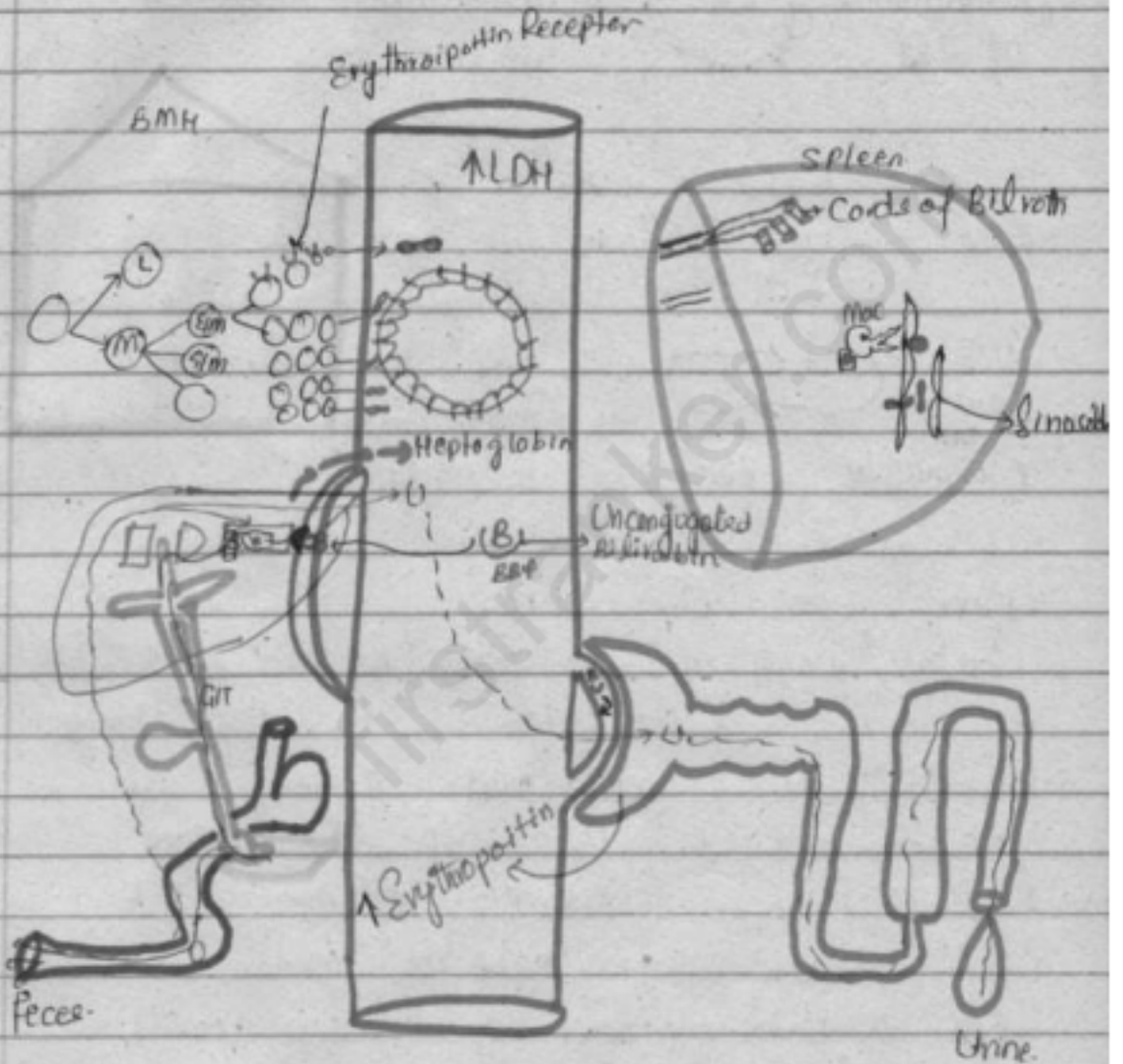
HEMOLYTIC ANEMIA



① Evidences of Hemolysis

Jaundice → (UCHB)
↑Urobilinogen → Urine
Dark Stool
↑LDH
Iod free Heptoglobin

② Accelerated Erythropoiesis

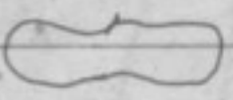
- Reticulocytosis
- Slight Macrocytosis
- polychromasia
- Hyper cellular BM

Cytoskeleton of RBC 

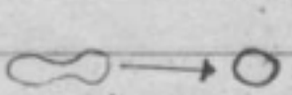
Most Imp Protein among them are Spectrin & enkaline

