NAS and FPQC:

Reflections after the State *Ad Hoc* NAS Advisory Committee

September 9, 2013

Effect of Opioids on Fetus/Child

- Slight increased risk of certain types of congenital heart disease (conotruncal defects, AV canals, hypoplastic left heart syndrome), neural tube defects (anencephaly, spina bifida), gastroschisis – odds ratios are 1.8-2.7
- Difficult to identify a clearly independent effect on fetal growth, but preponderance of evidence suggests a mild effect
- Profound neurobehavioral abnormalities at birth due to opioid withdrawal
- Emerging evidence for increased risk of behavioral problems, attention deficit issues in school age child; older children with ? memory/perception issues
- Studies on longer term executive functioning or IQ are lacking

Questions with Uncertain Answers Requiring Research

- Under what circumstances might detoxification be a safe and effective alternative to opioid maintenance therapy?
- What is the distribution of etiologies for NAS in Florida?
- What are the most effective primary prevention strategies?
- Is there a role for universal maternal or infant drug testing?
- What is the rate of recurrence of NAS in a subsequent sibling?
- Is there a way to predict which infants are at lower (or higher) risk for severe NAS?

Questions with Uncertain Answers Requiring Research

- What is the correlation of NAS as defined by particular ICD-9 hospital discharge codes for NAS vs. NAS as diagnosed by chart review using a rigorous case definition of NAS?
- What is the optimal non-pharmacologic and pharmacologic treatment strategy for NAS in infants?
- What is best approach to “outliers”?
- What is the role of the mother/family rooming-in at the hospital?
- Under what circumstances might neonatal outpatient treatment be safe and effective?
- What is the long-term outcome of infants exposed to opioids in the womb and continuing after birth?

Maternal Detoxification

- ACOG recommendation: Detoxification during pregnancy is not advised due to risk of spontaneous abortion, fetal demise, high rate of recidivism.
- But: in some communities, hard choices are necessary.
- New thoughts: in Stanhope TJ, Gill LA, Rose C. Chronic opioid use during pregnancy: maternal and fetal implications. Clin Perinatol 2013; 40:337-350.
  - In motivated patients, optimal time is second or third trimester.
  - Careful monitoring once dose is tapered.

Etiologies of NAS: Tennessee, Jan-Aug 2013

• Supervised OMT	43.9%
• Supervised pain therapy	21.6%
• Supervised psyciatric/neuro therapy	8.2%
• Opioids without a physician prescription	38.8%
• Use of illicit drugs (e.g., heroin)	27.8%
• Signs of NAS without evidence of exposure	2.0%
• No response provided	2.5%

More Mothers on Prescription Opioids

- Single provider obstetric practice (Mayo Clinic, Rochester)
- Retrospective study 1998-2009; 26,314 deliveries
- Rate of chronic opioid use increased by a factor of 5 (from 2 to 10 per 1000 deliveries)
- Cancer; chronic pain; GU pathology; headaches; orthopedic pathology
- NAS occurred in 5.6%
- Tennessee: Opioid use in first trimester rose from 8.6% of pregnancies in 1995 to 20.1% in 2009

Kellogg A et al. Am J Obstet Gynecol 2011;204:259.e1-4.

Factors for Rise in Prescription Rx

- Development of extended-release opioids
- Pharmaceutical company promotion
- Higher social acceptability
- Perception of less harm

National Survey on Drug Use and Health

http://www.samhsa.gov/data/NSDUH/2k11Results/NSDUHresults2011.htm

Recent Use (within 1 month of survey)	Illicit Drug Use (%)	Alcohol Binge or Heavy Drinking (%)	Cigarettes (%)
US Population ≥ 12 Years	8.7 MJ 7.0 COC 0.5 HAL 0.4	22.6	26.5
US Pregnant Women 15-44 Years	5.0 0.2% LM HER 0.9% LM RX Pain	2.6	17.6

National Survey on Drug Use and Health 2011

DEPENDENCY OR ABUSE BY U.S. POPULATION

- MARIJUANA 4,200,000
- PAIN RELIEVERS 1,800,000
  - FRIEND/RELATIVE (free) 54% (4/5 from single MD)
  - PRESCRIBED BY 1 MD 18%
  - FRIEND/RELATIVE (bought) 12%
  - OTHER 5%
  - STOLEN 4%
  - DRUG DEALER 4%
  - PRESCRIBED BY > 1 MD 2%
  - INTERNET PURCHASE 0.3%
- COCAINE 821,000

Lower prescription drug use, resurgence of illicit drug use?

- A new report by the Substance Abuse and Mental Health Services Administration (SAMHSA) shows that people aged 12 to 49 who had used prescription pain relievers nonmedically were 19 times more likely to have initiated heroin use recently (within the past 12 months of being interviewed) than others in that age group (0.39 percent versus 0.02 percent). The report also shows that four out of five recent heroin initiates (79.5 percent) had previously used prescription pain relievers nonmedically.

Lower prescription drug use, resurgence of illicit drug use?

- The number of people reporting that they have used heroin in the past 12 months rose from 373,000 people in 2007 to 620,000 people in 2011. Similarly, the number of people dependent on heroin in the past 12 months climbed from 179,000 people in 2007 to 369,000 people in 2011. The number of people starting to use heroin the first time in the past 12 months also increased from 106,000 people to 178,000 people during the same period.

