Letter to the Editors

Integrating pharmacology and clinical pharmacology

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Linked Article The following response from J.K. Aronson, together with the letter by Tucker & Miners published in this issue (<http://dx.doi.org/10.1111/j.1365-2125.2010.03817.x>), should be read in association with previously-published letters by C. Page (*Br J Clin Pharm*, **70**: 912–913; <http://dx.doi.org/10.1111/j.1365-2125.2010.03769.x>) and J.D. Fitzgerald (*Br J Clin Pharm*, **71**: 471–472; <http://dx.doi.org/10.1111/j.1365-2125.2010.03842.x>). The correspondence in its entirety relates to A manifesto for clinical pharmacology from principles to practice (Aronson JK. *Br J Clin Pharm*, **70**: 3–13; <http://dx.doi.org/10.1111/j.1365-2125.2010.03699.x>).

I here reaffirm some of the points that I made in the manifesto for UK clinical pharmacology [1], in response to letters from others. Much of what I wrote in the manifesto addresses points that correspondents have made, but as some of the important points may not have been clear on a first reading, I shall reiterate them and add clarifications.

I am surprised that Professor Page [2] should think that I have taken no cognizance of the erosion of the discipline of pharmacology in recent years. Nothing that I said, wrote or did, while I was President-Elect and President of the British Pharmacological Society (BPS) during 2006 to 2009, should have given that impression. If he doubts this, and my commitment to the integration of all pharmacological science across the clinical and non-clinical spectra, he may want to reread some of my articles in the newsletter of the BPS, previously called *pA*, now called *Pharmacology Matters* [3, 4], and indeed the manifesto itself, where I wrote that 'the importance of integrating pharmacology and clinical pharmacology cannot be overestimated'.

In relation to this, I strongly believe that the distinction that many make between basic and applied science is a false dichotomy. As I wrote in the manifesto, 'functions in biology emerge... as a result of integration of different components of relevant systems at different levels.' This is true of pharmacology and clinical pharmacology. Although it is sometimes useful to refer separately to basic and applied science, it is the crosstalk between them, at all levels and from one level to another, that is important. I have recently had the opportunity to make these views known more widely, in my opening plenary lecture at WorldPharma 2010, the 16th World Congress of the International Union of Basic and Clinical Pharmacology (IUPHAR). The contents of that lecture have been posted on the BPS's website [5].

Clinical pharmacology and clinical pharmacologists

As the manifesto again makes clear, I believe that it is important to distinguish between the *discipline* of clinical pharmacology, to which many can contribute, whatever their qualifications, and the *practitioners* of the discipline, who should be medically qualified practitioners. My definition of a clinical pharmacologist has two distinct parts:

- 1 A statement that a clinical pharmacologist is a medically qualified practitioner. A medical qualification is essential, as I argued in the manifesto and shall argue further here.
- 2 An outline of the main categories of activities that clinical pharmacologists undertake: teaching, research, the framing of medicines policy, the purveying of information and advice about the actions and proper uses of medicines in humans, and implementation of that knowledge in clinical practice.

Professors Tucker and Miners [6] suggest that as there are five categories in this list, clinical practice forms only 20% of the whole, the implication being that it is but a small part of the discipline. That is not so. Clinical knowledge, experience, practice, and above all, insight permeate all of the activities of a clinical pharmacologist, and there can be no simple division of attributes such as they suggest.

It is undoubtedly true, as Professor Page asserts, that one does not have to be medically qualified or clinically experienced to contribute work that is of relevance to drug action in humans, and many who are not medically qualified practitioners have made major contributions to the discipline of clinical pharmacology. When I suggested that some of those 'could be described as, say, "applied pharmacologists"', I was thinking specifically of the small

number of academics in the UK 'who are regarded [by themselves and others] as clinical pharmacologists but who are not clinically qualified'. Some of them are called professors of clinical pharmacology, although they could instead be called professors of pharmacology, systems pharmacology, applied pharmacology or some other suitable title.

However, it is self-evidently true that, as Professors Tucker and Miners concede, only medically qualified practitioners can perform *all the functions* of a clinical pharmacologist, such as the activities listed in the manifesto, which include inpatient and outpatient medical care, drug prescribing and the formulation of prescribing policies, and all aspects of the conduct of clinical trials, including the management of adverse events during human studies [7]. There are certainly many others who can fulfil one or a few of these functions. However, being, for example, a pharmacist prescriber or a statistician who designs and takes part in clinical trials does not make you a clinical pharmacologist. Only a medically qualified practitioner with pharmacological expertise can fulfil all the criteria that operationally define a clinical pharmacologist [8], as I discussed in the manifesto.

