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THE CHANGING PREVALENCE OF ASTHMA?

P Burney

Introductory article

Continued increase in the prevalence of asthma and atopy

SH Downs, GB Marks, R Sporik, EG Belosouva, NG Car, JK Peat

*Aims: To describe the change in the prevalence of wheeze, diagnosed asthma, and atopy in Wagga Wagga, NSW, Australia, between 1992 and 1997, and to compare this to the increase in prevalence reported between 1982 and 1992. Methods: A cross sectional study of the prevalence of respiratory symptoms and atopy in schoolchildren aged 8–11 years (n=1016, response rate 71%) in 1997 compared with studies of similar design in 1992 (response rate 83%, n=850) and 1982 (response rate 88%, n=769). Main outcome measures were respiratory symptoms measured by parent completed questionnaire and atopy measured by skin prick tests. Results: Between 1992 and 1997, the prevalence of wheeze increased by 5.1% (95% CI 1.2 to 9.0), asthma diagnosis by 8.1% (95% CI 3.8 to 12.4), and atopy by 6.7% (95% CI 2.2 to 11.2). Similar increases in prevalence had been found between 1982 and 1992. Conclusions: The prevalence of wheeze, asthma diagnosis, and atopy in Wagga Wagga has continued to increase. (**Arch Dis Child** 2001;84:20–3)*

The first person to plan studies to estimate the changing prevalence of asthma was John Morrison Smith. He began his studies in Birmingham in the 1950s and published a summary of his results in 1976.[1] In order to come to a conclusion on whether the burden of disease is changing, at least two well conducted studies of prevalence are required from at least two different periods using the same definitions of disease and the same populations. By the mid 1990s many such studies were available to support his conclusion that diagnosed asthma and symptoms associated with asthma had been increasing.[2] Taken singly, a number of these studies had potentially serious limitations.[3] Some looked at single areas which might have been subject to major population changes over the time of the study, as had Birmingham over the period of John Morrison Smith's studies. The majority of studies—though not Morrison Smith's—relied on only two points of measurement which, taking each study on its own, might be regarded as giving an inherently unreliable measurement of trend. Some studies introduced small changes in methodology that could have introduced an artefactual change in prevalence. However, there were some studies to which none of these limitations applied.[4] The fact that more than 20 studies had a remarkable consistency in reporting an increase of the order of 5% per annum over the period of the observations strongly suggested that there was a true change that needed explanation.

REAL CHANGE OR ARTEFACT OF REPORTING?

The nature and importance of these changes have, however, been more strongly debated. The first issue that has been raised is whether the changes described could simply reflect changes in diagnosis. From the mid 1980s a series of papers reported that "asthma" was underdiagnosed.[5] The argument was a pragmatic one. Children who did not have a diagnosis of asthma, even though they had disabling wheezy illness, were unlikely to be treated with bronchodilators and were more likely to lead a restricted life and miss school. Altering the diagnosis altered treatment patterns and significantly reduced disability. These findings were soon widely incorporated into treatment policies and it was argued that this could have increased the prevalence of diagnosed asthma without any change in the prevalence of the disease. There is little doubt that such changes did occur and that there was some artefactual increase in the prevalence of "asthma". Where studies measured changes of both symptoms and diagnosed asthma, the greater increase was in diagnosed asthma.[4] Nevertheless, on its own, this could not account for the increase in reported symptoms, and these were also increasing, albeit at a slightly lower rate.

P Burney
Department of Public Health Sciences, King's College London, London SE1 3QD, UK;
peter.burney@umds.ac.uk

The second argument is more difficult to test. It is possible that people might have become more inclined to report possibly trivial respiratory symptoms and that this might account for the increase. There is relatively good evidence against the hypothesis that the increase was confined to relatively trivial disease. The increase that has occurred has been at all levels of severity. Lewis *et al*[6] showed increases in all levels of severity when 16 year old subjects in the 1958 and 1970 national British birth cohorts were compared. The same has been shown more recently in a comparison of two local studies undertaken in Leicestershire in 1990 and 1998.[7]

This of itself does not exclude the possibility that reporting of all symptoms is now exaggerated compared with a decade ago, and this possibility is less easy to examine directly. Some studies have sought evidence for changes in the prevalence of airway responsiveness. Although such studies are still uncommon, some have reported increases in airway responsiveness that are commensurate with the increases noted in symptoms.[8 9] These also suffer from all of the general limitations of similar studies of symptoms other than those of reporting bias. They mostly rely on only two sets of measurements each, and standardisation of the measurement of airway responsiveness is difficult over long periods of time. These limitations weaken the force of the evidence. Moreover, one study in adults found both an increase in symptoms and a reduction in airway responsiveness.[10] The same limitations apply to this study as to the others and, in addition, the sampling of the population studied was clearly different on the two occasions. Other studies of military recruits in Israel[11 12] and Belgium[13] have come to the conclusion that changes in airway responsiveness are at least compatible with a true increase in prevalence of disease. However, the measurement of airway responsiveness was carried out on subsamples of recruits selected for their symptoms and the results still leave some room for arguing that they are compatible with no true increase.

