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News and Notes

New leprosy treatment, *TDR News*

The following article appeared in No. 38 of *TDR News*:

Large-scale trials began in February 1992 of a new, rapid drug treatment that could help to wipe out leprosy, which today still affects an estimated 5–6 million people worldwide, including 2–3 million people who have deformities as a result of the disease.

The treatment, which is given orally, combines a new antibiotic, ofloxacin, with rifampicin, an antibiotic discovered in the 1960s and the mainstay of standard leprosy (and tuberculosis) therapy. Scientists believe the combination of the two drugs will be the most powerful treatment yet discovered for leprosy.

The combination promises to shorten duration of therapy to only 1 month, as against the 6 months to 4 years required by the standard multidrug therapy. 'This should make leprosy treatment far more acceptable to the many patients who balk at taking drugs for months or years and brings the possibility of wiping out the disease much closer, 'says Hiroshi Nakajima, the WHO Director-General.

Multidrug therapy was introduced by WHO 10 years ago and involves the administration of 2 drugs (dapsone and rifampicin) for patients with mild (paucibacillary) leprosy and of 3 drugs (dapsone, clofazimine and rifampicin) for those with severe (lepromatous) leprosy. Over the past 5 years it has cured over 2 million of the world's known leprosy patients in 91 countries where leprosy is a public health problem.

'Such rapid and effective use of drugs is certainly a remarkable achievement,' says Dr Nakajima. 'Its only a first step though. There are still about 40 to 50% of leprosy patients who are not receiving drug treatment. Our task now is to ensure that *all* leprosy patients across the globe have access to multidrug therapy.'

The trials of the new ofloxacin-rifampicin treatment, which are being organized by TDR and the WHO's Leprosy Unit, will take place in 7 countries—Brazil, Kenya, Mali, Myanmar, Pakistan, the Philippines and Viet Nam. They will compare the new regimen with the standard multidrug therapy. Results of the trials, which will involve about 4000 patients, should be available in 4 or 5 years.

'If successful, this ofloxacin-rifampicin regimen would represent a major advance in the treatment of leprosy,' says TDR director Tore Godal. 'The first drug used against the leprosy bacillus was dapsone and for many patients it had to be taken every day for life. Then came multidrug therapy, which brought treatment time down to 4 years at most. And now we're talking about 4 weeks' treatment.'

Ofloxacin was launched in 1985 by the Japanese pharmaceutical firm Daiichi Seiyaku for the treatment of infections, particularly of the urinary and respiratory tracts: it has cured between 70 and 98% of the 1·5 million patients who have already received the drug, producing mostly mild side-effects in only a few patients.

Ofloxacin kills the leprosy bacillus by inhibiting an enzyme that controls the way DNA coils itself inside the bacillus. In 1986, French researcher Jacques Grosset of the Pitié-Salpétrière

Hospital Medical School in Paris found ofloxacin to be second only to rifampicin in the speed and efficacy with which it killed leprosy bacilli in laboratory animals.

The present trials were set up on the assumption that ofloxacin should be able to kill any mutant bacilli resistant to rifampicin much more quickly than do the other components of multidrug therapy. Shaik K Noordeen, chief of the WHO Leprosy Unit believes that if the new treatment is shown to work, it could be extremely useful for patients living in outlying communities for whom compliance with months or years of multidrug therapy is a problem. Initially, the rifampicin-ofloxacin 4-week treatment would be administered under medical supervision in clinics or health centres. But as experience with this treatment grows, community-based or even home treatment could be envisaged.

Ofloxacin and rifampicin are much more expensive than dapsone and clofazimine, making the new 4-week treatment about the same price as the standard 2-year or 6-month multidrug therapy. But again, with increased use, the price, particularly of ofloxacin, could be expected to fall.

Selected annotated bibliography on essential drugs: WHO

This publication (WHO/DAP/90.3) comes from the WHO Action Programme on Essential Drugs and Vaccines, WHO, 1211 Geneva 27, Switzerland. It has 214 pages and includes author, country and subject indexes. The introduction reads as follows:

The literature on the rational use of drugs has become more complex since the early 1970s. Within the last decade, interest has increased in developing a conceptual framework for the rational use of drugs. Governments, international and non-governmental organizations, universities and individuals have been actively involved in the many different aspects, including the formulation of the concept of essential drugs and the development of mechanisms to increase the availability of appropriate drugs at different levels of health care. National policies and programmes have been developed which determine the type and quantity of drugs needed, their rational use and the means to procure and distribute them effectively, taking into account local economic, social and political environments.

