JSC “Astana Medical University”
Department of Internal Disease

IWS

Theme: Hemolytic anemia

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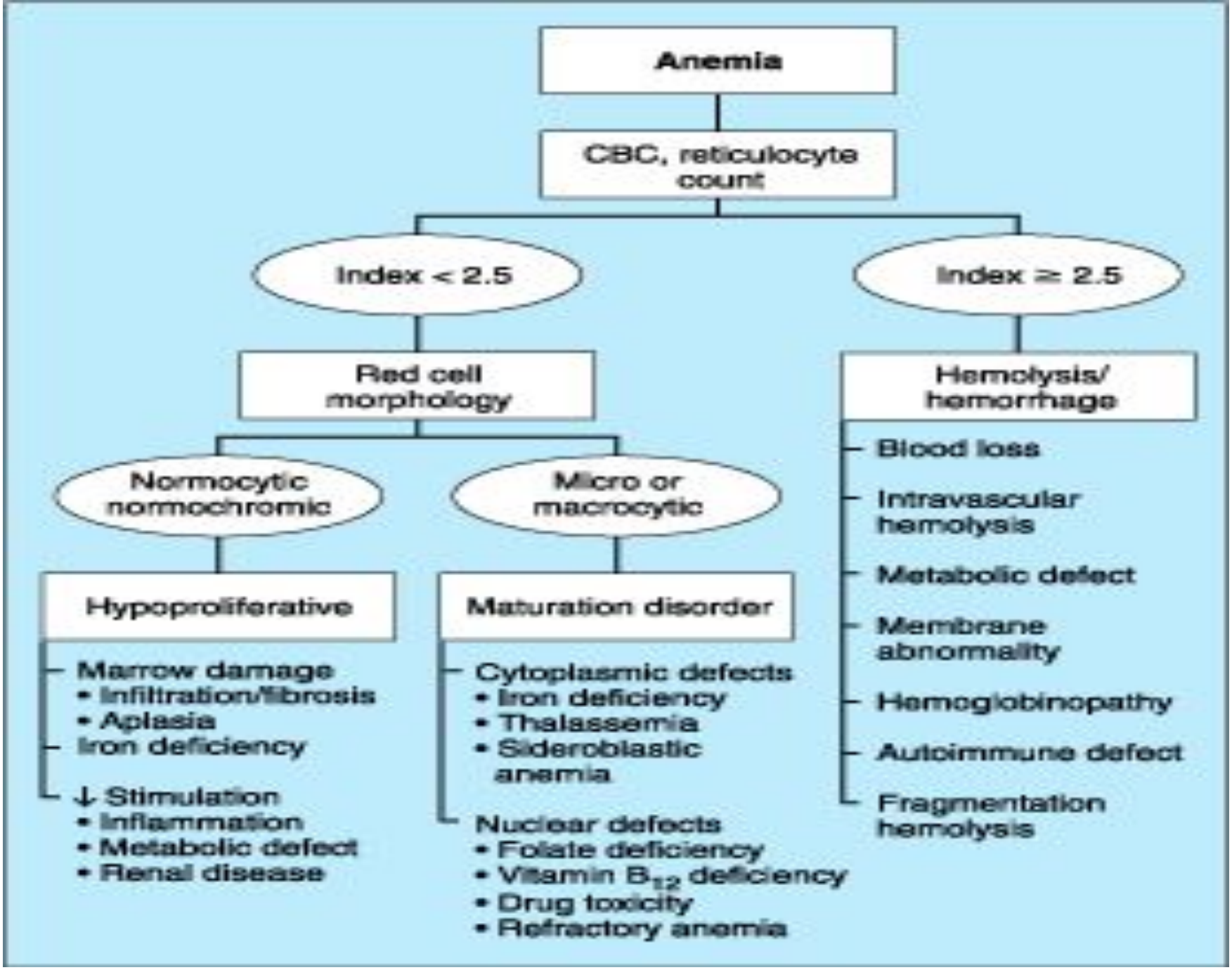
Astana 2018


Anemia
CBC, reticulocyte count
Index < 2.5
Index ≥ 2.5
Red cell morphology
Hemolysis/ hemorrhage
Normocytic normochromic
Micro or macrocytic
Hypoproliferative
Maturation disorder
Blood loss
Intravascular hemolysis
Metabolic defect
Membrane abnormality
Hemoglobinopathy
Autoimmune defect
Fragmentation hemolysis
Marrow damage
• Infiltration/fibrosis
• Aplasia
Iron deficiency
↓ Stimulation
• Inflammation
• Metabolic defect
• Renal disease
Cytoplasmic defects
• Iron deficiency
• Thalassemia
• Sideroblastic anemia
Nuclear defects
• Folate deficiency
• Vitamin B_{12} deficiency
• Drug toxicity
• Refractory anemia

