UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

ALCOHOL BIOMARKERS

JOSEPH SKOWRONSKI MD

UW ADDICTION MEDICINE FELLOW

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

SPEAKER DISCLOSURES

I have no conflicts of interest.

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

Mark Duncan MD
Rick Ries MD
Kari Stephens PhD
Barb McCann PhD
Anna Ratzliff MD PhD
Betsy Payn MA PMP
Esther Solano
Cara Towle MSN RN

UW PACC

OBJECTIVES

1. Review the standard alcoholic drink.
2. Learn how alcohol is digested and metabolized in the body.
3. Discuss sensitivity and specificity.
4. Explore commonly and less commonly known alcohol biomarkers.

UW PACC

AMOUNT OF ALCOHOL IN A STANDARD DRINK

Light Beer	Regular Beer	Micro Brew	White Wine	Red Wine	80 Proof
4.20% AbV	5.00% AbV	6.70% AbV	12.0% AbV	15.0% AbV	40.0% AbV
1 drink = 14 oz	1 drink = 12 oz	1 drink = 9 oz	1 drink = 5 oz	1 drink = 4 oz	1 drink = 1.5 oz

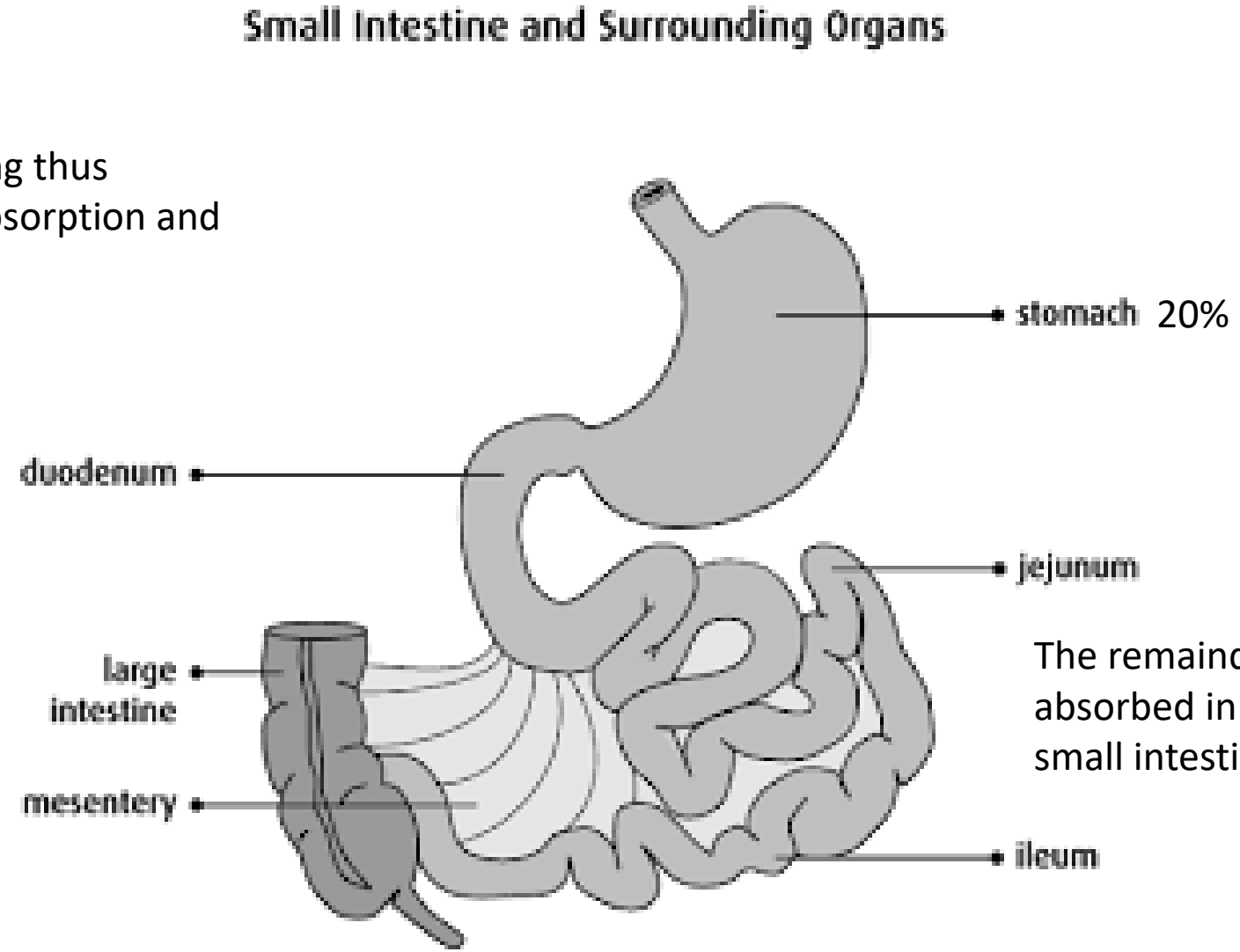
All these standard drinks are equivalent in pure ethanol content: about 0.6 ounces, 18 mL, or 14 g.

