Newborn Drug and Alcohol Testing

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Agenda

1. Drug Testing History
2. Current Fetal Drug Testing Methods
3. Umbilical Cord Assay
4. Maternal Drug/EtOH Testing
Diagnosing Fetal Drug & Alcohol Exposure

- Prior to early 1970’s, diagnosis relied on maternal self-report
- 1972 Physical diagnosis on facial dysmorphology for FAS published
- 1972 EMIT urine immunoassays introduced.
Diagnosing Fetal Drug & Alcohol Exposure

- Mid 1970’s EMIT allows newborn & maternal urine tests for drugs of abuse
- Maternal testing requires informed consent
- Newborn testing does not require maternal consent
- Newborn urine testing slowly adopted
Diagnosing Fetal Drug & Alcohol Exposure

- 1982 Cocaine babies arrive
- Huge demand for newborn testing starts
- Only 50% of urine tests ordered on NICU admits actually administered.
- Good data on drug exposure for neonates needed, but not being obtained
- Outcome measures deficient due to lack of true exposure data
Diagnosing Fetal Drug & Alcohol Exposure

- Outcomes originally ascribed to maternal drug use - just wrong.
- Urine lacked a long term direct marker for alcohol exposure
- Many cocaine effects were actually fetal alcohol effects
- A clear need arose for improved neonatal drug and alcohol exposure testing
Diagnosing Fetal Drug & Alcohol Exposure

- 1988 1st report on meconium screening for drugs of abuse
- 1990 1st report on meconium GC/MS confirmation for cocaine
- 1991 Meconium 5 drug panel available from reference lab (MecStat-5sm)
Diagnosing Fetal Drug & Alcohol Exposure

- 1992  1st experiments for determining Fatty Acid Ethyl Esters in meconium for alcohol exposure
- 1996  NIAAA funds SBIR phase I grant for FAEE’s in meconium
- 1998  FAEE’s in meconium available from reference lab (MecStat-EtOH^{sm})
Diagnosing Fetal Drug & Alcohol Exposure

- 2002: Expanded panels in meconium for prescription Rx’s (Oxycodone)
- 2005: NIDA funds SBIR phase I then phase II grants for drugs in umbilical cord
- 2007: Umbilical cord drugs of abuse 12 panel available from reference lab (CordStat™)
Diagnosing Fetal Drug & Alcohol Exposure

- 2007 NIAAA funds SBIR phase I grant for Phosphatidylethanol (PEth) in U-cord
- 2007 NIAAA funds SBIR phase I then Phase II for EtG in hair/nails
- 2010 Dried blood spot PEth available from reference lab (PEthStat\textsuperscript{sm})
- 2011 Hair/nails EtG available from reference lab (NailStat-EtOH\textsuperscript{sm})
Drug Test Sample Matrices

- Urine
- Hair
- Meconium
- Breast Milk
- Umbilical Cord
- Nails
- Oral Fluid
- Vernix
<table>
<thead>
<tr>
<th>U-Cord &amp; Meconium Drug Panels</th>
</tr>
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<tbody>
<tr>
<td><strong>5-Drug Panel</strong></td>
</tr>
<tr>
<td>Amphetamines</td>
</tr>
<tr>
<td>Cannabinoids</td>
</tr>
<tr>
<td>Cocaine</td>
</tr>
<tr>
<td>Opiates</td>
</tr>
<tr>
<td>PCP</td>
</tr>
</tbody>
</table>
Prescription Drug Abuse

- Prescription drug abuse now rivals the abuse of illegal drugs in the United States.

BBC News March 1, 2006
Figure 2.5 Lifetime Nonmedical Use of Selected Pain Relievers among Young Adults Aged 18 to 25: 2002-2004

- Any Pain Reliever
- Vicodin®, Lortab®, or Lorcet®
- Percocet®, Percodan®, or Tylox®
- Hydrocodone Products
- OxyContin®
- Oxycodeone Products

- 2002
- 2003
- 2004

α Difference between the 2003 estimate and the 2004 estimate is statistically significant at the .05 level.

