Saturday 17 May 1997



# Learning from asthma deaths

Need to relate deaths to prevalence, severity, and treatment in different populations

See p 1439

There seems little doubt that the prevalence of asthma in children and adolescents is increasing all over the world,1 and several epidemics of deaths in the past 30 years have aroused vigorous debate about the possible causes. Awareness of the importance of decreasing death rates in the 1980s led to the development of asthma management plans or guidelines, first at national level, such as those for Australia<sup>2</sup> and England,<sup>3</sup> then at international level, and now globally.4 The aim of these plans was to achieve better care. One of the signs of this is decreasing death rates, especially in young people, in whom deaths are mostly avoidable (as shown by the falling rates in the presence of increasing prevalence of the disease). Since it is widely stated in the lay press that death rates from asthma are rising worldwide, the paper by Campbell et al in this week's BMJ (p 1439), showing that the mortality from asthma is decreasing in those under 65 years in England and Wales, is timely.5

Caution is needed in interpreting data from death certificates, especially in elderly people,6 as fashions for diagnosing airway diseases change. However, in people under 35 death certificates are thought to more accurately reflect asthma deaths, and records over the past 100 years show periodic swings in mortality in this age group. The recent pattern has been of an increase in mortality between 1975 and 1983 and subsequently a decrease. This has been seen in England and Wales, Australia (where mortality peaked in 1986), Germany, and most dramatically New Zealand (peaking in 1979 with a high of 4.1/100 000 in 5-34 year olds).8 In Japan and the United States mortality is continuing to increase.9 In the United States the absolute rates are much lower than elsewhere, although the reasons for this, and the continuing rise, are not clear.

It is hard to interpret changes in mortality without knowing about changes in prevalence and severity of asthma in the different age groups within the population. However, the fact that the death rates in young people are decreasing as the prevalence of asthma in young people in England is increasing suggests either that the new asthmatic patients have mild disease or that treatment has improved. Overall it seems likely that improvement in long term management has occurred, although direct evidence for this from studies of severity of the disease in the community is lacking.

Campbell *et als* data on seasonality are also of interest.<sup>5</sup> They show that there is an increase in death rates in young people in the summer. It is unlikely that

this is due to viral infections, and in fact viral infections rarely cause death from asthma in young people. It seems more likely that the deaths are due to sudden severe attacks and, as the authors suggest, are the result of exposure to allergen. The authors are correct in drawing attention to this possibility, which is overlooked by many pulmonary physicians. Death from asthma is a rare event, and individual doctors are unlikely to notice that there are more deaths during the summer. Many groups have studied the risk factors for death, but there has not been much interest in seasonality. This is an important risk in addition to the well described risks of psychiatric caseness and noncompliance, 11 12 which are year round phenomena.

Campbell *et al* did not examine sex differences, which may be relevant. Deaths have been increasing in young males in Japan and in young black people in the United States. In Australia deaths in children below the age of 15 years are predominantly among boys, whereas after the age of 15 most deaths occur in young women. The authors also did not comment on the fact that there was a big fall in death rates between 1983 and 1984, not only for asthma but for other respiratory deaths. No explanation is offered for this. It is not clear from the data whether 1983 was a peak year or whether something happened to reduce the number of deaths drastically in 1984.

What can be learnt from studying asthma mortality? It seems that in order to interpret the figures we need to know prevalence, severity, treatment regimens, and allergic status of the population. Furthermore, we need this information from different populations. Already there is some indication that the high death rate among black people in America's inner cities results from difficulties with providing appropriate care rather than from a higher incidence of the disease. A study of the deaths in Saskatchewan showed that a small dose of inhaled corticosteroids protected against death,<sup>13</sup> and the data from Campbell et al support this theory by showing that there has been a proportionate increase in the use of inhaled steroids as the death rates have fallen.5 The debate about the place of inhaled  $\beta$  agonists in treatment could be helped by more data that relate deaths to prevalence, severity, and treatment. Eventually it may be possible to set up registers of severe asthmatic patients (such as those who have ever needed treatment at a hospital) so that more information is available to compare populations. However, most asthma is mild, fluctuates with time, and is hard to define. As a result, most patients and many doctors are unaware that it can be fatal and

that those at risk need to be identified, the severity of their disease documented, and appropriate treatment given until the disease is controlled. It is important therefore to keep examining the trends in mortality, to report them, and to continue to emphasise the fact that this is a fatal disease.