This second edition of the annotated bibliography builds on the publication issued in May 1988 and contains 173 additional references. It provides an entry point to the literature on these diverse activities. It directs the reader to key reports, articles and books related to essential drugs. The bibliography is not exhaustive. Some publications were excluded because of space and time constraints, and because of their limited circulation and accessibility. In addition, most of the material is from English language sources only.

The publications are organized in alphabetical order by author/corporate author and each is placed, according to its main focus, into one of 13 sections: assurance of quality; audiovisuals; drug information; economics and finance; health aspects; human resources and training; monitoring and evaluation; periodicals; pharmaceutical industry; policy and regulation; selection; supply; use. Keywords highlight specific subject areas and countries that are covered in each publication. A list of keywords pertaining to each section follows this introduction. The material is indexed by author, corporate author, subject area and country.

Most of the WHO publications should be available in national libraries. In case of difficulty it is suggested that the libraries of the WHO Regional Offices be approached for assistance.

WHO depository and reference libraries in each country (addresses available from WHO Headquarters) hold copies of all WHO publications. WHO publications may also be purchased from the WHO sales agents or the Distribution and Sales Office in WHO Headquarters. Please note that WHO documents are not for sale and may only be requested from the headquarters programme or regional office indicated in each bibliographic reference.

Blister–calendar packs for leprosy and tuberculosis in the Philippines

Dr A Galvez, Consultant in Chronic Diseases, WHO, Regional Office for the Western Pacific, United Nations Avenue, PO Box 2932, Manila, the Philippines, has written with details of multidrug therapy experience using blister–calendar packs (BCPs) for leprosy and tuberculosis. BCPs were originally introduced in 2 provinces of the Leprosy Control Programme, and after evaluation they were adopted nationwide for all patients. Procurement is at national level and allocation is based on registered patients and expected new patients in each province, per year. Distribution is through existing field health units at regional, provincial, municipal and barangay (village midwife) levels. Patients collect their antileprosy drugs in BCPs on a monthly basis, with supervision of the monthly medication. Empty packs are returned on each occasion, in return for a new supply. Patients are questioned at the time of collection about drug intake and visits are made to the patients' homes during each monthly period. Following this experience in leprosy, the Philippine Tuberculosis Control Programme adopted the use of BCPs for their drugs, using short course regimens of rifampicin, isoniazid and pyrazinamide (first 2 months), followed by rifampicin and isoniazid (4 months). These packs, issued at weekly intervals, and with appropriate monitoring by health staff for any adverse reactions, are available in all field health units and hospitals, nationwide.

Treatment of severe colitis in Behçet's syndrome with thalidomide

This case report was reported in the *Journal of Internal Medicine*, 1990, **228,** 405–7. Written by H Larsson of Lund University, Sweden it describes the use of thalidomide in a 35-year-old male patient suffering from severe Behçet's syndrome since 1979, as 'a final pharmacological measure to avoid colectomy during a severe attack of Behçet colitis.' The effect was dramatic and the patient was discharged from hospital 3 weeks after starting the treatment; at 5 months, the patient's condition was still satisfactory. The discussion includes the proposal that this drug should be considered as a first-line treatment in colitis associated with Behçet's syndrome.

Global evaluation of the introduction of multidrug therapy

This 58-page document, published jointly by the WHO and the Department of Epidemiology, Catholic University of Louvain, Brussels, Belgium and in consultation with ILEP 'presents information on MDT from 173 countries and territories worldwide . . . and is intended to be a stimulus for all those in charge of leprosy control programmes to implement MDT in the field and to collect the necessary information to monitor the process.'

The report is divided into 5 parts: summary of statistics by WHO regions; detailed statistics by WHO regions; annual trends by WHO regions; summary of statistics by country; and detailed statistics by country.

World leprosy atlas

This 200-page annual publication is a very useful reference document. It includes data on leprosy patients from 173 endemic countries and territories. 'Information about the last available statistics on population, registered leprosy cases and newly detected cases at national level and by administrative division was requested from the Ministries of Health of all these countries during 1991. A total of 79 answers were obtained by early December. As far as possible, figures presented in the Atlas only concern patients registered for, or still requiring, treatment. Patients under surveillance after treatment, or registered for care, are thus not taken into account.' For further details write to: EPID 30/34, Ecole de Santé Publique, Clos Chapelle-aux-Champs 30, 1200 Bruxelles, Belgique.

