

Table 2

| Tuberculosis risk (%) in population treated | NNT |
|---|-----|
| 1.0 | 125 |
| 2.5 | 50 |
| 5.0 | 25 |
| 10.0 | 12 |

NNT = number needing treatment to prevent one case.

positive tuberculosis in the UK National Contact Study² was 2.5%, giving an NNT of 50. Interestingly, an NNT of 50 is the figure that Dr Harding arrives at via extrapolation from her quoted US data ("980 out of 1000 receive no benefit").

Similar considerations apply to other high risk groups such as new, young, tuberculin positive immigrants.

Risk-benefit analysis favours chemoprophylaxis because it is a low risk intervention. A decision in the individual is best taken after discussion and agreement between physician and patient or parent on the basis of information available.

With regard to cost effectiveness, this depends on other competing demands for resources. If the competition is within a tuberculosis control programme, chemoprophylaxis comes a long way behind case detection and treatment in terms of cost effectiveness, so that it is inappropriate in a country where resources are severely limited, but in the UK where case detection and treatment are not limited by resources other elements of a control programme, such as chemoprophylaxis and selective BCG vaccination, are appropriate. Prevention of a single case of tuberculous meningitis with permanent neurological deficit in itself represents an enormous cost saving.

Finally, the risks of tuberculosis in unvaccinated children who are tuberculin positive before BCG vaccination in the schools programme are too slight to justify a policy of routine chemoprophylaxis and the guidelines do not recommend it.

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- 1 Seaton A, Seaton D, Leitch AG. In: *Crofton and Douglas's Respiratory Diseases*. 4th edn. Oxford: Blackwell Scientific Publications, 1989:373.
- 2 British Thoracic and Tuberculosis Association. A study of a standardised contact procedure in tuberculosis. *Tubercle* 1978;59:245-59.

Air pollution and COPD

A number of factors in the panel study reported by Higgins and colleagues (February 1995;50:149-55) need to be addressed before any conclusions can be made as a result of this study.

The most important concern is the method of analysis. Whittemore and Korn¹ have shown that the most appropriate method for panel study analysis is individual regression calculation with summary analysis of the individual regression coefficients being used to determine whether or not an effect of an environmental factor has occurred. They found that the greatest predictor of a change in symptoms was whether or not an individual had an attack or was symptomatic on the previous day, and recommended that this needed to be addressed in further studies. They also showed a clear cut effect of season and included in their model temperature and relative humidity.

Higgins and colleagues have not addressed seasonal influences and have only looked at mean temperature rather than mean and minimum or dew point temperatures.

In addition, no allowance has been made for the effects of autocorrelation (the tendency for adjacent observations *within* subjects to be more similar than those *between* subjects), a very important factor in air pollution epidemiology. Failure to allow for this can result in spuriously "positive" results.

There is no measurement of particulate matter either as PM₁₀, TSP, or black smoke. Although the authors acknowledge this in their discussion, it is well recognised that levels of sulphur dioxide and particulates can co-vary, particularly in areas near power stations. Consequently, even if the missing confounding variables are addressed, any association which might remain with sulphur dioxide may in fact be attributable to particulates.

The OPSIS system gives values recorded many metres above street level and will thus report higher levels of ozone than at street level. Without measurements of particles or street level ozone levels, causal attribution to ozone would be unwise.

We have published an effect of sulphur dioxide and British smoke on hospital admissions that showed an association which we were clear to point out was an association without necessarily implying causality.² Subsequent correspondence^{3,4} reinforced this cautious approach.

We have also shown⁵ that maximum hourly sulphur dioxide levels correlate with the following morning's peak flow in patients with severe asthma, but we have had difficulty in deciding how to interpret these data without hourly values of PM₁₀ and consequently this has not been published in full; again a more cautious approach.

The first Birmingham panel study, published in abstract form,^{6,7} shows a very limited effect of ozone on symptoms in adult asthmatic subjects in the summer, but a more significant effect of aerosol strong acid (which Higgins and colleagues did not measure) in the summer although less so in the winter.

The authors also state that nitrogen dioxide has been shown to cause respiratory effects in challenge studies. If the authors read the full literature on nitrogen dioxide challenge they would see that effects are only seen with extremely high levels of exposure, considerably above those normally seen in ambient air.

We would encourage the authors to re-analyse their data using the Wittemore and Korn analysis, accounting for autocorrelation and adequately controlling for confounders to see if there is any residual association. Until then these data are very difficult to interpret and the conclusions drawn by Higgins and colleagues will remain untenable.