Universal drug testing at Cincinnati

- All pregnant women delivering in Greater Cincinnati will be tested for drugs (Greater Cincinnati Health Council).
- University of Cincinnati Medical Center, Cincinnati Children's Hospital Medical Center, TriHealth's Good Samaritan and Bethesda North hospitals, Christ Hospital Health Network, Mercy Health's Anderson and Fairfield hospitals and St. Elizabeth Healthcare.
- NAS increased from 11 per 1,000 births in 2009 to 36 per 1,000 births in 2012
- Not meant to be "punitive", but "designed to help the family, the mother and the infant."
- Ensure that the hospital can monitor the infant after birth and provide the appropriate care if the infant begins to show withdrawal symptoms.

Role of genetic factors

- Single nucleotide polymorphisms (SNPs) of OPRM1 and COMT genes predict higher risk of addiction in adults
- OPRM1 118 AG/GG (about 12-15% in whites) associated with decreased LOS (by 8.5 d) and decreased need for pharm rx (48% vs. 72%) vs. AA
- COMT 158 AG/GG (about 50% in whites) associated with decreased LOS (by 10.8 d) and decreased need for 2 drugs (18% vs. 56%) vs. AA

Neonatal Treatment of NAS

- What is appropriate environment of care (physical; composition and roles of caretakers)?
- When is optimal time to begin pharmacologic treatment (role of NAS scoring)?
- What is optimal drug regimen?
- How should “outliers” be treated (those infants who do not respond to high doses of 2 drugs)?
- What is optimal weaning regimen?
- What is the role of outpatient management?

Primary Drug Treatment

- Methadone vs. morphine?
- NIH funded trial, PI Jonathan Davis at Tufts
  - Powered for decreased in LOS, n=184, 5 centers
  - Oral methadone: high EtOH equivalent to 3 beers/week. Had to compound methadone powder.
  - Oral morphine: Many solutions with high propylene glycol. Preservative free preparation more expensive.
- Also will look at long term outcomes.

Dr. Armstrong's Charge to Committee

- To provide insight and recommendations on strategies for data collection and reporting
- To determine what data DOH should collect to have the greatest impact on disease trends
- To advise how best to obtain requisite data

Prevention of NAS

- Primary:
  - Prevent non-medically indicated opioid use
  - Prevent pregnancy
- Secondary:
  - Screen pregnant women for opioid use; ensure good prenatal care
- Tertiary:
  - Treat pregnant women
  - Treat infants with NAS

Some considerations for NAS as a "reportable condition"

- What is the accuracy of surveillance?
  - What is the gold standard for the case definition
- What is the appropriate timeliness of reporting and analysis?
  - Hospital discharge codes
  - Medicaid claims data
- How is confidentiality maintained but yet provide enough information to make correlations with other databases?

Case definition?

- "Clinical diagnosis"
  - Combination of motor, autonomic, gastrointestinal signs consistent with opioid withdrawal
- Laboratory confirmation
  - Maternal urine; infant urine, meconium, hair, umbilical cord
- History of maternal drug use
- Categories:
  - Confirmed – Clinical diagnosis and lab confirmation
  - Probable – Clinical diagnosis, negative lab, positive history
  - Suspected – Clinical diagnosis only

Purposes of reporting

- Public health surveillance: follow trends in NAS over time by county: fairly straightforward
  - How accurate; how timely?
- Etiology of NAS: more complex, requires more data than is present in hospital discharge or claims data – e.g.,
  - What drugs
  - Why drugs
- Research initiatives: most complicated, perhaps done selectively, voluntarily
  - Link to type of treatment, genetics, LOS, multiple drug use, infant survival, etc.

Can we supplement hospital discharge and Medicaid claims database?

- Laboratory tests
- Maternal drug prescriptions
- Maternal in-hospital drug treatments
- Infant in-hospital drug treatments

Ad Hoc Committee Recommendations

1. Add Neonatal Abstinence Syndrome (NAS) to the Florida DOH roster of reportable conditions and diseases

Ad Hoc Committee Recommendations - 1

- Recommend that hospitals assume greater responsibility for including ICD-9 code (779.5) in the final discharge diagnoses for babies with signs of NAS

- Task the ad hoc committee to develop educational materials that:
  - Provide a clear case definition of NAS for hospital reporting purposes
  - Address confidentiality concerns associated with reporting
  - Distinguish and clearly decouple disease reporting from the process of reporting abuse and neglect

Ad Hoc Committee Recommendations - 1

- Work with Dr. Armstrong and partners (e.g., FHA, FMA, FOMA) to ensure that hospitals and physicians are adequately alerted and trained about the reporting requirements.
- Publish semiannual descriptive summaries and trends of NAS cases by county
- Develop a legislative budget request to seek funding to support educational efforts, data management, and promulgation of data summaries

ICD-9 Codes

- 779.5 Drug withdrawal syndrome in a newborn of a drug-dependent mother
- 760.62 Narcotics afffecting fetus or newborn via placenta or breast milk
- How many infants develop signs of withdrawal after hospital discharge that are not recognized, not treated, or not reported?

Ad Hoc Committee Recommendations

2. Validate the sensitivity and specificity of hospital discharge data through an CDC Epi Aid project (collaboration with CDC has begun)

Ad Hoc Committee Recommendations

3. Ask the Attorney General and the AG Task Force to develop procedures that would safeguard mothers from punitive actions that might result from NAS reporting