St Francis Leprosy Guild, London

The St Francis Leprosy Guild (founded 1895) exists to help missionaries, doctors, nurses and other workers care for the victims of leprosy. The 1992 Report records financial support for 92 different centres in Angola, Bangladesh, Bolivia, Brasil, Cameroon, Egypt, Ethiopia, India, Indonesia, Jamaica, Kenya, Korea, Madagascar, Mauritius, Myanmar (Burma), Nigeria, Pakistan, Papua New Guinea, the Philippines, Sri Lanka, Sudan, Tanzania, Thailand, Uganda, Vietnam, Zaire and Zambia. Including certain special grants and educational grants (the latter include support for medial medical student electives). The total dispensed in 1991 was £396, 231.

National Leprosy Organization Workshop of Voluntary Leprosy Institutions of Andhra Pradesh, India, 1991

The Meeting was opened by Dr K V Desikan, describing 'the present national scenario'. Shri S P Tare delivered the keynote address which covered all the session topics: Care after cure; rehabilitation; problems of voluntary organizations; and people's participation. Some very interesting points are made in this short 6-page report, e.g. 'The rigorous MDT schedule of drug delivery has also affected attention to individual patients.' Shri A Parathasarathy expressed the view, 'that the function of a physiotherapist is not to dress ulcers, but to prevent deformities'.

Copies are available from: Gandhi Memorial Leprosy Foundation, Hindinagar, Wardha 442103, India.

Bombay Leprosy Project celebrates 15 years

At the above celebration the Bombay Leprosy Project was congratulated on its work of the past 15 years. A brochure distributed at the Meeting contains contributions from the fields of surgery, rehabilitation and medicine which show among other achievements 'how the services of BLP have helped in increasing the acceptance of leprosy patients in their institutions'.

National Leprosy Organization Diary

This diary has now been published for 11 years. It includes many facts on leprosy including: definition, signs of the disease, classification, prevalence in India and further reading.

Copies may be purchased from: National Leprosy Organization, Hindinagar, Wardha 442103, India.

Disability in the developing world, IDEA

This is a multidisclipinary, 5-day course to share information and experience and to extend the debate on disability and development issues. It is an opportunity to discuss and learn more about the challenges facing disabled people and service providers in developing countries. The Course is relevant to people from all professional backgrounds who are concerned with disability, and will take place between 7 and 11 December 1992 in London (accessible venue).

Application forms and further information on this and other courses from: M. Greenhalgh, IDEA, William House, 101 Eden Vale Road, Westbury, Wilts BA13 3QF, UK. Tel: 0373 827635.

14th International Leprosy Congress, Florida, USA, 1993

There is great hope that the WHO resolution to eliminate leprosy as a public health problem by the year 2000 can be achieved. The questions remain: Is present technology sufficient? Are social, economic, and political conditions of endemic countries adequate? What will happen to patients with social and physical disabilities? The 14th Congress will address these issues and formulate plans of action.

For further details of this Congress, to be held between 29 August and 4 September 1993 in Orlando, Florida, USA write to: ILA Congress, c/o ALM International, 1 ALM Way, Greenville, South Carolina 29601, USA.

Leprosy Courses, Fontilles, Spain, Autumn 1992

Sanatorio de Fontilles are running 2 courses which are to be held in Fontilles, Alicante, Spain: (1) for auxiliary staff between 13 and 24 October 1992; and (2) for paramedical workers between 2 and 7 November 1992.

For further details write to: Dr J Terencio de las Aguas, Sanatorio San Fco, de Borja, 03791 Fontilles, Alicante, Spain.

WHO model prescribing information: drugs used in mycobacterial diseases, 1991

This is the third in the WHO's series of model prescribing information, which is produced to assist national authorities, particularly in developing countries, when preparing drug formularies, data sheets, and teaching materials. This volume covers some 13 essential drugs used for the prevention and treatment of tuberculosis, for the treatment of leprosy, and for the treatment of diseases caused by nontuberculous mycobacteria, including localized cutaneous lesions, pulmonary disease, lymphadenitis and disseminated disease.

Model prescribing information is presented in 3 main chapters. The first, devoted to tuberculosis, opens with a detailed overview of the disease, its clinical features, and the main principles of prevention, tuberculin testing, and chemotherapy. The special problems of diagnosis and treatment of HIV-infected patients are briefly discussed. Readers are also given detailed information on the properties of antituberculosis drugs, preferred treatment regimens, monitoring of patient compliance and therapeutic response, and the treatment of relapsing and unresponsive disease.

Against this background, model prescribing information is presented for 10 drugs used in vaccination, chemoprophylaxis, and chemotherapy. Each drug is profiled in terms of its clinical uses, dosage and mode of administration, contraindications and precautions, use in pregnancy, adverse effects, and possible interactions with other drugs.

Drugs used in the treatment of leprosy are covered in Chapter 2, which also features background information on the disease and the main principles of multidrug therapy. The final chapter provides prescribing information for drugs used to treat nonspecific mycobacterial infections.

