CHAPTER 11

Our Conclusions in Context

We do not know of any other study which has been specifically designed to compare the effects of being born too soon (regardless of birthweight) with those of being born too small (and not too soon). Nor do we know of any other study which has used such a wide range of tests of performance to assess any group of children at all comparable to ours (*e.g.* 'low birthweight'), or used multivariate analysis to identify the effects of such a comprehensive range of associated factors, so as to avoid drawing false conclusions about the effects of the factors of primary interest. But there are several studies whose data include material sufficiently relevant to ours, and clearly we must try to place our findings in context with those studies before we draw any final conclusions about their meaning. In this context we are not specifically interested in studies whose interest was confined to the incidence of frank neurological or intellectual handicap (*e.g.* Lubchenco *et al.* 1972, 1974; Davies and Tizard 1975).

The British population studied by McDonald (1967) was defined in terms of a birthweight of 4lbs (1800g) or less. The population was divided in relation to gestational age, those whose birthweight was more than two standard deviations below the mean being called 'small for dates'. The main concern of the study was with grosser types of defect, but the children's IQ was measured by the Stanford Binet test, and, after allowing for social class, was found to be (insignificantly) lower in the small-for-dates than in the remainder of this very low-birthweight population. Surprisingly, the IQ of this remainder (in the absence of severe defects) "did not differ appreciably from that of the general population" (of Britain). This study is, as far as we know, unique in finding no intellectual impairment at all in babies of such low birthweight, but there is a suggestion of relative impairment among the children who were light-for-dates.

The Baltimore population studied by Wiener (1970) had a full range of birthweights, and was assessed between the ages of eight and ten years by a battery of psychological tests (including intelligence), the results of which were subjected to analysis of covariance, making allowance for the effects of socio-economic factors and of race. But the biological significance of the findings has been obscured by the method of analysis and presentation, which illustrates the drawbacks of an outdated nomenclature (and associated methods of thought). The population was first divided into two main groups—those with a birthweight below 2501g, and the remainder ("full term"). Each of these groups was then subdivided into three subgroups according to whether the gestation was of "short", "modal" or "long" duration—but before doing this the low-birthweight group had been subdivided into three horizontal weight subgroups (<1500g, 1500 to 1999 and 2000 to 2500g), and different definitions of the gestational-age intervals were applied within each of the weight subgroups. The results for the low-birthweight and the full-term children were presented separately,

and two conclusions were derived from them:—
(1) "gestational age does not result in differential impairment (of intelligence, etc.) within a given low-birthweight group" and
(2) "infants whose birthweights were greater than 2500g and whose mothers had reported a shortened gestational age had significantly lower IQ scores . . . . . These findings were unexpected".

Fortunately, it is possible to re-interpret the published results in terms of the ideas concerning intra-uterine growth which we have adopted—and they appear to agree remarkably closely with our own results. The children in four of the six main subgroups have mean scores significantly below those of the remaining two—whose birthweights were more than 2500g after "modal" or "long" gestations (38 to 40 or 40 weeks). The children in the four groups with the depressed scores would appear to have been either light-for-dates or of short gestation (or both), and where the use of the terms seems justified by the information supplied, the very light-for-dates had lower scores than the rather light-for-dates. The similarity of these findings to those of our own study is all the more interesting because the Wechsler type of intelligence test was used in both investigations.

The investigation reported by Eaves *et al.* (1970) focussed upon children with a birthweight of less than 2041g (4½ lbs), dividing them into various birthweight and gestational-age groups, but included controls with a birthweight of more than 2500g (5½lbs). Allowance was made for some social factors, and IQ was measured by a Wechsler test at the age of 6½ years. There was certainly an excess of severe mental subnormality among the low-birthweight children who were light-for-dates compared with those who were "truly premature", but in those who could be fully tested, social factors were of overriding importance and those whose low birthweight fell between the 25th and 75th centiles scored rather better than those below the 10th centile. Because the index cases were primarily defined by a horizontal birthweight criterion, these findings are difficult to interpret in biological terms since those below the lower centiles were by definition of greater gestational age, and vice versa. Similar problems of interpretation apply to the contrary findings of Drillien (1970), who reported higher scores among her low-birthweight children aged 10 to 12 years if their weight fell below the 10th centile than above the 25th.

