

prescribed for long periods, accelerates progression of the disease because it might be a source of free radicals and hence might hasten the degeneration of already fragile dopaminergic neurons.³ If so, is the toxic effect one of irreversible damage leading to cell loss? Or is it just cell dysfunction, which may temporarily or permanently contribute to the occurrence of the side-effects?

To address these questions, a meeting of 25 experts was held in Paris (Jan 8–9, 1998) to discuss studies of levodopa toxicity done in tissue culture, animal models of parkinsonism, and human beings, and to try to arrive at some agreement on whether or how the findings should influence prescribing of the drug. The detailed discussion, together with published conflicting findings, will appear elsewhere. The main conclusions can be summarised as follows.

- Levodopa is still the most effective treatment for parkinsonian symptoms, and it decreases mortality rate from this disease.⁴
- There is no evidence that long-term administration of levodopa contributes to or worsens the underlying neurodegenerative brain lesions in patients with Parkinson's disease.⁵
- Levodopa-induced motor complications result from both degeneration of brain dopaminergic systems (a process for which there is no means of prevention) and the repeated administration of levodopa⁶ (which can be modified according to the condition of the patient).
- There is no convincing evidence that therapeutic doses of levodopa result in nerve-cell death in animal models of parkinsonism.⁷
- Levodopa can induce cell death in vitro but only when high concentrations are used in the absence of glial cells;^{8,9} however, the relevance of in-vitro work to patients with Parkinson's disease is uncertain.

In sum, there is no cause for concern that levodopa is dangerous for patients. How and when to prescribe levodopa should be influenced not by fear that the drug is toxic, but by how the patient reacts to the drug.

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WHO's tuberculosis research initiative

Although essentially curable, tuberculosis kills up to 3 million adults every year, more than any other infectious disease. Compounding the situation is a vast disparity between the burden of human disease attributable to tuberculosis (3% worldwide) and the amount spent on tuberculosis research (an optimistic guess is 0.2% of the health research budget). To establish a rational approach to setting priorities for research, the WHO global tuberculosis programme (GTB) has started the global tuberculosis research initiative (GTRI).

Under GTRI, tuberculosis researchers, policy-makers, and representatives of national programmes met in Geneva on March 3–5 to start priority setting. Their recommendations emphasise the need for research into optimising the delivery of directly observed therapy, short-course (DOTS), the strategy that lies at the heart of the WHO tuberculosis-control programme. The need to improve the delivery of DOTS is based on knowledge that the strategy works, but that only about 12% of tuberculosis patients worldwide are covered by DOTS and that most large key epidemic countries have low DOTS coverage. The GTRI recommendations stress the importance of developing operational-research capacity in the countries worst affected by tuberculosis and of coordinating research with the routine functions of national tuberculosis programmes. Another need is to make operational research more “glamorous”, to attract funding and the best scientists. For strategic research the priority areas are improvement in the accuracy of surveillance and epidemiological data, identification of drug-resistance trends, and development of new diagnostic tools, drugs, and vaccines. However, strategic research might take decades to bear fruit, hence the emphasis placed on operational research.

GTB must disseminate widely the GTRI recommendations and take account of the views of tuberculosis scientists and fieldworkers, particularly those in developing countries. The essential next step is to establish the mechanisms to turn GTRI recommendations into actions once they have passed through a Byzantine series of WHO committees. It would be a shame if bureaucracy inhibits the good intentions of the GTRI.

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The Lancet and the Internet, mark II

The pace of change is nowhere quicker than on the Internet. Return to the worldwide web (the multimedia section of the Internet) after an absence of a few months and you will find a landscape transformed in richness and variety. As a medium for academic publishing the Internet now offers opportunities unimaginable in paper. *The Lancet Interactive* website (<http://www.thelancet.com>) launched this week is a step forward in our challenge, according to Tony Delamothe in the supplement that accompanies this issue, to the “paper mindset”. Rapidly updated readers' comments form an integral part of the site, and we look forward to publishing research supported by video and sound.

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