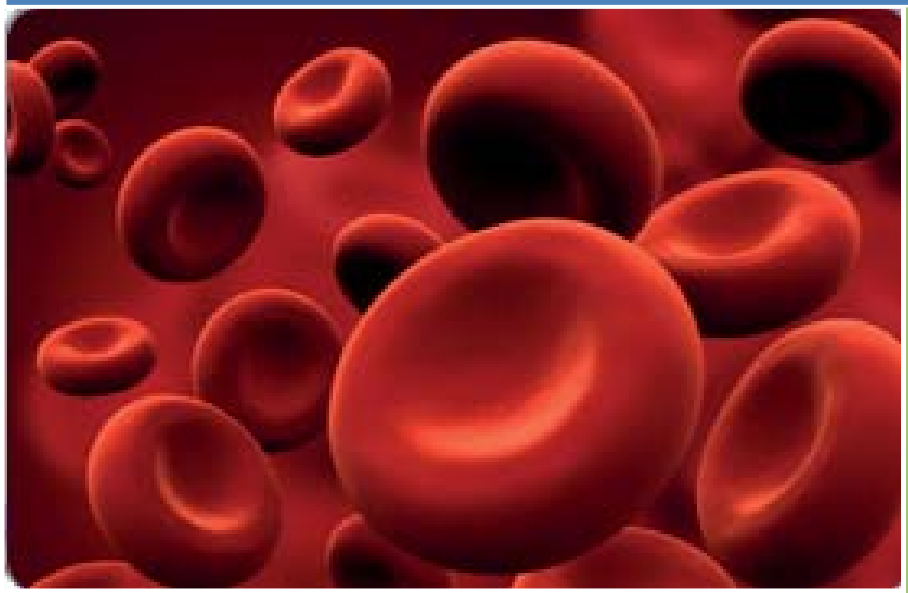
Medical Committee
The University of Jordan