Davie *et al.* (1972) divided their population in terms of biologically meaningful criteria, and found an excess of children with handicaps, educational backwardness and poor copying-design scores in both their short-gestation and their light-for-dates groups. They did not directly compare the two abnormalities of intra-uterine growth, but they did illustrate the effects of social class and ordinal position.

The children studied by Francis-Williams and Davies (1974) all weighed 1500g or less and the small-for-dates group's mean gestational age was 31 to 32 days longer than that of the appropriate-for-dates group, yet the latter group scored significantly better in IQ tests. There is also some suggestion that the latter group benefitted from improved management of food intake and environmental temperature, but the differences observed were not statistically significant.

In attempting to reach a final conclusion concerning the main question which we set out to answer, therefore, our findings appear to be supported by the few published results which we can interpret in a relevant way (bearing in mind that none of the investigations from which they are derived had been specifically designed to answer any of the questions to which we have addressed ourselves). The tests of cognitive function used by Wiener (1970) were the same as some of ours, and he allowed for some of the associated factors which we have grouped under 'family factors'. His results were published in sufficient detail so that we can re-interpret them (see p. 107) as showing that children aged eight to ten years who were of short gestation (regardless of birthweight), or light-for-dates (but not of short gestation) scored significantly less well than other children, and that those who were very light-for-dates scored less well than the rather light-for-dates of similar gestational age. In other words, his results are similar to ours. Davie *et al.* (1972) assessed the quality of the children in their large study population by relatively crude criteria, but showed clearly that there was a uniform tendency to poor performance at the age of seven years among those who were either of short gestation or light-for-dates. In so far as they can be compared, therefore, their findings also agree with ours. But in neither study can we directly compare the effects of the two abnormalities of intra-uterine growth and it is not possible to identify groups of children who suffered a comparable degree of shortening of gestation, or impairment of intra-uterine growth, respectively, in any of these studies to which we have referred.

Better Too Soon Than Too Small

We therefore have to base our conclusions concerning this key question on our results. We showed in Chapter 8 that, after allowing for the effects of six associated factors in a two-stage analysis of covariance, there was only one significant individual difference between our two extreme groups—the weight increment between birth and seven years in the very light-for-dates group was significantly less than in the short-gestation group (Table 8.3, p. 69). In two other instances (height at seven years, and Bender-Gestalt test of visuo-motor errors) the short-gestation group's advantage was on the verge of conventional statistical significance. But the fact that the direction of the difference was the same in all 13 instances, the short-gestation group being at an advantage in every case, was taken as the basis for a further analysis in which the over-all difference in the performance of this group was shown to be significantly superior to that of the very light-for-dates group. Even among children whose postnatal care was of the standard available in this City in 1960 to 1962, those who were born too soon were at a meaningful advantage in their later development in comparison with those who were born too small.

We have suggested in our text (Chapter 8) that better neonatal provision of food and warmth (as they could now expect to receive) might have increased the advantage of the children in the short-gestation group: but we acknowledge that our own information concerning these factors is too scanty and unreliable to be of use to us in supporting this suggestion directly. We have therefore looked for support in the literature. Davies and Davis (1970) demonstrated that such provision did indeed improve the subsequent head-growth of very small babies whose very low birthweight was appropriate for their dates (so that their gestational age was significantly less than the small-for-dates, upon whose head-growth the better neonatal care had no effect). However, Francis-Williams and Davies (1974) were not able to show a comparable effect upon the IQ of the same children when tested at about six years of age, and Davies and Tizard (1975) were unable to confirm that the disappearance of spastic diplegia after 1964 was attributable to this particular aspect of improved care. Lubchenco *et al.* (1974), however, showed a reduction in neurological handicaps among children of very low birthweight who had received intravenous fluid and calories after birth, and such evidence as exists all seems to point in the same direction—that it is advantageous to babies of short gestation to be kept on as good a plane of nutrition as is consistent with safety during the period when they should still have been receiving adequate nutrition across the placenta. It also seems possible that, perhaps because they have already experienced too long a period of malnutrition before birth, but at a comparable gestational age, some of the light-for-dates babies are incapable of benefitting to the same extent.

