AN APPROACH TO THE AETIOLOGY OF PREMATURITY.

A Study of the Obstetric Histories of Mothers of Premature Babies.

With an Appendix on the Progress and Development of Premature Children.

A Thesis Submitted for the Degree of

Doctor of Medicine

By

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September,1957.

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This thesis was prepared during the tenure of a Lectureship in the Department of Public Health and Social Medicine, University of Glasgow.

C O N T E N T S.

I N T R O D U C T I O N

The steady decline in the infant mortality rate since the end of last century has been satisfactory in most respects, but it has thrown into relief the importance of prematurity as a cause, or contributing cause, of infant deaths. This has stimulated interest in the aetiology of prematurity, but in spite of this quickened interest little real progress has been made towards a fuller understanding of the causes of prematurity.

The problem is, in some ways, made more difficult by the definition of prematurity which is now in general use. According to this definition, any infant who weighs at birth 5½ lbs. (2,500 G.) or less is classified as premature. This has certain advantages, but it has to be recognised that whereas the word 'premature' implies a measurement of time, the accepted definition substitutes a measurement of weight, and so-called premature children are in fact children of low birth weight. Now it is true that most children with birth weights of 5½ lbs. or less have been born prematurely, but quite a substantial proportion of them are simply full-time children of low birth weight. This must be borne in mind in considering any aspect of prematurity, and it is particularly important in considering aetiology.

The most firmly established view on the aetiology of prematurity is that in about half of all cases the cause is unknown/

unknown, and the other half are caused by such conditions as multiple pregnancy, toxaemia of pregnancy and ante-partum haemorrhage. Obviously an explanation of prematurity which accounts for only half of all cases is not satisfactory and further, many of the conditions which are said to cause prematurity are themselves of unknown aetiology and the ways in which they cause prematurity are not clearly established.

In recent years a number of large-scale surveys have been undertaken to investigate in detail the circumstances in which premature births take place. As a result of these surveys it has been shown that prematurity is more likely to occur in certain circumstances than in others, and a large number of factors such as maternal age, parity, social class, and legitimacy have been implicated in the aetiology of prematurity. While some of these surveys have added considerably to our knowledge of the subject, the large number of factors involved and the difficulty of reconciling these factors with any single hypothesis has prevented them from bringing us much nearer to a full understanding of the causes of prematurity.

In nearly all these works, however, one aspect of the problem has been ignored, or has received only passing mention. This is the possibility that a mother who has had a premature child on one occasion might have had other premature children on earlier occasions, or might have other premature children/

children later. Attention has usually been concentrated on one particular pregnancy which resulted in a premature child, and the circumstances associated with that pregnancy have been studied without much regard to the previous or subsequent obstetric history. The present investigation was designed mainly to explore this aspect of the problem, while taking account of the factors which are already known to play some part in the aetiology of prematurity.

As well as being concerned with prematurity because of its association with infant deaths, increasing attention has also been paid in recent years to the progress of those premature children who survive. At one time it was thought that a large proportion of them became physical and mental defectives and although more careful investigation has shown that this extremely pessimistic view is not justified the fact remains that in certain respects the progress and development of premature children is not as satisfactory as that of mature children. The present investigation provided an opportunity to obtain information about various aspects of the health and development of premature children up to the age of 5 years, and this information has been presented as an appendix.

PART I. - REVIEW OF LITERATURE.

THE PROBLEM OF PREMATURITY

In recent years interest in prematurity has increased considerably. There are good reasons for this. The principal one is that the neo-natal mortality among premature infants is much higher than among full-time infants, and as the most striking improvement in infant mortality in recent years has been in the 1 - 12 months age group, the importance of neo-natal mortality has become relatively greater. As so much of the neo-natal mortality is associated with prematurity, it can be said that "one of the major causes of infant deaths, though perhaps ill-defined pathologically, is prematurity" (British Medical Journal, Leading Article,1956). Indeed, in U.S.A.Baumgartner (1951) has stated that prematurity is the eighth most important cause of death among persons of all ages.

The changing pattern in infant mortality is illustrated in Table 1 (see p.148) derived from the Annual Report of the Registrar General for Scotland for the year 1955. This shows clearly that while infant mortality as a whole has improved, the improvement has been mainly during the later part of the first year of life and in particular there has been very little improvement in the death rate in the first week of life. Consequently the neo-natal component of infant mortality is now a greater proportion of the whole than formerly. For example, among/

among males the total infant mortality rate (i.e. deaths under 1 year of age per 1000 live births) during the period 1931-35 was 90.3 and the neo-natal mortality rate (i.e.deaths under 1 month of age per 1000 live births) was 30.9, so that deaths during the first month of life accounted for 34.2% of infant deaths. During the period 1951-55 the total infant mortality rate was 36.8 per 1000 and the neo-natal mortality rate was 23.5 per 1000 so that during this period neo-natal deaths accounted for 63.9% of infant deaths. Similarly, among females, deaths in the first month of life accounted for 46.0% of infant deaths during the period 1931-35 and 61.8% during the period 1951-55. This experience accords with that in other countries in which the infant mortality rate has fallen rapidly in recent years (Baird,1945a).

Many authorities can be cited to show the very strong association between neo-natal mortality and prematurity. In "Maternity in Great Britain" (1948), a survey undertaken by a Joint Committee of the Royal College of Obstetricians and Gynaecologists and the Population Investigation Committee, it is stated that 52% of neo-natal deaths occur in premature children, and this fact raises the neo-natal death rate from 12 per 1000 for all single mature births to 24 per 1000 for all single births, mature and premature combined. Expressed in another way (Douglas,1950), premature babies, who account for only 6% of total live births, are responsible for 52% of neo-natal deaths. Remarkably similar figures have been re-

ported/

reported from Chicago by Potter and Adair (1939).

Information about the incidence of prematurity in Scotland is not available, but since 1953 the Local Authorities in England and Wales have asked that the birth weights of all children be given when the births are notified to the Medical Officer of Health. From the information so obtained it is possible to publish annually, in the Annual Report of the Chief Medical Officer of the Ministry of Health, the incidence of prematurity in England and Wales, together with additional information about the number of such children who die within the first twenty-eight days. From this source figures are available for the three years 1953-54-55. The incidence in actual numbers and per hundred live births is shown in Table 2. Two further facts can be derived from these Reports: first, that more than half the neo-natal deaths in England and Wales in the last few years have been among premature babies (Table 3) and second, that about half the still-births (Table 4) have also been among premature babies. The present investigation is concerned with premature live births only, and therefore further discussion of the problem of stillbirths among premature babies will be omitted.

The certified causes of these neo-natal deaths need not concern us deeply for present purposes. In many cases the certified cause does not indicate the true underlying pathology, but merely indicates the mode of dying (Stewart,Webb and/

and Hewitt,1955). The number of deaths certified as due to prematurity alone has declined rapidly in recent years, but this is undoubtedly due to an attempt at greater accuracy in certification, and does not reflect accurately the actual decline in deaths among premature children. A few years ago it was stated that prematurity was the most frequent single stated cause of death in the first month of life, but it was recognized that the records greatly understated the importance of prematurity because usually, if it was possible to assign any other cause, a death would not be ascribed to prematurity ("Infant Mortality in Scotland," H.M.S.O.1943).

Nevertheless, it seems clear (Thomson,1955) that the deaths in which no other cause can be found are associated with poor social class, small stature of the mother and poor maternal general health and nutrition.

Of the remaining deaths, for which a cause other than prematurity is found, McNeil (1942) lists, in order of importance, asphyxia, infection, haemorrhage (mostly intracranial) and congenital abnormality, in that order. However, while the causes of death are of some interest, the primary and most important fact is that premature babies have an extremely high neo-natal death rate and whatever the exact mechanism of death it is reasonable to assume that the majority of those who died would not have died if they had not been premature.

The outstanding feature of this excessive neo-natal death rate among premature babies is its inverse relationship to the birth weight. This has been shown repeatedly. One of the earlier workers to point this out was Capper (1928), and Drillien (1947) showed that the early survival rate rises rapidly with increasing birth weight up to the group weighing 5¾ lbs. - 6 lbs. and then remains fairly steady at 97% until a birth weight of 10 lbs. is reached, when it begins to fall again. Douglas (1950) also showed this relationship very clearly and pointed out that there is a sharp difference between the mortality of babies of 4½ lbs. - 5½ lbs. and those of 5½ lbs. - 6½ lbs., the ratio being 4:1.

Statistics in the Annual Reports of the Chief Medical Officer of the Ministry of Health enable us to study the relationship between birth weight and neo-natal mortality from year to year, although this of course refers only to England and Wales. The figures for the three years 1953-54-55 are shown in Table 5 and the relationship between birth weight and neo-natal mortality is quite clear.

At the same time other factors influence survival during the neo-natal period. For instance, length of gestation, apart from its influence on birth weight, appears to have an independent effect on survival rates (Steiner and Pomerance, 1950). These authors also showed that premature babies born of/

of multiple births had lower mortality rates than single-born babies of similar birth weight, and the same finding was reported in this country by Record, Gibson and McKeown (1952). It appears then that birth weight is not the sole determinant of survival during the neo-natal period, but it is the main one. This touches, however, on the difficult question of the relationship between birth weight and maturity, of which more will be said later.

The principal effect of prematurity on the infant mortality rate takes place in the neo-natal period, but it does not end there. Douglas and Mogford (1953b) showed that the excessive mortality among premature babies continued at a lessening rate up to the age of 4½ years, and that this later excess was due to bronchitis and pneumonia, congenital abnormality and nephritis. This was carried a stage further by Alm (1953), who was able to follow up a group of male premature babies and a group of controls in Sweden to the age of 45. He compared mortality rates for 5-year periods up to the age of 45 and found that, while there was a significantly higher mortality rate among the prematures in the first five years, thereafter there was no significant difference at each subsequent five-year period, although if all the deaths after the age of 5 years were considered together there was a tendency to a higher mortality rate among the prematures.

Enough has been said to show the considerable effect of prematurity/

prematurity on the infant mortality rate and it is hardly necessary to emphasize that it is now the greatest single challenge in attempting to reduce infant mortality.

A further reason why prematurity merits study is the question of the fate of the survivors. This has excited interest for some time and the practical aspect of the problem is summed up in the title of one paper on the subject - "Is the Premature Baby Worth Saving?" (Crosse,1954). Interest in the fate of surviving premature children is enhanced by the fact that with improved methods of caring for prematures it is possible to increase the survival rates. For instance, in Chicago (Hess and Lundeen,1941), as a result of a thorough city-wide scheme the early mortality was reduced from 42.6% in 1935 to 20.8% in 1940, and similar results were reported from the University of Michigan Hospital (Barnes and Willson,1942). For the United States as a whole the number of neo-natal deaths due to prematurity fell from 13.8 per 1000 in 1939 to 10.8 per 1000 in 1948 (Children's Bureau Statistical Series,No.6). There is no evidence of any reduction in the incidence of prematurity and it seems most likely that the reduced mortality was due to improved care. It is therefore apparent that the number of premature children who survive can be increased by improved care and it is important to know whether this will lead to any untoward consequences at a later date.

Up/

Up till fairly recently a very gloomy view was taken of the fate of premature babies who survived. In 1928 Capper declared that "the immature infant becomes the backward school child and is a potential psychopathic or neuropathic patient and even a potential candidate for the homes for imbeciles and idiots", while as recently as 1940 Sir Robert Hutchison suggested that a large proportion of premature children became physical and mental defectives and he doubted whether they were worth saving. These views were undoubtedly excessively pessimistic, but the fact remains that premature babies as a group do not do as well as full-time ones.

The differences can be considered most conveniently under three headings - morbidity, physical development and mental development.

There is no doubt that in the first few years of life the morbidity among premature children exceeds that among full-time children. In one investigation (Drillien,1948) it was found that there was a high incidence of naso-pharyngeal infections and in the first year of life the pneumonia rate among the prematures was six times as high as the rate among the children in the control group. This excess of respiratory infections was confirmed in a later investigation (Douglas and Mogford,1953b) which showed that it took the form of bronchitis and pneumonia and although affecting mainly/

mainly the first year of life it persisted into the second year. It was particularly noted in those of low birth weight and in males. The same workers also showed that the amount of hospital care required by premature children in their first 4¼ years of life was definitely excessive for those whose birth weights had been less than 5 lbs. and the hospital care required by males exceeded that required by females. This agrees with the findings of Asher (1946) that males are less able to withstand the effects of immaturity than females. When the total time spent in hospital was considered it was found that premature children required 11% of all hospital care for children under the age of two years.

It is naturally difficult to obtain information on the later morbidity of premature children, but some indirect light is shed on this by the work of Alm (1953). Using the standard of fitness for compulsory military service in Sweden to compare a group of premature males with a group of normal males, he found that the proportion who were able to fulfil the standards for military service was significantly higher in the normal group. Unfortunately he was not able to give the reasons for rejection and this referred only to males. Some of the rejections may have been due to inadequate height or weight, but it is not unlikely that many of them were associated with ill-health.

Then the rather special problem of retrolental fibroplasia is closely linked with prematurity. There is an association/

association between its occurrence and the use of oxygen therapy and it is therefore found most commonly in children of very low birth weight. Terry (1945) discussed the condition as it affects U.S.A. He found that there is an incidence of 600 new cases per annum and this accounts for one-third of all blindness in children. Others have confirmed that this is a major cause of blindness in children in U.S.A. (Corsa, Pugh, Ingalls and Gordon,1952). In this country the position was investigated recently in England and Wales (Annual Report of the Chief Medical Officer of the Ministry of Health for 1953) and it was found that out of 6925 premature babies with birth weights of not more than 4 lbs. 6 oz. and surviving not less than two months, 127 cases of retro-lental fibroplasia occurred, an incidence of 1.8%. More recently (Potter,1954) it was shown that 51.2% of blindness in the Sunshine Homes (84 cases out of 164) was due to retro-lental fibroplasia so that the condition is responsible for a substantial amount of blindness among children in this country also. While careful control of the use of oxygen reduces the incidence (Forrester, Jefferson and Naunton,1954) it cannot be denied that retro-lental fibroplasia is a serious complication of prematurity.

Finally, so far as morbidity is concerned, there is a higher incidence of congenital defects among surviving premature babies than among surviving full-time babies. In a Birmingham/

Birmingham survey (Crosse,1954), 1% of the prematures and 0.5% of the controls suffered from defects which were definitely congenital in origin and 0.8% of the prematures and 0.4% of the controls from defects which might have been either congenital or acquired. In the same survey the surviving premature children showed an increased susceptibility to complications resulting from birth injury, kernicterus and, of course, retro-lental fibroplasia.

In its physical development there is no doubt that the premature child lags behind the mature one, at least in its early years and possibly indefinitely. It was shown in Vienna (Capper,1928) that premature children remained subnormal in height up to the age of 15, and particularly up to the age of 7, and it appears to have been accepted at this time that if a premature child survived its first few difficult years it eventually made up its deficiencies in height and weight (Hess, Mohr and Barthelme,1934). Later Illingworth (1939) compared 150 children whose birth weights had been 5½ lbs. or less with 150 children whose birth weights had been 8½ lbs. or more and showed that at varying ages up to 12 years, 86% of the premature children were underweight, compared with only 34% of the controls, and he also found that the differences tended to increase with age rather than decrease. The samples, however, were not random, as they were taken from patients attending a hospital out-patient department.