Hemolytic Anemia

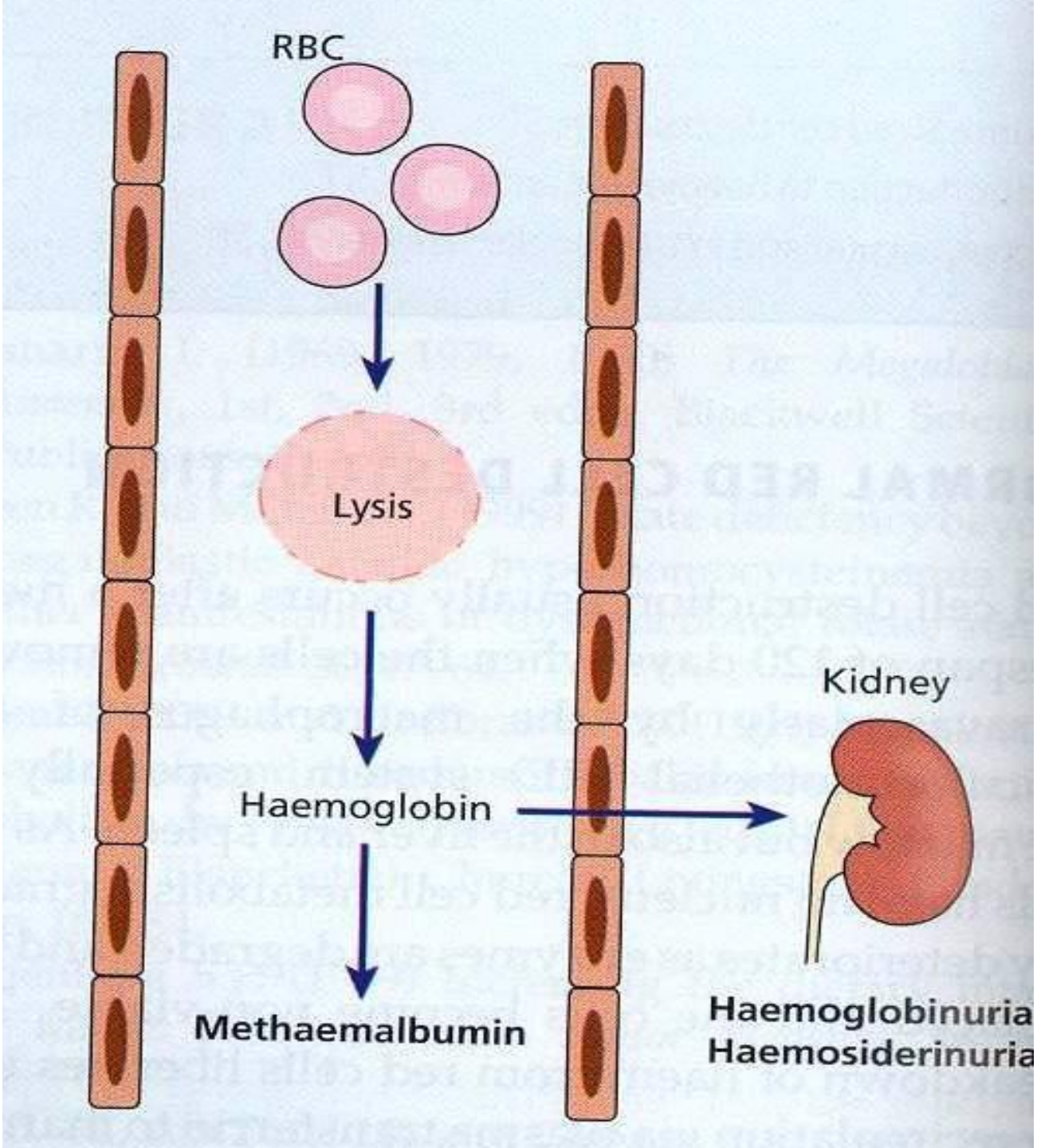
- Definition:
  - Those anemias which result from an increase in RBC destruction

- Classification:
  - Congenital / Hereditary
  - Acquired

Classification of Hemolytic Anemias

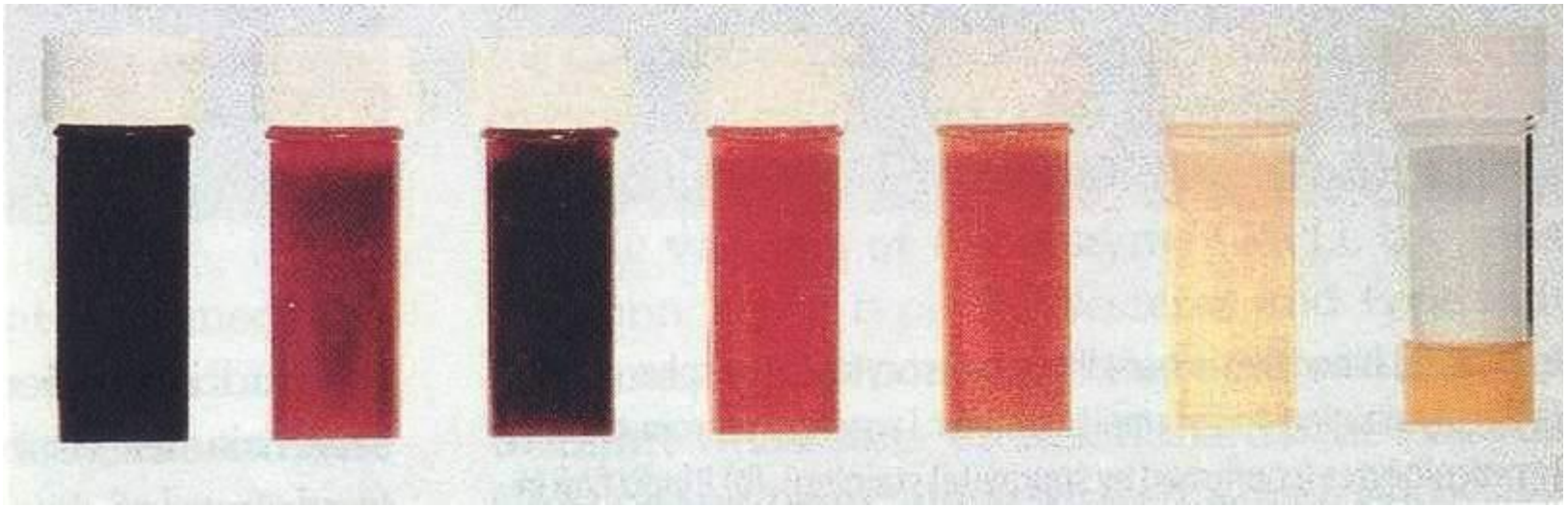
Hereditary	1. Abnormalities of RBC interior a.Enzyme defects: G-6-PD def,PK def b.Hemoglobinopathies 2. RBC membrane abnormalities a. Hereditary spherocytosis etc. b. PNH
Acquired	c. Spur cell anemia 3. Extrinsic factors a. Hypersplenism b. Antibody: immune hemolysis c. Mechanical trauma: MAHA d. Infections, toxins, etc

