CHAPTER 10

Conclusions Directly Based on Our Findings

We have carried out a very comprehensive and detailed programme of tests at the ages of five, six and seven years in three main groups of children, selected to represent approximately the 5 per cent of our population who were born before reaching a gestational age of 255 days (born too soon), the 10 per cent with the lowest birthweights related to a gestational age of 255 days or more (born too small), and the remainder of the population (random control). For most purposes we have subdivided those who were born too small into two groups—those whose birthweights fell between the 5th and 10th centiles (rather light-for-dates), and those below the 5th centile (very light-for-dates). In the latter subgroup, therefore, there was approximately the same degree of impairment of the rate of intra-uterine growth as there was of its duration in the short-gestation group. But in neither group was the over-all abnormality of intra-uterine growth at all severe, as illustrated by the fact that the mean birthweight of the babies in each group was about 2400g—and between them they were representative of 10 per cent of the children born to mothers living in our City between 1st June 1961 and 31st May 1962. Either through our own observations, or through the data made available to us by the Newcastle Survey of Child Development (Neligan *et al.* 1974), we have accumulated a great deal of information concerning biological, clinical and family (associated) factors which might have modified the performance of our groups of children, and so either exaggerated or suppressed the true effects of the abnormalities of intra-uterine growth in which we were primarily interested.

We have carried out a series of simple statistical analyses to identify any such effects in the areas of psychometric, behavioural, temperamental and neurological assessment, and of physical growth, and to identify the modifying effects of two associated factors—the child's sex and social class (Chapters 3 to 6). We have then carried out two much more complex series of analyses (by covariance and by multiple regression), firstly to identify the effects legitimately attributable to the abnormalities of intra-uterine growth, after allowing for those accounted for by 15 associated factors, and secondly to identify the relative importance of the individual effects of 18 or 19 associated factors.

Conclusions

As a result of these procedures, we have been able to reach a number of firm conclusions.

(1) *Both the short-gestation and the very light-for-dates groups of children perform significantly less well than those in the random sample* over the whole range of measures of performance which we employed at the ages of five, six and seven years. This is the straightforward conclusion suggested by the simple analyses in

Chapters 3 to 6, in which we allowed for the effects of no associated factors, or only those of sex and social class separately. The more complex analyses reported in Chapter 8 do not significantly alter this conclusion. Even when allowance is made for the combined modifying effects of 15 associated factors, reduced for the final analysis to the six most important (see Table 8.2, p. 66), the relationships between the groups' scores are unchanged except that the behaviour of the very light-for-dates group, as reported by the teacher, is no longer significantly worse than that of the control group.

(2) *The suggestion that (prenatal) impairment of growth may be directly responsible for the later impairment of performance is strongly supported by our findings.* Wherever we can assess it, the degree of intra-uterine growth impairment (reflected in depression of the birthweight after correcting for gestational age) is proportional to the degree of impairment of later performance. This is a striking feature of the simpler analyses in Chapters 3 to 6, in which the scores of the children in the rather light-for-dates group are almost all intermediate between those of the very light-for-dates and the random controls, not only in terms of the over-all scores but also in the individual subtests. This relationship persists almost intact after allowing for the six associated factors in Chapter 8. This is all the more surprising since the difference between the mean birthweights of the children in our rather and very light-for-dates groups is only some 300g (the difference between 2701g and 2397g—see Table 2.1, p. 10). A further piece of supporting evidence is the finding, reported in Chapter 9 and illustrated most clearly in Figure 14, that the birthweight makes an important contribution to the over-all performance scores of the children, not only in the random sample and short-gestation groups (in which the full range of weights is represented) but also in the very light-for-dates group (in which the range is restricted to the lowest 5 per cent of birthweights at gestational ages of more than 255 days). Such a constant relationship is most simply explained as causal: but our data do not rule out the alternative possibility of a common cause, such as intra-uterine infection, giving rise to the impairment both of intra-uterine growth and of later performance, at least in some children, However, it is most unlikely that such mechanisms have played any significant and unsuspected part in groups of children selected by criteria which are so very far from extreme, and it is also scarcely conceivable that such a common cause could produce such a constant relationship between two of its effects.

