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Coverage by selective neonatal BCG vaccination should be monitored

EDITOR,—Meirion R Evans raises important points relating to the provision and uptake of neonatal BCG vaccination by babies at increased risk of tuberculosis.[1] This matter has been addressed in Dudley, where we have increased the uptake of neonatal BCG vaccination in identified ethnic minority babies to 93·5% and have introduced a system for monitoring the coverage among ethnic minority groups.

The department of public health medicine reviewed the effectiveness of both neonatal and infant BCG vaccination and the relative benefits of the two methods of vaccination. The findings were used to support the introduction of a programme of neonatal BCG vaccination with the percutaneous multiple puncture method for babies at increased risk of tuberculosis; the programme was based in maternity units.[2]

During the first six months of the programme it proved extremely difficult to monitor the coverage among ethnic minority groups. By using the Office of Population Censuses and Surveys' weekly birth returns to identify the place of birth of both parents and their surnames, however, we estimated that the coverage among ethnic minority babies was 87% (95% confidence interval 82% to 92%). Dudley Health Authority recognised the need to continue to monitor coverage and introduced ethnic monitoring of births in its contracts from April 1995, to coincide with the ethnic monitoring of adults. The authority now has a system that is used to monitor the uptake of and coverage by BCG vaccination in higher risk groups and simultaneously allows us to arrange for further follow up of any baby who misses BCG vaccination. The quality, efficiency, and cost effectiveness of the neonatal BCG programme in Dudley have increased considerably.

We support Evans's call for increased emphasis on selective neonatal BCG vaccination. The Department of Health should urgently consider the introduction of a national system for monitoring coverage by infant BCG vaccination among those babies at higher risk of tuberculosis. In Dudley we have shown a simple method by which this may be achieved.

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Standards for control may not be consistent across United Kingdom

EDITOR,—Meirion R Evans's analysis of the control of tuberculosis in the United Kingdom raises several pertinent issues.[1] The joint tuberculosis committee of the British Thoracic Society (whose members treat nearly 90% of all patients with tuberculosis in the United Kingdom) has produced detailed guidance on chemotherapy and management,[2] the interaction between tuberculosis and HIV infection,[3] prevention and control,[4] and promoting awareness of and education about tuberculosis. The committee agrees that the surveillance system for tuberculosis needs to be changed from limited notification and short, cross sectional, five yearly surveys. An enhanced continuous surveillance system proposed by the Public Health Laboratory Service Communicable Disease Surveillance Centre has the committee's support.

Whatever the position on the unselective BCG programme in schools, for which England and Wales meet some of the international criteria for cessation,[5] the committee shares the concerns about the variable coverage and quality of selective BCG programmes. To stop the unselective programme without comprehensive and effective selective programmes being in place would be dangerous. In addition, without a continuous surveillance system we do not have a sufficiently reliable reporting system to enable the annual incidence of active tuberculosis to be determined by age and risk group; this is a prerequisite for considering stopping unselective BCG vaccination.

The "port of arrival" system for identifying new immigrants performs poorly. It should be replaced by the capture of complete data at ports and their rapid electronic transmission to the consultant in communicable disease in the district of intended residence, so that early health screening can be carried out locally. This too has been strongly urged on the Department of Health.

The concern regarding undernotification of patients with both tuberculosis and HIV infection was addressed by a circular from the Department of Health to all physicians in genitourinary medicine and will form a substantial part of revised guidelines on notification of tuberculosis to be issued soon by the joint tuberculosis committee.

A system for continuous monitoring of drug resistance has been set up by the Public Health Laboratory Service. All the above issues are being assessed by a working party at the Department of Health, of which I am a member. Whatever the working party's recommendations, however, because many purchasing decisions are now taken by local health care consortiums it may be impossible to ensure that adequate resources are devoted to local programmes to control tuberculosis unless local experts ensure that minimum standards for provision[4] are met.

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Treatment should be free for everyone

EDITOR,—Meirion R Evans believes that an action plan for tuberculosis is urgently required in the United Kingdom.[1] We are codirectors of the East London Tuberculosis Service, an organisation that is concerned with making sure that the highest possible standards of care are achieved for patients with tuberculosis. Antibiotic treatment for six months is an essential part of a programme to control tuberculosis. To encourage compliance we need to make it as easy as possible for patients to obtain such treatment. Many of our patients have free prescriptions because of their social circumstances or their age. Refugees and those not eligible for free treatment under the NHS remain a public health risk to the rest of the population. This small group of patients should also receive free treatment if we are to limit the spread of tuberculosis. We believe that free treatment would encourage compliance and is an essential part of the strategy to control the spread of tuberculosis.