Ref : Harrison's


RBC
Lysis
Haemoglobin
Methaemalbumin
Kidney
Haemoglobinuria
Haemosiderinuria

Laboratory Evaluation of Hemolysis

	Extravascular	Intravascular
HEMATOLOGIC		
Routine blood film	Polychromatophilia	Polychromatophilia
Reticulocyte count	↑	↑
Bone marrow examination	Erythroid hyperplasia	Erythroid hyperplasia
PLASMA OR SERUM		
Bilirubin	Unconjugated	Unconjugated
Haptoglobin	↓, Absent	Absent
Plasma hemoglobin	N/ ↑	↑↑
Lactate dehydrogenase	(Variable)	↑↑ (Variable)
URINE		
Bilirubin	0	0
Hemosiderin	0	+
Hemoglobin	0	+ □severe cases



Hemoglobinuria

Features of HEMOLYSIS

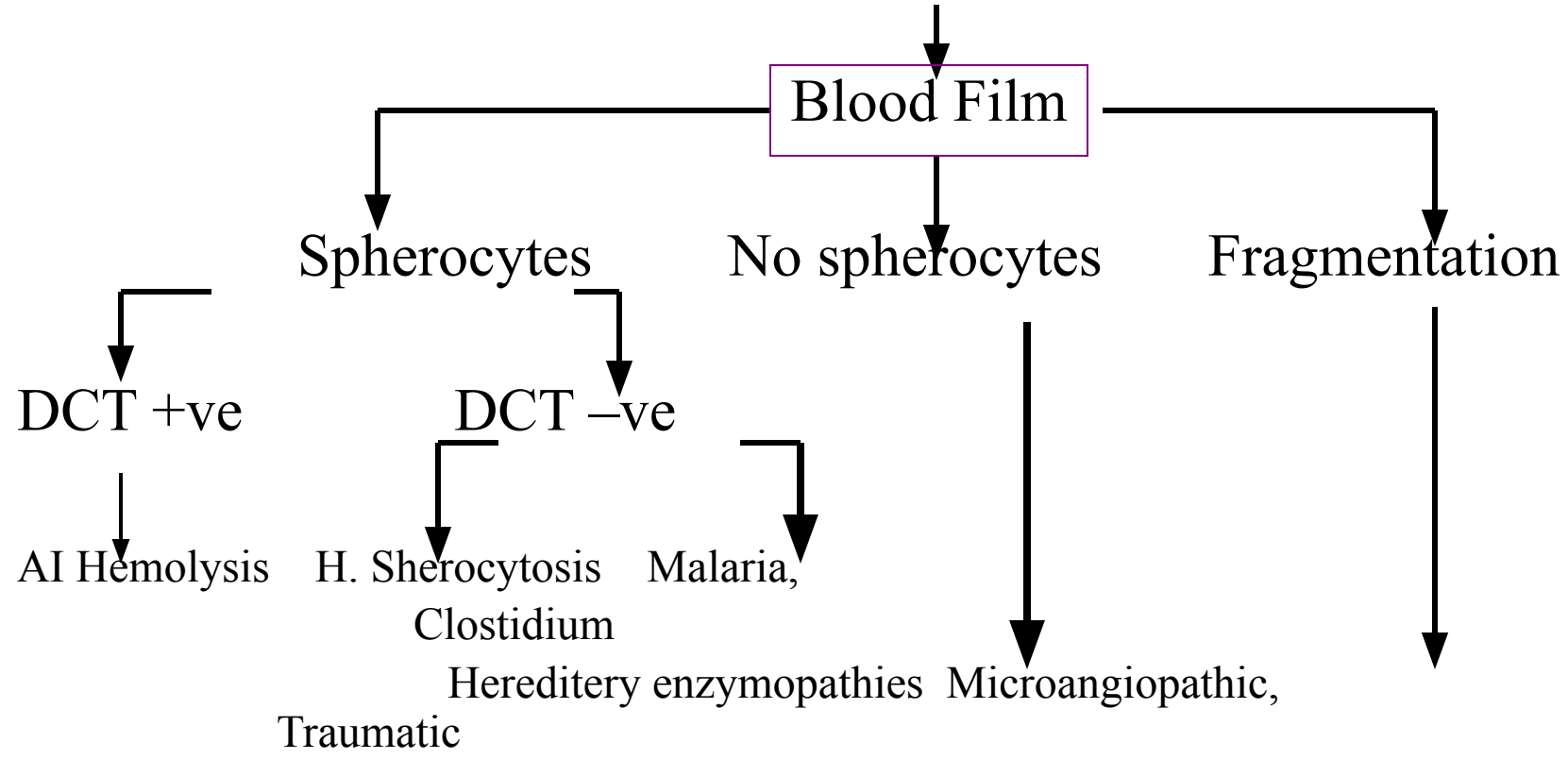
↑ Bilirubin

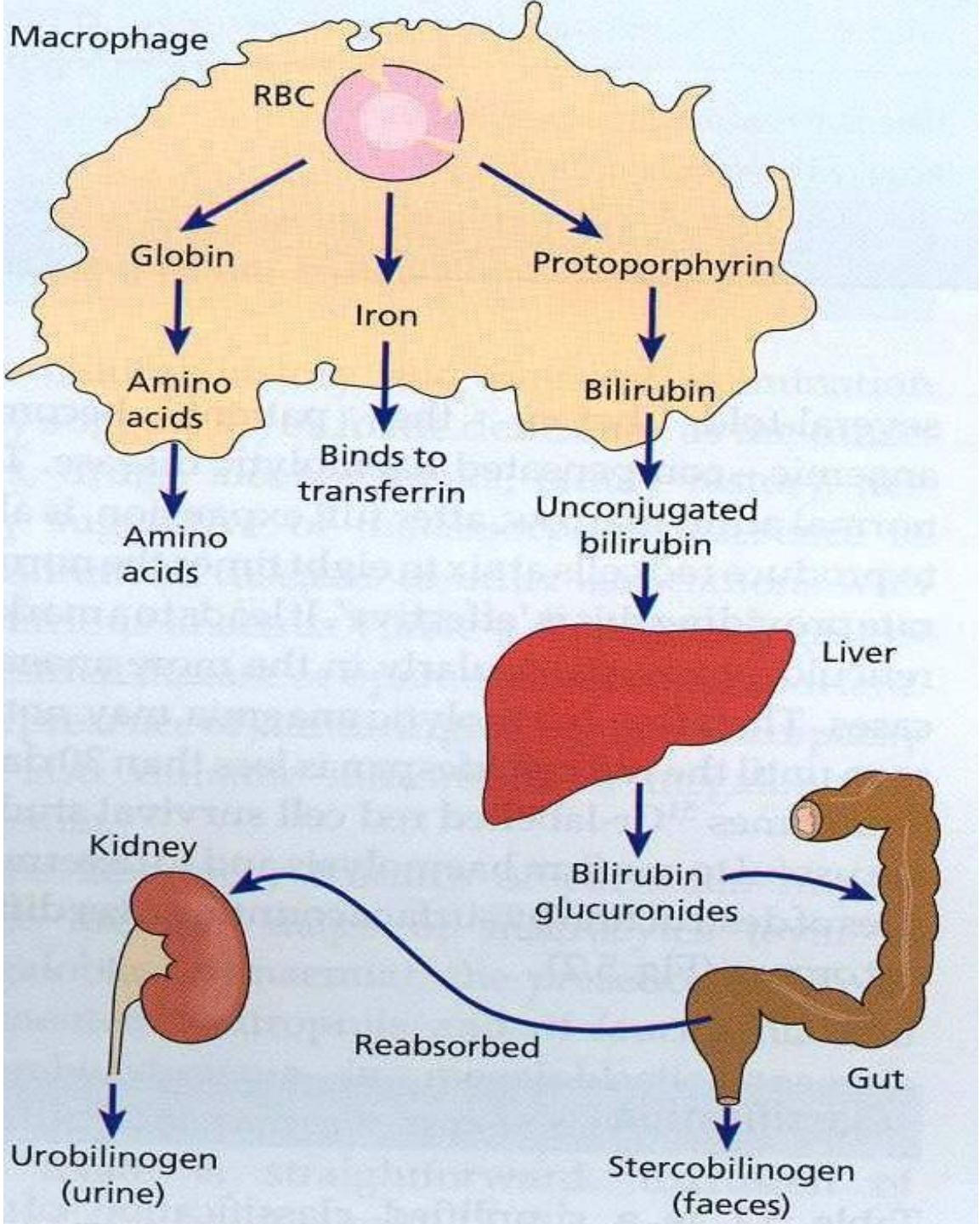
↑ LDH

↑ Reticulocytes, n-RBC

↓ Haptoglobulins

+ve Urinary hemosiderin, Urobilinogen

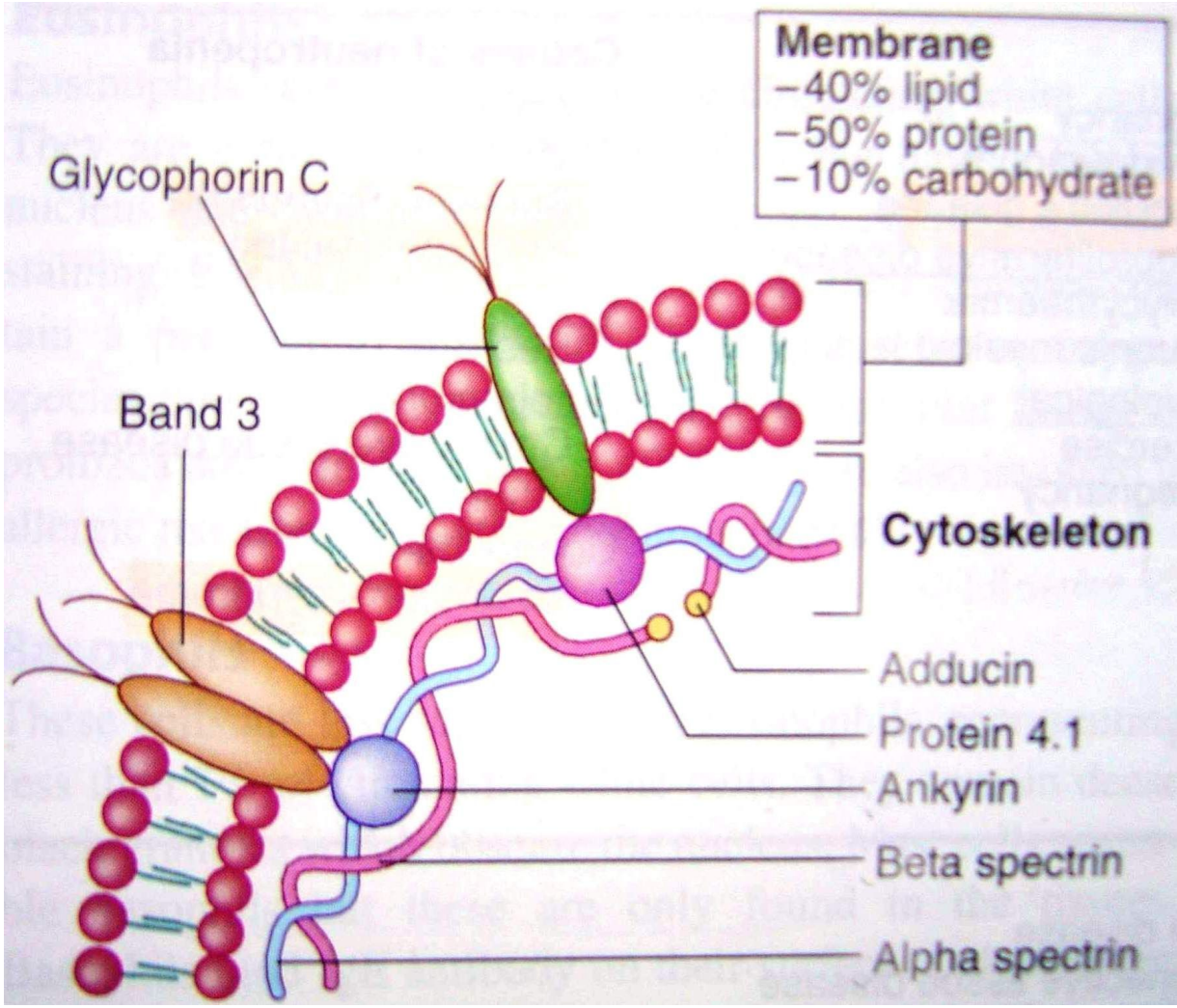



Macrophage
RBC
Globin
Iron
Protoporphyrin
Amino acids
