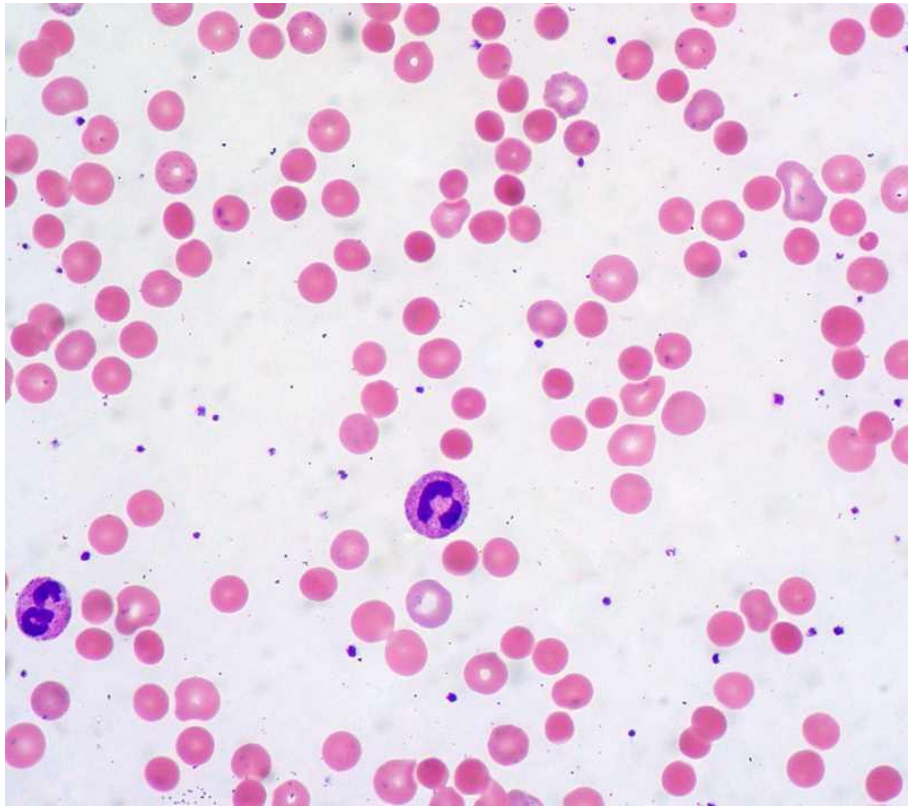
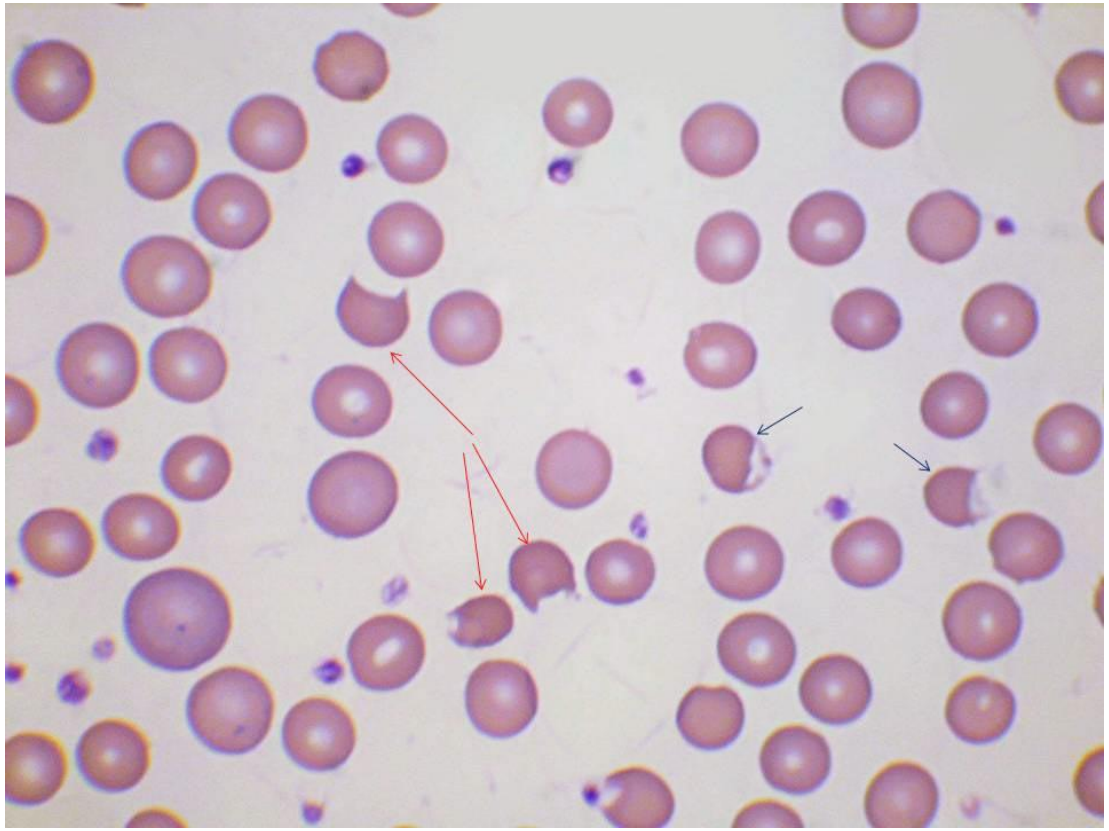
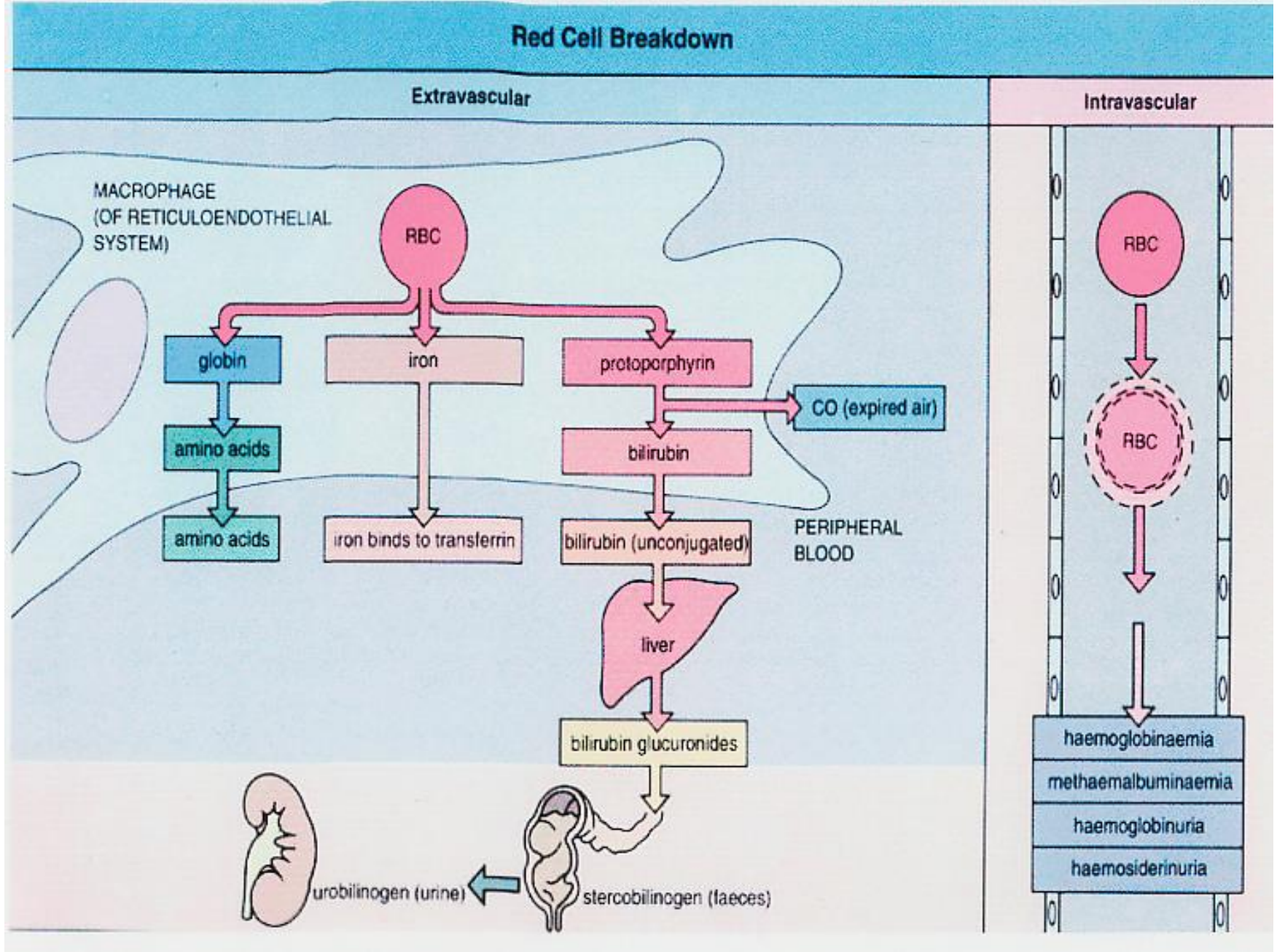
HS & G6PD





