

Screening for alcohol use in pain management and primary care: it's about time

Presented by:

Jeffrey Gudín, MD

Jack Kain, PharmD, Medical Science Liaison



Quest Diagnostics

- The abuse and misuse of alcohol, prescription and illicit drugs remains an epidemic in the US
 - A properly implemented drug and alcohol testing program is an important step in tackling drug misuse and abuse
- Quest Diagnostics is your trusted lab source
 - Serves 1 in 3 adult Americans and half the physicians and hospitals in the United States
 - Has the world's largest database of clinical lab results with diagnostic insights that help improve health care management
 - By performing more than 10 million drug tests annually, Quest Diagnostics has the experience to help you implement a successful prescription drug monitoring program—one that helps protect your practice, safeguards your patients, and keeps your community safe
 - Rx Tox line available to help clinicians with test ordering or result interpretation

Drug and alcohol misuse and abuse

- Alcohol, opioids, benzodiazepines, and skeletal muscle relaxants are among some of the more commonly utilized central nervous system (CNS) depressants
- Concurrent use of alcohol and opioid analgesics is common among patients with chronic pain
 - Co-ingestion causes additive and potentially synergistic effects leading to drowsiness, confusion, respiratory depression, and eventually coma and death^{1,2}
- Alcohol is the leading preventable cause of death in the US (after tobacco products use and poor diet and physical inactivity)³
- Prevalence rate of alcohol use, misuse, and alcohol use disorders (AUD) are alarmingly high and unfortunately overshadowed by opioids and cannabis
 - Centers for Disease Control and Prevention (CDC) reported that excessive alcohol consumption results in approximately 88,000 deaths annually across the US

Alcohol use is common with opioid and benzodiazepine abuse

- According to the 2017 national survey on drug use and health (NSDUH), 70% of respondents reported that they drank alcohol in the past year and 56% reported that they drank in the past month⁴
- Centers for disease control (CDC) show that in 2010, 18% patients who visited the emergency department (ED) due to opioid analgesic abuse overdose had consumed alcohol concurrently. Similarly, alcohol consumption was involved in 27% of benzodiazepines drug abuse related—ED visits⁵
 - The percentage of deaths due to concomitant use of alcohol and opioid pain relievers and alcohol and benzodiazepines drug abuse were around 22% each
- Abuse of tobacco, alcohol, prescription and illicit drugs is costly
 - US costs estimated at more than \$740 billion annually related to crime, lost work productivity, and health care

Most guidelines recommend screening to determine risks of drug abuse

- Tools include questionnaires (CAGE, AUDIT), PDMPs and urine (or other matrix) drug testing
- Although self-reported and clinician-administered screening tools are available, patients tend to under-report their consumption of alcohol, opioids, and other controlled substances
- Urine drug testing provides objective evidence for medication compliance, alcohol consumption, and aberrant drug behavior
 - Objective tool that informs clinicians what drugs or substances a patient has consumed
 - Detects and confirms presence of prescribed and illicit drugs
 - Most clinicians are not aware of options other than breathalyzer or blood alcohol content (BAC) testing

Testing for alcohol

- The majority of consumed ethanol undergoes a catabolic pathway in the liver where alcohol degrades to acetaldehyde by alcohol dehydrogenases
- Breathalyzer testing detects ethanol for a number of hours following alcohol use
- Advances in laboratory medicine have allowed for the identification of specific minor alcohol metabolites or biomarkers formed by pathways in the liver, including ethyl glucuronide (EtG) and ethyl sulfate (EtS)
 - Estimated to account for only approximately 1% of alcohol elimination¹
 - These direct, water-soluble metabolites remain detectable for a longer time window (up to 80 hours in urine) after the elimination of alcohol from the body^{1,7}
 - More sensitive than the nonspecific hepatic biomarkers (AST, ALT)
 - Results dependent on time and amount of alcohol consumed

Potential biomarkers for alcohol screening⁸

Biomarker	Abbreviation	Biological Sample Type	Marker Characteristics
Ethanol	EtOH	Blood Urine Breath	Restricted to conditions where ethanol is still present in circulation
Ethyl glucuronide/ Ethyl sulfate	EtG/EtS	Urine Serum Cerebrospinal fluid Vitreous humour Hair Nails	Ethanol metabolite, which remains positive in urine samples 2-5 days after stopping ethanol use. Window of detection dependent on sample type
Phosphatidyl ethanol	PEth	Blood Dry blood spots	Ethanol metabolite, which remains detectable 1-2 weeks after alcohol use. Measured by LC-MS or immunological techniques
Fatty acid ethyl esters	FAEE	Plasma Hair Meconium	Ethanol metabolite derived from a combination of fatty acid with alcohol
Acetaldehyde adducts and associated immune responses	AA-Ab	Blood Tissue specimens	IgA response toward acetaldehyde adducts most specific for alcohol-related disorders

Factoids for consideration

- Levels of EtG in urine cannot be used to determine how much alcohol a person has ingested, when they last consumed or whether they are under the influence of alcohol⁹
- Detection times vary based on several factors, including how much and what type of alcohol a person ingested
- While higher amounts of EtG might indicate greater alcohol consumption, the exact EtG level is influenced by several factors, including how recently alcohol was consumed, genetics, medications, and other factors (liver disease, chronicity of exposure, etc)
- Incidental exposure can cause a+ result; testing detects EtG and EtS regardless of the source
 - Personal products, mouthwashes, cold preparations, hand sanitizers, and other common household items will produce positive EtG results
- Ethyl glucuronide can be produced in the body, usually in the face of a urinary tract infection in a patient with diabetes. This in-vitro formation of EtG occurs when excess glucose in the blood is excreted into the urine and can be fermented into alcohol by microbial organisms, usually by *E coli* bacteria¹⁰