Binds to transferrin
Bilirubin
Amino acids
Unconjugated bilirubin
Liver
Kidney
Bilirubin glucuronides
Reabsorbed
Gut
Urobilinogen (urine)
Stercobilinogen (faeces)

Red Cell Membrane Defects

1.Hereditary Spherocytosis

- Usually inherited as AD disorder
- Defect: Deficiency of Beta Spectrin or Ankyrin Loss of membrane in Spleen & RES becomes more spherical Destruction in Spleen



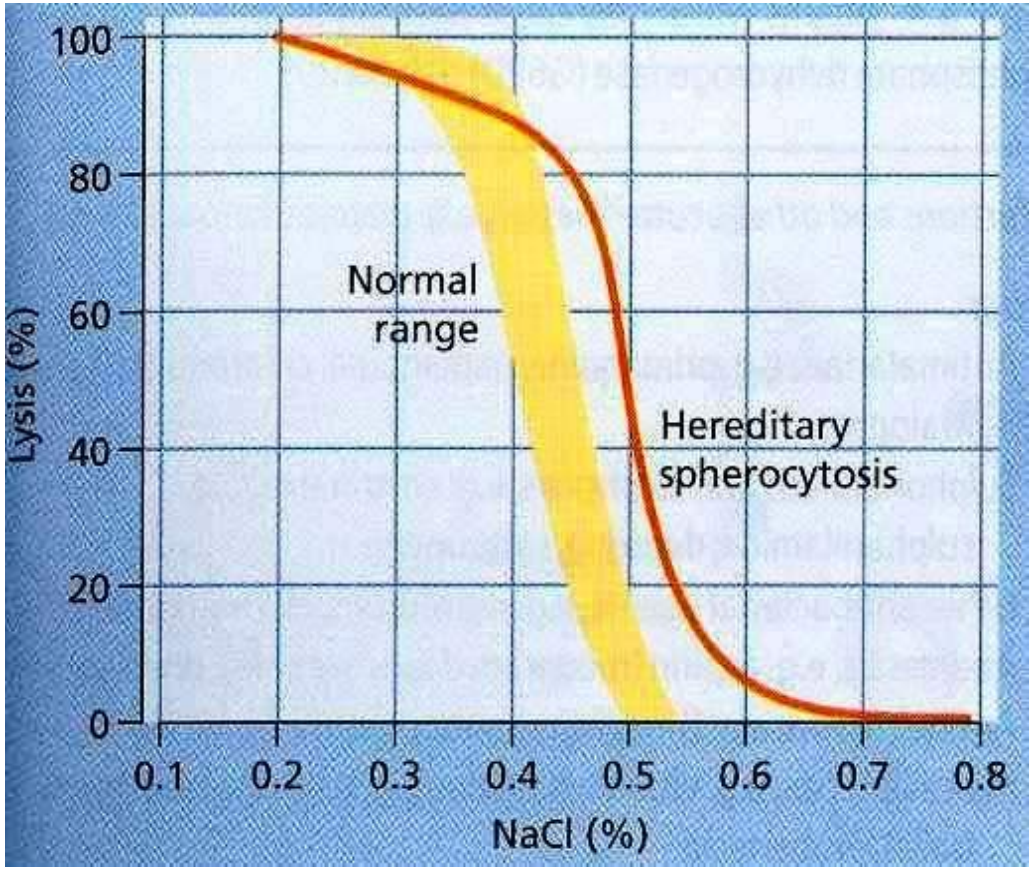
C/F:

