

ABNORMAL LABORATORY RESULTS

Drug screens

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SYNOPSIS

The two types of drug screens are rapid tests and specific assays. Rapid tests are for a restricted range of substances (usually just drugs of abuse) and have limited sensitivity and specificity. When there are important medicolegal considerations, the results must be confirmed by more specific assays. Specific assays are labour-intensive tests that can detect most drugs but take much longer to perform. They are required where the concentration of the drug may lead to specific interventions (such as in certain overdoses). Conversely, even the most comprehensive negative screen cannot entirely rule out drug ingestion as some substances are difficult to detect. The knowledge of the laboratory staff should be utilised when ordering and interpreting the tests.

Index words: diagnostic tests, drug abuse, poisoning, therapeutic drug monitoring.

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Introduction

'Drug screens' are simply tests for a range of drugs or other substances. They have a wide variety of uses and almost any bodily fluid can be screened. Routine use of drug screens does not improve clinical outcomes, but selective use may assist patient management and occasionally yield an unexpected diagnosis.

Types of drug screens

There are two main types of drug screens. Immunoassays screen for a limited range of selected substances. These assays are relatively quick and some can even be performed at the bedside. They are commonly used to detect drugs of abuse or to test for commonly ingested substances in overdose. There may be cross reactivity with some chemically related substances and the test cannot detect uncommon or unsuspected drugs. Different brands of immunoassays have different problems with sensitivity and specificity. These problems should be outlined in the product information of the assays.

The second form of drug screening involves chromatography with or without mass spectrometry. This can detect most substances that are present in significant concentrations. Testing is relatively expensive and is heavily dependent on the skill and experience of the laboratory staff. Unless only specific substances are of interest, the turnaround time varies from days to weeks, so these tests are less likely to influence the acute management of a patient.

Screening tests most commonly use urine, but serum can also be used. In forensic studies, vitreous humour, pleural effusions, hair, bone or nails may be screened. Saliva, breath, sweat and breast milk can also be screened when looking for drugs of abuse.

Indications for screening

Overall, screening is most frequently used in medicolegal situations. These include determining cause of death, detecting performance-enhancing drugs in athletes, and detecting drug abuse in the workplace, drug and alcohol rehabilitation programs or psychiatric patients. In most cases, detecting a drug, in any concentration, gives sufficient information.

In acute poisoning and other toxicological screening the drug concentration may be important so screening the urine may not be the appropriate investigation. Drug screens of the urine do not reveal the amount of drug or the time it was taken because the urinary concentration correlates poorly with serum concentrations. Detecting the presence of a drug does not tell you if it is at a toxic concentration or explain the clinical status of the patient. In these circumstances, serum may be a better body fluid to screen. This is particularly so for substances such as paracetamol, salicylates, anticonvulsants, alcohol, ethylene glycol, methanol, lithium and theophylline as their concentrations determine the treatment. In these situations specific assays are usually more appropriate than a 'drug screen'. Paracetamol is so commonly taken in overdose that a routine specific assay in unconscious patients is generally warranted. However, routine specific assays for other substances are not indicated unless there are signs or biochemical changes that raise suspicion of their ingestion. Quantitative screening for drugs is also important in patients with suspected brain death.

Performing drug screening

To optimise the usefulness and the cost-effectiveness of drug screens there are several important factors. These include selection of a screening test appropriate to the patient, correct collection of samples, communication with the laboratory and follow-up tests where appropriate.

Selection of an appropriate screen

The most common clinical reason for requesting a drug screen is suspected ingestion of an unknown substance or substances. Examples include suspicions of overdose (e.g. coma, seizures, acidosis), malingering or child abuse (e.g. unexplained

hypoglycaemia or ataxia), or illicit drug abuse (e.g. psychosis, mood swings). Where possible, the drug screen should relate to the patient's clinical presentation. For example, a patient with severe acidosis may be suspected of taking a number of substances. However, most immunoassay techniques do not detect many of the drugs and poisons that lead to acidosis. They are designed to detect only commonly used drugs of abuse and drugs that lead to coma, such as alcohol, benzodiazepines, opiates, amphetamines, tricyclic antidepressants, LSD, cocaine and marijuana. A 'negative' drug screen of the urine in a patient with acidosis would be largely unhelpful or misleading. Specific screening of the serum for ethylene glycol, methanol and salicylates, and chromatography to detect other unusual substances may be quicker and much more useful investigations.

In many cases drug screens are done for legal or quasi-legal purposes and the screen must accurately detect substances relevant to that purpose (for example, drugs that might impair driving). Testing for other substances is irrelevant.

Communication with the laboratory

Most laboratories performing drug screens do large numbers of tests for non-clinical reasons. If you anticipate that the drug screen may alter your clinical management it is important to discuss the case with the laboratory. A history of the drugs the patient is known to take will help the laboratory to identify the substances you are not concerned about. Knowing which specific substances are suspected on clinical grounds helps the laboratory to tell you whether or not it can identify such substances, for how long they can be detected after ingestion and whether serum or urine is preferred. The laboratory may also alter the methods used to prepare the sample to maximise the sensitivity of the testing for those substances.

Collection of sample and follow-up tests (medicolegal cases)

Correct and explicit identification of the patient and sample, prevention of tampering during collection and a secure chain of custody are very important in medicolegal cases. If the result has important medicolegal implications the accuracy of the result should be confirmed by using a more specific and accurate method such as gas or liquid chromatography and mass spectrometry. Depending on the drug involved these tests are done on the same specimen or a different specimen.

Results

False positives

The most common cause of false positive results in clinical settings is the therapeutic use of barbiturates, benzodiazepines and/or opiates for sedation, anaesthetic induction or analgesia. Many immunoassays do not differentiate between drugs in these classes and may cross react with related therapeutic substances. For example codeine (and poppy seeds) may lead to positive opiate reactions, and decongestants such as pseudoephedrine and phenylpropanolamine may lead to positive amphetamine reactions. Only discussion with the laboratory and further specific testing can clarify such results.

False negatives

False negatives can relate to the time of sampling (too soon or too late), the body fluid tested or the method used. Immunoassays test for a restricted range of chemically related substances. Even within pharmacological drug classes they may not detect substances that have identical effects but an unrelated chemical structure. For example, most immunoassays for opiates do not detect the structurally unrelated methadone, dextromethorphan or pethidine. Metals (e.g. mercury, arsenic) are not detected by the commonly used drug screens and require specific tests. Some toxic substances (insulin, succinylcholine, potassium) cannot be detected by any method, as any avid reader of crime fiction knows.

Other problems of interpretation

The detection of one substance does not exclude the presence of others which cannot be detected by the same method. Drugs with similar chemical structures, but different toxicities, may give the same result. For example, within the drugs in the amphetamine class (methamphetamine, MDMA, PMA, fenfluramine and pseudoephedrine) there is a non-overlapping spectrum of peripheral and central nervous system stimulant effects and serotonergic effects which lead to quite different toxicological syndromes. Failure to appreciate that some positive immunoassay screens for amphetamines could indicate ingestion of any or all of these drugs may lead to inappropriate management.

Conclusion

Drug screens are a useful clinical tool if you are selective in their use, have realistic expectations of their sensitivity and specificity, and discuss the clinical setting and suspected drugs with the laboratory staff. Otherwise you may be better off disposing of the urine in the traditional and less expensive manner.

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FURTHER READING

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Self-test questions

The following statements are either true or false (answers)

5. A drug screen for amphetamines may be positive in someone taking pseudoephedrine.
6. When testing for a specific drug, immunoassay is a more accurate method than chromatography.