

- I. Objectives of lecture
  - A. Review epidemiology
  - B. Review importance of substance use disorders
  - C. General overview of medical complications of substance use disorders
  - D. Complications specific to substances
  
- II. Epidemiology
  - A. Prevalence – at least 18% lifetime prevalence of alcohol/drug use disorders
  - B. Economic cost in US - \$414 billion
  - C. 20% of patients in general medical clinics
  - D. 35% of psychiatric patients
  - E. 20-40% of hospital admissions
  - F. 50-75% of trauma cases
  - G. 25,000 deaths per year from alcohol related MVAs, 2 million non fatal injuries
  - H. 25% of US health care budget – alcohol and drug related illnesses
  - I. Substance related illnesses
    - 1. 90% of some forms of liver disease and Ca of head and neck
    - 2. 72% pancreatitis
    - 3. 41% seizure disorders
    - 4. 13% of breast cancer
  
- III. Medical and neurological consequences of alcohol/substance use
  - A. Direct effects of ingestion of the substance
    - 1. Toxicity of substances of abuse
    - 2. Toxicity of contaminants
  - B. Indirect consequences
    - 1. Infectious diseases
    - 2. Trauma
    - 3. Nutritional deficiencies
    - 4. Other consequences resulting from intoxication/withdrawal states
      - a. Consequences from hypertension, hyperthermia, cardiac arrhythmias
      - b. Consequences from respiratory compromise
      - c. Consequences from hypoglycemia

#### CASE #1

A 43 year old woman presents to the family practice clinic with complaints of dyspepsia, epigastric burning and anxiety symptoms. She has a past history of “mild hypertension” but denies any other medical problems.

Medications: Atenolol 25mg qd

Review of systems – unremarkable – no history of PUD, no history of elevated cholesterol, not diabetic, never had these symptoms in the past

Lab data in the record from the past year – CBC, routine chemistries – all normal

Family hx – unremarkable

Social – married, works for an accounting firm, thinks she’s just nervous about “tax season” – but wanted to “make sure”

Physical exam:

P: 102 regular

BP: 155/101

Respirations, temp – normal

Exam remarkable for slight tachycardia – no other significant findings

She seems extremely anxious in your office and explains her “shaky, cold, clammy hands” because she is “nervous with new doctors.”

#### IV. Alcohol

- A. Most extensive consequences of all drugs of abuse – affects almost all organ systems
- B. Women are more susceptible
- C. Increased risk of death – shortens life expectancy by 15 years (alcohol dependent persons)
- D. Risk of medical consequences increases with
  - 1. >2 drinks per day (women); > 3 drinks per day (men)
- E. 20-40% of persons admitted to general hospitals have alcohol-related medical problems
- F. Most severe damage – liver – frequent cause of death in alcoholic patients
- G. Nutritional consequences
  - 1. Alcohol can account for up to 50% of dietary caloric intake
  - 2. Displaces intake of normal nutrients
  - 3. Malnutrition
  - 4. Vitamin deficiencies
    - a. Thiamine
    - b. Folate
    - c. Other B vitamins
  - 5. Alcohol impairs activation and utilization of nutrients
  - 6. Maldigestion – from GI complications
  - 7. When caloric intake of ETOH exceeds 25-30% of daily requirements – significant decrease in carbohydrate, protein, fat and vitamin intake occurs
  - 8. Wide variation in nutritional states noted in alcoholic patients
- H. Specific nutritional deficiencies
  - 1. Thiamine
    - a. Common deficiency
      - i. Replacement necessary - minimum of 50mg per day
      - ii. Consequences
        - a. Wernicke-Korsakoff
        - b. neuropathies
  - 2. Folate
    - a. Megaloblastic anemia
    - b. Replete by replacement and normal nutrition
  - 3. B12
    - a. Not usually a complication of alcohol dependence
  - 4. Vitamin C
    - a. May be deficient with high alcohol intake
  - 5. Vitamin A
    - a. Deficiency is hard to assess and treat

