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Time trends in twin perinatal mortality in northern England, 1982–94

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The dynamics of perinatal mortality rates (PNMR) and causes of death in twin pregnancies over 13 years in the Northern Region of the National Health Service in England is described. All twin perinatal deaths occurring between 1982–1994 were identified from the Northern Region Perinatal Mortality Survey. The twinning rate increased from 9.9 per 1000 maternities in 1982 to 12.0 in 1994. There was a total of 10734 twin pregnancies and of these 421 resulted in 530 perinatal deaths. The perinatal mortality rate in twins significantly decreased over time (1982–87, 55.4 per 1000; 1988–94, 44.4 per 1000; P = 0.01). The PNMR was significantly higher for twins from like-sexed than from unlike-sexed pairs (53.5 and 34.4 per 1000 respectively, P < 0.001). Despite no improvement in birthweight distribution in the twin population, birthweight-specific perinatal mortality rates for both like and unlike-sexed twins decreased for each birthweight category in 1988–94 compared with 1982–87. Twins with very low birthweight (< 1500 g) comprised 69%, and preterm twins (< 37 completed weeks of gestation) 74.9% of all twin perinatal deaths. The major immediate cause of early neonatal death was pulmonary immaturity (63%); antepartum anoxia caused 76.9% of antenatal deaths. Unexplained preterm labour and intrauterine death were the leading obstetric factors underlying death in twins. Despite a decrease over the 13 years, the perinatal mortality rate in twins in the Northern Region remains high. Continued monitoring of trends in twinning and mortality rates is needed to inform health care planning.

Keywords: twinning, birthweight-specific perinatal mortality, monozygotic and dizygotic twins, prematurity, low birthweight

Introduction

Twin pregnancies account for about 12/1000 of all pregnancies[1] but their contribution to all perinatal deaths is disproportionately high, over 10%.[2,3] It is well known that perinatal mortality in twins is 4–6 times higher than that of singletons[2,4–8] and has not declined as rapidly as it has in singletons over the past 20 years.[4] Whilst the improvement in neonatal mortality for preterm (< 34 gestational weeks) twins has been remarkable, the stillbirth rate has shown little change,[4,5] in fact there has been a rise in antepartum deaths.[4] The improvement in neonatal outcome of twin pregnancies has been achieved mainly by the increased survival of preterm and very low birthweight newborns, not by preventing preterm births. Among twins, monozygotic, especially monochorionic, twins are particularly at risk.[9–11]

The leading causes of poor outcome for twin pregnancies are preterm delivery and intrauterine growth retardation, as well as complications associated with these conditions.[12–14] Approximately one half of all twin births result in low birthweight (less than 2500 g) compared with 6–8% of singleton births,[6,8,15] and between a third and a half of twin deliveries occur before 37 weeks of gestation.[2,5,6,15–17] However, it is not only preterm twins who require special medical attention; among infants of birthweight 2500 g and over, twins also have a higher risk of mortality compared with singletons.[2,6,7] Thus, the disproportionate contribution of twin deaths to overall perinatal mortality and childhood disability is a matter of concern, especially in countries with relatively low perinatal mortality rates, as the trend in multiple birth rates all over the world is upward.

Data from an ongoing population based register (the Northern Region Perinatal Mortality Survey–PMS) have been used to study time trends in twinning and perinatal mortality rates in twins from 1982 to 1994, and to describe the main causes of death in twins.

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Materials and methods

Study sample

The former Northern Region (now part of the Northern & Yorkshire Region) was one of the 14 administrative regions into which the National Health Service in England and Wales was divided before its reorganisation in 1994. The region is a well defined geographical area comprising five counties (Tyne and Wear, Cleveland, Cumbria, Durham, and Northumberland) with a population of over 3 million and approximately 40000 deliveries per year. The PMS collects information on late spontaneous abortions, therapeutic abortions, stillbirths and infant deaths among babies born to mothers resident in the region. Cases are notified from multiple sources enabling almost complete case ascertainment. Details of the system for monitoring perinatal death in the Northern Region, which has been in operation continuously since 1981, have been described elsewhere.[18] All perinatal deaths, ie all stillbirths (see definitions below) and all liveborn babies delivered after the 20th week of gestation resulting in an early neonatal death, occurring in the region between 1982–1994 were identified from the PMS database. As information on zygosity is not recorded in the PMS, twinning rates by zygosity have been estimated by applying the Weinberg rule,[19] ie the number of dizygotic (DZ) twin pairs was calculated as twice the number of unlike-sexed twin pairs, and the number of monozygotic (MZ) pairs was calculated by subtracting the estimated number of DZ pairs from the total number of twin pairs.

