LASACT Presentation – Outline
Pregnancy & Addiction
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Goals

- Develop a common language between medicine and counseling therapy
- Develop a platform for discussion
- Provide up-to-date information about addiction and pregnancy
- Foster a multidisciplinary clinical approach
- Encourage sharing and networking between professions

Topics

- Pregnancy terminology
- Drugs and development
- Mothers variables
- Neonatal Abstinence Syndrome NAS)
- Long term effects to the child

Physicians' dilemmas
Where to refer
How to refer
What to convey
How to interface

Therapists' dilemmas
Where to refer
How to refer
Why did the doctor do that?
Medical provider frustrations

Fertilization age

- Time from the moment of fertilization
- Also called embryonic age
- Mostly a biological research term
- For humans we referred to gestational age

Gestational Age

- Also called menstrual age
- Based on first day of last menstrual period (MP)
- Add 40 weeks from last MP to estimated due date
- 5% accuracy for the exact date
- Use the app!

Embryo

- "That which grows"
- Start time
    - First cell division
    - Day of differentiation (Day 4)
- Until week eight when it has developed to the point of being recognizable as a human fetus

Stages of pregnancy - trimesters

- First trimester - organs and systems are formed
- Second trimester - fetus begins to grow in both size and in the development of its features
- Third trimester - rapid growth and the ending of the child's feature growth

Length of Pregnancy

- Preterm: 37 Weeks
- Early Term: 37 – 39 Weeks
- Full Term: 39 – 41 Weeks
- Late Term: 42 Weeks

Neonatal Abstinence Syndrome (NAS) - a group of problems that occur in a newborn who was exposed to addictive illegal or prescription drugs while in the mother's womb

Developmental Trajectory

- Trajectory: a path or line of progression
- Developmental Trajectory: the course of a behavior over age or time.
- There are factors that support or undermine children's health and development across the early life course.
- Nature and/or Nurture

Developmental Milestones:

- Skills such as taking a first step, smiling for the first time, and waving "bye bye" are called developmental milestones.
- Center For Disease Control And Prevention – (CDC) - Milestone Checklist

Postpartum:

- Acute Period (first 6–12 hours postpartum)
  - Postpartum hemorrhage, uterine inversion, amniotic fluid embolism, and eclampsia.
- Secondary Period (2–6 weeks)
  - " This the traditional "postpartum" period
- Delayed Period
  - Can last up to 6 months

Perinatal Period

- Occurring during, or pertaining to, the periods before, during, or after the time of birth
- From the 20TH OR 22ND week of gestation through the first 28 days after delivery.

Prescribed Medications vs. Illicit Drugs

Birth Weight (BW)

- Low BW = Less Than 5.5 Pounds
  - Premature
  - Mother Health (Starvation)
  - Placenta Problems
  - Sudo
  - Greater Risk For Health Problems
- High BW = Over 8.8 Pounds
  - Big Parents
  - Mother Diabetes
- Average BW = 7.5 Pounds
- Expect A 5–10% Initial Wt Loss

Child Abuse Prevention Treatment Act (CAPTA)

- Requires states to establish policies and procedures for reporting cases of newborns exposed to substances of abuse
- Infant Toxicology
  - Meconium
  - Placenta
  - Hair
  - Breast milk

Meconium

- Meconium is a thick, green, tar-like substance that lines a baby's intestines during pregnancy.
- This substance is baby's first "poop" released after birth
- Meconium contains the amniotic fluid swallowed by the fetus in the last half of pregnancy and is released as the first stools after birth – if released before may indicate fetal distress.
- Can detect mother's drug use over the last 20 weeks

Fetal Alcohol Spectrum Disorders - FASD

- Physical, neurological and mental conditions caused by mother drinking alcohol
- Fetal Alcohol Syndrome (FAS)
- Fetal Alcohol Effects (FAE)
  - Alcohol-Related Neurodevelopmental Disorder (ARND)
  - Alcohol-Related Birth Defects (ARBD).

