that influenza infection has preceded and not coincided with meningococcal disease.

We believe that our study confirms the previously suggested association between influenza A infection and meningococcal disease. During an influenza epidemic, public health authorities should be prepared to alert medical practitioners and the public to an increased risk of meningococcal disease in the following month.

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VIEWPOINT

Is Africa lost?

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During a World Health Organisation (WHO) tuberculosis meeting last year Africa was described as "lost". No one questioned this description, which was taken to mean that there was no way of dealing with coinfection with the human immunodeficiency virus (HIV) and the tubercle bacillus. Although at present there is little other than education and use of condoms that can help prevent the spread of HIV, are we really helpless against *Mycobacterium tuberculosis*?

Desperate problems may need desperate remedies, but the longer we delay these measures, the more difficult it will be to make them work. We can no longer think of 6 or 9 months as the minimum period of treatment for tuberculosis but must accept that a course of only 2 months (ie, just the initial three or four drug phase) has to be the maximum. Across sub-Saharan Africa there are now so many people with tuberculosis, 2·4 million of them coinfected with HIV, that there is no chance that sufficient funds or personnel will be made available to achieve even this.

In the prechemotherapy days, many patients with tuberculosis recovered spontaneously, but spontaneous recovery cannot be expected in those coinfected with HIV. Nonetheless, most cases of tuberculosis in HIV-positive persons occur before all immunity has been lost.[1] A very short course of chemotherapy followed by injection of an immunotherapeutic agent capable of reducing the amount of immune-mediated tissue necrosis should massively reduce the infectiousness of tuberculosis patients and might be sufficient to achieve a cure in a good proportion.[2] At the end of this abbreviated treatment, patients should be asked to come back to the treatment centre if their symptoms return.

The future of tuberculosis control no longer lies in those elegant studies of the Medical Reseach Council,[3] for perfection has to give way to expediency. What is now urgently required is for WHO to set up an immediate action group against tuberculosis with the power to design and initiate studies undreamed of in the past (see figure). We

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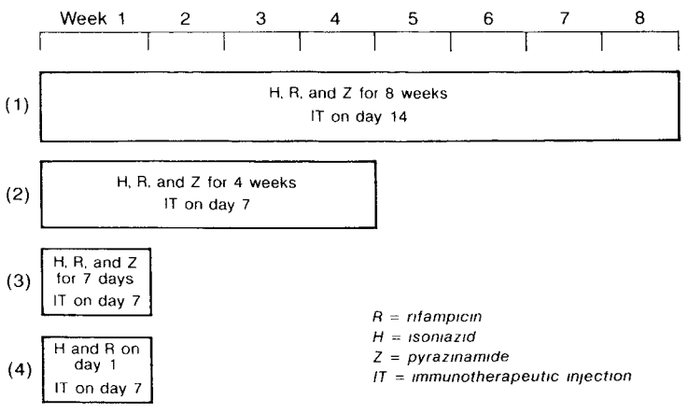

Schedules for investigation of revolutionarily short treatments for tuberculosis in countries with extensive HIV and *M tuberculosis* coinfection.

urgently need comparisons of regimens incorporating chemotherapy and immunotherapy and lasting no more than a month. Perhaps just 7 days of isoniazid, rifampicin, and pyrazinamide (which would kill 95% of bacilli) with immunotherapy on day 7 would suffice. Sights must be set not on the idealised but impractical target of 99% efficacy but on the best that can be achieved—perhaps a cure rate of no more than 80%. A high cure rate, with fewer than 20% of relapses over a 5-year follow-up period, can be achieved with a 3-month course of chemotherapy alone.[4] This could be the beginning of the achievement of control over the disease, and Africa might be regained.

Prevention of disease must also be a priority. BCG (bacille Calmette-Guérin) vaccine has to be given to as many children as possible, and a rapid decision has to be made on what to do with known contacts of patients. Protection could be offered to apparently healthy people in a patient's household either as preventive chemotherapy or as preventive immunotherapy. Preventive chemotherapy with isoniazid has been widely used in the USA and has been effective there.[5] But how could it be used in Africa? It is doubtful whether a single-month course of isoniazid would be sufficient to destroy bacilli that have already infected the recipient, and if he had not contracted tuberculosis while living with the index case before diagnosis, why should he do so during the short time in which chemotherapy makes a patient non-infectious? A longer course of isoniazid preventive chemotherapy would be too expensive, would run into problems of compliance, and is unlikely to make any useful contribution towards the prevention of tuberculosis. What, then, of preventive immunotherapy? Although hardly tried, it is the only approach that could make a major difference to the whole region within the available budget.

What is preventive immunotherapy? The term refers to the use of a vaccine-like injection, which has to achieve two aims. First, it must lead to the elimination or long-term stasis of infecting bacilli and, second, it must leave the individual protected as far as possible from reinfection. Such a treatment must be safe, cheap, stable, and easy to administer, and must not consist of live organisms because of the risk that the recipient might be infected with HIV.

The effects of suspensions of killed *M vaccae*[2,6,7] indicate that this might be a suitable preventive immunotherapeutic agent. This is supported by additional unpublished studies from The Gambia, India, Iran, and Vietnam. Intradermal injections of 10^8 *M vaccae* can be given to tuberculin negative or positive individuals without significant side-effects,[8] and in non-HIV-infected persons such injections have an effect on skin-test responses still seen after 8–10 years.[9] Since the same reagent, but at the higher dose of 10^9 bacilli, is recommended for immunotherapy of active tuberculosis,[7] there would be no danger if it was given to a person with unrecognised tuberculous disease. Experience with *M vaccae* in HIV-infected people is very small now but is rapidly growing.

Although the immunotherapy might produce a small increase in the number of T cells and, perhaps, a resulting increase in HIV replication, this is unlikely to be beyond that occurring in response to minor daily trauma. It would be more than offset by the reduction in the production of tumour necrosis factor (TNF), which is one of the major cytokines involved in the Koch response,[10] the basis of the immunopathology of tuberculosis,[11] and a known stimulator of HIV replication.[12] Thus switching off the Koch phenomenon in tuberculosis[11] should produce a net reduction, rather than an increase, in virus production.

A tremendous amount of money and research is going into tuberculosis today, but just how much of it is relevant to the problems of the real world? Elegant means of diagnosis are regarded as desirable, but what good are they really going to do? When we cannot treat all the cases that can be diagnosed clinically or by smear in the developing world rather less emphasis should be given to the elimination of the last few cases from those countries scheduled to be free of tuberculosis early in the next century. Despite the WHO's Alma Ata declaration of Health for All by the Year 2000, sub-Saharan Africa will be lucky if the tuberculosis problem is not far worse in that year than it is today.

In conclusion, we are facing one of the greatest public-health disasters since the bubonic plague. If the third or fourth treatment schedules in the figure could be made to work, perhaps it could be overcome.

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