Commentary

An agenda for UK clinical pharmacology

Developing and delivering clinical toxicology in the UK National Health Service

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Clinical toxicology concerns the investigation, diagnosis and management of suspected poisoning. It is an important discipline because of the frequency of suspected poisoning, including drug overdose. In the UK, most episodes are managed by nonspecialists, with support provided online or by telephone from the National Poisons Information Service. Leadership and clinical support for this is provided by a small number of clinical toxicologists, who are almost invariably accredited specialists in clinical pharmacology and therapeutics. Priorities for maintaining and enhancing clinical toxicology as a subspeciality in the UK include:

- 1 Maintaining funding for poisons centres. This is essential in spite of current budgetary pressures.
- 2 Formal training in the discipline. The 1 year optional training module in clinical toxicology approved in 2011 as part of the clinical pharmacology and therapeutics curriculum represents important progress, but funding for appropriate programmes and accreditation for trainees from other relevant disciplines is needed. Arrangements for registration and revalidation are also required.
- 3 An improved evidence base for management of poisoning. Priority areas include continued surveillance of the epidemiology and outcomes of poisoning, including syndromic surveillance, more rapid characterization of the human toxicity of newly introduced medicines and better clinical evidence on use of antidotes and other treatments; for example, acetylcysteine and lipid emulsion therapy.

Introduction

Clinical toxicologists are physicians with detailed knowledge and experience of toxicology relevant to the investigation, diagnosis and management of people who have been exposed to potential toxins. Clinical toxicology is important because of the frequency of suspected poisoning requiring medical assessment, the large numbers of deaths that occur as a result of the effects of poisoning and the wide range of substances that can be involved. Clinical toxicology is concerned not only with direct clinical effects on individual patients but also with the impact of chemicals on the environment and the public health aspects of toxicology. Advice to Government and regulatory and international bodies has become an increasingly important role for the clinical toxicologist. In some countries (for example the USA), the term 'medical toxicologist' is the preferred term to describe clinical toxicologists who are physicians.

A substantial proportion of all cases of poisoning relate to therapeutic medications, especially in developed coun-

tries. Clinical pharmacologists are therefore well placed to develop expertise in clinical toxicology and, at least in the UK, most physicians with clinical toxicology responsibilities have specialist training in clinical pharmacology and therapeutics (CPT), usually with general internal medicine.

Background

The importance of clinical toxicology is underlined by the frequency of cases of poisoning or suspected poisoning that present to hospital. For example, in England during the 2009/2010 financial year, there were over 127 000 presentations to Accident & Emergency departments with suspected poisoning, of which drug overdose was a major contributor [1]. Although severe morbidity or mortality is uncommon in hospital, with only a few hundred deaths each year [2], considerably more deaths occur out of hospital; the total number of deaths annually owing to drug poisoning is about 3000 (Figure 1), and a similar number occur as a result of exposure to chemicals or gases [3].

Figure 1

Deaths related to drug poisoning in England and Wales, 1993–2009. Source: Office of National Statistics [3]

Substantial contributions to poisoning mortality come from deliberate poisoning, accidental exposures and recreational drug use. The most common drugs involved in fatal poisoning in England and Wales in recent years have been heroin and morphine, methadone, antidepressants, sedatives and paracetamol [3, 4]. Presentation to hospital with suspected poisoning is also common in children, especially boys aged 1–4 years. Most episodes do not result in morbidity, but there have been 15–45 deaths annually due to poisoning in children in recent years, a minority of which relate to medicines.

There are international differences in the patterns of poisoning. For example, paracetamol poisoning is more common in the UK than in most other developed nations. In developing countries, poisoning with therapeutic medications is less problematic, but envenomation and poisoning with pesticides, herbicides and other chemicals is much more common and carries a higher case fatality rate.

