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Test Result
Interpretation

Interpreting Urine Cannabinoid Results: Renewed vs Residual?

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Attempts to Avoid Detection by Urine Dilution

Laboratory forensic toxicologists are increasingly aware of drug users' attempts to thwart drug use detection. Consuming excessive amounts of fluid a few hours prior to submitting a urine specimen, drug users have a misguided conception that the excess fluid will "flush" or "cleanse" the drug from the body. Instead, the elimination of excess water dilutes the concentration of drug in the urine specimen, despite the fact that the kidneys filter the same amount of drug. Effectively, a combination of low urine drug levels and excess fluid consumption shortly before testing may sufficiently dilute specimens so that test results fall under the specified assay cutoffs and yield negative results. Although drug assays have, nonetheless, provided the correct analytical results on diluted specimens, rather than consider them as false negative analytical results, they should be considered as false negative interpretive results.

Typical urine levels for drugs such as cocaine, methamphetamine, and opiates are on the order of tens of thousands to hundreds of thousands of nanograms per milliliter and higher. The standard screening assay cutoffs for these drugs are only 300, 1000, and 2000 ng/mL, respectively; therefore, an immediate attempt to dilute a urine specimen, will unlikely help a user avoid detection. (refer to figure 1)

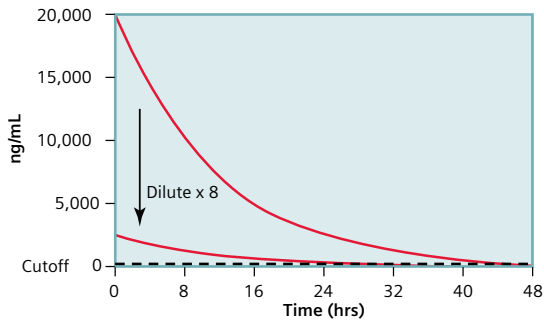


Figure 1: Example of Urine Dilution of a Cocaine Specimen

However, if a user dilutes a urine specimen 1 or 2 days after drug use, then urine drug levels may be close enough to the cutoff to allow for escape from detection.

In contrast to the drugs mentioned above, cannabis urine levels typically found after use are only on the order of a few hundred nanograms per milliliter, and occasionally higher. Given the standard cannabinoid screening assay cutoff of 50 ng/mL, even a recent cannabis user may be able to avoid detection by dilution. (refer to figure 2)

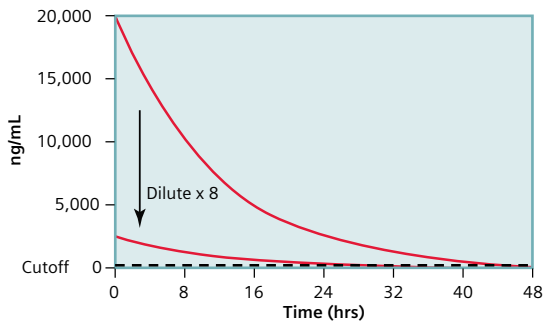


Figure 2: Example of Urine Dilution of a THC Specimen

The Kidney Response to Excess Fluid Consumption

Studies of kidney function in response to fluid intake show that drinking a liter of fluid over a relatively short time period (ie, 30 minutes) effectively dilutes a urine specimen 8-fold. A typical urine production rate by the kidneys is 1 mL/min; but this rate can easily and quickly increase 10 to 20 fold shortly after an acute water load of 1 to 2 liters. The urine rapidly becomes diluted (within 30 minutes) and can remain highly diluted for several hours. Although many manufacturers of drug test thwarting products claim to help drug users free their bodies of “toxins,” the “special properties” of the product do not affect the results; rather, the large amounts of water that the product literature instructs users to consume leads to the dilution observed. (refer to figures 3 and 4)

