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USDTL®
The Leader in Newborn Toxicology
QUARTERLY NEWS

Detecting Fetal Exposure To Heroin Using CordStat®

By Douglas Lewis, President, Scientific Director USDTL

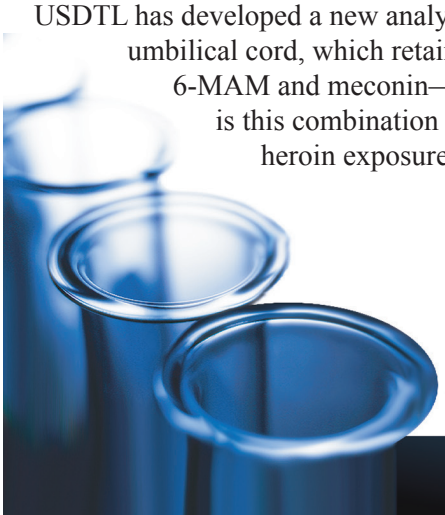
Since it has been possible to routinely screen newborn specimens for the presence of opiates, the chief complaint from clinicians and social service personnel to our laboratory has been "Why can't you tell us if this baby has been exposed to heroin?"

The question is certainly legitimate. The problem in the past was that, in many cases, the mother was given morphine during labor and delivery which caused the lab to report an opiate positive with morphine confirmed. Such a result stated the obvious- mom had morphine in her system- but could not provide any historical information for the newborn who went on to exhibit all the signs and symptoms of Neonatal Abstinence Syndrome (NAS).

With no further proof, mandatory reporters were stuck with only maternal self-report to verify heroin exposure. Mothers seldom provide such admissions voluntarily.

The primary reason the lab tests failed to identify heroin or its metabolite 6-monoacetylmorphine (6-MAM) was due to the extremely short life span of these two compounds in the body. Both heroin and 6-MAM have reported half-lives of less than ten minutes leaving the active metabolite, morphine, the compound that is most often identified.

To overcome this problem of detecting actual heroin use, USDTL has developed a new analytical test utilizing baby's umbilical cord, which retains trace amounts of 6-MAM and meconin—a heroin biomarker. It is this combination that is proof positive of heroin exposure.



By increasing both the sensitivity and the breadth of the opiate analysis, CordStat can identify more heroin-exposed newborns than ever before.

The improvements in the sensitivity begin in the initial screening for the opiate class using ELISA technology. By carefully adjusting the conditions, USDTL has been able to reduce the screening cutoff from 2.0 ng/gm to 0.5 ng/gm. The opiates that are cross-reactive are morphine, codeine, hydrocodone, and hydromorphone. The confirmation cutoffs have been reduced on LC-MS/MS from 2.0 ng/gm each to 0.5 ng/gm for morphine, codeine, hydrocodone, and hydromorphone and to 0.2 ng/gm for 6-MAM and meconin.

In the process USDTL also lowered the oxycodone, oxymorphone, cocaine and benzoylecgonine cutoffs as well. These sensitivity enhancements have improved diagnostic acumen to help you provide your tiniest patients with the most appropriate care.

Douglas Lewis is president and scientific director of USDTL. He began developing new specimens such as meconium for use in diagnosing substance-exposed newborns in 1991, establishing USDTL as *The Leader in Newborn Toxicology.*®

Ask a Toxicologist

Q: What is Meconin and why is it important in newborn toxicology?

A: Morphine is the predominant metabolite of heroin, but morphine is also a stand alone drug and a metabolite of codeine. Some mothers are provided morphine during delivery. Historically, there have been instances where heroin using moms could not be distinguished from moms given morphine during delivery. Meconin is a contaminating constituent from poppy that is present in heroin. Therefore, like Monoacetylmorphine - a metabolite of heroin, the presence of Meconin indicates the use of heroin and when found in umbilical cord tissue indicates fetal exposure to heroin.

Early Identification Improves Outcomes in Newborns Exposed to Alcohol During Pregnancy

by Bob Demaree, Clinical projects Manager, USDTL

Maternal consumption of alcohol during pregnancy can result in a spectrum of life-long disorders for the newborn. These negative outcomes include physical characteristics like abnormal facial features and reduced height and weight. Central nervous system issues related to attention deficit or physical coordination may also be present. Other factors like maternal age, parity, nutritional status and drinking patterns can impact individual outcomes in the neonate.

