Clinical In-Service:

Addictions Treatment: Pharmacotherapy

May 2008

Donald Avoy, M.D.
Mark Stanford, Ph.D.
Deb Stephenson, M.D.

Addiction Medicine and Therapy Program
Santa Clara Valley Health & Hospital System,
Department of Alcohol & Drug Services
ADDICTIONS
PHARMACOTHERAPY
A Study in Complexity
SIMPLE ANSWERS WORK ONLY FOR SIMPLE PROBLEMS

• GOAL--TO UNDERSTAND THE COMPLEXITY OF ADDICTIVE DISEASE--AND THE COMPLEXITY OF ITS TREATMENT
FOR CONSIDERATION

• EVOLUTION--FITNESS
• CULTURAL CONTEXTS FOR PSYCHOACTIVE DRUG USE
• EFFECTS OF DRUGS ON OTHER SPECIES--COMMON NEUROBIOLOGICAL PATHWAYS
• BALANCE--HOMEOSTASIS AND ALLOSTASIS
FOR CONSIDERATION

• STRESS AS A TRIGGER FOR RELAPSE

• THE HUMAN GENOME AND ADDICTION
EVOLUTION

• WHAT DRIVES EVOLUTION?

• PRESERVATION OF THE SPECIES IN A CHANGING, COMPETITIVE ENVIRONMENT
  – FITNESS
EVOLUTION

- The mechanism is mutation--transcription errors in translating genetic code information
  - ATG-----ATC Wrong amino acid sequence

- Natural Selection is the process
EVOLUTION

- THE MOST CONSTANT ENVIRONMENTS SUPPORT THE MOST SIMPLE ORGANISMS
  - TEMPERATURE
  - OXYGEN SUPPLY
  - pH
  - LIGHT
  - FOOD
EVOLUTION

• TO MAINTAIN FITNESS IN COMPLEX CHANGING ENVIRONMENTS ORGANISMS MUST HAVE ADAPTIVE CAPACITY

• Adaptation does not mean genetic change, it is built into the genetic code
EVOLUTION

• IN OCEAN -- ALMOST CONSTANT
  – TEMPERATURE
  – OXYGEN
  – LIGHT
  – HUMIDITY
  – FOOD AVAILABILITY

• ON LAND -- ENORMOUS VARIABILITY
EVOLUTION

• The greatest concentration of organisms and species is at the equator

• The fewest live at the poles

• In the temperate zones, there is the greatest variability in temperature, light, humidity
• Evolution is conservative--it continues to use the things that work
• Structures in our bodies are virtually identical to those in bacteria
• The similarity makes it possible to understand human biology by studying other species
EVOLUTION

• BY THE TIME MAN APPEARED, MOST OF THE SYSTEMS HAD BEEN WELL WORKED OUT--
  – ENZYMES
  – NEUROTRANSMITTERS
  – HORMONES
EVOLUTION

• THE HUMAN BRAIN AND NERVOUS SYSTEM--THE JEWEL IN THE CROWN OF EVOLUTION--THE MOST POWERFUL ORGAN ON THE PLANET
HUNTING/GATHERING

- FOLLOWING HERDS
- EATING WHAT HERDS EAT
- EXPERIMENTING
- DEVELOPING CULTURAL WISDOM--USE OF POISONS
- INTEGRATING PSYCHOACTIVE SUBSTANCES--TRIBAL RITUALS
HISTORICAL PERSPECTIVE

• Domestication of Plants and Animals

• Identification of Toxic Plants and Poisons--Cultural Memory

• Identification of “Mind Altering” Substances
HISTORICAL PERSPECTIVE

- IVENTIVE PROCESSING--
  - CORTICAL ACTIVITY
    - Fermentation--8000 years ago--Mesopotamia
      - Beer
      - Wine
    - Distillation--800 A.D.--Arabia
HISTORICAL PERSPECTIVE

• Opiates--Papaver somniferum
  – Sumeria--4000 BC
  – Egypt-2000 BC

• Use of Poppy juice

• 19th Century began chemical extracts
HISTORICAL PERSPECTIVE

• 20 Century--Chemically altering extracted compounds
• Synthesis of new compounds by pharmaceutical companies for legitimate medical use
• Synthesis of compounds for illicit use
• Higher dosage--direct injection
HISTORICAL PERSPECTIVE

• Do we have control?
  – Parental
  – Cultural
    • Spiritual
    • Legal
    • Medical
NEUROBIOLOGY

• A quick, superficial look at the human brain

• A quick, superficial look at what opiates do to the brain
NEUROBIOLOGY

HOW, WHAT, WHERE
INDIVIDUAL NEURONS.

- **soma**
- **axon**
- **dendrite**
- **terminal**
A neural neighborhood

Each neuron synapses with approximately 1,000 other neurons making for about 100 trillion synapses that regulate homeostasis.
How do we study the brain?

• Human Studies
  – Observation of anatomic lesions, imaging, surgery or postmortem
  – Observation of functional deficits or behavioral abnormalities
  – Correlations

• Clinical Research
NEUROBIOLOGY

How do we study the brain?

