BJCP British Journal of Clinical Pharmacology

DOI:10.1111/j.1365-2125.2012.04244.x

Commentary

An agenda for UK clinical pharmacology

UK medicines policy: the role of clinical pharmacologists

David J. Webb

Queen's Medical Research Institute, The University of Edinburgh, Room E3.22, Edinburgh EH16 4TJ, UK

Clinical pharmacologists are the only medical specialists whose training focuses specifically on the safe, effective and cost-effective use of medicines, underpinned by an understanding of drug discovery, drug regulation, pharmacology, translational medicine and the performance of clinical trials. This unique perspective has allowed them to provide expertise and leadership in medicines regulation, medicines policy, health technology assessment and drug pricing. Clinical pharmacologists assisted in the creation of the Committee on Safety of Medicines (now the Commission on Human Medicines), the Yellow Card Scheme, the National Institute of Health and Clinical Excellence (NICE) and related organizations in Scotland and Wales, and contributed to clinical guidelines (through the Scottish Intercollegiate Guidelines Network) and the British National Formulary. Their research work has contributed substantially, through translational medicine and therapeutics, to the development of new medicines and, as a result, creation of health and wealth in the UK. Their work in medicines policy has served to protect patients from harms associated with the use of medicines. A reduction in the number of able junior doctors attracted to a career in clinical pharmacology, a reduction in the number of training posts, and an ageing population of academic trainers, puts the future of the specialty, and its contribution to patient safety and UK wealth creation, at substantial risk. Urgent measures are needed to convince the NHS and government that these essential skills should be protected and nurtured.

Introduction

In this article, I describe the roles played by clinical pharmacologists in informing and influencing national medicines policy. At the population level, and in relation to prescribing guidance to aid treatment of individual patients, clinical pharmacologists aim to promote the rational use of medicines. Using the right medicine, at the right dose, at the right time, in the right patient, and discontinuing medicines promptly when they are no longer needed, serves to maximize the balance between benefit and harms in relation to the use of medicines, and to improve patient safety. Clinical pharmacologists also take an interest in how medication errors occur and how to prevent them, and how to use medicines in a cost-effective and clinically effective manner. With this focus on medicines, specialists in clinical pharmacology have played a central role in creating and developing UK medicines policy in a number of ways, both at local and national level, since the creation of the discipline after the Second World War.

Here I focus on some of the major ways in which clinical pharmacologists are involved in national policy making. Whereas drug regulation (licensing and pricing) is a reserved matter, which is addressed by government on behalf of the UK as a whole, some aspects of health (and so medicines) policy have been devolved to Northern Ireland, Scotland and Wales, where different approaches have sometimes been used. I shall mention these when they are relevant.

Medicines' regulation

Following the thalidomide tragedy of the late 1950s, the Dunlop Committee was established in 1963, under the chairmanship of Sir Derrick Dunlop, Christison Professor of Clinical Pharmacology in Edinburgh, to examine the control and introduction of new medicines in the UK. Subsequently, based on his report to the Department of Health, a Committee on Safety of Drugs was established under his chairmanship [1]. Initially a voluntary system, in 1971 this committee was replaced by a statutory system under the Medicines Act of 1968, which established the Medicines Commission. The Commission, under Section 4 of the Act, established the Committee on Safety of

Medicines (CSM) which, for some 40 years, advised the UK licensing authority on the quality, efficacy and safety of medicines. The Medicines Commission and the CSM were, in turn, replaced by the Commission on Human Medicines (CHM), in 2005 which combines the functions of the two previous advisory bodies.

The creation of the CSM was associated with the recognition that there was a need for specially trained doctors in academic departments of medicine (clinical pharmacologists) to teach about the efficacy and safety of medicines, and for specially trained doctors in pharmaceutical companies to assist in the development of new medicines (pharmaceutical physicians). The CHM is now part of the Medicines and Healthcare products Regulatory Agency (MHRA), which was formed in 2003 from the merger of the older Medicines Control Agency and Medical Devices Agency.

The MHRA is the government agency responsible for the assessment and authorization of medicinal products for sale in the UK. It also operates post-marketing surveillance for reporting, monitoring and investigating adverse reactions to medicines and incidents with medical devices. Its role is to promote the safe use of medicines and devices. The Chairman of the MHRA, Professor Sir Alasdair Breckenridge, and its Chief Executive, Professor Sir Kent Woods, are both clinical pharmacologists. It is entirely appropriate that clinical pharmacologists hold such key positions in the regulation of medicines and healthcare products, because of the focus of the clinical specialty on the safe and effective use of medicines. Indeed, Kent Woods, who has been a European Medicines Agency (EMA) board member since 2004, has recently been elected as Chair of the management board of the EMA, providing wider influence on medicines regulation in Europe.

