

## Book

### Over the rainbow: the pot of gold for neglected diseases

Over a hundred people in developing countries will have died of infectious or parasitic diseases by the time you have finished reading this article. Many could have been saved by access to viable vaccines and drugs, and much pain and suffering could have been avoided. Yet, barely 1% of global expenditure on pharmaceuticals goes into the research and development of products for diseases affecting 90% of the world's population. It is a sign of hope, of frustration, and of the craving for human dignity that the best way to redress this imbalance is currently under wide-ranging—and sometimes argumentative and painful—debate.

Michael Kremer and Rachel Glennerster's *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, part of a larger body of work by the Washington-based Center for Global Development, is an important contribution. They begin with a succinct summary of the problem—the pity is that it needs repeating. But it does. Of the dramatic improvements in health and life expectancy in developing countries consequent on relatively cheap medical advances, the extreme cost-effectiveness of vaccines stands out. Vaccines (in particular for HIV, tuberculosis, and malaria) are thus the focus of this book.

British readers of a certain age will be familiar with the notion of “strong medicine” as a drastic root-and-branch operation on the body economic. The spin here is much less radical: the body pharmaceutic is deemed to be in robust health, just in need of a little nip and tuck, as it were, in the shape of “advance purchase commitments”, which are sort of blockbuster end-of-the-rainbow pots of money to be divided between vaccine developers, paid for later by taxpayers. “Strong” refers to the alleged superior strength, dollar for dollar, of this mechanism compared

with current approaches: up to four-and-a-half times “stronger” than publicly funded research and joint ventures. But, after a 6-year campaign to get this policy proposal to the top of the heap, it is disturbing to find so little of the underlying mechanism laid bare, and no evidence to support the assertion that the mechanism is indeed “strong” for these vaccines. In fact, the authors pro-

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mote advance purchase commitments in much the same way that some pharmaceutical companies promote “wonder drugs”: emphasising the positives, burying the negatives, and ending up suggesting that we now have all the answers—or rather just the one answer—that we need. This is a shame, because the underlying idea has potential as part of something greater.

Kremer and Glennerster expend most of their firepower on early-stage vaccines (where there are no viable vaccines on the horizon and many scientific problems have not been resolved) and this is the main source of *Strong Medicine's* weakness. To strengthen their case, they simplify the state of difficult and unpredictable science to one that it is fixed at basic and applied levels with, among other artifacts, no benefits from information sharing, no patents on anything except end products, no coordination problems across public and private sectors in research or vaccine purchase decisions, and an idealised set of financial mar-

kets. Once these simplifications are thrown out—and we enter the real world—we face an elaborate trade-off between, on the one hand, inflexible rules based on expectations of future vaccine science, and on the other, layers of discretionary committees, treaties, and centralised control of the global public research process.

The authors' core justification for their approach is that it massively improves the choice of research leads. They deliberately favour large pharmaceutical firms over small and new biotechs and not-for-profit, university-based, and developing-country-based research. Yet, they present no empirical evidence that such firms are the most efficient at vaccine research. As the only evidence of the “plague” of failure of current programmes, we get the USAID Malaria Vaccine Program debacle of the early 1980s (which wasted a couple of ten-thousandths of 1% of the total US National Institutes of Health budget of the past 25 years). This is sad. And ungenerous to the many who, often at great personal sacrifice, give their lives to research into these difficult areas.

In its cloak of strong patents and secrecy, *Strong Medicine* also sets up an unnecessarily confrontational stand-off with those who argue for more open, collaborative approaches. The Gates Foundation and the G8 have been exploring these alternatives, following the recent proposal of a “Global Vaccine Enterprise” (*Science* 2003; **300**: 2036–39) along the lines of the successful human genome project. The strongest setting for a purchase commitment for a complicated vaccine like HIV is likely to be as a fairly late, and small, part of a much larger package of measures, with the information revealed by earlier collaborative mechanisms used to set the terms of “contingent” purchase commitments. This would allow for more guidance on



**Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases**

Michael Kremer, Rachel Glennerster. Princeton University Press, 2004. Pp 152. \$24.95. ISBN 0-691-12113-3

the quality of vaccines, fewer institutions and rules, more control over the eventual intellectual property, products priced pretty close to production costs, and quicker release to competitive generic producers. The real challenge is to work out how each part of this larger mechanism creates and handles information and risk, and how different parts fit together to reduce overall costs, speed up discovery, and ensure high-quality vaccines.

