

How a VOICE for clinical pharmacology turns into a RECIPE for its development

Jeffrey K Aronson*

Centre for Evidence Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford, Woodstock Road, Oxford OX2 6GG, UK

*Correspondence: Jeffrey K Aronson; E-mail: jeffrey.aronson@phc.ox.ac.uk

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Pharmacology is the study of the actions of synthetic or semisynthetic chemicals or naturally occurring substances on molecules, cells, tissues, and living organisms, as seen in physiological and pathological systems, seeking to establish order, pattern, and sequence among them, aiming ultimately to determine the rules by which pathophysiological information can be coded into molecules, allowing prediction of both beneficial and harmful consequences. Clinical pharmacology is the application, informed by an understanding of pharmacology, of all aspects of the study and use of medicines in humans, whose practitioners, normally medically qualified, teach, do research, frame policy, and give information and advice about the actions and proper uses of medicines in humans and implement that knowledge in clinical practice. Clinical pharmacology expanded in the UK during the 1960s and 1970s and maintained a steady state during the 1980s, but thereafter started to decline. Since 2006 this decline has been halted and partly reversed through the efforts of the British Pharmacological Society, by demonstrating the need for clinical pharmacology in clinical practice, teaching, research, and policy making, and bringing that need to the attention of medical colleagues, regulators, government, and the public. Efforts continue to maintain and enhance this recovery, using the VOICE paradigm, which involves improving and maintaining the *Visibility* of the specialty, *Outreach* to advertise its attractiveness to potential trainees and creating a public image for the specialty, *Integration* with other disciplines, encouraging *Coverage* of neglected areas, and the use of *Emissaries*, particularly younger members of the discipline, to promote it, both within medicine and in the wider world. Fortuitously, translation of the five elements of this paradigm into Korean, and back-translation into English, with the addition of a sixth element, provides a RECIPE for the future of clinical pharmacology and therapeutics.

Introduction

The history of the development of clinical pharmacology has been described in many different countries.[1-19] In this article I shall concentrate on developments in the UK, which offers lessons for practitioners in other countries.

After several years of growth during the 1960s and 1970s and a period of maintenance during the 1980s, clinical pharmacology in the UK started to decline between 1990 and 2006. However, thanks to the efforts of the British Pharmacological Society the

downward trend has started to reverse and efforts are being made to make further progress. Here I describe how this has happened.

Defining pharmacology and clinical pharmacology

Defining any scientific subject is hard. The word “define” etymologically means to draw a boundary around something, and in defining any subject one tries to encompass its essence, to include everything that the subject involves and to exclude, at least by implication, everything that it does not. This raises the possibility that something important may be omitted or that something irrelevant may be included. Nevertheless, a well-crafted definition can help to direct attention to what is relevant

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and important about a subject.

When Desmond Laurence, at that time Professor of Clinical Pharmacology in University College London, sought to define pharmacology by consultation, he found it hard to reach a satisfactory conclusion, and what emerged was a descriptive statement rather than a proper definition.[20] His experience demonstrates, in my view, that well-crafted definitions cannot be manufactured by committees or general consensus. To my knowledge, no pharmacologists have since done what Laurence suggested at the end of his article, namely direct their minds to producing something better than he offered. I have elsewhere described a fourfold method for crafting definitions, exploring etymology, usage, previous attempts at definition, and exploration of the operational aspects of the subject being defined.[21] However, for the time being, short of a concerted investigation of this sort, I propose an interim definition of pharmacology, based on Laurence's findings and the credo of one of pharmacology's Nobel prize winners, Sir James Black[22]:

Pharmacology is the study of the actions of synthetic or semisynthetic chemicals or naturally occurring substances on molecules, cells, tissues, and living organisms, as seen in physiological and pathological systems, seeking to establish order, pattern, and sequence among them, aiming ultimately to determine the rules by which pathophysiological information can be coded into molecules, allowing prediction of both beneficial and harmful consequences.