In the promotion of patient safety, the MHRA supports the CHM and the British Pharmacopeia Commission and hosts the General Practice Research Database (GPRD: http://www.gprd.com). It also hosts a number of other expert advisory bodies. Important among these is the Pharmacovigilance Expert Advisory Group, chaired by Professor Munir Pirmohamed, and the Herbal Medicines Advisory Committee, chaired by Professor Philip Routledge; both clinical pharmacologists. Clinical pharmacologists are also represented on the Expert Advisory Group on Clinical Trials and on the Independent Scientific Advisory Committee (ISAC) for MHRA database research. Clinical pharmacologists have also played important roles in developing the broader use of the GPRD to support research on the safety of medicines.

The MHRA and CHM together support the Yellow Card Scheme (yellowcard.mhra.gov.uk) for pharmacovigilance, introduced in 1964 after the thalidomide tragedy highlighted the urgent need for routine monitoring of medicines. The scheme receives more than 20 000 reports of suspected adverse drug reactions each year from healthcare professionals and, more recently, from patients. It also contributes to the WHO's database of information about adverse drug reactions, housed at the Uppsala Monitoring Centre. There are four regional Yellow Card Centres in the UK (in Birmingham, Cardiff, Edinburgh and Newcastle), with responsibility for education and research concerned with Yellow Card reporting. Each of the Centres is run by a clinical pharmacologist: Professors Robin Ferner, Philip Routledge, Nick Bateman and Simon Thomas, respectively. These groups also run the National Poisons Information Service (http://www.npis.org), providing expert clinical advice in the management of complex poisoning. In this work they are supported by Toxbase (http://www.toxbase.org), an online database, developed and run by the clinical pharmacology team at the Royal Infirmary of Edinburgh, which provides information for registered users about the appropriate management of poisoning with over 14 000 medicines or other hazardous substances.

Cost-effectiveness assessment

Supported by an Audit Commission report in England highlighting an NHS drugs budget rising well above the rate of inflation [2], and with politicians' concerns about so-called 'postcode' prescribing (by which a new and expensive medicine might be made available in one area but not in another close by), the National Institute for Health and Clinical Excellence (NICE: http://www.nice.org.uk) was established in 1999. The aim was to undertake health technology assessment (HTA) to establish the cost-effectiveness of new treatments and create clinical guidelines to inform clinicians on best practice [3]. The Scottish Medicines Consortium (SMC) was established in Scotland in 2001 and the All Wales Medicines Strategy Group in Wales (AWMSG) in 2002. All of these institutions undertake HTA and were created and led from the outset by clinical pharmacologists: Professor Sir Michael Rawlins, Professor David Lawson and Professor Philip Routledge, respectively. Over the last 10 years, a number of other senior clinical pharmacologists have held key roles within these organizations, and clinical pharmacologists provide key leadership, based on their strengths in assessing the safety, efficacy and clinical effectiveness of new agents, coupled with a broad understanding of clinical medicine and an ability to make complex clinical judgements. Most of these individuals have not started with expertise in health economics, but have learned about the strengths and limitations of this important area of applied science, to ensure that they can fully inform clinical judgements.

In England, NICE reviews medicines that are referred by the health ministers, often examining broader disease areas and focusing on diseases and clinical areas recognized as being of major importance for health. Its reviews take around 18 months to complete. Because of concerns about this timescale, which does not necessarily start at

the time of the UK drug launch, NICE has now introduced, for a selected group of technologies (mostly drugs for cancer treatment), a single technology assessment (STA) process that is more streamlined and of shorter duration. By contrast, the SMC looks at all new medicines, all new formulations of existing medicines and all major new indications for existing medicines, aiming to do so within 3–4 months of launch. This may have the benefit of shaping rather than changing prescribing behaviour, and has proved an extremely cost-effective process for assessing new drugs, in large part because the submission comes from the manufacturer, who bears the burden for making the case for clinical and cost-effectiveness [4]. The AWMSG largely focuses on agents that are not reviewed by NICE. Thus, the activities of all of these bodies can be seen as complementary. The SMC provides an early view, which can be refined with the passage of time, allowing the growth of a larger evidence base, so that a new drug can be seen in the context of broader disease management. The decisions that these groups have taken have been broadly similar, based on similar thresholds for acceptable cost per quality adjusted life year (QALY), and they benchmark well against other international organizations that undertake HTA assessments of new medicines.

