Introduction to Alcohol Use Disorder: Epidemiology, Diagnosis and Treatment

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I. Introduction

A. Alcohol use is common and fluctuates along a continuum of risk [SLIDE 2]

1. 80% of US population ♂; 60% ♀ ever drank[1]

2. 30-50% ever had alcohol problems[1,2]

3. Lifetime prevalence alcohol use disorder (AUD—defined later) = 12%[3]

B. Alcohol use costly [SLIDE 3]

1. AUD-related problems costs US $223.5 billion/yr[5]

2. Problematic alcohol use has been linked to:

   a. Motor vehicle accidents[6]

   b. Poor academic performance[7]

   c. ↑ risk suicide[8]

   d. ↑ violence, including with intimate partner [9]

   e. ↑ overdose deaths[10]

   f. ↑ sexually transmitted infections (STIs) including HIV[11-13]

C. AUD is under-recognized and under-treated [SLIDE 4]

1. Only 25% with AUD ever seek help

2. <10% with AUD receive treatment[3,14]

4. ID AUDs helps assessment & Rx other probs

D. Introducing Caroline [SLIDE 5]

E. Therefore, this lecture will cover AUD [SLIDE 6]

1. Diagnosis, prevalence and course

2. Pathophysiology

3. Screening and treatment

II. AUD Dx, prevalence, & course: Beginning with diagnostic criteria

A. Diagnostic and Statistical Manual of Mental Disorders (DSM-5) definition of withdrawal[15] [SLIDE 7]

1. Stopping alcohol use after heavy, prolonged use

2. 2+ of the following:

a. Autonomic hyperactivity:

1’ Sweating

2’ Racing heartbeat

b. Hand tremor

c. Insomnia

d. Nausea or vomiting

e. Hallucinations; unreal sensations generated in the mind (seen only in EtOH delirium)

f. Agitation

g. Anxiety

h. Seizures

3. Symptoms cause impairment or distress

4. Symptoms not due to another medical, psychiatric condition or another substance

B. DSM-5 definition of AUD[15] [SLIDE 8]

1. 2+ within same 12 months

2. Including:

a. Drinking more or for longer than intended

b. Unsuccessful efforts to ↓ or stop

c. Spending a large amount of time drinking or recovering from effects

d. Craving (i.e., strong desire/urge) for alcohol

e. Drinking → failure to fulfill life obligations (e.g., missing work)

f. Drinking → giving up important activities (e.g., exercise/ family birthday parties/etc.)

g. Drinking in hazardous situations (e.g., while or before driving)

h. Continued drinking despite social/interpersonal problems

i. Continued drinking despite physical/psychological problems

j. Tolerance (e.g., needing to drink ↑ to get same effect)

k. Withdrawal symptoms (i.e., ↓ or stop → > day of hands shaking/nausea

C. Update on Caroline [SLIDE 9]

D. Prevalence of AUD[16]

1. Lifetime risk for men = ~ 15%
2. Lifetime risk for women = ~ 10%

E. AUD course [SLIDE 10]

1. Intensity fluctuates[17]

   a. Heavy drinking & problems

   b. Stop drinking (happens to almost all at times, i.e. after crisis)

   c. Temporary control drinking

   d. 20% long term remission without treatment

   e. <10% able to drink without problems

2. If continues:[17] [SLIDE 11]

   a. ↓life ~15 years

   b. ↑ heart attacks/strokes

   c. ↑ cancer GI/breast/head & neck, etc.

   d. Liver disease (~80% do not have cirrhosis[21])

3. Common temporary (but severe) substance induced conditions

   a. Alcohol induced major depressions [SLIDE 12]

      1'. Seen in 40% with AUD

2’. Looks ID to major depressive disorder

3’. ~10% commit suicide in this state

4’. Begins during heavy drinking

5’. Greatly improves or disappears within 1 month abstinence

6’. Antidepressant meds not needed

b. Other psychologic syndromes in context of intoxication or withdrawal [SLIDE 13]

1’. Panic attacks in > 20% (disappear in days to weeks)

2’. Paranoia and/or hearing voices in ~ 3%--also disappear with abstinence

III. Pathophysiology of AUD [SLIDE 14]

A. Alcohol metabolism [SLIDE 15]

1. ~10% excreted via lungs/urine/sweat

2. 90% metabolized stomach and liver enzymes

a. Alcohol dehydrogenase (ADH) metabolizes alcohol → acetaldehyde

b. Aldehyde dehydrogenase (ALDH) metabolizes acetaldehyde → carbon dioxide and water