β Difference between the 2002 estimate and the 2004 estimate is statistically significant at the .05 level.
Newborn Urine Drug Testing

- Difficult to collect
- Limited window of exposure
- High false negative rate
Meconium Drug Testing

- Easier to collect than urine
- Up to 20 week window of exposure
- Drugs stable for up to 2 weeks
- Accepted standard for 15 years
Meconium Limitations

- Meconium not available in 8-20% of births
- Stressed babies in greatest need of testing
- Some newborns take several days to pass meconium
<table>
<thead>
<tr>
<th>Drug</th>
<th>2004</th>
<th>2005</th>
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<tbody>
<tr>
<td>Cannabinoids</td>
<td>16.4 %</td>
<td>14.7 %</td>
</tr>
<tr>
<td>Ethanol</td>
<td>10.5 %</td>
<td>13.7 %</td>
</tr>
<tr>
<td>Cocaine</td>
<td>10.1 %</td>
<td>10.3 %</td>
</tr>
<tr>
<td>Opiates</td>
<td>4.8 %</td>
<td>6.9 %</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>6.6 %</td>
<td>6.0 %</td>
</tr>
<tr>
<td>Methadone</td>
<td>5.0 %</td>
<td>5.0 %</td>
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</table>
Meconium Positivity Rate

\[
\begin{array}{ccccccccccc}
\text{AMP} & \text{COC} & \text{OPI} & \text{PCP} & \text{THC} & \text{BAR} & \text{BZP} & \text{MTD} & \text{PPX} & \text{FAEE} \\
\end{array}
\]

\[
\begin{array}{ccccccccccc}
0 & 2 & 4 & 6 & 8 & 10 & 12 & 14 & 16 & 18 & 20 \\
\end{array}
\]
Umbilical Cord

- Sample available in almost all cases
- Easier to collect than meconium
- Results may be reported sooner
Diagnosing Fetal Drug & Alcohol Exposure

• Testing Umbilical Cord
  – Provides ~ Equal Sensitivity as Meconium
  – Available on Every Newborn at birth
  – Provides More Rapid Results
  – Lowers Nursing Costs
  – Lots of specimen - virtually no QNS’s
NIDA Phase I Umbilical Cord Study

- Study to identify correlation of drug levels in cord vs meconium samples
- 118 paired meconium and cord samples collected
- Cord samples screened for NIDA-5 Panel
Meconium vs Umbilical Cord Agreement

- Amphetamines: 96.6%
- Opiates: 94.9%
- Cocaine: 99.2%
- Cannabinoids: 90.7%
Methamphetamine

- 3 samples positive in cord but negative in meconium
- Cord results confirmed by GC/MS
- Cord may be more sensitive for detecting methamphetamine
Umbilical Cord v. Meconium

AMPHETAMINES

<table>
<thead>
<tr>
<th>UCORD</th>
<th>MECONIUM</th>
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<tr>
<td>+</td>
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<tr>
<td>-</td>
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%AGREEMENT = 96.6
Umbilical Cord v. Meconium

OPIATES

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<th>MECONIUM</th>
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<td>+</td>
</tr>
<tr>
<td>-</td>
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<table>
<thead>
<tr>
<th>UCORD</th>
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</thead>
<tbody>
<tr>
<td>+ 7 4</td>
</tr>
<tr>
<td>- 2 99</td>
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%AGREEMENT = 94.9
Umbilical Cord v. Meconium

<table>
<thead>
<tr>
<th></th>
<th>COCAINE</th>
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<tbody>
<tr>
<td></td>
<td>MECONIUM</td>
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<table>
<thead>
<tr>
<th></th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCORD</td>
<td>+</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>-</td>
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%AGREEMENT = 99.2
Umbilical Cord v. Meconium

CANNABINOIDs

<table>
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<tr>
<th>MECONIUM</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
</tr>
<tr>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>UCORD</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>-</td>
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<table>
<thead>
<tr>
<th></th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>-</td>
<td>2</td>
<td>93</td>
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</tbody>
</table>

%AGREEMENT = 90.7
### Umbilical Cord v. Meconium

**Phencyclidine (PCP)**

<table>
<thead>
<tr>
<th>UCORD</th>
<th>+</th>
<th>-</th>
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</thead>
<tbody>
<tr>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>-</td>
<td>0</td>
<td>99</td>
</tr>
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</table>

**%Agreement = 100**
Phase II Umbilical Cord Study

- Extraction procedures now optimized
- Samples were collected from mixed ethnic, socioeconomic, & geographic populations
- Screening & confirmation methods were validated
Umbilical Cord Drug Panels

- U-Cord-5 Drug Panels became available October 2007
- U-Cord-7,9 &12 became available 2nd and 3rd Quarter 2008
- U-Cord buprenorphine available 3/2011
- U-Cord-EtOH (Phosphatidylethanol) under further development
Cord Collection
Cord Collection
Cord Collection
Send to laboratory

Specimen to Lab
Drug Detection Times

- Meconium
- U-Cord
- Hair
- Amniotic fluid
- Blood
- Urine
Current & Pending Studies 2011