In 1946 Asher suggested that premature babies gain at the/

the same rate as normal babies so that they never regain the weight handicap with which they started. A similar suggestion had been advanced many years earlier by Schwarz and Kohn (1921).

However, since then there has been a large survey in this country (Douglas and Mogford,1953a) in which the children were followed up to the age of 4 years and matched with carefully selected controls. This survey showed that at the age of 4 years 36% of premature children had made up their weight handicaps and 44% ~~of~~ their height handicaps, but it also showed that the smallest children were often the most successful in making up their handicaps and there appeared to be no relation between success in making up the handicaps and length of gestation, or the presence or absence of complications during pregnancy. Also, children in better homes did not make up their handicaps any more quickly. The most important factors in determining whether normal height and weight were reached appeared to be the height and weight of the mother - if these were normal the child tended to make up its handicaps. Other recent work shows that a child's gain in weight in its first few years is independent of its birth weight (Lowe and Gibson,1953).

Information about physical development of premature children at later ages is scanty, but Hess (1953) reported a follow-up of 445 premature infants born in Chicago between 1922 and 1952/

1952 whose birth weights had been less than 1250 G. He was able to account for all but 30 of them. It was known that 45 had died, but of the remaining 370 survivors, 200 were reported to be physically average or better than average, and a further 116 showed only slight deviations from normal.

We are therefore left to conclude that the average height and weight of prematurely born children are less than those of mature children, at least for some years, but the factors which determine this retardation are not clearly known - the height and weight of the mother play some part and the birth weight apparently plays no significant part at all.

When we come to consider mental development we are on more difficult ground. It is only recently that a clear picture has begun to emerge, although as long ago as 1862 Little discussed the relationship between premature birth and some types of mental and physical defect. Several papers published in the earlier years of the present century (Capper,1928) were based on work in Central Europe and took a very gloomy view of the mental development of premature children, but much of this work was done against a poor economic background, with low follow-up rates, and with no controls.

Later work tended to be much more optimistic, but one of the major difficulties has been to distinguish those children who are suffering from the effects of intra-cranial haemorrhage and neurological damage so that it can be determined whether

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or not, apart from this factor, prematurity alone has any effect on intelligence. Alm (1953) showed that there was a significantly greater incidence of mental deficiency, epilepsy and spastic paralysis among the premature children in his investigation than among the normal ones, and he attributed this to intracranial haemorrhage. A similar finding emerged from an investigation of the birth weights of children attending different types of school in this country (Asher and Roberts, 1949). It was found that educationally sub-normal children and mental defectives had a lower mean birth weight than the children at normal schools. This was due to excess of low birth weights among them and not to an alteration in the frequency distribution as a whole. This excess, however, was only such as to indicate that 10% of children with very low birth weights (less than 3 lbs. 4 oz. in boys and 2 lbs. 12 oz. in girls) are defective. It seems clear, therefore, that premature children, particularly of very low birth weight, contain more than their share of children showing severe mental handicap. Much of this is associated with birth injury or developmental abnormality and the question still remains whether, in the absence of such defects, there is any relationship between prematurity and intelligence.

The earlier evidence on this point is conflicting. Mohr and Barthelme (1930), using intelligence tests, concluded that the premature children gave average results, compared with controls, but others (Asher, 1946) thought that prematurity was probably/

probably associated with a low Intelligence Quotient (I.Q.). In a more recent survey (Douglas,1956) the intelligence of prematures and matched controls was tested at the age of 8 years. Three tests were used - mechanical reading,vocabulary and picture intelligence. In each of the tests the premature children made scores slightly but significantly lower than their controls.

It thus seems that premature children contain a higher proportion of mental defectives than would be expected, and the evidence suggests that the intelligence of the non-defective children is lower than average.

Importance of Reducing Incidence of Prematurity

From all that has been said it is apparent that if the incidence of prematurity could be reduced we could expect a marked reduction in the neo-natal mortality rate, a lesser reduction in the post-natal mortality rate, a reduction in early childhood morbidity, particularly from lower respiratory infections, with concomitant reduction in the amount of hospital care required, and some reduction in the amount of mental deficiency due to neurological damage. There would probably be no difference in the incidence of congenital abnormalities,as these may stand in causal relationship to the prematurity which accompanies them, and the effect on height and weight and intelligence is problematical. We may accept - and probably must accept - that these are all lower in premature children than in full-time children, but until we have some knowledge of/

of why this is so we can hardly estimate the effect of reducing the incidence of prematurity on these measurements.

Nevertheless enough has been said to show that a fall in the incidence of prematurity would be an improvement of the first magnitude in the field of child welfare.

Before the problem of preventing prematurity can be tackled thoroughly a great deal remains to be learned about the causes of prematurity and before going on to consider this something must first be said about the definition of prematurity.

DEFINITION OF PREMATURITY

As Ellis and Lawley (1951) have aptly pointed out, "In the last analysis prematurity represents an abnormally short period of intra-uterine life." In spite of this, estimations of the length of gestation have seldom figured in attempts to define prematurity. The reasons for this are not hard to find. A satisfactory definition of prematurity is required for three main purposes which overlap one another to some extent. The first is clinical, to determine whether or not particular infants should be regarded as premature for treatment purposes; the second is administrative, so that statistical information can be collected and related to various circumstances connected with the prematurity, as is done in England and Wales at present; and the third is for research purposes, so that various investigations into causes and effects of/

of prematurity will deal with the same things. It is obviously desirable that, if possible, the same definition should be used for all three purposes, and it is essential that it should be a simple objective measurement which can be made with the minimum of disturbance to the child, and should not require the use of judgment or expression of opinion.

In spite of its drawbacks birth weight comes nearest to satisfying these requirements. Birth weight has been used as the basis for definitions of prematurity since the 1860s (Alm, 1953) and it was in 1919 that Ylppo first suggested that an infant weighing less than 2,500 G. at birth should be regarded as premature. This gradually came to be accepted generally and was adopted by the American Academy of Pediatrics in 1935 when the following resolution was passed (Hess and Lundeen, 1941):-

> "For statistical purposes, and comparison of results of care, a uniform standard for diagnosis of prematurity is important. A premature infant is one who weighs 2,500 G. or less at birth (not on admission) regardless of the period of gestation. All live-born premature infants should be included, evidence of life being heart beating or breathing."

This definition was recommended by the Committee on Hygiene of the League of Nations in 1937, and was accepted in 1938 by the British Paediatric Association, with the concurrence of other interested bodies, but with the reservation that it was impossible to define prematurity satisfactorily and the definition was only accepted to facilitate comparisons between different/

different published works (British Medical Journal, Leading Article,1938). In this country 5½ lbs. is taken as the equivalent of 2,500 G. It is now recognized by the World Health Organization (Technical Report Series No.27,1950). As it has been so widely accepted no alteration should be considered without good reason, but this should not prevent us from realising its faults.

The principal fault obviously is that we are using a standard, not of prematurity, but of low birth weight. It is perfectly true that the majority of children with birth weights of 5½ lbs. or less are premature, but we are including a proportion of children who are full-time but of low birth weight, and similarly excluding others who are premature but whose birth weights are over 5½ lbs. It is the presence of these small but not immature children in any group investigated as premature that may confuse the findings and obscure our search for the real social relationships of true immature birth (Miller,1955). The small mature infants of low birth weight may account for about 30% - 40% of the so-called premature children in a sample being investigated (Baird,1945b; Douglas,1950; McKeown and Gibson, 1951a; Martin,1954).

At the same time we must recognize that this criticism would apply to a greater or lesser extent to any objective measurement or measurements. It has been suggested that three standards should be used (Ellis and Lawley,1951) - viz. birth weight,/

weight, crown rump length and head circumference - and that only infants satisfying at least two of these standards should be regarded as premature. If this is done the error will undoubtedly be reduced but although this would be an advantage it is difficult to see how these additional measurements could be made accurately on a large scale. Martin (1954), after discussing the defects of the weight definition of prematurity, mentioned that his sample was re-analysed using various different criteria of prematurity without making any difference in the relations between prematurity and the sociological variables with which he was concerned. It would therefore appear that, in the absence of reliable means of estimating the gestation period there is no acceptable alternative to the birth weight definition.

There are, however, certain other important criticisms. No account is taken of the fact that the average birth weight of female children is 4 oz. less than that of males, and an excess of female children will inevitably be classed as premature for this reason alone. In fact the incidence of prematurity is higher among females than among males (Anderson, Brown and Lyon,1943; Drillien, 1947; "Maternity in Great Britain",1948) and it has been suggested that a different weight standard should be used, according to sex. This suggestion, however, has not been adopted. Then again, no attempt is made to differentiate between single-born children and the products of multiple births - and the prognosis in the latter case suggests/

suggests that these babies are more mature than their birth weights would indicate. Further, the average birth weight in different races varies and no allowance is made for this, although it has been suggested that different standards should be used (Anderson, Brown and Lyon,1943; Salber and Bradshaw, 1951; Taback,1951; Llewellyn-Jones,1955). However, as far as the present survey is concerned the usual standard of 5½ lbs. or less has been used, but it will be seen that anomalies do arise.

Another defect of the definition, which has been pointed out by several authorities, is that there is no lower weight limit. This means that we must include as premature babies a varying number of very small live-born children whose chances of survival are negligible and whose gestation periods may have been very short (McNeil,1942), and the inclusion of these 'living abortions' does not give a proper conception of the problem. McNeil used a lower limit of 1½ lbs., but Henderson (1945) suggested that foetuses with a birth weight of less than 2¾ lbs., which is the average weight at 28 weeks, should be regarded as previable and the fact that they might be born alive should be ignored. Later Henderson (1946) showed that out of 118 babies with birth weights of less than 2¾ lbs. born in the Simpson Memorial Pavilion in Edinburgh in 6 years, only 4 survived. Several workers, mainly American, have in fact set their own lower limits (Murphy and Bowman,1932; Dana,1946).

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The effect of this is to exclude from the category of live births a number of very small children who will almost certaintly die soon after birth, and hence the reported neo-natal death rate will be reduced. While this would appear better, it makes little difference to the community whether a potential citizen is lost as a late 'living abortion' or as an early neo-natal death, and the net result would be to obscure still further the true extent of pregnancy wastage.

In conclusion we are bound to concede that the birth weight definition of prematurity is the best available and it will be used in this survey, but the anomalies and defects must be borne in mind.

AETIOLOGY

The aetiology of prematurity is generally obscure. In a few individual cases the cause may be fairly obvious, in other cases the prematurity is associated with some condition which might have a bearing on its aetiology, but the fact remains that in about one-third or one-half of all cases of prematurity the cause is unknown (Diddle and Plass,1942; Sandifer,1944; Baird,1945b). Bearing in mind that the definition is based on birth weight it is obvious that premature infants are a mixed collection and Crosse (1954) describes them as "a very heterogenous group resulting from such vastly different causes as congenital malformation, plural birth, trauma, pre-natal complications and small parents; and as a group they include an/

an excess of females and babies of parents in poor financial circumstances." It would therefore seem unreasonable to expect to find a single cause, or even a few causes of prematurity, but the number of factors which have been invoked as causes or contributing causes of prematurity is bewilderingly large. They are listed by Conway (1951) as "the age of the mother, her height, social class and state of nutrition, the amount of work done in pregnancy, the adequacy of antenatal care, illegitimacy, parity, birth spacing, multiple pregnancies, toxaemias of pregnancy, placenta praevia, hydramnios, the induction of premature labour, version of a breech presentation, local pelvic diseases, infections in pregnancy and constitutional diseases." There is, of course, evidence to show that each of these factors plays a part in the aetiology of prematurity, although some of them occur so infrequently that their contribution to the total problem of prematurity must be very small.

In the cases for which a medical cause can be found "toxaemia and twin pregnancy are the two most important factors, followed by ante-partum haemorrhage, placenta praevia, foetal deformity and various maternal conditions" (Ellis,1950). This summarizes the findings of most authorities.

While it is usual to describe multiple pregnancy as a cause of prematurity, it is not correct to regard prematurity, by birth weight definition, as an abnormal condition in multiple pregnancies./

pregnancies. McKeown and Record (1952) showed that the mean birth weight of single-born children in Birmingham was 7.43 lbs., the mean birth weight of twins 5.27 lbs., and the mean birth weights of triplets and quadruplets even less. It therefore follows that the majority of twins, triplets and quadruplets are bound to be classified as premature. McKeown and Record (1952) showed that there are two reasons for the low birth weights of these children. One is the earlier onset of labour which is common in multiple pregnancies, and the other is a retardation in the rate of foetal growth in multiple pregnancies after a certain stage of gestation. Thus low birth weight among children born of multiple pregnancies can be regarded as a normal characteristic of these children and although it means that most of them are classified as premature, it would be wrong to regard this as an abnormality. It is therefore proposed to limit further consideration of the aetiology of prematurity to its occurrence among single-born children.

This leaves us with toxaemia as the main known 'cause' of prematurity. Even this, however, is hardly satisfactory. In the first place, in some of these cases the child is prematurely born because labour has been induced, and although premature labour may very well have occurred in any case, this introduces an element of doubt. Apart from this, it has to be admitted that a cause and effect relationship between toxaemia/

toxaemia and prematurity has not been clearly established and we are dealing in fact with an association which has been demonstrated statistically - that prematurity occurs more often in the presence of toxaemia than in its absence. All that can properly be deduced from this is that there is some association between the two. Although there is no evidence to indicate the nature of this association, there is adequate evidence to show that it exists. One group of workers in Cincinnati (Brown, Lyon and Anderson,1946a) showed that 11% of infants of toxaemic white mothers were premature, compared with a prematurity rate of 8.7% in a series of mothers who showed no evidence of toxaemia during pregnancy. Further, when they divided their toxaemic cases into three grades of varying severity it was found that the more severe the toxaemia the higher the prematurity rate. In this country Drillien (1947) concluded that "a mother with a complication of pregnancy is more likely to give birth to a small baby than a mother without complications." Conway (1951) showed that in primiparous women at University College Hospital over a seven-year period the over-all prematurity rate was 5.9%, but among those who had a systolic blood pressure above 150 mm. of mercury it was 18.6% and he considered that a systolic blood pressure of more than 150 mm. was one of the most important factors influencing the prematurity rate. That there is an association between toxaemia and prematurity is/

is therefore fairly clear, although its nature has yet to be demonstrated.

Essential hypertension may also be associated with premature labour but the true extent of its contribution is uncertain because of the probability that it is confused with pre-eclampsia, which might supervene in any case. As only 1% of pregnancies occur in women who have a blood-pressure of 140/90 or over, either before they become pregnant or in the first trimester (Carey,1955) the contribution from essential hypertension is probably small.

Accidental haemorrhage has been cited as a cause of prematurity. Baird (1945a) stated that accidental haemorrhage without toxaemia was responsible for 3.9% of premature labours in his series of cases, and Morison (1952) states that accidental haemorrhage of doubtful origin accounts for less than 10% of premature labours. Conway (1951) found that ante-partum haemorrhage occurred significantly more often in association with premature births than with full-time births. Here also the exact relationship with prematurity is obscure, as the haemorrhage may be either a manifestation of toxaemia or may simply be the expression of the mechanism of abortion (Donald, 1955).