https://www.abc.ca.gov/education/licensee-education/alcohol-facts/#:~:text=Alcohol%20does%20not%20require%20digestion,intestine%2C%20where%20absorption%20is%20faster.

UW PACC

ALCOHOL DIGESTION AND ABSORPTION

Food slows gastric emptying thus decreasing the speed of absorption and subsequent intoxication.

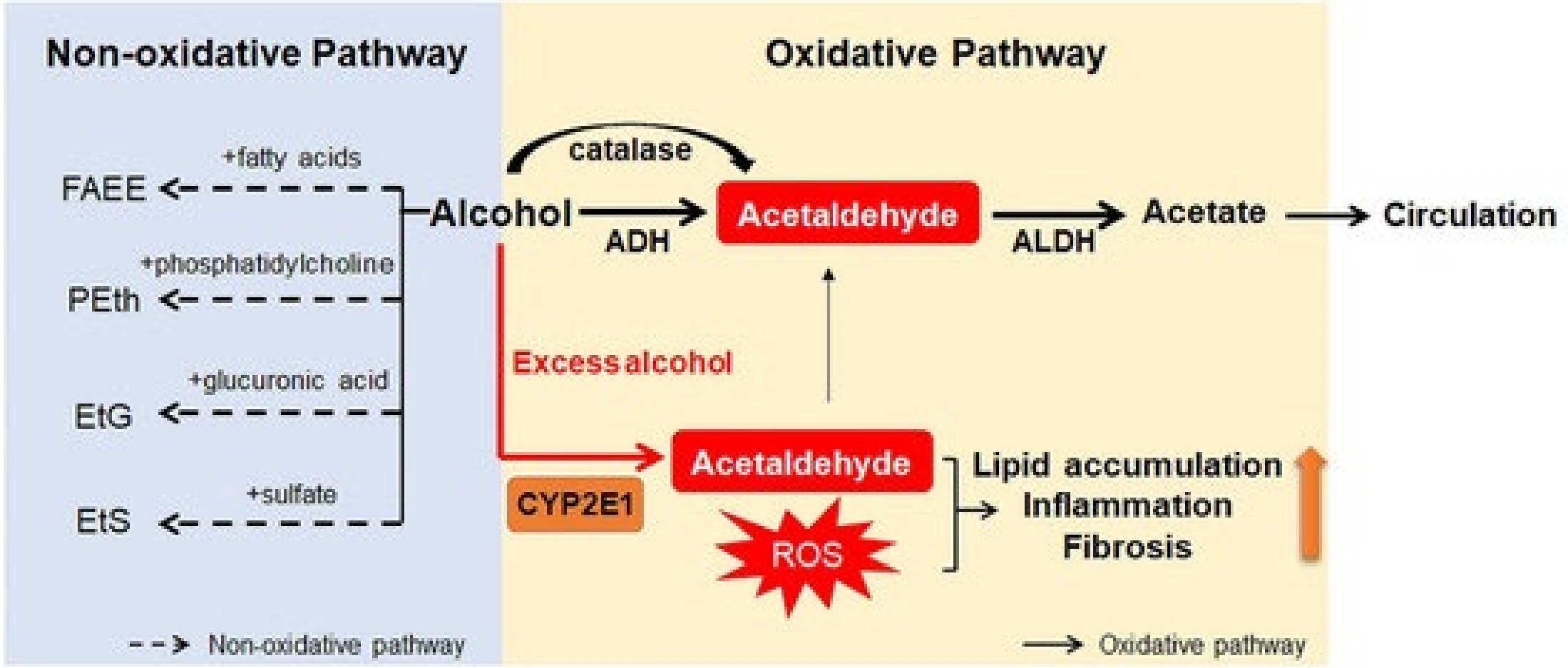


20%

The remainder is absorbed in the small intestine.

https://pharmacyimages.blogspot.com/2020/09/Smallintestinediagram-Simplesmallintestine-Smallintestinefunction.html?m=1

ALCOHOL METABOLISM PATHWAYS



https://www.mdpi.com/1422-0067/22/11/5717

A QUICK REVIEW OF SENSITIVITY AND SPECIFICITY

	Sensitivity	Specificity
Definition	Proportion of patients with a disease who test positive	Proportion of patients without the disease who test negative
100% (1.0) Means	The test correctly identify every person who has the target disorder	The test correctly identify every person who does not have the target disorder
Statistical Outcome	True Positive	True Negative
Ideal Test Result	Negative Test Result	Positive Test Result
Test Interpretation	They are definitely not positive → They DON'T have it	They are definitely not negative → They DO have it
The Rule	Rule Out (SnOut)	Rule In (SpIn)

https://www.aaronswansonpt.com/sensitivity-and-specificity/

UW PACC

REASONS TO CHECK ALCOHOL BIOMARKERS

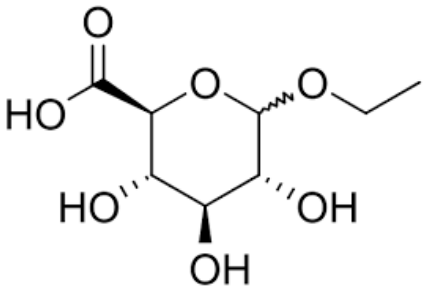