That *Strong Medicine* has "growing political support" is a testament to the persuasiveness of drastically simplified ideas, the lack of desire to think through tough issues, and the political appeal of programmes for which the payment can be pushed way off into the future. One of Kremer and Glennerster's main criticisms of the current system is that if publicly funded re-

searchers don't have to prove the worth of what they're doing by results, vested interests will lead them to overstate the chance of success. Their book is an excellent demonstration of this principle in action. We will never truly know whether early-stage advance purchase commitments will work for HIV, tuberculosis, and malaria until after they have been tried. Given the authors' assertion that public-sector failure is at the heart of the current system's inadequacies, it would be ironic indeed if such failure happens when choosing the mechanism itself. Kremer and Glennerster should refuse to tolerate political support that comes without awkward questions or demands for solid empirical evidence.

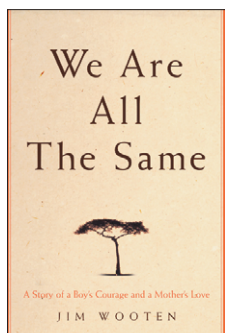
All sides in the debate over the funding for neglected diseases exaggerate to get noticed; it is always nice to think

that one's ideas are those chosen by policymakers. Disagreement is part of the discovery process. When, at the end of Hans Christian Andersen's tale, a small child squeals that the emperor has in fact got no clothes on, the emperor cringes but carries on the procession to its bitter end, while his chamberlains continue to hold up the train of his cloak, even though they know that it is not actually there. Let's hope that, after reflection, policymakers do not uncritically swallow all of *Strong Medicine*. It will make them feel better for a while, but the effect would be short-lived. Sooner or later, we will need to develop something stronger.

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**We Are All the Same: A Story of a Boy's Courage and a Mother's Love**

Jim Wooten. Penguin Press, 2004. Pp 192. \$19.95. ISBN 1-59420-028-9.

## In brief

### Book Same but different

*We Are All The Same* is not the normal scientific fare of the readership of *The Lancet*. In the jargon of the book trade, it is, however, a good read, and far more than, as its subtitle promises, "A Story of a Boy's Courage and a Mother's Love". It is the human story of millions of people in the developing world who learn of and experience HIV/AIDS in their personal lives and deaths. It is the story of the political struggle for freedom, human rights, and equity of access to health care in South Africa beyond the establishment of the outward form of a new democracy. Above all, by telling the story of Nkosi Johnson and his adoptive white mother, Gail, it raises (but does not seriously try to answer) the question of why, at this late stage in the new South African democracy, the struggle for access to effective treatment for AIDS was necessary at all.

The bare bones of the story are well known in South Africa. Nkosi was one

of the children infected at birth for whom antiretrovirals came too late. His engaging personality is captured, as are the contributions to his happiness from other players in the dramas through which he and Gail move: the HIV-positive people in the shelters who love him, the voluntary workers who raise funds to run these shelters, his two families, and his special school friend.

Jim Wooten is one of many journalists who ensured that Nkosi's story reverberated around the world. Nkosi has taken on, as Nelson Mandela has suggested, the mantle of an AIDS icon. He has become a symbol of the ethical responsibility for treatment to reach poor countries as speedily and effectively as possible. Why and how one person is raised above hundreds (even millions) of others to epitomise a particular social category or movement is a sociological question that may be raised in the mind of the more thoughtful reader. In Nkosi's case,

among many other reasons might have been his appearance as a speaker with President Mbeki at the opening of the 13th International AIDS Conference in 2000. The fact that it was the first time this meeting had been held in Africa, and the President's obdurate stand on HIV/AIDS, drew the media like flies to honey. Wooten tells this story graphically and builds the opening words of Nkosi's speech into a recurring refrain that gives the book both its title and a tragic coherence.

