

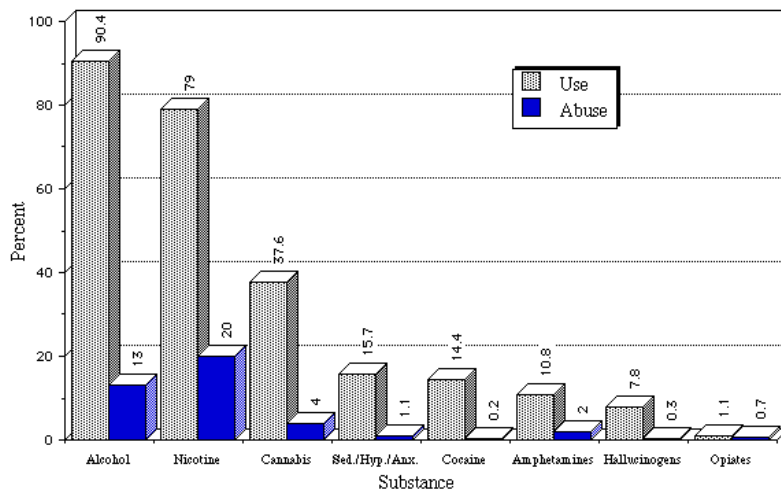
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**ALCOHOL USE NOW CAN BE DETECTED FOR DAYS RATHER THAN HOURS USING A NEW TEST, ETHYL GLUCURONIDE**

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Alcohol abuse is the single most preventable health care problem in the United States; however, this disease often goes undetected until its advanced stages, injuring not only the individual but the family, the workplace and community as well. It is estimated that alcohol abuse costs our economy well over a 150 billion dollars a year in accidents, injuries, crime, lost productivity, workman's compensation and subsequent illnesses. Alcohol and other drug abuse problems exist between 7-13% within the general population, including health professionals such as physicians, nurses, and pharmacists (see chart below).

*Lifetime Substance Use and Abuse Among American Adults*



Note. Data on "use" from National Institute on Drug Abuse 1985 National Household Survey; Data on "abuse" (includes dependence) from 1981-85 community studies reported by the American Psychiatric Association. Graph by Gordon E. Kenney, Ph.D.  
Sed./Hyp./Anx. = Sedatives/Hypnotics/Anxiolytics.

The effects of alcohol on our social structure are as equally devastating. For years criminal justice figures report that approximately 80% of child abuse, domestic assaults and violent

crimes are committed under the influence of alcohol and/or other drugs. Although there is great media attention on stopping the spread of cocaine, marijuana, and other “street” drugs, the effects of drug abuse in our society are a decimal fraction of the devastation of alcohol abuse.

Alcohol is an addictive drug, a gateway drug that is often abused with other drugs, increasing the danger to the individual and our society. It has often been suggested that if we want to solve the drug problem in the United States we first must begin with the alcohol problem.

Health professionals are not immune from drug and alcohol abuse. A great concern has risen within our health care system due to reported diversions of drugs by health professionals from patients going for operations, or patients who are on medications for chronic pain. A recent case captured national attention when an increased amount of infections were noted in an intensive care unit, caused by an impaired health professional diverting medications and using non-sterile techniques.

Clearly a great concern exists today over the effectiveness of our health care system due to a constricting economy and increased costs. But an even greater concern is emerging over the public safety in our health care system if impaired professionals are not properly monitored. This is compounded by the lack of health professionals, such as nurses and pharmacist, in the market, and the re-entry of impaired health professionals who have undergone treatment for drug or alcohol abuse, are in monitoring programs, and are again treating patients.

Alcohol use is culturally acceptable within America today but the dangers of alcohol abuse have long been a topic of public concern and even legislation during prohibition. In the early 1980s drug treatment programs were thought to be successful if the patients abstained from drugs but “only drank alcohol.” This is no longer the case; individuals identified with an addictive disorder are advised to abstain from not only their drug(s) of choice but alcohol as well. This is because there is a high incidence of problems with alcohol in this population, and return to other drug use following alcohol consumption. This phenomenon is called “cross addiction.”

Education of the dangers of alcohol and early detection of the abuse of alcohol, especially in recovering individuals, are the best means of limiting this problem in our society. Education campaigns, such a MADD, and SADD, along with driver sobriety testing, has had a marked effect on increasing the safety of our roadways and bringing individuals into treatment in the early stages of alcohol abuse or relapse.

Federal regulations now require safety sensitive individuals such as pilots, drivers and mechanics involved in the transportation industry to be tested randomly and post accidents for alcohol. Increasingly more and more licensing boards for professionals such as physicians, nurses and pharmacists require follow up testing once a drug or alcohol problem is identified. Unfortunately, these programs are not uniform in testing technologies like the transportation industry, leaving gaps in the monitoring of impaired health professions, especially with the testing of alcohol.

