

**Adolescent Addiction:
Where It All Starts**

**Satellite Conference and Live Webcast
Tuesday, October 8, 2019
12:00 – 1:00 p.m. Central Time**

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Faculty

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**DISCLOSURE OF RELEVANT
FINANCIAL RELATIONSHIPS**

Name	Commercial Interest	Relevant Financial Relationships: What Was Received	Relevant Financial Relationships: For What Role	No Relevant Financial Relationships with Any Commercial Interests
None To disclose				
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- Objectives**
- That childhood has multiple critical periods of brain development.
 - Vulnerability of adolescents to the disease of addiction.
 - Intervention and treatment.
 - To review current trends in drug use nationally in adolescents.
 - To discuss the implications of the above.


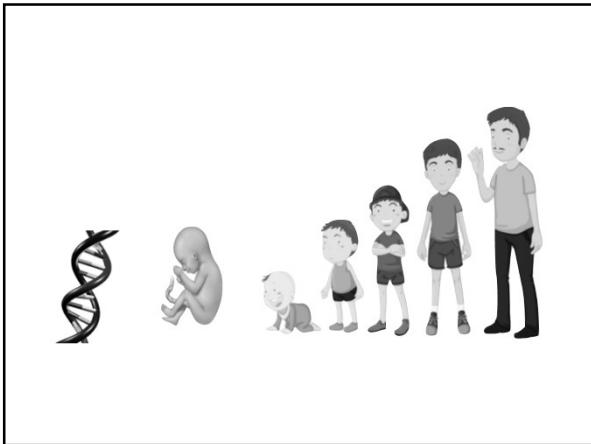
Where Have All the Children Gone.

We hope they're hiding

We hope they're playing a game but we know this is really happening.

Where have all the children gone?

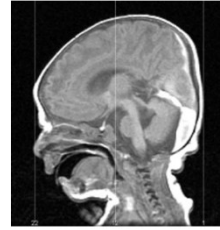
Joseph Kerschbaum

Addiction is a Brain Disease...



The Developing Brain...



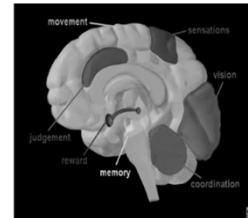
What happens when you expose the developing brain to drugs during childhood?

Prefrontal Cortex

- Has long been associated with impulse control
- Abnormalities are associated with greater risk of substance use disorder.
- Dysfunction may result in
 - Preferential motivational response to the pro-dopamine effects of drugs.
 - An unchecked progression of the neuroadaptive effects of drugs leading to compulsive drug seeking.

The Adolescent Brain is Still Developing

- The reward system is responsible for seeking natural rewards that have survival value
 - seeking food, water, sex, and nurturing
- Dopamine is this system's primary neurotransmitter



The Adolescent Brain is Still Developing

- During adolescence, the brain is undergoing dramatic transformations.
- In some brain regions, over 50% of neuronal connections are lost.
- Some new connections are formed.
- Net effect is pruning (a loss of neurons).

Adolescent Development

- Brain circuitry is establishing itself.
- Behaviors are developing.
- Risk taking and novelty seeking necessary for “sculpting” of brain.
- Risk taking and impulsivity are influenced by inherited factors.



The Critical Period

- “The adolescent brain is a critical period of vulnerability for disruption of brain regions important for individual development.”
 - Critical periods = windows during development when nature and nurture interact to establish functional characteristics.
- “Environmental alterations in gene transcription are unique during adolescence and likely impact the active remodeling of synaptic connections.”

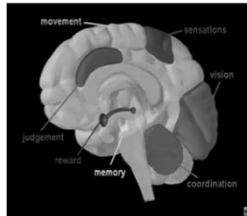
And, if that’s not enough!

- PFC takes time to develop & then addiction causes it to “regress.”
- Risk taking is high during developmental years.



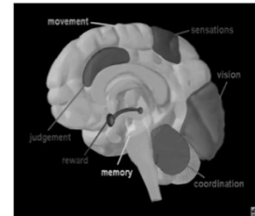
Drugs Hijack the Brain’s Reward Circuits

- Immediate effect of drug is an increase in dopamine.
- Continued use of drugs reduces the brain’s dopamine production.



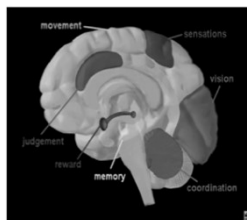
Drugs Hijack the Brain’s Reward Circuits

- Because dopamine is part of the reward system the brain is “fooled” that the drug has survival value for the organism.



Drugs Hijack the Brain’s Reward Circuits

- The reward system responds with “drug seeking behaviors.”
- Craving occurs and eventually dependence.

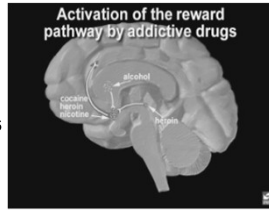


Dopamine

- When released into the nucleus accumbens is associated with motivational stimuli, subjective reward, thought, and learning of new behaviors.
- Influences the response of the nucleus accumbens to glutamatergic input.
- Children and adolescents operate at higher levels of baseline dopamine.

