



With a **new body formed** that is dedicated to **clinical toxicology**, we ask what comprises the discipline and why it has historically been **under represented**.

As far back as 1500BC, it was documented that hemlock, opium and certain metals could poison enemies and be deployed in state executions.

In the well-known example of Plato's account of the death – by drinking hemlock – of Socrates in 399BC, the doomed Senator is advised: “You have only to drink this and to walk about until your legs feel heavy, and then lie down; and it will act of itself.”

The discipline of toxicology emerged during the Renaissance and the Age of Enlightenment. For example, Paracelsus (1493–1541) recognised the importance of a dose-response relationship, observing: “All substances are poisons... The right dose differentiates a poison from a remedy.” And in 1814 *Traité des poisons* [*Treatise of Poisons*] by Paris-based Dr Joseph Orfila (1787–1853) – regarded by many as the father of modern toxicology – was published. Orfila's lectures were attended by the University of Edinburgh's Dr Robert Christison (1797–1882), and on

returning there from Paris, he was appointed in 1822 to the Regius Chair of Medical Jurisprudence and Medical Police (public health).

What is clinical toxicology?

Modern toxicology encompasses three distinct specialties: environmental, forensic and clinical. Environmental toxicology focuses mainly on the harmful effects of chemicals encountered in the atmosphere, the food chain, or occupational/recreational environments, whereas forensic toxicology addresses medico-legal aspects of the harmful effects of chemicals or poisons.

Clinical toxicology, however, is concerned with “the toxic effect of agents whose intent is to treat, ameliorate, modify, or prevent disease states, or the effect of drugs which, at one time, were intended to be used as such.”

Dr Stephen Morley is a medical consultant who specialises in clinical chemistry and toxicology at University Hospital Leicester. As well as running a large clinical and

post-mortem toxicology laboratory, he also manages patients who present with acute poisonings. “Clinical toxicology,” says Stephen, “is a very broad church within, primarily, clinical biochemistry, but with cross-over in haematology, microbiology and immunology. It covers drug assays as well as routine biochemistry and haematology tests, such as liver function tests and full blood counts.”

Stephen explains that drug assays range from those that are run in every acute hospital – such as paracetamol, salicylate and digoxin – to drugs that require therapeutic drug monitoring (TDM); these include immunosuppressants, anti-coagulants, and anti-microbial/anti-fungal drugs. “There are also more esoteric drugs,” he points out, “that require measurement in overdose cases, but are not available in every hospital.

Examples include ethylene glycol and trace elements/metals; and now there is the evolving field of drug compliance, such as anti-hypertensive drug compliance.”



Clinical toxicology and other disciplines

As Stephen suggests, clinical toxicology extends into other laboratory disciplines, even those in which drug measurement is not a standard procedure: "For instance, the routine laboratory must be able to perform tests, such as those for liver function, international normalised ratio for paracetamol, glucose for insulin overdose, and full blood counts for clozapine monitoring."

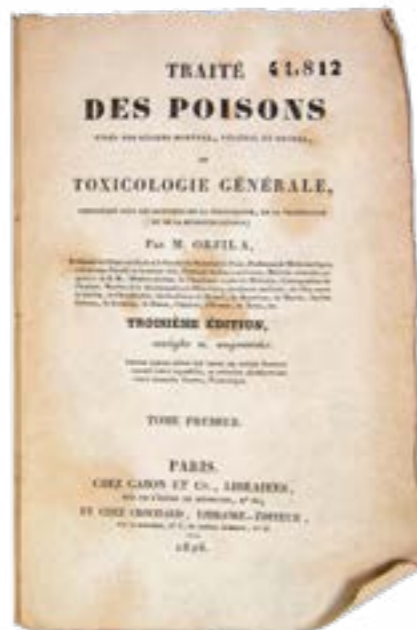
Stephen also observes, however, that although clinical toxicology may be a small part of every clinical laboratory, the discipline is as large as, say, microbiology with regard to the number of patients and staff who may be influenced by the test results: "We are working alongside the National Poisons Information Service (NPIS) to ensure that laboratory testing is fit for purpose, and as part of this we are in the process of updating the NPIS/ Association for Clinical Biochemistry and Laboratory Medicine (ACB) guidelines on the laboratory provision for poisoned patients."

