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The Value of PEth as a Biomarker of Prenatal Alcohol Exposure

By Joseph Salerno, Scientific Writer, USDTL

Recent research demonstrates the usefulness of the direct alcohol biomarker phosphatidylethanol (PEth) for prenatal alcohol exposure testing. In a study published in April, PEth testing was able to positively identify maternal drinking with a 100% sensitivity when measured in newborn dried blood spots.[2] PEth outperformed four maternal urine biomarkers (GGT, CDT, EtG, and EtS) and fatty acid ethyl esters (FAEEs) measured in newborn meconium specimens.

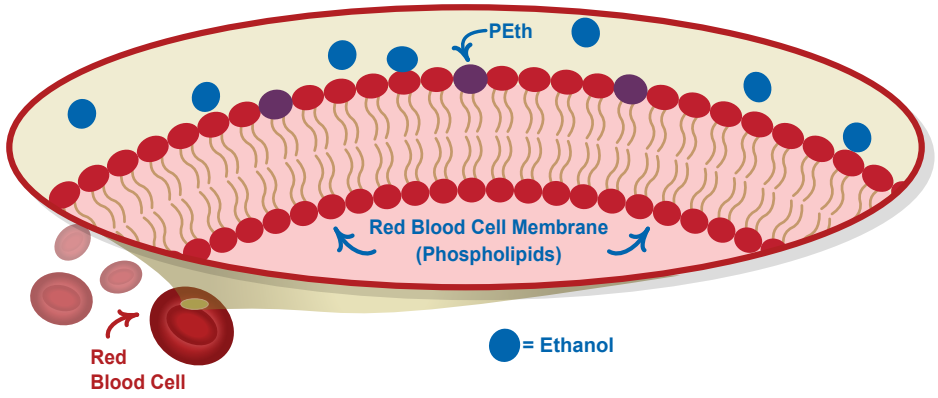

Figure 1. PEth is a direct alcohol biomarker produced and stored in the red blood cell membrane when ethanol is present in the body. Illustration by Michelle Lach, USDTL.

PEth is a direct biomarker of alcohol consumption that is only formed when ethanol is present in the body. As ethanol encounters the red blood cell membrane it becomes incorporated and trapped in the phospholipid molecules of the membrane bilayer (Figure 1). PEth can be measured in blood for 2-3 weeks following ethanol exposure, the period of late pregnancy. Research suggests the levels of PEth created and stored in red blood cells is not affected by age, gender, or disease, unlike indirect alcohol biomarker levels, which are often confounded by these factors.

The easiest method for PEth testing involves the collection of dried blood spots such as those collected from newborn heel sticks for genetic screening. This method of collection fixes the red blood cells to a filter card and prevents any further creation of PEth in the sample, ensuring an accurate measure of PEth levels.

Specimen availability and collection is often a problem for prenatal alcohol exposure testing using conventional sample types like meconium. Meconium is available only in approximately 80% of newborns, while dried blood spots are universally available. Meconium testing often requires multiple collection times to gather a complete specimen, as opposed to the single collection event for dried blood spots.

The value of PEth as a marker for prenatal alcohol exposure lies not only in its high sensitivity to alcohol exposure, but also to its low cost and ease of collection, shipping, and storage.

The collection of dried blood spots from newborns for genetic testing is routine in hospitals today. Bakhireva et al. were able to demonstrate the feasibility of collecting a second dried blood spot card for PEth testing, with sufficient sample volume to screen and confirm for the presence of PEth.[1] Their research also showed that PEth testing in newborn dried blood spots was half the cost of fatty acid ethyl ester (FAEE) testing in newborn meconium.

The collection of dried blood spots also ensures ease of sample shipment and storage, much more so than with meconium or whole blood samples. Dried blood spots can be shipped by any means and do not require special handling procedures. When stored as dried blood spots, the PEth biomarker degrades less than 5% even when stored at room temperature for as long as 30 days.[3]

To access more information about PEth testing in dried blood spots, including a fully annotated bibliography of PEth research, visit our website at www.USDTL.com/testing/blood-drug-test-labs.

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Neonatal Abstinence Syndrome And Variations in Expression, Part 2

By Loretta P. Finnegan, M.D.

This is a continuation of Dr. Finnegan's feature article. The first half of this article was published in the January 2014 issue of Perinatal Quarterly News. You can download our January issue at www.USDTL.com.

Medications provided for the treatment of opioid dependence in pregnant women (methadone or buprenorphine), although providing many benefits to the maternal-fetal-newborn triad, also have the potential risk of abstinence/withdrawal in the newborn. Exposure to methadone *in utero* can precipitate NAS in about 60-80% of those exposed. Dose of methadone has not been shown to be associated with the severity of NAS. Timing of the doses (once daily versus two or three doses) has been seen to influence the incidence and severity of symptoms. For buprenorphine, NAS has been reported in varying degrees of severity and incidence. Many early studies did not control for other drug abuse concomitant with buprenorphine treatment. NAS occurrence was significant in those studies that included other drug use, however, studies in Austria and the United States have shown minimal abstinence symptoms from buprenorphine alone.

