

Alcohol-Associated Liver Disease

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UMKC FAMILY MEDICINE

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Jordan

- ▶ 28yo male bar tender presents with c/o acute "stomach pains".
- ▶ History of increasing drinking past 3yr, now up to 1/2 of a fifth of vodka daily
- ▶ Diagnosed with alcoholic cirrhosis and hepatitis
- ▶ Hospital dy 25 has 40lb wt loss and severely ill.

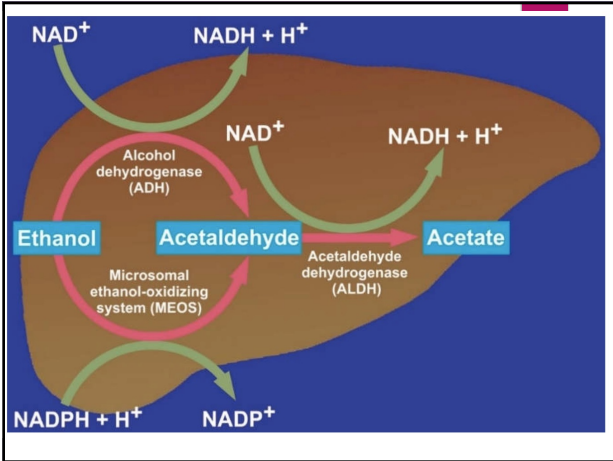


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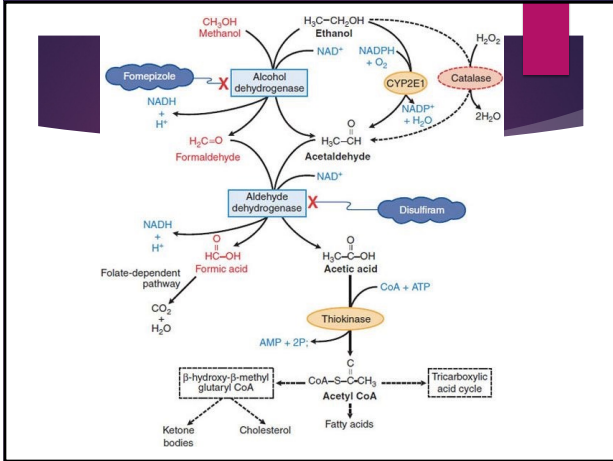
Epidemiology of ALD

- ▶ Affects about 123 million people globally
- ▶ Contributes to about 25% of deaths from cirrhosis and to 60% of hospitalizations for liver failure
- ▶ Cofactor in progression of viral hepatitis and NAFLD
- ▶ Accounts for about half of all alcohol related deaths

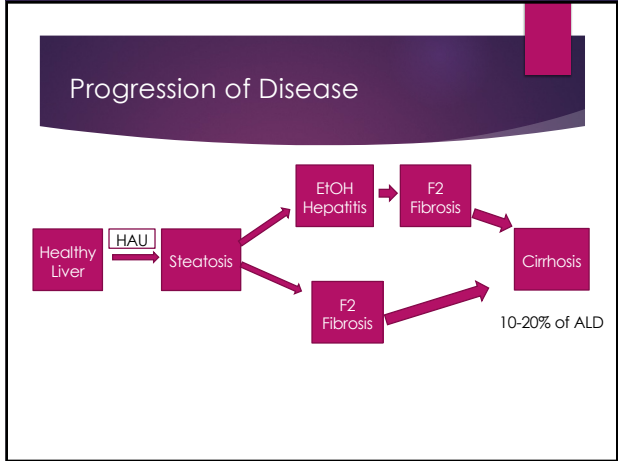
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Diagnosis of Alcohol Associated Liver Disease

- ▶ 12mo HAU (May use AUDIT-C screening)
- ▶ Liver disease (clinical, biochemical, imaging)
- ▶ Not caused by: viral, autoimmune, genetic
- ▶ 90% asymptomatic or vague sx like fatigue

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BOX 2

The diagnostic criteria for harmful alcohol use, according to the ICD-10 (F10.1) (e9)

- There is clear evidence that substance use is largely or wholly responsible for mental and/or physical harm, including impaired judgment or abnormal behavior, that can cause impairment or adverse consequences in interpersonal relationships.
- The nature of the harm caused by the substance should be clearly specifiable and describable.
- The pattern of harmful use has been present for at least one month or repeatedly over the past twelve months.
- The diagnostic criteria for another mental or behavioral disorder caused by the same substance are not simultaneously satisfied (with the possible exception of acute intoxication, F10.0).