*We Are All The Same* is a potent advocacy tool for access to antiretrovirals. At a personal level it is a celebration of courage and humanity. In this, this short book might constitute rewarding and important reading for all in the medical profession.

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## Historical keywords

### Nerve

Originally, “to nerve” meant to endow with physical strength, as in “to nerve the strong arm”. But by the 19th century, E Bulwer-Lytton could write of “nerving your mind to the exertion”. The transition to the more figurative use indicates the ambivalence in the meaning of nerve and its derivatives. “Nerve” bridges the body and the mind; it gestures to a pre-Cartesian cosmos that did not recognise a distinction between the two.

Nerve is derived from a Greek term that could also refer to tendons. Although the Alexandrian school differentiated between the two, this anatomical indeterminacy persisted until the 18th century. Other fields also appropriated the term. As late as the 19th century, the vessels of plants might be deemed to be nerves. In medicine, by 1800, nerve was used to subserve sensation or motion. As such, nerves and the nervous system remained liminal entities, intermediaries between the outside world and perception. In common use, they were associated with mental and moral qualities. According to Robert Browning, soldiers needed “nerves of steel”, while for George Orwell, pilots required “exceptional good nerve”. By the end of the 19th century, possessing nerve might also imply impudence, as in “you’ve got a nerve!” Such colloquial uses had little to do with the esoteric language of medical science, where from the 18th century, to have nerves or be nervous connoted a psychological predisposition. But when someone was said to have “touched a nerve” a physiological property was evoked to express an emotional response. If an experience was “nerve-racking”, the implication was that, as the nerves were stretched and made taut, so the mood became increasingly tense.

By the 19th century, a “nervous disposition” might lead to disordered mental states and behaviour. Generally, these conditions fell short of insanity, occupying a realm where peculiarities deemed to lie within the bounds of the normal might creep into the realms of the pathological. Women were especially prone to “nerves” that in extreme cases led to a “nervous breakdown”. By the end of the 19th century, these conditions were “neuroses”, and specialists for these complaints emerged: nerve doctors, or neurologists. Although this specialty is now mostly concerned with organic complaints of the nervous system, it is noteworthy that many early neurologists spent much of their time treating neurotics.

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## Lifeline

**Raoul Fransen** is the co-founder of Young Positives, an international advocacy network of young people living with HIV/AIDS. After setting out to be a medical doctor, he eventually received a masters in public health. He worked as a policy adviser for health-care institutions, then became policy officer at the Dutch AIDS Fund, dedicated to improving the Dutch response to HIV/AIDS.



**What has been the greatest achievement of your career?**  
Combining my career with personal motivation by being involved in issues around HIV/AIDS at a global level but still working with grass-roots communities.

**And the greatest embarrassment?**

Failing to acknowledge early on the relative simplicity and necessity of achieving access to antiretrovirals in poor countries.

**What do you think is the most neglected field of science or medicine at the moment?**

Research on the long-term effects of antiretrovirals.

**Which patient has had the most effect on your work?**

My now-best-friend Dieudonné, a young refugee from Burundi who saw his parents being executed. When I met him in one of our clinics in rural Zambia, he had nothing except for the clothes he was wearing and a picture of his father. 4 years on, he has graduated as a pharmacologist.

**What part of your work gives you the least pleasure?**

When I find myself in a 5-star hotel in the guise of fighting disease and poverty, surrounded by people who seem to make a career going from one of these events to another.

**If you had not entered your current profession, what would you have liked to be?**

A pilot with the Flying Doctors or a puppeteer on *The Muppet Show*.

**What is the best piece of advice you have received, and from whom?**

“Smell the flowers while you can” by U2’s Bono.

**What is your greatest regret?**

That, in spite of my incredible good fortune—being born in the Netherlands, a safe childhood, access to all basic needs—I am not able to make a bigger difference.

**What is the least enjoyable job you’ve ever had?**

I once worked for a rent-a-car company. I quite enjoyed it, but they fired me when they learned I was HIV-positive.

**What was your first experiment as a child?**

With a friend in primary school, I tried to make gunpowder. We had to re-paint his parents’ garage.

**What was the most memorable comment you received from a referee?**

“People in developing countries will never be able to adhere to antiretroviral therapy” (1997).