- Asymptomatic
- Fluctuating hemolysis
- Splenomegaly
- Pigmented gall stones- 50%

Clinical course may be complicated with Crisis:

- *Hemolytic Crisis*: associated with infection
- *Aplastic crisis:* associated with Parvovirus infection

- Inv:
  - Test will confirm Hemolysis
  - P Smear: Spherocytes
  - Osmotic Fragility: Increased



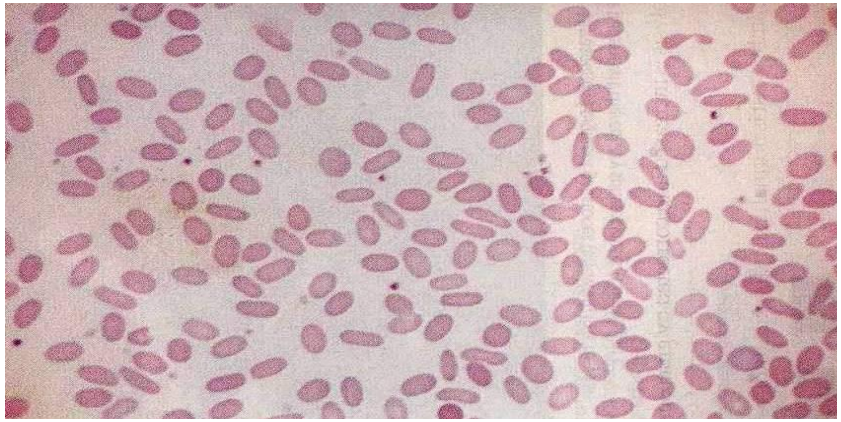
Osmotic Fragility

2.Hereditary Elliptocytosis

- Equatorial Africa, SE Asia
- AD / AR
- Functional abnormality in one or more anchor proteins in RBC membrane- Alpha spectrin , Protein 4.1
- Usually asymptomatic
- Mx: Similar to H. spherocytosis
- Variant:

  3.SE-Asian ovalocytosis:

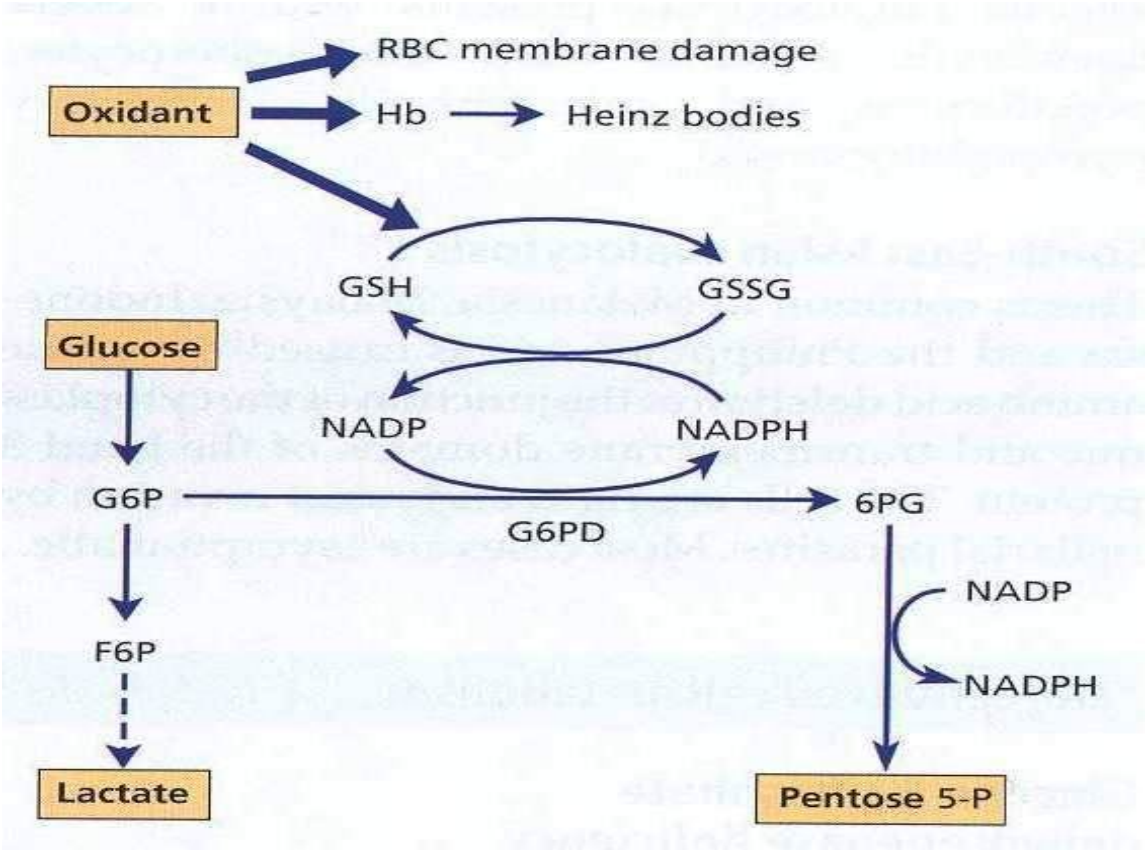
  - Common in Malaysia , Indonesia…
  - Asymptomatic-usually
  - Cells oval , rigid ,resist invasion by malarial parasites