The perinatal mortality rates for England and Wales, the total number of twin births and the birthweight distribution among twins and singletons born in the Northern Region were obtained from the Office for National Statistics (ONS). All data are based on the date of occurrence.

Definitions

Prior to October 1992 all foetal deaths were registered as stillbirths if they were delivered after the 28th week of pregnancy. After October 1992, the gestational age for stillbirth registration was lowered to 24 weeks as a result of a change in legislation in England and Wales.[20] This change is reflected in the PMS. Early neonatal death is the death, following livebirth, of a baby before completing seven days of life. Perinatal mortality rate (PNMR) is the total number of stillbirths and early neonatal deaths per 1000 registered births. Stillbirth rate (SBR) is the number of stillbirths per 1000 registered births. Early neonatal mortality rate (ENMR) is the number of early neonatal deaths per 1000 livebirths.

Immediate causes of stillbirth and neonatal death are presented using the 'Extended Wigglesworth Classification',[21] which identifies pathological conditions in the baby leading to death.

Statistical analysis

Analysis was carried out using the Statistical Package for the Social Sciences (SPSS for Windows).[22] χ^2 tests were used to test differences in proportions.

Results

Twinning and perinatal mortality rates

There was a total of 10734 twin births (5367 twin maternities) during the 13-year period with an average twinning rate of 10.5 per 1000 maternities. Table 1 shows twinning rates in the Northern Region during 1982–94. Although the twinning rate fluctuated by year, it increased from 9.9 per 1000 maternities in 1982 to 10.4 in 1991, rising further to 12.0 in 1994. As presented in Figure 1, the increase in the twinning rate from 1991 was due to the increase in the DZ rate, with the MZ rate remaining fairly constant during this period.

A total of 530 perinatal deaths (195 antepartum stillbirths, 38 intrapartum stillbirths and 297 early neonatal deaths) in twins were notified to the PMS. Stillbirth, early neonatal and perinatal mortality rates in twins during 1982–94 are presented in Table 2. Although the rates were lower in 1994 than in 1982, there were considerable variations in the SBR, ENMR and PNMR rates during the observed period (differences between maximum and minimum in SBR, ENMR and PNMR were 17.2, 22.8 and 26.5 per 1000 respectively). As a result of these variations and to investigate trends over time, the period was divided into 1982–87 and 1988–94. Comparison of the PNMR in twins for 1982–87 and

Table 1 Twinning rates in the Northern Region, 1982–1994

	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	Total
No. of twin maternities	388	403	356	430	421	429	422	390	398	427	446	439	418	5367
No. of total maternities	39170	38932	39148	40651	40042	40160	39875	38897	40446	40861	39723	38279	34772	510956
Twinning rate per 1000 maternities	9.9	10.4	9.1	10.6	10.5	10.7	10.6	10.0	9.8	10.4	11.2	11.5	12.0	10.5

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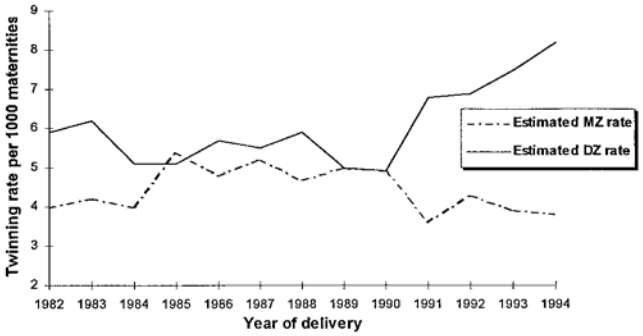