Alcohol testing in urine is dissimilar to drug testing whereas the drug or its metabolite is detectable for days, and in some cases months after a single use. This is why drug-testing

programs are successful, and are a major deterrent to relapse when the individuals know their drug use will be reliably detected for days. This is not the case for alcohol testing.

Breath and saliva are the most widely used samples in testing for alcohol because the results correlate directly with concentration of alcohol in blood, the standard of the industry. Blood is not used as often, as it requires a skilled medical technician to draw a sample, special handling for the collection, and the risks of trauma and infection in the donor are always present. Breath or saliva testing is important in detecting intoxication at work or on the highways, but is not effective in detecting violation of an abstinence agreement in a known alcoholic or drug addict whose ability to return to work is contingent upon remaining abstinent from all drugs of abuse.

The detection of alcohol for impairment, in blood, breath, and saliva is well documented in the literature. Blood alcohol is a routine procedure in the clinical laboratory where the same technology can easily detect alcohol in urine as well. In the field, breath and saliva alcohol tests are commonly used by law enforcement and in federally mandated programs. The standard of greater than 0.08% is fairly uniform in State DUI (Driving-Under-the-Influence) programs for intoxication and greater than 0.04% in federally mandated programs for removal from duty and evaluation.

However, among individuals with an identified history of substance abuse that have made a commitment to abstinence, detection of alcohol is problematic. This is due to the fact that alcohol is rapidly eliminated from the body at a rate of approximately one drink per hour. Whether looking for alcohol in breath, blood, saliva or urine, no matter what the technology used, this rapid elimination limits the detection of alcohol to a few hours under the very best conditions.

Consider the following example: an individual who was “under the influence” of alcohol using standard technologies (breath or saliva > 0.8%) at 10 PM would likely test negative the next morning at 9 AM due to the rapid elimination of alcohol from the body. This presents a significant problem for clinicians who are monitoring individuals in recovery programs for alcohol abuse and need to ensure their abstinence. This becomes a matter of public safety when recovering physicians, nurses, pilots or drivers are in monitoring programs and no effective testing technology is available to detect alcohol relapse, especially the early stages when the behavioral effects of drinking are not apparent.

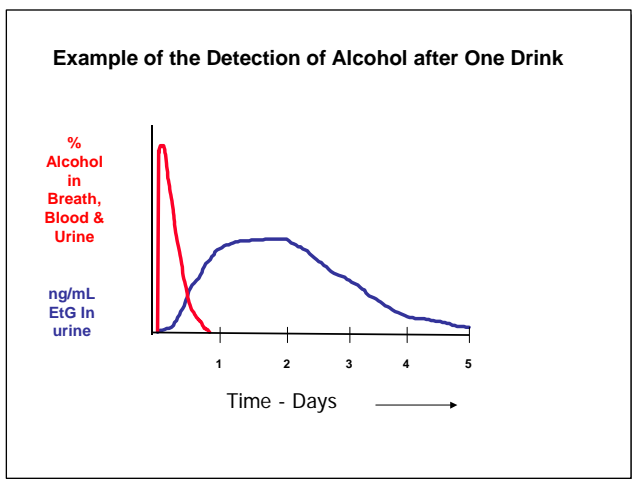
In the last decade, the refinement of drug testing under the Federal Guidelines, established by the Department of Health and Human Services (DHHS), established nationwide standards for collection, chain of custody, analysis and reporting of drug and alcohol tests. This has insured uniformity from one DHHS certified lab to another. Although urine is used for the testing of marijuana, cocaine, opiates, amphetamines and PCP, the DHHS established standards for alcohol testing using only breath or saliva.

Although urine does contain alcohol after drinking, the correlation with blood levels and impairment is not as direct as is saliva or breath samples. There is also the problem of alcohol being produced in a sample that is transported due to fermentation of glucose in some diabetic patients’ urine samples.

Because of all this, the most common technologies for alcohol testing are the breathalyzer, using breath as a sample, and various saliva testing technologies, all measuring alcohol directly at the point of collection. A limitation of breath and saliva technologies is that they are not offered everywhere that a urine sample could be collected. Also, depending upon the technologies and equipment used, a permanent record might not be produced for the alcohol test. Finally, there still exists the difficulty of combining a breath or saliva result with the result of the urine drug test into a single report for a health professional monitoring program's files. This is due to the fact that urine drug screenings for health professionals are often sent, due to their complexity, to a specialized laboratory, whereas alcohol in breath and saliva is measured at the point of collection.

Although appropriate for federally mandated and law enforcement programs where alcohol testing is done primarily to detect intoxication or impairment, it became apparent in the last few years that all the available technologies and samples were not appropriate for programs that monitor recovering alcoholics or drug addicts where there is a requirement to abstain from all drugs of abuse, especially alcohol.

