1. Management of microcytic anemias
2. Iron overload disorders

MBCHB IV lecture series

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Lecture outline

- Microcytic anaemias
  - Aetiology
  - Epidemiology of iron deficiency
  - Clinical features
  - Investigations
  - Treatment
- Iron overload
  - Sideroblastic anaemias
  - Haemochromatosis

Microcytic Anaemias

- Red cells that are smaller than normal
- MCV < 76.0 fL (80fL)
- Defect in haemoglobin synthesis (cytoplasm affected)

Iron + Protoporphyrin

↓

HAEME + GLOBIN (Ribosomes)

↓

Haemoglobin

Differential diagnosis of microcytosis.

1. Iron deficiency (most impt in our setting)
2. Thalassaemias, other haemoglobinopathies
3. Blockade of haem synthesis:
   Lead, Pyrazinamide, Isoniazid, Pyridoxine deficiency
4. Sideroblastic anaemias
5. Chronic inflammatory states/anaemia of chronic disease (may also give a normocytic normochromic picture)
6. Others e.g. Congenital atransferrinemia (very rare)

Epidemiology of ID & IDA

Anemia:HB concentration below the lower limit for a normal population of the same gender and age range

- **Iron deficiency**: A state in which there is insufficient iron to maintain normal physiologic functions
- IDA is the commonest type of anaemia worldwide – especially in the LMIC
- Several factors acting together contribute to its development
- Epidemiological factors are important

Epidemiology contd:

- Prevalence associated with dietary, tradition practices, physical environment, agricultural practices and tropical diseases.
- Age, gender factors
- Socioeconomic status, education influence nutrition
- Prevalence varies from locality to locality in a given country.

EPIDEMIOLOGY cont.

- In developing countries ID is most common in women of childbearing age and young children
- In postmenopausal women and adult men ID is uncommon in absence of bleeding
- ID cause solely by diet in adults is uncommon
- Dietary deficiency is an important cause in young children

EPIDEMIOLOGY cont.

- Poverty, war, poor agricultural practice, irrigation schemes, social and religious factors may be implicated as causes of iron deficient diets

- Iron deficiency predominant in Coastal and arid lowlands, Lake basin, Western Highlands

- Less in Central and mid west highlands

Aetiological factors for IDA

Usually >1 implicated

- Nutritional deficiency
- Increased physiological requirements
- Pathologic causes – Blood loss
- Defective absorption

Nutritional deficiency

- Due to iron-poor foods, factors reducing bio-availability of iron
- Especially in children and women (reproductive ages)
- In women poor iron intake compounded by menstrual losses, losses related to reproductive function
  - Increased requirements for iron not met by dietary intake

Aetiological factors for IDA cont….

