



Understanding Alcohol Use Disorder

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Lecture objectives

- ✦ To discuss clinical presentations, prevalence and healthcare implications of alcohol use, alcohol use disorder (AUD), and their complications
- ✦ To review biopsychosocial underpinnings of AUD as the basis for differential diagnosis and an integrated pharmacopsychosocial approach to treatment

Excessive Drinking Causes 10 Percent Of Deaths In Working-Age Adults

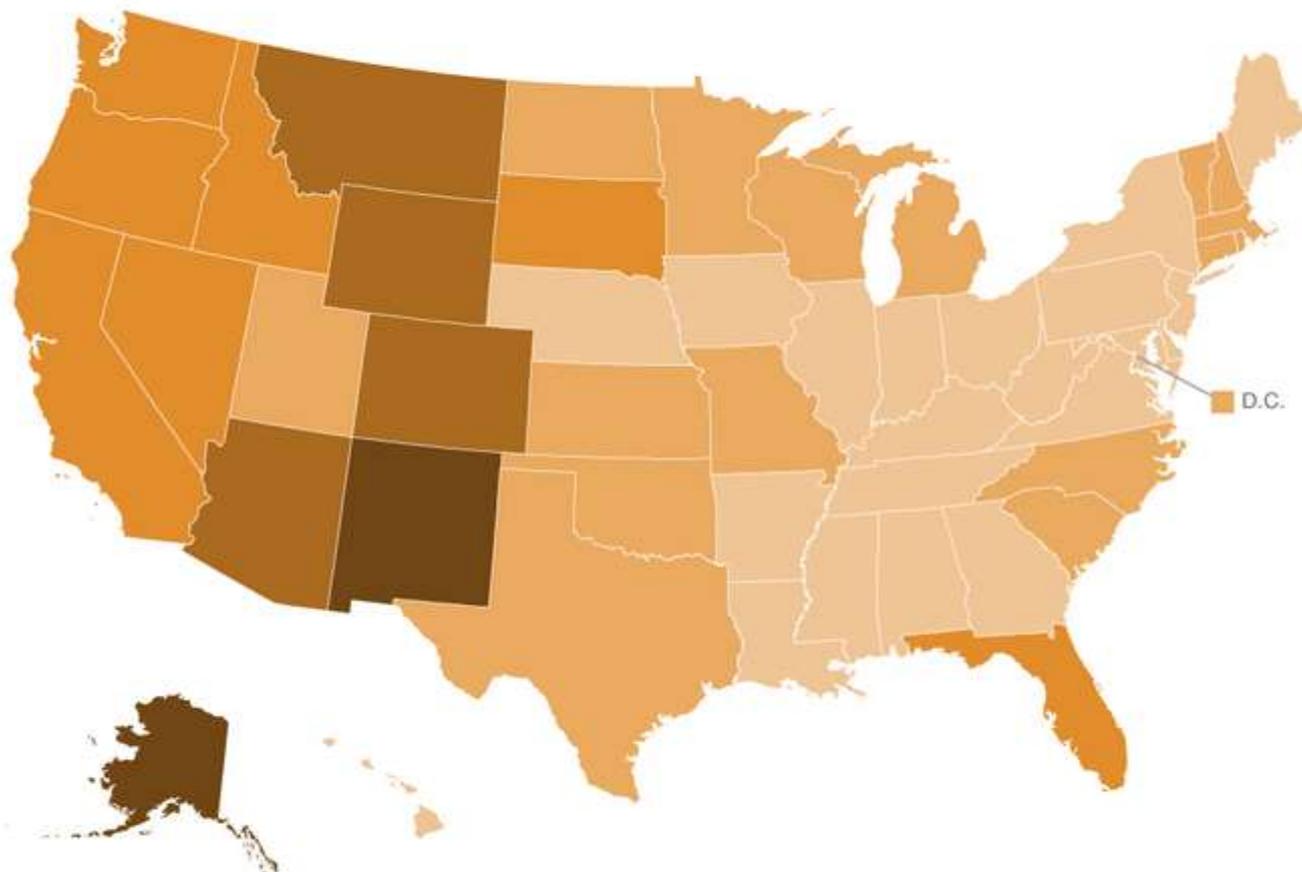
by NANCY SHUTE

June 26, 2014 1:59 PM ET



One in 8 adults binge drinks, and that plays a role in most alcohol-related deaths.

**Percent of deaths among adults age 20-64
that are attributable to alcohol (2006-2010)**



Source: Preventing Chronic Disease
Credit: Alyson Hurt/NPR

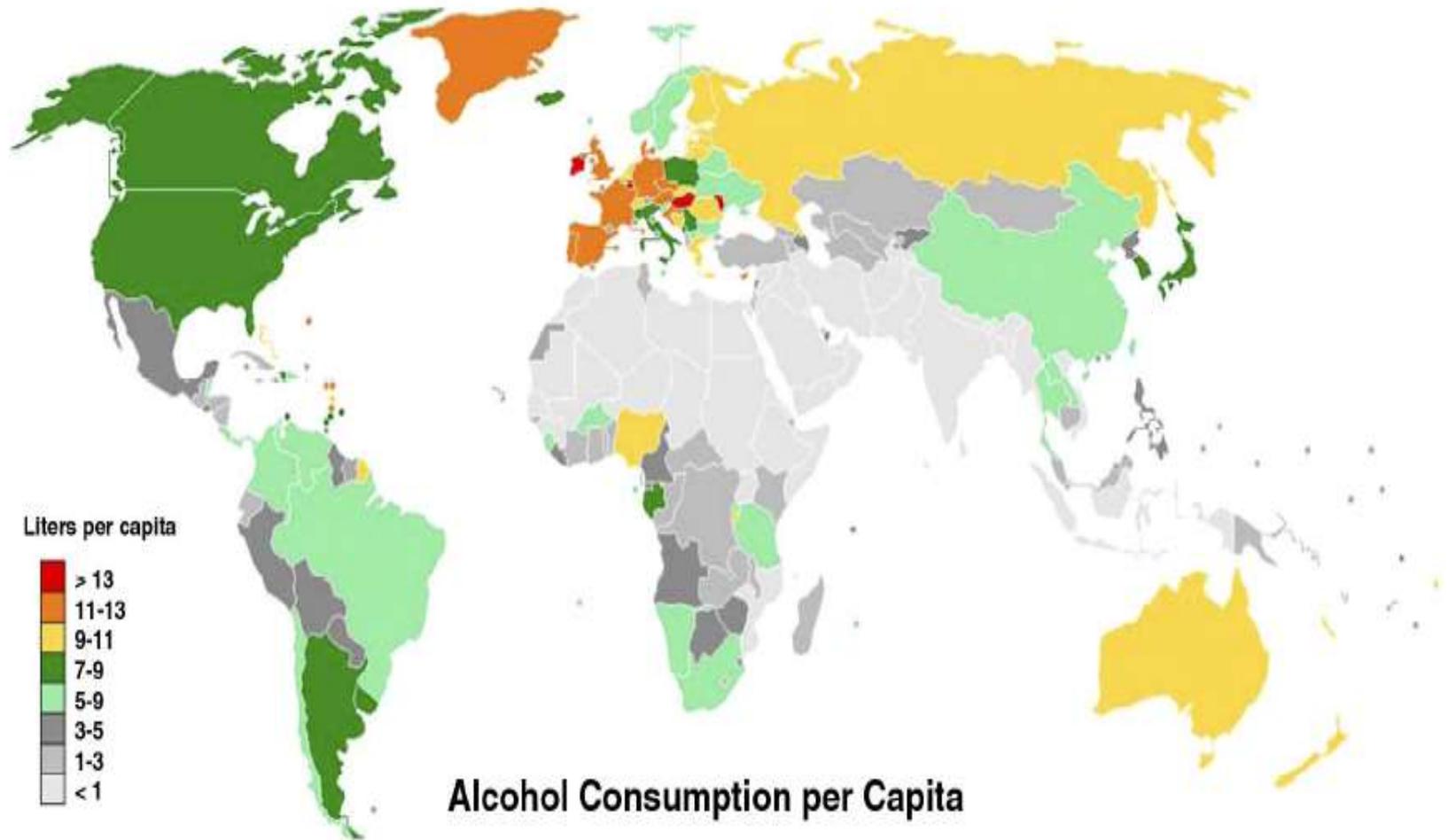
Archeological Evidence of Medicinal Wine on Shard of Pottery (Abydos, Egypt, 5000 BCE)



Credit: German Archaeological Institute of Cairo

Medical, religious, or recreational uses for indigenous psychoactive substances are as old as mankind—there is archeological evidence of alcohol use going back at least 7000 years.

Alcohol is Used Worldwide



Alcohol use disorder (AUD) – drinking to pathological use (alcoholism)

- ★ AUD is easily confused with or complicates diverse medical and psychiatric conditions, hence, the need for careful **diagnostic assessment**
- ★ Development of AUD and its complications is multi-factorial with interactions of biopsychosocial factors via **genes and environment** through:
 - ★ fundamental brain mechanisms (learning/ memory, drives, perception, mood, and cognition)
 - ★ personal history (life stresses, experiences, and interpretations)

Molecules to Man to Society

National Survey on Drug Use and Health (NSDUH), 2010

Current (past month) use - At least one drink in the past 30 days.