It can hold the Membrane of RBC with Substance of RBC

enlarged Surface (Membr) helps in Transfer Capacity along Membrane

Side view 

Normally RBC is flexible but when it undergo repated injury in Circulation it become stiff Now when such RBC pass through Circulation it never change its shape b/c old protein are degenerated So when RBC pass through such Narrow opening it will stuck & leave a piece of RBC Membrane & move further Now RBC become globular / Spherical



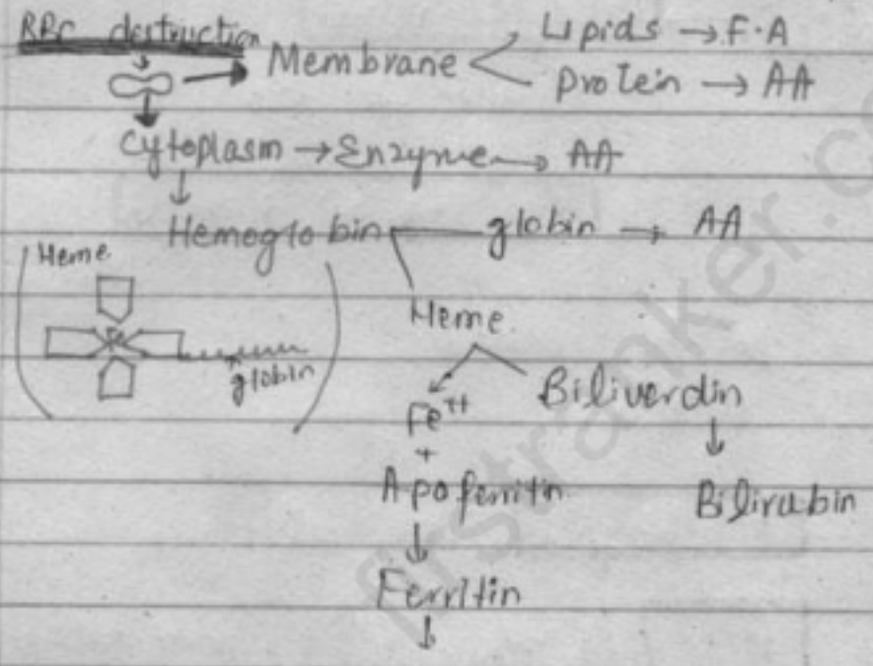
Na will retain in cell along with Na H2O will also retain

So RBC swell up

Normaly blood enters into Spleen whenever old RBC is stuck to Cords of Billroth there are Macrophages in it is walls

Mac → phagocytosed such RBC.
& new RBC will easily pass through slits.