In general, these initiatives have been well received, or at least are becoming better accepted, by physicians. There has been a growing recognition that prescribing autonomy is no longer appropriate, and that we have to use NHS funds wisely, effectively and cost-effectively, based on the available evidence [5]. Indeed, much of the additional cost of new medicines at around the time that NICE, the SMC and the AWMSG were established had been taken up by relatively expensive me-too agents, rather than in meeting the cost of developing drugs that provide major innovation or that meet a major clinical need [6], and a curb on this spending would seem justifiable. From a politician's point of view, the problem of 'postcode' prescribing has largely disappeared as a major media issue since the creation of these bodies.

Pharmaceutical price regulation

For more than 50 years the government has run a Pharmaceutical Price Regulation Scheme (PPRS), a pharmaceutical industry profit- and price-control system, which, it can be argued, has sustained a large and thriving body of pharmaceutical research in the UK [7]. Following an Office of Fair Trading (OFT) Market Study on the PPRS [8, 9], there has been a focus on a future policy of 'value-based pricing', in which the price of a drug is dictated by the value it offers to patients. Such a scheme will allow drugs that provide sufficient value to be prescribed by clinicians for their patients, whenever they are justified clinically. In such a scheme, agents that give good value for money would be supported, whereas others that come at too high a price for the value offered would be the subject of discussion between government and the relevant pharmaceutical company about a reasonable price that would offer acceptable value for money. The OFT and the Government have proposed that the health technology bodies (AWMSG, NICE and SMC) would be integrally involved in the process of assessment of value for money (linked to cost per QALY) [10]. Although health economic assessment will play a key part in this process, decisions will undoubtedly require complex clinical and scientific judgements to be made. It is likely that clinical pharmacologists will continue to play a central function in this process for the foreseeable future.

Prescribing guidance

Another key area of medicines policy is prescribing guidance. Perhaps the most important piece of work in this area has been the British National Formulary (BNF: http://www.bnf.org), a joint publication of the British Medical Association and the Royal Pharmaceutical Society), first issued at the birth of the health service in 1948, and a direct descendent of the National War Formulary (created in 1939) [11]. The BNF provides the most influential and authoritative advice on prescribing in the UK. It is widely used by physicians and is often described as a therapeutic 'bible'. Until white coats were abandoned, it was usually found in every junior doctor's pocket and copies are still within reach on hospital wards and on doctors' desks. The BNF provides UK healthcare professionals with the key information needed to prescribe all of the medicines currently available in the NHS, with authoritative and practical information on the selection and clinical use of medicines in a clear, concise and accessible manner. Indeed, it is widely recognized internationally as a key medical and pharmaceutical reference text.

The BNF is widely used not only by doctors in primary care and hospital settings, but also by a range of other healthcare professionals, including dentists, nurses and pharmacists, and find it a useful source of advice, along with patients and coroners. It provides highly relevant information, including indications, contraindications, adverse reactions, doses and legal classification, together with the names of available proprietary and generic formulations, all accompanied by an indication of price. It now also mentions NICE, the SMC and other guidance and guidelines. Importantly, the BNF complements local formularies, which indicate the preferred drugs used in a particular setting, and is now available in various electronic forms as well as in the paper copy that is issued twice a year. There is now also a BNF for Children, published annually, and there have been editions focused particularly on nurse prescribers.

Clinical pharmacologists have played key roles in creating and developing the BNF, and its Joint Formulary

Committee, which includes a number of clinical pharmacologists, has always been chaired by a clinical pharmacologist, currently Dr Derek Waller. Although the BNF is likely to have to move with the times, and will become increasingly used in electronic rather than paper form, its contents are likely to remain at the forefront of prescribing guidance, and it represents an excellent example of very effective collaboration between pharmacists and clinical pharmacologists.