A recent study using MRI scans found changes in brain growth patterns in children exposed to alcohol/ethanol while *in utero*. Lebel et al. found decreased cortical volumes and reduced brain plasticity in children, ages 5 to 15, whose mothers drank heavily while pregnant.[3]

These children demonstrated lower intelligence, an increased level of facial dysmorphology, and little change in brain volume over time. Dr Lebel stated "These findings further illustrate the need for early intervention, as they demonstrate that effective treatments may not only address current difficulties, but may also impact developmental trajectories during childhood and adolescence in a positive way".

Therefore, early identification is key to improving negative factors resulting from maternal drinking. The CDC references a number of treatment options for alcohol-exposed newborns, these include medication, behavior and education therapy, as well as parent training.

Streissguth et al also identified a group of protective factors that may limit Fetal Alcohol Spectrum deficits. These include early diagnosis, involvement in special education, social services, as well as a stable and nurturing home life – free of violence.[2]

Unfortunately the majority of alcohol-exposed newborns lack any physical characteristics related to this exposure.[1] In the past, physical characteristics along with maternal self report have been the only way to diagnose alcohol exposure leading to FASD. Therefore, confirmation of maternal alcohol use in pregnancy, depended, to a large extent, upon maternal self report.

Now the identification of alcohol biomarkers in umbilical cord tissue provides an objective method for identifying prenatal exposure.

In January 2013, USDTL introduced a new BloodSpot ™ assay using an abnormal phospholipid, phosphatidylethanol (PEth), as a marker of fetal alcohol exposure occurring in the last 2-4 weeks of pregnancy. PEth is only present following a binge of 5 or more drinks. The assay can help identify a heavy drinking life style as it is unlikely that a mother would begin binge drinking after week 35 of gestation.

Umbilical cord blood can be spotted on filter paper at birth. The sample is then immediately placed into the USDTL BloodSpot™ drying box–no waiting necessary. BloodSpot assays are easy to collect, stable in shipment and simple to store. Results are available 1-3 days after the sample is received by USDTL.

In a study to be published in early 2013, Bakhireva et al. reports a 6.5 percent positivity rate when using the USDTL BloodSpot-EtOH assay in a high risk population.[4]

This BloodSpot-EtOH test method can also be used to monitor women in antenatal treatment programs. In this case, the sample is collected from a finger stick provided by the mother.

Please contact Bob Demaree, at bob.demaree@usdtl.com, for additional information regarding this new test method.

References:

1. Streissguth AP, Bookstein FL,Barr HM, et al. (2004). Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. Developmental and Behavioral Pediatrics, 5(4), 228-238

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4. Kasten CH. 2012. The National Children's Study. Abstracts of the National Children's Research Study Research Day 2011. Am J Med Genet Part A 158A:2385-2390

Ask a Toxicologist

Q: Is there a test that can differentiate between fetal exposure to heroin and fetal exposure to morphine during the birthing process?

A: Yes. The umbilical cord from a baby whose mother was administered morphine during delivery will only be positive for morphine. The umbilical cord of a baby that is positive for Meconin and/or Monoacetylemorphine in addition to morphine is indicative of heroine exposure.

Knowing the difference can help doctors and nurses provide a better outcome for baby's treatment plan.

In The News:

Nov. 14, 2012 — Relatively small levels of exposure to alcohol while in the womb can influence a child's IQ, according to a new study led by researchers from the universities of Bristol and Oxford using data from over 4,000 mothers and their children in the Children of the 90s study (ALSPAC) and published November 14 in PLOS ONE.

Current advice to pregnant women about moderate alcohol consumption during pregnancy is contradictory, with some official guidelines recommending complete abstinence and others suggesting that moderate use is safe. Previous studies have produced conflicting and inconsistent evidence on the effects of moderate alcohol intake on a child's IQ. This may be because it is difficult to separate the effects of moderate alcohol consumption from other lifestyle and social factors, such as smoking, diet, affluence, mother's age and education.