Available in English (French and Spanish editions in preparation) from: World Health Organization, Distribution and Sales, 1211 Geneva 27, Switzerland. Price: Sw. fr. 9./US$8.10, and in developing countries Sw. fr. 6.30.

Breakthrough in leprosy surgery

Research funded by LEPRA has produced an exciting breakthrough in rehabilitative surgery for leprosy patients, according to an article published in *The Lancet* at the end of last year.

Success in dramatically restoring lost sensation to nerves paralysed by leprosy provides new hope for many thousands of people disabled by this ancient disease.

This new surgical technique has been applied to disabled leprosy patients for the first time in a co-operative project involving the Royal College of Surgeons in London, a southern India leprosy centre and LEPRA. Using muscle grafts to replace damaged nerves, early results show a 70% success rate in restoring sense of touch and temperature to damaged feet and hands.

While strong antibiotic drugs now provide an effective cure for leprosy—and the search for a preventive vaccine continues—millions of patients have been permanently disabled through infection, and tens of thousands are added to this total each year because damage to their nerves prior to drug treatment leaves them prone to continued injury and disability.

In addition to the purely practical disadvantages faced by disabled leprosy patients, they also have to cope with deep-rooted prejudice which can lead to loss of families, homes and jobs. This new technique offers the hope of preventing injuries which specifically identify leprosy sufferers and therefore could contribute to a reduction in the age-old stigma attached to the disease.

The paper published in *The Lancet*, written by 3 doctors based at the Royal College of Surgeons and 3 working at the Sacred Heart Leprosy Centre in Tamil Nadu, describes the successes achieved in operations on 10 leprosy patients in India. This follows extensive initial research in London at the Royal College.

Sections of nerve up to 6 cm long have been replaced by tubular muscle fibre, which provides a route encouraging the regenerating nerve to grow and bind, restoring lost sensation. The technique was developed from surgery originally carried out in the U.K. to repair nerve damage suffered by accident victims.

'For the first time we have a technique to restore protective sensation in selected leprosy patients with severe nerve damage' said one of the paper's authors, Dr Jerome Pereira.

'For individual patients, regaining the protective sensation which allows them to feel stones and thorns underfoot will mean the difference between dependence and independence. We are very hopeful that this relatively simple technique will eventually be widely available in the areas where it is most needed.'

The encouraging results achieved in India will now be tested further in multicentre trials in Ethiopia, Brazil and again in India to determine the effectiveness of the technique in all types of leprosy.

Handbook of leprosy, W. H. Jopling and A. C. McDougall (in Portuguese)

This title is once again available in Portuguese from Livraria Atheneu, Rua Bambina 74, Rio de Janeiro, RJ, Brazil. Price: US$22 approx. Of the 1200 copies printed over 500 have already been sold, almost entirely in Brazil. The English edition is available from the publisher, Butterworth–Heinemann, Halley Court, Jordan Hill, Oxford OX2 8EJ, U.K.

Ofloxacin for the treatment of leprosy

The following is the summary of a publication on the above subject by B Ji and J Grosset in *Acta Leprologica* (1991) **7**, 321–6:

Among the major commercially available fluoroquinolones, ciprofloxacin was inactive against *M. lepr*ae in mice; pefloxacin was active, 50 mg/kg daily showed bacteriostatic activity but 150 mg/kg daily displayed bactericidal activity; ofloxacin was more active than pefloxacin, 50 mg/kg daily exerted the same level of bactericidal effect as pefloxacin 150 mg/kg daily, and ofloxacin 150 mg/kg displayed profound killing activity. Two clinical trails with 6 months of pefloxacin and/or ofloxacin in 31 previously untreated lepromatous patients have been completed. Pefloxacin 400 mg twice daily or 800 mg once daily or ofloxacin 400 mg once daily were equally effective; definite clinical improvement with drastic decrease of morphological index to the baseline were observed in all patients at 2 months after beginning of treatment; about 99·99%, or 4 'logs', of organisms viable on Day 0 were killed by 22 doses of either pefloxacin or ofloxacin. The side effects from the 2 trials were rare and mild, and the patients tolerated extremely well the combinations of pefloxacin/ofloxacin plus multidrug therapy (MDT) regimen for multibacillary leprosy recommended by WHO. The amount of rifampicin-resistant mutants in lepromatous patients before treatment are no more than 4 'logs', thus, all rifampicin-resistant mutants may be eliminated by 22 doses of either pefloxacin or ofloxacin. It is, therefore, possible that the combination of ofloxacin and rifampicin may considerably shorten the required duration of MDT.