Two studies of the later effects of the (postnatal) 'pure' starvation associated with hypertrophic pyloric stenosis seem relevant here. Berglund and Rabo (1973) used data obtained in 180 boys at the time of enlistment for military service to assess the possible later effects of postnatal starvation associated with 'medical' management of the condition. They found a significant impairment of height and fertility, and reductions in IQ and adaptability scores which were not quite statistically significant. Klein *et al.* (1975) compared 50 survivors of surgically treated pyloric stenosis with 44 siblings and 50 matched controls, testing them between five and 14 years of age. They found no impairment of growth, but significant impairment of learning abilities in the index cases. These studies of the effects of neonatal starvation due to a cause which is not associated with social deprivation lend strong support to the possibility of long-term and irreversible organic consequences, such as we have postulated in the case of both our short-gestation and very light-for-dates groups.

Effects of Associated Biological Factors

Since we have demonstrated that some of the associated biological, clinical and family-environmental factors produce much greater effects upon the later performance of the children in all the three groups whose results we have illustrated in Figures 11 to 14, we would also like to look at these findings in the context of the literature.

Of the factors which we have classified as 'biological', the mother's age should perhaps have been classified as part of the 'family factors'. Illsley (1967) clearly showed that both increasing age of the mother and lower birth rank have a favourable effect upon the intelligence-test scores of children aged seven years. In each case this effect is more or less the opposite of the known effect upon perinatal mortality (which is presumably a direct 'biological' effect) and is presumably due to environmental consequences of the specified factor. Our findings agree with those of Illsley (1967) with respect to both these associated factors, and we know of no other published report of the effects of maternal age. Similar findings with regard to the effects of ordinal position in the family have been reported by Davie *et al.* (1972).

The effect of the mother's height upon the child's birthweight is so well recognised that no specific reference to the literature is necessary, and it is generally agreed that the mechanism concerned is environmental (through the size of the uterus) rather than genetic. However, genetic effect upon the child's growth is well marked by the age of three years (Hewitt 1957-8), and is the likely explanation of the relationship between the mother's height and the child's height and weight illustrated in Figure 11. We know of no published report which can throw light on the relationship between mother's height and the verbal and performance IQ and language quotient of the short-gestation group, after allowing for the effects of birthweight, which we have illustrated in Figure 12.

The mother's smoking during pregnancy was reported by Davie *et al.* (1972) in their national sample of children to have an adverse effect upon reading attainment and social adjustment after allowing for birthweight and a number of other associated factors (but these did not include any specific assessment of the mother's personality). There is no other published evidence that we know of which could help to explain our isolated positive finding of the adverse effect of maternal smoking upon the short-gestation children's behaviour as reported by the teacher, even after allowing for the child's birthweight and 16 other associated factors, including several types of assessment of the mother's personality. It is tempting to suppose that this effect in our short gestation-group, and the effect upon social adjustment in their whole population reported by Davie *et al.* (1972), may both be explained by aspects of the smoking mothers' personalities which have not been separately identified and allowed for in either study.

