

The price of hope

What's the benefit to drug companies of making medicines for the poor?

Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases

by Michael Kremer & Rachel Glennerster
Princeton University Press: 2004. 152 pp.
\$24.95, £15.95

Pierre Chirac

Access to essential drugs for poor people in developing countries has made headlines several times during the past few years. Most of the media attention has centred on a few specific topics within this broad theme: the debate about access to antiretroviral drugs against AIDS; the hot economic and political topics of patents and the World Trade Organization agreements; and the lack of research and development (R&D) to create desperately needed new drugs for 'neglected diseases', conditions that predominantly affect poor people in developing countries.

The central theme that links these issues together is how to encourage research and development for new drugs and ensure that everyone has quick access to the medicines they need. Only a few years ago the sole paradigm, recognized not only by industry but also within most academic circles, was 'patent + market → R&D'. But now alternative or at least complementary paradigms are being considered. Michael Kremer and Rachel Glennerster, the authors of *Strong Medicine*, favour the latter route. In their approach, they fall between those who still think (or at least claim) that the current system only needs minor adjustments and those who want to see complete change on a global scale.

Kremer and Glennerster's aim is to find practical ways to restart R&D for these neglected diseases. They believe that market and public bodies have failed to motivate R&D — only 1% of drugs launched onto the market during the past 25 years target such diseases. They are convinced that appropriate policies and public commitment could motivate private investment in this area. This strategy has already been followed with rare diseases, through 'orphan drug' legislation passed in rich countries, which grants tax incentives and guaranteed periods of exclusivity to companies that invest in R&D for drugs to treat rare conditions.

The authors comment on the various tools that have been suggested or tested to influence R&D. 'Push' mechanisms refer to financing research inputs such as grants to academics, or tax credits for specific R&D activities. 'Pull' solutions mean financing research outputs, such as a commitment to create a profitable market for the expected



Cost of living: who will pay for new drugs to combat 'neglected diseases' such as sleeping sickness?

products. Kremer and Glennerster tend to favour pull solutions, because these are less bureaucratic and are closer to market-like solutions (which the authors prefer in general). After a short discussion of various pull solutions, the authors opt for one in which somebody creates the market by committing to purchase a certain quantity of drugs at a fixed price.

And this is where this book becomes really original. Kremer and Glennerster enter into a computation for assessing the amount of sales that would be enough to motivate private companies to embark on such a deal with a sponsor. Their conclusion is that the system could work with a guaranteed price of \$15–20 per complete vaccination for the first 150–200 million individuals vaccinated, the rest of the vaccine supply being priced at a modest mark-up over production cost.

Who should pay for all this? Kremer and Glennerster believe that this kind of spending would be popular with governments of rich countries, as public money would only be invested in concrete outcomes — not in research that might lead nowhere. They also mention the World Bank and the Bill and Melinda Gates Foundation (from which they acknowledge financial support). Finally, they believe that a modest co-payment from recipient countries would be desirable.

The book does have some limitations. First, the reasoning is mainly based on vaccines and focuses mostly on the three biggest killers: AIDS, malaria and tuberculosis. These targets are worthwhile, but they are also the easiest, because vaccines generally

need only a few jabs to create a long-term benefit, and because hundreds of millions of people are affected by these diseases. It may be more difficult to convince the public and private sectors to do R&D for the most neglected diseases, such as sleeping sickness or Buruli ulcer.

Another important limitation is that the solution proposed by Kremer and Glennerster is mainly a tool. They recognize that a long-term political commitment will be necessary, but they do not elaborate on how to achieve this. This will frustrate those who believe that such a long-term commitment needs to take the form of an international framework or treaty for neglected diseases. Some people within the World Health Organization and Médecins Sans Frontières remember how difficult it was to mobilize the few million dollars necessary to secure the production of a new combination vaccine against meningitis, just a few months before the 2004 epidemic in Africa. It would have been much easier if some kind of global R&D fund had been available.

Thus, some people might criticize this book for stopping mid-way. But Kremer and Glennerster's solution does imply that the private drug R&D activity could be more appropriately directed by public will and money — something that others might consider a step too far already.

This book should interest anyone involved in international public health, politics and economics. It is a valuable effort to find a practical solution to a major problem, and most readers, when they've finished the

book, will probably say "Let's just try it!" ■
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The other evolutionist

The Heretic in Darwin's Court: The Life of Alfred Russel Wallace

by Ross Slotten
Columbia University Press: 2004. 648 pp. \$39.50, £26.50

An Elusive Victorian: The Evolution of Alfred Russel Wallace

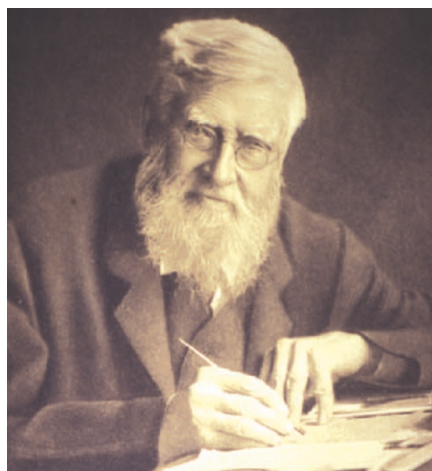
by Martin Fichman
Chicago University Press: 2004. 416 pp. \$40, £28

George Beccaloni

Lying ill with fever on the remote Mollucan island of Halmahera in February 1858, the English naturalist Alfred Russel Wallace puzzled over the phenomenon of 'species transmutation' — a subject that had rarely been absent from his thoughts for the past 13 years. Three years earlier he had published an important but largely unnoticed paper on this topic, now known as evolution, in which he strongly argued that organisms must have evolved from earlier forms. But the mechanism of this process had so far eluded him — as it had (virtually) everyone else.

