Controversies in BCG Immunization

A. Parthasarathy

Abstract. Despite controversies BCG vaccination has stood the test of time. World Health Organization continues to recommend its use in infant immunization programme in countries with heavy endemicity and where threatening HIV epidemic in an emerging problem >85% efficacy have been established in recent years against hematogenous spread of the disease and ≥50% efficacy even against pulmonary tuberculosis. Host related factors, agent related factors, vaccine related factors and inadequacy of evaluation tests determine the BCG vaccine efficacy. Identification of complete BCG genome in 1998 has opened new vistas in newer BCG vaccine development. Adoption of a '5C' concept viz. Case detection, Chemotherapy short course, Contact elimination, Chemoprophylaxis and lastly control in BCG vaccine will be a desirable national approach in combating adult and childhood TB. **[Indian J Pediatr 2003; (7) : 585-586]** ***E-mail : apartha2000@yahoo.com***

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Ever since its introduction in Infant Immunization, BCG vaccine has attracted more controversies than any other vaccine. A vaccine in general is adjudged on two important parameters: (a) Ability to protect the individual from the particular disease and (b) Control of the disease at the community level and possibly eliminate/eradicate the same.

BCG is now being used routinely in over 100 countries in their National Immunization Programme. The main objectives are to prevent disseminated and other life-threatening manifestations of *M. tuberculosis*. However, BCG does not prevent infection with *M.tuberculosis*. Because of genetic changes in the bacterial strains that have occurred over many years, various BCG Vaccines used throughout the world differ.[1] However, identification of complete BCG genome in 1998, has facilitated further research in development of more effective vaccine alternatives.[2]

From the earlier observation of 0 to 80% efficacy, recent meta analysis have shown greater efficacy of ≥ 80% against meningeal and miliary tuberculosis in children and in one meta analysis ≥50% efficacy was recorded even against pulmonary tuberculosis.[1] In short, endemicity of the disease, heavy bacillary load, constant contact with open TB case, concomitant HIV disease etc. are some of the factors which might affect the efficacy of BCG vaccine. Hence it is important that any attempt to contain and control tuberculosis should aim at "5C" concept viz. Case detection, Chemotherapy short course, Contact elimination, Chemoprophylaxis and Control with BCG vaccine.

In India, BCG vaccine is produced from Danish Strain 1331, based on the Copenhagen technology and standards. However, in the National Immunization Programme BCG vaccine produced from other strains are also supplied sometimes. Ever since the introduction of Universal Immunization Programme in 1985, BCG vaccine, coverage has been uniformly stepped upto >85%. Sentinel centers under UIP have been constantly reporting low/nil incidence of meningeal TB, miliary tuberculosis and disseminated tuberculosis which denote the field efficacy of BCG vaccine in controlling the hematogenous spread of childhoodtuberculosis.

The identification of complete genome sequence of *M. tuberculosis* in 1998 have opened new vistas in developing newer anti-tubercular vaccines. Currently this research is mainly directed towards : [4-9]

1. Purification of synthesis of protein peptide and non-peptide antigens for *M.tuberculosis*
2. Creation of rationally attenuated mutant antigens from *M.Tuberculosis*

Table 1. Determinants of BCG Vaccine Efficacy.[3]

1. Host related factors
a) Delayed vaccination, beyond infancy1
b) Chronic or severe malnutrition
c) Genetic differences?
d) Presence of Helminthic infestations
e) Concomitant anti-tubercular therapy
2. Agent related factors
a) Highly endemic regions-increased chances of repeated exogenous infections
b) High virulence and dose of primary infection
c) High prevalence of non-tubercular mycobacterial infections
d) Unexplained geographical reasons
3. Vaccine related factors
(a) Strains used for vaccine
(b) Dose and viability of vaccine
(c) Methodological inaccuracies
4. Inadequacy of evaluation tests

Reprint requests : Dr. A. Parthasarathy, 166/42, Park Road, Anna Nagar, Western Extention, Chennai-600101.

3. Development of DNA vaccines based on published genome sequence.
4. Development of a suitable vehicle for these potential subset vaccines using living vaccine carrier strain (Solmenella, Varicella virus) or artificial vaccine vectors.
5. Development of recombinant vaccines aimed at mucosal immunity.

The field efficacy of BCG vaccine in averting hematogenous spread of the disease in children has today been well established. Vaccinated individual infants are definitely protected from miliary tuberculosis, TB meningitis, disseminated tuberculosis etc. Hence, BCG vaccine available today has been recommended universally in TB endemic countries for infant immunization by the World Health Organisation especially in the wake of threatening HIV epidemic.

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