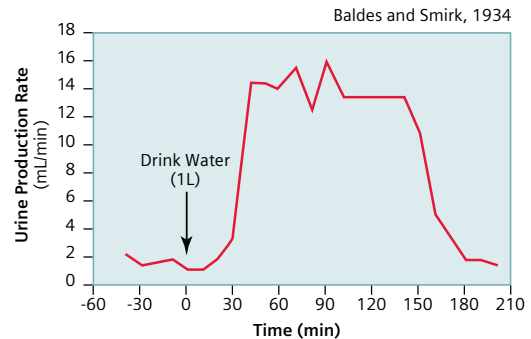
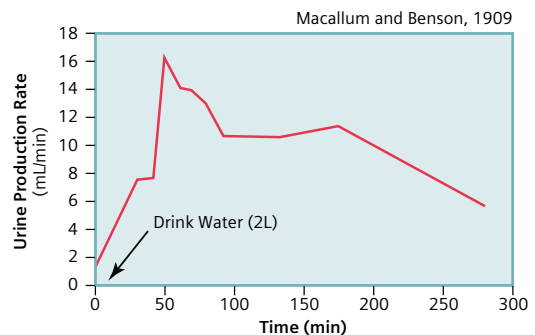


Figure 3: Urine Production Rate After Water Loading



The Use of Creatinine and/or Specific Gravity to Measure Urine Dilution

To identify a drug user's attempt to thwart detection, laboratories and on-site testing methods have the ability to measure creatinine and specific gravity in urine specimens. Creatinine is a natural by-product of skeletal muscle that the body eliminates at a fairly constant rate, depending on some daily factors such as biological function, exercise, and hydration. Typical creatinine levels are about 150 mg/dL. Because 20 mg/dL is an accepted lower limit for normal creatinine concentration, results below this level are suspicious. Another measure of urine dilution is specific gravity, which measures the relative density (amount of dissolved materials) of a urine specimen compared to pure water, which, by definition, has a specific gravity of 1.000. A typical urine specimen has a specific gravity of about 1.025. The current lower limit for a normal specimen in federally regulated workplace drug-testing programs is 1.003. Note that use and interpretation of such cutoffs may differ between federal agencies. For example, drug-testing policies of the Department of Transportation and the Department of Health and Human Services policies require both creatinine and specific gravity to be below the lower limits, to label a specimen as "dilute," whereas the Nuclear Regulatory Commission policy requires that only one of these markers to be below the specified limits.

Urine Drug Level Adjustment: Determining Renewed Drug Use or Residual Drug

Drug treatment programs or drug-testing laboratories often evaluate scientific-study participants over a period of days, weeks, or months by examining the relative levels of the test results from participants' specimens. Such examinations of sequential positive results, may help distinguish renewed drug use from residual levels. Nevertheless, drug concentrations in the urine can fluctuate by a factor of two or three, as fluid consumption and elimination can vary significantly throughout the day. Hence, laboratories must be alert to the nuances of increases and

decreases in urine drug levels presented in test results, in order to distinguish renewed from residual levels.

To account for the fluctuation in fluid consumption, laboratory professionals can "adjust" or "normalize" the level of drug detected by the level of urine dilution or concentration by using creatinine as a marker. Such adjustments to urine drug concentrations are neither new nor unique to urine drug testing, and, in fact, have been widely used in occupational medicine when checking for heavy metal exposure. Laboratory personnel divide the actual urine drug level (either as immunoassay screening results or GC/MS specific analyte results) by the observed creatinine level to make the appropriate adjustment. The calculated result provides the amount of drug in the specimen; not in terms of per unit volume (eg, ng/mL), but, rather, in nanograms of excreted drug per milligrams of creatinine. In this way, laboratories can more fairly compare sequential test results for increasing or decreasing levels, independent of fluctuations in fluid consumption. (refer to figure 5)

$\frac{\text{ng Cannabinoids/mL}}{\text{mg Creatinine/dL}}$	$\times 100$	$\frac{\text{ng Cannabinoids}}{\text{mg Creatinine}}$
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Figure 5: Formula for Urine Drug Level Adjustment

Even after correction for dilution, however, increases and decreases in the results still may not always provide an accurate indication of renewed use. As an alternative, some studies recommend the use of a specimen ratio—a calculated ratio of creatinine-adjusted drug concentration on two sequential specimens from a single donor.