Suddenly, a flash of insight led him to the idea of natural selection as the mechanism driving evolutionary change. Once he had recovered enough strength, he fleshed out his ideas in an essay entitled "On the Tendency of Varieties to Depart Indefinitely from the Original Type". Knowing that his occasional correspondent Charles Darwin was also keenly interested in the 'species problem', he sent the essay to him on the next mail boat that departed from the neighbouring island of Ternate. Unknown to Wallace, Darwin had in fact discovered natural selection some 20 years earlier and, urged on by the geologist Charles Lyell, he was slowly writing a huge tome in which he planned to present his 'heretical' theory to the world.

The events that unfolded following Darwin's receipt of Wallace's essay have become legendary. Realizing that Wallace had independently reached the same conclusion as himself, Darwin was thrown into a state of confusion and despair. He wrote to Lyell: "Your words have come true with a vengeance ... all my originality will be smashed." Lyell contacted another of Darwin's influential friends, the botanist Joseph Hooker, and together they sought to remedy the awkward situation as best they could.



Alfred Russel Wallace wrote some 700 articles and 20 books on a wide range of subjects.

Without first asking Wallace's permission, they arranged for his essay to be read at a meeting of the Linnean Society in July 1858, along with an abstract of an unpublished manuscript on natural selection that Darwin had written in 1844, and an abstract of a letter outlining the concept of descent with modification that Darwin had sent to the American botanist Asa Gray the year before. By arranging these texts in the order in which they had been written, Lyell and Hooker secured Darwin's priority, and when they were published a month later, Darwin's name naturally appeared as first author of what became the first publication to explicitly propose the theory of evolution by natural selection. This, together with the fact that Darwin's *Origin of Species* (an abstract of his "big book") was printed only a year later, are two of the reasons why Wallace often receives little or no recognition for the discovery.

The Heretic in Darwin's Court by Ross Slotten and *An Elusive Victorian* by Martin Fichman are the latest in a recent spate of books that examine Wallace's fascinating life and often controversial work. Slotten's book is a conventional, chronologically arranged biography, whereas Fichman's aims to provide "a contextualist and analytical study of Wallace's major intellectual and cultural views and activities".

Slotten's book is the most detailed study of its kind published to date and provides a vivid account of Wallace's rich 90-year life. It covers his early impecunious years at school in Hertford (he left school aged 13) and his training as a land surveyor; his four years collecting biological specimens in the Amazon basin (many of which were destroyed when his ship sank on the way back to Britain); his eight years collecting in Southeast Asia (he sent back 126,000 biological specimens, including 1,000 species new to science); and his years in England, during which he wrote some 700 articles and 20 books on an eclectic range of subjects and made a prodigious number of seminal contributions to the fields

of biology, geography, geology and anthropology, among others. Slotten attempts to produce a "three-dimensional portrait of a man whose forays into spiritualism, socialism, antivaccinationism, and other unorthodox 'isms' have been caricatured, overanalyzed, or ignored by specialists in the academic world". However, like most previous biographers, Slotten seems perplexed by some of Wallace's seemingly crackpot beliefs, and although he discusses them at length, he makes little attempt to analyse them in depth.

Fichman, in contrast, tries to do just that and adopts a thematic approach to scrutinize each of Wallace's major interests in turn. He argues that Wallace sought to integrate his beliefs into a single internally consistent world view, which he calls Wallace's "teleological evolutionary cosmology", and he maintains that many of Wallace's putative unorthodoxies are in fact artefacts of historiography. From a modern perspective, it may seem inappropriate for an 'objective' scientist to espouse beliefs such as spiritualism, as Wallace did, but in the late nineteenth century and the early part of the twentieth it was entirely acceptable for scientists to do so.

Fichman's book is the more challenging read and is likely to appeal mainly to serious Wallace scholars. But to understand why a book like Fichman's is needed in the first place, anyone unfamiliar with Wallace's work should probably study a biography such as Slotten's. ■

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Cycles of life

Nutrient Cycling and Limitation: Hawai'i as a Model System

by Peter Vitousek
Princeton University Press: 2004. 232 pp. \$79.50, £51.95 (hbk); \$35, £22.95 (pbk)

David Schimel

The regulation of growth by nutrient availability and the control of cycling of the elements through living communities are basic ideas in the field of ecology. Nutrient cycling, or biogeochemistry as it is known, is now a rich research field with a vast literature linked to disciplines as disparate as ecology, soil science and atmospheric science. It forms a bridge between the life and earth sciences, both of which are concerned with the cycling of elements but for vastly different reasons.

The ecological or process-oriented approach to nutrient cycling largely traces back to seminal work in New England in the 1960s and 1970s. In that oeuvre, Peter Vitousek's work for his doctoral thesis began