Hematology

Biochemistry



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Slide #6

Dr.Nayef Karadsheh

Hematology

Prenatal Detection of HbS

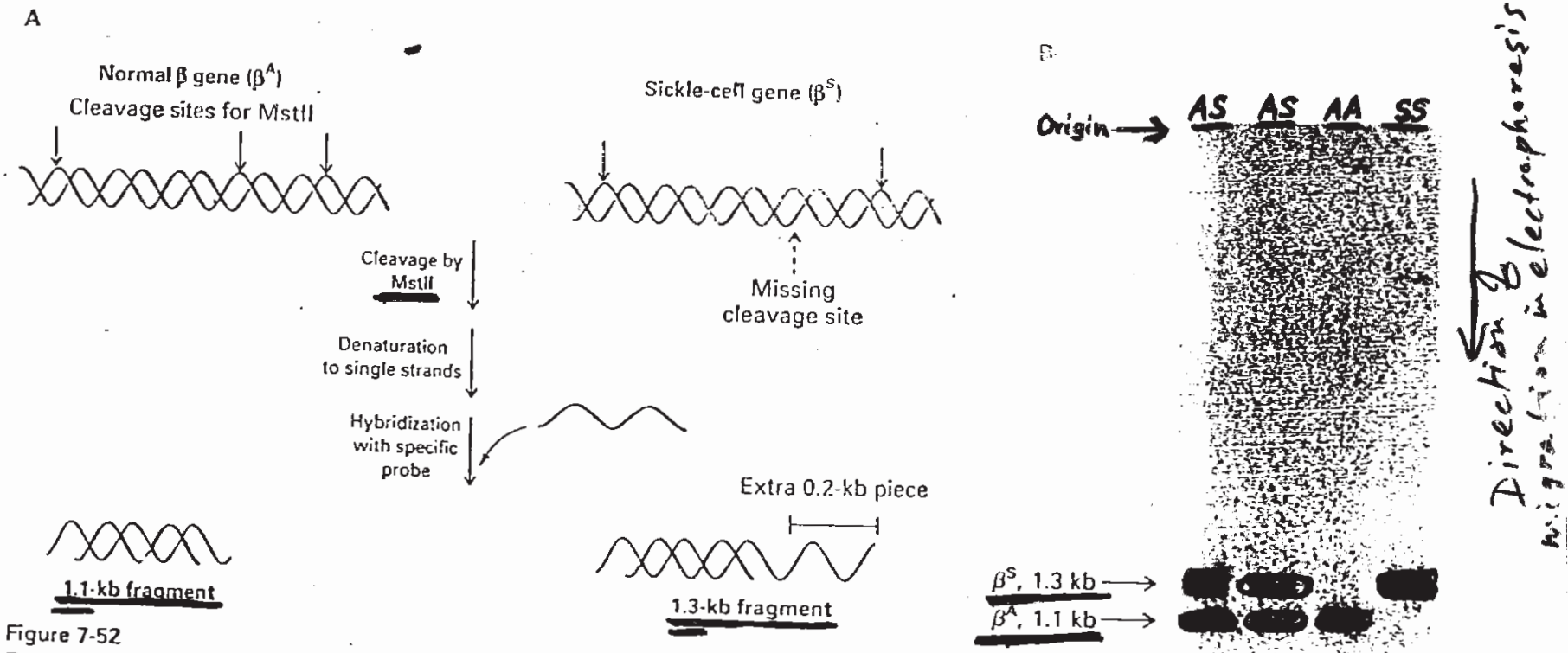
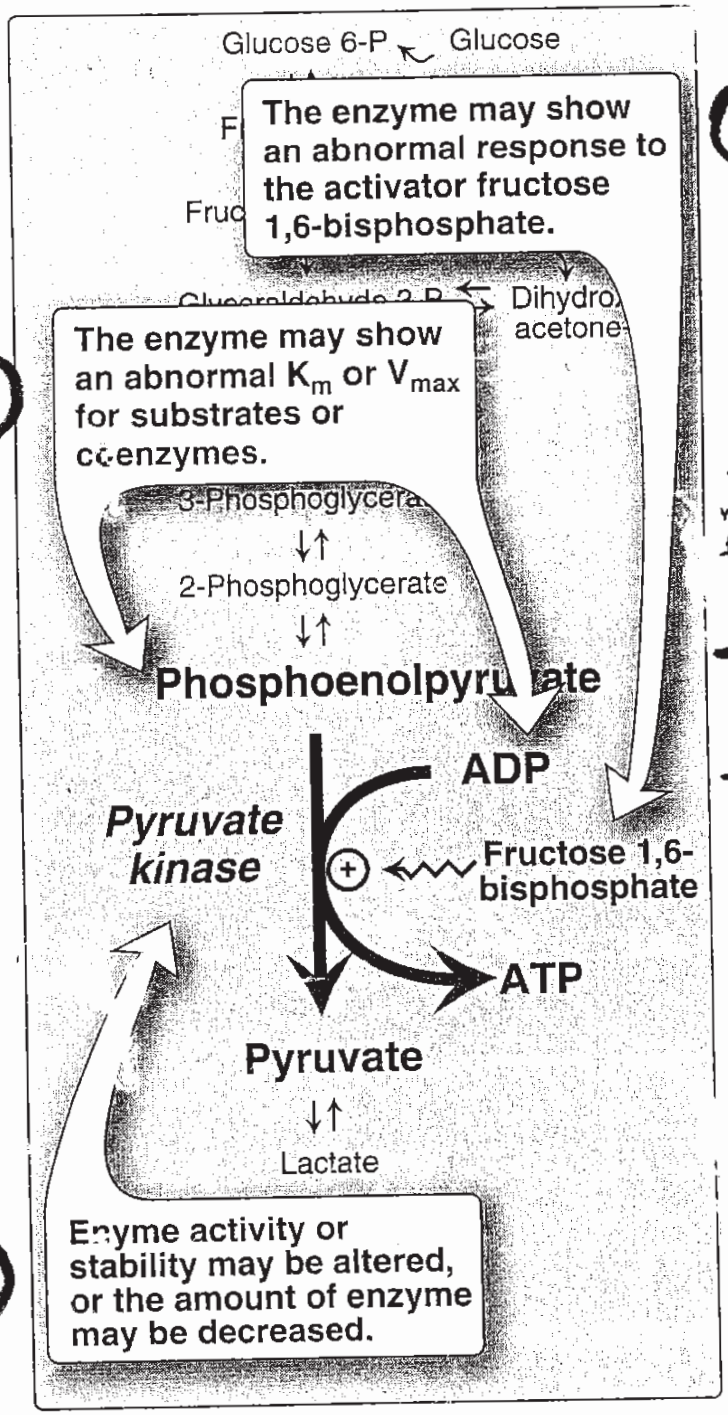


