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Mini Review

Mission-oriented Research Leads Frequently to a Product for Industry

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Abstract

This article reviews research which we undertook to combat Leprosy, of which the largest number of patients are in India. We had to learn first why a person becomes victim to this disease while more than 98% of us are immune to it. The defect is their inability to react to some key antigens of M. leprae. Having found that, the next issue was whether we can do anything to overcome this defect.

We developed a vaccine against Leprosy which is based on a cultivable, non-pathogenic mycobacteria originally coded as Mw. The gene sequence of Mw has been determined and it has been named as *Mycobacterium indicus pranii* (MIP), Pran is my family name and nii, the National Institute of Immunology from where trials were carried out.

Heat killed MIP given as adjunct to standard drugs expedites recovery of patients. It also renders a high percentage of multibacillary patients Lepromin positive from otherwise permanent Lepromin negativity status. Patients treated with MIP recover free of ugly blemishes which Drugs alone fail to achieve.

MIP is also effective in treatment of Category II, Difficult to treat tuberculosis patients. It is a potent invigorator of immune response and enhances significantly antibody titres of the anti-hCG vaccine under development for control of pregnancy. At the All India Institute of Medical Sciences, New Delhi, it has been used for curing ugly ano-genital warts.

Keywords: Mycobacteria; *Mycobacterium indicus pranii*; WHO

Mission-Oriented-research is geared to lead to a Product, which a Company has to produce and make it available to the 'Needy' for use. It has a purpose and utility. In the early stage of their career, most Scientists carry out basic research to publish good Papers making ground for their promotion to reach the top position, i.e. Professorship in an academic Institution.

A transition came in my life in 1970, when I was Professor of Biochemistry at the All India Institute of Medical Sciences, New Delhi. I was working with my students and scholars on the Mechanism of action of Growth-Promoting Developmental Hormones. Our work was quite exciting and was getting published in top Journals of the World. A team of famous Immunologists, Elvin Kabat, Barry Bloom and others came along with Howard Goodman, the Chief of Immunology at WHO, Geneva to ask me to take over the Headship of a WHO Research and Training Centre in Immunology for India and South East Asia which they were proposing to set up. I was reluctant. They informed me that India has the World's largest number of lepers. Do we expect Americans to come and solve your Problems? This shocked and ashamed me and I did not hesitate signing the Papers.

Our next task was to learn why people get Leprosy. The majority of us (98%) do not become victims to this disease, the few who fall victims, develop a spectrum of the disease varying from Paucibacillary Tuberculoid type of Leprosy to Multibacillary Lepromatous type. Along with 2 of my students and a Mobile lab, I spent 2 Summer vacations in 'Danish Save the Children Leprosarium' at Aska and Pogiri in Orissa to learn why people become victims to this hideous disease. Our findings are published in the entire Golden Jubilee Issue of "Leprosy in India" and elsewhere. The susceptible lack the ability to react against some key antigens of M. leprae [1]. The patients react normally to cholera, typhoid and other pathogens.

Having found the Nature of Defect in the immune system of those who contract leprosy, the next obvious issue was whether we can do something to protect these individuals from becoming victims to leprosy. Why not make a vaccine that can invigorate their immune response?

We collected 17 non-pathogenic cultivable mycobacteria and tested each for their ability to react with the immune system of multibacillary leprosy patients. Five atypical mycobacteria were short-listed. These underwent further investigations to zero in to a Mycobacteria coded as Mw. After doing Toxicology, Phase I/II/III clinical trials were carried out with Mw vaccine with due permission of Ethical and Drugs Regulatory Authorities. Encouraging results were obtained. Field trials were also carried out in a leprosy endemic District in Kanpur Dehat along with experts from JALMA Agra. The Vaccine based on the Mycobacteria coded as Mw, received approval of the Drugs Controller General of India and passed on to M/s Cadilla Pharma for making it available to Public.

The gene sequence of Mw was determined by a team of Profs Anil and Akhilesh Tyagi and Prof. S. Hasnain. Being hitherto an undescribed mycobacteria, it was deposited in an International Depository. It has been named as *Mycobacterium indicus pranii* (MIP). Pran is my first family name and nii, the National Institute of Immunology from where clinical trials were conducted and of which I was the Founder Director.

Figure 1 gives an Atomic Force Microscopy perspective of this marvellous unique bacteria.

Figure 1: Atomic Force Microscopic imaging of MIP.

Figure 2 shows a handful of patients who received MIP (Mw) in addition to the usual MDT treatment. Inclusion of MIP not only shortened the period of recovery, but most patients on full recovery lost the ugly blemishes of leprosy normally not cleared with drugs alone.

Tuberculosis

Tuberculosis is a major disease of the country. Interestingly *Mycobacterium indicus pranii* (MIP, Mw) reacts with not only M. leprae but also with M. tuberculosis which causes Tuberculosis, a major disease in many parts of the world. A vaccine was developed by Drs Calmette and Guerin at Institut Pasteur Paris about 100 years back based on a Bacillus named after them Bacillus Calmette Guerin (BCG). BCG is employed in India (and elsewhere) for immunizing children. However it has genetic restrictions of response. It is effective somewhere and not effective elsewhere.

