Newborn Screening for G6PD Deficiency: Value Beyond Malaria

April Grace D. Berboso, MD, DPPS
Pediatrician/Clinical Geneticist

Unit Head
Newborn Screening Center-NIH
Topics to be Discussed

• Brief History of Newborn Screening in the Philippines
• Current Status of the Philippine Newborn Screening Program
• G6PD Deficiency Newborn Screening Data
• Clinical Implications of G6PD Deficiency
• Diagnosis of G6PD Deficiency
• Confirmatory Centers for G6PD Deficiency
The Newborn Screening Act of 2004

• RA 9288 is also known as the "Newborn Screening Act of 2004," was approved on April 07, 2004.

• It is the Philippine law promulgating a comprehensive policy and a national system for ensuring newborn screening.
Newborn Screening Act of 2004 is based on....

- The policy of the State to protect and promote the right to health of the people, including the rights of children to survival and full and healthy development as normal individuals.
History of Newborn Screening in the Philippines

1996

- Research study for obstetricians and pediatricians for 24 Metro Manila hospitals

- Laboratory that coordinated the collection of dried blood spots (DBS) samples per month to be sent to Newborn Screening Laboratory in NSW
Participating Hospitals as of 1996

Started in 18 private and 6 gov’t hospitals

Newborn Screening Study Group

Philippine Newborn Screening Project

METRO MANILA
Capitol Medical Center
Cardinal Santos Medical Center
Children’s Medical Center
Chinese General Hospital
De Los Santos Medical Center
Dr. Victor R. Potenciano Medical Center
FEU-NRMF
Manila Doctors Hospital
Mary Chiles General Hospital
MCU-FDTMF
Medical Center Manila
Metropolitan Hospital
Ospital ng Maynila
Our Lady of Lourdes Hospital
Perpetual Help Medical Center
Philippine Children’s Medical Center
Philippine General Hospital
Quezon City General Hospital
Quirino Memorial Medical Center
Rizal Medical Center
St. Luke’s Medical Center
St. Martin de Porres Hospital
UERMMMCMC
United Doctors Medical Center
History of Newborn Screening in the Philippines

• The disorders tested were:
  1. Congenital Hypothyroidism (CH)
  2. Congenital Adrenal Hyperplasia (CAH)
  3. Phenylketonuria (PKU)
  4. Galactosemia (Gal)
  5. Homocystinuria
History of Newborn Screening in the Philippines

1997
- Begun the in-house operation (NSC-NIH)

1998
- Homocystinuria was removed from the panel of disorders due to absence of confirmed cases
- Glucose Phosphate Dehydrogenase Deficiency (G6PD) was added to the panel of disorders

1999
- Priority program of the Department of Health
5,000+ facilities
Jan 2015
## Prevalence of Disorders in the NBS Panel

(1996 to 2014)

<table>
<thead>
<tr>
<th>DISORDERS</th>
<th>CONFIRMED</th>
<th>SCREENED</th>
<th>CUMULATIVE PREVALENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) CAH</td>
<td>431</td>
<td>6,107,742</td>
<td>1: 14,171</td>
</tr>
<tr>
<td>(2) CH</td>
<td>2,285</td>
<td>6,107,742</td>
<td>1: 2,673</td>
</tr>
<tr>
<td>(3) G6PD Deficiency</td>
<td>116,629</td>
<td>6,028,644</td>
<td>1: 52</td>
</tr>
<tr>
<td>(4) Gal (all types)</td>
<td>164</td>
<td>6,107,742</td>
<td>1:37,242</td>
</tr>
<tr>
<td>GAL - Classical</td>
<td>20</td>
<td>6,107,742</td>
<td>1:305,387</td>
</tr>
<tr>
<td>GAL - Non Classical</td>
<td>58</td>
<td>6,107,742</td>
<td>1:105,306</td>
</tr>
<tr>
<td>GAL - Variant</td>
<td>86</td>
<td>6,107,742</td>
<td>1:71,020</td>
</tr>
<tr>
<td>(5) MSUD</td>
<td>37</td>
<td>2,494,177</td>
<td>1:67.410</td>
</tr>
<tr>
<td>(6) PKU (all types)</td>
<td>62</td>
<td>6,107,742</td>
<td>1:98,512</td>
</tr>
<tr>
<td>PKU - BH4 Defects</td>
<td>7</td>
<td>6,107,742</td>
<td>1:872,535</td>
</tr>
<tr>
<td>PKU - Classical</td>
<td>13</td>
<td>6,107,742</td>
<td>1:469,826</td>
</tr>
<tr>
<td>PKU - Hyperphenylalanemia</td>
<td>29</td>
<td>6,107,742</td>
<td>1:210,612</td>
</tr>
<tr>
<td>PKU - Mild</td>
<td>13</td>
<td>6,107,742</td>
<td>1:469,826</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td><strong>119,834</strong></td>
<td><strong>6,107,742</strong></td>
<td><strong>1.92%</strong></td>
</tr>
</tbody>
</table>
G6PD 1996-2014 National Data