Figure 7-52

Restriction endonuclease method for detecting the sickle-cell gene. (A) Target site in the gene and fragments produced by digestion. (B) Electrophoretic pattern of a digest from parents who are heterozygous for the gene (lanes labeled *AS*), a normal child (*AA*), and a child with sickle-cell anemia (*SS*). [Part B is from Y.-W. Kan. In *Medicine, Science, and Society*, K.J. Isselbacher, ed (Wiley, 1984), p. 297.]

- Pyruvate Kinase Deficiency

95% of glycolytic enz deficiency cases



- severe deficiency requires blood transfusion

→↑ 2,3-BPG

→↓ ATP

- PGI (4% of glycolytic cases)

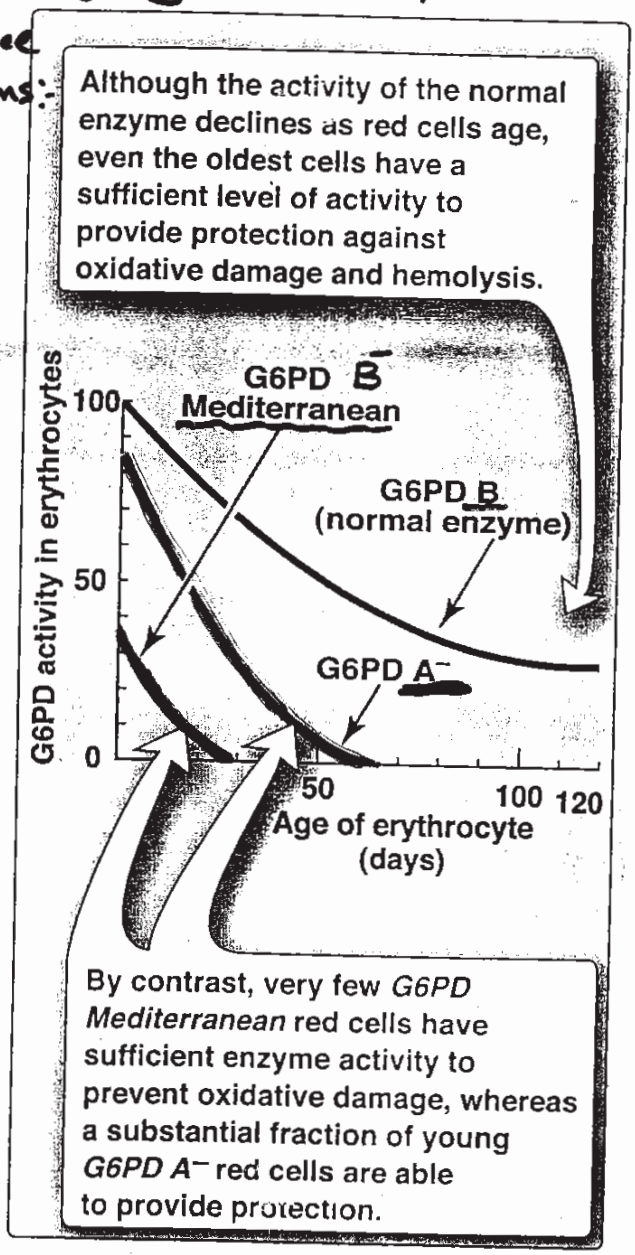
Properties of the G6PD Variant Enzymes 7

1- Classification of G6PD Variants

Class	Clinical symptoms	Residual enzyme activity
I	Very severe	<2%
II	Severe	<10%
III	Moderate	10–50%
IV	None	60–150%

→ Chronic nonspherocytic hemolytic anemia CASE A⁻
e.g. → Med. Variant B⁻
→ e.g. A⁻ (African)

2- Decline of erythrocyte G6PD activity with cell age for three most common forms:



- Precipitating factors in G6PD Deficiency :-

1- Oxidant Drugs

AAA

A = antibiotic e.g. sulfamethoxazole, chloramphenicol

A = Antimalaria primaquine

A : Antipyretics

Acetanalid, but not acetaminophe.