what happens to RBC in Mac of Spleen



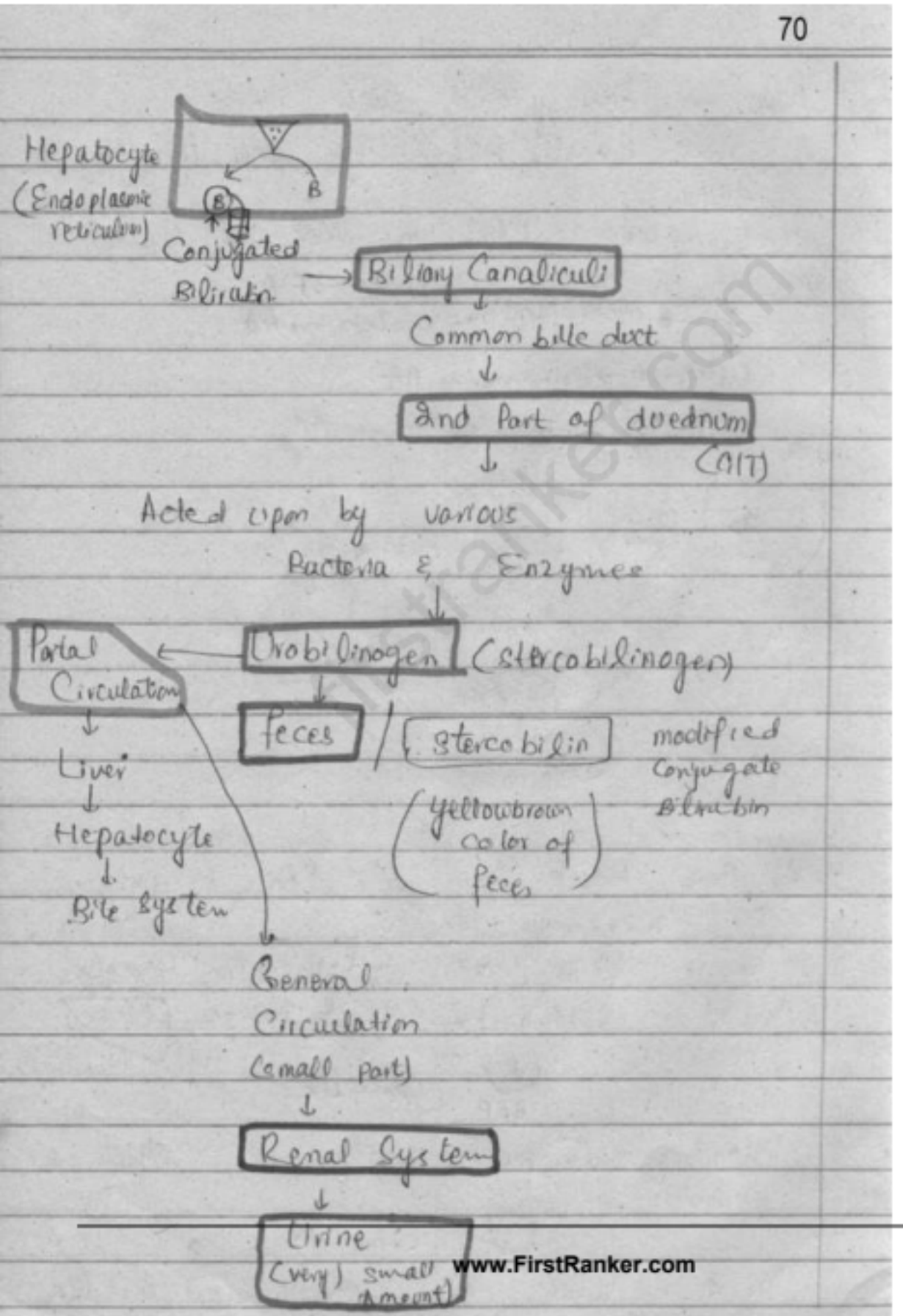
As this break down of RBC occurs in Macrophage.
this is known as Extravascular Hemolysis
Bilirubin → blood ← Bilirubin Binding PR ← Liver

(B) BBP] Complex

Hepatocyte Express another PR which binds

(B) BBP] Complex

& this will be Internalized into liver

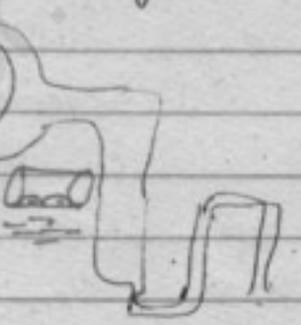


Hemolytic Anemia

Break down of RBC prematurely
(If break down occurs after 120 days it is physiological break down)

↑ Hemolysis → ↓ed. Hb → ↓ O_2 Sopply to
↑ Erythropoitin ← Renal System

Erythropoitin is secreted by Endothelial cells of peritubular Capillaries



Erythropoitin → Blood
↓
B.M. House
↓
Erythro blast & Pro Erythro blast have Receptor for Erythropoitin
↓
Erythropoitin binds with Receptor
↓
Erythropoitin ⊖ Apoptosis
↓
Cells Survive for more time & form more RBC

① Erythropoitin → keeps H_2O → BM → Red & hypercellular.
ie Erythroid Hyperplasia

So Large No of RBC enters into Circulation B.M ↑es its hemopoetic activity 8-10 times
If large No of RBC are hemolysed but body respond by ↑ing the formation of RBC we have should say that pt have

Compensatory Hemolytic disease

e.g
Life of RBC = 20 days
& Hemolysis rate = 120/20 = 6 times destruction

- If Rate of Hemolysis become so much that Compensatory mech fail
  Hb & RBC ↓es So we say pt have

Hemolytic Anemia.

- If eg pt have 1/2 life of RBC = 30
  i.e $\frac{120}{4} = 30$

Hemolysis Rate is 4 times
but If due to any reason B.M will Compensate only for 2times then still there is
Hemolytic Anemia

- ↑ed Hemolytic Anemia → ↑ level of Unconjugated Bilirubin

we Say

Unconjugated Hyperbilirubenemia

S/S

yellow discoloration of → skin, Sclera, mucous Membrane

This Condition is called

Hemolytic Jaundice

Usually this is Mild. b/c Normaly liver have Capacity to ↑es its Bilirubin ~~hemolytic~~ holding activity & more of B will be lost in feces.

