Self-poisoning in the UK: epidemiology and toxidromes

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Self-poisoning may be deliberate or accidental (as in most paediatric cases and many cases of drug abusers who overdose on their drugs of abuse). Either type of self-poisoning may be fatal, although the vast majority are non-fatal, particularly in children. Poisoning by some drugs can produce characteristic clinical syndromes (toxidromes) that may assist in determining to what a patient has been exposed, if the individual is unable or unwilling to divulge this information.

Epidemiology

Data on fatal self-poisoning are recorded nationally via the coroner in England, Wales and Northern Ireland and via the Procurator Fiscal in Scotland. Cases usually receive, and are categorised in the national databases under, a verdict of suicide, accidental or undetermined ('open verdict') death. In addition, *International Classification of Diseases* (ICD)-9 304 and 305 (pertaining to the dependent and non-dependent abuse of drugs, respectively) take precedence over other codes in the UK Office for National Statistics, and thus represent further areas in which self-poisoning mortality statistics may 'hide'.

Fatal self-poisonings

Suicides tend to be quoted together with open verdicts, to a greater or lesser extent, in many epidemiological studies due to the widely held belief that most open verdicts are actually 'missed' suicides.[1] In Scotland in 2000, 200 males and 94 females were fatally self-poisoned (predominantly by ingesting drugs or gassing themselves) under both categories (*source*: www.show.scot.nhs.uk); in England and Wales in 1999, there were 1,271 males and 662 females (*source*: www.statistics.gov.uk). Given that the ratio of the population of England and Wales to that of Scotland is approximately 10:1 (*source*: www.statistics.gov.uk), there are clearly geographical differences in the self-poisoning suicide rates around the UK.

The suicide rate (all causes combined) has been falling in the UK for many years in all age groups and for both genders, with the notable exception of young males in whom the rate significantly increased in the 1980s and has remained high ever since.[1,2] The most popular means of committing suicide currently is hanging (the numbers being heavily influenced by the preponderance of males in the overall figure), but young males as a group prefer self-poisoning: gassing (mostly using car exhaust fumes) and drug overdoses, roughly in a 2:1 ratio. Other groups that prefer self-poisoning for suicide, primarily by drug overdoses, include most females, medical professionals and drug addicts.[3,4] The most common drug taken in overdose resulting in suicide in the UK is co-proxamol.[5]

The number of deaths in England and Wales during 1999 attributable to *accidental* self-poisoning was 749 males and 280 females (*source*: www.statistics.gov.uk), about 50% of which involved opiates. In one study of teenagers in England and Wales, the accidental death rate attributable to drugs was found to be increasing by 27% a year.[6]

Non-fatal self-poisonings

Data on non-fatal self-poisonings are not routinely collected nationally, so epidemiological information is largely derived from the deliberate self-harm (DSH = self-poisoning and/or self-injury) admission/presentation records of various hospitals in the UK. Of note, hospitals vary as to whether their definition of DSH includes or excludes figures

Key Points

- **Self-poisonings may be accidental or deliberate, fatal or non-fatal**
- **Self-poisoning as a method of suicide is popular in all females, young males, drug addicts and doctors**
- **Co-proxamol is the prescription drug most commonly associated with suicide**
- **Opiates are responsible for the majority of deaths due to accidental self-poisoning**
- **Paracetamol is the drug most commonly associated with non-fatal deliberate self-harm (DSH)**
- **DSH is increasing in the UK, the largest increase being among young males**
- **Legislation limiting the availability of paracetamol appears to be reducing the death rate from paracetamol overdose in England and Wales, but not yet in Scotland**
- **Certain drugs in overdose produce toxidromes (characteristic constellations of symptoms/signs and results of investigations)**
- **The appearance of some toxidromes may be delayed due to the effects of absorption, distribution, metabolism and time taken to exhaust cellular/organ reserves**

KEY WORDS: deliberate self-harm, epidemiology, overdose, poisoning, suicide, toxic syndrome, toxidrome

