

Short reports

Cystic fibrosis mortality in England and Wales and in Victoria, Australia 1976-80

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SUMMARY Mortality from cystic fibrosis throughout childhood is more than twice as high in England and Wales than it is in the State of Victoria, Australia. Possible reasons for this difference are reviewed.

While there has been a notable improvement in survival from cystic fibrosis during the last 20 years, what has caused this change is far from certain. In the hope of identifying some of the factors, the mortality from cystic fibrosis has been compared in England and Wales and in Victoria, Australia. The incidence of the disease is similar in the two countries, but there are substantial differences in the approach to its management. In Victoria, 90% of children and adolescents are managed in the one clinic. In England and Wales most children are looked after by their local paediatrician and only a small number attend specialist clinics in referral centres.

Material and methods

There has been a long term epidemiological study of cystic fibrosis in the state of Victoria since 1955.^{1,2} An attempt has been made to identify every diagnosed patient and to record date of birth, mode of presentation, date of diagnosis, and date of death. On the basis of this information, the incidence has been calculated at 1/2556 live births and has not changed appreciably over a 24 year period.² Details were available on all known live born patients who died between 1976 and 1980 inclusive, and this information was used to calculate age specific death rates.

Data for England and Wales for the same 5 year period were obtained from the Office of Population Censuses and Surveys (OPCS). Age specific death rates were calculated based on those deaths in which cystic fibrosis (or meconium ileus) was registered as the principal cause of death. Nearly half the deaths registered between 1976 and 1980, however, had all

the conditions mentioned on the death certificate coded for computer analysis by OPCS, and a study of these deaths showed that in about 4% of the cases where cystic fibrosis received a mention somewhere on the death certificate, it was not listed as the 'underlying cause of death'. The rates given in the Table, underestimate, therefore, the actual mortality attributable to cystic fibrosis by at least 4%.

Using the calculated age specific death rates and published data on the incidence of cystic fibrosis in Victoria, Australia² and England and Wales,³ an estimated survival curve was calculated from the method of Armitage.⁴

Results

The Table shows the age specific death rates for cystic fibrosis in the two communities. A model based on a Poisson distribution showed that there was a significant difference in death rates in Victoria and England and Wales ($P < 0.0001$), and that the death rates in the different age groups were consistent with an hypothesis that a similar factor or

Table *Death and age specific death rates from cystic fibrosis in England and Wales and Victoria, Australia, 1976-1980*

	Age (years)				
	0-1	1-4	5-9	10-14	15-19
<i>Victoria</i>					
Number	4	2	7	7	6
Population at risk ($\times 10^3$)	295*	1254	1771	1715	1720
Mortality rate (per 10^6)	13.6	1.6	4.0	4.1	3.5
<i>England and Wales</i>					
Number	99	73	146	162	128
Population at risk ($\times 10^3$)	3044*	12 203	18 329	19 983	21 115
Mortality rate (per 10^6)	32.52	5.9	8.0	8.1	6.1

* Livebirths.

factors were contributing to the differences in death rates in each age group.

In Victoria, Australia one death in 125 between the ages of 1 and 14 years is in a child with cystic fibrosis, and in England and Wales the equivalent figure is one in 44 (before correcting for deaths in which cystic fibrosis was not listed as the main cause of death).

Estimated survival curves are shown in the Figure. These indicate that a newborn child with cystic fibrosis has an 80% chance of surviving to age 9 years in England and Wales but a similar chance of surviving to age 20 years in Victoria.

Discussion

This study indicates that the death rate from cystic fibrosis during childhood and adolescence is substantially higher in England and Wales than it is in Victoria. In Victoria, it is thought that the ascertainment of patients is close to 100%.⁵ Every infant dying within the first 28 days of life is the subject of specific enquiry by the Victorian Consultative Council on Maternal and Perinatal Mortality, and over 85% of these babies had a full necropsy for the study period. No case of cystic fibrosis that was not already known from other sources was found in the files of the consultative council, but in the years before the study two newborn infants dying on the first day of life from complex congenital anomalies were reported to the council as also having typical pathological changes of cystic fibrosis. During the study period an experienced paediatric pathologist (Dr A L Williams) conducted necropsies on almost all babies aged over one month and children less than 14 years who died unexpectedly in the Mel-

bourne metropolitan area (70% of the population of Victoria). He did not find a single case of cystic fibrosis despite specifically looking for this disorder. It is unlikely therefore that the Victorian data underestimate appreciably the mortality from cystic fibrosis.