So ↑B either in liver disease or some other causes.

Anemia → skin → Pale

Jaundice → " → yelloco.

Anemia + Jaundice → " → Lemon yellow

↑B → ↑ Conjugated Bilirubin → ↑ Stercobilin in feces → Dark color of Feces

↑ed abs → ↑ excretion in Urine

As Unconjugated B. Bilirubin is v. large 9t does not appears in urine such a Jaundice In which Bilirubin does not appear in Urine is called Acholuric Jaundice

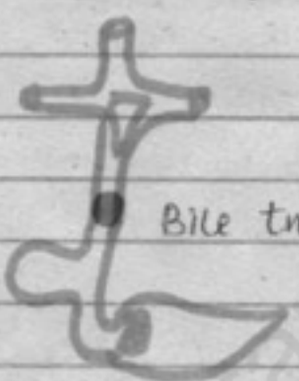
① There is hemolysis ?
- Jaundice
- ↑Urobilinogen
- Dark Stool
- ↑LDH

- If due to any obstruction in Biliary tree then conjugated Bilirubin will enters into blood

Conjugated Bilirubenemia

This Conjugated Bilirubin → Enters into Urine → Choluric Jaundice

So No Urobilinogen form → feces will be Light Color



Obstructive Jaundice

Along with Conjugated Bilirubin Bile acid also fall back into Circulation
Go into Skin → ⊕ Mast cell → Produce Itching

- RBC destruction → ↑LDH level in blood
- Liver → Heptoglobin in blood (free Hb binding Pr)

If RBC hemolysis occurs in Blood → (Hb) → Taken up by Liver cells Macrophages

Cause No tissue destruction

Heptoglobin → Slightly ↓ → Extravascular Hemolysis

① Accelerated Erythropoiesis ? (Compensatory mech)
(Fresh RBC → Reticulocyte)

Reticulocyte

Larger Size
Stained blue color
(due to presence of Still Ribosome & RNA)

Mature RBC

Smaller Size
Stained Red color

• In Normal Person RBC enters into Circulation 1-2% are Reticulocyte.

① So there is Reticulocytosis

② MCV → ↑
Slightly Macrocytic

③ Polychromasia

④ BM Biopsy → BM → hypercellular

⑤ Hemolysis < Extravascular / Intravascular ?

Extravascular
• Splenomegaly

Intravascular
• ↓ Haptoglobin
• Hemoglobinemia
• Methemalbumin (oxidized Hb in blood)
• Hemoglobinuria

Hb dimers in blood → Renal System
↓
Taken up by P.C.T cells (endocytosis)
↓
Break down to Iron
↓
destruction of P.C.T
↓
Acute Tubular Necrosis ATN
+
Heamoglobinuria

④ Hemolysis is Acute or Chronic ?

Acute	Chronic
• Free Hb in Urine	• Gall stone. Hemosiderinurea

↑ed Extravas Hemolysis Chronic ↑U.Bilirubin in blood
↓
↑ed Conjugated B in liver
↓
↑ed Bile Stone / Gall Stone formation

↑ed Intravas Hemolysis Chronic
small Hb taken by P.C.T (Renal Sys)
↓
Converted to Ferritin
Hemosidrin

Hemosidrin containing cells → Urine
↓
Prussian blue Staining
↓
Hemosiderinuria ← Shows Hemosiderin (blue stained granules)

Classification of H. Anemia

- Intrinsic H.A or Intra corposcular H.A
- Extrinsic H.A or Extracorpuscular H.A

Intrinsic H.A

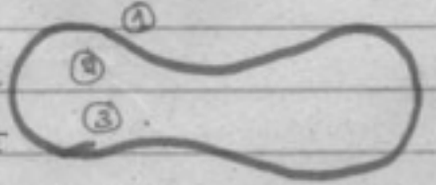
Hemolysis occurs due to defective RBC

Causes

① Inherited ② Acquired

→ Membrane defect

→ Enzyme defect

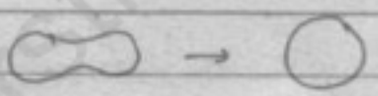


→ Hb Synthesis defect

Membrane defect:-

As RBC passes through Arterial Sys it is under excessive stress some of Microcirculation have small diameter

e.g Cords of Billroth in Spleen have a diameter just 2 µm.
So when RBC passes through such Membrane RBC undergo twisting.
Biconcave shape of RBC is due to Extra membrane on RBC so that gas exchange can be done this is Extramembrane also helps in Twist, torn & fold.
If Membane is lost RBC shape also decreased changed but Cytoplasm remains same.



