Leader

Detection of drug misuse—an addictive challenge.

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Abstract

It is now accepted that drug misuse is a large and growing problem in the United Kingdom, some estimates of the number of regular illicit drug users being as high as three million. The aim of this paper is to provide insight into the methods used to detect drug misuse. The strategy adopted by one laboratory is described and methods of screening for, and identification of, a wide range of compounds are provided. No claim is made that this is the best approach or that the list of drugs detected is comprehensive; the range of drugs encountered is always increasing and the lists are constantly updated. It is hoped that users of toxicology laboratory services will gain an appreciation of the capabilities and limitations of the techniques available; and that those who may wish to provide such a service will find the necessary information in a readily accessible format.

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The only way to establish the limits of what is possible is to test the boundaries of the impossible.

Why look for drugs of abuse?

For hundreds, indeed thousands of years, the use of chemicals for recreational or religious purposes has been part of most cultures. Even in Victorian Britain, laudanum and opium were used by respectable members of society, and cocaine was readily available in preparations such as Vin Mariani and the original Coca-Cola. More widely within Western society, the use of alcohol and nicotine as an aid to relaxation and social discourse has been generally accepted, apart from the abortive attempt by the government of the USA to impose prohibition of alcohol through the Eighteenth Amendment to the Constitution in the first half of this century.

Ever since the early days of a modern youth culture in the late 1950s and early 1960s the use of stronger drugs for recreation has been developed. These chemicals include illicit preparations such as heroin, Ecstasy (3,4-methylenedioxy-N-methylamphetamine, MDMA), and cocaine (as the hydrochloride, or as free base: "crack"). In addition to these illicit compounds various drugs intended for medical use have been "adopted" into misuse. In particular the benzodiazepines (diazepam and temazepam) are widely misused, as are opiates including diamorphine (heroin) and dihydrocodeine. Ketamine, methadone, tricyclic antidepressants, and dextropropoxyphene are further examples of prescribed drugs encountered in individuals who have not been prescribed them. The casual use of these drugs may never be a problem and is, for many, a natural part of recreational activity. The use of these drugs becomes a problem only if the individual involved becomes a habitual user and suffers longer term physical problems (illness and infections) and psychological problems which make them unable to be fully active and productive members of society.

The statistics of drug addicts notified to the United Kingdom Home Office (London: Government Statistical Service) give some evidence of the continued growth in the use of drugs of abuse (at a rate greater than 10% per annum) as measured by the number of addicts notified to the Home Office and by the number of drug seizures. The statistics for numbers of abusers only include those seeking help from statutory bodies and give no indication of the overall number of users. A more meaningful indication of the scale of the problem comes from calculations made by Atha and Blanchard (in preparation for publication) to be found on the internet site of the Institute for the Study of Drug Dependence (http://www.isdd.co.uk): the estimated number of regular drug users in the United Kingdom has increased from approximately 1 million in 1982/84 to 2.5–3 million in 1995.

Drug abuse has effects not only on the user but on the whole of society. This can take the form of crime related to the acquisition of drugs, and danger to other members of society resulting from the modification of the behaviour of drug users, who may become dangerous or irresponsible. Drug abuse will also cause an increased risk of the spread of transmittable diseases not only between addicts but also into associated populations.

The circumstances in which screening for drugs of abuse may be required are diverse. A request may be made by casualty departments simply to exclude the presence of drugs in a patient who has been admitted unconscious,

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with a decreased level of consciousness, or displaying bizarre behaviour. In most situations the demonstration of the presence of a drug which the patient should not be taking is sufficient. However, in a minority of cases it may be necessary to perform quantification in order to establish the degree of clinical effect of the drug and this will present a problem which must be considered by any potential service providers.

Clinics offering support and advice to drug addicts are widespread and include drug dependency units, community drug teams, and outreach services. These require regular drug checks on their clients in order to establish appropriate further treatment and they provide the most significant demands for the routine toxicology laboratory.

Finally, though rarely encountered in the past, screening for drugs of abuse is now increasingly performed both as a prerequisite before employment and randomly during employment.