The October 1998 edition of the Journal of Analytical Toxicology presented an article on the application of specimen ratios. This article describes an acute cannabis dosing study, examining the excretion profile of cannabinoids and creatinine from six

marijuana users who smoked two doses of marijuana over a 4-week period. Sequential positive results are either from a single use or are positive results from renewed marijuana use at least a week after the first dose. Based on the ratio of sequential positive results, the scientists determine if renewed use had occurred.⁵

The scientists' findings demonstrate that if sequential, positive, creatinine-normalized/cannabinoid test results (at least 24 hours apart) increase by a factor of two, then one could conclude with 100% confidence that the second positive test result represents renewed use rather than residual levels from prior use. Further, the scientists determined that a ratio of 0.5 provides the best overall accuracy in the detection of renewed use while minimizing false accusations. In other words, one would expect that sequential creatinine-normalized cannabinoid levels would decrease by at least 50% over 24 hours or more after occasional use. (refer to figure 6)

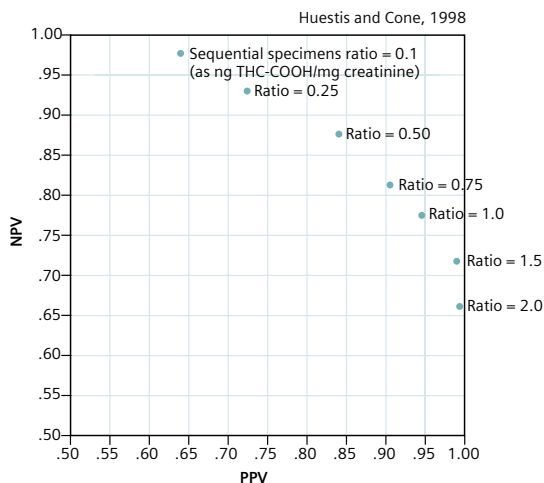


Figure 6: Sequential Specimens Ratio

The greater the ratio between the sequential creatinine-normalized specimens, and the greater the time between the specimens, the greater the certainty that the second positive result represents renewed use. Using a higher ratio to be more certain

that a second positive is, in fact, due to renewed use, however, also leads to lower sensitivity in detecting all of the instances of actual renewed use. In contrast, using a lower ratio allows for better detection of actual renewed use, but has a correspondingly increased likelihood of erroneously interpreting positives from prolonged residual excretion. Accordingly, a compromise must be reached when using a sequential specimen ratio as a cutoff for determining renewed use or residual levels. The selection of the ratio for the cutoff becomes a compromise between sensitivity in the detection of renewed use and providing adequate due process to chronic users who may be falsely accused due to extended periods of drug elimination, caused by deep reservoirs of stored cannabinoids.

Note that the above study describes the elimination of drug after occasional use, rather than elimination after the cessation of documented chronic use. Nonetheless, the study indicates the unlikelihood of prolonged elimination as the cause of sequential positive results. Also, note that these ratios compare sequential positive test results from at least one day apart. In most testing programs, a donor would unlikely submit a test specimen on two consecutive days; rather, more likely, drug testing programs would request a specimen at least several days apart. Accordingly, one would expect greater declines in cannabinoid levels after several days; therefore, the use of an even smaller ratio would be more appropriate. Therefore, using a ratio of 1.5 for sequential results at all times more than one week apart is a conservative approach, reducing the risk of false accusations of renewed use. Indeed, in an earlier study, scientists proposed a sequential specimen ratio of 1.5 based on creatinine-adjusted levels of immunoreactive cannabinoids on sequential weekly specimens.¹⁵

Conclusion

Although drug users may attempt to mask their drug use by diluting their urine specimens through excessive fluid intake, the availability of both on-site and laboratory tests to measure creatinine and

specific gravity minimize the effectiveness of such attempts. Furthermore, objective information on the extent of dilution may be used to assist in the interpretation of positive test results.

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Biography

Dr. Kadehjian is an independent biomedical consultant in Palo Alto, California, primarily lecturing and writing on the clinical, scientific, regulatory, and legal issues in drugs of abuse testing. He has provided consulting services for a wide variety of both private and public sector drug programs worldwide. He has special experience with on-site testing programs and provides oversight of the U.S. Federal Courts' onsite drug testing programs. He also serves on the faculty of the National Judicial College, lecturing on the neurobiology of addiction and drug testing issues, and has provided nationally broadcast live satellite television seminars for the Federal Judicial Center. An internationally recognized speaker, he has earned an Outstanding Speaker recognition from the American Association of Clinical Chemistry and has provided expert testimony in court and labor arbitration. Born and raised in Boston, he received his Bachelor's degree in Organic Chemistry from M.I.T. in 1972 and his Ph.D. in Biochemistry from Stanford University in 1977.