<table>
<thead>
<tr>
<th>Row Labels</th>
<th>Sum of INITIAL POSITIVE</th>
<th>Sum of CONFIRMED</th>
<th>Sum of NORMAL</th>
<th>Sum of SCREENED</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSC-CL</td>
<td>61688</td>
<td>14392</td>
<td>1636</td>
<td>791160</td>
</tr>
<tr>
<td>NSC-M</td>
<td>55224</td>
<td>16417</td>
<td>1281</td>
<td>887673</td>
</tr>
<tr>
<td>NSC-NIH</td>
<td>126003</td>
<td>67667</td>
<td>18296</td>
<td>2974053</td>
</tr>
<tr>
<td>NSC-V</td>
<td>81898</td>
<td>16195</td>
<td>815</td>
<td>1219637</td>
</tr>
<tr>
<td>NSC-SL</td>
<td>9747</td>
<td>1958</td>
<td>282</td>
<td>156121</td>
</tr>
<tr>
<td>Grand Total</td>
<td><strong>334560</strong></td>
<td><strong>116629</strong></td>
<td><strong>22310</strong></td>
<td><strong>6028644</strong></td>
</tr>
</tbody>
</table>

Note: 138,939/334560 → only 41.53% return rate for confirmatory testing
Brief Background on G6PD

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common disease-producing enzyme deficiency affecting 400 million people worldwide.
- It has a global prevalence of 4.9% which correlates highly with geographic areas endemic to malaria which include Africa, Mediterranean Europe, Southeast Asia, and Latin America.

Clinical Manifestations of G6PD Deficiency

- **Neonatal Jaundice**
  - risk of developing neonatal jaundice is much greater in G6PD-deficient neonates than in G6PD-normal ones

- **Acute hemolytic Anemia (AHA)**
  - anemia is from moderate to extremely severe, due largely to intravascular hemolysis
  - G6PD-deficient subjects are at risk of developing AHA in response to three types of triggers: fava beans, infections, and drugs.

Luzzatto. haematologica/the hematology journal | 2006; 91(10) | 1305 |
Clinical Manifestations of G6PD Deficiency

• Chronic non-spherocytic hemolytic anemia (CNSHA)
  - a very small minority of subjects with G6PD deficiency has chronic anemia of variable severity.
Glucose-6-Phosphate Dehydrogenase Deficiency in Filipino Neonates with Jaundice

**Subjects:** 102 neonates at PGH with neonatal jaundice

**Methods:**
- 102 clinically jaundiced neonates admitted to the nursery of the Philippine General Hospital were included in the study.
- Blood samples in individual microtainers were quantitatively tested for G6PD activity using a commercial G6PD assay kit.
- The clinical presentation and hospital courses of patients were statistically compared using the t-test for single proportions.

**Results.** G6PD deficiency was diagnosed in 17 of 102 cases [16.7% (95% CI: 10.0 to 25.3)], which is significantly higher than the normal population (p<0.001).