Liz (FASD) at 21 Years Old

- Cognitive problems
- Learning problems
- Social integration
- Vulnerability
- Impaired insight
- Poor executive functions
- Alcohol risk

FDA PREGNANCY CATEGORIES

- Category A – HUMAN STUDIES NO RISK
- Category B – ANIMAL STUDIES – NO RISK – BUT no adequate and well-controlled studies in pregnant women. (amoxicillin, HCTZ)
- Category C – Animal studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. (Tramadol, trazodone, gabapentin)
- Category D - There is positive evidence of human fetal risk in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks. Alprazolam, clonazepam, BZDS
- Category X - Studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.(anticancer agents, statins)

PREGNANCY & LACTATION LABELING RULE(PLLR)

- Effective Date June 2015
- Implementation – Full Swing 2018
- Subsections In Narrative Format:
  1. Pregnancy
  2. Lactation
  3. Reproductive Health - male & female

Pregnancy Subsection - The Pregnancy subsection provides information about dosing and potential risks to the developing fetus and registry information that collects and maintains data on how pregnant women are affected when they use the drug.

Lactation Subsection

- The Lactation subsection Information includes drugs that should not be used during breastfeeding.
- Information on active metabolites in milk, as well as clinical effects on the infant
- Information may include data on metabolism or excretion, a risk and benefit section, and timing section

Female/Male Reproduction

- Recommendations on pregnancy testing or birth control before, during or after drug therapy
- Medication's effect on fertility or pregnancy loss will be provided when available

Teratogens

- Factors that can alter normal intrauterine development
  - Fetal growth,
  - Anatomic structures
  - Physical functioning
  - Postnatal development.
- Environmental / Chemical exposures
- Maternal medical disorders
- Infectious agents
- Genetic conditions

EPIDEMIC VS. PANDEMIC

HISTORICAL REVIEW

- Past Opioid Epidemics & Cycles
- Addiction in China
- China's "War on Drugs"
- China/ British Opium Trade & Wars

Chairman Mao's War on Drugs:

- 1950's
- 10,000,000 Addicts Sent To Compulsory Treatment
- Dealers Are Executed
- Opium Crops Replaced
- Opium Production Went Below Southern Border – Golden Triangle

Opium Epidemic in USA – Civil War

- Chronic Pain Issues
- Phantom Limb / Neuropathies
- Musculoskeletal Injuries
- Chronic Bone Infections
- Post Concussion Syndromes
- PTSD
- Gastrointestinal issues
- Treatment was more opiates

The Doctors' Opinions

- US Doctor: Opiates are an all-healing panacea, which in all quantities always does good, and can never do harm (1866)
- Doctors who resort too quickly to the needle are : lazy, incompetent, poorly trained, behind the times (1895)

Harrison Narcotics Act 1914

- Enforcement began 1915
- A doctor could not prescribe opiates to an addict, since addiction was not considered a disease
- Criminalized addiction
- Opiate availability declined
- Opiate price increased
- Opiate use declined
- Addicts had withdrawal, craving, illicit use

Set Up Short Term Narcotic Dispensary Clinics

- Rid society of the Narcotic Evil
- Relieve suffering of the poor wretches
- Free them from predators
- Give the addict narcotics to make him/her a productive & responsible citizen
- Then reduce and/or stop their drug intake

The Results of the Shreveport Clinic

- Few wanted reduction or detox
- Clinic increased number of addicts
- Addicts increased dosage
- Addicts blame clinic - "I would have stopped if not for clinic."
- Diversion was a major issue
- Encouraged illegal traffic
- Addicts from Texas moved to Shreveport
- Continued to take "underworld narcotics"

Chicago Hipster Heroin Epidemic

New York Heroin Epidemic Late 1950s – 1960s

Vincent Dole, MD – Methadone for Opiate Addiction

Vietnam & Opioid Addiction

High Risk Factors

- Young age – average age 22 years old
- Vietnamese - Allies and Enemies
- "Limited conflict"
- Anti-war sentiment in USA*
- Drug availability
- Level of acceptance

Vietnam & Opioid Addiction

- 20% Self Identified As Opium Addicts
- 95% Of The Vietnam Veterans Who Self Identified As Heroin Addicts Stopped Using

Vietnam & Opioid Addiction

- Home environment
- Peace vs. War zone
- Less drug availability
- Less acceptance + increased consequences

