BCG VACCINATION

Pages with reference to book, From 150 To 151

Ghazala Moihyuddin Arain (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

BCG vaccine, is the oldest routinely used vaccine which owes its origin to in vitro attenuation by Calmette Guenn, between the years 1906 and 1919, of a strain of Mycrobacterium bovis[1]. It came into widespread use during the 1950's and 1960's with the support and encouragement of the World Health Organisation. Most countries of the world, and the expanded programme in immunization recommend its routine use in childhood immunization[2]. The major exceptions to this rule are the United States and Holland which never encouraged widespread use of BCG vaccines[2]. The strains marketed under the name of BCG are by no means bacteriologically identical[1]. Almost all current BCG vaccines are available as freeze dried preparations of viable bacilli and are administered by intradermal injection. There has been a lot of controversy regarding the protective effect of BCG, which has been based on its variation in efficacy and is related to differences in risk of infection. Trials of BCG vaccine are aimed at seeing the efficacy and protective effect of the vaccine. There have been 10 major trials against tuberculosis and 4 against leprosy; vaccine efficacy is the percent reduction in risk of disease in vaccinated individuals when compared to non-vaccinated controls. There is a lot of variation in the result of these different trials. The poor effectiveness shown by two different but highly reputed vaccines in the trials of Chingleput district in south India has convinced most people that there is no simple global answer to the problem of BCG efficacy[3]. It has been found that a higher proportion of strains of M. tuberculosis from Chingleput area of south India are of low virulence in guinea-pigs than those found elsewhere in the world, and it has been suggested that this might explain the low efficacy imparted by BCG in south India[4,5]. Related to this observation there are several publications suggesting that BCG's protection against tuberculosis is a function of disease due to endogenous reaction versus exogenous reinfection[6,7]. According to this information, BCG's action is to protect against haematogenous spread of infection. If this were so, then protection would be greater against systemic, i.e., miiary disease than against pulmonary disease, a prediction which is consistent with some recent studies[8]. It has also been found that BCG protects better against endogenous infection than against exogenous pulmonary disease. This maybe the explanation for its failure in the south Indian trial population; because the population is exposed more to exogenous reinfection type as has been inferred from the high prevalence of tuberculin sensitivity. Another old controversy over tissue damaging hypersensitivity versus antimicrobial immunity has never been resolved and lies at the heart of the induction of protective immunity by BCG. Over the few years we have built up a strong body of evidence from immunological knowledge[9] of human[10] and experimental animal[11] sources that there are two superfacially similar but quite distinct patterns of cellular response to mycobacteria[12]. These are referred to respectively as the listerian type and the Koch- type of responses. Contact with environmental mycobacteria will induce one or the other types of response and BCG vaccination will enhance it. Thus in those places where the environmental species prime for the listerian type of response (Mycobacterium non chromogenicum, M. vaccae, & M. leprae) subsequent BCG vaccination will afford good protection from both tuberculosis and leprosy. Where the Koch-type of response results from environmental contact BCG will be ineffective. Thus cell mediated immunity to mycobacteria can be of two types, one of which provides much better protective immunity from infection than does the other. Dependent upon the species present in the environment and the frequency with which they are met, either type of response can be induced and this will be boosted by subsequent BCG immunization. These principles provide a reasonably logical solution to the old controversy of

tissue damaging hypersensitivity versus protective immunity and they provide a basis upon which the conflicting results of BCG trials can be interpreted and investigated. On this basis where Koch-type of response results from environmental contact BCG will be ineffective. On the genetic level there are two schools of thought. One says that there is a gene on chromosome 2 in man which regulates the immune response to BCG as has been seen in mice also[13,14]. On the other hand there is no evidence that variation in protection imparted by BCG is related to genetic factors in human population. A study done in southern United States showed that protective efficacy was more for Whites than Blacks but the difference was not statistically significant[15]. A recent study done in Asian infants vaccinated in Britain show that the efficacy is as high as in the Caucasian population[16]. After seeing the various view points it seems more reasonable to accept that several mechanisms may be involved, and that masking by atypical mycobacterial infection; variation in BCG strains, and geographic variation in pathogenesis, all play a role in showing a variation in BCG's efficacy. The puzzle of its varying efficacy will remain an important problem in coming years. This importance is enhanced by recent efforts to develop new vaccines against tuberculosis and leprosy, a task which would be facilitated greatly if we understood why sometimes some BCG's in some population work so well and in other areas so poorly. This question has been in the air long enough but now with introduction of new epidemiological methods sufficient data may be provided to solve the problem.

REFERENCES

1. Frappier, A., Protelance, V. S., Pierre, J. and Painsset, M. 8CC strains; characteristic and relative efficacy, in status of Immunization in tuberculosis in 1971. Chamberlayne EC, ed. Forgartylsit. Cent. Proc. 14. Washington, CHEW, 1972, P. 157.
2. Expanded programme on Immunization. Global Status Report. WHO Weekly EpidemiologyRec., 1987; 62: 241.
3. Tuberculosis prevention, firstreport. lndianJ.Med. Res., 1980;72 (suppl):I.
4. Mitcbison. D.A. The virulence of tubcrcle bacilli from patients with pulmonary tuberculosis in India and other countries. Bill. Int. Union. Tuberc., 1964; 35: 287.
5. Prabhakar, R., Venkatraman, P., Villishayee, R.S. es al. Virulence, for guinea-pigs of tubercle bacilli isolated from the sputum of participants in the 8CC trial, Chingleput District, South India. Tubercle, 1987; 68: 3.
6. ten Dam, H.G. Research on 8CC vaccination. adv. Tuberc. Res., 1984; 21:79.
7. ten Dam, H.G. and Pio,A. Pathogenesis of tuberculosis and effectiveness of 8CC vaccination Tubercle, 1982; 63:225.
8. Smith, P.C. Case control of the efficacy of BCG against tuberculosis. Proc. 26th World Congresa of the International Union against tuberculosis. Singapore 4-7, November, 1986.
9. Rook, GA. and Stanford,J.L. Therelevance to protection of three forms of delayed skin-test response induced by M. Leprae and other mycobacseria in mice. Correlation with the clarical work in guinea pig. Parasite Immunio., 1979; 1: 111.
10. Stanford, J.L., Shield, Mj. and Rooks, G.A. Mycobacterium leprae, other mycobacteria and a possible vaccine. International Congress Series No. 466 Leprosy. Proceedings of the XI International Leprosy Congress, Mexico City, Excerpsa Media, Ameaterdam, 1978.
11. Rook, GA. Three forms of delayed skin-test responses evoked by mycobacteria. Nature, 1978; 27:64.
12. Rook, GA., Bahr, G.M. and Stanford, J.L. The effect of two distinct forms of cell-mediated response to mycobacteria on the proactine efficacy of 8CC. Tubercle, 1980; 62:63.
13. Fine, P.E. Immunogenetics of susceptibility to Leprosy, tuberculosis and leish meniasis. Epidemiological perspective. Int.J. Lepr., 1981; 49:437.

14. Blackwell, J.M. Bacterial infections, in genetics of resistance so bacterial and parasitic infections. Wakelin D., Blackwell J.M. eds. London, Taylor & Francis, 1988.
15. Comsiock, G.W. and Palmer, CE. Long-term results of 8CC vaccination in the southern United States. Am. Rev. Respir. Dis., 1966; 93: 171.
16. Packe, G.E., Innes, J.A. Protective effect of 8CC vaccination in infant Asians; a case control (submitted for publication).