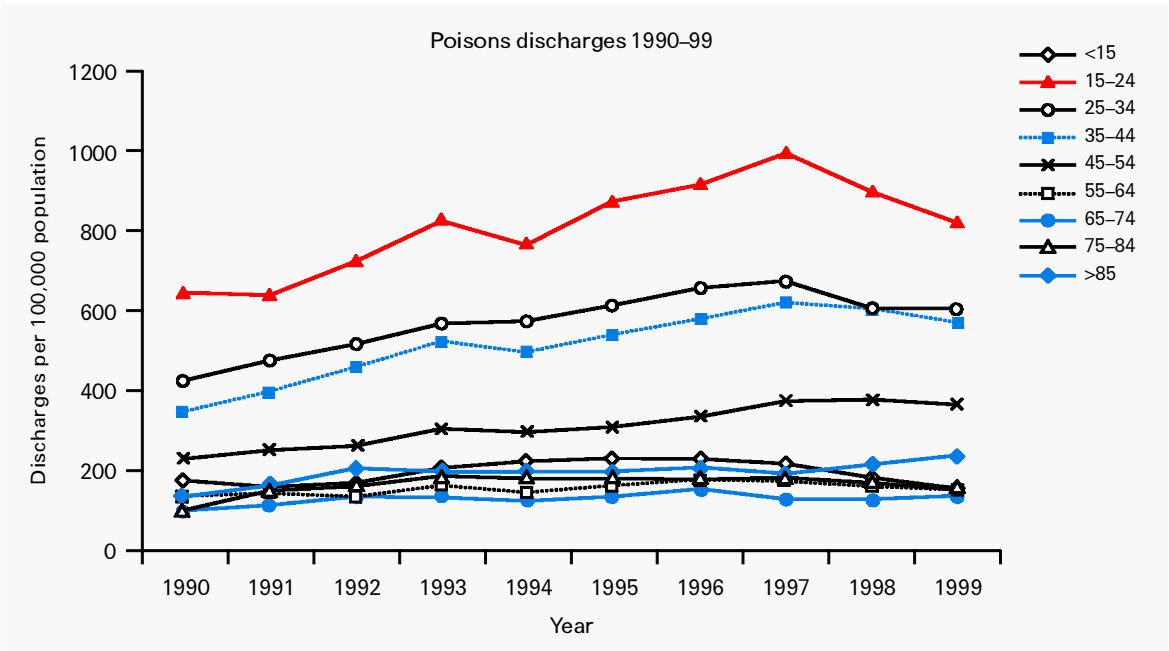

Fig 1. Trends in male self-poisoning discharges from Scottish hospitals by age 1990–99.[9]

on accidental self-poisoning following the recreational use of drugs.[7,8] National figures for non-fatal self-poisonings in Scotland (population 5.1 million), based on hospital discharges, gives the rate in 1999 as 349 males and 390 females per 100,000 population.[9]

The incidence of DSH appears to be increasing with time, with young males again the demographic group in which the increase is greatest (Fig 1).[7,9] Approximately one-third of self-poisoners take only one drug when they overdose and two-thirds take more than one drug.[7,8] Being able to complete a psychiatric assessment following an episode of DSH appears to reduce the annual re-presentation rate in these patients from approximately 38% to 18%.[10]

Table 1. The 10 drugs for which there were the most common enquiries to TOXBASE in the year 2000 (frequencies expressed as a ratio to frequency of paracetamol (*Source*: Scottish Poisons Information Bureau).

Rank	Drug	Frequency
1	Paracetamol	1.000
2	Diazepam	0.299
3	Aspirin	0.278
4	Ibuprofen	0.262
5	Zopiclone	0.250
6	Ecstasy	0.232
7	Amitriptyline	0.201
8	Dothiepin	0.199
9	Temazepam	0.176
10	Co-proxamol	0.171

Paracetamol overdosage

The most common drug employed in non-fatal self-poisonings in the UK is paracetamol (either 'pure' or within a combination preparation). The annual figure for paracetamol poisonings in the UK has been estimated at 70,000.[11] To give an idea of the other drugs used in self-poisonings, the 10 drugs about which there are the most common enquiries to the National Poisons Information Service secure toxicology website (TOXBASE) are listed in Table 1.