- Workup for a patient with altered mental status
- Hepatic injury screening for concerning use
- To aid in alcohol use counseling, especially in patients who may be less forthcoming about their use
- Legal system
- Forensic medicine during an autopsy
- Insurance underwriting

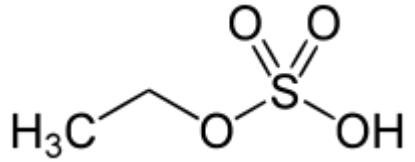
UW PACC

ETHANOL

- Ethanol is the main drug causing impairment in alcohol.
- It can be measured in blood, exhalation, saliva, urine, sweat, and hair.
- Longest detectable test is hair and can be detected up to 90 days.
- Typically metabolized/excreted at about 0.015 g/dL/hr, but this is quite variable by sex, genetics, tolerance, and other factors.

ETHYL GLUCURONIDE (ETG)
ETHYL SULFATE (ETS)





- EtG exists in the blood for approximately 36 h and in urine for 3–5 days after heavy alcohol intake, whereas EtS is noticeable in urine for 24-36 h.
- When individuals test positive, it is likely that they were drinking alcohol, even if there is no ethanol detected, but an exact minimum level is unclear.
- Along with urine and blood, these can be found in other body liquids, body tissues, and hair.
- EtG measurements in hair have quite a high sensitivity and specificity in the recognition of alcohol use: 80–95% and 70–90%, respectively.
- Incidental exposition to alcohol (e.g., hand sanitizers, mouth wash) might lead to EtG and/or EtS detection.