Dr Fitzgerald [9] suggests that no practitioner can be expected to be skilled in and knowledgeable about all of the specialized topics that constitute my extensional definition of clinical pharmacology. If he means that no practitioner can be expected to carry out high-class research in all of those topics, I agree. However, every clinical pharmacologist needs to have a basic understanding of the whole range of topics that the discipline affords as part of his or her clinical practice. This is necessary as part of the interactions that clinical pharmacologists have with consultant colleagues, junior doctors and medical students, demanding inquirers that they are. In addition, as I have discussed elsewhere, it is the depth of the subject, as well as its breadth across all medical specialties, which I have referred to as the waterfront, that makes clinical pharmacology such an intellectually rewarding career to follow [10]. Dr Fitzgerald is wrong, incidentally, to suggest that clinical pharmacology, as a speciality in the UK, lacks recognition; it is a recognized speciality and has its own training programme and specialist certification status. It is noteworthy that this is administered by the Joint Royal Colleges of Physicians Training Board (JRCPTB).

No one would question a definition of, say, a cardiologist or a psychiatrist, a neurosurgeon or an obstetrician that stipulated that they were medically qualified practitioners, although many who are not so qualified have contributed to cardiology, psychiatry, neurosurgery and obstetrics. Conversely, it is not the case, as Professor Page suggests, that there are clinicians who fulfil the definition of a clinical pharmacologist without being one. I know of no clinicians in any other specialties who are knowledgeable about clinical pharmacology across the waterfront, including, for example, pharmacodynamics and pharmacokinetics, pharmacovigilance and pharmacoeconomics, in

the way that clinical pharmacologists are, even though many are highly knowledgeable about the uses of medicines in the areas of their own expertise.

Professors Tucker and Miners suggest that it will be to the detriment of the future of clinical pharmacology if those who are not medically qualified cannot be called clinical pharmacologists. That suggestion does not withstand scrutiny. Had their own titles been otherwise, they would still, I have no doubt, have made eminent contributions to clinical pharmacology, as they have done over many years, including, in Professor Tucker's case, a major contribution to the success of the British Journal of Clinical Pharmacology. In contrast, as I shall argue below, if the title of clinical pharmacologist is *not* restricted to those who are medically qualified, the subject *will* suffer, and indeed already has done.

When it comes to defining a pharmacologist, Professor Page claims that it is 'drugs that distinguish pharmacologists from physiologists or many other branches of medical science'. But, as James Black pointed out in stating his credo, all biomedical researchers use drugs as tools [11], and many in other disciplines have contributed to pharmacology. Being a physiologist studying, for example, the mechanism of action of cardiac glycosides [12] does not necessarily make you a pharmacologist. Black proposed other criteria that he thought define a pharmacologist.

Being a medically qualified practitioner

I cannot stress how important I consider it, for the future of clinical pharmacology in the UK, that clinical pharmacologists be pharmacologists who are medically qualified practitioners. Dr Fitzgerald wonders why the number of UK clinical pharmacologists has declined in recent years [13]. The reasons are clear. A major factor, as he recognizes, has been that some of those responsible for allocating posts in universities, by whom most clinical pharmacologists in the UK are employed, have acquired the perception that some of the work that clinical pharmacologists do, particularly the teaching of therapeutics and giving therapeutic advice, could be done by others who are not medically qualified, such as pharmacists. The use of teaching expertise from pharmaceutical companies, even when afforded by pharmacists, in the absence of guidance from clinical pharmacologists [14], is also to be regretted, but is evidence of this trend. I yield to no one in my regard for pharmacists and the work that they do, but without the medical training, experience, and above all, clinical insight that being medically qualified gives, they cannot fully substitute. A symbiosis of clinical pharmacologists and pharmacists has been fostered in some centres and should be strengthened everywhere, each discipline supporting the other in teaching and the provision of therapeutic guidance.

A second and related factor has been a difficulty in recruiting trainees. This is partly because there is a perception that careers are hard to forge in the discipline. That this is not so is illustrated by the fact that pharmaceutical companies are desperately short of clinical pharmacologists; this was highlighted as a skills gap in the previous Government's 'Life Sciences Blueprint' [15]. I have recently noted advertisements in only three editions of the BMJ for nearly 30 research training posts and one consultant post in clinical pharmacology in the UK. But a medical student or a junior doctor will not see the point in training hard to become a clinical pharmacologist in the face of competition from non-medically qualified individuals who can gain the title of clinical pharmacologist more quickly and with no medical experience, which takes many years to accumulate. Those who are medically qualified will prefer to opt for other specialties, in which such competition does not exist and where they can work with senior colleagues who are medically qualified.