**Table 1. Etiologic distribution of hyperbilirubinemia**

<table>
<thead>
<tr>
<th>ETIOLOGY</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G6PD deficiency</td>
<td>17</td>
<td>16.67</td>
</tr>
<tr>
<td>Infection</td>
<td>15</td>
<td>14.71</td>
</tr>
<tr>
<td>ABO incompatibility</td>
<td>3</td>
<td>2.94</td>
</tr>
<tr>
<td>Cephalhematoma</td>
<td>2</td>
<td>1.96</td>
</tr>
<tr>
<td>Down Syndrome</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Gastric Outlet Obstruction</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Anemia of prematurity</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Infant of diabetic mother</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Thickly meconium stained</td>
<td>1</td>
<td>0.98</td>
</tr>
<tr>
<td>Unknown</td>
<td>59</td>
<td>57.84</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>102</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

Silao, Padilla, Uy, Delos Reyes Acta Medica Philippina Vol. 43 No. 2 2009
Glucose-6-Phosphate Dehydrogenase Deficiency in Filipino Neonates with Jaundice

• The prevalence of G6PD deficiency among jaundiced neonates was found to be higher than the normal population thus, early detection of this enzymopathy, regardless of sex, and close surveillance of the affected newborns is important in reducing the risk of severe hyperbilirubinemia.

Silao, Padilla, Uy, Delos Reyes Acta Medica Philippina Vol. 43 NO. 2 2009
Diagnosis of G6PD deficiency in the Philippines

• Newborn screening (included in the NBS panel since 1998)
• Confirmatory testing
• Molecular-based tests – target in the future
Diagnosis of G6PD deficiency in the Philippines

• Screening test
  - kit-based quantitative determination of G6PD activity in blood specimens dried on filter paper
  - test is not designed to screen for heterozygous G6PD deficient females
Diagnosis of G6PD deficiency in the Philippines

- Screening test

Reaction pathway:

\[
\text{G-6-P + NADP}^+ \xrightarrow{\text{G6PD}} \text{6-PG + NADPH}^* + H^+ \]

* = Fluorescent
Diagnosis of G6PD deficiency in the Philippines

• Screening test Quality Control
  1) Internal Controls
     Abnormal and Normal controls are included in the kit, to be performed daily.
  2) External Quality Controls
     NBS Laboratory receives 10 G6PD QC samples every 2 months from Veterans General Hospital- Taipei, Taiwan
Diagnosis of G6PD deficiency in the Philippines

- Confirmatory test
  - kit-based enzymatic determination of G6PD activity in red blood cells by kinetic method
  - by Scientific Biotech Specialties Inc.
Diagnosis of G6PD deficiency in the Philippines

• Confirmatory test

\[ \text{G-6-P} + \text{NADP}^+ \xrightarrow{\text{G6PD}} \text{6-PG} + \text{NADPH} + \text{H}^+ \]

Nicotinamide adenine dinucleotide phosphate (NADP) is reduced by G6PD in the presence of G-6-P. The rate of formation of NADPH is proportional to the G6PD activity and is measured spectrophotometrically as an increase in absorbance at 340nm. Production of a second molar equivalent of NADPH by erythrocyte 6-phosphogluconate dehydrogenase (6-PGDH) according to the reaction:

\[ \text{6-PG} + \text{NADP}^+ \xrightarrow{\text{6PGD}} \text{Ribulose-5-Phosphate} + \text{NADPH} + \text{H}^+ + \text{CO}_2 \]

is prevented by use of maleimide, an inhibitor of 6-PGDH.
Diagnosis of G6PD deficiency in the Philippines

• Confirmatory Test Quality Control

1) Internal Controls

2) External Quality Controls

   Participates in the External Quality Assurance Program of Preventive Medicine Foundation (PMF) in Taiwan
The 20 G6PD Confirmatory Centers