UW PACC

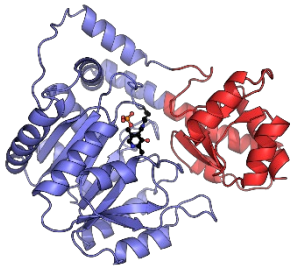
DETECTABLE ETG IN URINE OF ABSTAINING SUBJECTS

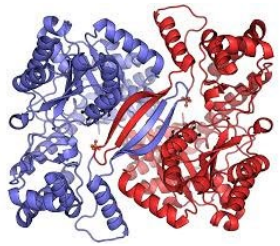
- Collected urine samples from children and abstaining adults
- EtG was detectable in both groups, and those who used hand sanitizer daily did not have significantly higher detectable amounts.
- Endogenously produced ethanol in the digestive tract likely leads to detectable EtG.
- Auto-brewery syndrome (ABS)- rare condition where overgrowth of specific bacteria/yeast leads to endogenous fermentation and ethanol production in susceptible patients

Rosano TG, Lin J. Ethyl glucuronide excretion in humans following oral administration of and dermal exposure to ethanol. *J Anal Toxicol*. 2008;32(8):594-600. doi:10.1093/jat/32.8.594

UW PACC

ASPARTATE AMINOTRANSFERASE (AST)
ALANINE AMINOTRANSFERASE (ALT)





- Levels may be elevated after heavy consumption of alcohol and remain elevated after alcohol use for as long as 2–3 weeks.
- Individuals with heavy alcohol use, but no alcohol-associated liver disease, do not have elevated ALT or AST.
- Elevated levels of ALT and AST <500 U/L may be indicative of alcohol-associated liver disease.
- The ALT/AST ratio may help differentiating alcohol-associated liver disease from other causes of hepatic dysfunction and inflammation.

UW PACC

CONFOUNDERS IN ELEVATED AST/ALT

AST

- Found in liver, heart, skeletal muscle, kidneys, brain, RBC, and gallbladder.
- AST can be elevated in myocardial infarction, acute pancreatitis, hemolytic anemia, burns, renal disease, MSK disease, and trauma.
- AST was historically used to evaluate for possible myocardial infarction.

ALT

- Primarily found in the liver, but also in the kidneys, heart, and skeletal muscle.
- More specific test than AST for liver injury, but it can be elevated from several liver pathologies besides chronic alcohol use.

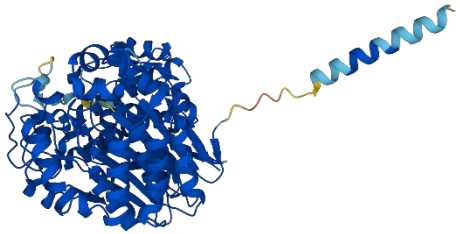
UW PACC

AST/ALT AND ALCOHOL-INDUCED LIVER DISEASE

- AST/ALT ratio in hepatocytes is about 2.5/1
- AST is cleared in 18 hours vs. ALT in 36 hours leading to relatively similar serum levels.
- Serum AST can be higher than ALT early in alcohol-induced liver disease but may be the same or less in advanced disease.
- While a ratio of 1.5-2 of AST/ALT classically indicates alcohol induced liver injury, it is not always present or particularly sensitive.

UW PACC

GAMMA-GLUTAMYL TRANSFERASE (GGT)



- A glycoprotein enzyme that aids in digestion and is found in the liver, bile ducts, kidney, spleen, and pancreas.
- After heavy alcohol consumption, GGT levels in the blood increase and stay elevated for several weeks (between 2 and 6 weeks).
- Specificity is reduced with comorbid medical conditions such nonalcoholic liver disease, biliary disease, nephrotic syndrome, and pancreatitis.
- Several medications, such as barbiturates, anticonvulsants, TCAs, and NSAIDs can cause an enzymatic induction of GGT.
- More sensitive than ALT and AST in detecting heavy alcohol use since ALT and AST elevate later in disease progression.