In all of the situations outlined above some control of sample integrity is desirable, but in the case of employment screening it is imperative, as the consequences of an incorrect result have far reaching consequences. Chain of custody documentation must be used and the samples (in duplicate, one to be tested and one to remain sealed to be used in the event of a problem—usually a challenged positive finding) must be in tamper proof containers.

What sample to use?

If we were interested in monitoring therapeutic drugs we would, in most cases, wish to monitor concentrations present in the blood of the patient and relate the results to established therapeutic windows. However, in cases of drug misuse our interest is primarily in establishing their presence and identity, and analysis of blood is not generally used.

In very acute cases, vomitus or stomach washings may be useful if there is evidence that the drug has been taken orally. In some situations sweat may be screened for drugs of abuse (as is proposed in the case of roadside testing by the police) but limitations in the amount of sample available for further procedures restrict the value of this approach. There are also published methods for hair analysis, particularly where a longer term assessment of drug use is desired; such analyses are, in our experience, difficult and outside the remit of a routine laboratory.

Drugs are usually recognised by the body as being foreign and not capable of being utilised, and are rapidly processed for excretion. In general they may be found readily in urine either in their original state (sometimes at concentrations as much as 100 times that found in blood), or in a conjugated form or as metabolites. Furthermore, because of the ease of obtaining a urine sample, the longer time scale for detection, and the ease of analysis owing to the practical absence of proteins, urine has proved to be the sample of choice for illicit drug screening, and a random urine sample in a plain 20 ml container is adequate. Staff involved in obtaining samples in the employment screening or clinic situation should be made aware that sample substitution by drug misusers (the use of a more "appropriate" urine sample from the clients/patients point of view) is relatively common.

Some liaison with the members of staff involved in obtaining the sample can be desirable, especially as they can often be junior medical staff faced with a possible drug addict for the first time. In addition, because a screen for drugs is open ended (it is never possible to prove the absence of all drugs) it is useful to be given a clear indication as to whether the presence of any particular substance or group of substances is suspected.

The initial screen

Commercially prepared immunoassay systems are now widely available for initial screening of urine samples. These include EMIT (the enzyme multiplied immunoassay technique), for instance the Dade-Behring system (Walton Manor, Milton Keynes, UK), FPIA (fluorescent polarisation immunoassay) offered by Abbott (Maidenhead, UK), and chemiluminescence offered by DPC (Immulite) (DPC, Llanberis, UK). A simple though expensive "dipstick" system supplied by Roche (Welwyn Garden City, UK), "Ontrak", uses the principle of microparticle capture inhibition to provide a screen for use within clinics, and the introduction of similar systems for roadside testing (using samples of perspiration) has been proposed. The microparticle capture inhibition system is also available in a more economical version for use within the laboratory (Roche Cobas/Integra).

The instrumentation that may be used ranges from simple dedicated machines, such as the Dade-Behring ETS, to more generally used machines, such as Olympus or Roche analysers.

Our experience has been with the Dade-Behring EMIT system using the ETS dedicated system; therefore the following description is based upon our experience with this. Our initial screen is for a panel consisting of opiates, methadone, amphetamines, barbiturates, benzodiazepines, cocaine metabolite, and cannabinoids. The ETS is simply calibrated using calibration standards provided at three levels: negative, cut off, and high. Samples which display activity below the cut off are designated negative and those that display activity above the cut off are designated positive. The concentration of drug which is used as the cut off level has been selected to provide optimal detection of positives while minimising the generation of false positives which may occur with any immunoassay screening system.