- Phase II U-Cord vs Meconium - Completed
- Phase II Alcohol Biomarker in Hair/Nails
- Phase II PEth (Alcohol Biomarker) in U-Cord
- NICHD U-Cord Stillbirth Study - Completed
- Phase II PEth in Newborn dried blood spots
Drug use among pregnant women aged 15-44

<table>
<thead>
<tr>
<th>Report Date</th>
<th>Time Period</th>
<th>Drugs</th>
<th>Alcohol Use</th>
<th>Binge Alcohol</th>
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<tbody>
<tr>
<td>Jan 04</td>
<td>2002</td>
<td>3.0 %</td>
<td>9.0 %</td>
<td>3.0 %</td>
</tr>
<tr>
<td>June 05</td>
<td>2002-2003</td>
<td>4.3 %</td>
<td>9.8 %</td>
<td>4.1 %</td>
</tr>
<tr>
<td>Jan 06</td>
<td>2004</td>
<td>4.6 %</td>
<td>11.2 %</td>
<td>4.5 %</td>
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Laboratory Studies
FAEE’s in Meconium

Quartiles

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Hawaii</th>
<th>Utah</th>
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<tbody>
<tr>
<td>1st Qtr</td>
<td>1059</td>
<td>1139</td>
</tr>
<tr>
<td>2nd Qtr</td>
<td>3133</td>
<td>3076</td>
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<tr>
<td>3rd Qtr</td>
<td>6628</td>
<td>7674</td>
</tr>
<tr>
<td>4th Qtr</td>
<td>62115</td>
<td>50143</td>
</tr>
</tbody>
</table>

ng/g
FAEE’s in Meconium Limitation

- Sensitivity is only ~ 70%

- Meconium available on only ~ 80%
  - Need a more universal specimen
  - Need better clinical sensitivity

- Best current candidates are DBS PEth and U-Cord PEth
Phosphatidylethanol (PEth) in Umbilical Cord

• Phosphatidylethanol is a unique, pathological phospholipid only formed when EtOH is present within cells
• Humans have no enzyme to destroy PEth
• PEth incorporates into cell membranes and remains until it spontaneously decomposes.
Phosphatidylethanol (PEth) in Umbilical Cord

- Current NIAAA grant to determine feasibility of PEth in umbilical cord as diagnostic test.
- 200 paired meconium-umbilical cord specimens from drug/EtOH suspected exposed newborns.
- Results currently under statistical analysis.
Phosphatidylethanol (PEth) in Umbilical Cord

- PEth found in red blood cells and virtually all tissues of heavy EtOH users
- PEth concentrations closely follow EtOH dosing
- Umbilical cord forms PEth
- PEth in umbilical cord is extractable and detectable.
Phosphatidylethanolol (PEth) in Dried Blood Spots

- DBS are universally collected for medical genetics testing
- PEth now detectable from blood spots
  - Requires only 3 punches from single spot
  - Can use same collection as genetics card
- In U-cord PEth Phase I DBS data available
- DBS PEth may be the best marker for dangerous EtOH exposure
Phosphatidylethanol (PEth) in Dried Blood Spots

- Ethyl Alcohol is so simple a drug
  - It is extremely difficult to monitor long term use
  - Direct Biomarkers work in adults
- PEth in blood spots now used to confirm urine EtG/EtS positives in Physician Health programs
- DUI study showed blood PEth correlated best with ignition interlock breath data
Dried Blood Spots - New Tests

• Opioid blood levels for pain management
  – Fentanyl, morphine and hydromorphone
  – Levels measured from heal stick DBS
• Ketamine and methadone in development
• Buprenorphine and propofol under consideration
Maternal Drug/EtOH Monitoring

• 1st - Requires specific consent by Mom
  – Ferguson v. City of Charleston 2000
• If Mom consents, then testing available
• EtOH monitoring follows a 3-3-3 modality
  – ~ 3 day window for urine tests
  – ~ 3 week for DBS PEth
  – ~ 3 month window for hair/nails tests
• Drug monitoring follows a 3-3modality
  – Same windows for urine and hair/nails
  – No blood equivalent for 3 week window
Maternal Drug/EtOH Monitoring

• What can be inferred from a Positive
• It is NOT reasonable to infer from a single test:
  – Timing of dose
  – Frequency of dose
  – Amount of dose
• Data on DBS PEth and hair/nail EtG do indicate a relationship of dose to threshold (but depends on how one drinks)
QUESTIONS
&
PRINTABLE SLIDE NOTES

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