In England and Wales there are no similar data. Unless there is a full necropsy by an experienced paediatric pathologist, infants dying from respiratory infection may have unrecognised cystic fibrosis.⁶ If reporting of death from cystic fibrosis in England and Wales is incomplete, the mortality rate may well be higher than that calculated and the difference from that in Victoria more notable.

There are a number of factors that may explain the difference. As most deaths from cystic fibrosis are due to respiratory infection, differences in climate and socioeconomic conditions in the two communities may lead to more respiratory infections in England and Wales. To test this hypothesis, the age specific death rates from respiratory infections and sudden infant death syndrome from ages of 1 month to 1 year and 1 to 4 years inclusive were calculated for the two communities. There has been a recent fall in the number of deaths from respiratory infection in both communities and an increase in the number of sudden infant deaths that almost certainly reflects changing terminology. Deaths from these two causes were therefore combined. Mortality rates from age 1 month to 1 year and 1 to 4 years were 1.9 and 2.0/1000 live births in Victoria and in England and Wales respectively. These figures do not support the hypothesis that the difference in mortality from cystic fibrosis in the two communities results simply from a different incidence of serious respiratory infection. The rate in Victoria is lower in the 1 to 4 year age group than in England and Wales (0.054 and 0.087/1000 respectively) but the numbers were small (68 deaths in Victoria over the full 5 year period) because death from respiratory infection is rare after the first year of life.

Climatic factors may be important, apart from affecting the incidence of respiratory infections: the opportunity for children to play outdoors is greater in Victoria than in England and Wales. The survival of patients with cystic fibrosis in Victoria,⁷ is however, very similar to that reported from the Hospital for Sick Children, Toronto⁸ and Cleveland, United States of America;⁹ two cities with severe winters that restrict outdoor activities for many months of the year.

There is a major difference between England and Wales and Victoria in the form of care provided for children with cystic fibrosis. It has been claimed in North America that management in a specialist

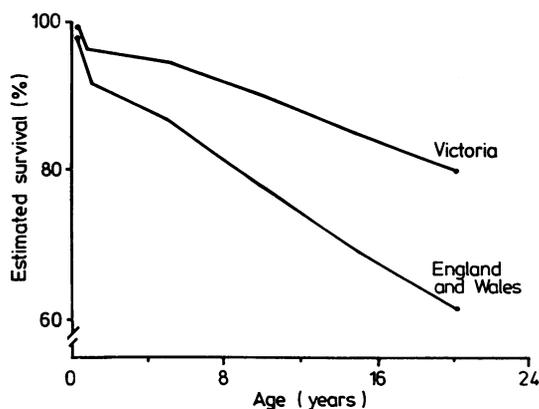


Figure Estimated survival curves for cystic fibrosis in England and Wales and Victoria, Australia derived from mortality data for the years 1976-80.

centre, as in Victoria, is essential for optimal care;⁹ and recent data from Denmark¹⁰ indicate a much better survival among patients attending a specialist clinic compared with those looked after by their local paediatrician, as happens for most children in England and Wales.

The results of this study indicate a need for further research in England and Wales into the reasons why the death rate in cystic fibrosis seems to be substantially higher there than in Victoria, Australia, and also, probably, in major referral centres in North America.

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Pancuronium bromide induced joint contractures in the newborn

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SUMMARY We report three infants paralysed with pancuronium bromide as an adjunct to mechanical ventilation, who developed multiple joint contractures. In two term infants, gentamicin and phenobarbitone given together with pancuronium may have potentiated its effect, and in one preterm infant contractures, which became more severe after paralysis, were present at birth.

Pancuronium bromide (Pavulon) is a non-depolarising muscle relaxant increasingly used in neonatal intensive care units to facilitate the management of infants undergoing mechanical ventilation. We report here the development of joint contractures in three of 13 infants, seen over an 8 month period, who received this drug as an adjunct to ventilatory treatment.

Patients

Between July 1982 and February 1983, 13 infants

admitted to the Leicester Royal Infirmary Neonatal Intensive Care Unit received intermittent bolus injections of pancuronium bromide (0.1 mg/kg body weight per dose as needed) to minimise spontaneous movement and facilitate mechanical ventilation. During the course of ventilation regular chest physiotherapy and four hourly changes in posture were undertaken in all infants. Details of these infants are shown in the Table. Three infants aged between 5 hours and 3 days died. Of the remaining 10, three developed contractures described in more detail below.

Case 4. Pancuronium bromide was started at 3 hours and continued until 27 hours of age in one girl. Initially she had a full range of joint movements. Seizures were treated with phenobarbitone, which was started on day 2. On day 8 she was noted to have limited extension of both knees and restricted abduction of both hips. Intensive passive stretching exercises were instituted but at 4 months of age full extension in the right knee was still limited by 20 degrees.