This study, believed to be the first substantial one of its kind, used genetic variation to investigate the effects of moderate (<1-6 units of alcohol per week) drinking during pregnancy among a large group of women and their children. Since the individual variations that people have in their DNA are not connected to lifestyle and social factors, the approach removes that potential complication.

Four genetic variants in alcohol-metabolising genes among the 4,167 children were strongly related to lower IQ at age eight. The child's IQ was on average almost two points lower per genetic modification they possessed.

But this effect was only seen among the children of women who were moderate drinkers. There was no effect evident among children whose mothers abstained during pregnancy, strongly suggesting that it was the exposure to alcohol in the womb that was leading to the difference in child IQ. Heavy drinkers were not included in the study.

When a person drinks alcohol, ethanol is converted to acetaldehyde by a group of enzymes. Variations in the genes that 'encode' these enzymes lead to differences in their ability to metabolise ethanol. In 'slow metabolisers', peak alcohol levels may be higher and persist for longer than in 'fast metabolisers'.

It is believed that the 'fast' metabolism of ethanol protects against abnormal brain development in infants because less alcohol is delivered to the fetus, although the exact mechanisms are still unclear.

Previous studies have relied on observational evidence, but this is problematic. Observational studies often find that moderate drinking is beneficial compared to abstention, but this is because mothers who drink in moderation during pregnancy are typically well educated, have a good diet and are unlikely to smoke -- all factors which are linked to higher IQ in the child, and which mask any negative effect that exposure to alcohol may have.

This study, on the other hand, looked at moderate (rather than high) alcohol intake in over 4,000 women and used a novel technique known as Mendelian randomization, which is a scientifically robust way of investigating the links between exposures and later diseases, using genetic variants which modify exposure levels and which are not influenced by lifestyle or other factors.

The mothers' alcohol intake was based on a questionnaire completed when they were 18 weeks' pregnant. It included questions on the average amount and frequency of alcohol consumption before the current pregnancy, during the first trimester, and in the previous two weeks or at the time when they first felt the baby move. One drink was specified as one unit of alcohol.

Around 32 weeks of gestation the mother completed another questionnaire in which she was asked about her average weekday and weekend alcohol consumption, from which weekly intake was derived. Any woman who reported drinking, even if it was less than one unit per week either in the first trimester or when she felt the baby first move was classified as drinking during pregnancy.

At approximately 18 and 32 weeks of pregnancy, the women were also asked on how many days during the past month they had drunk two pints of beer (or the equivalent amount of alcohol). Any women who reported doing this on at least one occasion was classified as a binge drinker for the purposes of this analysis and were excluded.

The children's IQ was tested when they were aged eight using a shortened version of the Wechsler Intelligence Scale for Children from which an overall age adjusted total score was derived.

Speaking about the findings, the report's main author, Dr Sarah Lewis, said: 'Our results suggest that even at levels of alcohol consumption which are normally considered to be harmless, we can detect differences in childhood IQ, which are dependent on the ability of the fetus to clear this alcohol. This is evidence that even at these moderate levels, alcohol is influencing fetal brain development.'

Dr Ron Gray from the University of Oxford who led the research added: 'This is a complex study but the message is simple: even moderate amounts of alcohol during pregnancy can have an effect on future child intelligence. So women have good reason to choose to avoid alcohol when pregnant.'

Story Source:

The above story is reprinted from materials provided by University of Bristol.

Journal Reference:

1. Sarah J. Lewis, Luisa Zuccolo, George Davey Smith, John Macleod, Santiago Rodriguez, Elizabeth S. Draper, Margaret Barrow, Rosa Alati, Kapil Sayal, Susan Ring, Jean Golding, Ron Gray. Fetal Alcohol Exposure and IQ at Age 8: Evidence from a Population-Based Birth-Cohort Study. PLoS ONE, 2012; 7 (11): e49407 DOI: 10.1371/journal.pone.0049407

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- February 27-March 30 – Gravens – Clearwater Beach, FL
- March 7-8 – March of Dimes – Lisle, IL
- March 14-15 – Drug Exposure During Pregnancy – Louisville, KY
- March 21, 22, 23 – Obstetrical Challenges – Phoenix, AZ

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