - If suppression occurs: this is pituitary adenoma, next step is pituitary MRI.
      - If suppression fails: this is lung cancer, next step is chest CT.

   b. **Corticotropin Releasing Hormone (CRH) stimulation test:** CRH is a hormone produced by hypothalamus to activate production of ACTH from pituitary. In this test we give the pt CRH, and then we measure cortisol level:
      - If Cortisol level increases: pituitary adenoma.
      - If Cortisol level does not increase: lung cancer (lung cancer does not have CRH receptors, so CRH has nothing to do with lung cancer).

      i. **Inferior petrosal sinus sampling:** a sample taken from inferior petrosal sinus which is a dural venous sinus that drains the pituitary gland, if ACTH level in the sample was high then the cause is pituitary adenoma, but this test is rarely done.



- **Treatment:** according to the cause:
  - Cushing diseases: if micro-adenoma remove it surgically, if macro-adenoma do bilateral adrenalectomy.

📄 **NOTE:** The most important side effects of bilateral adrenalectomy is Nelson Syndrome, it is hyperpigmentation due to loss of negative feed-back inhibition of cortisol on ACTH, so level of ACTH becomes high, but ACTH has melanocyte activating action, leading to hyperpigmentation.

  - If pt is not fit for surgery give:
    1. Ketoconazole: is an anti-fungal drug that increases metabolism of cortisol.
    2. Metyrapone: inhibits production of cortisol by inhibiting an enzyme in the pathway of cortisol production.

❖ Hyperaldosteroneism:

Aldosterone reabsorbs sodium and secretes potassium.

- **Causes:**
  - Hyperkalemia.
  - Renin.
  - High levels of ACTH (normal levels of ACTH does **not** induce production of aldosterone).
  - Hypovolemia and renal ischemia: because they induce renin secretion.

- **Types:**

1. *Primary hyperaldosteronism:*

I. Conn's syndrome:
- It is adrenal adenoma produces high levels of aldosterone, Renin level is Low.
- It is the most common cause of hyperaldosteronism.

II. Familial Glucocorticoid remediable aldosteronism (Familial GRA):
- In this disease aldosterone is sensitive to ACTH, in other words normal levels of ACTH induces production of aldosterone.
- Called glucocorticoid remediable because it is treated by glucocorticoid (steroids causes negative feed-back on ACTH, so levels of ACTH decreases, and this decreases aldosterone).

2. *Secondary hyperaldosteronism:*

Is caused by high levels of renin, this includes any cause of renal ischemia, e.g. reno-vascular diseases (renal artery stenosis), hypovolemia, liver cirrhosis (although there is fluid overload in liver cirrhosis, but the fluid is extravascular, and circulating blood is low), nephrotic syndrome, heart failure, etc.

- **Clinical features:**
  - Hypertension + hypokalemia.
  - Sodium level is high (Aldosterone increases reabsorption of sodium).
  - Alkalosis.

- **NOTE:** صبة

- K^+ and H^+ are both present in the blood, if any disturbance occurs, one should enter the cell.
- If there is low level of K^+ (hypokalemia), H^+ will enter the cell causing Alkalosis.
- If K^+ level was high (hyperkalemia), K^+ will enter the cell causing Acidosis.
- If H^+ level was high (Acidosis), H+ will enter the cell and K^+ will not, this causes hyperkalemia.
- If H^+ level was low (alkalosis), K^+ will enter the cell causing hypokalemia.

→ So, hypokalemia causes Alkalosis, and hyperkalemia causes acidosis.

- Acidosis causes hyperkalemia, and Alkalosis causes hypokalemia.

- **Investigations:**
  - Renin aldosterone ratio: if renin is high this is secondary hyperaldosteronism, and if renin is low this is primary hyperaldosteronism.
  - If it is primary hyperaldosteronism, do CT or MRI for adrenal gland looking for adenoma (i.e. Conn's syndrome).
  - Sodium and potassium level.

- **Treatment:** according to the cause:
  - Conn's syndrome: Adrenalectomy.
  - Adrenal hyperplasia: bilateral adrenalectomy.
  - Familial GRA: cortisol.
  - If pt has heart failure it must be treated.
  - You can give aldosterone antagonists: e.g. diuretics (spironolactone), Amiloride, or Eplerenone (Amiloride and Eplerenone block epithelial sodium channels (aldosterone act on epithelial sodium channels to reabsorb sodium)).
  - N.B. there is a disease called Gitelman syndrome. In this disease epithelial sodium channels are very active. It is treated by Amiloride and Eplerenone.

❖ Hypoadrenalism: It could be:

1) Primary: Addison's disease.
2) Secondary: due to pituitary insufficiency causing low ACTH. ما مهم

❖ Addison's disease:

➢ **Causes:**

1. *Destruction of adrenal gland by:*

a. Auto-immune destruction: the most common cause.
b. Metastasis to adrenal gland.
c. Infections: TB, CMV in AIDS pts, and *Neisseria Meningitidis* (*Neisseria Meningitidis* causes acute form of Addison's disease called Waterhouse-Friderichsen Syndrome).

TB adrenalitis is the only absolute indication of steroid in TB pts "see indications of steroids in TB".

2. *Anti-phospholipid syndrome;* there is venous thrombosis, if this thrombosis occurs in adrenal vein pt will develop Addison's disease (the case in exam: a female with history of DVT, and she develops features of Addison's disease, the cause is usually Anti-phospholipid syndrome)

➢ **Clinical features:**

1. Vague symptoms, e.g. weakness.
2. Features of Auto-immune disease (key word in exam): e.g. vitiligo, Pernicious anemia, DM type I.
3. Hyperpigmentation (**common in OSPE**): due to high level of ACTH, and ACTH has melanocyte stimulating activity. Note that hyperpigmentation occurs only primary hypoadrenalism.
4. Hypotension: long term hypotension causes small heart.
5. Eosinophilia and neutropenia.

🖹 **NOTE: Effect of cortisol on blood cells:**	
- It increases RBCs. - It increases platelets. - It increases neutrophils.	- It decreases basophils. - It decreases eosinophils. - It decreases lymphocytes.

- Cortisol decreases immunity by increasing the number of neutrophils. Because normally in acute inflammation neutrophils migrate to site of inflammation, cortisol prevents this migration, and causes neutrophils to return back to the blood. I.e. there is neutrophilia with failure of migration.
- So cortisol is both anti-inflammatory and anti-immunological factor.
- In Cushing disease and in steroid therapy there is neutrophilia.

Addisonian Crisis:

- Hypotension and fever that is precipitated by stress in pts with Addison's disease.
- During stress cortisol maintains the vascular tone in the body, pts with Addison's disease has low levels of cortisol, so they develop hypotension during stress.
- Addisonian crisis is treated by fluids to support circulation mainly dextrose (cortisol is a counter regulatory hormone, and low levels of cortisol lead to low levels of glucose), also give hydrocortisone (Dexamethasone) and synthetic aldosterone (Fludrocortisone) [Note that although the name fludrocortisone suggests that it is a derivative of cortisol, but it is a synthetic aldosterone].

➢ **Investigations:**

- Sodium level: low.
- Potassium level: high.
- Acidosis.
- **Short ACTH stimulation test (also called Synacthen test):** Normally if you give a person ACTH, cortisol levels will increase. But in pts with Addison's disease there is failure of stimulation (i.e. cortisol level dose not increase) because the adrenal gland is already destroyed.
  Note that ACTH stimulation test is positive in Addison's disease but it is NEGATIVE in secondary hypoadrenalism, because in secondary hypoadrenalism adrenal gland is normal, so ACTH stimulates cortisol production (negative test results) (but if it persists for long time adrenal gland will be atrophied the test result will be positive).
- Serology: Anti 21-hydroxylase Antibody detection in the blood; because the most common cause of Addison is autoimmune disease.

§ Diseases of adrenal medulla:

❖ Pheochromocytoma:

- Adrenal medulla is a modified sympathetic ganglion that produces adrenaline and nor-adrenaline.
- Pheochromocytoma is a vascular tumor of adrenal gland (chromaffin cells) that produces high levels of adrenaline and nor-adrenaline.

➢ **Role of 10:**

- 10% is bilateral.
- 10% is malignant.
- 10% occurs in children.
- 10% is familial (part of MEN ''see below'').
- 10% is extra-adrenal (Chromaffin cells are found in adrenal medulla and in sympathetic ganglia, so Pheochromocytoma may be adrenal (90%), or extra-adrenal (10%)).

➢ **Associations of Pheochromocytoma:**

1. MEN.
2. Von Hippel Lindau disease (VHL): is cerebellar and retinal hemangioblastoma. VHL may be associated with renal tumors.
3. Neurofibromatosis.

➢ **Clinical features:**

1. <u>Paroxysm</u> of: (due to increased sympathetic activity)

I. Palpitation.
II. Sweating (diaphoresis).
III. Headache: due to vasoconstriction of vessels.

2. Secondary hypertension (vasoconstriction).
3. Panic attacks.

➢ **Investigations:**

- **24 hours urinary Catecholamines** (adrenalin and nor-adrenaline), or better, you can measure their metabolites in urine (Venyl Mandylic Acid (VMA), Homo Valenic Acid (HVA), metanephrine, and noremetanephrine): if catecholamines or their metabolites are increased, then do CT or MRI to localized the tumor, or better do *MIBG scan*. MIBG scan can identify chromaffin cells, so it is very useful in extra-adrenal tumors because CT and MRI will be negative.

- **Management:**
  Surgical removal, but you should give α blockers before surgery to control hypertension [Note that hypertension in Pheochromocytoma is treated by α blockers].

❖ Multiple Endocrine Neoplasia (MEN):

- Is a group of tumors that occurs in the same time.
- Has three types:

- **MEN 1:** 3Ps
  1. Parathyroid hyperplasia or adenoma.
  2. Pancreatic tumor (e.g. insulinoma or gastrinoma).
  3. Pituitary tumor.

- **MEN 2 ''A'':**
  1. Medullary thyroid carcinoma.
  2. Pheochromocytoma.
  3. Parathyroid hyperplasia or adenoma.

- **MEN 2 ''B'':**
  1. Medullary thyroid carcinoma.
  2. Pheochromocytoma.
  3. Neuroma (nerve tumor).
  4. Marfanoid features (N.B main D.D. of Marfan is Homocysteinuria ''see cardiomyopathies in cardiac system chapter'').

Diabetes Mellitus:

- **Types:** Primary diabetes has two types:
  1. Insulin Dependent Diabetes Mellitus '' Type 1 DM'': Autoimmune destruction of β islet cells of pancreas leading to insulin deficiency (diabetes present after destruction of 90% of β cells).
  2. Non-Insulin Dependent Diabetes Mellitus ''Type 2 DM'': relative insulin deficiency due to insulin resistance.

» **MODY (Maturity Onset Diabetes of Young):**
- It is type 2 diabetes in pts younger than 25 years.
- Inherited as Autosomal Dominant.
- Treated by Sulfonylurea.

» **LADA (Latent Autoimmune Diabetes of Adults):**
- It is type 1 diabetes in older pts.
- Positive antibodies and negative C-peptide ''see below''.
- Treated by insulin.

- **Difference between type 1 and type 2 DM:**
  1. Type 2 DM is more common than type 1.
  2. Onset of type 1 is during childhood, and before puberty.
  - Onset of type 2 is usually after age of 40 years.
  3. Genetic role is stronger in type 2 ''Very common exam question''.
  4. Pts with type 1 DM have antibodies in their blood: type 1 DM is an auto-immune disease, examples of these antibodies include Anti- β islet cells antibody (endocrine pancreas consist of α, β, and δ cells. β cells are responsible for insulin production), and Anti- GAD antibodies (Glutamic Acid Decarboxylase is an enzyme involved in insulin production).
  - Pts with type 2 DM have **C-peptide** in their blood: insulin is produced in β cells as pro-insulin that consist of insulin and C-peptide. Pts with type 1 DM have their β cells destroyed, so they do NOT have neither insulin nor C-peptide. But pts with type 2 have C-peptide in their blood.
  5. Weight of pt: in type 1 pt is usually thin, but in type 2 pt is usually obese.
  6. DKA occurs in type 1.
  - Hyperglycemic hyperosmolar state occurs in type 2.
  7. Oral hypoglycemic drugs are used in type 2, but they have NO ROLE in type 1.

- **Diagnostic criteria of Diabetes Mellitus:**
  1. Presence of symptoms:

  Polyuria, polydipsia, and weight loss + one of the following lab results:

     I. Random blood sugar ≥ 200.
     II. Fasting blood sugar ≥ 126.
     III. 2 hours post prandial (Glucose Tolerance Test (GTT)) ≥ 200.

     - With presence of symptoms, presence of one of the above lab results in <u>one occasion</u> is sufficient to diagnose diabetes.

  2. Asymptomatic pt with one of the above lab results in <u>more than one occasion</u>.
  3. HbA1c > 6.5%. الهيموقلوبين التراكمي

- **Notes about diabetes laboratory tests:**
  - Normal levels of fasting blood sugar is <110.
  - Normal levels of 2 hours post prandial is <140.
  - Impaired fasting blood glucose: fasting blood glucose level between 110 and 126.
  - Impaired GTT: 2 hours post prandial between 140 and 200.
  - Impaired GTT is more dangerous than impaired fasting glucose, because most pts with impaired GTT will develop diabetes eventually.
  - Pre-diabetes: means that there is impaired tests (either GTT or fasting blood glucose), those pts does NOT need any drug, just life style modification + annular review.

➢ Treatment of Diabetes mellitus:

❖ Oral hypoglycemic drugs:

❶ Sulfonylurea:

- E.g. Gliclazide.
- It increases insulin secretion, that is why they are used in type 2 DM.
- Side effects: 1. Hypoglycemia, 2. Weight gain (note that pt is already obese).
- Contra-indicated in pregnancy and breast feeding.

❷ Biguanide:

- Most important one is Metformin.
- It decreases hepatic gluconeogenesis, so pt is not able to store glucose to use when glucose level is low.
- This means that fasting blood glucose is low.
- Metformin is the first line hypoglycemic drug, especially in obese pts, pts with polycystic ovary disease, and alcoholic fatty liver disease.
- Metformin does not cause weight gain, that is why it used in obese pts.
- The most common side effect is GI upset: nausea and vomiting.
- The most dangerous side effect is Lactic acidosis in pts with renal failure.
- Contra-indicated in pts with renal failure (impaired renal function).

❸ Thiazolidineione (Pioglitazone):

- Side effect is fluid retention.
- Contra-indicated in heart failure.
- May cause bladder cancer, and fractures. It also causes liver impairment.

❹ New Agents:

- Dipeptidyl peptidase-4-inhibitor (DPP4 inhibitor).
- Glucagon like peptide 1 (GLP-1) [Note that glucagon is anti-insulin, but GLP-1 is not].
- Meglitinides: for pt with erratic behavior. الزول بيصحى نص الليل ياكل

- If pt is diagnosed as type 2 diabetes, start with life style modification ± Metformin.
- An MCQs question:
- When do you add another hypoglycemic drug? if HbA1c was > 6.5%. (e.g. pt is taking metformin and his HbA1c was > 6.5%, you add another hypoglycemic drug (e.g. Sulfonylurea)).
- When do you add insulin? If HbA1c was > 7.5%.
  [So, when HbA1c is > 6.5% and < 7.5% add hypoglycemic drug, and if it exceeds 7.5% add insulin].

❖ Insulin:

- Insulin has 4 classes:

① **Rapid Acting Insulin (Ultra-Short):** e.g. insulin Lispro, Insulin Aspart.

- Can be taken during the meal.

② **Short Acting Insulin:** الإنسولين الصافي

Also called Regular insulin, or Soluble insulin

- Taken 15 minutes before the meal.

③ **Intermediate Acting Insulin:** الإنسولين العكر

- NPH, or Zinc insulin, or insulin isophane.

④ **Long Acting Insulin:** Glargine (Detemir).

⑤ **Mixed insulin:** Short + Intermediate acting insulin. المخلوط

- In all of them the concentration of the drug starts as low concentration, then it peaks and then it declines, EXCEPT long acting which has basal (steady) concentration.

- **Frequency of administration:**
  1. Twice per day:
     - Two doses, in each one give either short acting + intermediate acting or give mixed insulin.
     - Given as morning dose and evening dose. Morning dose consist 2/3 of the daily required dose, and evening dose consist 1/3 of the daily required dose.
  2. Four times per day:
     - One morning dose of Long acting insulin (glargine); because it has basal level.
     - Then with each meal give one dose of rapid acting insulin.
     - This method of administration is better than the first method, but it is not available in Sudan.
- **Side effects of insulin:**
  1. Hypoglycemia (diabetes medications that causes hypoglycemia are insulin and sulfonylurea).
  2. Lipid dystrophy (local effect): either hypertrophy or hypotrophy.
  3. Weight gain.

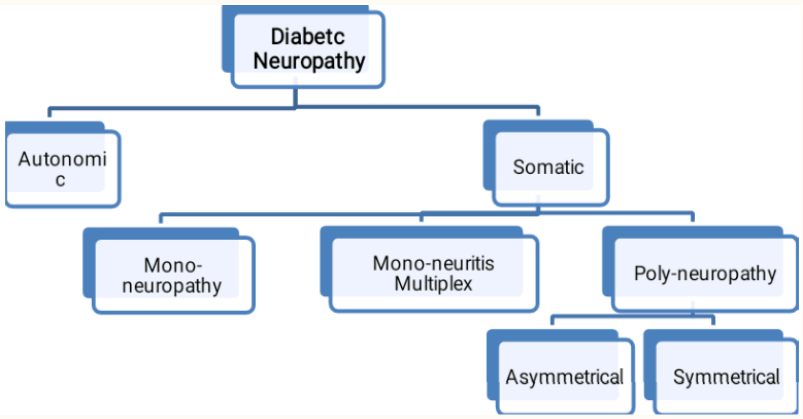
➢ Complications of diabetes mellitus:

❖ Acute complications:	❖ Chronic complications:
1. Hypoglycemia: in both types 1 and 2. **2. Diabetic ketoacidosis (DKA): in type 1.** **3. Hyperglycemic hyperosmolar state: in type 2.**	1. Diabetic neuropathy. 2. Diabetic nephropathy. 3. Diabetic eye disease. 1, 2, and 3 are Micro-vascular 4. Vascular diseases (Macro-vascular): stroke, MI, chronic limb ischemia.

1. Diabetic Neuropathy:

- Two types: 1. Somatic, 2. Autonomic.
- Somatic has three subtypes:

I. Poly-neuropathy: symmetrical and asymmetrical.
II. Mono-neuritis multiplex.
III. Mono-neuropathy



♦ **Somatic neuropathy:**

➢ **Mono-neuritis multiplex:**
- More than one nerve are affected in the same time.
- Example: Mono-neuritis multiplex of cranial nerves.

➢ **Mono-neuropathy:**
- Affect single nerve at a time.
- E.g. median nerve affection in carpal tunnel syndrome.

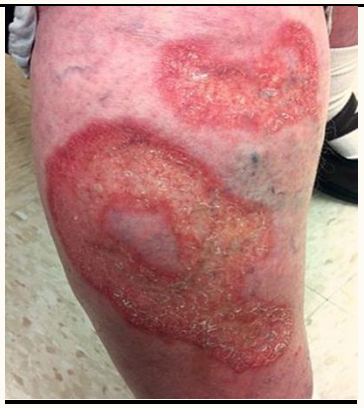
➢ **Poly-neuropathy:**
- **Symmetrical:**
  - Mainly distal neuropathy (All peripheral neuropathies are distal except Guillain Barré syndrome).
    [N.B. most common cause of death in Guillain Barré is respiratory failure, followed by arrhythmia].
  - It is sensory.

- Clinically pt present with peripheral neuropathy: numbness, loss of sensation in gloves and stocking pattern (i.e. distal pattern of sensory loss), + areflexia or hyporeflexia.
- Treatment:

- First line: Duloxetine, or Amitriptyline.
- Second line: Gabapentin, or Pregabalin.
- In MCQs exam you may be given a choice of one of the above drugs and another choice of multivitamin complex, multivitamins are given for pt with symmetrical poly-neuropathy but not as first line and not as second line.

- **Asymmetrical:**
  - Mainly <u>proximal</u> neuropathy.
  - It is <u>motor</u>.
  - That is why it is sometimes called Diabetic Amyotrophy.
  - Pt present with weakness, and wasting of quadriceps muscle. ما قادر يقوم
  - Treated by tight glycemic control.

♦ **Autonomic neuropathy:**
- Can affect **CVS** causing orthostatic hypotension or arrhythmia.
- Can affect **GI** system causing gastroparesis (decreased motility).
- Can affect **genital** system causing erectile dysfunction, retrograde ejaculation, and impotence.
- Can affect **urinary** system causing urine retention due to Atonic bladder.

Necrobiosis lipoidica diabeticorum **In diabetic patients –** **Skin manifestation of DM**	

NOTE: Difference between Spastic and Atonic bladder:

- Sympathetic outflow is Thoraco-lumbar. - Parasympathetic outflow is Cranio-sacral.
- Control of micturition is parasympathetic.
- Parasympathetic sacral nuclei are found in S_2, S_3, and S_4.
- When bladder is full, sensory impulses are send to sacral parasympathetic nuclei in S_2, S_3, and S_4, these nuclei send impulses to Detrusor muscles in the wall of bladder to contract, and bladder get empty (urinate).
- These impulses are inhibited by the brain, which sends inhibitory impulses to parasympathetic nuclei in S_2, S_3, and S_4.
- If there is lesion in S_2, S_3, and S_4: when bladder is filled with urine it will send impulses to S_2, S_3, and S_4, but NO impulses will be send back to Detrusor muscles → bladder becomes Non-contracting (i.e. Atonic bladder), pt will have urine retention with overflow incontinence.
- If there is lesion above S_2: the inhibitory impulses from the brain to parasympathetic nuclei will be lost, but the impulses from parasympathetic nuclei in S_2, S_3, and S_4 to Detrusor muscles are not affected. So if one drop of urine gets into the bladder, an impulse will be send to parasympathetic nuclei, and parasympathetic nuclei will send impulses to Detrusor muscles to contract, this bladder is always contracted (i.e. Spastic bladder).

- **Treatment of Autonomic neuropathy:**

اهم شي هو علاج القاستروباريسس لانو بجي كتير في الام سي كيوز

- First line in treatment of gastroparesis: Anti-emetics: pts suffering from gastroparesis has decreased GI motility, so they are given anti-emetics, because anti-emetics increase GI motility (e.g. Domperidone, and metoclopramide).

NOTE: Pts suffering from migraine are given Analgesic + Metoclopramide. Importance of metoclopramide here is not to prevent vomiting, but to increase GI motility in order to facilitate analgesics absorption. ''see nervous system chapter''

- Second line in treatment of gastroparesis: Erythromycin (erythromycin increases GI motility).
- If no response: Pacemaker by GI surgery.

2. Diabetic Eye Disease:

1. Retinopathy.
2. Cataract.
3. Glaucoma: due to Rubeosis Iridis which is formation of new vessels in Iris, it may lead to blockage of channels that absorbs aqueous humor causing Glaucoma.

♦ Diabetic retinopathy:

- Has 4 classes:

Class 1: it is called Background retinopathy:

I. Dot haemorrhages (it is a macro-angioma).
II. Blot haemorrhages: it is rupture of aneurysm leading to haemorrhage. It should be ≤ 3.
III. Hard (lipid) exudate.

Class 2: Pre proliferative retinopathy:

I. Blot haemorrhages > 3.
II. Soft exudate (infarction): called Cotton Wool spot.
III. Venous beading. زي السبحة

Class 3: proliferative retinopathy:

- It is formation of new blood vessels in retina
- (Noevascularization in retina (NVR)) or in optic disc (NVD).

Class 4: Maculopathy (the worst stage): there is decrease in visual acuity.

- Management of class 3 and 4 is by Laser photocoagulation.
- When to start screening?
  - Presentation of type 1 DM is early (because insulin deficiency is severe), but presentation of type 2 DM is late (you can't predict when did the disease start because insulin deficiency is relative).
  - In type 2: start screening immediately at time of diabetes presentation.
  - In type 1: start screening 5 years after initial presentation with diabetes.

3. Diabetic Nephropathy:

- Has 5 stages:

Stage 1: Increase in GFR with kidney enlargement.

Stage 2: Increase in GFR with changes in renal biopsy.

Stage 3: Micro-albuminuria

Stage 4: Frank albuminuria and hypertension + Sclerosis in renal biopsy (characteristic). It could be diffuse sclerosis, or nodular glomerular sclerosis called Kimmelstiel-Wilson lesions.

Stage 5: End stage renal disease.

NOTE: In diabetic pts:
- Urine Albumin of zero – 30 mg → Normal.
- Urine Albumin of 30 – 300 mg → Microalbuminuria.
- Urine Albumin of more than 300 mg → Macro (Frank) albuminuria (Nephrotic range).
- Urine dipstick: Is negative in micro-albuminuria, and positive in Frank albuminuria.

- **Management of diabetic nephropathy:**

1. Tight glycemic control: it is the best way to prevent diabetic nephropathy, if pt was taking oral hypoglycemic drugs shift to insulin.
2. Control of blood pressure: if pt has both diabetes and hypertension give him ACEI.
3. Decrease proteinuria: by ACEI ''see above''.
4. Statin: to decrease cardiovascular risk.

- Risk factors of diabetic nephropathy:

1. Poor control.
2. Long duration of disease.
3. Hypertension or other micro-vascular complications.
4. Family history of diabetic nephropathy.

Diabetic Nephropathy occurs ONLY after Diabetic Retinopathy. In other words, 100% of pts with Diabetic Nephropathy have also Diabetic Retinopathy (An MCQs question).

❖ Acute complications:

1. Hypoglycemia:

- Diabetic pt with blood sugar less than 70 mg/dl.
- Clinical features:
  - Autonomic symptoms: tremor, tachycardia, and sweating.
  - Neuro-glycopenic symptoms: seizures, coma, … etc.
- Hypoglycemia is classified into 2 types according to pt ability of self-treatment:

1. ***Mild hypoglycemia:***

- Pt is able to treat himself (by eating ☺).
- Give him short acting carbohydrates ((☺مازا) سكر), followed by long acting carbohydrates (عيش أو بسكويت).

2. ***Severe hypoglycemia:***

- Pt is either unconscious or conscious but can't treat himself (العيان ما مجمع أو ما قادر ياكل).
- If pt is conscious: give him honey or jam in buccal mucosa (يمسحها في خشمو و ما يبلعها), followed by long acting carbohydrates.
- It pt is unconscious: treatment should be parenteral by: IV dextrose, or IM glucagon, after he gains consciousness give him long acting carbohydrates.
- Long acting carbohydrates are mandatory in both mild and severe hypoglycemia, because if they are not taken pt will develop hypoglycemia again.

2. DKA:

- Occurs in type 1 DM.
- Called **D**iabetic because blood sugar is > 200, Keto because there is **K**etonuria, and **A**cidosis because pH is < 7.35 or bicarbonate is <15.
- Type of acidosis is metabolic acidosis with high anion gab ''see renal system chapter''.
- **Clinical features:**

1. Severe symptoms of diabetes.
2. Dehydration (dry membranes and hypotension; due to excessive polyuria).
3. Rapid deep breathing called Kussmaul breathing with acetone smell (rapid breathing to wash CO_2 before it gets converted to acid, Acetone smell is due to presence to ketone bodies).
4. GI symptoms: e.g. nausea, vomiting, and abdominal pain. (D.D. acute abdomen).
5. CNS symptoms (seizures, and coma).

- Insulin decreases lipolysis, to enhance consumption of glucose rather than lipids.
- Ketone bodies are the end product of lipolysis.
- So when there is insulin deficiency, lipolysis will be active, and so there is high amount of Ketone bodies.

- **Risk factors:**
  1. Wrong dose of insulin or missed dose.
  2. Stressful conditions (because they increase counter regulatory hormones):
     - *In children:* stress is mainly due to infection.
     - *In adults:* stress is mainly due to MI (that is why we need to do ECG).

- **Investigations:**

Random blood sugar.	pH.
- **Ketone in urine and blood**	- Look for infections.
- **ECG.**	

- **Management:** مهمة في البيدياترك
  1. IV fluids.
  2. Insulin: IV by infusion pump, if there is no infusion pump give insulin IM (absorption is not good if given SC because pt is dehydrated).
  3. Correction of electrolyte disturbances: mainly K^+ (DKA starts as hyperkalemia (Due to acidosis), then pt loses potassium in urine due to polyuria leading to hypokalemia → (correction of electrolytes) ± Bicarbonate correction
  4. Treat the underlying cause, e.g. MI or infection.

3. Hyperglycemic hyperosmolar state (HHS):

- Occurs in type 2 DM.
- Pt is usually old and not able to drink (severe dehydration).
- SEVERE hyperglycemia (hyperglycemia in HHS is more severe than hyperglycemia in DKA).
- NO ACIDOSIS.
- Most likely there is NO ketonemia and NO ketonuria.

📄 **NOTE:** As mentioned previously insulin decreases lipolysis.

- Pt with type 1 DM has No insulin → lipolysis is active → high amounts of ketone bodies are produced → Acidosis.
- But in pts with type 2 DM, insulin is present → insulin inhibits lipolysis → few or No production of Ketone bodies → No Acidosis (Because ketone bodies are not enough to cause acidosis).
- That is why it was previously named hyperosmolar non-ketotic coma

It is very important to differentiate between HHS and DKA, because it is a common question in exams (the main difference is that in HHS there is **NO ACIDOSIS**).

- **Management:** Same as DKA, with **aggressive IV fluids.**

📄 **NOTE:** Insulin is excreted by kidneys.

- If diabetic pt presents with recurrent attacks of hypoglycemia, this does not mean that pt is responding to insulin and his diabetes is cured, but it means that the pt is developing renal failure, and because insulin is excreted by kidneys, he becomes unable to excrete insulin, resulting in *recurrent attacks of hypoglycemia.*
- So this hypoglycemia does not mean cure.

يلزمك أنْ تستغفِر كَثيراً حَتّى تَهدأ
روحك. ♡

Contents:

INFECTIVE ENDOCARDITIS (IE)

- Hallmark of IE is: Fever + murmur.
- **Infective endocarditis is divided into Acute and Subacute:**

♦ **Acute:**	♦ **Subacute:**
○ **Occurs in a normal valve.** ○ **Most commonly caused by Staph Aureus.** ○ **Has poor prognosis (High mortality).**	○ Occurs in a diseased valve. ○ Most commonly caused by Strep. Viridans. ○ Has better prognosis.

➢ **Risk factors:**

1. Previous history of IE "most important''
2. Heart problem (CHD, MVP, Prosthetic valve, valvular heart disease): occurs mainly in subacute IE.
3. Host factor (IV drug abuser or immunocompromised pt): occurs mainly in Acute IE.

➢ **Most common organisms that cause infective endocarditis:**

1. Most common organism overall is ***St. viridans.***

2. Most common organism in acute IE, in IV drug abusers, and Rt. Sided IE (I.e. Tricuspid valve IE): is ***S. aureus*** (this is because S. aureus lives as commensal in the skin, IV drug abusers inject drugs in veins, which drains to the Rt. Side of the heart).

3. Most common organism after colonic resection is ***Bacteroides.***

4. Most common organism in pts with colorectal Cancer is ***St. bovis.***

NOTE: this is an MCQs question; You have a pt with IE and you did blood culture and the organism isolated was *Strep. bovis*. What is the best next step?
Answer: screen for colorectal cancer.

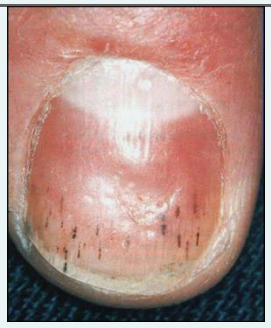
5. In pt. with prosthetic valve:

a) Early post-operative (2 months or less); the most common cause is Staph. Epidermidis.

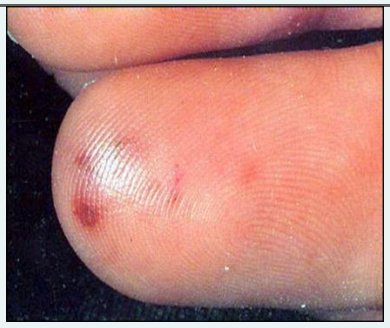
b) Late (more than 2 months); like other population (i.e. St. Viridans).

- **Diagnosis of IE:**
  1. Clinically: Fever + murmur
  2. Lab.: ***Diagnosis is by DUKE's criteria***: To diagnose IE you should have **ALL** Major criteria, **OR ALL** Minor criteria, **OR** 1 Major criterion + 3 Minor criteria.

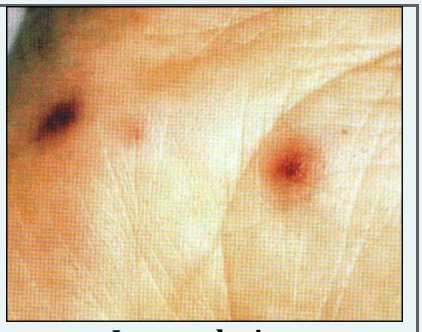
A. Major:	B. Minor:
1- **Typical blood culture:** I. Presence of a typical organism in **two** cultures taken from 3 sites, in 3 different times, each time 2 bottles (total of 6 bottles), within 24 hrs, 2 hrs apart. (Typical organism means the organisms mentioned previously (the most common organisms to cause IE) + HACEC group of organisms). II. Persistent bacteremia: presence of an organism (may or may not be typical) in two cultures, 12 hours apart. 2- **Typical echo:** I. Vegetations (Vegetation is the Hallmark of IE, It consist of platelets and cellular debris including the bacteria). II. Aortic root abscess. III. New regurgitation (detected by Echo Not by auscultation). IV. Prosthetic valve dehiscence.	**1- Fever >38 C°.** **2- Risk factor: e.g. IV drug abuse, CHD, immunocompromised.** **3- Immunologic OR Vascular (embolic) phenomena in examination:** **Immunologic phenomena:** **The presence of one of the following:** **I. Glomerulonephritis: due to immuno-complex deposition.** **II. Splinter hemorrhage.** **III. Osler nodes: it is PAINFULL Nodules at the tips of fingers).** **IV. Roth spots: it is retinal hemorrhage.** **Vascular (Embolic) phenomena:** **The presence of one of the following:** **I. Janway Lesions: it is PAINLESS Nodules at the palm of the hand).** **II. Infarction in any organ: due to embolism caused by the vegetations, e.g. kidney or spleen infarction.**



Splinter hemorrhage



Osler node



Janway lesion

NOTE: Presence of more than one of the above six phenomena is counted as only **one** minor criterion (i.e. If a pt for example has splinter hemorrhage this is one minor criterion, and if he has splinter hemorrhage and Janway lesions he still has only one minor criterion).

4- Atypical echocardiography findings: i.e. there is abnormality but it is not vegetation, not aortic root abscess, not new regurgitation, and not prosthetic valve dehiscence.
5- Atypical culture findings: i.e. positive blood culture but does not meet the criteria of typical blood culture.

- **Investigations**:

(Always when you are asked about any investigation, mention the finding you are expecting)

1. CBC (Anemia of Chronic diseases; ↑ ESR).
2. Blood Culture.
3. Echocardiography.
4. Urinalysis (hematuria; indicating GN or kidney infarcts).
5. Complement level for prognostic purpose (↓ C3, ↓ C4).
6. ECG: 1st degree heart block in aortic root abscess, or STEMI.

- **Treatment:**

IV Bactericidal Antibiotics for 4-6 weeks according to culture.
Empirical according to local regimen until culture:
IV vancomycin + gentamicin (add rifampicin in prosthetic)

- Criteria of antibiotics used in treatment of IE:
  - IV drug.
  - Bactericidal.
  - Can be used for 4 to 6 wks.
  - Sensitive to bacteria according to culture and sensitivity.

- **Types of Penicillin:** (is a common OSCE question)

- IV Penicillin G (Benzyle penicillin) and Oral penicillin V (phenoxy benzyle penicillin): narrow spectrum, active against gram positive organisms mainly Strep. infections (eg. In Rheumatic Heart Disease prevention).
- Aminopenicillins: **Amoxicillin** and **Ampicillin** → Wider spectrum but still sensitive to B-lactamase, active against gram negative organisms (Amoxicillin is used in treatment of **UTIs caused by E. coli** and H. pylori triple therapy).
- Aminopenicillins (e.g. amoxicillin) + lactamase inhibitors (clavulinic acid) = Amoclan.
- Lactamase resistant penicillins: Dicloxacillin, Nafcillin. Used against Staph. Aureus.
- Benzathine penicillin: IM depot (long acting) used in secondary prevention of rheumatic fever.
- Anti-Psuedomanal penicillins: e.g. Ticracillin.

- **Indications of surgery in IE:**
  1. Failure of Medical Treatment. مساكة
  2. Occurrence of Complications:
     - Heart failure (due to destruction of valve leading to regurgitation, this regurgitation causes heart failure).
     - Recurrent embolization (due to vegetation).
     - arrhythmia (caused by heart block that occurs due to development of aortic root abscess (Prolonged PR interval), the abscess compresses the myocardium and the conductive system leading to heart block).
  3. Impending complications: large vegetation.
  4. Special situations: e.g. Fungal IE, Prosthetic valve IE.
- **Causes of culture negative IE**:
  1. Recent Antibiotic treatment.
  2. Special Organisms: HACEK, Fungi, Brucella (because they need special media for culture).

NOTE: there are two types of Echo; transthoracic and transeosophageal. Transeophageal Echo is better in IE because transthoracic Echo can't see vegetations < 2 mm.

- **Poor Prognostic features:**
  1. S. aureus: acute IE.
  2. Fungal IE.
  3. Prosthetic Valve.
  4. Low complement →indicates heavy bacteremia (i.e. large number of bacteria that consume complement).

Jugular Venous Pulsation (JVP)

- It indicates the amount of fluid in Rt atrium.
- Measured in the internal jugular vein.
- It differs from arterial (Carotid) pulsations as it is: (common OSCE question)
    1. Wavy.
    2. Compressible.
    3. Not palpable.
    4. Biphasic: 2 waves per each arterial pulsation.
    5. Increased by hepato-jugular reflex.

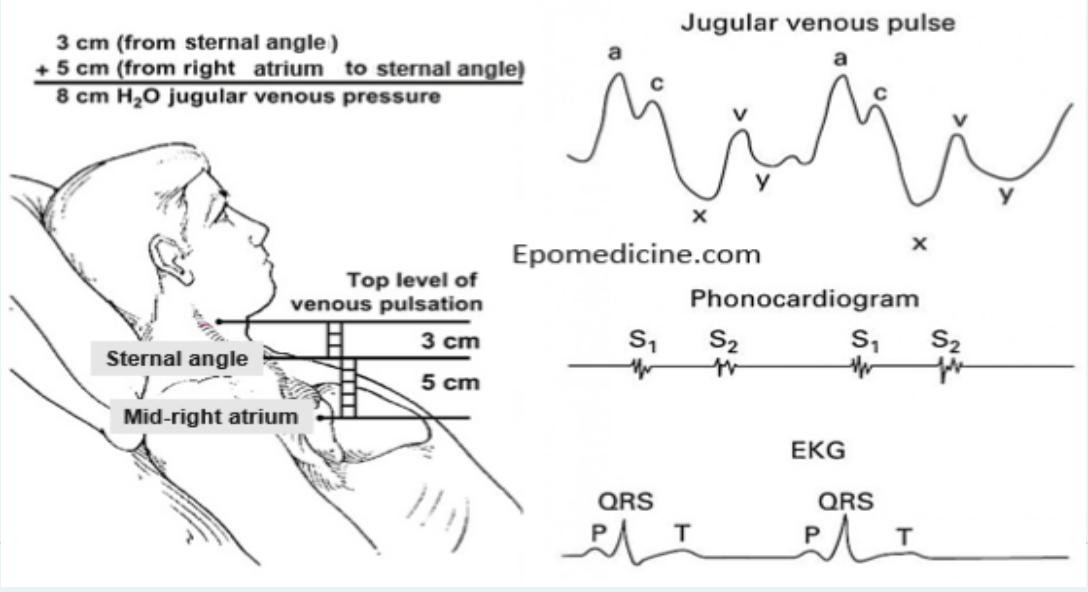
➢ **Waves of JVP:**

It has 2 large waves (''a'' and ''c'' wave), and 2 descents (''x'' and ''y'' descents):

- ✓ ''**a**'' wave indicates: **a**trial systole (during atrial systole pressure of internal jugular increases creating ''a'' wave of JVP).
- ✓ ''**c**'' wave indicates **c**losure of tricuspid valve (closure of tricuspid leads to slight increase in JVP, so ''c'' wave is a small wave).
- ✓ ''x'' decent indicates ventricular systole (Ventricular systole leads to decrease in pressure of jugular vein, leading to formation of ''x'' descent).
- ✓ ''**v**'' wave indicates **v**enous return to atria.
- ✓ ''y'' decent indicates opening of tricuspid valve.

➢ **Abnormalities of JVP:**

1. **Raised JVP:**
    - The JVP is raised but all the waves are normally present (i.e. Pulsatile).
    - It occurs in Rt sided heart failure and in fluid overload.



2. **Raised JVP without pulse (Non pulsatile JVP):**
   - The JVP is raised without waves (i.e. Non pulsatile).
   - Occurs in superior vena caval obstruction (superior vena cava syndrome) in lung cancer (see chapter of respiratory system).

- **Abnormalities of JVP waves:**
  1. **Absent "a" wave**: absent atrial contraction i.e. atrial fibrillation.
  2. **Large "a" wave:** indicates that the atrium is contracting against resistance, occurs in:
     1. Tricuspid stenosis.
     2. Pulmonary stenosis.
     3. Pulmonary HTN.
  3. **Canon "a" wave:** is a very large ''a'' wave, occurs when the Rt atrium is contracting against very high resistance, meaning that the tricuspid valve is totally closed while atria contract (i.e. atrium is contracting without coordination with the ventricle):
     1. Complete heart block (3rd degree heart block).
     2. ventricular tachycardia.
  4. **Large "v" wave:** Tricuspid regurgitation (because it increases venous return).
  5. **Deep "x" and "y" descents:** occurs in constrictive pericarditis.
  6. **Absent ''y'' descent:** Cardiac tamponade.

NOTE: Normally JVP decreases with inspiration and increases with expiration, but in both cardiac tamponade and constrictive pericarditis JVP increases with inspiration (this sign is called Kussmaul's sing). the difference between them:

Cardiac Tamponade:	absent "y" descent
Constrictive pericarditis:	deep "x" and "y" descents

Valvular Heart Diseases

- **NOTES:**
  - Valvular heart diseases are **the commonest** station in CVS examination on OSCE exam.
  - You must know the cause of any one of them.
  - Stenosis affect the chamber preceding the valve.
  - Regurgitation affect both chambers, the preceding one and following one.
  - The most common valvular abnormality is mitral valve prolapse.
  - During your examination, when you palpate the **apex**, you should comment on:
    1) Site 2) Character

1) Site of apex beat:	2) Characters of apex beat:
a) Displaced: there is eccentric hypertrophy (the wall becomes thick and moves outward), occurs in volume overload (MR and AR). **b) Not displaced: there is concentric hypertrophy (the wall becomes thick, but it does not move outside, it moves inside), occurs when there is pressure overload (AS).**	**1. Heaving:** a) **Ill sustained heave (Thrusting apex):** in volume overload (eccentric hypertrophy as in: MR & AR), result in displaced apex beat. b) **Well sustained heave:** in pressure overload (concentric hypertrophy as in AS & in HTN), apex is not displaced. **2. Tapping**: occurs in MS.

Heart sounds:

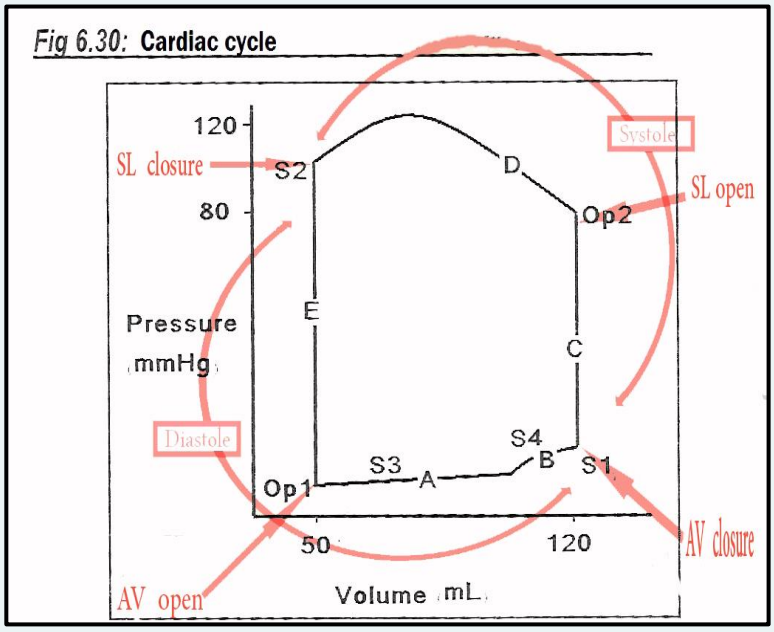
- S1 is the sound of closure of AV valves (mitral and tricuspid).
- S2 is the sound of closure of SL valves (aortic and pul.).
- LOUD S1: MS.
- Soft S1: MR.
- Soft S2: AS & AR.

[i.e. all valvular abnormalities cause **soft** heart sounds except MS which causes loud S1].

Notes about murmurs: ''See diagram of cardiac cycle''

- Murmur occurs due to turbulence of blood flow.
- **In case of stenosis**; murmur is heard when the valve is open (closed valve does not produce murmur because there is no blood flow).
- In mitral and tricuspid Stenosis murmur occurs during diastole (AV valves open during diastole), [that is why murmur of tricuspid and mitral stenosis are diastolic (mid diastolic)].

- In aortic and pul. Stenosis murmur occurs during systole (SL valves open during systole), and the murmur is systolic [ejection (mid) systolic].

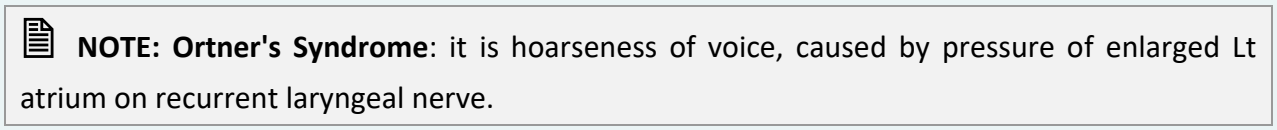


- **In case of regurgitation**; murmur occurs when the valve is closed.
- So, murmur of AV regurgitation is systolic (AV valves are closed in systole).
- Murmurs of SL valves regurgitation occur during diastole (SL valves are closed in diastole).

NOTE During inspiration diaphragm goes down → intrathoracic pressure decreases → venous return increases → blood goes to Rt side of the heart. That is why murmurs of Rt side **increase with inspiration** and **decrease with expiration** and vice versa.

1. MITRAL STENOSIS:

- **Valve area:** Normally from 4 to 6cm, symptoms occur when it is less than 2 cm.
- **Causes:** Almost always due to rheumatic heart disease.
- **Symptoms:**
  - Symptoms of pulmonary congestion (i.e. presence of fluid in the lung): Dyspnea, orthopnea, paroxysmal nocturnal dyspnea, cough with frothy sputum, hemoptysis.
  - Pressure symptoms: because the Lt atrium is the most posterior chamber, it may compress recurrent laryngeal nerve (causing hoarseness of voice, called Ortner's syndrome), or it may compress esophagus (causing dysphagia).



NOTE: Ortner's Syndrome: it is hoarseness of voice, caused by pressure of enlarged Lt atrium on recurrent laryngeal nerve.