Elsewhere I have proposed intensional and operational definitions of clinical pharmacology and clinical pharmacologists.[23,24] The following combines the various aspects of these definitions that I have previously discussed:

Clinical pharmacology is the application, informed by an understanding of pharmacology, of all aspects of the study and use of medicines in humans, whose practitioners, normally medically qualified, teach, do research, frame policy, and give information and advice about the actions and proper uses of medicines in humans and implement that knowledge in clinical practice.

This definition has been approved by others[25] and is in tune with other similar statements.[26] It should be kept in mind when reading the rest of this paper.

The history of clinical pharmacology to 1960

Anatomy, pathology, physiology, and pharmacology, the four pillars of medical sciences, antedate all other specialties.[27] The first recorded instance of the word "pharmacology" in English was in 1704, when Thomas Curteis described it as a "boundless field" in his *Essays on the Preservation & Recovery of Health*. Clinical pharmacology was at that time called "materia medica", a term that was first recorded in English in 1663, and which originally meant "the remedial substances and preparations used in the practice of medicine [or] a list of these", but later came to mean "The branch of medicine that deals with the origins, preparation, and use of the materia medica".[28] The latter

meaning seems to have been in general use by the 18th century—Tobias Smollett, for example, mentioned it in his medical novel *Humphry Clinker* in 1771. "Toxicology" first appeared in 1799. All other clinical ologies appeared later.

The term "materia medica" was originally a direct translation of the title of a five-volume herbal treatise by the Greek physician and botanist Pedanius Dioscorides, written in the first century AD, Περὶ ὕλης ἰατρικῆς (*peri hulēs iatrikēs*), which literally means "about things that heal". In its Latin form, *materia medica*, it was incorporated into the titles of textbooks, such as William Cullen's *A Treatise of the Materia Medica* (1789), referring to the substances themselves. The first textbook to my knowledge to use the term "materia medica" to mean the subject that we now call clinical pharmacology was *Elements of Materia Medica and Therapeutics* (1845) by Edward Ballard and Alfred Baring Garrod.

I was a medical student in Glasgow in the 1960s, and although the subject that we studied was called "materia medica", the recommended textbook was *Dilling's Clinical Pharmacology*. It was first published in 1884 by John Mitchell Bruce, who taught *materia medica* at the Charing Cross Hospital in London, under the title *Materia Medica and Therapeutics. An Introduction to the Rational Treatment of Disease*. Later, this was amended to *The Pharmacology and Therapeutics of Materia Medica* (Bruce and Dilling's *Materia Medica and Therapeutics*), after Walter J Dilling became a co-author, and in 1960 the 20th edition was published as *Dilling's Clinical Pharmacology*, written by Stanley Alstead, Professor of *Materia Medica* in Glasgow University. The first edition of Desmond Laurence's textbook *Clinical Pharmacology* also appeared in 1960, and these two are the earliest books to have used the precise term "clinical pharmacology" in their titles. There are, however, two other earlier books of note. First, Louis Lewin's monograph *Die Nebenwirkungen der Arzneimittel. Pharmakologisch-klinisches Handbuch* (1881). Secondly, a textbook by Hans Horst Meyer and Rudolf Gottlieb, *Die experimentelle Pharmakologie als Grundlage der Arzneibehandlung*, which was translated by John Taylor Halsey in 1914 as *Pharmacology, Clinical and Experimental*. Not quite "clinical pharmacology" in either case, but very close. The term "klinische pharmakologische" is also to be found in the text of Paul Martini's 1932 textbook *Methodenlehre der Therapeutischen Untersuchung*. [29,30]