Reinforcement

- First use to “feel good.”
- Some continue to compulsively use because of the reinforcing effects (e.g., to FEEL NORMAL”)
- Changes occur in the “reward system” that promote continued use.



Reward-Related Learning

- Future behavior is shaped by past experiences associated with rewards.
- Rewards are “stored” by means of neuroplastic changes in the nucleus accumbens.
- This can be driven by repeated drug-provoked dopamine release.
- These processes may underlie behavioral sensitization.
 - Reward becomes stronger as it is repeatedly experienced.

Prenatal Risk Factors for SUD



- Parents and transmission of altered gene expression (epigenetic)
- Substance/alcohol use in mother
- Birth trauma-anoxia, nutritional

Prenatal Drug Exposure



- It is unknown if drug exposure from mother causes SUD.
- Does increase risk of learning disabilities and other co-morbid issues which increase the risk of SUD?

Prenatal Alcohol

- Not much research on contribution to addiction (maybe the most under diagnosed factor leading to SUD).
- Predicts higher risk of alcohol “abuse.”
- Increase impulsivity.
- Higher number in juvenile justice system.



When you drink alcohol, your unborn child drinks it, too

Fetal Alcohol Syndrome (FAS)

- Most common non-inherited cause of intellectual disability.
- 0.5 to 3 per 1000 births.
- Six fold increase since 1979-93 as drinking more socially acceptable?
- Many without typical facial features may be less recognized.



Prenatal Opioids



- Neonatal abstinence syndrome.
- Opioid withdrawal syndrome during pregnancy can lead to fetal distress and premature labor owing to increased oxygen consumption by both mother and fetus.

Prenatal Opioids



- Even minimal symptoms in the mother may indicate fetal distress, as the fetus may be more susceptible to withdrawal symptoms than the mother.

Methadone & Buprenorphine

- Results indicate cognitive impairment in patients receiving maintenance treatment with buprenorphine or methadone compared with healthy controls.
- Both patient groups were significantly debilitated compared to controls in working memory and verbal list learning.
- Long term effect: ???

Heroin and Other Opioids

- HIV, Hepatitis C
- Overdose and brain injury
- Cognitive issues

Prenatal Marijuana

- Cognitive deficits - IQ, attention, and visual spatial deficits.
- Increased risk for substance abuse, externalizing behaviors and psychiatric disorders.



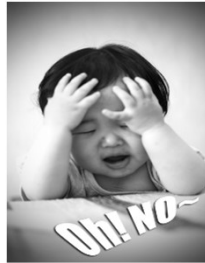
Prenatal Use of Tobacco

- Possible increase ADHD and conduct disorders?
- Lower IQ
- Impairment of visual, spatial, perceptual performance.



Methamphetamine and Ecstasy Neurotoxic Effects

- Single dose of amphetamine can damage nerve terminals in the dopaminergic regions of the brain – animal studies.
- Single dose of ecstasy can result in persisting psychosis, depression and cognitive issues.



Prenatal Cocaine

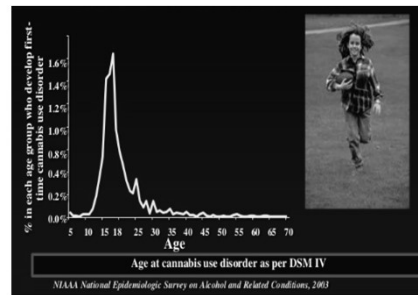
- Cocaine once thought to be a major cause of problems but more likely related to tobacco, marijuana, alcohol exposure and environmental issues.
- Can recover -> better home environment improved low IQ.

Fetal Distress

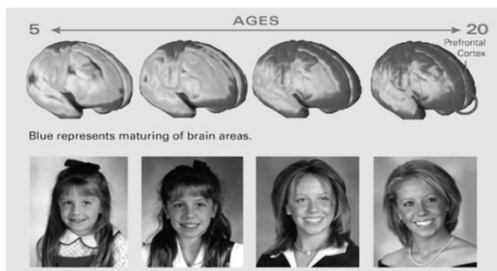
- Fetal distress, hypoxemia increases risk for ADHD and/or learning disabilities which increase risk for SUD.



Addiction is a Developmental Disorder



Exposure to drugs of abuse during adolescence could have profound effects on brain development and brain plasticity



Adolescent Substance Use

- In vulnerable individuals, the teenage years seem to be the greatest risk period for the development of substance use disorders (SUD'S).
- 20% of problem drinkers are adolescents.
- There are 42 million adolescents in the United States ages 12-19.

Stages of Addiction to Drugs of Abuse

- Drug taking invariably begins with social drug-taking and acute reinforcement and often, but not exclusively, then moves in a pattern of use from escalating compulsive use to dependence, withdrawal, and protracted abstinence.
- During withdrawal and protracted abstinence, relapse to compulsive use is likely to occur with a repeat of the cycle.

