

# The man who knew doses

John Gaddum did much to define what it means to be a pharmacologist.

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When Sir John Gaddum, born 100 years ago, began his career in pharmacology it was a fledgling discipline, dating back only to the beginning of the twentieth century. Gaddum played a vital part in establishing the field, which he described as “a mingling of materia medica with physiology”, as a separate entity with its own viewpoint and set of questions. Of his many seminal research contributions, his work on the standardization of drugs and the theory of competitive drug antagonism were probably the most influential. His labs in London, Edinburgh and Cambridge were of international renown and played host to some of the finest experimentalists of the century.

In the 1950s, Gaddum’s address “The Science of Pharmacology” to the American Society for Pharmacology and Experimental Therapeutics was a manifesto for the emergent discipline and an agenda for future research. Among his top priorities were “finding out how drugs work” and expunging remedies of dubious provenance and efficacy from the bloated pharmacopoeias.

Gaddum was an accomplished mathematician who believed that no scientific discipline had come of age until it was quantitative. The statistical techniques he introduced provided the tools for pharmacology, and he once joked that materia medica was the only field of knowledge “that has become smaller as it has advanced”. Other tasks set by Gaddum for his colleagues included the study of drug toxicity and pharmacokinetics, and the participation with clinicians in the design of clinical trials (for which he also laid much of the theoretical foundations). Discovering new drugs was, of course, also on Gaddum’s agenda, but to him this was a secondary goal. This may seem odd, but perhaps it reflects his early interest in sailing, which taught him that one must know one’s position to plot an accurate course to one’s destination.

Has pharmacology lived up to Gaddum’s expectations, and is his agenda still valid? In the 1930s, Gaddum briefly occupied the chair of pharmacology at Cairo University and it is salutary to remind ourselves how few really effective drugs there were at that time. His wife, Iris, who worked there as a dermatologist, later recalled that only morphine, aspirin and coal tar were available in her clinic. Apart from making a diagnosis, there was little that she could do for her patients except to ensure adequate nursing care. Topical steroids later revolutionized dermatology and many other



Jack of all trades: Gaddum realized that many disciplines are needed to discover and understand drugs.

therapeutic triumphs have since fundamentally changed other branches of medicine. Even Gaddum later remarked that pharmacologists had been “almost too successful”. Ironically, those very pharmacopoeias that he and his contemporaries strove to prune have burgeoned in size once again.

There has been good progress over the past 50 years with another item on Gaddum’s agenda — discovering how existing drugs actually work. Aspirin and morphine, for example, have yielded up many, if not all, of their secrets. But as the 1998 Nobel Prize in Physiology or Medicine shows, there is still much to learn about even such apparently simple drugs as nitrates.

The fundamental problems of pharmacology remain as Gaddum defined them half a century ago, although the intellectual landscape is very different. Gaddum’s early research training was in physiology at a time when, as a colleague put it, all he needed to do to become a pharmacologist was “to learn doses”. He later did much to define exactly what it means to be a pharmacologist; his 1940 textbook *Pharmacology* ran to five editions in several languages.

Gaddum always maintained that phar-

macology is truly interdisciplinary by its very nature, describing the pharmacologist as a “jack of all trades”. To ask how a drug works, what changes it produces and how it can be improved is to invite the assistance and insights of specialists from many other disciplines. This is truer today than ever, for of course the future of pharmacology is inextricably linked with that quintessentially millennial activity, the Human Genome Project, and will depend on many new professional alliances.

Many medical schools have sought to encourage this type of research by abolishing the traditional departmental structures, but Gaddum was concerned about organized ‘team’ science. His concept of collaboration was a synergistic interaction between specialists, and he might have argued that this could not be achieved simply by changing the names on laboratory doors, but rather by building upon the unique contributions that each separate discipline can make to the business of drug discovery and to an understanding of drug action. ■

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