PAPERS AND ORIGINALS

Perinatal mortality and one-year infant morbidity

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Summary and conclusions

Perinatal mortality in Southampton and South-west Hampshire Health District fell from 20.8 per 1000 total births in 1970 to 11.3 per 1000 in 1976. This was attributable mainly to a fall in the stillbirth rate, but also to a recent fall in the neonatal death rate in the first week. All infants born in 1975 who had any problems in the perinatal period were followed up for one year. Of the 12 children identified at one year as having a major handicap, eight suffered from problems of prenatal origin, two from problems associated with preterm delivery, and two from other conditions acquired during the perinatal period. As two-thirds of the major handicaps arose from congenital abnormalities, preterm delivery and low birth weight were not the main causes of major handicap.

Introduction

Many reports have emphasised the improved prognosis of infants with specific perinatal problems, particularly those of low birth weight, treated with modern methods of intensive care.¹⁻⁴ Many centres reporting follow-up results, however, are referral centres, and it is difficult to evaluate from their figures the effect of modern neonatal care in a given community. We have tried to examine, in a well-defined population, the effect of neonatal care on long-term handicaps that have their origin in or before the perinatal period.

Methods

The case notes of all infants born in 1975 with a problem identified during the perinatal period were analysed in detail. These included

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all babies admitted to the special care nursery, all babies referred directly from the labour ward or peripheral units to specialist surgical units, and some babies from the lying-in wards. Case notes were examined when surviving infants reached the age of about 1 year, and the children were assigned to one of three groups—no handicap, minor or possible handicap, and major handicap—and details of any handicaps were noted. Major handicap was defined, according to the definition of Stewart *et al.*,⁵ as the presence of a disability that was likely to prevent the child from going to a normal school or cause serious interference with normal function in society.

All surviving infants who had weighed 1500 g or less at birth were examined at the age of 1 year or more by CEMJ.

Details of perinatal deaths occurring in 1970-6 were analysed. Data on perinatal mortality were obtained from the proceedings of our monthly perinatal mortality meetings, supplemented when necessary by data from ward admission books and necropsy reports.

Population studied and delivery policy—Southampton and South-west Hampshire has a population of about 380 000. All high-risk deliveries are concentrated at the maternity unit, Southampton General Hospital, and about 30% of the total deliveries are carried out in several small peripheral units or at home. Antenatal and intrapartum fetal monitoring were well established in 1975. The special care nursery has 25 cots for babies needing a high or low degree of care and is staffed medically by a full-time registrar and two senior house officers. Since 1974 one of our senior house officers has been resident at all times in the unit.

Results

PERINATAL MORTALITY 1970-6

The fall in perinatal mortality from 1970 to 1976 is shown in table I. This fall was largely due to a decrease in the stillbirth rate, which was halved over the seven years, but in 1976 it was also helped by a sharp fall in the neonatal death rate in the first week. Further analysis

TABLE I—Perinatal mortality in Southampton

Year	No of live births	Stillbirth rate per 1000 total births	First week neonatal death rate per 1000 live births	Perinatal mortality rate per 1000 total births
1970	5965	12.4	8.5	20.8
1971	6039	12.7	10.8	23.4
1972	5778	12.8	9.2	21.9
1973	5714	12.1	9.1	21.0
1974	5383	12.1	9.1	21.0
1975	5078	8.2	8.9	17.0
1976	4739	6.2	5.1	11.3

showed that this was due mainly to a decreased mortality from respiratory causes (table II).

TABLE II—Cause of neonatal deaths in first week

Year	First week neonatal death rate per 1000 live births	Lethal congenital malformations per 1000 live births	Deaths from respiratory causes* per 1000 live births	Deaths from other causes per 1000 live births
1970	8.5	2.0	5.4	1.2
1971	10.8	2.8	5.6	2.3
1972	9.2	1.2	5.2	2.8
1973	9.1	2.1	3.8	3.2
1974	9.1	1.9	5.6	1.7
1975	8.9	3.5	4.1	1.2
1976	5.1	1.9	2.1	1.1

*Includes intracranial haemorrhage as a result of respiratory causes and apnoea of prematurity.

MORBIDITY OF INFANTS AT ONE YEAR

The case notes of 536 infants with various perinatal problems were reviewed. These were subdivided according to whether the problem was acquired during the perinatal period or was of prenatal origin (congenital abnormality).

Infants with congenital abnormalities

Of the 71 infants with congenital abnormalities identified during 1975, 26 died in the neonatal period. Of the 45 survivors, eight seemed to have a major handicap at one year, 34 had a possible or minor handicap, and three died a month to a year after birth (table III). Two of the children with a major handicap had spina bifida; one had a ventriculoatrial shunt and both showed considerable generalised developmental delay. Two other children with spina bifida were among the 34 infants with minor or no handicaps at one year. Both showed normal development for their age but it was too early to assess fully bowel and bladder function.