Campbell et al suggest that part of the fall in mortality might be due to the increased use of inhaled corticosteroids.<sup>5</sup> It is not clear what proportion of the drugs prescribed for asthma inhaled corticosteroids should represent because there is a large group of people with mild disease who do not require steroids and most asthmatic patients need more than one drug. Nevertheless, criteria for the use of inhaled corticosteroids are becoming clearer, and the Saskatchewan study showed clearly that those who took more than 400 µg of beclomethasone were protected from death.<sup>13</sup> Thus regular use of low dose inhaled corticosteroids seems to be the factor that is most important and most protective and should be advocated until we understand better how to prevent deaths.

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# Valvular heart disease: putting guidelines into practice

Letting symptoms guide management is no longer acceptable

ike many areas of medical care, the management of valvular heart disease has undergone a revo-Ilution within the practising lifetime of many doctors. As improved interventions have become available, so has the need to investigate correctly and identify better those who could benefit from such interventions. Recommendations for investigating and managing valvular heart disease have recently been published by Britain's Royal College of Physicians.<sup>1</sup>

Much of what we know about the natural course of valvular heart disease comes from an era before surgical intervention, when patients presenting with symptomatic disease were unlikely to survive more than five to 10 years.<sup>2 3</sup> Few investigative tools were available and management decisions were based on the patient's symptoms. It has now become clear that symptoms alone are not an adequate guide, since the lack of symptoms does not predict an uncomplicated course. For example, patients with severe left sided regurgitant lesions can remain relatively asymptomatic while the left ventricle dilates and develops irreversible functional impairment. Left ventricular dysfunction continues to predict a poor outcome in spite of technically successful valve surgery.<sup>4 5</sup> Similarly, patients with severe aortic stenosis may remain completely asymptomatic but are at risk of sudden death.6

In an era of non-invasive two dimensional echocardiography and Doppler examination, it is no longer appropriate to wait for change in symptoms to guide management. The guidelines' recommendations for mitral or aortic valve regurgitation-consider surgery

when end systolic dimension is greater than 5.5 cmemphasise echocardiographic variables. The guidelines repeatedly recommend an echo-Doppler examination as the pivotal tool in decision making: to exclude valvular heart disease in those with innocent systolic murmurs, to secure a diagnosis and judge severity in those with established valvular heart disease, to establish the cause, and (using serial measurements) to determine deterioration.

If echocardiography is fundamental to evaluating valvular heart disease it must be performed to a high diagnostic standard. Those performing echo-Doppler examinations must have appropriate instruments, skills training, quality assurance, and recognition. The onus is on all institutions performing such investigations to provide appropriate diagnostic standards, systematic examinations with accurate recording of cardiac chamber dimensions in a standardised manner,<sup>7</sup> accurate assessment of Doppler gradients, appropriate professional supervision, accurate reporting, and access to echo-Doppler examinations without undue delay. Since these instruments by their very nature are safe and non-invasive they should be widely available in the community-for example, in district hospitals-but this demands reliable diagnostic standards.

Although there may be minor disagreement over details of management and investigation, guidelines must remain broadly stated. If at first presentation or routine reassessment doubt exists over whether further intervention is required it is always appropriate to seek further specialist investigation and evaluation. Transoesophageal echocardiography and invasive cardiac catheterisation are required to assess complex situations such as coexisting valvular and ischaemic heart disease, or suspected dysfunction of prosthetic heart valve. Although echocardiographics examination may be reassuring, further evaluation at a cardiac surgical centre should always be considered in those with valvular heart disease when unexplained syncope or pulmonary oedema occurs, or if significant angina develops. Suspected prosthetic valve endocarditis or the possibility or occurrence of pregnancy in a patient with valvular heart disease should also prompt similar review.

As surgical and catheter based interventions improve, recommendations of this sort may require revision. Clearly, if prosthetic heart valves were highly durable and free of long term complications such as thromboembolism and endocarditis, valve surgery would be considered in patients with even mild valvular lesions. As yet this goal has not been realised, but excellent long term results with newer mechanical valve prostheses and low perioperative mortalities in experienced surgical centres have clearly tipped the balance towards earlier intervention, when symptoms are less severe.<sup>8</sup> Excellent results in appropriately selected patients from surgical mitral repair<sup>9</sup> and balloon valvuloplasty<sup>10</sup> for mitral stenosis have also led to early intervention.

Broadly applicable recommendations for investigation and management, such as those in the summary of the guidelines, <sup>11</sup> should be widely circulated and read by all those concerned with the care of patients with valvular heart disease. A widely agreed systematic approach should allow all those who can potentially benefit from intervention to receive it.

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# Antenatal HIV testing: what now?