UW PACC

MEAN CORPUSCULAR VOLUME (MCV)

- Chronic and excessive drinking leads to enlarged red blood cells due to direct toxic effects of alcohol and its metabolites on both red blood cells and bone marrow, interaction with erythrocyte metabolism, and poor nutrition, including folate and vitamin B12 deficiencies.
- Slightly elevated in individuals with excessive alcohol use and remains high even after several (about 2–4) months of abstinence.
- Some alcohol-related conditions are associated with microcytosis, which along with alcohol-induced macrocytosis, may lead to two cell populations (dimorphic anemia) with an averaged MCV within the normal range (may have elevated RDW).

CARBOHYDRATE-DEFICIENT TRANSFERRIN (CDT)

- A glycoprotein transferrin that is deficient in the carbohydrate sialic acid due to ethanol interference.
- Highly sensitive to heavy alcohol consumption above 40 g per day, or about 5–7 standard drinks per day, and can be used to assess excessive drinking.
- Elevated for up to 3 weeks after alcohol consumption and individuals with chronic alcohol use have higher levels of CDT, compared to those who do not drink alcohol.
- CDT, in combination with GGT, can be even more useful in confirming alcohol use, identifying abstinence and relapse, as well as differentiating individuals with chronic and heavy alcohol use (> 280 g of ethanol per week) from those with lower levels of drinking.

Summary characteristics of traditional alcohol biomarkers.

Parameter	g-Glutamyl Transferase (GGT)	Alanine Amino-Transferase (ALT)	Aspartate Amino-Transferase (AST)	Carbohydrate-Deficient Transferrin (CDT)	Mean Corpuscular Volume (MCV)
Type of drinking characterized	Probably at least 5 drinks/day for several weeks	Unknown, but heavy and lasting for several weeks	Unknown, but heavy and lasting for several weeks	Probably at least 5 drinks/day for c.a. 2 weeks	Unknown, but heavy and lasting at least a few months
Dose-response of alcohol	80–200 g/day	≥40 g/day	≥40 g/day	>50 g/day	≥60 g/day
Time to elevation	24 h–2 weeks	3–7 days	3–7 days	1–2 weeks	>4–6 weeks
Time to descent to normal levels	2–6 weeks of abstinence (T½ = 14–26 days)	2–4 weeks of abstinence (T½ = 37–57 h)	2–4 weeks of abstinence (T½ = 12–24 h)	2–3 weeks of abstinence (T½ = 15 days)	4 months of abstinence
Sensitivity for detecting excessive alcohol consumption	37–95%	5–40%	25–60%	55–90%	40–50%
Specificity	18–93%	50–57%	47–68%	92–97%	80–90%
Relapse sensitivity	50%	Not reported	Not reported	55–76%	20%

Fakhari S, Waszkiewicz N. Old and New Biomarkers of Alcohol Abuse: Narrative Review. *J Clin Med*. 2023;12(6):2124. Published 2023 Mar 8. doi:10.3390/jcm12062124

Sensitivity and specificity of biomarkers in detecting harmful or heavy alcohol consumption[105-107]

Biomarker	AST	ALT	MCV	CDT	CDT + GGT	CDT + GGT + MCV
Sensitivity	47%-68%	32%-50%	45%-48%	63%-84%	83%-90%	88%
Specificity	80%-95%	87%-92%	52%-94%	92%-98%	95%-98%	95%

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; MCV: Mean corpuscular volume; CDT: Carbohydrate-deficient transferring; GGT: Gamma-glutamyltranspeptidase.

Torruellas C, French SW, Medici V. Diagnosis of alcoholic liver disease. *World J Gastroenterol*. 2014;20(33):11684-11699. doi:10.3748/wjg.v20.i33.11684

FATTY ACID ETHYL ESTERS

- Non-oxidative metabolites of ethanol that are produced from triglycerides or free fatty acids by FAEEs synthases and other enzymes.
- Present in the blood for 24–99 h after alcohol consumption, particularly among individuals with chronic excessive alcohol use.
- Compared to FAEEs in the blood, measurement of FAEEs via scalp hair is considered a more precise method for detecting exposure to alcohol.

