

News and Notes

African Medical and Research Foundation (AMREF)

The African Medical and Research Foundation (AMREF) is Africa's largest indigenous health charity. Based in Nairobi, Kenya, AMREF employs 500 people, 97% of them African. It supports communities in their own efforts to improve their health and well being. It also runs comprehensive training courses for health professionals at all levels and a unique laboratory support programme. AMREF is also the parent organisation of the Flying Doctors' Service.

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's total annual budget is over £10.5 million, to which AMREF UK contributes over £1 million.

AMREF News is published by the UK office of the African Medical and Research Foundation.

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BBC World Service Trust: leprosy media campaign in India

From *Connect*, the Newsletter of the International Federation of Anti-Leprosy Associations (ILEP), No 1, Autumn 2000:

The BBC World Service Trust is nearing the end of its 12-month leprosy media campaign in India. The India project is phase two of their 5-country media campaign for leprosy. The Nepal phase was completed in 1999. The campaign aims to transform health programming into dynamic entertaining media that engages audiences in matters of crucial importance to them. The project also aims to make sustainable changes to programme design, build technical capacity and skills, and generate momentum around health issues. Working in partnership with local media companies Doordarshan TV and All India Radio, the BBC project has used the cultural sensitivity skills, and imagination of local programme makers. Project output included:

- 27 TV spots and 146 radio spots in 20 languages
- 13 TV dramas
- 53 radio dramas
- Total of 808 TV and 5545 radio broadcasts
- For media dark areas—2175 song and drama performances, 5455 video van screenings and 150 000 posters

Following an independent survey of audience responses commissioned by the BBC, results have been encouraging. Two important successes of the campaign have been highlighted. 176 000 patients have come forward for treatment, and there has been a real impact on attitudes to leprosy. Radio and TV spots

were seen by 48% of the total population in the five targeted states (Bihar, Madhya Pradesh, Orissa, Uttar Pradesh, West Bengal), representing 224 million people. Of these, 79% correctly recalled one or more messages.

As the Indian phase of the campaign comes to an end, an independent evaluation survey will now take place, while the Brazil, Ethiopia and Indonesia campaigns are being prepared. If you would like more information on this campaign or the preparation of future campaigns in this project, please contact the BBC Health Projects Director, Mr. Roy Head at roy.head@bbc.co.uk

New publication and leprosy organization from India

We were delighted to receive Vol 1 No 1, January 2001 of the *Bulletin of the Leprosy Elimination Alliance* (LEA) which includes the following information:

Welcome to the *Bulletin of the Leprosy Elimination Alliance!* It will be out every 3 months, and will be available free of charge to everyone who wishes to fight and eliminate leprosy. Through this bulletin, the LEA hopes to communicate with a large number of leprosy workers, and help them—and learn from them—in fighting the disease, especially in India.

The Bulletin will carry news, reportage, analysis and in-depth reviews of various facets of leprosy and the war against it. We promise facts and figures and revealing charts and maps. We will also go beyond the cold statistics to carry warm personality accounts of and interviews with men and women who are at the forefront of the eliminate-leprosy campaign. We will talk about current trends and developments, and update old information. We will discuss specific issues. We will focus in-depth on what's going on at particular locations—in India and abroad.

We appeal to leprosy workers to use the Bulletin as their forum for highlighting operational and technical problems in the war against leprosy. Tell us about your experiences, your views, give us your ideas and insights.

Our approach at all times will be positive and constructive. We will not shun controversy.

But in presenting and analysing controversial issues, we will make clear the distinction between fact and opinion. You will have your own opinions—please feel free to air them in our 'Readers write' column.

We reserve the right to abridge and edit any article before publication. The Editor's decision in this respect will be final. Please address all correspondence to Editor, Bulletin of the Leprosy Elimination Alliance at:

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A word about the Leprosy Elimination Alliance (LEA). It was launched in Chennai in August 2000, with Dr S K Noordseen, formerly Director of the Action Programme for Elimination of Leprosy at the World Health Organization headquarters in Geneva as its Chairman.

The main objectives of the organization are (a) to promote the cause of leprosy elimination (b) to promote exchange of information and ideas on leprosy elimination among leprosy workers and others (c) to monitor progress towards leprosy elimination and assist towards development of better strategies and methods to achieve the goal in collaboration with other interested parties and (d) to produce and distribute among leprosy workers and others interested, publications on leprosy elimination.