Stages of Addiction to Drugs of Abuse

- Genetic factors, environmental factors, stress, and conditioning all contribute to the vulnerability to enter the cycle of abuse/dependence and relapse within the cycle.

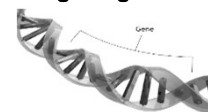
Host Factors

- Genetic risk (family history).
- Sixty percent of the likelihood of developing addiction is in the genes.
- Personality traits.
- Co-morbidities.
- A major factor in treatment response for *addiction treatment* is the presence of co-occurring psychiatric disorders and participating in/response to psychiatric treatments.

Inheritance - Genes

- No single gene results in drug addiction.
- Many genes may influence desirability of a drug, pleasure derived from a drug, impulsivity and restraint.
- Different levels of neurotransmitters like dopamine and/or type and amount of dopamine receptors in various areas of the brain might influence drug usage.

60%



Are adolescents more susceptible to alcoholism than adults? Most certainly YES

- Reduced sensitivity to intoxication.
- Increased sensitivity to social disinhibitions.
- Greater adverse effects to cognitive functioning.
- Medicates "excitability."

Age of Onset of First Alcoholic Symptoms Among Alcoholics

Age (years)	%
• 10 – 14	3
• 15 – 19	39
• 20 – 24	22
• 25 – 30	15
• 30 – 34	5
• 35 – 40	4

Natural History of Primary Alcoholism

	Years
Age at first drink	12-14
Age at first intoxication	14-18
Age at first minor problem	18-25
Usual age of onset	23-33
Usual age of treatment entry	40
Usual age of death*	55-60

* Leading cause: Heart or liver disease, Cancer, Accidents, Suicide

Age of Onset and Risk

- Alcohol use begins:
- 11-12 -> 13.5% abuse, 15.9% dependence
- 19-20 -> 2% abuse, 1% dependence
- Alcohol use before 15 compared to beginning after 21, "4" times more likely to be alcoholic.



Age of Onset and Risk

- Increased risk with earlier drinking over and above genetic risk.
- Earlier drinking initiates the more rapid progression of disease.



Adolescent Brain Changes

- Earlier drinking more likely to result in alcohol dependence independent of family history.
- Exposure of alcohol may indeed cause alterations in brain chemistry.... There are studies indicating heavy drinking during adolescence causes memory and neuropsychological changes.
- Alternative explanation that early use may be a marker for high novelty seeking behavior which is associated with the risk for alcohol dependence.

Examples

- Most adult smokers began smoking before age 18 in the US.
- 40% of adult alcoholics had symptoms of alcoholism before the age of 19.
- 16 is the median age of initiation of drug use in adults with SUD.
- Adolescents show higher rates of tobacco dependence with fewer cigarettes smoked per day than adult smokers.

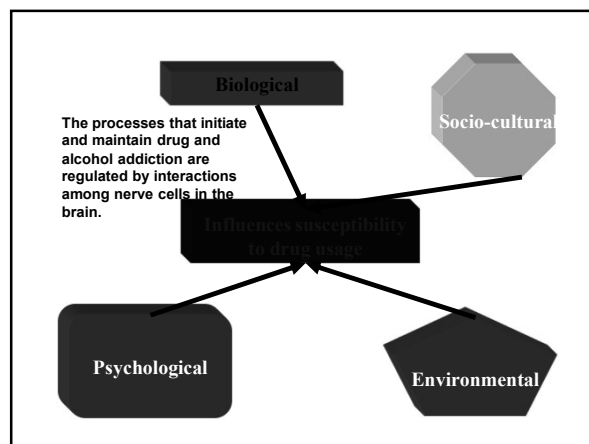
Family & Peers Influences

- Parent modeling increases notion that drugs are safe.
- Peers more powerful than parents.
- May also be associated with risk-taking.

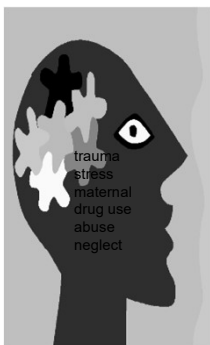


Adolescence: A Critical Period

- Adolescents exhibit higher rates of experimental use and SUD than adults.
- SUD in adults most commonly have onset in adolescence.
- The earlier the onset of substance use, the greater the predicted severity and morbidity.
- Adolescents have heightened biological vulnerability.



Co-Occurring Disorders



- Seldom does any patient with a SUD develop it without some significant precursors in their developmental history.
- Psychiatric comorbidity may increase the risk or speed of transition from substance use to SUD (ASAM text 2014).