Quest Diagnostics approach

- The primary benefit of an EtG test is to demonstrate sobriety. A negative EtG test is solid evidence that the individual is maintaining sobriety. On the other hand, a positive EtG result does not necessarily mean an individual has been drinking
- Remember, no clinical test is 100% reliable. Clinicians are encouraged to interpret alcohol metabolite test results in light of the clinical picture
 - Investigate other potential causes and use caution when reacting to a positive test when the donor denies drinking
 - A SAMHSA Advisory in 2012 recommended programs use additional corroborating evidence of drinking rather than relying only on a single positive EtG result
- Accuracy testing for alcohol metabolites is greater when **both** EtG and EtS are included
 - As mentioned, EtG may be produced *in vitro* when ethanol-producing bacteria are present in the urine specimen
 - Presumably, there is no *in vitro* production of EtS, so detection of EtS indicates *in vivo* alcohol presence, thereby improving the specificity of the test
 - Quest does not report a positive EtG result unless the EtS concentration is ≥ 100 ng/mL

How to order, how Quest Diagnostics tests

- How to order: Quest code 90079:
 - Drug toxicology monitoring alcohol metabolites, quantitative, urine
 - Chromatography/mass spectrometry
 - Reference Range(s): ethyl glucuronide (ETG) <500 ng/mL, ethyl sulfate (ETS)<100 ng/mL
- A high cut-off level (500 ng/mL) should help rule out incidental contact as the cause for a positive test
- LC-MS/MS is the preferred methodology for EtG and EtS analysis, since immunoassay methods are subjected to cross reactivity with analytes

Summary

- EtG and EtS are useful biomarkers to monitor alcohol use
 - The advantages over the traditional alcohol tests like breathalyzers and nonspecific LFTs
 - Early recognition of problem drinking is critical for intervention for alcohol use disorders and safety when prescribing concomitant opioids or benzodiazepines
- Quest Diagnostics offers testing for alcohol biomarkers with a longer detection window
 - A positive EtG results provide a strong indication that a person has recently been exposed to alcohol, even when ethanol is no longer detectable
 - The detection window for a urine EtG test ranges from 24 to 80 hours, depending on cutoff and usage patterns
 - Specimens that screen presumptively positive for EtG are confirmed by LC/MS/MS for both EtG and ethylsulfate (EtS), a process that improves result reporting

Quest Diagnostics

- The abuse and misuse of alcohol, prescription and illicit drugs remains epidemic in the US
 - A properly implemented drug and alcohol testing program is an important step in tackling drug misuse and abuse
- Quest Diagnostics is your trusted lab source
 - Serves 1 in 3 adult Americans and half the physicians and hospitals in the United States
 - Has the world's largest database of clinical lab results with diagnostic insights that help improve health care management
 - By performing more than 10 million drug tests annually, Quest Diagnostics has the experience to help you implement a successful prescription drug monitoring program
 - Rx Tox line available to help clinicians with test ordering or result interpretation
 - Call 1.877.40.RXTOX (1.877.407.9869)
 - Visit [QuestDrugTesting.com](https://www.questdiagnostics.com/questdrugtesting) or subscribe through your favorite podcast venue

References

1. Paulozzi LJ, Ryan GW. Opioid analgesics and rates of fatal drug poisoning in the United States. *Am J Prev Med.* 2006;31(6):506-511.
2. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *Jama.* 2008;300(22):2613-2620.
3. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *Jama.* 2004;291(10):1238-1245.
4. National Survey on Drug Use and Health. Substance Abuse and Mental Service Administration. U.S. Department of Health and Human Services. RTI International. (2017)
5. Jones CM, Paulozzi LJ, Mack KA. Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths - United States, 2010. *MMWR Morb Mortal Wkly Rep.* 2014;63(40):881–885.
6. Walsham NE, Sherwood RA. Ethyl glucuronide and ethyl sulfate. *Adv Clin Chem.* 2014;67:47-71.
7. Hoiseth G, Yttredal B, Karinen R, Gjerde H, Morland J, Christophersen A. Ethyl glucuronide concentrations in oral fluid, blood, and urine after volunteers drank 0.5 and 1.0 g/kg doses of ethanol. *J Anal Toxicol.* 2010;34(6):319-324.
8. Nanau RM, Neuman MG. Biomolecules and biomarkers used in diagnosis of alcohol drinking and in monitoring therapeutic interventions. Published 2015 Jun 29. Accessed January 13, 2020 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4598755/>
9. Helander A, Böttcher M, Fehr C, Dahmen N, Beck O, Detection times for urinary ethyl glucuronide and ethyl sulfate in heavy drinkers during Alcohol Detoxification, *Alcohol and Alcoholism*, Volume 44, Issue 1, January-February 2009, Pages 55–61, <https://doi.org/10.1093/alcalc/agn084>
10. Redondo AH, Körber C, König S, Längin A, Al-Ahmad A, Weinmann W, Inhibition of bacterial degradation of EtG by collection as dried urine spots, *Anal Bioanal Chem.* 2012 Mar;402(7):2417-24. doi: 10.1007/s00216-011-5687-7