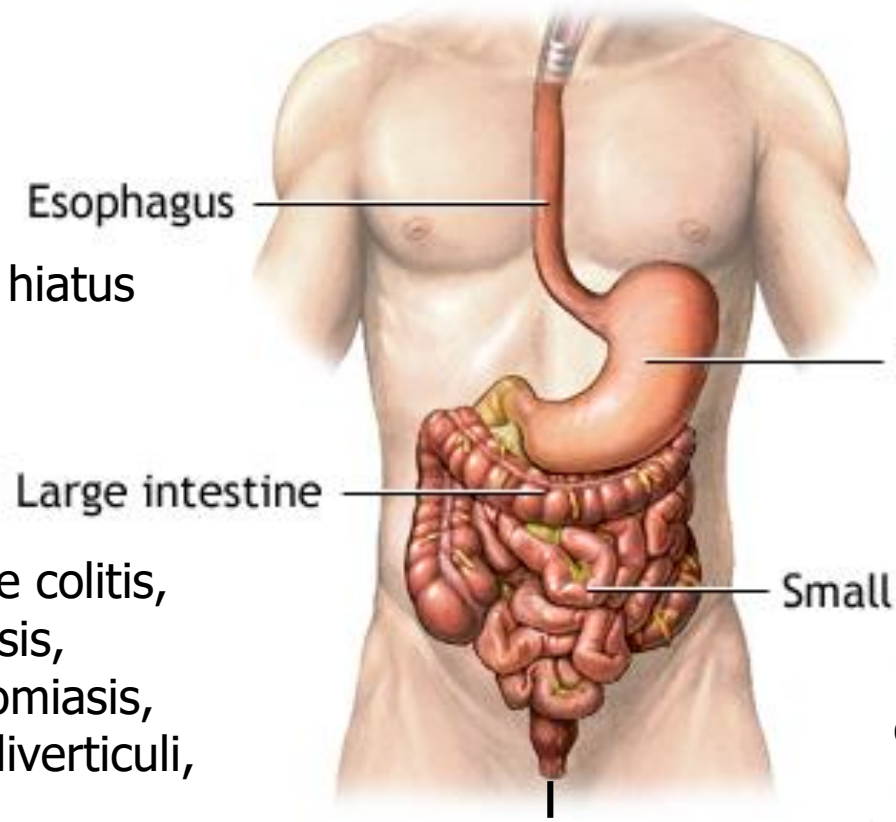
Increased physiological requirements

- Growth – Esp. preterm, neonate, childhood, adolescence
- Menstruation
- Pregnancy: increased RBC mass 35%, iron transfer to foetus, blood loss at delivery
- Lactation
- Frequent blood donation (250mg iron lost per unit of blood donated)

Pathological causes of iron loss

- Blood loss (haemorrhage) – Chronic blood loss is one of the most common causes for IDA
- Remember blood loss may be overt or occult
- Gatrointestinal blood loss and uterine blood loss are commoner sites for blood loss

Blood loss from GI Tract



Varices, ulcer, carcinoma, gastritis

Varices, hiatus hernia

ulcerative colitis, amoebiasis, schistosomiasis, cancer, diverticuli, vascular abnormalities

Ulcer, Helmenthiasis, enteritis, polyps, meckel's diverticulum, vascular abn. intussusception

haemorrhoids, ulceration, cancer

CAUSES OF GENITO-URINARY BLOOD LOSS

- Menstrual bleeding (menorrhagia etc)
- Uterine fibroids
- Neoplasm’s
- Renal stones
- Inflammatory renal disease
- Urinary schistosomiasis

CAUSES OF BLOOD LOSS FROM RESPIRATORY TRACT

- Recurrent haemoptysis
  - Chronic infection e.g. P.T.B.
  - Lung cancer
  - Valvular heart disease

