Lepr Rev (2000) **71,** 400–416

News and Notes

The genome mapping of the leprosy bacillus completed

The genome of the leprosy bacillus has been completely sequenced thanks to collaboration between Stewart Cole's team at the Institute Pasteur in Paris, and the Sanger Centre in the United Kingdom. The comparison with the genome of the tuberculosis bacillus (whose genome sequencing was published by the same teams in 1998) provides essential information on the two diseases, as Professor Stewart Cole will explain during the international seminar *Genomes 2000*, being held this week at the Pasteur Institute in Paris. Keep in mind that WHO estimates there are around 800,000 new cases of leprosy in the world each year, and that 2 million people suffer from severe disabilities as a consequence of this disease.

Comparative studies on comparing the TB and Leprosy Bacillus genomes have already begun. This could help to identify the growth factors absent in leprosy that would make its study easier, which would be useful in the eventual production of a vaccine.

Some genes present in the leprosy bacillus are not found in the TB bacillus. These genes could be used to provide diagnostic tools for skin tests to detect leprosy, and might also provide information on the nerve damaging characteristics of the bacillus.

The comparative approach being used might allow the identification of new therapeutic targets and could be useful in the rational creation of drugs for the treatment of leprosy.

Blocking natural killer cell activity

The latest issue of *Isis Innovation News*, University Offices, Wellington Square, Oxford OX1 2JD, United Kingdom, e-mail innovation@isis.ox.ac.uk; Web: http://www/isis-innovation.cm/ carries the following report from Professor Andrew McMichael's group in the *Institute of Molecular Medicine*, Oxford:

Recently acquired knowledge of the molecular interaction between HLA-E molecules and Natural Killer (NK) cells yields commercial opportunities for quantitating and manipulating these cells in vivo and ex vivo, screening for pharmacophores which block NK action, as well as to explore a genetic engineering approach for improving the 'take' of transplanted donor organs.

Background

Natural Killer cells, accounting for up to 15% of blood lymphocytes, are cytotoxic cells capable of mediating the immune response by recognizing and killing, for example virally-infected and tumour cells. Their ability to kill is generally considered to be inversely correlated with the expression of Class I major histocompatibility (MHC) molecules on the target cell surface. A subset of T Cells also expresses NK receptors.

The Oxford Invention

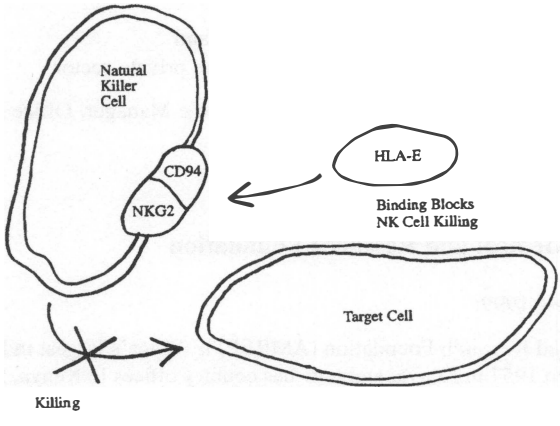
Professor Andrew McMichael and his team at the Institute of Molecular Medicine, Oxford have discovered that HLA-E, a non-classical MHC molecule, acts as a ligand for the CD94/NKG2 receptor

complex in the NK cell surface membrane. The interaction blocks NK cell killing, and hence may be exploited in order to modulate the immune response, for example to suppress or activate NK cell activity, or to identify and isolate NK cells, as set out below:

1. Diagnostic Reagent. HLA-E tetramers (biotinylated HLA-E molecules linked via streptavidin) provide a convenient NK-specific reagent, allowing NK cells to be separated by FACS analysis. This approach would enable monitoring for NK cell levels in, for example, patients with lymphoma, leukemia or other cancers, infectious diseases and transplantation, where NK cells may mediate graft-versus-host disease.
2. Depletion and Killing. HLA-E tetramers, coupled to toxins, can be used to deplete NK cells, for example, in bone marrow grafts prior to transplantation.
3. Isolation. Recovery of NK cells is feasible using the HLA-E/CD94/NKG2 interaction. This may be of value in patients with low NK cell levels, the isolated cells being expanded *ex vivo* and re-infused.
4. Screening. An *in vitro* cell assay system is available for screening combinatorial libraries of small molecules to identify pharmacophores capable of inhibiting NK cell activity.
5. Genetically-Engineered Resistance *In Vivo.* Immunotherapy for transplantation applications is envisaged whereby gene vectors encoding HLA-E sequences are integrated into target cells of donor organs in order to invoke NK cell 'resistance'.

Commercialization

Professor McMichael and his group welcome expressions of interest from manufacturing companies interested in co-developing products under the various applications of this invention.



Alliance For Health Policy and Systems Research

An information brochure from WHO carries the following introduction:

'The Alliance for Health Policy and Systems Research promotes the widest possible participation of institutions using and producing health policy and systems research to ensure a bottom-up source of direction and advice for its activities. The Alliance benefits from the support of a Board under the auspices of the Global Forum for Health Research.

WHO will implement this initiative through the Global Programme for Evidence on Health Policy.

This ensures the Alliance close collaboration and co-ordination with WHO activities for HPSR, and links WHO directly to a widespread collaborative network of institutions for the ground-up expression of demands and views related to HPSR.

The Alliance seeks the partnership of institutions in countries involved in the production or use of health policy and systems research, particularly when it relates to developing countries. Interested institutions can apply for partnership either by mailing the attached form, by mailing a separate letter of intent or by completing the Web site notice.

A contribution will be requested from partners, with an exemption for institutions in low-income countries. The contribution will be requested from institutions from the second year after joining the Alliance and its amount will be established in consultation with partners.'