Figure 1 Monozygotic and dizygotic twinning rates in the Northern Region during 1982–94. Monozygotic and dizygotic twinning rates have been estimated by applying the Weinberg rule[19]

1988–94 revealed a significant decrease (55.4 to 44.4 per 1000 twin births; $\chi^2 = 6.66$, $P = 0.01$), despite the lowering of the gestation for registration of stillbirth in October 1992. SBR declined significantly from 25.3 per 1000 in 1982–87 to 18.7 per 1000 in 1988–94 ($\chi^2 = 5.2$, $P = 0.02$). By using the old definition for stillbirths (28 weeks and over) for the later period, a decrease in SBR would be even more apparent: 25.3 vs 17.7 per 1000 ($\chi^2 = 7.12$, $P = 0.008$). The decrease in ENMR (30.9 to 26.2 per 1000) did not reach statistical significance ($\chi^2 = 1.92$, $P = 0.17$). As shown in Table 2, twin perinatal deaths accounted for 10.6% of all perinatal deaths in the region, and there was no significant change in their contribution to total perinatal deaths between 1982–87 and 1988–94 (10.7% and 10.4% respectively; $\chi^2 = 0.11$, $P = 0.77$). The PNMR in twins for the Northern Region in 1982–94 was significantly higher than that for England and Wales during the same period (49.4 and 39.7 per 1000; $\chi^2 = 24.36$, $P < 0.001$).

In singletons, the PNMR decreased from 9.5 per 1000 singleton births in 1982–87 to 8.3 per 1000 in 1988–94 ($\chi^2 = 20.96$, $P < 0.0001$). In contrast to twins, the SBR did not decline significantly between 1982–87 (5.5 per 1000) and 1988–94 (5.2 per 1000; $\chi^2 = 2.39$, $P = 0.12$), whilst the decline in ENMR was highly significant (4.1 in 1982–87 vs 3.2 per 1000 in 1988–94; $\chi^2 = 28.11$, $P < 0.0001$). However, when using the 28th week of gestation as a cut-off for stillbirth definition during 1988–94, a decrease in SBR appeared to be highly significant (5.5 in 1982–87 vs 4.8 per 1000 in 1988–94; $\chi^2 = 11.7$, $P < 0.001$).

Outcome of pregnancy in like and unlike-sexed twin pairs

Table 3 shows the number of births in like-sexed and unlike-sexed pairs and the number of perinatal deaths by year of delivery. The PNMR was significantly higher for twins from like-sexed pairs (53.5 per 1000) than for unlike-sexed pairs (34.4 per 1000; $\chi^2 = 17.03$, $P < 0.001$). In like-sexed pairs, males had an increased PNMR (57.7 per 1000) compared with females (49.1 per 1000), although the difference was not statistically significant ($\chi^2 = 2.61$, $P = 0.11$).

Birthweight and gestational age

Figure 2 shows the birthweight (BW) distribution among perinatal deaths in twins and singletons. Twins with very low BW (< 1500 g) comprised 69% of all twin perinatal deaths. Low BW (< 2500 g) twins constituted 90.4% of all twin perinatal deaths. Among singleton deaths, over one third (37%) weighed less than 1500 g at birth, but nearly the same proportion of deaths (36%) occurred in the normal BW category.

Table 4 shows the BW distribution and birthweight-specific PNMR for like and unlike-sexed twins in 1982–87 compared to 1988–94. The total PNMR in both like and unlike-sexed twins decreased over time. This finding cannot be attributed to the improvement in BW distribution in twins over the observed period as there was a 30% increase in the proportion of extremely low BW (< 1000 g) babies between 1988–94 compared with 1982–87. The PNMR was lower in both like and unlike-sexed twins for each BW category in 1988–94 compared with 1982–87.

Preterm twins (< 37 weeks of gestation) comprised 74.9% of perinatal deaths. In early neonatal deaths, 88.9% (264/297) of twins were born preterm, of which 65.9% (174/264) were born at a gestational age of < 28 weeks. The majority of early neonatal deaths (81%) had very low BW. The proportion of babies with extremely low BW (< 1000 g) was 63.6%, of which 92% were born at a gestational age of < 28 weeks. As data on gestational age for the twin population are not available (not collected by the ONS), it is not possible to present gestational age-specific PNMR over the observed time period.