Table 1 The relative retention times of volatile compounds on Chromosorb 101

Compound	*Relative retention time*
Methanol	0.60
Ethanol	0.69
Acetone	0.78
Propan-2-ol	0.82
Propan-1-ol	1.00
Chloroform	1.39
Toluene	3.00

Table 2 Relative retention times (as measured against SKF 525a) of drugs detected after basic screening

Compound	Relative retention time	Major ions
Amphetamine (amfetamine)	0.215	44, 91
Meprobamate artefact	0.219	84, 56, 55
Norfenfluramine	0.224	86, 159
Phenethylamine	0.229	91,121
Phentermine	0.238	58, 91
Methyl amphetamine	0.251	58, 91
Fenfluramine	0.287	44, 72, 159
Chlormethiazole (clomethiazole)	0.294	112, 161, 85
Labetalol artefact	0.295	91, 132, 117
Cathine	0.353	44, 77
Norephedrine	0.359	44, 77
Nicotine	0.363	84, 133, 162
Propofol	0.370	163, 178
Ephedrine	0.388	58, 77
Pseudoephedrine	0.400	58, 77
Meprobamate artefact 2	0.452	84, 56, 55
MDA	0.466	44, 77, 136
Methyl ecgonine	0.471	82, 182, 96
Diethylpropion	0.477	44, 72, 77
MDMA (Ecstasy)	0.506	58, 135
Ibuprofen	0.511	161, 177, 220
Methylthioamphetamine	0.539	33, 138
MDEA (Eve)	0.540	44, 72, 135
Dextropropoxyphene artefact	0.562	208, 115, 117
Ibuprofen metabolite	0.615	119, 118, 178
Metronidazole	0.628	54, 81, 124
Dextropropoxyphene artefact	0.629	208, 115, 193
Ibuprofen metabolite	0.651	193, 105
Pethidine	0.659	71, 70, 172
Ibuprofen metabolite	0.661	161, 119
Norpethidine	0.679	57, 56
Paracetamol	0.687	109, 151
Norketamine	0.705	153, 194
Meprobamate	0.707	55, 83, 56
Caffeine	0.711	194, 109
Norfluoxetine	0.713	42, 146, 91
Diphenhydramine	0.739	58, 73
Thiopentone (thiopental)	0.742	172, 157, 173
Lignocaine (lidocaine)	0.743	86, 58
Phencyclidine	0.748	200, 91, 84
Ketamine	0.749	180, 182, 209
Fluvoxamine	0.751	71, 276, 56
Fluoxetine	0.754	44, 309, 104
Etomidate	0.756	105, 104, 244
Primidone metabolite (PEMA)	0.770	163, 148
Meptazinol	0.776	84, 58, 233
Orphenadrine	0.786	58, 73
Tramadol	0.786	58, 128
Desmethyltramadol	0.795	188, 135
Carbamazepine artefact	0.801	193
Baclofen	0.803	138, 195, 140
Naproxen metabolite	0.821	185, 244
Psilocin	0.822	58, 204
Chlorpheniramine (chlorphenamine)	0.824	203, 58, 205
Theophylline	0.832	180, 95, 68
Cyclizine	0.834	99, 194, 167
Nefopam	0.837	58, 179
Methadone cyclic metabolite	0.838	277, 276, 262
Metoprolol	0.842	72, 107, 223
Norcyclizine	0.846	167, 207
Venlafaxine	0.869	58, 134, 179
Dextromorphan	0.897	59, 257
Diclofenac	0.904	371, 373, 336
Methadone	0.905	72
Norvenlafaxine	0.907	58, 120
Propranolol	0.910	72, 100
Procyclidine	0.919	84, 204
Methaqualone	0.921	235, 250, 233
Dextropropoxyphene	0.928	58
Butriptyline	0.929	58
Amitriptyline	0.934	58, 202
Mianserin	0.937	192, 264, 72
Mefloquine	0.939	84, 56
Cocaine	0.940	82, 182, 96
Nortriptyline	0.942	44
Trimipramine	0.945	58, 235
Imipramine	0.950	58, 85, 234
Doxepin	0.952	58, 165, 279
Ethylbenzoylecgonine	0.954	196, 82, 83
Naproxen	0.955	185, 229, 170
Desipramine	0.959	44, 71, 195
Nordoxepin	0.960	44, 165, 178
Flecainide	0.961	125, 201
Moclobemide	0.971	100, 113, 56
Primidone	0.972	190, 146
Pentazocine	0.977	259, 110, 244
Promethazine	0.978	72, 56, 73
Bupivacaine	0.981	140, 84, 96
Zuclopenthixol	0.989	234, 235, 270
Trimeprazine (alimemazine)	0.994	58, 298
Benztropine	0.999	140, 83, 82
SKF 525A (internal standard)	**1.000**	86
Carbamezapine	1.002	193, 236
Maprotiline	1.004	44, 277, 70
Phenytoin	1.019	180
Sertraline	1.026	274, 276, 159
Dextropropoxyphene metabolite	1.027	220, 44, 205
Dihydrocodeine	1.028	301
Codeine	1.029	299
Dothiepin	1.032	58
Dextropropoxythene metabolite	1.033	44,220
Citalopram	1.037	58
Clomipramine	1.043	58, 85
Dextropropoxyphene metabolite	1.051	44, 220
Norclomipramine	1.056	269, 229
Diazepam	1.059	256, 284
Dipipanone	1.073	112, 113
Chlorpromazine	1.084	58, 86, 318
Nordiazepam	1.108	242, 270
Norpropoxyphene	1.116	44, 220
Paroxetine	1.131	44, 192, 138
Chloroquine	1.157	86, 139
Metoclopramide	1.158	86, 99
Tamoxifen	1.180	58, 72
Lormetazepam	1.182	305, 307
Quinine	1.243	136, 137, 81
Prednisolone	1.260	122
Clozapine	1.268	243, 256, 192
Dextromoramide	1.296	100, 128, 265
Diltiazem	1.307	58, 71
Haloperidol	1.312	224, 237, 123
Cholesterol	1.361	386
Thioridazine	1.406	98, 70
Strychnine	1.430	334
Verapamil	1.448	303
Trazodone	1.544	182, 254, 56
Lofepramine	1.595	58, 193, 234