The *Bulletin of the Leprosy Elimination Alliance* plays an important awareness and networking role in the drive to eliminate leprosy.

Veterinary Laboratories Agency, UK: research on *M. bovis*

The following is taken from the *Annual Review 1999/00: Working for Animal Health* of the Veterinary Laboratories Agency, New Haw, Addlestone, Surrey KT15 3NB, United Kingdom, www.maff.gov.uk/vla:

BOVINE TUBERCULOSIS

Sequencing the Mycobacterium bovis genome

A collaborative project between VLA, the Sanger Centre and Institut Pasteur, jointly funded by MAFF* and the Wellcome Trust, was initiated to sequence the *M. bovis* genome. The project represents a highly cost-effective approach to supporting the MAFF initiative on *M. bovis* vaccine development. Sequencing has started and a database of assembled sequences greater than 1 kb is already available at the Sanger Centre, Cambridge.

Tuberculosis vaccine research

A major programme of *M. bovis* vaccine development is currently under way. The objectives are to produce a vaccine that protects against infection and a diagnostic test that differentiates between vaccinated and infected animals. The VLA is a member of the animal models task force for the World Health Organisation global programme for TB vaccination, whose aim is to improve co-ordination with human TB vaccine research.

Potential live vaccine candidates are now being screened using an aerosol challenge model. In collaborative work with the Centre for Applied Microbiology and Research (CAMR), two auxotrophic mutant candidates of BCG were shown to confer similar protection against *M. bovis* as BCG without compromising the ability of current tests to diagnose true infection. These are promising results and further work in this area is in progress.

Work on subunit vaccine development centred on DNA vaccination using immuno-dominant *M. bovis* genes is on-going. Also collaborative work with the National Institute of Medical Research (NIMR) demonstrated the possibility of a therapeutic vaccine against a pre-existing *M. bovis* infection. In cattle, the immunizing effects of DNA vaccination were improved when the vaccine was administered intramuscularly rather than intradermally. Several DNA vaccination schedules have now been developed, none of which compromises the diagnostic tuberculin skin test.

In collaboration with AgResearch of New Zealand, an intratracheal *M. bovis* challenge model for cattle has been validated. This will be used in immunological diagnostic test development and in vaccine evaluation.

Molecular typing of M. bovis

Spoligotyping of *M. bovis* isolates is now a routine test activity for MAFF. Additional discrimination between types is desirable and a second PCR-based technique known as variable numbers of tandem repeats (VNTR) under development at the VLA promises to provide this.

Diagnostic assays for bovine tuberculosis

VLA has developed an *M. bovine* antigen-specific lymphocyte proliferation assay for wildlife. This is now being used in collaborative work in the Republic of Ireland where a study of immune responses in wildlife inoculated with BCG is in progress.

Steps are also being taken to produce a wildlife gamma interferon assay. This will be an ELISA-based test similar to that available for cattle. In cattle, studies have concentrated on developing tests to differentiate vaccinated and infected animals. Experiments using mixtures of various *M. bovis* components have indicated the potential for specially designed peptide cocktails to allow the required discrimination.

* Ministry of Agriculture, Fisheries & Food, UK.

Epidemiological research

The Epidemiology Department, in collaboration with several universities, is currently performing two inter-related MAFF-funded studies, both utilising geographic information systems. The first is examining the locations of past tuberculosis incidents and assessing the possible role of environmental risk factors, such as climate, trace elements and wildlife. The second is a molecular epidemiological analysis examining the spatial distribution of *M. bovis* sub-types.

Two case-control studies, funded by the Milk Development Council and MAFF respectively, are also in progress examining a range of possible variables, particularly husbandry factors, which might contribute to the risk of a herd developing tuberculosis.

Surveillance activities

VLA provides a range of surveillance services to MAFF, including the supply of tuberculin. Over 5 million doses of tuberculin have been supplied to Animal Health Offices throughout the country. VLA also provides a post mortem examination service and in the process of isolating *M. bovis*, has cultured and typed over 5000 cattle samples.

PubMed Central: creating an Aladdin's cave of ideas

From the *British Medical Journal*, 322, 6 January 2001:

Starting this week, research articles from the *BMJ* will be freely available from PubMed Central, the new web based repository that will archive, organise, and distribute peer reviewed reports from biomedical journals (<http://pubmedcentral.nih.gov>). This will be in addition to their continuing free availability on bmj.com. The *BMJ* articles join those from 15 other journals. More are expected to follow suit.