Causes of death for the different pregnancy outcomes

The immediate causes of death in twins are shown in Table 5. The most common causes of perinatal death were pulmonary immaturity and antepartum anoxia. In singletons, the contribution of antepartum anoxia and congenital malformations was higher (44.9% and 18.2%, respectively) than in twins. In contrast, pulmonary immaturity, the third leading cause in singletons, accounted for 14.7% of perinatal deaths compared to 35.3% in twins.

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Table 2 Stillbirth, perinatal and neonatal mortality rates in twins in the Northern Region, 1982–1994

	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	Total
No. of twin births	776	806	712	860	842	858	844	780	796	854	892	878	836	10734
Stillbirths	24	19	18	24	18	20	13	12	15	16	18	12	24	233
Stillbirth rate[a]	30.9	23.6	25.3	27.9	21.4	23.3	15.4	15.4	18.8	18.7	20.2	13.7	28.7	21.7
Early neonatal deaths	26	28	16	19	35	22	19	26	17	23	24	24	18	297
Early neonatal mortality rate[b]	33.5	34.7	22.5	22.1	41.6	25.6	22.5	33.3	18.8	26.9	26.9	27.3	21.5	28.3
Perinatal deaths	50	47	34[c]	43	53	42	32	38	32	39	42	36	42	530
Perinatal mortality rate[a]	64.4	58.3	47.8	50.0	62.9	49.0	37.9	48.7	40.2	45.7	47.1	41.0	50.2	49.4
Contribution of twin deaths to all perinatal deaths (%)	10.7	11.0	7.7	10.4	12.4	12.0	8.6	10.4	9.7	9.8	12.3	9.6	12.1	10.6
Perinatal mortality rate (England & Wales)[a]	45.4	44.7	42.8	41.0	44.3	41.1	40.6	38.0	36.9	36.6	31.9	36.7	40.4	39.7

[a]Per 1000 twin births; prior to October 1992 stillbirths were registered after 28th week of gestation, after this date stillbirths were registered after 24 completed weeks of gestation.
[b]Per 1000 twin livebirths.
[c]This figure is one case different from that in the Northern Region Twin Survey, 1984[35] because of a difference in registration.

The major obstetric factors underlying perinatal death in twins were unexplained preterm labour (36.3%) and other unexplained deaths (27.7%) of which one third were with intrauterine growth retardation. Unexplained deaths not associated with preterm birth occurred mostly in the antenatal period accounting for two thirds of antenatal deaths. The commonest identifiable causes of perinatal losses in twins were twin-to-twin transfusion, antepartum haemorrhage and toxaemia of pregnancy with or without antepartum haemorrhage. In comparison, the leading obstetric factor in singletons was other unexplained deaths (36.1%). The second and third major causes were congenital malformations (18.2%) and antepartum haemorrhage (15.6%). Unexplained preterm labour in singletons contributed to a lesser extent to perinatal deaths than that in twins, accounting for 12.8% of deaths.

Discussion

Population-based studies from the USA, Canada, Japan, UK and Denmark report a rise in multiple birth rates during the past 10–20 years.[23–27] The observed change in multiple birth trends may be associated with the increased use of ovulation-stimulating drugs for infertility treatment or other methods of assisted conception. Another possible explanation for the increase in twinning rates, or cessation in their decline, may be an increase in 'natural' twinning rates. This latter explanation has been put forward to account for part of the recent increase in England and Wales and in Belgium.[27] In 1982–94 the twinning rate in the Northern Region showed an overall upward trend, although the annual rate varied considerably. Since 1991, the increase in the twinning rate has resulted from the increase in the estimated DZ rate. This increase in DZ rate may be partially attributed to a higher proportion of women aged 30 years and over giving birth during 1991–94 compared with previous years (29.6% vs 23.4%), as DZ rate is known to be affected by increasing maternal age. However, this slight increase in the proportion of older mothers cannot account for the increase in the twinning rate from 9.8 per 1000 maternities in 1990 to 12.0 in 1994. Information on parity, an additional factor influencing DZ twinning, is not available from the PMS. Based on the above findings, we suggest that the increasing trend of the estimated DZ twinning rates in the region is mainly due to a wider use of methods of assisted reproduction.