Talwin Panic 1978

- Introduced – 1967 (Pentazocine)
- Non-addictive opioid morphine substitute
- Heroin supply decreased (US/Turkey)
- T's & Blues increased
    - Talwin
    - Tripelenemine
- Poor substitute for heroin
- Talwin + Naloxone (1983)

OxyContin History

- FDA application 1995 – no advantage over other opioids
- OxyContin was Introduced in 1996
- FDA - approved label that iatrogenic addiction is "very rare" 1996
- In 2001, FDA – re-labels label that addiction risk "data is not available"
- Liberalization of use of opioids for Chronic Non Cancer Pain

OPIOID MEDICATION DURATION AND RISK FOR LONG TERM USE

- Less than 3 days -minimal risk of long term opioid use
- Risk Of Long Term Opioid Use Increases For Each Added Day
- Day 8 14% Will Have Additional Opioid Use Over The Next Year
- Day 31 - 30% Will Have Additional Opioid Use Over The Next Year

Over-prescribers & Mis-prescribers

- Misinformed
- Duped
- Unethical
- Incompetent
- Greedy

Oxycontin History FDA Re-label 2001 – (Chronic Non-Cancerous Pain Patient Fallout)

- False Promises
- False Hope
- Real Consequences

Oxycontin History

- Market budget for 2012 = $2,000,000
- Physician profiling – high prescribers
  - 94,000
  - Indiscriminant physician
- Starter coupon – free oxy*
  - 1996 – 2001
  - 34,000 free Oxy coupons issued
- Drug rep bonus systems
- Minimal risk of addiction
  - Less than 1%
  - Only 4 out of 11,882 opiate patients get addicted

REVIEW OF PUBLIC OUTRAGE

- Series of slides - examples

Susceptible Host

- Younger
- Nature/Nurture
- Pain – Acute vs. Chronic
- Stressful Environment
- PTSD
- Mood Disorders

The Cottage Industry of Drug Dealing – Discussion slide

The Status of Our Epidemic

- Supply shift – legal to illegal
- Focus on opioid epidemic to the exclusion or minimization of the other epidemics
  - Alcohol
  - Marijuana
  - Methamphetamine
- Medication Assisted Treatment vs. Medication Only Treatment

ADDICTED AND PREGNANT

Provider Bias

Consequences of Provider Bias

- Negative perception of birthing process by patient can cause PTSD
- Risk Factors of PTSD
  - Hx previous sexual trauma
  - Perinatal Depression
  - Perinatal Anxiety
- Postpartum PTSD consequences
  - Decreased bonding and post natal care

Provider Bias:

- 76% felt anger toward the mother
- Most lacked training on addictions
- Most did not know or have access to support services
- Education decreases bias
  - Foundation of Understanding
  - Decreases frustration
  - Improves care

Disease Prevention Model - Primary Prevention Means We Prevent The Disease

- Eliminate Pathogen
- Limit Exposure
- Immunize The Population
- Awareness

- Assessment Of Risk
- Acceptability
- Alternatives

Salient Event

- Stands out!!!
- Attentional mechanism
- Learning mechanism
- Survival mechanism
- Focus selectively on continuing/ re-experiencing the event

Executive Emotive Model

- Executive processing Prevails
- Emotive Processing yields to executive
- Adaptive, Goal Oriented, Reward Based, Pain Avoidant, Functional Behaviors
- Euthymic, Productive, Have Purpose

Emotive Executive Model

- Emotive processing prevails over executive function
- Executive processing yields to Emotive processing
- Maladaptive, Goal Oriented, Reward Based, Pain Avoidant, Dysfunctional Behaviors
- Reactive lifestyle with constricted focus

Staying Sane with Insanity:

Maslow's Pyramid & Addiction Paradigm – slide series – illustrations of high jacking & self delusion

Maslow's Pyramid & Addiction Paradigm

- Opioids are the foundation required to satisfy your basic physical needs
- Having a supply of opioids overrides all other needs
- This need creates constant stress
- Opioids relieve this stress and opioids become the primary coping skill

