SESSION IV

Chairman: Dr M. W. McNicol, F.R.C.P.G., F.R.C.P.

Future policy for BCG vaccination in Britain

IAN SUTHERLAND

MRC Statistical Research and Services Unit, London

Summary

The reduction in tuberculosis to be expected from mass BCG vaccination in Britain during the next few years has been assessed. It is concluded that mass BCG vaccination in adolescence should very soon be replaced by a selective vaccination policy aimed at groups at particular risk of exposure to tubercle bacilli.

BEFORE we can consider what future BCG vaccination policy should be, we must know both how much tuberculosis there will be to prevent, and how much of it will be preventable by BCG. I shall take the second of these two points first.

It might be thought that there is no question about the efficacy of BCG in preventing tuberculosis. The magic figure of 80% protective efficacy has been upheld through a series of reports on the MRC trial, and has withstood various dastardly attacks from those outside this country whose experience of BCG vaccination has frankly been disappointing. Few people here would doubt the continuation of the same high efficacy of British BCG in British (and immigrant) schoolchildren. And yet I propose to do just that today.

You have probably seen a table like Table 1 before, summarizing the findings of the main trials of BCG vaccination in various countries. They show an enormous range of efficacy for BCG, from nothing at all in one of the Georgia trials to 80% in North American Indians. You are probably also aware of the 'explanation' put forward by Dr

Carroll Palmer for these differences (Palmer & Long, 1966), namely that in populations with much atypical mycobacterial infection, such as the southern United States, and South India, this infection provides a partial natural vaccination, to which BCG can add relatively little. You may remember Dr D'Arcy Hart's (1967) detailed appraisal of this proposition, showing that on available evidence it was inadequate to account for such large differences, and postulating differing potencies of the vaccines used in the various trials, to bridge the remaining gaps.

I first prepared a tabular comparison of these trials myself over 4 years ago and have been looking at it, and lecturing on it, at intervals since. Yet it was only a few weeks ago that an alternative and much simpler explanation for the differences occurred to me (Table 2).

I have here rearranged the trials in order, according to the amount of tuberculosis developing in the unvaccinated group. The percentage efficacy is almost exactly in step with this order—there is only one reversal. So close a concordance, if the two sets of figures are not associated, has a chance of occurring of only one in 360. Even if you legitimately object that the bottom two trials were made in the same population with vaccine from the same source, and so should be regarded as one, the chance of as close a concordance is still one in sixty.

Now this, though intriguing, is not wholly convincing, because there are certainly many other differences between the trials than the amount of tuberculosis experienced by the population; in

TABLE 1. Seven controlled trials of BCG vaccine

Trial	Intake (date)	Vaccine	Observation period (years)	Percentage protection from BCG
N. American Indians	1935-38	Phipps	9-11	80
Chicago infants	1937-38	Tice	12-23	75
Georgia schoolchildren	1947	Tice	20	Nil
Puerto Rican children	1949-51	N.Y. State	5½-7½	31
Georgia, Alabama, population	1950	Tice	14	14
British schoolchildren	1950-52	Danish	15	78
S. Indian rural population	1950-55	Madras	2½-7	60

TABLE 2. Incidence of tuberculosis and efficacy of BCG vaccine

Trial	Tuberculosis in unvaccinated (per 1000 per year)	Percentage protection from BCG
N. American Indians	15.6	80
Chicago infants	2.2	75
British schoolchildren	1.3	78
S. Indian rural population	0.86	60
Puerto Rican children	0.43	31
Georgia, Alabama, population	0.13	14
Georgia schoolchildren	0.11	Nil

particular the factors advanced by Palmer and Hart probably do contribute to the differences in efficacy. Suppose we look within the MRC trial itself, at the findings in different areas. The same (Danish liquid) vaccine was used throughout the trial, and as far as the evidence goes, there are no important regional variations in atypical mycobacterial infections in Britain (Pollock, Sutherland & Hart, 1959) (Fig. 1).

