INDOOR ALLERGENS AND ASTHMA

POST 152
Post Note December 2000

The number of people diagnosed as having asthma has more than doubled in the last 30 years. Similar trends are seen with other allergic disorders such as hay-fever and eczema. This has led to speculation that increased exposure to allergens - particularly those found indoors - might be a factor behind the trends.

This briefing looks at recent trends in asthma, examines the possible factors behind them and discusses the issues that arise.

ASTHMA

What is it?

Symptoms of asthma include wheeze, shortness of breath, cough and tightness of the chest. The vast majority of cases are associated with inflammation in the network of airways that carry air in and out of the lungs. This can cause reversible narrowing of the airways, responsible for the symptoms described above. It can also leave the airways in a hyper-responsive state, where exposure to one of a range of factors may 'trigger' an asthma attack. There is a close link between asthma and **atopy** – where the immune system 'overreacts' to common allergens.

Trends

Data on the number of people with asthma (prevalence) or on how often it occurs (incidence) are available from a number of sources.

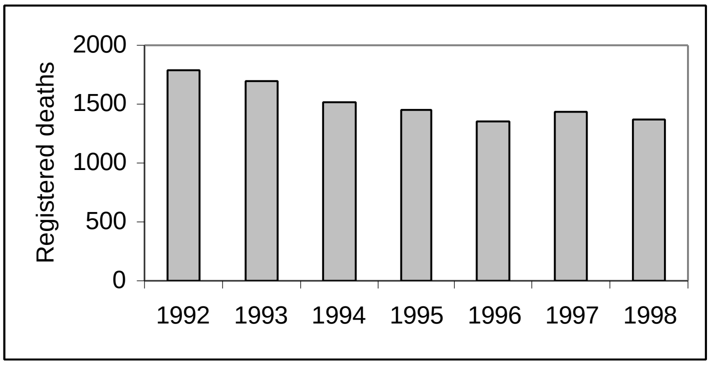
Deaths attributed to asthma rose during the 1980s, but have been in decline since the early 1990s (**Figure 1**), remaining stable since 1995.

Hospital admissions of patients with a primary diagnosis of asthma declined from ~95,000 in 1989/90 to ~70,000 in 1998/99 (in England).

10 yearly GP consultations survey – every 10 years the Royal College of General Practitioners (RCGP) collects detailed information from 92 'spotter' practices in England and Wales on all GP consultations over a period of 12 months. The last such survey found a 139% increase in visits to GPs because of asthma between 1981/82 and 1991/92. Over the same period, the number of people consulting GPs about asthma tripled.

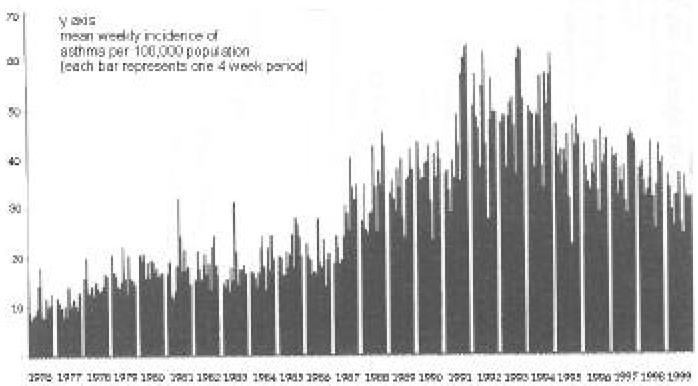
Weekly GP consultations – the same practices report acute disease to the RCGP's Research Unit every week (**Figure 2**). Overall, the trend shows a rise in average weekly incidence up to the mid 1990s, followed by a slow decline thereafter. Seasonal variations show spring and summer peaks (in young age groups) coinciding with peak levels of tree and grass pollens respectively as well as winter peaks (all ages) coinciding with respiratory infections.