- **Signs**:
  - Pulse: Normal, and if pt develops AF pulse becomes irregular irregular (AF is a complication of MS).
  - Face: malar flush.
  - Apex: 1) not displaced. 2) Tapping.
  - Loud S1.
  - Murmur: rumbling mid diastolic murmur, At apex area, with presystolic accentuation.
  - Opening snap (is heard after S2).
- **Sings of Severity:**
  1. Opening snap close to S2 (the closer the snap to S2, The more sever the disease is).
  2. Longer duration of murmur.
  3. Pul. HTN:
     - Findings in clinical examination of pt with Pul. HTN:
       a) Palpable P2.
       b) Raised JVP.
       c) Lt parasternal heave.
     - Pul. HTN can cause Graham-steel murmur ''see below''.
  4. Rt ventricular failure (because pul. HTN increases the load on Rt ventricle, so it becomes filled with blood and dilated, then tricuspid regurgitation may occur).
- **Complications:**
  - AF & Embolization.

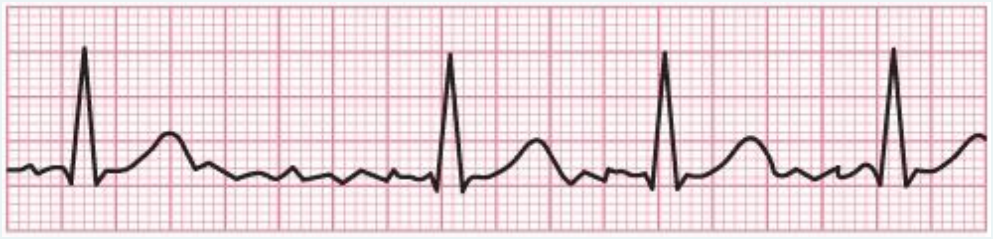
NOTE: Graham-steel murmur is murmur of pulmonary valve regurgitation due to pulmonary HTN " end diastolic murmur''.

- **Investigations:**

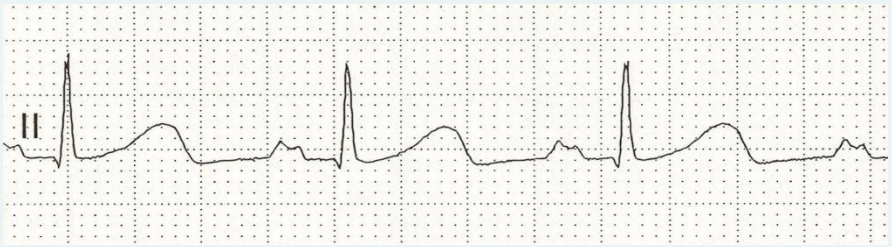
1. **ECG:**

AF, P mitral (P wave becomes bifid like the letter M, due to left atrial dilatation), and P pulmonale (indicates Rt atrial dilatation).

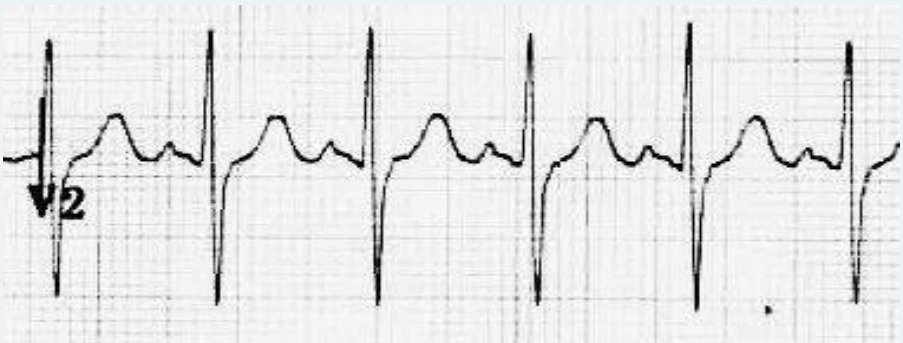
How could the Rt atrium gets enlarged in MS? MS causes enlargement of Lt atrium → blood goes back to lungs → blood goes from lungs to Rt ventricle → blood goes from Rt ventricle to Rt atrium → Rt atrium gets enlarged.



Fig(1): Atrial Fibrillation in ECG.



Fig(2): P mitral in ECG, Indicating left atrial enlargement (has bifid, "M" shape, M= mitral).



Fig(3): P pulmonale in ECG, indicating right atrial enlargement.

2. **Chest X-ray:** Findings include:
   I. Mitralization (Straightening) of Lt heart border (due to Lt atrial enlargement), normal left heart border is concave.
   II. Splaying (widening) of carina due to Lt atrial enlargement (Carina is the bifurcation of trachea).
   III. Double shadow of Rt side of the heart: In normal cardiac X-ray you see shadow of Rt atrium, but here in addition to this shadow you will see shadow of the enlarged Lt atrium.

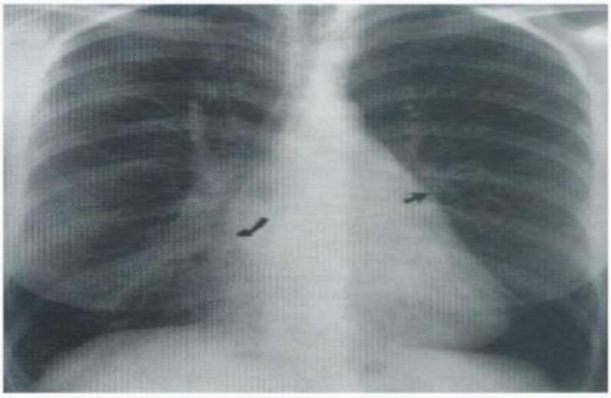
3. **Echocardiography:** is the DIAGNOSTIC test, you see valve area, chambers, and ejection fraction.

- **Management:** 3 options
  1- Closed/ percutaneous balloon valvuloplasty (widening of the narrow valve without open surgery (blindly)).
  2- Open valvotomy.
  3- Valve replacement.

- **Criteria Required to perform balloon valvuloplasty:**
  1. Valves are not calcified (detected by x-ray).
  2. Echo confirms **NO** Lt atrial thrombus.
  3. Not associated with mitral regurgitation.
  4. Significant symptoms.

NOTE:
- Right side murmurs increase with inspiration, left side murmurs increase with expiration

Mitral Stenosis (MS)



Plain X-ray of Mitral Stenosis, showing enlarged Lt. atrium as a double contour at the Rt. heart border (curved arrow), & enlarged Lt. atrial appendage (straight arrow)

2. Mitral Regurgitation:

- **Causes:**

I. Causes of valvular regurgitation [i.e. Any valvular regurgitation and NOT only mitral regurgitation], divided into acute and chronic:

- **Acute causes of regurgitation:**
  1. Infective endocarditis.
  2. IHD.
- **Chronic causes of regurgitation:**
  1. Connective tissue diseases: e.g. Marfan syndrome.
  2. Functional regurgitation: occurs in cardiomyopathies → the chambers of the heart get dilated.

II. The **most common** cause of MR is Rheumatic heart disease.

III. Another cause of mitral regurgitation is Mitral valve prolapse.

> **NOTE:** Rheumatic heart disease mainly affects mitral valve, the most common lesion in adults is mitral stenosis, and the most common lesion in pediatrics is mitral regurgitation.

- **Symptoms:**
  - Regurgitation affect both chambers, the preceding and following [in this case the Lt atrium and ventricles].
  - Symptoms of mitral regurgitation are not specific (Not important for exam): congestion of the lung causes dyspnea, orthopnea, paroxysmal nocturnal dyspnea. If Lt ventricle gets dilated it becomes non effective and pt develops heart failure (e.g. Low COP, fatigue).

- **Signs of MR:**
  - Pulse: Not characteristic.
  - Face: Not characteristic.
  - Apex:
    - **Site:** displaced (Regurgitation Causes volume overload → eccentric hypertrophy).
    - **Character:** ill sustained heaving apex beat (Volume overload).
  - Murmur: pan systolic murmur in apex radiates toward the axilla.
  - Soft S1.
  - S3 gallop: due to rapid ventricular filling.

NOTE:

- S3 is Physiological in: 1- children 2- Pregnancy (Due to fluid overload).
- S3 is Pathological in: 1- characteristic heart failure 2- MR (most important sign of severity).

- **signs of severity in MR:**
  1. S3.
  2. Pulmonary HTN.
- **Investigations:**
  - Echo is diagnostic.

    الباقيات ما مهمة , ممكن تستنتجها، مثلاً :
  - In ECG there is Lt atrial and ventricular enlargement → Lt axis deviation , you may find AF.
  - X-ray: Lt atrial and ventricular enlargement.
- **Management**:
  - Open repair.
  - Valve replacement.

3. Mitral Valve prolapse (MVP):

- ❖ The most common valvular abnormality.
- ➢ **Causes:** either congenital (Connective tissue diseases e.g. Marfan and Ostoegenesis Imperfecta), or acquired.

- ➢ **Symptoms:**
  - Mostly asymptomatic.
  - Symptoms: atypical chest pain (See Criteria of typical chest pain in page__) and palpitation.
- ➢ **Signs:** MVP produces mid systolic click, with progression of the disease it causes late systolic murmur.
- ➢ **Complications:**
  1. Mitral regurgitation.
  2. Embolization: e.g. stroke.
  3. Arrhythmia (palpitation).
  4. Sudden cardiac death.
- ➢ **Management:** According to symptoms, e.g. For chest pain and palpitation you need to decrease heart rate by β blockers, or surgery " valve repair".

4. Aortic stenosis (AS):

- **Causes:** are classified according to site of stenosis as either supra-valvular, valvular or sub-valvular:
    - Supra-valvular: William syndrome (associated with transient hypercalcemia, mental retardation and characteristic faces "elfin face'' in addition to supra-valvular AS).
    - Valvular: According to age of the pt;
        - Young pt → rheumatic heart disease.
        - Early adults (<65 yrs)→ **bicuspid** aortic valve calcification (aortic valve is normally tricuspid).
        - Elderly (>65 yrs) → senile calcification of normal aortic valve.
    - Sub-valvular: Hypertrophic Obstructive CardioMyopathy (HOCM).

- **Symptoms of Aortic stenosis:** triad of (severity increases in order):
    1. Angina (chest pain).
    2. Syncope on exertion.
    3. Dyspnea /HF.

Mechanism of		
Angina	**Syncope on exertion**	**Dyspnea**
Stenosis of aortic valve → pressure of Lt ventricle increases → Lt ventricular hypertrophy → blood demand increases → blood supply can't be increased to meet the demand of this hypertrophied ventricle because of the stenosis →Angina. (so, Angina is due to increased demand of the hypertrophied left ventricle).	Normally COP increases with exertion, but in this pt COP can't be increased because of the stenosis, so blood supply to the brain is not sufficient → Syncope (so, Syncope on exertion is due to failure to increase COP during exercise).	Any dilation occurs at the expense of function. In AS type of hypertrophy is concentric (I.e. muscle size increases without dilation) that is why early in the disease there is no dilation and no dyspnea, dyspnea and heart failure occurs later on when dilation occurs if the pt develops MR)**.**

NOTE: the most serious symptom of AS is dyspnea because it occurs in advanced cases (an MCQs question).

- **Signs of aortic stenosis:**
  - Pulse: Slow rising pulse.
  - Pulse pressure (difference between systolic and diastolic): Narrow pulse pressure.
  - Apex:
    - Site: Not displaced.
    - Character: well sustained heaving apex beat.
  - Heart sound: Soft S2, you may hear S4 but not usually.
  - Murmur: Ejection (mid) systolic murmur at aortic area 1, radiating towards the carotid.

- **Investigations:**
  - ECG: Strain pattern, it indicates ischemic changes due to hypertrophy (Also occurs in HTN), Also there is ST depression.
  - Echocardiography.

- **Management:**
  - If asymptomatic: No need for treatment, only follow up.

- **indications of surgery:**
  1. Symptomatic: any of the above symptoms.
  2. Pressure gradient across the valve (measured by cardiac catheter) > 50 mmHg even if pt is asymptomatic.
  - Type of Surgery: Valve replacement not repair (because repair is not available in Sudan).

5. Aortic Regurgitation

- **Causes:**
  - **I.** Causes of valvular regurgitation [i.e. Any valvular regurgitation And NOT only aortic regurgitation], divided into acute and chronic:
    - **Acute causes of regurgitation:**
      1. Infective endocarditis.
      2. IHD.
    - **Chronic causes of regurgitation:**
      1. Connective tissue diseases: e.g. Marfan syndrome.
      2. Functional regurgitation: occurs in cardiomyopathies → the chambers of the heart get dilated.
      3. Another cause of AR (Specific for Aortic valve) is Syphilitic aortic aneurysm and any inflammation in ascending aorta (ascending Aortitis) [it is a functional regurgitation].

NOTE about aortic aneurysms: the most common site of aortic aneurysm is infra-renal abdominal aorta (occurs in atherosclerosis), but when aneurysm occurs in ascending (thoracic) aorta it is usually due to syphilis.

- **Signs of AR**
  - Pulse: High volume collapsing pulse (water Hammer pulse).
  - Pulse pressure: wide pulse pressure.
  - Apex:
    - Site: displaced due to volume overload.
    - Character: ill sustained heaving apex beat.
  - Heart sound: soft S2.
  - Murmur: early diastolic murmur heard best at aortic area 2, with pt sitting up (increase with expiration شيل نفس و اكتم).
  - **De Musset's sign:** head nodding with each heartbeat.
  - **Muller's sign:** movement of uvula with each heartbeat.
  - **Corrigon's sign:** carotid pulsation in supra-sternal notch.
  - **Quincke's sign:** pulsations in capillary bed of nails
    ''الضفر بيحمّر بعداك ببقى أبيض''.
  - **Traube's sign:** (also called Pistol Shot Femoralis) a load sound like a pistol shot heard by auscultation of femoral artery.
  - **Duroziez's sign:** if you put the stethoscope on femoral artery after occluding it proximally by finger, you will hear a murmur.

- **Signs of Severity in AR:**
  1. Austin Flint murmur: mid diastolic murmur (the regurgitation is so severe that it causes blood to move back to Lt ventricle, then from Lt ventricle to Lt atrium then to Lt ventricle again)
  2. Dyspnea: it means that ejection fraction starts to drop and the heart starts to fail (Any dilation occurs at the expense of function).
- **Treatment:** treatment is given if pt is symptomatic or if ejection fraction becomes less than 50% even if pt is asymptomatic.

❖ Types of valve replacement:

- There are two types of valve replacement: Mechanical (prosthetic) and biological (bovine):
  - **Mechanical valve:**
    - Can be used for long time (lifelong).
    - Pt needs Warfarin for life.
    - Used for young pts.
    - Causes audible click. زي صوت الساعة، ممكن تتسمع حتى بدون سماعة .
  - **Bovine valve:**
    - Can't be used for long time.
    - Pt does not need warfarin.
    - Used for old pts.
    - Does not produce click.

NOTE: pulmonary and tricuspid valves are not important in exam].

❖ The Table below summarizes valvular heart diseases:

		Mitral stenosis	Mitral Regurgitation	Aortic stenosis	Aortic Regurgitation
Pulse		Normal or Low volume and if AF occurs it is irregular irregular.	Not characteristic	Slow rising	High volume collapsing pulse
Apex	**Site**	Not displace	Displaced	Not displaced	Displaced
	Character	Tapping	Ill sustained heaving	Well sustained heaving	Ill sustained heaving
Heart Sound		- Load S1 - Opening snap	- Soft S1 - S3	- Soft S2 - Sometimes S4	- Soft S2
Murmur		Mid diastolic murmur at the apex with presystolic accentuation.	Pan systolic murmur at the apex, radiating toward the axilla	Ejection systolic murmur at aortic area 1, radiating toward the carotid.	Early diastolic murmur at aortic area2, (with the pt sitting up).

Heart Failure

- It is failure of the heart to maintain COP adequate for tissue perfusion.

➢ **Classification:**
  - Right side vs Left side.[MOST IMPORTANT]
  - Systolic vs Diastolic.
  - High output vs normal and low output.
  - Acute vs Chronic.

- **Lt side heart failure: ''**is a disease of symptoms**''**
  - Symptoms are similar to MS because in both of them there is fluid buildup in the lungs; Dyspnea, orthopnea, paroxysmal nocturnal dyspnea, cough with frothy sputum, and hemoptysis.
- **Rt side heart failure:** ''is a disease of signs''
  - Raised JVP, tender hepatomegaly, Ascites, lower limbs edema.

- **High output heart failure:** causes; are the same causes of hyper-dynamic circulation (e.g. Anemia, thyrotoxicosis, pregnancy, Paget's disease, AV malformation, Beriberi diseases (thiamine deficiency)).

- **Systolic heart failure:** due to myocardial infarction.
- **Diastolic heart failure:** the most important cause is hypertension, but can be caused by constrictive pericarditis, and cardiac tamponade.

NOTE The most important causes of heart failure generally are HTN and IHD.

- **The currently used classification:**
  - Heart failure with preserved ejection fraction (i.e. > 40).
  - Heart failure with low ejection fraction.

➢ **Poor prognostic features in heart failure:**
1. High BNP (released from ventricles when there is fluid overload).
2. High uric acid.
3. Hyponatremia.

4. Anemia (low hemoglobin).

NOTE: BNP has High negative predictive value, (this means that positive result does **NOT confirm** the diagnosis, while negative result **excludes** the diagnosis), so if you have a pt with dyspnea and you do not know if the dyspnea is due to respiratory or cardiac cause; do BNP, if positive it may be cardiac, but negative result means that the cause is definitely NOT cardiac (i.e. it is respiratory dyspnea).

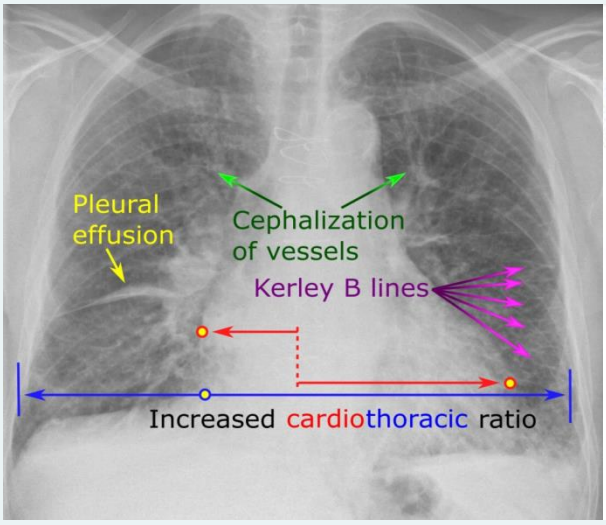
❖ Acute Heart Failure:

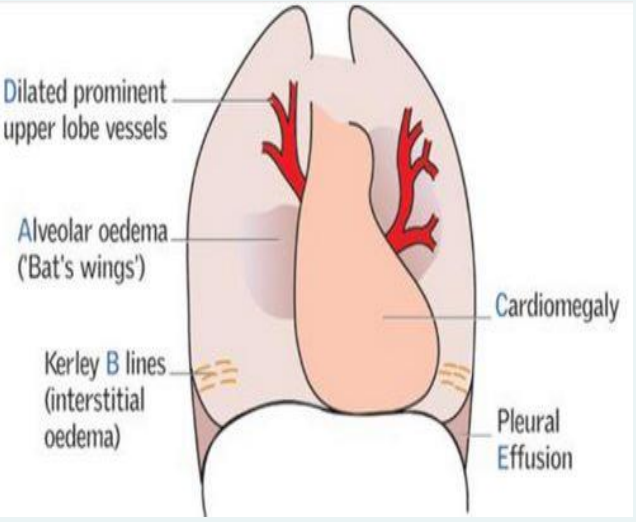
- Also called cardiogenic pulmonary edema.
- Presents with dyspnea, orthopnea, paroxysmal nocturnal dyspnea.

[NOTE: this edema is different from pul. edema due to fluid overload**].**

- **Characteristic CXR findings in Acute heart failure (pulmonary edema):** ABCDE
  - **A**lveolar edema (also called bat wings).
  - Kerly **B** lines (horizontal lines in lung, indicates interstitial edema).
  - **C**ardiomegaly (Cardiothoracic ratio is higher than 50%).
  - Upper lobe **D**iversion: Normally vessels of the lower lobe are more prominent than that of the upper lobe due to gravity, but in acute heart failure, because the lung is filled with fluid, fluid shift to upper lobe vessels, so vessels of upper lobe are more prominent than lower lobe.
  - Pleural **E**ffusion (fluid move from the lung to the pleura).

NOTE: This x-ray finding can also be found in chronic heart failure but to a lesser extend, because in chronic heart failure the long duration of disease allows lymphatics to drain this fluid.





- **Management of acute heart failure:** VERY IMPORTANT

1. Admission to ICU in cardiac bed.
2. Give O_2.
3. Give morphine.
4. Give IV furosemide (loop diuretic).
5. Give sublingual nitrate.
6. Give inotrope according to systolic blood pressure, as follow:
    a) If systolic blood pressure is more than 100 → continue nitrate, but give it by infusion instead of sublingual.
    b) If systolic BP is between 100 and 70 and there is NO signs of shock (i.e. Tachycardia, tachypnea, dry membranes, …….) → give dobutamine (weak inotrope).
    c) If systolic BP is Between 100 and 70 with signs of shock → give dopamine.
    d) If systolic BP is less than 70 → give noradrenaline (very strong inotrope).

When the pt is stabilized, and is to be discharged, he should be given treatment of chronic heart failure:

- **Management of chronic heart failure:**

1. Decrease salt intake, decrease fluid intake, encourages exercise and life style modification.
2. Treat the undelaying cause.
3. Prevent taking the precipitating factors (e.g. NSAIDs because they cause fluid retention and increase the load on an already diseased heart).
4. Furosemide (loop diuretic): only treats symptoms, it does NOT reduce mortality.
5. ACEI (the most important drug) (e.g. Enalapril) or Angiotensin receptor blocker (ARB) e.g. Losartan.
6. β blockers.
7. If you give the above 3 drugs without improvement → add either spironolactone or digoxin.
8. If there is NO improvement → do resynchronization therapy.
9. If there is NO improvement → do cardiac transplantation.

NOTES: When ACEI are contra-indicated, give vasodilator such as hydralazine.

- Very important NOTE: β blockers are contra-indicated in acute heart failure, and are only given after the pt passes the phase of acute heart failure and pul. edema. So β blockers are Only given in chronic heart failure starting with low dose and then increase it gradually.

NO BETA BLOCKERS IN ACUTE HF, BUT CHRONIC. (SIMILAR: NO ACEI IN ACUTE KIDNEY INJURY BUT CHRONIC)

An MCQs question: What are the drugs used in treatment of chronic heart failure but they do **not** reduce mortality?

1. Digoxin
2. Furosemide

   [if both are present select digoxin]

β Blocker is the most effective in reducing mortality.

- **New York Heart Association classified heart failure as (NYHA classification):**

Class I: Dyspnea on Exertion (i.e. No limitation of activity).
Class II: Dyspnea on ordinary activity eg:- when pt go to mosque
Class III: Dyspnea on less than ordinary activity " e.g. wearing dress", going to bathroom
Class VI: Dyspnea at rest.

➢ **Angiotensin Converting Enzyme Inhibitors:**

- ACEI blocks ACE which converts angiotensin I to angiotensin II, it also prevents degradation of bradykinin (so bradykinin is high in pts taking ACEI).
- Example of ACEIs: Captopril, Enalapril.

▪ **Side effects of ACEIs:**

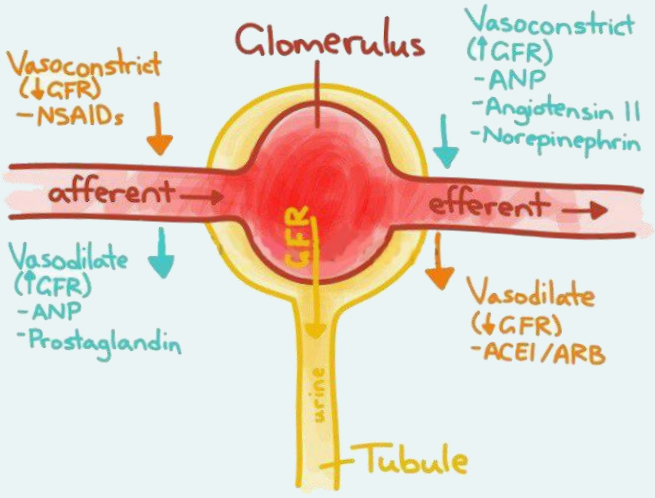
1. First dose hypotension: Captopril causes first dose hypotension more than Enalapril, that is why Captopril is sometimes used to treat hypertension.
2. Cough: caused by bradykinin, because ACEI prevents degradation of bradykinin. ARBs does NOT prevent degradation of bradykinin, so if you have a pt on treatment with ACEI and he develops cough, replace ACEI by ARB.
3. Hyperkalemia: Because blockage of angiotensin leads to blockage of aldosterone which releases K^+.

   So, ACEI decreases Aldosterone, decreased Aldosterone leads to high potassium.
4. Angioedema: can be fatal.
5. Acute kidney injury in pt with renal artery stenosis: each nephron has afferent arteriole, glomerulus, and efferent arteriole.

   The afferent arteriole is a continuation of renal artery. Afferent arterioles are maintained open by vasodilator prostaglandin (NSAIDs causes fluid retention because they antagonise prostaglandin → constriction of afferent arteriole → decrease GFR → fluid retention).

   Efferent arterioles are constricted by angiotensin II (constriction of efferent arterioles has the same effect of dilation of afferent arterioles, because both increase blood in glomerulus and hence increase GFR).

When a pt has renal artery stenosis and you give him ACEI, vasodilation of efferent arterioles occurs, this decreases GFR (because ACEI increases blood OUT-flow from the glomerulus, so blood supply to glomerulus decrease, but the glomerulus already has low blood supply because of the stenosis),
This leads to acute kidney injury.



Contra-indications of ACEI:	
○ **Absolute CI:**	○ **Relative CI:**
- **Bilateral renal artery stenosis.** - **Pregnancy: because it is teratogenic and affects kidney of fetus.**	- Unilateral renal artery stenosis.

➢ Digoxin toxicity: "an exam case"

- **Precipitants of digoxin toxicity:**
  - Hypokalemia "MOST IMPORTANT"
  - Hypomagnesemia.
  - Hypercalcemia.
  - Low albumin level

In exam pt is usually old, or a child who took his grandfather pills.

- **Symptoms:**
  - GI symptoms: nausea, vomiting.
  - CNS symptoms: Visual disturbances (Yellow-green vision) characteristic, disorientation.
  - CVS symptoms: arrhythmia.
- **Treatment:**
  - Stop digoxin.
  - Check K^+ level and correct it.
  - Give digoxin Fab Antibody (the antidote).
- **Investigations: ECG** shows characteristic "reverse tick" sign.

Fig: ECG showing "reverse tick" sign on Lead II indicating digoxin toxicity.

Hypertension (HTN)

Blood pressure more than 140/90

- **Causes:**

1. Essential (idiopathic), 95%

2. Secondary, 5%.

- **Causes of secondary hypertension:**

I. Renal causes (80% of secondary hypertension): e.g. Reno-vascular diseases (renal artery stenosis), Glomerulonephritis, and adult type of PCKD.

II. Endocrine causes: Conn's syndrome (Hyperaldosteronism), Cushing syndrome, acromegaly, pheochromocytoma.

III. Others: e.g. Coarctation of aorta and drugs (MAOI).

- **Stages of HTN:**

Stage 1:	Stage 2:	Stage 3:
From >140/90 to 160/100.	From > 160/100 to 180/110.	> 180/110.

Next step in stage 3 → start antihypertensive immediately.

Next step in stage 1&2 → Do ambulatory BP monitoring:

- If <135/85: pt is normotensive. No need for treatment, just life style modification.
- If >135/85 and <150/95: consider giving antihypertensive if:
    1. Cardiovascular risk is more than 20% per 10 years.
    2. Pt has end organ damage (e.g. CKD).
- If >150/95: treat immediately.

- **Management of HTN:**

I. Life style modification: [in any disease when we say life style modification we mean 1. Diet. 2. Exercise. 3. Habits].

1. Diet: decrease salt intake.
2. Exercise and weight loss.
3. Habits: quit smoking.
4. Control hyperlipidemia.
5. Control diabetes.

II. Antihypertensives:

- <55 years: first line is ACEI.
  If > 55 years or black regardless of his age: CCBs " first line in Sudan".
- Not controlled then give both ACEI & CCBs
- Still not controlled then **ADD** diuretic (e.g. thiazide).
- Still not controlled "refractory HTN" (refractory HTN is HTN resistant to three or more drugs) → **add** a fourth drug (e.g. Another diuretic, or α blocker or β, or α and β Blocker).
- If still not controlled add a fifth drug: use centrally acting anti-hypertensive e.g. **monoxydine** (Note that Minoxydil is a vasodilator, so do not be confused☺).

- **Special situations:**
  - HTN + DM: ACEI.
  - HTN + Chronic kidney disease: ACEI.
  - HTN + proteinuria: ACEI.
  - HTN + Heart Failure: ACEI.
  - HTN + angina: β blocker (to decrease contractility (heart rate) in order to decrease the load on the heart).
  - HTN + pheochromocytoma: α blockers.
  - HTN + Benign Prostatic Hyperplasia: α blockers.
  - HTN + pregnancy: methyldopa (which is a centrally acting antihypertensive).

- **β Blockers contra-indications:**
  1. Asthma.
  2. COPD.
  3. Bradycardia (because it decreases the heart rate).
  4. Acute HF.
  5. Variant angina.
  6. Diabetes is a relative contraindication (because it masks symptoms of hypoglycemia) ''see endocrine''.

- **Thiazides diuretics:** are contra-indicated in pt with gout because they increase the level of uric acid.

- **Grades of hypertensive retinopathy:**
  - Grade 1: dilated tortuous vessels.
  - Grade 2: Arteriovenous nipping الاوردة و الشرايين بتتوسع.
  - Grade 3: flame hemorrhage "Cotton Wool spots ".
  - Grade 4: papilledema.

❖ Hypertensive urgency vs. emergency vs. malignant hypertension:

In all of them there is very high blood pressure (more than 180/120)
في الغالب بيحصل الميتينات

✓ Hypertensive urgency:	✓ Malignant hypertension:	✓ Hypertensive emergency:
- **Very high BP without end organ damage.** - **Give oral atenolol.**	- Very high BP with End organ damage in the eye (i.e. retinopathy (grade3 or 4, usually papilledema). - Give oral Atenolol, and don't lower vigorously, or corneal/renal insufficiency will occur. Even if there is hepatic insufficiency or HF, lower BP to 150/90 in the first 24/72 hrs.	- Very high BP with end organ damage other than eye: e.g. Kidney (AKI), Heart (HF), Brain (Encephalopathy). - Give two drugs by IV route: furosemide + labetolol or Na nitroprusside. - Labetolol is superior to Na Nitroprusside because Na Nitroprusside is a vasodilator, which increases blood flow to kidneys.

❖ **Goals of treatment in HTN: بتتغير كل سنة ، فالا بس شوف كلام المحاضرة**

- General aim is to reduce BP to <140/90.
- If diabetic, target is <130/80 to protect kidney.
- If pt has proteinuria target is <125/75.
- If old (= 80 years) target is <150/90 [because old pt are more likely to have episodes of hypotension, so we want to have a higher systolic pressure].

[**NOTE:** Isolated systolic HTN → more dangerous than regular HTN: has same management].

Target with ambulatory BP:

	Diabetes	No Diabetes
Clinical	<130/80	<140/85
Ambulatory	<130/75	<130/80

[Note: The most important risk factor for stroke in elderly is Hypertension].

Aortic dissection

- Aortic dissection is shear in tunica intima; blood accumulates between intima and media.

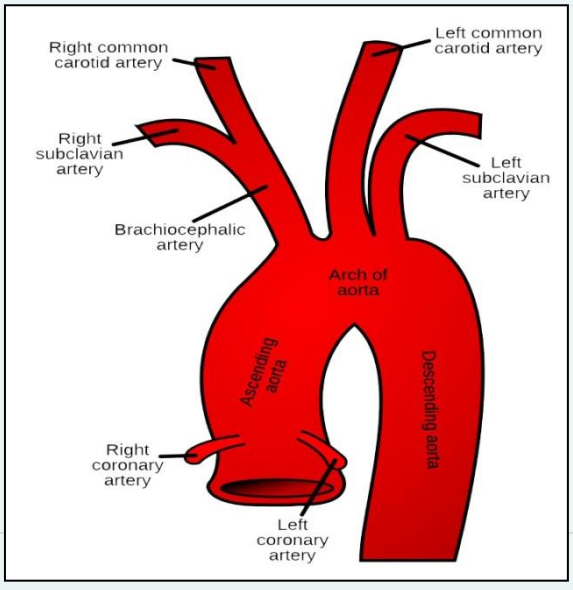
- **Causes:**
  1. HTN.
  2. Marfan's Syndrome.
  3. Trauma.
  4. Pregnancy.

''The first two causes are the most important"

- **Types Of Aortic Dissection:**
  - **Type A:** Aortic dissection involving ascending aorta (more dangerous).
  - **Type B:** Aortic dissection involving descending aorta (The accumulating blood leads to compression of renal artery and pt presents with oliguria).

- **Complications:** either due to forward tear or backward tear.
  - Due to Forward tear:
    1. Stroke: when dissection reaches carotid artery.
    2. Unequal BP between Rt and Lt arms: when dissection reaches subclavian artery (Unequal BP between Rt and Lt arms also occurs in Takayasu arteritis).
  - Due to Backward tear**:**
    1. MI: when Tear reaches coronary sinuses.

NOTE: in this type of MI thrombolytics are contra-indicated, it is the ONLY type of MI in which thrombolytics are contra-indicated ''see below''.



2. Aortic regurgitation: when it reaches aortic valve [That is why in any pt with AR history of back pain is very important (MCQs question)].
3. Cardiac tamponade: when it reaches the pericardium.

[**NOTE** Complications are more likely to occur in type A rather than type B, that is why type A is more dangerous].

- **Management:**
  - Management of type A:
    - Surgical management, but give IV Labetalol while pt is waiting for surgery (IV Labetalol reduces risk of hypertensive emergency).
  - Management of type B:
    - Just IV Labetalol and no need for surgery.

- **Clinical Presentation of aortic dissection:** Central chest pain radiating to the back, in type B the accumulating blood lead to compression of renal artery and pt presents with oliguria.

- **Diagnosis:**
  - Chest X-ray: wide mediastinum on chest X-ray (characteristic).
    - **Differential diagnosis of wide mediastinum:**
      2. mediastinal tumor.
      3. mediastinal lymphadenopathy.
      4. right aortic arch.
  - CT aortography: the DIAGNOSTIC test.

NOTE:

Marfan syndrome

Clinical Features:

- Tall stature.
- Arm span > height.
- Normal Mental function.
- Arachinodactyly.
- Ectopia lentis (lens is displaced upward).
- Cardiac features (Aortic Regurgitation & MVP)''see above''.

Differential Diagnosis of Marfan: homocysteine-urea (same appearance except for ectopia lentis where the lens is displaced downward, they have mental retardation, also cardiac involvement in Homocysteine-urea is NOT usual).

Pericardial diseases

1. Acute pericarditis:

- **Causes:** ما مهمة
  1. Idiopathic.
  2. Infection [viral (most common); Coxsackie virus, Fungal, or bacterial; TB].
  3. Uremia (uremic pericarditis in renal failure is an indication for dialysis).
  4. Hypothyroidism.
  5. MI.
  6. Autoimmune arthritis and SLE.
- **Clinical presentation:**
  - **Symptoms:** pleuritic chest pain that gets worse by lying flat and relieved by sitting forward, (An MCQs question) [this is because when a pt is lying flat, friction between parietal and visceral pericardium increases].
  - **Signs: O/E:** pericardial friction rubs.

NOTE:

Chest pain may be cardiac or pleuritic:

Cardiac chest pain:

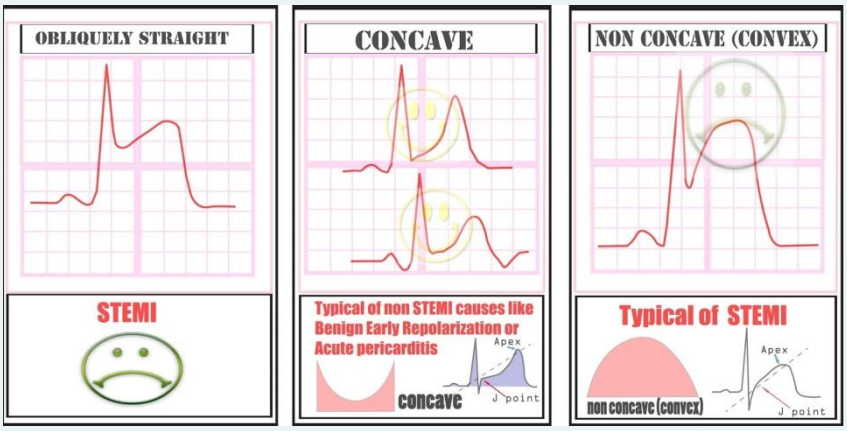
1. Central, crushing, radiating to jaw or Lt arm.
2. Increases by exercise, heavy and fatty meals, stress and emotions, and cold.
3. Releived by rest, or sublingual nitrates.

Pleuritic chest pain:

1. Sharp, localized pain.
2. Aggravated by deep inspiration and cough.

- **Investigations:**
  1. CBC, ESR.
  2. ECG:
     - Global concave (saddle shaped) ST segment elevation (An MCQs question).
     - But the most specific ECG finding is PR depression.

Differential Diagnosis of ST segment elevation:



1. **Pericarditis:** ST elevations is global (in all leads), and Saddle (concave) shaped.
2. **MI:** ST elevation is localized to certain leads, and it is convex in shape.

- **Management:**
  - First line: NSAID (Ibuprofen) + treatment of underlying cause.
  - Second line is colchicine (colchicine prevents WBCs migration to site of inflammation) + treat underlying cause.
  - Steroids are only given in severe cases because it decreases immunity.
  - If viral? stop Ibuprofen.

2. Pericardial effusion:

- **Causes:**
  - Same as acute pericarditis.
- **Clinical features:**
  - Ewart sign: bronchial breathing in the base of Lt lung, (because the pericardium contains fluids that compress the base of Lt lung (Lt lung looks like it is collapsed)).
- **Diagnosis:**
  - ECG: Two findings:
    1- Low voltage QRS (because there is a large gap between the heart and the site of recording (the skin)).
    2- Electrical Alternans: This short QRS complex has an altered height, sometimes it is short and sometimes it is even shorter, this is because the heart is floating on water and has an instable, fluctuating position.
  - CXR: enlarged heart (cardiomegaly), because there is fluid around it.
  - Echo: the DIAGNOSTIC test, there is echo free zone around the heart.

- **Treatment:**
  - By treating the underlying cause.
  - Pericardiocentesis may be used as diagnostic and therapeutic.

3. Constrictive pericarditis:

- **Definition:** Stiffness of the wall of pericardium that limits contractility of the heart.
  - **Causes:** TB is the most common cause in Sudan.
  - **Clinical features:** Symptoms & Signs of Right sided HF.

NOTE: Constrictive pericarditis and Restrictive cardiomyopathy have the same clinical presentation of Rt sided heart failure.

  - **Kussmaul's sign:** paradoxical rise of JVP with inspiration [Normally JVP decreases with inspiration because the intrathoracic pressure becomes negative → venous return increases → and JVP decreases. But in constrictive pericarditis stiffness prevents the increase of venous return].
  - Deep x and y descents in JVP.
  - **Investigations:** imaging [CXR, CT, MRI → Calcified pericardium].
  - **Management** is pericardiectomy.

4. Cardiac tamponade:

- **Causes**:
  1. Aortic dissection.
  2. Trauma.
  3. Anticoagulants (Warfarin).
  4. Post cardiac biopsy.
- **Clinical features:**
- **Beck's triad:** 1. raised JVP, 2. low BP, 3. muffled heart sounds.
- No ''y'' descent in JVP (the difference between cardiac tamponade and constrictive pericarditis in JVP is that in constrictive pericarditis both ''x'' and ''y'' descents are present (and they are deep), while in cardiac tamponade ''y'' descent is absent).
- Kussmaul's sign is present.
- Pulsus paradoxus: [Normally with inspiration the pulse and blood pressure drop, because the decrease in intra-thoracic pressure increases venous return, and blood accumulate in the heart. But this drop in BP is NEVER larger than 10 mmHg, (for example if it was 90, with inspiration it normally becomes 80 or above but never less than that). In pulsus paradoxus there is weak impalpable pulse or the drop in BP is more than 10 mmHg]. So, pulsus paradoxus is an exaggeration of a normal response.
- **Investigations:** Same as investigations of pericardial effusion and similar findings (both of them are due to fluid accumulation).

- **Treatment:** Pericardiocentesis (drainage) + treatment of underlying cause.

Cardiomyopathies

1. Dilated cardiomyopathy (DCM):

Is a global enlargement and dilatation of heart chambers.

- **Causes:**

1. Idiopathic (most common).
2. Pregnancy (peri-partum and post-partum dilated cardiomyopathy).
3. Alcoholism (thiamine (Vitamin B1) deficiency).
4. Beriberi (thiamine deficiency).
5. Hemochromatosis.
6. Drugs (doxorubicin (a drug used in treatment of cancer)).
7. Genetics: X-linked.
8. Duchenne Muscular Dystrophy.

- **Clinical features:**

- Symptoms and signs of Congestive heart failure.

NOTE: In Dilated cardiomyopathy there are signs and symptoms of congestive heart failure. In Restrictive cardiomyopathy there are signs and symptoms of Rt side heart failure.

- Systolic Failure (decreased Ejection Fraction).

NOTE: dilated cardiomyopathy is the only cardiomyopathy in which the type of heart failure is systolic. In restrictive cardiomyopathy and HOCM it is diastolic.

- Apex is displaced.

- **Diagnosis:** By echocardiography: there is enlarged heart.
- **Complications:**

1. Thrombosis and embolization; due to stasis of blood that occurs due to weak contraction.
2. Arrhythmias: when the dilatation of chambers involves the conductive system.

- **Treatment:**
  - Treatment of heart failure.
  - ICD (implantable cardiac defibrillation) can be done.
  - Resynchronization therapy.
  - Cardiac transplantation.

2. Restrictive cardiomyopathy:

- **Causes**:
  1. Idiopathic.
  2. Amyloidosis (the deposits in Amyloidosis decrease efficacy of diastole).
  3. Sarcoidosis.
  4. Haemochromatosis.
  5. Endo-myocardial fibrosis and fibro-elastosis (occurs in children): fibrosis of endocardium and myocardium.
  6. Loffler's syndrome (there is eosinophilic infiltrate that causes deposition similar to that of amyloidosis).

- **Clinical features:**
  - Similar to Rt side heart failure.
  - There is Diastolic Failure.

- **Diagnosis**:
  - Myocardial biopsy through cardiac Catheterization.

- **Management:**
  - Cardiac transplantation.
  - Prognosis is very poor.

3. Hypertrophic Obstructive cardiomyopathy [HOCM]: اهم واحد

- **Causes:** Autosomal dominant mutations in sarcolemma proteins (Contractile proteins, e.g. myosin binding protein c, tropomyosin, troponin, β myosin heavy chain).
  This mutation is associated with Friedrich's Ataxia ''see nervous system chapter'' (the cause of death in pt with Friedrich's ataxia is HOCM).
  (Duchenne causes DCM).
- **Clinical features:**
- **Symptoms:** same triad of aortic stenosis [Syncope on exertion, Angina, and Dyspnea].
- **Signs:**
  - Pulse: jerky pulse.
  - Apex: double apex beat, due to obstruction ''see causes of obstruction below''.
  - Ejection systolic murmur at the lower part of sternum.

NOTE:

How can you Differentiate between murmur of HOCM and murmur of aortic stenosis?

- The decrease in venous return leads to increase in murmur of HOCM, and vice versa. Also, the increase in venous return leads to increase in murmur of aortic stenosis, and vice versa.

- The increased venous return decreases murmur of HOCM because it dilates the Lt ventricle, and this deceases the obstruction by moving the septum away from outflow area ''see the figure below'', this decreases the murmur. But in Aortic stenosis the increased venous return increases blood flow through heart valves, the increase in blood flow through the stenotic aortic valve increases the murmur (murmur is turbulence of blood flow).

◊ **Valsalva maneuver** (expiration against closed epiglottis) increases the intrathoracic pressure → decreases venous return. So, Valsalva maneuver increases murmur of HOCM and decreases murmur of aortic stenosis.

◊ The same thing occurs when **standing from sitting**, because blood goes downward → this decreases venous return. So, standing from sitting increases murmur of HOCM and decreases murmur of aortic stenosis.

◊ The reverse occurs during squatting; because during squatting muscles act as a pump that squeezes blood → this increases venous return → murmur of HOCM decreases. So, squatting decreases murmur of HOCM and increases murmur of aortic stenosis].

	HOCM	AS
Valsalva maneuver and standing from sitting	Increase murmur	Decrease murmur
Squatting	Decrease murmur	Increase murmur

- **Causes of obstruction in HOCM:**
  1. Asymmetrical septal hypertrophy: hypertrophy occurs in both the free wall of the heart and in the septum, but the septum is more hypertrophied than the free wall, that is why it is called asymmetrical septal hypertrophy. Asymmetrical septal hypertrophy changes the position of septum, and this blocks outflow to aorta.
  2. Sub-valvular stenosis.
  3. Systolic anterior motion (SAM) of mitral leaflets: SAM is displacement of the distal portion of the anterior leaflet of mitral valve toward the Lt ventricular outflow area.

- SAM is present in a normal heart, but pt suffering from HOCM already has another two causes of obstruction, and SAM makes the obstruction worse.
- That Vasodilators are contra-indicated in obstructive lesions (HOCM and AS), because when blood vessels are dilated, blood get stored in veins, this decreases venous return, making the obstruction worse.

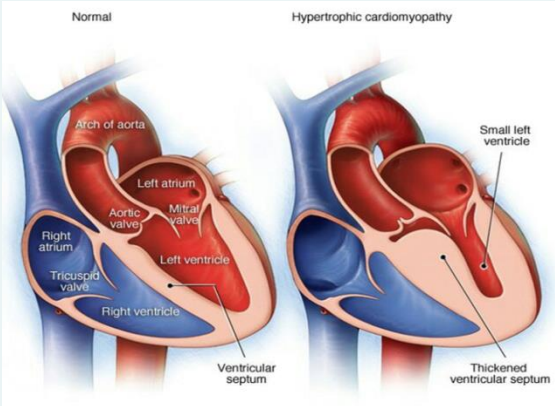
- **Diagnosis**: By Echo: *Mnemonic: MR SAM ASH*
  1. **A**symmetrical **s**eptal **h**ypertrophy.
  2. **S**ystolic **A**nterior **m**otion of mitral leaflet.
  3. Functional **m**itral **r**egurgitation.
  - Exercise test (measurement of BP during exercise): to assess risk of SCD.
  - Halter ECG monitoring (24 hrs ECG monitoring): to assess risk of SCD.

HOCM is the most common cause of sudden cardiac death in young athletes.

- **Factors that Increase risk of sudden cardiac death (SCD):**

I. Young age (< 14 yrs).
II. Family history of sudden cardiac death.
III. Syncope at presentation.
IV. Septum thickness more than 3 cm by echo (most important factor).
V. Exercise test: abnormal BP changes during exercise.
VI. Halter monitoring: Short running of ventricular tachycardia.

- **Management:**
  - **Medical:**
  - Most important drug is **β blockers** (because they have angina**).**
  - Remember that vasodilators are contra-indicated.
  - **Surgical**
  - Septal myomectomy.
  - ICD if there is high risk of sudden cardiac death.



Ischemic heart diseases

Ischemic heart diseases present clinically as angina.