Despite guidelines, infections remain undetected

f a pregnant woman has access to antiretroviral treatment she and her unborn child may benefit greatly from her knowledge of her HIV status early in pregnancy. Zidovudine given during pregnancy and to the infant has been shown to reduce the rate of vertical transmission from 25% to 8%.1 Furthermore, since antiretroviral therapy can produce impressive and sustained reductions in viral load, and low levels of circulating virus are associated with reduced vertical transmission<sup>2</sup> as well as slower rates of disease progression,<sup>3</sup> there is a strong case for early diagnosis. While mothers should always retain the right to decline an HIV test, every effort should be made to avoid undetected infection in pregnancy. To this end, the departments of health in the United Kingdom have recommended that obstetric units should offer an HIV test to all pregnant women ("universal testing") in areas of high HIV prevalence<sup>4 5</sup> and have provided guidance on how this should be done. Is this policy being implemented effectively?

MacDonagh and colleagues recently reported on the effectiveness of antenatal HIV testing in 1994 in London, where some centres have the highest prevalences of HIV infection in Britain (up to 5 per 1000).<sup>6</sup> Effectiveness was expressed as the detection rate of HIV infection among women previously undiagnosed. Among 13 units offering the test to all women (median HIV prevalence 2.9 per 1000) and 14 units offering it to selected groups (median HIV prevalence 0.8 per 1000) median detection rates were 3.8% and 0% respectively.<sup>6</sup> The authors investigated the process of implementing testing programmes in these units, reporting that (a) few had written protocols, (b) written material for patients did not contain all the relevant information, (c) counsellors and midwifery staff received little training, (d) practice was inconsistent, and (e) documentation was poor.<sup>7</sup> Since the discovery of zidovudine's impact on vertical transmission in 1994 some improvements in procedure may have occurred, but the worryingly low detection rates probably have not improved greatly.

Implementing antenatal HIV testing in London is particularly difficult. High levels of staff turnover in midwifery result in greater training requirements. Furthermore, staff need the skills to communicate difficult concepts to women whose first, and perhaps only, language is not English. This is especially important since most pregnant women whose infections remain undetected are likely to be from countries in Africa where HIV is endemic.<sup>8</sup>

Internationally the tactics adopted to achieve effective antenatal HIV testing vary. In France since 1993

units undertaking antenatal care have been required by law to offer a test to all pregnant women (F Hamers, personal communication). The US Congress recently passed legislation stating that the standard care of all pregnant women should include counselling and HIV testing; the situation will be reviewed in 1998, when targets may be set for uptake of HIV testing or reduction in the proportion of infants who are HIV antibody positive.9 Sweden's "universal opt out" approach requires women actively to decline an HIV test. In this small, culturally homogeneous, HIV knowledgeable population the uptake rate is 99%.<sup>10</sup>

Elsewhere in Europe, policy across and within countries varies between universal, selective, and "on request" testing.11 These different approaches have not been evaluated, though a randomised trial of different methods of offering an HIV test to pregnant women at low risk of HIV infection is underway in Edinburgh. Outcome measures will include the uptake rate, yield of previously undetected infection, and patient satisfaction.

Antenatal HIV testing programmes are expensive.<sup>12</sup> Limited resources should be channelled into places where prevention is most needed. In parts of London, universal testing should be standard. Imaginative approaches to offering the test-for example, the use of videos and group discussions-should be considered and best practice shared. Programmes should be implemented methodically, costed, and evaluated. Additional resources should be made available as a matter of urgency for programmes which ensure that pregnant women from countries where HIV is endemic receive appropriate, sensitive counselling on antenatal HIV testing. We believe such targeting within the context of a universal approach is pragmatic and discriminates positively to the benefit of mother and child.

In Britain outside London most results from unlinked anonymous testing studies show that HIV prevalence among childbearing women is low, at around 1 per 10 000.8 13 Only in Dundee and Edinburgh, where most infections are associated with injecting drug use, is it higher, at around 1-2 per 1000. Dundee's universal policy achieves HIV test uptake rates of over 90%14 and Edinburgh's selective approach achieves rates of less than 1% (F Johnstone, personal communication). In both cities, however, only the occa-

sional maternal infection goes undetected-because of prenatal diagnosis as well as antenatal testing. Even if every pregnant woman outside London was tested for HIV, the maximum number of vertical transmissions prevented would be very low. Outside London, selective testing, coupled with a test available on request, appears acceptable.