This brings us to another association with prematurity, which has not yet received much prominence, but which is of considerable aetiological interest. Turnbull and Walker (1956) found that in a series of booked hospital cases in Aberdeen the incidence/

incidence of prematurity among the patients who had a history of bleeding before the twenty-eighth week was 20.9%, compared with 6.5% for all booked cases. A similar finding was reported in a series of cases in U.S.A. (Brown, Lyon and Anderson,1946b) in which a prematurity rate of 14% was recorded among the women with a history of mild uterine bleeding, compared with 7% among the women with no uterine bleeding during pregnancy. With more severe bleeding the prematurity rate was higher. Naturally this raises the question of whether an early instability of the placental attachment, which might have resulted in abortion in the early part of pregnancy, can at a later stage result in premature labour. This involves an aetiological relationship between abortion and prematurity and more will be said of this shortly.

An uncertain proportion of premature births, stated to be 2.3% (Morison,1952), are due to placenta praevia, and other conditions such as hydramnios, foetal abnormality and syphilis add a small quota. Bearing in mind the incidence of these conditions it is unlikely that their contribution is numerically important.

Acute illness in the mother has always been cited as a cause of prematurity, and taking acute illnesses together (syphilis, gonorrhoea, pneumonia, acute respiratory tuberculosis, contagious diseases, and rheumatic heart disease), Conway (1951) found that the incidence of all these conditions combined was/

was greater in the mothers of premature children than in the mothers in the control series ($P < 0.05$) and there can be no doubt that on occasion they are responsible for prematurity. Drillien (1947) notes similar findings about acute and chronic diseases in the mother, and then goes on to say " ... but the effect is not so well established, nor anything like so important quantitatively as that observed with complications of pregnancy itself such as toxaemia and ante-partum haemorrhage." Sandifer (1944) made a similar statement - "The vast majority of the cases with some definite cause had an obstetric cause, non-obstetric associated conditions being rare - syphilis, accident or injury, and heart disease - the incidence of these conditions being no higher in cases of premature birth than in mature birth." We can therefore conclude with some degree of certainty that of the known 'causes' of prematurity toxaemic complications of pregnancy are the most important.

However unsatisfactory this may seem, it is even less satisfactory that these known 'causes' account for only about half the incidence of prematurity. This state of affairs is probably the main reason why a number of large-scale surveys concerned with prematurity have been undertaken in recent years. These surveys have been concerned mainly with the social background to prematurity and, while they provide a mass of useful data, they require very careful interpretation. The general conclusions of these investigations have been summarized/

summarized by Miller (1955) - "All workers agree that the incidence of all prematurity is least at the top and greatest at the bottom of the social scale; but it is more doubtful if it shows a steady increase down the social scale. The highest incidence is in the wives of semi-skilled and unskilled workers, while the wives of 'artisan' workers have a prematurity experience nearer that of the 'middle class'. All are agreed that premature infants are more likely to be born to the youngest and eldest mothers, whereas the least incidence is from 21 - 30 years. 'Unexplained' cases of prematurity show a steeper social gradient than all prematurity: that is, premature birth in upper social groups is more often associated with a recognised medical cause."

It has been shown repeatedly that the prematurity rate is higher in the lower social classes. In Aberdeen (Baird, 1945b) it was found that the incidence was 8.38% in hospital cases, 7.4% in the domiciliary midwifery scheme, 5% among nursing home patients and 4% among those able to afford specialist attention. Further, it was shown that the cause was unknown in 51.9% of the hospital cases, compared with only three out of twenty (15.0%) having specialist care.

Later it was found, in a national survey ("Maternity in Great Britain",1948), that the prematurity rate among the wives of professional and salaried workers was 4.3%, compared with 6.5% among the wives of black-coated wage earners, and 6.6% among/

among the wives of manual workers, while for illegitimate births it was 9.7%. Similar social class differences were found in a further large-scale survey in England (Martin,1954). More recently the same social class variations in the incidence of prematurity have been reported from Edinburgh (Drillien and Richmond,1956), where it was also shown that the prematurity rate among illegitimate children was 8.67% compared with a rate of 6.39% among legitimate children. These findings are not limited to this country and similar results have been reported from U.S.A. (Rider,Taback and Knobloch,1955). There is therefore no doubt that there is an association between social class and prematurity.

The reason for this association is not quite clear, but one possible explanation has been put forward by Baird and Illsley (1953) - "While there is a marked relationship between social class and prematurity this relationship is by no means straightforward, for there exists an equally strong association with (maternal) height within each social class. While we have as yet insufficient cases to understand fully the effects of age, the indications are that the prematurity rate among primiparae is highest among those who are under 20 or over 30 years of age. The rate is particularly high among the very young in Social Classes IV and V, a group which contains a high proportion of small women of poor physical grade. This fact, rather than extreme youth, is probably responsible for the high prematurity rate." In an earlier work Baird (1945b)/

(1945b) had shown that the mothers who had their babies in hospital (i.e. the lower social classes) were smaller than the mothers who had their babies in nursing homes and it was suggested that this was due to poorer nutrition in childhood. Martin (1954) feels that this 'stunted growth' theory has not been adequately proved, and that the possibility of an interpretation in genetic terms of these social class differences cannot be lightly dismissed.

However, whatever determines the social class differences in maternal height, we are still left with the interesting question of why there should be a relationship between maternal height and prematurity, and it is important, of course, to remember that by prematurity we really mean low birth weight. The question therefore is why should small mothers have small babies, and what, in the absence of abnormalities, determines birth weight?

It is well enough known that adult height is largely determined genetically and that both parents make an equal contribution. There has perhaps been too ready a tendency to assume that all human measurements, including birth weight, are determined in this way, but it has recently been shown (Tanner,Healy,Lockhart,MacKenzie and Whitehouse,1956) that although the growth curve from conception onwards is apparently genetically determined, the child maybe deflected very considerably from this curve towards the end of intra-uterine life by/

by the characteristics (both genetic and environmental) of the mother. Thus the mother makes two distinct contributions to the growth curve of her child - first, the straightforward genetic contribution which is the counterpart of the contribution of the father, and second, a modifying contribution during the later part of pregnancy which results in the child's birth weight being related to her own stature, and is quite distinct from her genetic influence on the child's ultimate height and weight. This was demonstrated in a rather dramatic fashion by experimental matings between Shire horses and Shetland ponies (Walton and Hammond,1938), and the conclusion drawn from these experiments is of considerable interest:-

> "Although the offspring differ genetically from their respective maternal parents, as is shown by subsequent growth, at birth the size of the foetus is approximately that to which the mother would normally give birth. The degree of maternal regulation of size in these experiments is very marked. It is however not absolutely complete; the cross-breds from the large mother are perhaps not quite so large at birth as normal Shires, and the limbs are relatively shorter. In the small mothers regulation appears to be more complete."

The last sentence is particularly interesting. Although it may be unwise to assume that what happens in one species will happen in another, it seems likely that the same maternal regulation of foetal size occurs in man. Thomson (1951) found that among full-time infants the average birth weights increased with increasing maternal height.

It is therefore quite reasonable to expect that small mothers/

mothers will have small babies, and if we use a birth weight definition of prematurity it is inevitable that small mothers will have a higher prematurity rate than the taller mothers.

The possibility has already been mentioned that poor maternal nutrition during childhood, by stunting the mother's growth may be associated with later prematurity. It has also been suggested that maternal nutrition during pregnancy plays some part in the determination of prematurity and this, of course, might account to some extent for the social class differences. The evidence on this point is conflicting. On three occasions in different places (Ebbs, Scott,Tisdall,Moyle and Bell,1942; People's League of Health,1942; Cameron and Graham,1944) it was reported that the prematurity rate could be reduced in groups of mothers both by giving them advice on their diets during pregnancy and by giving them various dietary supplements. Dean (1950) analysed German data for the years 1937-48 and showed that there was a sharp fall in the average birth weight of children born in 1945, when the war-time food shortage was at its worst. This would, of course, influence the prematurity rate. On the other hand, Speert, Graff and Graff (1951) compared the dietary history, haematology and blood chemistry of 70 mothers of live-born premature infants with 67 control mothers of term infants and found no evidence to support the theory that nutritional deficiency is a common cause of premature labour. Scrimshaw (1950) has emphasized the need for care/

care in interpreting the evidence from experiments of this sort and has pointed to the dangers in inferring nutritional status from dietary intake. It seems impossible to draw any firm conclusion about the influence of diet during pregnancy on the occurrence of prematurity, although most of the evidence suggests that it does play a part.

It is however certain that the incidence of prematurity varies with parity. In "Maternity in Great Britain" (1948) it was stated that the prematurity rate was 8% in first pregnancies and 5.3% for subsequent pregnancies. Similar figures are given in other studies (Karn,Lang-Brown,MacKenzie and Penrose,1951; Drillien and Richmond,1956). High birth rank also appears to be associated with a high prematurity rate. There is a paucity of information about this, but Drillien and Richmond (1956) showed that in social classes III,IV and V the prematurity rate for sixth and subsequent births was nearly 18%.

Maternal age also influences the chance of the occurrence of prematurity. This was expressed very clearly by Douglas (1950) when he said that the risk of prematurity is least in primigravidae between the ages of 25 and 35 and highest below the age of 20. For later births the risk is least between the ages of 26 and 35, but is also affected by birth spacing, being least when this is between two years and six years and particularly high when the birth interval is less than two years. The influence of age has been corroborated by other workers/

workers (Conway,1951; Martin,1954; Drillien and Richmond, 1956). In one publication (Drillien,1947) it is stated that the prematurity rate in primiparous mothers rises with increasing maternal age, but this was based on hospital patients which may explain the different conclusion in this instance.

The influence of birth spacing has been mentioned. Another related finding, which has been mentioned in recent work (Martin,1954; Drillien and Richmond,1956) is that there appears to be a relationship between delay in conception and prematurity, suggesting that subfertile mothers are more likely to have premature babies.

Two other factors of less certain influence have been discussed in relation to prematurity - ante-natal care and work during pregnancy. In "Maternity in Great Britain" (1948) it was suggested that premature births were least frequent among those receiving adequate ante-natal care, where adequacy was assessed on the number of attendances and the stage of pregnancy at which ante-natal care began. When the material was analysed further (Douglas,1950) it was found that, when the date of commencing ante-natal care was related to the expected date of delivery, the mothers of premature babies came under supervision at approximately the same stage of pregnancy as did the mothers of the 'controls', but it was still felt that, judging by the adequacy of the records kept, ante-natal supervision of the mothers of premature children had not been as thorough/

thorough as that of the mothers of the mature children. Following this point up in a later enquiry, Martin (1954) found that, as far as primiparous mothers were concerned, the shorter gestation period accounted for the reduced duration of ante-natal care, but he was not able to take the quality of care into account. In U.S.A.Eastman (1947) reported that the prematurity rate among those of his patients who had no ante-natal care, or poor ante-natal care, was 24.9%, whereas in women who had good care it was only 7.8%. He dismissed racial factors, emergencies, and differences in instruction regarding diet and hygiene, as explanations of this difference. He thought that "A more rational explanation would seem to lie in the general characteristics, as a class, of those patients who habitually neglect to receive medical attention, such as pre-natal care, though it is known to be available. They are, in the main, the shiftless and improvident of our population notorious to every social worker; and their habits of living in general are doubtless just as ill-managed as their habits in relation to pre-natal care." If there is a relationship between ante-natal care and the occurrence of prematurity this may well be the explanation and it would be a mistake to place too much emphasis on the possibility of reducing the incidence of prematurity simply by improving ante-natal care.

The relationship between work during pregnancy and prematurity/

prematurity is in much the same uncertain state. Evidence has been produced to show that work during pregnancy is associated with a high prematurity rate (Douglas,1950; Ferguson and Logan,1953; Stewart,1955) but other publications show that there is no such association (Illsley,Billewicz and Thomson, 1954; Martin,1954). Again the possibility arises that the relationship, if it exists, is not a direct one and Martin's observation that the proportion of primigravidae in employment had risen steeply between the time of the national survey (1946) on which the work of Douglas (1950) was based and the time of his survey (1953) may have some bearing on the interpretation of the results of these enquiries. At any rate,no very definite conclusions can be drawn at present about the influence of ante-natal care and work during pregnancy.

So far we can conclude that although certain factors such as social class, parity, maternal age, diet during pregnancy, ante-natal care and employment during pregnancy are related to the incidence of prematurity and although some of them are associated with low birth weight, the causes of prematurity are still largely unknown, and most of the so-called causes, such as toxaemia of pregnancy, do not have a proven causal relationship to prematurity.

The majority of investigations, from which evidence has been quoted, have been concerned mainly with attempts to relate the occurrence of prematurity on any particular occasion to the circumstances, medical and social, of that occasion. These investigations have not met with any real success in establishing/

establishing the aetiology of prematurity, and it is perhaps not surprising that several writers have suggested the possibility that certain women might have a constitutional tendency to have premature children. Martin (1954) spoke of the "concept of a biological predisposition to premature delivery," and Drillien and Richmond (1956) say that " .... it seems probable that subfertile mothers and those with an increased liability to miscarriage are also more likely to produce a premature infant."

In exploring these possibilities we must attempt to take into account all that is known of a woman's reproductive history and regard the outcome of each individual pregnancy as the resultant of two sets of forces - the mother's reproductive tendencies, as indicated by her whole reproductive history, and relevant modifying factors.

Before such an approach would be justified it must be shown that women do in fact have reproductive tendencies - that is to say, that in any given woman the character and outcome of one pregnancy would be influenced by the character and outcome of her other pregnancies. There is evidence in the literature that such tendencies exist with regard to both abnormal and normal characteristics of pregnancy.

If we consider the abnormal characteristics first it is logical to begin with early pregnancy and discuss abortion. It is widely accepted that abortion tends to be repetitive in certain women. Malpas (1938) in a paper entitled "A study of abortion/

abortion sequences", concluded that if the general abortion incidence is 18%, then of every 100 pregnant women, approximately 17 will abort for casual or random causes, and approximately 1 because of the pressure of a recurrent cause. Probably an abortion incidence of 18% is too high an estimate, and a later assessment suggested that the spontaneous abortion incidence lies between 7% and 11% (Papers of Royal Commission on Population, Vol.IV,1950), but this does not affect the general line of reasoning. Speert (1954) thought that the evidence to support the view that abortion has a strong tendency to recur was not conclusive, but he based his own findings on a series of 121 cases. In a much more extensive survey (Yerushalmy, Bierman, Kemp, Connor and French,1956), involving 6039 women, it was shown that there was a very large increase in the incidance of early foetal death (i.e. less than 20 weeks' gestation) when the immediately preceding pregnancy had also resulted in an early foetal death. This finding gives considerable support to the view that if one pregnancy terminates in abortion this will influence the probability that the other pregnancies of the same woman will terminate similarly. In order to account for this Malpas (1938) postulated two types of causes of abortion - a casual or random type which did not tend to recur, and a recurrent type which caused certain women to have a sequence of abortions. It is, however, reasonable to doubt whether the division is clear-cut. In a recent study of/

of habitual abortion (Wall and Hertig,1948), in which habitual abortion was defined as two or more consecutive abortions before the twenty-eighth week of gestation, it was found that 58% repeated the same aetiology, and the pathologic or blighted ovum constituted by far the largest group with common aetiology. More interesting, however, was the finding that when the aetiology of the 100 habitual cases was compared with the aetiology of 1000 spontaneous abortions, described in an earlier paper (Hertig and Livingstone,1944) the following emerged:-

(1) In both series the percentages for any given factor are closely parallel.