- b. Normal doses of Vitamin A may be hepatotoxic in patients consuming alcohol
  - 6. Vitamin K
    - a. Deficiency is seen with impaired fat absorption
  - 7. Vitamin D
    - a. Abnormalities of Ca, Phos, and Vit D are noted
    - b. Decreased intake
    - c. Poor absorption
    - d. Insufficient sunlight
    - e. Consequences
      - i. decreased bone density
      - ii. decreased bone mass
      - iii. increased osteoporosis
      - iv. increased fractures
  - 8. Magnesium
    - a. Usually repleted with normal dietary intake
- I. GI Complications
  - 1. Liver damage
    - a. Direct toxic effect of alcohol on hepatocytes – not secondary to nutritional deficiency
    - b. AST > ALT
    - c. Range of disease
      - i. Fatty liver
      - ii. Alcoholic hepatitis
      - iii. Fibrosis
      - iv. Cirrhosis
      - v. Alcoholic hepatitis
        - a. Fever, increased WBCs, RUQ pain and tenderness; increased transaminases
        - b. Rx – abstinence, supportive care
    - d. ETOH accelerates progression to cirrhosis in patients who are HCV+
    - e. Increased risk of acetaminophen toxicity
  - 2. Pancreatitis
    - a. Often occurs after 10-15 years of heavy drinking
  - 3. GI bleeding
    - a. Gastritis
    - b. Peptic ulcer disease
    - c. Esophageal varices
    - d. Esophagitis
    - e. Duodenitis
- J. Neurological complications
  - 1. Wernicke's encephalopathy
    - a. Necrotic lesions of mammillary bodies and thalamus
    - b. Clinical presentation
      - i. Delirium

- ii. Ataxia
  - iii. Ophthalmoplegia
- c. Clearly related to thiamine deficiency
- d. 50-84% of Wernicke's patients also have Korsakoff's psychosis
- e. Few regain normal cognitive function
- 2. Korsakoff's psychosis
  - a. Shares common pathology and etiology with Wernicke's
  - b. Severe chronic memory impairment for recent and ongoing events
  - c. Patients may confabulate, often apathetic, lack initiative, lack insight
  - d. Other intellectual functions may be preserved
  - e. Once established – not very responsive to thiamine – but should treat with thiamine
- 3. Alcoholic dementia
  - a. Deterioration in all cognitive abilities
  - b. Most prominent effects on frontal cortex and putamen
  - c. Impairments – range from mild and transient to fixed deficits and severe dementia; there is extreme individual variability
  - d. Etiology
    - i. Direct toxicity to nerve cells
    - ii. Effects on neurotransmitters and second messengers
    - iii. Vitamin deficiencies
    - iv. Metabolic derangements
    - v. Decreased cerebral blood flow
    - vi. Damage to other organs indirectly affecting the CNS
  - e. Cognitive impairments
    - i. Abstract thinking
    - ii. Problem solving
    - iii. Visual, spatial, perceptual motor abilities
    - iv. New learning
    - v. Remote memory
    - vi. Personal neglect
  - f. “Blackouts” – Transient anterograde amnesia
  - g. Other neurological complications
    - i. Increased risk of ischemic stroke – HTN, smoking, trauma, cardiomyopathy
    - ii. Increased risk of cerebral trauma
    - iii. Metabolic encephalopathies
    - iv. Alcohol cerebellar degeneration
      - a. Primarily affects lower limbs
      - b. Broad based gait
    - v. Peripheral neuropathies
      - a. Often caused by nutritional deficiencies and/or trauma
      - b. May be sensory, motor or autonomic
      - c. Degeneration of myelin sheath on pathology
      - d. Start distally and move proximally
      - e. “Stocking-glove” distribution of deficits

- K. Hematologic complications
  - 1. Fe-deficiency anemia from GI bleeding
  - 2. Megaloblastic anemia – folate deficiency
  - 3. Anemia, thrombocytopenia, granulocytopenia
    - a. Direct toxic effect of alcohol on hematopoiesis
- L. Musculoskeletal system
  - 1. Rhabdomyolysis – prolonged periods in one position
  - 2. Increased fracture risk – osteopenia
  - 3. Myopathies
  - 4. Muscle wasting
  - 5. Weakness
- M. Dermatologic complications
  - 1. Facial edema
  - 2. Rosacea
  - 3. Rhinophyma
  - 4. Psoriasis
  - 5. Eczema
- N. Cardiovascular complications
  - 1. Alcoholic cardiomyopathy (congestive)
  - 2. Hypertension
  - 3. Supraventricular arrhythmias
  - 4. Increased levels of triglycerides
- O. Metabolic and endocrine complications
  - 1. Increased levels of uric acid – gout
  - 2. Decreased testosterone levels
  - 3. Menstrual cycle abnormalities

## CASE #2

A 39 yo man presents to the emergency room with crushing substernal chest pain. He is diaphoretic, appears to be in distress. He denies any past medical history.