Organization of the management of poisoning in the UK

Most acute hospitals that admit patients in the UK do not employ a specialist clinical toxicologist. The significant workload associated with suspected poisoning is managed by clinicians from a range of disciplines, including emergency medicine, acute and general medicine, paediatrics, intensive care, anaesthetics, renal and liver medicine and occupational medicine. Owing to the frequency of self-harm in this context, specialists in psychiatry are also commonly involved. Most patients who present to hospital with poisoning come directly to the Emergency Department, from which they may be discharged if there is no acute medical risk, usually after a review by the Liaison Psychiatry or Crisis Teams if there is an element of self-

harm. A proportion of patients require admission for observation and/or treatment, which may take place in a short-stay ward in the Emergency Department or in an admissions or medical ward. Length of stay is generally very short, usually less than 24 h. Occasional patients require transfer to specialist services, including critical care or specialist wards, such as nephrology for dialysis or hepatology for management of liver failure, for example in the context of paracetamol overdose.

Role of poisons centres

Most episodes of poisoning are managed effectively by clinicians without specialist training in clinical toxicology, but they need information on the very large numbers of substances to which patients may have been exposed and the clinical effects that these might provoke, as well as advice on appropriate management strategies. This is the role of poisons centres, which in turn need clinical support to ensure that the advice provided by them is clinically appropriate.

Poisons centres have an important and proven role in supporting the management of the poisoned patient, preventing unnecessary hospital attendance or admission when there is a low risk from the suspected ingestion, facilitating early discharge from the Emergency Department and shorter hospital stays for those who are admitted. International evidence suggests that the resulting cost savings are substantial, making poisons centres highly cost-effective [5–8]. It is also likely that advice from poisons centres improves the quality of clinical management, resulting in better patient outcomes and reduced use of unnecessary investigations and treatments.

In the UK, poisons information is provided by the National Poisons Information Service (NPIS), which provides information and support to health professionals via its Internet database TOXBASE and a 24 h telephone service for use when online information is insufficient to manage the individual case. The service is currently commissioned by the Health Protection Agency, although arrangements will soon change, with the establishment of Public Health England. There are currently four poisons centres providing telephone information in the UK, in Birmingham, Cardiff, Edinburgh and Newcastle. The NPIS is available only to health professionals; the public are directed elsewhere, for example to NHS Direct in England and Wales, or to NHS 24 in Scotland, who may in turn seek advice from the NPIS.

Over the last decade there has been a sustained growth in requirement of online information via TOXBASE for supporting the care of poisoned patients; there were 1.3 million product accesses for TOXBASE in 2009–2010 and over the same period there has been a planned fall in telephone enquiries to 53 300 (Figure 2) [9].

Figure 2

Telephone enquiries and TOXBASE sessions from 2000 to 2009/10 (data for 2000–2003 by calendar year; thereafter, by financial year) [9]

Clinical toxicology in the UK

Clinical toxicologists in the UK are almost all clinical pharmacologists who have acquired specialist training by attachments to NPIS units or other centres of clinical toxicology expertise. All have a part-time commitment to clinical toxicology and in addition have other roles in internal medicine and/or academia. All are involved in the management of poisoned patients in their own hospitals, which is essential for maintaining their expertise. Their major funded clinical toxicology role is in providing clinical support for poisons centres, including clinical input to information held on TOXBASE, acting as a source of advice for episodes of difficult or unusual poisoning. In addition, they are involved in arrangements for antidotes, including appropriate use and supply, advice on the appropriate use and interpretation of laboratory assays relevant to toxicology, teaching NHS staff about appropriate management of poisoned patients and performing research directed at improving the care of poisoned patients. Clinical toxicologists also provide advice to official organizations, including the Department of Health, the Medicines and Healthcare products Regulatory Agency, the Home Office, the Advisory Council on the Misuse of Drugs and the National Institute for Health and Clinical Excellence. This results in a varied and rewarding job, with a balance of clinical, managerial and academic components.

Currently, there are 16 consultant clinical toxicologists working in NPIS units or providing clinical support at a consultant level to the service, and the Health Protection Agency invests just over 60 programmed activities (or six whole-time equivalents) in consultant support for NPIS, including 24 h consultant cover across the UK.

