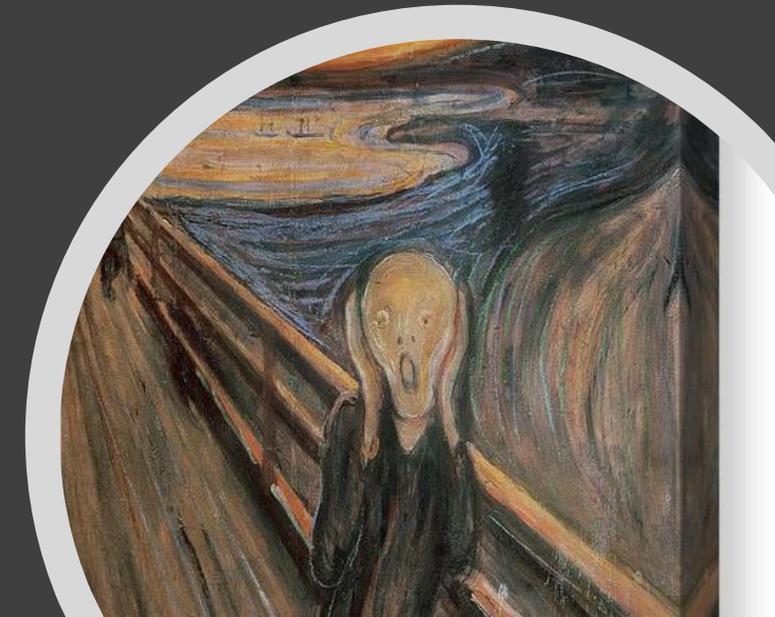


Psychiatric Emergencies Due To Substance Abuse

Rob Campbell, MD

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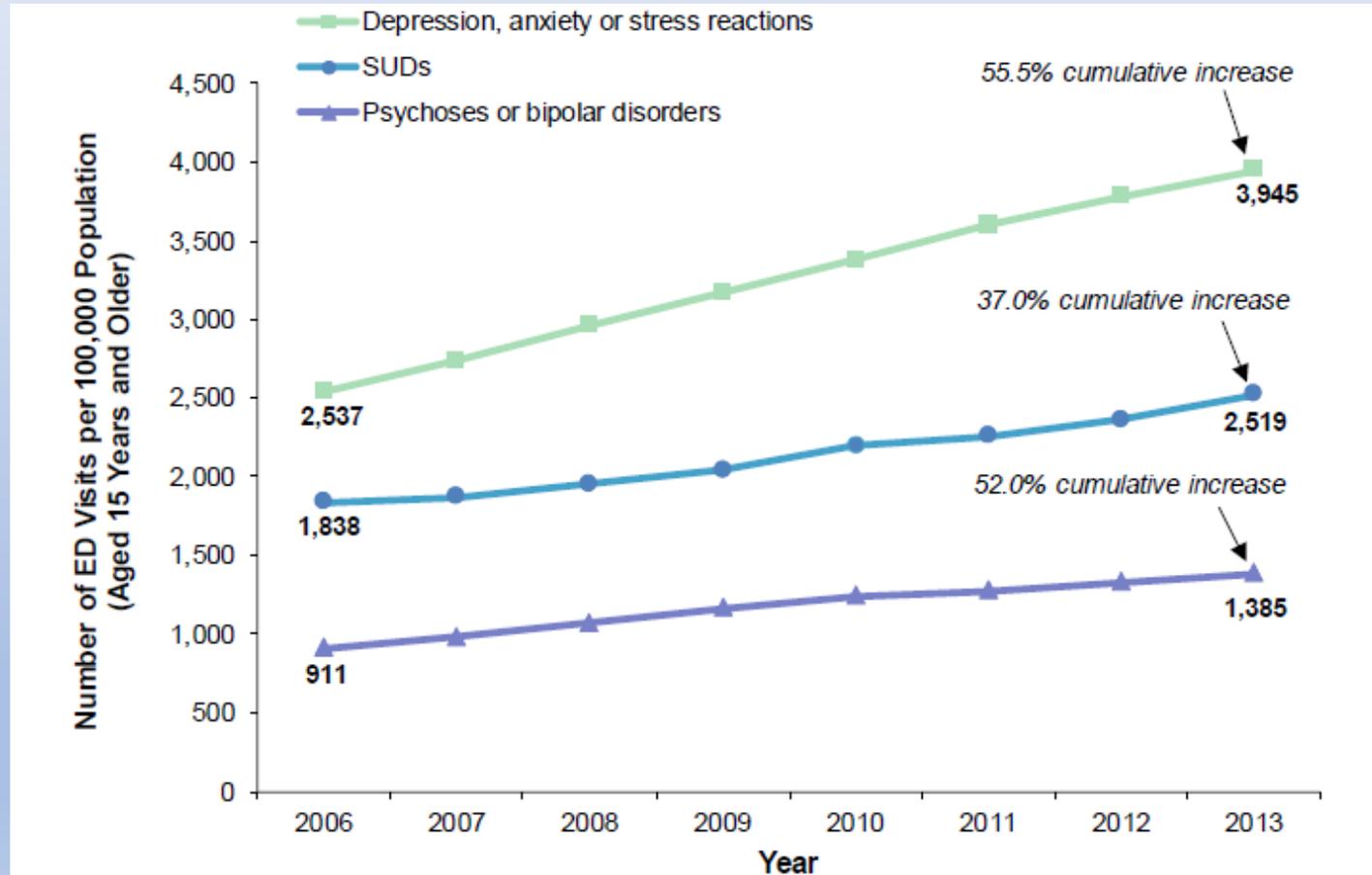