However, it is thought that the English term "clinical pharmacology" was first used by Harry Gold, who was appointed the first Professor of Clinical Pharmacology in Cornell in 1947 and pioneered clinical pharmacological studies of cardiac glycosides from the 1920s onward. John Gaddum called his Walter Ernest Dixon Memorial Lecture, given to the Royal Society of Medicine on 8 December 1953, "Clinical pharmacology".[31] "I propose," he wrote, "to discuss some of the clinical implications of pharmacology. I had already decided that the title of my lecture would be 'Clinical Pharmacology' when I found that Dr Harry Gold (1952) had used the same words to describe the same thing." There is also a paper from March 1952 describing,

in Spanish, the clinical pharmacology of Aureomycin (chlortetracycline).[32]

Although by the 1960s the term “clinical pharmacology” had prevailed, “human pharmacology” was for a short time a competitor. In 1959 Desmond Laurence edited the proceedings of a 1958 symposium titled “Quantitative methods in human pharmacology and therapeutics”.[33] Gold contributed. His lecture was called “Experiences in human pharmacology”. “Many of you,” he said, “are probably familiar with Dr Gaddum’s Dixon Memorial Lecture under the title ‘Clinical Pharmacology’, but I believe your term ‘Human Pharmacology’ is a better one, free of the meanings of the term ‘clinical’, which tend to identify it with the art of therapeutics, the practical care of patients.” A strange comment this, coming from one who had contributed so much to therapeutics. But the newly fledged clinical pharmacologists were very practical, as they continue to be, and “clinical pharmacology” as a descriptive term triumphed. This is as it should be—“human pharmacology” is a useful term to use in referring to the study of basic pharmacology in humans, but it does not fully capture the essence of the clinical activities that make clinical pharmacology such a distinct subject. Nevertheless, as a translational discipline, clinical pharmacology spans everything that can be termed pharmacological, from human pharmacology to applied pharmacology.[4]

These days, and fully reflecting Gold’s observation, “clinical pharmacology” is usually twinned with the much older term “therapeutics”. The noun “therapeutic” (singular), meaning the art of healing, first occurs in a text of 1541. In its now usual plural form it first occurred in William Salmon’s book *Synopsis medicinae, or a compendium of physick* (1671), where he wrote that “the Therapeuticks, or active part of Physick, is either Material, or Relative”. The word comes from the hypothetical Indo-European root DHAR, meaning ‘to hold’, which gave the Greek

word *θεραπεία* (therapeia), meaning attendance, service, or treatment.

Changes in clinical pharmacology in the UK 1960–2015

During the 1960s and 1970s increasing numbers of departments of clinical pharmacology were established[34] and the British Pharmacological Society introduced a clinical section in 1970.[35] It was the expressed desire of the Society “that all who are concerned with studying drug activity in man should be able to share in the activities of the section”. It was also hoped “that this initiative will provide the much-needed focus for clinical pharmacologists in this country”. Collaboration between basic and clinical pharmacologists, encouraged by this societal symbiosis, has been beneficial to the development of both aspects of pharmacology. Its strength is evidenced by the fact that in 2006 I was the first practising clinician to be appointed President-elect and then President of the Society, since when basic and clinical pharmacologists have alternated in those positions.

Clinical pharmacology flourished in the UK until the early 1990s, but then, under what many consider to have been the malign influence on UK research in science and the humanities of research assessment exercises,[36–40] the number of core clinical pharmacologists in the UK started to fall, mainly owing to reduced support from universities. The decline continued until 2006, but since then, mainly through the efforts of the members of the British Pharmacological Society (BPS), there has been a turnaround. The latest data show an increase in the number of posts in the discipline. The data are shown in Figure 1, compiled by combining two sources[41,42]; since 2006 there has been a steady increase in the numbers of consultant clinical pharmacologists, following the steady decline from 1993–2006.