3. Genetic variations ↓ risk alcohol-related problem risk [SLIDE 16]

a. Mutation in ALDH in 40% Asians → ↑ acetaldehyde and skin flushing

b. ADH mutation in ~20% Jews and blacks → ↑ acetaldehyde (less intense than ALDH)

B. Effects on brain [SLIDE 17]

1. Acute alcohol → ↑ inhibitory γ-aminobutyric acid (GABA) system[17,24]

2. GABA → muscle relaxation, somnolence, and intoxication

3. Acute alcohol ↓s excitatory N-methyl-D-aspartate (NMDA) stimulation[25]

4. Withdrawal associated with the reverse (↓GABA & ↑NMDA)[25]

5. All drugs →↑dopamine and reward feelings: ↑craving[26-28]

C. Alcohol-related organ damage

1. Central nervous system (CNS; especially brain) [SLIDE 18]

a. ↓memory: Blackout if alcohol level high (forget all or most of an evening drinking)

b. Sleep impairment[32,33]

1'. Worsens sleep apnea (breathing temporarily stops during sleep)

a' Alcohol →↓drive to breathe, ↓rate and depth of breath

b'. Alcohol relaxes throat muscles → ↑likelihood of airway collapse

2'. Trouble falling asleep

3'. Frequent awakenings in second half of night

4'.All of the above ↑ AUD relapse risk

5'. These are true of all depressants (e.g., benzodiazepine-type drugs).

c. Wernicke-Korsakoff Syndrome (WKS) [SLIDE 19]

1' WKS in <1% of AUD[17,31]

2' Wernicke Encephalopathy (WE): severe acute thiamine deficiency

a' Triad: confusion, ataxia (uncoordinated movement), and nystagmus (quick eye movements)

b' Potentially reversible with Rx: thiamine, nutrition and hydration

3' Korsakoff Syndrome (KS) is a chronic neurologic sequela of WE

a' Anterograde amnesia (cannot form new memories) – confabulation (made up memories)

b' Permanent brain damage

3. Cardiovascular system [SLIDE 20]

a. Leading cause of early death in AUD

b. 3+ daily drinks - ↑ blood pressure (BP), cholesterol, heart muscle damage risk[34,35]

c. Heavy drinking ↑s risk of temporary heart beating irregularities [35]

4. Cancer [SLIDE 21]

a. 2nd leading cause of early death in people with AUD[36]

b. ~75% of those with head and neck cancers have AUD[17,36]

c. AUD – 2x risk of esophagus, stomach, rectum and breast cancers[36]

5. Other disorders[37,38]

a. Gastrointestinal (GI) bleeding [SLIDE 22]

1’ Acute hemorrhagic gastritis

a’ Damages gastric mucosa (stomach lining)

b’ Can “ooze blood”; or develop to severe upper GI bleeds

2’ Forceful vomiting → Mallory-Weiss tear of esophagus

b. Pancreatitis

1’ Acute pancreatitis

a’ Pathophysiology not entirely understood

b’ Binge drinking linked with ↑ risk of acute pancreatitis

c’ Heavy drinking ↑s risk of repeated episodes of acute pancreatitis

d’ Upper abdominal pain radiating to back, tenderness, nausea/vomiting, fever

2’ Chronic pancreatitis

a’ Repeated episodes of acute pancreatitis → permanent damage

b’ ~70% of chronic pancreatitis due to long-term heavy drinking

c’ Cigarettes ↑ alcohol’s harmful effects on pancreas

c. Alcohol-related liver disease: fatty liver, alcoholic hepatitis and cirrhosis [SLIDE 23]

1’ Fatty liver

a’ Earliest stage of alcohol-related liver disease

b’ ↑fat inside liver cells → ↓liver function

c’ Usually asymptomatic; can have enlarged liver and abdominal discomfort

d’ Potentially reversible if stop drinking

2’ Alcoholic hepatitis

a’ Liver inflammation associated with destruction of liver cells

b’ ~35% of heavy drinkers develop alcoholic hepatitis (mild-severe).

c’ Symptoms: fever, jaundice, nausea, vomiting, abdominal pain and tenderness

3’ Cirrhosis

a’ Normal liver tissue replaced with scar tissue

b’ ~10-20% of heavy drinkers develop cirrhosis, after >10yrs drinking

c’ Scarring of liver → ↑ BP in the liver (portal hypertension)

d’ Symptoms: ascites, esophageal dilated veins (varices), mental confusion, enlarged spleen