Trends in ED visits involving mental and substance use

- An estimated 45 million adults aged 18 years or older in the United States have a mental, behavioral, or emotional disorder in any given year
- represents almost 20% of all U.S. adults (18 years and older)
- 1 in 8 visits to EDs in the United States involves mental and substance use disorders (M/SUDS)
- Over the past five years this rate has increased by 20%
- Rate of hospital admission is twice that of the non-M/SUDS patient



Population rates of ED visits involving mental and substance use disorders, 2006-2013



Psychiatric emergencies defined

- Any DSM-5 disorder whose symptoms have become so severe that the patient seeks emergency treatment

Psychiatric emergencies which may present as primary disorders or secondary to substance abuse

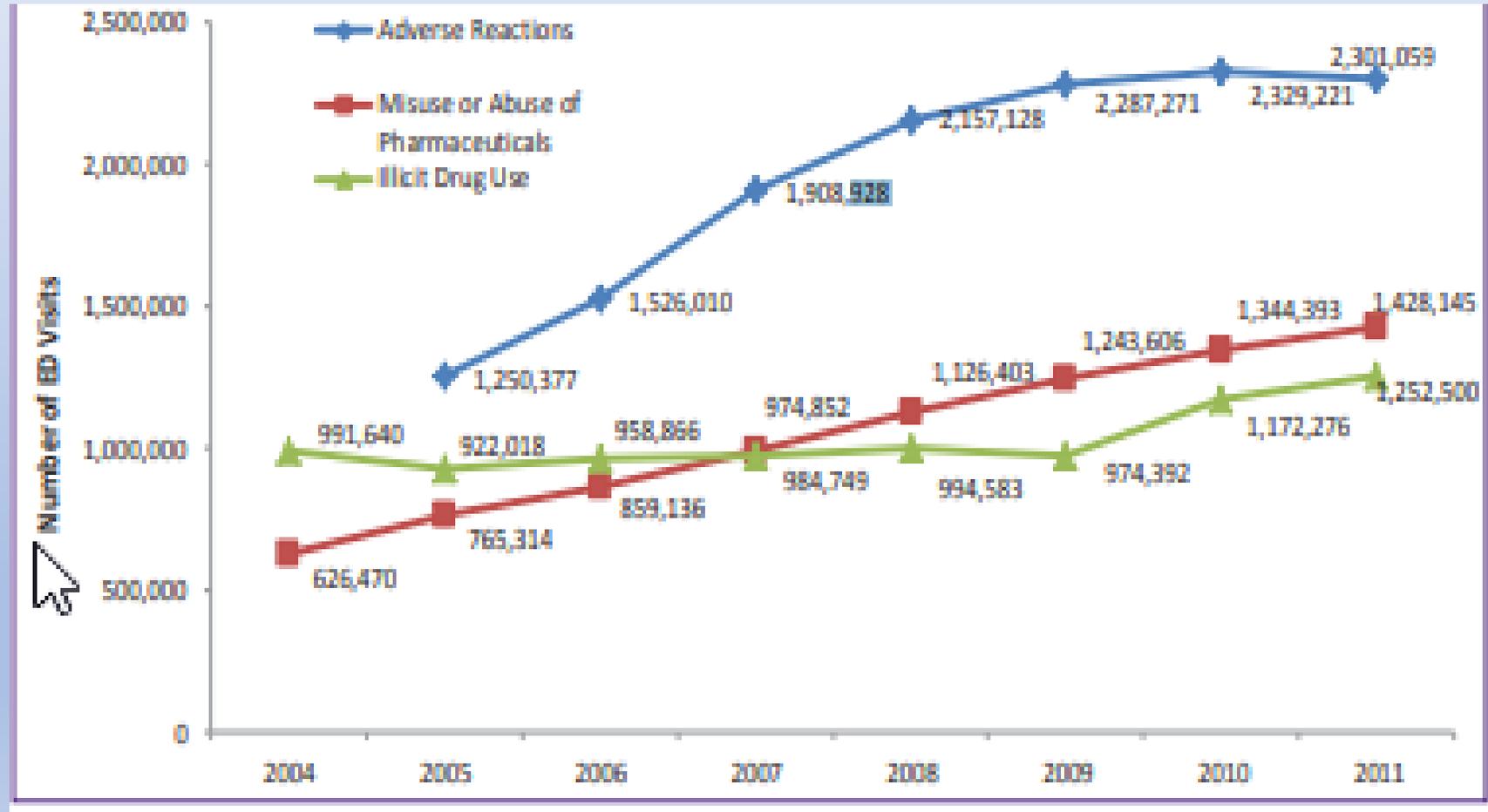
Primary psychiatric

- Depression
- Anxiety
- Stress reactions
- Psychosis
- Bipolar disorder
- Delirium

Psychiatric comorbid with SUD

- Depression
- Anxiety
- Stress reactions
- Psychosis
- Bipolar disorder
- Delirium
- Intoxication
- Withdrawal

Drug-related ED visits by type 2011



What about alcohol?