Cagayan Valley Adventist Hospital, Isabela
Mariano Marcos Memorial Hospital, Ilocos Norte
Ilocos Training Regional and Medical Center, Parian, San Fernando City, La Union
Angeles University Foundation Hospital, Pampanga

MCU-FDT Medical Foundation Center, Caloocan City
Univ. of Perpetual Help Medical Center, Las Pinas
Our Lady of Lourdes Hospital, Manila
National Institutes of Health, Manila
Batangas Regional Hospital, Batangas City
The Medical City, Pasig City, Metro Manila
Makati Medical Center, Metro Manila
Lipa Medix Medical Center, Batangas

Cebu Doctor’s University Hospital, Osmena Blvd, Cebu City
Mayor Hilarion A. Ramiro Sr., Regional Training
Dr. Pablo O. Torre Sr. Memorial Hospital (Riverside Medical Center)

La Vina General Hospital, Bukidnon
General Santos Doctors Hospital, General Santos City
Mayor Hilarion A. Ramiro Sr. Regional Training and Teaching Hospital, Maningcol, Ozamis City
Tagum Doctors Hospital, Davao del Norte
Polymedic Medical Plaza, Cagayan de Oro City
Molecular Basis of G6PD Deficiency

• Knowledge of the molecular basis of G6PD deficiency helps in the diagnosis and understanding of G6PD deficiency and its management.
Molecular basis of glucose-6-phosphate dehydrogenase deficiency among Filipinos

- Mutations in exon 11 of the G6PD gene were screened by Multiplex polymerase chain reaction (PCR) using multiple tandem forward primers and a common reverse primer (MPTP) in five unrelated Filipino cases with G6PD deficiency.

Molecular basis of glucose-6-phosphate dehydrogenase deficiency among Filipinos

• Results of the 5 patients:
  4 screened positive for a mutation in the gene
  Sequencing of the amplified products confirmed that
  3 cases had a C→T substitution at nucleotide (n.t.) 1360 (C1360T) resulting in an amino acid change of arginine to cysteine at position 454 (G6PD Union)

• 1 had a silent single base substitution C→T at nucleotide 1311.

Molecular basis of glucose-6-phosphate dehydrogenase deficiency among Filipinos

- G6PD Union has been found not only in the Philippines but also in Vanuatu Archipelago in the Southwestern Pacific, Italy, Hawaii, China, Thailand, Laos, and Gypsies in Spain.

Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

- A total of 200 cases confirmed to have G6PD deficiency, 180 males and 20 females, were identified through the Philippine Newborn Screening Program from 2001-2003.
Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

• 148 (74%) of 200 Filipino newborns with G6PD had detectable mutations/polymorphisms in exons 5, 6, 9, 11, and 12

• Mutations were uncharacterized in 15% of cases

### Distribution of g6pd mutations and polymorphisms among Filipino newborns

<table>
<thead>
<tr>
<th>G6PD variant</th>
<th>Mutation/Polymorphism</th>
<th>Number</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viangchan/Silent</td>
<td>871 G&gt;A/1311 C&gt;T</td>
<td>56</td>
<td>32.9</td>
</tr>
<tr>
<td>Union</td>
<td>1360 C&gt;T</td>
<td>36</td>
<td>21.1</td>
</tr>
<tr>
<td>Vanua Lava</td>
<td>383 T&gt;C</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Chatham</td>
<td>1003 G&gt;A</td>
<td>16</td>
<td>9.4</td>
</tr>
<tr>
<td>Canton</td>
<td>1376 G&gt;T</td>
<td>6</td>
<td>3.5</td>
</tr>
<tr>
<td>Union/Viangchan</td>
<td>1360 C&gt;T/871 G&gt;A</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Mediterranean/Silent</td>
<td>563 C&gt;T/871 G&gt;A/1311 C&gt;T</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Union/Chatham</td>
<td>1360 C&gt;T/1003G&gt;A</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Mahidol</td>
<td>487 G&gt;A</td>
<td>2</td>
<td>1.1</td>
</tr>
<tr>
<td>Vanua Lava/Silent</td>
<td>383 T&gt;C/1311 C&gt;T</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Union/Vanua Lava</td>
<td>1360 C&gt;T/383 T&gt;C</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Viangchan/</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vanua Lava/Silent</td>
<td>871 G&gt;A/383 T&gt;C/1311 C/T</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Viangchan/Canton</td>
<td>871 G&gt;A/1376 G&gt;T</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Union/Canton</td>
<td>1360 C&gt;T/1376 G&gt;T</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Coimbra/Silent</td>
<td>592 C&gt;T/1311 C/T</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Silent</td>
<td>1311 C&gt;T</td>
<td>22</td>
<td>12.9</td>
</tr>
<tr>
<td>Uncharacterized</td>
<td></td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>200</td>
<td>100</td>
</tr>
</tbody>
</table>
Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

