

## News and Notes

### **TDR: Four TDR diseases, including leprosy, can be ‘eliminated’**

The following is extracted from the March issue of *TDR News*, 1996:

The means are now available to ‘eliminate’ four of TDR’s original eight target diseases as public health problems (meaning reducing the cases of the diseases to a small and routinely manageable number), a TDR expert meeting has concluded.

This is a wonderful success for the Programme—and the world—but, interestingly, in no case did the tools arise out of TDR-sponsored basic research. Rather, they arose from TDR’s judicious and timely use of large-scale, multicountry field trials of largely pre-existing drugs and simple control tools, combined with cost-effective epidemiology. The trials sharpened evidence of the tools’ effectiveness and impact, identified or confirmed the best combinations of different tools, improved means of delivery and implementation, and, not least, generated an international consensus on intervention.

Basic research is likely to bring still greater benefits—such as anti-parasite vaccines or genetically disabled vectors—but only in the longer term, even in the case of the most advanced candidates. Meanwhile, however, basic science is making ‘spin-off’ contributions towards elimination in providing cheap and simple diagnostics, such as dip-sticks for detecting Chagas infection in blood banks, and a recently-developed day-time fingerprick test for lymphatic filariasis (where night-time blood samples were once required).

The diseases slated for elimination with existing tools are leprosy (using multidrug therapy), onchocerciasis (ivermectin), lymphatic filariasis (DEC and ivermectin) and Chagas disease (rational use of insecticides and control of blood banks), leaving malaria, schistosomiasis, leishmaniasis and African trypanosomiasis awaiting better tools.

TDR’s contributions to leprosy included mapping and quantifying growing dapsone resistance (the lifelong monotherapy of the 1970s), developing clinical protocols for dapsone’s great successor—multidrug therapy (MDT)—and establishing large-scale ‘post-marketing surveillance’ of MDT. Now, WHO and partner organizations are well on their way to their target of reducing leprosy to one case per ten thousand population in each affected country by the year 2000.

From the same issue we reproduce:

### **Leprosy: from elimination to eradication?**

Through the increasingly widespread distribution of multidrug therapy (MDT), and its effectiveness, the prevalence of leprosy (measured by numbers of registered cases) has been reduced from 5·4 million cases in 1985 to 1·3 million in 1995.

But there is much work still to do to reach the target of the 1994 ‘Hanoi Declaration’—the reduction in prevalence (registered cases) to one in 10,000 people in each endemic country by the year 2000. Countries numerically furthest from this ratio in 1995 were Brazil (10 per 10,000), Chad (10), India (9), Mozambique (9) and Nepal (8). Moreover in 1995, only 75% of those registered were receiving therapy, with treatment ratios worst in Africa. The largest total numbers of untreated registered cases are to be found in India (around 200,000) and Brazil (60,000).

And there is a further gap between the numbers registered and the estimated actual number of cases; this number of undetected cases is believed highest (in total) in India (150,000) and Bangladesh (120,000), with the proportion worst in Bangladesh, Indonesia, Viet Nam, Mali, Niger and Sudan. Globally, it is estimated that some 600,000 to 1 million cases escape detection.

The number of cases actually detected and registered per year has remained roughly constant for ten years, and stood at around 530,000 in 1995; it reflects a difficult-to-estimate combination of true incidence rates, delays in diagnosis, specificity and sensitivity of diagnosis, self-healing rates—and of the efficiency of control programmes.

However, recent studies suggest that only 10% of these newly detected cases are true incidence cases (new infections of that year); 75% started 3–5 years earlier and 15% as much as 5–10 years before.

Moreover, Special Action Projects for the Elimination of Leprosy (SAPEL) have been launched to accelerate MDT coverage in hard-to-reach areas (such as among forest workers and fishermen in Amazonas in Brazil, and nomads in eastern Chad). Other campaigns are being conducted to detect 'hidden leprosy cases of consequence' (hidden highly infectious cases); and officers of the WHO Action Programme for the Elimination of Leprosy (APEL) believe that, with the current determination being demonstrated among countries and NGOs, the goal of the Hanoi Declaration is achievable.