(2) In both series all factors are in approximately the same proportion to one another.

The authors concluded that the similarity of these two series suggested that the aetiological factors responsible for spontaneous abortion might also be responsible for habitual abortion. This is of some interest because a similar argument will arise about prematurity when the findings of the present enquiry are discussed, and it will be dealt with in detail then. The main point at the moment is that if a woman has aborted once she is more likely to abort during other pregnancies than would otherwise have been the case.

There is comparable evidence that if one pregnancy terminates prematurely this influences the probability that the other pregnancies of the same mother will also end prematurely. One of the earlier attempts to investigate the recurrence of prematurity/

prematurity was made from the records of Buffalo City Hospital (Gardiner and Yerushalmy,1939). They obtained information about 2,337 births to mothers who had at least one earlier pregnancy - that is to say, all the cases had a previous obstetric history. Of these 2337 births, 2116 were full-time and 221 premature. The previous births to the mothers of these infants were distributed as follows:-

This Birth.	No. of Births.	Previous Births.		
		Full-time.	Premature.	Miscarriage or abortion.
Full-time	2116	7120	144	686
Premature	221	777	49	139

From this it is obvious that the incidence of prematurity is much higher in the previous history of the mothers of premature babies than in the mothers of full-time ones. About the same time the results of a study in Finland were published (Brander, 1939) and in this case information was available about the earlier and later pregnancies of 376 women who had had premature babies. Of the other single-born children of these women (i.e. the siblings of the premature children in question),20.8% had also been premature. At this time the general incidence of prematurity in Finland was 12.8% and Brander therefore concluded that the siblings of premature children are more likely than usual to be premature. Similar results emerged from a study of prematurity in Glasgow (Ferguson,Brown and Ferguson, 1952) in which information was available about all the pregnancies/

pregnancies of 692 women who had a single-born premature child during 1943 or 1944. From the figures given it emerges that these women had 1554 full-time pregnancies and 329 premature births in addition to the one in 1943 or 1944, so that the incidence of prematurity among the live-born siblings of these premature children was 17.5%, a figure which again suggests that the siblings of premature children are more likely than usual to be premature. Other findings which have been reported have referred mainly to the number of mothers of premature babies who have a previous history of prematurity, without giving the actual incidence among their pregnancies. For example, Anderson, Brown and Lyon (1941) noted that 14.1% of mothers of babies under 5½ lbs. had a previous history of prematurity. Baird (1945b) found that "the tendency to prematurity of unknown cause is more common in women who have had previous premature babies. For example, in 81 women who had one previous pregnancy, 20 (25%) had an unexplained premature baby and 16% had had an abortion previously. In a group of 82 having had two, three or four previous pregnancies, 31 (38%) had had previous premature babies, 12 (15%) had previous abortions. Some had as many as two or three premature babies. Out of 25 who had five or more previous pregnancies, 17 (68%) had had either a previous premature baby or an abortion." One of the interesting points about these figures is the way in which the number of women who had previous premature babies apparently increased/

increased with the number of previous pregnancies which they had had, suggesting the possibility that the chance of any of these women having a previous history of prematurity was directly related to the number of children that she had had, and habitual prematurity might not be limited to a few women. More will be said about this when the figures from the present investigation are considered.

Dana (1946) found that 12.4% of the mothers of premature babies at the Women's Clinic of the New York Hospital had a history of previous premature delivery, compared with 4% in the total clinic group, but the incidence of previous abortions in the two groups was exactly the same. Conway (1951) also found that prematurity was often repeated and whereas only 6.75% of the multiparous mothers of full-time babies had a previous premature infant, 21% of the multiparous mothers of premature infants had a previous history of prematurity. So also did 21% of the mothers of still-born babies, thus illustrating the close connection in some women between the factors causing death in utero and a live-birth at an unusually low weight. More recently, Folsome, Stone, Hirsch and Krumholz (1956) in reviewing 380 premature births in New York, observed that 81 or 33.2% of the multiparous women gave a definite history of prior premature delivery. It has also been shown (Karn,Lang-Brown,MacKenzie and Penrose,1951) that the chance of a child being underweight (less than 5½ lbs.) at birth was 14.1% when the earlier born child was underweight, compared with 3.2% when the earlier born child/

child was not underweight.

From this it seems that prematurity, like abortion, has a tendency to be recurrent. Thus a history of one of these abnormalities would increase the probability that the same abnormality would occur in other pregnancies. There is, however, conflicting evidence on whether a history of one of these abnormalities influences the probability that the other one will occur in other pregnancies. The evidence of Gardiner and Yerushalmy (1939), given on page 43, suggests that it does and Conway (1951) found that habitual abortion (two or more successive abortions) had been more frequent among the mothers of premature infants than among the mothers of full-time infants. The evidence of a relationship between threatened abortion and premature birth, to which reference has already been made (Turnbull and Walker,1956), also supports the belief that there is a relationship between abortion and prematurity. On the other hand Dana (1946) found that the mothers of premature and non-premature babies gave histories of previous abortions with the same frequency. Speert (1954) in criticizing the work of Gardiner and Yerushalmy, remarks that ".... the presumed biological relation between abortion and premature labour has validated in the minds of some students the application to one phenomenon the characteristics of the other." Finally,there was the work of Yerushalmy and co-workers (1956), conducted on a large scale on one of the Hawaiian Islands. These workers investigated/

investigated the tendency for reproductive wastage to be repetitive, and they divided this wastage into three groups - early foetal (up to twenty weeks), late foetal and neo-natal, and post-neo-natal. They then showed that while there is a familial tendency to repeated pregnancy losses, the tendency is specific for the three components of loss, and they concluded that these different components represented distinct and independent manifestations of reproductive wastage and suggest that different sets of causative factors may be responsible.

There is, however, a possibility that the aetiological relationship between abortion and prematurity, if it exists, should be extended to include toxaemia, a condition which also has a tendency to be repetitive. The fact that toxaemia is to some extent recurrent has been appreciated for some time (Kellog,1924), but various estimates have been made of the extent to which it recurs. The question has been obscured by uncertainty about the nature of toxaemia, and about whether there is a special form which recurs and, if so, how it differs from the form which does not. The most recent and probably the most accurate estimate of the incidence of toxaemia and the chance of recurrence was that made in Liverpool (Gemmell,Logan and Benjamin,1954), in which it was shown that 15.3% of multiparous women with a history of toxaemia previously have toxaemia again, whereas only 3.2% of multiparous women with no such history have toxaemia.

The/

The relationship between toxaemia and abortions and prematurity lies in the fact that certain women are believed to show a tendency to all three complications at the same or different times. That such a group of women exists has been pointed out on several occasions, and perhaps the clearest description and exposition was given by Young (1927) in a study of 220 successive cases of toxaemia and accidental haemorrhage at the Royal Maternity Hospital,Edinburgh. Dealing first with the cases which had eclampsia, he says that "In a considerable number of these eclamptic cases there occurs a phenomenon which, lacking a better term, we may call the abortion - premature birth - toxaemia complex or sequence. This defines the condition in which, in association with one or more eclamptic pregnancies, there occurs an unbroken succession of gestations which end as abortion, premature or still-birth, sometimes in combination with accidental haemorrhage." This statement refers only to cases in which two or more successive pregnancies terminated in these abnormalities, so that the existence of the complex in these cases can be inferred with reasonable certainty. To quote again - "There are cases in which abortion or premature birth occurs one or more times in the reproductive cycle of toxaemic cases, butwhen, because of the interpolation of normal pregnancies, it is impossible to exclude so certainly the operation of other irrelevant factors. That,however, the same factors may be acting in the case, at least,/

least, of some of these damaged pregnancies is not improbable." Malpas (1938) found that there was evidence of recurrent toxaemia in 17.4% of his cases of sequential abortion and says, referring to recurrent toxaemia, "It is of course impossible to say with certainty in every case that the toxaemia will certainly recur in every pregnancy. Every now and then a woman will have a normal pregnancy intercalated in an abortion - still-birth sequence due to recurrent toxaemia." Young, to revert to his work, showed that 23.2% of the earlier pregnancies of eclamptic patients ended in abortion, premature or still-birth, compared with 10.2% of the earlier pregnancies of 'normal' parous women. To quote further - "The next fact of importance which has emerged from these studies is that frequently in the pregnancies that go to form the sequence complex there is no history of toxaemia. When the patients were under treatment in the Hospital during these preceding pregnancies there is sometimes positive evidence of an absence of toxaemia.

"We are thus led to conclude that women with an eclamptic history commonly have resident within their body some morbid influence which is not inconsistent with good health between their pregnancies, but which is inconsistent with the normal continuance of pregnancy to term. Many of the damaged pregnancies in such women end in abortion, some end in premature birth or still-birth, but only in comparatively few such pregnancies does this constant and imminent X factor culminate in a/

a toxaemic attack..... The demonstration also that the sequence is not secondary to the toxaemia makes necessary a revision of our views regarding the recurrent disaster to the foetuses which is so tragically common in such cases."

Young then goes on to say that the same relationship to the recurrence complex is exhibited by accidental haemorrhage, and by the condition which was then called non-convulsive toxaemia.

The effects of the complex were summed up by Shute (1942) - "If the patient is able to avoid the Scylla of abortion or miscarriage she exposes herself to the Charybdis of prematurity, toxaemia, and monstrosity."

We can therefore say that abortion, prematurity and toxaemia all show tendencies to recurrence and there is possibly a relationship between all three, but several important points are not clear. The first is whether each of these conditions can properly be divided into two separate types, non-recurrent and recurrent. This point has arisen mainly with reference to abortion, because it is customary to stipulate that abortion is only habitual if a woman has had two or three consecutive abortions. If the number has been less, or if normal pregnancies have intervened it is usually assumed that the abortions were due to non-recurrent causes. Reference has already been made to the fact that Wall and Hertig (1948) found that the aetiology in 100 cases of habitual abortion was similar to the aetiology/

aetiology in 1000 cases of spontaneous abortion, and from this they concluded that the aetiological factors involved in each group might be the same. This suggests that there might not be any fundamental difference between abortions which apparently occur at random and abortions which occur in sequence, and we must consider whether the absence of any difference would be consistent with observed facts. We know that the over-all incidence of abortion is about 10% of all pregnancies (Papers of Royal Commission on Population,Vol.IV,1950). Let us suppose for a moment that the risk of abortion applies equally to all pregnancies. Then if a woman has one pregnancy the probability that it will end in abortion is 1 in 10, if she has two pregnancies the probability that both will end in abortion is 1 in 100, and if she has three pregnancies the probability that all three will end in abortion is 1 in 1000. Therefore it is not absolutely necessary to postulate the existence of a special recurrent type of abortion to account for certain women having two or even three abortions in succession. It must be admitted that, on this basis, it would not happen very often, but it is probably wrong to assume that the 1 in 10 risk of abortion applies equally to all pregnancies. Crew (1949), after discussing the actions of lethal and sub-lethal genes in experimental animals and plants, said that "it is safe to postulate that in man also such genes are responsible for much embryonic/

embryonic and early foetal death and thus for much abortion and apparent infertility." If this is the case it means that although the over-all risk of any pregnancy ending in abortion is 1 in 10, the risk to pregnancies resulting from certain matings will be higher than this, and the risk to the pregnancies resulting from the remaining matings will be correspondingly lower. This uneven distribution of risk would not affect the apparent over-all probability of 0.1 that if a woman had one pregnancy it would end in abortion, but it would increase the probabilities that two or three successive pregnancies would end in abortions. This might account for all the observed cases of habitual abortion and would make it unnecessary to postulate the existence of two different types of abortion, spontaneous and habitual. This study is not primarily concerned with abortions, but the same problem arises in connection with prematurity.

The second point is this. If the abortion - premature birth - toxaemia sequence is a real entity, and certain women, or rather certain matings, are likely to have a sequence of abortion, premature birth and toxaemia, are these abnormalities when they occur as part of this sequence any different from the same abnormalities when they apparently occur alone? Again the evidence which will be presented refers only to prematurity.

So far we have considered only the tendency for certain abnormal characteristics of pregnancy to be recurrent, but it is/

is also relevant to consider whether or not another characteristic of pregnancy with which we will be deeply concerned - namely birth weight - shows any consistent trends in the different pregnancies of the same mother, assuming of course that no abnormality has interfered with the course of the pregnancy. The finding referred to earlier (Tanner,Healy,Lockhart,MacMenzie and Whitehouse,1956) that the mother exerts an influence on the birth weight would suggest that this is likely.

The subject was investigated recently by Karn,Lang-Brown, MacKenzie and Penrose (1951) and it was found that the correlations indicating degree of likeness between the birth weights of sibs were of sufficient magnitude to be compatible with the assumption that birth weight depends on the genetic constitution of the parents or might be due to maternal conditions or environment. From other work (Walton and Hammond,1938; Morton, 1955; Robson,1955; Tanner et al.,1956) it appears that maternal conditions and environment are more important than genetic constitution, but this is beside the point at the moment. It is, of course, known that birth weight increases in successive pregnancies (McKeown and Gibson,1951b) and in this investigation (Karn et al.,1951) it was found that the highest correlations were obtained for birth weights of second and third infants - that is, those in which neither member of the pair was first-born. The investigation did not take into account infants after the third, but even so it is of considerable interest in showing that a degree of likeness in birth weights can/

can be expected in children of the same mothers.

An extreme example of likeness in birth weights of sibs has been described (Penrose,1952) in which all the seven infants of a sibship had birth weights over 13 lbs.

It therefore seems clear, from what is known of certain abnormal and normal characteristics of pregnancy that mothers do have reproductive tendencies. It would thus be reasonable in investigating the aetiology of prematurity to take into account not only the circumstances of the pregnancies which resulted in the premature children, but also the whole of the mothers' reproductive histories, as indications of reproductive tendencies. This is the aim of the present study, but before going on to consider how this was attempted it will be useful to recapitulate briefly what is known at present about aetiology.

Summary.

The outstanding fact is that no precise cause can be defined in about half the cases of prematurity which occur. Of the remainder, most are 'caused' by complications of pregnancy, but the way by which this is brought about is not known; all that can be said is that "It is presumed that such complications are effective in causing premature labour" (Lewis,1956). It is important to point out that this is only a presumption. Only a very few cases can be ascribed to such causes as acute and chronic illness in the mother.

A large number of factors such as social class, maternal age/

age and parity, influence the prematurity rate, but it must be remembered that up to one-third of 'premature' children are in fact small full-time children of low birth weight.

Finally, prematurity tends to be repeated and this tendency may be related to a tendency to abort and to show signs of toxaemia.

PART II - PRESENT ENQUIRY

AIMS, MATERIAL AND METHODS

The principal aim of this study was to examine the occurrence of prematurity against the background of the reproductive tendencies of the mothers of premature children. To do this thoroughly it would have been necessary to limit the investigation to mothers whose years of child-bearing were over, but in practice it would be very difficult to assemble a large series of such mothers and obtain accurate information about reproductive histories stretching back over twenty years or more. It was therefore decided to take as the starting point those mothers who had had a premature baby in Glasgow during the calendar year 1950, and whose homes were within the city. It was hoped that it would be possible to trace most of these mothers so that details could be obtained of all their pregnancies before and after 1950. As the first of these mothers was not visited until December, 1955, a period of five years had elapsed since the births of the premature children.