Broader prescribing guidance is provided in the form of clinical guidelines, covering the management of diseases and therapeutic areas. The first major development in this area was the creation of the Scottish Intercollegiate Guidelines Network (SIGN: http://www.sign.ac.uk) in Scotland. SIGN was established in 1993, through an initiative led by an Aberdeen clinical pharmacologist, Professor James Petrie. Its objective was to improve the quality of healthcare for patients in Scotland, by reducing variations in practice and outcomes, through the development and dissemination of national clinical guidelines containing recommendations for effective practice based on current best evidence. SIGN has delivered a programme of evidence-based clinical guidelines covering a wide range of topics, many related to the NHS priority areas of cancer, cardiovascular disease and mental health. These guidelines are derived from systematic reviews of the scientific literature and are designed as vehicles for accelerating the translation of new knowledge into action. Their success has spawned the development of many similar guidelines groups, the largest of which in the UK is part of NICE, and initiated by a clinical pharmacologist, Professor Sir Michael Rawlins. The two organizations share information and work together to produce complementary work programmes. NICE has a very substantial work programme, which also covers other areas, such as HTA and public health, including guidance on health promotion and avoidance of ill health. NICE, perhaps because of its remit in HTA, was importantly the first to incorporate evaluations of cost-effectiveness into its appraisals.

A perspective

It is clear that the training that clinical pharmacologists undergo, and its focus on the safe and effective use of medicines, provides this group of specialists with a particular set of skills that are crucial to maintaining and developing UK medicines policy, and there is little doubt that these skills are valued by government. Currently, however, clinical pharmacology is contracting [12], and this raises the concern that core expertise may be lost if the specialty contracts further. It would be a disaster if the contribution of clinical pharmacologists to patient safety, and appropriate and cost-effective prescribing, is only fully recognized at a point when it is hard to reverse the loss of critical mass of clinical pharmacologists needed to train the next generation. It is crucial that clinical pharmacologists use every opportunity to make the case for the critical work that clinical pharmacologists undertake on behalf of the NHS in the UK [13, 14].

Competing Interests

There are no competing interests to declare.

REFERENCES

1 Cuthbert MF. Control of new drugs in the United Kingdom. Agents Actions 1978; 8: 410–2.

2 Audit Commission. A spoonful of sugar: medicines management in UK hospitals. December 2001. Available at http://www.audit-commission.gov.uk/SiteCollection Documents/AuditCommissionReports/NationalStudies/ nrspoonfulsugar.pdf (last accessed 16 March 2012).

3 Rawlins MD. The decade of NICE. Lancet 2009; 374: 351–2.

4 Dear J, O'Dowd C, Timoney A, Paterson KR, Webb DJ. Scottish Medicines Consortium: an overview of rapid new drug assessment in Scotland. Scot Med J 2007; 52: 20–6.

5 BMA Board of Science. Evidence-based prescribing. Science and Education Department, British Medical Association. May 2007. Available at http://www.bma.org.uk/health_ promotion_ethics/drugs_prescribing/evidencebased prescribing.jsp (last accessed 16 March 2012).

6 Morgan SG, Bassett KL, Wright JM, Evans RG, Barer ML, Caetano PA, Black CD. 'Breakthrough' drugs and growth in expenditure on prescription drugs in Canada. BMJ 2005; 331: 815–6.

7 Pharmaceutical Price Regulation Scheme: Third Report to Parliament 1999. Available at http://www.publications. doh.gov.uk/pub/docs/doh/pprs3.pdf (last accessed 16 March 2012).

8 UK Office of Fair Trading. The Pharmaceutical Price Regulation Scheme: an OFT market study. February 2007. Available at http://www.oft.gov.uk/shared_oft/reports/ comp_policy/oft885.pdf (last accessed 16 March 2012).

9 Webb DJ, Walker A. Value based pricing of drugs in the UK. Lancet 2007; 369: 1415–6.

10 Webb DJ. Value-based medicine pricing: NICE work? Lancet 2011; 377: 1552–3.

11 Wade OL. British National Formulary: its birth, death, and rebirth. BMJ 1993; 306: 1051–4.

12 Maxwell SRM, Webb DJ. Clinical pharmacology – too young to die? Lancet 2006; 367: 799–800.

13 Aronson JK. Clinical pharmacology and therapeutics in the UK: a great instauration. Br J Clin Pharmacol 2010; 69: 111–7.

14 Aronson JK. What do clinical pharmacologists do? A questionnaire survey of senior UK clinical pharmacologists. Br J Clin Pharmacol 2012; 73: 161–9.

RECEIVED
18 January 2012

ACCEPTED
30 January 2012

ACCEPTED ARTICLE PUBLISHED ONLINE
23 February 2012

CORRESPONDENCE
Professor David Webb, Queen's Medical Research Institute, The University of Edinburgh, Room E3.22, Edinburgh EH16 4TJ, UK.
E-mail: D.J.Webb@ed.ac.uk