The Priorities for HPSR are listed as follows:

The Alliance Board proposes the following general priorities, identified through consultations in 1998–99:

Health system functions of regulation, organisation, financing and delivery of services.
Social and economic policies with consequences for health care system development and reform.
Policy implementation in the context of global trends influencing policies, yet differing country health systems and needs.
Health system equity in financing, coverage, access, use and quality of care, conceived as risk factors for health.

These priorities are consonant with the work of WHO's cluster on Evidence and Information for Policy, particularly with the following tasks of the Global Programme on Evidence for Health Policy:

- measuring health system performance, especially responsiveness, fair financing and equity
- improving health system descriptions
- analysing health financing and organizational methods, and
- developing evidence to support public policy towards the private sector.

Further information: Miguel A. González-Block, Programme Manager, Office No. 3148, WHO, 1211 Geneva 27, Switzerland.

AMREF: African Medical and Research Foundation

From the *Annual Review* 1999:

The African Medical and Research Foundation (AMREF) is Africa's largest indigenous health charity. AMREF was founded in 1957 in Kenya, and now has country offices in Kenya, South Africa, Tanzania and Uganda. AMREF also has field offices in Ethiopia, Mozambique, Rwanda, Somalia and Sudan.

AMREF UK is one of 11 international offices in Europe and North America that raise funds to support the charity's work in Africa. AMREF has 500 staff representing 15 nationalities; 97% of them are Africans. Its annual total budget is over £10·5 million, to which AMREF UK contributes over £1 million.

AMREF is about innovation. It is about research, and it is about communities. But above all, AMREF is about health—good health.

AMREF works with East Africa's poorest and most vulnerable people. Our goal is for them to gain the knowledge, means and power to improve their own health.

For 42 years, AMREF has pioneered effective health care in East Africa. The innovation continues. This year we appointed a new Director General and a new professional, international Board. Working from our Nairobi headquarters, they will focus on increasing our impact all over Africa.

After successful work in South Africa, AMREF has also opened offices in Mozambique, Ethiopia

and Southern Sudan. There, we train district health teams to pass on affordable and appropriate schemes to local health workers and villagers.

This year too AMREF won the prestigious $1 million Conrad Hilton Prize, given for the first time to an African organisation. Smithkline Beecham and AMREF have also started work on a major $1 million project to teach basic hygiene and sanitation at primary schools throughout Kenya.

Intercapital, the UK's largest derivatives broker, supported AMREF with a share of the £1·3 million raised at their annual charity day. Chairman Michael Spencer summed up the reason why his company chose AMREF. 'It makes sense to enable local experts, in partnership with communities, to get on with what really works for them, rather than providing what we in Britain imagine they require.'

Further information:
AMREF
4 Grosvenor Place
London SW1X 7HJ
Telephone 0207 201 6070
Facsimile 0207 201 6170
E-mail amref.uk@amref.org
Website www.amref.org

'Molecular Pathology' edition of the *Journal of Clinical Pathology* (UK)

Molecular Pathology is a bimonthly edition of *Journal of Clinical Pathology*. It is a multi-disciplinary journal which draws together in one publication basic molecular research and new molecular techniques relevant to diagnostic pathologists and scientists.

The journal publishes original articles of molecular studies on human material relating to pathogenesis and disease processes, expert reviews, brief communications, a regular Demystified series and occasional focused issues such as the August 1999 issue on Cell Adhesion Molecules. Molecular Pathology is fully refereed.

Molecular Pathology is indexed in ISI Current Contents, Index Medicus, Excerpta Medica and is available through Ovid, BIDS/Ingenta, and OCLC.

Papers should be submitted to:
The Editors
Molecular Pathology
Department of Histopathology
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham B9 5SS
Fax: 0121 773 1182
Email: molpath@bhamheartlands.freeserve.co.uk

WHO Liaison: newsletter of the WHO Library and Information Networks for Knowledge

Liaison is published three times a year in English, French and Russian by the World Health Organization, Library and Information Networks for Knowledge, 1211 Geneva 27, Switzerland.

Telephone: Int. code 41—(22) 791 20 68
Cables: UNISANTE GENEVA

Fax: Int. code 41—(22) 791 41 50
Telex: 415 416
E-Mail: LIBRARY@WHO.CH

Editors: Mrs I. E. Bertrand and Miss V. L. Paterson

The latest issue received carries articles on:

(1) lack of resources for research libraries in developing countries, (2) managing information in research institutions: the role of the library, (3) the state of the world's refugees, (4) new books and journals for the WHO 'Blue trunk libraries' and (5) Internet tips (subject catalogues, search engines and meta search engines).

TDR: *Special Initiatives to Support Academic Programme Development*

The February 2000, No. 61 issue of TDR News carries the following information:

TDR's Research Capability Strengthening programme supports the development of selected academic programmes in developing countries in line with TDR's policy of promoting training within a trainee's own country or region. Current initiatives include support to three MSc programmes in clinical epidemiology and biostatistics in Africa (National University of Benin, University of Witwatersrand—South Africa, Makerere University—Uganda). The University of Witwatersrand programme commenced in January 2000, with the other two programmes expected to enrol their first student by October 2000. Past initiatives have included two regional MSc programmes in health economics (University of Capetown—South Africa, Chulalongkorn University—Thailand).

Further enquiries: TDR News: UNDP/World Bank/WHO Special Programme for Research + Training in Tropical Diseases, WHO, 1211 Geneva 27, Switzerland.

The Heiser Program for Research in Leprosy and Tuberculosis

The current 2000 information brochure opens as follows:

Dr. Victor George Heiser devoted his life to the study and treatment of tropical diseases, leprosy in particular. An associate director of the international health division of the Rockefeller Foundation, he circled the earth 17 times on his medical missions, and recounted his experiences in a best-selling autobiography, *An American Doctor's Odyssey*, published in 1936.