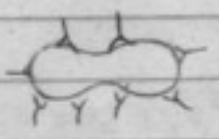
Normaly when RBC passes through Narrow Circulation some of its Membrane is shed this can be prevented by Spectrin & Actin which bind inside of RBC with Lipid bilayer Membrane & prevents its shedding.

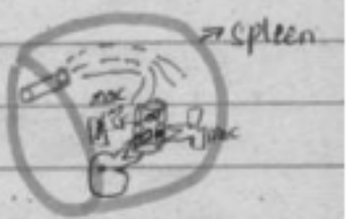
If Mutation occurs in genes of Cytoskeleton.
Then this stability will be lost when such RBC passes through Circulation Membrane will be lost but Cytoplasm remains intact

Such diseases are called
Hereditary spherocytosis
bc Such altered RBC will be stuck in Circulation (cap) & will undergo Hemolysis.
(they mostly have defective Vertical Pr)
Some times problem is in horizontal pr RBC shape changes to elliptical

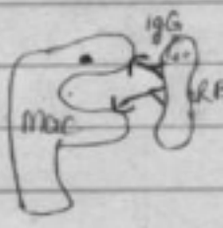
Hereditary Elliptocytosis

Spherocytosis also occures in





- Immune Mediated Hemolytic Anemia
- Spherocytosis also caused by Snake Venome



- Spherocytosis → also occurs in Clostridial Infection.

[Acquired] (Membrane defect)

Paroxysmal Nocturnal Heamoglobinuria

This is due to Mutation in gene → that form special Cuttle on surface of RBC (WBC, platelets) → that

cuts the Complent System. So Complement Sys will attack on these cells & cause dysfraction).
Later on we find that most of those pt have problem which is not Paroxysmal they also have problem at day time not only at Night & there is not only Heamoglobinuria but also Neutroperia & Thrombocytopenia

Enzyme defect

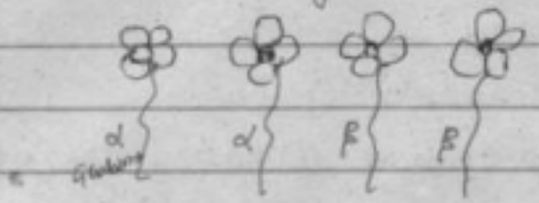
- Glycolysis
  - Hexokinase
  - Pyruvate kinase
- H.M.P. Shunt
  - G6P dehydrogenase
  - Glutathione Synthase

Glucose
Hexokinase →
G6P dehydrogenase
G-6-P → [HMP]
NADPH
Pyruvate
Lactate

NADPH → GS → $2H_2O$
NADH ← GSH ← H_2O_2

attack RBC Membrane
H_2O_2
Oxidative Crisis
→ Infection
→ Drugs
→ Fava bean

Hb Synthesis defect



Globin chain Syn defect
- Quantitative (Thalagemia)
- Qualitative (Hemoglobinopathies)

Thalasemia:

Are Heterogenous group of defect in which there is defective globin chain Synthesis

α Globin chain not produced = α Thalasemia
β " " " " = β "

Extrinsic H-Anemia

- Immune Mediated Hemolysis
  - Iso Antibodies
    - ABO Incompatibility
    - RH "
  - Auto Antibodies
    - Idiopathic
    - Infection
    - Malagnancies
    - Drugs
- Non Immune Mediated Hemolysis

ABO Incompatibility

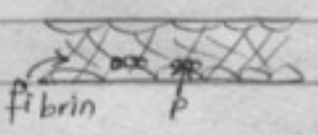
It is the donor RBC that is destroyed in recipient body but recipient RBC are not destroyed b/c donor Antibodies are diluted in recipient blood

Non Immune Mediated

Mechanical Cause

→ Cardiac Mechenical valve

→ DIC (wide spread damage → Vas Endo + platelate adh + fibrin accumulation



→ Thrombotic Thrombocytopenic purpura

Endo damage
↓
Platelate
Accumulation
↓
Ved platelate

→ March Hemoglobinuria
(In soldiers during March there foot touches with hard sole RBC is chrushe dinCap → Hemoglobinuria)

→ Cratas

Infection

e.g Malaria

Clostridial Infection

Chemical Injury

Lead

Splenic Sequestration

(Splenomegaly)

Infection Malegnancies Portal HTN