Each one of the approximately 75,000 babies born each year in Missouri is tested for galactosemia, a genetic disorder of galactose metabolism caused by deficient activity of the enzyme galactose-phosphate uridylyltransferase (GALT). With early identification and a switch to a lactose-galactose restricted diet, complications of liver failure, sepsis, neonatal death, and mental retardation can be prevented. The incidence of true classic galactosemia in Missouri is about one in 40,000, according to state newborn screening laboratory data, meaning one to two affected babies per year are identified. Kansas also screens for galactosemia.

Newborn screening is, as the name implies, screening. When an infant is identified as having a lower than normal GALT enzyme profile by the state, more definitive testing is required to rule out false positives and to assess whether the baby is deficient enough to require a diet change. This involves biochemical testing to measure GALT enzyme activity, which may give a continuum of activity ranging from classic galactosemia to carrier to normal. What complicates both biochemical testing and clinical management is a mild mutation, N314D, which causes only a 50% reduction in enzyme activity, a profile called the Duarte phenotype. Since galactosemia is a recessive disorder, an affected individual will have two mutated alleles. The possible combinations are provided in the table to the right.

Given the large overlap between the carrier and Duarte ranges, molecular genetic testing is a useful part of the GALT panel offered at CMH to distinguish between Duarte and classic mutation carriers. Molecular genetic testing is also useful for genotype/phenotype correlation, genetic counseling, and prenatal diagnosis. CMH is one of only three laboratories in the country that offers GALT mutation analysis.

Molecular testing is done in two steps:

1. The two most common mutations, Q188R and N314D are first tested. This panel resolves most abnormal enzyme profiles.

2. If the patient is negative for these two mutations but biochemical testing indicates the patient carries a mutation, an extended panel of five additional mutations is done, including S135L, Y209C, L195P, F171S, and K285N. Approximately 75% of galactosemic patients will test positive for at least one of these mutations.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Interpretation</th>
<th>GALT enzyme range</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/N</td>
<td>Normal</td>
<td>11 - 16</td>
<td>None</td>
</tr>
<tr>
<td>D/N</td>
<td>Duarte carrier</td>
<td>8 - 14.5</td>
<td>None</td>
</tr>
<tr>
<td>D/D</td>
<td>Duarte homozygote</td>
<td>6 - 10</td>
<td>None</td>
</tr>
<tr>
<td>G/N</td>
<td>Classic mutation carrier</td>
<td>6 - 10</td>
<td>None</td>
</tr>
<tr>
<td>D/G</td>
<td>Duarte plus classic mutation carrier</td>
<td>2 - 5</td>
<td>May or may not be necessary</td>
</tr>
<tr>
<td>G/G</td>
<td>Classic galactosemia</td>
<td>0 - trace</td>
<td>Yes</td>
</tr>
</tbody>
</table>
News From Histology
by Solvey Chapman, HT

Formalin Exposure: What You Should Know

YOU ARE EXPOSED TO FORMALDEHYDE ALMOST EVERY DAY AND MAY NOT EVEN KNOW IT. It is one of the most common chemicals in use today. Formaldehyde is used as a preservative in paints, dyes for clothing, building materials, and many other items you may have never thought of. The U.S. Department of Labor estimates that over 2 million workers are exposed to formaldehyde and its relative solutions each year. Formaldehyde is also widely used in the healthcare industry, primarily as a preservative for tissues. Following is some information that may help you better understand what formaldehyde is and how to protect yourself, as well as others, if you have it in your office.

Formaldehyde is a colorless, pungent gas most commonly used in a solution form as a disinfectant and preservative. The liquefied form is more commonly known as formalin. There are various strengths of formalin, but 10% is the most commonly used. The Histology lab uses 10% formalin to preserve tissue samples. These samples may come from a doctor’s office or most often, directly from surgery. Because it is colorless, it can be mistaken as water or alcohol. It is imperative that proper labeling alerting that the bottle contains formalin as well the percentage of formalin, be used on all containers for the safety of all persons handling the sample.

Several studies performed by the National Cancer Institute conclude that formaldehyde is a potential human carcinogen linked to leukemia, brain cancers, and nasopharyngeal cancers. In low levels of exposure, irritation of the eyes, nose and throat are experienced. In higher levels, of exposure, the central nervous system is affected. It may also be a strong sensitizer to both respiratory tract and skin, which may induce allergic reactions. Severe exposure may cause burns to the skin, cornea of the eyes, and could result in death.

The risks involved with handling formalin and possible long-term exposure cause the hospital to utilize various safeguards to keep its employees and visitors safe. The Histology lab is monitored on a regular basis to ensure that the levels of formaldehyde do not exceed the allowable amount set forth by OSHA, which is 0.75 parts per million. Personal protective equipment, such as gloves, lab coats, aprons, and eye protection, is supplied, and its use is mandatory. Gloves should always be worn when handling formalin since it can be absorbed through the skin. An MSDS (material safety data sheet) on formaldehyde needs to be in every area where formalin is used and handled. The sheet contains information pertaining to the chemical and how to correctly handle the chemical. The MSDS advises what to do if you are exposed. It also instructs on how to clean up a spill and what to use.

Formaldehyde is a potentially dangerous chemical that needs to be handled with great care. Safeguards have been given to ensure your safety while handling this chemical. If you follow the rules, you can be sure that your risks will be greatly decreased.

Laboratory CME Series
Tuesday, January 21, 2002
12:00 p.m.-1:00 p.m.
Location: Laboratory Conference Room #2206.10
Speaker: Dr. Uttam Garg