(3) *The over-all performance of the children in the very light-for-dates group is significantly worse than the short-gestation group* when directly compared after allowing for the effects of six associated factors. Only in the weight increment between birth and the age of seven years is the difference for a single measure of performance highly significant, as shown in Table 8.3, p. 69, but the difference between the two scores is uniformly favourable to the short-gestation group in every one of the 13 comparisons shown in that Table, and this difference very nearly reaches conventional levels of statistical significance in the case of height at the age of seven years and the Bender-Gestalt test. When the 13 scores for each group are dichotomized and added together, the difference between the two groups is highly significant. The conclusion is inescapable that, in the population which we have studied, impairment of the nett rate of intra-uterine growth has had a direct adverse effect upon the later per-

formance of our children which is greater than the effect of a comparable degree of shortening of its true duration. The results of our analyses point directly to this conclusion, in spite of the fact that we have not allowed for the effects of certain factors of our selection procedure which must have introduced a bias in favour of the very light-for-dates group (see p. 85).

Our own data do not enable us to say with any confidence whether a more modern approach to the early feeding of the smaller babies in our population would have increased the later advantage of those who were born too soon, by protecting them from a period of relative postnatal malnutrition. The possibility that their later impaired performance is due to a mechanism of this kind, corresponding to the intra-uterine malnutrition of the very light-for-dates group, is suggested by the remarkably similar pattern of impairment in the two extreme abnormal groups (as illustrated by the Figures in Chapter 3, for instance). Although we lack detailed information concerning the calorie intake of these babies, very few had any intravenous supplementation of what they were offered by gastric tube or by bottle, the volume of which was judged by their clinical ability to tolerate it; and we have reported a trend towards delay in regaining birthweight in the short-gestation group (at the end of Chapter 6). However, the results for weight increment between birth and the age of seven years suggest that any postnatal malnutrition experienced by the short-gestation group was not sufficiently severe to deflect their growth from its normal path, whereas the intra-uterine malnutrition of the very light-for-dates group was (see Tables 8.2, p. 66 and 8.3, p. 69).

(4) *The effects of some of the associated factors which we have investigated appear to be of much greater magnitude than those of the variations in intra-uterine growth which are our main concern,* and their relative importance tends to differ in the different groups (compare magnitude of coefficients of individual determination for birthweight or gestational age, illustrated in Figures 11 to 14, with those for other factors).

In the simpler analyses reported in Chapters 3 to 6, the only associated factors whose effects we have investigated are the child's sex and social class of origin as derived from the father's occupation. In the psychometric test results, the boys are consistently superior to the girls but appear more vulnerable to the adverse effects of abnormalities of intra-uterine growth (Chapter 3); this greater vulnerability is more definite in the results of the tests of temperament and behaviour (Chapter 4), the neurological abnormality scores (Chapter 5) and the measurements of physical growth (Chapter 6). The modifying effects of social class are much more obvious in the psychometric test results than in the other measures of performance, although the children in social classes, I, II and III have better scores than those in classes IV and V in all our three main groups of children in almost all the comparisons reported in Chapters 3 to 6.

However, the most important results are those reported in Chapters 8 and 9, because only there have we used techniques which enable us to take account of the well-recognised tendency to 'clustering' of favourable or unfavourable factors. Numerous examples of this tendency are apparent in Tables 2.2 (p. 12), 2.3 (p. 12) and 2.4 (p. 13); there is an excess of adverse biological, clinical and environmental factors in those groups of children whose intra-uterine growth was impaired, either in duration or in rate. The conclusions which we have alluded to so far could well be false, in the sense that the adverse effects which we have attributed to the disturbances of intra-uterine growth could well have been caused, in whole or in part, by these clusters of associated adverse factors. But in Chapters 8 and 9 we have used techniques of analysis which enable us to identify and allow for the effects of 15 or more associated factors simultaneously: the conclusions which we are able to draw from these results are therefore comparatively free of this risk of distortion by associated factors.

(5) *The impaired performance of the children in the two extreme abnormal groups persists with very little modification after the effects of six biological, clinical and environmental associated factors have been allowed for* (Table 8.2, p. 66). In the results of the first stage of the analysis of covariance (Table 8.1, p. 65) there are one or two surprises when we compare the relative importance of the different adverse factors, but we will be returning to this point when we discuss the conclusions to be drawn from the results of the multiple regression analysis (see section (6) below).