• The G6PD Union 1360 C>T on exon 11 is the 2nd most common mutation.

Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

- The Filipinos may have also inherited the G6PD variants Vanua Lava, Chatham, and Canton from neighboring countries possibly due to intermarriage and migration.

Characterization of Mutations and Polymorphisms in the G6PD Gene Among Filipino Newborns with Glucose-6-Phosphate Dehydrogenase Deficiency

• Results of this study demonstrated that molecular heterogeneity underlying G6PD deficiency among Filipino newborns.

• Further molecular analyses need to be done to find yet undefined mutations in other exons of the G6PD gene.

Ongoing Research...

• A descriptive research that describes the mutations and polymorphisms in the G6PD gene by whole gene sequencing among Filipino children aged 0-12 months old with G6PD deficiency.
Ongoing Research...

• Contribute to the growing databank of knowledge on genes and their role in health and disease among Filipinos

• For the development of a **low cost confirmatory molecular-based assay** that can detect most of the common G6PD mutations in the Filipino population
Quarterly G6PD Symposium

- The NSC-NIH conducts a quarterly parents and experts symposium on G6PD
- Parents of 150-200 newly diagnosed G6PD babies are invited to attend the symposium
- A Pediatric Hematologist and a Clinical Geneticist give the lectures and answer questions from the parents
G6PD Brochure

oxidative substances during severe infections or illnesses such as typhoid fever, pneumonia, or kidney failure. Most drugs with strong oxidative effects are of kinds:
1. antibiotics of the sulfonamide group
2. medicines for malaria
3. some medicines for fever

How is G6PD deficiency treated?
When a child has taken oxidative substances and suddenly shows the signs and symptoms of hemolytic anemia, he is said to have a hemolytic crisis. During such crises, the goal of doctors and nurses is to prevent the harmful effects from getting worse. Blood transfusion, oxygen, and folic acid may be given. The ultimate treatment for G6PD deficiency is gene therapy (replacing a defective gene with a good one), but this is not yet available at the present time.

As parents, what should I do to prevent a hemolytic crisis?
1. Tell your child's pediatrician that your child has G6PD deficiency. This is very important so that he will not prescribe oxidative drugs in case your child gets ill. He would also be able to watch out for hemolytic crisis and would immediately know what to do just in case it happens.
2. Keep your list of oxidative substances in a handy place. Better yet, post it in a convenient spot on the kitchen wall. Always double-check food, beverage, and medicine labels against the list.
3. Memorize the signs and symptoms of hemolytic anemia: paleness, dizziness, headache, difficulty in breathing, rapid and strong heartbeats, tea-colored urine, and abdominal or back pain. Bring your child to his pediatrician as soon as these signs and symptoms appear.
4. Do not ignore infections. Persistent fever signals an infection. Bring the child at once to his pediatrician.
5. As your child gets older, honestly and gently tell him about his condition and teach him to be careful about what he eats.
What is G6PD deficiency?
Glucose-6-phosphate dehydrogenase deficiency, or G6PD deficiency for short, is the most common enzyme deficiency worldwide. This is an x-linked inherited disorder which means that from the time a baby is born, there is already something wrong with how his body makes and breaks important ingredients. According to statistics, about 400 million people have G6PD deficiency, and it is most common in Africa, Southeast Asia and the Middle East.