Psychiatric Comorbidity

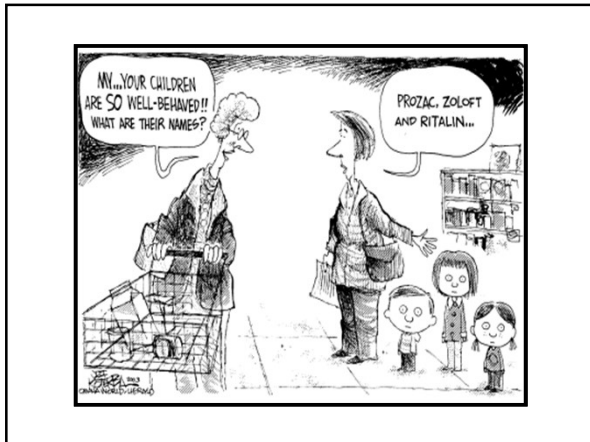
- Comorbidity of adolescent substance use disorder and other psychiatric disorders is common.
 - Young adults with a history of an anxiety or depressive disorder are shown to have twice the risk for later substance abuse.
 - Individuals with onset of substance use disorders during adolescence are 3 times more likely to be depressed, 4 times more likely to attempt suicide than later onset.

Why the High Incidence of Comorbidity


- Biological and psychosocial factors may predispose to both alcohol addiction and emotional disorders (i.e., uncontrollable trauma, schizophrenia, affective disorders)

Common Psychiatric Diagnoses Occurring With Substance Use Disorders

- Affective disorders
- Anxiety Disorders
- Personality Disorders
- Psychotic Disorders
- Organic and Neurological Disorders
- ADHD



Developmental Trauma/Stresses Associated With SUD



"It shouldn't hurt to be a child."

What do we define as "trauma"?

- "Individual trauma results from an event, series of events, or set of circumstances that is experienced by an individual as physically and/or emotionally harmful or threatening and that has lasting adverse effects on the individual's functioning and mental, physical, social, emotional, and spiritual well-being." (SAMHSA)


Early Traumatic Life Experiences

In childhood:

- Neglect/abandonment
- Lack of food, money, homelessness, adoption
- Abuse: sexual, verbal, emotional, physical
- Death of a parent
- Divorce or separation
- Family life with drug addiction, alcoholism, domestic violence
- Serious medical illness or disease


Conditions Associated High Number of Adverse Childhood Experiences

- As the number of adverse childhood experiences (ACE's) increases, the risk for the health problems increases including (but not limited to):
 - Substance use disorder/addiction
 - Anxiety disorders



Conditions Associated High Number of Adverse Childhood Experiences

- Depression
- Diabetes
- Heart disease
- Obesity
- Suicide attempts
- Increased risk for intimate partner violence



Trauma, SUD/Addiction and Co-Occurring Disorders

- Two thirds of adults in SUD treatment report child abuse and/or neglect.
- Survey of adolescents in SUD treatment >70% had a history of trauma exposure.
- The most common co-occurring disorders in patients with SUD include mood disorders, various anxiety disorders, eating disorders, and personality disorders.

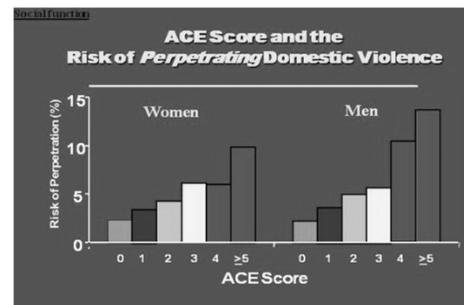
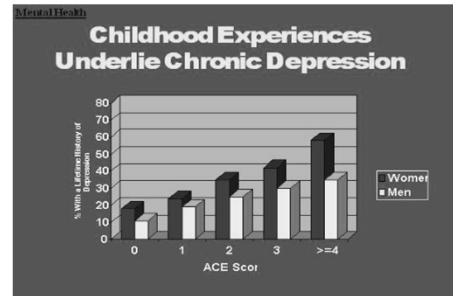
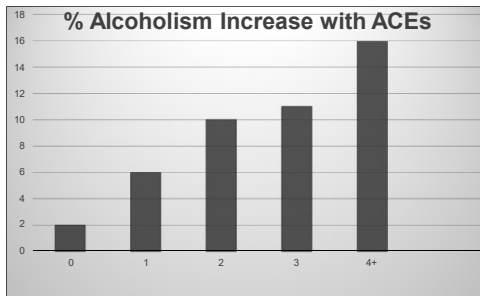
Adverse Childhood Experience (ACE) Questionnaire
 Finding your ACE Score (0-10)

