科技资料

The Very Low Birthweight Infant

A Challenge to Neonatology and Obstetrics

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Edited by G. Duc, A. Huch, R. Huch

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Prof. Dr. Gabriel Duc
Prof. Dr. Albert Huch
Prof. Dr. Renate Huch
Departments of Neonatology and Obstetrics
University Hospital
Frauenklinikstraße 10
CH-8091 Zürich

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Foreword

About seven years ago the first symposium in Zurich on the very low birthweight infant was held. Since then, changes have taken place at a rapid pace in this very area of perinatal medicine. When we organized this second symposium, all three of us realized that it would not be realistic to try to review either all of the recent progress or all of the implications of the large number of interventions in obstetrics and neonatology that are now used in the management of very immature fetuses and neonates.

The decision was thus made to limit the discussion to certain individual aspects. For one thing, a line had to be drawn concerning the birthweight. For the obstetrical considerations, the upper limit was set at 1,500 g, whereas for the neonatal discussions, it was set at 1,000 g. In addition, certain selected areas of interest were given priority.

Both in the symposium and in these proceedings, the "natural order of events" was reversed. Postnatal problems were discussed before prenatal management was considered. The reason for this is our belief that prenatal decisions are very dependent on an estimate of the chances for a successful outcome expressed in probabilistic terms.

The neonatal part of the symposium was mainly devoted to the problem of long-term morbidity of the survivors with a birthweight below 1,000 g. We are aware that we thus restricted the discussion to a very small proportion of the total neonatal population. We feel, however, that this group is of particular interest today because the neonates below 1,000 g are at the highest risk among the prematures, and data concerning their long-term morbidity are still sparse despite the fact that there has been a spectacular decrease in mortality reported in a number of neonatal units over the past 15 years.

It was not our intention to initiate an intensive debate about how "success" should be defined in order to justify intensive care, in particular the use of mechanical ventilation, for neonates below 1,000 g. Our goal was to establish a kind of summary of the data available in 1989 concerning intellectual, psychological and motoric impairments, visual defects and chronic pulmonary disorders. Together with mortality data, this should provide a measure of the effectiveness and efficiency of modern perinatal intensive care for this special group of infants. Moreover, it was our hope that this data would provide a basis for the discussions of the major ethical questions concerning the justification of intensive care in order to give a "previable" human a chance to live.

For obstetrics, the theme that was posed for discussion could best be summarized by a question: Where is the best location, and what is the best method of delivery for the very low birthweight premature infant, to ensure that the neonate can be turned over to the pediatrician in the optimal condition and with the best possible "starting chance"? The main points of discussion were aspects of clinical organization and equipment, regionalization, transport in utero versus neonatal transport, the influence of the mode and place of delivery on mortality and morbidity, various techniques of the Cesarean section and the significance of the anesthetic procedure.

Living proof for the justification of active obstetrical management and neonatal intensive care was seen in Sarah (1,200 g at birth), Sereina (1,120 g), Deborah (1,010 g), Sandra (1,002 g), Coy (950 g), Elena (930 g), Marino (860 g), and Simone (840 g), who delighted all those present with their lovely children's songs at the beginning of the symposium and so vividly embodied the most positive aspect of the many-faceted spectrum of medicine in this "frontier" area. Although the reader who was not there cannot see this before his eyes, it is our hope that the informative and constructive exchange of the various experiences and the thoughts of renowned experts invited from many areas of the world who participated in the symposium and in the chapters of this book will enable him to be better informed about what can be done today to help very low birthweight infants and to capture something of the excitement and continuing challenge in this field.

G. Duc A. Huch R. Huch

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Cerebral morbidity in the extremely low birthweight infant

Ann Stewart

Most neonatal intensive care units claim that they are admitting increasing numbers of extremely low birthweight infants weighing less than 1,000 g (ELBW). It seems likely that these increases are a consequence of the improvements in mortality among ELBW infants which many units mention. Dunn (4) showed this effect very clearly in 1985. He reported that the rate of admissions of ELBW infants in Avon Health Districts, UK accelerated immediately the units began to get survivors and the staff felt confident enough to offer intensive care to all ELBW infants without congenital malformations arriving in their units. If the Avon Health District experience indicates what is happening in all neonatal intensive care units, there is an urgent need for up to date ELBW mortality and cerebral morbidity data. This presentation reviews the available reports in the literature and gives some unpublished data on neurodevelopmental morbidity in older ELBW children aged 4 and 8 years who were cared for in the Neonatal Unit of University College Hospital London (UCH) between 1979 and 1983.

