

Cystic fibrosis in Leeds

J M Littlewood, S P Conway, R L Page

There has been exciting progress in the management of cystic fibrosis in the 1980s. Important advances in management include new and effective antipseudomonal antibiotics, pancreatic enzyme microsphere preparations, successful enteral feeding regimens, and heart-lung transplantation. Several potentially valuable therapeutic advances are under trial, including nebulised amiloride and ursodeoxycholic acid for liver disease. We now have an expanding and ageing population, with a median survival of 27 years in the best centres—results which compare favourably with those in North America.¹ Assessment of present practices must examine three areas: paediatric, transitional adolescent and adult care. It is important to know whether resources and knowledge in the United Kingdom are being used to deliver optimal care to patients.

Antenatal diagnosis

Expert genetic counselling and antenatal diagnosis are already available through a network of regional genetic services. The impending availability of population screening, after identification of the remaining gene mutations, raises serious ethical issues. Responsible medical practice demands that before mass screening is instituted an adequate infrastructure of education and counselling be developed in the NHS, although this may be difficult in the present financial climate.

Neonatal screening

The value of neonatal screening remains unproved and is not routinely available in the United Kingdom. Diagnosis more often follows investigation of symptoms, by which time irreparable lung damage and unnecessary parental anguish may have occurred. Unfortunately a large controlled study did not include specialist care in cystic fibrosis centres for the infants detected by screening.² This omission may be an important factor in the failure of this study to show benefit from the neonatal screening programme. Opponents of neonatal screening cite the potential damage that diagnosis in neonates may have on parent-child bonding and dispute claims that symptomless children in whom the disease is diagnosed earlier benefit from early treatment. We have screened all births in the Eastern District of Leeds since 1975, identifying 28 infants with cystic fibrosis, and we have not found that bonding suffered. Prevention of the very early nutritional abnormalities in such infants³ and the advantages of established management make further studies unnecessary.⁴ We would welcome the adoption of routine neonatal screening in the United Kingdom, but financial constraints make this unlikely for the foreseeable future.

Cystic fibrosis centres

The observation that survival was better in Victoria, Australia, than in England and Wales⁵ prompted the formation of the British Paediatric Association Working Party on Cystic Fibrosis in 1982. Before 1980 there were few specialised cystic fibrosis units in the United Kingdom, and these were mostly in London. Most patients attended their local district general hospital. In 1985 the working party report dealt with survival and patterns of current and proposed care for people with cystic fibrosis in the United Kingdom and recommended the establishment of one or more cystic fibrosis centres in each health region.⁶ This recommendation has been supported by the British Thoracic Society and the Royal College of Physicians.⁷ The Association of Cystic Fibrosis Adults requested that specialist centre care be available for all adults with the disease in the United Kingdom.⁸ It is surprising that the concept of a concentration of skills offering optimal up to date treatment to the patient is not generally accepted in this country and that debate continues between individual paediatricians and physicians. Provision of patient care in a cystic fibrosis centre, either total or shared with the staff at the district general hospital, is crucial to the provision of optimal care.

The diagnosis should be confirmed in all patients to avoid the comparatively common mistakes that continue to arise from poor laboratory sweat testing techniques.⁹ The recent identification of the cystic fibrosis gene and recognition of the remaining mutations may permit centralised laboratory confirmation of the diagnosis in all patients within the foreseeable future.

Available evidence shows improved survival of patients attending specialist centres; physicians should also strive to reduce morbidity and improve the quality of life of their patients. This is most likely to be achieved by a consultant led team of doctors, nurses, physiotherapists, dietitians, social workers, and laboratory staff each with the time, interest, and skill to attend to minute details of treatment. Only by working with such a team is the indispensable nature of its component parts in achieving optimal patient health appreciated. Above all else, patients with cystic fibrosis require time. They cannot be adequately reviewed in a busy routine general outpatient clinic.

Up to 50% of people with cystic fibrosis in the United Kingdom have no contact with a specialised unit.⁶ Existing patterns of care include receiving all supervision at a large unit or at the local district general hospital; receiving care at the district general hospital with occasional visits to the cystic fibrosis unit, the cystic fibrosis physician doing clinics at the district general hospital; or attending the cystic fibrosis unit only when a difficult problem arises. The latter is the most unsatisfactory as earlier intervention may often have prevented insoluble complications.