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Public health legislation should be changed

EDITOR,—We were interested in Meirion R Evans's article about tuberculosis in the United Kingdom.[1] A problem recently arose in this district concerning the screening of contacts of a patient with multidrug resistant tuberculosis acquired in a nosocomial outbreak in the Chelsea and Westminster Hospital.[2] The contacts identified were sent several invitations to attend the tuberculosis screening clinic, but they failed to attend despite intervention by their general practitioners and the tuberculosis health visitor. As a last resort, the feasibility of applying for an order from a magistrate for compulsory medical examination under section 35 of the Public Health (Control of Disease) Act 1984 was considered. Although this legislation is rarely used, the threat of implementation is occasionally useful.

To obtain an order under section 35 several criteria need to be fulfilled. These include (para 1(a)) that there is reason to believe that a person (*i*) is or has been suffering from a notifiable disease or, (*ii*) though not suffering from such a disease, is carrying an organism that is capable of causing it. Clearly, para 1(a)(ii) may be applied to the contacts of patients with notifiable diseases. Under regulation 4 of the Public Health (Infectious Diseases) Regulations 1988, however, this paragraph is specifically excluded in relation to tuberculosis. Since the aim of contact tracing in tuberculosis is to identify infected people before they become clinically ill, use of section 35 would seem not to be appropriate in this context. Section 20 of the same act, which enables a person to be excluded from work, might be applicable but would not be useful for diagnostic purposes. This would be an expensive option for the local authority, which would be required to compensate for loss of earnings.

The lack of appropriate legislation is of particular concern in view of the recognised association between tuberculosis and HIV infection. People infected with HIV are at greatly increased risk both of reactivation of latent tuberculosis and of acquiring tuberculosis from contact with infected patients. It has been shown in the United States that the proportion of patients with multidrug resistant tuberculosis is relatively high among patients with HIV infection.[3] We hope that the long awaited parliamentary debate after the review of public health legislation[4] will adjust the law to meet this threat to the public health.

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System for screening new immigrants is inadequate

EDITOR,—Meirion R Evans rightly points out the lack of a national policy for control of tuberculosis in the United Kingdom.[1] The impact that this has had on the allocation of resources for control is unknown, but the lack of evidence of the effectiveness of some elements of current control measures does not help.

Evans states that "active measures to detect clinical disease are necessary in tuberculosis contacts, immigrants, and other high risk groups." The epidemiological basis for including immigrants as a high risk group is the relatively high rate of notifications in this group, especially within five years of their arrival in the United Kingdom. There is conflicting evidence, however, on the contribution made by ethnic minority groups to the recent increase in notifications of tuberculosis in the United Kingdom. More importantly, the justification for screening immigrants should be based not on the potential but on the actual detection of previously undiagnosed cases of disease. A published audit of screening of immigrants in Blackburn showed that only 0·1% of those screened were found to have active disease,[2] which is the same as the detection rate resulting from examinations at the port of arrival.[3] In Birmingham no active cases were detected from screening 226 immigrants in one year.[4] There is little evidence that improvements in the system for screening immigrants will have any impact on the control of tuberculosis.

The present system for identifying and following up new immigrants for screening is inadequate, and a critical review of its value as a control measure is long overdue.

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Tuberculosis as a predictor of survival in AIDS

Study had several flaws

EDITOR,—Several problems with Thomas V Perneger and colleagues' paper on whether the onset of tuberculosis in AIDS predicts shorter survival challenge their findings.[1] Firstly, the title is misleading. The study evaluated people diagnosed as having AIDS during a 13 year period, whereas the title implies a 13 year follow up. This potential misinformation should be clarified by the reporting of median follow up in the text. Mean follow up, which the authors report, can be heavily skewed by a few subjects with lengthy follow up.

Studies of the prognosis of disease require that subjects be identified at a uniform point in the course of the disease. Given the history of the AIDS epidemic and the fact that the study began in 1979, this requirement was not met. Most AIDS defining illnesses were not identified or used as criteria until the mid-1980s, so many people with AIDS during the early years of the epidemic would not have been diagnosed as having the disease (and therefore not included in this cohort). A later start point should have been chosen. Additionally, inception cohorts are affected by referral patterns, which are not described for the 52 centres that participated in the study.