Medications – none

Review of systems – no history of any medical issues; denies complaints except chest pain which he rates as 10/10. No history of diabetes, hypertension, coronary artery disease, hyperlipidemia, nonsmoker, denies any risk factors for coronary disease

Family hx – no history of coronary artery disease; parents are alive and well – in their 70s

Social hx – single, works as a sales manager for a large company

Physical exam:

P: 126 regular

BP: 178/115

Temp: 38

Diaphoretic

No other significant findings

Labs: CPK = 6000

    Creatinine = 3.5

EKG: sinus tachycardia, ST elevations in anterior leads

## V. Cocaine and other stimulants

A. Can cause serious and widespread toxicity

### B. Cocaine

1. Sleep deprivation
2. Paranoia, psychosis
3. Sympathetic hyperactivity
  - a. Hypertension
  - b. Hyperthermia
  - c. Tachycardia
4. Cardiovascular complications
  - a. Angina, myocardial infarction
  - b. Cardiac arrhythmias
  - c. Chronic cardiomyopathy with congestive heart failure
  - d. Sudden death
5. Neurologic complications
  - a. Seizures – single or multiple – may be dose related
  - b. CVAs
    - i. Increased risk - CNS aneurysms and AVMs
  - c. Dystonic reactions – decreases threshold for dystonic reactions in patients on antipsychotics
  - d. Headache
6. Miscellaneous effects
  - a. Intranasal use – perforated nasal septum from ischemic necrosis
  - b. Smoking – hypoxia, pulmonary edema, pulmonary infarction
  - c. GI ischemia
  - d. Massive hepatic necrosis
  - e. Severe muscle contraction, hyperthermia, muscle rigidity, rhabdomyolysis, myoglobinuria and acute renal failure

### CASE #3

A 20 year old college student is home for spring break. His parents bring him to the clinic because he seems depressed, anxious, irritable, is not interested in doing anything with the family, isolates himself in his room but has profound insomnia and complains of itching. He has a variety of erythematous skin lesions on his face, arms and other exposed areas. His family states this behavior is different than 6 months ago and that the skin lesions are also new. You have known this patient for 10 years and agree with the family's assessment.

Medical history – unremarkable

Family history – unremarkable

Physical exam – entirely normal except for the skin lesions; he does seem a bit depressed and anxious but denies any problems to you. Mental status exam is otherwise unremarkable.

You are baffled by the skin lesions and refer the patient to dermatology

- C. Amphetamines (methamphetamine)
  - 1. Many complications similar to cocaine
  - 2. Cognitive changes
  - 3. Dermatologic lesions

#### CASE #4

A 28 yo man is brought to the ER by his friends after having a witnessed grand mal seizure. One of the friends is a medical student – he confirms the presence of tonic-clonic seizure activity. The patient has no medical history other than a history of a femur fracture in a motor vehicle accident one year ago – per the friends he still complains of pain from the injury – but they don't know if he is seeing anyone for the pain or taking any pain medication. According to the friends he doesn't smoke, drink or use any recreational drugs they are aware of. The medical student privately tells you his friend was recently prescribed fluoxetine for depression. There was no history of head trauma with the motor vehicle accident and no recent history of any head trauma. The friends has not noted any abnormalities in his behavior prior to the seizure.

Family history, review of systems – unremarkable

Social history – single, has a long term girlfriend, works part-time as a veterinary assistant and attending college.

Physical exam – somnolent, appears post-ictal, otherwise unremarkable

Neurologic exam – unremarkable except for somnolence and disorientation which seem to be resolving

Labs – unremarkable

Has another grand mal seizure while you arranging an emergency CT scan – you treat this successfully with IV diazepam. The CT scan is normal.

