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Commentary

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There has been a pronounced improvement in the outlook for children with CF during the last 20 years and major clinics in North America and Australia now report an 80% survival to late adolescence and early adult life whereas 30 years ago fewer than 10% were alive at age 5 years. However, CF remains an important cause of morbidity and premature death, being responsible for 1 in 40 deaths between 1 and 14 years of age in England and Wales.

It was hoped that early diagnosis and prompt institution of treatment would retard or even prevent progressive lung disease. On this basis there has been considerable interest during the last 10 years in the development of newborn screening. Measurement of immunoreactive trypsin in a dried blood spot seems to have acceptable sensitivity and specificity as a screening procedure.[1] Dodge and Ryley make a strong plea for its widespread use.

However, before such a programme is introduced it is important to assess critically evidence in its favour, particularly the possible benefit of early diagnosis. Data in the literature are inconclusive.[2] We have been interested in this problem in Victoria, Australia, where there is a long-term epidemiological study of CF.[3,4] Data are available on 580 patients born in Victoria between 1955 and 1978 and diagnosed by the end of 1979. The median age at diagnosis in the group was between 7 and 9 months and 68% of them were diagnosed before 12 months. It is believed that nearly all diagnosed patients are included and because of the nature of paediatric services in Victoria the number of patients dying undiagnosed is probably small. Such an unselected population provides considerable advantages for study over groups from clinics which see only referred patients.

In Victoria the survival of 39 patients diagnosed by 6 months because of family history and before the development of lung disease was not appreciably better than that of their 36 symptomatically diagnosed older siblings, nor was it better than that of other CF patients. Currently 95% of children and teenagers in Victoria with CF are managed in one clinic. Lung disease in 28 presymptomatically diagnosed children was not significantly less extensive than in other CF children. Sixteen presymptomatically diagnosed patients with living older CF siblings did not have significantly less extensive lung diseaase than those siblings.

The failure to demonstrate benefit from early diagnosis probably reflects the great variability of CF and the palliative nature of present treatment.

Dodge and Ryley suggest that newborn screening may prevent parents undertaking a further pregnancy if they already have an undiagnosed child with CF. In Victoria between 1967 and 1979 24 such children from 22 families were diagnosed as a result of finding the disease in a sibling. During the same period a total of 328 children presenting with symptoms or found by case detection was diagnosed so that at

the most 7% of CF children could have been prevented by newborn screening.

The availability of a large group of asymptomatic infants to provide subjects for controlled trials of therapeutic regimens is perhaps a further justification for screening. However, with the current marked improvement in prognosis and the fairly insensitive measures of the progess of lung disease in early life, large numbers of patients (100 or more) followed for at least 5 years would probably be needed to detect what are likely to be small differences. The dubious value of multicentre trials is accepted by Dodge and Ryley.

Cystic fibrosis is different from the other two conditions, phenylketonuria and hypothroidism, for which newborn screening is widespread. In hypothyroidism, parents can be told that treatment will lead to an essentially normal life style. Even in phenylketonuria, although treatment is demanding, the differences from absent or delayed treatment are striking. Currently, no treatment can be offered for CF that will prevent premature death. Even if the parents are given an optimistic outlook at diagnosis, and it is important that such be given, the very serious implications of CF should also be made known to them. The effect on bonding when parents are told that the infant they perceive as perfectly normal has CF and the inevitable discovery that he will die prematurely may be considerable. Perhaps a period of prediagnosis anxiety when the child has worrying symptoms makes the acceptance of the diagnosis easier even though as Dodge and Ryley note there may be guilt and anger as well.

There are many measures that can improve the outlook. Experience in North America and Australia indicates that the best results come when patients are managed in large regional centres. Dodge and Ryley seem to dismiss the need for such management. Perhaps the development, where appropriate, of major regional clinics for comprehensive care by a specialist team will give a better quality of life than the introduction of a newborn screening programme.

Almost no aspect of the current regimens used to treat CF has been subjected to careful scientific assessment. Consequently there is great uncertainty as to the factors responsible for improved prognosis. To compound the unscientific approach to the management by the introduction of widespread screening on the basis that it might do some good and on the unproved assumption that it will do no harm seems unwise. Demonstration that the natural history is favourably altered by presymptomatic treatment, that there will not be new psychological problems, and that there is definite cost benefit seem essential prerequisites particularly at this time of severe restriction on health care spending.

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