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LETTERS TO THE EDITOR

BCG vaccination of schoolchildren in England and Wales

We read with interest the article by Drs V H Springett and I Sutherland (February 1990;45:83–8) and would like to support from our own experience in Avon their conclusion that when the school BCG scheme is stopped the consequences will not be "epidemiologically disastrous" for young adults.

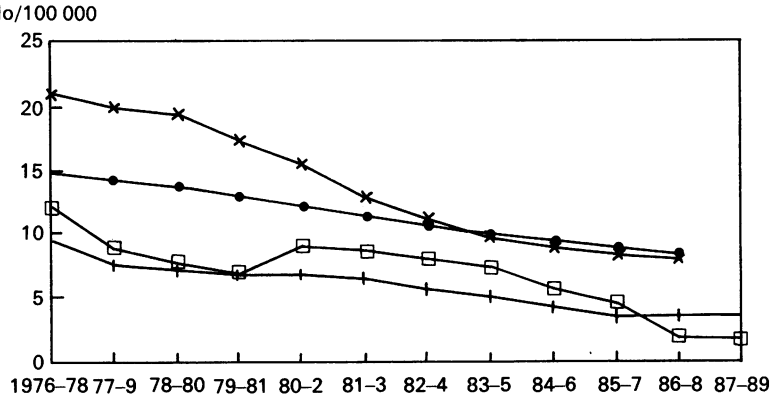
Tuberculosis notification rates in Avon have always been lower than the rates for England and Wales and thus it was one of the first area health authorities to discontinue routine BCG vaccination in children in 1976, except for at risk neonates. Recently we have reviewed all cases of tuberculosis in Avon (except Bath) since 1976 from the notification register and Hospital Activity Analysis. The accompanying graph shows respiratory tuberculosis notification rates for all ages and all (respiratory and other) tuberculosis notifications for the 15–24 year age group in England and Wales and Avon. In view of the wide fluctuation in yearly rates among the 15–24 year age group in Avon due to very small numbers, we have calculated all the rates as a three year rolling average from 1976–8 to 1987–9. As expected, the notification rates among the 15–24 year age group in Avon—that is, the group most affected by the policy change—show a slight increase in 1980–2 and subsequent slowing of the rate of decline. On the whole, however, it would appear that cessation of routine BCG vaccination in 1976 had no significant deleterious effect on the tuberculosis notification rate in Avon.

No routine tuberculin skin tests have been performed in Avon since 1976, so we propose to do a tuberculin sensitivity survey in children aged 12–13 years to determine the current natural conversion rate in Avon.

The results will give a measure of the transmission of the infection in the community and provide us with valuable information at a time when there is considerable debate about the future policy of the schools BCG vaccination programme.

SYED AHMED
W J POULSOM
Frenchay Health Authority, Frenchay Common, Bristol BS16 1ND

1 Office of Population Censuses and Surveys. *Key population and vital statistics*. Series VS: Nos 3–15. London: HMSO, 1976–88.
2 Office of Population Censuses and Surveys. *Statistics of infectious diseases*. Series MB2: Nos 3–15. London: HMSO, 1976–88.



Tuberculosis notification rates/100 000 population: respiratory tuberculosis at all ages and all tuberculosis at 15–24 years from 1976–8 to 1987–9. ●—● All ages, England and Wales; ×—× 15–24 years, England and Wales; +—+ All ages, Avon; □—□ 15–24 years, Avon.

Concentrations of cefixime in bronchial mucosa and sputum

Dr D R Baldwin and colleagues (May 1990; 45:401–2) have presented data on concentrations of the new oral cephem antibiotic cefixime in blood, sputum, and bronchial biopsy material. The concentrations of cefixime were below the assay limit in 13 of the 28 sputum specimens tested, but higher ones were noted in the bronchial biopsy specimens. Because of these findings, the authors believed that cefixime might have a role in the treatment of acute exacerbations of chronic bronchitis.

