CASE HISTORY

- A 14 years old boy was admitted to hospital complaining of dysuria, frequency and a suprapubic pain. Urine test confirm UTI. The patient was treated by Trimethoprim oral tablets twice daily.
- Three days later the patient said that the urine was dark, and the following day it was almost black. He complained of weakness and abdominal and back pain. His sclerae were yellow. The treating doctor requested the following laboratory investigations on admission and 10 days later:

	On admission	10 days later	Normal range
Hb, g/dl	8.2	14.5	14 - 18
RBC $\times 10^{12}$/l	3.5	5	5
Retics, %	12	4	0.5 - 1.5
Bilirubin, mol/l	340	23	2 - 14
Red cell G6BD, units /g of Hb	normal	low	13 - 19

Lecture_6

G6PD & Spherocytosis

fourth year students

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Haemolytic anaemia

1.Inherited

a) Red cell membrane abnormality

- Hereditary spherocytosis
- Hereditary elliptocytosis

b) Haemoglobinopathy

Thalassemia, sickle-cell disease

c) Red cell enzyme deficiency

Pyruvate kinase deficiency, G6PD

2.Acquired

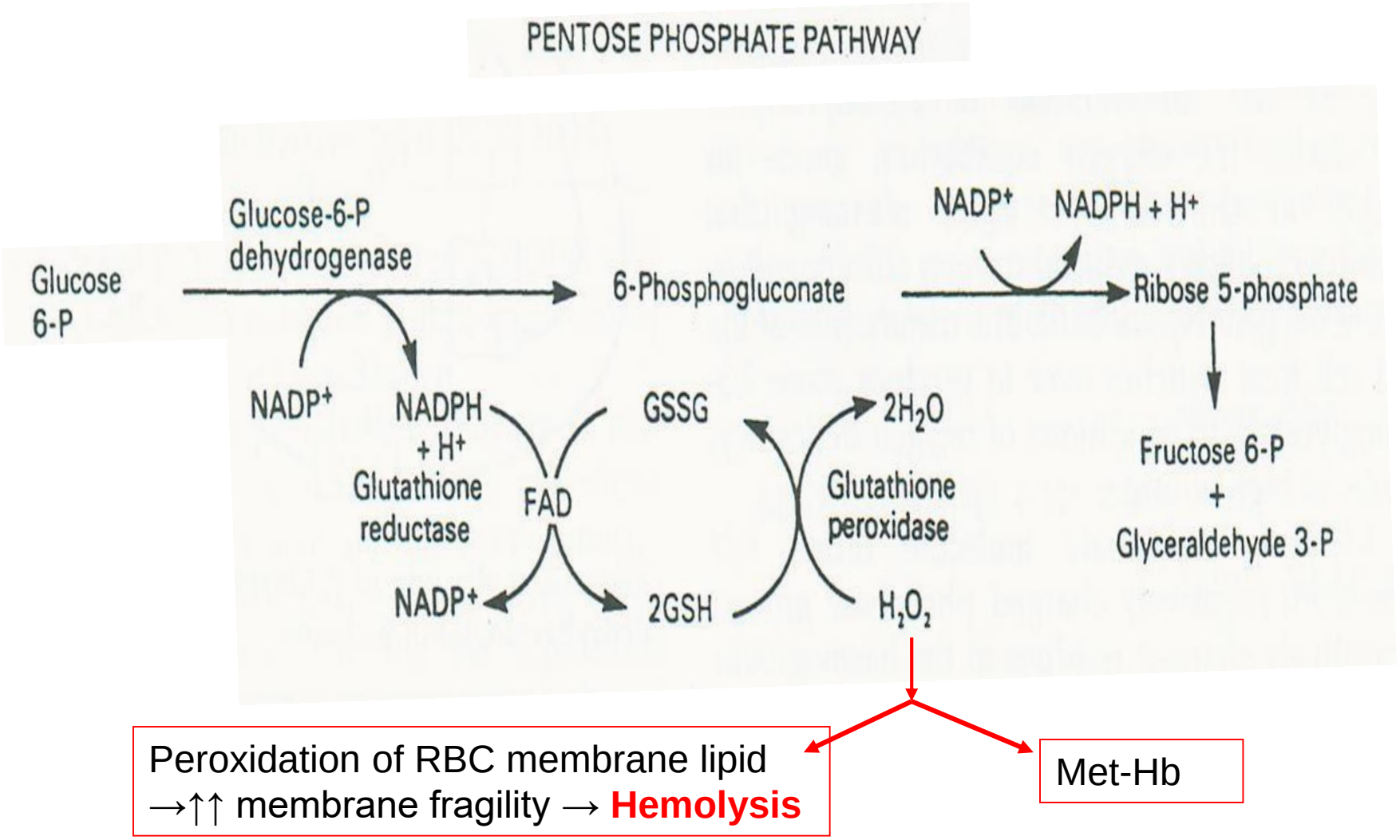
a) Immune

b) Non-immune

Hallmarks of hemolysis

- ↓ Hb
- ↑ Unconjugated bilirubin
- ↑ Lactate dehydrogenase **LDH**
- ↑ Reticulocytes
- ↑ Urinary urobilinogen


