9. Seki, M. *et al*., *Plant Cell*, 2001, **13**, 61–72.
10. Rabbani, M. A. *et al*., *Plant Physiol*., 2003, **133**, 1755–1767.
11. Casadaban, M. J. and Cohen, S. N., *J. Mol. Biol*., 1980, **138**, 179–207.
12. Silhavy, T. J. and Beckwith, J. R., *Microbiol. Rev*., 1985, **49**, 398–418.
13. Simons, R. W., Houman, F. and Kleckner, N., *Gene*, 1987, **53**, 85–96.
14. Töpfer, R., Pröls, M., Schell, J. and Steinbiß, H.-H., *Plant Cell Rep*., 1988, **7**, 225–228.
15. Hakkila, K., Maksimow, M., Karp, M. and Virta, M., *Anal. Biochem*., 2002, **301**, 235–242.
16. Vickers, C. E., Xue, G. P. and Gresshoff, P. M., *Plant Cell Rep*., 2003, **22**, 135–140.
17. Hooykaas, P. J. J. and Schilperoort, R. A., *Plant Mol. Biol*., 1992, **19**, 15–38.

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Role of BCG vaccination in tuberculosis control

Tuberculosis (TB) remains a major public health problem globally and its control is a daunting challenge in low-income country settings such as India. Our country contributes 20% of the global burden of new TB cases[1]. TB in children remains a major public health concern, especially as severe forms of the disease often occur, and there are many challenges to accurately diagnosing TB disease in children. BCG vaccination is an important component of the Universal Immunization Programme (UIP) in India and is administered at birth. However, the role of BCG vaccination in the prevention of the acquisition of TB infection amongst children and hence in TB control remains controversial. The protection provided by BCG vaccination against TB disease has been observed to vary between 0 and 80% across the many studies conducted on BCG in different countries[2]. The Tuberculosis Prevention Trial in South India reported that BCG did not offer any protection against adult forms of bacillary pulmonary TB disease[3]. A low protective effect of BCG vaccination (27%; 95% CI: –8 to 50%) against TB was observed recently amongst children vaccinated under the UIP[4]. Studies carried out amongst BCG vaccinated and non-vaccinated children have also shown that BCG vaccination does not affect the estimates of prevalence of infection and annual risk of TB infection (ARTI), thereby confirming that the children irrespective of BCG vaccination can be included into the overall calculation for prevalence of infection and ARTI estimates[5,6]. In view of this knowledge, we present the findings of a study which assessed the prevalence of infection and ARTI amongst BCG-scarred children as well as those with no BCG scar in the Central Indian State of Madhya Pradesh.

A community-based cross-sectional tuberculin survey was conducted amongst children from 11 selected districts of the state to estimate the prevalence of TB infection and ARTI. The children were tested using 1 tuberculin unit (TU) of purified protein derivative (PPD), RT 23, on the mid-volar aspect of the left forearm intra-dermally and the maximum diameter of the reaction sizes was read after 72 h. The number of infected children was obtained using the mirror-image technique by locating the mode at the right-hand side of the frequency distribution of reaction sizes of children. ARTI is defined as the probability of acquiring new tuberculous infection or reinfection over a period of one year, and was estimated using the formula ARTI = $1 - (1 - p)^{1/a}$, where p is the proportion of children infected and a the mean age of the children test-read.

Of the 4967 test-read children, 3150 (63.4%) had no BCG scar. The prevalence of infection and ARTI amongst vaccinated children was estimated to be 7.7% (95% CI: 6.4–9.0%) and 1.4% (1.2–1.7%) respectively (Table 1). The corresponding figures for non-vaccinated children were 6.8% (95% CI: 5.9–7.7%) and 1.3% (1.1–1.4%) respectively. Thus the prevalence of infection and ARTI was found to be similar in both groups of children, i.e. BCG-vaccinated and non-vaccinated, thereby suggesting that BCG appears to have had little, if any, impact on preventing the acquisition of TB infection by these children. Other studies conducted at various places in South India have reported similar findings amongst BCG-vaccinated and non-vaccinated children[5,6]. Our findings from amongst this population of Central India add further support to this observation.

Available information from different studies, however, indicates that in countries where BCG vaccination has been adopted, there was a decline in the incidence of the haematogenous form of TB in children (e.g. miliary and meningeal) and deaths attributable to these forms of TB[7,8]. Conversely, there was an upsurge of such cases in countries where BCG vaccination had been discontinued[9,10]. Recent studies have also demonstrated that BCG vaccination has a non-specific beneficial effect on infant survival and found that a BCG scar is a marker of better survival among children in areas with high child mortality[11,12].