The success of this elimination strategy may then lead to a desire—in some areas of the world—to totally eradicate the disease from these areas. This would require epidemiological surveillance and treatment of the small numbers of cases that may continue to occur, and, most importantly, surveillance of sub-clinical infection, and effective interventions to abort those infections.

This work would require new tools and new research, including a diagnostic test for sub-clinical infection. The most important consideration in the development of such tools, according to APEL, will be cost-effectiveness—which implies simplicity, affordability and acceptability to the whole community. Research is also needed on the rehabilitation and re-assimilation into the community of nerve-damaged and disabled patients.

Source: *TDR News*. UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, WHO, 1211 Geneva 27, Switzerland.

## Yemen makes progress in reducing the transmission of leprosy, WHO

The following is extracted from *LEPNews*, December 1995:

As in most countries, leprosy in Yemen has a long and unhappy past history. It is even recorded that, many centuries ago, one ruler collected large quantities of wood with every intention of solving the leprosy problem by burning the patients on a funeral pyre. Fortunately he died before carrying out this drastic 'cure'.

Even today, it is common for victims of leprosy to be obliged to get a divorce and be isolated from their own families; the moment the disease is diagnosed, they are considered socially dead. As recently as 1964, they were forced to live in unsanitary leprosaria.

Now a more enlightened attitude is spreading as the word gets about that leprosy is indeed curable by MDT. The country's case-load of leprosy has declined from a peak of 2314 registered cases in 1989 to 828 at the end of September 1995; 84% of these cases were multibacillary. Between January and September this year, 291 new cases were detected.

In 1992, an NGO called the Yemen Leprosy Elimination Society (YELEP) was formed to further the activities of the National Leprosy Control Programme (NLCP) and to provide material, financial and technical support to patients, including rehabilitation for former sufferers. Both the national programme and the NGO still face constraints; the stigma of leprosy continues even among health workers, control activities are not yet integrated in the health care infrastructure, and poor communications and difficult terrain impede the activities of field supervisors.

Nevertheless, the attitude of the community towards leprosy is gradually changing, thanks to intensive health education activities (including regular newspaper features and the screening of a special

TV programme on the disease each year since 1990). National health planners are confident that transmission of leprosy in Yemen will have been effectively halted within the WHO time-frame by the year 2000.

Source: *LEPNews*, WHO Action Programme for the Elimination of Leprosy, 1211 Geneva 27, Switzerland.

### **Mexico intensifies its strategy for the elimination of leprosy at sub-national level**

Having already achieved the elimination of leprosy (less than 1 case per 10,000 of the population) at national level, Mexico has now developed plans for the intensification of activities at state, health department and municipal levels. The State of Sinaloa in the western Pacific coastal area is due to start such activities in June 1996 and to pursue them intensively for 6 months, with the following main objectives: 1, discovery and treatment, to the maximum extent possible, of all hidden or occult cases; 2, examination of contacts of all registered cases; 3, identification of areas of high incidence and prevalence, with intensification of case-finding activities, including school children above the age of 9 years; and 4, orientation and basic training of health staff in peripheral health units in the recognition and referral of possible cases of leprosy, management of multiple drug therapy, and disability prevention.

It is anticipated that this intensive 6 months' project will reveal several hundred new cases (never treated before) and plans are already being made for similar activities in three other states in Mexico with relatively high prevalence. Sinaloa, for reasons which are far from clear, is currently the only state in the country with a prevalence of more than 1 case per 10,000; the figure is 4.9. It may be relevant that its population (2.5 million) has a high proportion of people of Chinese, Japanese, Philippine and European (mainly Spanish) origin, with a high degree of racial mixing, and from an epidemiological point of view the finding of numerous cases of Lucio leprosy ('smooth leprosy'; 'lepra bonita') could be of considerable importance; many of these cases are asymptomatic for long periods before diagnosis; do not develop nodules and frequently have little to show clinically except madarosis, despite positive smears at all sites.