The conclusions which we can draw from the results of the second stage of the analysis of covariance (see Tables 8.2 and 8.3) have already been mentioned briefly in sections (1) to (3) above. We have restated them here because they are of such overriding importance. Unless we can allow for the effects of adverse associated factors we cannot justifiably claim that the impaired later performance of groups of children such as those which we have studied is due directly to the effects of their abnormal intra-uterine or neonatal growth experience. When the 'clustering' of adverse factors is so marked—as it is well recognised to be in such groups of children (as illustrated in the abnormal groups as compared with the controls in Tables 2.2, 2.3 and 2.4)—only multivariate techniques of analysis can enable us to make the necessary allowances, and analysis of covariance seems to us to be the most appropriate for this particular purpose. The fact that making due allowance for the effects of 15 associated factors has made very little difference to our results, and none to our main conclusions, is beside the point: this result could not have been predicted before the analysis was carried out (and in fact a different result seemed more likely, in view of the different proportions of presumably adverse factors in the different groups). However, it must be be borne in mind that even the long list of confusing factors which we have allowed for is by no means comprehensive, and accounts for less than half the variance in most tests of performance (see Figures 11 to 13).

(6) *The associated factors which we have grouped under the heading of 'family factors' are of overriding importance in our randon sample and very light-for-dates group: biological and clinical factors combine to produce effects of almost equal importance in the short-gestation group.* This general conclusion is based upon the summed results illustrated in Figure 14, and takes no account of the detailed differences which can be seen in Figures 11 to 13. Those Figures make it clear that nearly all the larger summed effects of individual independent variables shown in Figure 14 are made up of a number of effects fairly widely spread over the full range of dependent variables, so that the general conclusion seems justified. Where the sum is made up of much more limited effects (as in the case of the mother's

height in the random sample, whose effects are confined to the two dependent variables by which the child's physical growth was measured) we can try to draw the reader's attention to this fact.

The most important conclusion, which is also new as far as we know, is that when we include other environmental factors which are more directly related to the child's upbringing, they may largely (or even entirely, in the case of our random sample) supplant the demonstrable effects of the child's occupational social class of origin. The most important environmental factor in two of our groups is the quality of the mother's care of her child: and we assume that the reason why the social-class factor assumes greater importance in the very light-for-dates group than in the other two groups must be that factors which we have not identified are producing a greater effect in this particular group. Whatever the explanation, however, it is clear that the relative importance of the 'family factors' as a whole, as an influence upon the children's subsequent performance, is even greater in the very light-for-dates group than in the random sample.

The 'biological factors' clearly come next in over-all importance. We have earlier pointed out that in the random sample the effect of mother's height is confined to the child's growth, and this draws to our notice the potential importance of heredity—a factor which has not been specifically identified either in our data or our results. The findings in the short-gestation group, where the mother's height has a very large effect indeed upon the results of the tests of cognitive function (Fig. 12), are much more difficult to explain, since the effect of birthweight has been allowed for separately.

The fact that birthweight has been assessed separately presumably explains the almost complete absence of harmful effects attributable to the mother's smoking during pregnancy (Fig. 14). Since the only important effect we have identified is upon the child's behaviour as reported by the teacher in the short-gestation group (Fig. 12), it seems likely that this is itself an indirect effect of some personality trait of the smoking mothers which we have failed to identify separately.

These and other conclusions which we would like to draw concerning individual biological and clinical factors seem best kept for further discussion in the next chapter, where they can be placed in the context of the relevant literature. But before we leave this summary of the conclusions which we think can be based upon our own findings, we think it only right to draw the reader's attention to the fact that the sum of the effects of the 18 or 19 associated factors which we have allowed for (shown as the multiple R^2 in Figures 11 to 13) account for only a proportion of the total variance of the scores of individual measures of performance; and this proportion is more than half in only three instances (the first three tests of performance in Figure 12), and less than a quarter in many instances. The rest of the variance must have been accounted for by other factors which we have not separately identified (of which a genetic factor is an obvious example, to which we have drawn attention above), together with unavoidable errors of measurement.