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- 1 Whittemore AS, Korn EL. Asthma and air pollution in the Los Angeles area. *Am J Public Health* 1980;70:687-97.
- 2 Walters SM, Griffiths RK, Ayres JG. Temporal association between hospital admissions for asthma in Birmingham and ambient levels of sulphur dioxide and smoke. *Thorax* 1994;49:133-40.

- 3 Ponce de Leon A, Anderson HR. Sulphur dioxide levels and asthma. *Thorax* 1994;49:1042.
- 4 Walters SM, Ayres JG. Sulphur dioxide levels and asthma. *Thorax* 1994;49:1042.
- 5 Rayfield DJ, Appleby RS, Giles B, Ayres JG. Peak flow assessment during an air pollution episode. *Thorax* 1992;46:314.
- 6 Walters SM, Ayres JG, Archer G, Harrison RM. Effects of aerosol strong acid on respiratory function in asthmatic patients: preliminary data from a panel study. *Am J Respir Crit Care Med* 1994;149:A661.
- 7 Archer GT, Harrison RM, Ayres JG, Walters SM. Acid air measurements in East Birmingham. *Thorax* 1994;49:399P.
- 8 Advisory Group on Medical Aspects of Air Pollution Episodes. Oxides of nitrogen. London: HMSO, 1993.

AUTHORS' REPLY Dr Ayres and Professor Harrison raise a number of points concerning our study and, in particular, question our method of analysis. We agree that this type of data presents its own particular analytical difficulties, but do not agree that there is only one way of dealing with this.

Whittemore and Korn describe their method of analysing panel data in a study in which records were kept for over two years.¹ From this prolonged record of symptoms estimates were made in each subject of the association between symptoms and pollution levels. A summary analysis of these individual data was then performed to determine the overall effect in the group. In our study records were kept for only 28 days. We therefore used an analysis which effectively combined the two steps of the Whittemore and Korn procedure using pooled data from all subjects to estimate the mean effect of pollutants in the group. This seems more appropriate for our data as we have a relatively large number of subjects followed for a relatively short period of time, and should give a reasonably robust estimate of the group regression coefficient. It is important to emphasise that differences between subjects are allowed for in this method, which is effectively that recently described by Bland and Altman.²

The relatively short period of observation is also relevant to the question of autocorrelation. The statistical methods for time series analysis are at their best when the number of repeated observations is large and the number of subjects is small. Furthermore, these methods do not overcome the problem of having to make assumptions about the error structure in the data. A series of simulations³ suggests that there is little to choose between the various statistical methods proposed for this experimental design. We have therefore deliberately used the simplest model available. However, we agree that in studies in which more prolonged measurements are made, tests for autocorrelation should be applied.

Regarding the possibility that the relationships demonstrated in our study are the product of confounding by covarying but unmeasured pollutants, we acknowledge this possibility in our paper, particularly with regard to particulates. At the time we performed our study the means to measure the whole range of potentially relevant pollutants was not available and, indeed, other work from that time, including that of Dr Ayres' group,⁴ considered only a limited number of agents. Happily the monitoring of an increased number of pollutants is becoming more widely available and interesting data should emerge.

The validity of measurements from the OPSIS system is also questioned. We had available the traditional measurement methods for sulphur dioxide and these

showed values consistent with the OPSIS measurements. The measurement methods for nitrogen dioxide before OPSIS did not give 24 hour levels and cannot be compared. At the time of the study the OPSIS system was the only one measuring ozone in the area. This criticism raises a more important point which we refer to in our paper but which deserves emphasis. In most epidemiological studies pollution measurements are made from a static monitoring site(s). Whether this is at a roadside or on a roof, it can only give an approximate estimate of the exposure of subjects who may spend time some distance away and who will spend much of their time indoors. Our study, previous Birmingham studies, and most similar work will suffer from this inaccuracy until individual monitors measuring multiple exposures are available.

We agree completely with the correspondents' comments about causality. A study such as ours can only demonstrate associations as stated in our paper, but we do not agree that we have been notably less cautious than the Birmingham group.

We are surprised by the remarks concerning nitrogen dioxide challenge. We mention challenge tests in our introduction but make it clear that, although changes can be identified in such tests, the circumstances in which they are performed are highly artificial. Nowhere do we imply that effects of nitrogen dioxide are seen in the laboratory at ambient levels.

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- Rogan JC, Keselman HJ, Mendoza JL. Analysis of repeated measurements. *Br J Math Stat Psychol* 1979;32:269-86.
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Fatal chickenpox pneumonia in asthma

The interesting case report of Drs Gatnash and Connolly (April 1995;50:422-3) reminds us that chickenpox may be fatal in an immunosuppressed patient. I agree with the authors' recommendations for prevention, but would add one thing. At-risk patients exposed to chickenpox or herpes zoster should seek urgent medical attention for antibody screening and, if antibody negative, should receive passive immunisation with varicella zoster immunoglobulin (VSIG).^{1,2}

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- Department of Health. *Immunization against infectious disease*. London: HMSO, 1992.
- Severe chickenpox associated with systemic corticosteroids. In: *Current problems in pharmacovigilance*. Committee on Safety of Medicines and the Medicines Control Agency, 1994;20:1-2.