Dr Durga Moratuwagama

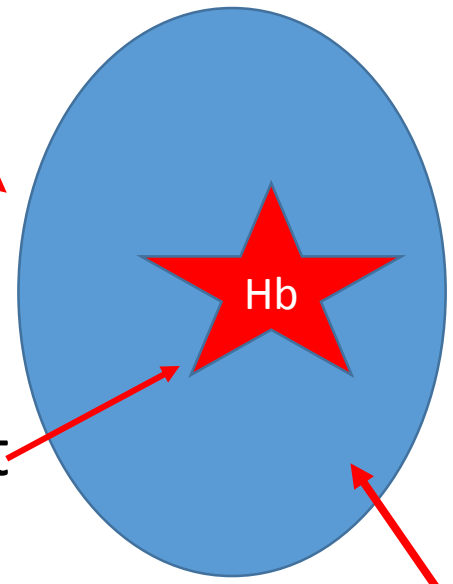

Red Cell Breakdown
Extravascular
Intravascular
MACROPHAGE
(OF RETICULOENDOTHELIAL
SYSTEM)
RBC
globin
iron
protoporphyrin
CO (expired air)
amino acids
bilirubin
amino acids
iron binds to transferrin
bilirubin (unconjugated)
PERIPHERAL
BLOOD
liver
bilirubin glucuronides
urobilinogen (urine)
stercobilinogen (faeces)
RBC
RBC
haemoglobinaemia
methaemalbuminaemia
haemoglobinuria
haemosiderinuria

HA

Congenital

Acquired

- Membrane defect
- Haemoglobin defect



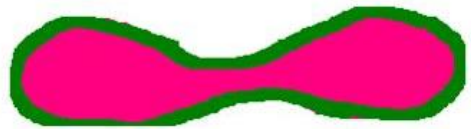
Enzyme defect

Hereditary Haemolytic anaemia

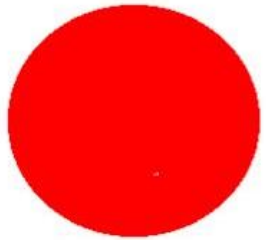
Membrane defects

- Hereditary spherocytosis is the commonest membrane defect
- Autosomal dominant
- Can present without a family history
- Males=Females
- Other examples: Hereditary eliptocytosis/ovalocytosis