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NEWS RELEASE

FOR IMMEDIATE RELEASE

Friday, January 12, 2018

NIH study shows steep increase in rate of alcohol-related ER visits

Increases were larger among females than males, providing more evidence of narrowing gender gaps in alcohol-related harms in the U.S.

The rate of alcohol-related visits to U.S. emergency departments (ED) increased by nearly 50 percent between 2006 and 2014, especially among females and drinkers who are middle-aged or older, according to a new study conducted by researchers at the National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health. The study findings are available online in the journal *Alcoholism: Clinical and Experimental Research*.

"In just nine years, the number of people transported to the ED annually for medical emergencies caused or exacerbated by alcohol increased from about 3 million to 5 million," said NIAAA Director George F. Koob, Ph.D. "These findings are indicative of the detrimental effects that acute and chronic alcohol misuse have on public health, and the significant burden they place on our healthcare system."

Researchers led by Aaron White, Ph.D., senior scientific advisor to the NIAAA director, analyzed data from the Nationwide Emergency Department Sample (NEDS), the largest ED database in the United States, and part of the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. The research team assessed trends in ED visits between 2006 and 2014 involving acute and chronic alcohol consumption among individuals 12 and older. Visits related to acute alcohol consumption were classified by standard diagnostic codes related to alcohol misuse over a short period of time, such as acute alcohol intoxication and

The rate of alcohol-related visits to U.S. emergency departments increased by nearly 50 percent between 2006 and 2014



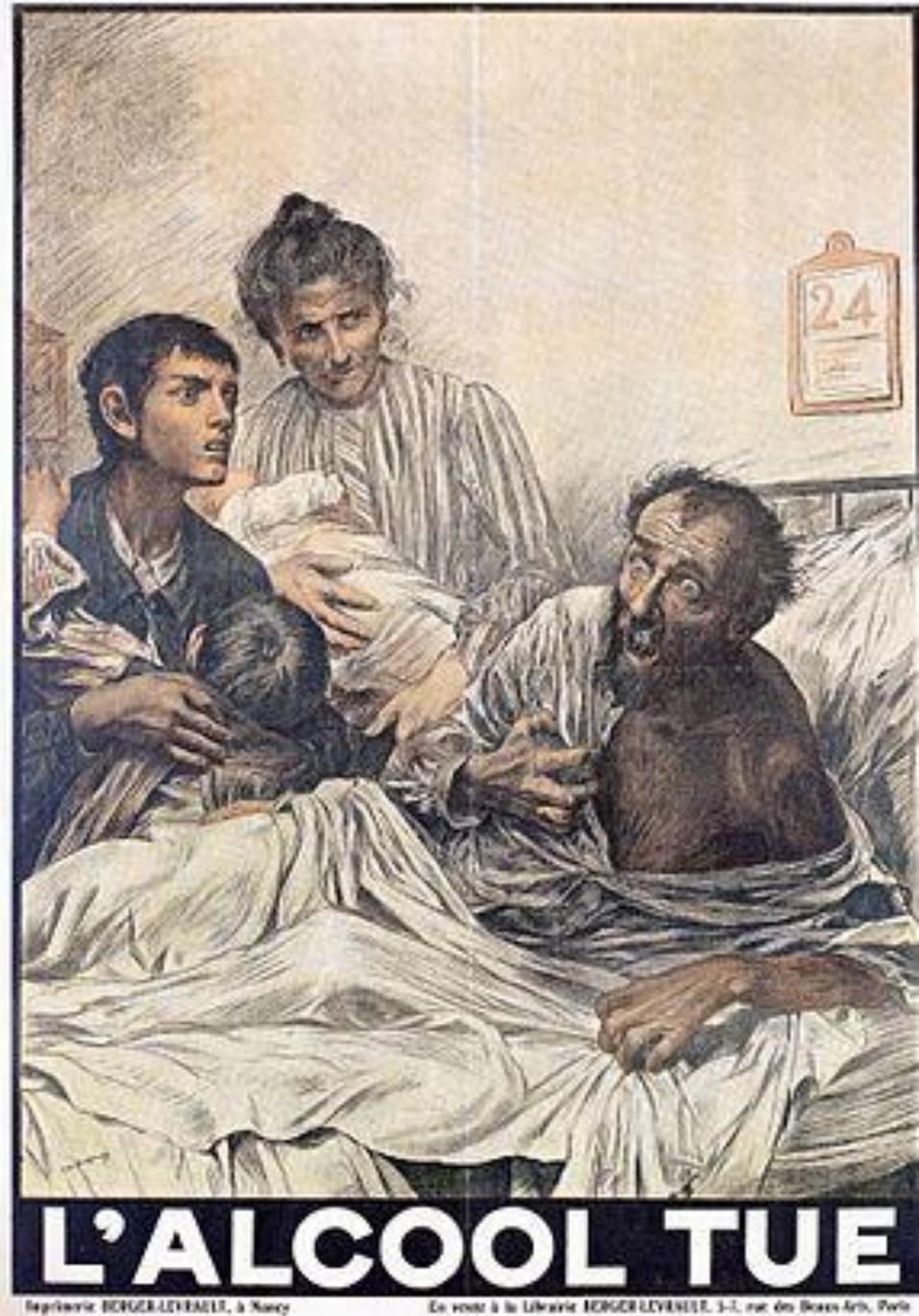
- 50% increase in ED visits secondary to alcohol over the past eight years
- Greatest increase:
 - ✓ Females
 - ✓ Middle-aged and older adults
- **Over the last 10 years the number of ED visits related to alcohol abuse has increased by over 2 million visits**

