CHAPTER 5

DRUG TESTS: THEIR USES AND LIMITATIONS

Introduction

In order to ascertain whether an individual has administered drugs of abuse or not, drug testing is commonly employed to check for the presence of any drug(s) of abuse or their metabolites in the donor’s biological specimen such as blood, urine, oral fluid, sweat or hair.

Urine has been and remains the mostly widely used body fluid specimen for routine testing for drugs of abuse, but oral fluid, sweat and hair are gaining scientific credibility as alternative specimens following advancement of testing technology. This chapter reviews the uses and limitations of different specimens for testing with respect to their time window of detection, ease of specimen collection and likelihood of adulteration.

Purposes of drug testing

Over the past several decades, drug testing has been used worldwide in a variety of disciplines including criminal justice, emergency medicine and clinical toxicology, and workplace [1].

Criminal justice

Drug testing plays an important role in facilitating the judicial sentence of drug abusers in courts, drug surveillance programmes of inmates who are detained under the custody of drug treatment centres, as well as the enforcement of the legislation of driving under the influence by police.

Emergency medicine and clinical toxicology

Timely and reliable drug test results are of prime importance in the field of emergency medicine and clinical toxicology. The objective of testing is focused on determining the class of drugs that has been inadvertently or purposely ingested or exposed to the patients. Mortalities and morbidities would then be greatly reduced by effective, appropriate and prompt antidotal treatment or supportive care.

Workplace

Pre-employment and workplace drug testing has increased rapidly over the last decade in western countries such as United States of America and United Kingdom. Federal organisations, government agencies, military and private corporations exercise drug testing either under mandatory legislation or corporate commitment as a measure to improve safety within the workplace.

Types of specimens for testing [2]

Blood

Blood is widely used for drug testing in clinical and emergency toxicology because it offers the best correlation between drug level and pharmacological impairments to the body. The time window for drug detection in blood is shorter, mostly within several hours, than in urine. For example, at a given dosage of cocaine, blood testing can detect use within 12 hours while urine testing can detect use within 48 to 72 hours. Even though blood is a good specimen for determining the presence of drugs, the concerns about invasiveness of the collection, ease of transportation and storage, and specimen stability greatly hamper its popularity in other fields of application even though substitution and dilution of specimen to tamper with drug testing are considered impossible.
Urine
By far, urine is the most widely used specimen for drugs of abuse testing because of the advantages of large specimen volume and relatively high drug concentrations that render drug detection comparatively easier than in other specimens. In addition, the technology used in urine testing is well developed and has withstood legal challenges. Furthermore, urine collection is considered non-invasive, and specimens can be collected by non-medical personnel. Urine is a matrix that remains stable over time and can be frozen to maintain the integrity of the sample. Drugs in urine are normally detectable up to 1-3 days. However, unless the urine sample is obtained under direct observation, adulteration, substitution or dilution to circumvent drug testing is possible.

Hair
Following the advancement of technology in detecting trace quantity of drug(s) in hair, hair testing has gained attention because of its ability in providing a longer window of detection from months to years when compared to other specimens. In contrast to providing short-term drug abuse profile through blood and urine testing, hair testing provides complementary information about the long-term drug abuse history of a donor. Furthermore, sampling head hair specimen is considered non-invasive and the drugs incorporated in the hair remain stable and bound for a long time leading to no concern about specimen adulteration. Head hair sampled from the scalp is preferred in order to obtain the retrospective chronological drug abuse history of a donor. Head hair tends to grow at a rate of about 1 cm per month, so a 3 cm section of hair would represent a 3 month history. However, testing for drug in hair is comparatively time consuming and costly, and it must be performed in the laboratory because of unavailability of on-site screening kits.

Oral fluid
Oral fluid is increasingly used for drug testing because the concentrations of many drugs in oral fluid correlate well with blood concentrations. Advancement of instrumental sensitivity makes oral fluid a suitable alternative to blood. Oral fluid is a non-invasive specimen that can be sampled under direct observation to prevent adulteration or substitution. The main disadvantage of oral fluid testing is its short window of detection, with most drugs being detectable within several hours only. This characteristic renders it suitable for determining very recent drug abuse, but weakens its ability in detecting use over time. For example, someone administered heroin a day ago is likely to be tested negative by oral fluid test, but positive by urine test.