A well controlled clinical trial (The MOTHER Study) compared the differences between the occurrence and severity of NAS from methadone and that from buprenorphine. No significant differences between methadone and buprenorphine were found in: overall rates of NAS needing treatment; peak NAS scores; and head circumference. There was a reduction of severity of NAS in buprenorphine-exposed neonates defined as: the total amount of morphine needed in mg; length of hospital stay; and number of days for treatment of NAS. These three items are inter-related in that, the more morphine that is needed, the longer the days for treatment and the hospital stay.

Methadone or buprenorphine exposure concomitant with heavy cigarette smoking is associated with greater compromised birth outcomes including obstetrical complications, intrauterine growth restriction, birth defects, and Sudden Infant Death Syndrome.

Heavier cigarette smoking has been found to be related to peak NAS score and amount of time to reach peak score in newborns exposed to methadone. Higher NAS severity scores were found with heavier smoking in neonates exposed to methadone, buprenorphine or slow release morphine. Although heavier cigarette smoking was associated with longer duration of NAS treatment in methadone exposed babies, the association was not found in buprenorphine exposed babies.

It has been shown that decreasing the amount of cigarettes smoked can decrease the effects upon pregnancy and the newborn. Since heavy smoking during pregnancy has consistently been found to compromise perinatal outcomes, if abstinence in the presence of opioid maintenance therapy is not possible, decreasing the quantity should be the goal.

Although there is much that we still need to explore concerning the treatment of Neonatal Abstinence Syndrome, what we do know will provide comfort for the baby and decrease the chances of associated complications such as aspiration pneumonia, dehydration, and seizures. Using supportive care will enhance the baby's ability to feed normally, gain weight and permit adequate sleep. Through appropriate recognition, assessment and treatment of Neonatal Abstinence Syndrome coupled with good orientation of the future caretaker, we can better assure a nurturing, healthy environment for the child with a good chance of normal developmental outcomes.

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Ask The Toxicologist

Q: Is it possible to determine how much or how often a mother has been using a substance of abuse based on the result of a perinatal drug or alcohol test?

A: This is a very common question, but, unfortunately, there is no reliable way to determine maternal drug or alcohol usage from the results of a perinatal drug test. There are simply too many variables involved to be able to make a determination of how often or how much a person is using a particular substance based on the levels that are reported in a drug or alcohol test.

Sample types such as umbilical cord and meconium are known as reservoir matrices. Over time, drugs will collect in a reservoir matrix, however, they can also degrade in the matrix. This build-up and break-down of drug and alcohol biomarkers happens at the same time, making it impossible to accurately determine the amount of substance ingested at any one time.

Personal metabolism also plays a large part in how drug and alcohol biomarkers are collected in reservoir matrices. Age, body mass, overall health, and other factors can all affect how much of a substance may get trapped in a reservoir matrix. The number of doses required to generate a positive test result is highly variable from one donor to the next. This is especially true for alcohol testing.

The level of drug or alcohol that a newborn is exposed to in the womb can also be affected by the mother's placenta. The placenta can function as a barrier between mom and baby to protect the growing fetus from foreign substances that may be in the mother's system. How much protective effect the placenta has varies greatly from one woman to the next, just like personal metabolism. It may also depend on the drug, as research studies have suggested that some drugs may have an easier time crossing the placental barrier than others.

When testing any reservoir matrix, you are unable to back-track and determine time, dosage, or frequency because there are simply too many variables involved. In the end, a drug test using a reservoir matrix only indicates the presence or absence of a drug or alcohol biomarker within an appropriate window of detection. Attempting to determined the amount, manner, or timing of substance ingestion from the test results is speculation at best. Care should be taken to avoid such assumptions.

How Can Delays be Avoided in Specimen Processing?

A Message From USDTL Client Services

Specimen collection, preparation and handling are essential steps in obtaining accurate test results. Proper procedures must be followed to assure the integrity of the specimen, its safe and expedient delivery to the laboratory, and accurate processing once in the laboratory. Each test has specific requirements for specimen collection. Visit our website at www.USDTL.com to download the most up-to-date collection instructions and review the specimen requirements for each of our tests.

How to prevent common collection errors:

- Collect a sufficient quantity of the test specimen.
- Be sure to use the correct container for specimen collected.
- Ensure proper and accurate labeling of the specimen to provide all pertinent information.
- Use the tamper resistant Custody Control Form (CCF) barcode sticker.
- Tighten specimen container lids, preventing leakage and/or contamination of specimen.
- Have the donor initial the tamper evident requisition form barcode sticker.
- Make sure the CCF donor identification information is the same as the information on the specimen container.
- Indicate the required test on the CCF.
- Ensure you have the collector signature on the CCF.

Collection supplies can be quickly and easily requested from our website at www.usdtl.com by clicking on the Collection Supplies link at the top of the page.

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Quarterly Perinatal Newsletter

Upcoming Events:

- May 29-June 1 – American Academy of Pediatrics District VIII Section on Perinatal Pediatrics 38th Annual Conference - Denver, CO
- June 14-18 – Association of Women's Health, Obstetric and Neonatal Nurses 2014 Annual Convention – Orlando, FL
- July 13-16 – Obstetric and Neonatal Dilemmas Conference – Jackson Hole, WY
- August 21-22 – Arizona Perinatal Trust Perinatal Conference – Flagstaff, AZ
- September 3-6 – 14th Annual National Neonatal Nurses Conference – New Orleans, LA
- September 10-13 – National Association of Neonatal Nurses 30th Annual Educational Conference – Phoenix, AZ

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