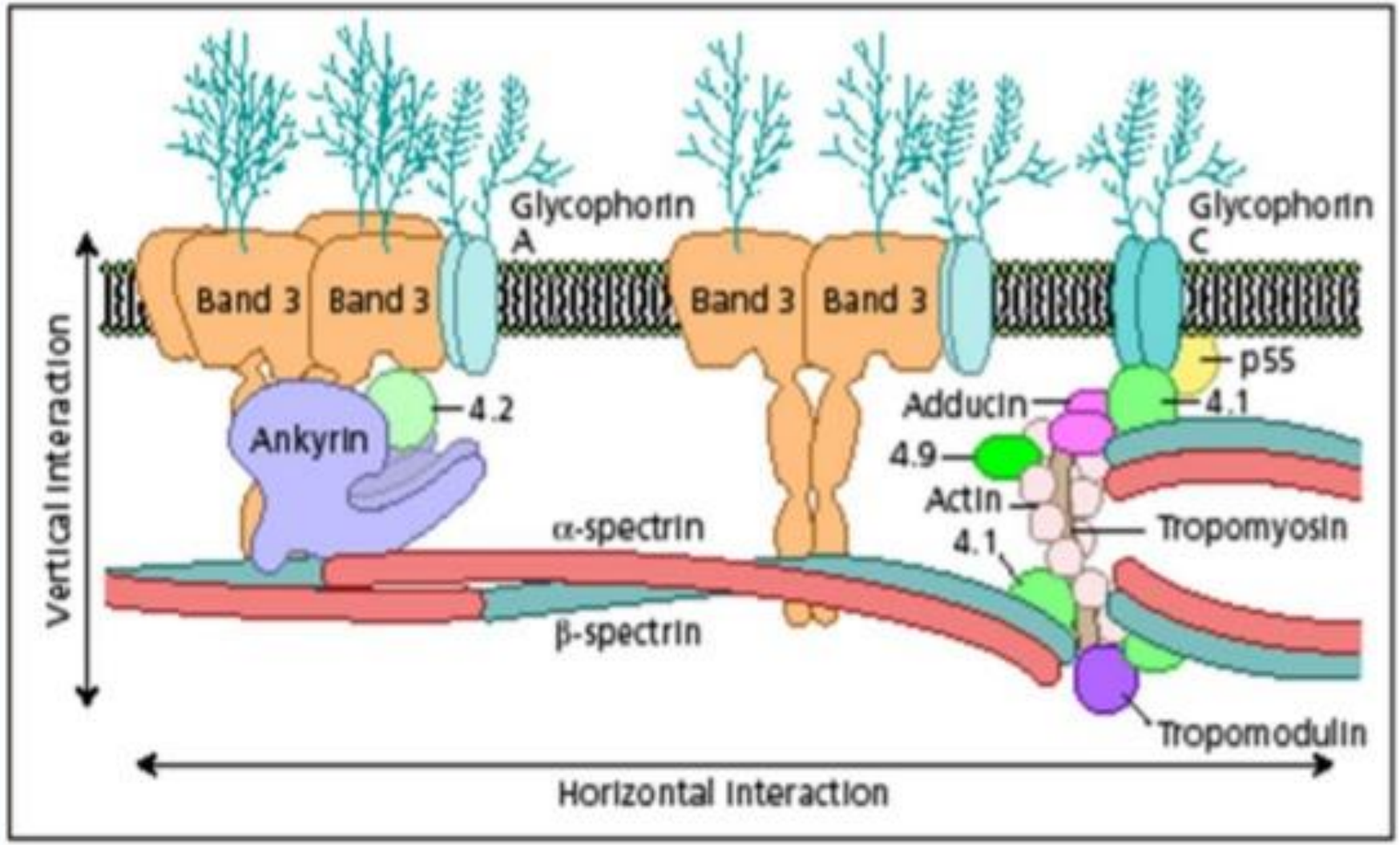
normal red cell



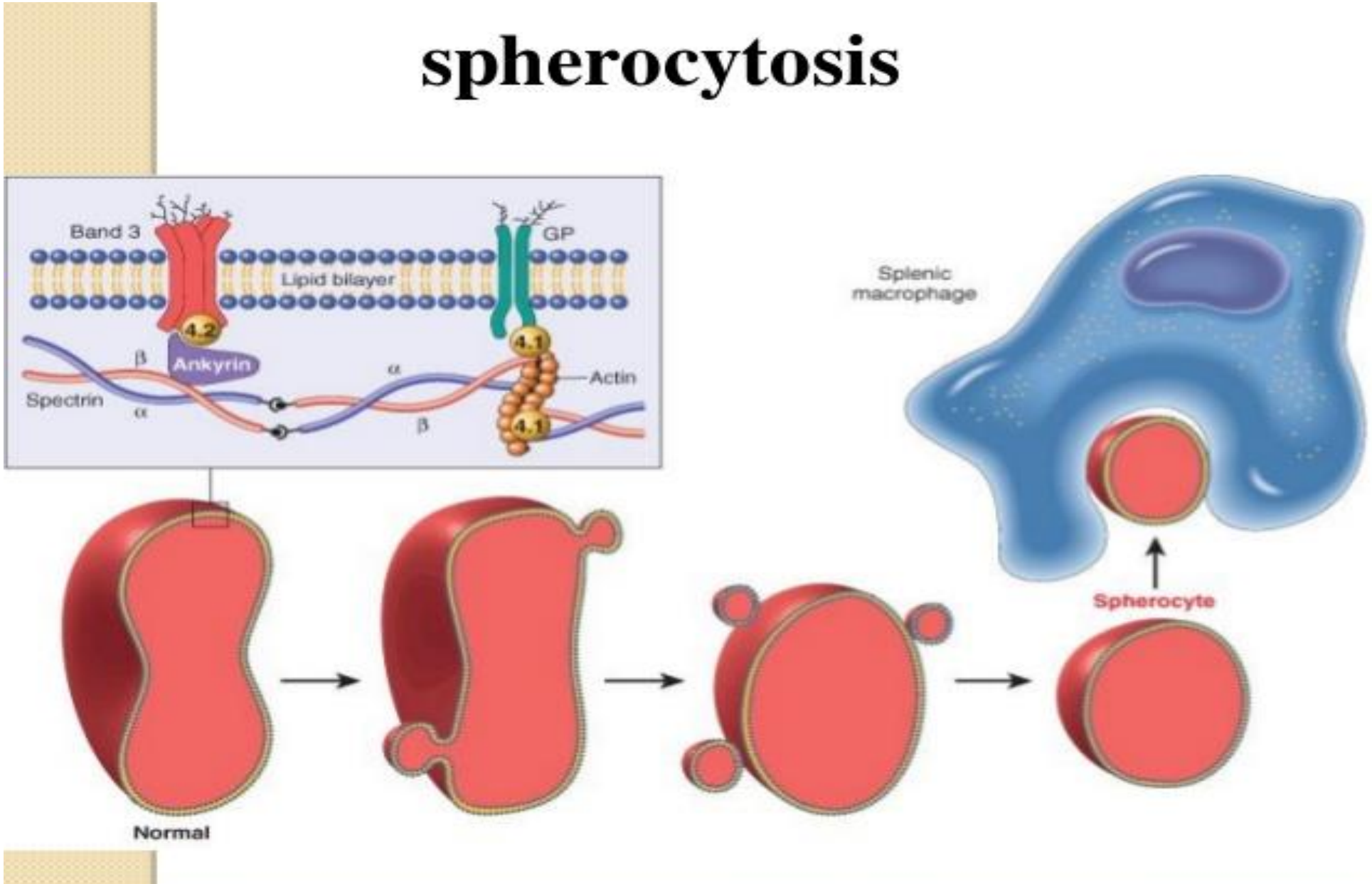
Spherocyte

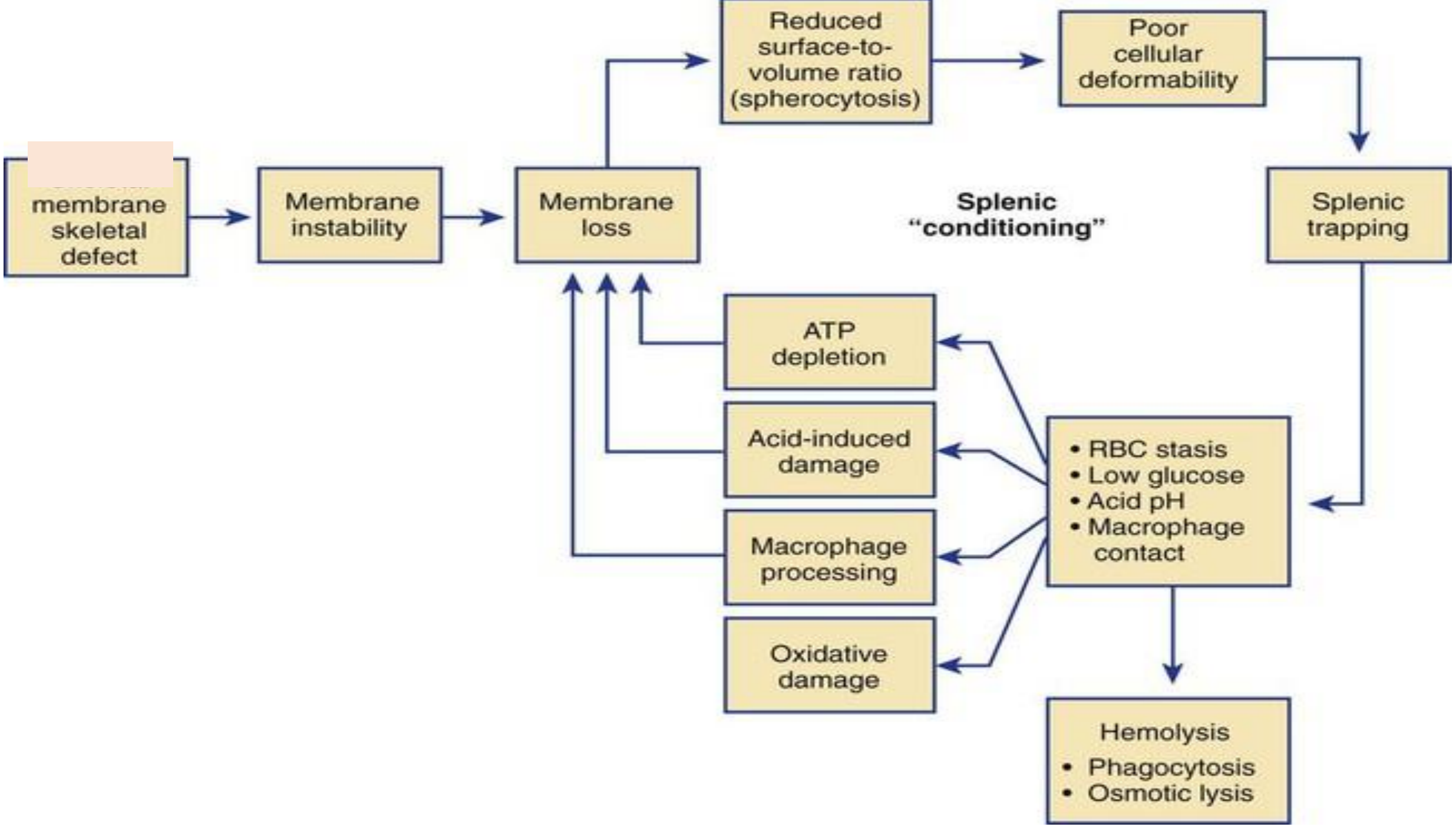


Structure of RBC membran



Pathogenesis



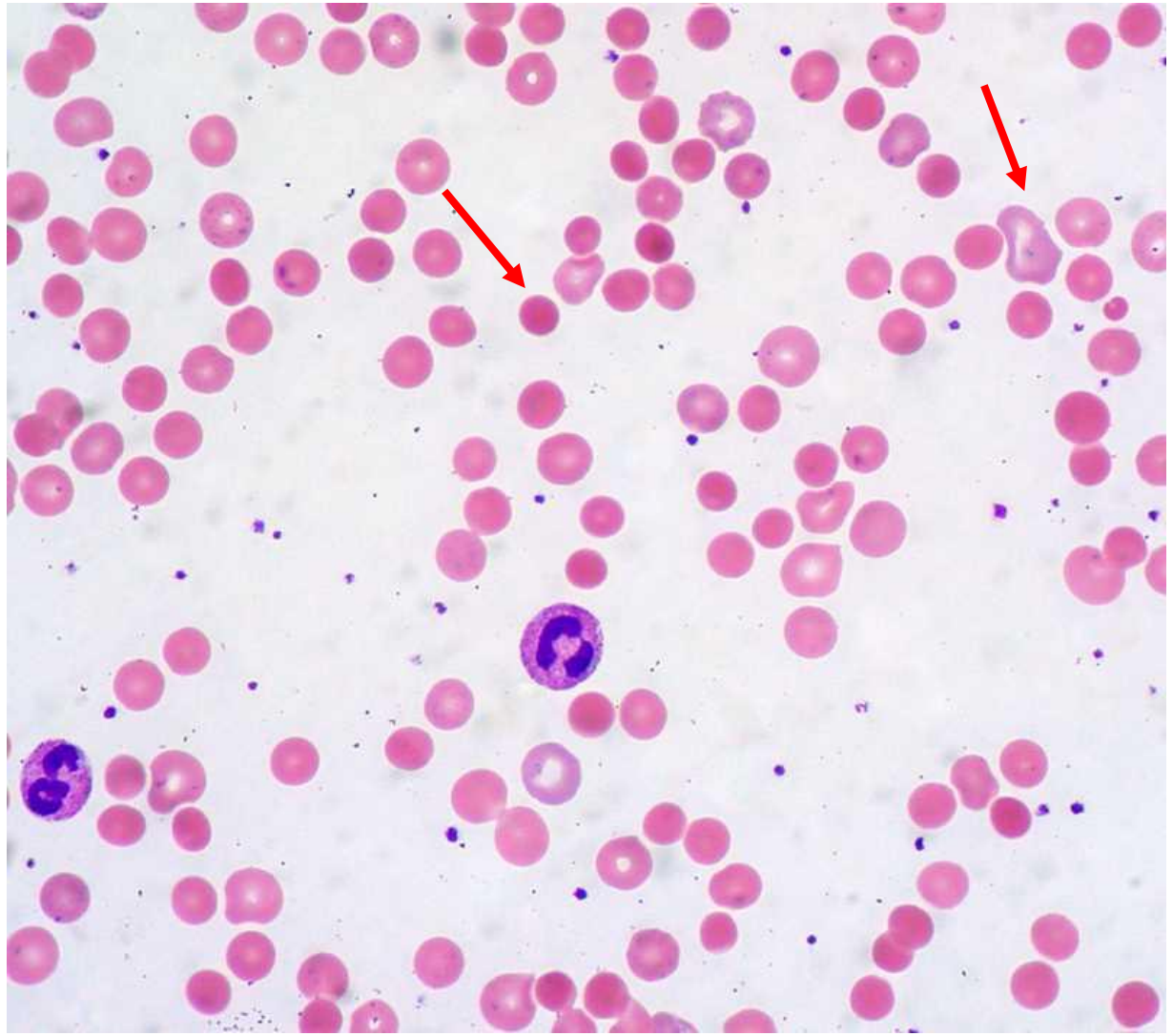

membrane skeletal defect
Membrane instability
Membrane loss
Reduced surface-to-volume ratio (spherocytosis)
Poor cellular deformability
Splenic trapping
Splenic "conditioning"
ATP depletion
Acid-induced damage
Macrophage processing
Oxidative damage
• RBC stasis
• Low glucose
• Acid pH
• Macrophage contact
Hemolysis
• Phagocytosis
• Osmotic lysis

Clinical features

- Present at any age-infancy-adulthood
- Symptoms and signs of anaemia
- Jaundice-Flactuate
- Splenomegaly
- Pigment gallsones
- Aplastic crisis-associated with parvo virus inf.
- Megaloblastic anaemia
- Leg ulcers

Investigations

- FBC-Low Hb /Increased MCHC
- Blood picture
- Retic count
- Haemolytic screen
- Coombs test