- **Causes of angina:**
  - **Decreased blood supply to the heart:** due to for example; atheroma, atherosclerosis, emboli, coronary spasm, or vasculitis.
  - **Increased demands:** either due to increased heart rate (e.g. in thyrotoxicosis) or increased contractility (in obstructive lesions (AS & HOCM)).
  - **Decreased oxygen carrying capacity of blood**: e.g. anemia and CO poisoning (CO has higher affinity than O_2, so it displaces O_2).

- **Criteria of Cardiac pain:**
  1- Central, crushing, radiating to jaw or left arm.
  2- Aggravated by exercise, heavy and fatty meals, stress, emotions, and cold.
  3- Relieved by rest or sublingual nitrates
  ➔ If the above 3 criteria are present: typical cardiac pain.
  ➔ If 2 present: atypical cardiac pain.
  ➔ If 1 or less: Non cardiac pain ''look for another cause''.

❖ **Ischemic heart diseases include:**
1. Stable angina.
2. Variant angina.
3. Acute coronary syndrome (ACS):
   I. Unstable angina.
   II. Non ST segment elevation myocardial infarction (NSTEMI).
   III. ST segment elevation myocardial infarction (STEMI).
   IV. Sudden cardiac death (SCD).

1. Stable angina:

Q: How to differentiate between stable angina and acute coronary syndrome?
A: In both of them there is atheroma, but in stable angina atheroma is fixed, while in ACS the atheroma develops an invent (e.g. rupture or hemorrhage).

➢ Classification:

›› You need to classify pts according to history of coronary artery diseases(CAD):

- **Pt with angina who has known history of CAD:**
  - If there is typical cardiac pain → start treatment immediately, no need to investigate (An MCQs question).
  - If there is Atypical cardiac pain → do functional studies:
  1. Exercise Echo: there is regional wall motion abnormality (i.e. decreased movement of muscles in the part of the wall that has decrease blood supply).
  2. Thallium scan (also called myocardial perfusion scan): decrease perfusion.
  3. Exercise ECG: not diagnostic, just gives probability of having angina.

- **Pt with angina who does not has any history of CAD:** We should calculate cardiovascular risk as follow:
  - Cardiovascular risk > 90% → start treatment immediately.
  - Cardiovascular risk 90 – 61 % → do angiography.
  - Cardiovascular risk 60 – 30 % → do functional studies.
  - Cardiovascular risk 29 – 10 % → do calcium CT score; high Ca CT score means that atheroma is small (atheroma consists of a lipid core and a fibrous cap), this fibrous cap consists of Calcium. High levels of Ca CT score means that the fibrous cap is thick and the lipid core is small).
  - Cardiovascular risk < 10% → consider another diagnosis.

- **Exceptions:**
  1. Male pt older than 70 yrs: (common MCQs question): you should start treatment immediately, whether the pain is typical or not, and regardless of cardiovascular risk.
  2. Any Female pt older than 70 yrs and with Cardiovascular risk less than 90%: do Angiography.

➢ **Management:**

1. Life style modification: diet, exercise, quit bad habits, Control risk factors (DM, HTN, hyperlipidemia).
2. Symptomatic drugs (monotherapy):
   I. Sublingual nitrate (GTN): Sublingual at home or as Spray, given when symptoms occur or as Prophylaxis.
   II. β blockers.
   III. Anti-platelet therapy: e.g. aspirin (to decrease mortality).

3. If not controlled by monotherapy:
   - Add Calcium channel blockers (CCB).
   - If still not controlled add a fifth drug while waiting for invasive procedures, this fifth drug may be:
     a) Potassium channel activator (Nicorandil).
     b) I_F channel blocker (Ivabradine): I_F channel blockers are drugs that block Funny channels. These are channels found in SA node and conductive system of the heart, if they are blocked conduction will decrease and hence the heart rate.
   - The invasive procedures are:
     a) PCI.
     b) Coronary Artery Bypass Grafting (CABG).

VERY IMPORANT NOTE:

There are two types of CCBs:
1. Dihydropyridines (e.g. Nifedipine): act on blood vessels causing vasodilation, this causes reflux tachycardia, which increases the load on the heart. So they are NEVER given for pts with angina alone, and should be combined with β blockers.
2. Cardio-selective (Verapamil and diltiazem): are CCBs that decrease contractility of the heart, so they can be given alone for pt with angina.

a) Percutaneous Coronary Intervention (PCI):

- Also called Percutaneous Transluminal Coronary Intervention (PTCI), and Percutaneous Transluminal Coronary Angioplasty (PTCA).
- Complications of PCI:
  I. Ischemia during procedure: prevented by giving glycoprotein IIB/IIIA inhibitor (tirofiban) ''see the note below''.

II. Thrombosis: occurs about one month after treatment, prevented by combination of aspirin and Clopidogrel (Note that in stroke combination of Aspirin and Clopidogrel is Contra-indicated).
III. Restenosis: occurs about 6 months after treatment, prevented by using drug eluted stents.
IV. Failure of the procedure: here we need to do emergency CABG.

So, any pt undergoing PCI should be given tirofiban before the operation, and the stent to be used should be drug eluted, then after the operation pt must be given aspirin and clopidogrel.

N.B: Drugs reduce mortality while PCI improves symptoms only.

b) Coronary Artery Bypass Grafting (CABG):

- Used in areas of the heart difficult to reach by PCI, for example:
  - ✓ Osteal disease.
  - ✓ Distal disease.
  - ✓ Triple vessel disease or more than triple (i.e. three arteries or more are affected).
  - ✓ Lt main stem disease.
- **Complications:** CNS complications (stroke).
- CABG is used once in life (streptokinase (a drug used in treatment of MI) is also used once in life).

NOTES about Anti-platelet drugs:

For platelet aggregation to occur, we need:
1. Thromboxane.
2. ADP.
3. Von Willebrand foctor.

- These three factors act together to activate a common pathway that end by activation of Glycoprotein II B/III A.
- So, Anti-platelet drugs:

A. Drugs that block thromboxane: e.g. Aspirin.
B. Drugs that block ADP: e.g. Clopidogrel.
C. Drugs that block the common pathway (are the most important group): Glycoprotein II B/ III A inhibitors, e.g. tirofiban**.**

2. Variant "Prinzmetal" angina:

- Caused by sudden spasm of coronary artery.
- **Clinically:** Pt is usually female, she develops angina at night (at rest).
- **ECG:** shows ST elevation.
- **Management:** CCBs acing on blood vessels (i.e. dihydropyridines)
- The following drugs are contra-indicated in Variant angina:
    1. Aspirin.
    2. β blockers (β blockers cause spasm of coronary artery).

  [Note that this two drugs are the first line in treatment of stable angina, so if pt with Variant angina was misdiagnosed as stable angina, Aspirin and β blockers may kill her].

3. Acute Coronary Syndrome (ACS):

- D.D. of ACS:
    I. Unstable angina.
    II. Non ST segment elevation myocardial infarction (NSTEMI).
    III. ST segment elevation myocardial infarction (STEMI).
    IV. Sudden cardiac death (SCD) انسوها.
        - In MI chest pain is > 20 minutes.
        - In MI there is myocardial cell death, cardiac enzymes leak, and can be detected in plasma.

  → So, if you want to differentiate between them:
    - In Unstable angina: there is No ST elevation and No cardiac markers.
    - In NSTEMI: there in No ST elevation but cardiac markers are elevated.
    - In STEMI: there is ST elevation and cardiac markers are elevated.

Myocardial Infarction (MI):

- Few words about ECG leads:
  - Bipolar leads:
    1. Lead I: between the two arms.
    2. Lead II: between the Rt arm and the Lt foot.
    3. Lead III: between the Lt arm and the Lt foot.
  - Unipolar leads:
    1. Limb leads: aVR, aVL, aVF.
    2. Chest leads: from V_1 to V_6.

- **Types of STEMI:**

1. **Anterior MI:**
   - Blockage is in the Lt anterior descending artery.
   - It is the most common type.
   - ECG changes: ST elevation in chest leads from V_1 to V_4.

2. **Lateral MI:**
   - Blockage is in the Lt circumflex artery.
   - ECG changes: ST elevation in the lateral leads (V_5, V_6, aVL, and lead I)
   -

3. **Inferior MI:** اهم وحدة
   - Blockage is in the Rt coronary artery.
   - ECG changes: ST elevation in aVF, lead II, and lead III.
   - Rt coronary artery supplies conductive system of the heart (AV node and SA node), that is why pt with inferior MI presents with heart failure with bradycardia and there is AV block.
   -

4. **Posterior MI:** ما مهمة
   - There is ST elevation from V_1 to V_6 in addition to V_7, V_8, and V_9 (these are the back leads).
   -

NOTE: AV block is one of the signs in inferior MI. But if you have pt with anterior MI and he has AV block, this is very bad sign which means that myocardial death progress from the anterior wall and reaches the conductive system.

- **Criteria of ST elevation:**
    1. More than 1 mm in limb leads.
    2. More than 2 mm in chest leads.

- **ECG changes in order:**
    1. Hyper acute T wave (tall T wave).
    2. Elevation of ST wave.
    3. T wave inversion.
    4. Formation of pathological Q wave (this wave lasts for long time, that is why it indicates an old infarct).

- **Cardiac markers:**
    - **Myoglobin** is the first to rise.
    - **Troponin** is the most sensitive, drops in 7 to 10 days.
    - **CK-MB** is used to detect re-infarction because it drops rapidly (in 3 to 5 days).
      So, if pt develops re-infarction do CK-MB because troponin of the previous MI has not drop yet (An MCQs question).

Management of acute coronary syndrome: مهم

1. ***Give MONA to all patients (Morphine, O_2, Nitrates, and Aspirin).***
2. Then do **serial ECG** and **serial cardiac markers,** then according to result:

I. **If ST elevation (STEMI):** after giving MONA, do reperfusion therapy:
    a. PCI ''see above'': always superior to thrombolytic therapy, the ideal time is 90 minutes.
    b. Thrombolytic therapy: by streptokinase or by tissue plasminogen activator (tPA), the optimum time is 30 minutes.
    - Streptokinase is used once a life (CABG is also used once a life).

NOTE: the difference between reperfusion therapy in MI and reperfusion therapy in stroke; is that streptokinase is used only in MI, in stroke there is NO role for streptokinase, only use tPA. سؤال امتحان.

Contra-indications to thrombolytic therapy:

A) Hemorrhagic stroke EVER.
B) Ischemic stroke in previous 6 months.
C) Upper GI bleeding in previous 1 month.
D) Major trauma or surgery in previous 3 weeks.
E) Pregnancy.
F) CNS tumors (because they are highly vascular).
G) Severe HTN.
H) Bleeding disorders.

II. **<u>If there is No ST elevation:</u>** this is either NSTEMI or unstable angina, both of them has the same treatment: after giving MONA, give heparin then assess the cardiovascular risk (according to GRACE score):

- **<u>If the pt has high risk GRACE score;</u>** give him glycoprotein II B / III A inhibitor, and do angiography in 4 days.

NOTE: High risk GRACE score:

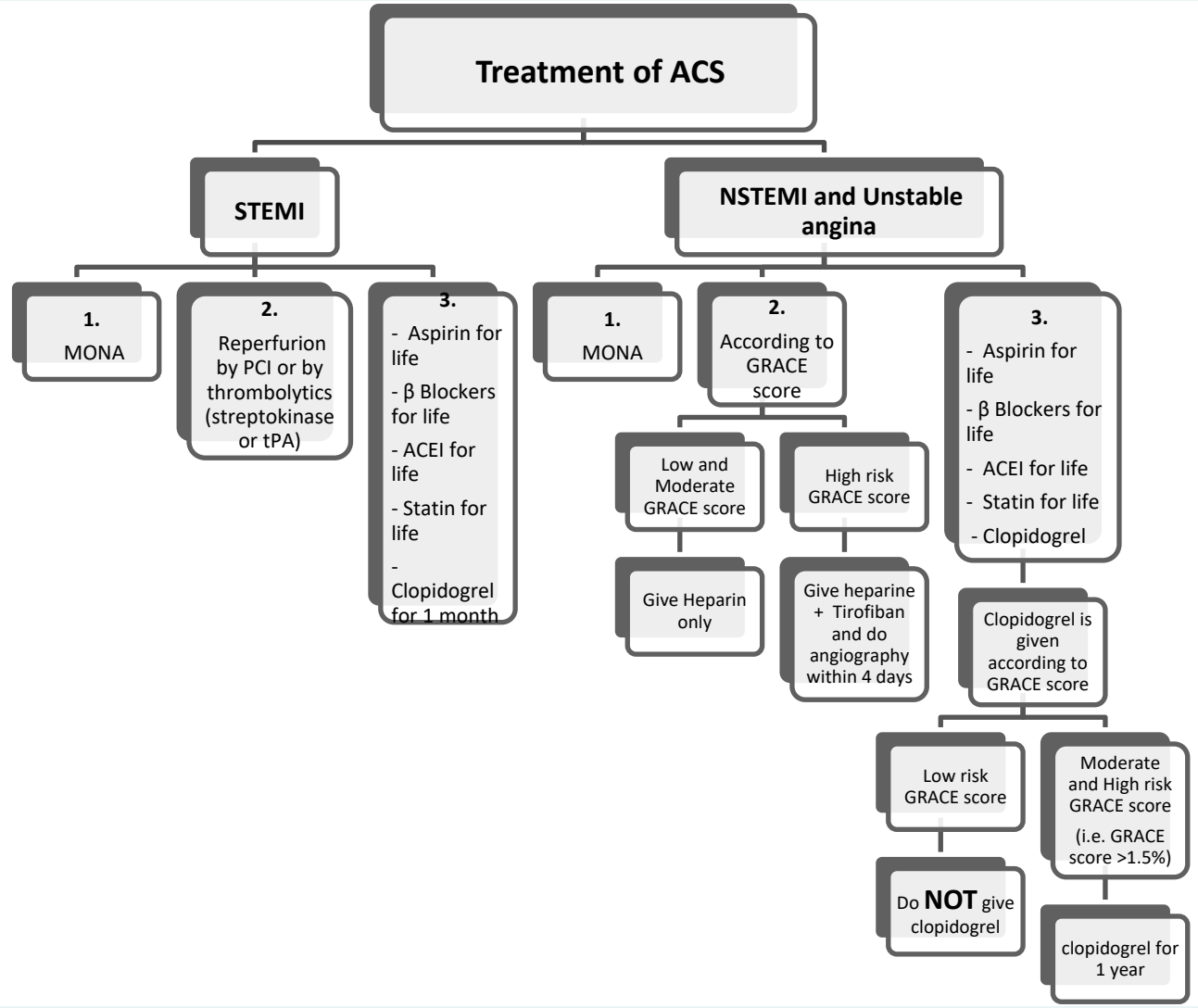
1. Diabetes.
2. ST depression.
3. High cardiac markers.
4. Persistent or recurrent ischemia.

3. Then give discharge medications:

The first 4 drugs are similar in all types of ACS.

1- Aspirin for life.
2- β Blockers for life.
3- ACEI for life.
4- Statin for life.
5- Clopidogrel: if STEMI give clopidogrel for 1 month, if NSTEMI or Unstable angina and the GRACE score is more than 1.5% give clopidogrel for 1 year.

Summary of treatment of ACS:



Complications of ACS:

1. Cardiogenic shock: treated same as heart failure.
2. Arrhythmias:

- The most common type of arrhythmia in pt with MI is ventricular extra-systole, it has two types; Bigeminal (more dangerous) and trigeminal.
- The most killer arrhythmia is ventricular fibrillation.
- AV block in anterior MI is dangerous and needs pacemaker.

3. Pericarditis: two types:
   a) Early (acute pericarditis); caused by spread of inflammation from the heart to pericardium.
   b) Late (Dressler's syndrome); occurs 1 to 3 weeks after MI, caused by antigen induced inflammatory response. Pt present -in addition to signs and symptoms pf pericarditis- with pericardial effusion, ascites, and elevated ESR (i.e. fluid accumulates in 3 chambers in the body; pericardium, pleura, and peritoneum). Treated by NSAID as first line (ibuprofen), and Colchicine as second line (first line in pt with renal failure), if very sever give steroids (steroids are not recommended because they decrease immune response and this decreases healing process).

4. Mural thrombus: stagnation of blood leads to formation of thrombi in walls of ventricles (same as dilated cardiomyopathy), it occurs most commonly after anterior MI, that is why any pt with anterior MI should be given warfarin for 3 months.

5. Rupture of Chorda Tendineae: leading to mitral regurgitation (pan systolic murmur).

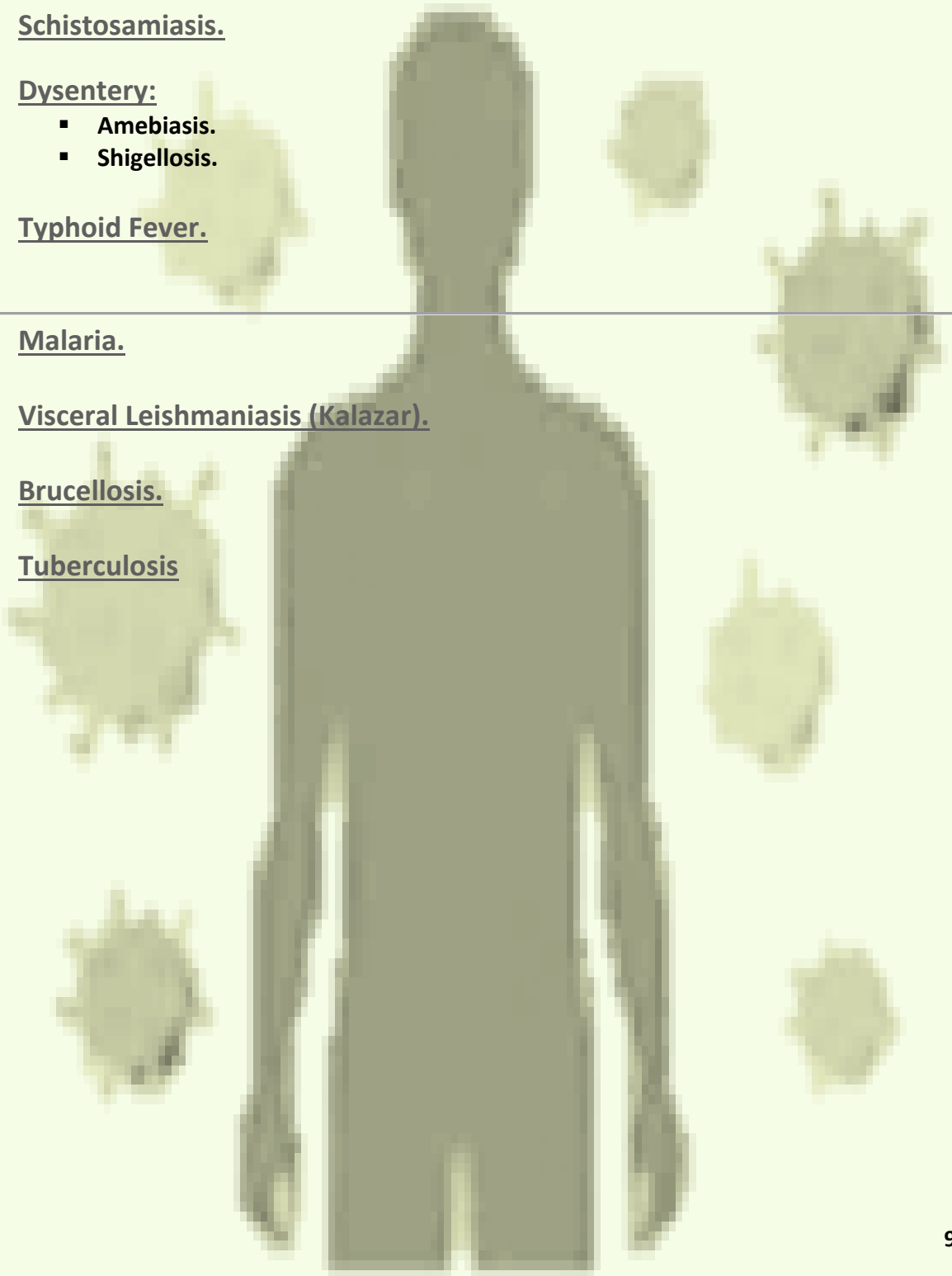
6. Rupture of inter-ventricular septum leading to ventricular septal defect (VSD) (also there is pan systolic murmur).
7. Rupture of free wall of the ventricle: leading to cardiac tamponade.

8. Ventricular aneurysm: occurs after 6 weeks, it may be complicated by thrombosis or embolization (because in aneurysm there is stagnation of blood), or it may rupture causing cardiac tamponade. It is diagnosed by PERSISTANT ST elevation for 6 weeks (i.e. pt with MI, but ST elevation persist and T wave did not get inverted).

قد ينظر الله إليك من فوق سبع سماوات
نظرة رضا فتطيب بها أوجاعك وكأنها
لم تكُن . ♡

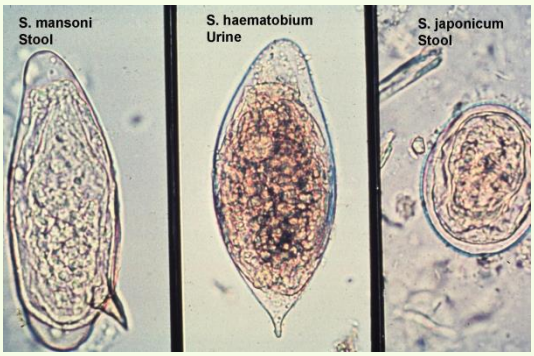
** Recorded on 25 Sep, 2 Oct. 2017

Contents



Schistosomiasis [blood flukes]

Sch. Hematobium → Terminal spine >> urinary
Sch. Mansoni → Lateral spine
Sch. Japonicum



Egg → miracedium → enters snail → cercariae(infective stage)→ penetration skin,, veins ,, Rt heart,, lungs,, left heart,, portal circulation (maturation to adult worm),,
Then mansoni to → mesenteric veins [Portal]
Or hematobium to vesical venous plexus [systemic]

Snails: Hematobium: bulinus Mansoni: Biomphalaria

Differences between species:

1- Prepatent period: from cercariae to production of eggs. In mansoni 1 month, hematobium 2-3 months
2- Location of adult worm
3- Host response to egg

N.B: adult worm doesn't multiply in body (eggs needs suitable condition to hatch)
Immunosuppression = No ↑ in of Adult worms

✓ The disease is mainly type 4 hypersensitivity reaction against eggs.

Clinical features:

1- **Swimmer's itch [Cercerial Dermatitis]:**
   - 1-2 days after penetration, more marked with non-human species. More marked in non-immune.

2- **Acute Toxemic Schistosomiasis (Katayama fever)**:
   - Common in S.Japonicum, rare in hematobium. Usually visitors to endemic area then after 2-6 wks.
   - Fever/ rigors, cough/ wheeze, diarrhea, lymphadenopathy and hepatosplenomegaly. And urticaria.
   - Mainly a disease of naive pts. --> Occurs from 2-6 weeks.
   - Blood: High eosinophils.
   - Characteristically negative stool [no eggs in stool/urine/tissues] but high antibodies.

3- **Established infection:**
   - Hepatosplenic schistosomiasis; Portal HTN, Pulmonary HTN.

 # Mansoni: may be asymptomatic

- ***Intestinal Schistosomiasis*;** bloody diarrhea and polyps (may bleed or cause intussusception. These polyps are treated by medical Rx and no need for surgery.
- ***Hepatosplenic schistosomiasis****; periportal fibrosis >> portal hypertension*

  - **Presentations of portal hypertension:** [may be asymptomatic]
  - Acute; hematemesis from varices.
  - Chronic: melena or anemia [Chronic Blood loss or Hypersplenism]
  - **O/E:** enlarged LEFT lobe of the liver, splenomegaly, venous hump and caput medusa. NO ASCITES.

N.B. Liver function test is normal in Schistosomiasis.
If abnormal either concomitant HCV infection, malnutrition or necrosis of hepatocytes due to ischemia (from shock).

N.B: **abnormal LFTs:** 1. Concomitant Hepatitis C infection.
2. Bleeding >> Liver necrosis. 3. Malnutrition

- **Complication of portal hypertension** is pulmonary Hypertension (occurs after opening of the Porto-systemic shunts and spreading of the ova to systemic circulation.)
- **SO** pulmonary hypertension always occur after portal hypertension

Dx:

- Stool examination looking for:- **viable** ova by hatching test (if negative but still suspicious do concentration method, if still suspicious do rectal snip)
- US looking for:-

1. Portal vein diameter (enlarged), 2. Splenomegaly 3. Fibrosis and its grading.

- Endoscopy:- esophago-gastric endoscopy for varices
- Serology for Abs (Circulating Cathodic Abs: CCA, Circulating Anodic Abs: CAA)
- Colonoscopy: for polyps.
- ECG, CXR : For pulmonary hypertension

Hematobium:

Clinical presentation:

1. Terminal hematuria
2. Calcification of ureter → hydroureter or hydronephrosis (AKI)
3. Calcification of bladder (Thimble bladder)
4. Squamous cell carcinoma of bladder (chronic irritation)

Dx:

- Urine Analysis for viable ova
- Imaging for kidney(hydroureter,hydronephrosis) +/-Renal function test
- Cystoscopy looking for calcification in bladder (sandy patches)
- Serology

N.B: Prolonged fever in schistosoma pt is most probably caused by ***schistosalmonillosis.*** Another cause is septicemia.

Rx:

- Mansoni: **Oxamniquine.** Dose 60mg/kg
- Hematobium: **Metrophonate**
- **Praziquantil** works for both

Drug SE: Oxamniquine:

1. Orange urine
2. CNS: epilepsy/ transient amnesia
3. Derangement of liver function (mainly ALP)

Metrofonate: increases acetylcholine (salivation, lacrimation, sweating and bronchospasm)

Praziquantil is effective against both adult worms and immature worms.
Dose is 40 mg/kg
1 capsule is 600 mg
Maximum dose is 2400 mg (4 capsules)
60 kg is as 600!!

Absent of viable ova after 3 months of treatment is the **Test of cure.**

Dysentery Amebic/ Bacillary

Amebiasis

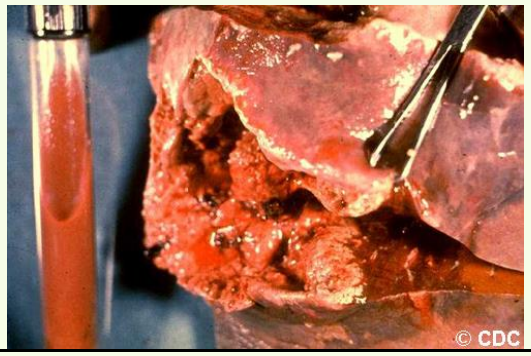
- Human amoeba types are E.histolytica: Pathogenic / E.dispar: non-pathogenic
- **Pathogenicity of E.Histolytica:**

1. Contact mediated lysis of the cells
2. Proteolytic enzymes.

- **2 forms:** cysts and trophozoites
- **Infective stage:** cyst [resistant to gastric acidity; secreted into environment.
- **Life cycle:** Human: Major reservoir; Cyst >> stomach >> intestine [ex-cystation into 4 trophozoites > > colon [encystation] >>> cyst in the environment

- Ameba affects **large** intestine → Presents with **bloody diarrhea**

Clinically: Intestinal .vs. Extraintestinal

Intestinal	Extraintestinal
1. Asymptomatic **2. Acute amebic colitis: fever, bloody diarrhea and normal WBCs (milder than bacillary dysentery)** **3. Fulminant amebic colitis: severe form may have dehydration, electrolyte disturbances and peritonitis.** • **Risk factor for fulminant colitis: steroids intake (make sure in case of suspecting UC) and children.** **4. Chronic colitis** **5. Ameboma**	**1. Amebic liver abscess:** - <50% →+ve stool for trophozoites on microscopy; usually 5-6 months after intestinal disease. - **C/O:** Acute .VS Subacute - Swinging fever [high grade], RUQ pain radiating to rt shoulder/ tender hepatomegaly - If in the left lobe epigastric pain radiating to left shoulder - **O/E:** 1. Tender Hepatomegaly 2. Mild jaundice in some cases *Full shiny intercostal spaces overlying the liver (characteristic).* **Subacute form:** no fever, no jaundice, +ve anemia 

(DDx: Pyogenic liver abscess, infected hydatid cyst, HCC, congestion "eg. Congestive HF and budd chiari"),

The abscess is sterile with low neutrophils.

*** Pseudo abscess:** because of the peripheral neutrophilia.

Difference from pyogenic abscess:

1. Not offensive
2. Anchovy-sauce color
3. Sterile from bacteria

****Risk of rupture of the abscess:** in the Pleura causing empyema, in the Bronchi causing hepatobronchial fistula, in Peritoneum causing peritonitis or in Pericardium causing tamponade.

Most common sites of rupture are those in the lung. & the most dangerous is the pericardium causing cardiac tamponade (most common in left lobe abscess)

2- Cerebral amebiasis: Abscess

3- Cutaneous amebiasis: Rupture of ALA > fistula or extension from rectal colitis

4- Genitourinary amebiasis: Renal & Genital Ulcers

Dx:

-For amebic colitis:

- Stool examination for microscopy & culture looking for cysts and **trophozoites containing RBCs.**

  Others: Ag & Ab detection by ELISA. PCR

- For amebic liver abscess:

1. CBC for neutrophilia,
2. Imaging: US: hypo echoic mass / CT: ring enhancing mass
3. Serology.
4. We can also use diagnostic aspiration (anchovy paste) (not used) [Differentiate it from pyogenic abscess]

N.B (Only less than 50% of people with Amebic liver abscess have positive abscess, 1/3 may got active disease)

Rx:

- **Luminal Amebicidal (kill cysts**): Paromomycin, Dinuoxnide Furate and Iodoquinolones.
- **Tissue Amebicidal:** metronidazole and tinidazole

*In Rx of amebic colitis and amebic liver abscess give tissue amebicidal followed by luminal amebicidal *Rx of carrier is by luminal

- ❖ Indications of therapeutic aspiration: 1. large cyst (more than 10cm) 2.left lobe abscess 3.failure of medical treatment.

Shigellosis

Bacillary dysentery

Difference between amebic and bacillary dysentery:

- Pt is **toxic, ill**
- WBCs highly elevated
- Pathogenicity is due to shigatoxin that's why bloody diarrhea is preceded by watery diarrhea.
- Diarrhea is of acute onset
- Odorless stool (offensive in amebic)
- Alkaline diarrhea (amebi**c** is acidi**c**)
- Can present with meningism or other CNS Sx in children
- Shigella has a low infective dose (ie; resist acidity of stomach)

Two peaks: children and elderly

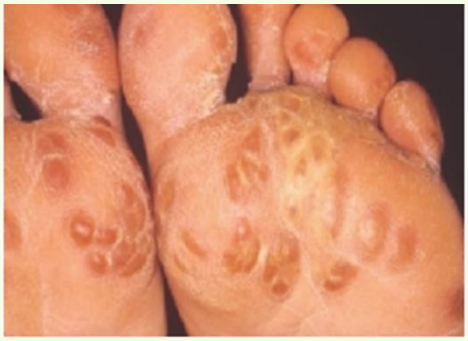
** In Children may present with features of meningism, CNS sx e.g. convulsion

May also cause fulminant colitis

Complications:

- **Local**: Perforation, toxic megacolon, intussusception or rectal prolapse (ie; ↑peristalsis)
- **Others:**
- **Rietter's syndrome:** conjunctivitis, urethritis and arthritis
- **Hemolytic uremic syndrome (HUS):** microangiopathic hemolytic anemia, AKI and thrombocytopenia. If plus + fever and neurological Sx that is Thrombotic thrombocytopenic purpura (TTP) treated by plasma exchange.
  -treatment of HUS is supportive.
- **Keratodermopleomerroghica:** keratinization of dermis + mucoid discharge. +/- Rietter

Keratodermopleomerroghica



Dx: stool examination for microscopy and culture

Rx: ciprofloxacin

Typhoid

Enteric Fever:

- Typhoid fever → Salmonella typhi
- Paratyphoid fever → Salmonella paratyphi A,B,C

Orofecal transmission.

Source: Only from human

Differentiate from shigella by its sensitivity to HCL.

Outcome of infection depends on:

1. Virulence of the organism(Vi antigen),
2. Infective dose
3. State of acidity (that is why it is higher in NSAIDs use and in gastrectomy pts).

Intestine→ Mesenteric lymph nodes→ blood (primary bacteremia)→ RES (10-14 days I.P.) {Incubation period} blood (secondary bacteremia)→any organ

2 important sites: 1. Gallbladder: cholecystitis & carrier

2. Peyer's patches in T.ileum: ulceration & perforation

Clinically:

Week 1 "week of Symptoms":

Fever, headache, myalgia and **constipation.**

Week 2 "week of signs":

- Fever (stepladder) with relative bradycardia "Faget's sign",
- Splenomegaly,
- Rose spots [in 50%](in lower chest and upper abdomen,
- Epistaxis (the only symptom)

Week 3 "week of complications":

- Delirium, affect the heart (basal Crepitations) and constipation changes to diarrhea (pea soap stool →green)
- Causes of death:

  1- Toxemia **#1**

  2- Myocarditis

  3- Local complications (bleeding and perforation)

Week 4 "convalescence":

Recovery: still intestinal complications can occure.

N.B: Salmonella resides in schistosoma [concomitant immunity] > prolonged fever (Schistosalmellonsis)

2 main problems in typhoid:

1- ***Relapses in typhoid:***

- Common: 10 -20% of tx. Pts! When? 1 – 3 weeks after Tx.
- Culture is positive while the ABs are high
- Milder than 1st attack. Quinolones ↓relapses

2- ***Carriers:***

- Fecal carriers: bacteria is in liver and gallbladder
- Urinary carriers: bacteria in bladder (less common)

Complications:

- **Intestinal:** Bleeding and perforation [↓Temp, ↓ BP]
- **Liver:** Hepatitis; GB: cholecystitis. Pancreatitis
- **CNS:** Acute confusional State / Psychosis [in convalesnce]
- **Cardio:** Myocarditis
- **Resp. :** Bronchopneumonia / Lobar pneumonia / bronchitis
- **Hem. :** DIC **&** Hemolysis with G6PD
- **Kidney:** Nephrotic Syndrome "with schistosoma"
- **Abdominal Muscles:** Zenker's degeneration of abdominal muscles
- **Bone:** osteomyilitis

Dx:

- **Blood:**
- **CBC for leukopenia**; anemia[normo normo]; mild thrombocytopenia
- **LFTs**: moderate increase
- **RFTs**: Mild proteinuria
- **Specific**:
- Isolation of the organism from **blood culture or bone marrow (better) culture** " in second week we can do urine culture and in third week we can do stool culture"
- Serology for Widal test: either high titer or rising titer

  Abs against O Ags [earlier > few months] & H Ags [later, longer period]

  False negative: in case of starting treatment, low immunity or simply in first week
  False positive: vaccination, past infection with other salmonella infections

Rx:

- Supportive: Admission; rest; soft diet; safe excreta disposal
- Antibiotics:

➢ **Ciprofloxacin for 14 days**

-Adv.: (Decrease relapse; effective against resistance. ** fever subsides in 3 -5 days.

-CIs: 1. pregnancy and children (affects cartilage) 2. elderly (tendon rupture "Achilles")

3. epileptic pts (decrease seizure threshold)

- Tx of carriers: Ciprofloxacin for 4 weeks.

➢ 3rd generation cephalosporin: IV except cefexime; can be used.

➢ in Pregnancy: Ampicillin/ amoxicillin

➢ Chloramphenicol: not used any more. Increased relapses and resistance.
Causes bone marrow aplasia and grey baby syndrome

❖ **Indications for steroids in typhoid:**

- CNS manifestations
- DIC
- Shock

N.B. Cholecystectomy is of no benefit in treatment of fecal carrier state.

Vaccines:

1- Killed vaccine: IM or S/C

2- Vi capsular vaccine: IM or S/C

3- Life attenuated vaccine: oral

**Immunity against typhoid is mainly cellular-mediated **

Malaria:

- **Cause is plasmodium:**
  - Plasmodium falciparum: malignant tertiary malaria
  - Plasmodium ovale and vivax: benign tertiary malaria
  - Plasmodium malarie: Quarten malaria

- Transmission through *female anopheles mosquito*
- Needs reservoir, adequate temp. (13-29)& high humidity
- Others are congenital & Blood Transfusion

  - Sexual cycle in mosquito
  - Asexual cycle in human (the intermediate host)
  - Sporozoites are the infective stage.

Two cycles for Sporozoites:

1) This is common between the four species:-
- sporozoites enter the liver (pre-erythrocytic schizogony, schizonts) rupture →releases merozoites in blood and → enters RBCs (where it is called erythrocytic schizogony).
- Here the duration taking the RBCs to rupture and release merozoites is the definer of the type of malaria (48 hrs = tertiary ... 72 hrs = quartan)

2) This is only for ovale and vivax→ Exoerethrocytic schizogony which gives the hypnozoites.

- Fate of merozoites: either the asexual cycle continues or they change into male and female gametocytes which are then ingested by the mosquito
- So infective stage for mosquito is gametocytes.

The most dangerous malaria is that of falciparum because of:-

1. Heavy parasitemia (increased number of merozoites)
2. Infect RBCs of different ages. (Vivax and ovale infect young RBCs (reticulocytes), malarie infect Old RBCs)
3. Cytoadherence (attachment if the RBCs to the endothelium), rosetting (attachment of infected RBCs to non-infected RBCs) and clumping (attachment of infected RBCs to other infected RBCs).

- Endemicity of malaria is measured by rate of splenic enlargement in children population; if less than 10% hypoendemic, 11-50% mesoendemic, 51-75% hyperendemic and more the 75% is holoendemic.

- **Natural Resistance to malaria:**

- Sickle cell trait (not disease)
- Thalassemia
- G6PD deficiency
- Duffy coat antigen negative (resistance for vivax as this Ag is the receptor for vivax)

- **Relapse:** Due to hypnozoites. Occurs in vivax and ovale.
- **Recrudescence**: all species but mainly falciparum. Due to inadequate treatment or inadequate immunity (incomplete clearance)

Clinically:

- 3 stages: cold stage (vasoconstriction, pale and increased BP and weak thready pulse), hot stage (vasodilation, hot and flushed, drop in BP and full volume pulse) and sweating stage.

**They don't really occur in real practice.

- **C/O in immune/Partially immune individuals:- Non-specific sx:**

  - Herpes Labialis, Tachycardia/Hypotension
  - Liver soft enlarged tender
  - Spleen soft enlarged tender after 10 days
  - Blood: anemia/ Leukopenia with relative lymphocytosis
  - Kidney: proteinuria/ Hyaline granular casts / ARF

N.B. Leukocytosis is Poor Prognosis
N.B: Causes of Anemia: 1) RBCs destruction in merogeny 2) BM suppression
N.B: Causes of Hypoglycemia: 1) Impairment of Gluconeogenesis "most important"
2) ↑ Glucose consumption by "Host/Parasite" 3) Quinine Effect

- Severe malaria is more in *Non immune, Non-Tx, or Partially Tx. And Heavy Parasitemia*.
- *Heavy Parasitemia: 5% of RBCs infected; >10% of them has >1 parasite; schizonts in peripheral blood*

Criteria of severe malaria:

1. **Head:** 1. Decreased level of consciousness (may reach unarrousable coma)
   2. Multiple convulsions (more than 2 in 24 hrs)
   3. Frustration (severe weakness pt unable to stand).
   [These are Sx of cerebral malaria].
2. **Eyes:** clinical jaundice.
3. **Mouth and nose**: abnormal spontanous bleeding
4. **Lungs:** ARDS (rapid deep acidotic breathing, or pulmonary edema by CXR).
5. **Kidneys:** creatinine more than 265. Or oliguria.
6. **Anemia**: Hb < 5 g/dL; / Macroscopic hemoglobinuria. HCT <15% + Parasite >10000
7. **Heavy parasitemia** (parasites infecting more than 5% of RBCs).(2% in non-endemic area)
8. **Hypotension**: systolic less than 70.
9. **Hypoglycemia:** glucose less than 40 (because the parasite is in the liver and can inhibit gluconeogenesis and also there is increased consumption of glucose. Quinine therapy also causes hypoglycemia).
10. **Lactic acidosis**: bicarbonate less than 15 or lactic acid more than 5. (Either due to anaerobic glycolysis, production by the parasite or decreased metabolism and clearance of lactic acid).

<u>Diseases:-</u>

1) Cerebral malaria:-

- Frustration, unarrousable coma and convulsions (generalized tonic clonic)
- It is a diffuse symmetrical encephalopathy (i.e. Focal neurological deficit is <u>rare</u>).
- There are no signs of meningism
- A characteristic feature is *absent superficial abdominal and Cremasteric reflexes.*
- Tone, Reflexes and Plantar response are variable Increased or decreased.

2) GI malaria:-

I. **Bilious remittent fever**: remittent fever (remit but doesn't reach baseline)
   - Hepatomegaly & jaundice + nausea and vomiting [coffee ground, bile]
   - Hepatic coma and fluid loss (causing kidney injury or shock) are the causes of death.
   - D.Dx: is Yellow Fever

II. **Dysenteric malaria:** Fever, epigastric pain, nausea and vomiting, and bloody diarrhea (red currant jelly stool)

III. **Choleric malaria**: fever, epigastric pain, nausea and vomiting, and profuse watery diarrhea / dehydration.

- Cause of death in coleric and dysenteric malaria is fluid loss (Shock) and ARF.

3) Algid malaria:- *(D.Dx is Acute adrenal insuffienicy)*

- Malaria + Sudden onset hypotension: shock (systolic less than 70)
- Most probable cause is gram -ve septicemia associated with malaria or spontaneous.
- Usually occurs during mild attack of malaria.

4) Black water fever:- ***ARF + Hburia(Black urine)***

- Hemoglobinuria due to severe intravascular hemolysis or due to quinine therapy (especially if given to pt with G6PD defficiency).

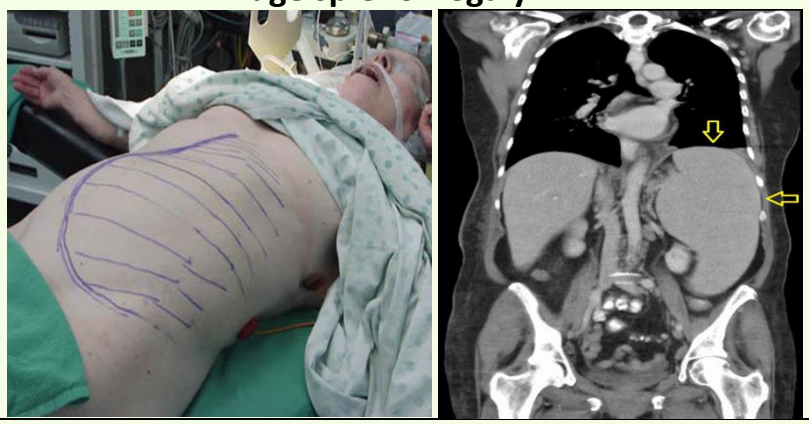
Chronic complications of malaria:-

1. **Hyper-reactive malarial splenomegaly syndrome: (Tropical Splenomegaly sX)**
   - Massive Splenomegaly (more than 8cm or reaching umbilicus) + positive IgM antibodies and negative blood film.
   - Pancytopenia due to massive spleen & -ve blood Film.
   - Death due to overwhelming sepsis.
   - Tx. Is with Antimalarial for life. Splenectomy if medical failed or severe hypersplenism

"N.B" - Causes of massive splenomegaly:

HMSS, kalazar, myeloproliferative disorders (CML), myelofibrosis, portal HTN. Brucellosis?

Huge splenomegaly DD



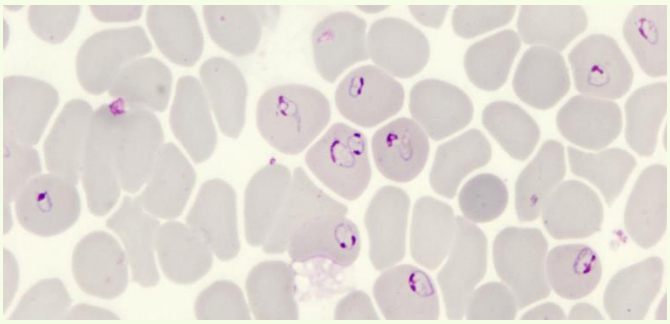
2. ***Quarten malaria*** **nephrotic syndrome:**
   - FSGS: nephrotic syndrome; hepatosplenomegaly (Antimalarials/ Steriods is of no use)

Dx:

1. **Thick blood film** by Giemsa stain to see whether there is a parasite or not
2. **Thin blood film** by leshman stain to see which parasite and how much parasites are there.
   - Falciparum: more than one ring trophozoite per RBC and banana shaped gametocytes.
3. Other method of Dx is ICT (for Ags or Abs) but usually done for screening.

N.B: if BF –ve and still suspicious = repeat up to 3 times, if still do BM biopsy.

Malaria blood film



Management:

NOTE: This section is updated according to "Sudan Malaria Treatment Protocol 2017"

Uncomplicated malaria:	Severe malaria:
○ **P.falciparum:** **First line: *Artemether + Lumifantrine (AL) (Quartum)*** **Second line: *Dihydroartemisinin + piperaquine (DHAP)*** **Alternative to second line *oral quinine*** ○ **P.vivax: *AL* followed by *Primaquine.***	○ ***IV Quinine OR Artesunate*** (if not accessible → IM Quinine OR Artesunate suppositories) - Drug which act on hypnozoites: ***primaquine*** - Gametocytes: ***primaquine*** - In first trimester **Pregnancy**; the first line in uncomplicated malaria is oral quinine (Avoid aretemisinin & mefloquine.) - In 2nd and 3rd trimesters it is similar to the usual regimen.

SEs of drugs:

- ***Quinine***:
    1. Cinchonism (deafness or tinnitus, disturbed vision, nausea and vomiting)
    2. Hypoglycemia (due to induction of insulin)
    3. Cardiac toxicity (can cause long QT syndrome)
    4. Black water fever (in pts with G6PD deficiency). Quinine is given IV with fluids (dextrose or normal saline)

**The only quinine contraindicated in pregnancy is halofantrine

- ***Chloroquine:*** pruritus, corneal & retinal deposits. Used in SLE, RA, ALA.
- ***Mefloquine:*** used as prophylaxis in sickle cell anemia pts. Doesn't have interactions in G6PD pts (unlike most other antimalarials). Mefloquine is cardiotoxic.

N.B. Be aware of using quinine after mefloquine prophylaxis (severe cardiotoxicity).

Visceral Leishmaniasis – Kalazar

- Cause is *Leishmania donovani* (sub-species in Sudan is leishmania donovani Donavan)
- Kalazar is a zoonotic disease except in India (where there is a large parasitemia) where it can be human to human.(can be diagnosed by blood film!)
- Vector **is female sand fly**; it is a night flier and it doesn't reach high altitude (so you can protect yourself by sleeping upstairs!!)
- Species of the sand fly: **in Sudan (old world); phlepotomas**. Outside (new world); luxomia.
- **Other modes of transmission:** congenital; blood transfusion; sexual.
- There are two forms of the parasite
  1- Promastigote: in culture and vector (in environment)
  2- Amastigote: in the human or animal (in the host).

Clinically:

- 100% of pts have fever: **fever intermittent and weight loss despite good appetite " حمى أم قدح"**
- Infiltration of RES causing **splenomegaly and hepatomegaly**.
- The splenomegaly (hypersplenism) can cause pancytopenia (bleeding, infections and anemia).
- There is also **lymphadenopathy painless (*epitrochlear lymph node enlargement is characteristic for kalazar)***
- **Edema (eg. Ascites**) in kalazar pts is usually due to malnutrition (decreases protein). Other cause of edema in kalazar is the protein losing enteropathy.
- The tongue is clean in kalazar

(Usually the tongue is clean in parasitic infections while coated in bacterial infections).