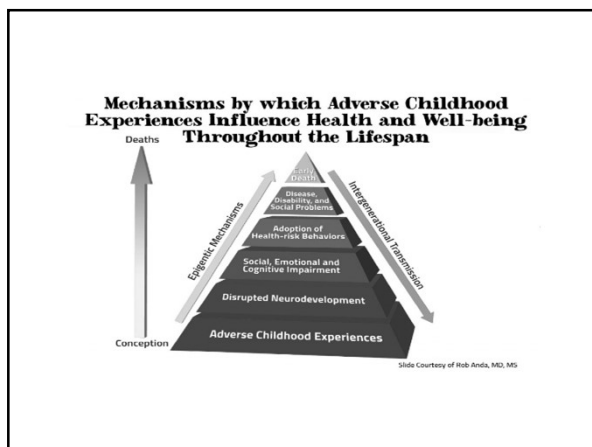
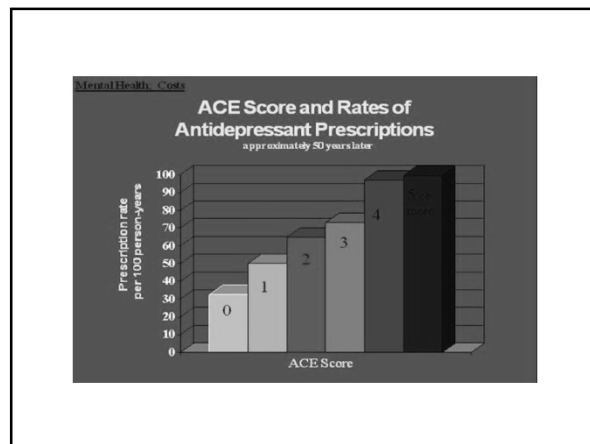
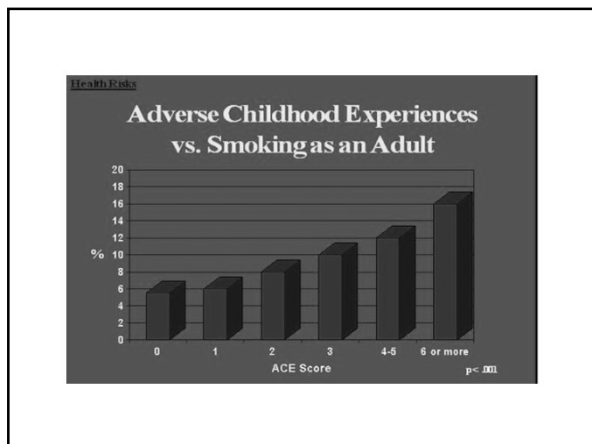
While you were growing up, during your first 18 years of life:

1. Did a parent or other adult in the household often or very often:
 - Swear at you, scold you, put you down, or humiliate you? Yes No If you enter 1 _____
 - Act in a way that made you afraid that you might be physically hurt? Yes No If you enter 1 _____
2. Did a parent or other adult in the household often or very often:
 - Push, grab, slap, or throw something at you? Yes No If you enter 1 _____
 - Ever hit you so hard that you had marks or were injured? Yes No If you enter 1 _____
3. Did an adult in your home at least 7 years older than you ever:
 - Talk to you about sex before you were ready to hear it? Yes No If you enter 1 _____
 - Try to have sex with you, or engage in sexual acts with you? Yes No If you enter 1 _____
4. Did you often feel that:
 - You were in your family would you or thought you were important or special? Yes No If you enter 1 _____
 - Your family did not love each other, but tried to reach out or support each other? Yes No If you enter 1 _____
5. Did you often feel that:
 - You didn't have enough to eat, had no one to rely on, and had no one to protect you? Yes No If you enter 1 _____
 - Your parents were too drunk or high to take care of you or take care of the house if you needed it? Yes No If you enter 1 _____
6. Were your parents ever separated or divorced? Yes No If you enter 1 _____
7. Was your mother or stepmother:
 - Often pushed, grabbed, slapped, or had something thrown at her? Yes No If you enter 1 _____
 - Sometimes or often kicked, bitten, hit with an object, or hit with something hard? Yes No If you enter 1 _____
 - Ever reportedly hit you or someone else in the household with a gun or knife? Yes No If you enter 1 _____
8. Did you live with someone who was a problem drinker or alcoholic or who used street drugs? Yes No If you enter 1 _____
9. Was a household member depressed or mentally ill or did a household member attempt suicide? Yes No If you enter 1 _____
10. Did a household member go to prison? Yes No If you enter 1 _____

Now add up your "Yes" answers: _____ This is your ACE Score


ACE and Adult Alcoholism Rates






What is Addiction? American Society of Addiction Medicine, April 2011

“Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.”



Definition of Addiction: American Society of Addiction Medicine April, 2011

“Addiction is characterized by the inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one’s behaviors and interpersonal relationships and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.”



- DSM-V Criteria for Alcohol and Substance Use Disorders**
1. Use in larger amounts/longer periods than intended
 2. Unsuccessful efforts to cut down
 3. Excessive time spent taking drug or alcohol
 4. Failure to fulfill major obligations
 5. Continued use despite knowledge of problems

DSM-V Criteria for Alcohol and Substance Use Disorders

- 6. Important activities given up
- 7. Recurrent use in physically hazardous situations
- 8. Continued use despite social or interpersonal problems
- 9. Tolerance
- 10. Withdrawal
- 11. Craving

DSM-V Addiction Severity Levels

- Mild: 2-3 criteria
- Moderate: 4-5 criteria
- Severe: 6 or more

Emerging Patterns



Categories of Drugs of Addiction

- Alcohol
- Cannabis
- Cocaine
- Opioids
- Sedatives
- Hypnotics
- Stimulants
- Hallucinogens
- Inhalants
- Nicotine