In 1969, he recalled that 'sixty years ago it became my responsibility and duty to gather up 10,000 lepers in the Philippines and transport them to a leper colony. The hope then was that isolation could reduce the incidence of the disease and perhaps eventually wipe it out. It didn't work. Now we have a new system—the clinic system—and that, too, has had practically no effect whatever in statistically reducing the incidence of leprosy. Indeed, it is apparently increasing in many parts of the world. But we must not sit idly by while so many people suffer from this horrible disease.'

The current world leprosy situation has vastly improved since Dr. Heiser's time. The World Health Organization has estimated that the total number of estimated and registered cases now stands at 1·3 million and 940,000, compared to 10–12 million and 5·4 million respectively, in 1983, and the WHO has set a goal of reducing the leprosy burden to one patient per 10,000 population over the next few years.

The Heiser Program for Research in Leprosy and Tuberculosis has made a major commitment of funds for the completion of the ongoing project for determining the DNA sequence of the entire genome of *Mycobacterium leprae*.

The Program will now commit funds in the form of research grants to accelerate WHO efforts to eliminate leprosy as a public health problem throughout the world.

Research grants provide limited support to scientists to allow them to contribute to the global goal of leprosy elimination.

Postdoctoral research fellowships support young biomedical scientists in beginning postdoctoral training for research in leprosy and/or tuberculosis.

Address applications and inquiries to:
Barbara M. Hugonnet, Director
Heiser Program for Research in Leprosy and Tuberculosis
450 East 63rd Street
New York, New York 10021 USA

'Drug-resistant tuberculosis can be controlled' says WHO

From the *British Medical Journal*, volume **320**, 25 March 2000, www.bmj.com:

The World Health Organization (WHO) has for the first time assembled hard evidence that the emergence of drug resistant tuberculosis can be held back by properly controlled treatment programmes.

It warns, however, that the 'window of opportunity' to prevent the spread of drug resistant strains will be missed if urgent action is not taken to persuade more health authorities and doctors to use its recommended treatment strategy, which still reaches only 1 in 5 patients with tuberculosis worldwide.

The warning comes in a global report released this week on World Tuberculosis Day at a ministerial summit in Amsterdam. It shows a disturbingly high prevalence of drug resistant strains of *Mycobacterium tuberculosis* in parts of eastern Europe and Asia.

By contrast, countries that have used the recommended treatment strategy tend to have very low rates of resistance. 'We only see significant drug resistance in countries without good control programmes,' said Dr. Marcos Espinal, an epidemiologist and head of the report's team of authors.

The WHO has been arguing for directly observed treatment, short course ('DOTS') for years on the basis of small scale studies that show it helps to prevent the emergence of resistance.

But this report is the first that allows it to show a clear inverse relation between the numbers of patients receiving DOTS and the prevalence of resistant strains in a widespread sample of populations. 'This conclusion is a ''no brainer'' to those of us who have been involved in DOTS, but now we have the evidence,' said a WHO spokesman.

The report is only the second global survey of the prevalence of drug resistant strains of *M. tuberculosis*. The first, in 1997, was based on just 35 sample populations.

The new report has data from 58 countries and other settings (such as provinces of China) and enough data to detect trends in 28. Its authors warn, however, that the picture is still incomplete. The scale of drug resistance is not fully known in the five countries with the highest incidence of tuberculosis worldwide: India, China, Indonesia, Bangladesh, and Pakistan.

As before, a high rate of resistance to one or more drugs was found in new tuberculosis cases in Estonia, with 37% of all strains resistant to any drug and 14% multidrug resistant. The prevalence of resistance in Estonia had grown substantially since the last survey, both in new cases and previously treated cases.

Other countries and settings with worrying rates of drug resistance included Latvia; two Russian 'oblasts' (territories); Iran; the Henan and Zhejiang provinces of China; and Tamil Nadu state in India. Germany and Denmark have both seen increases in drug resistance, but the scale of the problem is small.

In the parts of eastern Europe where rates of resistance are high, a tradition of treating patients for lengthy periods in hospital has encouraged resistant strains to flourish.

Anti-tuberculosis Drug Resistance in the World is available from the Publications Department, World Health Organization, 1211 Geneva 27, Switzerland.

TB: a clinical manual for South East Asia

This is a spiral-bound booklet of 145 pages, published by the World Health Organization in 1997. It is in fact an adaptation of a previous publication '*TB/HIV: A Clinical Manual*' by Mukund Uplekar, previously of the Foundation for Research in Community Health, Bombay, India and now with the Stop TB Initiative, WHO, Geneva. The reference number is WHO/TB/96.200 (SEA). The other authors are Anthony Harries, University of Malawi and Dermot Maher, Global TB Programme, WHO.

The main chapter headings are: background information on tuberculosis; diagnosis of tuberculosis in adults; diagnosis of tuberculosis in children; standardized TB case definitions and treatment categories; treatment of TB patients; side-effects of anti-Tb drugs; framework for effective TB control; background information on HIV/AIDS; HIV-related TB; diagnosis of HIV infection in adults with TB; diagnosis of HIV infection in children with TB; management of other HIV-related diseases in TB/HIV patients; coordinated care in different settings; prevention of TB.

Further information: Office of Publications, WHO, 1211 Geneva 27, Switzerland.