• Laboratory Studies
  – Anatomical
    • Surgical
    • Radiologic or other imaging
    • Functional Studies
Stimulation – Reward Studies
Neurotransmitters

• A. What are they?
• B. What do they do
Neurotransmitter chemicals and receptor sites are key to the psychoactive effects a drug has on behavior.
Neural Dynamics At Synapse

- Presynaptic membrane
- Neurotransmitter release
- Postsynaptic membrane
- Reuptake
- Enzyme degradation
- Binding at receptor site
The Neurobiology at Synapse: Behavioral Homeostasis
• THE HIGHER FUNCTIONS, CREATIVITY, COMMUNICATION, ABSTRACT THOUGHT ARE POSSIBLE BECAUSE WE DON’T HAVE TO WORRY ABOUT THE MORE IMPORTANT THINGS.
NEUROBIOLOGY

• Autonomic Nervous System
  – Deals with the most basic life functions, e.g. digestion, procreation, fight/flight
  – Highly evolved to maintain “fitness” with environment, e.g. land or water
  – Powerfully dynamic
NEUROBIOLOGY

- Control of vital functions, e.g. heart rate and
  - blood pressure

- Requires Precise instantaneous monitoring both to institute changes and assess the result—Instantaneous feedback mechanisms
Autonomic Nervous System
Two parallel systems

- **Sympathetic**
  - Speeds up Heart
  - Raises Blood Pressure
  - Stimulates Gastro-Intestinal system
  - Prepares CNS for being on ALERT

- **Parasympathetic**
  - Slows Heart Rate
  - Lowers Blood Pressure
  - Prepares for Digestion of food
  - Slows down CNS--Sedation
The Autonomic Nervous System Monitoring and Managing

a. Heart Rate
b. Blood Pressure
c. Oxygen/CO2
d. Temperature
e. Override/default
The reward Pathway
Figure 16-1. Neural reward circuits for various drugs (cocaine, amphetamines, opiates, nicotine, and alcohol) in a sagittal section of rat brain. A limbic–extrapyramidal motor interface is apparent. Dashed lines indicate limbic afferent inputs to the nucleus accumbens (NAc). A solid gray line represents efferent signals from the NAc believed to be involved in drug reward. Solid black lines indicate projections of the mesocorticolimbic dopamine system, which are believed to be critical substrates for drug reward. This dopamine system originates in the ventral tegmental area (VTA) and projects to the NAc, olfactory tubercle, ventral striatal domains of the caudate–putamen (C–P), and amygdala (AMG). Blue lines indicate opioid peptide-containing neurons, which comprise systems that may be involved in opiate, ethanol, and possibly nicotine reward; these systems include local enkephalinergic circuits (short segments) and the hypothalamic β-endorphin circuit of the midbrain (long segment). Blue areas indicate the approximate distribution of GABAergic receptor complexes, some of which may mediate sedative/hypnotic (ethanol) reward.
Mother Nature's Controls, the carrot and the stick

- A. Pain--To avoid destruction of the organism and the species

- B. Pleasure--To ensure the survival and perpetuation of the species
Endogenous Opioids
Keys that open locks

• A. Endorphins
• B. Enkephalins
• c. Dynorphins
Receptors--The locks

- A. The cell membrane
- B. Inside the Cell
Drug-induced plasticity might involve production of RNA- and ribosomal-binding proteins to alter mRNA stability and its translatability.

Regulation of post-transcriptional mechanisms by drugs of abuse.
Homeostasis and Addiction
• Homeostasis--A state of physiological equilibrium and balance. The raison d’être of the autonomic nervous system.

• Allostasis--An abnormal state of balance achieved in response to external stimuli.
HOMEOSTASIS
Effects of Opiates

- Sedation
- Slow the lower intestine—Constipation
- Slow heart rate
- Lower Blood Pressure
Autonomic Nervous System

Two parallel systems

- **Sympathetic**
  - Speeds up Heart
  - Raises Blood Pressure
  - Stimulates Gastro-Intestinal system
  - Prepares CNS for being on ALERT

- **Parasympathetic**
  - Slows Heart Rate
  - Lowers Blood Pressure
  - Prepares for Digestion of food
  - Slows down CNS—Sedation
Opiates’ Effects on Homeostasis
CNS RESPONSE TO OPIATES
CNS RESPONSE TO OPIATES

opiates  →  CNS
TOLERANCE

opiates

CNS
TOLERANCE

opiates

CNS
TOLERANCE

opiates

CNS
TOLERANCE

opiates

CNS
Opiate’s Effects on Homeostasis
Metabolism of Opiates
Opiate’s Effects on Homeostasis
Metabolism of Opiates
Symptoms of Withdrawal

- Agitation
- Sweating
- Nausea, cramps, vomiting, diarrhea
- Insomnia
- Elevated Blood Pressure, Heart Rate
Autonomic Nervous System
Two parallel systems