The fact that the child's sex has a wide range of effects upon test results, as shown in Figures 11 and 13, is not surprising, but the direction of the differences reported in the earlier chapters—where the boys in the random sample are shown to have very significantly higher scores than the girls both for full-scale IQ and language quotient (Tables 3.15, p. 35 and 3.16, p. 35) and lower behaviour abnormality scores than the girls at five and seven years (Table 4.8, p. 45)—is unexpected. The results reported in the literature are not consistent and differ according to the precise type of performance being assessed. Davie *et al.* (1972), for instance, found that their girls' reading attainment and social adjustment in school were clearly superior, although boys were slightly superior in arithmetic. In the total Newcastle population from which our children were derived, the girls scored better than the boys in assessments of general intelligence and behaviour (Neligan *et al.* 1974). This whole subject has been reviewed in detail by Hutt (1972). The girls in the total population were also reported to be less vulnerable than the boys to later adverse effects of breech delivery. It is tempting to suppose that there is a similar, presumably organic, basis for our own finding that the abnormalities of intra-uterine growth which we have studied clearly produce more adverse effects upon the boys' than upon the girls' intelligence and language quotients (Tables 3.15, p. 35 and 3.16, p. 35), their behaviour and psychiatric abnormality scores (Tables 4.8, p. 45 and 4.9, p. 46), their neurological abnormality scores (Table 5.3, p. 53), and their growth (Table 6.3, p. 59). Such findings would be consistent with the well-known differences in perinatal mortality rates, in favour of girls, which suggest that they are more resistant than boys to the lethal effects of adverse biological factors (for reasons which, as far as we know, are unexplained). They are also consistent with the evidence that the growth of girls can recover more satisfactorily than that of boys from the deleterious effects of transient adverse factors (Tanner 1970).

We have already discussed the significance of the finding that birthweight has important effects in all three groups of children and have reviewed the relevant literature in the Introduction.

Effects of Associated Clinical Factors

Our positive findings, summarised in Figure 14, show a logical pattern. In the random sample, where they were relatively rare (see Table 2.2, p. 12), antepartum haemorrhage, breech delivery or delay in onset of regular respiration produce no important adverse effect upon later performance. But in the abnormal groups, where they were relatively common (breech delivery in both, antepartum haemorrhage in the short-gestation and delay in regular respiration in the very light-for-dates) they produce important effects over a quite wide range of functions (see Figures 12 and 13). We know of no comparable data in the literature showing the effects of these clinical factors upon different groups of children, but there is evidence of a relationship between bleeding during pregnancy and later mental subnormality (Drillien 1965), and of relationships between breech delivery, delay in onset of regular respirations, low birthweight and low IQ in our whole Newcastle population (Neligan *et al.* 1974). Evidence of this kind gives us clues about ways in which improvements in perinatal clinical management can help to improve the quality of the survivors of the neonatal period.

However, the type of information which is of particular importance to those faced with the clinical decisions which are our main interest is concerned with the quantity and the quality of the survivors among babies of very low birthweight, for whom modern methods of perinatal care are available. Much alarm was caused by the findings of Drillien (1967) that percentage improvements in the survival of babies weighing less than 1362g (3 lbs) had been achieved at the cost of an even greater increase in the proportion of severely handicapped survivors. By contrast, more recent reports from units which have pioneered and developed the highest standards of modern techniques of neonatal care make it clear that the striking improvements in the percentage survival of these very small babies born during the past five to ten years have been accompanied by equally striking improvements in the quality of the survivors (Rawlings *et al.* 1971, Francis-Williams and Davies 1974, Davies and Tizard 1975). The technical advances that have produced these changes include improvements in nutritional and metabolic support, as well as the more dramatic aids to respiratory function, but the babies who appear most likely to benefit are those whose very low birthweight is due to shortening of the period of gestation. For those who have to make the clinical decisions, the implications of these advances appear to weight the scales in favour of active intervention to prevent prolonged malnutrition, either before or after birth.

Effects of Associated Family Factors

The factors which we have grouped under this heading are all reflections of the environment in which the children developed between birth and the age at which we tested them, and their effects upon the children's performance seem in principle more likely to have been produced by psychological than by biological mechanisms (see Introduction, p. xiii). There is also the possibility that some of the effects may be indirect—for instance if a factor modifies a child's cognitive function this in turn may modify his behaviour or his performance in a neurological test such as gesture imitation (p. 50).

Our main finding under this heading, that this group of 'family' factors has had a greater effect upon the over-all performance of our children than any other group (Fig. 14), includes the observation that in our representative sample the effects of gestational age and birthweight are so small as to appear trivial by comparison (Fig. 11). However, this does nothing to diminish the importance of the main finding of our whole investigation, namely that in the 10 per cent of our population of children who were born too soon or too small, but more significantly in the latter group, the abnormality of intra-uterine growth itself has produced widespread and non-specific impairment of performance at school age (Chapter 9).