Important contributing factors for the variable efficacy observed for the present BCG vaccine are said to include background immunity induced by non-tuberculous environmental mycobacteria, diversity of BCG strains, and over-

Table 1. Prevalence of infection and ARTI among BCG-vaccinated and non-vaccinated children

BCG scar	No. test/ read	No. infected			ARTI (%)	*P*-value
		Number	Percentage	95% CI		
No	3150	215	6.8	(5.9 –7.7)	1.3 (1.1–1.4)	NS
Yes	1617	124	7.7	(6.4–9.0)	1.4 (1.2–1.7)	
All*	4967	355	7.1	(6.4–7.9)	1.3 (1.2–1.5)	

*****Children with doubtful scar and no information on scar included.

attenuation of presently used strains[13]. The persistence of vaccine-induced sensitivity is also an important factor. A study in South India reported that the response to BCG wanes markedly 2.5 years after vaccination[3]. A quantitative analysis of the change in BCG efficacy in different randomized trials showed that there was no evidence that BCG provides protection more than 10 years after vaccination[14]. In order to reduce the current immense global burden of TB, new vaccines or vaccination strategies, or both, are urgently needed for primary prevention of infection and secondary prevention of the progression of latent infection to active disease. This is particularly urgent in view of the added challenges to RNTCP presented by MDR/XDR-TB and HIV-associated TB. In recent years, there has been a renewed interest in the development of new vaccines against TB[15]. However, there remains an urgent need to accelerate the search for additional vaccine candidates and/or vaccination strategies. Meanwhile, the current BCG vaccination policy needs to be continued in view of its beneficial effect in protecting children against the development of severe disseminated forms of the disease, such as meningeal and miliary TB.

1. Global TB Control. Surveillance, planning, financing. WHO Report, 2008, WHO/HTM/TB/2008.393.
2. Smith, D. W., Ernst, H. and Wiegeshaus, Edwards, M. L., *Mycobacterium Tuberculosis. Interactions with the Immune System* (eds Bendinelli, M. and Friedman, H.), Plenum, USA, 1998.
3. Tuberculosis Prevention Trial, Madras, *Indian J. Med. Res.*, 1980, **72**, 1–74.
4. Chadha, V. K., Suryanarayana, L., Suryanarayan, H. V., Srikantaramu, N. and Kumar, P., *Indian J. Pediatr*., 2004, **71**, 1069–1074.
5. Gopi, P. G., Subramani, R., Nataraj, T. and Narayanan, P. R., *Indian J. Med. Res*., 2006, **124**, 71–76.
6. Chadha, V. K., Banerjee, A., Ibrahim, M., Jaganatha, P. S. and Kumar, P., *J. Commun. Dis*., 2003, **35**, 198–205.
7. Ten Dam, H. G. and Hitze, K. L., *Bull. WHO*, 1980, **58**, 37–41.
8. Fillo, V. W., Castilho de, E. A., Rodrigues, L. C. and Huttley, S. R. A., *Bull WHO*, 1990, **68**, 69–74.
9. Romanus, V., *Bull. Int. Union Tuberc. Lung Dis*., 1988, **63**, 34–38.
10. Kelly, P., Mc Keown, D. and Clancy, L., *Eur. Respir. J*., 1997, **10**, 619–623.
11. Roth, A. *et al*., *Int. J. Epidemiol*., 2005, **34**, 540–547.
12. Garly, M. L. *et al*., *Vaccine*, 2003, **21**, 2782–2790.
13. Hoft, D. F., *Lancet*, 2008, **372**, 164–175.
14. Sterne, J. A. C., Rodrigues, L. C. and Guedes, I. N., *Int. J. Tuberc. Lung Dis*., 1998, **2**, 200–207.
15. Orme, I. M., *Vaccine*, 2005, **23**, 2105–2108.

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Occurrence of bryozoa *Chiplonkarina dimorphopora* (Chiplonkar 1939), in the Kakara Formation from type area Subathu, Himachal Pradesh: its stratigraphic and palaeogeographic significance

Late Cretaceous marine transgression occurred over large areas covering Garhwal–Himachal regions and deposited a unique lithounit that unconformably overlies different older lithounits of the Precambrian–Cambrian times (Table 1). This lithounit was recognized as the Kakara Formation[1] lying at the base of the Subathu Formation (Ypresian–Early Lutetian). Earlier this formation was recognized as a lithostratigraphic subdivision of the new Palaeocene Formation from Gambhar river section, Himachal Pradesh[2] (HP). Kakara Formation was considered as the uppermost lithounit of the Tal Formation[3] in the Lesser Garhwal Himalaya and various nomenclatures were used by earlier workers for this unit (i.e. Nilkanth, Singtali, Shell Limestone, Bansi, Shankerpur Formation, etc.).

The fossil record from the Kakara Formation in the present work from the type area Subathu indicates that the transgressive phase on the southern margin of Tethys took place during Cenomanian–Turonian and continued till Early Lutetian, during which the marine Kakara–Subathu succession was deposited (Figures 1 and 2). After deposition of the marine lithounits the area was uplifted and brackish to freshwater Dagshai–Kasauli succession was deposited. The biotic evidences recorded from the Kakara Formation indicate that tectonic activities in the southern margin of the Tethys facing towards the north, were substantially affected prior to the India–Asia collision, which took place along Indus Tsangpo Suture (ITS) during Late Ypresian (= 50 My).

Lithologically, the Kakara Formation in the Garhwal region is comprised of grey oolitic limestone, which is often shelly in the lower part. However, in the HP and Jammu regions, this formation comprises carbonaceous shale, intercalated by medium (in the Kakara area) to thinly bedded grey limestone in the