

Correspondence

Why study the epidemiology of asthma?

Dr Peter Burney (June 1988;43:425-8) was right to insist that epidemiological research is as necessary in the elucidation of the pathogenesis of asthma as study of the underlying mechanisms. More questionable, however, is his confidence that it will pay good dividends, for up to now epidemiology's contribution to our understanding of asthma has been disappointingly small.¹ Improvement will come only when it becomes possible to make valid comparisons between the findings in different populations or in a single population at different times, which will require standardisation of the criteria used to identify asthma in epidemiological surveys. Dr Burney's failure to allude to the problems arising from its heterogeneity and our present inability to define it with precision was a surprising omission.

Much greater integration between epidemiologists and clinicians will be essential, so that the former can observe asthma as it occurs in a clinical context—without which misconceptions about it inevitably arise. An example of such a conceptual misunderstanding is Dr Burney's assertion that asthma "is an acquired disease determined by the environment" and that "there is little evidence for its inheritance." Tacitly dismissing the evidence of twin studies, family studies, and the high prevalence of asthma in certain inbred populations,^{1,2} he supports his contention by the findings of a study by Townley *et al*, which showed that the transmission of *bronchial reactivity to methacholine* within families was inconsistent with single gene Mendelian inheritance; the authors themselves, however, stated that this did not "imply that there is no genetic component" in the transmission of asthma.

Hyperreactivity of the bronchi to challenge by methacholine is not identical to the natural phenomenon, exhibited by every patient with asthma, of bronchial *hyperresponsiveness* to various endogenous and exogenous stimuli that have little or no effect in normal persons. It is unfortunate that the two terms hyperreactivity and hyperresponsiveness have come to be used indiscriminately and as though they were synonymous, as it is now clear that hyperreactivity to artificial provocation by methacholine or histamine is not an invariable feature of asthma (LK Josephs and I Gregg, unpublished data).

It would seem that heredity determines only a predisposition to asthma and that this requires the agency of some environmental factor to transform it into a state of hyperresponsiveness in the bronchi, rendering them susceptible to stimuli that previously had exerted no effect. This would explain the occurrence of discordance for asthma in monozygotic twins, the observation that it may begin at any age, and its increased incidence in migrants. Moreover, the undoubted rise in the incidence and severity of asthma in some populations during the last 20-30 years must have been caused by some environmental factor. Whereas much is known about agents that provoke acute episodes of asthma, almost nothing is known about those associated with its inception, or about whether they can bring this about in people without an inherited predisposition. Exposure to

isocyanates is one of the very few environmental factors that have been recognised to induce asthma in people who have never had it during their previous life, but this could hardly account for a rise in incidence in the general population. A much more probable cause is to be sought in other developments of technology, particularly those that give rise to novel forms of outdoor and indoor atmospheric pollution. Dr Burney, however, is mistaken in believing that low prevalence rates of asthma are found in populations in developing countries who live in poor, rural areas. The highest rates anywhere in the world have been reported in the Western Caroline Islands, where 75% of children have asthma, and in Tristan da Cunha, where 39% of the islanders have had it. Its prevalence in children in the Maldivic Islands (21%) and in the Tokelau Atoll islands (11%) is higher than that reported in Scandinavian and several other European countries.⁴

Might I suggest that one of the principal aims in studying the epidemiology of asthma should be to identify the nature of the environmental agent or agents responsible for its increasing incidence and severity?

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- 1 Gregg I. Epidemiological research in asthma: the need for a broad perspective. *Clin Allergy* 1986;10:17-23.
- 2 Sibbald B. Genetic basis of asthma. *Seminars in respiratory medicine*. 1986;7:307-15.
- 3 Pauwels R, Joos G, Van der Straeten M. Bronchial hyperresponsiveness is not bronchial asthma. *Clin Allergy* 1988;18:317-21.
- 4 Gregg I. Epidemiological aspects. In: Clark TJH, Godfrey S, eds. *Asthma*. 2nd ed. London: Chapman and Hall, 1983:242-84.

AUTHOR'S REPLY Dr Gregg and I agree more than he seems to think even if we do have some residual differences of opinions. Most of the disagreements he finds arise from his misunderstanding of what I wrote.

I stated that asthma was an acquired disease *with one important exception*. The important exception is the largely inherited nature of atopy, which is a risk factor for asthma and airway hyperresponsiveness. The contrary evidence that Dr Gregg quotes is not "tacitly dismissed," but I know of no evidence that this is not explained by differences in atopic state. My comment on Townley's study was that it could not be "taken as definitive" but that "there is no better evidence for the alternative hypothesis." Dr Gregg has not convinced me that he knows of any either.

I am aware of the prevalence rates which he quotes from other underdeveloped areas of the world but these do not address the point that I was making: "The most striking evidence [for the acquired nature of asthma] is the large variation in asthma between similar populations living in different environments. Those in urbanised or Westernised areas have much more asthma than those in poorer areas..." Isolated reports are of interest but suffer all the handicaps of unstandardised measurement referred to by Dr Gregg when comparisons are made with other results.