Mortality

According to all the published reports of studies of ELBW infants, both 28 day and total mortality (all deaths up to 12 months of age) have been falling in the past 15 years. Table 1 shows pooled total mortality data from 22 reports made since 1972 and reviewed in 1986 (10). In order to look for trends, the results were divided into 3 groups, according to the year of birth.

Table 1: Mortality in the first year according to year of birth, calculated from pooled world literature data (2)

Years	Studies n	Infants n	Mortality⁺ %
1965 - 1974	4	416	75
1975 - 1979	8	623	68
1980 - 1982	11	1,593	63
1979 - 1984	UCH •	198	55

⁺ all deaths in the first year of life; • University College Hospital London

Analysis showed a definite downward trend in mortality over the 15 year period, but the changes were not very large. In the 5 years since the most recent of these reports was published, experience of many workers in specialist centres suggests that the downward

trend has accelerated and mortalities of less than 50% are often mentioned. However, it is too early to find confirmation in published reports.
A few workers have considered the effect of birthweight on mortality within the ELBW group. In one population study, mortality increased with every 100 g decrease in birthweight (8) (Table 2). A similar effect was reported from another population study (13), although actual numbers and values were not given. Other workers (6,10) have shown changes according to birthweight above and below 750 g.

Table 2: Mortality in the first year of life according to birthweight below 1,000 g

Birth-weight g	Hamilton (8) 1977 - 1980 Mortality n	%	Merseyside (6) 1979 - 1981 Mortality n	%	UCH* 1979 - 1984 Mortality n	%	UCH* 1987 Mortality n	%
1,000 - 901	63	29						
900 - 801	50	38	123	67	136	46	22	50
800 - 701	49	51						
700 - 601	52	69						
600 - 501	41	98	79	92	62	74	15	87

* University College Hospital London (unpublished data)

Interpretation of these data is difficult. The majority were obtained from studies reported from specialist centres; very few population-based studies appear to have been done. In addition, the accuracy of recording of ELBW births in all studies is likely to be affected by the lack of clear, unequivocal regulations for the reporting and registration of births down to the lowest limits of viability. Consider, for example, the situation in the UK. The lower limit of legal viability is still 28 weeks of gestation - one week after the gestation (27 weeks) at which the mean birthweight is 1,000 g. Thus, if a foetus is delivered at 25 weeks, it is counted as a live birth if it survives and is admitted to an intensive care unit. If that infant later dies, it is counted as a neonatal death. Foetuses of similar gestations who do not get admitted to an intensive care unit - for various reasons - are classed as abortions and do not appear in birth or mortality statistics. Even the most determined and meticulous attempts at population-based studies are subject to these biases. Until clear and unequivocal guidelines for recording births at the lower limit of viability are agreed and in operation the true ELBW mortality and morbidity will not be known nor can realistic comparisons be made between countries, regions or even individual units. All that can be done is to state what is happening in a particular place within a stated time period. Obviously, such statements are much better than no information - which is the alternative - provided the quality of the data and the consequent limitations, are recognised.

Cerebral morbidity

Definitions

Major impairments are generally defined as those which cause disability at the age of assessment. In young children aged 1 - 3 years, they include cerebral movement disorders ("cerebral palsy"), sensory neural hearing loss, blindness due either to cortical damage or retinopathy and overall developmental delay indicated by a developmental quotient of 2 or more standard deviations below the mean. And, of course, an infant may have more than one impairment.