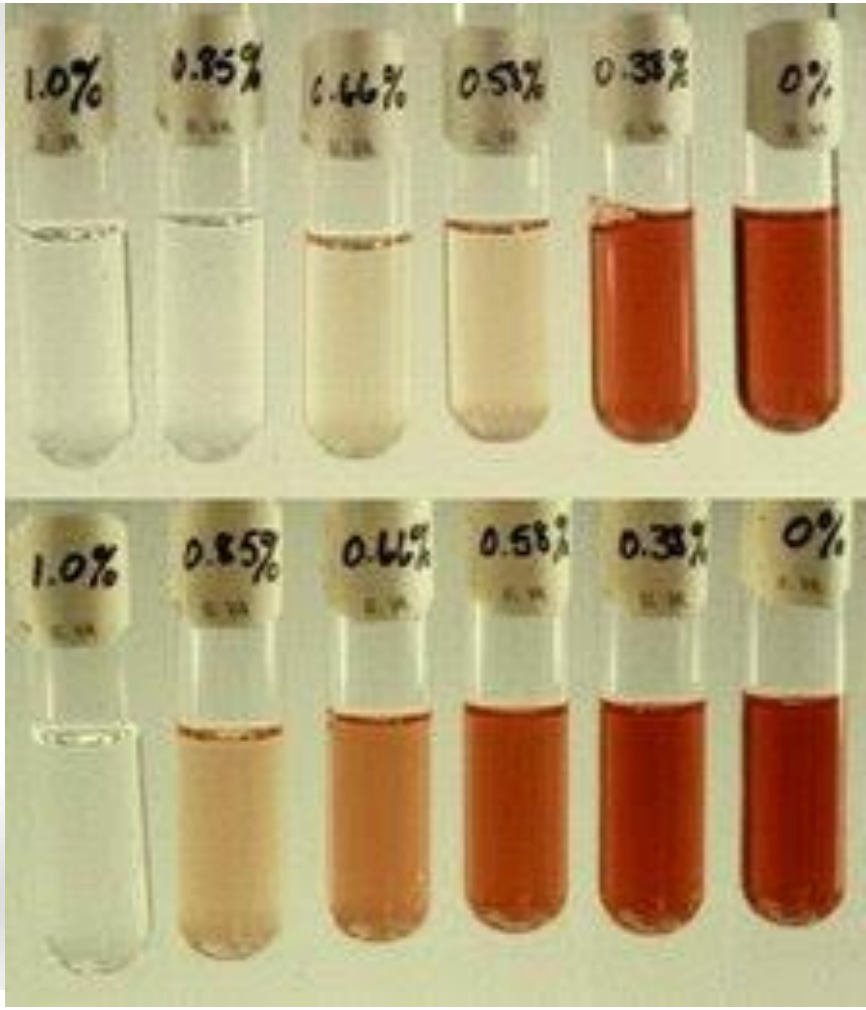
Spherocytes + Negative Coombs test + positive family history

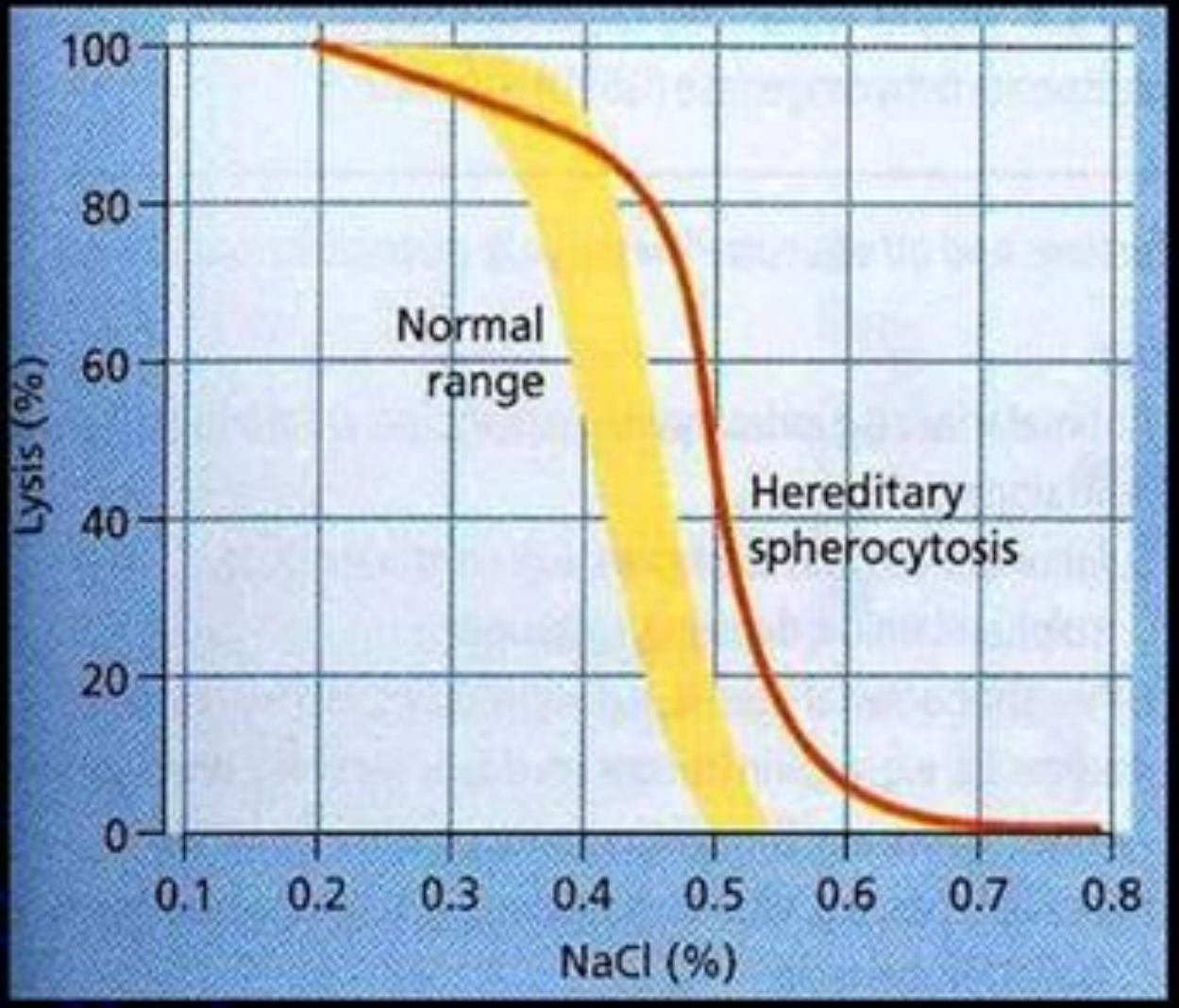
- Hereditary Spherocytosis

Other tests

Osmotic Fragility Test

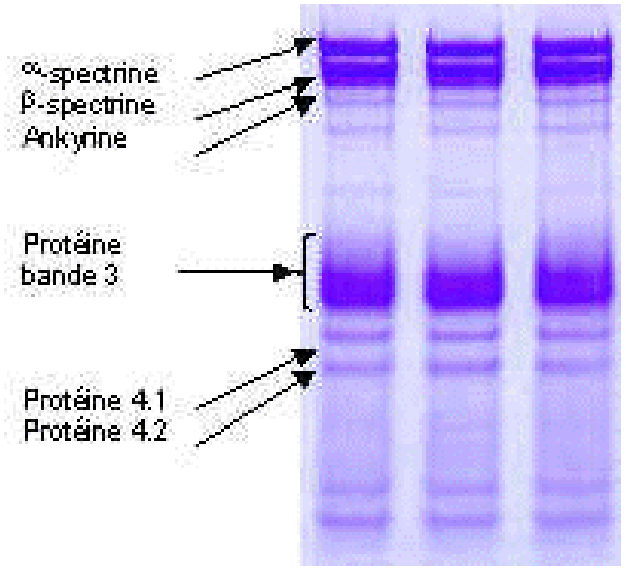
- It gives an indication of the surface area/volume ratio of the erythrocytes. As this ratio falls cells become more sensitive to osmotic lysis.
- Red blood cells that are spherocytic , for whatever cause, take up less water in a hypotonic solution before rupturing than do normal blood cells.