I entirely agree with Dr Gregg that this lack of standardisation has been a handicap to epidemiological studies. My reason for not discussing it as a special problem was a rather narrow minded attempt to answer the question posed in the title of the editorial. Some progress is now being made in this area by the International Union Against Tuberculosis and

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Lung Disease amongst others. It is, however, counterproductive to suggest that asthma needs to be *defined* with precision in some absolute sense. This is not possible either for epidemiological or for clinical studies, and is not likely to be possible until after the causes of asthma are more fully understood. What can be done is to standardise methods of diagnosis between studies and between researchers. This is an easier task.

On the interpretation of airway hyperreactivity, I have never held the view that this was the same as "asthma." I do, however, believe that it is a useful objective marker for the condition. Much is now being written on the imperfect association between asthma and airway hyperreactivity but caution is advisable in interpreting this, as there was in earlier times when airway hyperreactivity was thought by some to be almost synonymous with the condition. Firstly, there is the problem of defining asthma, which Dr Gregg mentions as a problem in epidemiological studies but not, evidently, in comparing "asthma" and airway hyperreactivity. Secondly, there is the inevitable discrepancy between two measures neither of which is perfectly reproducible. None of the studies that I know of in this area have addressed this problem.

Although I tend to believe, like Dr Gregg, that there has been an increase in the prevalence and severity of asthma, I hardly think that the rise is "undoubted"; and I am not sure that an epidemiological programme would be wise to make its major interest an explanation of this increase, as the data that would be required to support any such explanation have largely disappeared. Differences between contemporary populations are much easier to study.

As to the future, we will probably have to remain in disagreement until time tells whose assessment is more accurate. Dr Gregg's view that past failures must predict further failure seems unduly pessimistic. On the other hand, it may be an inevitable cultural prejudice that an epidemiologist sees more hope in understanding the epidemiological data than in disentangling the apparently limitless complexities that face the pathophysiologicalists. I remain relatively sure, none the less, that the pathophysiology will be easier to understand when the cause of the disease is known.

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- 1 PGJ Burney, JR Britton, S Chinn, *et al.* Descriptive epidemiology of bronchial reactivity in an adult population: results from a community study. *Thorax* 1987;42:38-44.

Reproducibility of walking test results in chronic obstructive airways disease

After we had read the interesting paper by Dr AJ Knox and others (May 1988;43:388-92) we found that some questions were unanswered.

In the study of reproducibility over three consecutive days the authors did not mention the time schedule of the test procedures: only the standardisation criteria for medication before the first walk of each study day were reported. They

found a decrease in mean visual analogue scale scores with day and an increase in walking distance both with day and with walk number. They did not report the visual analogue scale values at rest before each walk; possibly a change in breathlessness at rest could have influenced the results.

Furthermore, the authors studied the reproducibility over four consecutive weeks. We note the considerable difference in walking distance between study groups 1 and 2, despite the same spirometric entry criteria, and the opposite changes between groups 1 and 2 when only the first three walk tests are considered. They did not say whether daily activities during these four weeks were standardised; exercise training by the patient could perhaps have influenced the results. Moreover, the time schedule and use of bronchodilators were not mentioned.

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AUTHORS' REPLY We thank Dr Mostert and colleagues for their interest in our paper. With regard to the time schedule, the first walk on each day was always performed at the same time of day with one hour between each walk. Bronchodilators were not allowed between walks on any day.

With regard to visual analogue scale scores, we did not determine these before walks. It is conceivable that resting breathlessness may also have improved with repeated testing. This would be of interest.

Dr Mostert and colleagues point out that there was a difference in walking distance between our two study groups at the start of our study despite the similar spirometric values. There were also slight differences in spirometric values between the two groups (study 1: FEV₁ 0.7 l, forced vital capacity 1.7 l; study 2 FEV₁ 0.8 l, FVC 2.0 l) and these might account for the difference in walking distance. Nevertheless, it would not be surprising if two groups with similar spirometric values did have different walking distances as both our work and the work of others suggests that spirometry is a poor predictor of exercise performance.

Dr Mostert and colleagues also point out that there was a small decrease in walking distance between walks 2 and 3 in our second study. The trend over the 12 walks was upwards in the study, and the small difference between this pair of walks is most likely to reflect "noise." Our study 1 and the studies by McGavin *et al*, Swinburn *et al*, Butland *et al*, and Mungall and Hainsworth, which we quoted in our paper, have all shown increases over three walks.

With regard to the standardisation of daily activities, subjects were asked merely to continue their normal daily activities. While there is no way of ensuring that patients do not take additional exercise, the same is true in clinical practice when walking tests are used to assess treatment benefit. The message of our study is that improvement in walking distance occurs with repeated testing. While this improvement could be attributed to either a learning or an