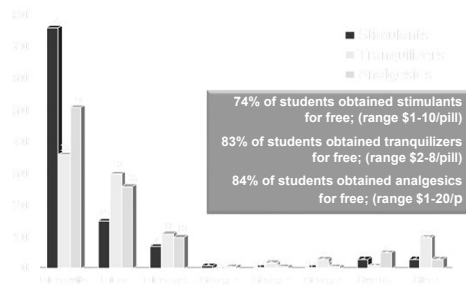
“Street Drugs 2019”

- Absinthe
- Alcohol
- Bath Salts
- Caffeine
- Cannabis
- Cocaine
- DXM
- DMT
- GHB
- Heroin
- Inhalants
- Ketamine
- LSD
- MDMA
- Mescaline
- Methamphetamine
- Mushrooms
- Kratom
- Opiates
- Peyote
- Salvia
- Spice
- Tobacco
- Tianna

Prescription Controlled Drugs

- Sedatives
- Opioids
- Hypnotics
- Stimulants
- Approximately 25% of teens report using psychoactive medication without medical supervision.

Source of Obtaining Prescription Drugs



Diagnosis of Addiction

- “Most of us have been unwilling to admit that we were real alcoholics. No person likes to think he is bodily and mentally different from his fellows. Therefore, it is not surprising that our drinking careers have been characterized by countless vain attempts to prove we could drink like other people. The idea that somehow, someday he will control and enjoy his drinking is the great obsession of every abnormal drinker. The persistence of this allusion is astonishing. Many pursue it into the gates of insanity or death.”

Diagnosis of Addiction

- “If when you honestly want to,
- (1) you find you can not quit entirely, or
- (2) if when drinking, you have little control over the amount you take,
- you are probably alcoholic.”

Big Book of Alcoholics Anonymous
 Third Edition Page 44

Assessment Basics

- Establish ground rules, especially regarding confidentiality (“your secrets keep you sick”).
- Interview patients, parents together and separately- need collateral history.

Assessment Basics

- Assessment must include questions about:
 - Relationships with parents and peers
 - Spirituality including belief in a “Higher Power”
 - Presence of family and personal secrets
 - Use of drugs/alcohol by other family members

Assessment and Treatment

Factors unique to adolescents that must be addressed:

- Entrenched denial
- Accelerated progression of disease
- Prevalence of dual diagnosis

Assessment and Treatment

- **Habilitation versus rehabilitation**
- **Need to provide comprehensive, individualized, adaptable and multidisciplinary continuums of care that include inpatient/outpatient treatment and ongoing care.**

Agents of Treatment

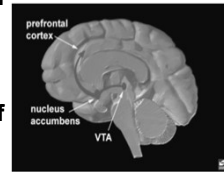
- **Withdrawal management**
- **Group therapy**
- **Educational lectures**
- **Individual therapy**
- **Spiritual component**
- **Family therapy**
- **Network therapy**
- **Recreation & exercise therapy**
- **Attendance at self help groups (AA, NA)**
- **Nutritional management**
- **Medical management**
- **Psychiatric management**

Agents of Treatment



Treat Both...

- **When treating other mental health disorder avoid mood altering drugs.**
- **Remember all drugs of abuse work through same pleasure area of the brain and may reactivate addiction.**



Following is a list of all drugs which are predictably effective for the treatment of addiction:

Any questions?

Medically Assisted Treatment (MAT)

- **Methadone**
- **Buprenorphine**
- **Naltrexone**
- **Naloxone**
- **Disulfiram**
- **Nicotine**
- **Varenicline**

Treatment Outcome

- In general, adolescent substance use treatment decreases substance use.
- Better outcome is associated with parental involvement, attendance at aftercare and treatment completion.
- Abstinence has been associated with improvement in multiple domains.
- Relapse rates for adolescents greater than adults.

Where are we now?

- By the time of the 8th grade, 1/3rd have used illicit drugs (including inhalants).
- 50% of high school seniors have tried an illicit drug.
- 27% of those who have used an illicit drug have used a drug other than THC.
- REMEMBER, in 1962 only 2% of population had ever used an illicit drug!!!

How Much Are We Missing?

National Center on Addiction and Substance Abuse

- 40% of pediatricians failed to diagnose illegal drug use even with classic presentation.
- 40% of substance using patients report that the primary care physician failed to diagnose addiction.
- Time constraints, patient dishonesty about use and poor reimbursement cited as greatest barriers to diagnosis.
- "Skepticemia" about success of treatment.