Global Tuberculosis Control. WHO Report 1999

This is a 179-page Report, WHO/CDS/CPC/TB/99.259 which reviews the global situation in great detail. The key findings were as follows:

- By the end of 1997, 85% of all TB cases were living in 102 countries which had adopted the WHO DOTS strategy for control.
- The key to meeting WHO targets lies in expanding case detection in high-burden DOTS countries: in 1997, 83% (2·5 million) of all unnotified TB cases were living in countries which have already shown that they can achieve high treatment success rates by using DOTS.
- The greatest number of cases without access to good treatment is in Asia, especially Bangladesh, India, Indonesia, Pakistan and Philippines.
- Only in Africa were treatment success rates relatively low (average 58%), because many patients did not complete treatment, or the outcome of their treatment was not evaluated.
- The number of new smear-positive TB cases notified by DOTS programmes has increased by an average of 100,000/year since 1994, reaching 16% of cases in 1997. By adding 250 000 extra cases each year (10% of the unnotified cases living in DOTS countries), the global target of 70% case detection could be reached by 2005.
- DOTS can succeed in a variety of settings: among major endemic countries showing relatively high treatment success ($\geq$70%) and case detection rates ($\geq$50%) were representatives from Africa (Kenya, Tanzania), Asia (Cambodia, Viet Nam) and Latin America (Peru).
- Marked upward trends in case notification rates from 1980 to 1997 variously reflect failing TB control (Eastern Europe), the impact of HIV (sub-Saharan Africa), and better case finding (China); marked downward trends (Western Europe) represent the direct (chemotherapy against TB) and indirect (general improvements in health) impact of TB control.
- Standardized short course chemotherapy, promptly delivered, can have a major impact on tuberculosis morbidity and mortality, but this impact has not yet been adequately quantified.

The *Technical Summary* reads:

Background and aims

This is the third global report on TB control, based on case notifications and treatment outcome data supplied by national control programmes to WHO. Four consecutive years of data allow us to present the most thorough appraisal of worldwide progress in TB control to date, focusing on 22 countries that account for 80% of all new cases. The main aim is to assess progress towards meeting WHO targets

for case detection (70%) and treatment success (85%). We also consider the potential of these data to assess the impact of control on cases and deaths averted.

Methods

Standard data collection forms A and B were sent to 212 countries via WHO Regional Offices. Part A requested, from DOTS areas, the number of types of TB cases notified in 1997, and treatment results for smear-positive cases registered in 1996. Part B is for areas that have not implemented DOTS, and required fewer details of notified cases and treatment outcomes.

Results

173 countries reported to WHO. 102 of these had satisfied the technical criteria for DOTS implementation by the end of 1997, including all 22 of the highest-burden countries except Brazil and Zimbabwe. The number of new smear-positive TB cases notified (detected) by DOTS programmes was 547,432 in 1997, or 16% of estimated global incidence. This number has increased by 100,000/year on average since 1994, though recruitment was slower in 1997. Among the 84% of smear-positive cases that were not notified under DOTS in 1997, 18% were living outside DOTS countries, 60% were living in DOTS countries but outside DOTS areas, and 23% were living in areas said to be covered by DOTS. Therefore 83% (2·5 million) of all smear-positive TB cases not detected under DOTS were living in countries which had partially implemented the WHO control strategy.

Whilst DOTS programmes have been reporting more cases each year, the total number of notifications has changed little: 3,368,879 TB cases were reported from all control programmes in all countries in 1997, 436,000 fewer (12%) than in 1996, and about the same as in 1995. A total of 1,292,884 sputum smear-positive cases was reported in 1997, about the same as in the two previous years.

Although case finding has been expanding slowly, most DOTS programmes have demonstrated that they can achieve high treatment success rates. The average for the 1996 cohort was 82% in the 22 high-burden countries (3% less than the target) and 78% globally. Only in Africa were treatment success rates relatively low under DOTS (average 58%); the reason is that many patients did not complete treatment, or the outcome of treatment was not evaluated.

Among the best performing, high-burden countries (case detection rate under DOTS, DDR $\geq$50%, treatment success rate, TS $\geq$70%) were representatives from Africa (Kenya, Tanzania), Asia (Cambodia, Viet Nam) and Latin America (Peru). Bangladesh, China, Ethiopia and Myanmar maintained acceptably high treatment success rates ($\geq$70%) whilst steadily expanding coverage (DDR 10–49%). India, Indonesia, Philippines, South Africa and Thailand have shown that they can achieve acceptable treatment success rates under DOTS, but case detection rates remained low (DDR $<$ 10%). Treatment success was low ($<$ 70%) or in doubt in Nigeria, Uganda and Russia. No data, or incomplete data, were supplied by Afghanistan, Brazil, DR Congo, Pakistan and Zimbabwe.

There were marked trends in case notification rates from 1980 to 1997 that differ by country and region, falling in Western Europe and Latin America, and rising in Eastern Europe, sub-Saharan Africa and Asia. A detailed analysis of new and re-treatment cases reported in China indicates that countries using DOTS cut the case fatality rate from 37% in 1991 to 6% in 1997.

Conclusion

Although treatment success needs to be improved in some countries, especially in Africa, the key to meeting WHO targets lies in expanding coverage in high-burden countries that have already implemented DOTS. The greatest number of cases without access to good treatment is in Asia, especially Bangladesh, India, Indonesia, Pakistan and Philippines. By maintaining the current rate of DOTS expansion, the WHO global target for case detection would be reached in 2015; by finding an

extra 250,000 smear-positive cases annually (10% of undetected cases in DOTS countries), the target could be reached a decade earlier. Trends in notification and cure rates portray, more or less clearly, the failures or successes of TB control. New indicators and methods of analysis must be developed to quantify the full impact of control on TB transmission, incidence, prevalence, deaths, and on the prevention of drug resistance.

What is DOTS? WHO 1999

This is the title of a 30-page publication, WHO/CDS/CPC/TB/99.270, sub-headed 'A guide to understanding the WHO-recommended TB Control Strategy Known as DOTS'. The Summary reads as follows:

DOTS (Directly Observed Treatment, Short-course) is the most effective strategy available for controlling the TB epidemic today. DOTS has five key components:

- Government commitment to sustained TB control activities.
- Case detection by sputum smear microscopy among symptomatic patients self-reporting to health services.
- Standardized treatment regimen of 6–8 months for at least all confirmed sputum smear positive cases, with directly observed treatment (DOT) for at least the initial 2 months.
- A regular, uninterrupted supply of all essential anti-TB drugs.
- A standardized recording and reporting system that allows assessment of treatment results for each patient and of the TB control programme overall.