Binge use - Five or more drinks on the same occasion (i.e., at the same time or within a couple of hours of each other) on at least 1 day in the past 30 days.

Heavy use - Five or more drinks on the same occasion on each of 5 or more days in the past 30 days.

Health consequences of Current, Binge, and Heavy use are quite different

Prevalence (%) of Alcohol Use and Alcohol Use Disorder in the Previous Year (persons 12 years or older)¹

Alcohol Use 50.3

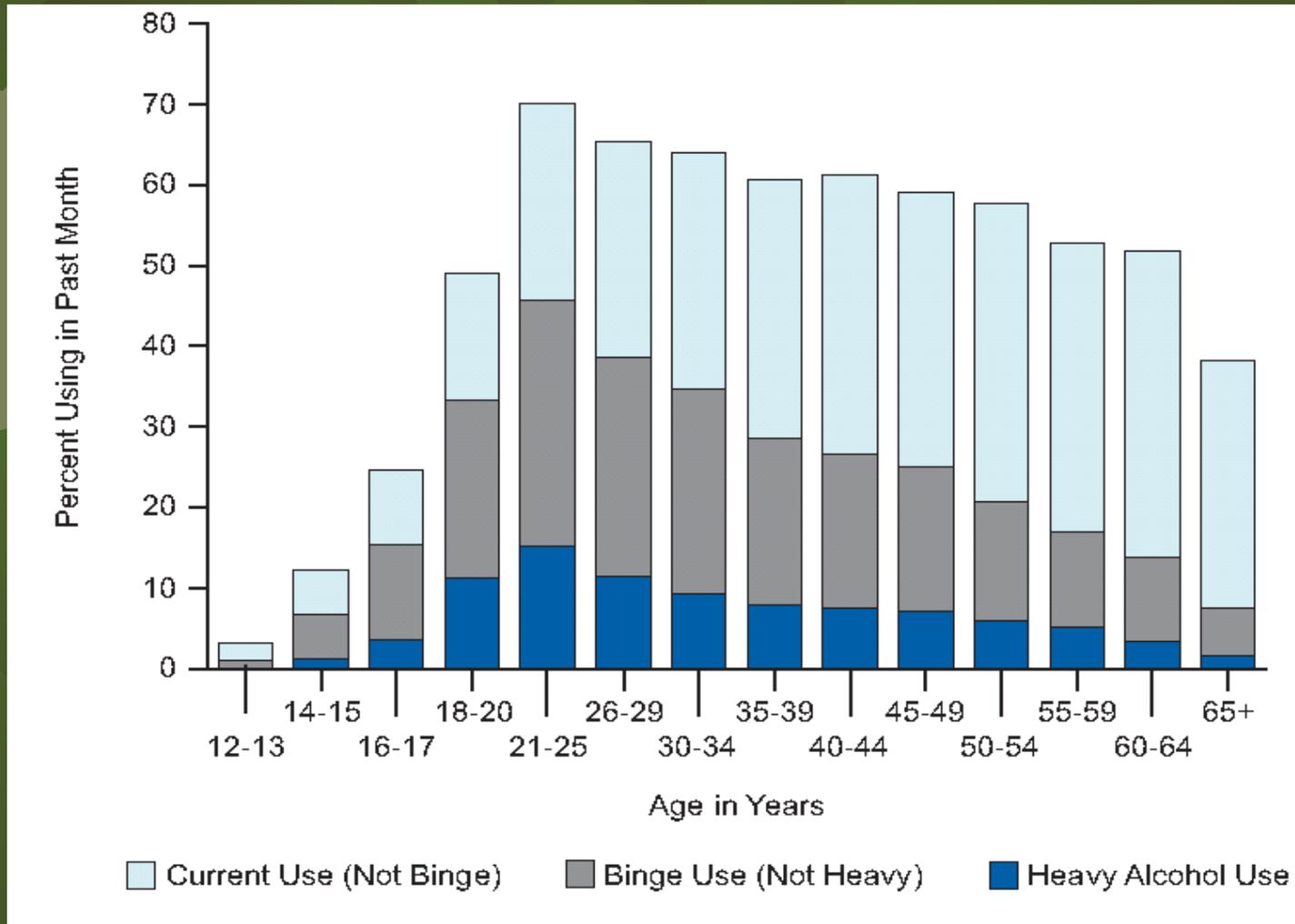
- Binge drinker 22.8
- “Heavy” drinker 6.9

Alcohol Use Disorder 7.8

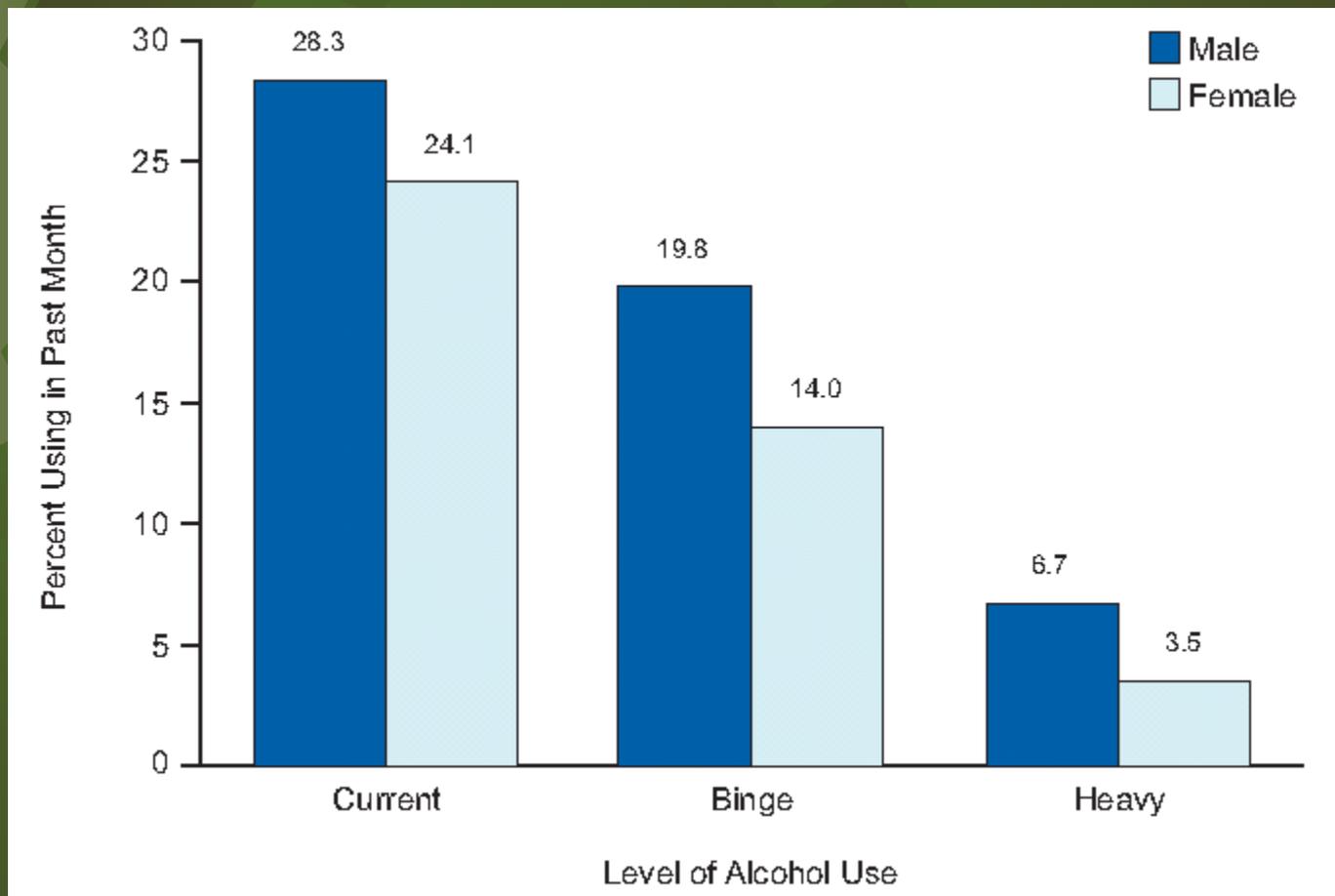
- Alcohol use disorder, *no* illicit drug use disorder 6.4
- Alcohol *and* illicit drug use disorders 1.4

¹Adapted from Substance Abuse and Mental Health Services Administration: 2004 National Survey on Drug Use and Health