PubMed Central's distinguishing characteristic is that it offers the full text of articles, free to users. Think of it as the logical extension of Medicine, which offers the bibliographic details of articles and their abstracts. It depends on publishers and societies transferring peer reviewed articles to PubMed Central, which, like Medline, is funded by the US National Institutes of Health.

A phenomenal advance

The *BMJ* has joined PubMed Central because we agree with Nick Cozzarelli, editor of the *Proceedings of the National Academy of Sciences of the United States of America* (also on PubMed Central), that 'free access to the scientific literature would be a phenomenal advance in scientific publishing—the greatest in our lifetime.'¹ We want to align ourselves with an initiative which if successful, will benefit science and so clinical medicine and patient care. From the *BMJ*'s point of view, we think that better papers might be submitted to us if we offer authors a route to publication both on paper and on PubMed Central. And we think that many people might see our original articles on PubMed Central and then jump to bmj.com to download PDF versions and for accompanying editorials, commentaries, and rapid responses—thereby increasing traffic to our site.

Whether the initiative will succeed is unclear; certainly most scientific publishers are hoping it will fail. But PubMed Central is the first initiative really to take account of how fundamentally the world wide web has changed the landscape of scientific publishing. On the face of it traditional scientific publishers have moved with the times, migrating their paper journals on to the web in their thousands. But most of these are no more than electronic facsimiles of the paper product. Some journals, such as the *BMJ*, have begun to exploit the properties of the web.² But access controls and the high costs of electronic subscriptions have reproduced the same fragmentation of information that was the despair of the paper world.

What the architects of PubMed Central realised was that the quality control and distribution functions of journals could be uncoupled on the web in a way unthinkable in paper. They recognised that the costs of peer review were relatively low—as most peer reviewers do it for nothing—and that the costs of electronic distribution were trivial compared with those of paper, printing, binding, and postage of the paper journal. If, say, US taxpayers would pick up the distribution costs (as they have done the costs of Medline) then publishers could dispense with this function entirely. Free information would mean that libraries could stop subscribing, thereby releasing money back to researchers.

Some of that money had previously ended up in publishers' profits, so unsurprisingly, publishers were loudest in their condemnation of PubMed Central. But when economic forces and the interests of the scientific community converge, publisher opposition may not succeed.

Sugar coatings; glycoproteins in immunity and protein folding

The *Wellcome Trust Review 2000* of research projects and major initiatives, volume 9, describes a wide range of exciting activities, supported by the Trust, in pursuance of its mission to '... foster and promote research' with the aim of improving human and animal health.' From an impressive list, one example has the above heading and a summary which reads:

'Many proteins have sugar molecules, essential to their form and function, attached to parts of their polypeptide chains. Such glycoproteins are particularly common on the surfaces of pathogens, so our immune system has sugar-binding proteins that initiate the destruction of invaders—a defence arm being investigated by Professor Kurt Drickamer and colleagues at the University of Oxford. Meanwhile, a collaboration between researchers in Bucharest, led by Dr Stefana Petrescu, and Oxford, led by Professor Raymond Dwek, is exploring the role of sugars in the folding of the enzyme tyrosinase, key to the production of the pigment melanin in human cells.'

The first paragraph continues:

'The recognition of sugars on the surfaces of microorganisms is one way in which the body distinguishes potential pathogens from its own cells. The sugar-binding proteins (animal lectins) that mediate this recognition are part of the first line of defence against infection, preceding the antibody-mediated (adaptive) immune response. If the lectin system fails at a critical time, such as during early childhood or in AIDS patients, the body's susceptibility to infections increases. At the Glycobiology Institute, University of Oxford, the animal lectins group—Professor Kurt Drickamer, Dr Maureen Taylor and Dr Russell Wallis—are working to understand how lectins neutralize pathogens, and how naturally occurring human mutations in the lectin genes affect the body's defences.'

Further information: The Wellcome Trust, 183 Euston Road, London NW1 2BE email: marketing@wellcome.ac.uk

Dora M. Scarlett MBE

Dora Scarlett, founder of Seva Nilayam, died on Wednesday March 28th after a short illness.