2- Favisim — Fava beans → Contain the glycosicles: vice + convicine → Produce the aglycones → dericine* + isouramil*

3- Infection

4- Neonatal jaundice

*oxidants cause rapid decline in GSH

- Properties of the Variant Enzymes

- Molecular Biology of G6PD

Majority missense mutation → Point mutations

Large deletions or frameshift mutations → not observed

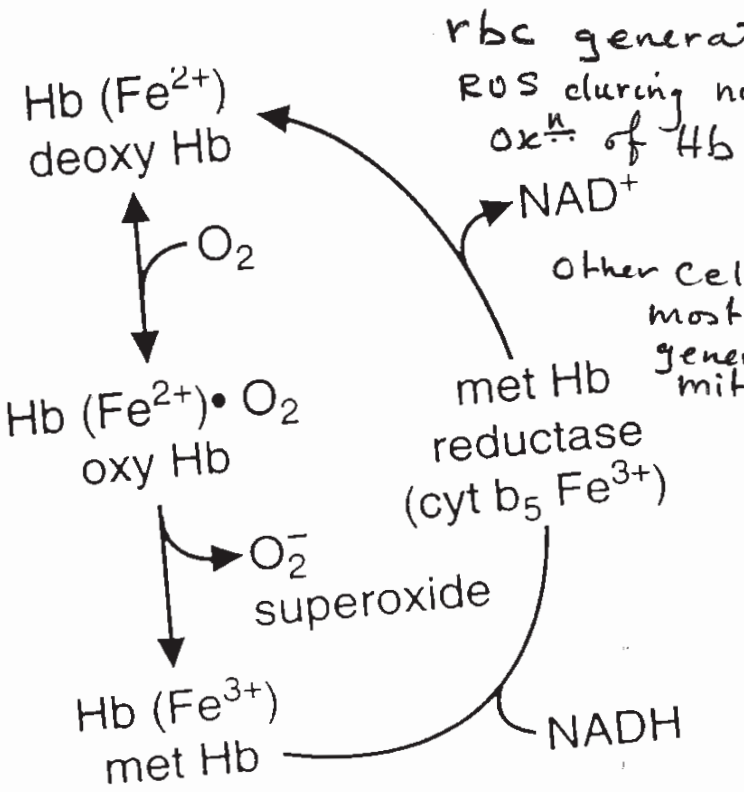