G6PD Deficiency



The function G6PD in the red cell is to generate NADPH → reduced glutathione → protect the RBCs from the oxidative damage by H_2O_2

Glucose-6-phosphate dehydrogenase deficiency

- Glucose-6-phosphate dehydrogenase enzyme-essential to counter oxidant stress to red blood cellsThe disorder is X-linked
- female are carrier and only affected if homozygous
- affecting 10% of the world's population
- G6PD deficiency does not cause any symptoms unless the patient exposed to oxidant stress causing rapid and often severe hemolysis and jaundice

Causes of hemolysis

- Acute drug-induced hemolysis to (e.g.):
  - Analgesics: aspirin, phenacetin
  - Antimalarials: primaquine, quinine, chloroquine, pyrimethamine
  - Antibiotics: sulphonamides, nitrofurantoin, ciprofloxacin
  - Miscellaneous: quinidine, probenecid, vitamin K, dapsone
- Infection or acute illness
- chemicals-naphthalene
- Favism, i.e. acute hemolysis after ingestion of broad beans

- Hemolysis begins 24 - 72 hours after exposure to oxidant stress

- When hemolysis is severe, patients present with weakness, tachycardia, jaundice, and hematuria

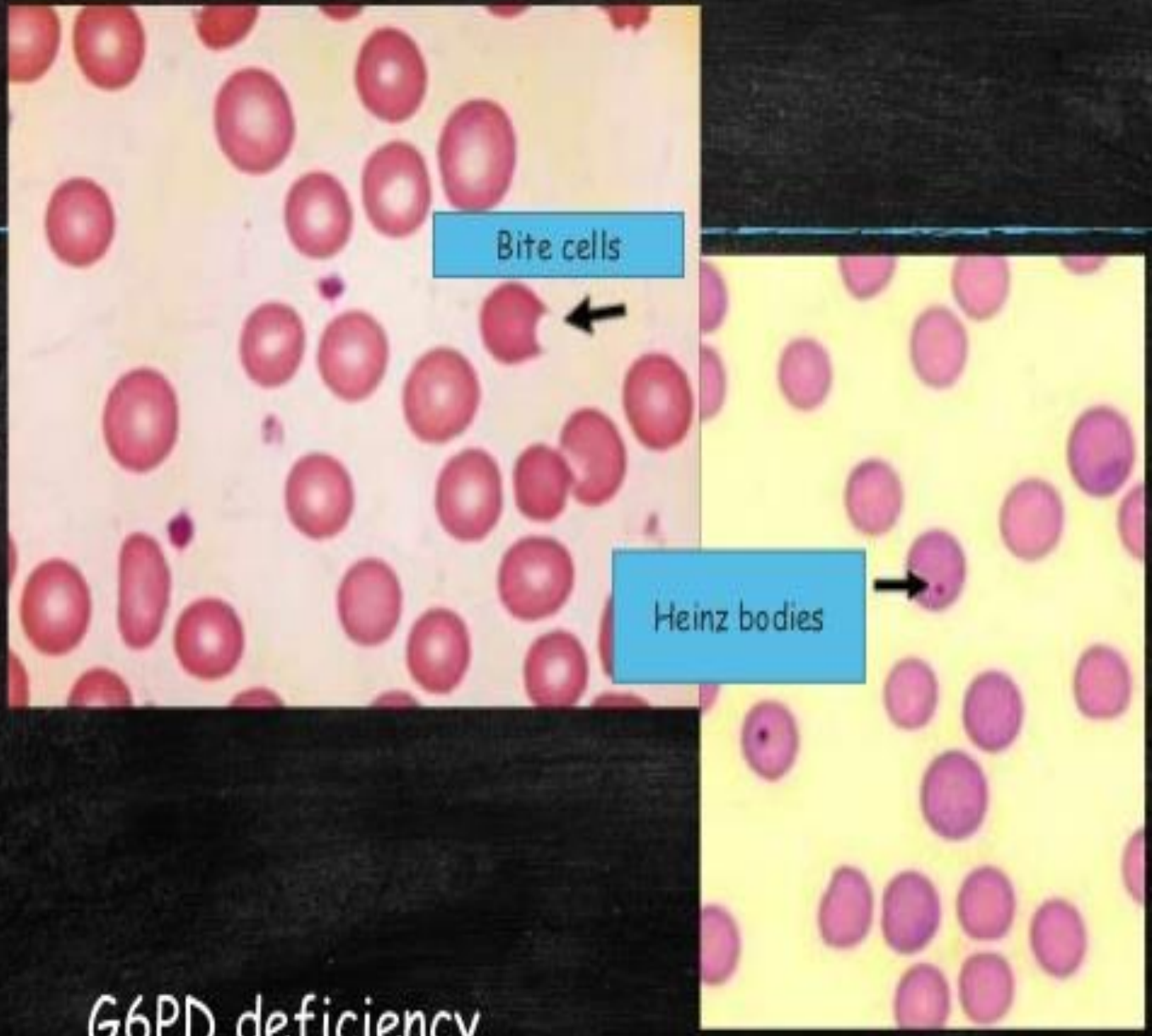
- Acute hemolysis is self-limiting, resolving after 8 -14 days

