the booklets. We thank the Department of Health and Social Security for funds which have made this project possible; the Imperial College of Science and Technology and the University of London for their computing facilities; and Professor W. W. Holland and Mr. H. S. Kasap for their helpful advice.

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Clinical Problems

Rapid Detection of Certain Basic Drugs in Urine

E. G. C. CLARKE

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Summary

Equipment costing only a few pounds can be used to detect a wide range of drugs in urine by anyone with a minimum of scientific knowledge. A run of tests takes about half an hour to perform and cost about 10p.

Introduction

Though the recent trend in toxicological analysis has been towards increasing automation and instrumentation, the growing problems arising from drug addiction have led during the past few years to the publication of a number of so-called simple methods for the detection of drugs in urine.¹⁻¹⁰ Most of these are based on thin-layer chromatography; all of them take several hours to perform and call for full laboratory facilities and considerable expertise. There are occasions, however, when these are not available, and specificity and sensitivity must be sacrificed to speed and simplicity. The method described below can be carried out anywhere by anyone with a minimum of scientific knowledge. The total cost of the equipment needed is less than £5. Each test costs about 10p and takes less than half an hour to perform.

Materials

Apparatus.—Wide-mouthed 8-oz (227-ml) bottles, Bakelite-capped. McCartney bottles (wide-mouthed, with plastic caps). White tile or pieces of white opal glass. Filter paper (Whatman No. 1; strips 6 by $\frac{1}{2}$ in; 15 by 1.3 cm). Small glass rods. Small dropping-bottles with glass stoppers and rubber teats. Forceps. Scissors. A small glass funnel and a spatula are useful but not essential.

Reagents.—(All chemicals of General Purpose Reagent grade.) Sodium sulphate, anhydrous. Chloroform. Sodium tetraborate.

Modified Marquis reagent—dissolve 200 mg of paraformaldehyde in 10 ml of concentrated sulphuric acid. Sodium sulphite solution 10%, freshly prepared. Sulphuric acid, concentrated. Sulphuric acid 2N. Potassium iodoplatinate solution—dissolve 25 mg of platonic chloride and 0.5 g of potassium iodide in 10 ml of water. Cobalt thiocyanate solution 5%. FPN reagent—mix together 0.5 ml of a 5% w/v solution of ferric chloride in water with 4.5 ml of 20% w/w perchloric acid and 5 ml of 50% w/w nitric acid. Ammonium vanadate—make a saturated solution of ammonium vanadate in boiling water, cool, and add an equal volume of 0.880 ammonium hydroxide solution. Paradimethylaminobenzaldehyde—dissolve 0.1 g of paradimethylaminobenzaldehyde in 10 ml of a mixture of ethanol and concentrated hydrochloric acid (10:1). Acetone:water, 20:1 (for chromatography).

Extraction

Place 75 g of anhydrous sodium sulphate and 1 g of sodium tetraborate in an 8-oz (227-ml) bottle (these bottles may be prepared in advance; provided the cap is screwed on tightly they keep indefinitely). Add about 30 ml (a full McCartney bottle) of chloroform. Shake briefly till the sulphate is wet. Add about 25 ml (a McCartney bottle, full to the shoulder) of urine. Shake immediately and continue shaking for two to three minutes. Allow to stand till the chloroform separates then decant into a McCartney bottle containing 1 g of sodium sulphate. If less than half the original volume can be obtained add a little more chloroform to the extraction bottle, shake again, and decant. Shake the McCartney bottle thoroughly. It is essential that the chloroform be absolutely dry; this is indicated by its being completely transparent. If there is any doubt add a little more sulphate and shake again. Decant the chloroform into another McCartney bottle.

By this procedure almost all basic drugs are extracted into the chloroform phase. They are now purified and concentrated by the acid-spot technique introduced by Morgan.⁸

Take a strip of filter paper 6 by $\frac{1}{2}$ in (15 by 1.3 cm) and mark it with a pencil 1 in (2.5 cm) from one end, then at every $\frac{1}{4}$ -in (1.9-cm) interval. At each pencil mark place a small spot, less than 1/10 in (2.5 mm) in diameter, of dilute sulphuric acid. This is most conveniently done by having the pipette of

the dropping bottle drawn out to a fine capillary point. The paper is now placed in the bottle containing the chloroform solution. It may be allowed to stand there for at least two hours (or overnight), but the result is obtained most rapidly if the bottle is shaken or agitated for about 15 minutes. Any basic drugs in the chloroform are extracted by the dilute acid and concentrated in the spot on the paper, but the extraction is not complete, and should additional tests be necessary a further extraction may usually be carried out with a second paper, agitating for half an hour.