Accurate ascertainment of primary cohort subgroups is also imperative in studies of prognosis. The paper notes that some cases of tuberculosis were diagnosed at necropsy. The authors do not state, however, whether all subjects in the cohort who died underwent necropsy. If they did not then underestimation of the rate of tuberculosis is likely.

Studies that use survival analysis should ensure that censoring is random (non-informative). This is partially accomplished by including in the hazards model all covariates that may show an association between the likelihood of follow up and either the predictor or the outcome under study. For example, socioeconomic status is probably associated with the likelihood of contracting tuberculosis, the likelihood of long term follow up being maintained, and the duration of survival. Yet it was not included in the model in the study.

Finally, many potentially confounding variables were not included in the model. These include the site of tuberculosis, presence or absence of infection with *Mycobacterium avium complex* (long term antituberculosis treatment may have prevented the development of this infection), AIDS defining illness, CD4 cell count, and frequency of follow up visits (patients with tuberculosis are likely to have been followed up more closely, which may have improved their care).

The identification of predictors of survival in people with HIV infection or AIDS is important. Future investigators may benefit from following guidelines for such studies.[2]

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Authors' reply

EDITOR,—Anyone who works with patients with AIDS is unlikely to believe that the phrase "over 13 years" in the subtitle of our paper referred to survival rather than to the study's duration. Similarly, only casual readers will have missed our reporting of median survival in both the results section and the abstract.

The Centers for Disease Control's 1987 definition of AIDS was used for all participants in the study. Because participants were identified a posteriori, from the medical records of all HIV positive patients, this definition was also applied to those who developed AIDS before 1987. We know little about referral patterns and agree that the cohort may not be representative of all European patients with AIDS. While this may bias estimates of the incidence of tuberculosis, we fail to see a plausible mechanism by which baseline referral patterns would have affected the observed association between tuberculosis and mortality later during follow up.

Necropsies were performed according to clinical need and local habits, not systematically. Thus we agree that the incidence of tuberculosis might have been underestimated in our study. Again, we are not sure whether this would have affected the association between tuberculosis and mortality, especially as only 5% of cases of tuberculosis were diagnosed at necropsy.

No survival analysis can ensure that censoring was random, for if we knew what happened to patients after censoring we would not have censored them. In our analysis most patients died during follow up; among the 26% who did not, most censoring occurred as a result of termination of the study. We are therefore confident that no major bias occurred. We wish that we had had indicators of socioeconomic status (we did not), but if poor patients with tuberculosis are more likely both to die and to be lost to follow up then the association of tuberculosis with mortality would have been even stronger had we obtained perfect follow up.

The spectre of hidden confounders looms behind every study. But raising the issue is not enough; one should also make a strong case that the putative confounder is a better explanation than that proposed for the observed association. Two of the authors' hypotheses regarding confounders (that *Mycobacterium avium complex* infections are prevented and care improved in patients with tuberculosis) suggest that differences in mortality between patients with AIDS with and without tuberculosis might have been even greater had we taken these variables into account. Nevertheless, as we stated in the paper, because of possible confounding (notably by immunodeficiency) we do not think that our study established a causal relation between tuberculosis and mortality.

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Standardised coding is needed for reports of adverse drug reactions

EDITOR,—Reports of adverse drug reactions make up a considerable proportion of the medical literature. Adverse reactions to recently marketed drugs may not have been detected during premarketing studies, and information about such reactions must be transmitted rapidly to all prescribers. This is usually achieved for serious reactions, but knowledge of milder reactions is often restricted to specialists.

Data on adverse drug reactions published in books and medical journals have to be taken into account when the role of drugs is assessed. It may, however, be difficult to retrieve and compile all the available published information since articles do not use standardised key words. For example, Medline (to which most journals refer for key words) lists only "drug hypersensitivity," "drug tolerance," and "drug interactions," although these represent only a small proportion of observed adverse drug reactions and restrict reported reactions to those due to particular mechanisms.

So that data can be compiled rapidly it is important to create and standardise coding for all adverse events attributed to drugs. Such coding should not be too precise since the knowledge of the mechanism of the reaction is often missing. Three to six key words could be given according to