#### VI. Opioids

- A. Relatively nontoxic when used as prescribed
- B. Impair gonadotropin release
- C. Heroin
  - 1. Noncardiogenic pulmonary edema
  - 2. Nephropathy – glomerulonephritis
  - 3. Neurologic complications and respiratory depression in overdose
- D. Seizures
  - 1. Meperidine – from normeperidine – toxic intermediary metabolite
  - 2. Tramadol – at doses greater than 400mg/day
- E. Other neurologic problems
  - 1. ?direct effect of drug, method of use, lifestyle of user or secondary to contaminants

#### CASE #5

An 18 yo high school senior is brought in by friends at 3AM. The friends seem quite concerned about the patient but also seem to want to leave before you speak with them – after you promise no to speak with their parents – they agree to stay. They admit that

they were out late at a “big party” when the patient seemed confused and disoriented; they say her skin was extremely warm; she didn’t seem to be sweating. They say she “danced a lot” at the party, it was quite warm at the location of the party and they are not sure what the patient had to drink during the evening and night. They admit alcohol and drugs were available at the party – they have no idea what the patient might have taken, if anything. They say she usually does not drink, smoke or use any drugs, is a good student, active in sports, well liked by her peers, parents and teachers.

Physical exam:

VS: T: 40 degrees

BP: 150/110

P: 140

Skin – hot, dry - physical and neurologic exams otherwise unremarkable except for delirium

Labs: Sodium – 129; Creatinine – 2.0 CPK – 600; SGOT – 755; SGPT – 886;

Blood alcohol level = 20 mg/dl

Urine drug screen (rapid toxicology screen) - negative

## VII. MDMA (methylenedioxymethamphetamine; Ecstasy)

### A. Effects produced by flooding the brain with serotonin

1. Stimulates release of serotonin
2. Inhibits reuptake of serotonin
3. Depletes up to 80% of CNS serotonin
4. Inhibits synthesis of new serotonin

### B. Usually mild stimulant

### C. Toxic effects

1. Delirium
2. Tachycardia, tachypnea, diaphoresis, hyperthermia
3. Acute renal failure, cardiovascular collapse
4. Disseminated intravascular coagulation, hepatic failure
5. Cerebral infarct or hemorrhage
6. Death
7. Toxic effects resemble serotonin syndrome
8. Risk increased in people lacking 2D6 or taking 2D6 inhibitors
9. Risk of long term deficiency in CNS serotonin and damage to serotonergic neurons
10. Hepatotoxicity
  - a. Fulminant hepatic failure
  - b. Delayed milder elevation of LFTs

## VIII. Marijuana

### A. Pulmonary toxicity - COPD

### B. Increased head and neck cancers

### C. Cognitive deficits

1. Short-term memory deficits
2. Poor attention
3. Slower information processing

- 4. Perceptual motor impairment
- 5. May be reversible
- D. Decreased immune response
- E. Decreased testosterone levels, menstrual abnormalities

#### IX. Inhalants

- A. Wide range of effects depending on substance
- B. Neurotoxicity, arrhythmias, pulmonary, hepatic, renal and hematologic effects
- C. Myelopathy
- D. Neuropathy

#### X. Nicotine

- A. Pulmonary effects
- B. Malignancies
- C. Cardiovascular disease

#### XI. Hallucinogens

- A. Direct toxic effects of LSD-type drugs are rare

#### XII. Sedative Hypnotics

- A. Respiratory depression
- B. Cognitive impairment – unclear whether deficits persist with abstinence
- C. Seizures – withdrawal states

#### XIII. Infectious disease complications

- A. Complications related to route of administration (use of needles, intranasal) and high-risk sexual practices
  - 1. HIV – affects approximately 25% of IV drug users
  - 2. Hepatitis
    - a. 65-90% of IVDU have antibodies to Hepatitis C
      - i. High incidence of chronic liver disease and cirrhosis
    - b. 50-70% have antibodies to hepatitis B
      - i. Many do clear the virus
      - ii. Lower incidence of chronic liver disease and cirrhosis
- B. Multiple potential local and systemic infections
  - 1. Cellulitis
  - 2. Abscesses
  - 3. Thrombophlebitis
  - 4. Systemic infections
  - 5. Endocarditis
  - 6. Osteomyelitis
  - 7. Septic arthritis
  - 8. Septic emboli

#### XIV. Summary