The above method has been devised primarily for urine but can be used for any suspect material such as powder or tablets; the latter should be wrapped in strong paper and crushed with a hammer. Place the material in a McCartney bottle. Add about 0.5 ml of dilute sulphuric acid and shake; half fill the bottle with water, shake vigorously, then treat as for urine.

The method is not suitable for cadaveric material, though it has been used successfully to identify strychnine in the stomach contents of a dog. It is designed for basic drugs only, and will not therefore extract cannabis or the barbiturates.

Identification

Remove the paper strip from the chloroform, allow it to dry, and examine it. If the spots appear purple the presence of a drug of the chlorpromazine type is suggested. Blue fluorescence under ultraviolet light (if available) may indicate that lysergide or some other ergot-type alkaloid is present, but these are unlikely to be detected in urine owing to the low concentrations usually found. Quinine alkaloids give a similar fluorescence. Cut the paper into six pieces midway between the spots. Put the two longer (end) pieces on one side for subsequent paper chromatography. Use the four remaining pieces for colour tests.

Place the first piece on a white tile and add a drop of the iodoplatinate solution. This gives a dark grey-purple (almost black) spot with nearly all basic drugs, including nicotine. Amphetamine, exceptionally, gives a white spot, forming slowly and not always easy to see. Now add a drop of the sodium sulphite solution. The red iodoplatinate bleaches immediately, but the rate at which the spot is decolorized depends on the compound forming it (see Table I). Nicotine and morphine, for example, fade almost at once, but methadone turns reddish and may persist for 15' minutes.

The second spot is treated with a drop of the modified Marquis reagent. Heroin (or morphine, in which form it is excreted in urine) gives a purple colour, as also does codeine. Chlorpromazine and various other phenothiazine derivatives give a rather more reddish colour but may be distinguished from the morphine-type drugs by the fact that they give an exactly similar colour with concentrated sulphuric acid, whereas the latter do not.

Amphetamine and methylamphetamine give an orange colour, rapidly turning brown with the Marquis reagent, but no colour with concentrated sulphuric acid. This distinguishes them from

amitriptyline, which gives an orange colour with both reagents. Diphenhydramine gives a bright yellow turning to brown with both reagents. This is important, as diphenhydramine is one ingredient of Mandrax and is easier to detect than methaqualone, the active constituent; but note that dimenhydrinate gives an identical colour.

If a positive result has been obtained with the Marquis test the third spot is tested with a drop of concentrated sulphuric acid for the purposes of differentiation described above.

The fourth spot (and the third if unused) may be treated with any of several reagents, the choice depending on the circumstances and on the results that have been obtained so far. The FPN reagent gives a red colour with chlorpromazine and several other phenothiazines, and blue with thioridazine and imipramine. The ammonium vanadate reagent is used by adding a drop of the reagent to the spot on the paper, allowing it to dry (a hair dryer is helpful here), and then adding a drop of concentrated sulphuric acid. Methadone gives a blue-green colour. The test is not, however, particularly sensitive, and low concentrations of methadone in urine may be missed. The paradimethylaminobenzaldehyde reagent gives a blue-purple colour, forming as the reagent dries, with lysergide and the ergot alkaloids, but again the test is not usually sensitive enough to detect these drugs in urine. It would, however, detect the pure substance and distinguish it from quinine.

Mixtures of drugs give confusing results which are sometimes difficult to interpret. These may often be resolved by a simple form of paper chromatography. One millilitre of the acetone: water mixture is placed in a McCartney bottle, and one of the longer papers placed in it with the spot at the lower end. After about one minute, by which time the solvent front will have risen $\frac{1}{2}$ in (1.3 cm) or so above the spot, the paper is removed, dried, and treated with several drops of the iodoplatinate solution to indicate the present position of the drug or drugs. These may remain at the point of origin—for example, nicotine—advance right up to the solvent front—for example, methadone—or occupy any point between them—for example, cocaine. Results are shown in Table II. Baseline + solvent front indicates a spot at each of these locations; baseline to solvent front indicates a streak between the two. No attempt has been made to give an R_f value, as this could not be reproducible under these conditions. Use of the Marquis reagent

TABLE II—Interpretation of Mixtures of Drugs in Urine

Drug	Paper Chromatography
Amitriptyline	Baseline to solvent front
Amphetamine	Baseline to solvent front
Chlorpromazine	Baseline to solvent front
Cocaine	Baseline to solvent front
Codeine	Baseline to solvent front
Diphenhydramine	Solvent front
Imipramine	Baseline + solvent front
Methadone	Solvent front
Methaqualone	Baseline + solvent front
Methylamphetamine	Baseline to solvent front
Methylphenidate	Solvent front
Morphine	Baseline
Nicotine	Baseline
Phenmetrazine	Usually invisible
Quinine	Baseline to solvent front
Thioridazine	Baseline to solvent front