There is bound to be some dispute about the best method of obtaining the names of these children. The names of the premature children born in hospital could have been requested from the maternity hospitals and units in the city, and we could have been reasonably sure of obtaining the names of all the premature babies born in hospital during the year, with accurate information about birth-weight and various other relevant matters. While this information would have been very valuable/

valuable as far as these children were concerned, it would only apply to about two-thirds of the premature children born in the city, the remaining one-third being born at home. Now the hospital group would have been selected in various ways and would contain an excess of primigravidae, mothers with complications of pregnancy, mothers from poor environments, and so on. To avoid selection it was essential to obtain the names of the babies born at home as well. It must be admitted that there is some doubt about the accuracy of the birth weights of babies born at home and the question which arises is whether this doubt is great enough to justify their exclusion. It is a choice between accuracy and selection on the one hand and a lesser degree of accuracy and little or no selection on the other. In this case it was decided to try to include all premature babies and avoid selection, even if this involved some doubt about the accuracy of birth weights in a proportion of cases. It was also felt that the names of all the cases should be obtained by the same administrative method - again to avoid selection.

The only single method available which covers all children is to use the records of the Medical Officer of Health. Since the passing of the Notification of Births Act (1907) and the Notification of Births (Extension) Act (1915) the Medical Officer of Health receives intimation of every birth in his area. Following/

Following receipt of notification of a birth a Health Visitor is sent to visit the mother about fourteen days after the birth of the child. At her first visit the Health Visitor completes a record for each child containing information about the delivery, birth weight, ante-natal conditions, previous obstetric history and housing and social conditions.

These records for all children born in Glasgow in 1950 were examined to find the names of those which were premature. It was intended to visit the homes of all the children who could be traced, to check and amplify the information on the Health Visitors' records and to obtain detailed information about the whole of the mothers' obstetric histories. At the same time inquiry would be made about the progress of the children who had survived and about the schools which they were attending. It would then be possible to obtain further information from the children's school medical records. Information about the progress of these children and details of their school medical examinations are presented in the appendix (p.131), and will not be discussed here.

It was realised quite early in the course of the study that it would not be reasonable to visit the mothers of the children who had died. Most of these deaths had occurred early in life and were sometimes only one of a series of obstetric tragedies and to visit the mother five years or more after the loss of a child and attempt to revive her memories of/

of that loss and of all her other pregnancies was not considered justifiable. It was therefore decided, reluctantly, to omit these children from the survey. As the children who died tended to be smaller than the children who survived this means that an unduly high proportion of small babies was omitted, but as the birth weight of the children born in 1950 was an important variable in the analysis of the findings it is unlikely that the omission of the children who died will make any difference to the ultimate conclusions. For reasons already given (p.25) the aetiology of prematurity among children born of multiple pregnancies is not being considered, but a number of premature twins were included in the investigation and information about their progress and development is given in the appendix.

We are left then to deal with the single-born children who had apparently survived the first few years of life. Scrutiny of the records produced the names of 670 such children whose birth weights were stated to be 5½ lbs. or less. Eleven of these were later rejected because the mothers were quite certain that they had weighed more than 5½ lbs. at birth. In four of these cases the error was obviously clerical, leaving seven unexplained. This reduced the number of cases to 659.

In addition to these, however, there were 258 children whose birth weights were not stated on the records but who were said to have been premature (without qualification), or whose period of gestation was less than thirty-eight weeks. This introduces/

introduces an element of doubt as there must have been an unknown number of full-time babies whose birth weights were not recorded but which were in fact 5½ lbs. or less, and on the birth weight definition of prematurity these children ought to be included. The absence of these children will be referred to again shortly.

To obtain some idea of the true loss (by weight definition) which might be caused by failure to record birth weight an attempt was made to trace half the 258 'premature' children of unknown birth weight - a total of 129. Of this number 71 were traced and 58 could not be found. Of the 71 who were traced, the mothers of 39 said that their birth weights had been 5½ lbs. or less, and the remaining 32 had been over 5½ lbs. From this it seems likely that about half of the 258 cases were in fact premature (by birth weight definition) and as 39 of these were found this means that there was a loss of roughly 90 (half of 258 less 39) from this group. The question then arises of whether or not these children differ from the children whose birth weights were given on the Health Visitors' Records. They appear to differ in one respect only. Using the 39 cases whose birth weights were obtained from the mothers as an indication of the birth weights of all the premature children in this group, it seems likely that the birth weight distributions differ. The birth weight distributions of these 39 cases and of the 659 whose birth weights had been recorded by/

by the Health Visitor, are shown in Table 6, and it is apparent that a higher proportion of the 39 cases are in the lower birth weight groups. The difference is significant. This suggests that the birth weights of the hypothetical 90 children who are missing are lower than those of the main body of premature children, but it must be remembered that there were some full-time children whose birth weights had not been recorded, and an unknown number of these will undoubtedly have had birth weights of 5½ lbs. or less and would be premature by definition. If these children could be included they might correct this bias, as most of them would fall into the upper weight groups of prematures. It seems unlikely, therefore, that the omission of these children whose birth weights are unknown will make any serious difference to the sample, since birth weight will be taken into account in analysing the results.

Of the 659 children whose birth weights were known from the records 483 were traced and 176 were not. Seven of those traced refused to co-operate so that complete information was obtained for 476 and was not obtained for 183. Failure to trace was due to the reasons shown in Table 7. Only 74 cases were completely unaccounted for, 95 were known to have left the city, and 7 had been adopted. The adopted children were omitted because it was felt that a difficult situation might arise if the adopting parents knew little about their child's background, and some of them might have been perturbed to find that/

that the child had been premature. In any case they would have been unable to give the desired information on so many points that visiting them would have been of limited value.

As might be expected the 183 children for whom complete information was not obtained differed from the other 476 in certain respects. The main significant difference was that a higher proportion of the 'lost' children were the children of first pregnancies (Table 8). The reason for this is probably quite simple - the parents of first children in 1950 were apt to be badly housed, or living in lodgings or with relatives, and thus less firmly rooted in the community. However, although this difference is significant the part played by parity as a variable will be considered in the analysis of the findings and it is unlikely that this element of selection will make any important difference.

The birth weight distributions of the two groups (those for whom full information was available and those for whom it was not) are shown in Table 9 and it will be seen that they are very similar.

In the analysis of the findings it is proposed to consider together the 476 cases whose birth weights were known from the Health Visitors' records and for which complete information was obtained, and the 39 cases whose birth weights were not known from the records, but which were successfully traced and said by the mothers to have been of 5½ lbs. or less. This gives a total of 515 cases, which constituted the material for the investigation.

The/

The method of investigation will now be described. In each of these 515 cases the mother was visited and questioned at some time between early December,1955, and the end of August, 1956. In the few cases in which the mother was dead or not available the person in charge of the child was seen instead, and occasionally the information obtained in this way was amplified by seeing relatives who had had charge of the child at other times. The information given by the Health Visitor about the pregnancy in 1950 was checked with the mother and elaborated and details were sought about her other pregnancies, including the dates, the result, the birth weight in the case of live born children, and if the child had not survived, then the age at death was noted. Details were obtained about the social background, housing, father's occupation and regularity of employment. Enquiry was also made about the progress of the child born in 1950 and its school medical record was seen at a later stage in the enquiry, but this part of the work is discussed in the appendix.

The accuracy of information obtained in this way might well be questioned, and the obstetric history in particular might be doubted. As far as abortions were concerned the Health Visitors had made a note of the number of abortions which had occurred before 1950, and it was possible to compare this with the history obtained about six years later. Occasionally a mother gave a history of abortion before 1950 which the/

the Health Visitor had failed to note, and conversely she sometimes did not give a history of abortion when the Health Visitor had noted that there was one. Generally speaking, however, the history given in 1955-56 tallied with the earlier history given in 1950. There is, of course, no check on abortions reported after 1950, but it is unlikely that this information will be any less accurate, and being more recent it might well be more accurate.

The other point on which doubt might well be cast is the accuracy of the birth weights reported by the mothers of the siblings of the children born in 1950. Much of the subsequent analysis is based on these weights, but absolute accuracy is not essential. These weights were used for two main purposes. The first was to decide how many of the siblings were also premature, i.e. had a birth weight of 5½ lbs. or less. While there is no direct check on the accuracy of the birth weights of the siblings it is known that as far as the 1950 children were concerned only 11 mothers out of 487 gave a birth weight which was substantially different from that recorded by the Health Visitor and in four of these cases the error was obviously clerical. It is true that in some other cases the weight given by the mother differed from the recorded weight, but not sufficiently to affect the classification of the child. This suggests that the mother's recollection is reasonably good.

It is relevant to consider the experience of others on this question. Illingworth (1953), compared the subsequent heights and weights of 150 premature children with 150 children whose/

whose birth weights had been 8½ lbs. or more. The mother's word was taken about the birth weight and he thought it was unlikely that in a series of 150 cases with controls the error arising in this way would be an appreciable one. In another investigation (Asher and Roberts,1949) into the birth weights of children then attending school it was found that the mothers gave reasonably accurate figures, although they tended to round off the weights to the nearest quarter pound. The present investigation involves a similar lapse of time and rounding off of birth weights would not make any serious difference. Parfit (1951) also relied on the mothers' accounts of birth weights in an investigation of weight increment. Douglas (1950) was able to check the birth weights originally given for the children in his survey, some of which were based on the mothers' statements, and found that out of 413 weights only 12 showed a discrepancy greater than 4 oz. On the other hand Illingworth, Harvey and Gin (1949) found that when 110 mothers were asked to give the birth weights of their babies born five years previously in a maternity hospital, 83.9% knew the birth weight to within 4 oz., but 10.4% made an error of over 8 oz. In Glasgow (Speirs,1956) it was found that only 24% of the mothers of a series of premature babies gave the correct birth weight, and only 37% of the mothers of the control series.

For our present purpose it seems likely that the mothers' accounts of birth weights are sufficiently accurate to be used with/

with confidence. They will be used simply to determine how many children fell into a few birth weight groups - mainly 5½ lbs. and less - so that absolute accuracy, although desirable, is not essential. The alternative to accepting the mothers' statements would be to attempt to trace a hospital or other record for each of their children, apart from the ones born in 1950, and this would involve a total of 1267 records of births which had taken place mainly during the last 10-15 years. It would be unlikely that an attempt to do this would meet with more than partial success and it would not justify the administrative trouble caused to several hospitals and to the Health and Welfare Department of the City. It was therefore decided to accept the mothers' accounts of the birth weights of their children.

Apart from interest in the number of the brothers and sisters of the premature children who were also premature, it was also of interest to try to gain some idea of how many of those who escaped prematurity had what might be loosely described as a 'normal' birth weight. It seemed reasonable to take as 'normal' a birth weight of 7 lbs. or more. It will be recalled that in Birmingham McKeown and Record (1952) found that the mean birth weight of single-born babies was 7.43 lbs.

Some of the other points on which information was obtained will be discussed more conveniently later, when their effects and associations are being considered.

Before/

Before analysing the figures obtained it is proposed to give a brief outline of the material, along with some of the salient features of the social background.

DESCRIPTION OF MATERIAL AND ITS BACKGROUND

The 515 premature children in the investigation consisted of 229 males and 286 females.

The birth weight distribution of these children, of each sex, and combined, is shown in Table 10. The weight groupings are the same as those used by the Ministry of Health in the Annual Reports of the Chief Medical Officer, and have the advantage of corresponding closely to convenient divisions on the metric scale. The birth weight distribution has undoubtedly been affected by the exclusion of children who died, most of whom would be in the lower weight groups.

The cases were divided into two groups according to whether or not there had been any complication of pregnancy in 1950. This was decided largely on the basis of the notes made by the Health Visitors in 1950, but this information was amplified by questioning the mother when she was seen five or six years later. There was no history of any complication in 323 (62.7%) of these 515 cases. In 107 (20.8%) there was a history of toxaemia, using this term to include pre-eclamptic toxaemia and eclampsia, essential hypertension associated with pregnancy, and chronic nephritis complicated by pregnancy. No attempt could be made to distinguish between these different components/

components of toxaemia, nor was any attempt made to assess the severity of the condition. Thirty-nine cases (7.6%) had an ante-partum haemorrhage, and again no attempt was made to ascertain the type of ante-partum haemorrhage involved. Thirty cases (5.8%) had a history of bleeding during pregnancy which had been regarded as threatened abortion, and 16 cases (3.1%) had other complications such as hyperemesis severe enough to require hospital treatment and hydramnios. All these cases (192 in all) will be regarded as a single group of complicated cases. One hundred and seven (55.7%) were cases of toxaemia, and some of the 39 (20.3%) cases of ante-partum haemorrhage were probably toxaemic in origin, so that it is likely that about two-thirds of the complications were toxaemic in origin.

The birth weight distributions of the uncomplicated and complicated groups of cases are shown in Table 11. It is apparent, as would be expected, that a higher proportion of the smaller children are the result of complicated pregnancies.

The birth weight distribution according to the number of previous pregnancies is shown in Table 12. The only point to which attention might be drawn is the slight tendency for the smallest children to be preceded by five or more pregnancies more frequently than the bigger children.

The distribution of the complicated and uncomplicated groups/

groups of cases according to the number of previous pregnancies is shown in Table 13. Although there appears to be a difference in the two distributions the difference is not significant.

Table 14 shows the place of delivery according to the birth weight and it will be seen that a higher proportion of the smaller babies were delivered in hospital. In thirty-eight cases it was known that labour had been induced and in twenty-eight cases delivery was by Caesarean Section.

A certain amount of the information which was obtained about the social background is worth mentioning at this stage.

In 13 cases the mother was dead at the time of interview, and in 9 cases the father was dead. In a further 11 cases it was not known whether the father was alive or dead. In 14 cases the child was illegitimate. This, however, does not give a true impression of the position because the illegitimate children were particularly difficult to trace and losses were high. In fact many of the illegitimate children who were traced were the children of men and women who were unmarried but living together as man and wife.

Only 393 of the fathers had been in continuous employment at the time of the pregnancies in 1950 and during the children's early years, and 73 of those not continuously employed had been out of employment for longer than would be accounted for by transitional unemployment. This suggests that there was an unduly/

unduly high proportion of shiftless individuals among them.

The housing of these children was unsatisfactory. When the premature children were born only 313 of the families were in houses of their own. One hundred and fifty-two were staying with relatives, 49 were in lodgings or rooms, and one was a squatter family. This, of course, refers only to the 515 who were traced five years later and the position of those not traced was probably worse.

Even so, 145 (28.2%) of the families traced were living in 1950 in one-roomed houses or one-roomed lodgings without the use of other parts of the house, and a further 185 (35.9%) were living in two-roomed houses, so that only the remaining 185 (35.9%) were living in houses of more than two rooms.

In terms of persons per room, the position just before the birth of the premature child, and not including that child, is shown in Table 15, along with the corresponding figures for all houses in Glasgow at the time of the 1951 census (Census 1951, One Per Cent.Sample Tables,1952), which was only a few months after the period with which we are dealing. A direct comparison cannot be made, but even so, the figures seem to bear out the impression obtained when visiting these homes that the housing conditions into which these children were born were worse than the average at that time.