Within the group of 'family' factors, the findings in the random sample are of particular interest because they show that the effects of social class (derived from the father's occupation) are virtually eliminated when compared with the effects of a number of factors derived from assessments of the mother at different stages of the child's life (Fig. 11 and 14). This is really what we might have expected, since the father's occupation cannot possibly have any direct effect upon his child's development, and its great value as demonstrated in a large number of previous studies (see Birch *et al.* 1970) must lie in its effectiveness as an indicator of the environmental factors which do produce direct effects. The most important of these in our random sample is the quality of the mother's care of her child as assessed by the City's health visitors when the child was three years old. We know of no exactly comparable observations, but several authors have recorded the effect of their assessment of the mother upon the child's performance. Wortis and Freedman (1963) noted a positive correlation between the mother's "growth fostering" score and both the motor and social development of young negro children. Drillien (1964) noted relationships between the mother's "efficiency" and her children's growth and illnesses, and between her "handling" of them and their behaviour. Douglas (1964) found that the level of "maternal care" in his national sample of British children "had a greater influence than social class on their chances of being put into the upper streams" at school. Miller *et al.* (1974) found that their Newcastle mothers' "standard of child care" produced an effect upon their children's test scores which was about equal to that of their father's occupation. Neligan *et al.* (1974) reported a similar finding in the total population from which our groups of children were drawn.

The importance of the child's ordinal position in the family in affecting his performance at school age is presumably a reflection of the fact that the child with fewer older siblings is likely to receive more individual attention and encouragement from his parents, and so to perform better. This observation has been confirmed repeatedly (*e.g.* by Illsley 1967 and by Davie *et al.* 1972), although the latter suggest that the total number of children in the family is even more important—and this seems likely. The other 'family factors' which we have listed (Fig. 14) do not seem to have been assessed in this way previously in relation to groups of children comparable with ours.

When we come to consider the differences between the three groups of children (summarised in Fig. 14) we do not know of any published work which can throw light on the problems mentioned in the previous chapter concerning the relative importance of biological, clinical and family factors, and the relative importance of social class within the latter group. However, there are a number of previous suggestions that babies of low birthweight are particularly vulnerable to the effects of adverse social factors (Wortis and Freedman 1965, Drillien 1970, Eaves *et al.* 1970). Certainly this seems to be the case in our very light-for-dates group.

Final Conclusions

On the basis of all the evidence now available to us, we feel that we can confidently answer the question which was the main focus of our investigation: both children who are born too soon and those who are born too small show some impairment of performance when they reach school age, but those born too small are at a greater disadvantage and appear less likely to benefit from recent advances in neonatal paediatric care. The adverse effects attributable to the disorders of intra-uterine growth cover a wide range of measures of performance, and show a similar (but not identical) pattern in our two extreme abnormal groups—which between them account for some 10 per cent of our child population. It seems likely that when a child is born too soon, but with an otherwise normal intra-uterine growth pattern, he will continue to develop normally if he can be protected from the dangerous neonatal complications of pre-term birth, and can be kept on an adequate plane of nutrition to continue his normal pattern of growth. However, when a child's growth pattern has already been seriously impaired by the time he is born, his whole subsequent development may be significantly impaired in a manner which cannot be remedied by improvements in postnatal care (although the situation may be aggravated if the neonatal complications of being light-for-dates are allowed to develop). These conclusions are of cardinal practical importance for the obstetricians and paediatricians who have to reach the relevant decisions about clinical policies.

Of more general interest is the mounting evidence that, when the absolute and relative importance of associated factors are assessed, those we have called 'biological' and 'clinical' are completely overshadowed by the group of environmental factors in a representative population of children. This group we have called 'family' factors because of the overwhelming importance of various attributes of the mother, and the structure of the family as a whole. Biological and clinical factors clearly affect the later performance of children in our two extreme abnormal groups to a greater extent than in our general population. Much further work is necessary to elucidate these complex inter-relationships.