BOOK NOTICES

A Colour Atlas of Respiratory Diseases. 2nd edition. D Geraint James and Peter R Studdy. (Pp 366; £71.00). London: Wolfe Publishing, 1993. 0 7234 1695 8.

This is the second edition of a very successful atlas. The first edition, published in 1981, lacked several important recent developments, particularly CT scanning and respiratory aspects of HIV and the immunocompromised patient which are now well covered. There are also new sections on sleep apnoea, MRI, parasitic disease and pulmonary vascular disease. The book appeals to a wide audience, including the more enthusiastic medical student, MRCP candidates, and respiratory nurse specialists. It won't harm senior thoracic physicians either!

The authors modestly refer the reader to other textbooks for details but the captions and brief texts accompanying the figures do, nevertheless, provide quite a lot of information. This is very adequate for the depth of knowledge that the respiratory nurse might want to acquire and a useful review for the MRCP candidate. There are many useful classifications and tables.

There is a major new contribution from Basil Strickland to the radiology in the atlas, particularly with the inclusion of CT images in all the conditions where this is an important investigation. Interpretation of the plain chest radiograph is also dealt with very well. This section is particularly commended to junior doctors who frequently seem to have difficulty in mastering the basic principles involved in distinguishing between major features such as collapse and consolidation - an unhealthy situation both for the patient and success in examinations!

This is a wonderful book to just browse through and represents a unique collection of slides from the authors and some 70 colleagues. It is a very good example of a picture being worth a thousand words and an excellent way to both learn and revise. It is strongly recommended for a wide readership. My only criticism is that the outside cover is not strong enough for the heavy use to which the atlas will be subjected. - MRH

Tuberculosis - A Clinical Handbook. Larry I Lutwick. (Pp 378; £25.00). London: Chapman & Hall, 1994. 0 412 60740 9.

This book, dealing with many aspects of tuberculosis, has a multi-contributor authorship which is entirely from the United States, mainly from New York. There are chapters on the history and epidemiology of tuberculosis, pulmonary and non-pulmonary disease in adults, paediatric aspects, and microbiology. Because of the all American authorship there is a major bias to the USA in management, ethics, and references quoted, which is both a strength and a weakness. The sections on the epidemiology and clinical aspects of multiple drug resistant tuberculosis are up to date, well referenced, and give a

good overview, with potential regimens in both HIV negative and HIV positive patients. Some of these regimens, however, are speculative and not evidentially based.

The section on ethical and legal aspects of tuberculosis control is virtually only applicable to the USA; that on infection control concentrates significantly on chemical agents, personal respiratory protection, and ventilation systems to levels which are not felt necessary on this side of the Atlantic except under exceptional circumstances, and are irrelevant for developing countries. For a UK readership there are significant gaps. Under tuberculin testing the Heaf test is barely mentioned, BCG vaccination and its pros and cons are only briefly covered, and the benefits of BCG vaccination for health care workers in particular are not given a balanced assessment. Non-tuberculous mycobacteria are covered individually in a separate chapter. This section does not explain the general principle that individual drug sensitivities are to be ignored, that clinical combinations often work even though the organisms are resistant in vitro, or that drug sensitivity tests using clinical combinations often show different results.

The book is cheaper than a number of other books on the topic, but does not add much for the UK reader which is not already available in other texts. The sections on multiple drug resistant tuberculosis will be of use in specialised situations and may be usefully consulted on such occasions. - LPO

NOTICES

RCN Tuberculosis Visitors Forum

The RCN Tuberculosis Visitors Forum is holding its annual conference in London on 18 October 1995. Topics include legal aspects of nursing/accountability, compliance with tuberculosis treatment, medications and their interaction with TB drugs, 1993 National Survey of Notification of TB in England and Wales. RCN members £47; Non-members £65. Application forms from Sandra Treadwell. Telephone 0171 409 3333. Fax: 0171 355 1379.

Fibres, particles and the lung: new perspectives

The British Association for Lung Research (BALR) Summer Meeting entitled "Fibres, particles and the lung: new perspectives" will take place at the Edinburgh Conference Centre, Heriott Watt University, Edinburgh on 11-12 September 1995. For further information contact Dr R Cullen, Institute of Occupational Medicine, 8 Roxburgh Place, Edinburgh EH8 9SU. Telephone: 0131 447 8460. Fax: 0131 447 2822.