Elliptocytosis

1. Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency

- Pivotal enzyme in HMP Shunt & produces NADPH to protect RBC against oxidative stress
- Most common enzymopathy -10% world's population
- Protection against Malaria
- X-linked



- Clinical Features:
  - Acute drug induced hemolysis:
    - Aspirin, primaquine, quinine, chloroquine, dapsone….
  - Chronic compensated hemolysis
  - Infection/acute illness
  - Neonatal jaundice
  - Favism

- Inv:
  - e/o non-spherocytic intravascular hemolyis
  - P. Smear: Bite cells, blister cells, irregular small cells, Heinz bodies, polychromasia
  - G-6-PD level

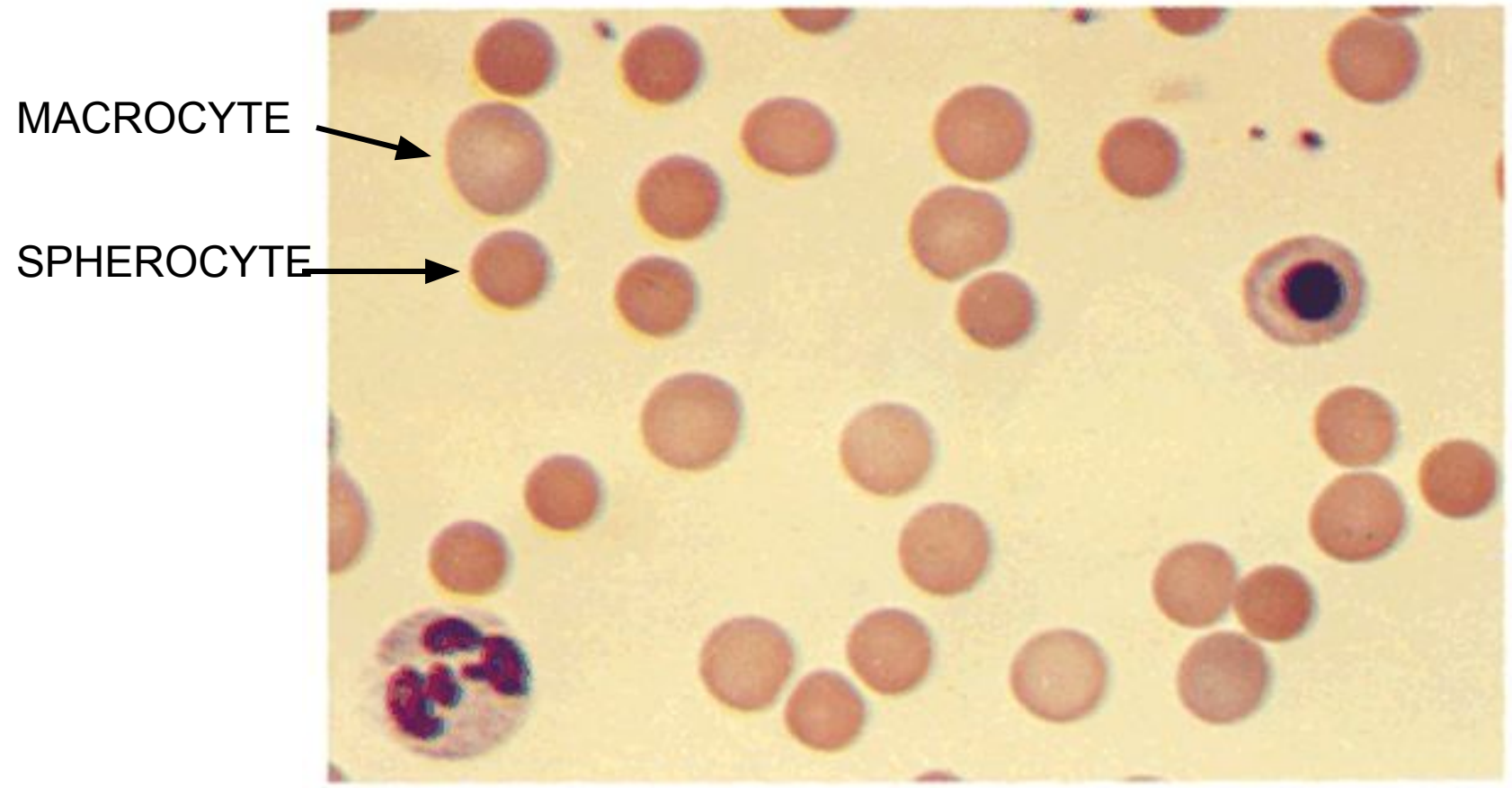
- Treatment:
  - Stop the precipitating drug or treat the infection
  - Acute transfusions if required