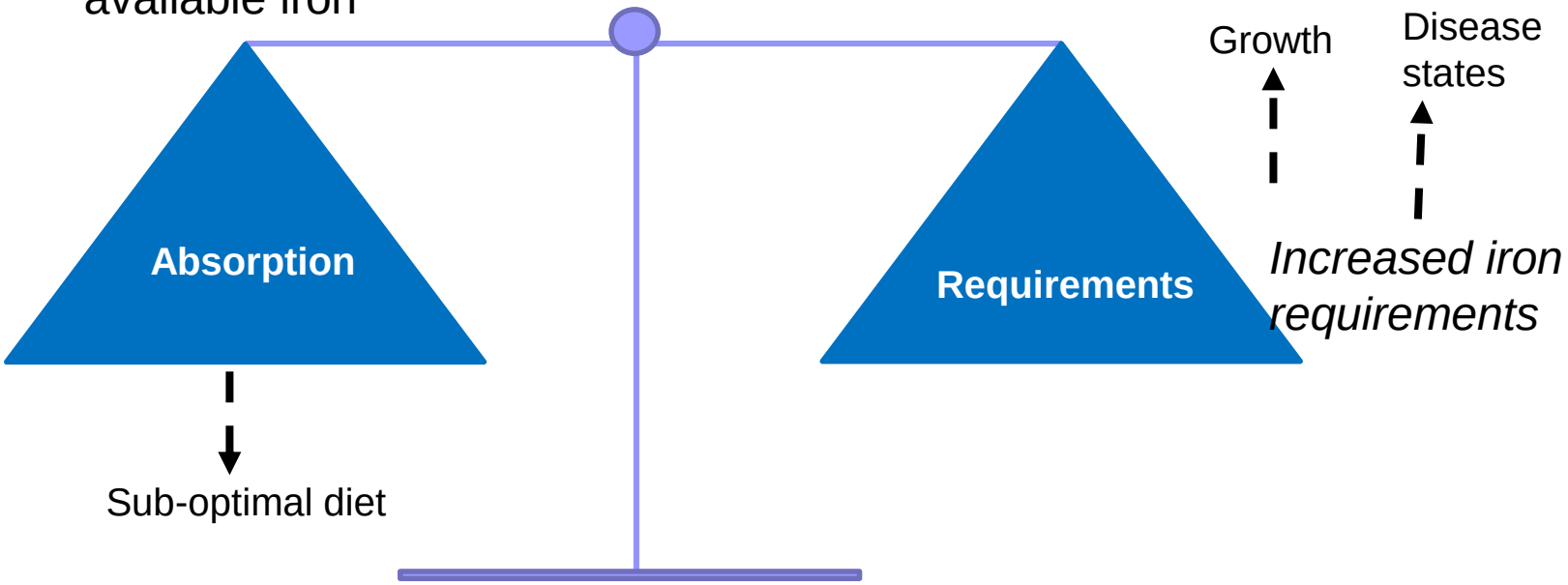
IMPAIRED ABSORPTION

- Gluten induced enteropathy
- Gastrectomy (partial/total)
- Atrophic gastritis

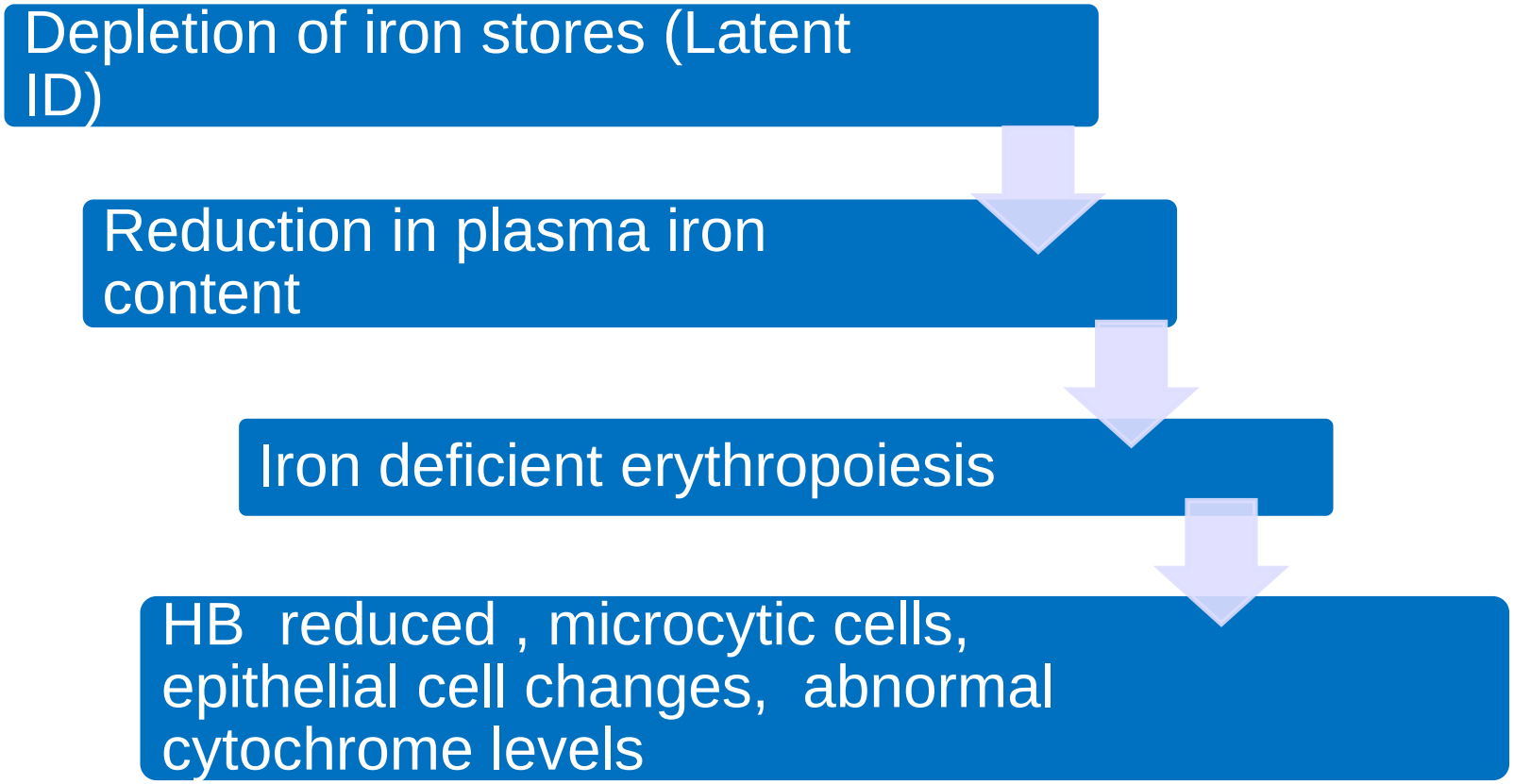
(Intestinal blood loss may also be present)