Sweat
Collection of sweat is undertaken by attaching a tamper evident patch, with underlying absorbent pad inside, to the skin over a relatively long period of time (10-14 days). Analysis of sweat must be performed in a laboratory and on-site test kits are not available. Sweat testing has not widely been used because of challenges of the potential contamination from the environment and from residual levels of drug in the skin from prior use.
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Characteristics of different specimens for drug testing
The advantages, disadvantages and time window of detection of different specimens are summarised in Annex 1.

Screening test versus confirmatory test
In order to undertake drug testing, there must be a cutoff level for each type of drugs to be tested, and such cutoff point serves as an administrative breakpoint in distinguishing a positive or negative result. Any sample that contains the drug/drug metabolite of interest at the concentration levels equal to or greater than the designated cutoff level is reported as positive, whilst a negative is reported for the concentration level less than the cutoff. Generally, a drug test can be categorised as either a screening test or a confirmatory test, with respect to the detection method and testing principle being employed [3].

Screening test
Screening test refers to the initial test undertaken to test for a broad class of drugs and their metabolites in the specimen with presumptive result, i.e. positive or negative. Generally screening test is rapid, sensitive, inexpensive with acceptable levels of precision and reliability, however, it lacks precise specificity and may be subject to a false positive result due to cross-reactivity with other non-targeted drugs of similar chemical structure.

Immunoassay, which works on the principle of competitive interaction between the antigen and antibody, is the common contemporary technology employed for screening tests.

Annex 1. Specimens for Drug Testing

<table>
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<tr>
<th>Specimen</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Window of detection</th>
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</table>
| Urine    | • Highest assurance of reliable results  
           • Least expensive  
           • On-site testing kits are available  
           • Acceptable in court to withstand legal challenge | • Susceptible to adulteration or substitution  
           • No dose-concentration relationship  
           • Test sometimes viewed as psychologically invasive or embarrassing  
           • Biological hazard for specimen handling and shipping to laboratory | Typically 1 to 3 days, except for cannabis (1 day to 2 weeks) |
| Oral Fluids | • Sample obtained under direct observation  
              • Minimal risk of tampering  
              • Non-invasive specimen collection  
              • Samples can be collected easily in virtually any environment  
              • Reflects recent drug use | • Drugs and drug metabolites do not remain in oral fluids as long as they do in urine  
              • Less effective than other testing methods in detecting marijuana use | Approximately 10 to 24 hours |
| Hair     | • Longer window of detection  
           • Greater stability (does not deteriorate)  
           • Can measure chronic drug use  
           • Convenient for transport and storage (no need to refrigerate)  
           • Collection procedure not considered invasive or embarrassing  
           • More difficult to adulterate than urine | • More expensive  
           • No on-site testing kit is available  
           • Inability to detect very recent drug use (1 to 7 days prior to test) | Months to year |
| Sweat    | • Non-invasive specimen collection  
           • Quick application and removal  
           • Longer window of detection than urine (a period of days to weeks)  
           • No sample substitution possible  
           • Provides cumulative measure of drug exposure | • Limited number of labs able to process results  
           • People with skin eruptions, excessive hair, or cuts and abrasions cannot wear the patch  
           • Passive exposure to drugs may contaminate patch and affect results | 1 to 4 weeks |
On-site screening test
Use of on-site immunoassay screening kits are highly popular in the fields of workplace testing and emergency toxicology because results are available within several minutes, with reliability similar to laboratory screening, at the site of specimen collection. Furthermore, these kits involve no calibration or maintenance, and no special skills are needed to perform the screening test. Most kits have built-in quality control zones in each panel, which ensures reagent integrity and testing validity. Nowadays, commercially-available on-site screening test kits are usually designed for urine and saliva specimens only, but not for sweat or hair as yet.

Laboratory screening test
Instead of on-site testing, drug screening may also be performed by instrumental immunoassay method in the laboratory by automated, sophisticated and high throughput analysers. Laboratory screening test is privileged by its capability of processing large numbers of samples, along with better instrumental logged quality control and integrity assurance when compared to on-site testing.

Generally, laboratory drug screening has to take at least 1-2 days before the results are ready for collection because of time taken in delivering the specimens to the laboratory, running the tests and preparation of test reports.

Confirmatory testing
Any specimen, which has been presumptively screened positive, should be subject to confirmatory testing in order to eliminate false-positive results that arise from cross reactivity. Confirmatory testing should employ highly specific and alternate chemical technique in order to obtain unequivocal and accurate analytical results. Gas chromatography/mass spectrometry (GC/MS) or liquid chromatography/mass spectrometry (LC/MS) are preferred confirmatory techniques because of their remarkable specificity and selectivity. When compared to screening testing, confirmatory testing is time-consuming, labour-intensive and more expensive.

