Identifying Alcohol-Exposed Newborns
By Charles Plate, PhD, Laboratory Director, USDTL

Alcohol is a teratogen (causes birth defects) and acts principally by inducing a variety of neurological defects in the developing infant brain. Consumption of alcohol by a pregnant woman results in a spectrum of fetal development disorders that is now referred to as the Fetal Alcohol Spectrum Disorder (FASD) which includes physical, clinical, and behavioral effects. In a recent study to determine the prevalence, patterns, and predictors of alcohol consumption prior to and during various intervals of pregnancy in the United States, it was found that 30.3% of women reported drinking alcohol at some time during the pregnancy. The most common pattern reported was to drink during the first month of pregnancy and then abstain for the remainder of the pregnancy (13.9%). The second most common pattern was to drink through all the trimesters of the pregnancy (2.7%), and the third most common pattern was to abstain until the third trimester and then resume drinking (2.5%).

An unfortunate fact about FASD is that it is not diagnosed until several years after birth, when the alcohol damage has become irreversible and permanent. Diagnosis of FASD shortly after birth would allow societal and clinical treatments to be applied and, while these treatments cannot reverse FASD, they can benefit the child by limiting mental impairments, improving health care, and enriching the learning environment.

For over 20 years United States Drug Testing Laboratories, Inc. (USDTL) has been offering fatty acid ethyl ester (FAEE) testing of a newborn’s meconium that, when positive, is an indicator that the newborn has been exposed to alcohol in utero. If FAEEs are formed only in the presence of ethanol, meconium is not always available for testing, or there is an insufficient amount, and this happens with anywhere from 9 to 27% of newborns.

In 2008 USDTL introduced umbilical cord testing to determine exposure of the fetus to drugs of abuse in utero. In 2010 USDTL introduced CordStat® EtOH which measured the direct alcohol biomarker phosphatidylethanol (PEtH) in umbilical cord tissue. PEtH is a biomarker of dangerous (binge3) drinking in the last two to four weeks of pregnancy. We have determined the frequency of PEtH in umbilical cord tissue to be less than 1%, which is consistent with 0.5% of women who binge drink in the third trimester.

Recent research at USDTL has revealed the presence of ethyl glucuronide (EtG), another direct alcohol biomarker, in some umbilical cord tissues. To determine the frequency of EtG in umbilical cord tissue, we have examined over one thousand umbilical cords and have found EtG present in approximately 2% of them. These findings indicate that EtG is detecting newborns that have been exposed to alcohol levels lower than what result from binge drinking in the third trimester. It is possible that EtG is detecting either those mothers who drink during all the trimesters of their pregnancy (2.7%), or those mothers who abstain until the third trimester, and then drink (2.5%). In either case EtG appears to be superior to PEtH in detecting a broader spectrum of drinking habits and, thereby, the number of infants exposed to alcohol that it detects.

3. What is binge drinking? According to the National Institute on Alcohol Abuse and Alcoholism binge drinking is defined as a pattern of alcohol consumption that brings the blood alcohol concentration (BAC) level to 0.08% or more. This pattern of drinking usually corresponds to 5 or more drinks on a single occasion for men or 4 or more drinks on a single occasion for women http://www.cdc.gov/alcohol/faq.htm#bingeDrinking

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Marijuana Use in Pregnancy

By Bob Demareae, Clinical Projects Manager, USDTL

Marijuana is the illicit drug most often used by women during pregnancy. The 2010 National Survey on Drug Use and Health reported that 4.4% of women used illicit drugs at some point during pregnancy; marijuana was the primary drug of abuse for this group. Reportedly marijuana use in the study increased by more than 20 percent in the years 2000-2010.1

While considered a benign substance by many people, an increasing number of studies have identified potential adverse effects during pregnancy. Thus and animal studies have identified issues with brain development and cognitive function. Marijuana use in pregnancy has been associated with low birth weight, prematurity, shorter birth length and an increased likelihood of admission to the NICU.2 Other studies have reported increased language delays, decreased performance on intelligence tests, issues with hyperactivity, attention, and impulsivity.3

Marijuana is often used in combination with other substances, primarily tobacco and alcohol. In a 2008 study, Rivkin et al. reported that alcohol, marijuana and tobacco, either alone or in combination, may affect brain structure. A group of 35 young adolescents with confirmed prenatal drug exposure were tested by volumetric MRI. The subjects exhibited reductions in gray matter and total brain volume. The study found that exposure to any of the individual substances had an adverse effect, which increased with combined exposure.4

United States Drug Testing Laboratories, Inc. (USDTL) has been involved in monitoring various forms of drug and alcohol abuse since 1991. Currently each newborn test panel for the meconium, umbilical cord and breast milk sample matrices offers assays to identify marijuana exposure. At this time USDTL offers synthetic marijuana testing in urine samples only. New assays could be introduced if interest grows in testing newborns for the synthetic cannabinoids.