MDA, 3,4-methylenedioxy amphetamine; PEMA, phenylethylmalonamide.

We also carry out a screen for ethanol. This could be performed with the ETS using an alcohol dehydrogenase based method but we choose to use head space analysis as this allows screening for some volatile compounds (table 1), though for solvent abuse screening a blood sample will usually offer greater sensitivity, and other analyses (such as measurement of hippuric acid/creatinine ratios in the urine) may prove necessary. The method as a screen for alcohol is simple. Into a 10 ml tube which has a septum in the cap put 200 µl of sample (or standard) and add 200 µl of internal standard (propan-1-ol, 4000 mg/litre in water), mix, and incubate at 60°C for 10 minutes. Using a gas tight syringe, inject 1 ml of vapour into a gas chromatography system with a Chromosorb 101 (100/120 mesh) packing and flame ionisation detection. We use a 1.5 m column and an oven temperature of 125°C.

A wide screen for basic drugs is provided by using a Hewlett-Packard gas chromatography/mass selective detector (GCMS) bench top system, consisting of a 5890 series II gas chromatograph with a 5971A mass selective detector. The extraction used has been described previously[1]: into a 1.5 ml microtube take 0.6 ml of sample and add 50 µl of concentrated ammonia (specific gravity 0.88) plus 200 µl of butyl acetate. This is mixed vigorously for 30 seconds and then spun in a microfuge for five minutes, after which 3 µl from the upper layer

Table 3 Data as in table 2 but presented in alphabetical order of the compounds listed