Review of our local amniocentesis register showed that one fetus with spina bifida, who would have been born in 1975, was aborted after antenatal diagnosis.

TABLE III—Further analysis of infants surviving neonatal period

Congenital abnormalities	No of infants	Acquired perinatal problems	No of infants
Major handicap:		Major handicap:	
Down's syndrome	4	Birth asphyxia or trauma ..	1
Microcephaly	1	Presumed cerebral	
Spina bifida	2	haemorrhage	1
Generalised connective tissue disorder	1	Preterm delivery	2
Possible or minor handicap:		Possible or minor handicap:	
Skeletal abnormalities—for example, cleft lip or palate, orthopaedic problems ..	7	Minor generalised developmental delay ..	3
Neonatal surgical problems—for example, tracheo-oesophageal fistula	8	Minor motor problems ..	5
Spina bifida	2	Possible squint	3
Others	17	Possible hearing deficit ..	2
Postneonatal deaths		Postneonatal deaths	
Down's syndrome—cot death	1	Bronchopulmonary dysplasia	1
Down's syndrome—atrioventricular canal ..	1	Cot deaths	3
Congenital heart disease ..	1		

Children with acquired perinatal problems

Altogether 434 of the 465 infants with acquired perinatal problems survived the neonatal period. Of these, 408 were considered to be normal either at one year or when discharged at an earlier age, 13 had possible or minor handicaps, four died during the year, five were lost to follow-up, and four (described below) had a major handicap at one year (table III).

Case 1—An infant was entirely normal at birth after a normal pregnancy and delivery but she suddenly collapsed on day 5 and started having fits. The presumed diagnosis was a massive intracranial

haemorrhage, for which no precipitating cause was defined. At one year she had gross developmental delay and fits that were resistant to treatment.

Case 2—An infant suffered from severe intrapartum asphyxia, and a technically difficult forceps delivery was followed by severe birth asphyxia. He had neonatal convulsions and at one year had considerable developmental delay.

Case 3—An infant weighed 1860 g at birth and was born at 36 weeks' gestation. Severe hyaline membrane disease was complicated by recurrent pneumothoraces. Prolonged intubation was required and tracheostomy was carried out at the age of 4 weeks. Developmentally he was thought to be normal at one year, and we expect that his tracheostomy will be closed by the time he is 2 years old. He is managed at home with occasional nursing help.

Case 4—An infant weighed 1100 g at 30 weeks' gestation and suffered from moderately severe hyaline membrane disease, which was treated by continuous positive airways pressure. Blood gases were monitored regularly, but in retrospect a fault in our oxygen electrode was suspected, and he may have received excessive oxygen for several hours. At one year he was developmentally normal and had useful vision, but he suffered from severe myopia, undoubtedly due to retrolental fibroplasia. He was too young to assess fully the extent of his visual handicap.

BABIES OF VERY LOW BIRTH WEIGHT

Of the infants born in 1975 who weighed less than 1500 g, 13 survived the neonatal period. These infants were all developmentally assessed according to the method of Sheridan at the age of 1 year or more, and 11 were found to be normal for their age. One infant (case 4) had a major visual handicap, and another, who weighed 1100 g at birth at 29 weeks' gestation, was intellectually normal but had a minor motor handicap with a mild right hemiparesis.

Discussion

Our object was to define the number of handicapped children who could be expected to enter the community as a result of our present policies on neonatal care and to predict how this could be expected to change as a result of changes in management of certain conditions.

The most obvious case is that of neural tube defects. In 1970 our local paediatric surgical policy was to operate on most children with spina bifida, but now a more selective policy is practised and mortality has consequently increased. Calculations from our figures suggest that this change in policy has probably increased perinatal mortality by about 1 case per 1000. The incidence of spina bifida in Southampton is near the national average at 3.2 per 1000 total births.⁶ In parts of the country with a higher rate of neural tube defects the effect will be proportionately greater. The increasing role of antenatal diagnosis may alter this figure.

The main feature to emerge from our study is that congenital abnormalities of prenatal origin accounted for a far higher incidence of severe handicap detected at one year than acquired perinatal injuries. In particular, preterm infants of low birth weight, who have traditionally contributed a high proportion of cases of major handicap, contributed only two cases of obvious major handicap, in neither of which there seemed to be any intellectual deficit. Both these infants had an iatrogenic component to their handicap, however, which serves as an unpleasant reminder of the hazards of neonatal care. Nevertheless, we have so far made only a crude estimate of handicap and it remains to be seen how much minor intellectual dysfunction has arisen from this group.