Monitoring HIV prevalence through unlinked anonymous HIV serosurveillance provides a way of evaluating the success of antenatal testing programmes and of rapidly detecting increases in prevalence which indicate the need for more active intervention. Its cost is only a fraction of that of "named" testing. Targeted, evidence based prevention is good public health practice and makes economic sense.

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### Helicobacter gastroduodenitis: a serious infectious disease

Antibiotic treatment may prevent deaths in the decades ahead

infection with *Helicobacter pylori* is the main cause of human gastritis,<sup>1</sup> the major cause of peptic ulcer,<sup>2</sup> and an important risk factor for gastric cancer.3 In 1994 the US National Institutes of Health recommended antibiotic treatment of *H pylori* for patients with gastroduodenal ulcers.<sup>2</sup> This approach has been swiftly adopted<sup>4</sup> and will surely accelerate as newer and more effective regimens are introduced. A more difficult dilemma, however, concerns the management

of the growing number of dyspeptic patients who are diagnosed with confirmed H pylori infection but no

No convincing evidence exists to suggest that eradicating H pylori improves the symptoms of non-ulcer dyspepsia,5 but as testing for the infection becomes part of the routine investigation of dyspeptic patients the question arises whether treatment should be given as an insurance against future, more serious, illness. Indeed, ethical, and perhaps legal, difficulties may confront the doctor who diagnoses a patient as H pylori positive and then fails to do anything about it. Even if serious sequelae are uncommon, is it appropriate to tell these patients that they have an infection which conveys no known benefit to them, that increases their risk of peptic ulcer and cancer, that may be transmitted to their children, but does not require treatment?

Commonly used regimens comprise a one week course of an acid pump inhibitor combined with two antibiotics (amoxycillin, clarithromycin, or a nitroimidazole). The clarithromycin-nitroimidazole regimen achieves eradication in 85-95% of cases<sup>6</sup> at a cost of around £20. Nevertheless, doctors are reluctant to treat *H pylori* in the absence of documented peptic ulcer for several reasons.

The major concern relates to the emergence of resistant organisms. These dangers have probably been exaggerated.<sup>7</sup> Nitroimidazoles (metronidazole) and macrolides (erythromycin) have been widely used for many years. In 1994 over 50 million antibiotic prescriptions were issued in England, amounting to more than one course for every person.8 A second concern is whether infection with H pylori might conceivably benefit the people infected with it.9 A recent study suggested that the eradication of *H pylori* from patients with peptic ulcer might precipitate gastro-oesophageal reflux.<sup>10</sup> More work on this is needed, but an alternative explanation is that reflux symptoms are unmasked when acid suppressive treatment is stopped.

The data required to determine the best management of patients positive for *H pylori* but without ulcers will eventually come from controlled clinical trials. Several trials are in progress or under discussion, though few are large or long enough to use cancer as an end point. Only clinical trials will provide the quantitative evidence of benefit to set against the cost of treatment, the problem of adverse drug reactions, and the microbiological consequences of widespread administration of antibiotics. Until such trials have been reported, one important factor to consider in evaluating the potential benefits of *H pylori* eradication is the risk of death from this infection.

In England and Wales over 7500 deaths occur each year from gastric cancer and over 4000 occur from peptic ulcer.11 Not all can be attributed to infection with H pylori. Nevertheless, three out of four gastric cancers may be attributable to the infection. 12 The contribution of H pylori infection to deaths from peptic ulcer is harder to assess. Although most gastroduodenal ulcers are caused by *H pylori* infection, the other major cause is non-steroidal anti-inflammatory drugs. Results from a recent large, multicentre study in Britain suggest that about 40% of the 10 000 peptic ulcer bleeds that occur in people over 60 are related to drug treatment.<sup>13</sup> In a high proportion, however, helicobacter infection probably also plays a part.<sup>14</sup> A conservative estimate is that 65% of these bleeds are attributable to *H pylori*.

These figures suggest that over 8000 deaths each year are caused by the infection. If we assume that half the population at risk is infected this translates into a cumulative risk of dying from the infection by 85 years of about 1 in 35 for men and 1 in 60 for women, after allowing for competing causes of mortality (1 in 51 for men and 1 in 96 for women from gastric cancer and 1 in 154 for men and 1 in 173 for women from peptic ulcer).

Few common infections in developed countries have a mortality this high, and if the deaths associated with *H pylori* gastroduodenitis occurred immediately rather than after many decades this situation would be medically unacceptable. Of course, whether treatment of the *H pylori* infection would prevent these deaths is unknown—which is why trials are essential. The current problem, however, merits debate: H pylori may be a dangerous pathogen and the infection not trivial.