High perinatal mortality in twins remains a major area of concern in perinatology not only because over 10% of all perinatal deaths are attributed to twins,[2,3,16] which is confirmed in our study, but also because of the lack of success in decreasing perinatal mortality in twins compared with singletons. The

Table 3 Perinatal deaths in like- and unlike-sexed twin pairs in the Northern Region, 1982–1994

	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	Total
No. of births (MM pairs)	286	276	268	338	330	312	318	288	312	278	336	300	294	3936
No. of births (FF pairs)	258	290	246	312	282	322	292	298	286	298	280	288	256	3708
No. of births (ULS pairs)	232	240	198	208	228	220	234	194	198	278	274	288	286	3078
Perinatal deaths (MM pairs)	16	18	11	16	38	19	14	20	12	20	14	9	20	227
Perinatal deaths (FF pairs)	21	14	13	14	9	16	11	14	17	11	14	16	12	182
Perinatal deaths (ULS pairs)	11	12	8	12	5	5	6	4	3	8	12	10	10	106

The perinatal deaths do not include 15 cases in which the sex of the co-twin was unknown. The total no. of twins with known sex was 10722. MM=like-sexed, male–male pairs; FF=like-sexed, female–female pairs; ULS=unlike-sexed pairs.

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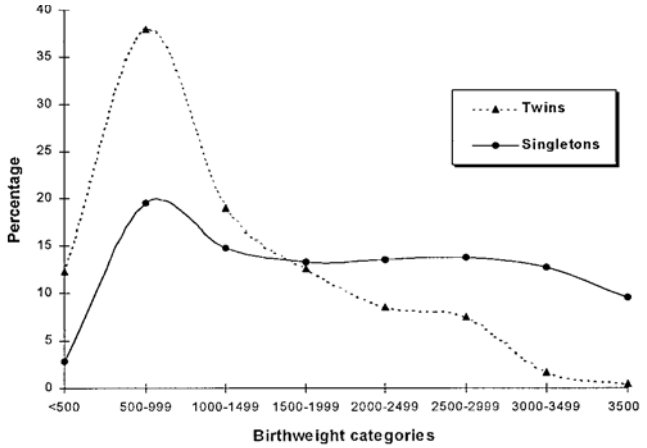

Figure 2 Birthweight distribution in twin and singleton perinatal deaths

recent increasing trends in twinning rates raise concern further.

In the Northern Region the average PNMR for twins during the 13 years was 49.4 per 1000. PNMR varied considerably probably as a result of the small number of losses occurring each year. We have shown a significant decreasing trend in perinatal deaths with time. Further, there was a significant declining trend in foetal mortality but not in early neonatal mortality. A possible explanation for this decline may be an increase in induced abortions for fatal congenital malformations, before 20 weeks of gestation, which may have reduced the stillbirth rate. When interpreting twin early neonatal mortality, it should be borne in mind that liveborn twins from pairs with a single antenatal stillbirth are at higher risk of mortality and morbidity than liveborn twins from pairs where both twins were livebirths.[28,29]

Perinatal mortality in MZ twins has been reported to be higher than in DZ twins.[9,11] When information on zygosity or chorionicity is not available, an indirect way to reveal differences in mortality between MZ and DZ twins is comparing mortality in like and unlike-sexed twins. In the Northern Region, perinatal mortality was higher in like-sexed compared with unlike-sexed twins due to the contribution of higher mortality of MZ twins to the like-sexed twin mortality, a finding consistent with previous studies.[9,11,30] The decrease in the PNMR in both like and unlike-sexed twins occurred in all BW categories in 1988–94 compared with 1982–87. The observed improvement in the PNMR may be partially attributed to advances in the antepartum management of twin pregnancies and also to a rise in the estimated DZ twinning since 1991. Although the downward trend in twin PNMR is encouraging, no obvious decrease in the total ENMR and the significantly higher PNMR in twins in the Northern Region compared with England and Wales, are evidence that there is still room for improvement. The PNMR in the Northern Region compared with England and Wales is also higher for singletons and this pattern for the region has been consistent since 1960. This disadvantage of higher perinatal mortality might be attributed to an unfavourable socio-economic situation in the region compared with the rest of England and Wales.[31]

