News and Notes

Leprosy bug provides clues to early nerve degeneration

Using myelin-forming primary nerve tissue cultures and mice genetically manipulated to lack two key immune system cells, researchers at Rockefeller University have shown that *Mycobacterium leprae*, the bacterium that causes leprosy, destroys the protective myelin sheath that surrounds nerve fibres. The nerve damage, a hallmark of leprosy previously thought to be a byproduct of the immune system’s response to the leprosy bacteria, now seems to be a direct result of the leprosy bug attaching itself to specialized nerve cells called Schwann cells, the glial, or supporting, cells of the peripheral nervous system (PNS).

The findings suggest that the body’s immune response does not play a significant role in the early stage of neurological injury. The damage is characterized by the disruption of the myelin sheath, the insulation on nerve cell connections that helps transmit rapid signals between the brain and the peripheral organs, for example, skin and muscles. Damage to myelin causes loss of sensation, disability and paralysis.

Using laboratory cell tissue cultures and mice genetically manipulated to lack two key immune system cells, the research team showed that *M. leprae* destroys the protective myelin sheath that surrounds nerve fibres and then hides out in the supporting cells that enclose non-myelin nerve fibres, poised to initiate later attacks.

The researchers found that, unexpectedly, *M. leprae* does not need to enter the cell to cause degeneration of the myelin sheath, and does not even need to be alive to demyelinate nerve cells. Similar results were obtained after cultured Schwann cells were exposed to bacteria that had been killed with radiation and to fractions of the bacterium’s cell wall.

As the damaged myelinated nerve cells repair themselves by generating new non-myelinating Schwann cells after attack, *M. leprae* sequesters itself in these non-myelinated nerve cells, waiting for a chance to attack again, once they multiply and escape from these cells. The researchers believe that this phenomenon accounts for the lasing/remitting characteristic of leprosy.

*M. leprae* is known to cause debilitating neurological injury in humans, but the clinical manifestation occurs years after a slow infectious process. Information about the pre-clinical mechanisms in *M. leprae*-induced demyelination may allow researchers to develop therapeutics and common diagnostic tests for early detection of demyelinating diseases of both infectious origin and unknown etiology, such as multiple sclerosis and Guillain-Barré syndrome.

Preventative treatment for leprosy on the way?

Vital new research is underway to find a preventative treatment for leprosy. A randomised-controlled trial is currently underway in Bangladesh to monitor the effectiveness of prophylactic rifampicin as a tool to prevent leprosy in people who are in close contact with the disease (i.e., family members of patients). The project, which follows a successful pilot study in northern Bangladesh, is a collaboration between TLM, American Leprosy Missions and the Erasmus University in Rotterdam, Netherlands.
Queensland researchers make malaria breakthrough

Scientists at the Queensland Institute of Medical Research have come one step closer to producing a vaccine to combat the world’s largest killer, malaria.

Researchers say their latest study suggests it is possible to rapidly immunize humans by infecting them with a low-dosage of parasites.

Professor Michael Good says the parasites are used to activate one of the body’s natural defence mechanisms called T-cells, which then fight the malaria. He says this latest research may also hold the key to developing vaccines for a range of infectious diseases. ‘This opens up an additional approach to developing a malaria vaccine,’ he said.

‘Up until now all the focus has been on stimulating protective antibodies but now we can also add to that repertoire molecules that stimulate T-cells, and that obviously broadens our entire strategy in developing a malaria vaccine.’

New malaria drug?

A drug with a new type of action against the malaria parasite has been reported. Codenamed G25, the drug stops the parasite making its cell walls when living inside red blood cells. Both in vitro, and in owl monkeys, it has shown remarkable activity and relative lack of toxicity compared to quinine.

Bioinformatics in disease endemic countries

Bioinformatics provides opportunities in health research and development. For new drug research and development, this includes identification of novel drug targets, structural predictions, tapping into biodiversity, reconstruction of metabolic pathways, and systems biology. Bioinformatics may also contribute to the identification of vaccine candidates through analysis of surface antigens and epitopes.

Bioinformatics is a window of opportunity for disease-endemic countries (DECs). It is ‘people-intensive’, and less affected by infrastructure and economics than other areas of biological research. Further, the ‘critical mass’ issue is less critical—a world-wide community is within reach through the Internet. Bioinformatics requires relatively modest hardware and technical support. There is a vast repository of public domain software for computational biology and individual accounts for remote access and data processing can be opened at high-performance computer facilities and bioinformatics regional centres including EMB network nodes, FIOCRUZ, SANBI, CеТCALУА (Venezuela), and ICGEB (Italy and India). Powerful searches are possible using public websites such as NCBI, EMB electromagnetic book nodes, Sanger Centre, Expasy/SwissProt, and KEGG database.