Practice Implications

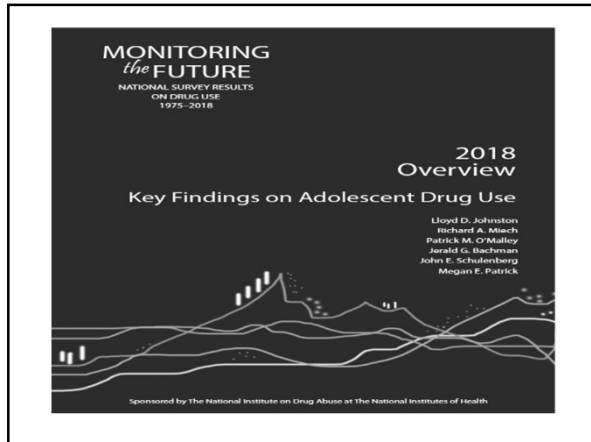
- Ask
- Urine drug testing at all well child exams.
- Urine drug testing for all initial psychiatric evaluations.
- Random urine drug screens as indicated.

Testing for Alcohol and Drugs

- Random
- Urine, hair and blood
- Observed urine samples
- Point of service
- Reference laboratory

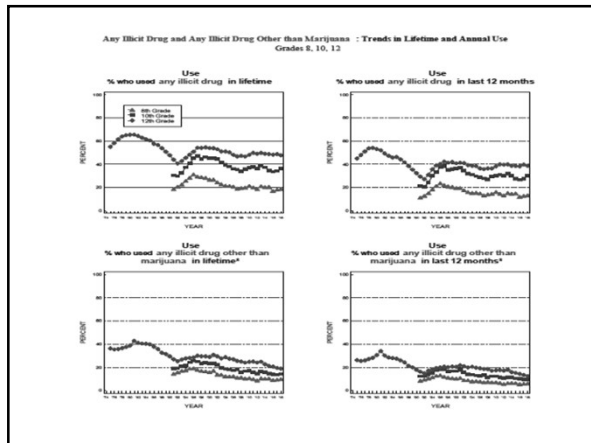
Implications

- Prevention
 - Primary
 - Prevent initiation
 - Secondary
 - Limit progression
 - Tertiary
 - Treatment at some level
- Medical education
- Residency training
 - All specialties
- Continuing education (CME)



Monitoring The Future Study

- Measures drug use in high school seniors since 1975.
- Included 8th and 10th graders since 1991.
- Funded by National Institute of Drug Abuse.
- Conducted by University of Michigan Institute for Social Research.



Substance Use Disorders United States 2018

- 21.5 million people aged 12 or older had a substance use disorder.
- 17.0 million people with an alcohol use disorder.
- 7.1 million with an illicit drug use disorder.
- 2.6 million who had both an alcohol use and an illicit drug use disorder.

Substance Use Disorders United States 2018

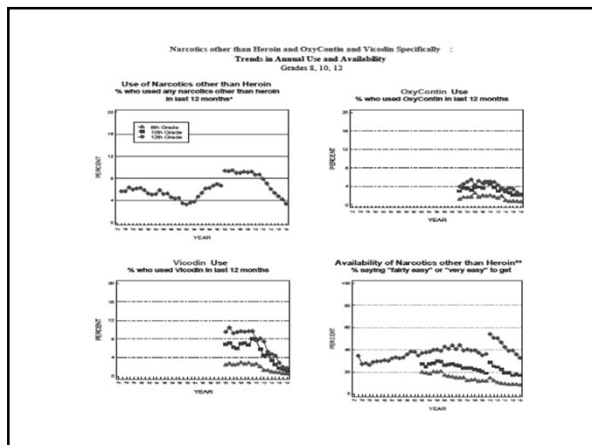
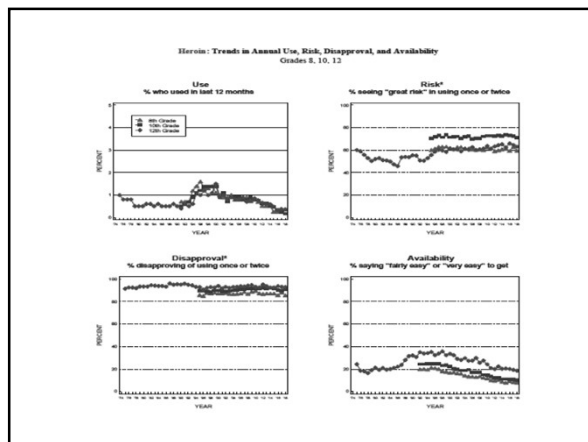
- The percentage of people aged 12 or older in 2018 who had a SUD (8.1 percent).
- An estimated 1.3 million adolescents aged 12 to 17 had SUD's in 2018, which represents 5.0 percent of adolescents or about 1 in 20 adolescents.

Opioid Use

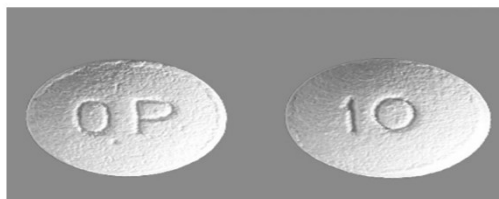
- In 2018, an estimated 467,000 adolescents aged 12 to 17 were current nonmedical users of opioid analgesics, which corresponds to 1.9 percent of adolescents, 168,000 having an addiction to prescription opioids.
- An estimated 28,000 adolescents had used heroin in the last year, 18,000 had a heroin use disorder.