• Sympathetic
  – Speeds up Heart
  – Raises Blood Pressure
  – Stimulates Gastro-Intestinal system
  – Prepares CNS for being on ALERT

• Parasympathetic
  – Slows Heart Rate
  – Lowers Blood Pressure
  – Prepares for Digestion of food
  – Slows down CNS--Sedation
Figure 5. Regulation of dendritic structure by drugs of abuse. The figure shows the expansion of a dendritic tree after chronic exposure to a drug of abuse, as has been observed in the nucleus accumbens and in the prefrontal cortex. The areas of magnification show an increase in dendritic spines, which is postulated to occur in conjunction with activated nerve terminals. Such alterations in dendritic structure, which are similar to those observed in other examples of synaptic plasticity such as long-term potentiation, could mediate long-lived sensitized responses to drugs of abuse or environmental cues.
OPIATE CYCLES

CONC

TIME
The Stress Hormone Cycle

When a person perceives an event as stressful, a hormone called corticotropin-releasing factor (CRF) is released from a structure in the brain called the hypothalamus...

CRF travels in tiny blood vessels to the pituitary gland directly below the brain where it stimulates the release of another hormone, adrenocorticotropic (ACTH)...

ACTH travels in the bloodstream to the adrenal glands, which sit atop the kidneys, where it triggers the release of still other hormones — principally cortisol...

When cortisol travels back to the hypothalamus and pituitary, it inhibits the further release of CRF and ACTH. If the person no longer perceives events as stressful, the stress hormone cycle stops at this point. If events continue to seem stressful, CRF continues to be released, and the stress hormone cycle continues.
Figure 5. Regulation of dendritic structure by drugs of abuse. The figure shows the expansion of a dendritic tree after chronic exposure to a drug of abuse, as has been observed in the nucleus accumbens and in the prefrontal cortex. The areas of magnification show an increase in dendritic spines, which is postulated to occur in conjunction with activated nerve terminals. Such alterations in dendritic structure, which are similar to those observed in other examples of synaptic plasticity such as long-term potentiation, could mediate long-lived sensitized responses to drugs of abuse or environmental cues.
Hypothalamic-Pituitary-Adrenal Brain Stress System

PFC
BNST
PVN
CRF
HPC
PIT
AMYG
ACTH
Adrenal Gland
Glucocorticoids
Extra Hypothalamic CRF Brain Stress System
METHADONE

THE HISTORY
METHADONE--HISTORY

• World War II
• The Germans respond intellectually
METHADONE-HISTORY

- Early Studies--Lexington
- Trails of Substitution Therapy
METHADONE-HISTORY

- Vincent Dole and his collaborators at Rockefeller
- Substitution Revisited--Methadone
- The Criminal Justice System Response
- Rockefeller fights back
METHADONE--HISTORY

- The Viet Nam War
- The Dilemma of the Nixon Administration
- New Diagnostics--SynVar
- The first Methadone Programs
Fighting Fire With Fire

Methadone Maintenance Treatment

Deborah Stephenson, M.D., M.P.H.

2/05/02
My Background

• National Board Certification in Preventive Medicine/Public Health
• American Society of Addiction Medicine Certification in Addiction Medicine
• Part of the DADS Treatment Team since 1992
The Problem: Addiction

- An overwhelming and irresistible urge to use despite negative consequences
- Characterized by compulsion and loss of control
- Associated with difficulties and loss in multiple areas of life
- Reward rather than punishment driven
The Drug: Heroin

- A short-acting opiate
- The delivery system results in rapid, intense exposure of drug to brain...the rush
- Highly addictive
- The short half-life necessitates multiple uses per day to avoid an intensely painful withdrawal
Heroin Addiction: The Downward Spiral

- Using for the high ends; Using to stay well begins and progresses to using to minimize the misery
- Expensive and illegal, regular use compromises the ability to work
- The addicts life is characterized by increasing dysfunction and chaos
Heroin: Medical Risks Associated with Injection

- Cellulitis
- Abscess formation
- Endocarditis
- Hepatitis
- HIV infection
The Goal: Recovery

- Freedom from compulsive use
- Stable relationships with family and friends
- Resolution of legal and financial problems
- Pursuit of education, vocational training or employment
- Appropriate use of medical/dental care
What is Methadone?

- A long-acting opiate which is taken orally
- A medication with a slow onset of action
- A medication that produces/perpetuates physical dependence
What is Physical Dependence?

- Physical dependence means that abrupt cessation after prolonged use results in symptoms of withdrawal.
- The severity, duration and nature of the symptoms varies by substance.
- Substances producing physical dependence may or may not produce addiction (Phenobarbital and Prednisone for example).
Why Use Methadone?

- Addicted patients benefit
  - Quit using heroin
  - Pursue education or employment
  - Work to regain/maintain family relationships

- Society benefits
  - Decreased transmission of HIV, Hepatitis B and C
  - Decreased criminal activity
  - Financial savings
Qualities of an Ideal Medication

• High efficacy
• No side effects
• Inexpensive
How does Methadone Compare?