IV. AUD Screening and Treatment [SLIDE 24]

A. Update Caroline [SLIDE 25]

B. Screening questionnaires for risky drinking (screening should be used in EVERY PATIENT) [SLIDE 26]

1. AUDIT (Alcohol Use Disorder Identification Test)[17]

a. 10 questions re drinking amount and problems

b. Takes 2-3min

c. Score 0-40 → risk level

d. 8+ = unhealthy alcohol use

e. 70% sensitivity, 80% specificity for severe problems

2. AUDIT-C (Alcohol Use Disorder Identification Test-Consumption Questions)[39]

a. 3 consumptions questions from AUDIT; briefer

b. Each question scored 0-4 points

c. Total score determines +/- for unhealthy drinking

1’ 4+ = (+) men

2’ 3+ = (+) women

3. CAGE

a. **C**ut down; **A**nnoyed; **G**uilty; **E**ye-Opener (each as yes or no)

b. ≥2 (+) responses indicate likely AUD

c. Best used in medical, surgical settings and with blood tests[21]

C. Biologic markers of heavy drinking [SLIDE 27]

1. Liver enzymes; AST, ALT (aspartate aminotransferase, alanine aminotransferase)

a. Indicate liver cell damage of any cause → not EtOH sensitive or specific[17]

b. AST:ALT >2:1 indicates alcohol related disease[18]

c. AST or ALT >500U/I associated with alcoholic hepatitis (liver inflammation)[18]

2. GGT (Gamma glutamyltransferase)[17]

a. >35 U/L indicates heavy drinking (eg. ~5+ drinks/day)

b. EtOH problem sensitivity and specificity ~75%

c. May not be good relapse measure[19]

3. CDT (carbohydrate deficient transferrin)[20]

a. >20 U/L indicates ~ 5+ drinks /day for ≥2 weeks

b. Heavy drinking indicated by >2.6%CDT

c. Can use to monitor abstinence

D. Treatment of AUD: treating withdrawal (definition given earlier in the lecture) [SLIDE 28]

1. Recognition and treatment of alcohol withdrawal following ↓ drinking or abstinence

a. ~50% AUD patients develop withdrawal[40,41]

b. Begins at 8h after ↓intake, peaks on day 2, substantially reduced at day 4 or 5[40]

c. Most: mild to moderate symptoms with mild tremors/no mental confusion/no seizures

d. Rx: educate re symptom course & consider Rx w benzodiazepines (e.g., diazepam [Valium]

e. Depressant meds given to point of ↓↓ high vital signs (VS) & ↓tremor; example is:

1'. Chlordiazepoxide (Librium) 25 mg PO up to 4 times on Day 1

2'. Extra 25 mg if still high vital signs; hold any dose if VS normal and patient very sleepy

3'. ↓ dose ~20% of Day 1 level each day to zero Day 4 or 5 for most patients

f. Can monitor via Clinical Institute Withdrawal Assessment (CIWA) scale [SLIDE 29]

1'. Rated by MD or nurses

2'. 10-item scale corresponding to common symptoms and signs of withdrawal

3'. Sum of item scores correlates to severity of alcohol withdrawal and benzo dosing

g. Oral or IV thiamine (e,g, 100mg daily) to prevent WKS (described above)

h. <5% have complicated & severe withdrawal [SLIDE 30]

1'. On Day 2 develop grand mal seizure (loss consciousness)

2'. Or develop delirium tremens (DT) : delirium & ↑↑ VS

3'. Requires intense medical monitoring (±intensive care unit)

4'. Rx very high doses depressant meds

5'. Details beyond scope of this lecture'[49]

E. Treatment: helping patients remain abstinent

1. Key approach based on cognitive behavior therapy (explained below)

a. Goals: change person's view of self and change behavior

b. Involves 1 on 1 &/or group Rx discussion of

1'. Person's responsibility to make changes or not

2'. Motivational Interviewing techniques (described below)

2. Choosing a treatment setting [SLIDE 31]

a. American Society of Addiction Medicine (ASAM) placement criteria re impatient or outpatient [42]

1' Based on patient needs, strengths & obstacles to Rx (↑ problems → ↑ likelihood need inpatient):

a' Acute intoxication and/or withdrawal potential

b' Biomedical conditions and complications (e.g. cirrhosis)

c' Emotional, behavioral or cognitive conditions and complications (e.g. very depressed)

d' Readiness to change

e' Doc sees ↑ likely to relapse or continue use

f' Recovery and living environment (e.g., lives on street or with heavy drinkers)