45-year-old male brought to ER by son in an agitated and disoriented state after having had a seizure. Blood pressure, pulse, respiratory rate and temperature are all elevated. What is the most likely diagnosis?

- A. Alcohol intoxication
- B. Cocaine intoxication
- C. Cannabis intoxication
- D. Opioid withdrawal
- E. Alcohol withdrawal

E. Alcohol withdrawal

- Typically begins 8-48 hours after last drink
- Peaks 48-96 hours after last drink
- Usually resolves in 7-10 days
- Characterized by agitation, tremulousness, auditory, visual, tactile hallucinations
- **DELIRIUM IS THE HALLMARK SYMPTOM**



DELIRIUM

The DSM 5 lists five key features that characterize **delirium**:

- ✓ Disturbance in **attention** (reduced ability to direct, focus, sustain, and shift attention) and awareness
- ✓ The disturbance **develops over short period of time** (usually hours to days), represents a change from baseline, and tends to fluctuate during the course of day
- ✓ An additional disturbance in **cognition** (memory deficit, disorientation, language, visuospatial ability, or perception)
- ✓ The disturbances are not better explained by another preexisting, evolving or established neurocognitive condition, and do not occur in the context of a severely reduced level of arousal, or medication side effect

Additional features that may accompany delirium and confusion include the following:

- ✓ **Psychomotor behavioral disturbances** such as hypoactivity, hyperactivity with increased sympathetic activity, and impairment activity, and impairment duration and architecture
- ✓ Variable **emotional disturbances**, including fear, depression, euphoria, or perplexity

Delirium by Other Names

- *ICU psychosis*
- *Acute confusional state*
- *Acute brain failure*
- *Encephalopathy*
- *Toxic metabolic state*
- *CNS toxicity*
- *Paraneoplastic limbic encephalitis*
- *Sundowning*
- *Cerebral insufficiency*
- *Organic brain syndrome*

Neuropathogenesis of Delirium

Neurotransmitter changes associated with delirium:

✓ Deficiency:

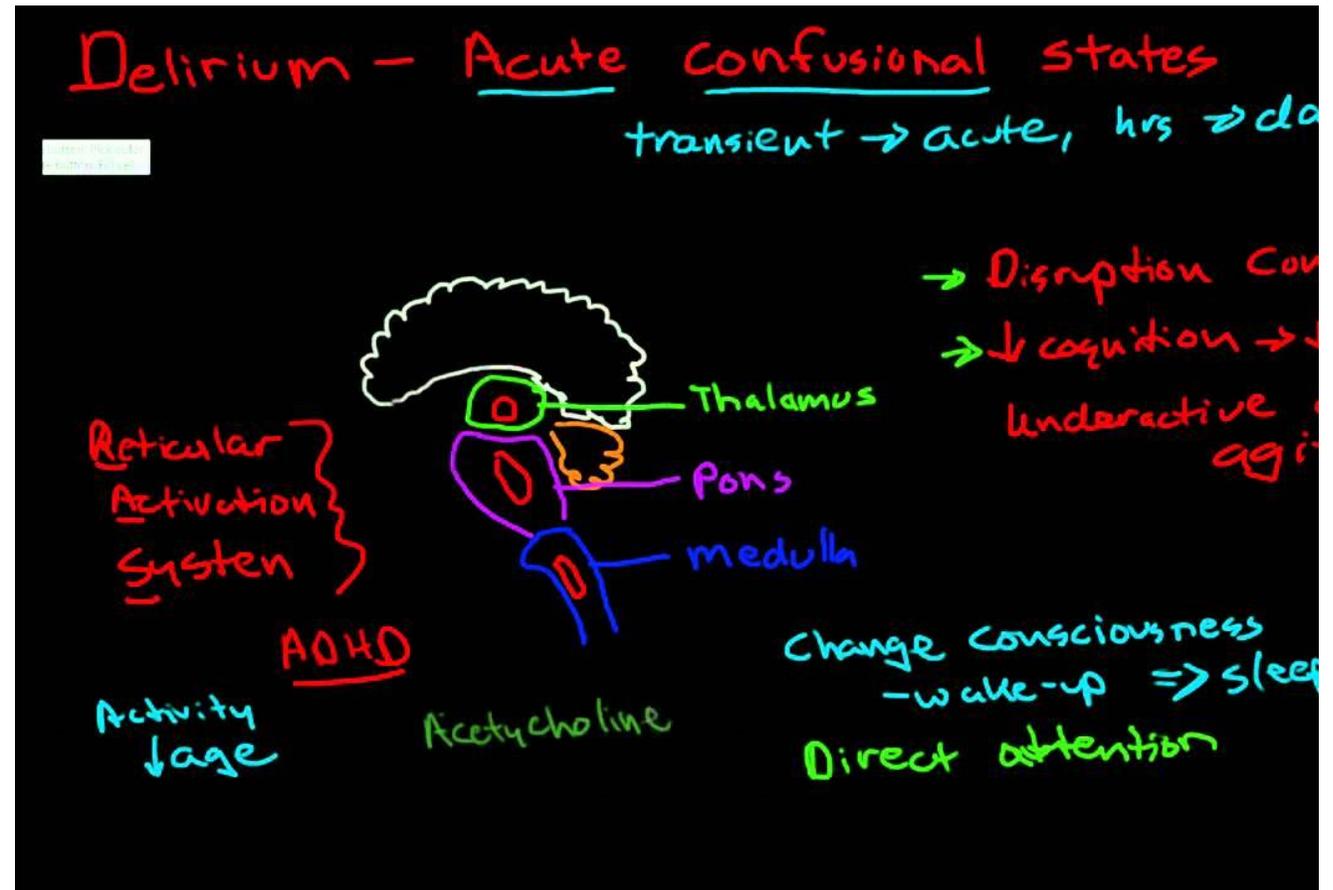
- Acetylcholine
- Melatonin

✓ Excess:

- Dopamine
- Norepinephrine
- Glutamate

✓ Variable alterations ↑ or ↓ depending on delirium presentation and cause:

- Serotonin
- Histamine
- GABA





Precipitating Factors

Drugs and Toxins

Prescription medications:

- Opioids
- Sedative-hypnotics
- Antipsychotics
- Mood stabilizers
- Skeletal muscle relaxants
- Antimicrobials
- Chemotherapeutic agents
- Polypharmacy in general (keeping medication interactions heavily in your mind, too)

Precipitating Factors

Drugs and Toxins

Non-prescription medications:

- Classic antihistamines (H1 blockers) like diphenhydramine
- H2 blockers (e.g., cimetidine, ranitidine, famotidine)
- Dextromethorphan
- Herbal supplements (e.g., kava, horny goat weed, ginkgo biloba, St. John's wort, others)

✓ Drugs of abuse:

- **Ethanol**
- Opioids
- Hallucinogens
- Stimulants (e.g., methamphetamine, MDMA, khat, kratom, others)
- Nonmedicinal abuse of prescription meds





Precipitating Factors

Drugs and Toxins:

✓ Withdrawal states:

- Ethanol
- Benzodiazepines
- Barbiturates
- GHB and others

✓ Medication side effects:

- Hyperammonemia from VPA
- Confusion from quinolones
- Serotonin syndrome
- others

✓ Poisons:

- Atypical alcohols (e.g., methanol, ethylene glycol)
- Inhaled toxins (e.g., carbon monoxide, cyanide, hydrogen sulfide, others)
- Plant derived (e.g., Jimson weed, Salvia, others)

54-year-old male brought to the emergency room by his family after they found him “acting strange” after an evening of drinking. He has been a longtime heavy drinker and often disappeared for days at a time but usually returns to normal when he is sober. He is ill appearing and has been losing weight. Today he was found by his family at a friend’s house where he began to get confused. The patient appears sleepy and is slow to respond to questions. In the emergency room his vital signs are normal. On exam he is somnolent, diaphoretic and tremulous, but no trauma is found. He often answers questions incorrectly or inappropriately. Neurologically, he has nystagmus. He has very poor short-term recall and has significant difficulty walking in a steady manner. What is the most likely diagnosis?

- A. Alcohol withdrawal with impending DTs
- B. Cerebellar stroke or hemorrhage
- C. Likely taking drugs other than alcohol
- D. Wernicke’s encephalopathy
- E. Partial complex seizures

D. Wernicke's encephalopathy

- **Wernicke's encephalopathy hallmark triad:**
 - ✓ Ophthalmoplegia
 - ✓ Ataxia
 - ✓ Confusional state
- Caused by thiamine deficiency
- Most common in chronic alcohol use disorder
- Intravenous thiamine is the treatment

A 43-year-old man with a history of alcohol, cocaine, and very heavy tobacco use was admitted to the Neuro ICU with a 4-day history of severe headache. He continued to smoke, drink, and use cocaine up to the day of his admission. CT head was performed and revealed subarachnoid hemorrhage. He was subsequently found to have an aneurysm at the tip of the basilar artery. On admission to the hospital, he had slight difficulty with concentration tasks but was fully oriented and had no short-term memory deficits or focal neurologic signs. He underwent successful clipping of the aneurysm on hospital day 1. On postop day 1 he was mildly disoriented and lethargic and answered simple questions slowly and intermittently. Over the following 5 days he developed bradycardia, severe restlessness, agitation, disorientation, paranoid delusions and a fluctuating level of consciousness. He was treated with haloperidol and four-point restraints, which were minimally successful in resolving his delirium. Finally on postop day 11 an agent was administered that resulted in complete resolution of his agitated delirium within 6 hours. What is the most likely treatment that was rendered?