This cost-effective strategy was developed from the collective best practices, clinical trials and programmatic operations of TB control over the past 2 decades.

Government commitment to sustained TB control is essential for the other four components to be implemented and sustained. This commitment must first translate into policy formulation, and then into the financial and human resources and administrative support necessary to ensure that TB control is an essential part of health services.

An important feature of DOTS is the basic management unit—usually covering a population of 100,000 to 150,000—that has the staff and resources to diagnose, initiate treatment, record and report patient treatment progress, and manage supplies. This basic management unit operates successfully within existing general health services, which is critical for the full integration and effectiveness of TB control services in the primary health care network, particularly during this era of health sector reform.

Another important feature is a recording and reporting system used by health care workers to systematically monitor patient progress and TB programme performance. This results-oriented system enables quality assurance of programme implementation and treatment and cure of TB patients. Data collected as part of TB management can be a useful indicator of access to and quality of the general health system.

Apply: Office of Publications, WHO, 1211 Geneva 27, Switzerland.

Guidelines for the control of tuberculosis in prisons

This is a publication of 83 pages, WHO/TB/98.250 produced by the World Health Organization and the International Committee of the Red Cross. The Preface reads as follows:

The World Health Organization (WHO) and the International Committee of the Red Cross (ICRC) have joined forces to produce these guidelines. The goal is to improve the control of tuberculosis in prisons and other institutions where people are incarcerated. The guidelines apply wherever people are in custody: prisons, police stations, remand centres, detention centres for asylum seekers, secure hospitals, penal colonies and prisoner of war camps.

Several international conventions (see Annex 1) guarantee the welfare of prisoners. Prisoners lose liberty but retain certain rights in prison. These include protection from harm and access to a standard of health care equivalent to that provided in the community. In practice, few prison authorities comply fully with these conventions. Low standards of general custodial care and of health care are common. Despite the often limited information available on the health of prisoners, there is increasing recognition of the health needs of prisoners, including the need to control tuberculosis. Contracting tuberculosis should not be part of a prisoner's sentence.

Tuberculosis is common in many prisons worldwide and treatment is often ill-informed and inadequate. Prisons form a reservoir of tuberculosis, including drug-resistant tuberculosis. Tuberculosis is a problem both inside prisons and outside in the wider community, since people enter, leave and re-enter prisons. There is therefore an urgent need to institute effective control of tuberculosis in prisons. Successful tuberculosis control in a country requires effective tuberculosis control in prisons. The WHO recommended strategy for tuberculosis control (known by the 'brand name' of DOTS) relies on the detection and cure of tuberculosis patients, with a priority for the infectious cases. The specific features of prisons and of prisoners necessitate specific approaches to implementation of the DOTS strategy. The prison health services must implement the DOTS strategy in close collaboration with national tuberculosis control programmes.

Practical guidelines are necessary for prison authorities to be able to implement the DOTS strategy. Policy-makers and decision-makers may be unaware of the extent of the problem of tuberculosis in prisons, the potential for spread to the wider community, and the emergence of drug-resistance. The guidelines therefore also highlight to policy-makers and decision-makers the need to control tuberculosis in prisons. Several countries, usually with low tuberculosis prevalence, have developed their own guidelines. However, there is a need for global guidelines for use in any country with high tuberculosis prevalence populations. WHO's Global Tuberculosis Programme (GTB) and ICRC contribute to these guidelines expertise in tuberculosis control and in the welfare of prisoners.

The objectives of the guidelines are the following: a) to describe briefly the burden of tuberculosis in prisons; b) to highlight the specific difficulties in implementing effective tuberculosis control in prisons; c) to outline the benefits of improved control of tuberculosis in prisons; d) to guide administrators in establishing and running tuberculosis control services in prisons; e) to guide prison health service staff in the detection and cure of prisoners with tuberculosis.

The guidelines are primarily for prison authorities (administration, health staff), policy-makers and decision-makers in relevant ministries (e.g. justice, interior, health), NGOs and donor agencies, and National Tuberculosis Programme (NTP) staff. Part I provides background information on tuberculosis and prisons, of particular relevance to prison authorities and decision-makers in relevant ministries. Part II provides guidelines for the control of tuberculosis in prisons, of particular relevance to prison health staff. Part III gives guidance to national prison authorities and NGOs on how to establish a prison tuberculosis control programme.

These guidelines require field testing in different situations. Comments on the guidelines are welcome and will help to improve future editions. Please send any comments to the WHO Global Tuberculosis Programme.

To order copies of these guidelines, please contact:

WHO Publications, Distribution and Sales, 1211 Geneva 27, Switzerland or ICRC Public Information Division, 1202 Geneva, Switzerland.

INASP-Health

INASP-Health is a co-operative network created by health information providers, for health information providers. Its goal is to facilitate co-operation across the health information community towards universal access to reliable information for healthcare workers in developing and transitional countries.

The network currently involves more than 600 participants. North and South, representing non-governmental organizations, international agencies, library services, publishers (print and electronic), and others. Visit our website at: www/inasp.org.uk for further information about our range of services and activities.

We welcome all those who are willing to share their experience and expertise with others to improve access to reliable information. Participation is free of charge and without obligation. Please write to:

Dr. Neil Pakenham-Walsh
Programme Manager
INASP-Health
27 Park End Street
Oxford OX1 1HU
UK

Tel: +44 (0) 1865 249 909
Fax: +44 (0) 1865 251 060
Email: INASP_Health@compuserve.com
WWW: www.inasp.org.uk

We are grateful to the following organisations for their support:

British Medical Association, Danida, Department for International Development (UK), CDSI (ICSU-Press), World Health Organization.