She attended hospital in Madurai 2 weeks before, after which she decided to return home to Seva Nilayam. She was 95.

Everything that Village Service Trust does as an organization originated with Dora. As many of you will know, Dora went to India in 1959 and founded Seva Nilayam in 1962, barely leaving India for the rest of her life. At first it was extremely simple: some everyday medicines handed out at the door of a mud hut. But over the years it developed; volunteer nurses came, funding was secured from agencies and individuals around the world, sister organisations Arogya Agam and Vasandham were launched, and the work grew from the original clinic to embrace tuberculosis and community health campaigns

and women's development and Aids. Work which has been replicated throughout Theni District, south India and beyond. None of this would have happened without Dora's forceful personality, tenacity and inspiration. All of us who worked with, met or corresponded with Dora will have special memories of her, and the way she touched our lives.

Dora was buried on Friday at Seva Nilayam. Hundreds of people attended her funeral that took place in the beautiful garden she had created and loved so much.

WHO: two new publications on the elimination of leprosy as a public health problem

1. Guide to eliminate leprosy as a public health problem. First edition 2000.

This a booklet of 39 pages, A5 format, with emphasis on the 'final push' to eliminate leprosy as a public health problem. The sub-heading to the title page reads: 'Multidrug therapy cures leprosy, stops transmission and prevents disabilities. Available free of charge at all health centres.' From the Contents list, the main headings are—the final push to eliminate leprosy; what is leprosy?; how to diagnose leprosy; treating leprosy; management and complications and how you can eliminate leprosy from your community. There are numerous, high quality illustrations of the most important aspects of the control strategy and excellent illustrations on pages 20 and 21 of the four blister calendar packs for multidrug therapy—PB adult treatment (green), MB adult treatment (red), PB child treatment (blue) and MB child treatment (yellow). The booklet has been developed in collaboration with the Global Alliance for the Elimination of Leprosy: Member States of the World Health Organisation, Danish International Assistance (DANIDA), International Federation of Anti-Leprosy Associations (ILEP), Nippon Foundation, Novartis Foundation for Sustainable Development and the World Health Organisation. WHO/CDS/CPE.CEE/2000.14

2. Eliminate leprosy from the world

This is a document of 32 page, A3 format, dealing with 'Communication, concepts and support material' in the form of a 'communication tool box', aiming to change the image of leprosy, with emphasis on elimination through case detection and the treatment of all cases with multidrug therapy. The opening page refers to the elimination of leprosy from Africa and some of the pictures are clearly African, with overall art direction from Madagascar, but the illustrations, concepts and support material have potentially valuable application almost worldwide. The subject matter covers posters, displays, patient information, booklets for community health workers and decision makers. Production: World Health Organisation and Novartis Foundation for Sustainable Development.

Biopsy of Skin Lesions in Leprosy by Kiyoshi Harada, Tokyo, Japan, 2001

This booklet of 74 pages is the second edition of the author's contribution on the above subject, with emphasis on stains, pathogenesis and classification. Apart from tables and diagrams, it includes 32 colour plates of high quality illustrating the histopathology of leprosy lesions, stained with conventional haematoxylin and eosin and the Fite-Faraco technique for bacilli, together with the author's own periodic acid-carbol pararosanilin or -silver stain. The most important parts of the Summary (page 71) read as follows:

For pathological studies of leprosy, Haematoxylin & Eosin and Carbol fuchsin 'acid fast' stain are commonly used.

However, mycobacteria are divided into acid-fast and chromophobic by their staining affinities.

The chromophobic bacilli are characterized by a complete loss of their carbon fuchsin stain and their carbol fuchsin 'acid-fastness' can be stored by prior periodic acid oxidation.

Harada has introduced the modification of Nyka's periodic acid-carbol fuchsin or Lillie's PAS allochrome stain, and of Gomori-Grocott's chromic acid-methenamine silver—periodic acid pararosanilin allochrome and periodic acid-methenamine silver—for demonstrating two types of mycobacteria.

The principle of the methods is that the first step is the oxidation of mycobacterial glycolipid to aldehydes $-\text{CHOH}-\text{CHNH}_2 \rightarrow -\text{CHO}$ and the second step is the demonstration of aldehydes with carbon pararosanilin or methenamine silver $\text{R}-\text{CHO} + 2\text{ArNH}_2 \rightarrow \text{R}-\text{CH}(\text{NHAr})_2$ or $\text{R}-\text{CHO} + 2[\text{Ag}(\text{NH}_3)_2] + \text{H}_2\text{O} \rightarrow -\text{COOH} + 2\text{Ag} + 4\text{NH}_3 + 2\text{H}$.

