Volume 72, Number 1
Printed in the U.S.A.
(ISSN 0148-916X)

COMMENTARY

What Is the Best Way to Use BCG to Protect against Leprosy: When, for Whom, and How Often?[1]

Earlier trials of BCG vaccine in the protection against leprosy addressed the question of whether or not BCG was effective against leprosy. BCG vaccine trials against leprosy in South America, Africa, and Asia have demonstrated that the BCG vaccine protects against leprosy ([4]). However the degree of protection conferred by BCG is variable between different populations as is its efficacy in the prevention of tuberculosis ([2]). Repeated doses of BCG confer additional protection against leprosy, but probably not against tuberculosis ([3, 5]).

The issue now is not whether BCG is effective but rather what is the best way to use BCG to protect against leprosy? Who should be vaccinated, when should they be vaccinated and how often? In this issue of the INTERNATIONAL JOURNAL OF LEPROSY, Sergio Cunha and colleagues describe a trial to compare two different BCG vaccination strategies. The one currently recommended in Brazil which is population neonatal BCG vaccination and vaccination of household contacts of leprosy patients, versus population neonatal BCG vaccination and vaccination of all school children aged 7 to 14 years.

Neonatal BCG vaccination is recommended in Brazil to protect against tuberculosis. The fact that BCG also protects against leprosy is a bonus. Indeed the degree of protection against leprosy may be greater than that conferred against tuberculosis ([5]). It would be difficult to justify the use of BCG at a population level on the basis of protection against leprosy alone because of the very low incidence rates of leprosy. The leprosy community is very supportive ([9]) of the continued use of BCG in leprosy endemic countries, particularly when the costs of the BCG vaccination program are not charged against the limited leprosy budget. The widespread use of BCG vaccine with high population coverage is considered to be a very important factor in the decline in the new case detection rates of leprosy observed in many countries. It is also estimated that the continued use of BCG will be a critical factor affecting the long term trends in incidence rate of leprosy ([6]).

The lack of a consistent protective effect of BCG re-vaccination against tuberculosis makes the policy of routine BCG re-vaccination in the whole population less economically viable. The most recent World Health Organization Expert Committee on Leprosy ([10]) did not recommend routine repeated doses of BCG to prevent leprosy because of poor cost-effectiveness, lack of acceptability to recipients, operational difficulties, and the fact that the vaccine (BCG is a live vaccine) is contra-indicated in patients showing symptoms of HIV infection.

In Brazil, neonatal BCG vaccination and selective BCG re-vaccination of household contacts of leprosy patients is recommended. The trial described by Sergio Cunha in this issue sets out to compare this current BCG strategy with an approach where all school age children are re-vaccinated. Similar research questions are being explored in the use of chemoprophylaxis ([1]); should chemoprophylaxis be give to whole communities or selectively to household contacts ([7]). A meta-analysis of chemoprophylaxis trials suggests that community coverage has greater efficacy but that selective household contact strategies are more cost effective ([8]). Analysis of the numbers needed to vaccination to prevent one case gives a simple esti-

[1] This article was received for publication 30 November 2003. It was accepted for publication 20 January 2004.

Reprint requests to: Professor of Public Health and Head of Department of Public Health, Polwarth Building, Medical School, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, Scotland. E-mail: w.c.s.smith@abdn.ac.uk

mate of the relative cost effectiveness of the different regimens. Household contacts are at higher risk of leprosy than the general population, but only a minority of new cases are from household contacts. Selective high risk approaches are more cost effective than population strategies, but they fail to prevent the majority of new cases. Clearly exposure to *M. leprae* occurs outside the household as well as within households, although the relative importance of household contacts compared with non-household contacts may vary between high and low endemic countries. It is very important that the analysis of this trial in Brazil includes economic appraisal as well as simply measuring vaccine effectiveness. The economic analysis is vital to inform future policy development. It is important to know not just about the effectiveness of the vaccine strategy but also, where resources are scarce, about its cost effectiveness.

This trial described in the journal uses a cluster randomised allocation to intervention groups rather than individual random allocation. This is a robust study design and is appropriate for evaluating public health interventions. The use of clusters as opposed to individuals influences the sample size calculation and this is discussed in the paper. This design also has implications for the analysis and will need to be taken into consideration in the presentation and the interpretation of the results; one important effect is on the size of the confidence intervals.

Tuberculosis is important for leprosy. It is unlikely that this Brazil trial would be taking place for leprosy alone. This is true of many other BCG studies and indeed for many aspects of leprosy research. There was a time when moving from leprosy research to tuberculosis was seen almost as an act of treason, now interchange between leprosy and tuberculosis research is essential. It is important that all future vaccine development for tuberculosis considers the impact on leprosy.

This Brazil trial illustrates the renewed interest in investigating strategies to prevent leprosy and in research that addresses transmission and incidence of leprosy. Other examples of this renewed interest are seen in the focus on chemoprophylaxis and development of new diagnostic tests. Multi-drug therapy (MDT) has had a very dramatic and global impact over the last decade in reducing the prevalence of leprosy. However, there has not been the same impact on new case detection rate. This has provoked renewed research interest in transmission, prevention and early diagnosis. This trial is a good example of the renewed commitment of the research community to explore approaches to the eradication of leprosy.

—W. Cairns S. Smith

Professor of Public Health and
Head of Department of Public Health,
University of Aberdeen, Scotland

REFERENCES

1. Bakker, M., Hatta, M., Kwenang, A., and Oskam, L. Prevention of leprosy by chemoprophylactic treatment of contacts. Int. J. Lepr. Other Mycobact. Dis. **70** (2002) 365–366A.
2. Colditz, G. A., Brewer, T. F., and Berkey, C. S., *et al*. Efficacy of BCG vaccine in the prevention of tuberculosis: Meta-analysis of the published literature. JAMA **271** (1994) 698–702.
3. Convit, J., Smith, P. G., and Zuniga, M. *et al*. BCG vaccination protects against leprosy in Venezuela: a case-control study. Int. J. Lepr. Other Mycobact. Dis. **61** (1993) 185–191.
4. Fine, P. E., and Smith, P. G. Vaccination against leprosy—the view from 1996. Lepr. Rev. **67** (1996) 249–252.
5. Karonga Prevention Trial Group. Randomized controlled trial of single BCG, repeated BCG, or combined BCG and killed *Mycobacterium leprae* vaccine for prevention of leprosy and tuberculosis in Malawi. Lancet **348** (1996) 17–24.
6. Meima, A., Gupte, M. D., van Oortmarssen, G. J., and Habbema, J. D. F. SIMLEP: a simulation model for leprosy transmission and control. Int. J. Lepr. Other Mycobact. Dis. **67** (1999) 215–230.
7. Richardus, J. H. A prospective study on contact transmission and chemo-prophylaxis in leprosy. http://www.eur.nl/fgg/mgz/mgzprojects/prjct1tm54/project045.html
8. Smith, C. M., and Smith, W. C. S. Chemoprophylaxis is effective in the prevention of leprosy in endemic countries: a systematic review and meta-analysis. J. Infect. **41** (2000) 137–42.
9. Velema, J. ILEP-organizations should strive for high BCG coverage in the communities under their care. Int. J. Lepr. Other Mycobact. Dis. **70** (2002) 181–182A.
10. World Health Organization. WHO Expert Committee on Leprosy—seventh report. WHO Tech. Rep. Ser. 874. 2002.