In the UK, the environmental and population aspects of toxicology, including management of chemical incidents, are generally dealt with by specialists in public health, while toxicity arising from exposure in the workplace may

be dealt with by specialists in occupational health medicine. There is considerable overlap in expertise, and NPIS-associated clinical toxicologists are involved in planning for chemical, biological, radiological or nuclear incidents and providing outpatient clinics for patients with suspected chronic toxicity, including occupational exposure.

Developing clinical toxicology

Enormous progress has been made in the establishment of careers in clinical toxicology over the last decade, catalysed by the formal network arrangements for the NPIS, instituted by the Health Protection Agency as part of its commissioning arrangements. Clinical toxicologists in the UK meet regularly, are involved together in continuing professional development, and often discuss clinical issues and policy. However, there is still much to be done to maintain and develop the specialty, such as the introduction of formal and appropriately accredited training programmes and arrangements for registration and revalidation. There is also a need to improve the evidence base on which clinical decisions are made. It is also essential that the current funding arrangements for poisons centres and their associated clinical toxicology support be maintained in the face of budgetary pressures. Two areas deserve particular consideration, namely training and research.

Training

In the absence of a specific training programme in clinical toxicology, training in the UK has been informal, with no traditional mechanism for specialist accreditation. However, many specialist training programmes have some clinical toxicology component. For example, it is appropriate that core medical training has a significant amount of basic clinical toxicology contained within it. Training in clinical pharmacology and therapeutics also has

Figure 3

Structure of the basic training programme in clinical pharmacology and therapeutics (CPT), showing how clinical toxicology training could be incorporated. Abbreviations: CCT, certificate of completion of training; FY2, second foundation year; GIM, general (internal) medicine; and MRCP, Membership of the Royal College of Physicians

knowledge, skills and behaviour outcomes relating to clinical toxicology and drug overdose, but even in this discipline, closely allied as it is to clinical toxicology, the level of detail required is not sufficient to allow an individual to achieve full training to practise independently as a consultant clinical toxicologist without additional training experience.

In the past, there has been an ambition to develop a separate training programme for clinical toxicology, analogous to the US fellowship programmes in medical toxicology. A 5 year training programme was developed before the initiation of *Modernising Medical Careers* (http://www.mmc.nhs.uk/medical_education/about_modernising_medical_care.aspx). However, this was not adopted, and such a training programme is unlikely to be viable in the future owing to the low numbers of consultant clinical toxicologists for whom funding is available.

A better alternative is to develop clinical toxicology training as optional modules that might be taken as part of specialist training in appropriate disciplines, such as clinical pharmacology and therapeutics, acute medicine, emergency medicine, paediatrics or public health. This would involve an additional training programme of 1 or 2 years. Using CPT training as an example, an optional special module in clinical toxicology could form part of core training or be provided as an additional period of out-of-programme training during or at the end of the training programme (Figure 3). Trainees completing this optional module would be able to demonstrate that they had met its educational objectives using their e-portfolio.

For clinical toxicology modules to remain viable and to maximize their impact on the quality of care, it is important that these are accredited by other relevant training programmes and made available to their trainees. This would

roll out advanced training much more widely, with the possibility of a higher proportion of acute NHS Trusts having a consultant with additional training in clinical toxicology. This might allow, for example, many Accident & Emergency departments to have at least one consultant with clinical toxicology training. This raises the risk to the speciality of CPT that specialist posts, for example working with NPIS, might become open to graduates of other training programmes who have completed the module. However, the benefits of this approach, involving much more widespread training with resultant improved patient care in clinical toxicology, are much more important. The influence and visibility of CPT would be enhanced by provision of a training programme attractive to a wide range of trainees.

Considerable progress has already been made in establishing a specialist module. A training curriculum has been approved by the CPT specialist advisory committee and has been endorsed by the General Medical Council. The next challenge is to persuade postgraduate deans to fund programmes; this will be more challenging when it involves a move between training programmes or deaneries.