It was also striking that of the families of the 515 children/

children traced, only 181 were still living in the homes in which they had been living when the premature children were born five or six years earlier. One hundred and two had moved within one year of the birth, and a further 53 within two years. Many of the later moves were due to rehousing in Corporation property and were satisfactory, but many of the earlier moves were not satisfactory and it was surprising how many had left good accommodation with relatives to live in overcrowded slum property in the older parts of the city.

An attempt was made to allocate each child to one of the five social classes (Classification of Occupations,1950) according to the occupation of the father at the time of the child's birth. In this way it was possible to determine the social class of 505 of the children out of the total of 515, and the distribution is shown in Table 16.

The social class distribution of each birth weight group is shown in Table 17, and it will be seen that the distribution in each group is approximately the same. The social class distributions of the uncomplicated and complicated cases are shown in Table 18 and there is a significant difference between them. A higher proportion of the uncomplicated cases are in the lower social classes. This is to be expected and is a reflexion of the usual finding that a higher proportion of prematurity in the lower social classes is 'unexplained' (Baird, 1945b).

The/

The foregoing has been presented to give a general impression of the material used in the investigation, and from what has been said here and in earlier sections, it seems to be free from any peculiarities which might influence the conclusions which will be drawn from it.

BIOLOGICAL PREDISPOSITION TO PREMATURITY

The first question to be considered is whether certain women show a predisposition to premature delivery. It has already been shown that while many factors apparently play some part in the aetiology of prematurity it is only rarely that in any particular case of prematurity the cause can be identified with confidence. From the evidence available in the literature it seems clear that women show tendencies to repeat certain characteristics in all their pregnancies and it has been suggested that prematurity may be a characteristic of this sort.

This possibility, that certain women have a tendency to have premature babies, can only be examined by considering the reproductive histories of a large group of mothers who have had a premature child. If it is found that a substantial proportion of the other children in these families are also premature then we might consider the possibility that some or all of these mothers have a tendency to have premature babies. The problem is, however, complicated by the fact that the prematurity on any particular occasion may have been due to the operation/

operation of factors peculiar to that particular pregnancy. For example, it has been shown ("Maternity in Great Britain," 1948) that the prematurity rate is 8% in first pregnancies and 5.3% in subsequent pregnancies. Therefore some at least of the prematurity among first pregnancies must be attributed to the fact that they were first, a circumstance which will not apply to the other pregnancies of the same mother. Similarly, it is known (Douglas,1950) that the risk of prematurity for births after the first is least between the ages of twenty-six and thirty-five. Therefore some of the prematurity which occurs among mothers under the age of twenty-six or over the age of thirty-five must be attributed to the effects of maternal age, and this particular risk will not apply to any other children which these mothers may have had between the ages of twenty-six and thirty-five. It is important that the risk of prematurity cannot be uniform throughout the whole of a woman's reproductive career, and the prematurity which occurs on a particular occasion may be due to special risks associated with that particular pregnancy.

It is, however, possible that, apart from the additional prematurity due to these special risks, certain women have a predisposition to prematurity. Let us suppose that, to examine this possibility, we have selected a group of women who have each had a premature child, and let us also suppose that we are able to identify and exclude those cases in which this occurrence/

occurrence of prematurity was associated with a known risk peculiar to this particular pregnancy. We might then examine the possibility that the prematurity in the remaining cases was due to a predisposition to prematurity. It is unlikely that any other causes would be found. We have already pointed out that it is doubtful whether complications of pregnancy should be regarded as causes of prematurity, and also that the number of cases in which prematurity can be attributed to ill-health during pregnancy is probably negligible. If, however, we discovered that a substantial proportion of the other children of these women were also premature we could argue that at least some of them showed a predisposition to prematurity. There would then be two possibilities to consider. In the first place we might be dealing with a mixed group in which some of the women had a predisposition to prematurity and therefore had a high proportion of premature children in their families, while the others did not have a predisposition to prematurity and therefore had only one premature child for reasons unknown but presumably peculiar to that one pregnancy. Alernatively we might be dealing with a homogeneous group in which all the women have the same predisposition to prematurity and the risk of prematurity to each child would be the same.

The material which we have available to examine this problem has already been described. It consists of 515 women who are known to have had a single live-born premature child in/

in Glasgow in 1950. Each woman was interviewed in late 1955 or the first half of 1956 and a history of all her pregnancies up to the time of interview was obtained. In this way it was found that these 515 women had had, in addition to the 515 premature children in 1950, another 1554 pregnancies either before or after 1950. Of these 1554 pregnancies, 1267 resulted in a single live-born child. The mothers were asked to give the birth weights of these children. This was not known in 48 cases, but of the 1219 children whose birth weights were known, 322 (26.4%) were said to have had birth weights of $5\frac{1}{2}$ lbs. or less, and were therefore premature by birth weight definition. That is to say, 26.4% of the single-born brothers and sisters of these 515 premature children were also premature. Some of these children had died, but dead children, of course, are always included in calculating the incidence of prematurity in these families. Two comparable figures are available from the literature and reference has already been made to both of them. Brander (1939) found that 20.8% of the single-born siblings of premature children were also premature and in Glasgow an incidence of 17.5% was found among the siblings of premature children (Ferguson, Brown and Ferguson,1952). When these figures are compared with a general incidence of prematurity in this country of the order of 6% or 7%, it is clear that when there has been one premature child in a family the chances that other members of the family will have been premature are considerably/

considerably greater than the normal probability of prematurity. It remains to be seen whether this increased probability applies to every family in which prematurity has occurred or whether it must be limited to a few families in which prematurity appears to be habitual. This is the problem which must now be examined.

Of the 515 women in the series 80 had no other single live-born children, apart from the premature one born in 1950, so that no conclusions can be drawn about predisposition to prematurity in these cases. The remaining 435 women had other single-born children, at least once, and in 191 (43.9%) of their 435 families prematurity had occurred more than once (i.e. in 1950 and on at least one other occasion). This means that the prematurity which occurred in 1950 was not an isolated event in these 191 families. Even this is perhaps a slight under-estimate of the true position, because many of the 48 children whose birth weights were not known were probably also premature - the most frequent reason given for the birth weight being unknown was that the baby was too small to be weighed. Nevertheless, the fact remains that in almost half of these 435 families the prematurity in 1950 was not an isolated event, whereas in slightly more than half of them it had not occurred on any other occasion. Does this mean that there are two groups of cases, in one of which the prematurity tends to be habitual, whereas in the other it does not? At first sight this/

this might appear to be the case, but on closer examination it will be found that it is only partially true.

We are considering at the moment 435 women who are known to have had a premature baby in 1950, and who have also had other children, a considerable proportion of which were also premature. Let us suppose that the prematurity in 1950 was due in every case to a predisposition to prematurity, and ignore for the moment the fact that certain factors such as parity and maternal age must have played some part. We would expect the predisposition to have applied to all the other pregnancies which these mothers had had with the same force as in 1950. Now we know that 26.4% of the other children were premature. Therefore, if the predisposition to prematurity was uniform the probability that each of these other children would be premature is 0.264, or approximately 1 in 4. If that is the case, and the probability that any one of the other children in these families will be premature is 1 in 4, it is not to be expected that many of the smaller families with only one or two children additional to the premature one in 1950 would exhibit prematurity on another occasion. So that the fact that slightly more than half of the 435 families did not show prematurity more than once does not necessarily mean that the mothers of these families were any less likely to have premature babies than the mothers of the families in which prematurity occurred more than once. Only by considering the distribution

of prematurity in families of different sizes will it be possible to decide whether or not there is any demonstrable difference between these groups of mothers.

At the moment we are overlooking the fact that some of these 435 premature children born in 1950 owe their prematurity to special circumstances which applied at that time and would not apply during all the other pregnancies of their mothers. If these cases can be satisfactorily excluded we might postulate that the prematurity in the remaining cases was due to a predisposition on the part of the mothers to have premature babies. It would follow that the same predisposition must apply to their other children. Therefore, it should be possible to show that the incidence of prematurity among the other children in these families is unduly high, and that there is no difference in the incidence among the children born before and after the child which was prematurely born in 1950, so that there can be no question of prematurity on this occasion predisposing to prematurity during later pregnancies. Further, if the predisposition applies equally to all pregnancies the probability that each of the other children will be premature should be the same as the average probability calculated from the incidence of prematurity among all the other children. Therefore it should be possible to show that the distribution of prematurity among families of different sizes does not differ significantly from the expected distribution on the assumption/

assumption that the average probability applies to each child. If these points can be demonstrated then it would be reasonable to postulate that the prematurity in these cases was due to a predisposition on the part of the mothers. The first problem is to identify those special groups of cases to which this hypothesis cannot be expected to apply, and show adequate reason for removing these cases from the data.

The first group which must be excepted consists of those mothers who were primigravid in 1950 - that is to say, the premature child in 1950 was the result of a first pregnancy. We have already quoted the evidence that the risk of prematurity in first pregnancies is greater than in later pregnancies and therefore it seems reasonable to assume that some of the prematurity among first children can be attributed to the fact that they are first, which is a non-recurring attribute. Therefore some of these cases of prematurity among primigravid mothers were presumably due to circumstances peculiar to the pregnancy in 1950 and cannot be due to a predisposition to prematurity, and we would not expect to find as much prematurity among the other pregnancies of these mothers as among the other pregnancies of mothers who were not primigravid in 1950.

Of the 435 mothers who had other children, 121 were primigravid in 1950, and these mothers had another 198 single live-born children of known birth weight, of which 34 (17.2%) were premature. By contrast, the remaining 314 mothers who were not primigravid in 1950 had 1021 other children of known birth weight/

weight and of these 288 (28.2%) were premature. This difference is significant (Table 19) and supports our assumption that some of the prematurity among first children can be attributed to the fact that they are first. Accordingly our hypothesis cannot be expected to apply to the mothers who were primigravid in 1950, and they must be removed from the data. This leaves 314 mothers who had 1021 children in addition to the premature ones born in 1950. If our hypothesis is correct, and the risk of prematurity to each of these 1021 children is the same, we would expect to find that the incidence of prematurity among those children born before 1950 would be the same as among those born after 1950. This was found to be true, with the exception of one important group of cases.

The number of additional single-born children which each of these 314 mothers had varied from 1 to 9 or more. Thus some of them had quite large families and as only five or six years had elapsed from the time of the birth of the premature child in 1950 to the time at which the mothers were interviewed it is apparent that when the family was large many of the children must have been born before the premature child in 1950, so that this child and any later ones would be subject to the disadvantages and dangers associated with high parity. There is very little information in the literature about the incidence of prematurity among children of high birth rank, but Drillien and Richmond (1956) showed that in social classes III, IV and V the prematurity rate for sixth and subsequent births rises

to/

to nearly 18%. Thus, to revert to our own material, in these cases in which the mother has had a large family, it is possible that the later members, often including the child born in 1950, were subject to an influence tending to result in prematurity, and the earlier pregnancies of these mothers would not be subject to this influence. This is borne out by the data. In Table 20 the 314 cases are divided according to the number of other single-born children which the mother had, varying from 1 to 9 or more. At each family size the incidence of prematurity among those children born before 1950 and among those born after 1950 are shown separately. (The few twins in these families have not been included in reckoning family size.) It is obvious that until the number of other children exceeds 5 there is no difference in the incidence of prematurity before and after 1950. When the total incidence of prematurity among those children born before 1950 in families in which the number of additional children did not exceed five is compared with the total incidence in these families after 1950 the difference is not significant (Table 21). When there have been six or more additional children the pattern is quite different, and with the exception of the few families in which there were nine or more additional children, the incidence of prematurity after 1950 is greater than before. When the totals are compared the difference is significant (Table 22).

Therefore it is apparent that in families which had six or/

or more additional children (i.e. total family of seven or more) a new influence leading to prematurity has begun to assert itself at some stage in the mothers' reproductive careers, so that it cannot be suggested that the risk of prematurity to the other children in these large families is uniform. The later children are obviously subject to a greater risk. We cannot therefore expect that the hypothesis will apply to these cases, and accordingly the 54 families containing a total of seven or more children must be withdrawn from the data.

We are now left with 260 mothers who had a total of 653 single-born children in addition to the one born in 1950, and of these 195 (29.8%) were premature. The ages of these mothers at the time at which they had the premature child in 1950 varied from under twenty years to thirty-five years or more. Now it has been shown that the risk of prematurity in births after the first is least between the ages of twenty-six and thirty-five years (Douglas,1950). Therefore some of these 260 mothers had their premature children in 1950 at a time when they were not within the age group with the least risk, and the prematurity on that occasion may have been due to the risk attached to the maternal age at that particular time. As this same risk would not apply at other periods in their reproductive careers it is probable that some of the other children of these mothers would be subject to a lesser risk of prematurity. Table 23 shows these/

these 260 cases divided according to the mothers' ages when the premature children were born in 1950. In each maternal age group the incidence of prematurity before and after 1950 is shown, along with the total incidence. The striking feature shown by this table is that when the mother had been thirty-five years or older in 1950, most of her other children had been born before this date, and the incidence of prematurity among them was less than among the other children of mothers who had been younger in 1950. When the incidence of prematurity among the other children of the mothers who had been thirty-five years or older in 1950 is compared with the incidence among the other children of all the younger mothers, the difference is significant (Table 24). We are therefore justified in concluding that some of the prematurity in 1950 among mothers who were then thirty-five years or older was due to the additional risks of maternal age, and as most of their other children had been born earlier, the risk of prematurity to the children of these mothers was not uniform and our hypothesis cannot apply to them. Accordingly, the fifty-eight mothers who were aged thirty-five or more in 1950 must be removed from the data.

We are now left with 205 mothers who were not primigravid in 1950, whose total family size did not exceed six single live-born children (i.e. the premature in 1950 and five others) and who were less than thirty-five years old in 1950. These

205/

205 mothers had a total of 514 other children of whom 163 (31.7%) were premature. The incidence of prematurity among the other children in these families is therefore unduly high, and by eliminating the large families we have been left with families in which the incidence of prematurity among the children born before 1950 is almost the same as among those born after 1950 (Table 21). It seems possible that all those cases in which some circumstance peculiar to the pregnancy in 1950 might have been responsible for the prematurity on that occasion have been eliminated, but before considering in detail the exact distribution of prematurity in these families it is necessary to consider a number of other factors which may be thought to have been responsible in 1950, although in fact none of them appears to be important.

In certain of these 205 cases it was known that labour was induced in 1950, or the child was delivered by Caesarean Section, or the mother at that time was not in good health. It might be held that these are features of the pregnancy in 1950 which are exclusive to that pregnancy, and if it is accepted that they might account for the prematurity in 1950, then we would not expect these women to have as high an incidence of prematurity among their other children as the remainder of the women.