• The most effective treatment available for heroin addiction...the most likely to produce sustained abstinence
• Two persistent side effects: constipation and sweating
• Inexpensive compared with the alternatives
Qualities of an Ideal Medication

• Safe
• Non-allergenic
• Easily absorbed after oral ingestion
How does Methadone Compare?

• Safe at appropriate dosage; Use caution if patient has severe respiratory or liver compromise
• Allergy rare
• Oral absorption very adequate
Qualities of an Ideal Medication

- Infrequent dosing schedule
- No interactions with food or medications
- Non-addicting and no physical dependence
How does Methadone Compare?

- Once a day dosing usually adequate
- Interacts with a small number of other medications; No known food interaction
- Low addiction potential; Produces physical dependence after about three weeks of use
Practical Considerations for Narcotic Replacement Therapy

- Is the patient opiate addicted?
- Is the patient safe to admit/dose?
- Is the patient appropriate for the outpatient setting?
Methadone Maintenance Verses Detoxification

• Detoxification is for patients who are newly and less severely addicted
• A 21 day detoxification is seldom successful
• Maintenance is for patients with long-standing addiction problems
The Candidate for Methadone Maintenance

• Has a moderate to severe addiction
• Has demonstrated an inability to achieve/maintain abstinence with other treatment modalities
• Has been physically dependent on opiates for longer than one year
• OR is physically dependent and pregnant
The Benefits of Methadone Maintenance

• Relieves symptoms of heroin withdrawal
• Eliminates cravings for heroin
• Promotes abstinence
• Decreases risky behaviors
• Blocks the effects of heroin
• Decreases illegal activities
• Promotes retention in treatment
Methadone Treatment is Heavily Regulated

• Must be provided by a licensed treatment program
• Legal to start/continue in the hospital only while treating another medical condition
• Unless pregnant, must have at least a one year history of physical dependence to qualify for admission
Methadone Regulations

- Generally require daily attendance in a clinic for dosing
- Some take-home privileges are possible if patients meet specific criteria
Regulatory Requirements for Admission to Maintenance

• Current physical dependence
  – Physical signs of opiate dependence
  – A lab test positive for an opiate drug
• Physically dependent for at least one year
• Continuous or episodic physical dependence for all or most of the year prior
Regulatory Requirements for Admission to Maintenance

- Voluntary participation/informed consent
- Greater than 18 years of age or consent of parent or guardian
- If 18 or younger, must have 2 documented attempts at short-term detoxification or drug-free treatment
Exceptions to Physical Dependence Requirement

- Incarcerated or institutionalized patients
  - If institutionalized for at least a month
  - If admitted within first month after release
  - Provided patient was eligible before entering institutional facility
- Pregnant patients at risk of relapse
- Previously maintained patients
  - If maintained for at least 6 months
  - If detox was voluntary
  - If admitted within 6 months of detox
Special Circumstances

• The State Regulatory Agency may allow admission of a patient not meeting all criteria if it would be life or health endangering to withhold treatment
• Patients with AIDS
• Patients with endocarditis, etc
Goals of Methadone Treatment

- Relieve symptoms of withdrawal
- Eliminate cravings
- Eliminate use of heroin
- Block action of illicit opiates (if necessary)
- Minimize side effects
  (constipation/sweating/decreased libido)
Admission to Methadone Maintenance Includes...

- Substance abuse interview
- Review of medical history
- Physical examination
- Lab studies including drug and infectious disease screens
- Referrals for primary medical/dental care
- Determination/administration of starting dose
Understand Patient’s Motivation for Treatment

• Reasons for seeking treatment
• Ability to dose in clinic daily
• Willingness to participate in program
• Interest in pursuing abstinence and recovery
Build Trust and Rapport

- Listen to patient’s story with empathy
- Withhold judgment
- Explain the process
- Maintain patient’s dignity
Inform about Methadone

- Necessity of dosing daily
- Continued physical dependence on an opiate
- Side effects
- Possibility of interaction with other drugs
- Long-term nature of treatment
- Consequences of premature and/or hasty withdrawal
Review and Discuss Patient’s Current Medications

- Ask about prescription and over-the-counter medications.
- Identify medications with abuse potential.
- Obtain patient’s consent to speak with prescribing physicians.
Consider Risk of Withdrawal from Non-Opioid Drugs

- Arrange for appropriate detoxification if there is physical dependence on alcohol, benzodiazepines or barbiturates
- Start methadone before referring unless the problem is imminently life-threatening
The Goal: A Therapeutic Dose

- Maximizes treatment efficacy
- Stops withdrawal symptoms and cravings
- Promotes abstinence
- Eliminates sedation
- May not eliminate side effects
If the Dose is Not Therapeutic

• Jeopardizes the success of treatment
• Under-dosing results in physical discomfort and ongoing use
• Over-dosing causes physical discomfort and over-sedation
Stabilization