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AUDIT-C

AUDIT-C

Please circle the answer that is correct for you.

1. How often do you have a drink containing alcohol?					SCORE
Never (0)	Monthly or less (1)	Two to four times a month (2)	Two to three times per week (3)	Four or more times a week (4)	_____
2. How many drinks containing alcohol do you have on a typical day when you are drinking?					_____
1 or 2 (0)	3 or 4 (1)	5 or 6 (2)	7 to 9 (3)	10 or more (4)	_____
3. How often do you have six or more drinks on one occasion?					_____
Never (0)	Less than Monthly (1)	Monthly (2)	Two to three times per week (3)	Four or more times a week (4)	_____
TOTAL SCORE					_____

Add the number for each question to get your total score.

Maximum score is 12. A score of ≥ 4 identifies 86% of men who report drinking above recommended levels or meets criteria for alcohol use disorders. A score of > 2 identifies 84% of women who report hazardous drinking or alcohol use disorders.

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Clinical Diagnosis of ALD

- ▶ Clinical
 - ▶ Firm, large liver
 - ▶ Splenomegaly
 - ▶ Muscle wasting
 - ▶ Spider angioma
 - ▶ Decompensation (ascites, jaundice, GI bleed, encephalopathy, hepatocellular carcinoma)

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Biochemical Diagnosis of ALD

- ▶ Biochemical
 - ▶ Early ALD
 - ▶ High MCV, Alk Phos, GGT, and AST/ALT >1 (both <400)
 - ▶ Advanced ALD- Above plus;
 - ▶ High Bilirubin or PT
 - ▶ Low albumin or platelets

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Imaging diagnosis of ALD

- ▶ Imaging
 - ▶ Steatosis
 - ▶ Portal Hypertension
 - ▶ Cirrhosis

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Fatty Liver

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ALD is Not Attributable to...

- ▶ Viral
 - ▶ HBV
 - ▶ HCV
- ▶ Autoimmune
 - ▶ Autoimmune hepatitis- ↑IgG, +ANA, ASMA
 - ▶ Primary biliary cholangitis- ↑Alk Phos, lipids, +ANA, AMA
- ▶ Genetic
 - ▶ Wilson's- ↓ceruloplasmin, ↑urine copper, KF rings, anemia
 - ▶ Hemochromatosis- Ferritin>1,000 and ↑tissue iron by MRI
 - ▶ Alpha 1- antitrypsin deficiency

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Complications of ALD

- ▶ Cirrhosis
 - ▶ Esophageal varices
 - ▶ Hepatorenal syndrome
 - ▶ Hepatocellular carcinoma
 - ▶ Loss of synthetic liver function (↓albumin and ↑INR)
- ▶ Jaundice of uncertain etiology
- ▶ Alcoholic hepatitis

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Clinical Diagnosis of Cirrhosis

- ▶ Advanced fibrosis with regenerative nodules
- ▶ Symptoms include anorexia, fatigue, hypogonadism
- ▶ Exam- jaundice, spider angioma, gynecomastia, testicular atrophy, ascites, splenomegaly, palmar erythema, clubbing, asterix, decreasing blood pressure.

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Cirrhosis

- ▶ Evaluations associated with survival
 - ▶ MELD (Model for End-Stage Liver Disease) score
 - ▶ Child Turcotte Pugh score
 - ▶ Presence of Decompensation
 - ▶ Diagnosis of Hepatocellular Carcinoma
- ▶ Evaluations for advanced fibrosis
 - ▶ Serological (Fib-4)
 - ▶ Ultrasonographic (transient elastography)

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MELD score

Model for End-Stage Liver Disease (MELD) Score

**MELD = 3.78 x log_e serum bilirubin (mg/dL) +
11.20 x log_e INR +
9.57 x log_e serum creatinine (mg/dL) +
6.43 (constant for liver disease etiology)**

NOTES:

- If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0
- Any value less than one is given a value of 1 (i.e. if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)