The incidence of cerebral palsy in Britain is about 2 per 1000⁷ live births, and Woods⁸ has claimed that about 78% of cases are of perinatal origin. If cerebral palsy is defined as a persistent but not unchanging disorder of posture and movement due to a dysfunction of the brain present before its growth and development are completed then only three cases in our survey so far seem to fit the definition (cases 1 and 2 and a further case of acquired minor handicap). Obviously not all cases of cerebral

palsy will be identified at 1 year, and it will be interesting to see how many of this group of infants with perinatal problems emerge with lesser degrees of cerebral palsy when they are older.

Of the 536 babies studied, four died from the sudden infant death syndrome. Three of these were of low birth weight (<2500 g) and one had Down's syndrome. Our district records indicate that 13 babies born in 1975 died in their first year from this cause out of just over 5000 live births. Therefore about one-third of the cot deaths occurred in our high-risk group.

Conclusions—The overall fall in perinatal mortality in Southampton and district has therefore been similar to the national average and has been caused largely by a fall in the stillbirth rate. In 1976 it was also helped by a fall in the death rate in the first week after birth. This occurred in spite of a changing surgical attitude to the active management of neural tube defects. Low birth weight and preterm delivery were not

the main causes of major handicap detected at one year, as two-thirds of the major handicaps arose from congenital abnormalities.

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Atopy and immunoglobulin E concentrations in Hodgkin's disease and other lymphomas

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Summary and conclusions

Serum immunoglobulin E (IgE) concentrations are increased in Hodgkin's disease (HD) but not in other types of lymphoma. The prevalence of atopic disease is similar to normal in both groups. Patients with high IgE concentrations and HD were separated into atopic and non-atopic groups, which were found to differ clinically. Atopic patients had a significantly lower incidence of night sweats, fever, and weight loss, and treatment had no significant lasting effect on their IgE concentrations. In the non-atopic group there was a striking correlation between high IgE concentrations and a histological appearance of nodular sclerosis, particularly in the presence of night sweats, fever, and weight loss. Successful treatment in the non-atopic group led to a noticeable fall in IgE concentrations, in most cases to normal, though on relapse of the disease they rose again.

Introduction

Early observations that atopic illness is less common in patients with cancer than in the normal population suggested that atopy might have a protective role in oncogenesis,¹⁻³ but subsequent controlled studies showed comparable incidences of atopy in people with and without cancer.⁴⁻⁶ With the identification of immunoglobulin E (IgE) as the major class of reaginic antibody⁷ the basic type I allergic response could be studied direct without relying on a history of atopy to indicate a genetic predisposition

to some but not all type I allergic manifestations—for example, hay fever, seasonal rhinitis, eczema, and asthma. With one exception, no valid study so far has shown any differences in serum IgE concentrations between people with cancer and those without.⁸⁻⁹ The one exception showed high concentrations in 11 out of 19 patients with Hodgkin's disease (HD).¹⁰ The high incidence of atopy (six of the 19 patients) in this small group was unusual, however, and the results could not be confirmed in a retrospective study by Steinberg *et al*.¹¹

Our study aimed to determine serum IgE concentrations in patients with active HD and other lymphomas, and to assess the relevance of atopic history, patient's clinical state, and treatment to the concentrations.

Subjects and methods

We studied 115 patients with active HD. Ninety were studied before treatment, and the remaining 25 were in relapse 10-28 months after undergoing radiotherapy as the sole treatment. The disease was staged by means of the Ann Arbor classification,¹² and histology accorded with the Rye modification of Lukes and Butler's classification.¹³ Radiotherapy for HD was given by "mantle" or "inverted Y" fields, 3500-4000 rads being delivered over four to five weeks.¹⁴ Quadruple chemotherapy was given in some cases.¹⁵

Sixty-eight patients with other lymphomas were also studied, all before treatment. Fifty-three had lymphocytic lymphomas (22 well-differentiated, nine chronic lymphatic leukaemic, and 22 poorly differentiated types); eight had histiocytic lymphomas; four had mixed histiocytic and lymphocytic lymphomas; one had reticulo-endotheliosis; one had a Burkitt-like lymphoma; and one had angioimmunoblastic lymphadenopathy. One hundred and eighty laboratory personnel, blood donors, and dental outpatients served as controls.

Patients and controls were regarded as atopic if they had a definite history of atopic symptoms, such as asthma, hay fever, perennial rhinitis, urticaria, and eczema. A history of drug reaction was not counted as an atopic manifestation. To ascertain that an atopic background had not been overlooked, patients with IgE concentrations above normal were prick-tested for immediate hypersensitive reactions to a large battery of common allergens—namely, pollens; yeasts and fungi; foods; furs, feathers, and danders; and house-dust mites. Twenty of the controls were found to be atopic; a further 57

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