(B) Med. 563 C → T 188 ser → phe

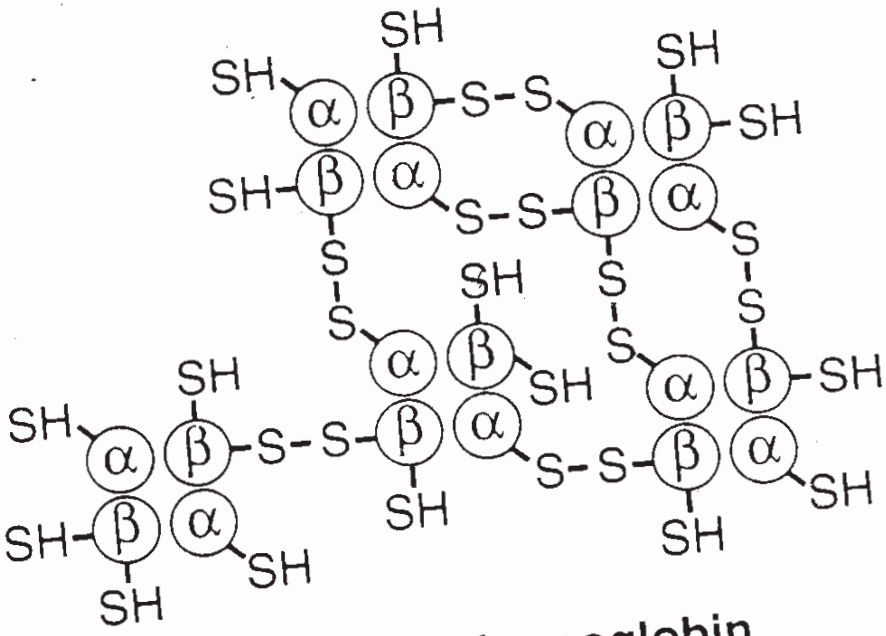
A+ → 376 A → G 121 Asn → Asp

A- → 376 A → G + 202 G → A

126 Asn → Asp 68 Val → Met.

Formation of Heinz-bodies in red blood cell 3

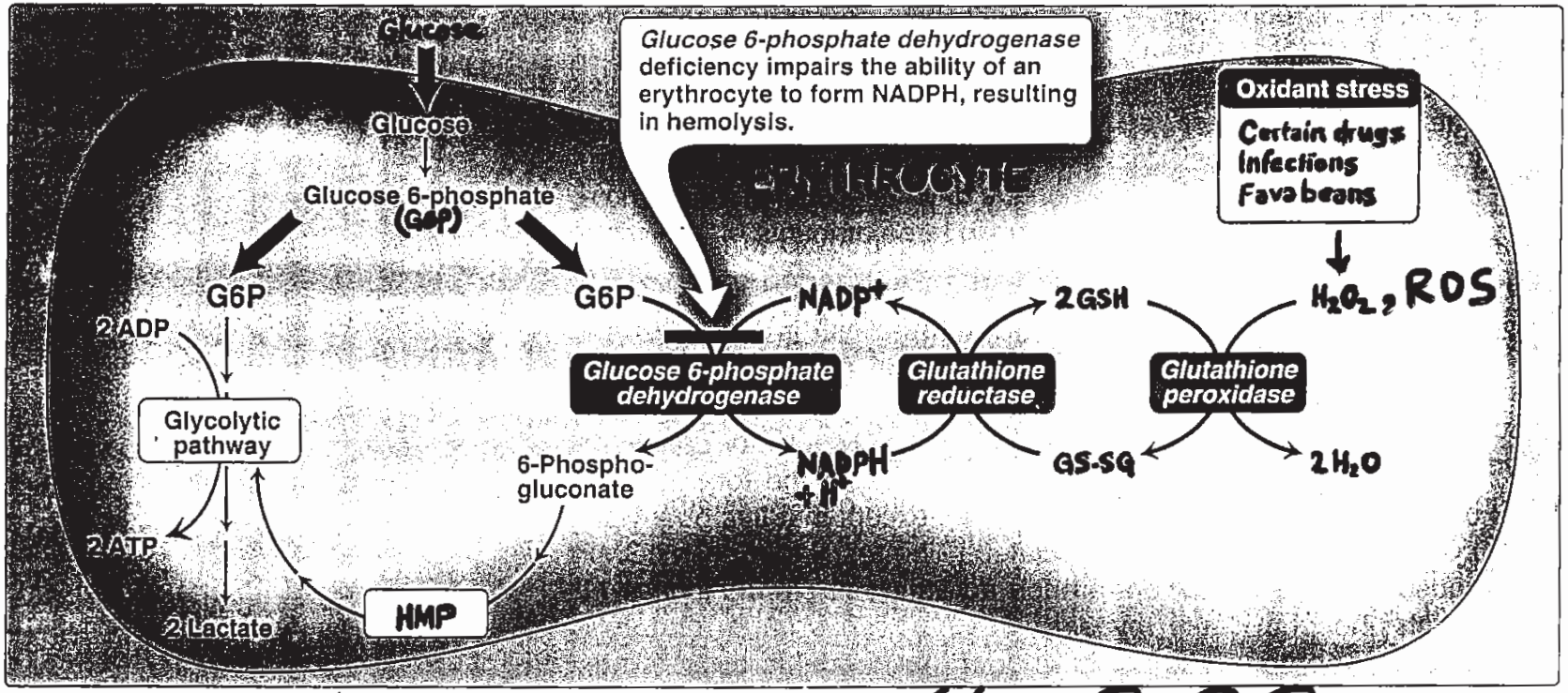




Cross-linked hemoglobin in Heinz bodies

G6PD Deficiency

Pathways of G6P metabolism in the erythrocyte

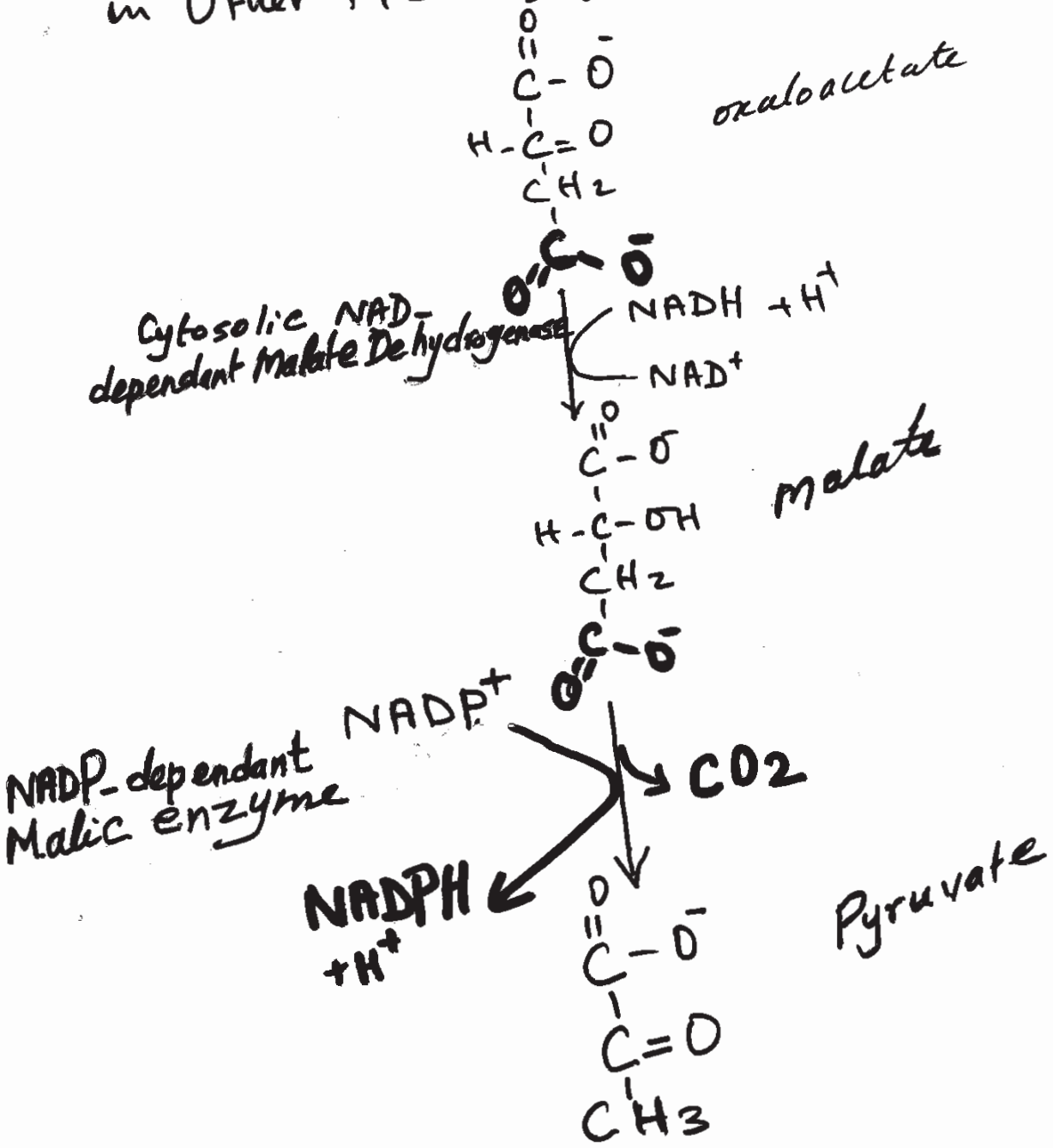


Hemolysis is caused by ROS

G6PD DEFICIENCY

- Introduction
  - location of the gene
- Geographic Prevelance of G6PD Deficiency
  - Middle East
  - Tropical Africa & Asia
  - Parts of Mediterranean
- Clinical Symptoms
  - Resistance to Malaria
- Role of G6PD in Red Blood Cells
  - ⟹ NADPH
    - Anti-oxidant
    - Heinz Bodies in deficiency
      - Oxn of membrane proteins → rigid & nondeformable