Iron Balance

ID & IDA result from Imbalance between iron needs and available iron



Stages of Development of Iron deficiency



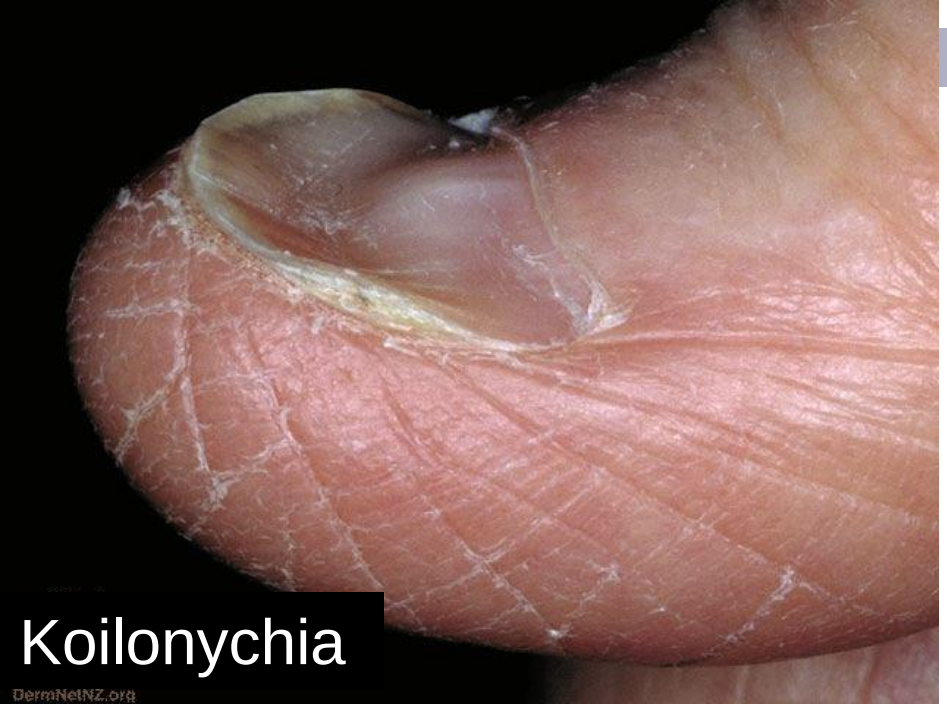
Clinical Features of Iron Deficiency

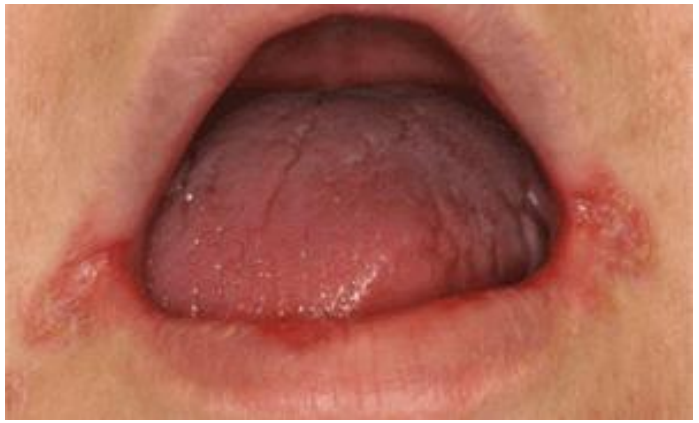
Clinical features of:

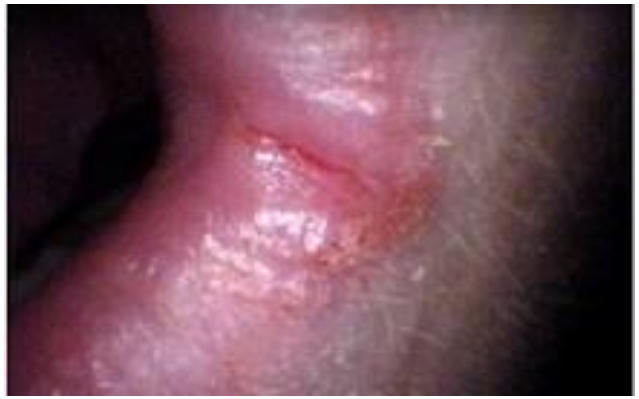
- Anaemia
- Effects of chronic iron deficiency
- Underlying/causative disorder

Epithelial tissue changes:

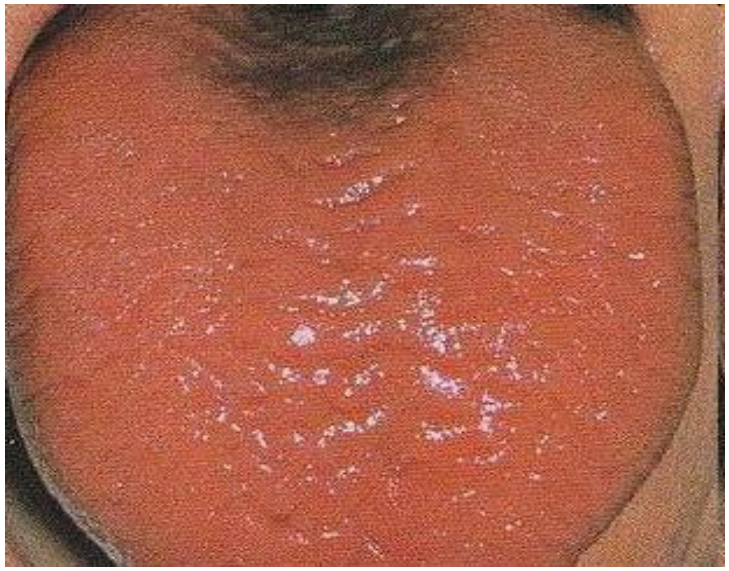
- Nails- Koilonychia
- Tongue - Atrophic glossitis
- Angular stomatitis
- Oesophageal webs- Kelly Patterson syndrome (middle aged females with chronic severe IDA)







Angular stomatitis



Atrophic glossitis

Management:

Diagnosis → History
Physical Examination
Investigations

Treatment → Symptomatic, supportive
Specific

Case Study

A 21-year-old female is seen in the clinic with a chief complaint of overwhelming tiredness and fatigue. Partial results of TBC:

RBC	$3.2x10^{12}/L$
Hgb	6.0 g/dL
Hct	18.7 %
MCV	58.1 fL
MCH	19 pg

Case Study cont.

Question:

This patient's anaemia would be classified morphologically as:

(a) Normocytic, normochromic

(b) Microcytic, hypochromic

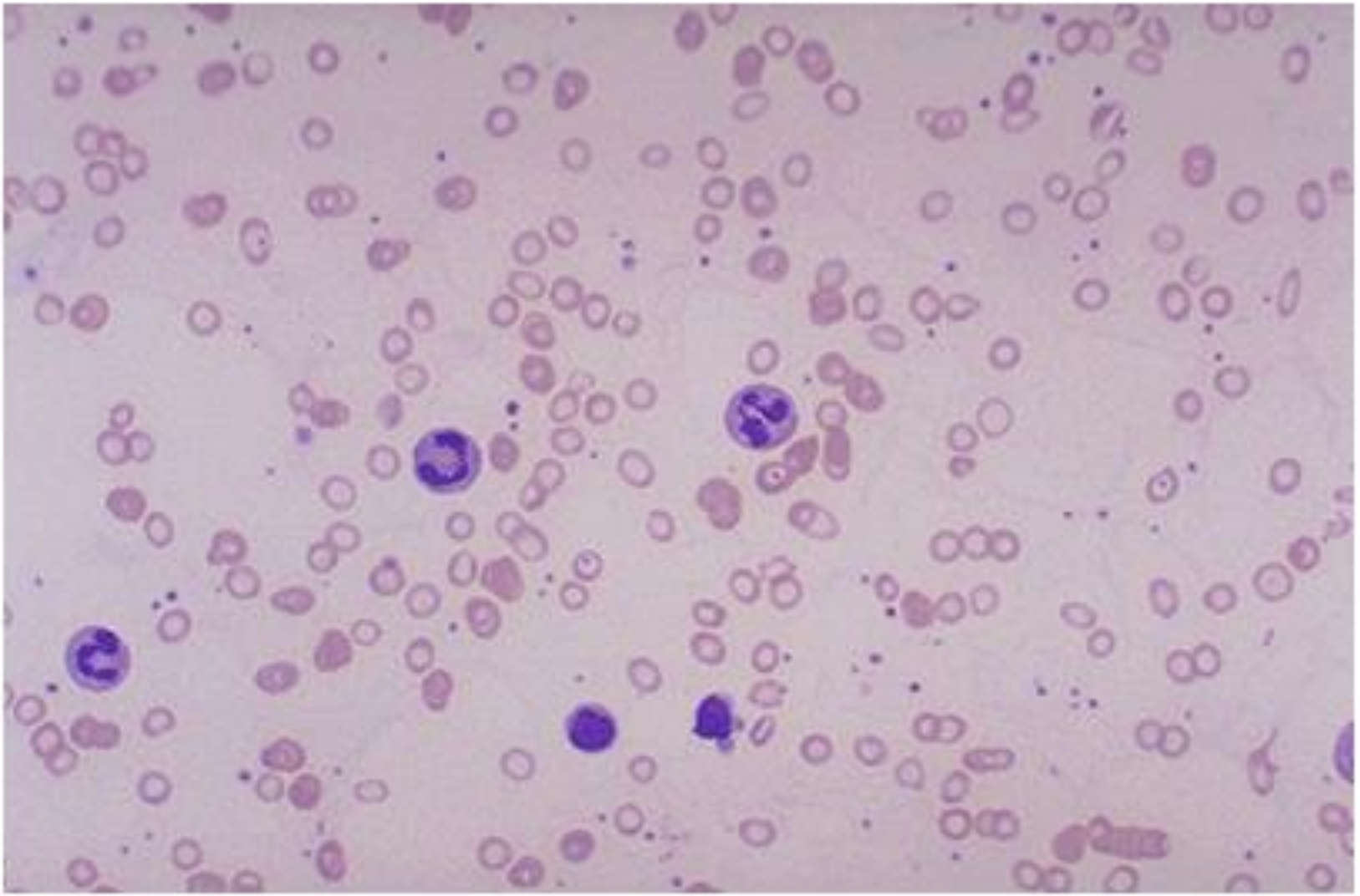
(c) Macrocytic, normochromic

(d) Microcytic, normochromic

LABORATORY FEATURES OF IDA.

1. FBC
   - Hb ↓
   - HCT ↓
   - RBC counts ↓
   - MCV ↓
   - MCH ↓
   - MCHC ↓

- WBC – Usually N
- PLTs – N or ↑
- Retic – Low*



Microcytic hypochromic cells.

3. Biochemical Features

- Serum Fe ↓ < 14 μmol/l (n= 14-29 μmol/l)
- Serum ferritin reduced < 15 μg/l
  - N average male 100 μg/l
  - N average female 30 μg/l

- Transferrin saturation reduced < 33%
- TIBC ↑
- Serum transferrin receptors ↑
- Red cell porphyrin ↑

Bone marrow iron stores

BME is **not** necessary for uncomplicated IDA

- Iron stain (Perl's reaction) – Absent stores
- Iron deficient erythropoiesis (micronormoblastic)

Iron stores present

Absent iron stores

Appropriate investigations for the cause of iron deficiency (guided by Hx/PE):

- Stools exam - O/C, occult blood
- Urine examination
- Endoscopy
- Pelvic examination
- U/S, other imaging studies etc.

TREATMENT: Principles-

- Bring Hb to normal
- Treat underlying disease
- Replace iron stores

Treatment Options:

1. Treatment with oral iron preps
2. Parenteral iron treatment
3. Blood transfusion

- Others in conjunction with treatment above includes dietary measures

Oral Iron:

- Preferred mode
- ~ 100 mg elemental iron daily
  - Ferrous sulphate : 200mg (67 mg iron) tds
  - Treatment needs to be for up to 6 months to restore iron stores
  - Other preps:
    - Combined iron and folate (ranferon)
    - Ferrous gluconate, ferrous fumerate
    - Care to ensure dose is correct with combinations
- HB rise of 1g/dL at day 14; (or HB should rise at 2g/dl every 3 weeks) and there should be a reticulocyte response

Parenteral Iron:

- Iron sucrose (IV); Iron dextran (IM); ferric gluconate; ferrous carboxymaltose (more recently approved)
- Indications: intolerance to oral iron, chronic blood loss, GI diseases aggravated by oral iron, rapid replenishment needed, impaired absorption

Transfusion

- Indications
  - Severe anaemia <5g/dl
  - CCF or impending CCF
  - Pregnant woman about to deliver, etc
- Transfuse packed cells, under diuretic cover