Babies with G6PD deficiency have very little or no enzyme called Glucose-6-Phosphate Dehydrogenase (G6PD). An enzyme is a kind of protein that speeds up chemical reactions in the body. The enzyme G6PD is especially important to red blood cells. If this enzyme is lacking or missing, red blood cells are easily destroyed. Another name for G6PD deficiency is favism because some people who have it, usually those living in the Mediterranean region, react very badly after ingestion of fava beans.

What causes G6PD deficiency?
In order to understand what causes G6PD deficiency, one must first learn a bit about genes and chromosomes. Genes are like the body’s blueprints. They contain instructions on how specific parts of the body are made. For example, the instructions in your hair genes say your hair is black, your hair will be black. Genes are packed into threadlike structures called chromosomes. A chromosome is very much like a beaded bracelet. The beads are the different genes that give instructions for different part of the body; the entire bracelet is the chromosome. Genes usually come and add in pairs. One member of a specific pair comes from the father, and the other member comes from the mother. The members of a pair are located on paired chromosomes.

All normal human beings have 23 pairs of chromosomes. Each of the first 22 pairs contains the same number and kind of genes. The last and 23rd pair is the sex chromosomes. They are different from the first 22 pairs in that they do not have the same number and kind of genes. The sex chromosomes contain the genes that determine whether a baby will be a girl or a boy.

If a baby girl gets one defective G6PD gene from either of her parents, she will not have G6PD deficiency because she has another G6PD gene that can do the work (remember: a baby girl has two X chromosomes, thus two G6PD genes). But if she gets two defective G6PD genes from both her parents, she will have G6PD deficiency. On the other hand, a baby boy whose G6PD gene is defective will surely get G6PD deficiency because the Y chromosome has no G6PD gene. A defective G6PD gene will give wrong instructions on how to make the enzyme G6PD. As a result, too little or none of it is made.

What are the harmful effects of G6PD deficiency?
G6PD has a very small but strategic role in protecting the body from substances that can cause damage to cells or oxidative substances. Because of this important role, G6PD is normally found in all parts of the body. To be sure, most parts of the body also keep a “spare” enzyme, one that can do the work of G6PD in case it is lacking or missing entirely. Unfortunately, this is not the case with red blood cells. They do not have spare enzymes that can do the work of G6PD. If a baby does not have enough G6PD, his red blood cells lack protection from the harmful effects of oxidative substances.

A baby with G6PD deficiency appears and remains healthy until he is exposed to a large amount of oxidative substances. When this happens, his red blood cells are destroyed, a process known as hemolysis. Red blood cells carry oxygen to all parts of the body. When they undergo hemolysis, the baby will have hemolytic anemia. The signs and symptoms of hemolytic anemia are paleness, dizziness, headache, tarry-colored urine, and abdominal or back pain or both. Hemolytic anemia, when very severe, can end in death.

Destroyed red blood cells are brought to the liver to be broken down to smaller pieces for disposal. One of the end products of this process is bilirubin, a yellowish substance that accumulates in different parts of the body when too much of it is produced. Quite often, bilirubin accumulates in the skin and causes it to appear yellowish. In the worst cases, bilirubin accumulates in the brain and causes mental retardation or death.

G6PD Brochure

What are the harmful effects of G6PD deficiency?
G6PD has a very small but strategic role in protecting the body from substances that can cause damage to cells or oxidative substances. Because of this important role, G6PD is normally found in all parts of the body. To be sure, most parts of the body also keep a “spare” enzyme, one that can do the work of G6PD in case it is lacking or missing entirely. Unfortunately, this is not the case with red blood cells. They do not have spare enzymes that can do the work of G6PD. If a baby does not have enough G6PD, his red blood cells lack protection from the harmful effects of oxidative substances.