WHO: drugs used in HIV-related infections

Under the broader heading of *WHO Model Prescribing Information*, this valuable document of 58 pages (WHO/DMP/DS1/99.2) complements WHO's *Model List of Essential Drugs*. The *summary* on the back cover reads:

WHO Model Prescribing Information is being prepared to provide up-to-date and independent clinical information on essential drugs, including details of dosage, uses, contraindications and adverse effects. It is intended as source material for adaptation by national authorities, in particular in developing countries, that wish to produce drug formularies, data sheets and teaching materials.

This update of the volume on HIV-related illnesses covers drugs currently used for the prophylaxis, treatment and palliative care of patients with opportunistic infections and other illnesses related to HIV infection. For further information on the drugs used in the treatment of early HIV infection see The implications of antiretroviral treatments WHO/ASD 97.2 and Guidance Modules on Antiretroviral Treatments WHO/ASD 98.1 UNAIDS 98.7.

Opportunistic infections:

Infectious diseases constitute the immediate cause of death in up to 90% of patients with advanced HIV. Some are caused by common pathogens, but many are *opportunistic*, meaning that they are caused by microbes which usually do not cause disease in the immunocompetent host. Knowledge of these is incomplete and new forms of opportunistic infections attributed to previously unrecognized and uncharacterized microbes are still being discovered.

The incidence and spectrum of these infections differ in important respects from those associated with other immunosuppressive disorders. Whereas *all* immunocompromised patients are vulnerable to *Toxoplasma* encephalitis, oral candidiasis and pulmonary tuberculosis, many opportunistic diseases including *Pneumocystis carinii* pneumonia (PCP), and systemic infections due to *Cryptococcus*

neoformans, cytomegalovirus (CMV), the *Mycobacterium avium* complex and *Cryptosporidium* species have occurred more frequently in people infected with HIV.

The pattern of infection varies between different socio-ecological settings. In some African countries as many as 50% of patients with advanced HIV disease will develop tuberculosis. In contrast, *Pneumocystis carinii* pneumonia is less frequent in these countries. This may be because many patients die before their immune defences are severely attenuated or because of under-reporting. In the immunocompromised patient infections often present atypically; disseminated disease is common and two or more infections may occur concurrently. The systems commonly involved in manifestations of the opportunistic infections are given below.

Other infections such as those due to *M. tuberculosis*, *Shigella*, and *Salmonella* species occur in people with normal immunity and are not classified as 'opportunistic infections'. They are, however, included as they occur with increased frequency in people with HIV.

Pulmonary tuberculosis:

Tuberculosis is the commonest cause of death in people with HIV infection world-wide. There are indications of a resurgence of tuberculosis almost everywhere where HIV is prevalent. HIV infection increases a person's susceptibility to infection with *M. tuberculosis* and is the most potent factor known to increase the risk of progression from *M. tuberculosis* infection to disease. In an individual infected with HIV the presence of other infections including TB allows HIV to multiply more quickly. This may result in more rapid progression of HIV infection.

The initial signs of disease may become apparent at any time during the evolution of HIV infection. In HIV-infected patients TB may be pulmonary or extrapulmonary. Pulmonary TB is still the most common form of TB. The presentation depends on the degree of immunosuppression. In advanced HIV disease the immune system is less able to prevent the growth and local spread of *M. tuberculosis*; thus, disseminated and extrapulmonary disease is more common, and unilateral or bilateral infiltrates in the lower lobes are seen more often than upper lobe lesions and cavities. The commonest forms of extrapulmonary disease are lymphadenitis, pleural effusion, pericarditis, miliary disease and meningitis.

The essential elements of tuberculosis control are the same in populations where HIV is common and where it is rare. The objectives are to decrease morbidity, mortality and transmission of tuberculosis, while avoiding the emergence of drug resistance. One of the essential elements of the WHO strategy is to provide short course chemotherapy under direct observation to at least all identified smear positive cases. The central strategy recommended by WHO is one of the most cost-effective of all health interventions.

Treatment regimens have an initial (intensive) phase and a continuation phase. The initial phase lasts for 2 months and utilises three or four drugs. During this phase there is rapid killing of TB bacilli, infectious patients become non-infectious within about 2 weeks and symptoms improve. The vast majority of patients with smear-positive TB become sputum smear negative within 2 months. Directly observed therapy is recommended in the initial phase to ensure that the patient takes every single prescribed dose. This protects against the development of drug resistance. The risk of drug resistance is higher during the early stages of anti-TB drug treatment when the number of TB bacilli is very high.

The continuation phase lasts for 4–6 months depending on the combination of medications used. During this phase the drugs eliminate the remaining TB bacilli. Killing the persistent bacilli prevents relapse after completion of therapy.

There is little evidence, as yet, of atypical patterns of antibiotic resistance in *M. tuberculosis* isolates from patients with HIV. However, reports from the USA describe clusters in which isolates shared multi-drug resistance. This is the result of the spread of TB infection with rapid progression of disease in this population. The limited data on treatment failure in TB/HIV dually infected patients and relapse rates following antituberculosis therapy are comparable to those prevailing in the population at large.

Mortality is, however, considerably higher in HIV seropositive than HIV seronegative TB patients. Furthermore, the incidence of adverse reactions may be substantially higher in TB patients with HIV infection. In particular, thiacetazone is associated with a high risk of severe, and sometimes fatal, skin reactions in HIV-infected individuals.

TB preventive therapy

There is evidence showing the efficacy of TB preventive therapy among HIV-infected people. TB preventive therapy can be given to people with HIV who have been screened to exclude active TB and who are PPD positive. Isoniazid is the recommended drug. A dose of 5 mg/kg (maximum 300 mg) may be given daily as self administered therapy for 6 months.