- A. Lorazepam 1-2 mg IV q1h
- B. Thiamine 100 mg IV bolus
- C. Physostigmine 1.5 mg IV q1h
- D. Baclofen intrathecal 50 mcg x 1 dose
- E. Nicorette® spray 2 mg intranasal q1h

Answer: E. Nicorette[®] spray 2 mg intranasal q1h

- Nicorette[®] is the proprietary name for one of the several brands of nicotine nasal spray, and is an FDA approved, over the counter, nicotine replacement product.
- Agitated delirium due to nicotine withdrawal is not well recognized and is frequently overlooked in hospitalized smokers who are not on NRT.
- Dramatic improvement of delirium due to nicotine withdrawal using NRT has been well-documented in the literature.
- All patients who smoke, especially if it is more than 10 cigarettes daily, or if they smoke their first cigarette of the day within 15 minutes should be offered NRT.

Regarding substance-induced psychotic disorders, the following statements are correct EXCEPT:

- A. Prevalence of psychosis among current methamphetamine users is 11 times higher than among the general population.
- B. Chronic IV use of methamphetamine rarely leads to prolonged psychotic symptoms.
- C. Prevalence of psychotic symptoms among methamphetamine users has been estimated to be between 13-23%.
- D. Psychosis during intoxication is common among those abusing cocaine, amphetamines, GHB and PCP.
- E. Substance-induced psychotic disorders are slightly less prevalent than primary psychotic disorders with concurrent substance use among patients presenting to psychiatric emergency rooms with psychotic symptoms.



B. Chronic IV use of methamphetamine rarely leads to prolonged psychotic symptoms.

- Methamphetamine psychosis in general has a better prognosis than a primary psychotic disorder.
- Studies conducted have shown that chronic IV methamphetamine use is associated with increased rates of prolonged psychosis persisting for several months to over 2 years.

Approximately what percent of patients with schizophrenia abuse drugs or alcohol excluding nicotine?

- A. 2.5%
- B. 6%
- C. 12%
- D. 24%
- E. 50%



SCHIZOPHRENIA AND ADDICTION:

CO-OCCURRING DISORDERS

Addiction Campuses

E. 50%

- Schizophrenia and substance abuse are more common with:
 - ✓ Younger age
 - ✓ Males
- Increased risk of schizophrenia is noted in:
 - ✓ Cannabis: 5.2 times
 - ✓ Alcohol: 3.4 times
 - ✓ Hallucinogens: 1.9 times
 - ✓ Sedatives: 1.7 times
 - ✓ Amphetamines: 1.2 times
 - ✓ Other substances: 2.8 times

35-year-old male is brought to the emergency room by police for erratic behavior. He manifests increasing agitation, paranoia, and persecutory delusions. He has small sores on his face and arms. He states that neighbors are conspiring against him and he has been spying on them. He is hostile and reports having anger issues, increased libido, insomnia, weight loss and anxiety spanning of the past 6 months.

- A. Cannabis intoxication
- B. Phencyclidine (PCP) intoxication
- C. Delirium
- D. First onset primary psychotic disorder
- E. Methamphetamine-induced psychotic disorder

METH PSYCHOSIS

UNDERSTANDING
METHAMPHETAMINE
PSYCHOSIS



E. Methamphetamine induced psychotic disorder

Signs of methamphetamine intoxication:

- ✓ Hyperactive behavior and speech
- ✓ Hypersexuality
- ✓ Anorexia
- ✓ Insomnia
- ✓ Inattention
- ✓ Labile mood
- ✓ Hostility
- ✓ Paranoia
- ✓ Auditory, visual and tactile hallucinations
- ✓ Skin picking or “punding” or “meth mites”

38-year-old male presents to the emergency room after having a witnessed seizure. Patient continues to seize upon arrival to the emergency department but is appropriately treated and discharged. Later the same day the patient re-presents to the emergency department after having two more seizures. Paramedics find a number of crushed blue pills as well as blue powder on his fingertips. Patient admits that he had also done the same thing prior to his first presentation of the day. What is the most likely substance that this patient is abusing?

- A. OTC “cold pills”
- B. Fluoxetine (Prozac)
- C. Ecstasy
- D. Adderall
- E. Bupropion (Wellbutrin)



E. Bupropion (Wellbutrin)

- Bupropion abuse via “snorting” and IV use has become problematic.
- Bupropion is structurally similar to amphetamines.
- Stimulant properties of bupropion are sufficient to allow treatment for ADHD.
- The patient in question describes a chemical euphoria similar to that with cocaine use.
- Bupropion is not a controlled substance...YET!
- Bupropion abuse or overdose commonly presents with psychotic symptoms as well as seizures.