63 year old male with microcytic hypochromic anaemia on oral iron treatment

Initial blood counts

- HB - 6.8 g/dl
- Hct - 20.9 %
- MCV - 64 fl
- MCH - 21 pg
- Retic - 0.1%

4 weeks later

- HB – 7.1 g/dl
- Hct - 21.4 %
- MCV - 66 fl
- MCH - 22 pg
- Retic - 5%

Comment on above and give course of action

Feature	Fe def	Chronic Dx
MCV	↓	N/↓
sFe	↓	↓
TIBC	↑	↓
Transferrin satn	↓	N/↑
Transferrin receptor	↑	N/↓
BM iron	Absent	Present
Serum Ferritin	↓	N/ ↑
Rbc protoporph	↑	↑

DIFFERENTIAL DIAGNOSIS:

- Distinguish between the other major differentials:
  - Anaemia of chronic disorders
  - Thalassaemias
  - Sideroblastic anaemias

IRON OVERLOAD STATES

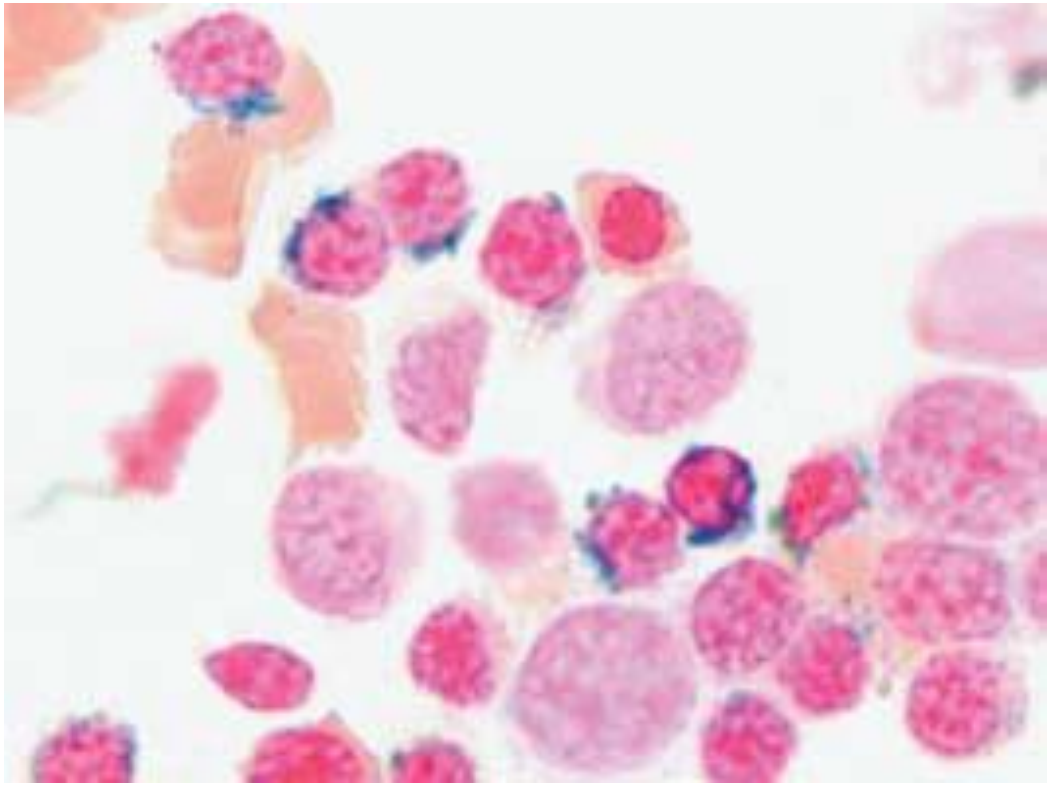
- Increased iron absorption:
  - Ineffective erythropoiesis e.g. thalassaemias, Sideroblastic anaemias
  - Hereditary haemochromatosis
  - Chronic liver disease
- Transfusion siderosis

Iron overload states

- Hereditary haemochromatosis
  - High incidence in Europeans – *HFE* gene; other genes also involved eg Hepcidin, transferrin receptor, ferroportin etc
  - High incidence in Black South Africans associated with increased iron consumption in alcoholic beverages and genetic factors
- Transfusion related siderosis - Iron deposition initially mainly in the RE cells then later in parenchymal cells.

