Glucose-6-Phosphate Dehydrogenase deficiency (G6PD)

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by SuRa Mostafa
Glucose-6-Phosphate Dehydrogenase

• Is the major enzyme in the pentose phosphate pathway
  (also called the phosphogluconate pathway or the hexose monophosphate shunt)
• which is a metabolic pathway parallel to glycolysis.
• Rapidly dividing cells, such as those of bone marrow, skin, and intestinal mucosa,
• Use the pentoses to make RNA, DNA, and coenzymes as ATP, NADH, FADH, and coenzyme A.
Glucose

Glucose 6 phosphate

\( \text{G6PD} \)

6-phosphoglucono-δ-lactone

Glutathione peroxidase

6-phosphogluconate

Ribose 5-phosphate + CO₂

Hexose monophosphate (HMP) shunt pathway or Pentose phosphate pathway

NADP

NADPH

GSSG

GSH

Glutathione reductase
Liver, adipose, mammary gland,

Erythrocytes---the electron donor NADPH, needed for

- reductive biosynthesis
- to counter the damaging effects of oxygen radicals by maintain reducing atmosphere (a high value of $[\text{NADPH}]/[\text{NADP}]$ and a high $[\text{GSH}]/[\text{GSSG}]$, GS = glutathione),
- prevent oxidative damage to proteins, lipids, and other sensitive molecules.
Glucose-6-phosphate $\rightarrow$ 6-Phosphogluconate

$\text{NADP}^+ \rightarrow \text{NADPH}$

GS-SG $\rightarrow$ 2 G-SH (reduced Glutathione)

Antioxidant Activity
Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency

• Halfway through the previous century, the anti-malaria drug primaquine was introduced.
• It was found that this drug can cause severe hemolytic anemia.
• In 1956, Carson and colleagues discovered that the hemolytic anemia was caused by glucose-6-phosphate dehydrogenase (G6PD) deficiency.
• Four hundred million people worldwide carry one or two deficient G6PD genes, making G6PD deficiency the most common enzyme pathology.
• Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is an inborn error of metabolism that predisposes to red blood cell breakdown.
• Is the most common human enzyme deficiency in the world; it affects an estimated 400 million people.
Glukose-6-Phosphatdehydrogenase-Mangel (G6PD-Mangel)

Glukose

Hexokinase (HK)

Glukose-6-Phosphat (G6P)

Glukose-6-Phosphat Isomerase (G6PI)

Fruktose-6-Phosphat (F6P)

Phosphofructokinase (PFK)

Fruktose-1,6-Biphosphat (FBP)

ATP

ADP

6-Phosphoglucono-δ-Lakton

Glukose-6-Phosphat Dehydrogenase (G6PD)

NADP

NADPH

Glutathionreduktase

Glutathion reduziert

Glutathionoxidiert

Glutathionperoxidase

H₂O

H₂O₂
Triggers of hemolysis in kids with G6PD deficiency include:

- **Diseases**, such as bacterial and viral infections
- some painkillers and fever-lowering drugs
- **antibiotics** (most often those with "sulf" in their names)
- **anti-malarial drugs** (most often those with "quine" in their names)
- allergic to Favism.
- **naphthalene** (a chemical found in mothballs and moth crystals)
- Mothballs can be very harmful if a child swallows one.
Triggers that Can Cause Hemolytic Anemia in G6PD Deficient People

- Intake of Fava Beans
- Ingestion of Certain Drugs
- Fever

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Favism
deficiency is inherited.

• Children who have it are born with it
• Causes by passed down in genes from one or both parents.
• The gene responsible for this condition is on the X chromosome.
• G6PD deficiency is a genetic disorder that most often affects males.
• Many females of African inheritance are carriers of G6PD deficiency.
• This means that they can pass the gene for the deficiency to their children but do not have symptoms.
G6PD DEFICIENCY

• It happens when the body doesn't have enough of an enzyme called 
  glucose-6-phosphate dehydrogenase (G6PD)
• .helps red blood cells work.
• also protects them from substances in the blood that harm them.
• In people with G6PD deficiency, either the red blood cells do not make enough 
  G6PD or what they do make doesn't work as it should.
• Without enough G6PD to protect them, the red blood cells break apart.
• This is called hemolysis
G6PD Deficiency

Normal Red Blood Cells

Damaged Red Blood Cells

For Information, Visit: www.epainassist.com
• Neonatal Hyperbilirubinemia
• Acute Hemolysis
• Chronic Hemolysis
• When many red blood cells are destroyed, a person can develop hemolytic anemia.
• This can cause tiredness, dizziness, and other symptoms.
• Red blood cells that don't have enough G6PD are sensitive to some medicines, foods, and infections.
• When these things trigger a quick loss of RBCs over a short time, it's called a hemolytic crisis.
• In these cases, the symptoms stop when the cause is gone.
Symptoms of Hemolytic Crisis

- situations such as fevers.
- ingestion of certain drugs such as aspirin, antimalarial drugs,
- certain antibiotics and other drugs,
- ingestion of foods such as fava beans cause the circulating red cells to breakdown with release of its hemoglobin (intravascular hemolysis).
- Part of the released hemoglobin pigment (which is red in color) is excreted in the urine giving the urine with a dark brown color (hemoglobinuria).
Drugs Causing Hemolysis in G6PD Deficiency

- The following drugs can cause hemolysis in a patient with G6PD deficiency and should be strictly avoided.