The reasons for this recovery, which has been brought about

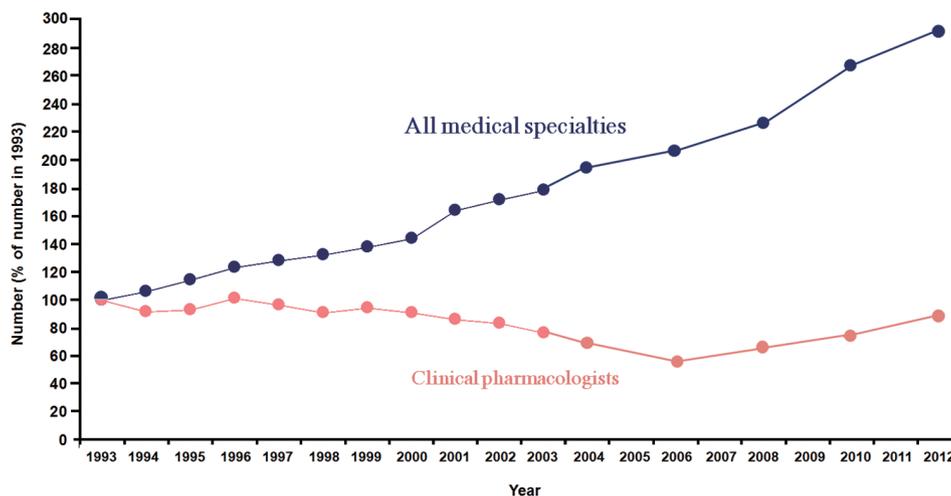


Figure 1. Changes in the UK in the numbers of consultant clinical pharmacologists (pink) and consultants in all other medical specialties (blue) in percentage terms since 1993; since 2006 there has been a steady increase in the numbers of consultant clinical pharmacologists, following the steady decline from 1993–2006; in the UK system a consultant is a senior hospital doctor

by the efforts of many members of the British Pharmacological Society, have been described in detail elsewhere.[43] The activities involved can be summarized under six general headings:

- research into students' attitudes to teaching of clinical pharmacology, demonstrating that while such teaching is regarded as being of high quality there was too little of it;
- discussions with medical regulatory bodies (such as the General Medical Council, the Medical Schools Council, the Royal College of Physicians of London, and the Association of the British Pharmaceutical Industry), leading to various independent research streams and reports outlining deficiencies in provision of clinical pharmacology and consequent concerns about adequate provision of health care;
- discussions with Government agencies, leading to further reports and recommendations;
- discussions with funding bodies, leading to new funding streams for training posts;
- inclusion in national recommendations of details of the minimum prescribing knowledge and skills required by newly qualified doctors and institution of a national examination in prescribing for final-year medical students;
- press briefings, leading to newspaper reports, highlighting the importance of clinical pharmacology.

Current efforts to maintain recovery and improve on it: the VOICE paradigm

Although the initial recovery in the numbers of UK consultant clinical pharmacologists is encouraging, there is no room for complacency, and the British Pharmacological Society continues to work on projects intended to further it. The latest efforts to promote clinical pharmacology world wide have been summarized as having the following aims:[6]

- to engage health system/services managers and policy makers to ensure that the full benefit from clinical pharmacology services is achieved;
- to put a monetary value on clinical pharmacology;
- to ensure adequate recruitment of doctors into the specialty.

These aims are all consistent with the VOICE paradigm, which was developed in June 2011, when 50 senior clinical pharmacologists, their junior colleagues, other medical specialists, and pharmacists gathered in Oxford to discuss an agenda for the future development of clinical pharmacology in the UK.[44] In June 2012, at a similar meeting in Erice, Sicily, 30 clinical pharmacologists from 19 different EC member states discussed the future of the subject in Europe as a whole.[45] The outcomes on the two occasions were strikingly similar and were summarized using the acronym VOICE:

- *Visibility* Improving and maintaining the visibility of the specialty among clinical colleagues.
- *Outreach* Advertising the attractiveness of the discipline to potential trainees and creating a public image for the specialty.
- *Integration* with other disciplines, where relevant.

- *Coverage* of neglected areas.
- *Emissaries* Encouraging all members of the discipline, but particularly younger ones, to promote it, both within medicine and in the wider world.