FIGURE 1 ASTHMA DEATHS 92-98 (ENGLAND & WALES)



Source: Mortality Statistics England and Wales, Series DH2

FIGURE 2 TRENDS IN MEAN WEEKLY INCIDENCE OF ASTHMA (4 WEEKLY PERIODS), 1976-99



Source: Dr Douglas Fleming, RCGP Birmingham Research Unit

Population studies – questionnaire-based studies repeated some years apart provide data on trends in prevalence of asthma (if the second study uses the same methodology as the first). A recent paper[1] reviewed 12 such studies published between 1983-97 (**Table 1**). All showed an apparent rise in the number of children/young adults reporting 'current asthma'[2] (and wheeze where assessed), although the extent of the observed increases varied considerably (Table 1). More recent research[3] investigated trends in lifetime asthma and hay fever among adults aged 45+. This study found the prevalence of asthma and hay fever rose between 1972/76 and 1996 (from 3% to 8.2% for asthma and 5.8% to 19.9% for hay fever) among UK adults who had never smoked. Among 'ever smokers' asthma rose from 1.6% to 5.3% and hay fever from 5.4% to 15.5%.

Prescriptions – drugs used to treat/prevent asthma (**Box 1**) are also used to manage COPD[4]. Data on the

1 Magnus P & Jaakkola, JJK, 1997. BMJ, **314**, 1795
2 Definitions of current asthma varied from one study to another – typical definitions included recent asthma and asthma within the last 12 months.
3 Upton MN et al, 2000. BMJ, **321**, 88-92.
4 Chronic obstructive pulmonary disease, a persistent breathing dysfunction.

use of such drugs collected by the Prescription Pricing Authority (PPA, see **Figure 3**) show a seasonal trend, peaking in the quarter to December. In the last 5 years, there was a small overall upward trend in total annual prescriptions (Figure 3), although it is not possible to distinguish whether these were for asthma or COPD.

Overall, the various sources of information suggest:

- An increase in the number of people suffering from asthma and in the number of cases between the 1970s and mid-1990s;
- Trends since the mid-1990s are less clear-cut. Drug prescriptions have risen slowly, death rates from asthma have remained constant while the number of visits to GPs for asthma has declined.
- The National Asthma Campaign (NAC) estimates that some 3.4M people in the UK (1 in 25 adults and 1 in 7 children) have asthma, at an annual cost to the UK of ~£2B per year (including costs to the NHS of ~£672M per year).

CAUSES

Underlying mechanisms

Most cases of asthma are caused by inflammation brought about by allergic responses to common allergens (atopy). Several types of cells are thought to be involved (**Box 2**). Atopic people are thought to have T helper cells (Box 2) that are sensitised to common allergens; this may occur in early infancy. When such cells are exposed to an allergen, they orchestrate an all out immune response to the perceived threat. This involves the release of biologically active factors (Box 2) that inflame and narrow the airways.

Allergens and other risk factors

Population studies have identified a wide range of risk factors linked to asthma (**Box 3**). These include predisposing (e.g. atopy), causative (e.g. indoor and outdoor allergens) and other factors (e.g. air pollution). The various factors shown in Box 3 can both initiate asthma and trigger it in those already sensitised. Each person's asthma is different: some individuals may be sensitive to one dominant allergen, others to a range of different allergens.

ISSUES

Factors behind the trends

So which of the factors outlined in Box 3 are most likely to be behind the observed trends in asthma? ***Genetic factors*** can be ruled out, since trends in asthma have occurred over too short a time (20-30 years) to reflect underlying genetic changes.

TABLE 1 STUDIES ON PREVALENCE OF ASTHMA

Location	Study 1		Study 2	
	Year	% asthma	Year	% asthma
Children				
UK	1973	4.2%	1988	9.1%
Pacific Asia	1974	1.3%	1985	5.1%
New Zealand	1975	5%	1989	8%
Finland	1977-79	1%	1991	2.8%
USA	1981	3.2%	1988	4.3%
Australia	1982	5.6%	1992	10.5%
UK	1982	3.3%	1992	8.9%
UK	1985	6%	1988	8.9%
Young Adults				
Sweden	1971	1.9%	1981	2.8%
UK	1972	1.3%	1989	2.8%
Israel	1981-83	1.7%	1987-89	3.3%
Israel	1986	5%	1990	5.9%

Source: Magnus P & Jaakkola, JJK, BMJ, 1997, 314, 1795.