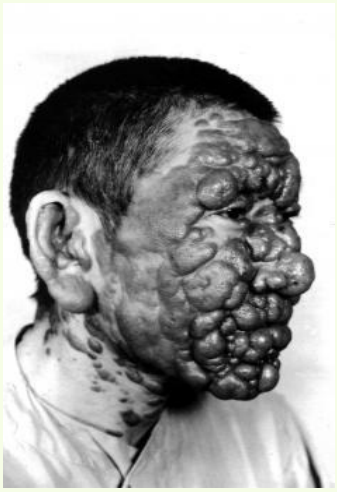
- Cause of death in kalazar: #1 ***is secondary bacterial infections***
  Following cause is ***bleeding.***
  N.B: Kalazar is gradual onset; with 2-6 months IP [Acute toxic is rare]

Complications of kalazar:

1. Secondary Infection:
   - Chest: TB/Lobar pneumonia
   - GI: Amebic /bacillary dysentery
   - Children: cancerum oris [التهاب الفم]
2. Bleeding
3. Anemia
4. PKDL: post kalazar dermal Leishmaniasis

- **PKDL:**

- Lesions in the face, usually occurring after kalazar but may occur during the disease (DDx is lepromatous leprosy and neurofibromatosis)
- Significance of PKDL is that it may act as a source of transmission of the infection.

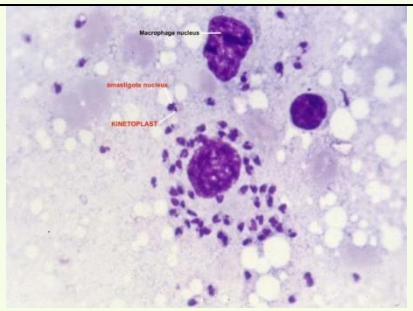


Dx:

- **CBC**: pancytopenia WBCs<4000 in 90% [↑WBCs is due 2ndry infections]
- Hypergammaglobulinemia by **formal gel test.**
- 3 figures ESR (DDx pulmonary TB, connective tissue diseases, multiple myeloma and nephrotic syndrome)

- **Demonstration of Parasite:-**

- LN Biopsy / BM / Splenic aspirate [Either most sensitive or specific is splenic (but there is a high risk of rupture)].
- The practical one & done in Sudan is the **epi-trochlear LN biopsy.**
- Biopsy from the RES looking for Leishman Donovan bodies or amastigotes.
- We can do culture in triple N (nickole- novie- Mc Neel) media.



Visceral Leishmaniasis- LD bodies

- **Serology**: DAT (good test), **RK39 detection test (best field test). RK 28 [new]**
- **N.B** Leishmanin test is –ve

Treatment:

- Antimony compounds: **sodium stibogluconate (Pentostam**) and negleomine Antimonate
- In the past the treatment was IV injections of Pentostam for 28 days
- Then changed into ***IV Pentostam + Paromomycin for 17 days***
  [↑renal toxicity; Anaphylaxis like reaction; toxic effect at end of tx; cardio Hepato toxicity (monitor by ECG daily); Pancreatitis]
- Liposomal amphotericin B [Less renal toxicity than Amphotericin]
- **Miltefusine (the only oral drug);** cytotoxic drug used for Breast Ca deposits in skin; not used in females of child bearing age
- Pentamidine

Response to treatment:

1. Fever subsides in 5-7 days.
2. Hematological indices return to normal in 1-2 months.
3. Normalization of albumin globulin ratio in 3-6 months.
4. Leishmanin test becomes positive in 3-6 months.

- ✓ In HIV Pt: check BM for parasites
- ✓ Failure of response is by Resistance or immunosuppression

Leishmanin test:

- Cutaneous Leishmaniasis: good immunity; positive test.
- Mucocutaneous: immunity decrease
- Visceral Leishmaniasis: poor immunity; negative test.
- In PKDL: immunity has returned; positive test.

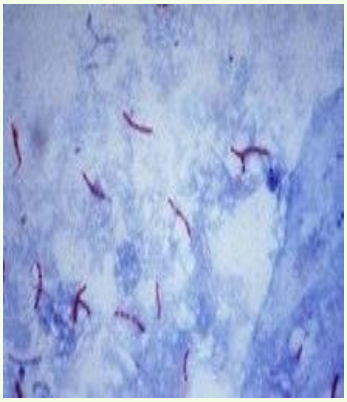
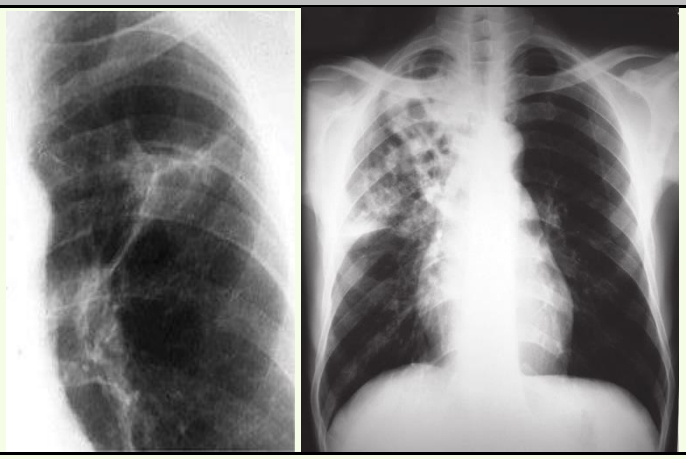
Tuberculosis

Pathogenesis:

- Caused by *Mycobacterium Tuberculosis*
- Methods of transmission:
  - Inhalation of droplets (common).
  - Ingestion of infected milk.
- Sites of primary TB: lung (inhalation), tonsils and intestine (ingestion).

Primary TB:

- Bacteria is inhaled to sub-pleural alveoli and attacked by alveolar macrophages and T cells causing granuloma and forming Ghon focus, it forms Ghon complex when it reach the draining lymph node.
- Usual location of primary TB is upper part of the lower lobe or lower part of the upper lobe.
- Primary TB Clinically: either asymptomatic (commoner) or symptomatic with allergic manifestations
- **Allergic manifestations**: fever, erythema nodosum, phlectinular conjunctivitis and pleural effusion.
- **Fate of primary TB**: either healing by fibrosis calcification or becoming dormant (latent
- TB), or progressive primary TB.

ZN stain	Ghon complex
	

Progressive primary TB: either:

- TB spread by bronchi causing bronchopneumonia.
- Spread to hilar lymph nodes causing enlarged LNs obstructing the bronchi (partially causing wheeze or completely causing atelectasis).
- Spread to the pleura causing pleural effusion.
- Spread through blood causing milliary TB.

"**N.B**" the most common form of pleural effusion is the allergic form; That is why if you find tuberculin test negative in a pt with pleural effusion you should exclude TB, as the immunity should be normal in allergic phase"".

Dx of primary TB:

- **CXR:** ghon's complex
- **Tuberculin test:** turns positive after 6-8 weeks.
- No sputum examination (there is no cough).

The primary TB pts then may either have reactivation (in countries where TB is not common) or reinfection (like in Sudan). Both are called secondary or post primary TB

Post primary or secondary TB:-

Either pulmonary or extrapulmonary

- **Pulmonary:**
  - Immune system has already encountered TB before that is why the immune response is aggressive.
  - This response results in cavitations and erosions reaching bronchi and causing cough (sputum positive).
  - Here the pt is infective.
  - It affects upper lobes.
  - Clinically: the classical presentation; fever, cough, weight loss, hemoptysis.
    It can also spread heamatogenously and cause milliary TB.
  - In post primary TB the immunity is good that's why the bacteria is localized to the lung and doesn't involve the lymph nodes (no lymphadenopathy).

"**N.B"** Think of TB in any pt with pyrexia of unknown origin (fever more than 3 weeks), chronic cough or any patient with non-resolving pneumonia""

N.B "Clubbing in a TB pt: either TB has caused empyema or bronchiectasis"

Dx:

- **Sputum examination**:
  - Microscopy by ZN stain or better by auramin stain...
  - Culture by Lowenstin jensin (LJ) media which takes 6 weeks or in BACTEC media which takes 2 weeks.

- **CXR**: you might find cavitations, consolidation, collapse, or pleural effusion, these indicate active disease. Fibrosis and calcification indicates old TB

- **Tuberculin test**: the problem is that it doesn't differentiate between active infection and latent infection.

N.B. Causes of false positive tuberculin test: Vaccination and infection by other mycobacteria""
False negative: immunosuppression and miliary TB, and also in early disease""

- **Interferon gamma release assay "Quanteferon":** in vitro, WBCs of the pt are exposed mycobacterium tuberculosis if they release IFN gamma that means that they have encountered them before.
- It doesn't react to vaccine proteins or to other mycobacteria so it is more accurate and avoids the causes of false positive tuberculin test.

- **ESR** is high (3 figures).

- **CBC**: anemia.

Extrapulmonary:

- Anywhere in the body: Pott's disease, meningitis, adrenalitis, skin, LNs,
- And can enter blood from any organ causing miliary TB.

Miliary TB:

- Mainly in children.
- Can occur after any of the previous forms.
- Bacteria spread through blood and cause miliary shadows in all organs.
- Clinically: classical symptoms (but usually cough is not present)
  - meningism
  - hepatosplenomegaly and lymphadenopathy +
  - choroid tubercles in fundal examination in children.

Dx:

- **CXR:** miliary shadows
- **Tuberculin test**: negative
- **Sputum**: usually not helpful as there is no cough.
- **Liver or bone marrow biopsy** to isolate the organism (instead of sputum) and do the sample tests from it (microscopy, culture)

Cryptic miliary TB:

- Mainly in elderly
- There are no chest symptoms so **sputum** Examination is not of use
- No choroid tubercles
- **CXR** is normal (no miliary shadow)
- **Tuberculin test** is negative
- Hard to detect
- Present with fever and weight loss
- You can do liver or bone marrow biopsy to isolate the organism
- Cryptic miliary TB is very fatal.

Management of TB:

Drugs:

- Most of the Mycobacterium bacilli are actively dividing: these are targeted by isoniazid (kills more than 90% of the bacteria).
- Some killed only by acid: pyrazinamide (it is an acid).
- Others have erratic behavior: targeted by rifampicin.
- Calcified bacteria do not need treatment.

- So the best bactericidal drug is ***isoniazid.***
- The best resistance preventer is ***isoniazid.***
- The sterilizing drugs are ***rifampicin and pyrazinamide.***
- The bacteriostatic drug is ***ethambutol***.

Case definition of TB:

- **Pulmonary TB:** divided into smear positive and smear negative.
- **Extrapulmonary TB:** divided into those with extensive diseases and those who don't have extensive disease.

Relapse VS defaulters VS treatment failure:

- **Relapse:** occurrence of the disease after adequate treatment.
- **Defaulters**: started treatment but stopped.
- **Treatment failure**: no response to treatment.

Categories of TB:

Category 1: The severe

- Smear positive pulmonary TB
- Extensive extrapulmonary TB
- HIV pts

Category 3: The mild

- Smear negative pulmonary TB
- Not extensive extrapulmonary TB

Category 2: pts who encountered the treatment before

- Relapse
- Defaulters
- Treatment failure

Category 4: drug resistant

- Multidrug resistant (MDR).
- Extensive drug resistant (XDR).

MDR: resistance to isoniazid and rifampicin or resistance to three drugs.
XDR: resistant to MDR (INH & Rif) + quinolones + aminoglycosides (eg, streptomycin) + one of the injectable second line drugs (eg, Amikacin).

Category 1 and category 3 are treated the same:

- (4x2)+ (2x4)
- Total is 6 months
- Initiation phase *INH, Rifampicin, Pyrazinamide and Ethambutol* for 2 months.
- Continuation phase by *INH & Rifampicin* for 4 months.

Category 2:

- (5x2)+ (4x1) + (3x5)
- Total is 8 months.
    - *INH, rifampicin, pyrazinamide, ethambutol and streptomycin* for 2 months.
    - Then withdraw streptomycin (nephrotoxic) and continue with the four drugs for 1 month.
    - Then withdraw *pyrazinamide* and continue with *INH, rifampicin and ethambutol* for 5 months

Category 4:

- Treatment is individualized.

N.B. Treatment is given by DOT method (direct observational therapy)

Monitoring:

- By sputum examination at end of initiation phase (2 mon), after 5 mon and after end of treatment.
- If pt was smear positive in 2 months and again smear positive in 5 months this is treatment failure.
- If the pt was smear negative and changed smear positive at any stage (2 or 5 months) this is also treatment failure.
- If the pt took treatment and completed the 6 months but didn't showed after the 6 months for sputum examination, this is called "received successful treatment" but you can't say "cured" as you didn't do the last sputum examination.

Special problems in TB:

- **Pregnant ladies**: streptomycin is contraindicated.
- *Streptomycin and ethambutol* are the two drugs that affect the kidney but are also the two drugs which are not hepatotoxic.
- **In pt with renal failure**: avoid streptomycin. Ethambutol is either given in smaller dose or used with regular monitoring
- **If pt developed hepatotoxicity**: first thing is to stop all drugs until there is no jaundice, bilirubin normal and enzymes normal (till clearance of disease). Then you have two choices: either you introduce all drugs at full dose or introduce one by one.
- **Hypersensitivity reactions of the drugs**: it is a spectrum: erythema multiforme, Steven Johnson (worse) or toxic epidermal necrolysis TEN (the worst).
- In pt with hypersensitivity reactions; stop all drugs until the pt is normal and then introduce one by one gradually to see which one is causing the hypersensitivity (don't introduce them all together)

TB and HIV:

- TB is a febrile illness. Fever increases replication of the virus and make the disease worse.
- HIV reduces immunity and cause severe TB as the immunity is reduced. TB here is also non-classical. But the response to drugs is fortunately normal.
- "" any pt with TB (kalazar also) should be tested for HIV""

Indications of steroids in TB

- Definitive indication is replacement therapy in pts with TB adrenalitis
- Non definitive: TB laryngitis (to prevent edema), serosal membranes (eg, pericarditis and pleural effusion), genitourinary TB (to prevent healing by fibrosis and loss of fertility), TB lymphadenitis,TB meningitis and hypersensitivity reactions.

Brucellosis

(Malta Fever/Indulent Fever)

****N.B. This Topic was written from Dr.MUSA M. KHAIR lecture record****

Species:

*Aerobic gram –ve bacilli or coccobacilli ,not motile, do not form spores

- B. abortus [cattle]
- B. Miletensis [goats/sheeps/camels]
- B. suis [pigs] -B. canis

Transmission:

- Zoonosis: "Direct contact / Inhalation / **ingestion of raw milk #1**"
- Others: congenital / Blood transfusion/ Labs/ cut wounds

**↓gastric acidity & ↑infectivity

C/O: Acute .v.s Chronic [>1yr] (Incubation period 2-4 weeks)

- **Acute:**
  - Step ladder fever
  - Perfuse sweating(DDx;Lymphoma)
  - Splenomegaly; hepatomegaly; Lymphadenopathy,pneumonia …etc

- **Chronic:** > 1 yr

  Complications:

  1. **Neurobrucellosis:** remember Depression + suicide (↓evidence)
     CN palsies (2,6,8)

  2. **Joints/Bones:** Lumbar spine / Sacroiliac joint → Sciatica
     tender spine (due to vertebral destruction and new bone formation)

  3. **Heart:** IE "Fatal" .

N.B;

- Not cause of Female infertility.
- All age groups can be affected.
- Intracellular organism → cellular immunity → non caseating granuloma

Causes of Death:

- IE "84%"
- Suicide
- Liver cell failure

Dx:

- Blood Culture: +ve 70% in B.meletnsis. 50% in others
- CBC “Anemia, WBCs “relative lymphocytosis””
- LFT: ↑ ALP, Slight ↑ in transaminases; ↑ globulins

Specific:

- Isolation in Blood or **Bone Marrow [90% sensitivity]**
- Immunology:
  - ✓ Widal Test: (IgM agglutination), maybe –ve by prozone phenomenon
  - ✓ Mercapto-ethanol (IgG agglutinin) +ve at lower titer
  - ✓ Antihuman globulin (Coomb’s Test) – non-agglutinin
    - Doesn’t differentiate between recent & past infection
    - ELISA / PCR

N.B: Hepatosplenic calcification: characteristic for Brucella

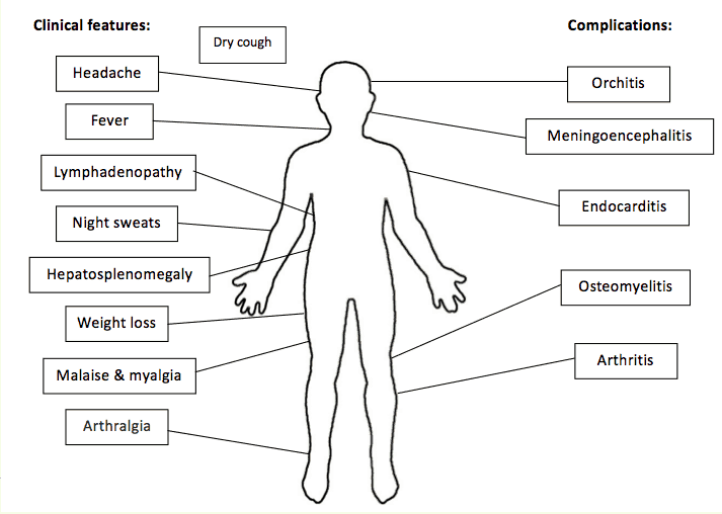
- ❖ X-ray → Snaw flack calcification in spleen “Pathognomonic”

Tx:

- Should be in combination
- **BEST** according to WHO→ Doxycycline + Streptomycin (1^{est} 3weeks combination, 2^{end} 3weeks doxy. Alone)
- if **Neuro. OR Skeletal manifestation** same combination for 12 weeks
- If **Endocarditis** : + 3^{ed} generation cephalosporin +/- valve replacement
- **Children** : Rifampicin + Cotrimoxazole
- **Pregnancy**: Rifampicin alone for 6 weeks (1^{est} trimester), if passed : Rifampicin + Cotrimoxazole

N.B.: Streptomycin > IM ; painful / Doxycycline > oral , after food with ↑water ie; irritant

N.B.: treatment can cause Jarisch-Herixheimer Reaction; tx by steroids.



Contents

GIT 1 (Esophagus; Dyspepsia; Malabsorption; IBD)

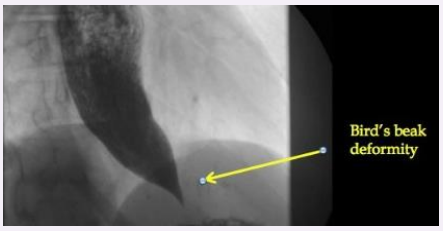
Esophagus:

GERD:-

- ***Def***: Reflux of gastric contents to the esophagus causing severe Sx affecting life or complications.
- **RFs**: sliding hiatal hernia (*the other type of hiatal herial is paraesophgeal*)
- **Clinically**:
  - **Esophageal Sx:** heart burn (increased with bending forward and after meals; decreased by antacids) / regurgitation (lead to acid brash) → water brash (*caused by excessive salivation)*
  - **Atypical Sx:** asthma (in severe resistant case → treat the GERD first) / hoarseness (laryngitis) (acid reach the laryngeal) / teeth decay *(acid reach the teeth)* /chronic bronchitis / chronic sinusitis
- **Complications:** reflex esophagitis (causing odynophagia), / peptic stricture due to fibrosis (causing dysphagia), / Barrett's esophagus (can change to adenocarcinoma)
- **Dx:** The gold standard is **24 hrs PH monitoring**
- **Rx:** life style modification (frequent small meals, no late meals, bed elevation, weight loss, avoid drugs and meals increasing GERD)
  - Antacids or PPIs
  - Nissen's fundoplication (S*urgery : wrap the funds of the stomach around the lower esophageal to act as a sphincter)*

Barrett's esophagus:	Achalasia:
Def: Metaplasia of the lower esophagus from stratified squamous to columnar epithelium **Rx: take biopsy -> (**_dysplasia)_** ○ **If low dysplasia: PPIs for 8-12 weeks** ○ **If high grade dysplasia: excision or cryotherapy**	**Def:** Failure of relaxation of the lower esophageal sphincter with absent peristalsis in the lower esophagus and increased resting lower esophageal sphincter tone → Due to absence of ganglia in the Auerbach's myenteric plexus. → (***Myenteric plexus → motility / Submucosal plexus → secretion*) - Dysphagia is for liquids at beginning (functional dysphagia), may start with both solids and liquids. - Risk for squamous carcinoma

Dx: Gold standard is **manometry** (absent peristalsis and increased lower sphincteric tone)
→ Grossly dilated esophagus proximally with distal smooth tapering (rat tale or bird beak appearance) on **barium swallow.**



Rx:

- first line: botulinium toxin injection
- Others: endoscopic pneumatic dilatation
- Surgery: Heller's cardiomyotomy + antireflux procedure (eg, partial fundoplication).
- Other medical treatments: Ca channel blockers and nitrates. (Not of use)
- (****avoid food** *that increase the reflux → coffee / chocolate / spicy food.*
- ***Avoid drug*** *that relax the LES → Nitric oxide / anticholinergic drug).*

N.B: Other Diseases diagnosed by manometry:-(Systemic Sclerosis & Diffuse Esophageal Spasm)

•Systemic sclerosis:	•Diffused esophageal spasm:
Either limited systemic sclerosis (CREST syndrome) 80% or diffused 20% **(*Limited means involve the face, neck, parts of legs and hands /Diffuse means reach the trunk).*** **** CREST Syndrome:*** ▪ **Calcinosis: calcified nodules in skin** ▪ **Raynaud's phenomena (**_cyanosis in peripheral parts with cold_)** ▪ **Esophageal motility disorder (**_replaced the muscle by fibrous tissue = no contractility_)** ▪ **Sclerodactily (**_fibrosis in digits_)** ▪ **Telangiectasia** **- On myometry: absent peristalsis + decreased LES tone.**	"Arrhythmia of the esophagus" (*Sudden uncoordinated contractions)* - Chest pain due to sudden contractures (**DDx**: angina) - Crock screw appearance on barium swallow - On manometry: abnormal contractures (may be normal during episodes)

❖ *Dyspepsia:-*

Def: Recurrent vague Sx ***involve***; abdominal pain, nausea, post prandial fullness, early satiety.

Causes:

1. Esophageal: GERD, esophagitis
2. Stomach: gastric ulcer, gastritis, gastric cancer
3. Duodenum: duodenal ulcer, duodenitis
4. Other organic causes.

- When these causes are excluded it is called *functional dyspepsia (non-ulcer dyspepsia) = (**main symptom)*

ALARMS *(Anemia (IDA); Loss of Wt.; Anorexia; Recent onset Symptoms; Melena or Hematemesis; Swallowing Difficulty)*

Treatment of patient with dyspepsia	
Age more than 55 years or ALARMED features	**Age less than 55 and no ALARMED**
Do endoscopy => (***suspect cancer)*** **NOTE:** ***(Dyspepsia + epigasteric mass => also for endoscopy)*** **ALARMED:** - **Anemia (IDA)** - **Loss of weight** - **Anorexia** - **Recent onset symptoms** - **Malena or hematemesis** - **Epigastric mass** - **Dysphagia**	• lifestyle modifications & antiacids and return after 4 weeks; • if still symptomatic *do H. Pylori test* • If negative *give PPI or ranitidine (H2 blocker)* • If positive *treat H. Pylori* ➢ *then return after 4 weeks* • *If not improved → **endoscopy***

- **H.pylori eradication therapy:**
- **Triple therapy (*Clarithromycin based therapy*) :** PPI + Clarithromycin + metronidazole or amoxicillin for 1-2 weeks
- **Quadrable therapy:** PPI + bisthmus + tetracyclin + metronidazole for 2 weeks.
  - Test for eradication every 4 weeks
- ***H.pylori associated disease:***
  1- **Duodenal ulcer** (+ve H. Pylori in 90% of pts)
  2- **Gastric ulcer, gastric carcinoma** and **gastric MALToma (**nonhodgkin's lymphoma) and **chronic gastritis type B** (atrophic gastritis).

NOTE: (MALToma = mucosal associated lymphoid tissue lymphoma
- **Acute gastritis presented as hemorrhagic anemic gastritis / caused by NSAID , Burn , Head trauma**
- **Chronic gastritis: type A (caused pernicious anemia) / Type B (caused by H.pylori)**

- **Diagnosis of H.pylori:** Best is biopsy and then invasive tests:

Invasive tests:	**Non-invasive tests:**
1- Culture (most specific) **2- Histology** **3- Urease**	2- Urea breathe test (used in monitoring) 3- Stool Ags 4- Serology (not good as ABs persist)

NOTE: *before urea breath test the pt should not be on ABs in the 4 weeks or PPIs in the past 2 weeks.*

- **Indications to start quadruple therapy before trial of triple therapy:**

1- Areas of high resistance
2- Renal transplant pts taking cyclosporine (due to interaction with clarithromycin)

- **Rx** of gastric MALToma is by treating H. Pylori.

Hodgkin's lymphoma	Non-Hodgkin's lymphoma
- Characterized by Reed Sternberg cells **- Localized to lymph nodes and presents with B symptoms: fever, night sweat, weight loss; that is why it is detected early.** **→ *just Nodal involvement***	- Affect other areas e.g. stomach (*MALToma)* and jaw (*burkets lymphoma*), doesn't present with B symptoms and that is why it is of poorer prognosis as it is discovered late. **→ *Extra-nodal involvement***

❖ *Peptic ulcer disease:*

Gastric ulcer	Duodenal ulcer
- Pain increases with food (*post prandial pain*) **- Patients have weight loss** **- Most common site of gastric is Antral lesser curvature**	- Pain increases with hunger (*most common*) - Most common site of duodenal is first part of duodenum - Aim of management is reducing risk of recurrent ulcers & healing the ulcer.

- **Causes:** 1. H.Pylori 2. NSAIDS
- **Complications:** (Post. Ulcer tend to bleed; ant. Ulcer tend to perforate)

1. *Bleeding* (posterior **Gastroduodenal ulcer**; Gastroduodenal artery), If bleeding from **gastric ulcer** then the artery is the left gastric artery.)
2. *Perforation* (anterior duodenal ulcer).
3. *Stricture* causing Gastric outlet obstruction.

NOTE: Refractory ulcer (*resistant ulcer after 2 treatments***):** more than 8 weeks if duodenal or more than 12 week if gastric

- This ulcer needs **endoscopy**
- **Causes** of refractory ulcer: non-compliance, bacterial resistance, malignancies, Zollinger Ellison syndrome.
- If these causes are excluded go for surgery → (*vagotomy)*

❖ Zollinger Ellison syndrome:

- Gastrinoma tumor secreting gastrin causing increased HCL secretion. Most common sites are duodenum and pancreas.
- Could be a part of **MEN1** (*multiple endocrine tumor type 1 → involve duodenum / pancreas / PTG)*

- **Clinically**:
  - peptic ulcer + diarrhea (due to increased acidity Defunctioning pancreatic enzymes causing malabsorption and hence diarrhea)
  - Refractory multiple peptic ulcers in unusual sites + diarrhea
- **Dx**:

✓ **Best screening test** is serum gastrin level; very high.

✓ **Best diagnostic test** is Secretin stimulation test (very high gastrin after secretin administration "Secretin decreases level of HCL").
(*Secretin normally secrete from S cell in duodenum → ↓HCL).*

✓ **Best test to localize** is Somatostatin receptor syntography (Cells secreting gastrin have somatostatin receptors).
(*The function of somatostatin is to inhibit Gastrin → So any cell secrete gastric should have somatostatin receptor)*

✓ **Others** to localize: CT or endoscopic US

- **Rx**: High dose PPI + octreotide until surgery

- Definitive Rx => surgery +/- chemotherapy

N.B: "Most common cause of elevated gastrin is hypo or Achlorhydria" so exclude before doing the test (*monitor the stomach PH → if high "alkaline" that means No acid due to achlorhydria)*

IBDs: (Chron's Disease & Ulcerative Colitis (UC):

Crohn's disease	**UC:**
All GI from mouth to anus, Mainly ileum	Only colon, Mainly **rectum**
Skip lesions	Continuous lesions
Macroscopic: Cobblestone appearance **Microscopic: Transmural -all layers - (fistula as a complication)**	**Macroscopic**: Pseudopolyps (*the area around is depressed*) **Microscopic** :Only mucosa and submucosa
(ulceroconstrictive disease) → stricture ***Incerease in goblet cell*** **(The hallmark is non-cascating granuloma, so intestinal obstruction one of the complications)**	(**ulceroinflammatory disease**) → crypt abscess Decreased goblet cells. (*Due to inflammatory factors that cause abscess and destruct the goblet cells)*
Clinically: watery diarrhea with intestinal obstruction + (*Weight loss*)	**Clinically**: bloody diarrhea with tenesmus (*sense of incomplete evacuation)*.
Imaging: string sign	**Imaging**: narrow short colon with loss of haustrations (lead pipe colon).
Smoking increase it.	Smoking is protective.
Complications: intestinal obstruction, malabsorption, fistula, Perianal disease and apthous ulcers	**Complications**: bleeding, perforation, toxic megacolon and colorectal cancer.

- **Extraintestinal manifestations:**
  - ✓ **Skin:** erythema nodosum, pyoderma gangrenosum.
  - ✓ **Eyes:** episcleritis, anterior uveitis, conjunctivitis
  - ✓ **Joints:** arthritis, ankylosing spondylitis, sacroilietis, osteoporosis
  - ✓ **Liver: Clubbing, PSC (Primary Sclerosing Cholangitis)**
  - Episcleritis, erythema nodosum, pauciarticular arthritis and osteoporosis → ***indicates activity of the disease.***
- **Precipitating factors for toxic megacolon:**
  1- Hypokalemia (*cause muscle weakness and increase the diltations)*
  2- Anticholinergics, antidiarrheal (both decrease the motility and aggregate the problem)
  3- Opioids
  4- Hypomagnesemia.

- **Treatment**

➢ **UC:**	➢ **Crohn's Mx:**
Acute Attack Classification of Ulcerative Colitis: **1- Mild: <4 bowel motions/day, with minimal blood loss** **2- Moderate: 4-6/day + moderate blood loss** **3- Severe: >6/day with fever, tachycardia, High ESR, low Hb and low albumin (*systemic feature)*** *** For mild and moderate:** **- 1st Line: 5- aminosalycilic acid (e.g. methalazine or sulphasalazine) → *topical (rectally)*** **- 2nd Line: Steroids.** *** For severe: *Resuscitation + IV steroids and topical (rectal) steroids + heparin(to prevent the risk of thromboembolism)*** *** Absolute indications for surgery (*Proctocoloctomy) are:* perforation, massive bleeding and failure of medical treatment.** *** Maintenance for UC is by 5- aminosalycilic acid (Methasalazine)**	- Dietary management (NG Tube or TPN); smoking cessation **- 1st line** is steroids **- 2nd line** is azathioprine o For chronic **Maintenance** by azathioprine / *stop smoking* o Perianal disease: metronidazole o Fistulating disease: infliximab.(anti TNF) **N.B.** If the pt is in maintenance therapy and he developed epigastric pain radiating to back think of **acute pancreatitis** due to azathioprine.

N.B: Risk Factors for developing CA colon in UC:

- Long standing colitis (more than 10 years).
- Started before 15 years of age. - Pancolitis - Non-remitting
- Noncompliance to treatment - Family Hx of ca colon.
- Associated PSC (Primary Sclerosing Cholangitis) **(very important in MCQs)**

Malabsorption:

- **Hallmark** is steatorrhea and weight loss *(also associate by VitA deficiency / hypoalbumenima / anemia)*
- Steatorrhea: bulky greasy offensive stool hard to flush.

➢ **Causes**:

1- **Pancreatic:** chronic pancreatitis, cystic fibrosis
2- **Biliary system**: biliary obstruction *(like PSC/ PBC)*, Ilial diseases (alteration of enterohepatic circulation).
3- **Bacterial overgrowth:** increase desaturation of bile salts.
4- **Intestinal (mucosal):** celiac, Whipple disease, tropical sprue, giardiasis, short bowel syndrome.

❖ Celiac disease:-

- Immunological hypersensitivity to **gluten** (*autoimmune disease)*
- An important **association** is dermatitis herpitiformis → (10% of pts with celiac disease have dermatitis herpitiformis (*vesicles in the knee)* ; all pts with dermatitis herpitiformis have celiac disease),
- Also associated with other autoimmune diseases *(DM , thyroid disease)*

- **Features:**

1- Steatorrhea, weight loss, features of vitamins deficiency,
2- Vit D: osteoporosis,
3- Vit K: bleeding,
4- Iron and folate: anemia,
5- Hypoalbuminemia,
6- Malnutrition,
7- Sub-fertility,
8- Growth failure (*short stature / delay puberty*).

- **Complications**: enteropathy associated T cell lymphoma (**_non Hodgkin) /_ and adenocarcinoma of small bowel.
- **Invx:**
  Serology**: Abs:**
    - Anti-tissue transglutaminase (anti-TTG IgA Abs) "**best**" (but can be negative as these pts are IgA immunodeficient → _false negative result_)
    - Anti endomysial IgA Abs
    - Anti gliadin IgA & IgG Abs
  - **Best test to diagnose** is biopsy (_from mucosa of the jujenum_) showing : villous atrophy, crypt hyperplasia and intraepithelial lymphocytosis(_T Cell - lymphocyte infiltrate lamina propria)_
- **Rx: gluten free diet.**

❖ Whipple disease:

- **Caused** by T. Whipple bacteria
- It is a **multisystem disease:** 1- _GIT:_ malabsorption, 2- _joint:_ arthritis, 3- _Skin_: hyperpigmentation, _4- LN_ -lymphadenopathy, 5- _CNS_ (occulomasticatory myorrythmia; **pathognomonic**→ _means nystagmus + arrhythmia in jaw & eye_)
- **Dx**: jeujenal biopsy showing lamina propria infiltration by PAS positive macrophages. (bacteria stain by PSA)
- CSF analysis → PCR
- **Rx**: IV penicillin or ceftriaxone for two weeks followed by Cotrimoxazole for 1 year.

❖ Tropical sprue:

- Pt went to **T**ropics and returned with malabsorption.
- **Rx**: **T**etracyclin for 6 months

❖ Bacterial overgrowth syndrome _(Blind blue syndrome) :-_

- _take place in the small intestine_
- **RFs**:
  - decreased acidity (eg, PPIs for long duration)
  - decreased motility (eg, scleroderma, diabetic neuropathy),
  - anatomical disturbances (small bowel diverticulae or blind loop) → (_cause stagnation for the flow of the secretions)_
  - coloenteric fistula.
- **Invx**: screening: xylulose or hydrogen breath test (double wave of CO2 _**the second wave result from bacteria of the small intestine & Co2 result from bacteria of xylulose_)
- Best is: jeujenal aspiration and send for quantitative culture (_quantities of bacteria)_

- **Rx**: empirical antibiotics

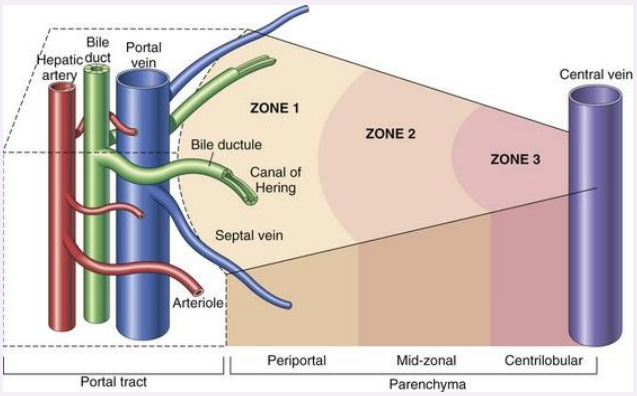
❖ Chronic pancreatitis:

Acute pancreatitis → fibrosis → destruction of exocrine and endocrine pancreas.

- **Clinically**: epigastric abdominal pain radiating to the back + Malabsorption (due to destruction of exocrine pancreas)
- If reached endocrine pancreas can cause diabetes
- Most important **cause** is alcohol intake.
- (Other **causes:** *cystic fibrosis / hereditary/ autoimmune)*
- **Dx**: imaging by CT or X-ray looking for calcification (*indicate chronic inflammation*)
- Then **test** for pancreatic function: decreased fecal *elastase* due to pancreatic exocrine insufficiency **Rx**: analgesia and enzyme replacement
-

GIT 2 (Liver)

Introduction:



- **Blood Supply of Liver:**

1- Portal vein 80% 2- Hepatic Artery 20%

- **Cells of Liver:**
  - Hepatocytes; Sinusoids "in the capillary"
  - Between them there is "Space of Disse" :
    → which contains Ito cells = fibrosis
  - Hepatic Lobule
- Central (Hepatic) vein & Portal Triad in the periphery (Hepatic Artery, Portal Vein & bile duct)
- **Zones of Liver:** Zone (1) = Periphery = High O_2 Supply
  Zone (3) = Central = Low O_2 Supply
- <u>Functions of Liver</u> Include: Metabolism of CHO, lipids & Proteins. Synthesis of Clotting Factors (1972). Storage of vitamins. Detoxifocation …etc

Liver Function Tests (LFT):-

1. **Functional tests:**
   *(**The liver function is to conjugate bilirubin and synthesize albumin)*
   - **Serum bilirubin** (with differential), (N: Total 0.1 – 1.2 mg/dL (3 – 20umol/L))
     Direct Less than 0.3mg/dL (5.1µmol/L)
   - **Serum albumin**: Half-life of albumin is 2 weeks so it <u>is *not used*</u> *to detect acute liver failure (N: 3.5 – 5.5 g/dL (35 – 55 g/L)*

2. **Enzymes**: **ALT & AST**
   - ALT is the one specific for the liver; When they are both increased → ***hepatitic LFT pattern*****;** except in Alcoholic Liver Cirrhosis AST>ALT
     ALT (7 – 56 IU/L) AST (5 – 40 IU/L) ALP (30-130IU/L)

3. **Other enzymes**: ALP & GGT
   Both are canalicular, so increased in obstruction → ***cholestatic LFT pattern. (Obstructive cholestatic pattern)***

N.B: **GGT** if increased Alone: Enzyme inducing drugs (rifampicin) and alcohol increases GGT without others.

4. **Clotting tests:**
   PT ; (INR): Used to monitor acute liver failure (half-life hrs to days)
5. **Imaging:** (US, MRCP, ERCP…etc)

6. **liver biopsy**:

CI for percutaneous biopsy are:

1- Deranged bleeding (Abnormal Bleeding Pattern):
   - INR > 1.4 (*N: 0.9-1.1 , INR measure PTserum/PTcontrol ratio*)
   - PT > 4 sec
   - PLT < 60,000 or 80,000
   - Substitute by trans-jugular liver biopsy

2- Ascites (*fluid make it difficult)*
3- Uncooperative pts
4- Hemangioma
5- Hydatid cyst
6- Biliary obstruction → (*biliary peritonitis*)

•**Non-invasive markers for liver fibrosis:**

1- Fibroscan (US shockwave)
2- Serology (eg, metalloproteinase)-> (***in fibrosis it secrete in blood in large amount)*

7. Hematological: CBC

(Normocytic normochromic anemia = recent GI Hemorrhage; Microcytic hypochromic = chronic blood loss; Macrocytosis = Alcohol)

N.B: Hypersplenism: Pancytopenia but Platelets are more depressed due to Decreased production. (No Thrombopoietin)

Liver injury is either acute or chronic

Injury	Acute Injury	Chronic Injury
Mild	Abnormal LFTs	Abnormal LFTs
Severe	Jaundice	Chronic Liver Disease (Cirrhosis) *(typically not associate with jaundice)*
Very Severe	Fulminant Hepatic Disease *(encephalopathy is a main feature)*	Decompensated liver disease: - Jaundice - Ascites (Hypoalbuminemia) - Variceal Bleeding *(low clotting factors)* - Hepatic Encephalopathy

- Both mild and moderate liver injury cause abnormal LFT
- Severe acute injury appears as jaundice
- Severe chronic injury appears as chronic liver disease ie, cirrhosis.
- If very severe acute it is fulminant hepatic disease
- If very severe chronic it is decompensated liver disease: jaundice, ascites (hypoalbuminemia), variceal bleeding (low clotting factors) and hepatic encephalopathy.

Acute liver failure (fulminant): Encephalopathy within 8 weeks (in some texts 12 weeks) from onset of jaundice in the presence of healthy liver.
(The only exception is Wilson Disease; liver is damaged but still it is acute liver failure).

- Divided into:*(according to the period between the onset of the jaundice and encephalopathy)*
  - 0-7 days: hyperacute
  - 8-28 days: acute
  - 28 days- 8 weeks: subacute

Causes:

1- Acute viral hepatitis (Esp. Hep. E in Pregnancy)
2- Drugs: Antituberculous, antifungals, and paracetamol toxicity (MC outside Sudan)
3- Toxins (fungi: amantida phylloid)
4- Others. (Budd- chiari Syndrome (Hepatic Vein obstruction); Wilson Disease; Fatty Liver in Pregnancy)… etc

Grades of encephalopathy:

- Grade **4**: coma
- Grade **3**: drowsy, stupporosed, gross disorientation to time, place and person
- Grade **2**: decreased concentration and slurred speech, flapping tremor
- Grade **1**: reversed sleep pattern *(sleep during the day and awake at night)*, apraxia.

4 signs in hepatic encephalopathy:

1) Fetor hepaticus *(distinctive breath odor "breath of the dead" due to accumulation of the toxin "thiol" in the blood)*
2) Flapping tremor
3) Constructional apraxia *(inability to do simple learned tasks; can't draw a circle)*
4) Hyperreflexia with bilateral positive Babinski sign *(up going planter reflex)*

Complications:

1- Cerebral edema (cause of death) → *first complication*
2- Hypoglycemia
3- bleeding (mainly variceal)
4- Sepsis
5- Hepatorenal syndrome.
6- Stress ulcers

Management of Fulminant Liver Failure:

- Admission to ICU with head elevation *(to prevent cerebral edema)*
- 10% IV dextrose *(to prevent hypoglycemia)*
- Abs metronidazole (neomycin in the past) to sterilize the gut
- Bowel enema to wash the bowel
- Lactulose (*oral*): decrease pH , so prevent absorption of ammonia *(which is toxic to the brain, it's source from intestinal bacteria)*
- IV PPIs → *(to prevent stress ulcer)*

- IV Vit. K (for bleeding tendency)
- If cerebral edema occurred: hyper ventilation *(to washout CO2)* and give 20% mannitol

Poor prognostic features of ALF:

1. Age <10 yrs or >40 yrs
2. Non A non B hepatitis *(all type of hepatitis except A&B +drugs → are poor prognostic feature)*
3. Grade 3&4 encephalopathy
4. Acute and subacute types
5. (Abnormal bleeding pattern): prolonged PT (25-50 seconds); INR Deranged (>3.5)

1- Ascites:

- Accumulation of Fluid in the peritoneal Space; Signs: (Distended abdomen, Full flanks, Everted umbilicus, SHIFTING DULLNESS, FLUID THRILL +ve)

Causes: Old classification:

Transudative: protein < 30	Exudative: protein >30
○ **Increased hydrostatic pressure: Rt HF & *congestive HF*** ○ **Reduced protein: nephrotic syndrome, malnutrition, chronic liver disease *(& portal HTN)* , hypothyroidism**	○ Infections (Eg, abdominal TB) ○ Malignancy ○ Acute pancreatitis *(*rare) *(NB, Peritoneal disease like infection and malignancy)*

New classification is according to SAAG (Serum Ascites Albumin Gradient):

- Ascites with SAAG > 1.1 g/L (11.1g/dL): **Transudative**
- Ascites with SAAG < 1.1 g/L (11.1g/dL): **Exudative**

*(**NB**. SAAG " serum albumin : ascitic albumin if **> 1.1g/L** that mean the ascitic fluid contain low albumin , if **< 1.1g/L** that mean the ascitic fluid contain high albumin)*

Invx:-

1- **CBC:** for pancytopenia *(can be feature of hypersplenism due to CLD & PHTN)*
2- **LFT** *(may indicate the cause)*
3- **Abdominal US:**
   1-confirm ascites 2- portal vein diameter *(if increased the cause is PHTN)*
   3- spleen size 4- search for masses *(if the cause is malignancy)*
4- ***Diagnostic paracentesis (Ascitic Tap):***
   a) Albumin & protein *(for classification)*
   b) WBCs total and differential
   c) Staining and culture*(for infection)*
   d) *C*ytology for malignancy
   e) Amylase if suspecting acute pancreatitis.

Rx:

- Salt restriction if mild
- If not responsive → add diuretics: spironolactone 100 mg/day *(starting dose)* and furosemide 40 mg/day *(starting dose)*
- Double the dose up to 4 times *(if patient in a good compliance)*
- Spironolactone 400 mg/day or furosemide 160 mg/day
- If still not responsive check compliance (Refractory ascites)
- Then **2 options**:
    - Serial paracentesis: after draining 5L add 6gm albumin infusion for every further 1 L drained. OR
    - TIPSS (Trans jugular Intrahepatic Portosystemic Shunt)

Complications:

1. **Spontaneous bacterial peritonitis (SBP):**
    - Presents with fever, abdominal pain and tenderness (peritonism).
    - **Dx** is with WBCs > 5000 (Neutrophils >250/mm^3)
    - Main organism is E.coli; *(due to translocation of colonic bacteria)*
    - **N.B.** Complicated Ascites for renal causes is caused by strept. Pneumoniae. *(If there is more than one organisms indicate perforated viscus)*
    - **Rx**: **IV cefotaxime** followed by norfloxacin prophylaxis
    - Definitive management is liver transplant

2. **Hepatorenal syndrome:**
    - Renal failure in the presence of severe liver disease with exclusion of other causes.
    - It is a pre-renal failure *(toxemia)* due to splanchnic vasodilation and renal vascular constriction *(due to disruption of auto regulation)*. *(NB Renal parenchyma is intact)*
    - Type 1 (worst, rapid RF) & type 2 (better prognosis)
    - **Rx**:
        - **Type 1**: terlipressin (Vasopressin) + albumin infusion *(preserve the blood in the circulation)*
        - **Type 2**: TIPSS
    - **Definitive management** is liver transplant.

Chronic liver disease:

Stigmata of chronic liver disease:-

- Leukonychia, clubbing, terry nails *(white nail proximally with telangectasia distally)*
- Palmer erythema and Dupuytren's contractures (esp. in alcoholic)
- Xanthelasma *(usually occur in PBC)*
- Parotid enlargement (esp. in alcoholic)
- Spider naevi, gynecomastia and loss of body hair
- Testicular atrophy

Hyperestrogenemia causes (Gynecomastia, Testicular Atrophy, Loss of Body hair, spider naevi)

- **Cirrhosis**:-
  - Irreversible liver diseases characterized by fibrosis and nodular formation leading to distorted architecture of liver.
  - The loss of architecture will distort the vessels causing ischemia and further damage (and the cycle continues).
  - Responsible cells are Ito cells (Stellate cells) present in the space of Disse.

- Micronodular (<1mm = Alcohol), or Macronodular (variable= viruses)

Causes:

1. Chronic Alcoholism
2. non- alcoholic steatohepatitis (NASH)
3. Chronic hepatitis
4. Genetic causes: hereditary hemochromatosis, alpha 1 antitrypsin defficiency and Wilson disease
5. Biliary and autoimmune: PSC, PBC and autoimmune hepatitis., secondary obstruction .
6. Budd chiari syndrome *(**thrombosis of the central vein)*

Complications: Decompensated Liver Failure; Portal HTN; HCC

1- Decompensated liver failure (encephalopathy, jaundice, bleeding, and ascites):-

Precipitating factors:

1- Increased protein (e.g. upper GI bleeding represents a large protein meal when it is absorbed)
2- Electrolyte disturbances (eg, after diuretics)
3- Sedatives *(avoid morphine in cirrhosis pt)*
4- Constipation
5- Infection

CHILD PUGH classification:

Each one of the five parameters is given a score 1, 2 or 3 and then the overall score is calculated.