In 1997, 9% of paracetamol overdoses were above the treatment line for acetylcysteine (3% for those reporting less than 12 g ingested and 20% for those reporting more).[12] From September 1998, legislation limiting the availability of paracetamol was introduced into the UK (Table 2), following which a 21% reduction in the death rate from paracetamol has been reported in England and Wales.[13] Even though the overall number of poisoning episodes has declined since 1998 (Fig 1), no corresponding reduction in paracetamol deaths has yet been reported in Scotland.[14]

Toxidromes

Self-poisoning by certain drugs can produce characteristic constellations of symptoms, signs and results of

Table 2. UK legislation limiting the availability of paracetamol (16 September 1998).

- Pharmacies to sell a maximum of 32 (× 500 mg) tablets in a single transaction (but up to 100 tablets in justifiable circumstances)
- Other retail outlets (eg supermarkets, garages) to sell a maximum of 16 tablets
- Specific warnings of the dangers of overdose to be printed on packets and on leaflets within packets
- Blister-packs for tablets in almost all circumstances

Table 3. Toxidromes associated with common categories of drugs taken in overdose.

Drug	Mechanism	Toxidrome
Opiates	Opioid receptor agonist	Nausea, vomiting, constricted pupils, drowsiness, respiratory depression, hypotension, bradycardia, absent bowel sounds *NB*: some opiates have additional properties that alter their toxicological effects, eg dextropropoxyphene (QT prolongation), tramadol (5HT effects), morphine and codeine (histamine release causing urticaria)
Salicylates	Acidic compounds, central respiratory stimulant, uncouple oxidative phosphorylation, disturbance of carbohydrate metabolism increasing lactate and pyruvate	Vomiting, tinnitus, vertigo, deafness, sweating, tachypnoea, haematemesis, hyperpyrexia, mixed respiratory alkalosis and metabolic acidosis, hypoglycaemia, hypokalaemia, thrombocytopenia, renal failure, coma
Tricyclic antidepressants	Anticholinergic, amine reuptake inhibitors, direct membrane action on sodium channels	Tachycardia, reduced sweating, dry mouth, urinary retention, dilated pupils, nystagmus, dysconjugate gaze, ataxia, convulsions, drowsiness, hyperreflexia, hypertonia, extensor plantars, prolongation of QRS on ECG
Selective serotonin reuptake inhibitors	5HT reuptake inhibitors	Nausea, vomiting, agitation, tremor, nystagmus, drowsiness, convulsions, hypertension, tachycardia, arrhythmia 'Serotonin syndrome' (hyperpyrexia, hypertonia, rhabdomyolysis, renal failure)
Amphetamines	Direct catecholamine receptor action and indirect via amine release	Euphoria, agitation, sweating, hallucinations, delusions, convulsions, hyperpyrexia, tachycardia, rhabdomyolysis, renal failure, CVA
Ecstasy	Amine release, 5HT-like effect	Nausea, hypertonia, dilated pupils, sweating, dry mouth, hypertension or hypotension, tachycardia, tachypnoea, confusion, convulsions, coma, hyperpyrexia, rhabdomyolysis, hyponatraemia, renal failure, hepatic failure
Ethylene glycol/methanol	Conversion to toxic aldehyde and acids	Metabolic acidosis, pulmonary oedema, renal failure, blindness, dilated pupils coming on after 24 hours or more (longer if ethanol also consumed)
Iron	Metabolic toxin	Nausea, vomiting, abdominal pain, diarrhoea, haematemesis within 6 hours Quiescence/latency from 6–24 hours Drowsiness, convulsions, metabolic acidosis, circulatory collapse, hepatic necrosis and renal failure after 24 hours Gastric and pyloric scarring some weeks after recovery

CVA = cardiovascular accident; 5HT = 5-hydroxytryptamine (serotonin).

investigations, called toxidromes (Table 3). This information may be useful in determining which agent has been taken in order to guide clinical management, particularly if patients are unsure, incapable or unwilling to provide this information themselves. Certain toxidromes will suggest the use of specific antidotes, such as naloxone for opiates or desferrioxamine for iron overdoses.