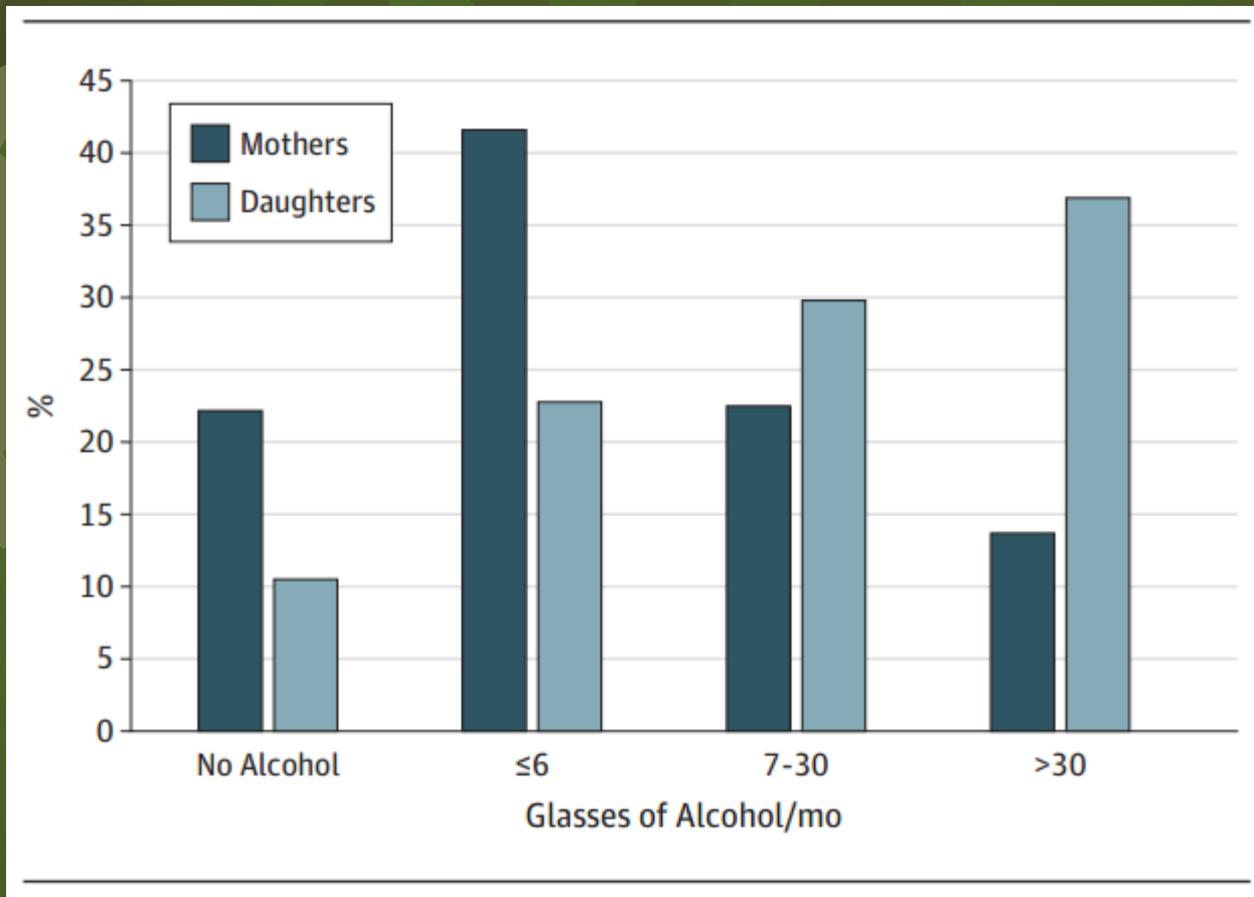
Current, Binge, and Heavy Alcohol Use by Age, 2010



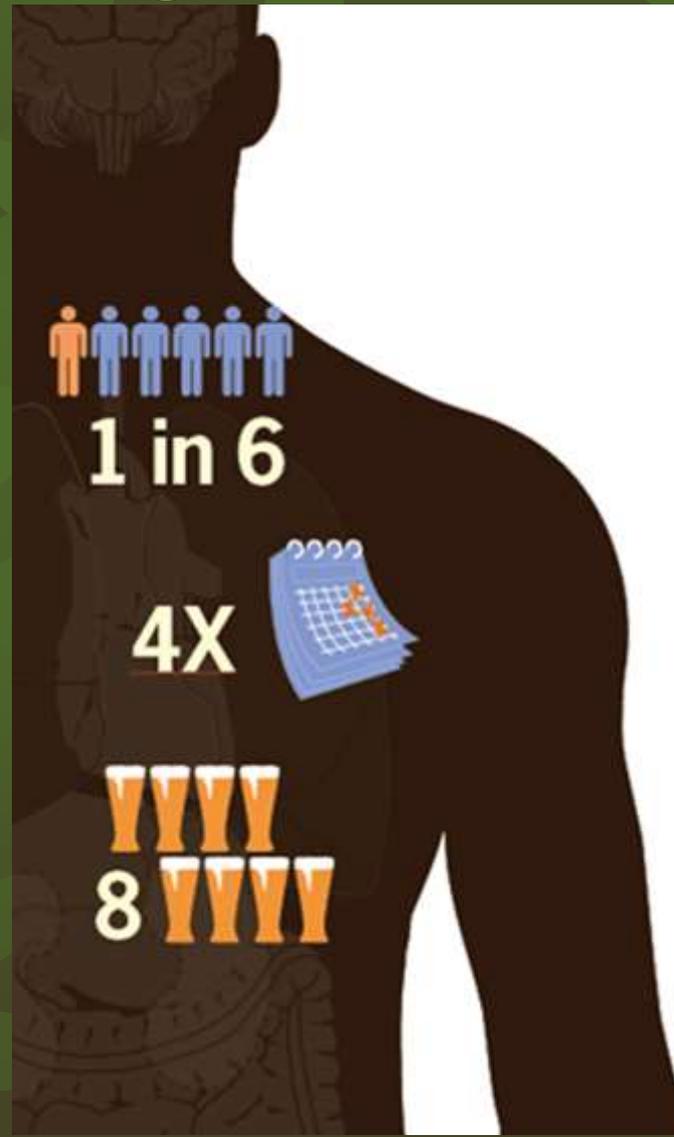
Current, Binge, and Heavy Alcohol Use, by Gender, Persons Aged 12 to 20, 2010



Drinking Levels of Australian Mother-Daughter Dyads (n=1053) at Age 18-25



More than **38 million** US adults binge drink.



Consequences of binge drinking



Binge drinking
can lead to

- Motor Vehicle Crashes**
- Violence Against Others**
- Spread of HIV and Sexually-Transmitted Diseases (STDs)**
- Unplanned Pregnancy**
- Fetal Alcohol Spectrum Disorders and Sudden Infant Death Syndrome (SIDS)**
- Alcohol Dependence**

Causes of Death Among Youth

- ☀ 70.6% of all deaths among youth and young adults aged 10-24 years result from only four causes:
 - ☀ motor-vehicle crashes (31.4%)
 - ☀ other unintentional injuries (12%)
 - ☀ homicide (15.3%)
 - ☀ suicide (11.9%)
- ☀ Each of these causes are significantly associated with use of **alcohol**/drugs

Only a fraction of drinkers (≥ 18 yrs) progress to severe AUD



Substance	Prevalence (%) of past-year use	Number of past-year users	% of past-year users with past-year dependence	Number with past-year dependence
Alcohol	65.44	136,035,000	5.82	7,911,600
Tobacco	27.66	57,503,000	46.13	26,525,000
Cannabis	4.07	8,468,000	7.96	673,900
Opiates	1.81	3,756,000	6.30	236,500
Sedatives	1.24	2,583,000	5.42	139,900
Tranquillizers	0.93	1,940,000	5.04	97,700
Hallucinogens	0.57	1,192,000	2.67	31,800
Cocaine	0.56	1,169,000	23.91	279,500
Amphetamines	0.49	1,019,000	14.34	146,000
Solvents/inhalants	0.11	231,000	1.04	2,400
Heroin	0.03	64,000	26.96	17,300

Alcoholic patient's concept of AUD:
"Alcohol makes you a captive."



Major Questions Concerning Alcohol Use Disorder

- ★ Why, in the face of **widespread availability** of alcohol, certain individuals develop a alcohol use disorder and others do not?
- ★ Why does alcohol use disorder **continue inexorably** to death in spite of treatment in certain cases, whereas in others, **drinking can be decreased** or arrested either spontaneously or with treatment?