Parameter	(1)	(2)	(3)
Encephalopathy	None	Grade 1 & 2	Grade 3 & 4
Ascites	None	Mild	Marked
Albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
Bilirubin (mg/dL)	< 2	2 – 3	> 3
PT (sec) **(INR)**	< 4 (<1.7)	4 – 6 (1.7 – 2.3)	> 6 (>2.3)

- ***Interpretation***:

▪ **< 7 → Class A**	▪ **7-9 → Class B**	▪ **> 9 → Class C**

2- Portal hypertension:

- Cardinal feature is splenomegaly
- Also ascites and features of Portosystemic shunting (esophageal varices, piles - Hemorrhoid- , caput medusa).
- Sign of portal HTN if severe is *venous hump*

3- Hepatocellular carcinoma

N.B: Causes of portal hypertension:

- Pre hepatic, hepatic (Presinusodial, sinusoidal and post sinusoidal) and post hepatic.

Prehepatic	Hepatic			Post hepatic
Portal vein thrombosis	**Presinusodial**	**Sinusoidal**	**Post sinusoidal**	Budd chiari syndrome, inferior vena cava obstruction, RT HF and congestive HF.
	Schistosomiasis	Liver cirrhosis	Venoocclusive disease	

Dx: Clinically →

1- US → for portal/splenic veins dilatation.
2- Measuring Hepatic vein wedge pressure (give indirect result)
3- Upper GI Endoscopy for Varices.

Specific Causes of Cirrhosis:

Hereditary hemochromatosis:-

- Inheritance is AR (autosomal recessive)
- Mutation in **HFE** gene
- Control of iron stores in the body is through control of absorption. HFE gene is responsible for control of absorption of iron so this mutation results in uncontrolled absorption.
- Increased iron in cells is hemosiderosis, when it causes tissue destruction this is hemochromatosis.
- It deposits in: **(Heart & Skin are reversible)**

✓ **Joints** causing arthritis/arthralgia (pseudogout *"deposition of Ca & phosphate"* ; chondrocalcinosis on x-ray)
✓ **Pancreas** causing diabetes
✓ **Skin**: bronze skin
✓ **Heart** causing DCM & RCM
✓ **Anterior Pituitary** causing Hypogonadotrophic hypogonadism

Dx: **By Iron profile**:

1- *Increased* ferritin *(normal in early stage , it's an acute phase reactant)* ,
2- *Increased* iron
3- *Increased* transferrin saturation
4- TIBC is *low*.

- Best *Screening* is by **transferrin saturation**
- Screening for <u>family</u> members is by **genetic studies**.
- <u>Gold standard</u> diagnostic test is **liver biopsy** (using perl's stain we can quantify amount of iron deposited)

Rx:

- **Venesection (phlebotomy),** also iron chelating agent (desferroxamin)
- Definitive management is liver transplantation.

Wilson disease (hepatolenticular degeneration):-

- AR
- Problem is mutation in the ATP transported needed for incorporation of copper into bile and also for incorporation of copper into ceruloplasmin *(in blood)*.

  Clinically:

  1- **Liver** disease (cirrhosis)
  2- **CNS**: basal ganglia symptoms *(chorea , dementia)*
  3- **Eyes**: Kayser Fischer ring (eye deposition)

  Dx:

  - **Increased 24 hrs urinary copper (Co++) (Most Important)**
  - Decreased ceruloplasmin
  - Liver biopsy
  - Genetic studies.

  Rx:

  - Penicillamine (copper chelatior).
  - Alternatives if CI; are zinc and trenitin hydrochloride
  - Definitive management is liver transplant.

Alpha 1 antitrypsin deficiency:-

- AR
- **Clinically**: cirrhosis and emphysema *(affect liver + lung)*
- **Dx**: decreased serum alpha 1 antitrypsin/ liver biopsy (with PAS stain) /genetic
  (N.B. PAS: periodic acid shift)
- **Rx**: supportive and transplant.

❖ *Cholestatic Liver Disease:*

• PBC (Primary Biliary Cirrhosis):- NEW NAME → Primary Biliary Cholangitis	•PSC (Primary Sclerosing Cholangitis):-
- **Autoimmune granulomatous disease affecting *intrahepatic canaliculi (bile duct)*** - **Occurs more in females** - **Associated with Sjogren's syndrome (80%); sicca syndrome** - **Other features: Xanthelasma and skin pigmentations** - **Clinically: obstructive jaundice** - **Dx: +ve AMA *(anti-mitochondrial Ab)* and liver biopsy.** - **Rx:** **1. <u>Cholestyramine</u> (for itching)** **2. Ursodeoxycholic acid (make improvement in LFT)** **3. Liver transplantation (only if bilirubin more than 100 or intractable pruritus)**	- **Fibroobliterative disease** - Onion skin appearance in histology - Affect both intra & extra hepatic channels - Occurs more in males - **Associated** with ulcerative colitis - **Complications**: colorectal cancer and cholangiocarcinoma. - **Clinically**: obstructive jaundice - **Dx**: **MRCP** or **ERCP** looking for beading, and liver biopsy. *(beading mean constriction - dilatation - constriction - dilatation)* ANCA antibodies may be found. - **Mx**: 1. <u>cholestyramine</u> (for itching) 2. <u>Ursodeoxycholic acid</u> (make improvement in LFT) 3. Liver transplantation (mandatory due to cancer association).

❖ Alcoholic & non- alcoholic fatty liver disease:-

- It is a spectrum:
  1) Steatosis is *reversible* (fatty liver) >>
  2) Steatohepatitis (Fatty liver with inflammation) >>
  3) Cirrhosis
- 1 Unit of alcohol equals 8 gram of Ethanol
-

In Alcoholic liver disease	In Non- alcoholic liver disease
- **Steatosis is reversible** - **Features of alcoholic steatohepatitis: AST>ALT, High GGT, macrocytosis (high MCV), Infiltration by neutrophils, Mallory B bodies** **(AST increased b/c it mitochondrial enzyme and alcohol destruct it causing AST release)** - **Rx of alcoholic hepatitis: *(severe)*** ○ **Stop alcohol** ○ **Steroids** ○ **<u>Pentoxyphylline</u>**	- Dx. Of Exclusion - Pt is obese, with DM, dyslipidemia "metabolic syndrome", - *(or pt with GI operation e.g. gastric bypass)* - Mx by controlling risk factors

❖ Autoimmune hepatitis:

- The scenario is *"Young female with amenorrhea has abnormal LFT & hypergammaglobulinemia" + Associated autoimmune diseases* (e.g Hypothyroidism + Vitiligo)
- **Dx**:
    - Hypergammaglobulinemia (↑Ig) esp. IgG
    - Antibodies:
        - Type 1: **ANA** (anti nuclear Ab) **& ASMA** *(anti smooth muscle Ab)*
        - Type 2: **anti LKM** *(anti liver kidney microsmoal Ab) → in pediatrics*
        - Type 3: **anti SLA** *(anti soluble liver Ag)*
    - liver biopsy
- **Rx**:
    - Steroids
    - Azathioprine
    - liver transplant

Viral Hepatitis:

❖ Hepatitis A&E:

- Orofecal transmission.
- Acute hepatitis (Doesn't cause chronic).
- Dx by antibodies (IgM)
- Complicated by (Fulminant Hepatic Failure (<1%); Cholestatic Hepatitis and Relapsing Hepatitis)
- Supportive treatment. (Avoid Alcohol, Drugs that's metabolized in Liver, No dietary Restriction)
- HEV causes fulminant disease in pregnant.

❖ Hepatitis B:

- Routes of transmission: Parenteral, sexual and mother to child
- Causes both acute and chronic hepatitis
- **Markers:**
  - HBsAg +ve is hepatitis B infection *(then differentiate by core Ab)*
  - If HBcIgM Ab +ve it is acute infection *(< 6 month)*
  - If HBcIgG Ab +ve it is chronic infection *(>6 month)*
  - HBsAb: immunization or resolved infection *(differentiate by anti-core IgG if +ve "past infection , if -ve " immunization ")*
  - HBeAg indicates infectivity *(viral load*)
  - In pre-core mutation pts: they have *high viral load* but *-ve e Ag*

- ***Window period*** *is the period between the drop in HBsAg and rise in HBsAb. The only positive marker in this period is* ***HBcIgM.***

  Extra hepatic Manifestations:
  - Polyarteritis Nodosa (PAN)
  - Cryglobinuemia
  - Serum Sickness (Fever, Rash, Arthralgia) >>> Acute
  - GN
- **Rx of chronic Hepatitis B:**
  - We check for
    1. US features and liver biopsy: for liver texture
    2. Viral load *(e antigen)*
    3. Liver enzymes
- Treat if fibrosis → increased liver enzymes and increased viral load.
- **Aim of Rx**: normalization of variables and reversing e antigen to e -ve.
- **Treatment**:
  - **1st Line:** Pegylated Interferon (interferon alpha) [C.I. In decompensated liver disease]
  - **2nd line**: oral drugs; Entecavir, Tenofovir, lamivudine.

"Note: HBV is an oncogenic virus (because it is a DNA virus), it can cause HCC without causing liver cirrhosis"

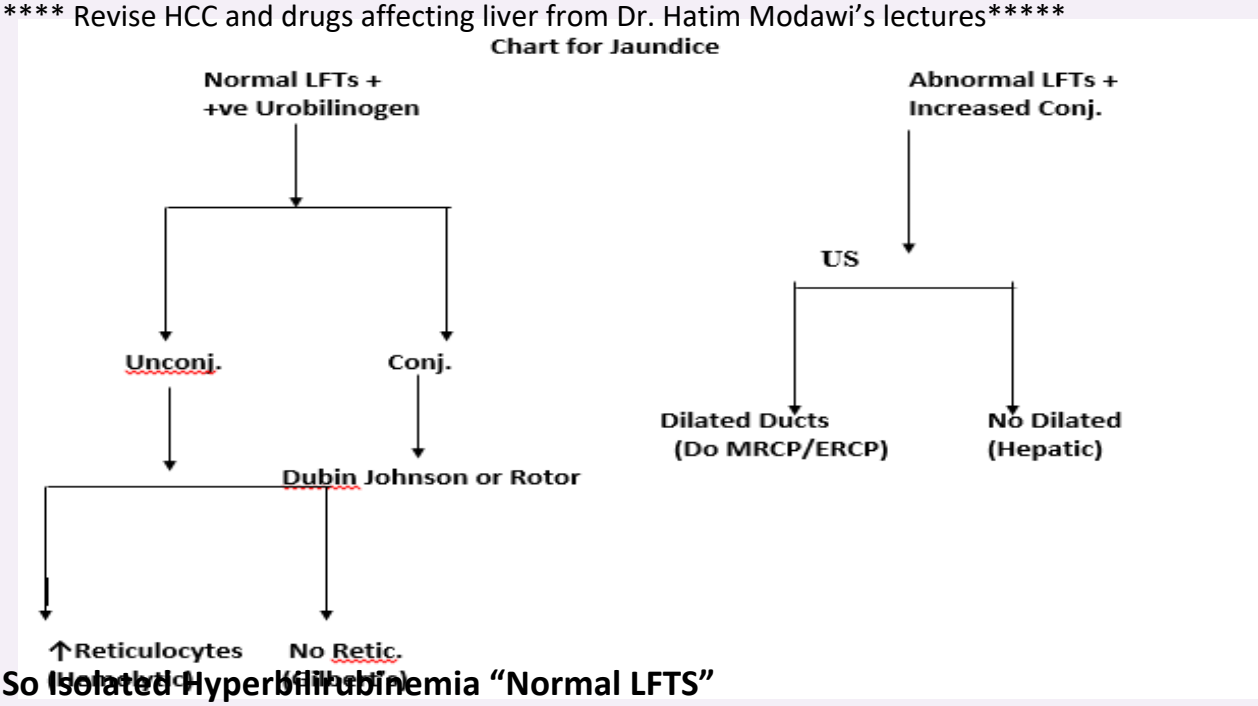
❖ Hepatitis C:

- Same routes of transmission as hepatitis B
- Acute or Chronic (85%)
- Chronicity is higher in Hep. C; but malignancy is higher with Hep. B
- **Dx**:
  1. Antibodies (Anti HC IgM; IgG)
  2. HCV-RNA >>>> Gold Standard
  3. Genotyping: (Worse is Genotype 1)
  4. Liver Biopsy for Histology
- Viral RNA detection has an important role here
- Genotyping is also important
- Genotypes 2&3 are given Rx for 24 months
- Genotypes 1&4 are given Rx for 48 months
- **Aim of Rx is "Sustained viral response (SVR)", viral load becomes 0 after 6 months of treatment.**
- INF-alpha & Ribavirin (Cause Hemolytic Anemia)

❖ Hepatitis D:

- Occurs as co-infection or super infection with hepatitis B.

**** Revise HCC and drugs affecting liver from Dr. Hatim Modawi's lectures*****



So Isolated Hyperbilirubinemia "Normal LFTS"

If Conjugated >>> Dubin Johnson or Rotor

If Unconjugated >>>> Gilbert's

Types of Jaundice:

Pre-hepatic	Hepatic	Post-hepatic
- (Increased Unconjugated) ○ **Hemolytic Disease** ○ **Gilbert's or criggler Najar**	Abnormal LFTs if Acute or Decompensated Chronic Liver Disease (Mixed Conjugated)	(Increased Conjugated + Itching, Dark Urine, Pale Stool, Cholesterol Deposition) ○ Biliary Obstruction (Stones, Ca Pancreas, PBC …etc) ○ Dubin Johnson's or Rotor

Hepatomegaly:

1- Viral Hepatitis
2- Congestion (HF / IVC obstruction / Budd Chiari)
3- HCC
4- Ameboic Liver Abscess / Pyogenic Liver Abscess

Massive Splenomegaly:

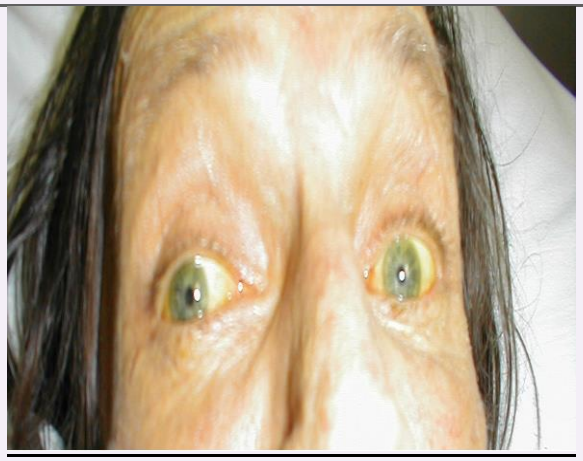
1- Hyper reactive Splenomegaly Syndrome (Malaria)
2- Visceral Leishmaniasis
3- CML
4- Myelofibrosis
5- Chronic Brucellosis

❖ Liver Tumors:

- Most common >> Secondaries (From Lung, GI & Breast)
- O/E Hepatomegaly; Hard & Nodular (D.Dx for Cirrhosis)

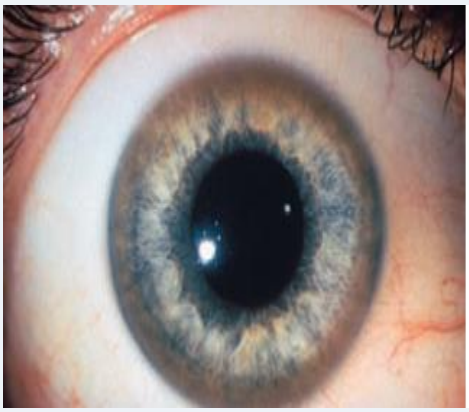
Benign		**Malignant HCC**	
➢ **Adenoma:**	➢ **Hemangioma**	**Risk Factors:**	**Treatment:**
- Female + Oral contraceptives or Anabolic Androgens **- Highly vascular>may cause Intraperitoneal Bleeding specially in Pregnancy** **- Dx by:** **1) α Fetoprotein: Normal (Doesn't Exclude HCC)** **2) US** **3) Biopsy: Mandatory** **- Tx: Surgical Resection (If symptomatic)**	- Most common benign - Biopsy is Contraindicated; Dx is by Triphasic CT-Scan	1) Cirrhosis (specially A1ATD, Wilson, NALD) 2) Chronic HBV 3) Afla toxin	- Resection if no cirrhosis; - Transplantation (if cirrhosis) - Surgery: Lesion < 5 cm or 3 Lesions < 3cm (Milan Criteria) - Radio-frequency ablation = small lesion - Trans-Chemo-embolization: Contraindicated in Multifocal - Percutaneous Ethanol Injection (Small Lesions) - Chemotherapy >>> End stage (Palliative; they are not responsive/ radio)

OSPE

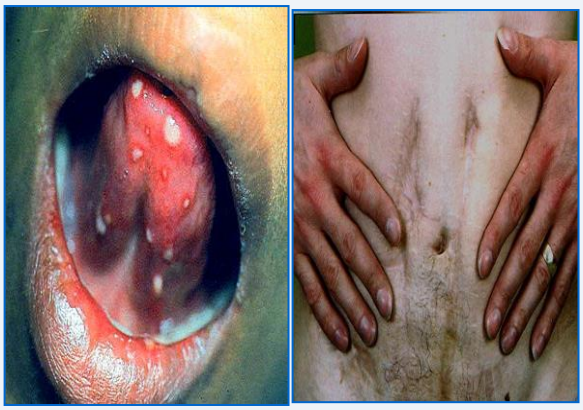


Jaundice

Ascites



Kayser fleischer ring
Wilson's disease



Aphthus ulcers + multiple scars in abdomen + clubbing
Crohn's disease

وإن ضاقت بك الأركانُ يومًا

فَرُكن الله رحبٌ لا يضيقُ. ♡

Neurology

**Recorded on 18, 26 Sep.2018

Contents

Localization:

- **Dominant hemisphere** is determined by speech areas (Wernick's and Broca's areas)

➢ Frontal lobe lesion:	➢ Parietal lobe lesion:
- Disinhibition. **- Emergence of primitive reflexes.** **- Preservation (repetition of other's speech), inability to follow task sequence,** **- Motor (afluent) aphasia Broca's, and anosmia.** **- N.B. Poor orientation, poor concentration and poor judgment.**	- Contralateral inferior Quadrantanopia. **Grestman syndrome:** - Lesion in dominant parietal lobe: present with acalcuria or dyscalcuria-- alexia or dyslexia -- agraphia or dysgraphia-- disorientation between left and right -- finger agnosia. - Non-dominant parietal lobe: **hemineglect... apraxia.**
➢ Temporal lobe lesion:	**➢ Occipital lobe lesion:**
- Contralateral superior Quadrantanopia. **- Fluent aphasia.** **- Auditory loss (1ry auditory cortex) or auditory agnosia (damage to 2nd and tertiary auditory cortex).** **- (Hippocampus) memory impairment.** **- Prosopagnosia (inability to recognize faces).**	- Contralateral homonymous hemianopia with macular sparing **Anton syndrome**: pt is unaware of his occipital lobe blindness.

Subarachnoid Hemorrhage [SAH]:

- *Ruptured Berry aneurysm* is most common cause (85%) & 2nd MCC is *AV malformation*.
- Most common artery in ***Berry aneurysm is the anterior communicating artery aneurysm.***
- Most common presentation of ACA aneurysm is ***bitemporal hemianopsia (heterogenous) similar to pitutary prolactinoma.***

N.B: In exam subarachnoid hemorrhage with *Oculomotor nerve affection* is → posterior communicating artery aneurysm.

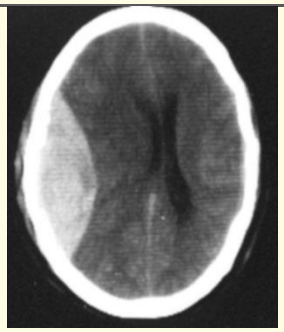
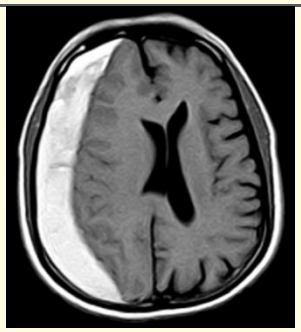
3rd nerve palsy: Ptosis, eye ball outward and downward, pupil dilated (from the mass effect of hematoma to outward parasympathetic fibers of 3rd nerve)

- Important associations are: ADPKD, Coarctation of the aorta, Ehlers Danlos and Marfan
- **C/O:**
  - Worst headache ever... thunder clap headache occipital.
  - Meningism (remember meningism in pituitary apoplexy)
- **Dx**:
  - CT: blood in CSF
  - If nothing, do LP after 12 hours (looking for xanthochromia)
- Most common cause of mortality is **rebleeding**
- Most common of morbidity is **ischemia (vasospasm)**
- 3rd complication is **communicating hydrocephalus when blood clots**
- 4th complication is **SIADH (hyponatriaemia)**
- Give **Nimodipine** to prevent ischemia and refer *for neurosurgical unit.*
- **Second cause SAH is** AV malformations (15%)

N.B: ***LP Contraindications:***

1) Signs of ↑ICP "Headache, Projectile Vomiting, Papilloedema"
2) Focal Neurologic Deficit.
3) Skin Infections / Congenital Lumbosacral Abnormalities /Meningocele.
4) Unconsciousness unless you do CT.
5) Bleeding Abnormalities, Platelets < 40 x 10^9, Anticoagulant Drugs.

Epidural Vs Subdural hematoma:

 **Epidural hematoma** - **Cause: arterial mainly trauma** - **Evacuated by burr hole?** - **Characterized by lucid interval**	 **Subdural hematoma** - **Cause: stretching of bridging veins due to brain atrophy or recurrent trauma** - **Occur in Old age... alcoholic... fluctuant consciousness** - **Crescent shape on CT** - **Hemicraniotomy to evacuate (blood is clotted)**

Intracranial Venous Thrombosis: Cortical V.S Dural.

➢ Cortical Venous Thrombosis [like stroke]:	➢ Dural Venous Thrombosis:
- Fever, Focal signs "e.g. Hemiparesis", headache ± Epilepsy (Unlike arterial Stroke)	- (Veins between 2 layers of dura) - **RF:** Hypercoaggulable state. - **Symptoms:** of raised ICP. ***- Cavernous sinus Thrombosis:*** o Affect 3rd , 4th ,ophthalmic of 5th , 6th CN , internal carotid A, sympathetic fibers. o Spread from facial Pustule or Follicle o Fever/ Red painful eye / Proptosis / Chemosis / Ophthalmoplegia, Horner's syndrome, sensation over ophthalmic division - *Lateral / Sagittal* >>> ↑ICP (Sagittal cause in vision)

- **Risk Factors:** 1) Pregnancy 2) OCP 3) Dehydration 4) Head Injury 5) Inherited/Acquired prothrombtic 6) Infection e.g. (from P.N sinuses)
- **Tx.** Heparin initially then Warfarin for 6 months.

- **Dx:** by MRI / MRV / MRA

Idiopathic intracranial HTN (IIH) or (Pseudo Tumor Cerebri):

- Young female, obese, taking a medication (COCs, vit A, Tetracyclin), papilledema, may be 6th cranial nerve palsy (↑ ICP), negative CT scan
- 2 D.Dx: ***either IIH or dural sinuous thrombosis***
- So next step is to do
    1) **MRV to exclude dural sinuous thrombosis**
    2) Then do **LP** to confirm (CSF Analysis: increased opening pressure but normal constituents)
    3) **CT** scan to exclude tumor (SOL)
- **Complications:**
    1. Blindness due to optic atrophy caused by chronic papilloedema.
    2. Abducent Nerve Palsy.
- **Tx:**
    1) Wt loss.
    2) CAI (Carbonic Anhydrase Inhibitor – **Acetazolamide**) ↓CSF.
    3) Serial LP.
    4) Surgical: - lumpoperitoneal shunting for CSF, optic sheath fenestration (Prevents Blindness)

Normal pressure hydrocephalus:

- Old man with triad of: urinary incontinence, ataxia, dementia
- **Dx:** CT shows dilated ventricles
- **Rx:** Ventriculoperitoneal shunt

N.B: dandy walker, chiari maformation, aqueduct stenosis → (non-communicating hydrocehallus)

Wernick's encephalopathy:

- ↓Thiamine (B1)
- CAN reversible Triad: ***Confusion, Ataxia and eye signs (Nystagmus and ophthalmoplegia)***
- **Risk factors:** alcohol, hyperemesis gravidarum
- **Dx** measuring RBCs transketolase (decreased)
- **Rx:** do not correct hypoglycemia before correcting thiamine (cofactor to glycolysis)
- Complicated by **korsakof psychosis** (irreversible): confabulations and amnesia.

Stroke:

- Sudden onset of focal neurological deficit lasting more than 24 hours or leading to death. (If less than 24 Hours → TIA).
- Etiology:

  * **Ischemic (85%) or Hemorrhagic (15%) or Others**

- Ischemic: focal + global (**watershed stroke** (due to anemia, recurrent hypoglycemia, hypotension))
- **(Vasculitis, Carotid Dissection, CADASIL, Venous thromboembolism)**

1. Ischemic	2. Hemorrhagic stroke
- Either thrombotic or embolic (Acute Onset; Enhancement on *CT by contrast*) **- Embolic is either from carotid stenosis or cardiac cause.** **- Cardiac causes: AF / valvular (prosthetic, IE, prolapse) / Ventricular mural thrombus following MI / Paradoxical emboli / atrial myxoma.**	**Causes are:** 1- HTN. 2- Chacort Poucharb aneurysm ass with HTN (due to hyaline arteriolossclerosis) m.c affected site is (basal ganglion, thalamus, and internal capsule). 3- AV malformations. 4- Bleeding disorders, Anticoagulant or Thrombolytic Therapy 5- **Other causes:** vasculitis, dural sinus thrombosis, thrombophilia.

- **Water-shed stroke: (Hypoperfusion)**
- **Lacunar stroke:**
  1. Penetrating arteries > Internal capsule "*lenticulo straia A of middle cerebral A*" → pure motor loss features (only paralysis)
  2. Thalamus → pure sensory loss (except olfaction)
  3. Sensory motor (1,2)
  4. Ataxic hemiparesis
  5. Clumsy hand syndrome

Risk factors of stroke:

- **Non Modifiable**: male, age and family history.
- **Modifiable**: DM, HTN, hyperlipidemia and smoking.

➢ Signs pointing towards **hemorrhagic:** decreased level of consciousness and signs of increased intracranial pressure.

N.B: **Carotid Dissection:** Neck Pain, Hyperextension of neck, Carotid Bruits on Examination, Horner's syndrome. Usually in young patients.

- Most common artery affected in stroke is the **Lenticulostriate artery of the middle cerebral artery causing lacunar stroke (affects internal capsule).**

- **Symptoms of Stroke is Divided into 2 Circulations:**

Anterior circulation:

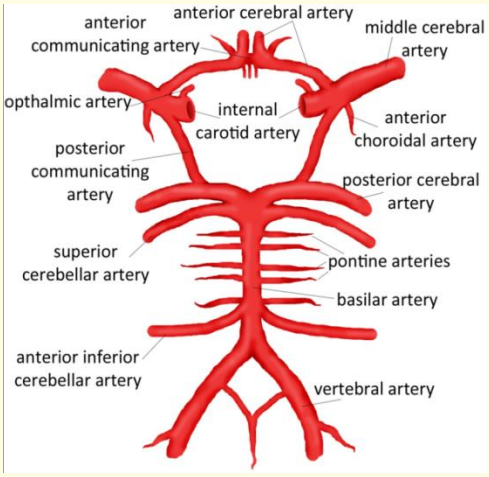
1. Anterior cerebral artery (ACA):

- Contralateral hemiparesis and hemi-sensory loss mainly in Lower Limbs. Also urinary incontinence. Also change in behavior as it affects the frontal lobe → (Premotor Area).

2. Middle cerebral artery (MCA):

- Supply UL and face + Broca's & Wernick's areas.
- lacunar stoke penetrating branches or lenticulostriate from MCA to (basal ganglion, internal capsule & thalamus)
- **Sx:**
  - Contralateral hemiplegia and hemi-sensory loss; mainly in the upper limb and face.
  - Contralateral homonymous hemianopia
  - Aphasia (motor and sensory) if dominant or hemineglect if non-dominant.
- If Sx of middle cerebral artery + blindness on ipsilateral eye that means the internal carotid artery (middle cerebral + ophthalmic)
- Internal Carotid Artery (ICA): MCA + Blindness "Ophthalmic Artery" of lacunar stoke:

Posterior circulation:



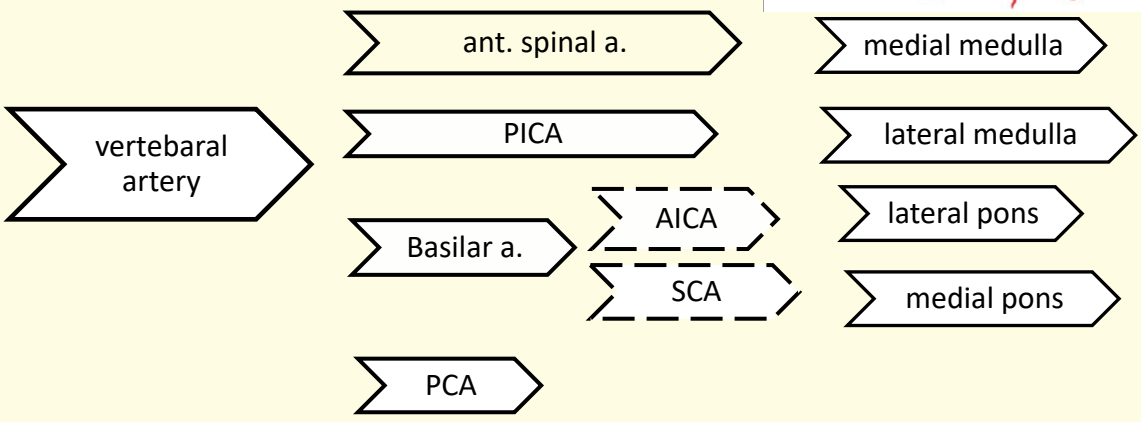
3. Posterior cerebral artery (PCA):

- Cortical Blindness

"Contralateral Homonymous Hemianopia + Macular Sparing)

Sub-syndromes:

1. **Posterior circulation:**



2. **Cranial nerves:**
   - 3,4 → Mid brain
   - 5,6,7,8 → Pons
   - 9,10,11,12 → Medulla
   - 6,12 (/6) → Medially

2M: Medial structures:	4S: Lateral structures:
1. **Motor (corticospinal and corticobulbar)** 2. **Medial leminiscus (vibration & proprioception)**	1. **S**ympathetic nuclei → Horner's syndrome. 2. **S**pinothalamic tract → Pain, temp contralateral. 3. **S**pinal nucleus of 5th CN → Pain, temp of face. 4. **S**pinocerebellar tract → N/V, Vertigo, nystagmus, ataxia.

- **Lateral medullary syndrome(LMA – PICA (Posterior Inferior Cerebellar Artery-Wallenberg Syndrome)):**
  - Contralateral loss of pain and temperature of the body
  - Ipsilateral: loss of the pain and temperature in face (trigeminal nerve affection);
  - Ipsilateral Horner (sympathetic fibers);
  - Ipsilateral nystagmus, vertigo and dizziness (vestibular nucleus), ipsilateral ataxia (cerebellum) and 9th, 10th, 11th CN palsy.
  - **Lesion** is in PICA (posterior inferior cerebellar artery).
- **Medial medullary syndrome:**
  - Contralateral weakness,
  - Contralateral loss of fine touch, position and vibration and *ipsilateral hypoglossal (12th) nerve palsy.*
  - **Lesion** is in the anterior spinal artery.
- **Midbrain syndrome:**
  - Ipsilateral Oculomotor N palsy + contralateral weakness: **Weber syndrome**
  - Ipsilateral Oculomotor N palsy + contralateral ataxia (red nucleus) + proprioception & vibration (medial leminiscus) **Benedict's syndrome**
- **Medial pontine syndrome:**
  - Same as above but the cranial nerve affected is abducent nerve (6th).
  - Lesion is in the paramedian branch of the basilar artery.
- **Lateral pontine syndrome:**
  - Same as above but cranial nerves affected are 7th and 8th (facial palsy and hearing loss).
  - Lesion is in the AICA (anterior inferior cerebellar artery)
- **Locked in syndrome:**
  - Bilateral pontine artery occlusion
  - (Tetraparesis + Loss of horizontal gaze; only vertical eye movement is found).
  - Occur in Central Pontine Myelinolysis (rapid correction of hyponatremia).

❖ Stroke management:

- **CT scan** to exclude hemorrhage (if hemorrhage refer to neurosurgeon)
- **Aspirin** 300 mg
- If presented within 3-4.5 hrs give **tPA** (streptokinase has no role here; only in MI)
- If ischemic; do ECG, Echo & Carotid Doppler (To see carotid stenosis)
- *Don't manage the blood pressure* except if blood pressure is more than 220/130 or hypertensive emergency or carotid dissection. If with AF; give Warfarin 2 weeks after stroke to avoid hemorrhagic transformation
- Keep **hydration** and **nutrition**

***N.B**: Revise Contraindications of Thrombolysis.*

CI to Thrombolysis: **1)** Hemorrhagic stroke ever **2)** Ischemic stroke within 6 mo **3)** GIT bleeding within 1 mo **4)** Trauma or major surgery within 3 wks. **5)** CNS tumor, pregnancy or severe HTN

- **Conservative:**
  - **Secondary prevention:**
    - Control risk factors, give statin, weight loss, exercise.
- If Carotid stenosis (more than 70%) carotid endarterectomy
- If Embolic start warfarin after 2 weeks
- **Clopidogrel** is the first line in secondary prevention but if the pt is not tolerating it give **aspirin + dipyradamol**.
- If the pt is already on aspirin just **add dipyradamol** (don't change to Clopidogrel)
- If the cause is AF give warfarin after 2wks from the attack.

Dipyradamol:
Is a phosphodiesterase inhibitor; which increase cAMP and decrease thromboxane A2.

❖ Complications: 4Ps ; 3Bs

- **P**neumonia, **P**E (Pulmonary Embolism), **P**ainful shoulder, **P**sychiatric problems,
- **B**owel incontinence, **B**ladder incontinence and **B**ed sores.

N.B:
A = Keep Airway patent and assess swallowing, if can't (NPO + NG tube).
B = O_2
C = Hydration + nutrition. Don't Lower BP unless → 220/120 or organ damage or encephalopathy or aortic dissection;
D = Glucose then bowel & Bladder Care

Epilepsy:

- **Seizure** is abnormal, synchronized electrical discharge from brain neurons.
- **Convulsion** is motor manifestation of seizure.
- **Epilepsy** is spontaneous (unprovoked) tendency to have recurrent seizures.

Etiology:

- Idiopathic
- Perinatal Problems → **Children** (Hypoxic Ischemic Encephalopathy + Metabolic disorders)
- Trauma, alcohol/Drugs, Infections → **Young**
- CVA, Neurodegenerative, Tumor →> **Old**
- ***Others:***
  - *Metabolic (↓Na^{+}, Glucose, Mg^{+2}, Ca^{+2}, Hypoxia) (No K^{+})*
  - *Developmental "Hippocampal Sclerosis = Temporal Lobe Epilepsy"*

Types:

1- Generalized	2- Partial (Focal)
- Tonic clonic (Grand-mal): ○ **Tonic: Laryngeal spasm (crying) & Tongue biting.** ○ **Clonic: Urinary or bowel Incontinence.** **- Atonic: Sudden loss of tone.** **- Myoclonic: (no LOC): Sudden shock-like jerky.** **- Absence "Petit-mal" :** ○ **LOC for <10 Secs. 20-30/day** ○ **Eyelid abnormal movement (blinking), hyperventilation** ○ **On EEG: 3 Hz spikes & waves.**	Simple or complex **- Simple:** Jacksonian march start at thumb then proceed proximally. **- Complex:** Temporal lobe epilepsy: automatism, Deja vu or jamais vu, hallucinations (mainly auditory). **3- Partial with secondary generalization**

N.B: Juvenile myoclonic epilepsy: (inherited epilepsy syndrome)

- 5 yrs. → absence seizure
- 15 yrs. → juvenile myoclonus
- Adult. → grand-mal epilepsy
- Need treatment for life

➢ **Triggers of epilepsy:** sleep deprivation, illness, lights, high sounds or music & alcohol.

DDx for epilepsy is pseudoseizure /syncope:

- **Syncope:** vaso-vagal or postural hypotension syncope.

1. **Vaso-vagal syncope:** Triggers: fear, unpleasant sight, severe pain.
2. **Postural hypotension**: drop more than 20 in systolic or 10 in diastolic when standing.

- **Cardiac syncope:** aortic stenosis, arrhythmias (heart block in stokes Adam attack), massive pulmonary embolism
- Syncope is short in duration, short post ictal phase, pt is pale, no tongue biting or urinary incontinence

Phases:

- **Prodrome**: 2-3 Days before seizures "Behavioral/Mood changes"
- **Aura:** more in Partial "e.g.: hallucination, déjà vu, jamais vu
- **Ictal**
- **Post-Ictal:** headache, confusion, Sleepiness, Todd's Paralysis "Jacksonian's Amnesia = Temporal Lobe"

Investigations:

- **MRI** "show posterior fossa tumor → superior to CT"
- **EEG:** if normal consider 24 hr Ambulatory EEG, or Videotelemetry
- Others to exclude cause: CBC, TWBCs, Serum Ca^{+}, Blood Sugar, RFT

Management of epilepsy:

- Don't give anti-epileptics from first attack except in case of:
  1. Focal neurological deficit
  2. Unequivocal EEG pattern
  3. Structural abnormality on MRI
  4. Patient request

Drugs:

- Generalized: ***Na valproate***
- Absence: ***ethosuxamide***
- Partial: ***carbamazepine***
- Myoclonic is treatment is life long and carbamazepine is contraindicated in it.
- Safest in pregnancy is **Lamotrigine**

- **Enzyme Inducers**: Phenytoin, Carbamazepine, Barbitone, Rifampicin, chronic alcohol >>> Contraceptive Failure
- **Enzyme Inhibitors**: Antibiotics (Macrolides esp. Erythromycin), Isoniazid, Azol anti-fungal, grapefruit juice & acute alcohol.

- Warfarin when given with Macrolide → Warfarin toxicity.

SEs of Anti-epileptics:

➢ **Na valproate: VALPROATE** **(Appetite Increased, Weight gain; Liver Failure; Pancreatitis; Reversible hair loss; Oedema; Ataxia; Teratogenicity, Tremor, Thrombocytopenia; Encephalopathy)**	➢ **Carbamazepine:** **SIADH and agranulocytosis**
➢ **Lamotrigine:** **Hypersensitivity rash "Steven Johnson syndrome " or even "toxic epidermal necrolysis"**	➢ **Phenytoin:** Cerebellar like syndrome (ataxia), gum hyperplasia, hirsutism or hypertrichosis and course facial features, interferes with vit D causing osteomalacia, interferes with folic acid causing megaloblastic anemia, and teratogenicity (cleft palate), peripheral neuropathy.

Status epilepticus:

- Episode lasting more than 30 minutes or multiple episodes without regaining of consciousness in between.
- **Rx**

- ABCs
- "Loading" IV lorazepam (best) or IV diazepam or Rectal diazepam
- After 10 min then "reloading" same above
- After 10 minutes "maintenance" IV phenytoin or bisphenytoin infusion
- After 10 min GA + intubation

Trigeminal neuralgia:

- Severe pain along trigeminal nerve distribution.
- Considered as a partial seizure that is why it is treated by **carbamazepine.**

Headache:

- **Primary headache:** (Migraine, Cluster, Tension, Trigeminal Neuralgia).
- **Secondary Headache *(dangerous)*:** (↑ICP, Infection, Hemorrhage, Giant cell Arteritis).

➢ Migraine:

Criteria to dx:

A. At least 5 attacks fulfilling following criteria:
B. Duration lasting 4-72 hours (if no tx used).
C. Unilateral, pulsatile, moderate to severe, interfere with daily activity.
D. Associated with nausea, vomiting, photophobia or phonophobia.
E. No underlying cause.

- Migraine with aura (25%) or without aura (common).
- Increased by **CHOCOLATE** (**C**heese, **O**CP, **C**affeine, **A**lcohol, **A**nxiety, **T**ravel, **E**xercise)
- Some **types:**
  - Hemiplegic Migraine: D.Dx for Stroke
  - Vertebro-basilar Migraine: Ataxia
- **Rx:**
  - **Acute:** simple analgesia (NSAIDs) or serotonin agonist (sumatriptan) + prokinetic drug (Metaclopramide) to increase the absorption.
  - **Prevention:** β-Blockers: propranolol (most important), Topiramate others like Na valproate and pizotifen (SE: wt gain, Anticholinergic Symptoms)

➢ Tension headache:

- Bilateral band-like, very mild; due to spasm of Scalp of Suboccipital Muscle.
- **Rx:** massage, ice packs and if severe give simple analgesia (NSAIDs).

➢ Cluster headache:

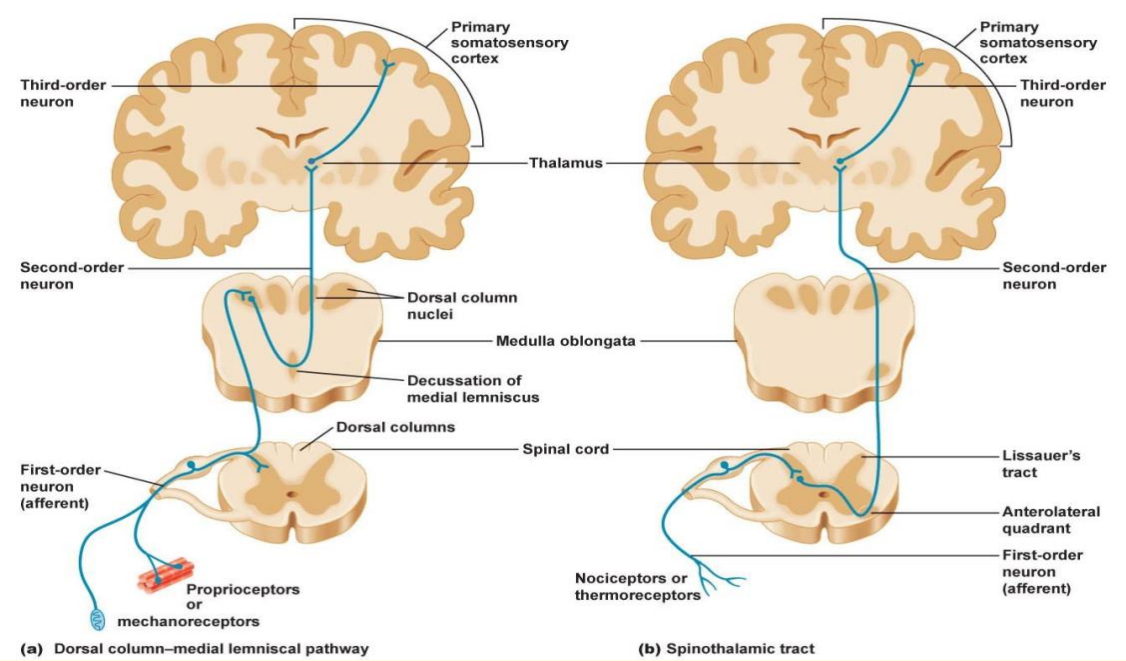
- Male, smoker, severe headache → (suicide), comes in clusters (frequent attacks → free period → attacks) at night, eye Sx (lacrimation, pain, and even Horner) and nose Sx (rhinorrhea and congestion)
- **Rx: ACUTE**: O2 + S/C tryptans
- **Prevention**: CCBs, lithium

➢ Temporal arteritis:

- Jaw claudication, cord-like temporal arteries, headache, high ESR.
- **Rx**: high dose steroids to prevent blindness.

Spinal cord

- 33 vertebrae: 7C, 12T, 5L, 5S, 3 or 4 C
- 31 segments: 8C, 12T, 5L, 5S, 1C
- Collection of cell bodies inside CNS: Nuclei
- Collection of cell bodies outside CNS: ganglia
- Sensory tracts: dorsal column tract and spinothalamic tract
- **Dorsal column tract:** decussate at the level of Medulla (Ipsilateral lesion)
- **Spinothalamic tract:** decussate at its level in the spinal cord (Contralateral lesion)
- Motor tracts: Corticospinal tracts



Upper motor neuron lesion (UMNL)	Lower motor neuron lesions (LMNL)
Weakness (paralysis or paresis), hypertonia, hyperreflexia, positive Babinski sign and clones.	Weakness, hypotonia, hyporeflexia, fasciculations and wasting. Most characteristic sign of LMNL is ***fasciculations***

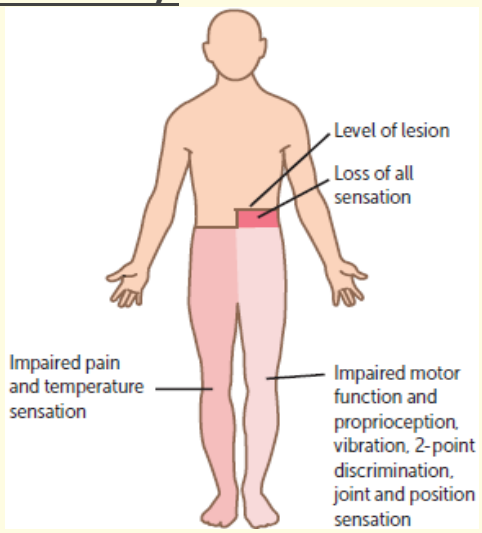
N.B: **Spasticity VS rigidity:**

Spasticity	Rigidity
<u>One</u> group of muscles. **Occurs with pyramidal lesions (clasp knife spasticity, e.g. stroke)**	<u>Both</u> groups of muscles (flexors and extensors). Extrapyramidal lesions, cog wheel (rigidity + tremor, e.g. Parkinsonism) or lead pipe (in all movement).

➢ Brown-sequard syndrome (hemisection of spinal cord):

- Ipsilateral weakness
- UMNL below the level of the lesion
- LMNL at the level of the lesion
- Dorsal column tract lost at the same side
- Spinothalamic tract lost in contralateral side 2 segments below the lesion.

- Spinal cord is supplied by anterior spinal artery (anterior 2/3) and posterior spinal (posterior 1/3).



➢ Anterior spinal artery occlusion (ASA):

- Acute loss of all tracts below the lesion except the dorsal column.
- Weakness and loss of spinothalamic sensations with preservation of dorsal column sensations.

➢ Conus medullaris lesion:	➢ Cauda Equina lesion:
- Both UMNL and LMNL (spinal cord lesion), sensory affection in form of sensory level at the saddle area (S2, 3, 4), early sphincteric and sexual disturbances.	- Only LMNL (only nerves), sensory affection in form of dermatomal loss, late sphincteric and sexual disturbances.

NOTE: Sphincteric disturbances.
- Lesion above S2 cause spastic bladder → urinary incontinence.
- Lesion in S2, 3 & 4 cause atonic bladder → urinary retention with overflow incontinence.