- The starting dose is seldom adequate to support abstinence
- The frequency and magnitude of dose changes are determined by the severity and time of onset of symptoms
- Abstinence hastens the process
Dose Evaluation: Review the Record

- Dose requirements during previous treatment episodes
- Methadone blood levels
- Substances of abuse
- Patterns of use
- Medical history
Dose Evaluation:
Examine the Patient

- Prior to dosing for signs of withdrawal
- 3-4 hours after dosing for signs of sedation
- Focus on pupils, skin, vitals
Dose Evaluation: Methadone Blood Levels

• The therapeutic range is 200-1000 ng/ml
• Patients often do best when trough ~ 400ng/ml
• The peak is usually twice the trough
• Patients may experience adverse effects when the peak is greater than 1.0
• Put blood levels into the perspective of the clinical picture
Methadone Treatment is More Effective With

- Counseling (individual/group)
- Urine testing
- Involvement in community recovery groups
- Lifestyle changes to support recovery
- Mental health evaluation/treatment
- Medical assessment/referral
Dosing Needs May Change

- Pharmacological issues
- Logistical issues
- Concurrent conditions
Pharmacological Issues

- New medications
- Recent dose changes
- New pattern of use
- New substance(s) of abuse
Logistical Issues

- Missing doses
- Change in schedule
- Newly in residential care
Concurrent Conditions

- Fatigue
- Stress
- Pregnancy
- Internal medicine problems
- Mental health problems
Evaluating a Patient’s Dose Change Request

- What is bothering the patient most?
- Is there one symptom or a constellation of symptoms?
- What is the counselor seeing?
Barriers to Stabilization

- Patients may not request dose adjustments for things that are dose related
- Patients may be reluctant to go up due to fear of being on a “high” dose
- Patients may be nervous about going down due to fear of experiencing withdrawals
Adjusting the Dose

- Safety is the top priority
- A 10% change will be discernable to most patients
- The peak effect of any one dose occurs 3-4 hours after ingestion
- Blood levels take about 5 days to stabilize
What is LAAM?

- Levo-alpha acetylmethadol
- A oral medication FDA approved in 1994 for the treatment of opiate addiction
- An opiate which is even longer acting than methadone
- Associated with cardiac complications in a small subset of patients
- Not available in Santa Clara County
Should a Patient on Methadone Maintenance Appear Sleepy?

- No
- Possible explanations include
  - Use of heroin/other drugs
  - Too much methadone
  - Recent cessation of stimulants, alcohol or heroin
  - Sleep deprivation
What is the Methadone Honeymoon?

- A mild euphoria experienced in the early weeks after induction which resolves due to the development of tolerance
- The better-than-normal feeling associated with instant disappearance of the physical misery associated with daily heroin use
- A phenomena which increases treatment retention and program compliance
Why are Some Patients Dosed Twice a Day (Split Dosing)?

• The maximum daily dose may be insufficient to suppress symptoms of withdrawal/support abstinence
• The patient’s blood levels may change dramatically over a 24 hour period producing a sick/drowsy cycle
What About Detoxification?

- Like insulin, methadone stabilizes a chronic illness, so can rarely be discontinued.
- The normal brain has an endogenous opioid system; Methadone acts as replacement therapy.
- 80% of patients withdrawn from methadone will relapse to heroin within 1 year.
Recognizing Recovery

- A commitment to sobriety
- A life coming to order; The chaos is diminishing
- Loss of connection to people and places associated with drugs
- Growing connections to a stable support system
Fighting Fire With Fire

Managing the Pregnant Heroin Addict
Deborah Stephenson, M.D., M.P.H.
2/05/02
Pregnant Women with Addiction

- Drug abuse markedly increases the risk of an adverse outcome
- Treatment has a prominent medical component
- Pregnant women seeking treatment through DADS are referred to a Perinatal Drug Treatment Program (Blossoms or PSAP)
PSAP: Perinatal Substance Abuse Program

- Located on the VMC campus
- Van transportation to and from program
- Individual and group counseling format
- Counselors, Program Manager, M.D., P.H.N., M.A., Health Educator, Parent Educator, Childcare Staff
- On-site childcare

- 2-4 days/week
- Recovery Education
- Recovery Support group
- Lifeskills
- Pregnancy Education
- Court Approved Parent Education
- Parenting support group
- 12 step meetings
- Healthy Relationships
The Patients of PSAP

- Pregnant women and women parenting young children or seeking reunification
- Many are addicted to more than one drug
- OPDF: Outpatient Drug Free
- Methadone Maintenance
Potential Negative Outcomes for the Fetus

- Physical anomalies
- Enduring behavioral problems due to affects on the developing nervous system
- Fetal or neonatal withdrawal or toxicity
- Miscarriage or stillbirth
Treatment Goals During Pregnancy

- Minimize fetal exposure
- Regular prenatal care
- Good nutrition
- Decrease risky behaviors
- Clean and sober at delivery
- Avoid neonatal withdrawal
- Safe and stable living environment
Establishing a Therapeutic Relationship is Vital