Partial Answers

- ✦ Alcohol use disorder is **heterogeneous**, either a primary psychiatric disorder in its own right, or the **final common pathway** for a variety of behavioral difficulties in diverse sociocultural contexts
- ✦ Pathogenesis of alcohol use disorder is conceptualized as **multiple simultaneous** variables interacting over time:
 - the manifest **psychopathology** of the individual
 - the **psychopharmacologic actions** of alcohol within the **sociocultural context**

Initiation and Progression of Alcohol Use Disorder

Antecedents/Socio-cultural Context/Consequences of Alcohol Use / Abuse / Compulsive Use

Psychopharmacologic Effects of Alcohol

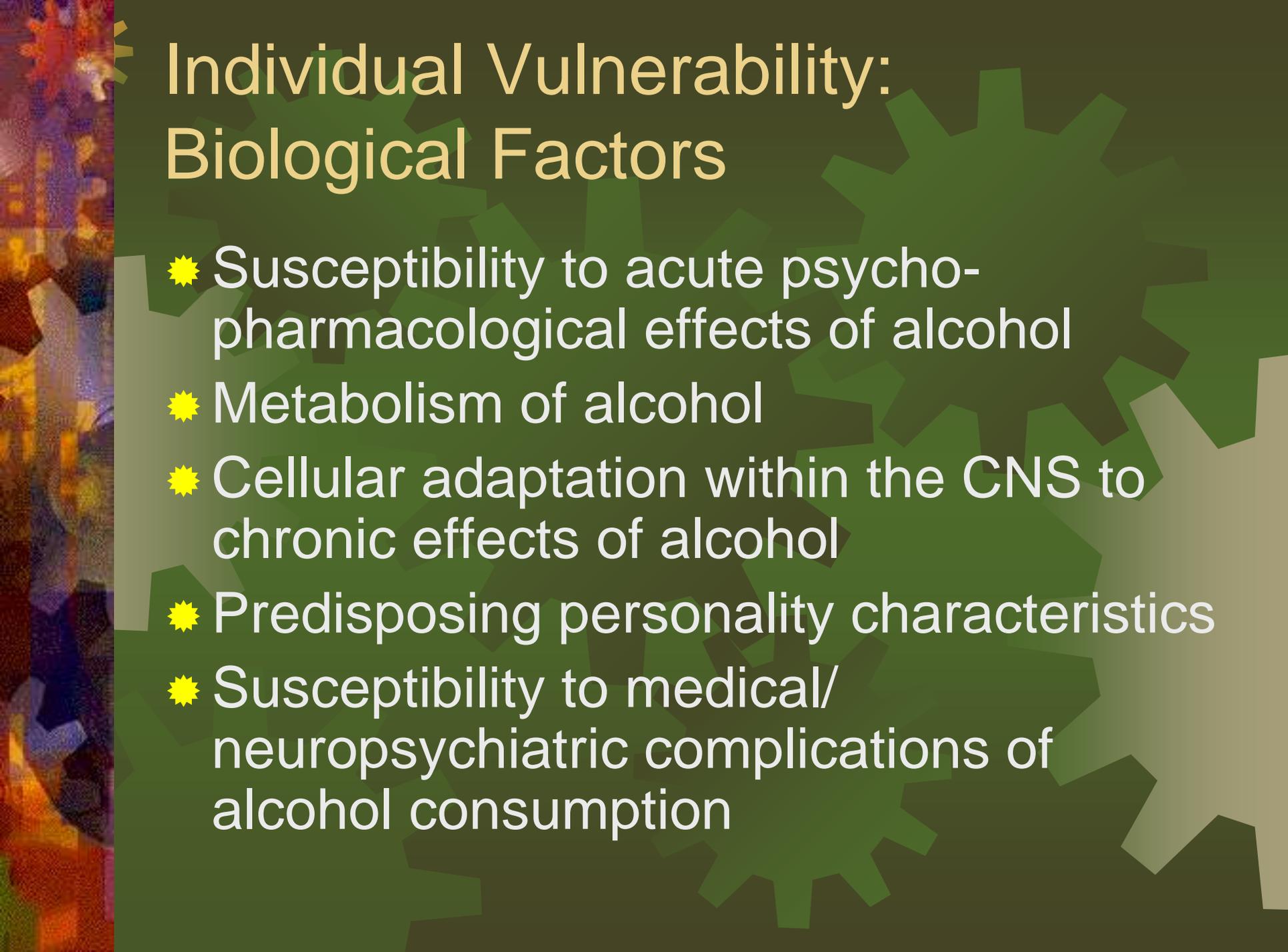
Vulnerable Individual

- Biological
- Psychological
- Social

Drug-seeking
Neuroadaptation
Dependence

Complications

- Social
- Neuropsychiatric
- Medical



Individual Vulnerability: Biological Factors

- ✦ Susceptibility to acute psychopharmacological effects of alcohol
- ✦ Metabolism of alcohol
- ✦ Cellular adaptation within the CNS to chronic effects of alcohol
- ✦ Predisposing personality characteristics
- ✦ Susceptibility to medical/neuropsychiatric complications of alcohol consumption

Individual Vulnerability: Psychological Factors

- ✦ Co-occurring psychopathology
- ✦ Medical illness (essential tremor, chronic pain, physical limitations)
- ✦ Severe stress (crime, battle exposure, sexual, economic)
- ✦ Post-traumatic effects of severe stress

However, it is also possible that susceptibility to psychological stressors and alcoholism actually share similar or common etiologies.

Individual Vulnerability: Social Factors

The following are potent contributors to the initiation of alcohol use and progression of alcohol use disorder:

- ✱ Peer group **attitudes** toward, and **shared expectations** of the **benefits** of drinking
- ✱ Availability of **competing reinforcers** in the form of educational, recreational, and occupational **alternatives to drinking**
- ✱ **Alcohol availability** during particular developmental stages

Alcohol use disorder (AUD) – drinking to pathological use (alcoholism)

Alcohol use disorder is easily confused with or complicate diverse **medical and psychiatric** conditions:

- ✱ Associated with other mental disorders
- ✱ Affects many (if not all) organ systems
- ✱ Multi-factorial pathogenesis (cause or consequence, primary *vs* secondary)
- ✱ Diagnosis requires a high index of suspicion

Molecules to Man to Society

Other Psychiatric Diagnoses that Frequently Co-Occur with SUD

DIAGNOSIS	Lifetime Prevalence Rates		
	ANY	ALCOHOL	DRUGS
SCHIZOPHRENIA	47 %	33.7	27.5
ANTISOCIAL	83.6		
ANXIETY DIS.	23.7	17.9	11.9
Phobias	22.9	17.3	11.2
Panic	35.8	28.7	16.7
OCD	32.8	24	18.4
MOOD DISORDERS	32		
Major Depression	27.2	16.5	18
Bipolar I Disorder	60.7	46.2	40.7

ECA Data. Regier et al. 199

“Hyperthymic” disorders (Bipolar, Cluster B personality disorders), in particular, seem to be associated with Substance Use Disorders.

Risk of Co-Occurring Psychiatric Diagnoses

- ★ OR=2.7 for mental disorder (alcohol and/or other drug use disorder vs no drug use disorder)
- ★ OR=5.8 for drug use disorder (alcohol use disorder vs no alcohol use disorder)
- ★ OR=4.2 for alcohol use disorder (drug use disorder vs no drug use disorder)
- ★ Thus, if any of these disorders is present in an individual, the likelihood that another is also present is significantly enhanced

Risk of Co-Occurring Psychiatric Diagnoses

☀ Clinicians should:

- have a **high index of suspicion** for diagnosing alcoholism in psychiatric patients
- be circumspect about prescribing **psychoactive medications with dependence liability**

☀ Implications for research:

- **Associations** of specific psychiatric diagnoses with alcoholism suggest theories of **common pathogenesis**

Differential Diagnosis of Alcohol Use vs Induced Disorders

- ✦ Timing of the **onset** of psychopathology with respect to initiation of alcohol use disorder
- ✦ **Persistence** of psychopathology when alcohol use has ceased – **duration of abstinence** at observation is a determining variable

Differential Diagnosis of Alcohol Use vs Induced Disorders

- ☀ Pharmacotherapy of a complicating psychiatric disorder is appropriate only if it is **independent** (primary), but not if it is a consequence of a alcoholism (secondary)
- ☀ Treating a co-existing psychiatric disorder using **medications with dependence liability** (e.g. benzodiazepines, methylphenidate, barbiturates, anticholinergics) or **failing to address the primary disorder** (alcohol use disorder) may be detrimental
- ☀ Some medications may do more **harm** than good (e.g., SSRIs in patients with hyperthymic or externalizing disorders, chronic opioids for pain/depression)

Social Stigma Associated with Alcohol Use Disorder

- ☀ “They do it to themselves.”
- ☀ “There is nothing that can be done.”
- ☀ “These people are not really worth the effort.”
- ☀ “Alcoholism is hopeless, but I can treat their depression, diabetes, or ulcers.”

Alcohol use disorder occurs in young people and can affect the trajectory of the person's life (if it does not cause death). Unfortunately, most physicians are not adequately able to manage or even recognize these patients. Many physicians compound the problem with inappropriate pharmacotherapy that actually may exacerbate the disorder.

Alcohol Use Disorder: “Classical” Presentations (Dramatic, Easy)

- ★ Acute and chronic **direct** pharmacologic and toxic actions of the substance:
 - ★ **Overdose**
 - ★ **Organ toxicity** (e.g., cirrhosis/ulcer/pancreatitis, angina/MI/cardiomyopathy, emphysema, stroke/seizures/dementia, depression/anxiety/ psychosis, hypogonadism/infertility/fetal)
 - ★ **Metabolic consequences** (gout, diabetes, hypoglycemia, hyperlipidemia)

Alcohol Use Disorder: Typical Presentations (Difficult to Dx)

- ☀ **Indirect effects** of drinking on life-style are most common:
 - ☀ family disruptions and emotional trauma
 - ☀ legal problems and physical trauma
 - ☀ self-neglect (e.g., malnutrition, infections)
 - ☀ inappropriate use of prescribed medication (e.g., analgesics, anxiolytics)
 - ☀ lack of compliance with medical regimens for coexistent illnesses, including smoking cessation
 - ☀ non-specific, poorly defined problems

Patients Rarely Complain of Alcoholism!