Compound	Relative retention time	Major ions
Amitriptyline	0.934	58, 202
Amphetamine (amfetamine)	0.215	44, 91
Baclofen	0.803	138, 195, 140
Benztropine	0.999	140, 83, 82
Bupivacaine	0.981	140, 84, 96
Butriptyline	0.929	58
Caffeine	0.711	194, 109
Carbamazepine	1.002	193, 236
Carbamazepine artefact	0.801	193
Cathine	0.353	44, 77
Chlormethiazole (clomethiaxole)	0.294	112, 161, 85
Chloroquine	1.157	86, 139
Chlorpheniramine (chlorphenamine)	0.824	203, 58, 205
Chlorpromazine	1.084	58, 86, 318
Cholesterol	1.361	386
Citalopram	1.037	58
Clomipramine	1.043	58,85
Clozapine	1.268	243, 256, 192
Cocaine	0.940	82, 182, 96
Codeine	1.029	299
Cyclizine	0.834	99, 194, 167
Desipramine	0.959	44, 71, 195
Desmethyltramadol	0.795	188, 135
Dextromoramide	1.296	100, 128, 265
Dextromorphan	0.897	59, 257
Dextropropoxyphene	0.928	58
Dextropropoxyphene artefact	0.562	208, 115, 117
Dextropropoxyphene artefact	0.629	208, 115, 193
Dextropropoxyphene metabolite	1.027	220, 44, 205
Dextropropoxyphene metabolite	1.033	44, 220
Dextropropoxyphene metabolite	1.051	44, 220
Diazepam	1.059	256, 284
Diclofenac	0.904	371, 373, 336
Diethylpropion	0.477	44, 72, 77
Dihydrocodeine	1.028	301
Diltiazem	1.307	58, 71
Diphenhydramine	0.739	58, 73
Dipipanone	1.073	112, 113
Dothiepin	1.032	58
Doxepin	0.952	58, 165, 279
Ephedrine	0.388	58, 77
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Fluvoxamine	0.751	71, 276, 56
Haloperidol	1.312	224, 237, 123
Ibuprofen	0.511	161, 177, 220
Ibuprofen metabolite	0.615	119, 118, 178
Ibuprofen metabolite	0.651	193, 105
Ibuprofen metabolite	0.661	161, 119
Imipramine	0.950	58, 85, 234
Ketamine	0.749	180, 182, 209
Labetalol artefact	0.295	91, 132, 117
Lignocaine (lidocaine)	0.743	86, 58
Lofepramine	1.595	58, 193, 234
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Maprotiline	1.004	44, 277, 70
MDA	0.466	44, 77, 136
MDEA (Eve)	0.540	44, 72, 135
MDMA (Ecstasy)	0.506	58, 135
Mefloquine	0.939	84, 56
Meprobamate	0.707	55, 83, 56
Meprobamate artefact 1	0.219	84, 56, 55
Meprobamate artefact 2	0.452	84, 56, 55
Meptazinol	0.776	84, 58, 233
Methadone	0.905	72
Methadone cyclic metabolite	0.838	277, 276, 262
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Norfluoxetine	0.713	42, 146, 91
Norketamine	0.705	153, 194
Norpethidine	0.679	57, 56
Norpropoxyphene	1.116	44, 220
Nortriptyline	0.942	44
Norvenlafaxine	0.907	58, 120
Orphenadrine	0.786	58, 73
Paracetamol	0.687	109, 151
Paroxetine	1.131	44, 192, 138
Pentazocine	0.977	259, 110, 244
Pethidine	0.659	71, 70, 172
Phencyclidine	0.748	200, 91, 84
Phenethylamine	0.229	91, 121
Phentermine	0.238	58, 91
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Tamoxifen	1.180	58, 72
Theophylline	0.832	180, 95, 68
Thiopentone (thiopental)	0.742	172, 157, 173
Thioridazine	1.406	98, 70
Tramadol	0.786	58, 128
Trazodone	1.544	182, 254, 56
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Trimipramine	0.945	58, 235
Venlafaxine	0.869	58, 134, 179
Verapamil	1.448	303
Zuclopenthixol	0.989	234, 235, 270

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are injected into the GCMS system. The column used is a Hewlett-Packard HP-5 capillary 25 metres in length with an internal diameter 0.32 mm and 0.17 μm film thickness.

The gas chromatography conditions used are initial temperature 85°C, initial time 1.5 minutes, rate 10°C/min, final temperature 280°C, and final time of nine minutes, giving a run time of approximately 30 minutes. The mass spectrometry conditions are scan range 40–500 and solvent delay 2.5 minutes.

Using this system we are able to screen for a the wide range of drugs indicated in tables 2 and 3. It is possible to use this method to screen for many of the commonly encountered abused/misused drugs, though this list should not be regarded as comprehensive and it is constantly being updated. To investigate unknown peaks detected during a run we use both a commercial library (Pfleger, Maurer and Weber: MS and GC data of drugs and poisons, available from VCH (UK) Ltd, Cambridge, UK) and our own library.