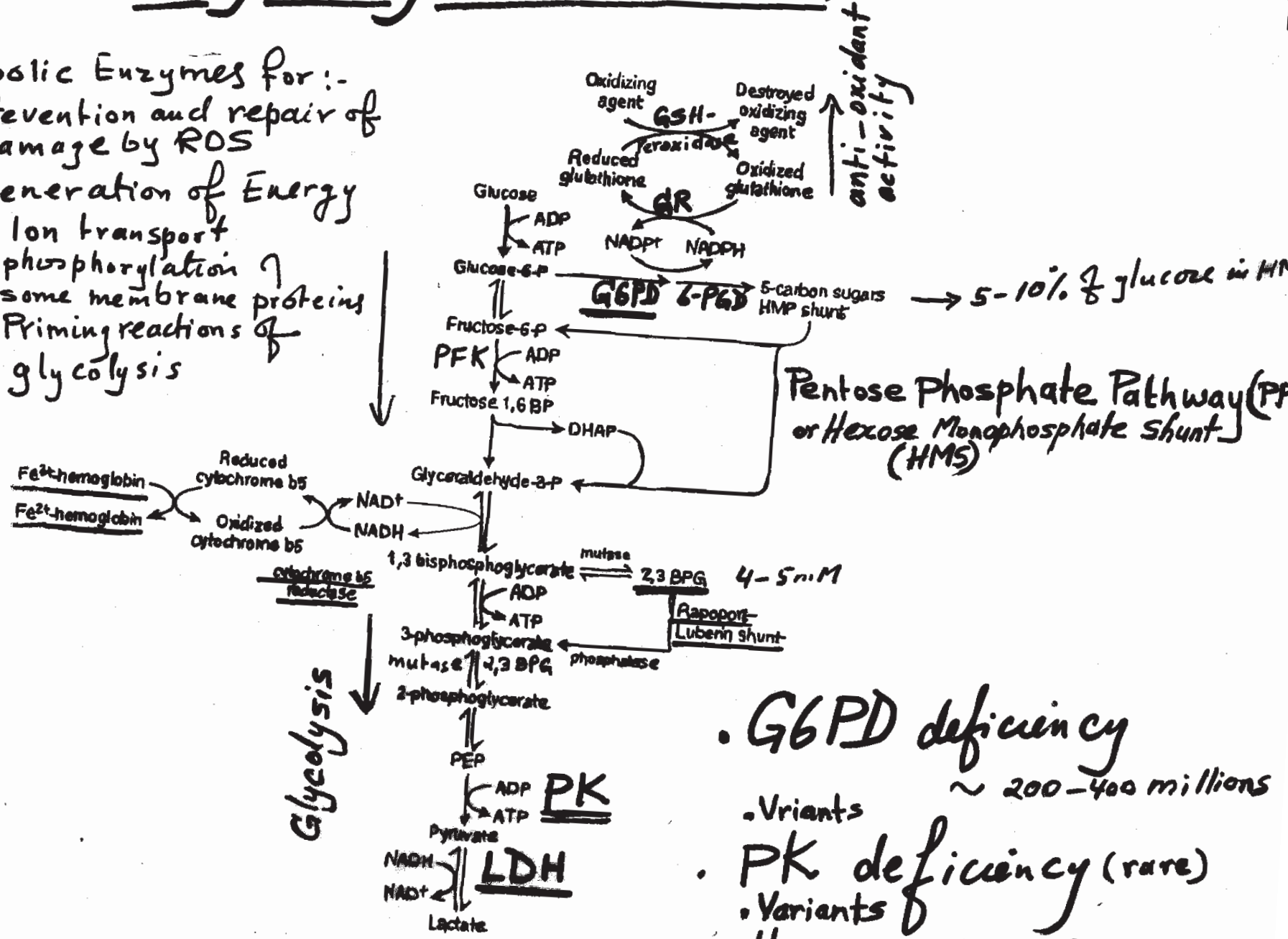
Alternative Sources of NADPH in Other Tissues :-



Erythrocyte Metabolism

Metabolic Enzymes for :-

1- Prevention and repair of damage by ROS
2- Generation of Energy
   - Ion transport
   - phosphorylation of some membrane proteins
   - Priming reactions of glycolysis



- G6PD deficiency ~ 200-400 millions
  - Vriants
- PK deficiency (rare)
  - Variants
- others are v. rare