Kits for on-site testing
Over the past 10 years, testing kits of different designs have been marketed in order to meet the growing demand for drug screening at point of collection. These on-site test kits are commonly used by healthcare professionals, and drug treatment and rehabilitation programme supervisors to help deter drug use by the patients and supervisees, respectively.

Dipcards and cassette kits that employ lateral flow immunoassay technology have been proven to be reliable and easy to use [4]. Recently, newly designed testing cups, also employing the same technology, with integrated test strips in the interior surface have grown in popularity because of their ease of testing and sanitary protection to the test operator, with the elimination of specimen transfer or direct contact with the specimen.

![Dipcard Cassette Testing cup](Source: First Test Ltd.)

Figure 1. Different kinds of kits for on-site testing.
Adulteration of specimens to interfere with testing

Amongst the four kinds of specimens discussed, urine may be subject to adulteration in order to circumvent drug detection. Meanwhile the chance of adulterating saliva, hair and sweat is relatively low because these specimens may be collected under direct observation. Adulteration and substitution of synthetic urine are the unscrupulous acts of tampering with a urine specimen with the intention of altering the test result. Generally adulterants are classified into three basic types:

i. Those that decrease the concentration of drugs through consuming detoxifying drinks/pills, and/or drinking excessive amount of water prior to urine sampling;
ii. Those that decrease the drug level in urine by covertly adding a large quantity of water soon after urine has been collected; and
iii. Those that break down the drugs or interfere with the ability of the assay through alteration of acidity (pH) by addition of household substances or detoxifying products.

Adulterants may be either household chemicals for domestic uses or detoxifying agents that can be purchased through the internet.

Consuming detoxifying drinks/pills and excessive quantity of water

A person may attempt to thwart a drug test by consuming detoxifying drinks/pills or diuretics such as herbal tea, and/or drinking excessive quantity of water so that the concentrations of drug metabolites in the urine are diluted to below detectable thresholds. However, the donor may experience water intoxication in cases of extreme conditions. Minimising the time duration allowed for the donor to drink fluids prior to testing is considered the best way to deter this unscrupulous attempt. Furthermore, the unusually low creatinine and specific gravity levels in urine may serve as indicators for alertness.

Diluting urine by adding in plenty of water

A negative result for the presence of abused drugs in a urine specimen does not necessarily mean that no drug is present. It is possible that the amount of drug is below the cut-off values used in the drug testing protocol. Diluting urine by adding in plenty of water is the simplest way to circumvent a drug test if the original concentrations of the drugs in the urine are not substantially high. The opportunity to dilute urine samples is minimised by not having a source of water in the test room or the water is coloured. Testing specific gravity and creatinine level remain as effective tools to counteract this dilution tactic.

Addition of oxidising chemicals or exogenous detoxifying agents

Many chemicals are often used to adulterate urine in order to avoid a positive test result. Bleach, hydrogen peroxide, laundry detergents, nitrite, pyridinium chlorochromate and iodine are the common oxidising adulterants used to break down the drugs and drugs metabolites in the urine. Also, addition of glutaraldehyde can give false negative screening results by disrupting the enzyme used in some immunoassay tests. Alteration of pH by addition of acid, lemon juice and vinegar is another way to interfere with the assay process. In addition, various detoxifying agents that are easily available through internet are alleged to be able to affect the results of a drug test after adulteration into urine samples.

Substitution by synthetic urine

Synthetic urine may be used to substitute the urine sample from a donor leading to a negative test result if sample collection is not supervised. Synthetic urine has all the characteristics of natural urine, with correct pH, specific gravity and creatinine level, but with a temperature unusually low when compared to body temperature. Some urine test kits have a built-in temperature measurement band to negate this substitution strategy, thus the testing operator should be alerted if the sample temperature is below 32 °C.
Test strips for detecting adulterants

In order to interfere with a drug test, someone may add adulterants into the urine specimen leading to the inability to run the test (an invalid test) or a false negative result. If the integrity of a urine specimen is in doubt, a urine adulteration test strip should be used to help assessment. Each test strip contains 6 to 7 chemical-treated reagent pads that will change colour upon dipping the testing strip into the specimen. Through colour comparison, the test strip can screen for irregularity of levels of creatinine, nitrite, glutaraldehyde, pH, specific gravity, oxidants and pyridinium chlorochromate in the urine specimen.

References