The other argument for supposing that this is not simply a change in reporting comes from a rather less direct approach to the problem. Over the same period of time that increases in prevalence have been reported, there has been a large increase in admissions to hospital for asthma.[14] This could also be due to changes in definitions of disease, changes in health care practices, or to changes in the prevalence or severity of disease. Further examination of the changes in admission rates, however, makes some of these explanations more likely than others. Changes over time can be the result of changes in the age structure of the population, changes in the admission rates that occur among all ages at the same time, or changes that occur from one generation (birth cohort) to another. It is possible to some extent to distinguish between these three explanations for the change. The evidence in relation to asthma admissions strongly suggests that the changes have been inter-generational, admission rates being more consistently associated with a group's date of birth than with the year that they are admitted to hospital.[14] This result is not easily compatible either with changes to the criteria for admission or with changes in diagnostic habits, both of which would be more likely to have affected all age groups at the same time. Much more likely would be a change from one generation to another in the prevalence or severity of asthma.

Does an increase in atopy explain the rise in asthma prevalence?

If the prevalence of asthma is increasing, the question arises why this should have happened. One broad question is whether this has been because all atopic disease has increased, or whether this is something that is specific to asthma. Even the answer to this broad question is not entirely clear.

Several of the studies that have reported changes in the prevalence of asthma have also dealt with the other atopic diseases—hay fever and eczema.[8 15] Where such studies have been done it is generally the case that an increase has been reported in all the conditions, not just in asthma. All the reservations that have been made about the studies of asthma can be repeated in the case of the other atopic conditions. There are, however, more studies that have investigated changes in the prevalence of biological markers of sensitisation. Most of these, particularly where they have used the more easily standardised measures of serum IgE to specific allergens, show increases in the prevalence of sensitisation over time.[16–19]

Nevertheless, there is mixed evidence on this issue and it has been hard to assess how far the increase in asthma has been secondary to an increase in atopy. Although in general the relative rate of increase in each has been approximately the same where it has been measured, there are exceptions where the increase in asthma has not been accompanied by a similar increase in atopy.[9] It is also clear from other evidence that atopy is not a sufficient explanation for asthma and that other factors must be important.[20] It is reasonable to infer from this that, whatever these other factors are, they could also have played a part in changing the prevalence of disease.

Some recent studies have contributed to this debate in different ways. One of them, the Introductory article by Downs and colleagues,[21] is a continuation of the work of Peat and colleagues that itself raised questions about the relevance of atopy to the increase in asthma in Australia.[9]

This paper reports on a series of cross sectional studies of asthma prevalence undertaken in primary school children aged 8–11 years in Wagga Wagga, New South Wales in 1982, 1992, and 1997. The prevalence is still shown to be increasing in the latter period, although there is a relative slowing of the increase in severe wheeze (more than three episodes in the previous year) and asthma treatment. The evidence on atopy from these surveys is informative but paradoxical. In the earlier period there had been a substantial increase in the prevalence of reported hay fever, but only a minor increase in the prevalence of positive skin tests. In the latter period there was virtually no change in the prevalence of hay fever but there was a substantial increase in the prevalence of positive skin tests. In this study the increase in cases during the 1990s is more or less equally attributable to an increase in atopic asthmatics (due to the increase in atopy) and an increase in reported asthma (but not wheeze) reported in non-atopic children. This is compatible with a true increase in atopic asthma secondary to the increase in atopy and an artefactual increase in non-atopic asthma due to relabelling of wheezy illness.

These findings are similar to those of Upton *et al*[22] who compared the prevalence of asthma, wheeze, and hay fever in 45–64 year old married couples living in Paisley and Renfrew, Scotland in the mid 1970s with the prevalence in their offspring aged 30–59 in 1996. The authors concluded that there had been an increase in the prevalence of reported hay fever of around 5.4% per annum and an increase in asthma of around 4.9% per annum. Further analysis suggested that the increase in reported asthma was explained by the increase in people reporting hay fever, among whom the relative risk of reporting asthma and wheeze was unchanged, and an increase in the reporting of asthma but

Learning points

- Reports are emerging for the first time in a quarter of a century of a slowing down in the increase in asthma. These, however, are not universal with some reports of increases in the prevalence of asthma during the 1990s
- Changes in the prevalence of asthma have been associated with changes in the prevalence of sensitisation, and these could explain part of the increase
- Some of the changes noted could be explained by changes in the way wheeze in non-atopic subjects is reported
- Increases in body mass, which are associated with asthma but not with atopy, do not explain the increases in asthma prevalence

crucially not of wheeze among people who had never smoked and who did not report hay fever, an observation suggesting a change in reporting. Overall this would suggest that, in Scotland over this period, and excluding the artefactual increase due to reporting bias, the real increase in asthma could be explained in terms of a change in atopic disease as a whole.