- Build trust and rapport
- Alert the patient to potential negative outcomes
- Patients who are addicted respond better to a carrot than to a stick
What If I Don’t Feel Neutral? Some Things to Consider

• Nobody plans to get hooked
• People tend to choose to engage in behaviors that feel good or meet a need
• Nobody likes who they are when addicted
• Most people do not want to be on a medication for the rest of their life
• These women feel guilt-ridden and ashamed
Heroin: Medical Risks Associated with Injection

- Cellulitis
- Abscess formation
- Endocarditis
- Hepatitis
- HIV infection
Heroin in Pregnancy: Obstetric Risks

- Stillbirth
- Fetal growth retardation
  - Low birth weight
  - Small head circumference
- Prematurity
- Neonatal mortality
- Note: 3-7 times higher rate for each
Heroin Addicts May Avoid or Delay Prenatal Care

- Ambivalence about the pregnancy
- Fear/quilt about exposing the fetus to drugs
- Previous unpleasant experience with medical providers
- Delayed awareness of pregnancy
Methadone Maintenance is the Treatment of Choice

- The most effective treatment for management of heroin addiction
- The safest treatment during pregnancy for a woman who is physically dependent on heroin
Opiate Detoxification is Not Recommended During Pregnancy

- Relapse rate is high (80%)
- Risk of intrauterine demise (death)
- Risk of premature labor/miscarriage
The Benefits of Methadone Maintenance

- Relieves symptoms of heroin withdrawal
- Eliminates cravings for heroin
- Promotes abstinence
- Decreases risky behaviors
- Blocks the effects of heroin (at a high dose)
- Decreases illegal activities
- Promotes retention in treatment
Additional Benefits During Pregnancy

- Provides a stable blood level of opiates
- Increases participation in prenatal care
- Reduces obstetrical complications
- Improves maternal nutrition
- Links women to a program with the opportunity for daily observation and ongoing follow-up
Admission to Methadone Maintenance Includes

- Substance abuse interview
- Review of medical history
- Physical examination
- Lab studies including drug and infectious disease screens
- Referrals for primary medical/dental care
- Determination/administration of starting dose
Medical Follow-up Includes

- Frequent M.D. visits until dose is stabilized
- Weekly drug screens
- Monthly M.D. visits while pregnant
- Verification of prenatal care
- Communication with hospital at delivery
- Post-delivery review
- Verification of post-partum check-up
- Verification of immunizations
The Methadone Dose During Pregnancy

- Doses are determined clinically
- Methadone blood levels may be helpful
- Must prevent symptoms of withdrawal
- Must enable complete abstinence
- May increase in the first and third trimesters and decrease after delivery
- Twice a day dosing is sometimes needed
Effects of Methadone on the Baby

- Used/studied for more than 30 years
- No known birth defects
- More likely to be born at term
- Lower birth weight/smaller head circumference at birth, normalizes by 1 year
- May experience developmental delay during the first year of life
- Potential for withdrawal at birth
Methadone Withdrawal in the Newborn

- Safer than heroin withdrawal in utero
- Experienced by 60-80% of exposed babies
- Occurs within the first 14 days of life
- Usually treated with an opiate
- Duration of treatment is days to months
- Can be life threatening without treatment
The Neonatal Abstinence Syndrome

- Hypertonicity (stiff muscles)
- High-pitched cry, irritability
- Poor feeding, vomiting, diarrhea
- Tremors
- Sneezing
- Sweating
- Occasionally seizures/death
Important Issues During Delivery

• Status in recovery
  – Ob needs to know if delivering patient is intoxicated or in withdrawal
  – Pediatrician needs to know if an intoxicated or sick baby is anticipated

• Toxicology testing
Pain Management

- Uncontrolled pain may trigger cravings and/or relapse
- Patients may need doses at the upper end of the therapeutic range
- Discharge medications may be appropriate
- Refill requests require careful patient evaluation by the prescribing M.D.
Breast Feeding Issues

- Consider the woman’s progress in recovery
- Review and consider infectious disease status
- Methadone maintenance is not a contradiction
Special Concerns in the Postpartum Period

• Relapse prevention
  – Ongoing connection with recovery program
  – Support system in the community
• Prompt recognition and treatment of post-partum depression
• Contraception
What About Detoxification After Delivery?