Secondary tests

Under this heading are included assays which arise from our initial findings. In considering the results of the immunoassay screens we will deal with each screen in turn.

In the case of opiates it is necessary to confirm the presence and the identity of the drugs. We use a system of solid phase

extraction followed by propionylation (SPE/MS), and a report on this has been published elsewhere.[2]

The presence of methadone does not usually require confirmation, but if it is requested the basic extraction described above is suitable. It is not unknown for addicts who have been prescribed methadone to sell it on and then adulterate their urine sample using a small portion of the prescribed methadone in order to achieve a positive finding when tested. Such adulteration is readily confirmed by performing the basic extraction and establishing the absence of the cyclic methadone metabolite.

The presence of "amphetamines" requires confirmation and identification, and we have described one approach elsewhere.[2] However, in many cases the basic extraction will suffice, as may be noted from table 2.

One problem with the Dade-Behring "amphetamine class" screen is the cross reaction with a whole range of non-amphetamines, particularly lofepramine metabolites, putrefaction products, and trazodone. Lofepramine metabolites and products of putrefaction such as benzenethanamine may be detected by using the basic extraction system as described above. Trazodone will be detected by using the SPE/MS propionylation system as described for opiates (relative retention time for propionylated trazodone, 0.975; major ions 166, 56, 252).

The presence of barbiturates in a sample is usually a result of the presence of phenobarbitone (phenobarbital), though other barbiturates may still be encountered. We generally use a simple acid extraction to confirm and identify barbiturates but have noticed improved sensitivity with ether extraction followed by methylation. Briefly, for a more sensitive screen for barbiturates, take 500 µl of urine and 500 µl of 0.1 M phosphate buffer pH 6.5, and add 25 µl of internal standard (Proadifen-SKF 525a, 100 mg/litre in methanol) and 8 ml of ether; after mixing for 10 minutes the phases are separated by centrifugation and the ether layer taken and evaporated to dryness. To the dry extract is added 70 µl of DMSO/TMAH (dimethyl sulphoxide/tetramethyl ammonium hydroxide, 20:1) and this is mixed for 30 seconds; 10 µl of iodomethane are then added and after brief mixing this is incubated for five minutes at room temperature. After methylation add 200 µl of 0.1 M hydrochloric acid and 1 ml of hexane to the tube and mix for two minutes using a vortex mixer. After allowing the layers to separate, take the hexane layer and dry it down. The resulting mixture is reconstituted in 100 µl of hexane and 3 µl are injected onto the GC/MS using the conditions described above for the basic extracts. We present our data for methylated barbiturates in table 4.

The presence of benzodiazepines and cocaine in urine does not normally require confirmation. The presence of benzodiazepines may be confirmed using a scaled up basic extraction (2.5 ml of urine, 200 ml of ammonia, 2 ml butyl acetate, and 25 µl of SKF 525a internal standard). Varian also publish a solid phase extraction method for benzodiazepines using their BondElut Certify columns which we have used with some success (available from Phenomenex, Macclesfield, UK).

Table 4 Relative retention times of methylated barbiturates as calculated against Proadifen (SKF 525a)

Compound	*Relative retention time*	*Major ions*
Barbitone (barbital)	0.379	169, 184, 126
Butobarbitone (butobarbital)	0.503	169, 184, 112
Amylobarbitone (amylobarbital)	0.540	169,184,112
Pentobarbitone (pentobarbital)	0.560	169, 184, 112
Quinalbarbitone (quinalbarbital)	0.588	196, 181, 169
Hexobarbitone (hexobarbital)	0.692	235, 81, 169
Phenobarbitone (phenobarbital)	0.717	232, 117, 146
SKF 525a (Underivatised)	1.000	86

The detection of the presence of cocaine is straightforward: the simple basic extraction is adequate for the detection of cocaine and the ecgoninemethylester metabolite (the second most dominant metabolite of cocaine). Though the immunoassay system is directed against benzoylecgonine (the major cocaine metabolite), this compound is not readily detected using a routine screening system. However, our experience has been that confirmation of a putative immunoassay positive finding has always been possible by searching for cocaine and ecgoninemethylester (the second most abundant cocaine metabolite) alone.