Executive/ Emotive Function in Addiction – slide series – illustrations

Dependency vs. Addiction

- After two weeks of scheduled opioid intake, physiological adaptation occurs
- Discontinuance results in OWS (usually mild)
- Chronic pain patients on opioids can be physiologically dependent (and impaired) but not addicted
- Chronic pain patients on opioids can be physiologically dependent and addicted

Disease Prevention Model I

- Primary – Prevent The Disease
  - Eliminate Pathogen
  - Limit Exposure
  - Immunize The Population
  - The War On Drugs Is A Declared Failure
  - We Are Writing Less Narcotics
  - Drug Dealing Is A Cottage Industry
  - We Have Many Awareness Campaigns
  - We Have Open Access To Narcan
- Secondary – Intervene Early
  - Early Diagnosis
  - Evidence Based Treatment
- Tertiary
  - Manage Chronic Disease
  - Decrease Relapses

Immunization

- Protective Factors
- Education
- Family Dynamics / Values/ Planning
- Citizenship
- Church Involvement
- Organized Sports
- Societal Attitudes

Disease Prevention Model II/ Secondary – Intervene Early

- Early diagnosis
- Evidence based treatment
- We have increased screening
- We lack evidence based treatment
- We have harm reduction
- We lack standardization
- Mal-aligned incentives exist

Early Dx & Rx

- Education
  - Patient & Family
  - Healthcare Providers
- Appropriate Referral
- Treatment
  - Matching (Least Intrusive, Most Effective)
  - Evidence Based Best Practices
  - Legitimate
- There is no single treatment that works for everyone

Disease Prevention Model III

- Tertiary
- Manage Chronic Disease / Decrease Relapses
- Legacy Pain Patients
- We Have Unstandardized Harm Reduction
- We Have Additional Ongoing Epidemics
- Mat (Opioid & Non-Opioid)

Tertiary

- Ongoing Treatment
- Ongoing Monitoring & Accountability
- Recovery Contract
- Develop Resource Base
- Rapid Intervention For Relapses
- Long Term Mat Consideration

Addiction

- Primary
- Progressive
- Detention/ Disability/ Dissolution/ Dementia/ Death
- Chronic
- Destructive

Treatment

- Outpatient
- Intensive Outpatient
- Partial Hospitalization
- PHP With Boarding
- Residential Treatment
- Sober Houses
- Most Follow A 12 Step Model

Professional Enabling

- Revolving Door
- Industry Issues
- Outcome Studies
- Best Practices
- Evidence Based
- Admission Criteria

Treatment Philosophy

- Abstinence Based Programs
- 12 Step Foundation Programs
- Cognitive Behavioral Models
- Faith Based Programs
- Aversion Medications
- Opioid Replacement/ Blockade Medications
- Outpatient – Long Term – Longer Term

Gender Bias

- Females Under-Represented (1:3)
- Women Become Addicted More Quickly Than Men
- Less Likely To Seek Treatment
- Judged Harshly – Cultural Bias
- Responsible For Raising Children
- Dependent On Spouse

Medication Assisted Treatment For Opioid Use Disorder

- Opioid Agonists (Narcotics) – Buprenorphine / Methadone
- Opioid Blockers – Naloxone/ Naltrexone (Vivitrol, Oral Tablets)
- Common Factor - All Act On Opioid Receptors

MEDICATION ASSISTED TX

- Methadone
  - Developed in 1937
  - Mid 1960's used as opiate substitution therapy
  - Special licensing / Barrier
- Buprenorphine
  - Discovered 1966
  - Approved 2002 for opiate addiction treatment
  - Office Based Opioid Treatment (OBOT)

OAT (Opioid Agonist Treatment) Medications

- Both MTD & BUP are relatively long acting
- Eliminate need for mother to dose multiple times per day (Except MTD in 3rd TM)
- Prevent opioid blood level fluctuations
- Fluctuations increase fetal distress due to multiple withdrawal episodes

OAT Is Harm Reduction

- Methadone
- Buprenorphine
- Both are harmful & addictive
- Cost benefit analysis
- Controlled dependency
- Minimize damage from lifestyle
- Anticipate outcomes more accurately
- Have opioid fetal impact (short & long term)