A baby with G6PD deficiency appears and remains healthy until he is exposed to a large amount of oxidative substances. When this happens, his red blood cells are destroyed, a process known as hemolysis. Red blood cells carry oxygen to all parts of the body. When they undergo hemolysis, the baby will have hemolytic anemia. The signs and symptoms of hemolytic anemia are paleness, dizziness, headache, tarry-colored urine, and abdominal or back pain or both. Hemolytic anemia, when very severe, can end in death.

Destroyed red blood cells are brought to the liver to be broken down to smaller pieces for disposal. One of the end products of this process is bilirubin, a yellowish substance that accumulates in different parts of the body when too much of it is produced. Quite often, bilirubin accumulates in the skin and causes it to appear yellowish. In the worst cases, bilirubin accumulates in the brain and causes mental retardation or death.

Oxidative substances during severe infections or illnesses such as typhoid fever, pneumonia, or kidney failure.

Most drugs with strong oxidative effects are of kinds:
1. Antibiotics of the sulfa group
2. Medicines for malaria
3. Some medicines for fever

How is G6PD deficiency treated?
When a child has taken oxidative substances and suddenly shows the signs and symptoms of hemolytic anemia, he is said to have a hemolytic crisis. During such crises, the goal of doctors and nurses is to prevent the harmful effects from getting worse. Blood transfusion, oxygen, and folic acid may be given. The ultimate treatment for G6PD deficiency is gene therapy (replacing a defective gene with a good one), but this is not yet available at the present time.

As parent, what should I do to prevent a hemolytic crisis?
1. Tell your pediatrician that your child has G6PD deficiency. This is very important so that he will not prescribe oxidative drugs in case your child gets ill. He would also be able to watch out for hemolytic crisis and would immediately know what to do in case it happens.
2. Keep your list of oxidative substances in a handy place. Better yet, post it in a convenient spot on the kitchen wall. Always double-check food, beverage, and medicine labels against the list.
3. Memorize the signs and symptoms of hemolytic anemia: paleness, dizziness, headache, difficulty in breathing, rapid and strong heartbeats, tarry-colored urine, and abdominal or back pain. Bring your child to his pediatrician as soon as these signs and symptoms appear.
4. Do not ignore infections. Persistent fever signals an infection. Bring the child at once to his pediatrician.
5. As your child gets older, honestly and gently tell him about his condition and teach him to be careful about what he eats.
## I. DRUGS TO BE AVOIDED

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Common Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Antibacterial</strong></td>
<td></td>
</tr>
<tr>
<td><em>Nalidixic acid</em></td>
<td>Macrodantin, Diafarm, Diapectolin, Furoxone, Furacin</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td></td>
</tr>
<tr>
<td>1. Nitrofurantoin</td>
<td></td>
</tr>
<tr>
<td>2. Furazolidone</td>
<td></td>
</tr>
<tr>
<td>3. Nitrofurazone / nitrofural</td>
<td></td>
</tr>
<tr>
<td>*P-a-minosalicylic acid</td>
<td></td>
</tr>
<tr>
<td><strong>B. Analgesic/ Antipyretic</strong></td>
<td></td>
</tr>
<tr>
<td>*Acetanilid</td>
<td></td>
</tr>
<tr>
<td><strong>C. Antihelminetic</strong></td>
<td></td>
</tr>
<tr>
<td>*B-napthol</td>
<td></td>
</tr>
<tr>
<td>*Niridazole</td>
<td></td>
</tr>
<tr>
<td>*Stibophan</td>
<td></td>
</tr>
<tr>
<td><strong>D. Sulfonamides and Sulphones</strong></td>
<td></td>
</tr>
<tr>
<td>Dapsone</td>
<td>Lepravir</td>
</tr>
<tr>
<td>*Glucosulphone sodium</td>
<td></td>
</tr>
<tr>
<td>Glyburide / Glibenclamide</td>
<td>Euglucon, Gluban, Lodulce, Orabetic</td>
</tr>
<tr>
<td>*Mafenide acetate</td>
<td></td>
</tr>
<tr>
<td>*Salicylazosulphapyridine/ Sulfasalazine</td>
<td></td>
</tr>
<tr>
<td>Stibophen</td>
<td>(2-(2-Oxo-3,5-Disulphonatophenoxy)-1,3,2-Benzodioxastibole-4,6-Disolphonate)</td>
</tr>
<tr>
<td>Sulphacetamide / Sulfacetamide</td>
<td>Cetaped, Sensocet</td>
</tr>
<tr>
<td>*Sulphadimidine</td>
<td></td>
</tr>
<tr>
<td>*Sulphafurazone</td>
<td></td>
</tr>
</tbody>
</table>