A 25-year-old male with a history of marijuana, amphetamine, nicotine, codeine, and alcohol abuse presents to the ED in a manic state and having increasing paranoid delusions and auditory hallucinations. He is highly agitated and violent. He admits to having used a large amount of cocaine the previous hour. Which of the following drugs when combined with cocaine makes it the most difficult for cocaine to be eliminated from the body?

- A. Marijuana
- B. Methamphetamine
- C. Nicotine
- D. Codeine
- E. Alcohol



E. Alcohol

Cocaine + alcohol →
cocaethylene

Cocaethylene:

- ✓ Pharmacological action similar to cocaine
- ✓ Much longer half-life
- ✓ Severely cardiotoxic
- ✓ Increases risk of myocardial infarction and malignant arrhythmias over cocaine alone
- ✓ **Increased risk of sudden death is 18 times greater than with cocaine alone!!**

The many faces of GHB

- 23 yo woman presents to ED with paranoid delusions and auditory hallucinations.
- Psychiatric history includes two brief psychotic episodes induced by amphetamines and marijuana several years ago.
- In the last 6 months, she has demonstrated bizarre behavior, isolation, apathy, poor ADLs.
- Patient reports occasional use of GHB but otherwise gives no history of recent drug use.
- UDS is negative so schizophrenia is diagnosed, and antipsychotics started.
- Patient develops tachycardia and hypertension lasting 24 hours.
- Severe agitation and confusion are also present.
- Restraints used and lorazepam used to stabilize her.
- Confusion resolves in less than 72 hours.
- Patient then reveals that she had been using GHB daily for the last six months.
- Stopped GHB abruptly 24 hours prior to the admission.

GHB

- Member of sedative-hypnotics
- **VERY ADDICTIVE**
- First synthesized as analog of GABA
- Acts on GABA-B and specific GHB receptors
- Causes CNS depression, stimulation, psychomotor impairment
- Response is dose-dependent
- Low-dose stimulates dopamine
- High dose inhibits dopamine
- Enhanced sexual response
- Altered states of consciousness
- Increased socialization 2° to oxytocin release
- OD → somnolence, stupor, coma, agitation, combative behavior, self injury, respiratory depression and **DEATH**



- 51yo male used high-dose GHB X 10 days then stops.
- No history of previous GHB use.
- No history of alcohol, cannabis, nicotine use.
- No symptoms of withdrawal day #1
- Reports “strange feelings” withdrawal day #2
- 4 days after cessation patient suddenly jumps the security gate at airport, runs to his car and collides with another car.
- Heads home, collides with three more cars, chased by police.
- Becomes very confused restless and nonsensical.
- Extremely anxious, highly agitated and combative.
- Complaints of abdominal pain.
- Waxing and waning attention and concentration.
- Finally responds to IV Valium.

Excited Delirium Syndrome

- Subtype of delirium characterized by aggressive and combativeness.
- AKA “Bell’s mania”.
- Usually due to stimulant abuse or psychotropic medication cessation in psychiatric patients (usually BPD).
- GHB withdrawal Sx usually 6-72 hrs. after cessation.
- Very rare after *recreational* GHB use.
- More common after withdrawal in GHB *dependence*.
- May require on-site use of ketamine or taser to subdue.
- **10% sudden death rate.**



29-year-old male with a history of chronic methamphetamine dependence presents to ED after suicide attempt via self-inflicted GSW to chest. After emergency surgery patient is stabilized. Postoperatively the patient is noted to have profound depression which he states was present preoperatively and led up to his suicide attempt. He is also agitated and having vivid dreams. What is the most likely etiology for his clinical presentation?

- A. Methamphetamine intoxication.
- B. Methamphetamine withdrawal.
- C. Major depressive disorder, recurrent, severe, w/ PF.
- D. Intoxication from another substance of abuse.
- E. Withdrawal from another substance abuse.

B. Methamphetamine withdrawal.

- Withdrawal symptoms occur in 90% of chronic methamphetamine abusers when they cease the drug.
- Withdrawal symptoms include:
 - ✓ Depression (often severe)
 - ✓ Hypersomnolence
 - ✓ Anxiety
 - ✓ Irritability
 - ✓ Inability to concentrate
 - ✓ Psychomotor slowing
 - ✓ Increased appetite
 - ✓ Paranoia

Stimulant withdrawal depression

- More common in females than males.
- More common in patients with DDx disorders.
- Due to chronic depletion of dopamine and serotonin.
- More common with methamphetamine withdrawal than cocaine withdrawal.
- **MAY ALSO BE SEEN IN OPIOID ABUSE AND WITHDRAWAL.**

It's New Year's Day 2015. In London a young woman pressed her palms to the chest of her comatose boyfriend and desperately pumped. On a coffee table strewn with beer cans were a few pills in a tiny plastic bag. They were red, triangular and stamped with Superman's symbol. The woman's mobile phone lay dashed to the floor. The last dialed number was 911.

Paramedics pronounced the boyfriend dead at the scene. 'Superman' pills killed three more men in Britain that day. They had all been duped. They thought they were buying MDMA - the drug known as Ecstasy. Instead they were sold the toxic imposter chemical PMMA.