Methadone vs. Buprenorphine

- Both are Addictive Opioids
- Both cause dependency & OWS
- Methadone
  - Full mu agonist / No ceiling effect
- Buprenorphine
  - Partial mu agonist/ Ceiling effect
- Neither approved in pregnant patient

Slide Series Illustrating Opioid Receptor and MAT

The Bupe Result

- Replaced a full opioid agonist with a partial opioid agonist.
- Replaced an addiction to opioids to a controlled dependency on an opioid
- Ceiling effect
- Long half life
- Absence of euphoria
- Blocking of other opioids

Office Based Opioid Treatment OBOT

- Waiver Prescriber is focus
- Patient
- Referral capability

Behavioral Clinic

- Focus in on counseling
- Has waivered prescribers
- Treatment team

Retention Rates

- Buprenorphine Outpatient Outcome Project
- "BOOP"
  - 40% retention at one month
  - 15% retention at 3 months
  - There was harm reduction by several measures
- Musical Chair Providers

Barriers To Treatment for Pregnant Addicts

- Pre-authorization (Subutex)
- Treating Addictionologist vs. Waivered
  - QUALIFIED VS. CERTIFIED
  - Work with OB
- Patient is high-risk, high exposure, requires more time and effort
- Home environment
- Unexpected interruptions

Maternal Variables

- Mom does not acknowledge pregnancy
- Interpret S/S of pregnancy as OWS and increase opioid dose
  - Fatigue, HA, N, V, cramps
- Amenorrhea is common in OUDO
- Lack of contraceptive use

Conspiracy of Silence

- < 30% are "honest" when asked
- Fear of consequences
  - DCFS
  - Legal Issues
  - Custody Issues
  - Safety issues
- Drug screening
- Motivational interviewing

Prescriber Legal Issues – MAT for Pregnant Patient

- High Risk Pregnancy
- Pregnancy Category "C"
- Pregnancy Rating USA (?)
- Evidence Based / Best Practice
- Projection & Blame
- Dept. Child & Family Services
- Prenatal Neglect Vs. Exp W/O Pnn

Epigenetics & Gene Expression

- Gene Expression - Genes are turned On and Off
- If Bad Genes are turned on a Disease is Expressed
- Many factors can cause gene expression
- The increased DNA methylation in sperm Of OPRM1 Gene may suggest a way of epigenetic heritability of opioid abuse or dependence phenotypes.
- THC alters sperm's genetic profile & alters two major DNA pathways occurs. This occurs in weekly users. The question is: What does this mean?

CDC OPIOID RX DATA 2008 – 2012

- Medicaid - 39 % of pregnant patients filled opioid prescriptions during pregnancy
- Private insurance carrier - 28 % filled opioid prescriptions during pregnancy
- 13,500 babies are born each year with NAS
  - Heroin Users - 60-70% of babies had NAS & Hospital stay >30days

Some of the Risks Of Not Treating Mom's OUD

- Miscarriage / Premature delivery
- Complications (Placenta Abruption)
- Fetal stress/distress/death
- Low Birth Weight
- Increased SIDS Risk = 2-3X
- More severe NAS
- Congenital heart defect
- CNS damage
- Infections

NAS Historical Perspectives - slides

NAS Risk Factors

- Type and amount of maternal drug use
- Maternal metabolism
- Low maternal weight (malnutrition?)
- Placental metabolism
- Net transfer across placenta
- Infant metabolism -
- Number of cigarettes smoked
- Infant birth weight - >BW=>NAS
- Age of gestation (>EGA+>IBW>NAS)

Why is there less NAS in Preterm?

- Immaturity of central nervous system
- Lower cumulative drug exposure
- Less placental transfer
- Delayed hepatic and placental metabolism
- Lower fat content = Less drug deposition
- Lack of validated scoring system
- For every increase of 1 wk GA from 36 – 40 wks, the odds of needing MS > by 88%

More Variables

- Bup + CYP2C8 > Nor-Bup (Preg Variation)*
  - > CYP2C8 > NorBup in mom
- Placenta* Bup + Cyp 19 > Nor-Bup
  - CYP 19 increases with Gestational Age
  - Increases significantly after 34 weeks
  - Genetic variation
- Placenta – individual expression of P-glycoprotein efflux active against Bup transport
- Different people make different amounts of nor-buprenorphine
- As gestational age increases the placenta makes more nor-buprenorphine – so longer GA means more NAS

NAS Assessment Tools

- Lack of high-quality evidence to guide management of exposed neonates
- There is limited data on the inter-observer reliability of NAS assessment tools
- Scoring is highly subjective
- Lack of a standardized approach.
- Non-pharmacologic interventions, particularly breastfeeding, may decrease NAS severity.