In this paper, periodic acid-carbon pararosanilin or -silver is used for demonstrating both types of bacilli and their host-parasite relationships.

Mycobacteriosis are characterized by tubercle formation or Yersin type of disease.

In most people, the leprosy bacilli fail to established themselves in the tissue; the disease, therefore, tends to be self-healing and self-limiting. Few people develops the disease 'leprosy'.

Leprosy is the atypical Yersin (lepromatous) type of mycobacteriosis. Histoid may be a true Yersin type of disease. It is confused by the presence of epithelioid cell granuloma in the nerves in the tuberculoid and borderline leprosy.

Moreover, leprosy is essentially a disease of peripheral nerves. In very early infection, Schwann cells of cutaneous nerves is a first identifiable target organ of mycobacterium leprae.

Also, leprosy is an immuno-defect disease for mycobacterium leprae. Even in tuberculoid leprosy there is an immunodeficiency.

As a result, in all types of leprosy, even in tuberculoid, lymphocytes could not be cooperated with infected macrophages. Macrophages, therefore, could not be activated, not capable to kill the organism and not ability to alteration into epithelioid cells. However, in the tuberculoid and borderline, lymphocytes could be cooperated only with infected Schwann cells of a nerve. Schwann cells could be activated, capable to kill the organism and transform to epithelioid cells and perhaps Langhans cells in tuberculoid and in less extent in borderline. Therefore, cell mediated immunity is of special importance in dealing with the infection and evolution of leprosy caused by mycobacterium leprae.

Hence, the pathological features of leprosy reflect the infection and response of the disease.

Interpretation of the evidence concerning pathological sign is as follows:

1. Schwann cells of a cutaneous nerve is a first demonstrable target organ of mycobacterium leprae.
2. In the evolution of disease
 - A. Without response, there is an evident of two ways of bacillary spread; a. infected to neighbouring Schwann cells in a nerve, terminally and centripetally and b. infected to accumulated macrophages around a nerve in subpapillary layer. c. alteration of bacillated Schwann cells and macrophages into Lepra cells. d. No focalization of lymphocytes around a nerve.
 - A'. In regressive stage of lepromatous, if immunity is more low, alteration of histiocytes into Yersin type of cells.
 - B. With response, a. accumulation of lymphocytes around an infected nerve b. alteration of Schwann cells into epithelioid cells and perhaps Langhans cells.

Further information: Kiyoshi Harada MD, Research Laboratory, National Sanatorium Tamazenseiyen, Higashimurayama, Tokyo, Japan.

Leprosy project promotes disabled meet

At a significant get-together function to mark the Silver Jubilee Year of Bombay Leprosy Project (BLP), patients affected by leprosy and other physically disabling diseases assembled to relate the job satisfaction they derived in working together without experiencing a feeling of isolation.

Dr R. Ganapati, Director, BLP observed that there are several ways of fighting stigma associated with leprosy and to a lesser extent with the visibly disabled patients in general. BLP has found that offering employment opportunities to such patients in an integrated manner without isolating them in institutions is the best way of avoiding social ostracism.

Dr T. Sreedhar, Deputy Director, All India Institute of Physical Medicine and Rehabilitation, Mumbai, The chief guest in his address informed even school and college principals were not aware of the Disability Act-1995 which recommends equal rights to the disabled persons. He recounted the story of a student who underwent post-polio surgery as a result of which she missed college attendance for more than three months, with the Principal refusing admission to her though the Disability Act 1995 prevailed upon all Institutions of learning to show the maximum possible concession to disabled persons. However, armed with a letter from Dr. Sreedhar, reminding the Principal of this Act, the child again sought admission and was permitted to join.

To Mr P. P. Hirani, the celebrated photo-journalist, who has visited several rehabilitation institution elsewhere, community based rehabilitation practiced by BLP was a novel experience. He referred to the disabled as 'Children of a Greater God' and confessed that these persons will spread the positive message.

The meeting concluded with a vote of thanks from Dr C. R. Revankar, Deputy Director, BLP.