For further information in the treatment of TB in patients with HIV infection see

(i) *TB/HIV. A clinical manual*. Geneva, World Health Organisation, 1996 (WHO/TB1996.2000).
(ii) *Treatment of Tuberculosis, Guidelines for National Programmes*. Geneva, World Health Organisation, 1997 (WHO/TB1997.220).

Further information: Office of Publications, WHO, 1211 Geneva 27, Switzerland.

AIDS cuts life-expectancy in sub-Saharan

From the *British Medical Journal*, volume 319 of September 1999:

The spread of HIV and AIDS in sub-Saharan Africa has far exceeded the worst projections, according to speakers at the 11th international conference on AIDS and sexually transmitted diseases in Africa. In 13 countries the prevalence of HIV infection is more than 10%, and in some it is as high as 30%. At the conference in Lusaka, Zambia, last week, the epidemic was described as an unprecedented threat to the region's economic development.

At the end of 1998, 22·5 million people out of the region's population of 600 million were living with HIV or AIDS; this number includes 1 million children. The epidemic in sub-Saharan Africa accounts for two thirds of the worldwide total of 34 million people with HIV/AIDS. About 7500 people are infected daily.

In only two countries, Uganda and Senegal, does the epidemic seem to be abating. Strong governmental leadership in these countries ensures that there is universal health education, that condoms are easily available, and that there is coordinated action from the government.

Life expectancy in the region has decreased from 64 to 47 years. Sixty five per cent of patients in medical wards in Zambia, and 75% in paediatric wards, are infected with HIV or have AIDS, and the underfunded health system is near to collapse. Even common drugs such as co-trimoxazole are scarce.

In Zambia, a 15 year old has a 60% chance of dying of AIDS. As the epidemic, which is driven largely by poverty, continues to grow, there is little sign of widespread change in sexual behaviour, especially among teenagers, one of the most vulnerable groups.

Tsepo Sitali, aged 8, described to the conference the anguish of her friend who will mark her eighth birthday without a mother or a father because both died from AIDS last year.

Tsepo's friend is not alone: the number of children orphaned by AIDS in Zambia is forecast to reach 500,000 by the year 2010. The epidemic affects children not only directly through infection being spread from mother to child but also through the deaths of their parents which results in their being forced into prostitution and other forms of exploitation.

Children, especially girls, are taken out of school to nurse sick relatives or because school fees are no longer affordable. Only an estimated 10% of the predicted illness and death has occurred: the full impact on people, communities, and economies is still to come.

St Joseph's Leprosy Hospital

The following history of St Joseph's Leprosy Hospital, Tamil Nadu, India, was supplied by the Superintendent.

St Joseph's Leprosy Hospital was started in 1949 by Mgr. Francis T. Roche, S. J. with the help of three sisters of the Institute of Franciscan Missionaries of Mary (F.M.M.). By the end of 1958 it had developed into a well-equipped hospital with 300 beds. The first Survey Education Treatment Unit was started with three roadside clinics in 1961 and the number of leprosy patients treated rose to 2245. In 1963 the entire administration was handed over to the F.M.M. Sisters, who now collaborate with the Government of India in its Leprosy Eradication Programme.

In 1972 the Leprosy Control Unit was extended, covering an area of 2160 sq. km. with 11 sub-centres and 28 roadside clinics, catering to a population of 2,20,000. In 1994 there were 13 main clinics with 54 roadside sub-clinics. From 1949 to 1998 a total number of 6950 leprosy patients were detected and treated by the Institution.

In 1998, we undertook Tuticorin Urban area which contains 2,04,000 population. This area is divided into 8 zones and one leprosy Inspector is posed in each zone.

Our service

The hospital provides in-patient care for the treatment of lepra reaction, stabilization on anti-leprosy drugs, treatment of trophic ulcer and other infections. Regular exercises are given to patients by the Physiotherapy Section to prevent deformities or to correct them. As a result of multi-drug therapy and ROM treatment patients are cured in a comparatively shorter period.

About half of the inmates of the Hospital are permanent residents, who are disabled and rejected by their families. A few of them are employed in gainful rehabilitation work like candle making, weaving, agricultural, poultry and dairy farming. We also have a shoe making unit where microcellular rubber foot wear are made to protect the anaesthetic feet of leprosy patients. In all our rehabilitation work we aim at allowing the patients to continue their work in their own environment.

All the patients in our hospital and clinics are treated free of charge, irrespective of caste, creed, community or social status. All in-patients are provided with food, clothing and shelter free of charge.

Owing to the successful implementation of the Leprosy Eradication Programme, the number of persons infected by leprosy in the area is now steadily decreasing. We have now launched into process of integrating a Tuberculosis Control Programme, Malaria, Aids along with the leprosy Eradication Programme. This will be a boon for Tuticorin, where a good number of people suffer from this disease.

Regional conferences of leprosy workers

The following is taken from the report of Mr Udary Thakar Secretary, Hind Kusht Nivaran Sangh, Maharashtra Branch, Mumbai.

Hind Kusht Nivaran Sangh, Maharashtra Branch has been organizing Regional Conferences of leprosy workers in Maharashtra for last several years. This has been with the primary objective of providing opportunities to grass root level workers to express their views and actual field experiences. This year, two regional conferences were organized, i.e. 1) Western Maharashtra region (Dist. Satara, Sangli, Kolhapur and Ratnagiri) at Richardson Leprosy Hospital, Miraj on 11th and 12th March 2000 and 2) Kokan region (Dist. Mumbai, Thane, Raigad and Sindudurg) at Kushtarog Nivaran Samiti, Cantina, Painful on 14th and 15th March 2000.