- ✦ Determine the **nature and extent** of alcohol, nicotine, and other drug use in each patient
- ✦ Conduct routine screening for alcohol/drug use **associated problems**, as well as **risk factors** for development of alcohol, nicotine and other drug dependence
- ✦ **Intervene** if indicated—never ignore or minimize drinking as a significant problem (even if patient *encourages* you to do so)
- ✦ **SIMPLY ASKING** reduces use and subsequent problems at follow-up by 10 to 30%

NIAAA's One Question Approach

Prescreen: *Do you sometimes drink beer, wine, or other alcoholic beverages?*

NO

Screening complete

YES

Ask the screening question about heavy drinking days:
How many times in the past year have you had...

5 or more drinks in a day (for men)

4 or more drinks in a day (for women)

History of Alcohol Consumption

- ☀ Number of drinks considered harmful in:
 - ☀ **men** > 14 drinks/week or > 4-5 drinks per occasion
 - ☀ **women** > 7 drinks/week or > 3-4 drinks per occasion
- ☀ Simple quantity/frequency questions are moderately sensitive (34-47%); certainly better than not asking

Screening with CAGE Questions

- ✱ **C**—have you ever felt you should **CUT DOWN** your drinking?
- ✱ **A**—have people **ANNOYED** you by criticizing your drinking?
- ✱ **G**—have you ever felt bad or **GUILTY** about your drinking?
- ✱ **E**—have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (**EYE-OPENER**)?

CAGE \geq 2, sensitivity=93%; specificity=76% for identification of problem drinkers (Bernadt et al)

Laboratory Tests for Diagnosis of Alcohol Use Disorder

- ★ **Gamma-Glutamyl Transpeptidase (GGTP)**: quite useful but can be elevated with liver disease
- ★ **Carbohydrate-Deficient Transferrin (CDT)**: heavy alcohol use impairs glycosylation of transferrin; most specific test available
- ★ **SGOT (AST)** more elevated than **SGPT (ALT)** (ratio > 2) in alcoholic liver disease
- ★ **Breathalyzer or BAL** can be unequivocal (e.g., if BAL > 0.15 but patient is not intoxicated)

Blood Ethanol Concentration: Effects on CNS Functions

Whiskey (Oz.) Beer (Drinks)	Blood Ethanol (mg/100 ml)	Impaired Function
0.5	15	Vision
1-1.5	30-40	Fine muscle coordination
2-3	80	Reaction time
4	100	Judgment



Signs and Symptoms of Alcohol Intoxication and Withdrawal

Intoxication

- ✱ Disinhibition (inappropriate sexual or aggressive behavior, impaired judgment, mood lability)
- ✱ Somnolence, stupor, or coma
- ✱ Impaired attention or memory
- ✱ Slurred speech
- ✱ Incoordination
- ✱ Ataxic gait
- ✱ Nystagmus

Withdrawal

- ✱ Anxiety or psychomotor agitation
- ✱ Tremor, hyperreflexia
- ✱ Craving
- ✱ Autonomic hyperactivity (pulse, BP, T, sweating, arrhythmia)
- ✱ Insomnia
- ✱ Sensory distortions or transient hallucinations
- ✱ Nausea or vomiting
- ✱ Seizures
- ✱ Delirium

Intoxication can be enhanced by GABA agonists and reversed with benzodiazepine antagonists, e.g. flumazenil.

ALCOHOL WITHDRAWAL PATTERNS



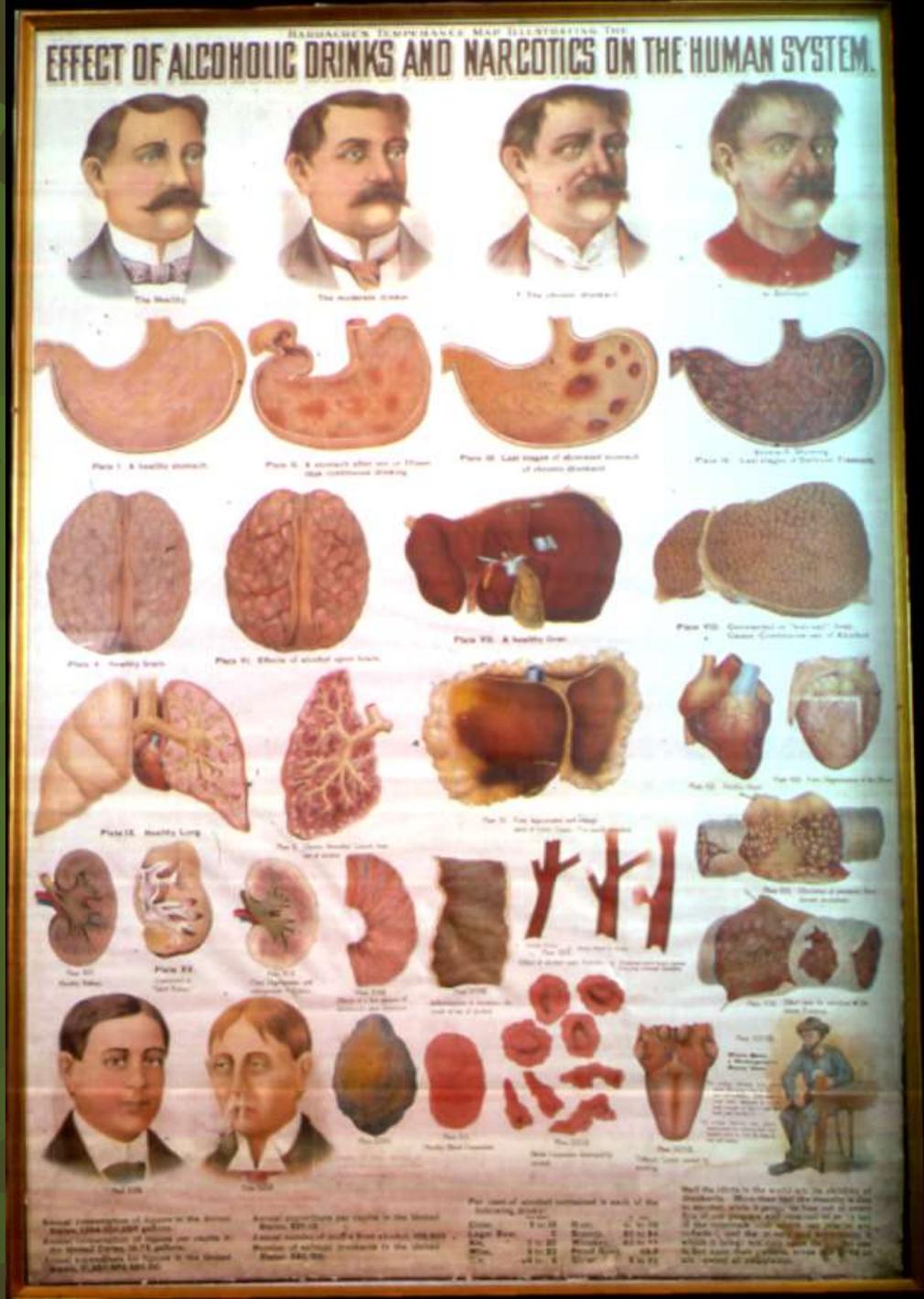
Alcohol Withdrawal: Treatment Objectives

- ★ Relief of symptoms
- ★ Prevention or treatment of complications of withdrawal (eg. seizures, arrhythmias, delirium)
- ★ Prepare patient for *post-withdrawal rehabilitation*

Medications for Treatment of Alcohol Withdrawal

- ★ Symptom-triggered (CIWA) diazepam administration is treatment of choice
- ★ Phenobarbital sometimes required when other central nervous system depressants involved
- ★ Other anticonvulsants sometimes
- ★ Alcohol taper—used but not recommended

"If you understand alcoholism, you understand medicine (and psychiatry, especially)."