It was known from the records that in twelve cases out of the 205 labour had been induced in 1950. It is possible that labour/

labour was induced in a few other cases also, but it is only in these twelve that the information is reliable. Now it is doubtful whether induction of labour is often responsible for prematurity which would not otherwise occur. For instance, Sandifer (1944), in analysing the causes of prematurity in 1000 cases of premature birth at Queen Charlotte's Hospital, stated that the cause was unknown in 372, that the prematurity was the result of induction of labour in 319 and that it was associated with abnormal maternal or foetal conditions without induction of labour in the remaining 309. In the 319 cases in which labour had been induced, the four main reasons for induction were toxaemia (205), placenta praevia (30), accidental ante-partum haemorrhage (20) and eclampsia (16). Of the 309 cases with an associated complication in which labour was not induced, multiple pregnancy accounted for 178. If these are excluded, the main complications in the remaining 131 were toxaemia (38), accidental ante-partum haemorrhage (28), foetal abnormality (18) and placenta praevia (13). Thus the same abnormalities appear in much the same order in both lists, and it seems reasonable to conclude that induction is usually resorted to when the child is likely to be delivered prematurely in any case, although perhaps as a premature stillbirth rather than as a premature live birth. In Sandifer's cases toxaemia is the main reason for induction, and also the commonest abnormality in the non-induced group. Donald (1955) states "It is to be noted that pre-eclamptic toxaemia is a cause/

cause of prematurity more through the need to terminate pregnancy than through its own direct effects on the woman although, less often, it may kill the baby in utero, thus causing the premature still-birth of a macerated foetus". It is thus open to doubt whether induction is frequently a cause of prematurity which would not otherwise occur, except perhaps in a few cases in which labour might be induced to prevent erythroblastosis foetalis, and possibly on rare occasions to prevent disproportion.

The problem at the moment is to decide whether or not to regard induction of labour in 1950 as a feature of that pregnancy which would cause prematurity on that occasion only, and would not influence the other pregnancies of the same mother. On the evidence available it seems more likely that induction is an indication of circumstances which might have resulted in prematurity in any case, and the same circumstances could arise during the other pregnancies of the same mother. In fact the incidence of prematurity among the other children of the mothers who had an induction of labour in 1950 was 21.4% (Table 25), which does not differ significantly from the incidence in the remaining cases.

Much the same argument applies to cases delivered by Caesarean Section. In this group of 205 women there were 10 such cases, which were delivered by Caesarean Section in 1950. The fact that this operation was undertaken at a time when the baby/

baby was still small probably indicates that a difficult premature delivery was anticipated or that there was a danger of foetal death which would have resulted in a premature stillbirth. In either case the operation cannot be regarded as the primary cause of the prematurity on that occasion, and the circumstances which led to the section being performed may on other occasions have led to premature delivery. The incidence of prematurity among the other children of the 10 mothers who were delivered by Caesarean Section in 1950 was 23.1% (Table 26), which does not differ significantly from the incidence in the remaining cases.

Since both induction of labour and Caesarean Section result in an artificial termination of pregnancy, and the numbers in each case are small, the cases have been combined in Table 27. Even combined the incidence of prematurity among the other children in these cases does not differ significantly from the incidence in the remaining cases.

In 44 cases the mother was suffering from some greater or lesser degree of ill-health at the time of the pregnancy in 1950. It is therefore possible that this was responsible for the prematurity on that occasion, and as it is unlikely that these mothers would all suffer from the same degree of ill-health during their other pregnancies, particularly when the illness had been an acute one, it might be thought that the incidence of prematurity among their other children would be less than among the other children of women who had been in good health in 1950. However, we have already drawn attention to the evidence (Sandifer,/

(Sandifer,1944; Drillien,1947) that maternal ill-health as a cause of prematurity has been considerably overrated, and the information available from the present investigation appears to agree with this.

In 33 cases the health of the mother was said to have been 'fair' in 1950. This was decided mainly on the evidence of the Health Visitor, who made her notes at the time, but it was checked by questioning each mother when she was seen in 1955 or 1956. These 33 cases consisted mainly of mothers who were said to have been anaemic or debilitated or who gave a history of minor illness during the pregnancy in 1950. In these cases the incidence of prematurity among the siblings of the child born in 1950 was 26.0% (Table 28) which was not significantly less than the incidence in the remaining cases.

In 11 cases the health of the mother was described as 'bad' in 1950. Several of these mothers had respiratory tuberculosis and the remainder had an acute illness such as pneumonia or severe chronic illness. In these cases the incidence of prematurity among the siblings of the child born in 1950 was 25.0% (Table 29), which was not significantly different from the incidence in the remaining cases.

Since the numbers were small, the 44 cases with 'fair' or 'bad' health have been combined, but again the incidence of prematurity is not significantly less in the families of these mothers than in the families of the remaining mothers who were in good health in 1950 (Table 30).

There is thus no reason to suppose that the mothers who had induced/

induced labour or were delivered by Caesarean Section in 1950, or who were not in good health at that time, were any less likely to have premature babies on other occasions than the remaining mothers who did not have any of these special characteristics in 1950,and these cases need not be removed from the data.

It therefore seems possible that our hypothesis could apply to this group of 205 cases, because there appear to be no extraneous circumstances associated solely with the pregnancy in 1950 which had any significant responsibility for the prematurity on that occasion. We can now proceed to examine the distribution of prematurity in these 205 families in more detail. Each family contained a premature child which was born in 1950, and the cases were originally selected because of this. This child must therefore be excluded from further consideration. In addition to these children, there were 514 other single live-born children,of which 163 (31.7%) were premature. But these 163 other premature children were all members of 105 families, so that the 205 families consisted of 100 families containing 223 additional children of known birth weight, none of whom had been premature, and 105 families containing 291 additional children of known birth weight,of whom 163 (56.0%) had been premature. Does this mean that the children in these 105 families were necessarily more likely to have been premature than the children in the 100 families in which prematurity had occurred only once, in 1950? In other words, we have to decide whether we can regard the mothers of these

205/

205 families as a homogeneous group, all showing a predisposition to prematurity, or whether we must divide them into a group of 105 showing habitual prematurity, and a group of 100 showing prematurity as an isolated and non-recurring feature of their reproductive careers.

We know that the number of additional children in each family varied from 1 to 5. Thus if all the mothers had a predisposition to prematurity the number of opportunities which they had to demonstrate this varied with family size. Let us suppose that the probability that any one of the additional children in these 205 families will be premature is the same in each case and that there is no difference between the 100 families in which none of the additional children were premature and the 105 families in which some of them were premature. If we denote the probability that a child will be premature by p, then since 31.7% of these additional children were premature, p in this case will have a value 0.317. Similarly if we denote the probability that a child will not be premature by q, then q will have a value of 0.683; $p + q = 1$. Now if under these circumstances a mother has one additional child there are two possibilities - either it will be premature or it will not. The probability that it will be premature is p and the probability that it will not is q. Now in this group of 205 cases 44 mothers had one additional child. Therefore, since the probability that each child will be premature is p, we would expect that 44 x p mothers would have had a premature child,/

child, and since the probability that each child will not be premature is q, then 44 x q mothers would not have had a premature child. If p has the value 0.317 and q has the value 0.683, we would expect that in 44 x 0.317 or 13.9 cases the child would be premature and in 44 x 0.683 or 30.1 cases it would not. In fact in 16 cases the child was premature and in 28 cases it was not, and these observed values do not differ significantly from the expected values on the assumption that the probability that each child will be premature is 0.317. These figures are shown in the first line of Table 31.

Let us consider now the mother who has two additional children. There are three possibilities in each family. Both children may be premature, one may be premature and one not, or neither of them may be premature. Reverting to the symbols p and q, the probability that any of these events will occur is given by the expansion of $(p + q)^2$. This gives us $p^2 + 2pq + q^2$, where p^2 is the probability that both children will be premature, 2pq is the probability that one will be premature and one not, and q^2 is the probability that neither of them will be premature. Out of this group of 205 families, 70 had two other children, so that we would expect that in $70 \times p^2$ cases both children would be premature. If p has the value 0.317 this gives an expected number of 7, compared with an observed number of 10. Similarly the expected number of cases in which one child is premature and one not is given by/

by 70 x 2 pq, which is 30.3 and the observed number is 22. Also, the expected number of cases in which neither child is premature is 70 x q^2, which is 32.6 and the observed number is 38. These figures are given in the second line of Table 31 and again the expected values and observed values do not differ significantly.

In the same way if a mother has three additional children the possibilities are that all three are premature, or that two are premature and one not, or that one is premature and two not, or that none are premature. The probability that any of these events will occur is given by the expansion of $(p + q)^3$. This gives $p^3 + 3\ p^2q + 3\ pq^2 + q^3$, where p^3 is the probability that all three will be premature, $3\ p^2q$ that two will be premature and one not, $3\ pq^2$ that one will be premature and two not, and q^3 that none will be premature. Now in the group of 205 families, 39 had three other children and giving p the value 0317 and q the value 0.683 we can calculate the expected number of cases showing prematurity three times, twice, once, or not at all, and this can be compared with the observed numbers. These figures are shown in line 3 of Table 31 and again the expected and observed values do not differ significantly. Similar calculations have been made for mothers having four and five additional children, and the expected and observed numbers are shown in lines 4 and 5 of Table 31. In neither case do they differ significantly.

Thus,/

Thus, looking at Table 31 as a whole, it has been shown that no matter how many additional children a mother may have had, the observed number of times each possible combination of premature and non-premature children occurs does not differ significantly from the expected number. There does, however, appear to be a tendency for the number of mothers with no premature children to exceed the expected number and also for the number of mothers with all their children premature to exceed the expected number, but even if the values of χ^2 for each line of the table are added the probability that these differences are due to chance is still greater than the significant value of 0.05. Therefore there is no reason why the hypothesis that the probability that each of these other children will be premature is the same should be rejected, and as the total number of cases, 205, is fairly large, this can be asserted with some confidence. This means that there is no reason to suppose that the children of the 105 mothers in whose families prematurity occurred more than once were necessarily any more likely to have been premature than the children of the 100 mothers who had a premature child once only. It is of course true that our method of selection may not have excluded all the cases in which the prematurity in 1950 was related to circumstances peculiar to that pregnancy, and it may be that there are a few cases in which prematurity really is habitual so that almost every child will be premature. Such cases may have accounted/

accounted for the slight and insignificant excess of women who had no other prematures and women who had the maximum possible number, but the number of such cases must be very small indeed.

To sum up the argument which has been presented so far, we started with 515 women who had premature babies in 1950. In 80 cases no conclusion could be drawn about predisposition to prematurity because they had no other single live-born children. Of the remaining 435 who did have other children, some of them had their premature child in 1950 in circumstances in which the risk of prematurity was increased. One hundred and twenty-one cases were excluded because the child was the result of a first pregnancy, 54 because the family contained a total of seven or more single-born children and 58 because the mother had been 35 years or older at the time her premature child was born in 1950. When these cases had been withdrawn from the data, we were left with 205 families, which contained 514 single-born children in addition to the premature children born in 1950, and of these 514 children 31.7% were premature. The hypothesis was then put forward that in these 205 families the probability that each of the other children (i.e.apart from the one born in 1950) would be premature was the same. As the distribution of prematurity throughout these families does not differ significantly from the expected distribution if the risk of prematurity to each child was the same, there is no reason for rejecting this hypothesis.

The/

The object of this section was to consider the proposition that, with certain exceptions, prematurity might be due to a predisposition on the part of certain mothers to have premature babies, and it was argued that if certain criteria could be fulfilled this would be a reasonable proposition. It is now submitted that if we allow the exclusion of those mothers who were primigravid in 1950, who had large families, or who were 35 years or older in 1950, these criteria have been fulfilled. It has been shown that the incidence of prematurity among other children in the remaining 205 families is unduly high, that it does not differ significantly before the premature child was born in 1950 and after, and that the distribution of prematurity throughout families of different sizes does not differ significantly from the expected distribution on the assumption that each child had an equal chance of being premature. Therefore the proposition that prematurity in these cases is due to a predisposition on the part of the mother is a reasonable one.

This conclusion of course applies only to the 205 cases which were left after the exclusion of all those cases in which factors associated with additional risk of prematurity might have operated in 1950. The method of exclusion was clumsy and arbitrary and involved the complete exclusion of all these cases. It was noted, however, that the incidence of prematurity among the other children of these excluded cases was also unduly high. For example, 17.2% of the later children of the

121 mothers who were primigravid in 1950 were premature, and 23.0% of the other children of the 58 mothers who were 35 years or older in 1950 were premature. It is therefore probable that in quite a substantial proportion of these cases the prematurity was also due to the same maternal predisposition, although such cases cannot be identified precisely. If this is the case, then it is possible that more than half of all prematurity is due to a predisposition on the part of the mother. It is important to consider the possible reasons for such a predisposition, but before doing so two other matters must be considered.

So far we have considered only the circumstances in which the pregnancy in 1950 took place and have ignored the characteristics of the pregnancy itself. For instance, it has already been mentioned that in any sample of premature children being investigated, 30%-40% of the so-called premature children are in fact small mature infants of low birth weight. The aetiology of 'prematurity' in these cases is obviously quite different from the aetiology in cases in which the period of gestation has been abnormally short. Since it has not been possible to disprove the hypothesis that the risk of prematurity to all the children of certain mothers is the same, it follows that the tendency for prematurity to occur several times in one family cannot be due solely to one or other of these two main types of prematurity, but must be a characteristic of both types./

types. Nevertheless it is important to examine in detail the birth weights of the other children in families in which these two main types of prematurity have occurred.

Further, although it has been shown that there is no good reason for supposing that prematurity is caused by obstetric complications, there is no doubt that there is an important association between them. It is therefore worth examining the data to see whether the presence of a complication during the pregnancy in 1950 has any relationship to the incidence of prematurity on other occasions.

These points will be examined in relationship to the 205 cases in which it appeared to be reasonable to presume that the prematurity in 1950 was due to a predisposition on the part of the mother. It has been shown that there is no reason to suppose that the risk of prematurity to each of the children of these mothers was not uniform. There is thus no reason to suppose that the 100 mothers who did not have any premature children apart from the ones born in 1950 were any less liable to have premature children than the 105 mothers who actually did have premature children more than once. It is therefore justifiable to compare the total incidence of prematurity among the additional children of different groups of these 205 mothers and if the difference is significant to conclude that one group is more liable to have premature children than the other.

This approach will be made to examine the incidence of prematurity in families in which it was due to low birth weight

at term as opposed to short gestation, and to examine the influence of complications of pregnancy in 1950 on the incidence of prematurity among other members of these families.

RELATIONSHIP BETWEEN BIRTH WEIGHT AND PREDISPOSITION TO PREMATURITY

The real purpose of this section is to compare the incidence of prematurity in those families in which the prematurity in 1950 was due to low birth weight at term with the incidence in those families in which it was due to an abnormally short period of gestation. The first difficulty which arises is that estimations of duration of pregnancy are not sufficiently reliable to be used to allocate individual cases into these two groups. It will be seen, however, from Table 32, that the majority of the full-time pregnancies have resulted in 'premature' children with fairly high birth weights and the majority of the short pregnancies have resulted in children with low birth weights. As birth weights are more reliable in individual cases than the reported duration of pregnancy it is more satisfactory to divide the cases according to birth weight, bearing in mind that the influence of the full-time children will be exerted mainly in the heavier weight groups.

In Table 33 the 205 children born in 1950 have been divided into four birth weight groups and the incidence of prematurity among the siblings of the children in each group is shown. The incidence of prematurity among the siblings of the lightest children is rather low (22.7%) but the number involved is small and/

and with this exception it appears that the mothers of the lighter children in 1950 are more likely to have premature children on other occasions than the mothers of the heavier children. For convenience the cases in the two lower weight groups have been combined and compared with those in the two higher weight groups. The difference in the incidence of prematurity among the siblings of children in these two combined groups is significant.