Representation of clinical toxicology

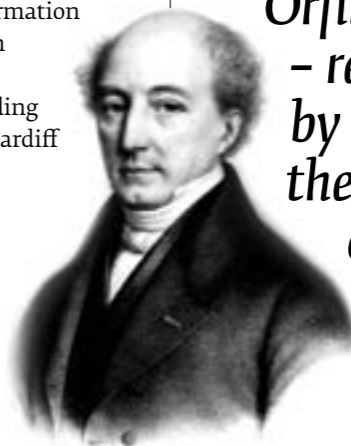
In response to increasing incidents of poisoning in Britain, the 1962 Atkins Report recommended the establishment of poisoning treatment centres and poisons information services. The following year saw the establishment of the Scottish Poisons Information Bureau in Edinburgh, which would later form part of an informal UK network providing similar services in Belfast, Cardiff and London.

Following a review and subsequent management changes in 1996 and 2005, respectively, the UK NPIS now operates from four units in Birmingham, Cardiff, Edinburgh and Newcastle.

A Toxicology Club, which ran from 1971 to 1979, was succeeded by the British Toxicology Society. Its aim is to facilitate discussion of toxicology-related issues throughout all areas of this wide-ranging discipline, and today it has around 700 members.



In 1814 *Traité des poisons* [Treatise of Poisons] by Paris-based Dr Joseph Orfila (1787–1853) – regarded by many as the father of modern toxicology – was published.



Historically, however, there has been no single organisation dedicated to clinical toxicology. But now, to fill this void, a new organisation of clinical toxicology professionals – the Clinical Toxicology Network UK (CTNUK) – has been formed.

CTNUK

One of the organisation's founders is consultant clinical scientist Dr Alexander Lawson, who specialises in clinical biochemistry and toxicology. Alex, based at Heartlands Hospital, University Hospitals Birmingham, runs a clinical and post-mortem toxicology service and has extensive experience in the development of assays for drug screening and quantitation using several chromatographic techniques with and without mass spectrometry.

When was CTNUK established? "The idea that a group dedicated to the laboratory aspects of clinical toxicology should be established has been discussed between several professionals working in this field for a few years," Alex explains. "We organised the first meeting in February 2018 and have had four more since then. Our meetings are open to all NHS staff working within the field of clinical toxicology. For more information, or if you would like to attend future meetings, please e-mail alexander.lawson@heartofengland.nhs.uk."

Why has clinical toxicology been previously under-represented? "Firstly," says Alex, "there are some organisations dedicated to the field of analytical toxicology – such as the London Toxicology Group and the UK and Ireland Association for Forensic Toxicology – but the focus of these groups is typically targeted at workplace or forensic testing and interpretation, with little time given to the types of clinical analysis routinely performed in NHS laboratories."

Alex explains that clinical toxicology in the NHS may be represented at more general clinical chemistry meetings, such as the IBMS congress or the ACB Focus

CTNUK: CURRENT ISSUES OF INTEREST

Topics covered at recent CTNUK meetings have included:

- Cut-offs and methods currently in use for drugs of abuse screening: are these appropriate for clinical use and can they be harmonised UK-wide?
- Coverage of urgent toxicology services listed in the NPIS guidelines
- Evidence behind critical limits for TDM
- The absence of relevant EQA services for important toxicology tests suggest topics for investigation to major research bodies: for example, the National Institute for Healthcare Research and the Human Tissue Authority
- Advise equipment manufacturers on key issues for toxicology and TDM in laboratory medicine
- Provide input into syllabus development in training in laboratory medicine (for example, Scientist Training Programme and FRCPath) and to promote and organise educational/continuous professional development activities relevant to clinical toxicology.

meeting, but is rarely given top billing, with discussion limited to more general aspects of toxicology: "In general, these groups are not chaired by professionals working within clinical toxicology," he comments.

Alex's second point is that in routine laboratories many people are involved with clinical toxicology but perhaps don't realise it, and if they want to learn more, they may not know who to speak to or which meeting to attend. He further notes that although it may seem specialised, most laboratory professionals working within clinical chemistry laboratories will have acquired some experience of clinical toxicology, whether through performing routine biochemistry or haematology tests on patients who have taken an overdose; measuring anti-epileptic drugs, such as phenytoin to manage their treatment;

or screening for drugs of abuse in urine: "We want to encourage staff who take an interest in these areas to attend our meetings," Alex says, "to participate in discussions, share their experiences and take back useful information to their laboratories. Biomedical scientists should have invaluable experience of the numerous analytical issues which may be affecting aspects of their service provision."

Stephen, who is the present Chair of CTNUK, agrees: "The most important message is that CTNUK is for all laboratory staff, from every hospital, and biomedical science staff are likely to be those carrying out the analyses, so they have the experience of what works and what doesn't work on a practical basis. I would

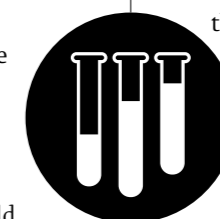
encourage as many of them as possible to take an interest in CTNUK."