PHOSPHATIDYL ETHANOL (PETH)

- Cellular membrane phospholipid that can be measured in the blood as a product of phospholipase D, which catalyzes the reaction between phosphatidylcholine and ethanol.
- Can be used to detect heavy alcohol consumption, or about 50 g of alcohol per day, for up to 3 weeks.

UW PACC

EMERGING BIOMARKERS

- N-acetyl-B-hexosaminidase (Beta-Hex)
- Macrophage migration inhibitory factor (MIF)
- D-dopachrome tautomerase (DDT)

UW PACC

CASE

- 35-year-old female comes to your clinic to discuss her alcohol use.

- What questions would you ask her?
- Would you order labs?
- If so, what labs would you order?
- How would you counsel her on her use?

UW PACC

LABS

- MCV- 105 (normal range: 80-98)
- Platelets- 225 (normal range: 150-350)
- AST- 150 (normal range: 10–40 U/L)
- ALT- 80 (normal range: 10–40 U/L)
- GGT- 125 (normal range: Female: 8–40 U/L)
- Total bilirubin- 1.0 (normal range: 0.3-1.0 mg/dL)

UW PACC

NOW WHAT?

UW PACC

SUMMARY

- Alcohol metabolism is more complicated than simply breakdown into acetaldehyde and acetate.
- Sensitive tests rule out disease and are good screening tests.
- Specific tests rule in disease and are good confirmation tests.
- While there are many different biomarkers to screen and monitor alcohol use, there is no single test to make or exclude the diagnosis.
- History from the patient/family/friends, physical examination, and laboratory tests are the goal standard for making this diagnosis.

ADDITIONAL QUESTIONS

- When would you order any of these biomarkers?
- Why should you order one test over another?
- How would you counsel your patients knowing the results of some of these biomarkers?
- Does any of this information change your practice?
- When would you consider ordering one of these more uncommon tests?

UW PACC

OPEN FORUM FOR QUESTIONS/DISCUSSION

UW PACC

CITATIONS

- Alcohol facts. Alcoholic Beverage Control. Accessed March 18, 2025. https://www.abc.ca.gov/education/licensee-education/alcohol-facts/#:~:text=Alcohol%20does%20not%20require%20digestion,intestine%2C%20where%20absorption%20is%20faster.
- Hyun J, Han J, Lee C, Yoon M, Jung Y. Pathophysiological Aspects of Alcohol Metabolism in the Liver. *International Journal of Molecular Sciences*. 2021; 22(11):5717. https://doi.org/10.3390/ijms22115717
- Tameez Ud Din A, Alam F, Tameez-Ud-Din A, Chaudhary FMD. Auto-Brewery Syndrome: A Clinical Dilemma. *Cureus*. 2020;12(10):e10983. Published 2020 Oct 16. doi:10.7759/cureus.10983
- Fakhari S, Waszkiewicz N. Old and New Biomarkers of Alcohol Abuse: Narrative Review. *J Clin Med*. 2023;12(6):2124. Published 2023 Mar 8. doi:10.3390/jcm12062124
- Harris JC, Leggio L, Farokhnia M. Blood Biomarkers of Alcohol Use: A Scoping Review. *Curr Addict Rep*. 2021;8(4):500-508. doi:10.1007/s40429-021-00402-7
- Rosano TG, Lin J. Ethyl glucuronide excretion in humans following oral administration of and dermal exposure to ethanol. *J Anal Toxicol*. 2008;32(8):594-600. doi:10.1093/jat/32.8.594
- Vroon DH, Israili Z. Aminotransferases. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990. Chapter 99. Available from: https://www.ncbi.nlm.nih.gov/books/NBK425/
- Harris JC, Leggio L, Farokhnia M. Blood Biomarkers of Alcohol Use: A Scoping Review. *Curr Addict Rep*. 2021;8(4):500-508. doi:10.1007/s40429-021-00402-7
- Torruellas C, French SW, Medici V. Diagnosis of alcoholic liver disease. *World J Gastroenterol*. 2014;20(33):11684-11699. doi:10.3748/wjg.v20.i33.11684

UW PACC