Our study confirmed that prematurity and its consequences in liveborn twins remain the major problem facing clinicians. Over half early neonatal deaths were born before 28 weeks of gestation and 89% were born prior to 37 weeks. Pulmonary immaturity was the main immediate cause of death in liveborn twins. Among obstetric antecedents, unexplained preterm labour was the primary factor leading to death in liveborn twins. Most perinatologists agree that preventing preterm birth in twin pregnancies is the best approach to reducing perinatal mortality and morbidity.[2,12,17,32–35] However, the effectiveness of measures for preventing and treating premature labour in twins (hospital bed rest, prophylactic cerclage, progesterone therapy and tocolytic agents) is controversial.[32] There is no evidence that any of these preventive measures significantly affect birthweight, preterm labour or perinatal mortality in twin pregnancies.[33,36] However, serial ultrasound assessment of foetal growth every two weeks after 24 weeks gestation suggested by D'Alton and Mercer in a prevention programme for preterm delivery in twin gestation, did result in significant reductions in the incidence of preterm delivery and of intrauterine and neonatal death.[37]

The results of the present study show that perinatal mortality in twins in the Northern Region remains high despite the advances in perinatal technology which have taken place during this period. Establishing why this continues to be so should be a priority for research in perinatology. As preterm labour of unknown aetiology and unexplained intrauterine death are the main obstetric factors leading to perinatal death in twins, further research should be directed towards searching for pathogenetic mechanisms underlying antepartum death and further assessing the effectiveness of existing measures for preventing and treating preterm labour. Thus, in January 1998, a Register of Multiple Pregnancies was established in the Northern Region. This will substantially extend the information on multiple pregnancies and enable research to be undertaken into the aetiology of higher mortality and morbidity in twins to identify ways to improve the outcome of multiple pregnancies.

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Table 4 Birthweight (BW) distribution in twins and birthweight-specific perinatal mortality rates (PNMR) in like-sexed (LS) and unlike-sexed (ULS) twins in the Northern Region

Birthweight category (g)	BW distribution (%)		PNMR in LS twins per 1000		PNMR in ULS twins per 1000	
	1982–87	1988–94	1982–87	1988–94	1982–87	1988–94
<1000	2.8	3.6	893.2	678.8	656.2	638.3
1000-1499	5.9	5.5	219.6	145.2	166.7	54.8
1500-1999	13.7	13.6	52.2	41.9	47.9	29.3
2000-2499	29.5	29.1	19.1	11.4	13.0	12.3
2500+	47.7	46.9	12.1	9.2	10.5	7.7
Total	100	100	58.2	40.0	40.0	30.2

Birthweight was missing in 0.3% of twins in 1982–87 and in 1.3% of twins in 1988–94.

Table 5 Immediate causes of death in twins by timing of death

Immediate cause of death[a]	Time of death			
	Antepartum stillbirth	Intrapartum stillbirth	Early neonatal death	Perinatal death
Congenital malformation	13 (6.7)	8 (21.1)	35 (11.8)	56 (10.6)
Antepartum anoxia	150 (76.9)	0	0	150 (28.3)
Intrapartum anoxia/trauma	0	24 (63.2)	37 (12.5)	61 (11.5)
Pulmonary immaturity[b]	0	0	187 (63.0)	187 (35.3)
Infection	2 (1.0)	0	12 (4.0)	14 (2.6)
Twin-to-twin transfusion	28 (14.4)	6 (15.8)	12 (4.0)	46 (8.7)
Other specific causes	2 (1.0)	0	10 (3.4)	12 (2.3)
Sudden infant death	0	0	1 (0.3)	1 (0.2)
Unexplained	0	0	3 (1.0)	3 (0.6)
All causes	195 (100.0)	38 (100.0)	297 (100.0)	530 (100.0)

[a]According to the Extended Wigglesworth Classification[21]
[b]Pulmonary immaturity also includes hyaline membrane disease and intraventricular haemorrhage and refers to liveborn twins only.

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