Medical Treatment of NAS

- Morphine
- Buprenorphine - Shorted hospital stay than MS
- Methadone
- Phenobarbital
- Clonidine

Dangers Opiates Pose To Pregnant Patients

- Opioid-dependent pregnant women are nearly five times as likely to die during hospitalization
- Addicted pregnant women have much longer hospital stays
- Babies born to opiate-dependent women are twice as likely to be stillborn, born prematurely or suffer poor growth
- Pregnant opiate addicts are also three times more likely to suffer a placental abruption

Methadone Pharmacokinetics

- Fate of substances in the body
- Differ between pregnant and non-pregnant women
- Changes significantly throughout pregnancy
- MTD half-life falls from 22 to 24 hours in non-pregnant women to 8.1 hours in pregnant women
- Compensate with split dosing

Methadone vs. Buprenorphine

- MOTHER - Maternal Opioid Treatment Human Experiment Research study
- Buprenorphine has advantage over MTD
  - Shorter hospitalization stay for mom
  - Shorter treatment duration for child
  - Less cumulative morphine required for NAS

Long Term Effects Opioid Use Disorder During Pregnancy

- Visual - Nystagmus, Stabismus, Low Acuity
- Delayed Motor Milestones
- Poor Motor Coordination
- Attention Problems
- Impaired Abilities - Verbal, Arithmetic, Reading

Nystagmus

- Repetitive uncontrolled movements
- Reduced vision
- Reduced depth perception
- Balance problems
- Coordination problems

Strabismus - Person cannot align both eyes simultaneously

Long Term Effects of MAT in Pregnancy - Buprenorphine vs. Methadone

- Follow up at 2 years old
- No striking differences between effects of BUP vs. MTD
- BUP - Lower rates of
  - Delayed motor function
  - Delayed social function
  - Delayed language skills

Methadone vs. Buprenorphine – Peripartum

BUPRENORPHINE BETTER THAN MTD

- Less relapse in later pregnancy
- Less relapse postpartum
- Easier access

Buprenorphine

- Buprenorphine/naloxone combination - Suboxone, Zubsolv, generic
- Street value $20 per 8mg/2mg
- Naloxone is absorbed
- Buprenorphine mono-therapy - Subutex
- Buprenorphine Metabolite - Nor-buprenorphine - Antidepressant Effect

EFFECTS OF OPIATE RECEPTOR BLOCKADE

- Opioid Growth Factor Receptors Modulate Brain Cell Development
- Perinatal Naltrexone
  - Decreased cells in cerebellum
  - Decreased nerve cell length
- This Is One Reason Why Vivitrol Is Not Used In Pregnancy

DETERMINING BUPRENORPHINE DOSE

- History
  - Maximization vs. minimization
  - Self-detox history (Kratom)*
  - "Meth"
- Physical Assessment
  - COWS
- Drug Screen
- Baseline Labs
- RX from other provider – PMR/ LBP

Follow Up Visits

- Follow up sessions – compliance, ADE
- Maintain Motivation
- Enlist healthy family member
- ROI for collaborative care
- Changes in Fetal Movement
- Fetal heart tone
- Pregnant MAT Support Group

Detox During Pregnancy

- There is no clear evidence to support the viewpoint that medical withdrawal is harmful in a pregnant opiate independent woman.
- Methadone detoxification treatment is not associated with risk of miscarriage in the second trimester or premature delivery in the third trimester.