➢ Localization of spinal cord lesions:

- Spinal cord ends at level of L1 vertebra
- **Vertebra: segment**
- Cervical: add 1
- T1-T6: add 2
- T7-9: add 3
- T10-12: sacral and lumbar
- L1: coccygeal

➢ Cord compression and transverse myelitis features:

1- Spastic paralysis
2- Sensory level
3- Sphincteric disturbances
4- Radicular pain

Transverse myelitis:

Causes:

- **Acute infection**: Schistosoma and TB
- **Post infection:** immunological reaction; measles, CMV, EBV, varicella.
- **Post vaccination**
- **Demyelinating diseases**: MS and NMO
- **Systemic autoimmune diseases**: SLE and Sjogren's syndrome

Invx: MRI spinal cord and infection screen
Rx: high dose steroid and treat underlying cause

Cord compression:

Causes:

- Vertebral: pott's, metastasis, disc prolapse
- Epidural: abscess or hematoma
- Extramedullary tumors: meningioma
- Intramedullary tumors: glioma

Invx: MRI spinal cord
Rx: high dose steroid and surgical decompression

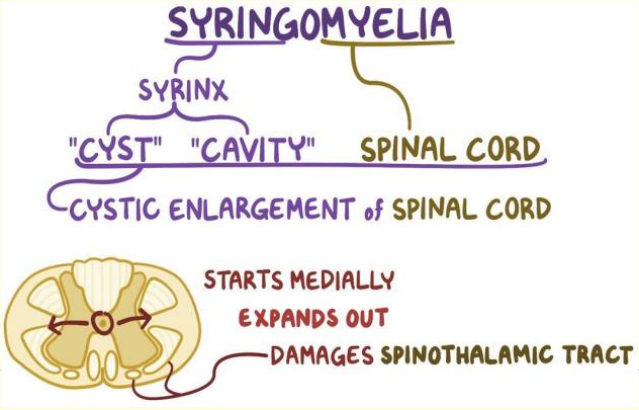
Syringomyelia:

- Fluid filled cavity in the central canal of the spinal cord
- Either *congenital* disease associated with Arnold chiari malformation type 1
- Or *acquired* by tumors or trauma

Sx:

- Suspended dissociated sensory loss (**Suspended:** affected segment; **dissociated:** only spinothalamic tract).
- LMNL features in upper limbs when the lesion extends to ventral horns (Upper limbs because mainly in cervical), loss of pain + temperature sensation → charcot joint.
- UMNL in lower limbs when it reaches the motor tracts.
- (So LMNL in upper limb and UMNL in lower limb).

Invx: MRI spinal cord → *Syrinx*
Rx: Surgery



Subacute combined degeneration of the cord (SACD):

- Caused by B12 deficiency
- **B12 deficiency first causes**
  1) Areflexia (peripheral neuropathy)
  2) Then cause **2)** SCDC: Presenting as spastic paralysis with loss of dorsal column tract
  3) Then it affect the **3)** Cortex causing dementia and psychiatric problems
  4) Optic atrophy
  5) Lastly it causes **5)** Autonomic neuropathy.

- Most common neurological presentation of B12 deficiency is **peripheral neuropathy**
- Most characteristic is **SCDC** (pathogenomic).
- *Dorsal column lesions are characterized by **positive Romberg sign →*** fall when close eyes *(differentiates it from cerebellar lesions)*

Motor neuron disease (MND):

- No sensory affection, degeneration of motor neurons.
- Characterized by *fasciculations (DDx Spinal muscular atrophy)*

1. **Amyotrophic lateral sclerosis (ALS)**: degeneration of motor neurons in cortex and anterior horn cells.
2. **Progressive muscular atrophy (PMA)**: only in anterior horn cells. Only LMNL
3. **Primary lateral sclerosis (PLS):** only Betz cells in motor cortex. UMNL only.
4. **Progressive bulbar palsy(PBP)**: LMNL in 9,10,11,12 cranial nerves in brain stem
   - Pseudobulbar palsy: when corticobulbar tracts are affected.
   - UMNL of the cranial nerves 9,10,11,12.

- Differentiate from bulbar palsy by the tongue:
  Bulbar palsy: LMNL, tongue fasciculations (bag of worms)
  Pseudobulbar palsy: UMNL, tongue is spastic and do not protrude.

- ***Most common is (ALS)***
- ***Most dangerous is (progressive bulbar palsy): risk of aspiration***

- **Dx:** clinically by exclusion of other causes
- **Rx:**
  - *Riluzole* increases survival by 3 months
  - *Non- invasive ventilation* increases survival by 7 months (so it is the most useful to prolong survival)

Role of 17 of cranial nerves:

CN **10** (uvular deviation) **+** CN **7** (facial deviation) → Deviation to opposite side of the lesion

CN **12** (tongue deviation) **+** CN **5** (jaw deviation) → Deviation to same side of the lesion

Spastic paralysis:

- **With sensory affection:**
  - **Sensory level:** cord compression and transverse myelitis
  - **With no sensory level:** SCDC or tapes dorsalis (both dorsal column), syringomyelia and anterior spinal artery occlusion (spinothalamic)

- **Without sensory affection:**
  - MND, parasagittal meningioma, hereditary spastic paraparesis and tropical spastic paraparesis

Flaccid paralysis:

Gullien barre syndrome and poliomyelitis

- ***Causes of mixed UMNL & LMNL:*** **MASTC**
  - **M**ND (motor Neuron Disease)
  - Friedreich's **A**taxia
  - **S**ub-acute combined degeneration of the cord (SACD)
  - **T**abes dorsalis (Syphilis)
  - **C**onus medullaris

Multiple sclerosis:

- Autoimmune disease causing demyelination in the CNS.
- "All cranial nerves are peripheral nerves except for the **optic nerve** which is a part of CNS".

Main sites of MS:

- Periventricular areas
- Optic nerve
- Cervical spinal cord
- Brain stem

Types:

1. Relapsing remitting (most common)
2. Secondary progressive
3. Primary progressive
4. Progressive relapsing
5. Unstandardized MS (NMO)

Clinically

- Can present with anything (palsy, hemiplegia,)
- But the most common presentation is unilateral **Optic neuritis;** *pain on eye movement, decrease visual acuity and color desaturation on central field*
- **Lehrmittie sign:** parasthesia on neck and back after neck flexion "shock wave sensation" → Indicate cervical spine MS
- **Utthof phenomena:** worsening of symptoms after hot bath
- **Bilateral internuclear ophthalmoplegia (INO):** damage in the medial longitudinal fasciculus causing disconnection between abducent nerve and oculomotor nerve; so ipsilateral ophthalmoplegia and Nystagmus of other when adduct ipsilateral (looking lateral to other eye) [Pathognomic]

  * First attack is diagnosed as **clinically isolated syndrome. (CIS)**

Dx: (Mainly Clinical)

1. MRI brain and spinal cord showing → plaques disseminated in time and place.
2. CSF analysis showing Oligoclonal bands of IgG (intrathecaly synthesized IgG).
   (DDx → GBS & Neurosyphilis)
3. Evoked potential showing decreased conduction

Use McDonald criteria to diagnose

Rx:

Acute attack: First line is **Steroids** (methylprednisolone) to decrease severity and duration of the attacks

Prevention of further attacks:

- Interferon β (not used now)
- Glatiramerer acetate
- Monoclonal ABs (Natalizumab)

Symptomatic management:

- **Spasticity:** baclofen (muscle Relaxant), dantroline, diazepam
- **Trigeminal neuralgia:** carbamazepine
- **Atonic bladder**: self-intermittent catheterization and methcholine
- **Spastic bladder**: (hyper responsive) oxybuterin (block parasympathetic)
- **Fatigue**: Amantadine (SSRIs)

Good prognostic features

- Typical cases have good prognosis:
- Females, relapsing remitting, long duration between attacks, optic neuritis, sensory Sx, young age

So, ***Poor Prognosis:*** Male, Elderly, Remission of relapse interval is short (may relapse early), ass. With other complication, 1ry progressive type (axonal loss), many MRI lesions, Motor symptoms at onset.

Neuromyelitis Optica NMO (Devic's disease):

- Bilateral optic neuritis with myelitis (>3 Segments affected)
- **Differ from MS by**:
  - Bilateral, Monophasic disease, severe attack but responds well to Rx
- **Dx:**
  1. MRI spinal cord lesion extending 3 or more segments (longitudinal myelitis)
  2. CSF analysis shows anti-aquaporin 4 Abs "in periventricular cells"
  3. MRI brain is normal
- **Rx:**
  - Steroids
  - If severe we can do plasmapheresis
  - Others: Anti CD20 Abs (rituximab), Micophenolate
- **Prognosis:** More aggressive than MS, Frequent attacks, severe progression.

Peripheral neuropathy:

- Most important sigh is **Areflexia**
- Usually affects ***distal muscles except GBS (proximal)***

Charcot joint:

- Painless swelling + loss of function
- Causes: according to affected joint
  - Ankle: DM
  - Knees: syphilis (tabes dorsalis)
  - Shoulder + Elbow: syringomyelia
  - wrist: leprosy (ulnar nerve affection)

Gullien barre syndrome (GBS) (AIDP):

- Acute inflammatory demyelinating polyradiculoneuropathy
- Autoimmune demyelinating disease of PNS.
- Usually preceded by infection (**campylobacter** is the most common poor prognosis)
- Others: mycoplasma, HIV, HepB,
- First symptom in GBS is **radicular pain**
- First sign is **areflexia**
- **Ascending flaccid paralysis (weakness)** ± sensory affection
- Sensory affection is not common (except for the back pain).
- Autonomic affection is rare and occurs late
- **Dx:**
    1. Nerve Conduction Studies: ***decreased conduction velocity***
    2. CSF analysis: ***albumin cell dissociation (increased albumin with normal cells)***
    3. ***Anti GM1 Abs in blood (poor prognosis)***
- **Rx:**
    1. 1. IV IGs or plasmapheresis (Equal in effect)
       Usually we do IVIG (easier and cheaper)
    2. **Respiratory support → Monitor by forced vital capacity every 4 hrs (Spirometry) or Chest Expansion.**

- **N.B.** DON'T GIVE STEROIDS
- Causes of death in GBS patients are **respiratory failure and arrhythmia (Autonomic Disturbance), and renal failure.**
- **Autonomic disturbances:**
    - Sphincteric and sexual disturbances, sweating problems, salivation problems and cardiac problems (arrhythmia and postural hypotension better IVIG to restore the circulation)
- **Poor prognosis in GBS:**

- Age more than 40 years
- Campylobacter jejini
- Anti GM1 Abs (granulocyte-monocyte Abs)
- Respiratory affection
- Rapid progression

Other variants of GBS

1. **Miller Fischer:** Traid of: ataxia + areflexia + ophthalmoplegia. Anti GQ1B Abs
2. **Polyneuritis cranialis:** affection of cranial nerves. (Bilateral facial palsy)

Chronic inflammatory demyelinating polyradiculoneuropathy: (CIPD)

- Prolonged course (months), less respiratory affection, less autonomic features and less cranial nerves affection. Responds to steroids

GBS → most patients will recover, it can cause Cranial Nerve Problems "e.g. *Bilateral Facial Palsy"*

DDx of bilateral facial nerve palsy: Leprosy, Lyme disease, Sarcoidosis

Muscular diseases (Myopathy):

1) Symmetrical proximal muscle weakness (e.g. difficulty in combing, climbing stairs, except Myotonia Dystrophia >> Distal affection, frontal bossing.
2) Gradual onset
3) Reflexes are normal

** **Myopathies** (Inflammatory, Dystrophies, Channelopathies, Myotonia, NMJ Problems, Acquired)

❖ Inflammatory Myopathies:

- C/O: Pain + Tenderness in muscle + Above Sx.

1. Polymyositis (PM): Myositis + systemic features (fever, wt. loss, malaise...etc.)
2. Dermatomyositis (DM): PM + skin manifestations
(Heliotrope rash = eye, Guttron's papules = knuckles, Shawl's sign = back, shoulder, Nail fold Erythema, Sub cutaneous calcification)

- If DM & PM is accompanied with *interstitial lung Fibrosis, Raynaud's, Cardiac Involvement, Mechanic hands* >> Anti-synthesase Syndrome +ve Anti-JO antibodies
- **N.B.** DM/PM usually points towards: Malignancy or SLE / RA

- **Invx:**
  1. ↑ muscle enzymes (e.g. CK-MB, LDH)
  2. EMG = Characteristic Pattern
  3. MRI of Muscles.
  4. Biopsy >>>> Gold Standard
  5. Malignancy Screen "CXR, A-U/S, PET scan"
  6. A/bs (ANA = SLE, Rheumatoid Factor = RA)

- **Causes of death:**
  i) Respiratory Failure ii) Cardiac Problems iii) GI Bleeding / Perforation

- **Tx:** Bed rest + limiting exercise
  ↓Inflammation by Steroids / Cytotoxic Drugs

❖ Channelopathies:

- Autosomal Dominant Defect in muscle membrane ion channels.

*** Hypokalemic Periodic Paralysis:**

- Diuretics exercise or heavy CHO meal >>> attack (**Invx**. $\downarrow K^+$ / **Tx:** IV KCl)

*** Hyperkalaemic Periodic Paralysis:**

- exercise >>> Attack (Invx: $\uparrow K^+$ / Tx: IV Ca^{2+} Gluconate

*Normokalemic variant is also found

❖ Muscular Dystrophies:

- Affect specific group of Muscles
- X-Linked >>>>> **Duchene's / Becker's**
- AD >>>>>>>>>> **Fascio-scapulo-humeral.**
- AR>>>>>>>>>> **Limb-girdle dystrophy (shoulder of pelvic girdle affection)**

* Duchene's:

- 4 yrs of Age → Clumpsy-movement
- Mention 3 signs: (Waddling gait; Pseudo hypertrophy of calf; +ve Gower sign)
- **Dx**: - Biopsy → Immunohistochemistry , ↓ Dystrophin. [Elevated Muscle Enzyme]
- **Causes of death**: (by Age of 20)
    - Cardiac complications (e.g: Dilated Cardiomyopathy)
    - Respiratory Failure (associated Kyphoscloiosis)
- **Tx:** Supportive

+ve Gower sign

* Becker's:

- mild form of Duchene's (Start at 10 yr)

* Fascio-Scapulo-Humeral:

Remember facial weakness "difficulty in puffing cheeks, chewing + winging of scapula"

- **Myotonia:**
- Congenita & Dystrophica.
- Prolonged contraction; delayed relaxation

- **Myotonic Dystrophy**:
    - AD (Autosomal Dominant)
    - **Dx:** EMG (Diagnostic Characteristic Pattern)
    - can be part of Syndrome "Cataract, Frontal …
    - Distal weakness of both upper & lower limbs.

Myasthenia gravis

Autoimmune disease, attacking nicotine receptors of Ach at NMJ.

<50 Years: Females, associated with other autoimmune disease, Thymic Hyperplasia.
>50 Years: Males, associated with Thymus atrophy, Tumor.

- Hallmark C/O is fatigable weakness [↑with exercise]
- First is eye muscles affection (ptosis and diplopia)
- Facial muscles (snarl face)
- Bulbar muscles
- Associated with thymic hyperplasia, thymoma and other autoimmune diseases.
    - Extraocular [Diplopia + ptosis] then Bulbar [dysphagia + dysarthria]

Dx:

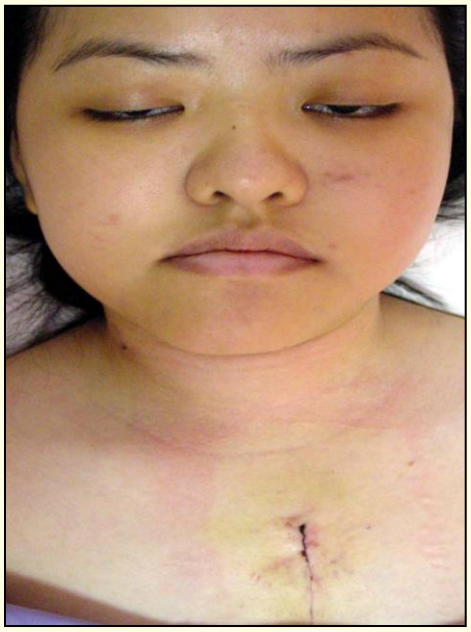
1. **Single fiber EMG:** increased single fiber jitter *(the most sensitive test)*
2. Serology: **anti-Acetylcholine receptor ABs** *(the most specific)*; and if negative do anti-MuSK. Anti-Striated muscles ABs indicates presence of thymoma
3. **EMG:** decremental response on repetitive stimulation
4. **Tensilon test** (now replaced by neostigmine eye drop)
5. **CT chest** for thymus.

Rx:

- Pyridostigmine [Anti-cholinesterase] for Sx. Control
- Immunosuppression → Prednisolone, Cytotoxic Drugs
- Thymectomy for all pts (in thymoma because it is a thymoma!! and in others as it improves the response)

	Myasthenic Crisis	Cholinergic Crisis
Preciptus	• Stress (eg, infection) or skipped drug [B-Blocker, CCB, Abs: Macrolide, Aminoglycosides & Antiarrhythmic] • Small dose of ttt.	Drug Overdose
Clinical	Worsening of Weakness	Worsening of weakness + signs of increased Acetylcholine (muscarinic Sx eg, meiosis)
Ttt.	Same + Resp. support + *plasmapheresis or IVIG*	*stop drugs*
Risk	Respiratory Failure	

In clinical practice you can differentiate them by pupil examination; constricted in cholinergic crisis and normal in myasthenic crisis.



Bilateral ptosis + surgical scar → MG?

Lambert Eaton myasthenic syndrome:

- Autoimmune or Para-neoplastic "Lung Ca"
- Abs attack presynaptic Voltage gated calcium channels
- Differentiate from MG:
  - **Improve with exercise**
  - **Areflexia and gait problems, autonomic involvement Sx. Occular and bulbar affection are rare**
- Indicate underlying malignancy (SCLC)

Dx:

- Serology: anti VGCC Abs (voltage gated calcium channels)
- EMG: incremental response on repetitive stimulation
- CXR to look for underlying malignancy

Rx: 3, 4 diaminopyridine (k+ channels blocker (-) delay the repolarization and prolong depolarization)

Parkinsonism

- Triad of:

1. **Bradykinesia** (shuffling gate, mask face, decrease arm swinging),
2. **Resting tremor "pill-rolling"**
3. **Rigidity (cog wheel)**

N.B: Types of tremors:

1. **Resting tremor →** Parkinsonism
2. **Action tremor (**muscle action**)**
    a. **Intention tremor →** cerebellar ataxia
    b. **Postural tremor (**in certain postures**) →** essential, thyrotoxicosis, anxiety

#Essential tremor:

Autosomal dominant, increased by stress, reduced by alcohol and treated by B blockers

- **Causes of Parkinsonism:**

1. Idiopathic = Parkinson's disease
2. Drugs (anti-psychotics and anti-emetics)
3. Trauma (dementia pugilistica)
4. Wilson disease
5. Parkinson plus syndrome

* **Other features in Parkinsonism**

- Constipation, autonomic features, sleep disorders, psychiatric problems (especially depression) and **anosmia (characteristic)**

"**N.B.**DM, GBS, parkinsonism and B12 deficiency are the most important causes of autonomic neuropathy"

Parkinson's:

- Prodrome "Yrs before Sx":
- Anosmia 90%
- Depression/ Anxiety 50%
- Sleep/Behavior disturbances
- **Pathogenesis:** Loss of Dopaminergic neurons in the Basal Ganglia "↓ Dopamine"

N.B. Asymmetric Sx. Points towards P.D "idiopathic form"

N.B. difference of bradykinesia of P.D from other bradykinesia: in P.D >> Developmental response on repititve movement.

Association: Dysphagia / Constipation / Seborrhea / Excessive Salivation

N.B. Myerson's sign: +ve Glabellar reflex

- **Dx:** Clinical

Rx:

1) **Levodopa + Carbidopa**
   - SE: is wearing-off effect That's why it is given in old age pts
   - Other SEs Long term: dyskinesia (treated amantidine), on and off phenomena (SC apomorphine) & psychosis.
2) **Dopamine agonists:**
   - Ergots derived: Bromocriptine (SE: serosal fibrosis). Non ergot: Cabergoline

Newer drugs: Ropinirole and Retigotine (SE dyskinesia and psychosis ,Binge behaviour)

- **Amantadine** is used to treat dyskinesia of levodopa
- On and off phenomena is treated by a sub cutaneous infusion of **apomorphine** (dopamine agonist)

Others:

- MAOIs: Selegline
- COMT inhibitors: Tolcapone and entecapone
- Antimuscarinics for Tremors: benzhexol and benztropine (for tremors)

Parkinson plus:

- Parkinson symptoms plus other features
- Symmetrical tremor (unlike of Parkinson asymmetrical)

1- Multiple system atrophy (shy dragger syndrome): + autonomic features and cerebellar ataxia. Divided to MSA-P (mainly parkinsonian features) and MSA-C (mainly cerebellar).

2- Progressive supranuclear palsy (SNP): + vertical gaze problem (especially downward gaze), early gate problems (recurrent falls) and cognitive impairment.

3- Lewy body dementia: + dementia and visual hallucination. Worsened by antipsychotics

4- Corticobasal degeneration: + sensory disturbances (apraxia and Stereognosis) and alien limb phenomena (invoulntory movement of hand)

5- Vascular Parkinsonism: in DM & HTN

Meningitis:

N.B: Meningism: Neck Stiffness + Photophobia + Phonophobia + +ve kerning's sign + +ve brudzinski sign

- **D.Dx of Meningism:**
  Meningitis, Subarachnoid Hemorrhage, Tremor & Intrathecal drugs.

- **Causative organisms** according to age of pt;
  - **0-3 months:** Str. Agalactia, E. coli and listeria
  - **3 months- 6 years:** Str. Pneumonie, H. Influenze and N. meningitides
  - **>6 years:** Str. Pneumonie, N. meningitidis and listeria
  - Immunocompromised, Alcoholic, cheese, old age or brain stem involvement: listeria

- **CSF analysis:**
  - Bacteria: high protein reduced glucose and neutrophilia
  - TB: same but lymphocytosis
  - Viral: high protein but normal glucose and lymphocytosis
  - Neisseria meningitidis: occurs in epidemics, meningococcemia, DIC and rash, can present by hypotension due to adrenal crisis (waterhouse frederichson).

- **Invx:**
  - LP + CSF Analysis: for Color & Proteins, glucose.
  - CBC [Leukocytosis]
  - RFT: ↓ Na^+ (SIADH)
  - Blood Culture: Especially if CSF –ve. +ve in 50%.
  - CT/MRI: meningeal enhancement.
- **Complications of meningitis**:
  - ↓LOC / Coma. - Convulsions
  - Obstructive hydrocephalus - Brain Abscess
  - SIADH
  - N. Mengitiditis: (Waterhouse Frederichson's syndrome)
  - Complications of Str. Pneumonie meningitis: subdural abscess and cranial nerve palsies
- **Rx:**
  - Admission.
  - IV A/b "3rd gen Cephalosporin (ceftriaxone) for 2 weeks.
  - Add ampicillin if suspecting listeria (Immunocompromised + Age >55)
  - Chloramphenicol can be used as second line for N. meningitidis
  - Contacts are given Rifampicin

- Cerebral Malaria >>>>>> -ve Brudziniski's; -ve Kernig's

TB Meningitis:

N.B: CNS TB: [Meningitis; Meningioma; Pott's Disease**]**

- **C/O**: S/s of TB + subacute (2-8 weeks)
- In **CSF Analysis:** ↑ cells but lymphocytes. Do ZN Staining, Culture in L.J medium
- **Others**: Tuberculin; CXR
- **Tx:** Anti TB drugs for 9 months, Exchange of Ethambutol by Streptomycin.

1. Steroids for:
   1) Hydrocephalus
   2) Deteriorating Conscious Level
   3) Progressing signs.
2. Surgery: - Hydrocephalus - Tuberculoma

Encephalitis:

- Differ from meningitis by Low grade fever, decreased level of consciousness and behavioral personality changes.
- (Localizing sign; Convulsions = more common)
- Herpes encephalitis is characterized by its temporal lobe involvement
- **Invx:**
  1. CT/ MRI brain: Exclude SOL "for LP".
  2. CSF analysis: normal Glucose & -ve culture.
     - And Remember PCR on CSF sample (faster). & Serology

N.B. in CT you may see Temporal Lobe abnormities or brain edema >> Herpes Simplex Virus

- **Rx:** - Supportive
  - Acyclovir + careful fluid balance
  - Steroids "if brain edema"

Notes:

❖ **Stroke**:

- Small vessel disease >>> Lipohyalanosis (HTN)
- Poor Prognosis:
  - Age > 70
  - > 1 Attack
  - Loss of Consciousness, Crossed Hemiplegia, Convulsions.
  - Neck Stiffness, Aspiration Pneumonia.
- Primary Prevention → Control Risk Factors.
- Secondary Prevention → Control Risk + Clopidogrel (Ischemic)
- Risk Factors: [HTN, DM, Smoking, ↑Lipids, Family Hx, Elderly, Alcohol, Polycythemia, Aneurysm, drug Abuse, Inta/Extracranial Atheroma]

❖ **Epilepsy:**

- Precipitation: Lack of sleep, emotional disturbances, infection, music, prolonged reading of calculation, sudden withdraw of Anti-epileptic.
- Pseudoseizures → Psychological, normal EEG, doesn't respond to Antiepileptics.
- **Status Epilepticus:**
- > 30min or repeated attack without regain of consciousness.
- Tx: ABC
  - IV Bolus Lorazepam 2-4mg [Repeat if not stopped in 1 min] or Buccal Midazolam
  - If failed: Phenytoin IV infusion or Fosphenytoin
  - Phenobarbitone; if failed GA + Intubation

❖ **Headache:**

- Migraine: Agg. By walking stairs or similar physical activity (unlike cluster headache pt. who is moving around)
- Other variants:
  1. Opthalmoplegic: Diplopia > Occulomotor Palsy
  2. Retinal: Acute persisting visual loss in one eye ± scotomatous field defect

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❖ **Mechanism of Nerve Injury:**

- Demyelination → Schwann cell damage e.g Gillian Barre.
- Axonal Degeneration → Axonal Damage.
- Compression → Focal demyelination [entrapment e.g: Compartment syn.]
- Infarction → Microinfarct of Vasa nervorum [Wallerian degeneration]
- Infiltration →Inflammatory cells e.g Leprosy & Granuloma

❖ Types of Peripheral Neuropathy [PN]:

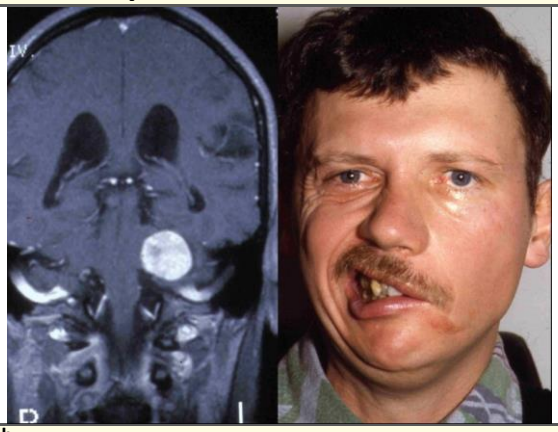
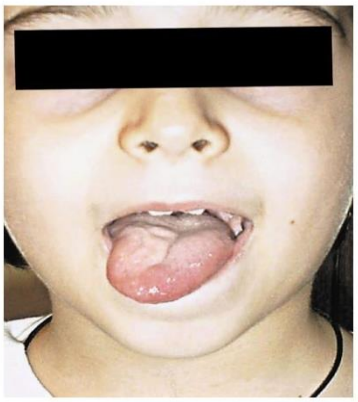
- Mononeuropathy → Single Nerve [Focal]
- Mononeuritis Multiplex → Several single nerve [Multifocal]
- Polyneuropathy → Bilateral Symmetrical Wide spread [Generalized]

❖ Causes of Peripheral Neuropathy [PN]:

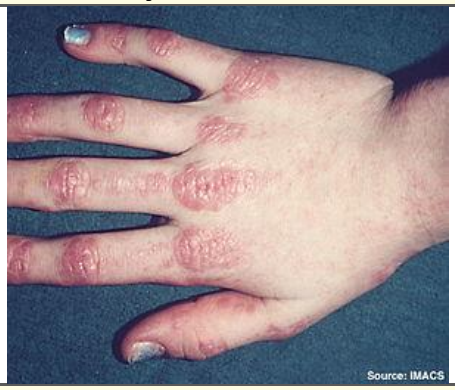
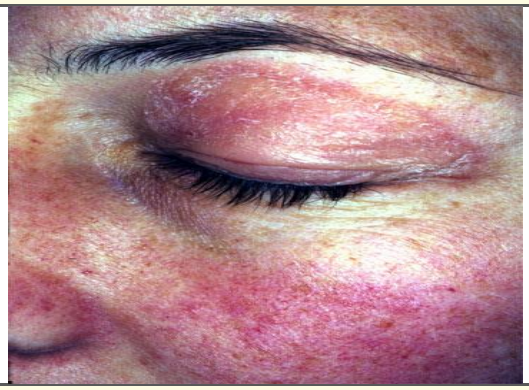
1. Inflammatory → GBS
2. Infectious → Leprosy
3. Malignancy → Lymphoma, MM
4. Metabolic → DM / B12 Defiency
5. Drugs & Toxins → Alcohol, Metronidazole, INH
6. Genetic → HMSN, F. Ataxia

- Acute PN → Onset over 4 Wks.
- Subacute PN → onset over 8 Wks.
- Chronic → onset over ≥3 months

❖ Nerve palsies

	
7th cranial palsy left LMN **Cerebellar pontine angle ➔ acoustic neuroma (NF)**	**Right sided hypoglossal nerve palsy of LMN**

❖ Dermatomyositis

	
Gottron papules	**Heliotropic rash**

يارب إني مُحسن الظن في تدبيرك
فتولّني. ♡

Respiratory System

**Recorded on 11, 18 Nov.2018 / 20Dec.2018

Contents

Pleural Effusion:

- **It is the accumulation of fluid in the pleural space i.e. between the parietal and visceral pleura.**
- **Normally there is 20-30 ml of fluid in this space for lubrication and to prevent collapse**
- Fluid in Pleural Space; 300 ml→ X-ray changes 500 ml →Symptomatic

Sx:

- Asymptomatic as incidental finding
- Pleuritic Chest Pain [Sharp, localized, ↑ by inspiration & coughing)
- Dyspnea most common symptom

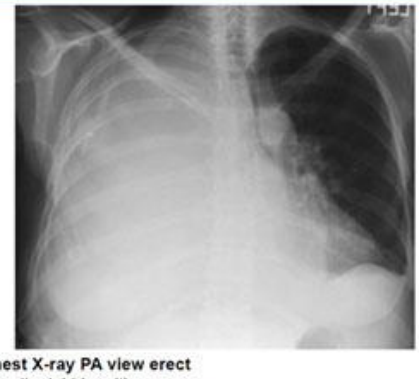
  Pleuritic chest pain sharp and localized, increased by deep inspiration and cough i.e. when pleura moves.

  Angina pain is crushing central retrosternal radiating to the left shoulder and jaw.

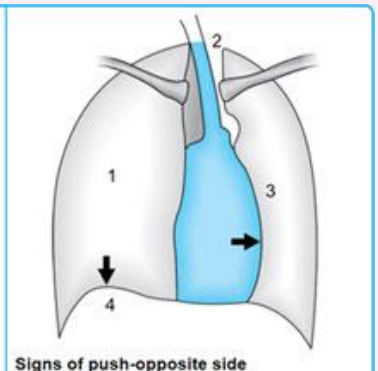
Signs:

- Side affected is moving less and bulging when you see the patient at the end of the bed *(in contrast to fibrosis where the side affected is moving less and depressed)*
- ↓ Chest Expansion *(decreased chest movement by palpation)*
- ↓ Breath sounds
- Stony Dull on Percussion *(stony dull is most important feature to pleural effusion, resonance is normal, hyper resonance in pneumothorax, dull in consolidation, pneumonia and fibrosis)*
- ± ↓ Tactile Vocal Fremitus / Vocal Resonance (like in pneumothorax they are also decreased but in contrast to consolidation and cavitation they are increased).
- ± Tracheal deviation to other side if massive
- ± Bronchial breathing on top of area of effusion

Pleural effusion



Chest X-ray PA view erect
Opacity right hemithorax
Right diaphragm dome obscured
Right cardiac border obscured
No air bronchogram/bronchovascular markings
Signs of push–mediacstinal shift to left tracheal shift to left widened, i.e. spaces
Increased thoracic volume right side



Signs of push-opposite side
1. Opacity right hemithorax
2. Tracheal shift to left side
3. Mediastinal shift to left-black arrow
4. Right diaphragm dome obscured-black arrow
5. Right cardiac border obscured

Right massive pleural effusion in tension

Causes:

Transudative .vs. Exudative

Transudative	Exudative
❖ **They are the causes of** **1. Increased hydrostatic pressure:** ▪ **HF** ▪ **Constrictive Pericarditis** **2. Decreased oncotic pressure:** ▪ **↓ Protein [malnutrition, Malabsorption; Liver disease; Nephrotic]** **3. Hypothyroidism** ***4.* Meig's Syndrome: Ovarian fibroma + Ascites + Rt. Pleural Effusion *(the cause of pleural effusion is unknown but it thought to be transmitted from ascites through the diaphragm).***	❖ **Infections and malignancy are the most two important causes** ▪ Infection: Pneumonia (it is called para pneumonic effusion), TB ▪ Malignancy: Ca Lung; Mets; Mesothelioma, lymphoma ▪ CTD: RA; SLE ▪ Pulmonary Infarction happen in PE ▪ Dressler's Syndrome happen in MI ▪ Yellow Nails Syndrome (v.rare) → 1ry Lymphedema (yellow nails + Bronchiectasis + Sinusitis + Pleural effusion (chylo) ▪ Yellow nail syndrome is a triad of (exudative pleural effusion + yellow nails + lymphedema) and usually in 60% of cases they have recurrent infections in a form of bronchiectasis and sinusitis. ▪ Pancreatitis & Chylothorax

Invx:

- Start with general investigations like CBC looking for signs of infection, etc.
- And then do specific investigations:

1. **CXR – PA** and lateral**:**
   - Homogenous Opacity + obliteration of costophrenic angle
   - + no air bronchogram (Meniscus sign) (if there is air bronchogram it means pneumonia)

2. **US & Diagnostic Aspiration:**

- US used to confirm there is fluid in pleural space and for aspiration guidance
- US to guide aspiration in Small effusion then Diagnostic Aspiration for:

  - Biochemistry: (Proteins / LDH / Glucose / pH / Amylase + Pancreatic enzymes)
  - Microscopy: (Staining gimsa and ZN + Culture & Sensitivity (TB))
  - Cytology: Malignant cells
  - ± Immunology: (RF ; ANA ; Complement levels)

3. **Pleural Biopsy (Best)**

- If inconclusive aspiration (Thoracoscopic or CT guided)
  - Protein < 25 g/L → Transudate
  - Protein > 35 g/L → Exudate
  - Protein 25 g/L – 35 g/L → Light's Criteria:
    - Exudate if any of: one is enough
      - Fluid protein / Serum Protein > 0.5
      - Fluid LDH / serum LDH > 0.6
      - Fluid LDH > ⅔ Upper limit of serum LDH

- **interpretation:**
  - **↓ Glucose (<3.3 mmol/L):** Empyema, TB, Malignancy, CTDs
  - Normal Mesothelial cells: PE
  - Abnormal Mesothelial cells: Mesothelioma
  - ↑ Amylase: Pancreatitis, Esophageal Rupture
  - ↑ Neutrophils: Pneumonia, PE (because it causes inflammatory process).
  - Bloody: Trauma, Malignancy, TB, PE
  - Turbid: Empyema

✓ IF Suspicious for Malignant Effusion → Do CT Scan

Ttt:

1. **Treat underlying cause.**
2. **Drain** slowly **(By needle or Chest tube) if:**
   - Symptomatic
   - Parapneumonic Effusion with (↓pH <7.2 or Pus drained or +ve culture) because they indicate empyema and it should be drained even if the pt is asymptomatic

- N.B: Empyema is drained by Chest Tube
- Slowly & Repeatedly ≤ 2L/24h
- N.B: in HF even if symptomatic Give Diuretics (no drainage)

3. **Pleurodesis (Sclerosing Agent**): for recurrent Effusion or Malignant effusion
   - Use Tetracycline; Bleomycine; Talc
4. **If all fails >> Surgery** for example pleurodectomy.

Pneumothorax:-

- **Spontaneous (Rupture of Subpleural Bullae) or Traumatic**

Spontaneous Pneumothorax	Traumatic Pneumothorax
▪ **Primary:** - **Thin, tall, young smoker male in healthy lungs, occur due to rupture of sub-pleural bleb.** ▪ **Secondary:** - **Lung disease: (Asthma; COPD) is more dangerous**	- **Is for surgery** ▪ **Iatrogenic:** - CVP - Pleural Aspiration - PPV ▪ **Accidental:** - RTA

N.B: If communication act as one-way valve = Tension Pneumothorax
If communication in both ways but close = Closed Pneumothorax
If continue to be open = Open Pneumothorax

Symptoms: the same symptoms of pleural effusion

- Asymptomatic.
- Dyspnea; Pleuritic Chest pain

Signs:

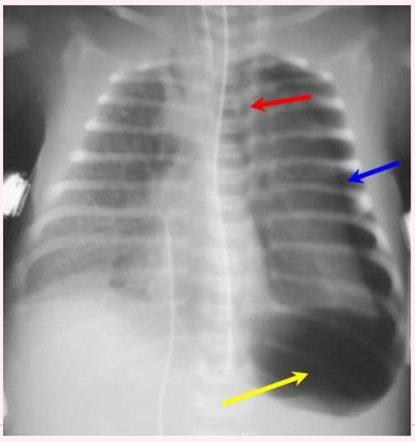
- ↓ Chest Expansion
- ↓ Breath sounds (you may find bronchial or vesicular breathing)
- **Hyper resonance on Percussion**
- ± Tracheal deviation (to other side if Tension Pneumothorax)

Diagnosis:

- CXR: increased Lung Translucency
  - Calculate rim of Air: between lung margin & chest wall to be used in management

N.B: If Tension Pneumothorax; don't do CXR; treat immediately by chest draining.

Pneumothorax



Management:

Primary	Secondary:
- **Asymptomatic or Rim of Air <2cm on CXR → Discharge & follow up in 2-3 wks.** - **<u>Otherwise</u>: (i.e. the pt is symptomatic and Rim of air is >2cm) → Aspirate with Percutaneous needle** ▪ **<u>If failed:</u> → Repeat Aspiration** ▪ **<u>If failed:</u> → Chest Drain**	- Age > 50 y and rim of air > 2cm on CXR and Symptomatic → **Chest Drain** by chest tube - **<u>Otherwise:</u>**→ Aspiration by percutaneous needle - After Aspiration = Admit for 24 hours & observe (.v.s discharge if 1ry) - **N.B:** 2ndry + Age <50 + rim <2cm → Aspiration ✓ **Recurrent Pneumothorax:** 1ry or 2ndry to (COPD; Marfan's)

❖ **After ttt:**

a) No diving for life
b) No air travel for 2 wks after ttt (Normal CXR)
c) Stop smoking

❖ **Surgical Advice in spontaneous pneumothorax:**

a. Recurrent ≥ 2 on the same side
b. Hx. Of pneumothorax on otherside
c. Bilateral spontaneous pneumothorax
d. Failure of Chest drain to inflate lung in 48 hours

❖ **When to remove drain?**

After 24 hrs from Reinflation + Stop of Bubbling

Pulmonary Embolism (PE):

Sources

- **Veins:**
  - DVT (Proximal Thigh i.e. above the knee) is the most common site. (most common site for atherosclerosis is infra renal abdominal aorta).
  - Rare: - Pregnancy it leads to thrombosis in unusual sites like portal and abdominal veins - CV line in upper extremity
- **Cardiac:**
  - Rt. Side Failure (mural thrombi after MI; or if it is caused by IE)
- **Amniotic Fluid** it causes DIC; air embolism after injection; Fat Embolism after fracture of long bones and it is associated with petechia

Risk Factors:

- Surgery: is the 2nd important one (Orthopedic especially of the lower limp, Abdominal)
- Malignancy: (Abdominal; Pelvic like pancreatic cancer) is the 4th.
- Conditions that increase estrogen level like Pregnancy and COCS is the 6th.
- Hx. Of VTE → Strongest is the most important risk factor 1st.
- Prolonged Immobilization (Stroke, Fracture, Travel) is the 3rd
- Thrombophilia is the 5th risk factor (or hypercoagulable state whatever if it is congenital like protein C & S deficiency or acquired like Antiphospholipid syndrome)
- OCP
- CVS →HTN, HF

Symptoms: differ according to size:

Massive PE	Acute, non-massive, segmental PE	Chronic, non-massive, segmental PE
- **Shock** - **Syncope** - **Signs of Pulmonary HTN: [↑JVP, palpable P2, left Parasternal Heave]**	- Dyspnea - ↑ RR; ↑HR - Pleuritic Chest Pain - *Low Grade Fever* - *Hemoptysis,* cough	- RHF (pt present with raised JVP, ascites and lower limb edema)

Invx:

General investigations:

- **1. CXR 2. ECG 3. ABG**

Specific investigations:

- **4. D-Dimer 5. CT-PA 6. V/Q Scan**

1. **<u>CXR:</u>** most likely it is Normal

   Or:

   - Elevated hemi diaphragm
   - wester mark sign (Oligemia, you know it by collapsed vasculature).
   - Hampton hump sign (Wedge Shaped opacity) it is triangular in shape its base is facing sub pleural space and its apex is facing toward the lung.
   - Linear Atelectasis or collapse
   - Pulmonary Effusion
   - Dilated Pulmonary Arteries

2. **<u>ECG:</u>**
   - Sinus Tachycardia is the most common finding
   - Rt. Axis deviation, RBBB
   - *(normally both lead I and lead II should be QRS positive in ECG, if one of them is negative it means that there is axis deviation, if lead I is negative and lead II positive, i.e. facing each other this is right axis deviation, and the opposite is left axis deviation i.e. lead I is positive and lead II is negative مقبلين بعيد من بعض)*
   - *(in bundle branch block in ECG you find wide QRS complex (>3 small squares) with M sign, if you find these changes in V1 it is right BBB, if you find it in V6 it is left BBB).*
   - S I Q III T III (20%) (deep S wave in lead I, pathological Q wave in lead iii, inverted T wave in lead iii)→ Characteristic is pathognomonic for PE

3. **<u>ABG:</u>** **Type 1 Respiratory Failure**
   - *Respiratory failure means there is hypoxia PO2 <8 KPa, <60 mmgh…*
   - *If normal CO2 or low it is type 1, if CO2 is high it is type 2.*

   - ***Causes of type 1 RF; anything that lead to V/Q mismatch like:-***
     - *Intrinsic lung diseases like pneumonia and pulmonary edema*
     - *Causes of airway obstruction like asthma and COPD*
     - *Causes of poor perfusion like PE*
     - *If there is anything between the membranes and it increases the thickness like fibrosis.*
   - ***Causes of type 2 RF; are any problem in respiratory apparatus from :***
     - *Brain stem (stroke) → spinal cord (any spinal cord disease) → peripheral nerves (GBS) → muscles (MG)*
     - *Any chest wall deformities like kyphoscoliosis.*
     - *In addition to any cause of RF type 1 can lead to type 2 RF if exhaustion occur like asthmatic patients for example.*
     - *Drugs that causes respiratory depression like opioid can also lead to RF type 2)*
   - ↓PO_2 , ↓PCO_2 (Hyperventilation + poor gas exchange)
   - Respiratory Alkalosis
   - If massive; Metabolic Acidosis with increased anion gab due to anaerobic metabolism

that increases lactic acid.

- ***Other causes for metabolic acidosis with increased anion gab:***
  - **I.** *DKA because it increases ketones*
  - **II.** *Aspirin toxicity: by its metabolite salicylic acid and the aspirin also increase the respiratory drive leading to respiratory alkalosis*
  - **III.** *Ethanol.*
- **N.B** this is explained in renal chapter.

4. <u>D-Dimer:</u>

- [**High –ve Predictive Value]** it means it is very sensitive → i.e. if you find it –ve you should role out the disease but if you find it +ve this will not confirm the disease. Like BNP in heart failure
- In low Risk Pts. If –ve → Send Home
- D-Dimer it is fibrin degradation product.

5. <u>CT-PA:</u>

- Gold Standard; may miss Peripheral Segmental Arteries. Angiography is better than CT-PA

6. <u>V/Q Scan:</u>

- *(it measure ventilation perfusion mismatch)* ↓ Perfusion Lung/Heart function should be normal
- May be abnormal if other Lung disease.
- Affected by COPD and Mitral disease
- High –ve Predictive Value; If –ve there is no PE.
- May be +ve in Vasculitis; Past PE; AVM

- ↓PO_2 , ↓PCO_2 (Hyperventilation + poor gas exchange)
- Respiratory Alkalosis

7. <u>Doppler US of Legs:</u> If DVT is the suspected cause

<u>Diagnosis:</u>

- **If High Probability PE: [Sx + RFs + no other DX]**
  - Treatment + CTPA
- **If Intermediate or Low Probability PE:**
  - D-dimer
    - If –ve: Send Home
    - If +ve: CT-PA & Treat if +ve

N.B: *Probability is by Modified Well's Criteria. <4 = unlikely; >4 = Likely*

Management: Divide the pts into:

1. **Hemodynamic Instability** (shock, hypotension caused by massive PE) →

Supportive management in form of IV fluids +/- inotropes + thrombolysis by TPA or streptokinase

- If contraindicated → Embolectomy + Venacaval filter
- Then treat as Stable

2. **If Stable** → LMW Heparin until INR is fixed at > 2.0 for 24 hours or until 5 days, Whichever Longer, then add Warfarin after 24 hours (continue warfarin for:

If known Cause → for 3 months, If Ca / Unknown cause → for 6 months, Thrombophilia → for Life) and continue both for 5 days

- After that Oral Anti-coagulation
  - For Life: Irreversible Cause.
  - For 6 months: Reversible Cause.

3. **Acute management:** → O_2 + IV Fluid + analgesia + ABCs

❖ ***If Massive:***

- IV Fluid; Inotropes
- Thrombolysis: tPA, Streptokinase → if failed: Embolectomy

❖ ***If Not Massive:***

- SC LMW Heparin until INR ≥ 2.0 for 24 hrs or until 5 days. (Whichever Longer)
- Start Warfarin: after 24 Hrs
  - If known Cause → for 3 months
  - If Ca / Unknown → for 6 months
  - Thrombophilia → for Life
- ***Aim is to keep INR 2.0 – 3.0***
- **Drug Interactions:**
  - Enzyme Inducers: Warfarin Toxicity:
  - Enzyme Inhibitors: Bleeding
  - All Antibiotics are Inhibitors except Rifampicin
  - All Antiepileptics are inducers except Na Valproate
  - If Taking OCP: Stop & Change to IUCD
- ***2ndry Prevention:***
  - Secondary prevention is by warfarin, if there is any problem with warfarin or CI use IVC filter (بالعربي اسمو المصفاة).
    - IVC Filter (if on Warfarin & Still get PE or if there's CI to Warfarin)
- **N.B:** LMWH → No Need to monitor & given SC.

Unfractionated Heparin → Monitor by APTT (2-3x) and if Renal Impaired.

Heparin:

- **Mechanism of action** → it works on two clotting factors active factor ii (thrombin) and active factor X (10) inhibiting them.
- **Unfractionated heparin** is taken IV and has short half-life and needs **monitoring by APTT**, and its action is reversible by *Protamine Sulphate*.
- It is then improved to **LMWT heparin** (like Enoxaparin and Dalteparin) which has longer half-life, taken subcutaneously, doesn't need monitoring and it is mainly works on factor X.
- Any pt on heparin and he is going to have surgery, LMWT heparin should be change to unfractionated heparin for its shorter half-life which can be stopped whenever we want for surgery.
- **Side effects:**
  1) Bleeding
  2) Osteoporosis
  3) heparin induced thrombocytopenia (HIT):

     Clinically present with thrombosis after 3-5 days after starting treatment and thrombocytopenia, antibodies are formed against platelet factor 4 which is attached to heparin, this complex (which is composed of platelet factor 4, heparin and antibody) will activate the platelets, leading to their consumption and thrombosis.