BOX1 ASTHMA MANAGEMENT/TREATMENT

Drugs - there are two main types of asthma medication, both of which are usually delivered via inhalers:

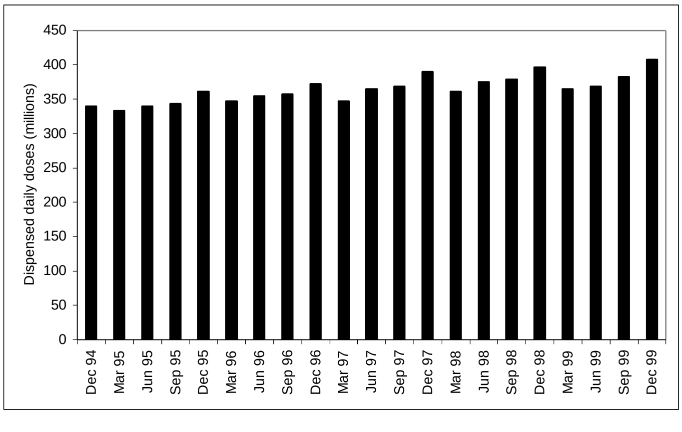
- Relievers – bronchodilators work by relaxing the muscles in the airways, thereby allowing the patient to breathe more easily. They are used to alleviate the symptoms of asthma when they occur, but do not reduce inflammation in the airways.
- Preventers – corticosteroids work over a period of time to calm inflammation in the airways and make them less likely to react to asthma triggers. They are taken on a daily basis.

Asthma management – guidelines for the management of asthma in the UK were first published in 1990, and have been updated in 1993 and again in 1997. The most recent guidelines from the British Thoracic Society (BTS), National Asthma Campaign (NAC) and Royal College of Physicians guidelines cover:

- avoidance of provoking features where possible;
- patient's involvement and education;
- selection of best inhaler device;
- treatment stepped up as necessary to achieve good control;
- treatment stepped down if control of asthma is good.

Five treatment steps are outlined, ranging from occasional use of bronchodilators (Step 1) to high doses of inhaled steroids plus regular bronchodilators plus regular steroid tablets (Step 5). Patients are prescribed a peak flow meter to allow their response to treatment to be monitored.

FIGURE 3 TRENDS IN ASTHMA/COPD DRUGS



Source: PACT Report March 2000, Prescription Pricing Authority

BOX 2 SOME CELL TYPES INVOLVED IN ASTHMA

T helper cells - the 'brains' behind normal immune responses. They orchestrate other cells by releasing chemical messengers (cytokines) and are responsible for memorising 'foreign' intruders (antigens) so that the immune system can mount a prompt response if it encounters them again.
Eosinophils – cells found in the blood that normally form part of the body's defence against parasites. In asthma, eosinophils move into the lung, releasing damaging inflammatory chemicals. This process is controlled by T helper cells.
Mast cells – large cells found in connective tissue that may also be controlled by T helper cells. Enzymes released by mast cells are implicated in over-secretion of mucus (a feature of asthma).
B cells – cells of the immune system found in the blood that manufacture and release antibodies. In asthma and other allergic conditions, exposure to inhaled allergens causes secretion of a certain type of antibody (immunoglobulin E – IgE).

Indoor allergens such as those produced by house dust mites, cats, dogs and cockroaches are often suggested as a factor behind the rise in asthma. This is plausible given recent trends in homes and lifestyles; more people live in centrally heated, well-insulated homes that encourage the growth of dust mites. Research shows that the majority (~80%) of children and young adults with asthma are allergic to one of the common indoor allergens. Other studies show that the higher the level of house dust mite allergen present in dust, the greater the chances of developing an allergy to it.