- Like insulin, methadone stabilizes a chronic illness, so can rarely be discontinued.
- The normal brain has an endogenous opioid system; Methadone acts as replacement therapy.
- 80% of patients withdrawn from methadone will relapse to heroin within 1 year.
Poly Drug Addiction

- Alcohol
- Cocaine
- Cigarettes
Fetal Alcohol Syndrome: Frequency of Occurrence

• Recognized in 1 per 500-1,000 deliveries
• May actually affect 3 per 1,000 births (12,000 babies per year)
• The most commonly identified cause of mental retardation
Fetal Alcohol Syndrome: Three Characteristics

- Growth retardation
  - Prenatal, postnatal or both
- Craniofacial dysmorphism
- Nervous system dysfunction
Fetal Alcohol Syndrome: Risk Factors

• 10% chance for women consuming two to four drinks per day (1-2 oz of absolute alcohol)

• 6-50% incidence in the offspring of chronic alcoholics
Signs of Alcohol Withdrawal

- Signs common to pregnancy and alcohol withdrawal
  - Hypertension
  - Nausea/vomiting
  - Restlessness
  - Seizures
  - Sleep disturbance
  - Tachycardia
  - Tachypnea, respiratory alkalosis

- Signs not commonly associated with pregnancy
  - Agitation
  - Distractibility
  - Fever
  - Hallucinosis
  - Impaired memory
  - Marked diaphoresis
  - Tremor
Untreated Withdrawal Symptoms Can Progress to

- Hyperpyrexia
- Electrolyte abnormalities
- Cardiovascular collapse
- Death
Alcohol Withdrawal: Evaluating the Risk

• History of withdrawals in the past, especially seizures or hallucinations?
• History of hospitalization for detox from alcohol?
• Are there physical symptoms if drinking is delayed or discontinued?
Alcohol Withdrawal: Evaluating the Risk

• Assume tolerance in women consuming more than 8 ounces of alcohol per day (one pint of liquor)
• Tolerance may be present in women consuming less especially if they are using other substances
Managing the Alcohol Dependent Pregnant Woman

- CSAT recommends a medically supervised detox in an inpatient setting
- The treating physician(s) should have training in Addiction and Obstetrics
- Disulfiram (antabuse) has been associated with birth defects and should not be used in pregnancy
Obstetric Complications Among Cigarette Smokers

- Spontaneous abortions (141,000/year)
- Low birth weight (61,000/year)
- Perinatal deaths (4,800/year)
- Premature rupture of membranes
- Preterm delivery
- Decreased birth weight
Medical Issues for the Children of Smokers

- Neonatal withdrawals
- Increased risk of SIDS
- Increase in the frequency and duration of respiratory illness
- Increased incidence of smoking initiation
Most Pregnant Women Express Interest in Smoking Cessation

- Offer assistance
- Behavioral approaches
- Smoking hotline: 1-800-7-no-butts
- Pharmacological intervention
Cocaine: Medical Complications

- Malignant hypertension
- Cardiac ischemia
- Cerebral infarction
- Sudden death
- Infections such as HIV, hepatitis B & C and other sexually transmitted diseases
Cocaine: Obstetric Complications

- Premature rupture of membranes (20%)
- Pre-term labor and delivery (25%)
- Intrauterine growth restriction (25-30%)
- Meconium-stained amniotic fluid (29%)
- Abruptio placentae (6-8%)
Cocaine Withdrawal

- Develops within hours to days
- Characterized by dysphoric mood, fatigue, vivid and unpleasant dreams, insomnia or hypersomnia, increased appetite and psychomotor retardation or agitation
- Often includes intense drug cravings
Cocaine Withdrawal: Treatment Issues

• In general medications have not proven efficacious in the suppression of withdrawal symptoms

• If depression persists for longer than a month after cessation of use, consider treating with an anti-depressant
Cocaine: Effects on the Fetus

- Decreased birth weight
- Spontaneous abortion
- Death in utero
- Increased frequency of microcephaly
- Limb reduction defects and genitourinary malformations
Cocaine: Effects on the Newborn

- Tremulousness and irritability
- Inability to suck properly
- Cognitive & neurobehavioral problems
- Lack of coordination
- Overstimulation
- Difficulty in tracking visual stimuli
- Treatment is supportive
RELAPSE & STRESS

Mechanisms and Insights
RELAPSE & STRESS

- Addiction is a chronic, relapsing neurobiologic disorder.

- Primal preservative instincts--Fight or Flight
The Stress-Hormone Cycle

When stress is perceived, the stress-hormone cycle is activated preparing the organism for fight-flight response.

The hypothalamus – pituitary – adrenal (HPA) axis initiates the stress response.

Corticotropin Releasing Factor (CRF) secreted by the hypothalamus trigger ACTH from the pituitary which stimulates cortisol release from the adrenal glands. Cortisol in turn completes the cycle and chemically turns the cycle off.

CRF and ACTH act as both hormones and neurotransmitters
The Stress Hormone Cycle

When a person perceives an event as stressful, a hormone called corticotropin-releasing factor (CRF) is released from a structure in the brain called the hypothalamus.

CRF travels in tiny blood vessels to the pituitary gland directly below the brain where it stimulates the release of another hormone, adrenocorticotropin (ACTH).

ACTH travels in the bloodstream to the adrenal glands, which sit atop the kidneys, where it triggers the release of still other hormones — principally cortisol.