Warfarin:

- Is taken orally, its action is inhibiting vit K dependent factors which are X, IX, II, VII (1972) synthesis in the liver and inhibit protein C &S also.
- Needs time to start its action because it works on enzymes level, it blocks enzymes that reduce vit K which is needed to be in the reduced form to be used in the synthesis of the clotting factors 1972.
- Warfarin is started after 24 hours not from the beginning, because it inhibits protein C & S which are anticoagulants leading to thrombosis initially which will make the condition worse → so we give heparin first alone and give it a time to work to prevent this thrombosis to occur. Warfarin later on will be a blood thinner (anticoagulant).
- **Warfarin monitoring is by INR.**
- **Warfarin toxicity (antidote)** is treated by *Vit.K injection* *(used to treat small amount of bleeding)* or fresh frozen plasma *(used to treat massive bleeding immediately).*
- Warfarin is metabolized by cytochrome P450, so any enzyme inhibitor will lead to bleeding (i.e. warfarin toxicity) most important one to remember are macrolides (azithromycin, erythromycin and clarithromycin)

Lung Cancer:

Risk Factors:

- Smoking (x10) most important risk factor!
- Chemicals: Asbestosis (x5) if Asbestos + smoking (5 x10 = 50 (Synergism)), arsenic...etc
- ✓ *From surgical and outcome point of view lung cancer is divided to two Types are SCLC (small cell lung cancer) (20%) which is more dangerous and Non SCLC [Squamous. Adeno, Large Cell). (in order of most common, squamous is most common then adeno then large cell cancer) (80%)*

Types:

- Most common lung cancer is Squamous Cell Carcinoma (SCC Lung), then Small C, then Adenocarcinoma then large cell carcinoma.

 # Squamous Cell Carcinoma:

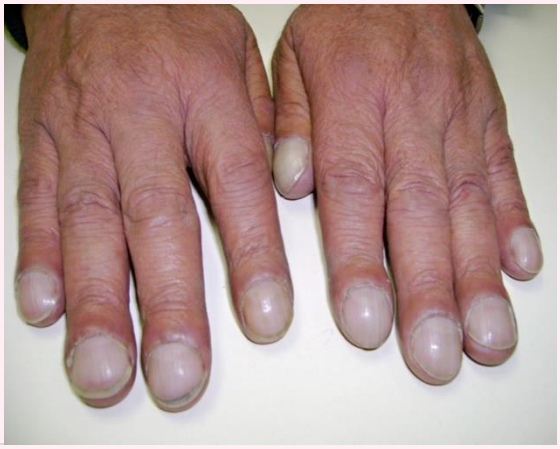
- Most common one, most common in smokers, mostly is located centrally near the bronchi, i.e. medially.
- Necrotic & Invasive. Squamous and small are Central; others are peripheral
- Paraneoplastic features are:
  - PTHrP (↑ Ca^{+}) **hypercalcemia** is the most important one, due to PTHrP release not PTH, PTH level is normal or low (unlike in small cell in which ACTH is released to get Cushing syndrome).
  - **Clubbing, HPOA**

✓ **N.B.** *squamous lung cancer is the most invasive type (like Pancoast tumor for example which invade sympathetic trunk, so any pt present with hoarseness of voice, tracheal or esophageal compression i.e. symptoms of invasion the squamous cell type is the most likely type, except superior vena cava syndrome which occur more with small cell type) and most one has skeletal features which is hypertrophic pulmonary osteoarthropathy, which is grade 5 clubbing, include: clubbing, wrest pain and x-ray features in form of new bone formation*.

✓ *Hoarseness of voice is due to recurrent laryngeal nerve invasion.*

- **Grades of clubbing:**

- **grade 1:** loss of angle
- **grade2:** fluctuation (there are different opinions on which is grade 1 and which is grade 2!)
- **grade 3:** increase longitudinal curvature
- **grade 4:** drum stick appearance (due to soft tissue swelling)
- **grade 5:** hypertrophic pulmonary osteoarthropthy



❖ **Respiratory causes of clubbing:**
- Lung cancer (squamous and mesothelioma)
- Cystic fibrosis
- Suppurative lung diseases: empyema, bronchiectasis and lung abscess
- Two of Interstitial lung diseases: idiopathic pulmonary fibrosis (IPF) and asbestosis.

 # Adenocarcinoma:
- Most common type in Non Smokers
- Location is Peripheral → Normal Bronchoscopy, so it can be missed on bronchoscopy.
- Paraneoplastic: Gynecomastia (Also in SCC)
- Subtype: Bronchoalveolar CA → Copious amount secretions (so it can be misleading as the common type of cough for lung cancer is dry cough) & Multifocal so it is difficult to do surgical resection for it.

 # Small Cell Lung carcinoma:
- Early Mets .. that is why it isn't treated surgically.
- Paraneoplastic syndromes are:
  - Cerebellar Ataxia [due to formation of Anti Purkinje Cells Antibodies]
  - Lambert-Eaton Syndrome
  - SIADH due to ADH release
  - Cushing syndrome [due to ACTH release].

Symptoms:
- **Primary Lesion**
  - Dry Cough – Most common presentation (Except Bronchoalveloar subtype of adenocarcinoma type)
  - Hemoptysis (not Massive)

N.B. Causes of massive hemoptysis:
1. *Bronchiectasis*
2. *Aspergilloma*
3. *Carcinoid syndrome in the lung (Endo bronchial carcinoid tumor)*
4. *Pulmonary infarction.*

Definition of massive hemoptysis: *large amount to the degree that impaired respiration or leading to hemodynamic instability*.

  - Dyspnea: [Obstruction + collapse / Ass. COPD / Pleural Effusion / Pneumonia (non-resolving; recurrent on same side)]
  - Wheezes: Monophasic, if bronchi is blocked.

***N.B**. Wheeze is a sound that is produced from passage of the air through narrow airways, it has two types if only one airway is blocked it will be monophasic wheeze like in cancer, if multiple airways are affected like in asthma it will be polyphasic wheeze.*

- Chest Pain: if Involvement of Chest Wall or Pleura (Pleuritic) has occurred.

- **Invasion: (mostly with Apical Tumors)** occur mostly with squamous type
  - Intrathoracic Spread: Phrenic Nerve; Pleural; Pericardium
  - Dyspnea, Stridor → Trachea
  - Dysphagia → Esophagus
  - Invasion to recurrent laryngeal nerve leads to hoarseness of voice
    - If unilaterally affected or can leads to vocal cord paralysis
    - If completely bilaterally affected and here the patient will present with aphonia
    - If partially affected bilaterally will lead to stridor and airway obstruction.

  - **Pancoast Syndrome:**
    - *Typically results from a malignant neoplasm of the superior sulcus of the lung (apical tumor) leads to destructive lesions of the brachial plexus roots especially C8, T1, T2 and cervical sympathetic nerves (stellate ganglion).*
    - *Patient presents with shoulder pain radiate to the scapula + wasting of small muscles of hand which are supplied with Ulner nerve myotom C8, T1 + Horner syndrome (Ptosis, Miosis, Anhydrosis)*
    - *Pain in the arm + wasting of small muscles of hand (Brachial Neuralgia) lesion in C8, T1*

  - **Horner Syndrome**: (Ptosis, Miosis, Anhydrosis)

  - **SVC Syndrome**: occur especially with small cell type (Oncologic ER)
    - Dilated neck veins; **<u>Pulseless</u>** raised JVP most important feature
    - Headache / Blurring of vision
    - Congestion (Swollen) of Face/Neck/Arms
    - Dyspnea, Orthopnea
    - Plethora, Cyanosis.
    - Pemberton's Test: lifting arms over head for > 1min: causes:
      - Facial Plethora / Cyanosis
      - ↑ JVP (non-pulsatile)
      - Inspiratory Stridor

- **Manage it:** IV high dose Dexamethasone *(to reduce the swelling, it's an inflammatory process)* + Heparin (or thrombolysis) (quick) then radiotherapy (if all this failed ❼ consider surgery (endovascular Stenting)
- **(Note:** some are chemo sensitive, so better if you do biopsy)

- **Metastasis**
  - **Brain:** Most common site, especially with small cell type
  - **Liver:** Jaundice & ↑ ALP
  - **Bones:** Exacerbate ↑Ca^{+}, bone pain
  - **Adrenals:** Hypoadrenalism, adrenal crisis
- **Paraneoplastic:**
  - **Endocrine:** SIADH, Cushing, Hypercalcemia
  - **Neuro:**
    - Cerebellar like syndrome
    - Dementia
    - Peripheral Neuropathy
    - Motor Neuron like Disease
    - Lambert Eaton Syndrome
  - **Skeletal:**
    - Clubbing
    - HPOA (Clubbing + Wrist Pain) (Dx by ↑ Uptake in bone scan; X-Ray: perositis) No limitation of movement
  - **Skin:**
    - Acanthosis Nigrans *(its common with lung and stomach cancers), it's a feature of insulin resistance, you can find it also in diabetes type 2, obesity and PCOS*
    - Dermatomyositis
    - Herpes Zoster
  - **Hematological:**
    - DIC
    - Thrombophlebitis Migrans
    - Marantic Endocarditis
    - TTP (Thrombotic Thrombocytopenic Purpura)
    - Selective Red-Cell Aplasia (Mets)

- **Non-Specific**: Bad Prognosis
  - Anemia
  - Malaise
  - Aches & pain
  - Fever
  - Anorexia
  - Wt. loss

Diagnosis:

- **General:**
  - CBC → ↓Hb, ↓Platelets. Electrolytes for Endocrinopathies
  - RFT: Electrolytes ↑Ca
  - LFTs: ↑ ALP + Jaundice (Mets)
  - Coagulation Profile → DIC
  - CXR for Staging (CT may not be needed, used to increase the clarity and to asses LN)
    - Mass +Slow resolving Consolidation
    - Collapse
    - Hillar Lymphadenopathy
    - Unilateral Pleural Effusion (D.dx: mesothelioma)

- **Tissue:**
  - **For Central →** Fibrooptic Bronchoscopy
  - **For Peripheral →** Percutaneous Needle Biopsy under CT guidance
    - **TTNA:** US/CT guided → comp: hemoptysis + pneumothorax
    - **TBNA:** Peripheral & hilar LN
    - **EEBS:(Endoscopic Endobronchial US): (Endoscope + US +Doppler)** Best; better
    - TBNA because you can see Vessels
  - **Mediastinoscopy** → Higher LNs
  - **Mediastinostomy** → Lower LNs (Sub-cranial)
  - **Others:** Sputum cytology + Pleural Asp cytology

- **Staging:**
  - CT / PET / MRI (Site/LN involvement/Mets TNM)

- **Fitness:**
  - Pulmonary Function Tests (FEV_1 >1L) most important one!
  - ECG
  - Echo

Treatment:

1. **NSCLC**

➢ Usually not responsive to Chemo, but Neoadjuvant Chemo is Used

- SURGERY is Curative for Stage 1 & 2a (Early) → Pneumectomy. If late stages -> radiotherapy
- If localized; early; candidate for curative surgery but poor health (IHD, COPD) → aggressive Radio/Chemo or both. (N.B: Poor: >70y, FEV1 <1.5L, <2 if lob
- Radiotherapy: Imp. In palliation
- Intraoperative Staging is important > (Could be non resectable)

Contraindications to surgery in NSCLC type:

1. Late stages (stage IIIB, stage IV), i.e. presences of metastasis.
2. Aggressive invasion: to SVC (SVC syndrome) or recurrent laryngeal nerve bilaterally (vocal cord paralysis) or to pleura (malignant pleural effusion).
3. Unfit patients: from his general health (for example pt with MI is unfit pt) or if his FEV1 <1.5 L.
4. Inoperable tumors: tumor near the hilum or within 2 cm from the bronchi.

2. SCLC

- Mets may not be seen on Imaging
- Chemotherapy & Radiotherapy
- No role of Surgery, because it metastasizes early, so at the time of presentation it has been already metastasized.

So NSCLC → Early: Surgery; Late: Radio. SCLC→ Radio&Chemo

N.B: Contraindications to Surgery:

1. Distant Mets / Intrathoracic Spread (e.g. SVC obstruction)
2. Poor Respiratory Function
3. Serious Illness: e.g IHD
4. > 65 yrs / but acc. To health status
5. Malignant Effusion
6. < 2cm from main bronchus (Hilum)
7. Hoarseness of Voice
8. Bilateral Tumor

Obstructive Disease: (Asthma; COPD; Pneumonia; Suppartive Lung):

- Asthma - COPD - Bronchiectasis
- 1 ISLD: Broncholitis Obliterans (Elderly)
- PFT: spirometer
- **In obstructive:** unable to get air out of the lung >> large lung
- **In restrictive:** unable to get air in >> small lung

Obstructive			Restrictive
PFT:	**FEV1 / FVC**	**↓ <70%**	**FEV1/FVC normal or high**
	FEV 1	**↓ <80%**	

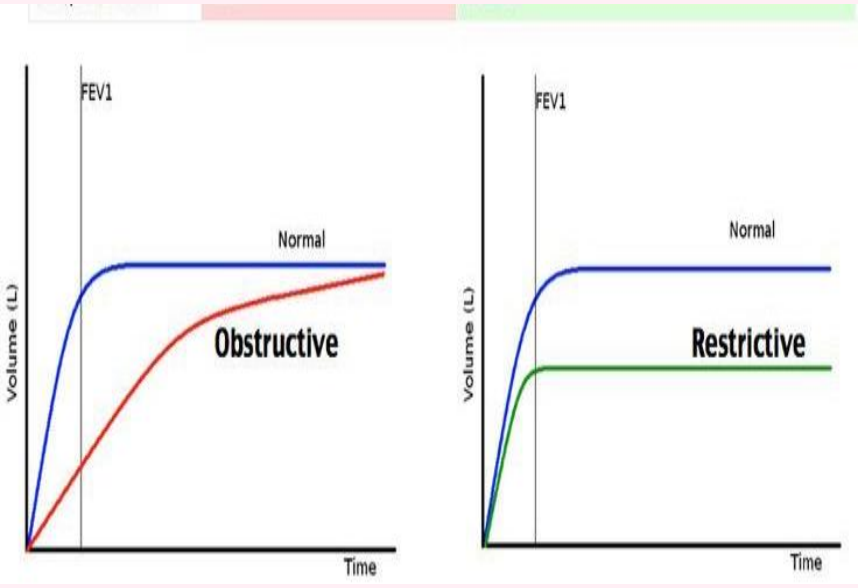
Reversibility with Salbutamol:

- FEV1 ↑ by 15% → Asthma
- FEV1 No Increase → COPD

DLCO: measure gas transfer through the alveolar membrane (CO2)

Interstitial & Emphysema: ↓DLCO (Diffusion Lung Capacity of CO2); in Asthma DLCO is ↑

Total lung capacity & Residual volume are high in obstructive; low in restrictive



Asthma:

- Inflammatory condition characterized by chronic hyper responsiveness of Airways to various stimuli causing reversible bronchoconstriction.
- **Phenotypes:**

Extrinsic	Intrinsic
- **(Atopic)** - **Child** - **+ve Skin test**	- No history of atopy - Child or adult - -ve Skin test

Atopy: (Rhinitis, Eczema, Hay fever …etc)

Main Triggers: *External allergens (e.g Dust), Exercise, Emotions, Cold Air, Drugs (B-Blockers, NSAIDs, Infections)

- ***When you suspect Asthma: Assess Probability:***
    1. Typical Sx: Dry Cough, Chest tightness, Dyspnea, Wheeze
    2. ↑ Sx at night (morning dipping & diurnal variation)
    3. Stimuli :Exercise/NSAIDs/B-Blocker/External Allergens: Cause
    4. FHx of Atopy
    5. Peripheral unexplained Eosinophilia

- ***If ↑ Probability →*** *Trial of Ttt.*
- ***If Intermediate →*** *Spirometry*
    - If FEV_1/FVC <70% → Asthma.
    - If >70% : Do Reversibility Test: if FEV_1 Improves by >15% (>400ml) after Bronchodilators → Asthma
- ***If ↓ Probability →*** *Other Dx.*
- Diurnal Variability (PFM): EFR(variation) >20% in 2 weeks: Asthma

Management:

Chronic Asthma: -

- *Avoid Allergens +* ***STEPWISE Management***

Step 1: SABA on Need (salbutamal)

Step 2: If use SABA more than one time/day or have night symptoms
add ICS (200 – 800 ug/day)
400 is the proper initial dose. - Dose according to severity

(Fluticasone = Lipophilic, ½ Dose of Budesonide, Beclamethasone)

Step 3: Add LABA (Salmeterol) + Assess control:

- **Good →** Continue
- **Partial →** ↑ ICS to 800ug/Day
- **Poor →** stop LABA + consider others:
  - (Leukotriene Receptor Antagonist or Theophylline)

Step 4: ↑ ICS to 2000ug/day or Add 4th Drug

Step 5: Above + Oral Prednisolone & Refer

Can try Steroid sparing drugs for 3 months (Methotrexate; Cyclosporine; Oral Gold)

N.B:

- Leukotriene Receptor Antagonist (Montelukast, Zafirleukocast)

  * Better in Aspirin induced Asthma

  * ↑ or cause Churg-Strauss (Eosinophilia + Asthma + Peripheral Neuropathy + Nephrotic Syndrome + Necrotizing Vasculitis) Tx: Steroids

Moderate Asthma:-

- PEFR >50%
- Normal Pulse, RR, Speech

Acute Asthma: (Severe V.S. Life Threatening)

- **Severe:**
  - PEFR 33 – 50 %
  - Can't Complete Sentence
  - RR ≥ 25
  - HR ≥ 110 bpm

- **Life Threatening:**
  - PEF < 33%
  - Hypotension / Bradycardia / arrhythmia
  - Exhaustion / Confusion / Coma
  - Silent Chest
  - Cyanosis
  - ABG:
    - SpO_2 < 92%
    - PaO_2 < 8.0 KPa
    - Normal $PaCO_2$ (4.5 – 6.0 KPa)

- **Near Fatal:**
  - ↑ PaCO2 (>6.0KPa)
  - pH <7.3
  - Intubate & Ventilate

Management of Acute Asthma: **SOS**

1. Nebulized **S**albutamol 5mg + high Flow $\mathbf{O_2}$.
2. **S**teroids (Oral Prednisolone or IV Hydrocortisone) [Both if very ill]

If Life-threatening: (Consider ICU)

3. Continue Nebulization + add Ipratropium every 15 mins.

Do CXR to exclude Pneumothorax

4. If needed:
    - IV $MgSO_4$ (RR should be >25)
    - Or IV Aminophylline
    - IV salbutamol
    - Or Nebulized B2 Agonist
    - Nebulized Ipratropium

If Failed: Transfer to ICU → Intubate & Ventilate (no Role for non-Invasive Ventilation (CPAP)

If Improving: Continue O_2 - Prednisolone for 5 – 7 days - Neb. Salbutamol 4 Hrly.

No Response to tx: - Wrong Dx: (COPD, Pulm. Edema, GORD)
- Non-compliance to ttt
- Wrong way of using ttt
- Steroid Resistant Asthma

Occupational Asthma:

- Improves in Holiday (Isocyanide Cobalt)
- Ttt: Quit Job/Minimize exposure

Exercise Induced Asthma:

- Dx: Spirometry before & after exercise
- Ttt: Bronchodilator before exercise

N.B:

- Nocturnal Asthma → ICS is the ttt.
- Brittle Asthma: (severe-life threatening attacks in mins/hrs)→ Special Program (risk of sudden death)
- Rescue Therapy after any attack: Prednisolone for 1-2 wks.

COPD:

- Preventable + treatable lung disease
- Characterized by Pulmonary & extrapulmonary manifestations
  - **Pulmonary:** Irreversible Airflow Limitation
  - **Extrapulmonary**:
    - Myopathy
    - Osteoporosis
    - Salt/Water Retention
    - CO_2 retention (Morning Headache, Bounding Pulse, Asterixis, Confusion)

Risk Factors:

- Smoking - Pollution (indoor & outdoor) - Genetic (a1-antitrypsin def.)
- In children: LBW, maternal Smoking, Recurrent infections…etc

Old Classification:

Chronic Bronchitis	Emphysema
- **Clinically** - **Productive cough in most days in at least 3 cons. Months in at least 2 cons. Yrs (increase in secretions)**	- **Pathologically** - Irreversible airway dilatation distal to terminal bronchioles with destruction of their walls. ↓ DLCO

Differences:

Main Sx: (cough +sputum/Dypsnea/Wheeze) **Chronic Bronchitis:** Productive Cough
Emphysema: Dyspnea

Signs: more in Emphysema

- ↓ Chest expansion [Vertical inflation]
- Hyperinflation & Hyperresonance on percussion, Barrel Chest
- Cricoid notch distance <3cm
- Tracheal Tug "Depression of trachea on inspiration = airflow limit."
- In Chronic bronchitis → Crackles

Complications: more in chronic bronchitis

- Acute exacerbation + infection
- Type II Resp. Failure
- Hypoxia >> Pulmonary HTN → Corpulmonale
- 2ndry Polycythemia - Pneumothorax - Bronchiectasis

2 varieties

Pink Puffers: emphysema	Blue Bloaters: chronic bronchitis
- **↑ Alveolar ventilation**	- ↓ Alveolar ventilation
- **Compensate by increasing RR**	- ↑ $PaCO_2$
- **Normal or ↓ $PaCO_2$**	- Compensate by shunting
- **Breathless/not cyanosed**	- Cyanosed / Not Breathless
- **RF Type 1**	- Corpulmonale

Investigations:

≥ 40 yrs, Smoker, Chronic Productive cough or SOB; do:

1. Post bronchodilator Spirometry (Reversibility): FEV1/FVC <70%
2. CBC: Polycythemia, ↑ WBCs (Infection or steroid Neutrophilia)
3. BMI: Metabolic Syndrome (weight loss)
4. CXR: Hyperinflation:
    - > 6 ribs anteriorly above the diaphragm in mid-clavicular
    - Flat hemidiaphragm
    - Bullae (air felled spade)
5. Sputum Ex. 6. ABG 7. HR-CT for Emphysema 8. ECG for p.HTN

Staging:

- by FEV1; so for severity not for Dx:

1: mild → $FEV_1 \geq 80\%$

2: Moderate → FEV_1 50 – 79%

3: Severe → FEV_1 30 – 49%

4: Very Severe → $FEV_1 < 30\%$

Treatment:

- Treat comorbidities
- General:
  - Stop Smoking
  - In B,C,D: Annual Flu-vaccination.
  - 5 yr vaccination for Pneumococcus
  - Encourage Exercise
  - SABA/SAMA as need for All
  - **In stage 1,2 (FEV1 > 50%) if not improve add LABA or LAMA**
  - **In stage 3,4 add (ICS + LABA) or LAMA**

	↓Sx.	**↑ Sx.**
↑Risk	C	D
↓ Risk	A	B

(↑Risk = 2 or more Exacerbation w/hosp.)
(↑ Sx = CAT 10 or more)
(↓ Risk = 1 or less Exacerbation /y, without hosp)
(↓ Sx = CAT < 10)

A Less Sx & less Risk

A → SAMA or SABA
B → LAMA or LABA
C → ICS + LAMA or LABA
D → ICS + LAMA &/or LABA

(SAMA: Ipratropium)
(LAMA: Tiotropium)
(SABA: Salbutamol)
(LABA: Salmeterol)
(ICS: Beclometasone)

Theophylline → Used earlier in COPD as it enhance Diaphragmatic muscle contractility
Mucolytic in Pts with thick sputum

<u>Drugs/ttt that Increase Survival:</u>

1. Smoking Cessation: Most important
2. Long Term O_2 Therapy (LTOT)
3. Surgery in Selected Pts. ($PaCO_2$ 4.5 – 6.0Kpa)

<u>LTOT:</u> O_2 Therapy >15h/day (Pt must be non-smoker On maximum ttt)

Indications:

- PaO_2 <55 mmHg (7.3Kpa) in 2 occasions, 3 wks apart)
- PaO_2 55 – 60 mmHg (7.3 – 8.0Kpa) &
  - 2ndry Polycythemia
  - Pulmonary HTN
  - Peripheral Edema
  - Nocturnal Hypoxemia

Benefits of LTOT:

- ↓ Polycythemia
- ↓ Sympathetic, ↓ Salt & Water Retention → Pul HTN
- Improves Sleep
- ↓ Arrythmia

<u>Acute Exacerbation of COPD:</u>

- M.C: - H. influenzae - S. Pneumoniae - M. Cattarhalis
- M.C viral: - Rhinovirus

Management:

1. O_2 (not high Flow; Start with 24 – 28% O_2 using Venturi Mask)
2. Nebulized Salbutamol **+** Ipratropium Bromide
3. Steroids
4. Abs if signs of Pneumonia / DVT Prophylaxis

- If no improvement or PaCO2 ↑ despite ttt:
  - Non-Invasive Ventilation (NIPPV) (endotracheal tube)
- If Failed:
  - Invasive Ventilation (Mechanical Ventilation)
- **<u>N.B:</u> O_2 Therapy aims to SaO_2 94%-98%, but in COPD the aim is 88% - 92% (unless normal CO2) [PaO_2 >8.0Kpa)**

<u>NOTE: Polycythemia:</u>

Primary: ↑ RBCs, WBCs, Platelets → Myeloid Lineage

Mainly: RBCs: PC rubravera → itch in hot bath, erythema
WBCs: CML
Platelets: Essential Thrombocytopenia

Secondary:

Hypoxia, HCC, RCC, Ovarian Fibroma, Pheochromocytoma,

Do O_2 Sat. ABG:

- **Normal: (RCC, HCC) →** do Abd. US
- **↓ Sat., PaO_2: Resp cause (e.g COPD) →** do Pul. Function test

Pneumonia:-

- Acute inflammation of the lung + recently developed radiological changes
- No radiological changes=no pneumonia

Types:

1. Community acquired pneumonia (CAP)
2. Hospital acquired pneumonia (HAP)
3. Pneumonia in immunecompromised
4. Aspiration pneumonia

***CAP:**

- Organisms: ***Most commonly step. pneumonie***, H.influenzee, L. pneumophila, viruses

RF:

1. extremes of age: >65 ,<16 years
2. comorbidities (malnutrition, HIV, CHD, DM, etc)
3. lung diseases(COPD, CF, bronchiectasis, etc)
4. life style: smoking, alcohol, IV drug abuse
5. corticosteroids therapy

C/O:

Acute onset,

Symptoms:

- High grade fever(39-40 C),
- Cough dry then productive(mucopurulent -/+ hemoptysis),
- Pleuritic chest pain(sharp and stabbing increased by cough and respiration)
- Dyspnea.

Signs: ↑Fever / Tachycardia / Tachypnea

- Consolidation: (DDX : lung collapse with patent main bronchus)
    - ↑or ↓ Chest expansion.
    - Bronchial breathing + Pleural rub
    - + Coarse crackles
    - Dullness on percussion,
    - increased TVF/VR ± whispering Pectorlioquy

DDx: Pulmonary infarction, pulmonary edema, TB

Specific features:

- **S. Pneumoniae:** Rusty sputum, herpes labialis, flu like illness before atypical pneumonia

N.B. Atypical pneumonia:

- walking pneumonia
- CXR worse than Sx.
- Bilateral patchy X ray changes

- ***M.pneumoniae:***

- Epidemics - Atypical - Dry Cough - Walking Pneumonia

- ***Extrapulmonary manifestations of M. pneumoniae:***
  - Hematology: Hemolytic Anemia (Cold Agglutinin)
  - CNS: Meningioencephalitis GBS Transverse Myelitis
  - CVS: Pericarditis Myocarditis
  - Skin: Erythema nodusum -Erythema multiforme; Steven Johnson syndrome Toxic Epidermal Necrolysis
  - Renal: Glomerulonephritis [Hematuria]

- **CXR:** worse than symptoms (Atypical Pneumonia) (Bilateral CXR changes; Patchy consolidation)
- **Dx**: Serology - Cold Agglutinin at 4 C
- **Rx**: Erythromycin / Clarithromycin

- ***L. pneumophila***:

- Coolers and showers - [Water source] No person to person contact
- Pneumonia and GI Sx. + Relative Bradycardia
- In elderly can present with confusion and recurrent falls.
- **Lab**: hyponatremia [SIADH], lymphopenia, increased CK, Abnormal LFTs
- **Dx** by urinary Ag,
- **Rx** by erythromycin.

- ***Klebsiella***:

- Characteristically affects the upper lobe (Rt, Upper lobe abscess) [Abscess: S.auerus; Klebsiella]
- Pt is Alcoholic, DM, Old
- Very high mortality (30%)
- Current jelly sputum

Investigations:-

1. **CXR:** Consolidation ± Effusion

- Consolidation "homogenous opacity" + air bronchogram “visible airway line due to surrounding fluid”
- Consolidation in Rt. middle and Lt. lingual lobes: silhouette sign to heart (loss of normal boarder)
- Consolidation in lower lobe: silhouette sign to diaphragm

2. **Sputum** (stain gram and ZN, microscopy & culture)
   I. In severe pneumonia ii. Not responding to ttt (C&S) iii. For epid.
3. **Blood**(CBC , U and E, culture)
4. **ABG**
5. **Serology**

Prognosis: -

- Pulmonary severity index :-

  CURB-65:

  Confusion, **U**rea ≥ 7, **R**espiratory rate ≥ 30 per minute, **BP** systolic ≤ 90 or diastolic ≤60, Age > **65**

- 0,1: outpatient, 2: hospital, ≥ 3 may need ICU
- 0,1: oral amoxicillin at home
- 2 : at hospital with oral amoxicillin & oral clarithromycin
- 3,4,5: ICU, IV macrolides & third generation cephalosporin or Amoclan (co-amoxuclav)

- ***Other poor prognosis features:***

Clinically:

1. 60 yrs
2. More than one lobe (or bilateral)
3. Comorbidities (e.g DM)
4. Respiratory Rate ≥ 30 [Resp. Failure: PaO_2 <8.0 KPa, SaO_2 <92%)
5. Hypotension: CVS Failure
6. Atrial Fibrillation

Lab:

1. Hypoxia: PaO_2 < 8.0 KPa (i.e < 60mmHg)
2. WBCs: Leukopenia < 4000. Or-brisk leukocytosis > 20,000
3. +ve blood culture → sepsis
4. ↑ Serum Urea: Marker of renal failure

- These Pts. Needs aggressive ttt → ICU. Needs Dialysis + ventilation + monitoring

Rx of pneumonia:-

- Oxygen for all hypoxemic pts. aim is SaO2 94-98%, if COPD 88-92% (loss of hypoxia drive)
- Supportive: Paracetamol/ Pethidine/ Morphine/ Chest physiotherapy , if retention of sputum
- Antibiotics: Empirical
    - Mild / Moderate: Oral Amoxicillin + Clarithromycin (if hospital adm.)
    - Severe: IV Coamoxiclav (or 3rd gen Ceph) **AND** IV Clarithromycin.
    - S. aureus → Clarithromycin + Flucloxacillin. If MRSA is suspected → add Vancomycin or Teicoplanin.

Other types:-

- **HAP: [Nosocomial Pneumonia]:**
  - Pneumonia occurring ≥ 2days after hospital admission, ***subtypes:***
    - ***a.*** Ventilator associated pneumonia
    - ***b.*** Health care associated pneumonia HCAP (admission ≥2 days, IV ABs, attended hemodialysis unit, stay in nursing home or other long term health care facility)
  - Organisms: Early: like CAP; Late: P. aeruginosa, Klebsiella, anaerobes, staph including MRSA
  - **Rx:**
    - **<5 day of admission**: Coamoxiclav / 3rd gen. Cephalosporins
    - **> 5 days of admission:** Anti-Pseudomonal: (Piperacillin + Tazobactam) or Ciprofloxacin or Broad spectrum (IV aminoglycosides + 3rd generation or anti-pseudomonas penicillin). If MRSA IV vancomycin

- **Aspiration pneumonia**
  - Anesthesia especially pregnancy (Menddson syndrome). - Stroke-bulbar palsy. Esophageal dilation – Alcoholic - Unconscious
  - Can cause lung abscess or bronchiectasis
  - **Rx**: according to culture

❖ **Pneumocystis Jervici Pneumonia:-**

- In IMC especially HIV , most common opportunistic infection in AIDS; post transplant
- Prevention if: Total CD4 < 200 give PCP prophylaxis [Cotrimoxazole]
- C/O: HIV + pneumonia sx + *rapid desaturation on exercise*

- **Dx:**
  - **CXR:** bilateral diffuse shadowing starting perihilary and extending in butterfly shape.
  - immunofluorescence on induced sputum
  - or Bronchoalveolar lavage then biopsy [Silver stain = cyst] as it presents with dry cough
- **Rx:**
  - Cotrimoxazole → 1^{est} line
  - Clindamycin + Primaquine → 2^{nd} line
  - IV Pentamidine in severe cases
  - Steroids if hypoxia, to reduce mortality

Complications of pneumonia

1. **Respiratory Failure [**ttt by O_2 + ventilation] if doesn't improve or CO_2 is rising progressively or Acidosis → ICU for ventilation.

2. **Para pneumonic effusion:** pus – Empyema

➢ ***Empyema:***

- Pus in pleural space, presents as continuity of fever and rising markers despite adequate Antibiotic therapy
- **Causes:** pneumonia, infection of hydrothorax, rupture of ALA
- **Signs of pleural effusion:** decreased chest expansion on affected site, decreased TVF/VR, stony dull on percussion, decreased air entry but normal vesicular , mediastinal shift away from the lesion , ***Clubbing***
- **Complications:** rupture:
  - To bronchi: broncho pleural fistula, copious sputum, pyo-pneumothorax.
  - To Skin and subcutaneous tissue: SC abscess, skin fissures
- **Rx of empyema :** Drainage by tube and underwater seal, IV ABs for 2-4 weeks

3. **Lung Collapse:**
   - Due to retention of sputum
   - **Collapse:**
     - Obstruction by LN (TB, CA).
     - By FB.
     - By retained secretions (post-operative)
     - by bronchial casts allergies broncho pulmonary aspergillosis
   - **signs:** collapse and patent main bronchus is same as consolidation but mediastinal shift towards the lesion
   - Collapse and obstructed main bronchus:
     - decreased chest expansion,
     - Air entry and decreased TFV/VR
     - Dull on percussion
     - Mediastinal shift towards the lesion

4. **Suppurative pneumonia and lung abscess:**
   - S.Pneumoniae can cause destruction of lung parenchyma and formation of micro abscess , collection of these result in lung abscess, other causes:
     - Certain pneumonia : staph aureus and Klebsiella
     - Septic emboli : IV drugs, right sided I.E. ,or ALA rupture
     - obstruction of airways
     - Lemmicis syndrome: fever + sore throat + swollen neck, results in LRTI + jugular vein thrombosis caused by Faso bacteremia
     - Infected pulmonary infarction
   - **C/F**: Swinging remittent fever, **clubbing**, cough, foul smelling purulent sputum
   - **CXR:** Air-filled cavity surrounded by wall
   - **Rx:** Co-Amoxiclav + Metronidazole then according to culture for 4-6 weeks

5. **<u>General:</u>**
   - Septicemia
   - Multiorgan failure “Circulatory collapse, ARDS, ARF”

N.B: if BP doesn’t improve with Tx → ICU for inotropes

- Other complications: AF, Cholestatic Jaundice, Myocarditis, Pericarditis, Meningioencephalitis , DVT → PE

Corpulmonale:-

- RHF due to Pulmonary HTN
- Pulmonary HTN: Pul. Arterial Pressure > 25 mmHg.
- **Causes:**
  - Chronic Lung disease: Asthma, COPD, Fibrosis
  - Pulmonary Vascular disease: PE, Vasculitis, ARDS, Sickle
  - Thoracic/Neuromuscular: Kyphosis, MG, GBS
  - ↓ Ventilation: Obstructive Sleep Apnea. High Altitude.
- **Signs:**
  - Loud/Palpable P2
  - Left Parasternal Heave
  - RHF signs
  - Graham steel murmur (Pul. Regurg. = early diastolic)
  - Tricuspid regurg (Pansystolic)
  - ↑ JVP + Prominent a & v waves. (a = Pul HTN) (v= Tricuspid reg.)
- **Dx:**
  - ECG: RVH "Strain Pattern"
  - CXR: Prominent Hilar pulmonary vessels + Oligemic Lung fields
  - ABG.
  - CBC "Polycythemia"
- **Tx:**
  - Underlying cause
  - Tx. Of respiratory Failure
  - Tx. Of HF "Diuretics"
  - Venesection if HCT > 55%.
  - Heart/Lung Transplant

Bronchiectasis:-

- Abnormal, permanent dilatation of the bronchi "Small to medium sized"
- **Causes:** Localized "Focal" or Diffused.
  1. ↓ Ciliary function:
     - Congenital: Immobile Cilia Syn (ICS) or Kartagner's: ICS + dextrocardia and situs invertus + Adrenoinsuffiency.
     - Acquired: Young's syn (Bronchiectasis + Sinusitis + infertility)
  2. Cystic Fibrosis
  3. Immunodeficiency
     - Congenital: Hypogammaglobulinemia, IgA defiency
     - Acquired: HIV
  4. Severe Infections:
     - Child: TB, Pertussis, Measles, S. aureus
     - Adult: Suppartive Pneumonia
  5. Obstruction: Foreign Body / Tumor
  6. Allergic Bronchopulmonary Aspergillosis (ABPA).

N.B: (CCII: Ciliary, CF, Infective, Immunodeficeny, others ABPA, obstruction, yellow nail syn)

- **C/O**: Productive Cough, foul smelling, purulent and copious amount. Mainly in the morning.

➢ N.B: can be changed by posture if localized
Clubbing / Recurrent Infections / Hemoptysis

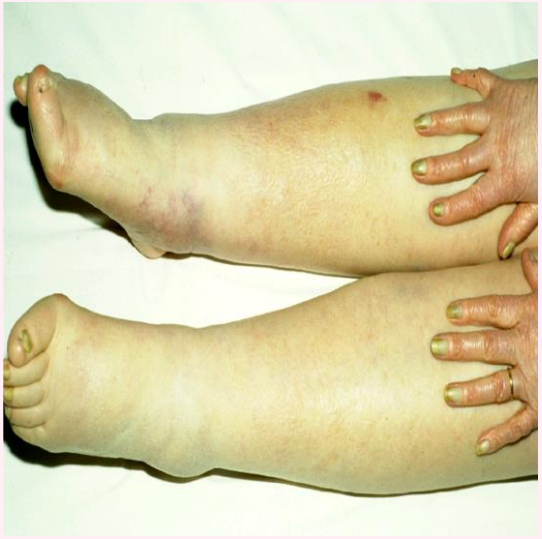
- **O/E: Coarse mid-inspiratory Crackles**

- **Dx:** Obstructive Pattern on PFTs
  1. CXR: Tram-track appearance "Dilated bronchi, thick walls ± cysts" or normal
  2. HRCT: best
     - Cut 1mm Assess extent & distribution - "Signet-ring sign"
  3. Sputum Examination
     - Most isolated organism is H.influenzee
  4. You can do Sweat Cl test (CF) / Test for Ciliary function "Nasal Saccharin test"

- **Tx:**
    1. Postural Drainage (at least 1/day)
    2. Physiotherapy (non CF pts)
    3. Antibiotics for acute exacerbations according to culture
    4. Surgery if localized disease or massive hemoptysis
    5. & Treatment of underlying cause if possible

N.B: “Add bronchodilators if with Asthma; Steroids if with ABPA”

- **Complications:**
    1. Massive Hempytsis
    2. Pneumonia / Pneumothorax/Empyema
    3. Metastatis Abscess “Brain”
    4. RF type 1
    5. Pul HTN → Corpulmonale
    6. Amyloidosis “Check for splenomegaly > chronic inflammation”



Bronchiectesis, AIDS, RA, chronic sinusitis,

chylothorax,, non-pitting edema

A triad of yellow nails+ pleural effusion+ lymphedema

Diffuse Parenchymal Lung Disease (DPLD) (Interstitial Lung Disease):

د. محمد ميرغني

Lung Parenchyma:

1. Alveolar Epithelium
2. Capillary endothelium
3. Space between them
4. Alveolar Space
5. Lymphatics

Etiology:

1. **Idiopathic:** Idiopathic Interstitial Pneumonia
   i. Idiopathic Pulmonary Fibrosis (Usual Interstitial Pneumonia)
   ii. Others: - Cryptogenic Organizing Pneumonia - Lymphocytic IP
2. **Immunological:** e.g "Sarcoidosis; Extrinsic Allergic Alveolitis"
3. **Occupational:** Pneumoconiosis
4. **CT diseases:** RA, SLE, Scleroderma…etc
5. **Drugs**: *Amidarone,* Nitrophenytoin, Methotrexate.
6. **Miscellaneous**: Lymphangitis Carcinomatosis
   "Diffuse infiltration & obstruction of pul parenchymal lymphatic channels by tumor, mostly AdenoCa "breast, lung, colon, stomach"

Symptoms:

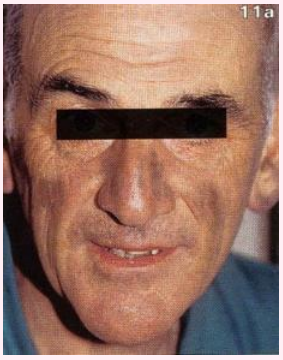
- Main is Dyspnea
- Cough (dry)
- Hemoptysis & wheezes are rare

Signs:

- Cyanosis "Type 1 RF"
- Clubbing [Asbestosis / Idiopathic Pulmonary Fibrosis]
- Late fine bilateral basal crackles
- Corpulmonale (if developed)

Dx:

1- CXR
2- HRCT
3- Lung Functions
4- Cardiopulmonary exercise test
5- Blood
6- BAL
7- Biopsy



Amidarone

CXR:

- Fibrosis & ↓ Lung Volume
  - Fibrosis: Linear, nodular, reticulonodular, reticular, cystic changes "honeycombing"
  - Early: nodular → reticular → Honeycombing.
  - Site:

- **Upper Zone:**
  - Ankylosing Spondylitis
  - Extrinsic Allergic Alveolitis
  - TB
  - Marfan's
  - Sarcoidosis
  - Silicosis

- **Middle Zone:**
  - Progressive Massive fibrosis
  - Alveolar Proteiniosis
  - Pulmonary Hemorrhage
  - Pulmonary Edema

- **Lower Zone:**
  - Idiopathic Pulmonary Fibrosis
  - Scleroderma
  - Asbestosis

TB causes upper zone fibrosis
CTD causes Lower Zone fibrosis; ***except Ankylosing Spondylitis Upper***
Pneumoconiosis causes Upper zone fibrosis; ***except Asbestosis Lower***

HRCT: early dx & Severity
Lung Functions:

- ↓ FEV1, ↓ FVC, ↔ Ratio [Restrictive Pattern]
- ↓ TLC, ↓Functional Residual Capacity
- ↓ DLCO (d.dx: emphysema)

Cardiopulmonary Exercise test with ABG: *how much distances can the patient walk for 6 minutes.*
Blood:

- **Hypercalcemia**: Sarcoidosis.
- **Rheumatoid factor** (25-30% of pts with ILD have +ve Rh. Factor), antinuclear factor, antinuclear ceruloplasmin, anti Jo.

Broncho-alveolar lavage (BAL):

- IPF: increased neutrophils.
- Extrinsic allergic Alveolitis and sarcoidosis: Lymphocytosis.

Definitive Dx → **Lung biopsy**
Treatment of ILD:

- General: Correct hypoxemia.
- Treat Complications (corpulmonale).
- Steroid: glucocorticoid +/- cyclophosphamide azathioprine.
- Lung transplantation.

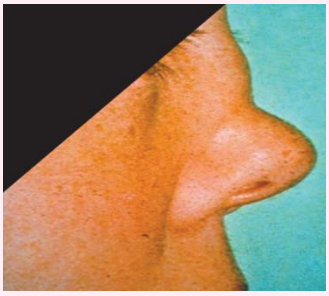
Sarcoidosis

- Multisystem granulomatous disease
- Non caseating granuloma with unknown etiology.
- African American have poor prognosis.

C/O:

1- **Asymptomatic 50-60%** **[**CXR: bilateral hilar lymphadenopathy**]**.
2- **Acute Sarcoidosis:**
   - **lofgreen syndrome:** Fever, BHL, erythema nodosum ± Polyarthalgia
   - Herrfordt's syndrome : Uveitis, parotid enlargement &facial nerve palsy bilateral
3- **Pulmonary Sarcoidosis:**
   - Dyspnea + dry cough, few crackles.
4- **Extra-Pulmonary Sarcoidosis.**
   1- **Eyes:**
      - Uveitis: both Anterior (Iridocyclitis)
      - Posterior (Chorioretinitis) DD: TB, CMV, leprosy, sarcoidosis.
      - Lacrimal & Parotid Enlargement [mickulick Syndrome]
   2- **Skin:** Erythema nodosum. Lupus pernio: infiltration of nose and cheeks.
   3- Lymphadenopathy / Hepatosplenomegaly
   4- **Cardiac**: Cardiomyopathy, complete heart block
   5- **CNS:** Bilateral lower motor neuron facial palsy:
      - DD: Guillain-Barre syndrome, Lyme disease, Sarcoidosis.
      - SOL/Neuropathy/DT/Meningitis
   6- **Renal:** Nephrocalcinosis: due to hypercalcemia.
   7- **Saddle Nose: ➔**

   DD: Sarcoidosis, syphilis, Leprosy, relapsing polychondritis.



   8- **Others**: Perforated hard Palate. / Sarcoid plaques/ Nodular lesions /Alopecia. Pigmentation/ hypopigmentation / Dactylitis: can cause bone cyst/ Hypopituitarism.

Dx:

- Same Investigations, but in Blood (hypercalcemia / **ACE** / ESR / Igs/↓Lymph)
- CXR is used for Staging:

  Stages on CXR:

  Stage 1: Symmetrical bilateral hillar lymphadenopathy [BHL]

  Stage 2: BHL + parenchymal Infiltrate.

  Stage 3: Infiltrate without hillar lymphadenopathy.

  Stage4: Fibrotic changes.

Causes of intra-thoracic lymphadenopathy:

- Sarcoidosis (bilateral+ symmetrical).
- Lymphoma (bilateral+ nonsymmetrical).
- Carcinoma (unilateral)
- Primary TB (unilateral+ para-tracheal).

N.B: Tuberculin test: -ve.

- Erythema nodosum + **positive** tuberculin test + hillar lymphadenopathy = Primary TB.
- Erythema nodosum + **negative** tuberculin test + hillar lymphadenopathy= Sarcoidosis.

Treatment:

- Observation: Asymptomatic + Lofgren syndrome, improve spontaneously.
- Acute Sarcoidosis: NSAIDs + Bedrest

- **Steroid indications:**
  - I- Cardiac / Neurologic involvement
  - II- Worsening Lung function + Paryncehmal lung disease
  - III- Uveitis
  - IV- Hypercalcemia

N.B: Mucocutaneous Sarcoidosis Treatment is by: Antimalarial: chloroquine phosphate. & minocycline.

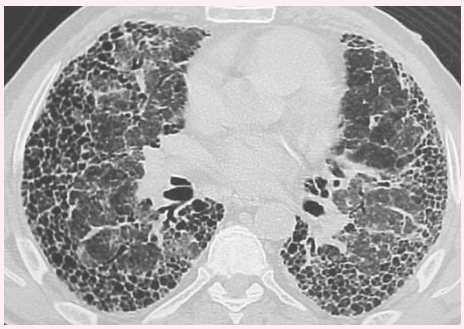
Poor prognosis:

Old (>40y), extapulmonary, stage 3/4 , African American

Idiopathic pulmonary fibrosis (IPF)
Cryptogenic fibrosing alveolitis (CFA)
Usual interstitial pneumonia (UIP)

- **Most common cause of DPLDs**
- **CXR:** reticulonodular pattern.
- **#** CXR with reticular pattern with honeycombing which is peripheral and basal: IPF.
- **Tx**: Is Lung Transplant

Interstitial lung disease –honey combing



Extrinsic allergic alveolitis
(Hypersensitivity pneumonitis)

- Inhalation of organic dust. Type III or type IV HSR.