Minor impairments may be defined as those which do not cause frank disability at the age of assessment. These impairments tend to be poorly described in reports concerning young children, presumably because standardised tests of neurological and motor function have not been widely available for pre-school children. In a later presentation, Dr. Amiel-Tison will discuss this problem and offer a solution. In our experience, neurological impairments which do not have gross motor consequences can be identified by the end of the first year of life; and these apparently minor impairments indicate neurological deficits which may be quantified later when fine and higher motor functioning and coordination skills can be measured (1,11). Once children are old enough for assessment of these and other more sophisticated functions including those of language, subtle deficits can be identified and clearly defined. For the purposes of this presentation, only major impairments will be considered among young children aged 1-3 years.

Young children (1 - 3 years)

Calculated as a proportion of the total ELBW births in population studies or of admissions in single centre studies, the prevalence of major neurodevelopmental impairments has been less than 10% since the earliest follow up report made in 1972. Table 3 shows mortality and morbidity data from the 22 studies already quoted in the mortality section, pooled and grouped according to the year of birth for analysis (10).

Table 3: Mortality in the first year and major morbidity aged 1 - 3 years according to year of birth, calculated from pooled world literature data (10)

Years	Studies n	Infants n	Mortality⁺ %	Morbidity# %
1965 - 1974	4	416	75	5
1975 - 1979	8	623	68	6
1980 - 1982	11	1,593	63	7
1979 - 1983	UCH •	145	55	7

⁺ all deaths in the first year of life; # major cerebral morbidity;
• University College Hospital London

The proportion of major neurodevelopmental morbidity changed very little during the 15 year period although mortality decreased and the proportion of children surviving without major impairments increased accordingly. However, these data are subject to the biases arising from possible inconsistencies of reporting and registering of ELBW infants which have already been discussed so must be interpreted with care.

In contrast to ELBW births, all survivors of a particular weight or gestation range who leave intensive care units can be identified. Thus, prevalence values for morbidities may be calculated as proportions of total survivors but interpretation, for example, of trends for change over time requires the same caution as interpretation of the mortality data. Calculated as a proportion of ELBW survivors aged 3 years or less, the prevalence of major cerebral morbidity also seems to have been more or less constant in the past 15 years, at around 20% (10) (Table 4).

These rates are higher than those usually reported, in the same period, for heavier infants weighing 1,001 - 1,500 g. Table 5 shows the major morbidity rates according to birthweight reported in two recent population studies (6,12) and those calculated from our own study at UCH.

Table 4: Major cerebral morbidity aged 1 - 3 years calculated as % of survivors from pooled world literature data (2)

Years	Studies n	Survivors n	Morbidity# %
1965 - 1974	4	102	21
1975 - 1979	8	207	18
1980 - 1982	11	594	20
1979 - 1983	UCH*	63	16

major cerebral morbidity; * University College Hospital London

Table 5: Major cerebral morbidity aged 1 - 3 years according to birthweight, calculated as a % of survivors from recent national, regional and single centre studies

Studies	501 - 1,000 g Morbidity#		1,001 - 1,500 g Morbidity#	
	n	%	n	%
Merseyside 1979 - 1981	46	15	276	11
Netherlands 1983	130	8	640	6
UCH* 1979 - 1983	63	16	166	10

major cerebral morbidity; * University College Hospital London

A few studies have examined major cerebral morbidity according to birthweight subgroups below 1,000 g, including two that were population-based. Table 6 shows the results according to 100 g increments from 501 g to 1,000 g from one population study (8), and above and below 750 g in a population study (12) as well as the results from a regional study (7) and from our own unit at UCH. It, however, must be emphasised that the UCH study is not a population-based one.

In all four examples the prevalence of major cerebral morbidity did not increase as birthweight decreased. These calculations were based on total cerebral morbidity. The prevalence of retinopathy of prematurity was not specifically mentioned in the reports, although if it caused blindness in appreciably larger numbers in the smallest infants, this would be expected to affect the overall total of morbidity. This question will be discussed in detail in another presentation.