Medical Complications of Alcoholism

☀ Metabolic and malnutrition

- ☀ Gout
- ☀ Hyperlipidemia and fatty liver
- ☀ Hypoglycemia
- ☀ Weight loss or obesity
- ☀ Immune compromise (opportunistic infections)
- ☀ Impaired protein synthesis
- ☀ Mineral and electrolyte imbalances
- ☀ Vitamin deficiencies
- ☀ Decreased blood clotting

☀ Gastrointestinal

- ☀ Esophagitis
- ☀ Gastritis or ulcer
- ☀ Pancreatitis
- ☀ Liver disease (alcoholic hepatitis, cirrhosis)
- ☀ Malabsorption
- ☀ Altered drug and carcinogen metabolism
- ☀ Increased cancer incidence

Medical Complications of Alcoholism

☀ Endocrine

- ☀ Pancreatic insufficiency (glucose intolerance)
- ☀ Increased ACTH, glucocorticoid, or catecholamine release
- ☀ Inhibited testosterone synthesis (male hypogonadism)
- ☀ Inhibition of ADH, oxytocin release

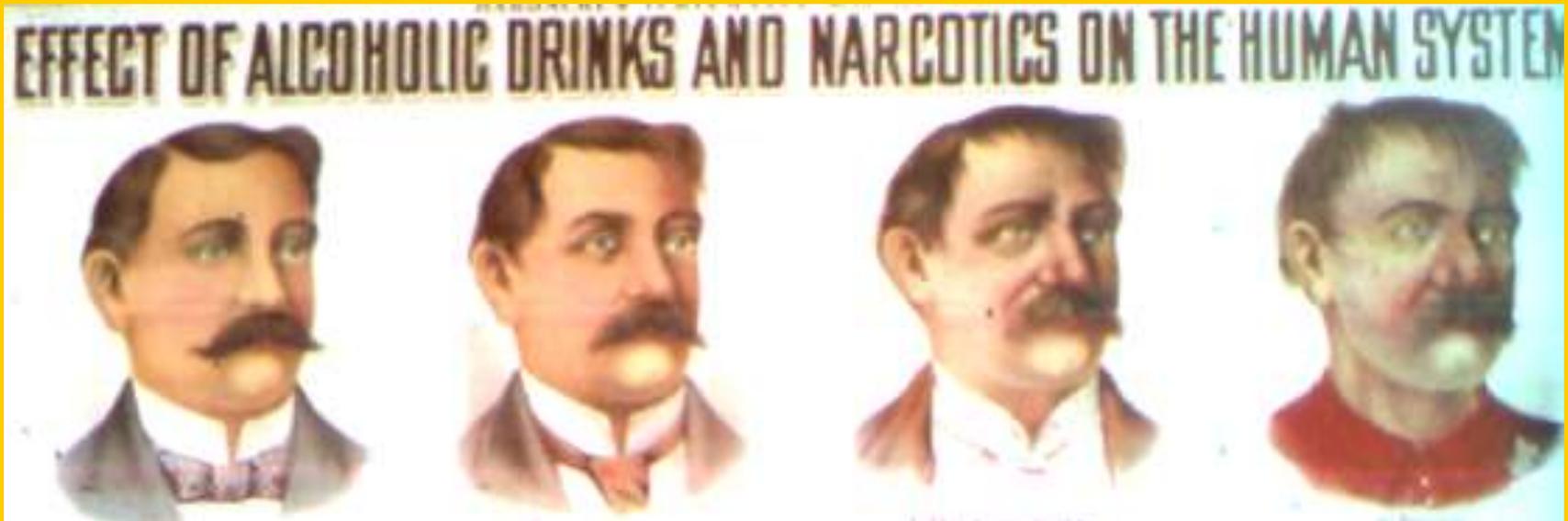
☀ Cardiovascular

- ☀ Hypertension
- ☀ Stroke
- ☀ Arrhythmias
- ☀ Coronary heart disease

☀ Neuropsychiatric

- ☀ Dementia
- ☀ Amnesia
- ☀ Cerebellar degeneration
- ☀ Fetal alcohol effects
- ☀ Neuropathy

It doesn't take a rocket scientist to recognize which of the patients below has alcohol use disorder! A good clinician can recognize the problem before it is obvious...



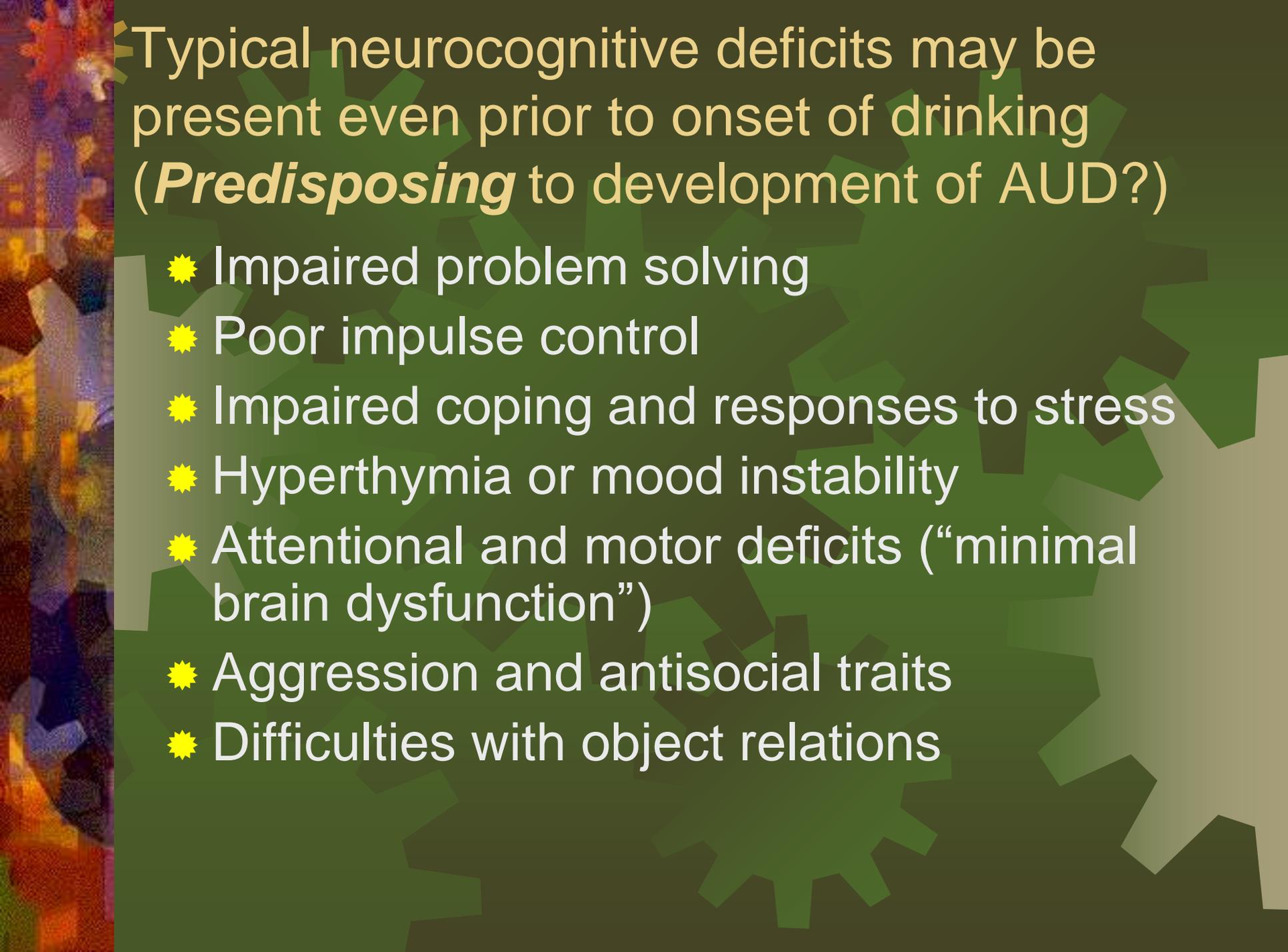
But when/to what degree is the brain first affected by alcohol consumption? Intoxication/drinking also change with years of out-of-control use...

Brain changes can influence the clinical course of alcohol use disorder (AUD)

- ★ AUD involves altered structure and function of the brain
- ★ Brain circuitry involved in adaptive motivated behavior, stress responses, and survival are affected by chronic alcohol consumption
- ★ These brain changes convey lifelong *vulnerability to relapse*, a powerful automatic behavioral (learned) action reflex
- ★ AUD may also cause more overt *neurocognitive deficits*, e.g. problem solving, memory, visuospatial and motor disturbances