We have studied 20 patients with an acute exacerbation of chronic bronchitis, 10 receiving 200 mg cefixime twice daily for seven days and 10 a 400 mg dose once daily. Sputum was cultured before, during, and after the treatment; concentrations of cefixime were measured microbiologically in serum and purulent sputum at standard times after the first drug dose. Mean peak serum concentrations of 2·5 mg/l after 200 mg and 6·2 mg/l after 400 mg were found, though one patient had no antibiotic in the blood despite supervised administration. Four patients given 200 mg and two given 400 mg showed no detectable concentrations in the sputum; the mean sputum concentrations in the other patients were 0·08 and 0·23 mg/l. Penetration from blood to sputum averaged just under 4%. The MIC_{90} values for *Streptococcus pneumoniae* rose from 0·25 mg/l (before treatment) to 4 mg/l (after treatment) and those for *Branhamella catarrhalis* from 0·06 to 0·5 mg/l.

Five of the 10 patients given 200 mg doses and four of those receiving 400 mg cefixime were assessed as treatment failures. *S pneumoniae* was responsible in four patients, *B catarrhalis* in three, and *Haemophilus influenzae* combined with *B catarrhalis* in one other. The patient with no cefixime in blood or sputum also represented a treatment failure. No unwanted drug effects were noted.

Our conclusion therefore differs from that of Dr Baldwin and his colleagues. In view of the above findings and our previous unfortunate experiences with cefuroxim axetil[1] and cefaclor[2] we believe that no oral cephalosporin has yet been found which is suitable for patients with acute purulent exacerbations of chronic bronchitis, for the following reasons: (1) poor or irregular absorption, (2) poor penetration into infected sputum, (3) instability in the presence of (*B catarrhalis*) β lactamases, (4) development of relative resistance during treatment, and (5) the high cost in relation to the results achieved.

F P V MAESEN
R COSTONGS
Department of Respiratory Diseases
B I DAVIES
Department of Medical Microbiology

De Wever Ziekenhuis, PO Box 4446, 6401 CX Heerlen, The Netherlands

1 Davies BI, Maesen FPV, Teengs JP. Cefuroxim axetil in acute purulent exacerbations of chronic bronchitis. *Infection* 1987;15:253–6.
2 Maesen FPV, Geraedts WH, Davies BI. Cefaclor in the treatment of chronic bronchitis. *J Antimicrob Chemother* (in press).

AUTHORS' REPLY The results of Dr Maesen and colleagues differ from those of a randomised double blind multicentre study[1] which compared cefixime 400 mg daily with amoxycillin 500 mg twice daily. A clinical cure was found in 13 of 22 patients treated with cefixime (59%) compared with 14 of 24 treated with amoxycillin (58%). All patients in the cefixime group and all but one in the amoxycillin group improved. All the 25 pathogens isolated were eradicated by cefixime whereas 24 of 29 were eradicated by amoxycillin. This study has the advantage of providing a comparison with established treatment.

With regard to the apparent rise in minimum inhibitory concentrations for the pretreatment and post-treatment isolates of *Moraxella* (previously *Branhamella*) *catarrhalis*, Dr Maesen and colleagues have not stated whether their MICs were obtained in parallel from pretreatment and post-treatment isolates or on different occasions. This is important when MIC data are being compared. The MIC_{90} values given are within the expected range for both β lactamase and non-β lactamase producers[2] and the observed differences could therefore be attributable to methodological factors. We would also point out that their use of the term MIC_{90} may be incorrect when so few strains have been included.

A recent paper[2] compared the relative in vitro activity of 39 antibiotics on 74 clinical isolates of *M catarrhalis*, of which 58 were β lactamase producing strains. The MIC_{90} of cefixime was 0·5 mg/l for both β lactamase and non-β lactamase producing strains, indicating that cefixime is relatively stable in the presence of β lactamase. The rise in MIC values for the pneumococci is curious but could be explained if the pretreatment and post-treatment isolates were not the same strains (that is, were not typed serologically). The mechanism of resistance is not clear as alteration in penicillin binding proteins, possibly by transformation, is very unlikely in four patients over such a short time period.

In view of the favourable in vitro activity of cefixime, it may have a role in the treatment of chronic bronchitis, particularly where resistance patterns preclude first line drugs.

D R BALDWIN
J M ANDREWS
J P ASHBY
R WISE
D HONEYBOURNE
Clinical Investigation Unit, Dudley Road Hospital, Birmingham B18 7QH