Air pollution from road traffic has also often been suggested as a factor behind asthma trends[5]. However, the current consensus among experts is that air pollution is not a significant factor in initiating new cases of asthma in healthy people. This is based on lack of evidence of cause (exposure to air pollutants) and effect (initiation of asthma) in laboratory and population studies. Some air pollutants can exacerbate asthma; indeed, DETR[6] runs an Air Pollution Information Service to provide regional information on levels of seven pollutants, as well as forecasts for the next day.

Hygiene hypothesis – this theory suggests that improved levels of hygiene may be a factor behind the trends. It is based on the idea that exposure to infections (viruses or bacteria) in early childhood may protect against developing allergies in later life. Early research focused on air-borne infections, whereas more recent studies[7] suggest food-borne infections may be more important (oral or food-borne infections in children may assist maturation of the immune system). However, further research is needed to verify the hypothesis.

BOX 3 RISK FACTORS LINKED WITH ASTHMA

Predisposing Factors
- Atopy
- Family history of atopy/asthma
- Gender/Age (male:female ratio ~1.5 in children, ~1.0 in adolescents and <1.0 in adults)

Causal Factors
- Indoor allergens (e.g. house dust mites, cats, dogs, birds, cockroaches, fungi)
- Outdoor allergens (e.g. pollens, fungi)
- Occupational sensitizers (e.g. isocyanates in some paints)
- Exercise

Other Contributory Factors
- Respiratory infections (e.g. rhinovirus)
- Maternal factors (e.g. maternal age, allergies, smoking)
- Birth factors (e.g. complications in pregnancy, small birth size)
- Diet (e.g. stopping breast feeding before 4 months, seafoods, shellfish, peanuts)
- Air pollution (e.g. indoor and outdoor air pollution)
- Smoking (e.g. both passive and active)

*Source: Adapted from Global Initiative For Asthma (www.gin asthma.com) and A J Newman Taylor, 1998, BMJ, **316**, 997-99.*

Other factors – a range of other factors has also been suggested to account for the observed trends in asthma. These include changes in the diet, improvements in treatments and the way they are delivered (e.g. the emergence of nurse-led asthma clinics), as well as variations in seasonal factors such as pollen counts and respiratory viral loads in the population at large. However, no single factor fits the observed changes over time exactly. For instance, the apparent decline in asthma since the mid-1990s may be partly due to reductions in the severity of the hay fever season and in respiratory viral loads, although it is not clear whether these were major contributors to the rising trend prior to the mid-1990s. Overall, the trends are likely to reflect the interaction of a complex combination of different factors.

Avoiding indoor allergens

Of the various environmental factors implicated in asthma trends, recent years have seen an increasing focus on the role of indoor allergens. A particular question arises over whether sufficient attention is currently being paid to patient education and allergen avoidance strategies in the prevention and management of asthma.

House dust mite allergens

Research (**Box 4**) has focused on measures to reduce exposure in patients' homes, where mites are found mainly in beds/bedding, carpets and upholstery. Various approaches have been developed including: physical barriers (allergen impermeable bedding covers); chemicals or dehumidifiers (to reduce mite numbers); steam/vacuum cleaners or air filters (to reduce mite/allergen levels in carpets and/or air);

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5 See POST Report Breathing in our Cities, February 1994 for further details.
6 Department of the Environment, Transport and the Regions. The pollutants monitored are sulphur dioxide, nitrogen dioxide, ozone, carbon monoxide, particles (PM_{10}), benzene and 1,3 butadiene.
7 See Matricardi., PM *et al*, 2000. BMJ, **320**, 412-417.

and other devices (beds that minimise exposure to allergens).

- Numerous small-scale clinical trials (Box 4) have attempted to assess the effectiveness of these approaches. Studies conducted to date have been too small and/or poorly designed to unequivocally demonstrate whether any of these approaches can lead to clinical benefits in asthma patients. However, they do provide some pointers as to which are worth evaluating in properly designed large-scale clinical trials. For instance:
- Mites live in different sites in homes, so multiple measures may be needed to reduce exposure.
- Effective integrated approaches may involve mite-impermeable barriers (particularly on beds and bedding), removing mite habitats (e.g. replacing carpets with wood flooring) and minimising dust (e.g. using vacuum cleaners with integral filters and double thickness bags).
- Single measures such as air filtration/use of ionisers (which do not address the main sources of mite allergen exposure) or chemicals that kill mites (but do not necessarily reduce exposure to the allergens) are less likely to be effective.