The inability of the staff at the district general hospital to remain completely up to date with

Leeds Regional Cystic Fibrosis Unit, St James University Hospital, Leeds LS9 7TF
J M Littlewood
Seacroft Hospital, Leeds
S P Conway

Correspondence to:
Dr Littlewood

developments in management is understandable but can largely be offset by an annual comprehensive assessment by the staff at a specialist unit (particularly doctors, physiotherapists, and dietitians with access to a specialised laboratory). The local team can then be advised on the fine details of care for that particular patient. The details of care differ between specialised units and many general clinics in local hospitals. Advice on the timing and intensity of treatment is the main contribution of the specialised unit. Infrequent input into management from a specialist centre may cause patient care to remain suboptimal. Results and conclusions of important national and international meetings are overlooked by many paediatricians and physicians who, although responsible for the care of a few patients with cystic fibrosis, never attend such meetings.

We have shown improvement in many areas with advice given after patient referral to a specialist centre.¹⁰ In particular, physiotherapy supervision and technique, nutritional management, clinical and laboratory monitoring, and antibiotic regimens have improved. For example, 75% of patients referred had received no specialised dietetic advice and consequently had a poor energy intake. Most had never had a faecal fat estimation, and poorly controlled intestinal absorption went unrecognised and untreated. Inadequate fat soluble vitamin supplementation resulted in low plasma concentrations. Patients cared for in district general hospitals are often seen by junior doctors who know less about cystic fibrosis than the patient or his or her parents. In a specialist centre the patient is usually seen by a doctor with specialist skills even when staff are absent through being on holiday, study leave, or ill.

The increasing involvement of the Cystic Fibrosis Research Trust in patient services, by funding staff in addition to its role in funding specific research projects, has improved management in the United Kingdom. We would support the categorisation of centres in the United Kingdom into three basic levels of care in addition to research centres and teaching resource centres as in the American model (Cystic Fibrosis Foundation, Rockville, Maryland).

In order to secure funding, such centres would need to maintain specified staff levels, laboratory facilities, and teaching and research programmes. Such a system would ensure the highest standard of care for patients with cystic fibrosis. Similarly, we believe that consultants appointed to positions involving a substantial amount of care of patients with cystic fibrosis should have had sufficient training so as to qualify for accreditation as physicians or paediatricians with a special interest in cystic fibrosis.

Adolescent and adult care

The necessity to plan for the increasing population of adults with cystic fibrosis is recognised by the British Thoracic Society in its recommendation of centre care by a professional caring team. Within the present decade adults

will outnumber children, the former increasing by 100 to 200 cases per year. Greater longevity means that previously uncommon problems now need to be faced and solved, including control of diabetes mellitus; advice on contraception and pregnancy; management of associated liver disease and oesophageal varices; and assessment for and postoperative management of heart-lung transplantation. These varied demands can be met only by all the facilities available at a cystic fibrosis centre.

The paediatrician and adult physician should establish a continuum of care with joint management over a transitional adolescent clinic. Although excellent care is provided in adult clinics in the United Kingdom by those who work to a strict age defined cut off point when care passes abruptly from the paediatrician to the adult physician, patients in our unit have expressed feelings of insecurity and a sense of being deserted when close links with the paediatric team are severed too abruptly.

Structure of care

In the United Kingdom, patients with cystic fibrosis benefit from a fully funded system of health care without personal concern of the cost of treatment or admission to hospital. This is a distinct advantage compared with what happens in the United States. The excellent facilities of the NHS have been increasingly applied to cystic fibrosis. The United Kingdom database of patients organised by Professor John Dodge and funded by the Cystic Fibrosis Research Trust is unique in its completeness. Centralisation of resources and agreement to restrict heart-lung transplantation to three centres at present has resulted in outstanding success in the programme. Local hospitals offer a high standard of general medical care and if they are willing to seek and accept advice on the fine points of management shared care can work in the United Kingdom, perhaps better than in countries such as Australia, Canada, and the United States, which of necessity developed specialist units at an earlier stage.

Conclusion

There have been impressive improvements in the care of cystic fibrosis in the United Kingdom over the past decade. We are optimistic that these improvements will continue. But the verdict on the current service must be "could do better."

- 1 British Paediatric Association Working Party on Cystic Fibrosis. Cystic Fibrosis in the United Kingdom 1977-85: an improving picture. *BMJ* 1988;297:1599-602.
- 2 Chatfield S, Owen G, Ryley HC, et al. Neonatal screening for cystic fibrosis in Wales and the West Midlands: clinical assessment after 5 years' screening. *Arch Dis Child* 1991;61:29-33.
- 3 Reardon MC, Hammond KB, Accurso FJ, et al. Nutritional deficits exist before two months of age in some infants with cystic fibrosis identified by screening test. *J Pediatr* 1984;105:271-4.