Osmotic Fragility

- Cryo haemolysis test-Cells from HS patients are particularly sensitive to cooling at 0° C in hypertonic solutions
- EM dye binding test
- SDS PAGE: Red cell membrane protein analysis
- Genetic testing



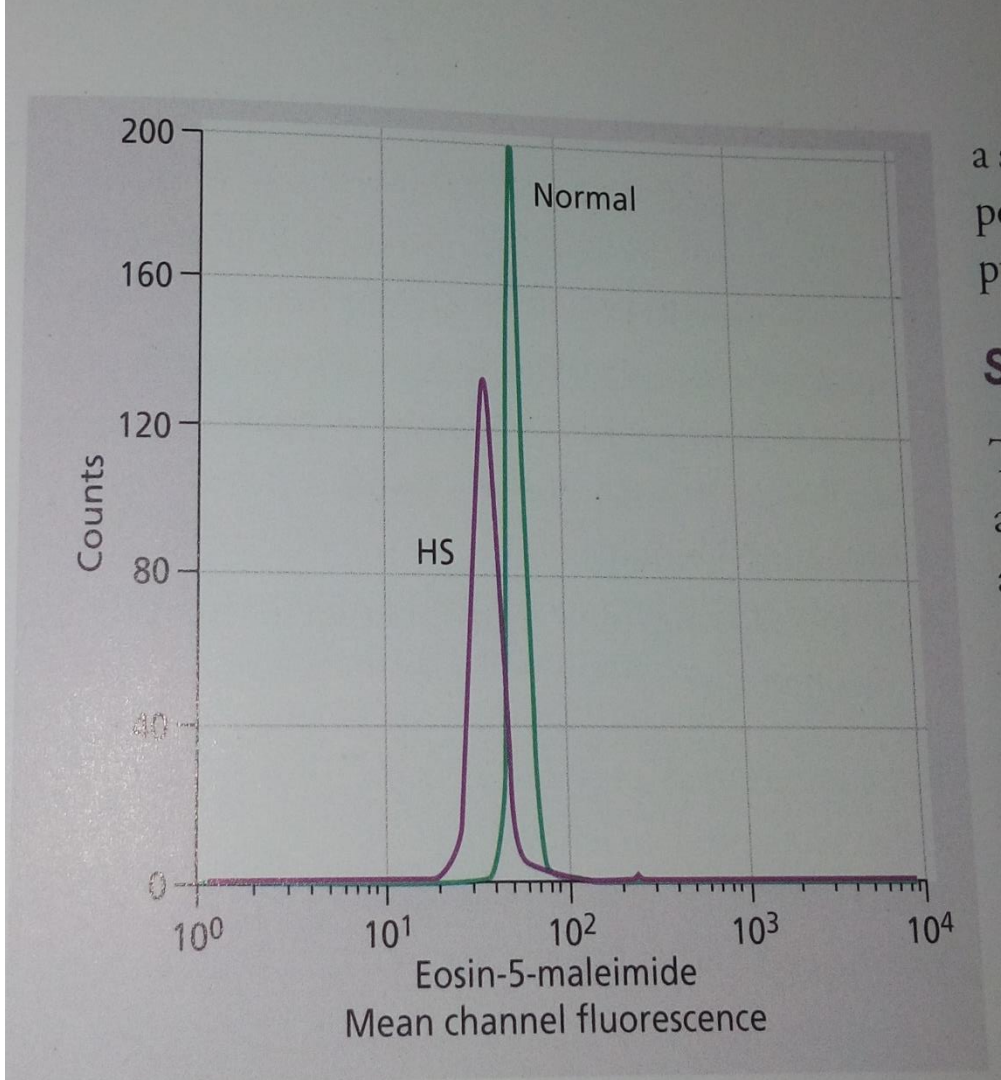


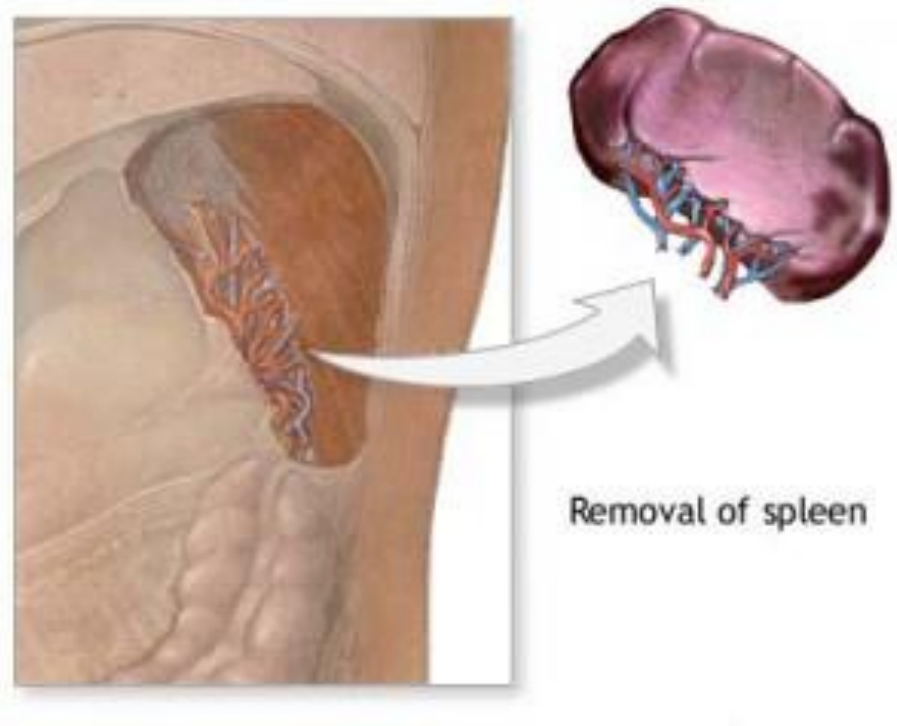
Figure 6.5 Eosin-5-maleimide staining in hereditary spherocytosis (HS) showing reduced mean channel fluorescence due to membrane band 3 protein deficiency. (Courtesy of Mr G. Ellis.)

Management

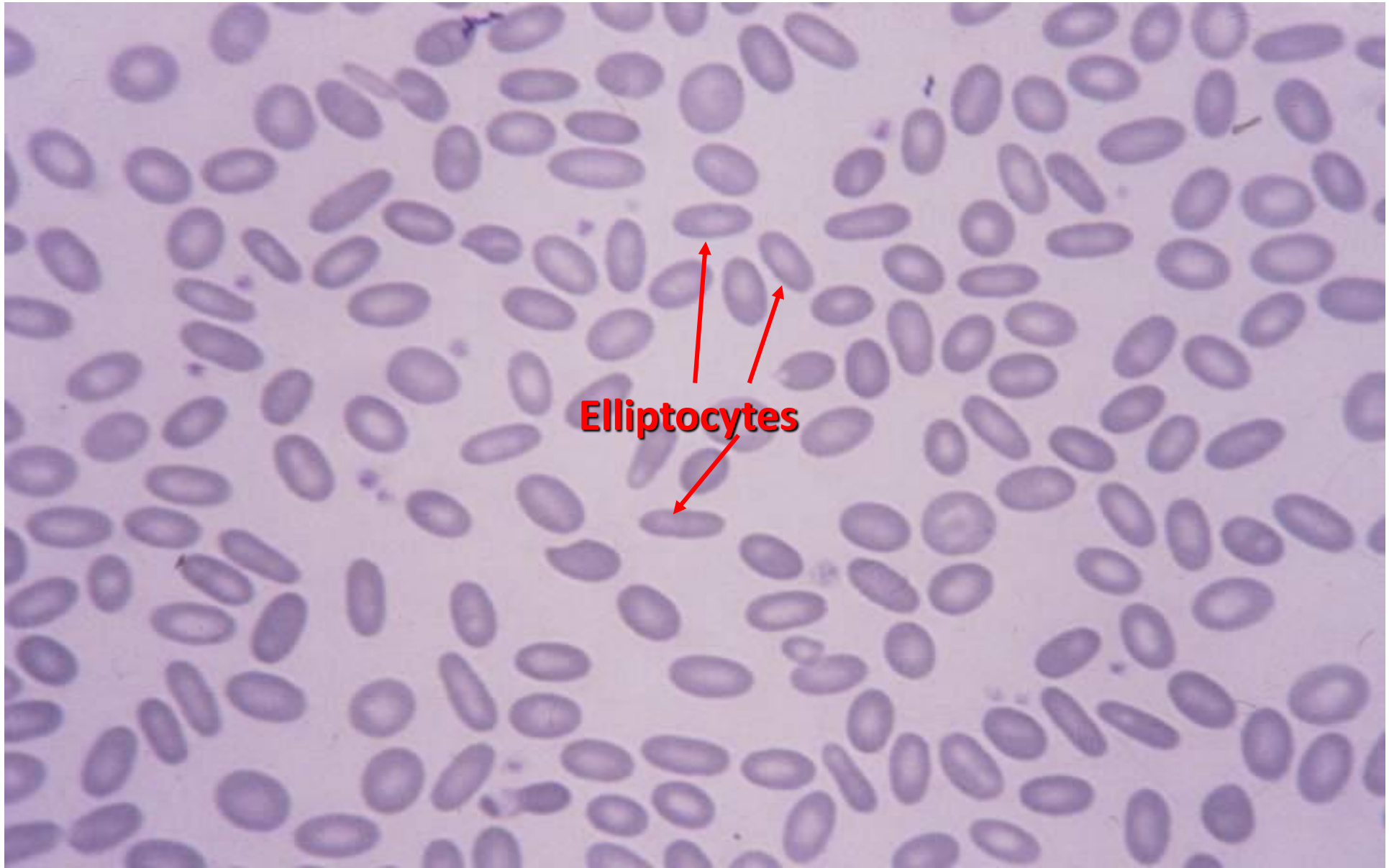
- Asymptomatic
- Symptomatic anaemia/Complications-Splenectomy
- Post splenectomy complications
- What are the complications?