Bakulesh Khamar In-Charge of the working of Cadilla Pharma, has carried out clinical trials in Category II, "Difficult to treat" tu-

Figure 2: Some representative cases of LL/BL multibacillary patients treated with MDT plus Mw (*Mycobacterium indicus pranii)* [2].

berculosis patients. Table 1 shows the high efficacy of using it along with the usual MDT. Also the Relapse rate of those treated with MIP is much lower (Figure 3).

Treatment Description	Cured	Cured (%)
MIP + MDT (n = 49)	48/49[a]	97.96
MDT alone (n = 27)	21/27[b]	77.77

Table 1: Outcome of the additive effect of MIP in comparison to MDT alone for therapy of Cat II "Difficult to treat" tuberculosis patients.

Notes: [a]One patient defaulter for 6 doses, sputum negative after intensive phase; [b] Six patients- No effect of therapy.

Abbreviations: MIP, *Mycobacterium indicus pranii*; Mw, Mycobacterium w; MDT, multidrug therapy.

An amazing healing action of MIP on Ano-genital warts

Mycobacterium indicus pranii (MIP) vaccine is promising for treatment of warts though the exact mechanism by which MIP acts

Figure 3: Relapse rate of Category II tuberculosis patients after treatment with MDT alone or MDT+ MIP.

is not known. Prof. Somesh Gupta at the Department of Dermatology, All India Institute of Medical Sciences, New Delhi, has published remarkable action of MIP in curing ugly ano-genital warts [3,4].

Patients of anogenital warts, were given MIP initially intradermally in deltoid area of both sides followed two weeks later by weekly intralesional injections into warts. Complete clearance was seen in 8 out of 9 patients with time for complete clearance ranging from 2 to 12 weeks [3]. Figure 4 and 5 give representative photographs showing clearance of ano-genital warts by MIP.

Figure 4: Effect of MIP on ugly anogenital warts. (a) A patient with giant condylomata. (b) The lesions completely subsided with intralesional immunotherapy with MIP.

Complete clearance in 83% patients of extensive cutaneous warts was seen with MIP vaccine with a mean time of complete

Figure 5: Action of MIP on ugly ano-genital warts (A) Before treatment (B) After treatment with MIP.

clearance of 9.7 weeks (Figure 6) [5]. A study on 30 patients with cutaneous warts at difficult to treat sites were given intralesional Mw vaccine, with complete resolution seen in 93.33% patients [6].

Figure 6: Cure by MIP of warts on feet. (A) Before treatment and (B) After 5 months of treatment with MIP.

A study comparing intradermal Mw vaccine with intradermal purified protein derivative (PPD) of tuberculin antigen in patients of multiple warts showed that MIP vaccine was much more effective than PPD [7]. Immunotherapy with MIP vaccine has proved to be an effective treatment modality for cutaneous warts and has potential as a first line treatment.

MIP is a potent invigorator of immune responses

MIP used as adjuvant in a potential Birth Control Vaccine against hCG enhances substantially antibody titres [8]. Figure 7 gives the titres with and without MIP.

Figure 7: Enhancement of antibody response to hCGβ-LTB vaccine in Balb/c mice by MIP. Mice were immunized intramuscularly with 2μg of the vaccine adsorbed on alum with or without MIP. Primary immunization consisted of 3 injections given at fortnightly intervals followed by a booster on day 60 or 120. The symbols represent the titres in a given mouse. Bars give the geometrical means [8].

Covid, the unexpected epidemic

Covid descended in all parts of the World caused by hitherto unencountered virus. It took an in numerable lives in all parts of the Word including India. Although 2 vaccines against Covid were made by 2 Indian companies M/s Serum Institute of India Pune and M/s Bharat Biotech, Hyderabad, immunization with 2 doses of the vaccine with an interval of one month demanded time for building up immunity. At the All India Institute of Medical Sciences, and related Institutions, a large contingent of 21 Doctors thought of using MIP(Mw) as an invigorator of Immunity as a supplement to their treatment.

In their preliminary paper, they report "In conclusion, the use of an immune-modulator Mycobacterium w in addition to standard care resulted in early clinical improvement compared to standard care alone [9].

Another trial conducted in Mumbai has reported that the use of Mw was observed to be associated with rapid recovery of 116/117 patients from Covid-19, who were discharged from the hospital within 10 days, a decrease in the levels of CRP and IL-6 was ob-

served after administration of Mw. This decrease was associated with improvement in the patients' condition. The use of Mw was seen to be associated with no side effects [10].

Conclusion

TO SUM UP, MIP, *Mycobacterium indicus pranii* (previously coded as Mw) is a wonderful discovery of which I am very proud of. It is of course highly useful for treatment of leprosy, for which it was originally made. It is also effective for the treatment of Tuberculosis without genetic restrictions. It is a potent invigorator of immune responses and is intended to be used as adjuvant in the unique Birth Control vaccine against hCG currently in clinical trial. Astonishingly recent reports of its utility in the current Corona virus infection have also been reported.

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Volume 5 Issue 7 July 2021