

real-world patients might be at higher risk for renal disease than individuals selected for the trials. These possibilities could be investigated further by looking at the risk profile of people who met inclusion criteria for the trials.

The costs of postoperative complications are high and conflicting evidence now exists about whether use of aprotinin increases⁸ or tends to reduce⁵ them. A large randomised trial comparing different antifibrinolytics seems fully justified, and we await the findings of the BART trial in Canada.¹³ Perhaps further trials of aprotinin are needed, but they should be designed to answer specific unresolved questions,² such as: what is the risk of adverse outcomes in high-risk groups?

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The rise and fall of sleeping sickness

Human African trypanosomiasis (HAT) (sleeping sickness), is much feared. Trypanosome parasites, transmitted by tsetse flies, proliferate in patients' blood, lymphatics, and later CNS, in which they induce progressive neurological dysfunction then death.¹ *Trypanosoma brucei gambiense* and *T brucei rhodesiense*² cause a chronic disease in central and western Africa and an acute form in eastern and southern Africa, respectively. More than 90% of cases are the gambiense form.

HAT was largely under control in the mid-20th century but by the 1990s was back with a vengeance.³ Wars in many African countries were rampant and national HAT programmes, chronically under-funded, were in disarray. The fragmented efforts of a few charities and non-governmental organisations were insufficient to contain the disease. Production of HAT drugs was in jeopardy.

By 1997, an estimated 450 000 people were afflicted. The most recent WHO figures now put numbers at no

higher than 70 000.⁴ A coordinated but sometimes precarious campaign has precipitated the decline. For example, in 1999, WHO received the licence for eflornithine, a compound registered for late-stage gambiense disease. But no one would make it until another condition materialised. Eflornithine suppresses the growth of facial hair, a disorder perceived as lucrative to Gillette. Médecins Sans Frontières, lobbying hard on access to essential medicines,^{4,5} fuelled public outrage. What clearer example of the failings of profit-driven drug-design could there be?

At this point, France's drug giant Aventis stepped in. They agreed to produce eflornithine for HAT. By May, 2001, Aventis made an unprecedented US \$25 million agreement promising all of their HAT drugs to WHO gratis for 5 years plus cash to underpin control activities. Their goal according to Jean Jannin: "to create the conditions enabling a process of disease elimination." Bayer also donated suramin. Another boost came in December, 2000, when the Bill & Melinda Gates

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Tsetse fly

Foundation funded a group centred at the University of North Carolina to develop DB289, a new orally available drug for early-stage trypanosomiasis.

Since 2001, awareness of the disease and surveillance have increased. Gates have extended their contribution in 2006, taking DB289 into phase III trials and funding the Foundation for Innovative Diagnostics, in collaboration with the neglected tropical diseases department at WHO, to develop new methods to detect and stage HAT. National programmes have been reinvigorated and other organisations, such as Médecins Sans Frontières, Malteser, WHO/Special Programme for Research and Training in Tropical Diseases, and Caritas have made great strides.

A clearer picture of HAT epidemiology has also emerged. The 1990s figures assumed that, with only 10% of the affected population under surveillance, a tenfold multiplication of reported cases was required to estimate true numbers. Increased surveillance means that today's figure of confirmed cases (17 500)⁴ requires a factor of only 3–4-fold to reach a credible estimate.

Coordinated efforts, backed by sufficient funds, can control HAT. What happens now though? HAT will undoubtedly resurge again if ignored. Luckily, the now merged Sanofi-Aventis renewed their commitment on the gratis provision of drugs in the past year, and are in discussions to provide more cash to sustain control programmes.

The available drugs are, however, unsatisfactory. Some are toxic, resistance is appearing, and all are difficult to administer. DB289, being orally available, will offer some benefits if registered, but it is suitable only for early-stage disease whereas it is for the late-stage disease that new medications are most urgently required.

A report⁶ from the London School of Economics painted an optimistic picture for new drug development. The emerging public-private partnerships (PPP)⁷ aiming at developing new drugs for various afflictions of the developing world are doing well. For example, just in the past month the Drugs for Neglected Diseases Initiative, the Geneva-based PPP that includes HAT in its remit, received £6.5 million from the UK Government. Britain's Wellcome Trust too retains tropical-disease control high on its agenda. They provided most of the funds required to sequence the trypanosome's genome,⁸ and they have just opened a drug-screening centre at the University of Dundee.

Buoyed by recent successes, the International Scientific Council for Trypanosomiasis Research and Control in Addis Ababa last September called on WHO to "launch an elimination programme for sleeping sickness".⁴ That in just 5 years we have moved from the abyss to a position where words like "elimination" can even be spoken is remarkable. A coordinated campaign to eliminate the scourge of sleeping sickness should begin.

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