2’ ASAM levels of care match intensity of Rx to patient needs: [SLIDE 32]

a’ Early intervention

b’ Outpatient treatment

c’ Intensive outpatient treatment or partial hospitalization

d’ Residential/inpatient treatment

e’ Medically-managed intensive inpatient treatment

3’ All levels of care include medical mgmt, pharmacotherapy and family support

4’ Effectiveness of treatment setting modest and diminish over time [43,44]

3. Caroline update [SLIDE 33]

4. Treatment of AUD - individual psychotherapies [SLIDE 34]

a. Cognitive behavioral therapy, to learn:[45]

1’ Triggers for drinking including:

a’ Being around friends or family who drink

b’ Negative feelings like being rejected by a partner or feeling like a failure

2’ How to handle situations where tempted to drink. For example:

a’ Making sure they have a realistic plan to confidently refuse EtOH

b’ Learning ways to cope with difficult feelings like exercise

b. Motivational enhancement therapy[45]

1’ People more likely to change when they want to vs being told what to do

2’ Approach helps patients ↑self-motivation to stop drinking

3’ Important to be empathic, respectful and not show frustration with patient

5. Adjuncts to AUD treatment – mutual help groups like Alcoholics Anonymous[17]

a. AKA “12-step” program because are 12 suggested recovery steps

b. Offers support 24 hours/day, 7 days per week

c. Can be a spiritual framework where a “Higher Power” is identified

1’ Higher power does not have to be “God”/ some groups not strong on “spiritual”

2’ Can be a meaningful to patient, like “humanity” or “love”

3’ Not all patients accept this step, but may still benefit from AA

6. FDA-Approved Medications[46] [SLIDE 35]

a. Naltrexone (Trexan, Vivitrol): medication that blocks opiate receptors

1’ ↓ cravings for EtOH

2’ If relapse, tend to drink less

3’ Rx orally (50mg/day) or as a monthly injection (380mg)

b. Disulfuram (Antabuse)

1’ Blocks alcohol metabolism at acetaldehyde (metabolite)

2’ Drinking on disulfiram → nausea and vomiting

3’ Can’t Rx if patient has heart disease, diabetes, etc

4’ MUST warn to avoid EtOH in any form, i.e. common foods

5’ → fear of effect of drinking; so hard to know if better than placebo

6’ A barrier to effectiveness is that people stop taking it

7’ Better outcomes with supervised dosing[47]

c. Acamprosate (Campral)

1’. Decreases glutamate activity in brain (might ↓ residual (protracted) mild withdrawal symptoms)

2’ Helps patients remain abstinent longer

3’ Side effects are mild nausea and diarrhea

4’ Drug not metabolized in liver (so might be OK if have liver disease)

5’ Common dose is 666mg 3x daily (is poorly absorbed)

6’ Three times a day dosing can ↓ compliance

7. Non-FDA Approved Medications (not currently recommended for clinical use) [SLIDE 36]

a. Topiramate (Topomax)

1’ Dose range 200-300mg/day, typically BID

2’ Many potential side effects – weight loss, cognition, acute closure glaucoma, kidney stones

3’ Gradual dose titration to minimize side effects

4’ Need to dose adjust if there is renal impairment

b. Gabapentin (Neurontin)

1’ Dose range 900 to 1800mg/day, BID or TID

2’ Need to dose adjust for renal impairment

3’ Monitor for misuse given abuse potential

8. APA Practice Guidelines for the Pharmacological Treatment of AUD[48] [SLIDE 37]

a. *Recommends* naltrexone or acamprosate for mod-severe AUD, and

1’ Have goal of ↓ alcohol consumption or abstinence;

2’ Pt prefer pharmacotherapy and/or not responded without meds

3’ Has no contraindications

b. *Suggests* disulfiram for mod-severe AUD, and

1’ Have goal of achieving abstinence;

2’ Pt prefers disulfiram and/or not responded without meds not responded to naltrexone/acamprosate

3’ Have no contraindications

c. *Suggests* topiramate or gabapentin for mod-severe AUD, and

1’ Have goal of reducing alcohol consumption or achieving abstinence;

2’ Prefer topiramate/gabapentin, or are intolerant/have not responded to naltrexone/acamprosate

3’ Have no contraindications

9. Caroline update [SLIDE 38]

IV. Conclusions [SLIDE 39]

A. Alcohol use is common and produces costly problems for society [SLIDE 41]

B. Problematic drinking leads to risk and damage to multiple organ systems in the body

C. AUD is under-recognized and under-treated

D. Treatment is effective, includes talk therapy and medication, and can be delivered in various settings

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