Causes:

- Mostly by: **Farmer's lung**: moldy hay. 4-6 hours after exposure.
- Bird fancier "Bird dropping"
- Cheese worker.
- Saxophone player.
- Byssinosis: cotton workers.
- Sugarcane: Baggasosis

C/O: Acute 4-6 hrs after exposure: fever + rigors, myalgia, SOB, dry cough, crackles, **no wheezes.**

- Chronic: Upper zone lung fibrosis
- Good prognosis if changed the job.
- N.B: +ve serum precipitin test: IgG Abs and showing precipitin lines.
-

Treatment

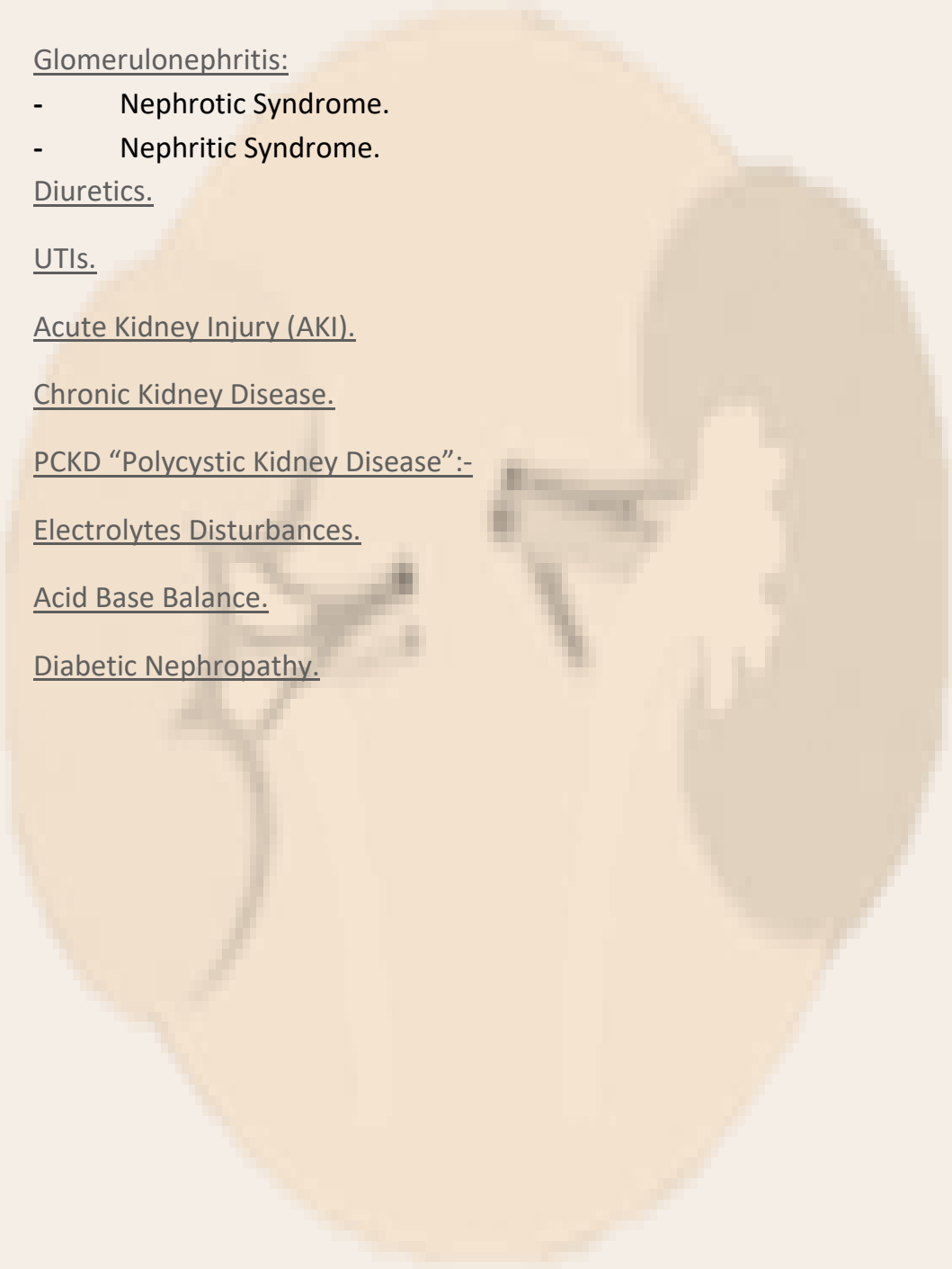
- Acute: Oxygen + remove allergens.
- Chronic: Change job, use mask, Steroids

ولستُ أصبر إلا لِيقيني بأن الله يرى كُل شيء وسيُحدث أمراً . ♡

Renal System

**Recorded on 28 Jan.2020

Contents



Glomerulonephritis:

- Nephrotic spectrum: Minimal change disease, FSGS, membranous GN, membranoproliferative GN.
- Nephritic spectrum: post streptococcal GN(Children) IgA nephropathy (Adults) ,Alport syndrome (familial)
- Rapidly progressive GN.

- **Nephrotic Triad:**
  1. Massive proteinuria > 3.5g/day or Albumine: creatinine ratio >200 (note: normal Albumine: creatinine <3. both are good for diagnosis but Albumine: creatinine ratio better cuz lower error +easy)
  2. Hypoalbuminemia
  3. Generalized Edema
     *Hyperlipdemia

- **Nephritic triad:**
  1. Hematuria ± RBC casts
  2. Hypertension
  3. Renal impairment (azotemia)

- **Rapidly progressive GN:**
  - AKI due to either nephrotic or nephritic.

Nephrotic syndrome:

➢ Triad of Massive proteinuria; Hypoalbuminemia and Generalized Edema

- **Proteinuria:** proteinuria more than 150 mg/day.
- **Massive proteinuria:** >300 mg/day
- ***Nephrotic range:*** more than 3g or ACR >200

- 24 hr urine protein was replaced by Albumin: creatinine ratio (ACR)

- **N.B:** ACR: Normally <2.5 (male) or < 3.5 (female)
- Microalbuminuria: 30-300 mg/day
- Or **ACR from 2.5 or 3.5 to 15**

Causes:

- Primary (idiopathic) or due to secondary causes.
- Primary Causes are: - Minimal Change Disease - FSGS
  - Membranoproliferative GN(MPGN) - Membranous
- Secondary to (DM, infections, Drugs, Malignancy, SLE, RA, Amyloidosis, Hereditary)

Minimal change disease:

- MCC of nephrotic in children
- Secondary causes: Hodgkin's lymphoma (Infectious Mononucleosis) and NSAIDs
- LM: no change no findings
- EM: effacement of podocytes
- Specific management: **Steroids**. (60 mg/day for 4 wks, 40mg/day on alternative day for 4 wks)
- 80% settle in 8 wks but:
  - 1/3 are treated... 1/3 infrequent relapsers ... 1/3 frequent relapsers.

Membranous GN:

- Most common cause in cocasion (الاروبيين)
- Secondary causes:
  - Malignancies solid tumors (usually; Lung Ca, Gastric & colon).
  - SLE [Class V]
  - Drugs (penicillamine) gold
  - Hepatitis B.
  - Diabetes.
- LM: diffuse thickening of the basement membrane.
- EM: sub-epithelial deposits with "spikes and dome" appearance.
- Specific management: steroids, chlorambucil and cyclophosphamide.
  - 1/3 end with ESRF

Membranoproliferative GN (MPGN) (Mesangiocapillary GN)

- 2 types:
- ***Type 1:***
  - Secondary to hepatitis C (due to Cryoglobulinemia).
  - EM: Subendothelial deposits.
  - Low C4 complement (characteristic)

- ***Type 2: [Dense Deposit Disease]***
  - Secondary to factor H deficiency (needed for regulation of complement) (partial lipodystrophy).
  - + Positive antibodies against C3 nephritic factor (C3 nephritic factor is required for stabilization of C3 convertase which activate the complement) resulting in hyperactivation of the complement and **low C3 level.**
  - EM: Intramembranous deposits (dense deposit disease) and tram track appearance due to mesangial proliferation.
  - 50% end in ESRF.
  - can occur after transplantation

Focal segmental glomerulosclerosis FSGS:

- Most common cause of nephrotic in adults African American
- Secondary causes: Malaria, *HIV, *Heroin, and secondary to other renal diseases, massive obesity ,(eg, IgA nephropathy)
- LM: sclerosis (hyalinosis) that is focal (not all glomeruli) and segmental (not the whole glomerulus)
- High recurrence after renal transplant.

Complications of nephrotic syndrome:

1. **Infections:** due to loss of Igs and complement in urine. Mainly due to Strept Pneumonia
2. **Thrombosis:** most important due to loss of anticoagulants (protein S, protein C, and antithrombin III)
   - Scenario: nephrotic syndrome complicated by hematuria and loin pain => **renal vein thrombosis**.
     N.B: Renal vein thrombosis, causes AKI, in US: enlarged edematous kidney
3. **Hyperlipidemia** (hypercholesterolemia): due to loss of protein in urine which stimulates synthesis of cholesterol and lipoproteins.
4. **Hypocalcemia;** due to loss of Vit D. ↓ Ca^{+2} binding proteins
5. **Chronic kidney disease.** **(**chronic Glomerulonephritis)

- *Best diagnostic test is biopsy*

General management of nephrotic syndrome:

- General treatment:-
  1. Treatment of proteinuria *by ACEIs* /ARBs (causes constriction in efferent arteriols)
  2. Treatment of generalized edema *by water restriction, salt restrictions, increase protein diet and loop diuretics*
  3. Rx of complications:
     - Pneumococcal vaccination
     - Statin
     - LMWH
  4. Rx of underlying cause.(eg: steroids with or without immunosuppressive)
  5. Specific management.

Nephritic syndrome:

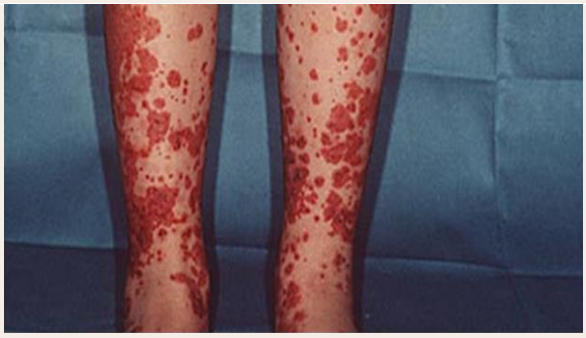
- Hematuria with RBCs casts ± dysmorphic RBCs, proteinuria, HTN, Oliguria and renal impairement (azotemia)
- General Mx:
  - Refer to nephrologist:
    - BP ≤ 130/80
    - If proteinuria >1g/day
  - Controlled by ACE-I or ARBs

IgA nephropathy:

- Most common GN in developed countries.
- Classically: young male with recurrent (gross) hematuria after one or two days of RTI.
- Differentiate from PSGN (occurs 3 weeks after pharyngitis)
- LM: mesangial proliferation
- EM: mesangial IgA deposition
- Poor prognostic features: Male... Old age... full spectrum of nephritic (hypertension and renal failure)... proteinuria.
- Hematuria is the main clinical finding but NOT a poor prognostic feature. N.B: Treatment: supportive.

Henosch - Schonlein purpura (HSP):

- Features of IgA nephropathy + purpura N.B: palpable purpura (on buttocks and extensor surfaces) + arthritis + abdominal pain
- Dx: either renal biopsy (better) or skin biopsy.



Alport Syndrome:

- X-linked dominant, collagene type 4 mutation gene.
- Histology: basket wave apperance for basement membrane.
- Clinically: kidney problem+ deafness+ eye problem.

Post streptococcal GN (diffuse proliferative GN):

- 1-12 weeks (but usually 3 weeks) after streptococcal pharyngitis.
- High ASO titer and low complement level.
- LM: diffuse increase in cellularity
- EM: sub-epithelial deposits (humps)
- Clinically: child with smoky (coca cola)+ periorbital odema, colored urine usually with proteinuria and hypertension following pharyngitis.
- Good prognosis.

Rapidly progressive GN:

- Clinically: AKI and systemic features
- Hallmark is crescents formation

- **3 types:**
    1. *Anti- GBM disease (Good-pasture disease if there is lung involvement):*
        - ABs against collagen type 4 in Kidney causing hematuria and lung causing hemoptysis
        - Linear deposits on immunofluorescence
    2. *Immunocomplex crescentric GN:*
        - Secondary to other nephritic causes and SLE.
        - granular immunofluorescence
    3. *Pauci-immune rapidly progressive GN:*
        - Associated with ANCA positive vasculitis (Wegner, microscopic polyangitis (P-ANCA)and Churg Strauss)
        - Negative immunoflurescence.
        - Clinically:
            - Wegner: lung and kidney involvement. But it reaches up to upper respiratory tract (eg, sinusitis)N.B: suddle nose, C-ANCA
            - Churge-strauss: asthma with eosinophilia and periferal neuropathy ,P-ANCA

- All three types are managed by high dose IV corticosteroids + cyclophosphamide ± plasma exchange.

Diuretics:-

1- Loop diuretics: most potent

- E.g: **Furosemide**
- Acts on loop of henle. Blocks on $Na^+/K^+/2Cl^-$ channel. N.B: Decrease medullary hypertonisity
- Strong diuretic used in *pulmonary edema, peripheral edema* and in severe hypercalcemia (it loose calcium).
- **SE:** hyponatremia, hypokalemia, hypocalcemia, hypomagnesemia, hypovolemia, metabolic alkalosis (H+ loss in urine) and ototoxicity (characteristic).

2- Thiazide diuretics:

- **E.g Chlorothiazide, bendroflumethiazide**
- Act on distal convoluted tubule. Block Na^+- Cl^- channel.
- SE: hypercalcemia, hyperglycemia, hyperuricemia (CI in gout) and some other side effects of loop diuretics. "↑glucose, ↑ lipids" N.B: hyper GLUC (Hyperglycemia, hyperlipidemia, hyperurecemia and hypercalcemia) , metabolic alkalosis.
- Uses: hypertension and prevention of calcium stones formation.

3- Potassium sparing diuretics

- **Spironolactone & eplirenone**"Aldosterone Antagonist ,epithelial Na channels" **and Amiloride &triamitrine**"Na^+/K^+ Blocker at distal tubule, epithelial Na channel blockers"N.B used in ledel syndrome.
- Aldosterone antagonists
- Used in combination with thiazides "causes ↓K". ascites and ↑aldosterone
- SE: hyperkalemia and gynecomastia (esp., spironolactone) N.B: metabolic acedosis.

4- Carbonic anhydrase inhibitors

- Eg, **Acetazolamide**
- Blocks HCO3 reabsorption in proximal convoluted tubules
- Only one that **causes metabolic acidosis (characteristic)**
- Other uses: pseudotumor cerebri and glaucoma.+ Alttitude sickness

5- Osmotic diuretics

- Eg, **mannitol**
- Used in cerebral edema

UTIs:-

Risk factors:

- Female
- Age: males in < 1 year due to posterior urethral valve. Then females 1-40 years. After 40 years incidence rises in males and become equal to that of females due to increased BPH and catheterization.
- Pregnancy: progesterone causes relaxation of ureters causing stasis predisposing to infections.
- Immunosuppression
- Diabetes
- Obstruction
- Manipulation (eg, catheter)
- Vesico-ureteric reflux

Divided into:

- **Lower UTI (Cystitis):** dysuria, urgency, frequency and suprapubic pain.

Upper UTI (Acute pyelonephritis): fever, rigors and loin pain + costovertebral angle tenderness.

Complicated vs uncomplicated UTI:

- Some divide UTIs as Complicated (pyelonephritis) and uncomplicated (LUTIs)

- Organisms: most common organism is E.coli

Dx:

For Cystitis

- Urinanalysis: 1/+ve Nitrate or +veleucocyte esterase in urine dipstick.
  2/ microscopy :Significant pus cells (7-10)
- N.B:No need for further investigaton unless : pregnant lady , recurrent cystitis, not responding to treatment. +Male need culture.
  *For Acute Pylonephritis:
- Culture (best diagnostic test): more than 10^5 cfu/ml. colony forming units (CFUs). Or only 1 CFU if suprapubic sample (bladder is sterile).
- US: children / Male / Pyelonephritis / Not responding to ttt

Rx:

- **Uncomplicated UTI: Cystitis:**
  - Oral drug: trimethoprim (for 3 days) Nitrofurantoin or amoxicillin (for 5 days).

- **Acute Pyelonephritis:**
  - IV broad spectrum antibiotics empirically (eg, 3rd generation Cephalosporins or Coamoxiclav for 10 days) until culture results come.

» **UTI management in pregnancy:**

- Amoxicillin or cephalosporin for 7 days.
- **CIs:** ciprofloxacin (absolute CI), trimethoprim (1st trimester) and Nitrofurantoin (3rd trimester)
- Asymptomatic Bacteriuria is **only** treated in pregnancy

- **Sterile pyuria:**

- Positive WBCs but no bacteria
- Causes:
  - **Infection related:** TB and other fastidious organisms, treated infection and appendicitis
  - **Non-infection related:** stone, malignancy, PCKD and acute interstitial nephritis

N.B: **Casts**

- **RBC Casts:** GN
- **WBC Cast:** acute pyelonephritis
- **Fatty Cast:** nephrotic syndrome
- **Muddy brown cast:** acute tubular necrosis
- **Hyaline cast:** normal finding... in dehydration.
- **Eosinophilic cast:** interstitial nephritis
- **Granular cast:** any chronic kidney disease.

N.B:

- Renal failure = increase blood urea nitrogen+ creatinine .
- If develop over hours to days = AKI . If more than 3 months= CKD
- Shared complication between AKI & CKD :
    1. Electrolytes disturbances (most important hyperkalemia)
    2. acid base disturbances(metabolic acedosis)
    3. uremic symptoms (nausia and vomitting ,pericarditis ,encephalopathy, bleeding)
    4. Fluid overload (pulmonary odema) .
- 2 complications occure in CKD : Anemia , bone disease
- CKD → small kidney in US

AKI:

- Rapid loss of renal function over hours to days, Usually reversible
- **Staging**: N.B: Depends on serum creatinine.

  Stage 1:
  - Serum creatinine > 1.5 x the baseline (>0.3g/dL in 48 hrs)
  - Urine output < 0.5 ml/kg/hr for 6 consecutive hrs

  Stage 2:
  - serum creatinine 2.0 – 2.9 x baseline
  - Urine output < 0.5 ml/kg/hr for 12 consecutive hrs

  Stage 3:
  - Serum creatinine >3 times baseline
  - Urine output < 0.3 ml/kg/hr for 24 hrs
  - Or anuria for 12 hrs at any time
  - **creatinine more than 354.4 umol/L is stage 3**

- **Other staging is RIFLE**
  - Stage 1: **R**isk
  - 2: **I**njury
  - 3: **F**ailure
  - 4: **L**oss, complete loss of renal function for more than 4 weeks
  - 5: **E**nd stage renal disease [ESRD], complete loss of renal function for more than 3 months

- **<u>Causes:</u>**
  - ✓ Prerenal most common.
  - ✓ Renal most commonly interstitial.

  Prerenal:
  - Most common
  - Any cause of hypovolemia "e.g: GE, hemorrhages, burns" or hypotension or renal vasoconstriction "drugs, Hepatorenal syndrome" or systemic dilatation .
  - N.B: Treatment : optimization of fluids status

  Renal:
  - Any cause of renal damage
  - Tubular: ATN (most important) ▪ Glomerular: GN
  - Interstitial: Acute tubulo-interstitial nephritis
  - Vascular causes "Atheroma, embolism, HUS & TTP, malignant HTN
  - N.B: Treatment of the underline cause.

Post renal:

- Any cause of obstruction "BPH",stones, bladder cancer. Obstruction must be bilateral to cause kidney failure. Treatment:relive obstruction(cathetarization/nephrostomy)

• **HUS "Hemolytic Uremic Syndrome":**

- Microangiopathic hemolytic anemia with thrombocytopenia & uremia
- Causes: E.coli 157:H7 and shigella
- Rx is supportive

• **TTP "Thrombotic Thrombocytopenic Purpura":**

- Same triad of HUS + fever and neurologic Sx
- Rx: plasmapheresis and supportive

• ***Acute tubular Necrosis:***

- Causes: ischemia (same causes of Prerenal) and toxins
- Toxins are either **endogenous**: hemoglobin (in intravascular hemolysis) and myoglobin (in Rhabdomyolysis)
- **Exogenous**: aminoglycosides, amphotericin and **contrasts(N.B: avoid in renal disease)**

Acute Interstitial nephritis (tubulointerstitial nephritis):

- Scenario: pt took drugs (eg, penicillin and Cephalosporins) and came with features of allergy "fever, rash, arthralgia" and AKI
- **Dx**: *eosinophilia in blood* and **eosinophiluria (pathognomic)** and eosinophilic casts.N.B:Causes of sterile pyurea.
    - Biopsy is best
- **Rx:** stop the drug and give high dose steroids.

• Pre-renal vs renal failure:

Parameter	Pre-renal	Renal
Urinary Na^+	< 20 meq/L	>40 meq/L
Fraction excretion of Na^+	< 1%	> 1%
U. osmolality	> 500	< 350
Specific Gravity	> 1.020	< 1.010
Urea: Creatinine Ratio	> 20:1	< 10:1

Normal Urea = 2.5 – 6.5 mmol/L (7 – 20 mg/dL)
Normal Creatinine = 70 – 150 mmol/L (0.6 – 1.2 mg/dL)

Investigations:

- Serum Urea & Creatinine (rise in serum creatinine is the most important predictor)
- BUN: creatinine ratio
- Above Prerenal & renal investigations
- Electrolytes: ↑ K^+, ↑PO_4, ↑Mg^+
- Abd US (post renal)

Complications of AKI:

- Electrolyte disturbances: Hyperkalemia
- Metabolic acidosis
- Fluid overload: either due to kidney injury or fluid therapy. May lead to **pulmonary edema**
- Infections
- Uremic complications: encephalopathy and pericarditis. Uremic Sx: nausea and vomiting, encephalopathy, pericarditis, peripheral neuropathy, pruritus and bleeding.

N.B: any oliguria: give furosemide

Mx: Correct fluids, treat pulmonary edema, treat hyperkalemia. monitor

Indications of dialysis in AKI:

1. Severe HyperKalemia: K+ more than 7
2. pH < 7.2
3. Pulmonary edema refractory to medical Rx
4. Uremic complications.
5. Urea > 300 mg/dL
6. Creatinine > 10 mg/dL

• CIs of dialysis•!!!!!!

Chronic kidney disease:

- Impaired renal function for more than 3 months, as evident by abnormal structure or function.
- Evidence of renal damage: abnormal sediment/ abnormal imaging/abnormal histology/transplanted
- Most important Invx is the **GFR**
    - It is best measured by inulin clearance. Or by creatinine. But both are not applicable.
    - We use estimated GFR [eGFR]:
        - Calculated by Creatinine Clearance [increased in body builders]
        - $\frac{(140-age)\ x\ weight\ in\ Kg.}{Serum\ Creatinine}$
        - If female same equation times 0.85 (prof. Alfadil).
        - Other methods:
            - Cockroft-Gault equation "most imp."wt ,ht, age , gender , serum creatinine.
            - Modification of diet in CKD [MDRD]; depends on age, gender, ethnicity & serum Cr. Better accuracy
            - CKD-EPI (best)

• Stages of CKD: important!!

Stage 1	**GFR > 90 ml/min with evidence of renal damage (eg, albuminuria, abnormal histology, structural abnormality, abnormal urine sediment or history of renal transplant) N.B: Treatment is to prevent progression**
Stage 2	**GFR 61 - 90 ml/min** with evidence of renal damage.N.B: Treatment is to prevent progression.
Stage 3a	**GFR 46 - 60 ml/min** no need for evidence of renal damage
Stage 3b	**GFR 30 - 45ml/min**
Stage 4	**GFR 15 – 29 ml/min ,** N.B: Treatment of stage 3 & 4 is to prevent progression + ttt of complication
Stage 5	**GFR < 15 or need for RRT ,N.B: End stage renal disease.**

N.B: Dialysis: renal dialysis and peritoneal dialysis
GFR is measured from serum creatinine.

Causes of CKD:

1. DM "most common and most important" "Esp. type 2"
2. Hypertension
3. Chronic Glomerulonephritis "specially IgA nephropathy"
4. Chronic Pyelonephritis
5. A-PCKD "most common hereditary"
6. Other causes of renal diseases

Screening for CKD:

- DM - HTN - CV diseas

- Multisystem disease may affect kidneys "SLE"
- Family Hx of Stage 5 CKD or known hereditary disease
- Structural abnormality "BPH, VUR"
- opportunistically dected hematuria/proteinuria

Investigations in CKD:

1. Serum Cr, urea, electrolytes.
2. Full Urinalysis
3. Abd kidney US "most important"shrunken kidney
4. PO_4/Ca^+/PTH: bone disease.
5. CBC check anemia

Management of CKD:

1. Dietary control "↓proteins: 0.88 gm/Kg/Day"
2. Life style modification: "Wt. loss, exercise, statins…etc"
3. **Reno protection:** tight control BP and control proteinuria. Glucose control (metformine is contraindicated: causes lactic acedosis)
   - Mainly by ACEI/ ARBs
   - Aim of BP control is less than 130/80
   - Or < 125/75 if DM/proteinuria
   - Proteinuria aim is A:Cr <30; P:Cr <50
4. Treatment of complications: "Renal Bone Disease, Anemia, uremia, others"

"Cholecalciferol, Phosphate binders, Erythropoietin"

- Most common cause of death in CKD is cardiovascular complications (eg, IHD, HTN, and HF), followed by infections

Special complications of CKD (differentiate it from AKI):

- Renal osteodystrophy
- Anemia

Renal osteodystrophy:

- most important, high parathyroid hormone[↑PO_4, ↓Vit D → ↓ Ca^{+2} → ↑PTH]
- *High phosphate level and decreased vit D result in increase in parathyroid hormone level!*
- *N.B : Mx: give ph binder + give Ca & vit D supplements (secondary hyperparathyroidism)*
- *resulting in:*
    1. **Osteomalacia** "↓ Vit. D"
    2. **Osteitis fibrosa cystica** (pepper pot skull on X-ray, subperiosteal erosions)
    3. **Osteoporosis:** due to malnutrition
    4. **Adynamic bone disease** (cessation of activity of both osteoblasts and osteoclasts due to unknown cause)
    5. **Osteosclerosis**: Rugger jersy spine. (Unknown cause)

Mx of RBD:

- Decrease phosphate in diet and give phosphate binders
- Give Calcium supplements and vit D "Cholecalciferol"

➢ **Anemia:**

- Causes:
    - Erythropoietin deficiency most important, Dietary "decrease hematinics", anemia due to chronic disease and uremic bone marrow toxicity
- ➢ **Rx:**
    - Check hematenics and correct them. "Iron & folic acid"
    - If normal,Give erythropoietin
        - **Erythropoietin SEs:**
            I. Hypertension (due to increased viscosity),
            II. EPO induced seizures "Encephalopathy"
            III. Abs formation against RBCs (leading to pure red cell aplasia)
            IV. Thrombosis & AV fistula(due to increased viscosity)
- Causes of no response to erythropoietin: deficiency of hematinics, inadequate dose, Abs formation, aluminum toxicity.
    - Aim of Tx: is Hb 10 – 12 gm/dL.
    -

N.B: normal Kidney size is 9 – 11cm, <9cm is small. In CKD Kidney is Small, unless:

- **Causes of normal sized kidneys in CKD:**
  1- DM - Diabetic Nephropathy, early diabetes*
  2- HTN
  3- Amyloidosis*
  4- PCKD*
  5- Obstructive uropathy*
  6- Infiltration "Rhabdomyolysis, Myoglobinuria"

Other complications of CKD:

- CVS: HTN, atherosclerosis, Pericarditis. Most common"Cause of Death"
- Metabolic: ↑ Cholesterol / "Gout"
- Endocrine: ↑ Prolactin
- CNS: Uremic Encephalopathy. Neuropathy. Myopathy
- Immune: ↑Infections

N.B: K+ levels 3.6 – 5.0 mmol/L (<3.0 Hypo, >5.0 hyper)

- **Rx of hyperkalemia:**
  1. If there are ECG changes or K^+ >6.0 give **10% IV Ca gluconate**
  2. Insulin + glucose (increase K entry into cells)
  3. Neb. Salbutamol (increase K entry into cells)
  4. IV furosemide (loose K)
  5. Potassium binding [ion exchange resins](loose K) >>> takes 1-2 days for action; Chronic management
  6. Dialysis

PCKD "Polycystic Kidney Disease":-

- Either autosomal dominant or autosomal recessive.
- The recessive type: chromosome 6, occurs in pediatrics, big kidneys, liver cirrhosis, dies early.

♦ Autosomal dominant PCKD – Adult Type:

- Type 1: "85%" → Chromosome 16... Rapid progression to ESRD
- Type 2: Chromosome 4... Slow progression to ESRD

♦ Berry aneurysm is the most important association but the commonest is HTN.

Dx:

- Screening and Dx by abdominal US
- **Criteria:**
  - if age < 30 years → 2 cysts are enough for Dx "uni or bilateral"
  - If age 30-60 years → 2 cysts bilaterally
  - If age > 60 years → 4 cysts bilaterally

- Screening is only done after 20 years as the rate of false negative is high before 20 years.
- **Indications of screening for berry aneurysm in a pt with PCKD: "by MRA"**
  1. Hx of ruptured berry aneurysm
  2. FHx of hemorrhagic stroke
  3. Presents with neurological Sx

- **Associations:**
  1. HTN "75%"
  2. Colonic diverticulae.
  3. Mitral Valve Prolapse, AR
  4. Berry's Aneurysm
  5. Liver/Spleen/Ovarian Cysts

N.B: it's like CKD: ↑PO_4^{-2}, ↓Ca^{+2} but ↔ or ↑ Hb = "↑EPO"

Tx: ACEIs & Regular follow up (Renal, BP)

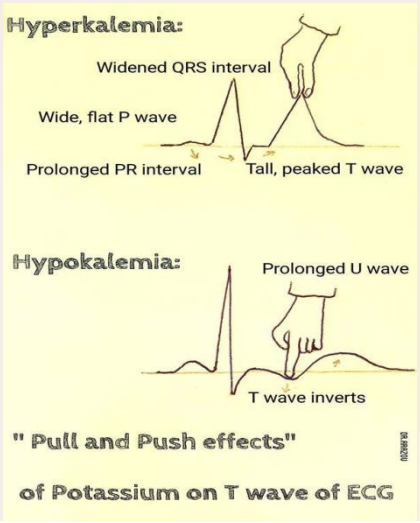
Electrolytes Disturbances:-

Hyperkalemia:-

- Normal range : 3.5-5.5 mmol\L
- exclude Psaudohyperkalemia:-
  - Artifacts(hemolysis during the procedure)
  - High blood cells count (Erythrocytosis, leukocytosis,..)

- **What are ECG changes in hyperkalemia?**
  - 1-tall T wave 2- wide QRS 3- prolonged PR interval 4- flat P wave
  - First change tall tented T wave. Then flat P wave and prolonged PR interval . Then wide QRS then (SINE pattern)

ECG changes in hyperkalemia



- **Management of Hyperkalemia :**
  - if ECG changes or K more than 6m → IV Ca gluconate to protect the heart .
  - K inter the cell → insulin + glucose, nebulized β2 agonist (salbutamol).
  - K out of the body → in urine by diuretics, Stool by K binding resine.or through kidney by dialysis(K >7).

Hypokalemia: -

- ECG changes: flat T wave and appearance of U wave.

Sodium:-

- SIADH causes euvolemic hyponatremia.
- Complications of hypernatremia: brain hemorrhage, in hyponatremia: causes cerebral edema.
- Rapid correction complications :

➢ From low to high your Pones will die. → Pt quadraplegic except : vertical gase + aware (reticular activating system)

➢ From high to low your brain will blow → Cerebral edema.

Acid base disturbances:

- **Normal Values:**
  - PH =7.35-7.45
  - PCo2 =35-45
  - bicarbonate= 22-28
  - Anion gap <12
- In the Exam: find PH first (acidosis/alkalosis)
- Low PH → high Co2(respiratory) or low bicarbonate(metabolic)

- **Anion gap:**
- In metabolic acidosis there are :-
  - High anion gap metabolic acidosis OR
  - normal anion gap metabolic acidosis

♦ **Anion Gap** = (Na+K) - (Cl + bicarbonate)

- Normal anion gap metabolic acidosis called hypercloremic metabolic acidosis (high Cl as a compensation for low bicarbonate)
- High anion gap metabolic acidosis (increase in unmeasured anion = lactic acid ,ketones, aspirin , methanol toxicity, uremia phosphate, iron ...) = normocloremic metabolic acidosis

- **Examples:-**
  - Respiratory Acidosis = ↓ PH , ↑Co2 high , ↑ bicarbonate
    - Causes: opioid overdose, GBS, Myasthenia gravis, ...(type 2 respiratory failure)
  - Respiratory Alkalosis :
    - Washout of Co2 ↑RR : hysteria , Aspirin(early stage of poisoning) ,PE
  - Metabolic Acidosis:
    - Normal anion gap 2 important causes : Diarrhea , renal tubular acidosis.+ Drugs(acetazoleamide)
  - Metabolic Alkalosis :
    - Vomiting , diuretics(loop diuretics, thiazides diuretics)

Renal Tubular Acidosis:-

Proximal renal tubular acidosis (Type 2):

- Defect is inability to reabsorb bicarbonate in proximal convoluted tubules =
- Metabolic acidosis = urine PH < 5.5
- Causes:-
- Fanconi Syndrome → generalized malabsorption Syndrome.
- Acetazolamide
- Note: Hypophosphatemic rackets association

Distal Renal Tubular Acidosis (Type1):

- Inability to secrete H+ in collecting duct (retention of H +) PH of Urine > 5.5
- Causes : Amphotericin B , analgesic
- Note;: Association : Calcium phosphate stones

♦ Hypokalemia in the 2 above types .

N.B: K+/H+: competition to enter the cells
Normally: in acidosis = Hyperkalemia
So in Alkalosis: low H+ = hypokalemia

N.B. All electrolytes disturbances cause CNS Symptoms **Except** K+ causes Cardiac symptoms.

Type 4 Renal Tubular Acidosis:

- hyperkalemia + metabolic acidosis
- Normal urine PH
- Defect in Renin Angiotensin Aldosterone pathway =>
  - DM: ↓renin
  - ACEI / ARB
  - Defect in Aldosterone : aldosterone antagonism (spironolactone)

Diabetic Nephropathy:

- No diabetic nephropathy without diabetic retinopathy.
- 5 stages :

- **Stage 1:** High GFR + big kidney (hyperfiltration hypernephrotic nephropathy)
- **Stage 2:** Normal GFR + early histological changes
  (glomerular basement membrane thickening + meningeal proliferation)
- **Stage 3:** microalbuminurea (30-300mg/day) -ve in dipstick.
  First sign of Diabetic Nephropathy
- **Stage 4:** overt nephropathy = protein urea + low GFR + High blood pressure .
  (Irreversible)
- **Stage 5:** End stage renal disease.

Rheumatology

Rheumatoid Arthritis:

Def: chronic, inflammatory, multisystem autoimmune disease

Female > Males

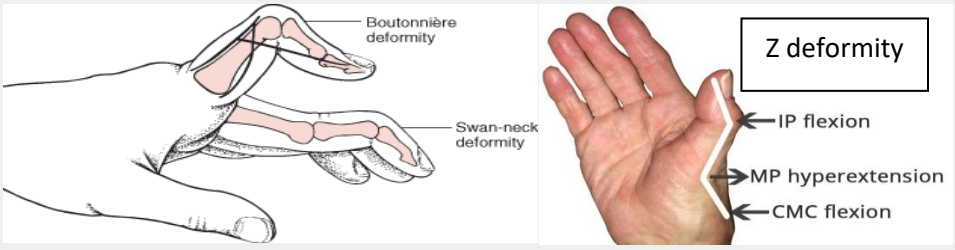
Associations:

1. HLA DR4, DR1
2. IHD (RA = Type II DM)
3.

Dx: **≥ 4 of:**

1- Morning stiffness >1hr (for ≥ 6wks)
2- Polyarthritis ≥ 3 joints
3- Symmetrical involvement
4- Hand Involvement (MCPJ "Metacarpal phalangeal Joints", PIPJ "Proximal interphalengeal joints", wrist
5- +ve Rheumatoid Factor (RF) → **IgM against Patient's IgG**
6- Radiological changes:
   - Early: Periarticular osteopenia
   - Late: bony erosions, subluxation
7- Subcutaneous nodules

- **Boutonnière and swan-neck deformities of fingers or Z-deformity of thumbs**



- In pathology of RA: **TNF** is a key factor
- **Some extra-articular manifestations:**
  1. Rheumatoid nodules "Pressure areas"
  2. Lung: Fibrosis, B.obliterans, Pleural Effusion
  3. Osteoporosis
  4. Depression
  5. Increased risk of infections (Proteus mirabilis)
  6. Increased risk of IHD
  7. Rare: Felty's syndrome (RA + Splenomegaly + neutropenia)

8. Rare: Amyloidosis

- Ocular: most common is Keratoconjuctivitis sicca
- Neuro: **Atlanto-axial Subluxation** (C2 → Sudden death) & Carpal Tunnel Syndrome.

- **Investigations:**
  - CBC: Anemia
  - ↑ESR ↑CRP
  - Rh F: +ve in 70%
  - Anti-CCP (Anti Cyclic-citrullinated peptide antibodies) = most specific 98%
  - Radiology
  - Joint aspiration: WBC
    - 20,000 – 50,000
      - 2,000 – 20,000 (Osteoarthritis "non-inflammatory")
      - 20,000 – 50,000 = (inflammatory "RA, gout")
      - >50,000 = Septic Arthritis
- **Poor Prognosis:**
  - Female
  - Insidious onset
  - HLA DR4 +ve
  - +ve RhF, Anti-CCP, Radiological changes
  - Extra articular features
- **Mx:**
  - Acute: Rest, NSAIDs, Steroids
  - Long term: **2DMARDs (one Methotrexate) + short term Glucocorticoids**

DMARDs: Disease-modifying antirheumatic drugs:

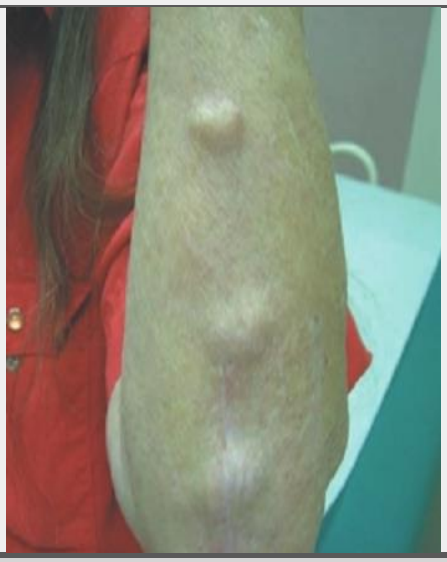
1. **Methotrexate:**
   - Most common
   - SE:
     1. Bone marrow suppression
     2. Liver cirrhosis
     3. Pneumonitis

2. Sulfasalazine (rash, ↓sperm, oral ulcers)
3. Hydroxychloroquine (Eye involvement; retinopathy … annual screening)
4. Lefluonimde (teratogenicity)

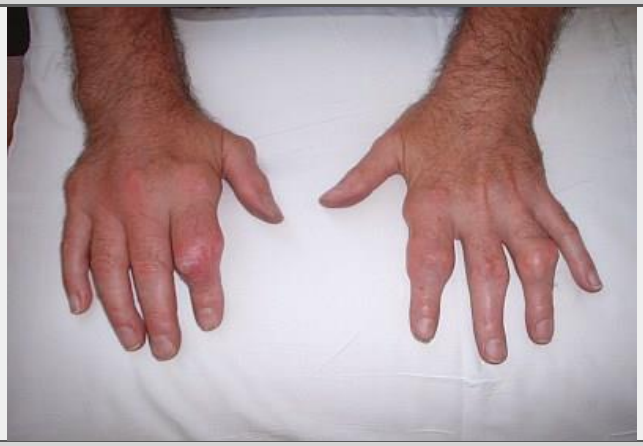
2nd Line: Biological Therapy (e.g TNFa inhibitors)

- Screen for TB, HepB,C, HIV before starting
- Started when resistance to 2 DMARDs (including methotrexate)
- Infliximab, Rituximab, Tocilizumab, Abatacept

N.B: in pregnancy NSAIDs & Methotrexate are contraindicated.



Rh nodules



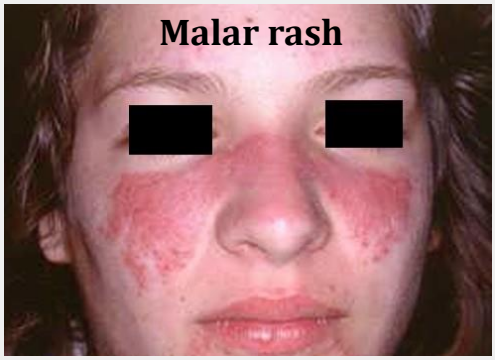
Boutonniere deformity in pip joint….Rh arthritis

Z thumb….Rh arthritis

SLE (Systemic Lupus Erythematosus):

- Females: Males 9:1

Dx: ≥ 4 of the following: (at least 1 clinical + 1 laboratory) or biopsy proven lupus-nephritis + +ve ANA or Anti-DNA



1. Malar Rash
2. Discoid Rash "commoner, scaling"
3. Photosensitivity rash
4. Oral ulcers
5. Serositis
6. Arthritis (≥ 2 peripheral joints)
7. CNS: seizures, psychosis
8. Hematological: Anemia, neutropenia, lymphopenia, Thrombocytopenia
9. Renal: (Persistent Proteinuria >0.5 g/day, casts)
10. Immunological: e.g +ve Anti-dsDNA, Anti-SM abs
11. +ve ANA

N.B: Abs in SLE:

- Most sensitive: ANA
- Most specific: Anti-Smith
- Follow-up: Anti-dsDNA
- Others: Antiphospholipid Abs [Anti-cardiolipin / Lupus anticoagulant]
  False +ve = syphilis

- 20% have +ve RhF
- For monitoring & follow up:
  1- Anti-dsDNA (-ve in drug lupus)
  2- Complement levels
  3- ESR

Multisystemic disorder + ↑ ESR but Normal CRP >> think of SLE

Lupus nephritis [LN]:

- **Stage I:** Minimal mesangial LN (No tx)
- **Stage II:** Mesangioproliferative LN (may need steroids)
- **Stage III**: Focal LN (<50% of glomeruli)
- **Stage IV:** Diffuse LN (>50% of glomeruli) **(Most common/most severe)**
- **Stage V:** Membranous GN
- **Stage VI:** Advanced Sclerosing LN (ESRD)

N.B: requires renal Biopsy to diagnose.

Tx: 3 – 6 of IV cyclophosphamide + IV high dose steroids ± RRT

N.B. SE of Cyclophosphamide: Hemorrhagic cystitis, Infertility.

Drug induced Lupus:

- Hydralazine, Procainamide, Penicillamine.
- N.b: OCP, Sulfonamides worsens Lupus
- Anti-histone Abs in 100
- **N.B**: Anti dsDNA is –ve

Lupus in pregnancy:

- Anti Ro- Anti La Abs = ↑ risk of neonatal complications (Heart block) [SSA]

Investigations:

- ↑ ESR - Normal CRP
- Abs___ - Complements: Low
-

Management:

- **Acute flares (e.g psychosis, nephritis)**
  - IV Cyclophosphamide + IV high dose steroids
- **Chronic [Maintenance]**
  - NSAIDs
  - Hydroxychloroquine
  - Steroid sparing agents (Azathioprine, Methotrexate, Mycophenolate)
  - Steroids

N.B: Raynaud's Syndrome:

- Teenage females + family hx = Primary
- Male / Female >30 yrs = think of secondary
- Differentiate by Ophthalmoscope to capillary nail fold loop

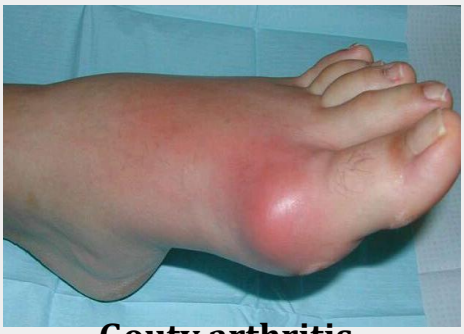
Livedo Reticularis: "see picture" SLE/APL

Gout:

- **Definition:** Deposition of monosodium urate (MSU) crystals in joints

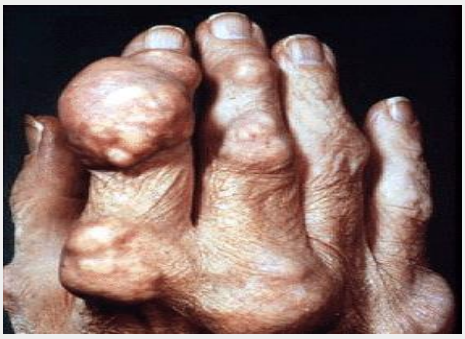
  - Typical Presentation: Acute attack of monoarthritis
  - 60% in Metatarsophalangeal joint of big toe (Podagra)
  - Long term: urate deposits (Tophi in pinna, tendons, joints)
  - More in males
- **Causes:**
  - Hereditary: Lesch-Nyhan syndrome (+ learning difficulties + RF)
  - Secondary:
    - Reduced Excretion: Renal impairment
    - Increased production: Myeloproliferative / Lymphoproliferative (e.g Leukemia)

      Cytotoxics (Tumor Lysis syndrome)



Gouty arthritis

- **Precipitants:**
  - Trauma/Surgery
  - Dietary: ↑ purine, Alcohol, starvation
  - Infections
  - Diuretics
- **Associations:**
  - HTN, IHD, metabolic Syndrome
  - Hyperuricemia



Gouty tophi

- **Complications:**
  - Tophi (e.g. ear pinna) - Urate renal stones
- **Dx:**
  - X-ray: soft tissue swelling, recurrent punched out erosions
    1. NB: joint space is preserved until late
  - Joint Aspiration: microscopy: -negatively birefringent needle shape urate crystals
- **Tx:**
  - High dose NSAIDS "e.g: Ibuprofen, indomethacin". **If CI (e.g PUD) → Colchicine**
  - if CI both (e.g renal impairment)→ Steroids

Allopurinol Indications:

1. Recurrent attacks (≥ 2/yr)
2. Tophi
3. Renal stones

- When to give: After 2 weeks from acute attack, under cover of NSAIDs/Colchicine
- Why? It precipitates attack first

- **Lifestyle modifications:**
  - Weight loss, ↓ Purines, avoid starvation, avoid alcohol

N.B: D.Dx for gout: Pseudogout/Septic arthritis

Pseudogout:

- Deposition of Ca^{+2} pyrophosphate dehydrate
- Large joints (Knee, wrist…etc)

Causes:

1. Hemochromatosis
2. Hyperparathyroidism
3. Hypothyroidism
4. ↓Mg^{2+} / ↓ PO_4^{2-}

- **Dx:** X-Ray: Chondrocalcinosis
- Joint fluid microscopy: Positively birefringent rhomboid shape crystals
- **Tx:** self-limiting. Can give NSAIDs

يارب إني مُحسن الظن في تدبيرك فتولّني.