The numbers of participants varied widely in the sixteen different sub-areas, and this is indicated roughly by the size of the points on the graph. (The circles represent larger areas than the blobs.) It has also been taken into account in fitting the line to express the variation in the percentage protection with the incidence of tuberculosis. The association shown by this line is significant at the 1% level.

It therefore appears very probable that the efficacy of a technically adequate BCG vaccine is not an immutable quantity, determined by the characteristics of the particular strain, but is closely dependent on the extent of superinfection of the vaccinated subjects. Perhaps the efficacy of the vaccine wanes rapid-

ly in the absence of boosting from virulent tuberculous infection. If this is indeed so, we can hardly expect BCG to have the same efficacy now as it did in the MRC Trial 20 years ago.

The discovery of this association suggests that we could get some idea of the likely future efficacy of BCG in Britain if we could first estimate what the incidence of tuberculosis will be in unvaccinated subjects. Let us consider the decade 1970-80. Unfortunately there is no good recent information on the risk of infection with tubercle bacilli in this country, derived from representative tuberculin surveys with standardized techniques. I shall therefore use the information obtained by the Tuberculosis Surveillance Research Unit for the Netherlands, but in applying it I shall assume that in terms of the trend of tuberculous infection Britain is lagging no less than 10 years behind the Netherlands. In other words I shall assume that what happened in the Netherlands in 1960-70 is what is going to happen in this country during the next 10 years.

Between 1960 and 1970 the annual incidence of primary tuberculous infection in the Netherlands for those aged 15 and over decreased from about 150/100,000 to about 40, with an average of about 80/100,000 during the period (Styblo, Meijer & Sutherland, 1969, p. 40). About 5% of young adults develop clinical tuberculosis within 10 years following infection (Sutherland, 1966), so that the average annual incidence of clinical tuberculosis in unvaccinated subjects was about 4/100,000, or 0.04/1000. This is the required estimate of the annual incidence of tuberculosis in unvaccinated subjects in Britain during the next decade. In his presidential address to the BTTA last week, Dr Springett (1971) made an independent estimate of this incidence, and arrived at the rather larger figure of 0.10/1000 for the net decade.

These two estimates are both just below the lowest figure in Table 2. If the relationship between efficacy and the amount of tuberculosis is validly summarized by the findings of these seven trials, we may therefore expect virtually no contribution at all to the reduction of tuberculosis from mass BCG vaccination in Britain from now on.

FIG. 1. Protection from BCG vaccine in sixteen areas in England.

Before you all conclude that the national scheme for mass BCG vaccination of schoolchildren should be abandoned forthwith, I would like to remind you of several imponderables in the situation. We do lack recent information on the risk of tuberculous infection in this country and its likely trend, and the MRC is planning a national tuberculin survey, to start in the autumn, which should rectify this situation and provide a much-needed basis for informed policy decisions of this type. If possible too, the relationship between the efficacy of BCG and the extent of super-infection needs to be clarified and quantified much more precisely than at present. As far as I am aware this is a completely new suggestion in relation to BCG, and I find this quite astonishing, considering that the vaccine has now been in use in man for 50 years.

Nevertheless, mass BCG vaccination must have a very limited future indeed as a control policy in this country. BCG will then retain an importance only in relation to groups at special risk of exposure to tubercle bacilli. Contacts in tuberculous households, medical students and nurses will be joined by the populations of overcrowded areas in our large cities, those going to visit or work in countries overseas with substantial tuberculosis problems, and other similar groups.

In conclusion, it is interesting to reflect how right the Americans have been to eschew a general vaccination scheme and how right they were to introduce selective vaccination schemes in high-risk areas in Chicago and New York; but how very wrong they

have been to send their troops to Vietnam without apparently even considering the possibility that BCG would protect them against the very high risk of tuberculous infection they encounter there (Elliott, Spaur & Sokolowski, 1969). It is fortunate, too, that the MRC trial took place just in time to establish the high efficacy of BCG in the tuberculosis situation which applied in this country in the early 1950s, as otherwise the value of mass vaccination in countries with even larger tuberculosis problems might well have been doubted by the World Health Organization.

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