Both the conferences were dedicated to the memory of pioneering efforts of Late Shri S. S. Naik, the past secretary, Hind Kutht Nivaran Sangh, Maharashtra Branch in starting this event for leprosy workers.

Over 150 field workers from Government and NGOs participated in the Conferences and presented 58 papers (25 papers at Miraj and 33 at Cantina) on various aspects of leprosy, i.e. Epidemiology, clinical aspects, MLEC, Rehabilitation and Social aspects etc.

The Conferences at Miraj and at Cantina were inaugurated by Shri Patil, Mayor of Sangli and by Shri Chandrashekhar Dharmadhikari, Ex. Chief Justice, respectively.

The highlights of paper material, discussion and the suggestions in both the Conferences were as follows:

1) The papers based on case detection in special groups of population like fishermen, prisoners, tribal population, commercial sex workers etc. showed significant high N.C.D.R. Hence, it was suggested to include these groups in routine surveys.
2) The results of last three MLECs in Maharashtra showed decline in New Case Registration. However, the experience with VRCs, this was encouraging.
3) Since the routine surveys do not reveal smear +ve cases, it was suggested to make special efforts to get the hidden smear +ve cases.
4) In case of smear +ve cases, along with the household contacts, the contacts at the work place, travel and at social activities should also be examined.
5) If properly trained, it was expressed, that leprosy patients can also disseminate information on leprosy.
6) In the conference, information on various rehabilitation schemes for leprosy patients was made available to the field workers for future references.
7) To solve the problem of duplication of registration and to trace the drop out cases who leave the area, it was suggested to create a State level Central Registry of leprosy patients.
8) All the field workers expressed that the Integration of Leprosy Services into General Health Services should be made only after proper training and motivation of general health workers.

In both the conferences, field workers participated in the deliberations with keen interest and expressed their views and experiences freely.

Leprosy Focus Group for Podiatrists

Mission statement

The Leprosy Focus Group for Podiatrists and Other Healthcare Professionals will clarify and develop the role of podiatry within the field of leprosy.

Aims

To link up a multinational group of podiatrists and other healthcare workers with an interest or experience in the leprotic foot and to facilitate the development of podiatry within the leprosy framework.

To bring the specialized skills of podiatry into leprosy project work throughout the world.

Objectives

1. To clarify and promote the role of podiatry within the field of leprosy.
2. To develop a comprehensive information pool regarding prevention and treatment of foot pathologies in people with leprosy.
3. To provide links between appropriately skilled podiatrists and leprosy organizations.
4. To act as a support mechanism for podiatrists and other related healthcare professionals working in the field.

5. To inform and update relevant professional bodies about the group's activities, and to gain their help in disseminating information through professional journals.
6. To promote the inclusion of leprosy and the role of the podiatrist in the prevention of disability into the undergraduate and postgraduate curriculum.
7. To encourage podiatric postgraduate research into leprosy.

Philosophy

We believe that podiatrists have specialized skills that can be utilized to benefit people with leprosy in preventing and treating disability.

We believe that podiatrists are obliged to broaden these skills to encompass all aspects of prevention of disability in people with leprosy.

To date the podiatry profession has not been used effectively in leprosy care and this situation can now only change with a positive, and mutual, input from the podiatry profession and leprosy organizations.

We believe that these specialized skills can be transferred via education and practical training to local staff at all levels leading to sustainable development.

We are a secular organization that respects all faiths and cultures.

If you wish to become actively involved with this group, please send an E-mail to the following address podiatry@lepra.org.uk

Poster contest on leprosy (Hansen's disease)

Leprosy of yesterday was shrouded in mystery and fear, and patients were isolated far from the community. Today, it is society's responsibility to inculcate confidence in the patient. Leprosy can only be eradicated if society throws away its baseless prejudices, and if the community works together with the Health authorities.

The role of Health Education has already been emphasized. People have to be closely associated with Public Health Programmes, as the health measures are for their benefit and that of their families. Local communities should be made aware of the scientific facts of leprosy to encourage individuals with early signs of the disease to come forward for treatment. It should then be the community's task to motivate patients to take treatment regularly, to care for their hands and feet, to provide retraining with job opportunities and to integrate them back into society.

In observance of 'anti-leprosy day', SWAPLAP (Society for the Welfare and Awareness of the Poor and Leprosy affected people) and We Care Trust, in collaboration with Directorate of Health & Family Welfare Services and AMICI were jointly organized a State level poster contest on leprosy on 30th January 2000 for school and college students, to bring about an awareness among youth. This poster contest was conducted at Media Centre, 96, Lavelle Road, 3rd Cross, Bangalore-1.

Aims of the contest

- To discover the extent of students' knowledge about leprosy.
- To allow them for practice in communication skills.
- To understand and respond to their needs on leprosy.
- To develop positive attitudes in participating leprosy awareness programmes.
- To give an opportunity to children and young people, who have the talent of creativity.
- To develop proper education and communication skills among children and young people which can change attitudes towards people living with leprosy.

The contest was conducted for School and College students. The response was indeed very good. There were in total 50 participants from various schools and colleges.

Results and findings of this contest

- Teenagers and adolescents are interested to learn about leprosy.
- Young people have their own language and it is important to learn that language.
- The right information will enable students to act responsible.
- It is not difficult to develop a sustainable leprosy programme in schools/colleges.
- It is more important to keep reference materials on leprosy in schools/colleges.
- Awareness programmes among youth has its own impact and effectiveness.
- More number of such programmes will definitely increase the awareness among more teenagers and adolescents.

It was indeed a very successful programme, under the able guidance of Dr. Jangay (leprosy), H & FWS, Karnataka, and the financial support given by We Care Trust, St Anthony's Friary, 86, Hosur Road, Bangalore-95 and AMICI, 58, 4th Cross, Kaveri Layout, Thaverekere Main Road, Dharmaram College Post, Bangalore.