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MELD score with prognosis

**Three Month Mortality
in Hospitalized Patients**

• MELD Score	• Death Rate
<= 9	4%
10-19	27%
20-29	76%
20-39	83%
>= 40	100%

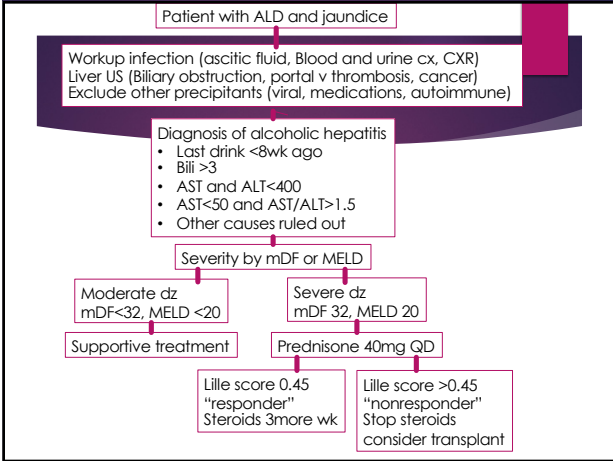
Kamath 2001

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Jaundice

- ▶ Patient presenting with jaundice see algorithm below
- ▶ ALD should be suspected, and workup should target precipitants
 - ▶ Infection- viral hepatitis, ascending cholangitis
 - ▶ Drug-induced liver injury – Medications, herbals, supplements
 - ▶ Portal vein thrombosis- unbalanced hemostasis and slowing of portal flow in cirrhotic patients

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MDF score

Discriminant Function (DF)

- Aka 'Maddrey score'
- DF = (4.6 x increase in PT sec.) + (serum bilirubin mg/dl)
- To assess prognosis in alcoholic hepatitis
- ✓ A value over 32 implies severe liver disease with a poor prognosis

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Lille score

The Lille model is based on a composite score looking at survival in patients with ETOH hepatitis.

- ▶ Lille formula:
- ▶ Lille Model Score = $(\exp(-R))/(1 + \exp(-R))$
- ▶ Where R = $3.19 - (0.101 \times \text{age}) + (0.147 \times \text{baseline albumin}) + (0.0165 \times \text{change in bilirubin level}) - (0.206 \times \text{creatinine}) - (0.0065 \times \text{baseline bilirubin}) - (0.0096 \times \text{prothrombin time})$

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Recent review of ALD

Review > JAMA. 2021 Jul 13;326(2):165-176. doi: 10.1001/jama.2021.7683.

Diagnosis and Treatment of Alcohol-Associated Liver Disease: A Review

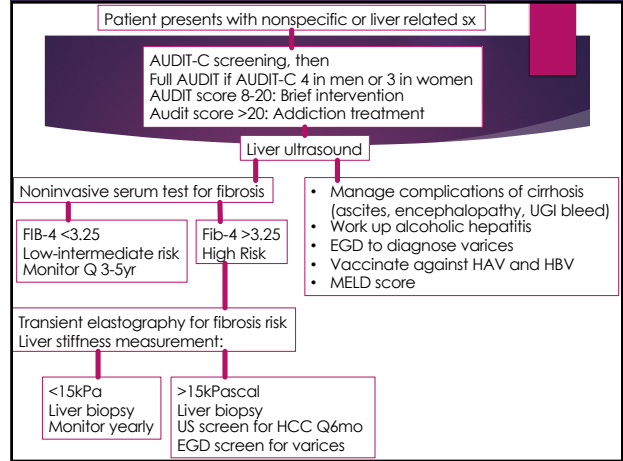
Ashwani K Singal^{1,2}, Philippe Mathurin³

Affiliations + expand
PMID: 34255003 DOI: 10.1001/jama.2021.7683

Abstract

Importance: Alcohol-associated liver disease results in cirrhosis in approximately 10% to 20% of patients. In 2017, more than 2 million people had alcohol-associated cirrhosis in the US. Alcohol-associated liver disease is the primary cause of liver-related mortality and the leading indication for liver transplant, representing 40% to 50% of all liver transplant in high-income countries.