Having done all possible, using an intensified, short-period approach, at health department and municipal levels in the above 4 states, attention will be given to any remaining areas or pockets with significant numbers of cases in other parts of the country. Rehabilitation centres with orthopaedic workshop facilities have been established in 18 endemic areas, with considerable help from Ciba-Mexicana and the Ciba-Geigy Leprosy Fund in Switzerland and these agencies have recently supported the printing and distribution of a revised edition of the *Manual of Procedures for Leprosy Control*, written by the Health Secretariat. In 1986, Mexico had 16,687 registered cases with a prevalence rate of 2.1/10,000. By March 1996 this had fallen to 5005 with a prevalence rate of 0.5/10,000. The control programme has exceptionally strong medical and political support and the prospects for still further reduction in prevalence, at sub-national level, are apparently excellent.

### **TB deaths reach historic levels, WHO**

The following is taken from WHO Press Release, March 1996, WHO/22:

More people died from tuberculosis in 1995 than in any other year in history, according to a report released today by the World Health Organization. According to WHO, nearly three million people died from TB in 1995, surpassing the worst years of the epidemic around 1900, when an estimated 2.1 million people died annually (see Figure 1 below).

The WHO warned that the TB crisis will continue to grow unless immediate action is taken. At current rates, up to a half-billion people could become sick with TB in the next 50 years. Increasingly, these people may become sick with often-incurable multidrug-resistant TB.

## Annual TB Deaths

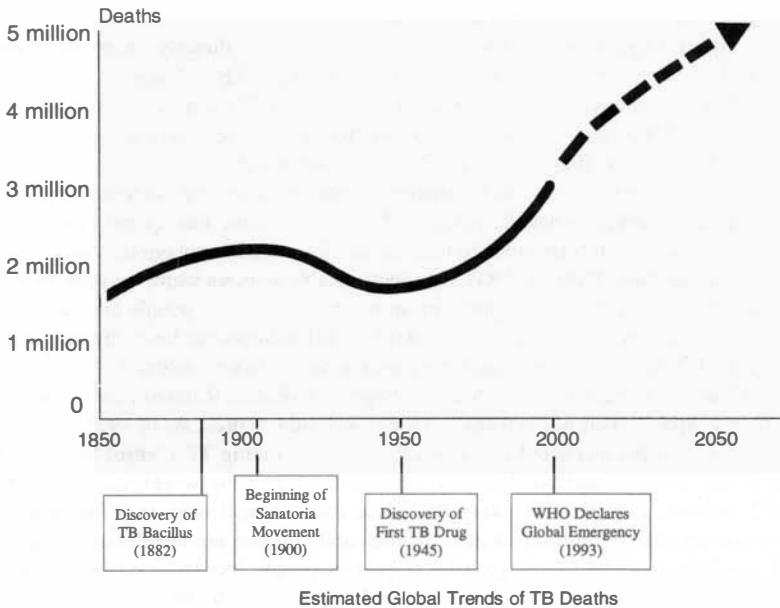


Figure 1.

'Not only has TB returned, it has upstaged its own horrible legacy,' said Dr Hiroshi Nakajima, Director-General of the World Health Organization.

According to the WHO report, entitled 'Groups at Risk', TB has increasingly assailed all segments of society. TB is now the leading infectious killer of youth and adults. It has become the principal killer of HIV-positive people and kills more women than all causes of maternal mortality combined. Nearly half of the world's refugees may be infected with TB. It is likely that no other infectious disease is creating as many orphans and devastating as many families.

