

## Leprosy is in principle eradicable – a possible approach

G. P. Talwar

Many years ago, India had the largest number of the leprosy patients in the world. A country-wide leprosy control programme based on multidrug therapy (MDT) has significantly reduced the current prevalence figure. However, the incidence of new cases each year is increasing. What is further worrisome is that some of the patients are becoming resistant to the drugs employed. Suggested below is an approach which can not only treat such patients, but also prevent the occurrence of new cases.

Leprosy is caused by a Mycobacterium, *Mycobacterium leprae*, which was discovered over a century ago by a Norwegian, Armauer Hansen. He was unable to culture it in any medium and his thesis is the shortest recorded in academic history. *M. leprae* requires a host cell to grow and divide. It is a slow grower and takes about 13 days to duplicate.

Most (nearly 99%) of the humans are resistant to *M. leprae* and do not develop leprosy on exposure to this bacteria. Those who develop the disease manifest it as a spectrum varying from tuberculoid (TT) to multibacillary lepromatous (LL) leprosy. The polar tuberculoid leprosy patients (TT) have limited, usually one lesion, with no live *M. leprae*. The immune system of such patients, though slightly deficient than the normal humans, who are totally resistant, limits the multiplication of *M. leprae*. On the other hand, the multibacillary leprosy patients are loaded with *M. leprae*. Their cells serve as a fertile soil for proliferation of *M. leprae*. Leprosy patients and those incubating the disease are the source of infection to others in the community. The causative microorganism being a slow grower, it takes 2 to 10 years for an infected person lacking immunity to this bacterium to manifest the disease.

### Proposition

It is proposed that every time a patient is detected as suffering from leprosy, he/she should be treated with not only the standard multidrug regime, but also immunized with autoclaved *Mycobacterium indicus pranii* (MIP, previously coded as Mw). The genome of this non-pathogenic Mycobacterium has been

sequenced<sup>1</sup> and being hitherto a non-described micro-organism in the World Data Bank, has been given this name<sup>2,3</sup>. MIP is a potent invigorator of immune responses<sup>4</sup>. It shares antigens with both *M. leprae* and *M. tuberculosis* and overcomes anergy of immune response to *M. leprae*, which is the nature of defect rendering a human susceptible to leprosy. The inclusion of MIP in the treatment regime accelerates bacterial clearance and shortens the recovery period<sup>5-7</sup>. It is effective in patients who are slow responders to MDT<sup>8</sup>. What is more notable is its ability to render LL patients who are lepromin negative to lepromin positive status. The conversion rates were 100% for TT, 71% for BL (in between TT and LL) and 70% for LL patients<sup>9</sup>. Lepromin is an index test for classification of leprosy patients to lepromatous leprosy category. The test is a reflection of the nature of defect in the immune responses of the patients. It stays negative even after the multibacillary LL

patient is made bacillary negative by drugs. Hence, immunization with MIP not only cures the patient faster, but also renders him somewhat responsive immunologically to some crucial antigens of *M. leprae* to which he was anergic previously. What is amazing is the elimination of granulomas and normalcy of physical appearance of many patients on recovery after receiving MIP + MDT<sup>10</sup>. Figure 1 is a graphic illustration of some patients suffering from multibacillary leprosy who were treated with a combination of multidrugs regime and MIP. It may be mentioned that MIP is approved by the Drugs Controller General of India and also by the US FDA. It is licensed to M/s Cadilla Pharma and is available to the public.

### Concentric zone of immunization

The proposition for eradication of leprosy demands immunization of not only the patient, but all of his family, friends



Figure 1. Some representative cases of LL/BL multibacillary patients treated with multidrug therapy plus *Mycobacterium indicus pranii*<sup>8-10</sup>.

and contacts to whom he could have transmitted the infection, so as to fortify the immune responses of individuals deficient in this respect and thereby liable to develop leprosy. It is a doable proposition. This was the way small pox was eradicated. The undertaking though appearing large is far smaller than what was done for polio. The achievement will be historical.

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*G. P. Talwar is in the Talwar Research Foundation, New Delhi 110 068, India. e-mail: gptalwar@gmail.com*

## COMMENTARY

# Indian pharmaceutical industry: policies, achievements and challenges

*Rajesh Kochhar*

The Indian pharmaceutical industry is a success story from a national as well as developing nations' perspective. India accounts for 10% of the world's production of pharmaceuticals and ranks third in the world in terms of volume. In value terms, however, its share is only 1.4% and the rank 14th (ref. 1). This statistics underlines the important fact that India produces world-class generic drugs at a low cost. Indian domestic pharma market, currently valued at US\$ 12 billion, is largely self-sufficient with patented drugs playing a minimal role. India exports both bulk drugs and formulations (tablets, etc.). For the year 2012–13, India's pharmaceutical exports stood at some US\$ 14.7 billion, registering a growth rate of 11% (ref. 2). About 55% of exports are to USA and to a lesser extent other regulated markets such as Europe, Japan and Australia. These countries primarily buy bulk drugs, but they are now increasingly buying formulations as well.

However, it is in the case of the poor and low-income countries that Indian generic drugs are playing an extraordinary humanitarian role. UNICEF's 2012 Supply Annual Report (p. 37) recognizes India as the largest supplier of generics<sup>3</sup>. About 50% of the essential medicines that UNICEF distributes in developing countries is sourced from India; Belgium which supplies vaccines comes a distant

second. India can justly be proud of the signal role it has played in suppressing AIDS in Africa and other poor countries. Nearly 70% of the medicines for AIDS patients in 87 developing countries purchased by various agencies, including UNICEF and Clinton Foundation since July 2005 has come from India. The independent international medical humanitarian organization Médecins Sans Frontières (MSF) rightly calls India the 'pharmacy of the developing world'.

In 1996, the US Food and Drug Administration (FDA) approved the combination antiretroviral (ARV) drug therapy for AIDS, which turned out to be effective indeed. By 1997, the number of AIDS deaths in USA had declined significantly. Unfortunately, the benefit of the therapy was denied to the poorer parts of the world. The drugs are patented in USA and marketed by pharmaceutical companies, in some instances as exclusive licensees of the US Government. Patents relating to AIDS drugs were granted across the globe, including in South Africa. The AIDS drug cocktail cost about US\$ 1000 a month, obviously beyond the reach of most patients and their governments. The patent-holding companies, refused to lower the prices. In 2001, the Indian pharma company Cipla, led by Yusuf Khwaja Hamied, offered to sell generic medicine at about US\$ 30 a month. The powerful Big

Pharma, using all legal and political weapons at its command, objected to the sale of generics in territories where it held the patents. Finally, thanks to a worldwide campaign led by a handful of dedicated people, Big Pharma was forced to retreat. By this time 10 million or more people had already unnecessarily died of AIDS. It is matter of record that AIDS-death rate in Africa showed a decline only in 2007, a full 10 years after the introduction of ARV (Table 1). How Africa coped with AIDS is the subject of a critically acclaimed award-winning 2013 documentary 'Fire in the blood'.

### Indian Patent Act

From 1972 till 2005, Indian drug manufacture was governed by the Patent Act of 1970 which refused to grant a patent for a product, thus encouraging drug companies to produce generic drugs through reverse engineering, unmindful of their patenting elsewhere. In 2005, India was obligated to allow product patents in accordance with Trade-Related Agreement on Intellectual Property Rights (TRIPS); but making effective use of the permitted flexibilities, the new system protects the interests of generic manufacturers as well as patients. The Indian patent regime does not permit ever-greening, that is patenting of minor