Chronic Alcohol Use Disorder: Syndromes of CNS Impairment

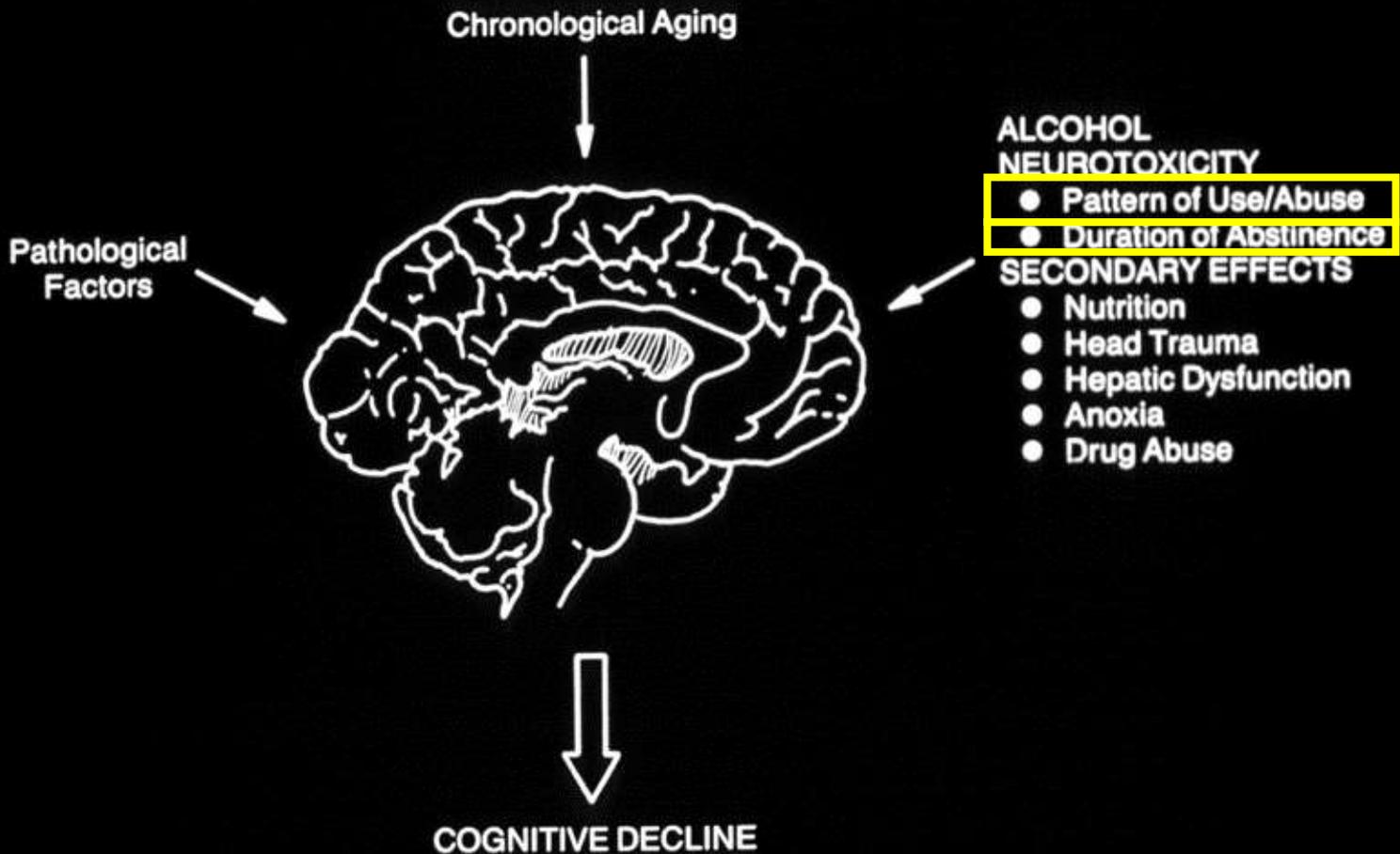
- ★ 50-70% of alcoholics have *mild to moderate deficits* in following domains:
 - Verbal
 - Abstracting/problem solving
 - Learning/memory
 - Perceptual/motor
- ★ 10% have *severe* brain dysfunction (Wernicke-Korsakoff syndrome or alcohol-induced persisting dementia)



Typical neurocognitive deficits may be present even prior to onset of drinking (*Predisposing* to development of AUD?)

- ✦ Impaired problem solving
- ✦ Poor impulse control
- ✦ Impaired coping and responses to stress
- ✦ Hyperthymia or mood instability
- ✦ Attentional and motor deficits (“minimal brain dysfunction”)
- ✦ Aggression and antisocial traits
- ✦ Difficulties with object relations

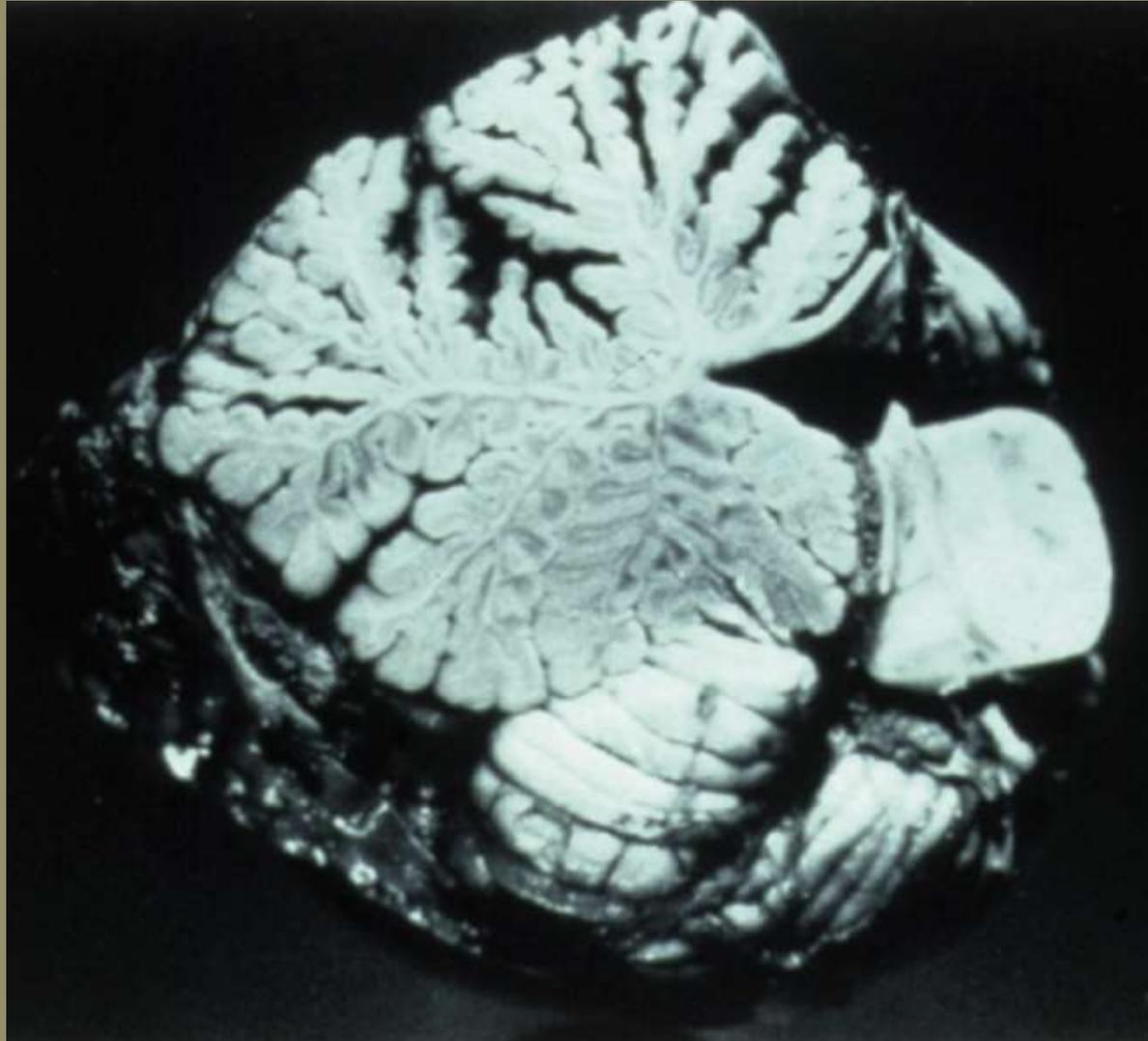
Alcoholism-associated Neurocognitive Deficits: Contributing Factors