How one is perceived by others is important. It is difficult, if not impossible, to gain the respect of one's clinical colleagues without being medically qualified. And without such respect, one cannot flourish as a pharmacologist practising in a clinical environment. Those who are outside the subject have once more started to recognize its importance [16], and we should all take advantage of that, to rebuild not only clinical pharmacology, but with it pharmacology as well.

I am not alone in defining a clinical pharmacologist as one who is a medically qualified practitioner. In a recent paper issued under the auspices of the International Union of Basic and Clinical Pharmacology [17], which I first saw in a late draft, the following (here slightly modified) definitions appear:

Clinical pharmacology The scientific discipline that involves all aspects of the relationship between drugs and humans . . . [and] . . . that may be of significant interest to a variety of professions, including physicians, pharmacists, nurses, and scientists in many different disciplines.

Clinical pharmacologist A physician who is a specialist in clinical pharmacology, having undertaken several years of postgraduate training in many aspects of the above relationship involving teaching, research and health care, and having as a primary goal that of improving patient care, directly or indirectly, by developing better medicines and promoting the safer and more effective use of drugs.

It is clear that these definitions do not 'fail to recognize the major contribution of non-medically qualified individuals to the discipline', contrary to what Professors Tucker and Miners assert. However, they are undoubtedly correct when they concede that it is necessary to include a medical qualification as part of the definition of a clinical

pharmacologist if increased support for specialist medical training in the discipline is to emerge. Recognizing that some who currently have the title of clinical pharmacologist are not clinically qualified, one could add the word 'normally' before the words 'a specialist' in the second definition.

Lost or found in translation?

I do not share Professor Page's dislike of the term 'translational medicine'. Although there is a large degree of overlap, it is misleading to suggest that translational medicine is all that pharmacology is, or that pharmacology is all that translational medicine is (there is, after all, translation in non-pharmacological areas, such as surgery [18]). However, I do have a real difficulty with the way in which the idea of translational medicine has been widely interpreted, in that it seems to have been generally assumed that it is a process that begins with omics rather than functional omics and proceeds in a linear fashion to practical outcomes. This diminishes the non-linear systems approach to translation, to which I referred in the manifesto and my plenary lecture to WorldPharma 2010, and it downplays the many ways in which clinical observations can lead to practical outcomes independently of science at more basic levels, and the to-and-fro interactions of science at all levels and across levels, each depending on the other [5]. The Scientific Management Review Board at the US National Institutes of Health (NIH) has recently recommended the creation of a new NIH centre focused on translational medicine and therapeutics (TMAT) [19]. Perhaps it is time for us to add the word 'translational' to our titles. We should certainly stress that pharmacology is highly suited for contributing in a major way to understanding translational processes.

A manifesto for pharmacology

I agree with Professor Page that we need a manifesto for all of pharmacology, in order to define its boundaries and those who practise it. A manifesto for non-clinical pharmacology could be devised analogously to the clinical manifesto, starting with a linear structure on which an extensional definition of pharmacology could be modelled. That in turn could be developed into a non-linear operational definition, extending that shown in figure 2 of the clinical manifesto [1], and as suggested there. I encourage Professor Page and his colleagues to do that, and I should be happy to discuss with them how such a manifesto could be combined with the clinical manifesto to create a manifesto for the whole subject.

To deal with Dr Fitzgerald's final question (what advice would one give to a recently qualified medical doctor as to whether this is a career with a stable attractive career

trajectory?) would take a whole paper in itself. My own optimistic view [16] is encapsulated in the title of the President's Lecture that I gave to the British Pharmacological Society in December 2009: 'Clinical Pharmacology: Past, Present, and (YES) Future'.

Envoi

Finally, although I consider nomenclature important, it is much more important to concentrate our efforts on further integrating and strengthening pharmacology and clinical pharmacology. This will be an important aspect of a James Black conference that the BPS will run in June 2011, titled 'Planning a 5-year agenda for UK clinical pharmacology'. I hope that those pharmacologists who are not medically qualified practitioners, whatever type of pharmacology they undertake, and those in other disciplines, particularly pharmacy, will support their medical colleagues in their endeavours to reinvigorate the subject of clinical pharmacology, after its recent vicissitudes. I believe that they will thereby find that opportunities will arise for strengthening pharmacology as a whole.

Competing Interests

J. K. A. is a clinical pharmacologist and a President Emeritus of the BPS; however, the opinions expressed here are not necessarily shared by other members of the Society.

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