Detox During Pregnancy

- Level of motivation
- Level of self-efficacy*
- Living environment
  - Home
  - Sober house (caveat emptor)
  - People, places, things
- Support system
  - Family
  - Sponsor (role)
- Level of involvement in treatment

Buprenorphine Detox During Pregnancy

- Evidence based data from systematic, controlled or prospective studies are sparse
- Begin in 2nd Trimester (Week 14-32)*
- Stabilized dose for at least two weeks
- Dose reduction at 1 to 2 mg every two weeks
- Reduction only as clinically tolerated – Craving / OWS
- Collaboration with other healthcare providers

Maternal Variables

- Social deprivation – Transportation, Unemployed, Housing / overcrowding
- Maternal Health - Physical and mental health / Delayed prenatal care
- Lifestyle issues

Does Maternal Dose Matter?

- **Short Term**
- Maternal Safety
- Maternal Compliance
- Reduce Complications
- Fetal Safety
- Reduce FAS

Does Maternal Dose Matter?

- **Long Term Goal**
- Maternal Safety
- Maternal Compliance
- Relapse Prevention
- Child Safety
- Child Development
- Fly System Stress

Does Dose Matter?

- Four year old children
- Exposed to MAT during gestation
- Impaired eye tracking skills
- Decreased visuomotor task performance
- Could inhibit cognitive function

Opiate/Opioid Receptors

  - **Opiate Receptor Location:** Brain, Spinal Cord, Gastrointestinal tract
- **Receptor Types**
  - **Delta** - antidepressant
  - **Kappa** - dysphoria
  - **Mu** - euphoria

Cigarettes & Pregnancy

- Nicotine concentration is higher in fetal compartment than maternal serum
- Increase Risk NAS in OUD
- Developmental Issues
  - 2 X Risk for SUID at one per day
  - Obesity
  - Conduct Disorders
  - SUDO
  - ADHD

Benzodiazepines & Pregnancy

- Decreased BZD/ GABA-A Receptors
- BZD Withdrawal
- Irritability
- Anxiety Disorder

Acute BZD Effects

- Hypotonia
- Poor suck reflex
- Hypothermia
- Apnea
- Hypertonia
- Hyperreflexia/Sz
- Tremor
- Irritability

Long Term BZD Fetal Effects

- The density of GABA A receptors is continually increasing during gestation
- Chronic BZD use reduces the number and density of GABA A receptors in the brain.
- Receptors appeared in the human brain as early as 8th week of gestation.
- The frontal cortex receptor density increases between 12 and 26 weeks of gestation.
- Prenatal diazepam caused chronic anxiety in animals

Gabapentin & Pregnancy

- Dysregulation of muscle formation
- Heart defects

Cocaine

- Neurotrophic roles of monoaminergic NTs
- Mal-development of brain structure & circuits
- Language defects
- Attention regulation
- Executive function
- Memory problems
- Aggression
- Gender specific differences

Cocaine & Pregnancy

- **NAS** not clearly defined
- Second or third postnatal day
- Irritability
- Hyperactivity
- Tremor
- High pitch cry
- Excessive sucking
- **Preterm**
- Placental abruption
- Fetal distress
- < IU Growth
- Cardiac abnormalities
- Long term CNS effects, behavior, cognition, dexterity

METHAMPHETMAINE & AMPHETAMINE

Follow up out to 16 years old

- Increased Emotional Reactivity
- Anxiety
- Depression
- Attention Problems
- Externalization (5yo)
- Aggression
- ABNORMAL BRAIN DEVELOPMENT
- White Matter Tracts
- Frontal Lobes
- Thalamus
- Hippocampus
- NAc

MARIJUANA - 20% Use MJ During Pregnancy - Effects On Child

- ADHD
- Conduct DO
- Depression
- Anxiety
- Learning Problems
- Memory Problems
- Less DA2r in NAc
- More + response to OPS
- There is no clear teratogenic effect

Maternal Marijuana - Mother MJ Detox

- 28 days
- Worse first week
- Mid-week
- Anger & agitation
- Day 3 – 7 peak
- Gabapentin

Co-Occurring Disorders

- PTSD
- Trauma exposure (childhood/adolescent/adult)
- Trafficked
- Anxiety Disorders
- MDD
- Borderline Personality
- Bipolar
- Antisocial