## II. CHEMICALS TO BE AVOIDED

- Methylene Blue
- Arsine
- Phenylhydrazine
- Toluidine blue
- Trinitrotoluene
- Aniline dyes

## III. FOOD/DRINKS TO BE AVOIDED

- Fava beans
- Dingdong nuts, Mr. Bean
- Red wine

## IV. DRUGS SAFE TO TAKE IN THERAPEUTIC DOSES

- Acetaminophen
- Paracetamol, tylenol
- Acetophenetidin / phenacin
- Alka-seltzer, Aspiltes, Cor-80, Cortal
- Ascorbic acid
- Chloramphenicol
- Chloromycetin, Chlоро-S, Chlorisig, Klorfen, Oliphenicol, Optomycin, Pediaclor, Penachlor, Speradex

## I. OTHERS

- Menthol
- Alaxan Gel, Ben-gay, Effisacent Oil, Listerine mouthwash, Listerine Pocketpacks, Megagen Oil, Mentopas Medicated Plaster, Omega Pain Killer
- Camphor
- Naphthalene
- Moth balls
- Henna
- Cattle gallstone bezoar, Honeysuckle flower, Chimonanthus flower, 100% pearl powder, Figwort flower, Acalypha indica
G6PD Parents Support Group

• A G6PD parents support group is slowly growing in number.
Now Offering Expanded NBS

IMPLEMENTATION OF THE EXPANDED NEWBORN SCREENING

6 DISORDERS → 28+ DISORDERS

(Option 1 - at P550) (Option 2 - at P1500)

To save more and more babies...

Hey! Can we get a little Expanded Newborn Screening over here?
Expanded NBS to Screen for 28+ Disorders

**Organic Acid Disorders**
- Carboxylase Deficiency (3MCC)
- Multiple Carboxylase Deficiency (MCD)
- Propionic Acidemia/Methylmalonic Acidemia (PA/MMA)
- Glutaric Acidemia Type I (GA1)
- Isovaleric Aciduria (IVA)
- Beta-Ketothiolase Deficiency

**Fatty Acid Oxidation Disorders**
- Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)
- Long Chain Acyl-CoA Dehydrogenase Deficiency (LCHAD)
- Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)
- Carnitine Palmitoyl Transferase Deficiency Type I (CPT1)
- Carnitine Palmitoyl Transferase Deficiency Type II (CPT2)
- Carnitine Uptake Defect
- Glutaric Acidemia Type II (GA2)
- Trifunctional Protein Deficiency

**Amino Acid Disorders**
- Hypermethionemia/Homocystinuria (MET/HCY)
- Tyrosinemia (TYR)
- Phenylketonuria (PKU)
- Maple Syrup Urine Disease (MSUD)

**Hemoglobinopathies**
- Alpha Thalassemia Trait
- Alpha Thalassemia
- Beta Thalassemia
- Hemoglobin C/D/E/S Trait
- Hemoglobin B/C/D/E/F/FE/H Disease
- Sickle Cell Disease

**Others**
- Cystic Fibrosis
- Biotinidase Deficiency
- Congenital Adrenal Hyperplasia
- Congenital hypothyroidism
- Glucose 6 Phosphatase Dehydrogenase Deficiency
- Galactosemia
Thank You!