- 4 Wilcken B, Chalmers G. Reduced morbidity in patients with cystic fibrosis detected by neonatal screening. *Lancet* 1985;i:1319-21.
- 5 Phelan PD, Hey E. Cystic fibrosis mortality in England and Wales and Victoria, Australia, 1976-1980. *Arch Dis Child* 1984;59:71-83.
- 6 British Paediatric Association Working Party on Cystic Fibrosis. Report. *Bull Int Pediatr Ass* 1988;7:439-44.
- 7 Royal College of Physicians of London. *Cystic fibrosis in adults. Recommendations for care of patients in the UK.* London: Royal College of Physicians, 1990.
- 8 Walters S. *A policy document of cystic fibrosis centres.* London: Association of Cystic Fibrosis Adults (UK), 1987.
- 9 Shaw N, Littlewood JM. Misdiagnosis of cystic fibrosis. *Arch Dis Child* 1987;62:1271-3.
- 10 Littlewood JM, Kelleher J, Rawson I, et al. Comprehensive assessment at a CF centre identifies suboptimal treatment and improves management, symptoms and condition. Amsterdam: Excerpta Medica, 1988:89. (Asia Pacific congress series No 74.)

Commentary

J A Dodge

We have reached a turning point in our approach to research in and management of cystic fibrosis. For more than a decade the main thrust of research has been to identify the gene, its corresponding protein, and the mutation(s) responsible for the disease. Though many of these goals were reached in 1989,¹⁻³ the implications of these discoveries in the control of cystic fibrosis are not yet clear. For the individual patient it is too early to talk about pharmacological treatment, although it may not be long before we discover exactly how the cystic fibrosis transmembrane regulator protein works, or in the case of cystic fibrosis why it does not work normally. If pharmacologists are able to design a drug that will restore normal function to the regulator protein it will clearly be of most value to those patients who can start treatment early in life. To make such treatment available to most patients would entail having a programme of population carrier screening or neonatal screening for affected infants. If prevention of cystic fibrosis by prenatal diagnosis and termination of pregnancy is regarded as a desirable objective currently available techniques for carrier detection already provide the means to reduce the burden of cystic fibrosis by at least half. But the unexpectedly large number of mutations poses a technical problem, even if the majority of carriers would opt for diagnosis and termination early in pregnancy. The success of screening programmes aimed at controlling thalassaemia and Tay-Sachs disease is often cited in support of carrier screening, but in both cases the populations affected were well aware of the disease and its implications. For this reason the use of cystic fibrosis as a model for teaching genetics to school children in the new biology course for the General Certificate of Secondary Education is very welcome.⁴ A remarkable amount of clinical and genetic information is presented very simply, including the speculation that it may eventually be possible to replace the mutant allele with a normal allele, perhaps by using techniques of genetic engineering on very early embryos. This will help to increase the basic knowledge of part of the population in whom screening is likely to be effective.

In the meantime, the cystic fibrosis population of the United Kingdom continues to increase at the rate of about 100 a year, being almost entirely made up of adults who are surviving longer.⁵ The authors of all three accounts of the management of cystic fibrosis in this issue refer to this improvement in outlook and agree that it is related to existing methods of treatment. However, Professor Phelan and Dr Bowes point to the considerable uncertainty about which factors are responsible and the paucity of double blind trials. They believe that the single most important factor has been the development of specialised clinics. The best evidence to support this contention probably comes from Copenhagen,⁶ although Drs Koch and Høiby curiously do not refer to the benefits of centralised care. They come straight to the point, suggesting that better survival relates to better treatment of respiratory infection. Their practice entails a high level of clinical and microbiological surveillance combined with aggressive antimicrobial treatment. The details of management contained in their article will repay careful study by directors of cystic fibrosis clinics elsewhere. Like Professor Phelan and Dr Bowes, I remain unconvinced that the excellent Danish survival record is related to the policy of regular admission for treatment; I suspect that it is much more closely related to their policy of monthly surveillance. If such close monitoring is possible in Denmark it should be possible in countries such as the United Kingdom, where travel to a regional centre is comparatively easy. Even in Australia, where a visit to the specialist clinic may entail a journey of several hundred miles, patients are reviewed every three months. The inconvenience of travel is outweighed by the fact that on arrival at the clinic patients in Australia can expect to see their own doctor. In Leeds they would expect to see a doctor with specialist knowledge of cystic fibrosis even during holiday times. In many clinics the continuity of care is less satisfactory. Staffing levels vary widely between different countries, and differences between chest clinics in Australia and the United Kingdom were highlighted recently.⁷ Drs Littlewood and Conway make the fundamental point that patients with cystic fibrosis require time above all else and that they cannot be adequately reviewed in a busy routine general outpatient clinic. In this context it is perhaps surprising that the patients in Melbourne are seen in a paediatric thoracic outpatient clinic "to avoid

Institute of Clinical
Science, Queen's
University of Belfast,
Belfast BT12 6BJ
J A Dodge

Correspondence to:
Professor Dodge