Table 6: Major cerebral morbidity aged 1 - 3 years according to birthweight below 1,000 g, calculated as a % of survivors

Birth-weight g	Hamilton (8) 1977 - 1980 Morbidity[#] n	%	Netherlands (12) 1983 Morbidity[#] n	%	Melbourne (7) 1977 - 1980 Morbidity[#] n	%	UCH[*] 1979 - 1983 Morbidity[#] n	%
1,000 - 901	52	17						
900 - 801	43	9	112	9	48	25	51	14
800 - 701	50	14						
700 - 601	60	10						
600 - 501	1	0	18	0	11	27	12	17

[#] major cerebral morbidity; [*] University College Hospital London

Older children (4 years and more)

There is very little information about ELBW children as they reach school age. The few studies that have been reported include only small numbers of children and tend to be incomplete with appreciable proportions of children lost to follow up. In several instances the children were born before full intensive care was generally available to ELBW infants, making their relevance to current survivors dubious (for review see 9).

This review will consider just two studies, from Lausanne (2) and our own from UCH (3). In both studies assessments of cognitive and higher motor functioning were carried out, including for example, tests of visuo-motor integration skills. No major impairments were found in the 32 ELBW infants studied by the Lausanne group at age 1 - 7 years. Our own study concerned the 63 ELBW children without serious congenital malformations from a large cohort of very preterm (< 33 weeks) infants born between 1979 and 1983. Among these 63 children, the proportion with major impairments was 16% at 12 months of corrected age and 22% at 4 years. The difference was due almost entirely to the emergence of cognitive deficits. The mean McCarthy General Cognitive Index (IQ) was 92% (range 50 - 125%). This may be compared to a value of 100% for the whole group of infants born before 33 weeks of gestation (11). 15 of these 63 ELBW children have been re-examined at 8 years; no additional major impairments were found. The mean IQ (WISC-R) of 13 of these 15 children was 100% (range 75 - 121%).

25% of the 63 ELBW children in our study had minor impairments at age 4 years, in addition to the 22% who had major impairments. It should be noted that almost half (6/16) of these children with minor impairments also had minor neuromotor impairments at 1 year of age. The proportion of affected ELBW children at age 4 years was larger than that (13%) found in the heavier children weighing more than 1,000 g at birth (3). No additional minor impairments were found in the 15 children examined at 8 years. In fact, 2 children judged to have minor impairments at 4 years on the grounds of low cognitive scores were functioning within the normal range (IQs of 94% and 95%) at 8 years and were considered to be making normal progress by both their parents and their teachers.

In the Lausanne study (2) also, 25% of the ELBW children had minor impairments including clumsiness, language disorders and myopia. The age of assessment of these children ranged from 1 to 7 years so the proportion of 25% with minor impairments is likely to be a minimum estimate. Although the proportions of minor impairments were the same in the two studies, the problems which the children had were different. For example, we found only 1 child with a specific language disorder. By contrast, children were usually categorised as having minor impairments on the basis of low scores in all aspects of the tests of cognitive functioning. Other minor impairments found in our study included poor fine motor skills and visual problems such as amblyopia. From the type of minor impairments that they found, the Lausanne group (5) suggested that ELBW children may be at particular risk of early school failure. While such predictions are reasonable there are as yet, insufficient reports of ELBW children old enough to include documented cases of school failure from which to draw firm conclusions.

Conclusions

Although the available data concerning the ELBW infant are both limited and difficult to interpret, two definite trends may be detected:

1. In ELBW infants who weigh less than 1,000 g, both mortality and the prevalence of cerebral morbidity are greater than in heavier very low birthweight (VLBW) infants who weigh 1,000 - 1,500 g. In particular, older ELBW children tend to have an excess of minor impairments when compared with their peers who were heavier at birth. These minor impairments are usually of cognitive functioning or other skills which are likely to affect learning and school performance. However, no evidence of an excess of school failure among ELBW children has yet been reported.
2. Among ELBW infants who weigh less than 1,000 g, mortality increases as birthweight decreases below 1,000 g but cerebral morbidity does not. The prevalence of morbidity remains constant. This may be the result of selection biases, but it is a consistent finding in all studies where the data are analysed. Thus, among ELBW survivors, the long term prognosis for an infant weighing 550 g is the same as it is for one weighing 995 g.