References

4. Rivkin MJ, Davis PE, Lemaster JL, Cabral HJ, Warfield SK, Mulkern RV, et al. MRI. The subjects exhibited reductions in gray matter and total brain volume. The study found that exposure to any of the individual substances had an adverse effect, which increased with combined exposure.4

Newborn Direct Ethanol Biomarkers

By Douglas Lewis, ScD; President and Scientific Director, USDTL

How can medical science accurately identify ethanol exposed newborns and do it in a manner timely enough to allow clinicians to take action and treat the ethanol affected babies to ameliorate the prenatal damage that the ethanol exposure may have produced? Since the first documentation of Fetal Alcohol Syndrome (FAS) and subsequent description of the continuum of Fetal Alcohol Spectrum Disorders (FASD), it has become increasingly imperative that newborns exposed to significant amounts of ethanol be diagnosed as early as possible and then treated early and intensively while the brain is most plastic and capable of new growth.

Historically, maternal self-report of ethanol consumption has been the principal means of obtaining fetal ethanol exposure histories. Maternal self reports, however, suffer from under reporting due to maternal anxiety, fear of potential consequences and reporting bias. The problems of self-report have been known for many years so a series of indirect markers of ethanol exposure were developed. These markers are actually somewhat non-specific markers of organ pathology that ethanol toxicity is the most likely agent, but not with any certainty. Of the many indirect pathological markers such as GGT, ALT, MCV, and CDT, CDT is considered the most specific but is less sensitive in women and of little value in umbilical cord blood, so it may not offer much self-report for histories in pregnancy.

The direct biomarkers, on the other hand, are not indirect measures of pathological damage but are direct measures of the non-oxidative metabolites of ethanol. These non-oxidative metabolites represent less than 1% of the total ethanol consumed, but since ethanol is consumed in hundreds of grams over time, the metabolites can reach significant and measurable concentrations in a variety of tissues. These direct ethanol biomarkers to be seriously studied in the past were the fatty acid ethyl esters (FAEE), a series of ethyl esters of various fatty acids that were known to be found in serum of adult individuals after consuming ethanol. Indeed, FAEE’s do appear in the meconium of newborns.

Unfortunately, FAEE’s appear at low concentrations in nearly all newborns and therefore required establishing a threshold level that would provide unequivocal evidence of ethanol consumption. This issue which reduced the sensitivity to about 60%, as well as the discovery that meconium, when exposed to ethanol post-passage, would synthesize FAEE’s in vivo without ethanol exposure. When coupled with the successful collection rate of only 70—80% of newborn cases, FAEE meconium analysis lacks sensitivity, specificity and universality for general use.

Another direct ethanol biomarker, Ethyl Glucuronide (EtG) also has been analyzed in meconium. While promising, the same lack of universality due to low collection rate for meconium applies here as well. EtG, however, has been analyzed in two much more universally available tissues, placenta and umbilical cord tissue in two separate laboratories in Italy and in the USA. Both labs have confirmed the utility of using EtG in these related tissues as a sensitive and specific marker for fetal alcohol exposure. EtG is currently the most reliable universally available ethanol biomarker available for diagnosing newborn ethanol exposure despite some gaps in the knowledge base. More research is being conducted to further define the level of drinking required to produce a positive and the time window reflected by a positive.

Much has been accomplished in the past twenty years to bring truly useful diagnostic tools such as the direct biomarker EtG, Ethyl Glucuronide to the forensic toxicologist practicing in the USA. This tool allows the forensic toxicologist to clinicians who desire to treat newborns exposed to high levels of ethanol during pregnancy. Much work remains to be done to further the diagnostic evaluations beyond just the diagnostic of fetal ethanol exposure and assist the clinicians with an understanding of the severity of the syndrome at the earliest possible moment. As we explore the various improvements in separation science and genetics, more breakthroughs are coming as we continue to push the frontiers of this rapidly developing area of toxicology.

Douglas Lewis, ScD, President and Scientific Director of USDTL for the past 21 years, spent five years in academia as an assistant professor of clinical pharmacology at Northwestern University Medical School while also serving as the head of the toxicology section at the Children’s Memorial Hospital in Chicago. He also began developing new specimens such as meconium for use in diagnosing substance-exposed newborns.

Announcing a New Area of Research

USDTL has made significant investments in laboratory detection of heavy fetal alcohol exposure through the use of Phosphatidylethanol (Peth) analysis of newborn blood spots. This ground-breaking achievement utilizes a universally available specimen thereby removing a major barrier of sample collection from newborns. A further challenge, however, is to determine the extent of damage that ethanol exposure may have caused. To explore the means to this diagnostic information, USDTL has launched a new area of research with the addition of Aileen Baldwin, Ph.D., M.P.H. Dr. Baldwin comes to USDTL following a post-doctoral fellowship at the Pasteur Institute in Paris, France and obtained her Ph.D. in Molecular Biology and Masters in Public Health at Northwestern University.

A tandem application to the NIH to investigate epigenetic changes in DNA from blood spots of newborns identified to have been exposed to excessive levels of ethanol as determined by detection of Peth in their blood spots.

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