Table 8.14

Drugs causing haemolysis in glucose-6-phosphate deficiency

**Analgesics**, such as:
- Aspirin
- Phenacetin (withdrawn in the UK)

**Antimalarials**, such as:
- Primaquine
- Pyrimethamine
- Quinine
- Chloroquine
- Pamaquin

**Antibacterials**, such as:
- Most sulphonamides
- Dapsone
- Nitrofurantoin
- Chloramphenicol
- Quinolones

**Miscellaneous drugs**, such as:
- Vitamin K
- Probenecid
- Quinidine
- Dimercaprol
- Phenylhydrazine
Some of the hemoglobin is processed in the liver and converted to bilirubin.

The high bilirubin levels result in jaundice with yellowish discoloration of the skin and eyes.

- oxygen transport to the various parts of the body is affected due to destruction of red blood cells,
- the person becomes anemic, tired and breathless.
- the condition is not recognized immediately
- blood transfused immediately
- it may sometimes result in death
Symptoms of G6PD Deficiency

• Most people without any symptoms.
• Others have symptoms of hemolytic anemia if many RBCs are destroyed.
• These can include:
  • paleness (in darker-skin kids, paleness is best seen in the mouth, lips or tongue)
  • extreme tiredness or dizziness
  • fast heart-beat
  • fast breathing or shortness of breath
  • jaundice (the skin and eyes look yellow)
  • an enlarged spleen
  • dark, tea-colored pee
Symptoms of G6PD Deficiency

- Jaundice
- Dark-colored Urine
- Rapid Heartbeat
- Enlarged spleen
• Mild symptoms usually don't need medical treatment.
• As the body makes new red blood cells, the anemia will improve.
• If symptoms are more severe, a child may need care in a hospital.
<table>
<thead>
<tr>
<th>CLASS</th>
<th>LEVEL OF DEFICIENCY</th>
<th>ENZYME ACTIVITY</th>
<th>PREVALENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Severe</td>
<td>Chronic nonspherocytic hemolytic anemia in the presence of normal erythrocyte function</td>
<td>Uncommon; occurs across populations</td>
</tr>
<tr>
<td>II</td>
<td>Severe</td>
<td>Less than 10 percent of normal</td>
<td>Varies; more common in Asian and Mediterranean populations</td>
</tr>
<tr>
<td>III</td>
<td>Moderate</td>
<td>10 to 60 percent of normal</td>
<td>10 percent of black males in the United States</td>
</tr>
<tr>
<td>IV</td>
<td>Mild to none</td>
<td>60 to 150 percent of normal</td>
<td>Rare</td>
</tr>
<tr>
<td>V</td>
<td>None</td>
<td>Greater than 150 percent of normal</td>
<td>Rare</td>
</tr>
</tbody>
</table>
## Comparison of the Two Most Common Variants of G6PD Deficiency

<table>
<thead>
<tr>
<th></th>
<th>G6PD MEDITERRANEAN</th>
<th>G6PD A–</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Health Organization class</td>
<td>Class II</td>
<td>Class III</td>
</tr>
<tr>
<td>Populations affected</td>
<td>Italian, Grecian, Spanish, Arabic, Jewish (Kurdish) descent</td>
<td>African descent</td>
</tr>
<tr>
<td>Neonatal hyperbilirubinemia</td>
<td>Yes, may be more severe</td>
<td>Yes</td>
</tr>
<tr>
<td>Favism</td>
<td>More common</td>
<td>Less common</td>
</tr>
<tr>
<td>Hemolysis with oxidative drugs</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Diagnose G6PD Deficiency

The diagnosis of G6PD deficiency is based on the following:

**History**

The diagnosis of G6PD deficiency may be made from a

- careful drug and food intake history with symptoms of jaundice
- tiredness and passing dark colored urine following ingestion of certain drugs or foods.
Diagnosis of G6PD Deficiency Hemolytic Anemia

Diagnosis of hemolytic anemia
  Complete Blood Count (CBC) & reticulocytic count

Screening:
  Qualitative assessment of G6PD enzymatic activity
  (UV-based test)

Confirmatory test:
  Quantitative measurement of G6PD enzymatic activity

Molecular test:
  Detection of G6PD gene mutation
• **Urine tests**
  The urine specimen
  • dark colored
  • positive for hemoglobin and hemosiderin

• **Blood film examination**
  Examination of a stained blood film under the microscope may show abnormal broken red cells (hemolytic RBCs).
  • Special stains show
    • denatured hemoglobin within red cells (**Heinz bodies**)
    • increased immature red cells (**reticulocytes**) due to formation of new red cells (erythropoiesis) by the bone marrow
  • If the abnormal cells have the appearance of a bitten piece they are termed **bite cells**.
• **Diagnostic tissue**

• For a complete diagnostic assessment of the G6PD deficiency rate, the following laboratory parameters are also important:
  • RBCs and reticulocyte counts,
  • total and indirect plasma bilirubin,
  • plasma iron and lactate dehydrogenase levels,
  • serum aptoglobin and ferritin amounts,
  • urine hemoglobin concentration.
Blood Film Examination Can Detect Heinz Bodies and Bite Cells in G6PD Deficiency
Treatment

• Treating G6PD deficiency symptoms is usually as simple as removing the trigger.
• Often, this means treating the infection or stopping the use of a drug.
• A child with severe anemia may need treatment in the hospital to get oxygen and fluids. Sometimes, a child also needs a transfusion of healthy blood cells.
• The best way to care for a child with G6PD deficiency is to limit exposure to anything that triggers symptoms.

• Check with your doctor for instructions, and a list of medicines and other things that could be a problem for a child with G6PD deficiency
Thank you for listening