UN says up to half the teenagers in Africa will die of AIDS

From the British Medical Journal, volume 321, page 67, 8 July 2000:

AIDS will cause early death in as many as half of the teenagers living in the hardest hit countries of southern Africa, causing population imbalances nearly without precedent, according to a report released last week by UNAIDS, the Joint United Nations Programme on HIV/AIDS.

Demographers predict that two thirds of the 15 year olds in Botswana will die of AIDS before reaching age 50. Although that is clearly the world's worst scenario, researchers predict that in any country where 15% of adults are now infected, at least 35% of those who are currently teenagers will eventually die of AIDS.

The AIDS epidemic is already measurably eroding economic development, educational attainment, and child survival—all key measures of a nation's health—in much of sub-Saharan Africa, according to the report.

The disease's ultimate toll on the region, however, is likely to be far more severe than what is evident today, the report found. "The demographic effects will only be getting worse in the coming years, even if by some miracle HIV infection suddenly stopped," said Peter Piot, director of UNAIDS. "I believe we are only at the beginning of the actual impact on societies of AIDS."

According to the report, there are now 34.3 million people infected with HIV worldwide, of whom 1.3 million are children under the age of 15. About 5.4 million people were infected last year.

Last year 2.8 million people died of AIDS; a total of 19 million have died since the epidemic was first recognized 20 years ago. About 13.2 million children, the vast majority in Africa, have lost at least one parent to the disease.

There are a few success stories in an otherwise grim picture. The infection rate in Uganda has fallen to around 8% of the adult population from a peak of 14% in the early 1990s, thanks to strong prevention campaigns and the increased use of condoms.

Despite earlier fears of an epidemic in Asia, the rate of infection remains generally low. In Thailand the heterosexual epidemic has been curbed, although the virus is spreading fast through shared needles and unprotected sex between men.

Strong campaigns in some of these countries have shown that it is possible to slow the epidemic. But the report also said that there must be a massive increase in political will. □

Report on the Global HIV/AIDS Epidemic 2000 is available from UNAIDS, 20 Avenue Appia, 1211 Geneva 27, Switzerland, or at www.unaids.org.

Full story in News Extra at bmj.com

Interleukin 2 increases CD4 T cell counts in people with HIV

The following account appeared in the *British Medical Journal* volume 321, page 196, 22 July 2000. bmj.com:

Adding interleukin 2 to anti-retroviral drugs substantially increases the CD4 T cell count and decreases the viral load of HIV, according to a multicentre trial sponsored by the National Institutes for Health (*JAMA* 2000;284:183–9).

The combination treatment may further extend the immune competency and therefore the life span of people infected with HIV. The two year study, led by Drs Richard Davey Jr and H. Clifford Lane of the National Institute for Allergy and Infectious Diseases, enrolled 82 patients and randomized them into two groups. Nearly all the patients were male.

Forty three patients received antiretroviral drugs alone, and 39 patients received antiretroviral drugs plus intermittent therapy with subcutaneous interleukin 2 at a starting dose of 7.5 mIU twice a day for five days every 8 weeks.

The choice of antiretroviral was left to the patients and their physicians, but both groups had similar proportions of patients who were taking protease inhibitors (89% of those in the interleukin group; 80% of those taking only an antiretroviral). Patients with serious AIDS defining illnesses were excluded from the study.

Enrolment criteria included either a baseline CD4 count of $200\text{--}500 \times 10^6$ or 14% of all T cells, a viral load of less than 10 000 copies of HIV-1 RNA, and no previous treatment with interleukin 2.

Additionally, patients had to be free of treatment with systemic steroids, chemotherapy, and cytotoxic agents for at least 4 weeks before the trial.

Of the initial 82 patients enrolled, 78 completed the study. After 1 year, patients who had been receiving both interleukin 2 and antiretroviral drugs sustained a greater increase in CD4 counts than those given antiretrovirals alone, with an average increase of 112% compared with 18%. Moreover, there was a dose related increase in CD4 count with increasing dose of interleukin 2. □

Full story in News Extra at bmj.com

Changes in the STOP TB Campaign

From *Connect*, the Newsletter of the International Federation of Anti-Leprosy Associations (ILEP)-No. 2, Winter 2000/01:

Changes to the STOP TB Campaign and the organization of TB activities in WHO have just been announced by the Director General, Dr Gro Harlem Brundtland. Dr J. W. Lee, formerly special Representative of the Director-General, is appointed as Director of SPOT TB, with intermediate effect. STOP TB will have two components—one of which will be the Secretariat of the STOP TB initiative, headed by an Executive Secretary, Dr Jacob Kumaresan. The second component will continue to fulfill WHO's normative and technical responsibilities in TB and will be coordinated by Dr Mario Raviglione. For further information, please contact the STOP TB Secretariat at stoptb@who.int

Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment

This is the title of an important and interesting article published in *The New England Journal of Medicine*, 1999;341:1174–9, by Annelies van Rie *et al.* from the University of Stellenbosch in South Africa, The Catholic University of Leuven in Belgium and the International Union against Tuberculosis and Lung Disease in Paris, France. The *Abstract* reads as follows:

Background For decades it has been assumed that postprimary tuberculosis is usually caused by reactivation of endogenous infection rather than by a new, exogenous infection.

Methods We performed DNA fingerprinting with restriction-fragment-length polymorphism analysis on pairs of isolates of *Mycobacterium tuberculosis* from 16 compliant patients who had a relapse of pulmonary tuberculosis after curative treatment of post-primary tuberculosis. The patients lived in areas of South Africa where tuberculosis is endemic. Medical records were reviewed for clinical data.

Results For 12 of the 16 patients, the restriction-fragment-length polymorphism banding patterns for the isolates obtained after the relapse were different from those for the isolates from the initial tuberculous disease. This finding indicates that reinfection was the cause of the recurrence of tuberculosis after curative treatment. Two patients had reinfections with a multidrug-resistant strain. All 15 patients who were tested for the human immunodeficiency virus were seronegative.

Conclusions Exogenous reinfection appears to be a major cause of postprimary tuberculosis after a previous cure in an area with a high incidence of this disease. This finding emphasizes the importance of achieving cures and of preventing anyone with infectious tuberculosis from exposing others to the disease.

Particularly if confirmed in other parts of the world, these findings in South Africa have important implications for our current efforts to control this disease. An extract from the *Introduction* reads:

‘Before the introduction of antituberculous medication, there was little recognition of the distinction between endogenous reactivation and exogenous reinfection in patients who had multiple episodes of tuberculosis, since untreated established tuberculous lesions may be alternately active and dormant. Effective treatment regimens made possible the sterilization of pulmonary lesions, but it was accepted that subsequent episodes of tuberculosis were almost invariably caused by endogenous reactivation. The complete sterilization of a lesion became possible with improved treatment regimens, especially with the introduction of rifampin, a drug with a potent sterilizing effect. With short-course combination therapy consisting of isoniazid, rifampin, and pyrazinamide, the relapse rate dropped from 21 percent to 1 to 2 percent. In this era of effective treatment regimens, the notion that multiple episodes of tuberculosis in one patient are almost always caused by endogenous reactivation may be questioned. It is now possible to characterize the genotype of *Mycobacterium tuberculosis* by DNA fingerprinting, which can show whether a new episode of the disease is caused by infection with the same strain that caused a previous episode or by a different strain.

In this study we used DNA fingerprinting to determine the relative frequency of endogenous reactivation and exogenous reinfection in patients with multiple episodes of postprimary tuberculosis. We aimed to determine the importance of this distinction in terms of the definition of cure, the efficacy of current treatment regimens, and the control of tuberculosis.’

And the closing paragraph of the *Discussion*—

‘The controversy with regard to endogenous as opposed to exogenous pathogenesis of tuberculosis is of importance in the planning of clinical trials and national tuberculosis-control programs. If, in areas with a high incidence of the disease, postprimary episodes of pulmonary tuberculosis after previous cure result predominantly from exogenous reinfection, as indicated by our results, the effectiveness of a drug regimen cannot be evaluated on the basis of the relapse rate without the additional information provided by RFLP analysis of bacterial isolates. In the evaluation of national tuberculosis-control programs for areas in which the disease is endemic, restriction fragment-length polymorphism (RFLP) analysis can prove the effectiveness of the currently used treatment regimens. “Cure” in a patient who later has another episode of tuberculosis is not necessarily an incorrect concept. The more likely possibility is that he or she has a new infection after the cure. The emphasis should thus be placed on achieving cure in patients and on prompt case detection to prevent reexposure to sources of active tuberculosis.’