Ethylglucuronide (EtG): A New Marker to Detect Alcohol Use in Recovering Physicians

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Alcohol is the most frequently abused "addictive substance" that causes impairment among physicians (see Table 1) and the most difficult to monitor. Once identified, alcoholic physicians usually undergo treatment and then long term monitoring to assure they can safely return to work. Medical boards in most states authorize "physician health programs" to promote early referral, intervention, evaluation and treatment, and to oversee monitoring. In 2002 more than 9,000 physicians were being monitored nationally in such programs.[1] The long-term success rate for physicians with alcohol and drug problems is very high and few cases of harm to patients have ever been documented.[2,3] However, a better test has been needed to monitor abstinence from alcohol use. The only reliable test, to date, with adequate specificity has been to test for ethyl alcohol itself in urine, breath or blood. Testing for the substance alcohol, although inexpensive and sometimes useful, is, however, inadequate — chiefly because it is so rapidly metabolized within hours after use, making it an insensitive marker of abstinence. Although rare, false-positive urine alcohol tests can occur (or can be claimed to have occurred) due to in-vitro fermentation, especially if glucose and yeast are present in the urine. Other markers have been sought, and these include blood CDT (carbohydrate deficient transferring), GGT (gamma glutamyl transferase), and others. These markers have attracted interest but they fail to provide adequate sensitivity and/or specificity to be clinically or legally useful. What is needed is a reliable test that can detect alcohol use for at least several days after use, a reliability standard similar to testing for other drugs of abuse.

Ethylglucuronide, EtG, has recently been introduced in the United States and an assay for EtG is now commercially available. EtG is a minor non-oxidative metabolite of alcohol formed by the in-vivo conjugation of ethanol with activated glucuronic acid in the presence of membrane bound mitochondrial UDP glucuronyl transferase in the liver. Only .02-.04 percent of alcohol is metabolized by this pathway, however, EtG can be detected in urine for up to three to five days following consumption of alcohol. EtG is not detectable unless alcohol has been consumed. Additionally, EtG offers the additional advantages of being detectable in body tissues and in hair following drinking.

Usefulness of the test was affirmed in one study involving psychiatric inpatients who had been hospitalized for crimes related to alcohol use. When these patients went home on pass, near the end of their confinement, they were checked for urine EtG, as well as other tests traditionally used to detect alcohol use (GGT, MCV, CDT and alcohol) upon their return. The findings were impressive. Of the 146 urine samples collected, 14 were positive for EtG. Alcohol was detected in only one case and none of the other markers were positive in any. In all 14 cases where the EtG was positive the patients, when questioned, admitted alcohol consumption of between 40-200 grams of alcohol (the equivalent of 3-15 standard drinks) within 12-60 hours prior to testing. Additionally, upon questioning the patients with the 132 urine samples negative for EtG and other markers, none admitted alcohol consumption.[4] The test appeared to be 100 percent specific and 14 times more sensitive than tests detecting alcohol in the urine.

Physicians with a history of substance-related disorders in monitoring programs develop a sophisticated understanding of the detection parameters for alcohol and other drugs by urine testing, and some attempt to circumvent monitoring by timing their drinking. It is known that some physicians "beat the system" by drinking during weekends or other times when testing is unlikely to occur. Physicians have admitted

drinking regularly for years without being detected by standard urine testing. Therefore, to evaluate the rate of positive tests for EtG among a group of physicians in monitoring, 100 sequential random urine samples were tested for EtG as well as standard testing. The physicians were not aware of the new test. Surprisingly, seven percent were positive for EtG. No other drug, including alcohol, was positive in these samples by standard testing.[5] Therefore, it appears that physicians may have a higher rate of covert surreptitious drinking while in abstinence monitoring programs than previously known. While it is not suspected that this discovery has a direct relationship to the degree of patient harm, it is likely that better testing methods that discourage covert use would increase success rates.

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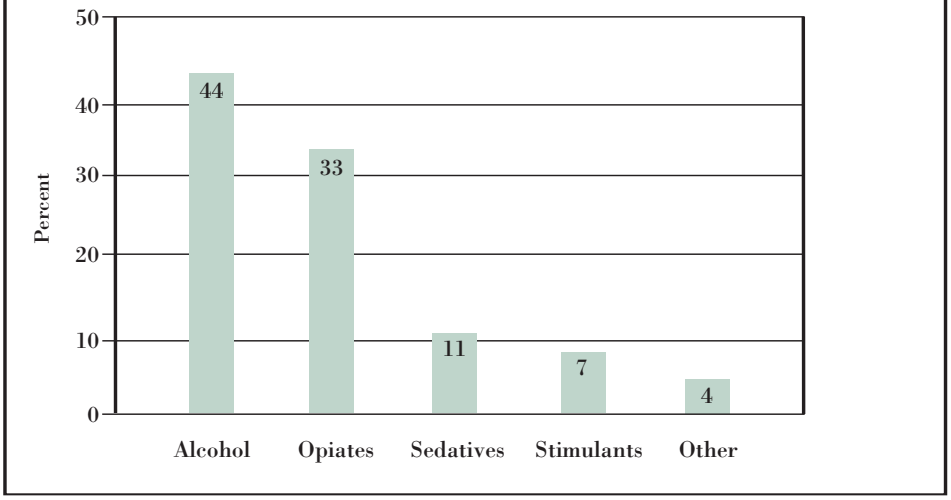
Because EtG testing is currently only possible using Liquid Chromatography and Tandem Mass Spectroscopy (LC/MS/MS) the test is relatively expensive, a factor that limits its use.[6] Development of an Enzyme-Linked Immunosorbent Assay (ELISA) screening test for EtG is under development and should greatly reduce the cost. Some physician testing programs are attempting to include EtG routinely in all urine panels. However, most are currently using the test selectively, primarily in three settings:

1. To confirm positive urine alcohol tests if alcohol use is denied.
2. "For cause" when there is a heightened concern (such as following a report of suspected "alcohol on the breath").
3. Randomly and more routinely in "high risk" individuals who have had multiple relapses. Physician health programs utilizing EtG testing are reporting its utility in detecting recent alcohol use is far superior to testing for alcohol in the urine.

For example, of the 18 EtG tests performed to date in Alabama, eight of eight tests performed "for cause" were positive for EtG but negative for all other drugs, including urine alcohol. All eight were confirmed

Table 1: Category of drug named as drug of choice by physicians (n=453) with substance-related disorders participating in the Alabama Physician Health Program from 1991-2003



positive by admission of drinking by the physician-participant when confronted regarding the positive test result. Of six tests performed to "confirm a positive urine alcohol," two were positive (and also confirmed positive by admission of drinking). None of four tests performed thus far, randomly, in participants considered "high risk" have been positive. Other states are reporting the apparent reliability and efficacy of this test for earlier detection of alcohol use in physicians. Questions regarding potential false-positive tests due to incidental exposure to alcohol (due to alcohol in food, such over-the-counter medications as cough syrup, communion wine, mouthwash, etc.) are being asked. Because such a small fraction of consumed alcohol is metabolized to EtG, a significant amount of alcohol must be consumed for EtG to be

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Table 2. Synopsis of results for those samples positive for ethyl glucuronide among the first 100 samples

Sample-no	EtG [ug/L]	Urinary ethanol	Other drugs tested positive
1	42,000	<LOD	None
2	1,300	<LOD	None
3	85,000	<LOD	None
4	196,000	<LOD	None
5	4,900	<LOD	None
6	4,100	<LOD	None
7	500	<LOD	None

Table 3. Synopsis of 18 EtG tests performed clinically during monitoring

Patient ID	Age	Sex	Date	Reason	EtG level ug/L	Confirmed + by patient
1	50	M	6/17/03	For cause	1,200	Yes
2	57	M	12/02/03	+ Ur Alc .01gm%	0	No
3	53	M	10/03/03	For cause	2,200	Yes
3	53	M	10/06/03	For cause	8,100	Yes
4	46	M	9/29/03	For cause	120,000	Yes
5	55	M	7/17/03	High risk	0	No
6	54	M	12/22/03	For cause	820	Yes
6	54	M	12/26/03	For cause	1,600	Yes
7	46	M	1/12/04	For cause	>100,000	Yes
7	46	M	1/14/04	For cause	80,000	Yes
8	55	M	2/18/04	High risk	0	No
8	55	M	3/02/04	High risk	0	No
8	55	M	3/04/04	High risk	0	No
9	54	M	7/02/03	+ Ur Alc .02gm%	17,000	Yes
10	36	M	8/02/03	+ Ur Alc .06gm%	2,400	Yes
11	58	M	9/15/03	+ Ur Alc .04gm%	0	No
12	46	M	10/02/03	+ Ur Alc .02gm%	0	No
12	46	M	9/01/03	+ Ur Alc .02gm%	0	No

detected in urine. However, cutoff levels for measuring EtG in urine have been set at between 100-250 ug/L to eliminate detection of incidental minor exposure to alcohol. Additionally, it is recommended that physicians in monitoring be advised and agree to abstain (in writing) not only from overt alcohol use, but also from any alcohol use in food, OTC meds, communion wine, etc., to avoid claims of potential false positive tests. Current analysis suggests that if the level of EtG in urine exceeds 500 ug/L incidental exposure is extremely unlikely. In any event, if testing is positive, as with any laboratory test, clinical correlation is important. In the case of physician monitoring programs it is advisable to refer physicians with positive tests for further in-depth evaluation by clinicians or programs skilled and adept at evaluating physicians.

In summary, utilizing the new alcohol marker, EtG, in urine testing programs makes it harder for recovering physicians to cheat. With the aid of this new test, the hope is that if physicians know detection is likely it will discourage their drinking. If physicians still choose to drink, earlier detection will help prevent harm to patients, appropriate referrals can be made and help may be sought for these individuals. For more information, see http://www.ethylglucuronide.com.

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