Some may argue that the serious consequences of infection, especially gastric cancer, are declining in incidence and therefore becoming less important. This is true, but only partly. Age standardised rates of gastric cancer are declining rapidly in many populations, 15 but this effect is counterbalanced, especially in the developing world, by population growth and an increasing proportion of elderly people. The absolute number of patients with gastric cancer is likely to increase globally despite decreasing incidence rates (D Forman, unpublished observations). Furthermore, much of the decline in mortality from gastric cancer is probably attributable to the fall in the prevalence of *H* pylori infection in recent decades. The individual risk to the infected patient will remain unchanged.

In summary, it is timely to consider H pylori gastroduodenitis as a disease in its own right, with ulcer and cancer as its important complications. About 85% of infected individuals will not develop complications, but until a reliable means can be found to identify the 15% who become seriously ill all those with the disease must be considered to be at risk of a potentially fatal outcome.

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# Sexual medicine

#### Towards an integrated discipline

exual dysfunction is common at any age. The most common problems are loss of sexual drive, anorgasmia, vaginismus in women, and erectile failure and premature ejaculation in men. Up to 38% of women report anxiety and inhibition during sexual activity, 16% complain of lack of pleasure, and 15% have difficulties reaching orgasm.¹ Up to 40% of middle aged men report some kind of sexual dysfunction.² The dysfunction may be purely psychological or physical but is usually a mixture of the two.³

Sexual dysfunction is a particular problem for physically ill or handicapped people. Half of middle aged men with insulin dependent diabetes report erectile dysfunction.<sup>4</sup> Between 50% and 90% of patients with multiple sclerosis will develop sexual difficulties.<sup>5</sup> Dyspareunia is twice as prevalent in women with inflammatory bowel disease as in healthy matched controls.<sup>6</sup>

Many patients use self help literature or are managed in general practice or family planning services, but an increasing number are referred to specialties, including urology, gynaecology, psychiatry, and psychology. Specialist psychosexual services have arisen to assess and treat sexual dysfunctions that are considered to have psychological causes.<sup>7</sup> This separation and specialisation sometimes deprives patients of a holistic approach to their difficulties.

Many people believe that their doctor is a suitable professional in whom to confide their sexual difficulties, but few doctors are taught how to manage them. Although several of Britain's royal colleges take the view that sexual medicine is an important part of training, there is little consistency about the quality or duration of training expected, or how such training might be achieved.

The Royal College of Obstetricians and Gynaecologists expects trainees to acquire skills in reproductive medicine and the ability to recognise, counsel, and refer psychosexual problems.9 The Royal College of Psychiatrists expects training schemes to include the opportunity of experience in psychosexual or marital therapy.<sup>10</sup> Although the Royal College of General Practitioners has no set curriculum, sexual health is regarded as an important issue and the college's quality network is about to set up a working party on this topic (Y Carter, personal communication). The Royal College of Physicians is currently revising its curriculum, in which sexual medicine is regarded as relevant to endocrinology, rehabilitation medicine, spinal injury, neurology, genitourinary medicine, and public health (D A Shaw, personal communication). The Royal College of Surgeons has no reference to sexual medicine in its curriculum (A R Mundy, personal communication). There are few specific institutions that provide a general training in sexual medicine for doctors. Most provide training based on approaches that are purely psychosexual (for example, the institutes of psychosexual medicine and psychiatry) or biological (for example, andrology or gynaecology services).

Attitudes to sexuality in society are becoming more relaxed, and people expect their doctor to be able to ask them about sexual problems. Many doctors, however, find it difficult to discuss the sexual details of their patients' lives. The development of sexual medicine is fragmented, and there is a lack of liaison between the royal colleges. Specialist clinics lead to fragmentary care with many referrals between clinics, which means delays for patients and unnecessary cost. The growth of sexual medicine in many medical specialties calls for closer integration. Joint clinics providing a multidisciplinary service are a promising approach for the future. Informal networks of interested specialists who wish to collaborate on clinical work, research, and teaching are arising spontaneously. One example is the Andrology Network at the Royal Free Hampstead NHS Trust.

In an editorial published more than 10 years ago in Canada, Maurice called for the development of sexual medicine as a new medical specialty. We suggest that a more appropriate way forward is closer academic and clinical integration of specialists working in gynaecology, urology, endocrinology, and psychiatry. Interdisciplinary clinics such as this are attractive to purchasers and providers alike, provide unequalled training opportunities, and may be the most cost effective option in our quest to improve the sexual health of the nation.

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