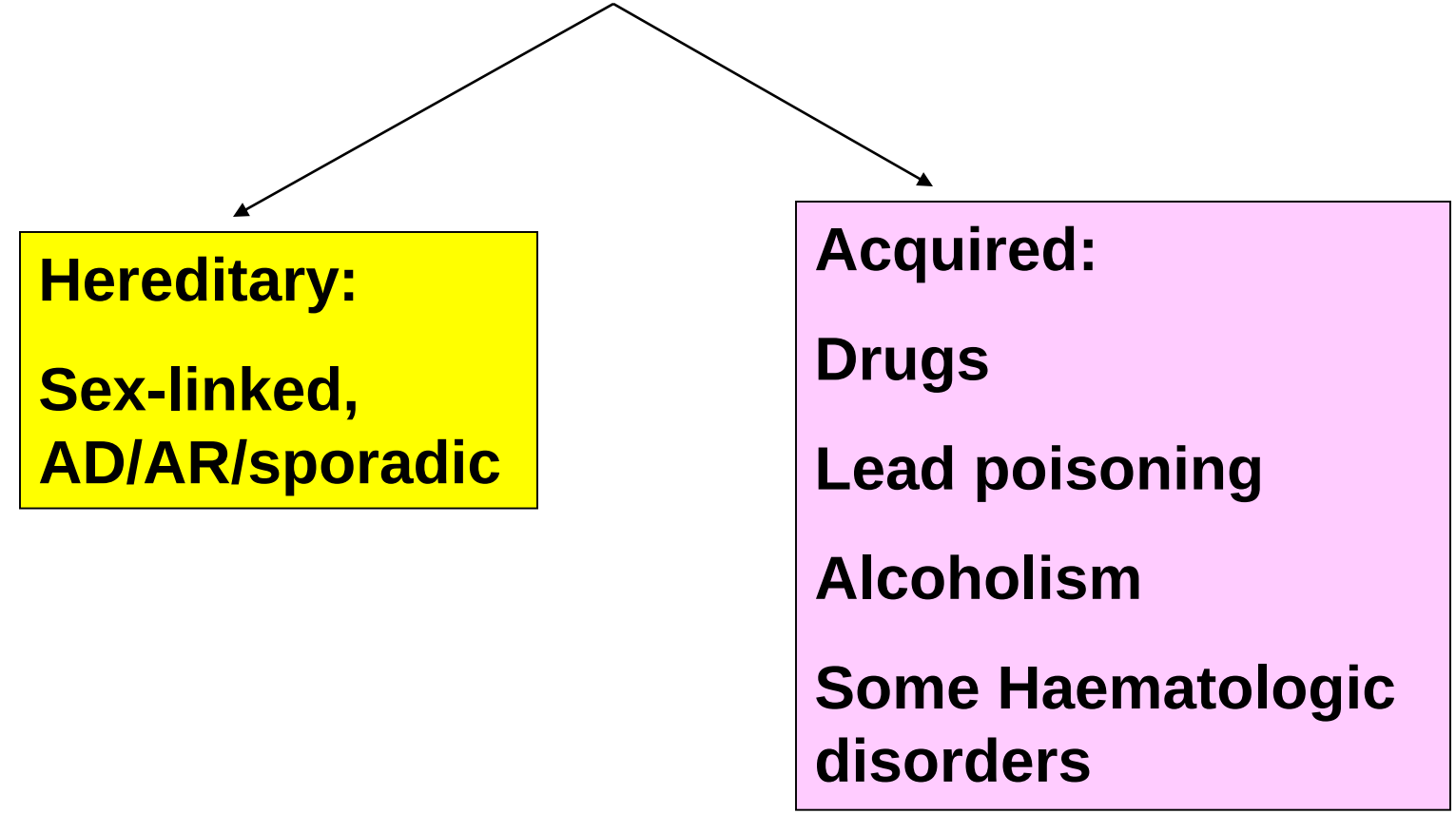
SIDEROBLASTIC ANAEMIAS.

- Characterized by ringed sideroblasts (RS) in bone marrow
- RS are developing erythroblasts with iron granules in the mitochondria arranged in ring around nucleus
- Disordered porphyrin and abn haeme synthesis is a common



Ring sideroblasts in Bone Marrow

Aetiology of sideroblastic anaemias



Lab features of iron overload

- FBC PBF
- BM - ↑↑ iron stores, ringed sideroblasts
- BIOCHEMICAL
  - Serum iron ↑
  - Serum ferritin ↑
  - Transferrin saturation 100%
  - TIBC ↓↓
  - Increased storage iron in tissues

Conclusion

- Iron deficiency (ID) is the most common and important cause for microcytic anaemia
- Causes of ID include blood loss, dietary deficiency and malabsorption
- Investigations include TBC, PBF, iron studies and investigation for cause of ID
- Oral iron replacement is treatment of choice
- Iron overload states may be due to conditions associated with increased iron absorption or chronic transfusion

Thank you!

Questions?