There is, nevertheless, room for optimism about funding, with a short training programme in Edinburgh already advertised and filled by a trainee in emergency medicine. Recently, a toxicology training module has also been funded by the Health Protection Agency, although this has a predominantly public health orientation with a limited clinical component, so graduates of this programme will be prepared to work in public health rather than in clinical toxicology.

Research

A second priority is the establishment of improved clinical research in clinical toxicology. This is underscored by the

Table 1

The 10 most common poisonings in the UK (data from Nottingham, 2006–2007) [11]

Position	Drug	Number of times used in overdose	Percentage of overdoses involving the drug	Percentage of all drugs used in overdoses
1	Paracetamol	679	42.5	25.1
2	Ibuprofen	277	17.3	10.2
3	Citalopram	107	6.7	4.0
4	Zopiclone	92	5.8	3.4
5	Fluoxetine	84	5.3	3.1
6	Co-codamol	81	5.1	3.0
7	Aspirin	79	4.9	2.9
8	Diazepam	78	4.9	2.9
9	Codeine	61	3.8	2.3
10	Diclofenac	60	3.8	2.3

weakness of the evidence base to inform the management of many poisons. Historically, there have been several examples of treatments used widely for treatment of poisoning that have subsequently been found to be of little benefit and sometimes to be hazardous. For example, gastric lavage was used extensively in the past, but evidence suggests an unfavourable benefit-to-harm balance for most patients, and the method has almost disappeared from clinical use in developed countries. Although often replaced by the use of activated charcoal, this technique is now also restricted to subgroups of patients who present early after clinically important episodes of poisoning; even in these circumstances, data emerging from clinical trials have not provided robust evidence of benefit [10].

There are many areas in which further research would be welcome, but three specific examples are given here.

First, there is a need for higher quality surveillance of the clinical effects of poisoning with newly introduced agents, including therapeutic medications. This would allow more rapid characterization of their clinical effects and provide more evidence of differential toxicity in humans. Better information on prevalent recreational drugs associated with clinical toxicity would also be obtained. Improved syndromic surveillance also offers better opportunities for early identification of the unusual patterns of poisoning that might be associated with occult chemical releases.

Second, paracetamol poisoning remains important, because of its frequency in the UK (Table 1) [11]. Although a highly effective antidote is used in thousands of patients each year, in the form of intravenous acetylcysteine, the optimal dose and administration schedule remain uncertain, because dose-ranging studies were never performed. The current licensed dose, although highly effective in preventing hepatotoxicity, is commonly associated with adverse reactions that might be avoided by less intensive infusion schedules. This might also allow use of the antidote in people at lower risk of hepatotoxicity, preventing

the occasional episodes of fulminant hepatic failure that occur rarely. Clinical trials of alternative administration schedules are badly needed, but significant investment is required, because of the substantial sample sizes needed to demonstrate improved tolerability and equivalent efficacy to the licensed regimen.

The third example is the use of lipid emulsion to treat poisoning with highly lipid-soluble agents. Persuasive case reports of benefits in individuals poisoned with a range of agents have been published; for example, local anaesthetics, for which the method is increasingly being adopted. This has stimulated enthusiasm for the use of lipid emulsion for poisoning with a wider range of products, with the risk of selective publication of cases with good outcomes. Higher quality research is needed, including randomized clinical trials, before the method should become commonplace.

It has been challenging to obtain funding for research in clinical toxicology in spite of the public health importance, perhaps in part owing to unsympathetic perceptions of the patients involved. There are signs of progress in this area, and significant grants have recently been obtained, including support for clinical trials to address some of the key issues facing clinical toxicologists. One particular challenge of research in clinical toxicology is the frequency with which patients present during unsocial hours. A round-the-clock research infrastructure is needed to maximize recruitment into clinical trials.

Conclusions

Although the available number of consultants is limited, clinical toxicology offers exciting and varied career opportunities, and it is appropriate for the subspecialty in the UK to remain firmly linked to CPT. There are mutual benefits, with clinical toxicology providing a limited number of career opportunities for clinical pharmacologists in

training and CPT offering an infrastructure on which to base training accreditation and revalidation into the future.

Competing Interests

There are no competing interests to declare.

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