Pet allergens

Research has also shown that up to 60% of asthmatics are allergic to cat and/or dog allergens. Inhalation of airborne particles is a major route of exposure for pet allergens (levels can rise fivefold when a pet enters a room). Carpets, upholstered furnishing, bedding, etc. can also harbour reservoirs of pet allergens. The single most effective measure for avoidance of pet allergens is removal of the pet from the home, although this is an option that owners may be unwilling to take. Other approaches include keeping the pet out of the main living areas and bedrooms, air filtration, carpet replacement, pet washing and other environmental measures. As with mite allergens, the clinical benefits of such measures are largely unproven.

Allergen avoidance & asthma management

Current asthma management guidelines (Box 1) acknowledge a role for allergen avoidance ("*avoidance of provoking features where possible*"), but place more emphasis on drug treatments. Some see an imbalance here, and have called for guidelines to be amended to place a greater emphasis on educating asthma patients to avoid indoor allergens. The problem is that allergen avoidance approaches have yet to be proven effective in properly designed clinical trials. Many thus see an urgent need for large-scale trials to assess the clinical effectiveness of allergen avoidance. Several such trials are now underway. For instance, the NHS is funding a multi-centre trial over 12 months involving some 2,000 adult asthmatics to assess whether impermeable bedding improves asthma control. Another NHS funded study, involving some 300 infants at high risk of developing atopy, will investigate whether living in a low allergen environment can reduce the risk of infants developing allergies in the first place.

BOX 4 AVOIDANCE OF HOUSE DUST MITE ALLERGENS

There have been two recent reviews of clinical trials of avoidance of house dust mite allergen in patient's homes. The first[1] looked at 31 studies; of these only 9 presented evidence that the measure taken had actually reduced levels of mites/allergen in the home (8 of these involved using impermeable covers on beds/bedding). Six of the 9 showed evidence of clinical benefit (e.g. improvement in lung function or symptoms, reduction in medication) to the patients. In the remaining 3 studies, the treatment was given over too short a time for clinical benefits to be shown. The review concluded that there was an urgent need for large-scale trials.

A second review[2] took the form of a meta-analysis (where a number of smaller studies are re-analysed as a single, larger, study). It looked at 23 studies designed to see whether patients diagnosed with asthma and sensitive to mite allergens benefited from reduced allergen exposure. These measured allergic/asthma symptoms and lung function in patients subject to 'treatments' to reduce exposure to mite allergens compared to 'control' patients. Overall, 41 of 113 treated patients improved compared to 38 of 117 in the control group. The review concluded "*current chemical and physical methods aimed at reducing exposure to allergens from house dust mites seem to be ineffective*". However, some have questioned the method used to assess lung function whereas others have taken issue with the studies selected for (or excluded from) the meta-analysis (only 6 of the 23 studies presented evidence that the measures taken had actually reduced allergen levels). Finally, even though this was a meta-analysis, it involved only 230 patients; considerably more would have been needed to detect small but significant improvements.

Sources 1. Custovic, A et al, Thorax, 1998; 53, 63-72
2. Gotzsche, PC et al, BMJ, 1998; 317, 1105-1110

In conclusion

- There is considerable evidence implicating indoor allergens – particularly house dust mite and pet allergens – as a cause of asthma (although many other factors are also known to cause asthma);
- A wide range of allergen avoidance products are available; in general, the benefits of such products have yet to be proven in clinical trials;
- In the absence of evidence from clinical research, bodies such as the NAC do not endorse specific allergen avoidance products.
- There is a need for clinical trials to assess allergen avoidance/patient education as a way of managing/preventing asthma.