'There is nowhere to hid from tuberculosis bacteria,' warned Dr Arata Kochi, director of the WHO Global TB Programme, 'Anyone can catch TB simply by inhaling a TB germ that has been coughed or sneezed into the air. These germs can remain suspended in the air for hours; even years. We are all at risk.'

TB has returned with a vengeance to wealthy countries, as increased air travel and migration have helped transport the disease throughout the world. Miltidrug-resistant TB, which has cost New York City hundreds of millions of dollars to fight, has now been reported in London, Milan, Paris, Atlanta, Chicago and cities throughout the developing world. In particular, the number of multidrug-resistant cases in Asia are expected to increase rapidly, unless TB control efforts are strengthened.

'The world is becoming smaller and the TB bugs are becoming stronger,' said Kochi, 'While international travel has increased dramatically, the world has been slow to realize the implications for public health. Only recently have wealthy governments begun to recognize that poor TB treatment practices of other countries are a threat to their own citizens.'

According to the WHO report, unprecedented levels of neglect during the 1970s and '80s helped to create this situation. In 1993, WHO declared a global TB emergency, prompting some governments to increase their response to TB. However, the TB epidemic continues to outpace these modest efforts.

'The scientists have done their part to help rid the world of TB' said Dr Kochi. 'But the politicians have yet to put these tools to use. The TB bacillus was discovered over a hundred years ago, and

medicines that can cure nearly every TB patient have been available for the past fifty years. But these tools are not being widely or correctly used. Many TB treatment programmes are so poorly supported that they are producing stronger bacteria and weaker patients.'

The World Health Organization endorses a strategy known as directly observed treatment, short-course, or 'DOTS', which has proven successful in fighting TB. Countries that follow WHO's recommended DOTS strategy, such as Tanzania, China, and Peru, have discovered that they can double the number of TB patients cured. The DOTS strategy can cure nearly 95 percent of TB patients, using medicines that cost less than \$11 in some parts of the world.

The secret to the success of the DOTS strategy is that it places the responsibility for curing TB patients on the health workers—not the patients. The TB epidemic has spread rapidly over the past decades because patients often forget to take their medicines, remain contagious, and continue to infect others in their communities. With the DOTS strategy, health workers watch as patients swallow their medicines and tracks each patient's progress, ensuring that contagious people are cured.

According to WHO, only 10 percent of the world's TB patients are being treated with the DOTS strategy. If the DOTS strategy were used throughout a dozen large countries—such as Bangladesh, Brazil, China, Ethiopia, India, Indonesia, Mexico, Nigeria, Pakistan, Russian Federation, South Africa, and Zaire—nearly three-fourths of the world's TB cases could be cured. As of 1995, only a few of these countries had aggressively committed to establishing and expanding TB control based on DOTS.

'The longer we wait to establish DOTS programmes around the world, the more expensive TB treatment will become, and the less likely it will be that we will ever stop this disease,' said Dr Nakajima. 'In the meantime, millions of men, women and children are needlessly dying.'

'The TB epidemic must be fought globally to protect people locally,' said Dr Kochi. 'It is in the interest of wealthy countries to help less-developed countries fight tuberculosis, before their own countries become the battleground.'

The World Health Organization is releasing this report prior to World TB Day, 24 March. World TB Day commemorates the day in 1882 when Dr Robert Koch officially informed the scientific community that he had discovered the TB bacillus. Yet Koch's discovery and the effective drugs that were later developed have seen limited use. As a result, TB has sent at least 200 million people to their graves since 1882.

For more information, contact Kraig Klautd or Colin Martin in London (21 March only) at (44) 171-798-4217 or Courtenay Singer or Richard Bumgarner in Geneva at (41) 22-791-2189 or (41) 22-791-4641.

## **Hepatitis A, B, C, D and E**

In view of the fact that several of the drugs used for the treatment of both leprosy and tuberculosis may be hepatotoxic, the following information on the terminology and clinical effects of the various forms of viral hepatitis may be of interest. It is extracted from a '*Workshop on Hepatitis C Virus*', an account of which was published in the *Proceedings of the Royal College of Physicians of Edinburgh*, October 1995, Volume 25, Number 4, pages 583–622.