Many of the efforts that the British Pharmacological Society has been making have been related to the VOICE paradigm, and currently the following activities are being undertaken, illustrating how the paradigm can be used:

Visibility

- Leading the annual Prescribing Safety Assessment in UK medical schools;[46] in 2014 the assessment was taken by over 7000 final year medical students.
- Raising awareness of the discipline among politicians and NHS decision makers via reports. "A prescription for the NHS"[42] was launched in the House of Lords in 2014.[47] More recently, the Society has published a second report, "Clinical Pharmacology: a Dynamic Medical Speciality Essential for UK Healthcare".[48] Both of these reports have shown how the diversity of clinical pharmacology means that it is uniquely placed to deliver the key strategic priorities for the UK's National Health Service (NHS), including: protecting patients; improving productivity and efficiency; leading research on medicines; promoting access to innovative medicines; ensuring that medicines are cost-effective and used to best effect; and training skilled, knowledgeable, and safe prescribers. The reports also highlighted the fact that clinical pharmacology gives excellent value for money. As an example, in one study for every £1 of investment, clinical pharmacology yielded £10 of savings.[49]
- Meetings with Health Education England and individual Hospital Trusts.
- Responding to consultation documents.

Outreach

- Supporting junior doctors training in clinical pharmacology.
- Presence at Medical Careers Days held by the London Royal College of Physicians.
- Producing careers leaflets and other materials.
- Funding regional postgraduate meetings and undergraduate societies.
- Using social media (such as Facebook, Linked-in, and Twitter) to highlight activities and key research.
- Providing media training.
- Liaising with the Science Media Centre to promote clinical pharmacology through press briefings and expert comment on news items.
- Supporting and organizing outreach events, communicating to the public, including schoolchildren.

Integration

- Strengthening links with learned societies and bodies with related medical and scientific interests, including pharmacists

in the Royal Pharmaceutical Society.

Coverage

- Encouraging work in experimental and translational medicine and disseminating information in the Society's three journals, its in-house magazine *Pharmacology Matters*, and newsletters.

Emissaries

- Funding a Pharmacology Ambassadors scheme, including an annual Pharmacology Ambassadors meeting.[50]
- Promoting pharmacology via outreach events (talks, school visits), including outreach grants.
- Supporting undergraduate and postgraduate students.

How the VOICE for clinical pharmacology becomes a RECIPE for the future of the subject

In 2015 I was privileged to be invited to discuss all of the above developments at the annual meeting of the Korean Society of Clinical Pharmacology and Therapeutics in Seoul. In describing the VOICE paradigm, outlined above, I thought that it would be helpful to translate each of its five elements into Korean. On

Original English	Korean translation	Backtranslated into English
Visibility	드러내고	Reveal (CPT)
Outreach	다가가며	Extend (reach out)
Integration	융합하고	Converge (with others)
Coverage	보완하며	Increase (subjects covered)
Emissaries	전파해서	Promote (CPT)
and thus	발전시키자!	Evolve (develop CPT)
VOICE	→	RECIPE

Figure 2. How the VOICE paradigm becomes a RECIPE for the future development of clinical pharmacology by translation into Korean and back-translation into English; CPT = clinical pharmacology and therapeutics (with thanks to Seonsam Na for help with the translations)

back-translating from Korean to English I found that, with the addition of an extra element, the VOICE became a RECIPE for future developments in the subject. This is illustrated in Figure 2.

Conclusion

After several years of growth during the 1960s and 1970s and a period of maintenance during the 1980s, clinical pharmacology in the UK started to decline between 1990 and 2006. However, thanks to the efforts of the British Pharmacological Society the downward trend has started to reverse and efforts are being made to make further progress. The efforts that are required to bring this kind of transformation about are considerable and involve actions on several fronts, including engagement with medical colleagues, regulatory authorities, grant-giving bodies,

government agencies, the press, and the public.

Conflict of interest

JKA is a President Emeritus of the British Pharmacological Society.

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