



## CHEM-643 Intermediary Metabolism

### Problem No. 1

## Inborn Errors of Metabolism

Image from: [http://www6.miami.edu/homepage/first\\_alert.htm](http://www6.miami.edu/homepage/first_alert.htm)

Each enzyme of intermediary metabolism catalyzes a specific chemical reaction. When all are functioning properly, as is usually the case, there are no problems. Even if the activity of one enzyme is ~50% of normal, the effects are usually minimal, such as when someone inherits a mutated gene encoding a defective enzyme from only one parent. However, if a person inherits the same mutated gene from both parents, there is virtually no activity for the encoded enzyme. This leads to serious metabolic problems that often are fatal. Such "inborn errors of metabolism" affect more than one in every 1000 births. While the prognosis is bleak in many cases, restricted diets can ameliorate the effects of some enzyme deficiencies. The key is early detection.

The *New York Times* reported (January 29, 2002, pF7) that newborn infants in some states are routinely tested for up to a dozen treatable defects. The tests require a few drops of blood taken from the heel at birth. Based on the month of your birth, please write a short paper (at least 4 pages double-spaced with figures) on one of the following treatable inborn errors of metabolism mentioned in the NYT article. See also *Ann. Rev. Genomics and Human Genetics* 1, 139-177 (2000). A superb source of information is the *Metabolic and Molecular Basis of Inherited Disease*, a four volume tome in the Morris library.

#### Your Birth Month

January or July

February or August

March or September

April or October

May or November

June or December

#### Your Assigned Inborn Error of Metabolism

PKU (phenylketonuria),

MCAD (medium-chain acylCoA dehydrogenase) deficiency

Biotinidase (multiple carboxylase) deficiency

Maple syrup urine disease (branched-chain ketoaciduria)

Galactosemia

Homocystinuria

#### This assignment has several purposes:

1. To familiarize you with one inborn error of metabolism
2. To review material from CHEM-641/642 and other courses.
3. To illustrate the importance of an understanding of metabolism
4. To demonstrate your ability to locate and use relevant information resources
5. To exercise your organizational and writing skills

**This assignment will be evaluated on the following elements:**

1. A clear description of the symptoms and consequences of the untreated disease.
2. The treatment and rationale for the treatment.
3. A discussion of the normal enzyme that is missing in the afflicted individuals (e.g. structural properties, reaction catalyzed with chemical structures, cofactors, mechanism, organ and sub-cellular distribution, any regulatory properties, etc.)
4. How deficiency is detected in newborn infants.
5. Relevant information cited appropriately in the text and the sources listed in standard *Journal of Biological Chemistry* format. A *minimum* of three **primary** references must be cited.
6. Turned in on time.
7. Bonus-Particularly outstanding work displaying unexpected elements or intellectual involvement above and beyond the assignment can earn an A<sup>+</sup>.

**Suggestions:**

1. Search your topic in PubMed and Web of Science. These are resources you should find helpful in other science courses as well.
2. Get started early and be considerate. Use your resources in the library and return them to the stacks so that others can use them.
3. Learn from the past:

Because this is your first assignment in CHEM-643, it is appropriate to layout my grading procedure and expectations from the start.

1. Typically I read and write comments on every paper before I go back and assign grades. That way I can get a sense of the range of quality in the answers and I can be more consistent in the grades I give. (Grading is subjective and never perfect.)
2. On this assignment in the past, students did a good job of locating relevant references and relaying the information they found. However, there are three issues (voice, sources, and chemistry) that many of them needed to address better and I suspect may be issues for you as well.
  - a. Many of the papers I read contained lots of good, accurate, factual material. However, it was not clear to me that that information also resided in the heads of the authors. Ideally, you need to read and understand, take notes, and then write *in your own words* your understanding, i.e. your own voice needs to be evident. Too often I feel I am reading the words or paraphrased comments of others. This feeling has been verified on several occasions when I put some finely crafted sentences into the Google search engine and discovered examples of whole sentences that also appear verbatim on web-sites. This is plagiarism. However, frequent close paraphrasing is not much better. The goal of education is for you to understand. This means more than finding the relevant information and repeating it with slight variations on a report.
  - b. Many students are unfamiliar with the distinction between **primary** and **secondary sources**. Primary sources are original sources, such as scientific articles, where new data are published and interpreted. Secondary sources summarize, reflect on, and review primary sources. They may contain original insights but they rarely contain new data. Web-sites are secondary sources unless they come from on-line journals. Some web-sites provide excellent resources but they should not be the only sources of information. As students in science, you need to become used to locating and reading primary sources such as the *Journal of Biological Chemistry* or the *Proceedings of the National Academy of Sciences*. Both are on line. Related to this, you will need to pay close attention to the citation and referencing conventions used in science writing.
  - c. Finally, and of considerable importance in this class, is the issue of chemistry. In the past I have been astonished when over half of the reports had no chemical structures or any figures despite the explicit request for them in the assignment. I don't know whether this meant the assignment was not read, students avoided the chemistry, or something else. In order to understand metabolism, biochemical compounds need to be more than words. I look for the chemical structures of substrates and products of enzymes, the chemistry of cofactors involved in particular reactions and metabolic pathways, the chemical rationale for various diagnostic tests, and so on. (If you haven't learn to use ChemDraw software, this is a good time to start. It is loaded on the HHMI computers.) What I read in many cases were clinical descriptions and not chemical descriptions. Both are important. I try very hard to make metabolism make sense to every student in CHEM-643 in terms of biochemistry, not only because this is a biochemistry course, but because this perspective is a very powerful way to understand health, medicine, and life in general.

Written by H. B. White. Revised 27 August 2010.