TDR has initiated a programme for developing capacity in bioinformatics, with the following objectives:

- To support 20–30 DEC scientists to a top level competence in bioinformatics (‘trainers’) with the capability to conduct local bioinformatics training in Africa, Asia and Latin America in the next 5 years.
- To further establish sustainable regional networks of centres and expertise for the promotion and integration of bioinformatics and DNA technology in basic research and management of tropical diseases in endemic countries.
- To establish a distance learning programme for bioinformatics in disease endemic countries.

The strategy is to build an integrated and sustainable network of centres in DECs utilizing existing and/or newly developed infrastructure including the World Bank’s Distance Learning Program, NCBI, SANBI, and ONSA centres. TDR’s activities started with a ‘train-the-trainer’ workshop in bioinformatics and applied genomics. The next steps are to initiate regional training courses in Africa, Asia and
Latin America, and a Bioinformatics Career Development Grant for exceptional individuals who emerge from these courses. In the longer term, Masters and Doctoral training programmes will be developed and/or expanded in DECs.

**New research institute for tropical diseases research**

Novartis, in collaboration with the Singapore Economic Development Board, has established a research institute for tropical diseases research in Singapore. Aimed at the discovery of novel treatment and prevention methods for diseases such as tuberculosis and dengue fever, the long-term aim is to help reduce the overall affliction of tropical diseases and improve the prosperity of developing countries. In those countries where the diseases are endemic, the Novartis Group intends to make treatments readily available and without profit. The Institute is looking to become a major centre of excellence and will offer exceptional teaching and training opportunities for postdoctoral fellows and graduate students.

**Breakthroughs in tuberculosis research**

A new drug against tuberculosis is being developed through a partnership between Chiron Corporation and the Global Alliance for TB Drug Development. The drug, codenamed P-824, is currently in pre-clinical development. It is a nitroimidazole and has a different type of action to any other anti-TB drug.

Clinical research with SCV-07, a compound that enhances the body’s immune system may lead to the production of an oral treatment for drug resistant tuberculosis, a particularly alarming strain.

SCV-07 was developed by SciClone Pharmaceuticals, of the US, and Verta, from Russia.

Clinical trials with hospital patients have been conducted in Russia, and the researchers reported that the patients showed a marked decrease in the presence of tuberculosis in the lungs. The patients also showed a significant reduction in ailments symptomatic of tuberculosis, such as fever, chest pain, and dry coughing. SCV-07 brought 80% to a non-contagious state, a primary goal in TB therapy and a critical step in reducing the spread of the disease.

The researchers plan to conduct further trials before bringing the compound to the market.

**Rehabilitation in China**

Four small-scale projects are being run by HANDA (the Hansen Damien Welfare Association) based in the city of Guangzhou to help leprosy sufferers in 63 high endemic villages in Guangdong province in southern China. The projects are supported by the Novartis Foundation, and had the following aims:

1. **Training young people in sewing skills, enabling them to find jobs in industry**

The project ran 3-month sewing courses in the Handa building in the city of Guangzhou which also served as a short-term residence for Handa members looking for jobs. Those completing the course were trained to operate high speed sewing machines. Most Handa members who sought factory jobs, found them at average wage levels for the jobs. Others went on to work in health care or as sewing teachers.

A few of the trainees came from cities but most were from those villages with a high incidence of leprosy in Guangdong province. Reports from local government officials as well as follow-up visits by Handa officials indicated that the trainees’ stay in a supportive environment had helped them greatly in developing their self confidence and in facilitating their social integration in the very different world of the city. For the minority who returned to their villages, the acquisition of a skill had improved their standing within their communities. In two years, the school trained 56 people from Guangdong and an adjoining province.
2. Village micro-enterprise sewing projects to provide income support for women

To provide support for young mothers and other women in remote villages, in 1997 the Foundation supported the provision of cloth and sewing machines to make quilts, using the Handa teachers to help with instruction. Several of the women taking part had themselves been trained in the Handa sewing school. Classes were held both at the school, in Leizhou and in two rural villages.

Progress towards the target of providing the women with the equivalent of a factory-level wage was slow, largely because of the depressed market in textiles. A number of the women taking part experienced difficulties as a result of their social insecurity but contact with the project personnel had some success in breaking this down.

3. Fruit growing and fish breeding projects to provide support for residents of the provincial leprosy hospital/settlement, most of them disabled

An agricultural project started in 1994 to help the remaining residents of the provincial leprosy colony at Sian, on an island in the East river had only limited success. The 87 residents, 75% of whom were disabled, were the last left in the settlement after the introduction of MDT in the 1980s allowed the discharge of hundreds of their fellow residents.