Gall stones /leg ulcers/Growth retardation

- Choleycystectomy
- Folic acid



HEREDITARY ELLIPTOCYTOSIS (HE)



HS

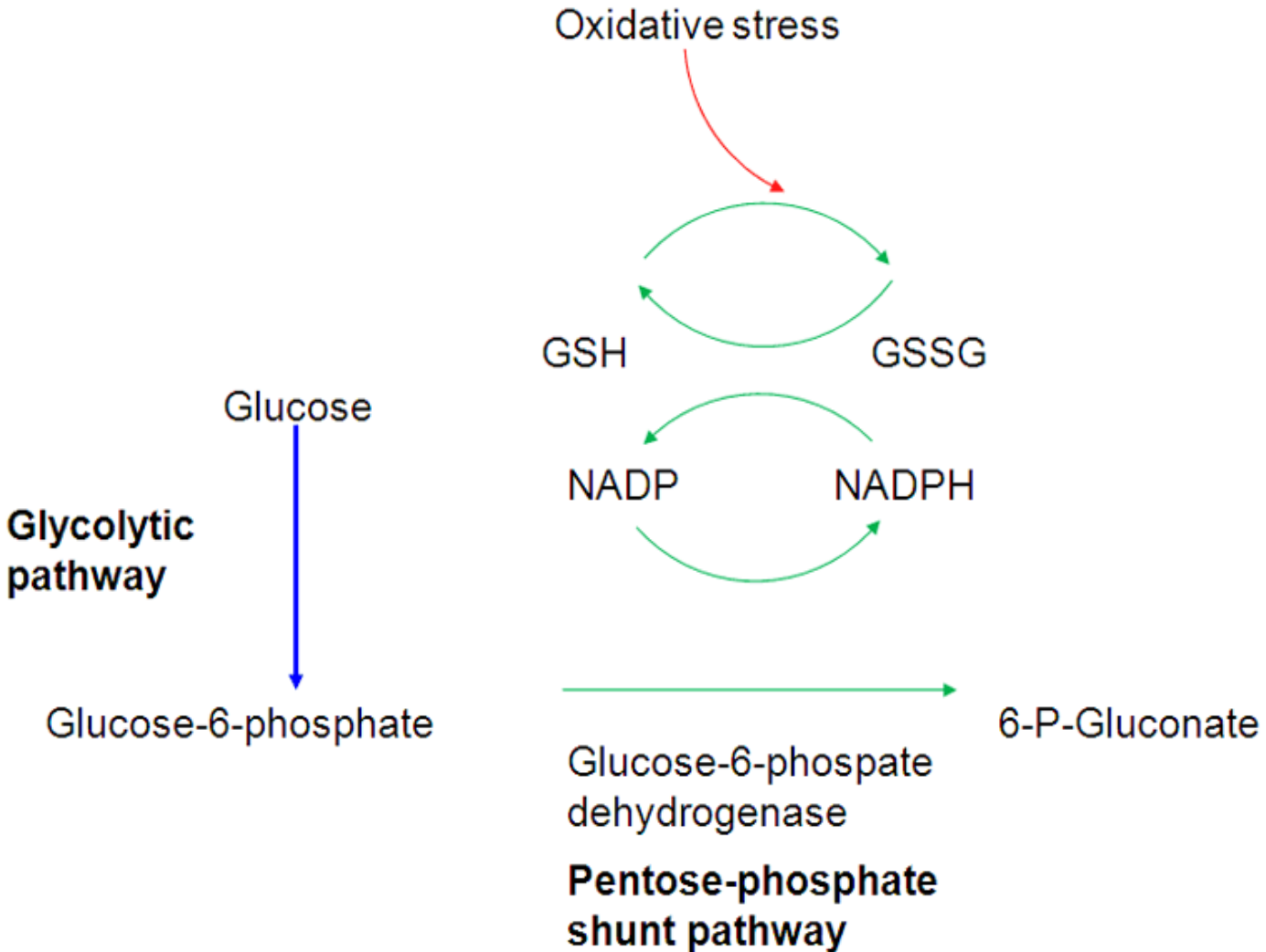
- Pathogenesis of HS
- Clinical features
- Diagnosis
- Management

G6 PD deficiency

- G6PD deficiency is the most common red cell enzymopathy world wide.
- Glucose-6-phosphate dehydrogenase (G6PD)
- Only source of NADPH
- NADPH is needed for the production of reduced glutathione

Deficiency renders the RBC

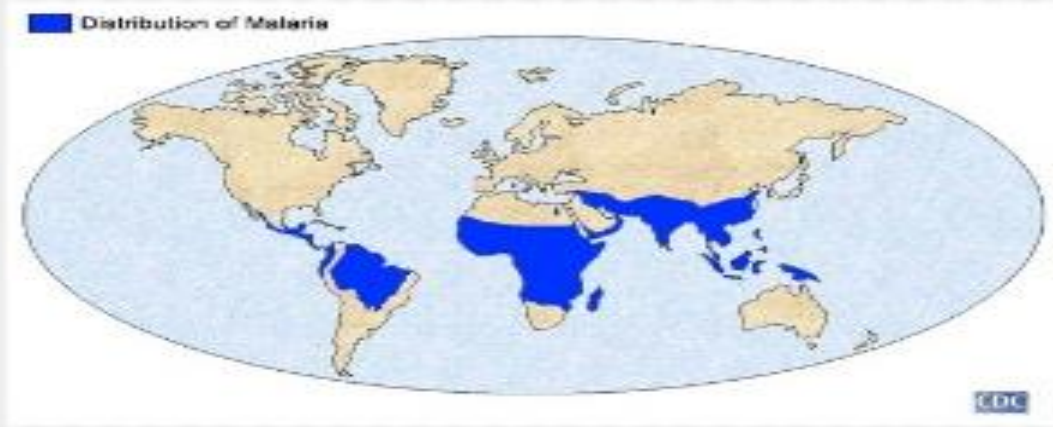
Susceptible to oxidant stress



- X linked
- Males are affected
- Females are carriers
- There are different variants and mutations that determine the severity of the disease -Mild-Black Africans

  Severe-Mediteranians

- Distribution of G6PD deficiency coincides prevalence of malaria



- G6PD deficiency may impart some degree of malaria resistance

- Most people with G6PD deficiency have no symptoms and are not anemic.
- Majority of affected individuals live out their lives unaware of their status.
- The disease is generally manifest when the red cells undergoes oxidative stress triggered by:
  - Certain drugs
  - Infections
  - Ingestion of fava beans
  - Medical conditions such as DKA, liver disease, renal disease

- G6PD deficiency usually presents as:
  - Acute Haemolysis drug/infection/favism-induced- √
  - Neonatal jaundice
  - Congenital non-spherocytic hemolytic anemia (CNSHA)

G6PD and haemolysis(IVH)

- The symptoms start after ingesting the offending drug by 2 to 4 days.
- Infection induced haemolysis occurs after 1-2 days from onset of febrile illness.
- Favism- Within 5 - 48 hrs from eating or inhaling fava beans
- **Fatigue, jaundice, pallor , abdominal or back pain, and dark urine.**
- Self-limiting, but may be prolonged in severe variants, with an average of 7 – 1o days after onset of hemolysis.

Drugs and G6PD deficiency

- Dapsone
- Methylene blue
- Toluidine blue
- Phenazopyridine
- Primaaquine
- Rasburicase
- Nitrofurantion

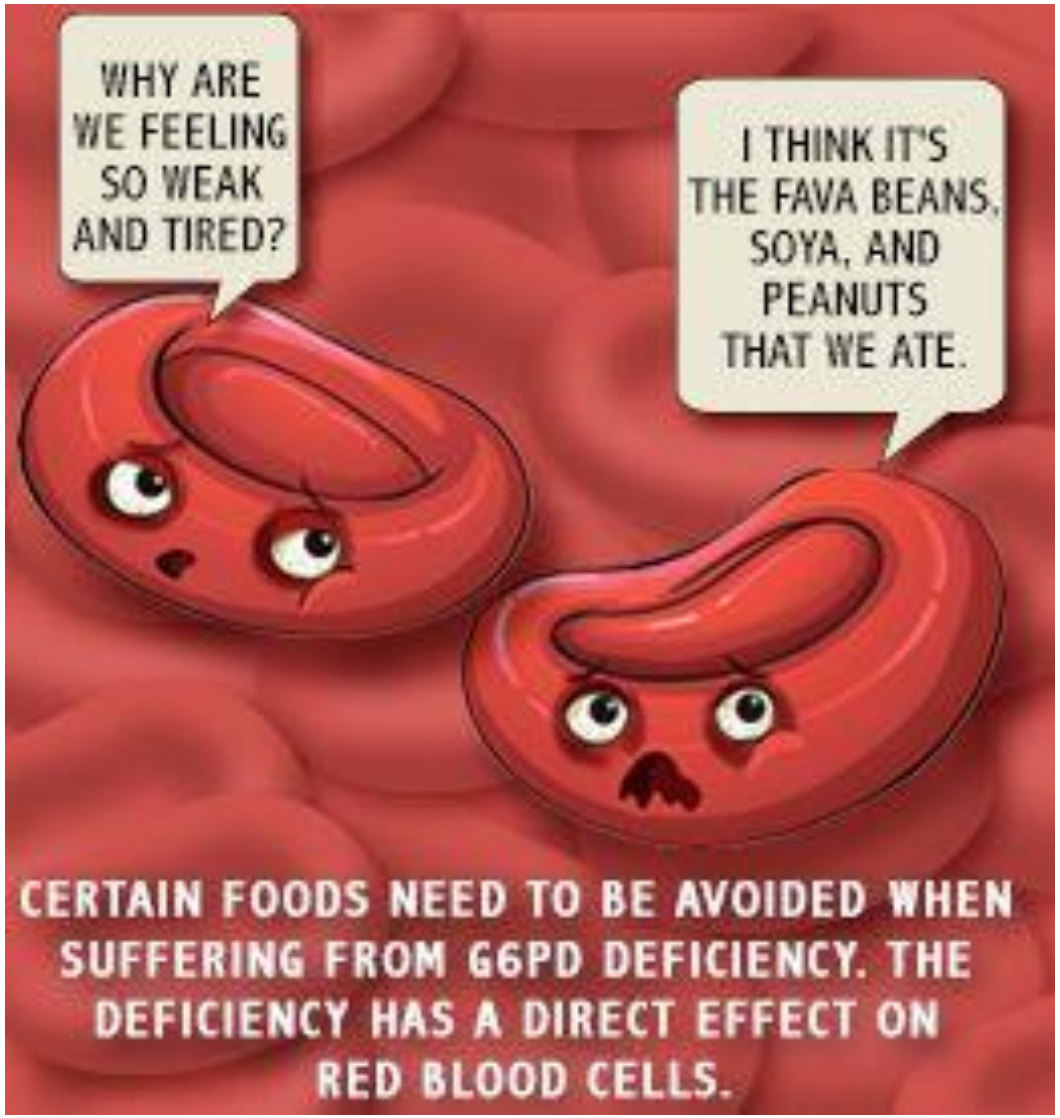
Table 1. Drugs and chemicals to be avoided by persons with G6PD deficiency