Mood During Pregnancy

- 50% have significant anxiety +/- depression
- 32% have less anxiety or depression
- 16% no change

Depression During Pregnancy – Child's Impact

- Neonatal distress
- Disrupt social development
- Language problems
- Decreased motor activity
- Decreased sleep
- Increased risk for autism

SSRI In Pregnancy-Baby Effects

- Autonomic dysfunction
- Motor dysfunction
- Sleep problems
- Decrease language development
- No apparent cognitive dysfunction
- Organ mal-development (small absolute risk)
- Withdrawal syndrome

SSRI During Pregnancy

- 12% take antidepressants during pregnancy
- Low or no reported risk
  - Citalopram
  - Sertraline
  - Escitalopram
- Fluoxetine – heart, cranium
- Paroxetine – heart, cranium, abd. wall

SSRI During Pregnancy

- Assessment - Medication, duration, dosage
- Infant Effects
  - Onset 1-2 days
  - Duration 1-2 weeks
- Drug Effect vs. WD
- Signs/Symptoms
  - Crying, irritable, restless, tremor, hypertonia, feeding, hypoglycemia, sz

Prenatal Depression – Effects on Child

- Untreated
  - Neurobiobehavioral dysregularity
  - Higher placental glucocorticoid
- SUID Risk
  - Tryptophan hydroxylase low
  - 5-HT low
  - Lower medullary 5-HT

Post Delivery Issues

- Breast feeding
- Postpartum depression
- Postpartum Psychosis
- Bonding issues
- Relapse Risk
- DCFS

Brexanolone – Zulresso

- Base on the hormone allopregnanolone
- Allopregnanolone amplifies GABA
- Rises during preg. and abruptly falls after delivery
- Brexanolone is analog of allopregnanalone
- It restores allopregnanalone levels
- Relieves PPD

Antipsychotic Rx & Pregnancy

- Inadequately controlled psychiatric illness is a risk to mother and child
- Increase risk of gestational diabetes
- Organ malformation in fetus
- Miscarriage
- Stillbirth
- Different effects at different times during pregnancy

Breast Anatomy Montgomery Gland

- Smell Stimulus Behavior
- Less arousal
- Calming
- Positive head turning
- Appetitive activity
- Directional behavior

Mother's Breast Milk Sets Tone Of Baby's Microbiota

Post Delivery Pain Mgt

- Buprenorphine Mat Mom - Less Hyperalgesia
- Methadone Mat Mom - May Require More Opioid Pain Rx
- Optional Pain Rx - Iv Tylenol Works!
- Resume Oat Asap

Pain Management Plan

- Addictionologist, OB MD and patient have agreement
- Option #1
  - Stay on MAT and supplement RX (IV Tylenol, NSADS)
- Option #2
  - DC MAT 12 – 16 hours before hospitalization
  - Routine treatment in hospital
  - Resume MAT 3 – 4 days post delivery

Relapse Prevention Plan

- Develop individualized plan
- Proactive NOT Reactive
- Third Party involvement - Hold & administer Rx
- Follow up visit made with addictionologist
- Discuss plan with therapist/group - Get feedback
- Limit amount of pain Rx prescribed

Stillbirth

- Increases risk for long term depression
- Monitor for 3 years
- Persists even after birth of another healthy child

Hep C – Also A Brain Disease

- HCV without cirrhosis (30% cog. dysfunction)
  - Decreased attention, concentration, working memory
  - Frontal subcortical dysfunction
  - Direct effect of virus on brain
  - Microglia cell dysfunction
  - Medication effect
- FATIGUE

Maintaining Motivation

- Accountability breeds compliance
  - Random UDS (EXPLOITATION ALERT)
  - AA/NA logs
- Positive reinforcement
- Earned Advocacy
- Realistic expectations
  - Sub acute signs of NAS may last up to 6 months

Urine Toxicology

- Oxycodone > Oxycodone & Oxymorphone (Opana)
- Codeine > Hydrocodone > Hydromorphone
- Codeine > Morphine > Hydromorphone
- Heroin > 6MAM
- Heroin > Morphine > Hydromorphone
- EtG (Ethyl Glucuronide) Cur off levels (100ng/mL vs. 500 ng/mL)