- Hemolytic episodes destroy aging RBCs that have the lowest levels of G6PD, New RBCs produced to compensate for anemia contain high levels of G6PD

- Young RBCs are not vulnerable to oxidative damage and so limit the duration of hemolysis

Laboratory features

- The blood film will show:
- **Bite cells** (red cells with a ‘bite’ of membrane missing)
- Irregularly shaped small cells
- Polychromasia reflecting the reticulocytosis
- Denatured Hb visible as **Heinz bodies** within the red cell cytoplasm with a methyl violet



G6PD deficiency

Management

- stop the intake of any precipitant drugs or foods
- treat any underlying infection
- Acute transfusion support may be life-saving in severe anemia
- Genetic Counseling- female carriers, male
- offspring, screen siblings/extended family, monitor neonates

Hereditary Spherocytosis:

- Most common hereditary hemolytic disorder (red cell membrane)
- Mutations of chromosome 8
- Defect in cytoskeletal proteins, spectrin
- Underestimate as mild forms not clinically significant
- Autosomal Dominant inheritance

Clinical features:

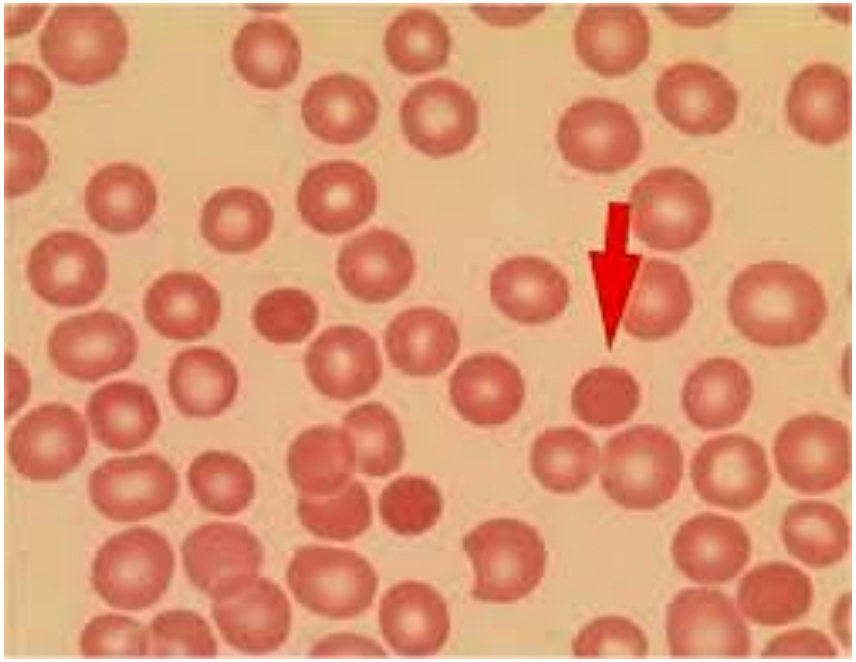
- Hemolytic anemia
- fatigue, jaundice, dark urine

The clinical course may be complicated by crises:

- **A haemolytic crisis** which can be severe, this is rare and usually associated with infection
- **A megaloblastic crisis** resulting from folate deficiency, or disease in pregnancy
- **An aplastic crisis** occurs in association with parvovirus (erythrovirus) infection

Investigations:

- Blood film
  - spherocytes, increased reticulocytes
- Elevated bilirubin, LDH
- Osmotic fragility
- Flow cytometry
- Gene tests not required



Treatment:

- Folic Acid supplementation
- Blood Transfusion as needed
- Splenectomy
  - indications: frequent transfusion, poor growth, massive splenomegaly with risk rupture
- Cholecystectomy
- Education and Genetic Counselling- genogram, likely inheritance and risk to future offspring

Hereditary elliptocytosis (ovalocytosis)

- is a rare autosomal dominant disorder
- RBCs are oval or elliptical
- Hemolysis is usually absent or slight, with little or no anemia
- splenomegaly is often present