It is important to note that some toxic effects are delayed in overdose due to:

- delayed absorption of drug
- redistribution effects
- time taken to form toxic metabolites, or
- the exhausting of cellular/organ reserves.

Examples of such delayed toxicity include:

- the four phases of iron intoxication: gastrointestinal effects within six hours, latency until 24 hours, progressing to severe metabolic and biochemical disturbances thereafter, followed by the late possibility of gastric scarring some weeks after recovery, and
- the central neurological effects of methanol that come on only 12–24 hours after ingestion.[15]

Knowledge of toxidromes may prevent false reassurance in these situations, particularly if delayed toxicities are preceded by a period of relative quiescence, and thereby allow patient and staff to be prepared for symptoms and signs of a particular overdose that are yet to come.

If several different agents have been ingested, an individual may occasionally display complex elements of several different toxidromes.

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Antidepressant poisoning

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Antidepressants are involved in about one in five cases of overdose. They cause significant morbidity and are the second most common cause of fatal drug overdose in the UK.

Tricyclic antidepressants

Tricyclic antidepressants account for most deaths from antidepressant overdose. Dosulepin and amitriptyline are particularly toxic. The mechanisms of toxicity are summarised in Table 1.

Clinical features

The clinical features of tricyclic antidepressants include anticholinergic, cardiovascular and neurological effects.

Anticholinergic effects. Serious anticholinergic effects that may be associated with poisoning include ileus, urinary retention, confusion, and postural hypertension.

Table 1. Mechanisms of toxicity of tricyclic antidepressants (adapted from Ref 1).

- Sodium channel blockade (membrane stabilising action or 'quinidine-like' effect)
- Anticholinergic activity at autonomic nerve endings and in the brain
- Inhibition of norepinephrine reuptake at nerve terminals
- Vascular α-adrenergic blockade

Cardiovascular effects. Tricyclics retard phase 0 cardiac depolarisation by inhibiting sodium channels. The delay in propagation of depolarisation in the atrioventricular (AV) node, His-Purkinje fibres and ventricular myocardium leads to prolongation of the PR and QRS interval (Fig 1). A right bundle branch block pattern may be seen, but second- or third-degree AV block is uncommon. In more severe poisoning, ventricular tachycardia can occur, especially in those with marked QRS prolongation or hypotension, and may degenerate into ventricular fibrillation.

Tricyclic antidepressants slow repolarisation and prolong the QT interval, predisposing to *torsade de pointes*. However this is uncommon; sinus tachycardia is usually the underlying rhythm in tricyclic poisoning, whereas *torsade de pointes* is a bradycardia or pause-dependent arrhythmia.

Hypotension results from a combination of diminished myocardial contractility and peripheral resistance. Refractory hypotension is a common cause of death.

Central nervous system effects. Severe neurological features include drowsiness, ataxia, hypertonia and hyperreflexia with extensor plantar responses. Respiratory depression and deepening coma may occur, especially when other CNS depressant substances have also been ingested. Severe agitation and delirium may be present, particularly during recovery.

Convulsions occur in more than 5% of cases and are more likely if there is QRS prolongation. Seizures may exacerbate hypotension and trigger ventricular arrhythmias by worsening acidosis and hypoxia.

Investigations

1 A *12-lead ECG* is essential. Prolongation of QRS interval predicts seizures (QRS >0.10 sec) and ventricular arrhythmias (QRS >0.16 sec).[2] A terminal R wave above 3 mm in lead aVR, or an R wave/S wave ratio of over 1.4 may be a better predictor than QRS