

# Post-mortem toxicology of commonly-abused drugs

Alexander R Allan

Ian S D Roberts

## Abstract

Post-mortem redistribution and other changes present major obstacles to the interpretation of drug concentrations in the dead. Nevertheless, reasonable assessments can still be made by the pathologist and toxicologist as to the contribution that commonly-abused drugs may have made to the death. The best assessments may be obtained by the implementation of the investigation along the following lines: (1) carefully select, store, preserve and utilize the post-mortem tissue samples intelligently for appropriate toxicological and histological analyses; (2) use as much information concerning the circumstances of the demise as possible to guide the procedures in step 1; (3) factor in prevalence of drug use and estimated fatality risks of such use within the particular group concerned to determine whether or not additional analytical work is required; (4) consider how these drugs behave in the body ante- and post-mortem, with and without disease states, together with any other factors such as tolerance; (5) consider the toxicological results in the context of macroscopic and histological autopsy findings.

**Keywords** drugs of abuse; fatal; post-mortem; pharmacokinetics; pharmacodynamics; redistribution; site sampling; toxicity; overdose

## Introduction

In order to assist the pathologist in his or her assessment of the contribution that drugs of abuse may have made in a death, it is important that the pitfalls of post-mortem toxicology are described for these substances. This review has been compiled to introduce pharmacological data, redistribution, sampling, toxicological and analytical aspects for the common drugs of abuse, together with associated autopsy findings as a guide to interpretation. This is not a comprehensive account of all drugs of abuse. The focus will be on those drugs most frequently implicated in deaths in the UK, as this reflects the authors' experience. The statistical data presented on the frequency of abuse will be restricted to the UK. It is acknowledged that patterns of drug abuse and toxicity differ in other parts of the world.

*Alexander R Allan PhD CChem FRSC CSci RFP is a Director at Triple A Forensics Ltd, PO Box 608, Oldham OL1 9GH, UK.*

*Ian S D Roberts BSc MBChB FRCPath is Consultant Pathologist, Oxford Radcliffe Hospitals at the Department of Cellular Pathology, John Radcliffe Hospital, Oxford OX3 9DU, UK.*

## Commonly-abused drugs and substances in the UK

Alcohol (ethanol)  
 Alkyl nitrites  
 Amphetamines  
 Barbiturates  
 Benzodiazepines (typically diazepam and temazepam)  
 Buprenorphine  
 Cannabis  
 Cocaine and 'crack'-cocaine  
 Codeine  
 Dihydrocodeine  
 GHB and GBL  
 Hallucinogens (LSD and 'magic mushrooms')  
 Heroin and morphine  
 Ketamine  
 MDMA – 'ecstasy', MDA and related phenethylamines MDEA, MBDB  
 Methadone  
 Volatile substances

**Table 1**

The current commonly-abused drugs in the UK are listed in [Table 1](#), based on data in the NHS Information Centre Statistics on Drugs Misuse in England, which can be found online in its statistical report for 2007.<sup>1</sup> This publication summarizes the types of drugs used and their prevalence of use, as well as trends and patterns in England. The types of drugs used are listed for adults (16–59 years) and children (10–16 years). Cannabis remains the most common drug used by adults, followed by cocaine (all types), MDMA – 'ecstasy', amphetamines, alkyl nitrites (incorrectly referred to as amyl nitrates) and hallucinogens (LSD and 'magic mushrooms'). In 2006 9% of children (11–15 years) in England reported taking drugs in the last month and 17% in the previous year, with cannabis being the most commonly taken drug at 10%. Four per cent of children reported that they had used a Class A drug in 2006.

Although only 0.1% of adults reported using opiates, their toxicity ensures that they are responsible for more deaths than the other drugs of abuse and so figure at or near the top of the tables for drug-related deaths in many countries (e.g. most of the Nordic countries<sup>2</sup>). Cannabis use, despite being the most widespread of the illicit substances, produces very few deaths due to its low toxicity, although in many cases it may be found in association with other abused substances. However, it should be noted that six deaths potentially caused by acute cardiac problems have been described in Norway.<sup>3</sup>

## Commonly-abused drugs

The range of commonly-abused drugs and substances in the UK is similar to that in many other developed countries and includes the substances listed in [Table 1](#), although there may be regional, temporal and societal differences in the particular favoured drugs and substances.

The abuse of alcohol still causes more deaths than any other substance and, because much literature has been devoted to the subject, it will only be touched upon briefly in this review.

### Geographical and temporal variation in the UK

A Scottish Statistical Office report summarizes the drugs of abuse deaths for Scotland in 2007 and for comparison, in earlier years.<sup>4</sup> The corresponding figures for England and Wales for this period are not available at compilation of this review, but there is no reason to doubt that the range of drugs involved in the death statistics is similar to that in Scotland, and to the period 1993–2004 for England and Wales.<sup>5</sup> Anecdotal information indicates that there may be local ‘hot-spots’ for particular types of abuse from time-to-time, although official surveys are not available to confirm these trends.