The land had traditionally been given over to banana cultivation and the project aimed to support diversification into mangos and other fruit as well as fish farming. The Foundation began its support in early 1997 but the project was vexed by local administrative and marketing problems, and the only benefit was the share of the new harvest kept for the residents. However, there has been one positive outcome, albeit an indirect one. The higher profile that Sian attained as a result of this project led to Handa establishing a kitchen for the disabled residents who could not cook for themselves, and helped to generate active participation from groups in Hong Kong in improving the welfare of the leprosy sufferers.

4. Assistance for comprehensive eye care provision in remote areas

When the Foundation donated a van to Handa in 1998, it enabled medical personnel to extend their activities to previously inaccessible areas. Around 75% of people in Guangdong province’s high endemic villages suffer from eye disabilities. The medical team included an ophthalmologist and within one year of operating the mobile clinics, it had completed a comprehensive eye project in 14 of these villages, treating a total of 577 patients.

Where possible, the activities of the mobile clinic were combined with those of the sewing project. For example, the premises in the city of Leizhou (600 km from Guangzhou) used to train the quilt makers, were also prepared for eye clinic operations. The van was used to transport patients needing operations. In the same way, sewing training workshops offered the eye team an opportunity to travel to remote villages not only to give treatment but also to train local doctors in techniques of blindness prevention.

Leprosy prevalence rate comes down

31 July 2002, Bhubaneswar, India
Source: The Newindpress

The number of leprosy patients in the State is declining steadily with the plunge in leprosy prevalence rate from 121 per thousand in 1982–1983 to 6.3 per thousand at present. However, this is still higher than the national rate of 3.7 per thousand and Orissa is the fourth State having highest number of leprosy patients.

Due to effective implementation of the National Leprosy Elimination Programme (NLEP), launched
in the State in 1982–1983, the number of leprosy patients has gone down considerably. Sources in the Health Department informed that the prevalence rate in Jharsuguda district is the highest (16.93 per thousand) and in Malkangiri it is the lowest (2.32 per thousand). Sources said as many as 23,759 active cases of leprosy are registered in the State at present, of which 13,465 are multi-bacillary, 10,266 are pauci-bacillary and 28 are single skin lesion.

The NLEP aims at bringing down the leprosy prevalence rate below one per 1000 through multi-drug therapy (MDT) method.

**Medico-Social commission’s new Chair**

At its June 2002 Meeting, members of the Medico-Social Commission of ILPE co-opted Dr Pieter Feenstra to act as Chair until their term in office ends in June 2004. A medical doctor and health services consultant, he is currently engaged by the Department of Health at the Royal Tropical Institute, KIT, in Amsterdam as Coordinator for the Leprosy Unit. Dr Feenstra worked in Ethiopia as WHO advisor to the National Tuberculosis and Leprosy Control Programme. He replaces Dr Etienne Declercq, who stepped down as Chair of the MSC in May.

**Ayurveda—the people’s medicine**

The following is taken from an article by Nimal D. Kasturiaratchi, Director, Medical Education, University of Peradeniya, Sri Lanka.

**Leprosy and Ayurvedic illness categories**

The importance of Ayurvedic practitioners in leprosy control activities is derived from the impact Ayurvedic ideas have on expressions of experiences with illness in Sri Lanka. *Sema, vata, pita, peenus, rakataya, rakta vata, hiri gatiya, and hiri vata* are common expressions of sickness among Sri Lankans. These expressions are essentially Ayurvedic illness categories for which it is not easy to find corresponding biomedical categories. The terms themselves refer to experiences with illness, and sometimes terms such as *sema* denote concepts of humoral imbalance described in Ayurvedic medical theory. Ayurvedic diagnoses are therefore elicited on the basis of particular experiences with illness and are not necessarily based on symptomatology used in biomedicine. The unsuspecting Ayurvedic physician may thus treat patients who have such complaints with Ayurvedic medicines, which are not effective against leprosy. Correcting humoral imbalances requires medication for a longer period. Leprosy patients who end up seeking Ayurveda assistance may receive treatment even longer, as their symptoms do not subside immediately.

When confronted with a vignette depicting a story and a picture of a leprosy patient, Ayurveda practitioners tended to come up with Ayurvedic diagnoses. Similarly, a greater time lag was reported before patients with numbness, etc. sought the services provided by the Anti-Leprosy Campaign. It has also been revealed that patients with numbness and certain types of infiltration and nodules seek treatment from Ayurvedic practitioners at some point in time. Similarly, deformities such as ulcers, foot drop, and claw hand may be treated by Ayurvedic medicine, as there are traditional medical practitioners who specialize in treating these conditions.