Autoimmune Hemolytic Anemia

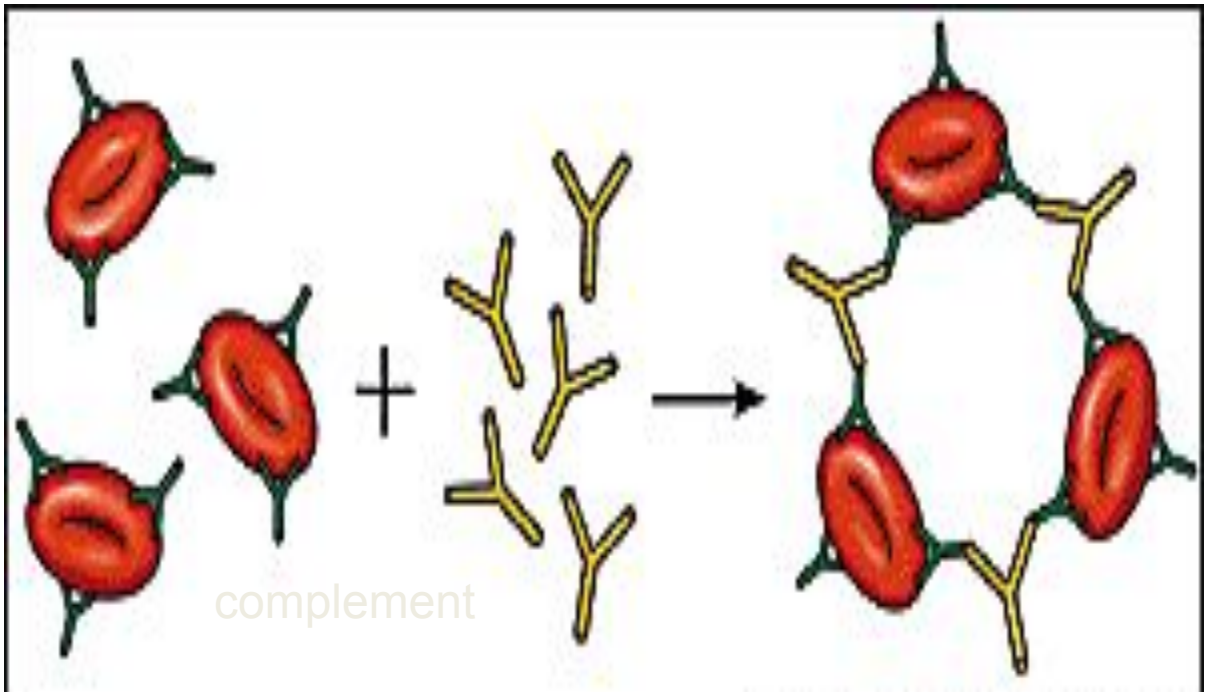
- Result from RBC destruction due to RBC autoantibodies: Ig G, M, E, A
- Most commonly-idiopathic
- Classification
  - Warm AI hemolysis:Ab binds at 37degree Celsius
  - Cold AI Hemolysis: Ab binds at 4 degree Celsius

1.Warm AI Hemolysis:

- Can occurs at all age groups
- F > M
- Causes:
  - 50% Idiopathic
  - Rest - secondary causes:
    1. Lymphoid neoplasm: CLL, Lymphoma, Myeloma
    2. Solid Tumors: Lung, Colon, Kidney, Ovary, Thymoma
    3. CTD: SLE,RA
    4. Drugs: Alpha methyl DOPA, Penicillin , Quinine, Chloroquine
    5. Misc: UC, HIV



IMMUNOHEMOLYTIC ANEMIA



Direct antiglobulin test

demonstrating the presence of autoantibodies (shown here) or complement on the surface of the red blood cell.

- Inv:
  - e/o hemolysis, MCV
  - P Smear: Microspherocytosis, n-RBC
  - Confirmation: Coomb's Test / Antiglobulin test

- Treatment
  - Correct the underlying cause
  - Prednisolone 1mg/kg po until Hb reaches 10mg/dl then taper slowly and stop
  - Transfusion: for life threatening problems
  - If no response to steroids Spleenectomy or,
  - Immunosuppressive: Azathioprine, Cyclophosphamide

2. Cold AI Hemolysis

- Usually Ig M
- Acute or Chronic form
- Chronic:
  - C/F:
    - Elderly patients
    - Cold , painful & often blue fingers, toes, ears, or nose (Acrocyanosis)

- Inv:
  - e/o hemolysis
  - P Smear: Microspherocytosis
  - Ig M with specificity to I or I Ag

Non-Immune Acquired Hemolytic Anemia

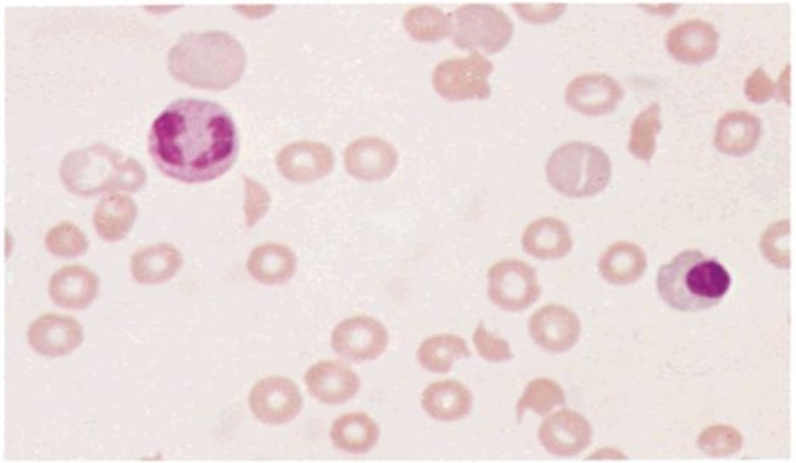
1. Mechanical Trauma

A). Mechanical heart valves, Arterial grafts: cause shear stress damage

B).March hemoglobinuria: Red cell damage in capillaries of feet

C). Thermal injury: burns

D). Microangiopathic hemolytic anemia *(MAHA):* by passage of RBC through fibrin strands deposited in small vessels disruption of RBC
eg: DIC,PIH, Malignant HTN,TTP,HUS



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