Positive cannabinoid results are not usually confirmed, though confirmation is required in cases where the implications of such a finding will be far reaching (for example, an isolated positive finding in a juvenile). We use a GC/MS method which has proved to be both reliable and sensitive. The method, described by Kemp *et al*,[3] involves hydrolysis to yield THC acid (11-nor-9-carboxy-Δ^9-tetrahydrocannabinol), which is then extracted and derivatised to form the trimethylsilyl derivative which may be detected using GC/MS.

Tertiary tests

There are certain drugs that are not easily detected as they are normally present in very low concentrations, for which the only convenient systems of analyses are specific immunoassays. In the case of LSD (lysergic acid diethylamide) there are other methods available (high pressure liquid chromatography with fluorimetric detection) but these are best regarded as reference methods rather than for routine use. Buprenorphine (Temgesic) and fentanyl are two other occasionally encountered drugs for which a specific immunoassay is the most convenient screening method.

Also within this category are compounds which are unsuitable for gas chromatography owing to their physical characteristics (high molecular weight, non-volatile, or highly polar molecules). No doubt the simpler to use and less expensive liquid chromatography/mass spectrometry systems now coming onto the market will facilitate the provision of a much better service with respect to these compounds.

Summary of procedures

The strategy for identification of drugs present in urine (or other samples as described above) should be:

1. *Ask for information*—From the staff who are dealing directly with the case. For samples provided routinely by clinics this discussion need only take place initially in order to establish their requirements. Samples from acute poisoning cases probably benefit from some discussion either on receipt or after initial screen. This could make the question you are being asked more specific.
2. *Screen*—Generally by some form of immunoassay. There is a wide range of options available and choice should be made based upon existing equipment and expertise.
3. *Further analysis*—A means of confirmation/identification of drugs in samples with putative positives from the screening stage is needed. We use GC/MS for confirmation purposes but other approaches, for example thin layer chromatography (TLC), have been used successfully (we used this approach initially). GC/MS will also provide the means of broadening the search to cover drugs not within the initial screen.
4. *Specific testing*—It must be accepted that it will be unlikely that a single system will provide a comprehensive, one shot screen for drugs at present. In the medium term with more sophisticated GC/MS and liquid chromatography/mass spectrometry such an ideal analysis will be more readily performed. In the interim, certain drugs will be tested for using specific assay systems, usually commercial immunoassay. The individual laboratory will have to decide which of these assays they will provide directly and which will be referred on for reasons of economy.

Conclusions

In this paper, we have described some of the systems that have evolved from lessons learned over eight years of providing a drug screening service. We hope that it will give the reader some insight into the problems and the solutions used. We make no claim that our approach is unique or the best, and other approaches have been reviewed.[4] Screening samples for drugs should be regarded as an open ended and evolving process. It should not be beyond the capacity of any district hospital laboratory, provided adequate funding is made available. In order to provide a useful service it is a prerequisite that the limitations of the system being used are fully appreciated both by the laboratory and by those using the service. Our approach has been to have clear analytical data for the commonly abused or misused drugs (for example, opiates, amphetamines, tricyclic antidepressants, and dextropropoxyphene) and to develop a wider range of cover as a natural progression. It is not possible to introduce a comprehensive service overnight.

The laboratory staff involved can make their own lives easier and provide a more effective service by having strong lines of communication with the staff who are dealing directly with the patients and—especially in the case of suspected overdoses—obtaining all possible information. This may be of particular importance when cases arise in which drugs not previously encountered by the laboratory have been used, and clear guidance from nursing and medical staff can be a considerable help in such circumstances. However, it would be wise to remember to expect the unexpected; in our experience the empty bottle or wrapping materials found in the vicinity of a patient can provided a false lead, and unexpected drugs will be found upon analysis of samples taken from the patient.

We hope this article has given readers some insight into the procedures involved in screening for drugs. The methods described will provide an effective starting point for those challenged into doing more work in this field, and also insight into what can and cannot be reasonably expected of a toxicology laboratory.

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Further reading:
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