This became abundantly clear in November of 2002 when Gregory Skipper M.D. and Friedrich Wurst M.D. reported, at an international meeting of the American Medical Society, that 7% of urine samples that reported negative for alcohol did in fact contain a metabolite of alcohol called Ethyl Glucuronide (EtG). EtG has been reported to stay in the urine for up to 5 days after drinking (up to 2 days for a single drink and up to 5 days after heavy drinking); well after alcohol itself has been eliminated from the body. (See chart below).



This was an important and alarming finding as the population they studied was recovering health professionals who were required to abstain from alcohol. Clearly a better way to measure alcohol use over a period of days, not hours, is needed as an early warning system to detect the beginning of a relapse before the individual can hurt himself or the communities they live and work in.

It has long been known that the limitations of existing technologies on detecting alcohol use almost encouraged those in recovery to drink, as their chances of being caught with an

alcohol test was at best, minimal. If found to be positive, the “fermentation excuse” was often used and difficult to resolve.

Instead of measuring alcohol directly in blood, breath, saliva and urine other markers and metabolites of alcohol have been intensely studied for the past 20 years. Liver tests such as GGT, blood cell tests such as MCV, or serum protein tests such as CDT were studied but all only

indicate long-term and/or large amounts of drinking. A recent marker HTOL/HIAA also holds promise but this indicator only detects the use of alcohol for a day.

EtG was initially determined to be a metabolite of alcohol in man in 1952 and has been studied at various universities internationally. These studies have been limited to research orientated universities with sophisticated instrumentation used in biomedical research, making the test out of the reach of clinicians.

In the last 10 years there has been a great amount of study on the biology of alcoholism. It is now apparent that a significant amount of human lives and costs to society could be saved if addictive diseases such as alcoholism could be detected early, treated and monitored effectively. EtG has emerged as the marker of choice for alcohol and due to the advances in technologies is now routinely available for clinicians.

There are now a substantial number of studies in the world literature that supports the clinical importance and reliability of EtG as a marker of recent alcohol consumption. This is especially important in the monitoring of the recovering health professional who knows the limitations of alcohol testing. "In the future it will be negligent not to test for EtG when monitoring recovering alcoholics," reported Dr. Skipper, Medical Director of the Alabama Physician Health Program.

In his recent article in Alcoholism: Clinical and Experimental Research, Dr. Friedrich Wurst, who serves as the Assay Center Director for EtG in the World Health Organization and International Society for Biomedical Research on Alcoholism concludes, "The findings emphasize the diagnostic and therapeutic usefulness of EtG as a marker of recent alcohol abuse. The health, social, and socioeconomic benefits arising from the future use of (EtG) is hard to overestimate."

Although extremely important as a marker for recent alcohol use in health professional and safety sensitive programs, EtG has applications in all recovery programs for any patient who suffers from the disease of alcohol and drug abuse as an early warning indicator of relapse and an effective deterrent for future abuse.

## References

1. Nishikawa, M., H. Tsuchihashi, A. Miki, M. Katagi, G. Schmitt, H. Zimmer, Th. Keller and R. Aderjan (1999): "Determination of Ethyl Glucuronide, a Minor Metabolite of Ethanol, in Human Serum by Liquid Chromatography-Electrospray Ioinization Mass Spectrometry," *J. Chromatogr. B.* **726**: 105-110.
2. Seidl, S., F.M. Wurst and A. Alt (2001): "Ethyl Glucuronide – a Biological Marker for Recent Alcohol Consumption," *Addiction Biology* **6**: 205-212.
3. Wurst, F.M., C. Kempter, J. Metzger, S. Seidl and A. Alt (2000): "Ethyl Glucuronide: a Marker of Recent Alcohol Consumption with Clinical and Forensic Implications," *Alcohol* **20**: 111-116.
4. Zimmer, H., G. Schmitt and R. Aderjan (2002): "Preliminary Immunochemical Test for the Determination of Ethyl Glucuronide in Serum and Urine: Comparison of Screening Method Results with Gas Chromatography-Mass Spectrometry," *J. Anal. Toxicol.* **26**: 11-16.
5. Goll, M., G. Schmitt, B. Ganssmann and R.E. Aderjan (2002): "Excretion Profiles of Ethyl Glucuronide in Human Urine After Internal Dilution," *J. Anal. Toxicol.* **26**: 262-266.
6. Stephanson, N., H. Dahl, A. Helander and O. Beck (2002): "Direct Quantification of Ethyl Glucuronide in Clinical Urine Samples by Liquid Chromatography-Mass Spectrometry," *Ther. Drug Monitor.* **24**: 645-651.
7. Wurst, F.M., Vogel, R., Jachau, K., Skipper, G. E., et al. (2003): "Ethyl Glucuronide Discloses Recent Covert Alcohol Use Not Detected by Standard Testing in Forensic Psychiatric Inpatients," *Alcoholism: Clinical and Experimental Research*, **27**: 471-476.
8. Dahl, H., N. Stephanson, O. Beck and A. Helander (2002): "Comparison of urinary excretion characteristics of ethanol and ethyl glucuronide," *J. Anal. Toxicol.* **26**: 201-204.