From the *Introduction* by the Editors:

'Older readers will remember that their textbooks in the 1930s contained a section on catarrhal jaundice which was distinguished from obstructive and haemolytic jaundice. The cause of the catarrh was unknown. The single diagnostic label was soon replaced by two, infectious hepatitis and serum jaundice, the latter being a common condition in patients being treated for syphilis with intravenous injections. When means were discovered for isolating and identifying viruses, these conditions were found to be due to separate viruses, hepatitis A and B (HAV and HBV). A third distinct virus with an affinity for the liver was yellow fever virus. Other identified viruses are hepatitis C virus (HCV), hepatitis D (HDV) and hepatitis E virus (HEV).

Yellow fever virus is spread by an arthropod vector from a pool of infection which still persists in

some jungle primates. HAV and HEV infection is spread from case to case by the faecal-oral route. Infection by HBV is transmitted via intimate (usually sexual) contact or parenteral injection through a contaminated needle or transfusion fluid. HCV is rarely transmitted by sexual contact, occasionally by needle stick injury but usually by infusion fluid.

There is extreme variation in the clinical manifestations of infection with hepatic viruses. A self limiting attack of fever with jaundice is the common presentation with yellow fever and with HAV and HEV infections, but is often absent with HBV and HCV infection. A fulminating, usually fatal, hepatitis is common in yellow fever, very rare with HAV, HCV and HEV, a well known tragedy with HBV infection. A persistent inflammatory response, with or without the continuing presence of virus, leading to cirrhosis and carcinoma is the main clinical feature of HCV infection and common in HBV infection. It is rare, if it ever occurs, in yellow fever or in HAV infection. Hepatitis D virus is strongly related to intravenous drug use but has similar epidemiological and clinical features to HBV with which it is often associated in time. In the immunocompromised patient, as with AIDS, the liver may be affected by other viruses, in particular cytomegalovirus, herpes simplex virus, measles virus in adults and Coxsackie virus B, all of which may give rise to hepatitis in occasional individuals.'

From a section entitled '*Historical Perspective*' under the heading '*Epidemiology of Hepatitis C*': 'In the 1960s, in Washington in the USA, a recipient of a blood transfusion had a 1 in 3 chance of developing post-transfusion hepatitis. In 1970 two things changed. Firstly, testing for hepatitis B became available, which reduced post-transfusion hepatitis by about 50%. Secondly, the blood donor service moved to an all-volunteer programme with a further significant reduction in hepatitis amongst recipients. In the 1980s, donors with raised ALT levels were excluded, but a rump of post-transfusion hepatitis cases remained. When testing for hepatitis C became available it became clear that 95% of non-A, non-B hepatitis was due to hepatitis C.'

In 1982, the Centre for Disease Control, Atlanta, set up a 'Sentinel Counties Study', looking into the risk factors for non-A, non-B hepatitis in sporadically occurring cases in the community. It soon became apparent that transfusion only accounted for 3% of such cases and in approximately 50% no risk factors could be identified. In the first year of this study, 13% of cases were associated with intravenous drug abuse, but by 1988 this figure had risen to over 40%. When second generation assays for HCV antibody became available, retrospective testing confirmed that HCV was responsible for 100% of cases acquired through intravenous drug abuse. In 1988, no source of infection could be identified for approximately one third of cases, and HCV was only identified in 52% of these. It should be noted that when testing for anti-HCV in patients with acute non-A, non-B Hepatitis, sufficient time must be allowed to elapse for seroconversion to take place. For example in one study only 10 of 20 (50%) patients who developed non-A, non-B hepatitis following blood transfusion and were tested within 6 weeks of the onset of illness, were found to be anti-HCV positive, compared to 19 of 25 (76%) who were tested 6 months after the onset of illness.'

