BIOLOGICALLY DISTINCT ISOLATES OF MYCOBACTERIUM TUBERCULOSIS IN PATIENTS WITH BACILLARY PULMONARY TUBERCULOSIS IN INDIA*

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Tubercle bacilli isolated from individuals living in south India have been found to vary in several biologically distinct features. Example of the biologically distinct features include: the ability to disseminate haematogenously (virulence); sensitivity to antibiotics; pattern of lysis by major and minor phage types; and restriction endonuclease pattern of their Deoxyribonucleic acid (DNA).1 In addition to the contributions derived from the study of host immune response to the infection, analysis of these biologically distinct features provides a powerful tool to further our understanding of the key events in the pathogenesis of bacillary pulmonary tuberculosis.

The unexpected findings of the BCG Trial in south India (Chingleput Trial) were the stimulus for an ICMR/WHO joint sponsored Scientific Working Group on Vaccination Against Tuberculosis, held in Delhi, in May 1980.2 Various proposals for further research work were put on record, including studies on the south Indian variant of Mycobacterium tuberculosis (M.TB); the role of infections with non-tuberculous (environmental) mycobacteria; and the role of exogenous superinfection.

Mitchison and co-workers3 reported extensive studies on the virulence of isolates from the sputum of patients living in Madras. Naganathan et al4 reported findings of a joint research effort between the National Tuberculosis Institute, Bangalore (NTI) and the Tuberculosis Research Laboratory, University of Wisconsin, Madison, which revealed the presence of a variant of M.tuberculosis in majority of individuals with pulmonary tuberculosis living in Bangalore, called the south Indian variant, this variant has a low capacity to disseminate haematogenously (low virulence) in guinea pigs. In contrast to the findings with isolates from sputum, the proportion of isolates with high virulence obtained from cerebro-spinal fluid (CSF) of tuberculous meningitis patients was significantly greater. A study by Mayurnath et al5 on tubercle bacilli isolated from individuals with bacillary pulmonary tuberculosis, living in the Kashmir valley in north India, indicated that the isolates were of high virulence. Except for these reports, the distribution of the south Indian variant in different regions of India and its epidemiological significance has not been established.


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With respect to infection with environmental mycobacteria, especially organisms in the Mycobacterium avium-intracellulare complex (MAC), Palmer & Long and Edwards et al. observed a substantial protective effect in guinea pigs immunized with MAC. Accordingly, a protective effect of BCG could not be demonstrated in a region having high prevalence of infection with environmental mycobacteria.

The hypothesis of exogenous superinfection appears to provide an acceptable explanation about disparity of the results observed in different BCG trials. But, it is quite difficult to distinguish between a disease in humans originating from a haematogenous implant and disease originating from an aerosol implant.

From a study conducted at NTI, Bangalore, Challu et al. recently reported the recovery of biologically distinct forms of tubercle bacilli from urine and sputum specimen in a number of individuals with smear positive bacillary pulmonary tuberculosis. These findings on small number of paired isolates (urine & sputum) has to be supported upon the completion of more extensive study. Smith and Wiegeshaus postulated that the evolution of cavitary pulmonary tuberculosis requires that bacilli reach the apical-subapical region of the lungs. Because in the pathogenesis of exogenous superinfection, the first infection protects against haematogenous dissemination from any subsequent implant, it is postulated that the bacilli reach the apical-subapical region of the lung directly via the airway following at least one, but perhaps several further episodes of infection. As a result, the sputum specimen could contain biologically distinct forms of tubercle bacilli. Moreover, if the first infection was with a high virulent isolate, followed by one or more superinfections, the urine of such individual could yield an isolate with different biological properties than the isolate from the sputum. Nardell et al. reported evidence of exogenous superinfection among persons living in a shelter for the homeless in Boston. The relative importance of exogenous superinfection in the pathogenesis of tuberculosis has been reported by Ten Dam and Pio.

In south India a number of factors are compatible with an important contribution of exogenous superinfection to the pathogenesis of bacillary pulmonary tuberculosis, including: high risk of infection, high prevalence of disease due to tubercle bacilli of low virulence; high prevalence of infection with environmental mycobacteria. However, further investigations are needed to identify the predominant pathogenetic pathway responsible for the development of tuberculosis under different epidemiological situations which exist in India.

"With latest techniques available at present, the key events in the pathogenesis of tuberculosis could be identified through sharing the expert opinion of various investigators. This knowledge can be utilised for evaluating the potential of new vaccines and also for the development of better immunodiagnostic tests, eventually aimed at efficient and effective control of tuberculosis disease".
REFERENCES

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