In contrast to the Australian and Scottish studies, a study by Kuehni *et al*[7] came to a rather different conclusion. This paper compared the prevalence of wheezy illness in young children under the age of five in two surveys in Leicestershire, UK in 1990 and 1998. In this young age group in central England the prevalence of wheezy illness was still rising during the 1990s. The authors made no direct assessment of atopy, but noted that the increase was approximately equal in groups classed by the number of attacks in the previous year, more marked in those with persistent wheeze, and greater in those reporting colds and exercise as precipitants for attacks than in those reporting attacks induced by common allergens or foods. Their conclusion was that some factor other than a change in the prevalence of atopy must have been implicated in this increase. The robustness of this argument must depend on the ability to distinguish atopic and non-atopic children at this age on these criteria.[23] Nevertheless, the observations provide an important caveat when interpreting the current evidence.

One promising explanation for the change in asthma prevalence that does not involve a change in atopy is the increased body mass that has been shown in several countries. High body mass index has been shown to be associated with an increased risk of asthma[24] and, like asthma, it is more common in small sibships. Most studies now show that body mass is not associated with atopy, but only with asthma, and this has been suggested as an explanation for the increase in asthma in the absence of an increase in atopy.[25] In spite of the plausibility of this argument, an important study suggests that this is an unlikely explanation for the increase in asthma in the UK. The National Study of Health and Growth is a mixed longitudinal study of primary schools in England and Scotland that has collected information on both body mass index and parent reported wheezing and asthma for over 20 years. Analysing these data from 1982 to 1994 when there were substantial increases both in wheezy illness and in body mass, Chinn and Rona[26] have shown that the change in body mass cannot explain the increase in asthma, at least in children.

Is the asthma epidemic coming to an end?

Two of the studies quoted here show a strong continuing growth in the prevalence of asthma during the 1990s.[7 21] Recently, however, some reports have suggested that the almost monotonic increases in asthma prevalence reported over the last quarter of a century are possibly coming to an end. One of the first of these reports came from British general practice where patient consultations for asthma, which had been increasing, levelled off and began to fall in the mid 1990s.[27] The fact that these were consultations led to at least the alternative hypothesis that this represented better control of asthma secondary to the very large increase in the use of inhaled steroids rather than lower prevalence. However, there has been some evidence of changes in prevalence from other sources including some preliminary data by Grize *et al* from Switzerland[28] and an Italian study by Ronchetti *et al*[29] which reported changes in the prevalence of asthma in primary school children (aged 6–14 years) in two schools in Rome during the 1990s. This study is particularly interesting in that it followed up two earlier studies undertaken in 1974 and 1992 which used the same methods and showed a substantial increase in asthma over the period compatible with other contemporary estimates of about 5% per annum. The latest survey showed no further substantial increase during the 1990s. However, it is too early to draw general conclusions from these studies. The studies by Kuehni *et al* and Downs *et al* show strong further growth in the prevalence of wheezy illness in two other areas—one in much younger children[7] but one also in primary school children.[21] It will take several more reports to confirm any general trend.

As with many such studies, the paper by Ronchetti *et al*[29] provides little further positive information that explains either the change over the last quarter of a century or the lack of change since. However, most other possible explanations that have been similarly tested by direct comparison in repeated cross sectional studies have been unable to incriminate any of the major risk factors so far identified. This was true also of the paper by Kuehni *et al*[7] and of other earlier studies.[6] These include changes in birth weight, maternal age, breast feeding, birth order, smoking, maternal smoking (especially in pregnancy), gas cooking, low home occupancy, lack of nursery care, and lack of pets in the home.

Conclusions

Studies over the last year have probably given more weight to the likelihood that the increases in asthma prevalence

recorded over the last quarter of a century have come about because of an increase in the prevalence of sensitisation to common allergens as well as an artefactual increase associated with redefining some non-atopic wheeze as "asthma". This does not put in doubt the importance of other factors in determining the prevalence of asthma, but it points more clearly to the likelihood that the increase in the prevalence of asthma noted in the market economies, where this has been most studied, is due predominantly to this change in the prevalence of sensitisation. It is not possible at this time to extrapolate this conclusion to poorer countries which have been less well studied and where the important drivers could be different. If we are to understand the recent epidemic of asthma, we need to focus more closely on the causes of the increase in sensitisation to common allergens.

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