### **Chemotherapy of leprosy. Report of a WHO Study Group**

The above booklet of 24 pp. is from the WHO Technical Report Series, No. 847 and was published in 1994:

Since the introduction of standardized multidrug therapy (MDT) for leprosy in 1981, over 5.6 million patients have been cured and the number of cases has been reduced by two-thirds. Although most countries are now aware of the critical role of MDT in leprosy control, there is still some uncertainty about the efficacy and optimum duration of such regimens.

The report contains the recommendations of a WHO Study Group on Chemotherapy of Leprosy, convened to review the performance of WHO's multidrug therapy regimens for paucibacillary and multibacillary leprosy. Intended for managers of leprosy control programmes, the report has five sections. The first reviews findings from several studies of leprosy chemotherapy involving large numbers of patients. The second section summarises accumulated data on the safety, efficacy, optimum

doses and costs of available antileprosy drugs. Recommended chemotherapeutic regimens are presented in the third section. The report concludes with practical advice on operational issues relevant to the quality of control programmes and reviews prospects for the development of new drugs.

Available in English, French and Spanish from: World Health Organization, Distribution and Sales, 1211 Geneva 27, Switzerland. Price: Sw.fr.6/US\$5.40, and in developing countries Sw.fr.4.20.

### **Leprosy data on-line through the Internet**

Essential information about leprosy and the efforts around the world to eliminate it are already available to everyone whose computers are plugged in to the Internet. WHO's Action Programme for the Elimination of Leprosy ensures that regularly updated statistics on the global burden of the disease can be brought on screen, as well as a brief summary of the situation in the major endemic countries.

*LEPNews* itself will be available on the net as soon as it is published. Other specific pages include: the disease and its treatment, the WHO Programme and its strategy for elimination, the most endemic countries, the Leprosy Information system, MDT drug supply monitoring and relevant publications.

Users need only to connect to the INET link [http://www/who.ch/programmes/lep/lep\\_home.htm](http://www/who.ch/programmes/lep/lep_home.htm).

Source: *LEPNews*, Vol. 5, No. 1, 1996, WHO, Geneva, Switzerland.

### **IV Congress of the College of Hansenology of the Endemic Countries/IX Congress of the Brazilian Association of Hansenology, 4–8 June 1997, Foz do Iguaçu, Brazil**

Topics to be covered: Elimination day: Diagnosis and treatment, Research methodology, and Social and educational aspects.

Conferences: Therapeutics, Immunology, Genetics, Rehabilitation, Elimination, and Neural lesions.

Seminars: Treatment, Reactions, Immunology, Epidemiology, Social Aspects, and Elimination.

For further details write to: Secretaria Executiva, IN TIME Promoções e Eventos Ltda, Av. Paulista, 2073 Horsa I cj 501 - CEP 01311-300 São Paulo, SP, Brazil. Tel: 55 11 285 5549; Fax: 55 11 283 5409.

### **Leprosy Review posters: ENL**

The A3 poster enclosed with this issue of *Leprosy Review* is the second in a series of four covering important areas of management and research in leprosy and is distributed free to subscribers to the Journal.

We hope subscribers will find these posters informative and useful. Displayed prominently in clinics, they should serve as a useful teaching resource and aide memoire for all those involved in the treatment of leprosy and its reactions and in prevention of disability work.

We would welcome feedback and comments (to the Editor please) on this series and suggestions for future topics. Additional copies of the poster in this issue and those in future issues will be available from LEPR, Fairfax House, Causton Road, Colchester CO1 1PU, England.

### **Erratum**

Development of life-threatening thrombocytopaenia in a patient on MDT and prednisolone. R. CROFT, Letter to the Editor, *Lepr Rev* (1996) **67**, 229. Please note that the author of the above Letter to the Editor is R. CROFT and not as printed.

paragraph 3, line 3 for 'crushingoid' read 'cushingoid'