The interesting story of counterfeit MDMA



- ***Safrole*** is an oil harvested from the sassafras tree in Southeast Asian rain forests
- Harvest has been outlawed in many countries
- Used in the synthesis of MDMA or Ecstasy
- ✓ Paranoia
- ✓ Psychosis
- ✓ Insomnia
- ✓ Bruxism
- ✓ Hypertension and tachycardia
- ✓ Cardiovascular collapse
- ✓ **DEATH**

PMMA and PMA

- Powerful serotonin release
- Unlike MDMA cannot be broken down by the brain
- Often sold as MDMA
- Rise of PMA and PMMA secondary to banning the harvest of safrole in countries like Cambodia and Australia
- Linked to 125 deaths in Britain in 2015 alone

20-year-old man with excellent premorbid functioning and no family history of schizophrenia experiences mild paranoia after smoking cannabis for the first time. He presents again one month later with paranoia, delirium, hallucinations, and psychosis. Symptoms resolve in four days after antipsychotic medications are given. What is most likely explanation for the etiology of his presentation.

- A. First break psychosis of schizophrenia
- B. First episode of bipolar mania with psychotic features
- C. Cannabis-induced psychosis
- D. Intoxication by unknown substance
- E. None of the above

C. Cannabis-induced psychosis

- Cannabis is the most abused drug by patients with bipolar disorder and schizophrenia.
- Delta-9 THC is the culprit for adverse psychoactive effects.
- Highly lipid soluble and accumulates in the brain.
- Peak brain concentrations occur 4-5 days after ingestion.
- Slowly released back into the body.
- Half-life is about 7 days.
- Poorly responsive to antipsychotic treatment.
- Generally only responds to the “gift of time”.



35-year-old female with a history of depression presents to the ED after several days of greatly increased fluoxetine (Prozac) and bupropion (Wellbutrin) use. Her medications include HCTZ, phenelzine, sumatriptan, and trazodone. She is delirious, has a severe headache, and fever of 103°, tachycardic and hypertensive as well as diaphoretic with vomiting and severe agitation uncontrolled by intravenous Ativan. What is her most likely diagnosis?

- A. Sepsis
- B. Allergic reaction to medication
- C. Serotonin syndrome secondary to medication combination
- D. Neuroleptic malignant syndrome
- E. None of the above

C. Serotonin syndrome secondary to medication combination

- Serotonin syndrome secondary to high concentrations of 5 HT
- Presents with:
 - ✓ Agitation
 - ✓ Tachycardia
 - ✓ Hypertension
 - ✓ Hypertonia
 - ✓ Hyperreflexia
 - ✓ Diaphoresis
 - ✓ Tremor
 - ✓ Potential cardiovascular collapse
 - ✓ **DEATH**

Serotonin Syndrome

Symptoms



anxiety



confusion



diarrhea and vomiting



sweating



tremor



muscle stiffness
(especially in legs)



difficulty with
balance



Serotonin syndrome

- **May be seen with:**
 - ✓ **SSRIs**
 - ✓ **SSNRIs**
 - ✓ **Other antidepressants**
 - ✓ Mood stabilizers
 - ✓ Antipsychotics
 - ✓ Anxiolytics and sedative hypnotics
 - ✓ Others

You are seeing a 23-year-old patient on the medical floor who was admitted for autonomic hyperactivity and hallucinations. He is new to you. Urine drug screen was positive for cannabis. Since admission he has been up every night and wandering around the unit. He tells you that he heard you last night conspiring to commit him. Which of the following is the definitive diagnosis?

- A. Paranoid schizophrenia
- B. Bipolar disorder, currently manic
- C. Substance induced psychotic disorder
- D. Alcohol withdrawal delirium
- E. You are unable to make an assessment at this point in time

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E. You are unable to make an assessment at this point in time

- **A new patient presenting with both psychotic symptoms and active substance abuse can be a diagnostic dilemma.**
- **Differential diagnosis must be broad.**
- **In evaluating psychotic symptoms clinicians must consider the possibility that these symptoms may be caused by:**
 - ✓ **Primary psychiatric disorder**
 - ✓ **General medical condition**
 - ✓ **Substance intoxication or withdrawal**
 - ✓ **Cognitive disorder such as dementia or delirium**

Give the patient a diagnosis they can live with!!!

- Current life expectancy for US in 2020 is **78.93** years.
- Average reduction in life expectancy in **bipolar** patients is **9-20 years**.
- Average reduction in life expectancy in **schizophrenic** patients is **10-20 years**.
- **Inaccurate diagnoses can have ramifications for the remainder of the patient's lifetime.**
- **It's hard to undo a psychiatric diagnosis.**
- **Be accurate.**
- **Be ethical.**
- **Be an advocate for your patient!!!**

Summation



- Severe psychiatric symptoms may be due to use and abuse of psychotropic medication and illicit substances.
- Timelines and contemporaneous use may be the key to proper diagnosis and determination of the etiology of these disorders.
- Pre-existing primary psychiatric disorders predispose patients to adverse effects of these drugs.

Questions or comments?