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ALD diagnosis and treatment

- ▶ Serum markers for advanced fibrosis
 - ▶ FIB-4 (Age x AST)/(plt x square root of ALT)
 - ▶ Result > 3.25 --> high risk of fibrosis
- ▶ Adequate Nutrition in 3 meals & 3 snacks
 - ▶ 35kcal/kg (60Kg needs 2100cal)
 - ▶ 1.2-1.5gm protein/kg (60Kg needs 90gm)
- ▶ Encephalopathic patients may need vegetable or dairy protein
- ▶ Avoid iron overload, without restricting dietary iron

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Emerging treatments

- ▶ Fecal transplant improves liver function and survival
- ▶ DUR-928- regulates genes controlling inflammation
- ▶ IL-22- Cytokine promoting hepatic regeneration
- ▶ Granulocyte colony stimulating factor- Also promotes hepatic regeneration

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Treatment of Alcohol Use Disorder

- ▶ **Counselling**
 - ▶ AUDIT score 8-20 → Brief counselling reduced episodes of HAU from 38% to 20%
 - ▶ AUDIT score >20 → CBT or motivational therapy (including 12-step) improved abstinence from 48% to 74%
- ▶ **Medications to improve abstinence**
 - ▶ Acamprostate (may consider in ALD)
 - ▶ Naltrexone
 - ▶ Disulfiram
 - ▶ Baclofen (may use in decompensated ALD)
- ▶ **Treat persistent mood disorders**

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The Alcohol Use Disorders Identification Test: Self-Report Version

PATIENT: Because alcohol use can affect your health and can interfere with certain medications and treatments, it is important that we ask some questions about your use of alcohol. Your answers will remain confidential so please be honest. Place an X in one box that best describes your answer to each question.

Questions	0	1	2	3	4
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times a month	2-3 times a week	4 or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	1 or 2	3 or 4	5 or 6	7 to 9	10 or more
3. How often do you have six or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
9. Have you or someone else been injured because of your drinking?	No	Yes, but not in the last year	Yes, during the last year	Yes, during the last year	Yes, during the last year
10. Has a relative, friend, doctor or other health care worker (even concerned about your drinking or suggested you cut down)?	No	Yes, but not in the last year	Yes, during the last year	Yes, during the last year	Yes, during the last year
Total					

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Alcohol and public health

- ▶ 3 Million die each year from harmful use of alcohol
- ▶ Over 280 million live with Alcohol Use Disorder
- ▶ Alcohol is the leading risk factor for premature mortality and disability among those aged 15 to 49 years, accounting for 10 percent of all deaths in this age group.
- ▶ Disadvantaged and especially vulnerable populations have higher rates of alcohol-related death and hospitalization.

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WHO action on alcohol

- ▶ May 2010- Adoption of the Global Strategy to Reduce the Harmful Use of Alcohol
- ▶ Feb 2020- Executive board calls for accelerated action
- ▶ **Focus on**
 - ▶ cross-border alcohol marketing
 - ▶ advertising and promotional activities
 - ▶ targeting youth and adolescents
 - ▶ adequately resource the work on the harmful use of alcohol.

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Cross-border marketing of alcohol

- ▶ Disregards social, economic, cultural environment of target country
- ▶ Largely carried out by transnational corporations
- ▶ Included prominent placement of alcohol in TV/ movies/ sporting events.
- ▶ Is unavoidable by people who do not wish to drink
- ▶ Is effective in producing an urge to drink

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Targets of advertising

- ▶ Groups who should be protected
 - ▶ Children and adolescents
 - ▶ People with alcohol dependence
 - ▶ People who do not wish to drink
- ▶ Women drink about 1/4 of alcohol consumed
 - ▶ Marketers see this as an opportunity and target women in ads
 - ▶ Domestic abuse is most likely when BOTH men and women drink

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Social Media

- ▶ Much growth in advertising of alcohol is on social media, and is made more effective by using in-depth knowledge of users' interests and behaviors
- ▶ Advertising is driven by influencers, often paid
- ▶ Promotion is targeted by highlighting products that "friends" have "liked"
- ▶ Advances in marketing via social media are sophisticated, vast, and have developed quickly

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WHO "SAFER" initiative

- ▶ Strengthen restrictions on alcohol availability
- ▶ Advance and enforce drink-driving countermeasures
- ▶ Facilitate access to screening, brief interventions and treatment
- ▶ Enforce bans or comprehensive restrictions on alcohol advertising, sponsorship and promotion
- ▶ Raise prices on alcohol through excise taxes and other pricing policies.

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Jordan and Gina

- ▶ Transferred to university hospital
- ▶ Four months later pt is home with his wife, abstaining from alcohol, and able to work.