Providing analytical and interpretative toxicology

What are the main issues that are relevant to the provision of analytical and interpretative toxicology? Alex explains: "In some respects the same things apply to analytical and interpretative toxicology as apply to any aspect of laboratory medicine. We need to ensure that the services offered by laboratories across the UK are of the highest quality. In that respect, one of the aims of CTNUK is to produce and promote consensus guidance for best practice in pre-analytical, analytical and post-analytical aspects of toxicology."



"Historically there has been no single organisation dedicated to clinical toxicology"



Alex also identifies a need to ensure that there are sufficient resources available for the delivery of urgent, specialised testing for poisoned patients – such as those poisoned by ethylene glycol – and that clinicians, in collaboration with the NPIS, are aware of the most appropriate use of these resources: “All laboratories are concerned with the UK Accreditation Service, and as such we need to identify specialised tests which may need External Quality Assessment (EQA) schemes, or similar, in order to gain accreditation. We also want to learn from each other, with discussion of interesting cases, emerging drug threats – such as New Psychoactive Substances (NPS) – and analytical issues.”

Nerve agent attacks and new threats

Two further topics under recent discussion by CTNUK members were the emergency provision of cholinesterase measurement in cases of nerve agent attacks, and emerging new threats and interesting cases.

Stephen expanded on these aspects. “As far as the role of cholinesterase management following nerve agent attacks is concerned,” he notes, “NHS laboratories are at present not in a



AIMS OF CTNUK

CTNUK aims to:

- Produce and promote consensus guidance for best practice, citing evidence where available, in pre-analytical, analytical and post-analytical aspects of toxicology and TDM in laboratory medicine
- Advise on the most effective use of existing tests and the likely utility of new tests
- Provide information for non-specialist laboratories on the selection, application and interpretation of core tests in toxicology and TDM.

position to undertake testing if there were to be a mass nerve agent attack. The service is primarily set up to support those families where there are problems with anaesthetics, although it can provide support when one-off poisonings occur.”


In terms of emerging threats, one issue of primary importance that concerns Stephen is that, with the movement of post-mortem forensic toxicology to

private providers, many of the larger centres are investing less in their toxicology services: “There is therefore a potential lack of individuals who are trained in clinical toxicology.”

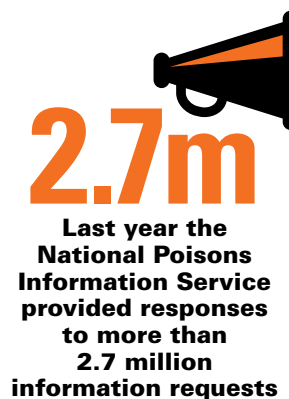
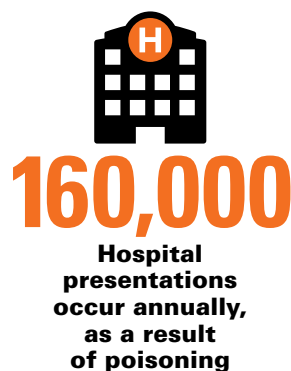
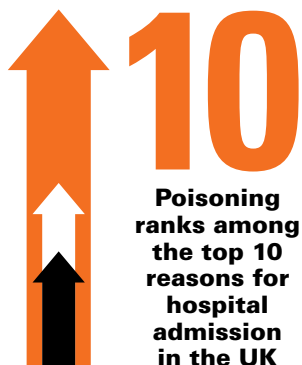
From a clinical perspective, one of the biggest concerns that Stephen has is the ever-changing NPS market: “No NHS laboratory can support or claim to be able to remain up to date with the drugs being used, and so, testing is not happening in the acute scenarios. Although here is a nationally-funded project looking at NPS, the uptake from Accident and Emergency departments to take samples is very poor, so the epidemiology of the problem is not understood.”


Continued evolution

The field of clinical toxicology has no shortage of interesting cases. Stephen emphasises that the cases of importance are those which change future practice: “An example of this is a child who was suffering with PICA, a psychological disorder where individuals develop an appetite for non-nutritive substances such as ice, hair, paint and soil. The child was eating paint from the bannisters in his house, and he died from lead poisoning. Although the house had been painted recently, the process had been to just re-paint over existing layers, and, as the house was Victorian, these layers dated back to before lead was banned from paint. The hospital changed its practice so that every child who presents with PICA is screened for metal toxicity, and several children have been identified as having high concentrations of lead.”

Finally, ongoing developments in areas such as molecular-, nano- and computational-toxicology, combined with the establishment of groups such as CTNUK, ensure the continued evolution of clinical toxicology. 

POISONING STATISTICS



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