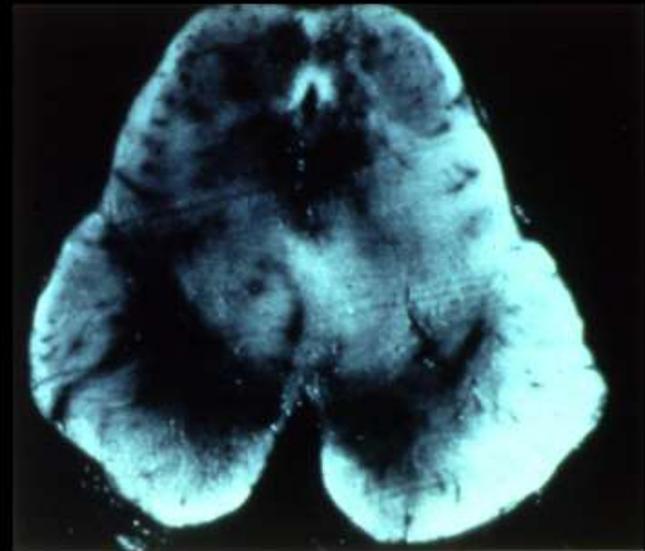
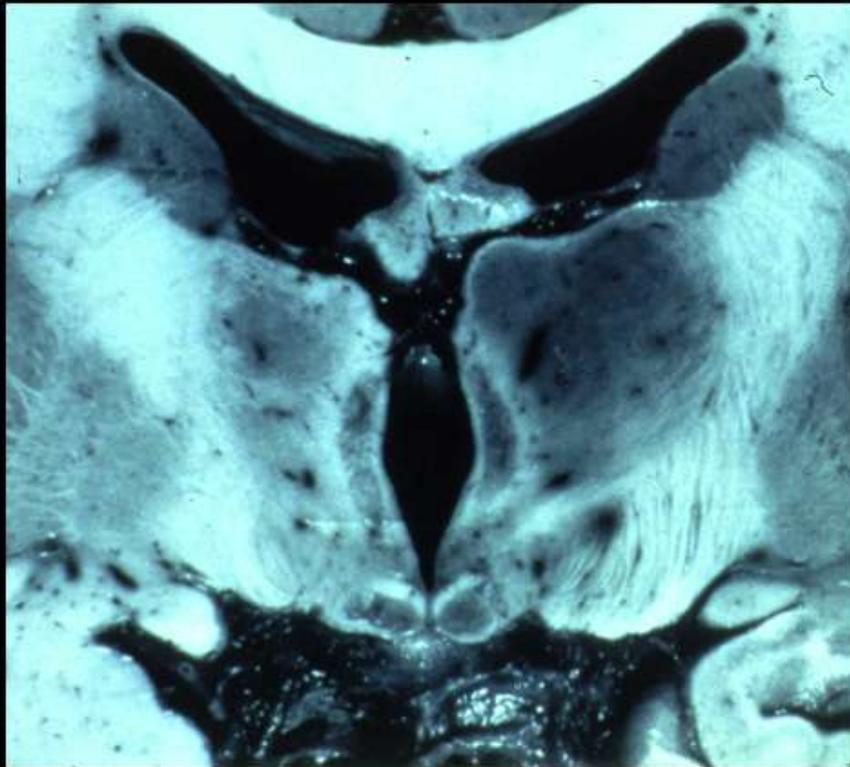
Neuropathologic Findings in Alcoholic Patients

- ★ Cerebellar degeneration (~50%)
- ★ Brainstem and diencephalic abnormalities of WKS (~13%)
- ★ Reduced brain weight and/or volume (frontal lobe WM)

Alcoholic Cerebellar Degeneration



Wernicke-Korsakoff Syndrome



1881—Confusion, ataxia,
external ophthalmoplegia

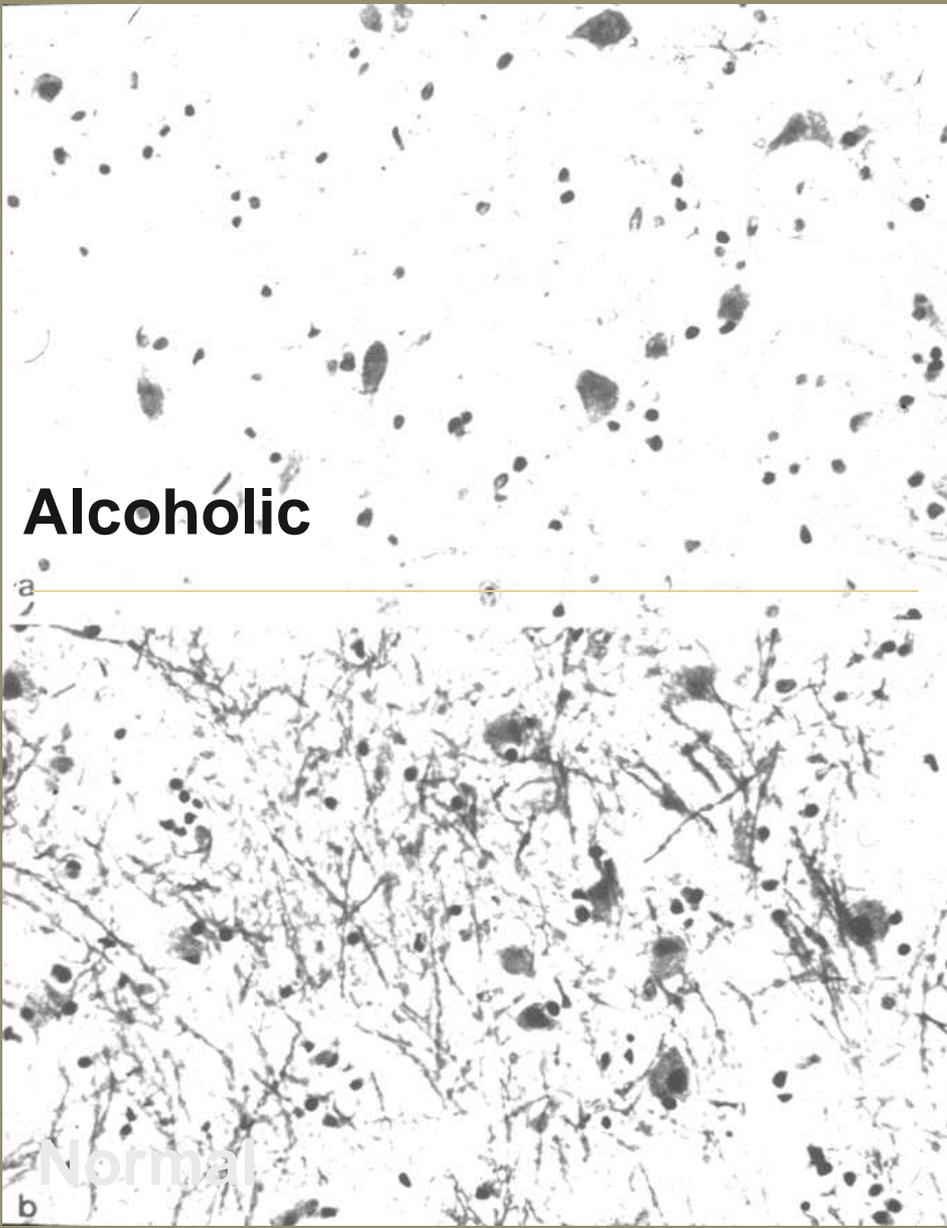


Carl Wernicke
1848-1905

1887—Amnestic state
± polyneuropathy



S.S. Korsakoff
1853-1900



Alcoholic

a

This panel shows a microscopic view of brain tissue from an alcoholic individual. The tissue appears pale and lacks the dense network of dark-staining myelin fibers seen in the normal control. The overall structure is less organized, indicating demyelination.

Normal

b

This panel shows a microscopic view of normal brain tissue. It features a dense, intricate network of dark-staining myelin fibers, which is characteristic of healthy brain tissue. The structure is well-organized and shows a clear pattern of myelination.

Demyelination of Mammillary Bodies in Non-WKS Alcoholics

Alling and Bostrom (1981)



Top row, slice images from three normal subjects. Bottom row, slice images from three alcoholic subjects showing the large amount of *ventricular enlargement and cortical and cerebellar atrophy*.

Alcohol-Induced Brain Injury May Act via Thiamine Deficiency [TD]

- ✦ Up to *80% of alcoholics* may have TD (reduced intake/absorption and altered metabolism/utilization)
- ✦ Reduced activities of *thiamine requiring enzymes* are also found in brains of *non-WKS alcoholics* (*Butterworth*)
- ✦ Thiamine *rapidly reverses signs of TD* (Wernicke's encephalopathy) in alcoholics potentially leaving residual neuropsych/pathologic deficits (Korsakoff's syndrome)
- ✦ *TD can mimic and potentiate histological effects of alcohol* in animal models; thiamine reverses neurochemical/histological and behavioral effects (*Langlais; Butterworth*)

Longitudinal Perspective on Treatment of Alcohol Abuse/Dependence

Antecedents/Socio-cultural Context/Consequences
Occasional/Regular/Compulsive

Brain Effects of Alcohol

Vulnerable Individual

- Biologic
- Psychologic
- Social

Drug-seeking

Neuroadaptation
Dependence

Complications

- Social
- Neuropsychiatric
- Medical

Pharmacopsychosocial Treatment
Varies with Stage of Disorder

Pharmacopsychosocial Treatment of Alcoholism



⚙ Medications Used in Treatment of AUD and Complications

⚙ Withdrawal

- ⚙ diazepam, lorazepam, clonidine, phenobarbital,

⚙ Craving/Relapse

- ⚙ disulfiram, naltrexone, acamprosate, topiramate, oxcarbazepine

⚙ Depression/Anxiety

- ⚙ fluoxetine, sertraline, paroxetine, etc

⚙ Mood instability

- ⚙ valproate, carbamazepine, oxcarbazepine, lithium, etc

⚙ Psychosis

- ⚙ haloperidol, risperidone, olanzapine, etc

Evidence-based Medication Treatments for Primary Alcohol Dependence

- ✦ Disulfiram (Antabuse)
- ✦ Naltrexone (Revia, Vivitrol)
- ✦ Acamprosate (Campral)
- ✦ Anticonvulsants
 - ✦ Topiramate (Topamax)
 - ✦ Carbamazepine (Tegretol)
 - ✦ Oxcarbazepine (Trileptal)
 - ✦ Gabapentin (Neurontin)