Ayurvedic practitioners are well aware of leprosy. They know leprosy as *lādur*, which is not an Ayurvedic illness category, and they will not recognize it in its clinical form. Given the low endemicity of leprosy in Sri Lanka, not many Ayurvedic practitioners have encountered *lādur* patients. They are reluctant to refer patients without trying some treatment on their own.
Integrating Ayurvedic practitioners in leprosy control

A training programme has now been designed for Ayurvedic practitioners by the Leprosy Elimination and Comprehensive Care (LECC) programme, so that they will be able to suspect ladura among complaints made by patients indicating Ayurveda diagnoses. The main thrust of the programme is to keep these practitioners from diagnosing ladura so that they will refer suspected leprosy patients. Under the terms of the programme, upon suspecting leprosy, Ayurvedic practitioners use a referral form designed by the programme to refer patients to the Anti-Leprosy Campaign Public Health Inspector (PHI), who makes arrangements to confirm the diagnosis and assure comprehensive care. Patients who are referred but confirmed to be free of leprosy will be referred back to the Ayurvedic physician.

Island-wide awareness programmes for all Ayurvedic practitioners in the country have been planned, and an initial awareness programme for provincial commissioners of Ayurveda has already been concluded. This will be followed up by training in an Ayurvedic trainers programme. An essential feature of this strategy is to strengthen the link between the field leprosy worker (PHI) and the Ayurvedic practitioner at the local level.

Tokyo Declaration

An extremely fruitful meeting, bringing together high-level staff from India, WHO and NGOs, was held 3 June 2002, jointly sponsored by SEARO and The Nippon Foundation. Discussions were intense and general commitment to leprosy control in India was achieved through the Tokyo Declaration which focussed on: the realization of the elimination goal as defined by the World Health Assembly; multi-drug therapy (MDT) for all; access to Prevention of Disability (POD) and Socio-Economic Rehabilitation (SER) services wherever feasible; cooperation of partners; and recognition of each partner’s peculiarities.

For the full text of the Tokyo Declaration contact: ilep@ilep.org.uk The SMHF are currently preparing a small booklet and CD of this meeting for distribution.

Update on the fight against lymphatic filariasis

Lymphatic filariasis (LF), also known as elephantiasis, is a condition that currently affects 120 million people worldwide and threatens a further 1.2 billion, mainly in poverty-hit areas. It is a disease transmitted from person to person by mosquito. Minute immature larvae swimming in a patient’s blood are ingested by a mosquito, develop into larvae in the mosquito and pass to another person during the mosquito’s next feed. Once inside the human host (humans are the only known carriers) the larvae migrate to the lymphatic system where, over the next 3–12 months they grow into thread like parasitic worms. The worms, which live for about 7 years, then nest in the human body, each 10 cm long female producing millions of microfilariae. A typical patient will have two or three nests but up to 15 nests have been found in some people.

The worms cause serious damage to the patient’s lymphatic system, by stopping the smooth passage of lymph fluid. When the worms die, the system is often unable to clear itself and swellings develop. Although the disease is not usually life threatening, the effects can be devastating.

The disabling consequences of LF are significant. In India, which accounts for 44% of the world’s cases, 10 million people seek help every year. Millions more should be seeking help but don’t because they fear that nothing can be done for them. Like leprosy, LF is disabling, carries with it a burden of stigma and shame and affects the same impoverished communities. It too can be simply eradicated with drugs. Mass Drug Administration (MDA) programmes, driven by the local communities, aim to interrupt transmission by killing off the microfilariae in the human body. But to be successful, MDA programmes require 70–80% of at risk communities taking two drugs once a year for between 4 and 6 years.
In May 2002, a workshop was held in Delhi, convened by The Global Alliance for the Elimination of Lymphatic Filariasis at which Non-Governmental Organisations (NGOs) discussed the roles they could play in eliminating the disease. The workshop concluded with a commitment to establish an information system allowing the activities of NGOs active in LF elimination efforts to be recorded. There was also a strong consensus that a focal point was needed to co-ordinate activities and that an inventory of interested NGOs should be established.

AIDS vaccine

An American pharmaceutical company has said that it may be able to produce a vaccine against AIDS within five years, and not ten as previously thought. The company, VaxGen, is due to announce the findings of its research this afternoon at an international AIDS conference in Barcelona.

In another development, the Swiss firm, Roche, in partnership with an American company, said that they have produced a drug that attacks the HIV virus before it gets into human cells, not after. That drug could be available next year.

But Seth Barclay, President of the International AIDS Vaccine Initiative, which promotes research into the illness, said that it would be some time before the treatment was readily obtainable.

There have been calls at the 14th International AIDS Conference for the disease to be put at the top of political agendas around the world. The head of the United Nations agency set up to combat AIDS, Dr Peter Piot, earlier said that leaders who did not take the fight against the disease seriously should be put out of office.