Acetanilid
Diaminodiphenyl sulfone
Furazolidone (Furoxone)
Glibenclamide
Henna (Lawsone)
Isobutyl nitrite
Methylene Blue
Naphthalene
Niridazole (Ambilhar)
Nitrofurantoin (Furadantin)
Phenazopyridine (Pyridium)
Phenylhydrazine
Primaquine
Sulfacetamide
Sulfanilamide
Sulfapyridine
Thiazolesulfone
Trinitrotoluene (TNT)
Urate oxidase

TABLE 6

Synonyms for Fava Beans

Bell beans	Horse beans
Broad beans	Pigeon beans
English dwarf beans	Silkworm beans
Fever beans	Tick beans
Haba beans	

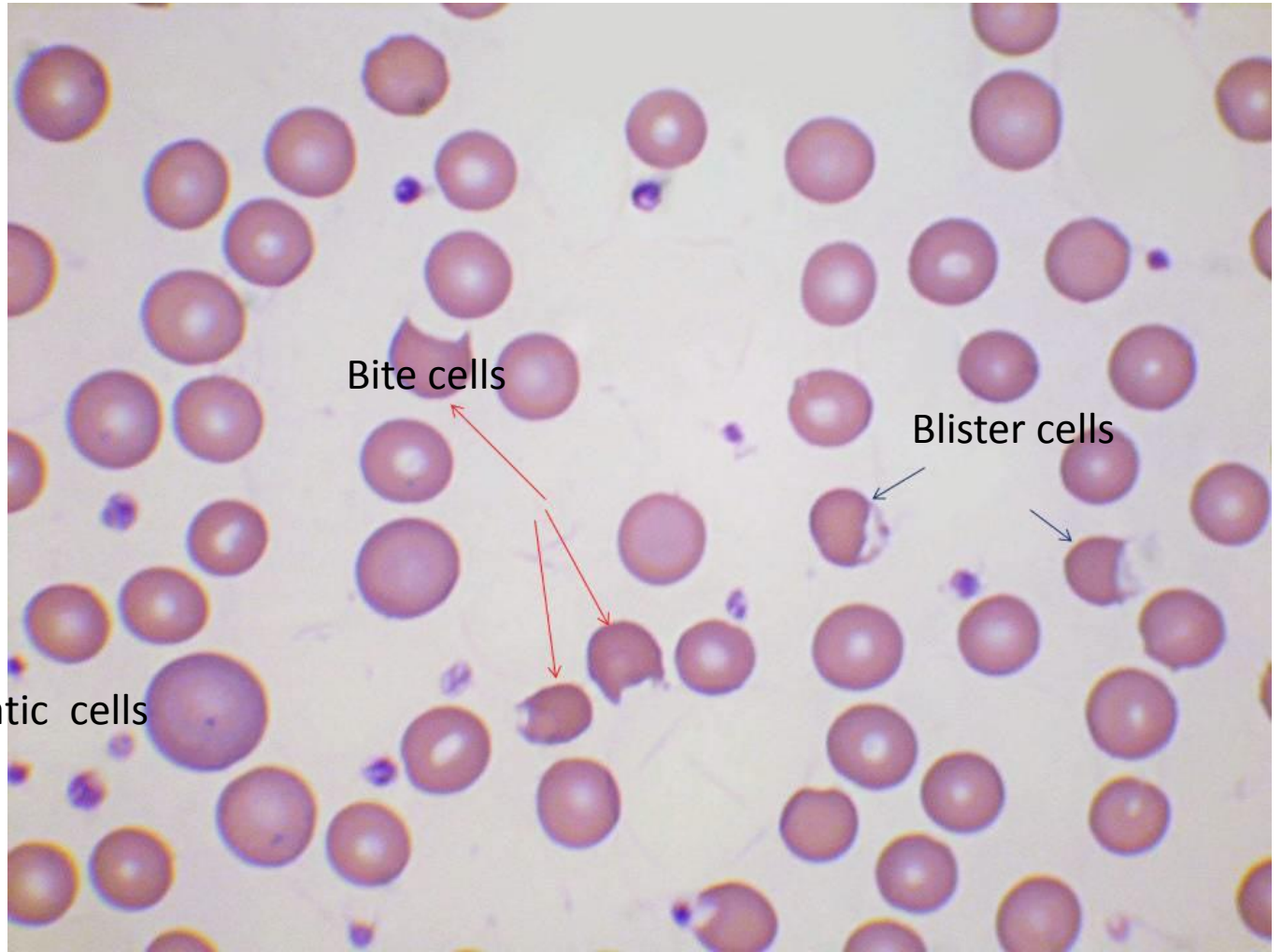


Broad beans

Kidney red beans

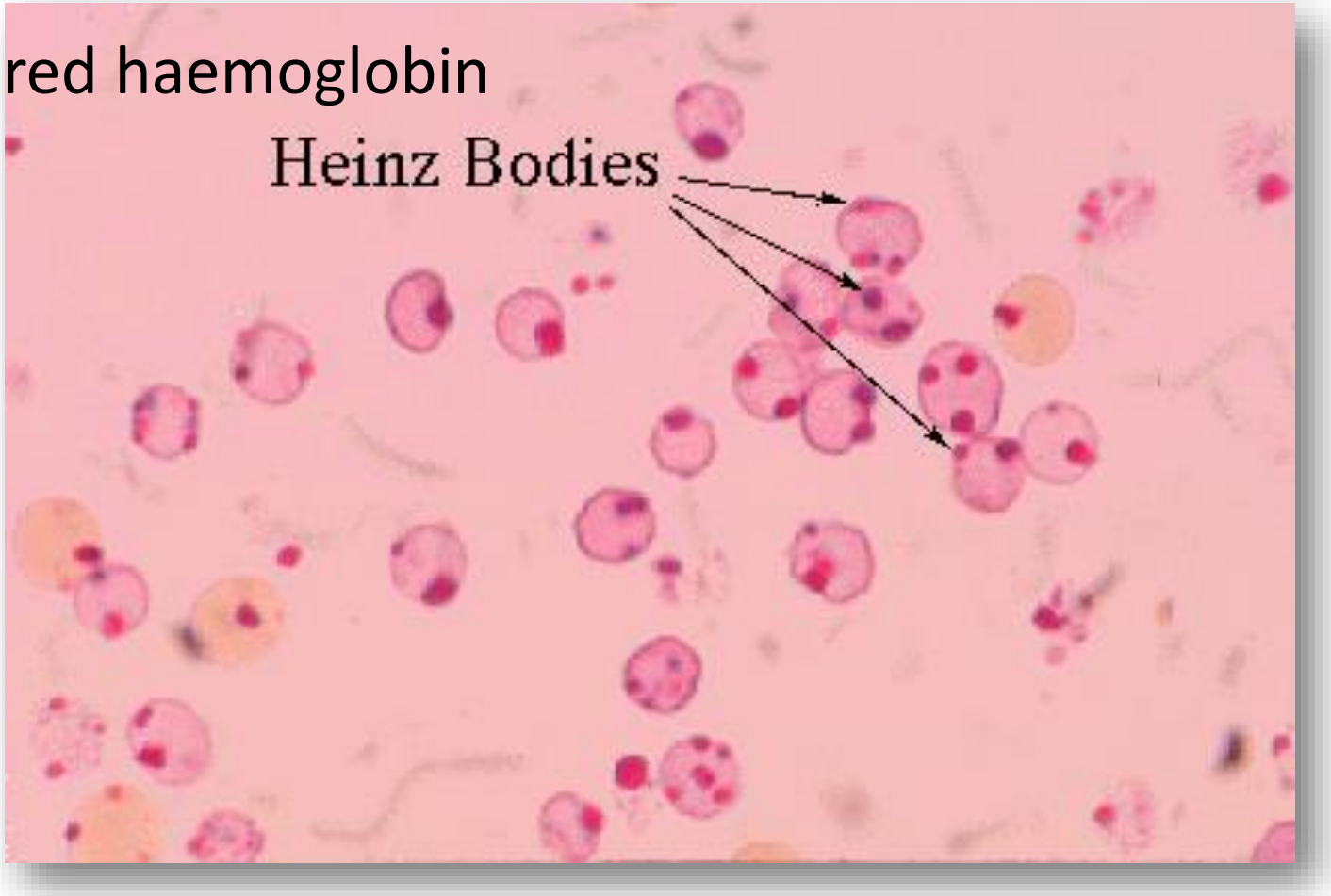
Diagnosis

- FBC+ BP+ Retic count
- Haemolytic screen-IVH
- Enzyme levels
- Brewers test

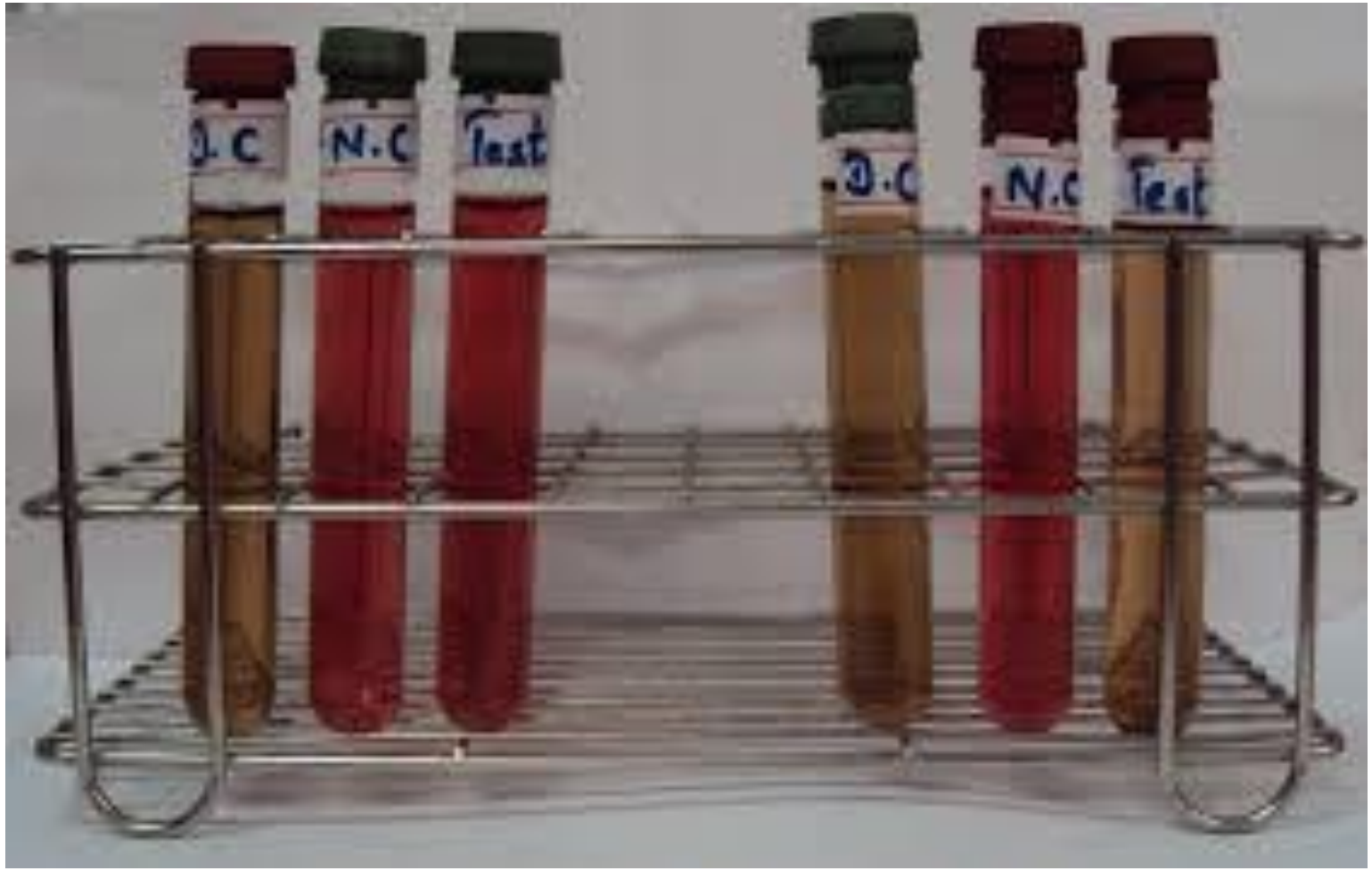


Heinz body preparation

- Oxidized denatured haemoglobin



Brewers test-HW

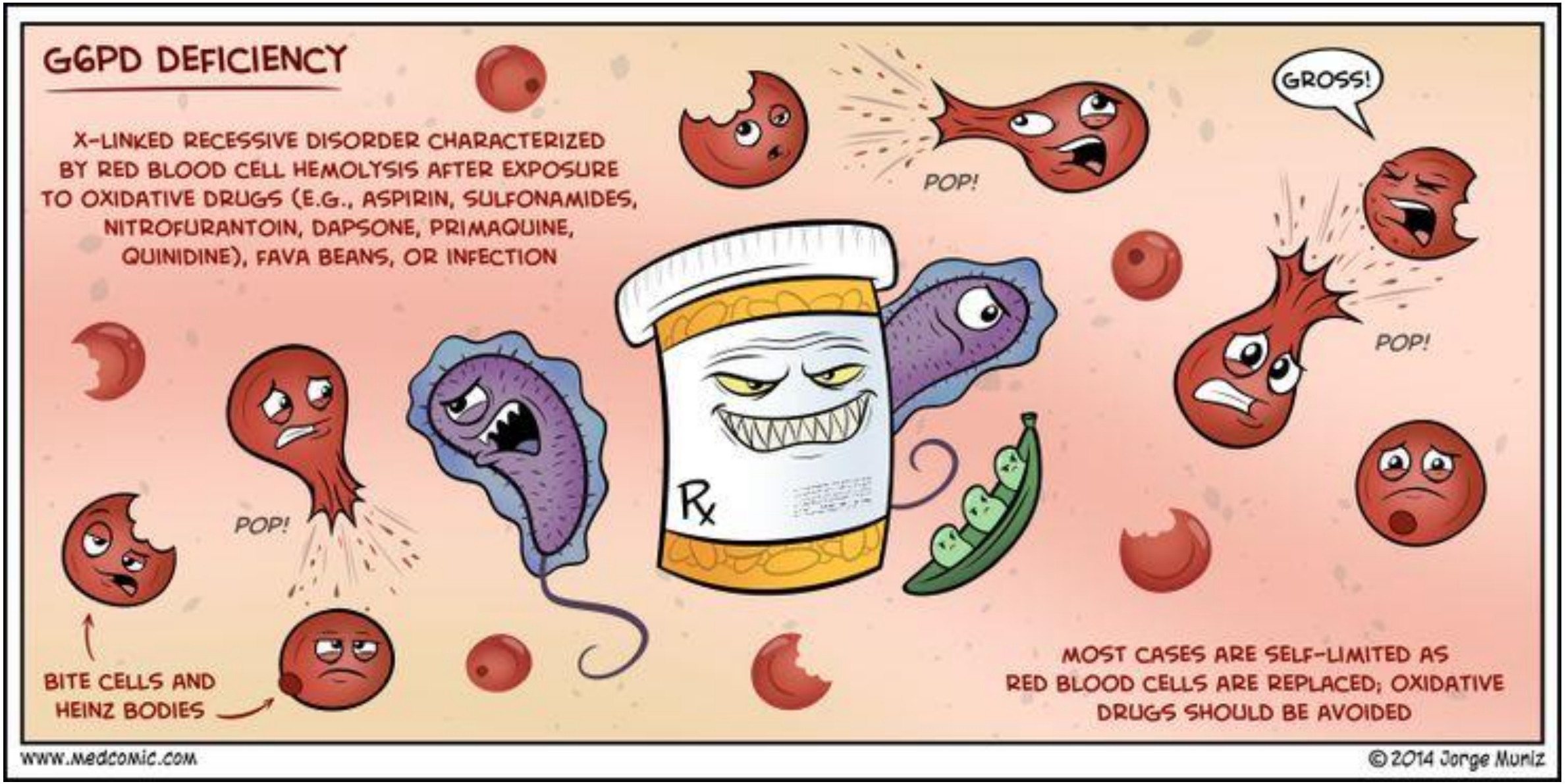


Limitations of the IX

- Young red cell contain a higher enzyme level
- During acute haemolysis- Increased young cells
- False normal results in enzyme assays and Brewers test

Management

- Straightfarward …
  - Stop the offending drug
  - Avoid fava beans, or any other oxidant stersses
  - Adequate intake of fluids
  - Treat infection with appropriate antibiotic
  - Blood transfusion if severe anemia
  - Phototherapy and exchange transfusion for neonatal jaundice
  - Folic acid supplementation


G6PD DEFICIENCY
X-LINKED RECESSIVE DISORDER CHARACTERIZED BY RED BLOOD CELL HEMOLYSIS AFTER EXPOSURE TO OXIDATIVE DRUGS (E.G., ASPIRIN, SULFONAMIDES, NITROFURANTOIN, DAPSONE, PRIMAQUINE, QUINIDINE), FAVA BEANS, OR INFECTION
POP!
GROSS!
POP!
POP!
Rx
BITE CELLS AND HEINZ BODIES
MOST CASES ARE SELF-LIMITED AS RED BLOOD CELLS ARE REPLACED; OXIDATIVE DRUGS SHOULD BE AVOIDED
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Thank you