Opioid Analgesics

- Most adolescents who misuse prescription pain relievers are given them for free by a friend or relative.
- The prescribing rates for prescription opioids among adolescents and young adults nearly doubled from 1994 to the present.
- People often share their unused opioid analgesics.



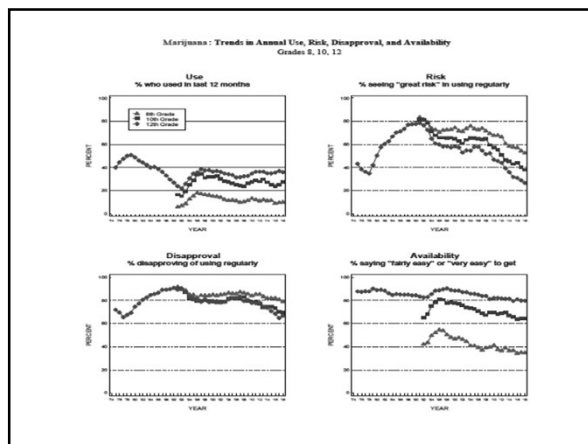
**FDA APPROVES OXYCONTIN
USE FOR CHILDREN AS
YOUNG AS 11
BY JESSICA FIRGER of
Newsweek ON 8/17/15**



The FDA says OxyContin is safe for children as young as 11.
NATIONAL INSTITUTES OF HEALTH

Cannabis sativa- Marijuana

Marijuana = mixture of leaves, stems, tops
THC = 1- 20-30%



Marijuana

- The average marijuana cigarette ('joint') contains 2.5-5.0 mg THC; about 50% is absorbed.
- 30 years ago marijuana was 1-3% THC by weight, as low as 0.5%.
- Now, marijuana is 5-10% THC by weight, but as high as 15 %.
- Some strains as high as 30% THC by weight and in edibles.

Is Marijuana a Gateway Drug?

- 60% of teens who use marijuana before age 15 will subsequently use other substances and/or alcohol.
- Teens who use marijuana are more likely to use substances and/or alcohol than teens who abstain.

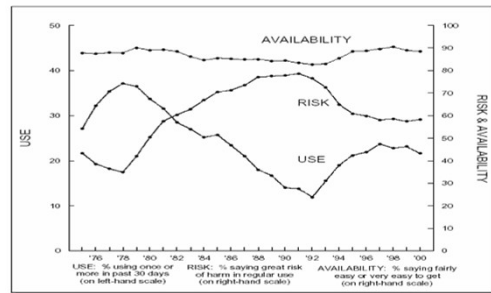
National Center on Addiction and Substance Abuse at Columbia University; October 27, 1997

Marijuana and Adolescents

- Use in early adolescence correlates with higher rates of adult addiction.
- ~ 60% of adolescents in drug treatment programs have primary diagnosis of marijuana use disorder.
- The percentage of middle-school students who reported using marijuana increased throughout the early 1990s.
- In the past few years, illicit drug use, including marijuana, by 8th-, 10th-, and 12th-graders has leveled off.

Perceived Risk vs. Use

Marijuana: Trends in Perceived Availability, Perceived Risk of Regular Use, and Prevalence of Use in Past Thirty Days for Twelfth Graders



Psychiatric Issues

- Naive users smoking high potency marijuana are most common to receive ER treatment (anxiety/panic, paranoia).
- Marijuana can precipitate anxiety/panic and even psychotic disorder in vulnerable individuals.

Psychiatric Issues

- Associated with other affective/mood disorders.
 - Increases suicide risk
- Estimated attributable risk of cannabis use was:
 - 13% for psychotic symptoms
 - 50% for any disorder requiring psychiatric treatment

Marijuana and Psychosis

- Heavy marijuana use may lead to earlier onset of schizophrenia in some adolescents.
 - Phenomenon is dose-response related.
 - Effect not due to self medication as no relationship found between early psychotic symptoms and risk of cannabis use.

Marijuana and Psychosis

- IV Δ^9 THC provokes dose-dependant positive and negative symptoms in people with schizophrenia.
- Marijuana use may account for ~ 10% of cases of psychosis in the general population.

Schizophrenia and Marijuana

- Marijuana is frequently used by persons with schizophrenia to self medicate?
- 13% of cases could be avoided without the use of marijuana.
- Use of cannabis more than 10 times was associated with 2.3 times greater risk of having schizophrenia.

Gateway Drug



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- **Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults, The Adverse Childhood Experiences (ACE) Study; Vincent J. Felitti MD, FACP, Robert F. Anda MD, MS, Dale Nordenberg MD, David F. Williamson MS, PhD, Alison M. Spitz MS, MPH, Valerie Edwards BA, Mary P. Koss PhD, James S. Marks MD, MPH, American Journal Of Preventive Medicine, Volume 14, Issue 4, May, 1998**