Of particular note, in the year 2007 Statistical Report by the National Health Service (NHS) surveying drug misuse in England, cocaine usage over the period 1996–2006 has increased 10-fold in England and Wales.<sup>1</sup> This report included self-reporting surveys from adults and could underestimate the respondents’ true usage, particularly for recent drug use and Class A drugs.<sup>6</sup>

The drug misuse death statistics for England and Wales over the period 1993–2004 show that heroin and morphine continue to be implicated specifically in more drug-abuse deaths than any of the other listed drugs; e.g. in 2004, out of the total of 1427 deaths attributed to drug misuse, 744 were reported to be due to heroin/morphine.<sup>5</sup> A slight downward trend noted for heroin/morphine deaths of 1% was noted over a period of 5 years from 1999 to 2004. However for cocaine, the figure of 147 deaths in 2004 represents a 68% increase over the 1999 total, reflecting the increased usage reported in the NHS survey.

Despite coming second, after heroin/morphine deaths, methadone deaths show a significant downward trend during the period 1999–2004, the figure for 2004 of 200 deaths involving methadone misuse being 33% less than the figure for 1999. This reflects a move to supervised dispensing, reducing the availability of diverted methadone.

Benzodiazepines continue to be used and abused to alleviate dysphoria and anxiety following abuse of other drugs, but although they rank close to methadone, being credited with involvement in 206 deaths in 2004, their relatively low toxicity indicates incidental involvement in most deaths.<sup>7</sup> It has been suggested that impairment of judgement may be a factor with mixed drug use.<sup>8</sup> Recent press coverage (September 2008) suggests that diazepam is becoming very popular as the supply of good quality heroin declines.

The involvement of amphetamines and dihydrocodeine in fatalities shows a marked decrease during the period, down by 35% (35) and 33% (81) respectively for 2004. On the other hand, MDMA and codeine show an increase of 85% (48) and 108% (54) respectively over the period 1999–2004.

The national programme on Substance Abuse Deaths (np-SAD) publishes online summaries of its 6-monthly surveillance reports for drug misuse deaths for the UK. For example, the 18th report covered the period January to June 2006.<sup>9</sup> As for previous surveys, most of the cases (76%) comprised males, about three-quarters being under 45 (74%). Ninety-six per cent were classified as white. Heroin/morphine alone or in combination with other drugs accounted for the highest proportion (47%) of the fatalities.

Although barbiturates are included in the NHS survey, being classified with benzodiazepines as ‘tranquillizers’, they seldom show up in the drug deaths statistics except in special

circumstances such as the suicide of a veterinary surgeon, since they are not readily available on prescription and, furthermore, due to their low frequency of occurrence, some laboratories may no longer routinely screen for their presence.

For other drugs, although no figures are available, various elements of society may favour particular substances, e.g. ketamine seems to be favoured by young men in parts of the West Country seeking the ‘K-hole’ experience. Substances such as alkyl nitrites (poppers) and GHB or GBL may be encountered particularly in individuals associated with the ‘gay scene’.

Alkyl nitrites, cannabis, ketamine, LSD and psilocybin are implicated in very few deaths and therefore pharmacological details of these substances will not be included in the tables.

### General points on the interpretation of post-mortem drug levels

The proper interpretation of any drug findings must be carried out with knowledge of the limitations and statistics of the analytical results, the nature of the particular samples used for the analysis (see below), cognisance of post-mortem changes and as much information about the victim and circumstances as possible.<sup>10</sup> In particular, tolerance to a drug is a crucial issue when dealing with suspected acute overdose cases and without such information interpretation may necessarily be only tentative. Analytical results are seldom of use without such information and the evidential value of the findings depends upon the types and numbers of tests and samples used and the prevalence of drug use in that particular population.<sup>11–13</sup>

Some authors urge extreme caution in the interpretation of any post-mortem drug data.<sup>14</sup> However, as long as the toxicologist and pathologist are aware of all the variables that may affect the results, and sufficient information about the victim and circumstances is available, then it is feasible to form a considered opinion that is almost always better than none, and essential for the death certificate. As the understanding of drug redistribution advances, allowances for the types of drugs that have the greatest propensity to redistribute can be factored into the assessment of contribution of that particular drug in the death.<sup>15</sup> The factors that predispose redistribution are described in more detail below.

If drugs of abuse are not involved directly in a death by overdose or atypical reactions, then the extent of their involvement may also be required by the Coroner or Procurator Fiscal to attempt to ascertain contribution to death in terms of impairment of behaviour or judgement, as described later.

Pharmacological data are of limited use in interpretation of the analytical data because they apply to live subjects, and post-mortem changes such as autolysis and putrefaction enhance drug redistribution.<sup>16</sup> Furthermore, saturation of metabolic pathways for some drugs in overdose may have to be considered. Additional problems of interpretation are generated by the fact that the clinical data usually apply to plasma or serum of quite small populations and seldom to whole blood. For drugs such as MDMA that are not used medicinally, information on expected levels from known dosage is not as extensive as drugs such as morphine, methadone and the benzodiazepines. Pharmacological data on drug metabolites are also extremely limited. In any case, pharmacological data of the parent drug often only apply

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