TABLE I—Colour identification of Drugs in Urine

Drug	Iodoplatinate	Sodium Sulphite	Marquis	Sulphuric Acid	Cobalt Thiocyanate	FPN Reagent	Ammonium Vandate
Amitriptyline	++	Red-brown > 15 min	Orange	Orange	Bright blue	—	Brown-purple
Amphetamine	White	Fades < 1 min	Orange	—	—	—	—
Chlorpromazine	++	Yellow > 15 min	Red	Red	Greenish blue	Red-purple	Red-brown
Cocaine	++	Fades < 4 min	—	—	Bright blue	—	—
Codeine	++	Fades < 1 min	Purple	—	Faint blue	—	—
Diphenhydramine	++	Fades < 10 min	Bright yellow	Bright yellow	Bright blue	—	Orange
Imipramine	+	Red-brown > 15 min	—	—	Blue	Blue	Green
Methadone	++	Red-brown > 15 min	—	—	Bright blue	—	Blue-green
Methaqualone	++	Fades < 1 min	—	—	Faint blue	—	—
Methylamphetamine	++	Fades < 1 min	Orange	—	—	—	—
Methylphenidate	++	Fades < 1 min	—	—	Faint blue	—	—
Morphine	++	Fades < 1 min	Purple	—	—	—	—
Nicotine	++	Fades < 1 min	—	—	—	—	—
Phenmetrazine	+	Fades < 1 min	—	—	—	—	—
Quinine	++	Fades < 2 min	—	—	Faint blue	—	—
Thioridazine	++	Fades < 1 min	Brown-purple	Blue*	Blue	Blue (runs)	Brown-purple

*Not changed.

on the second chromatogram will show up mixtures of morphine and amphetamine or morphine and chlorpromazine.

Discussion

It must be remembered that nearly 1,000 basic drugs are available, either legally or illegally. Most of these give a positive reaction with the iodoplatinate solution. Many of them give colours with the Marquis reagent.¹¹ Only the more important drugs of abuse and a few common tranquillizers have been included in Table I. Should other basic compounds assume a position of importance their characteristics can be determined for inclusion in the scheme. Further reagents may be added if this becomes necessary.

It must be emphasized that this method is in no way a substitute for normal toxicological analysis, and its results would not serve as legal proof in court. Owing to its speed and simplicity it should, however, be of service in providing confirmation of clinical or circumstantial evidence under conditions where normal laboratory facilities are not available.

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General Practice Observed

The Hallucinations of Widowhood

W. DEWI REES

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Summary

227 widows and 66 widowers were interviewed to determine the extent to which they had hallucinatory experiences of their dead spouse. The people interviewed formed 80.7% of all widowed people resident within a defined area, in mid-Wales, and 94.2% of those suitable, through the absence of incapacitating illness, for interview.

Almost half the people interviewed had hallucinations or illusions of the dead spouse. The proportion of men and women who had these experiences was similar. The hallucinations often lasted many years but were most common during the first 10 years of widowhood. Social isolation did not affect the incidence of hallucination, nor was it related to the incidence of known depressive illness. There was no variation within cultural groups and there was no variation with place of residence, whether this was within town, country, or village, or within England and Wales.

Young people were less likely to be hallucinated than those widowed after the age of 40. The incidence of hallucination increased with length of marriage and was particularly associated with a happy marriage and parenthood. Members of the "professional and managerial" group were particularly likely to be hallucinated,

while widows of "non-manual and sales workers" were the ones least likely to be hallucinated. The incidence was greater with hysteroid than obsessoid people. It was unusual for the hallucinations to have been disclosed, even to close friends or relatives.

These hallucinations are considered to be normal and helpful accompaniments of widowhood.

Introduction

The extent to which widowed people experience hallucinations and illusions of their dead spouse had not been previously investigated, so it seemed worth while to determine its incidence.

Method

The intention was to interview all widowed people resident within a defined area in mid-Wales. This area, centred on Llanidloes, is such that with few exceptions all residents are patients of one group practice. The practice has about 7,500 patients, and of these about 5,200 live in the survey area. The age and sex distribution of this survey group has been reported elsewhere by Rees and Lutkins.¹

The identity of most widowed people in the area was already known, but a further check was made with the aid of the practice secretaries, who had lived for many years in the area, district nurses, and local clergy. It was found that 363 widowed people resided in the area. Because of serious physical or mental defects 52 were considered unfit for interview and excluded from the sample. The age and sex distribution of those excluded

Llanidloes, Montgomeryshire

W. DEWI REES, M.B., M.R.C.G.P., General Practitioner