When cortisol travels back to the hypothalamus and pituitary, it inhibits the further release of CRF and ACTH. If the person no longer perceives events as stressful, the stress hormone cycle stops at this point. If events continue to seem stressful, CRF continues to be released, and the stress hormone cycle continues.
RELAPSE & STRESS

- The Hypothalamic/Pituitary/Adrenal Axis
  - Hormones as ligands
  - Feedback Loop
RELAPSE & STRESS

• The Adrenals
  – Adrenalin

  – Steroids
Extra Hypothalamic CRF Brain Stress System

- BNST
- CRF
- HPC
- PVN
- CRF
- AMYG

Behavioral Responses to Stress

Sympathetic Responses to Stress
- Cardiac output
- Stroke volume
- Peripheral vascular resistance
- Blood glucose
- Heart rate
- Blood pressure

Adrenal Medulla
- Epinephrine
- Gastric acid secretion
- Gastric emptying
STRESS & RELAPSE

• The Hypothalamus
  – POMC

• The critical balance between ACTH and endorphins
ProOpioMelanoCortin

- MSH
- ACTH
- B-ENDO
RELAPSE & STRESS

- The effects of Addiction
  - Downregulation of the mu opioid receptors
Drug-induced plasticity might involve production of RNA- and ribosomal-binding proteins to alter mRNA stability and its translatability.
RELAPSE & STRESS

- Endorphin imbalance
- Self-Medication
THE HUMAN GENOME

• Nucleotide pairing
  – A-------T
  – G-------C
  – T-------A
• Transcription
• Transcription errors
THE HUMAN GENOME

- The genetic code
- Translation--Stringing the amino acid beads
SNIPS--Single Nucleotide Polymorphisms

Mu opioid receptor Snips
  - Dosage effects
  - Susceptibility effects
REFLECTIONS ON THE FUTURE

• New Therapies

• New attitudes
  – Social Model Programs
  – Criminal Justice System
  – Regulatory Agencies
Why do some people become addicted in the first place, and others not?
### The Continuum of Use

<table>
<thead>
<tr>
<th>No Use</th>
<th>Experimental</th>
<th>Occasional</th>
<th>Regular Abuse</th>
<th>Dependency</th>
</tr>
</thead>
</table>

#### Gateway Drugs:

**Drugs of First Use**

- Nicotine
- Caffeine
- Marijuana
- Alcohol

- Loss of Control
- Compulsivity
- Can’t use despite adverse consequences
- Denial

**Who are Susceptible Host Populations?**
The disease of addiction is a chronic, progressive, relapsing, incurable and potentially fatal condition with genetic, psychosocial and environmental factors influencing its development and manifestations.

The disease is set into motion by experimentation with the drug by a susceptible host in an environment that is conducive to alcohol and other drug misuse.

The susceptible user quickly experiences a compulsion to use, a loss of control and will continue to use despite adverse physical, emotional or life consequences.

American Society of Addiction Medicine
Science has shown there are “susceptible hosts”, (people with a predisposition), for substance abuse disorders.

Those persons most at-risk for drug abuse problems have:

- A genetic predisposition (family history) and,
- An environment highly conducive to drug misuse.
- Persons with concurrent psychiatric illness.
Biogenetics & Increased Liability

- Genetic factors contribute up to 40% of AOD risk

- Those with an immediate family history of alcoholism and who also have a high tolerance for alcohol’s effects have a 60% greater liability for alcoholism disorders

- “Biological markers” can help identify specific individuals who are at highest risk (i.e. beta-endorphins, P-300 cognitive deficits)

- Environmental factors contribute greatly to risk
Biopsychosocial Risks:

• Biological:
  - Family history of addiction (inherited liability)

• Psychological: (co-occurring)
  - Depression,
  - schizophrenia,
  - early antisocial personality

• Sociological: (dysfunctional/incongruent environment)
  - environments conducive to drug misuse,
  - favorable attitudes toward drug use,
  - peers who use drugs,
  - family history of criminality or antisocial behavior,
  - age of first use
Susceptible Host Populations:

- Biogenetics and Increased Liability
- Environment and High Risk Behaviors
- Associative Conditioning Processes
- Comorbidity
Research in addictions treatment has established that the driving motivational force for the practicing addict is:

- The severity and intensity of drug craving behaviors,
- The desire to self-medicate the symptoms of drug withdrawal and,
- The compulsive need to change the way they feel.
The goals of addictions treatment are to:

- Establish and maintain abstinence from the illicit use of all psychoactive drugs,
- Foster development of (non-chemical) coping and problem solving skills to stop, and ultimately eliminate impulses to “self medicate” and,
- To enhance and sustain client motivation for change.
Addiction: A Bio-Psycho-Social Concern

- **Biological**
  - Tolerance
  - Withdrawal
  - Drug Craving
  - Medical Problems

- **Psychological**
  - Internal Factors:
    - Thoughts & Feelings
    - Distress
    - Psychiatric Problems

- **Sociological**
  - External Factors:
    - People
    - Places
    - Situations
    - Events

Cued reactivity, environmental triggers and conditioned behavioral responses

Treatment must address all 3 of the biopsychosocial domains of patient needs in order to be effective.
Wanna know more about What Science Says about addiction and treatment?

Go to the net!

www.drugabuse.gov
Thank You !!!