Since prematurity has been defined on the basis of birth weight this difference might simply mean that the siblings of the lighter premature children had a lower average birth weight than the siblings of the heavier premature children. The explanation, however, is more complicated than this, because it was found that lighter premature children also had a higher proportion of siblings with birth weights of 7 lbs. or more.

Reference has already been made to the significance which is attached to a birth weight of 7 lbs. or more. It is being used as a rough guide to the number of children who had a 'normal' birth weight, and although a few children may have a high birth weight because of post-maturity or maternal diabetes, the number of such cases must be small.

It is of course useful to consider the number of siblings with birth weights of 7 lbs. or more in relation only to the number of siblings which were not premature. This is done in Table 34 and it will be seen that the lighter children had

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a higher proportion of non-premature siblings with birth weights of 7 lbs. or more than the heavier children. The gradient is slightly different from the one shown for premature siblings in Table 33 and it is convenient to group together the cases in the three lightest birth weight groups and compare them with the cases in the heaviest group. When this is done the difference is found to be significant.

Thus, if we take these two findings together - the proportion of siblings which were premature and the proportion which had a birth weight of 7 lbs. or more - it is apparent that the lighter premature children had a higher proportion of both premature siblings and non-premature siblings with birth weights of 7 lbs. or more. That is to say, a higher proportion of the siblings were at one or other extreme of the birth weight distribution than was the case if the premature child in 1950 had been fairly heavy. The combined figures are shown in Table 35 and it will be seen that the variation in the total number of siblings which were either premature or 7 lbs. or more at birth is significant. Therefore, whatever the mean birth weights of the siblings may be, we can conclude that the birth weight distribution of the siblings differs radically with differences in the birth weight of the premature child born in 1950.

This difference is almost certainly due to the presence of most of the full-time children of low birth weight among the heavier premature children. We have already referred to the evidence (Karn,Lang-Brown,MacKenzie and Penrose,1951) that there is/

is a correlation or degree of likeness between the birth weights of the children of the same mother. Thus when a mother has had a full-time child of sufficiently low birth weight to be classified as premature, that is an indication of a tendency to have small babies. Therefore all the other babies of such a mother are likely to be small, some of them sufficiently so to be classified as premature, and few of them are likely to have birth weights of 7 lbs. or more. On the other hand, in the remaining cases of prematurity in which the pregnancy did not run its full course, the birth weight on that occasion is not a proper indication of the usual birth weights of the children of these mothers, and they do not necessarily tend to have children of low birth weight after normal pregnancies. Hence, many of the other children of these mothers, if they escape prematurity, have birth weights of 7 lbs. or more. What is perhaps more interesting is the fact that the mothers of these children also have such a high proportion of prematures among their other children. Thus no matter whether the prematurity in 1950 was due to low birth weight at term or to interruption of the pregnancy, there is a similar tendency to prematurity on other occasions. Since the two groups of cases are so radically different in origin we would expect that the prematurity on these other occasions would be due to the same causes as in 1950. Bearing in mind that the full-time 'premature'/

'premature' children tended to be of fairly high birth weight, and the premature children of interrupted pregnancies of low birth weight, it should be possible to show similarity between the birth weights of the children born in 1950 and any premature siblings which they had.

To show this the cases have been divided into two groups according to the birth weight of the child in 1950 - viz. up to and including 4 lbs. 15 oz. and over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz. (Table 36). The premature siblings were divided into the same weight groups and it was found that the majority of the premature siblings of the children with birth weights up to and including 4 lbs. 15 oz. were in the same birth weight group. Similarly the majority of the premature siblings of children who weighed over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz. were in the same higher weight group. This finding is significant. Thus in both cases the majority of the premature siblings fall into the same birth weight group as the child in 1950 and thus there is a tendency for the birth weights of all the premature children in a family to be similar. Therefore, if the prematurity in 1950 was due simply to low birth weight at term the prematurity which occurred among the siblings of such children would also be due, mainly, to low birth weight at term. This, of course, is not surprising, but it also follows that if the prematurity in 1950 was due/

due to the interruption of a pregnancy before term, then most of the prematurity which occurred among the siblings of these children was also due to the interruption of pregnancy before term.

Thus although it is still true to say that if prematurity has occurred on one occasion the chances that it will have occurred on other occasions during the reproductive career of that particular mother are much higher than usual, it is important to recognize that this is due to two different processes. On the one hand there is a tendency for certain mothers to have children of low birth weight, and on the other hand there is a tendency for the pregnancies of certain women to fail to go to term. This, however, does not interfere with the hypothesis that prematurity in these 205 cases was due to a predisposition on the part of the mothers to have premature babies. It merely shows that there are at least two different types of predisposition - one to have babies of low birth weight, and the other to have abnormally short pregnancies - both of which result in prematurity according to the currently accepted birth weight definition.

RELATIONSHIP BETWEEN COMPLICATIONS OF PREGNANCY AND PREDISPOSITION TO PREMATURITY

It has already been mentioned that 192 of the total 515 pregnancies which resulted in the birth of a premature child in 1950 were complicated, and the majority of these complications were toxaemic in origin. Of the group of 205 cases which are/

are being considered at the moment, 67 of the pregnancies in 1950 were complicated.

From evidence to which reference was made in the section on aetiology it is clear that there is a strong relationship between prematurity and complications of pregnancy, in that prematurity occurs more often in complicated pregnancies than in uncomplicated ones. It has been usual to assume that in these circumstances the prematurity was caused by the complications, but there is no proof that this is so. Nevertheless complications of pregnancy are important accompaniments of prematurity and it is worth examining the data to see whether there is any relationship between the presence of complications during the pregnancy in 1950 and the birth weights of the siblings.

The 205 cases have been divided into uncomplicated and complicated groups according to whether the pregnancy in 1950 was complicated or not and in Table 37 the incidence of prematurity among the siblings of each group of cases is shown. It will be seen that the incidence is greater when the pregnancy in 1950 was uncomplicated, and the difference is significant. This agrees with the figures reported by Brander (1939) who found that in his uncomplicated cases the risk of prematurity among the siblings was higher than in his complicated cases. He was unable to offer an explanation, and the interpretation is not straightforward, but it will be shown later that the mothers who had complicated pregnancies in 1950 had a higher incidence/

incidence of still-births and abortions among their other pregnancies than the mothers who had uncomplicated pregnancies and this excess apparently compensates for their deficiency in premature live births. The lower incidence of prematurity among these mothers should not be interpreted as a sign of better reproductive performance, but is rather the reverse. This will be discussed again when the incidence of still-births and abortions is considered.

Equally important, however, is the finding (Table 38)that when the pregnancy in 1950 was complicated a significantly higher proportion of the non-premature siblings had birth weights of 7 lbs. or more than was the case when the pregnancy in 1950 was uncomplicated. This is probably because the majority of the mothers who had full-time children of low birth weight would have had uncomplicated pregnancies in 1950, and these mothers had fewer children with birth weights of 7 lbs. or more than the others.

When the cases in the uncomplicated and complicated groups are considered according to the birth weight in 1950 it again appears that the differences which exist are largely due to the concentration of the cases of simple low birth weight in the uncomplicated group. First of all, in both groups of cases (Tables 39 and 40) it is apparent that the incidence of prematurity increases as the birth weight of the child born in 1950 decreases. In the group in which the pregnancy in 1950 was/

was uncomplicated the increase is fairly steady, except for the few cases which had birth weights of 3 lbs. 4 oz. or less and if the upper two birth weight groups and the lower two are combined, the difference is almost significant. On the other hand, when the pregnancy in 1950 was complicated the variation is less regular and although if the upper two birth weight groups and the lower two are combined and compared the difference is significant it is doubtful whether much importance should be attached to this.

The numbers of non-premature siblings with birth weights of 7 lbs. or more are probably more reliable (Tables 41 and 42). Again it is apparent that in both groups of cases the proportions with birth weights of 7 lbs. or more increase as the birth weight in 1950 decreases, but this is more marked in the uncomplicated group than in the complicated one and perhaps the outstanding feature is that the two heavier groups of premature children of uncomplicated pregnancies had only 42.2% of non-premature siblings with birth weights of 7 lbs. or more. This is much less than any other group of cases. This confirms the expectation that the 'premature' children which are actually full-time children of low birth weight are concentrated among the heavier children of uncomplicated pregnancies.

We can now consider the question of whether there are any differences in the reproductive histories of mothers with uncomplicated and complicated pregnancies in 1950 to suggest that there/

there is any fundamental difference between the aetiologies of prematurity in these two groups of cases. In the first place, there is less prematurity in the families in which the pregnancy in 1950 was complicated, but it will be shown that this is offset by more still-births and abortions. Apart from this the other differences appear to be due to the fact that those cases of 'prematurity' due to low birth weight at term are concentrated mainly in the uncomplicated group. Thus the only real difference appears to be that when the pregnancy in 1950 was complicated there is a tendency for pregnancies to end in still-births and abortions rather than in premature live births. It could be argued that this difference is one of degree and is not fundamental, but discussion of this will be postponed until the incidence of still-births and abortions has been considered.

STILL-BIRTHS AND ABORTIONS

When the mothers of these 515 premature children were interviewed in 1955-56 they were asked if they had had any still-births or abortions. In the case of still-births it was seldom possible to ascertain the period of gestation or the birth weight. However, for reasons which have already been given, it is felt that the information about the incidence of still-births and abortions is reasonably accurate. Abortion is taken to mean the expulsion of the products of gestation before the 28th week of pregnancy, unless of course the foetus survived and was regarded as a live birth, but it is probably

as well not to draw too firm a distinction between abortions and still-births.

The 205 mothers in the special group being considered at the moment had 654 pregnancies in addition to the 205 which resulted in the premature babies in 1950. Of these 654 additional pregnancies, 23 (3.5%) resulted in a still-birth, and 95 (14.5%) in an abortion. The incidence of abortions is thus higher than the estimated 7-11% given by the Royal Commission on Population (1950) so that these women are probably more liable than usual to have abortions.

The incidence of both these abnormalities is shown in Table 43, in which the cases have been divided according to the birth weight of the child born in 1950. The numbers of still-births are too small to show any trends, but there is a higher incidence of abortions among the pregnancies of the mothers who had the lighter children in 1950. If the lower two birth weight groups and the upper two birth weight groups are combined and compared the difference is significant. Thus the women who had the lighter babies in 1950 had not only a greater incidence of prematurity in their families than the women who had the heavier babies, but they also had a greater incidence of abortions.

The next point to consider is the difference between those cases in which the pregnancy in 1950 was uncomplicated and those in which it was complicated. The figures are shown in Table 44 and it will be seen that when the pregnancy in 1950 was complicated/

complicated the combined incidence of still-births and abortions is significantly greater than when the pregnancy was uncomplicated. This is in agreement with the findings of Bryans and Torpin (1949) who followed up 243 cases of eclampsia for an average period of 12 years and found that of their subsequent pregnancies 22.9% ended in still-birth or abortion, so that the foetal mortality was about twice as high as would have been expected. A similar conclusion was reached by Banister (1930) when he found that in about 30% of cases who had had either eclampsia or pre-eclampsia there was a tendency towards either recurrence of the same condition in subsequent pregnancies or towards some other complication of pregnancy such as antepartum haemorrhage, abortion, or intra-uterine death of the foetus in later weeks.

Now it was shown that the mothers who had complicated pregnancies in 1950 had fewer premature live births in their families than the mothers who had uncomplicated pregnancies (Table 37) and it has now been shown that they have more still-births and abortions. This leads to the question of whether we are entitled to regard prematurity, still-births and abortions as one entity and say that the excess of still-births and abortions compensates for the deficiency of premature live-births. Young (1927) has postulated that there exists an abortion - premature birth - toxaemia sequence, and that certain women have a succession of abortions, premature births, still-births,/

still-births and toxaemic pregnancies, but these same women are capable of having perfectly normal pregnancies. Young attributed this to an unknown "X" factor. Malpas (1938) described cases with recurrent toxaemia and sequential abortion and apparently accepted the existence of an abortion - still-birth sequence due to recurrent toxaemia. It has also been accepted by others (Breakey,1932; Bryans and Torpin,1949) although Young's conception of an "X" factor as a morbid influence is not necessarily accepted. However, if it is accepted that the abortion - premature birth - toxaemia complex is a real entity then we are bound to think in terms of a common aetiology.

In our own data the fact that the women who had the lightest children in 1950 had not only the highest incidence of prematurity among their other children but also the highest incidence of abortions suggests that there is some relationship between abortions and prematurity. Further, it is known from the Annual Reports of the Chief Medical Officer of the Ministry of Health that about half of all still-born babies are premature.

There is therefore some justification for regarding premature births, abortions, and still-births as part of one entity, and when this is done it is found (Table 45) that the combined incidence of prematurity, abortions and still-births among all the other pregnancies of mothers who had uncomplicated pregnancies in 1950 is 43.7%, while the incidence among the other pregnancies of mothers who had complicated pregnancies/

pregnancies in 1950 is 41.7%. There is thus very little difference between the incidence of prematurity, abortions and still-birth taken together and the real difference lies in the fact that when the pregnancy in 1950 was complicated there is a tendency for pregnancies to end as still-births or abortions rather than as premature live-births. There is therefore no quantitative difference in reproductive performance, but there is a qualitative one. Again there is nothing in this to interfere with the hypothesis that prematurity in these 205 women is due to a predisposition on the part of the mother.

DISCUSSION

The findings which have to be interpreted are briefly as follows. Certain women apparently have a tendency to have premature babies, and their reproductive histories are characterised by a very high incidence of prematurity, and by an incidence of abortions which is probably abnormally high, especially if their premature children were very small. At the same time these women have shown that they are perfectly capable of having babies of normal birth weight. Differences in the birth weight distributions of the children of different groups of mothers are largely due to two facts - that a number of full-time children of low birth weight are classified as premature according to the birth weight definition and that when the pregnancy in 1950 was complicated the quality of reproductive performance tended to be worse.

Any/

Any interpretation which is placed upon these findings must take into account the significance of the complications which occurred during some of the pregnancies in 1950. To hold that the complications which occurred in 1950 stood in causal relationship to the prematurity on that occasion would not allow a rational explanation of the observations, because it is then necessary to assume that the prematurity in the uncomplicated cases was due to other unknown causes. This is hardly consistent with the striking similarity in the reproductive performances of the two groups of mothers, the only difference being a tendency for the mothers who had complicated pregnancies to have still-births and abortions instead of premature live-births, and some differences due to the concentration of full-time children of low birth weight in the uncomplicated group of cases. There is, however, no sound justification for the belief that prematurity is due to the complications of pregnancy which often accompany it. It is more reasonable to suggest that the prematurity and complications have a common origin, and there is some evidence to support this view. Walker and Turnbull (1953) showed that the foetal haemoglobin is abnormally high in the presence of toxaemia and placenta praevia, or if there was a history of threatened abortion, and this of course indicated that the foetus had suffered from anoxia. They also found a high foetal haemoglobin in babies which were born prematurely and since the foetal haemoglobin was raised even in babies which were premature for unknown reasons/

reasons it could not be said that the foetal anoxia was due to the presence of complications. It seems more likely that the same process was responsible for both the prematurity and the toxaemia, which may appear separately or together, and interference with the oxygenation of the foetus was in some way part of this process.

On this basis a rational explanation of the observations in the present survey is possible. We are dealing with a group of mothers who apparently all have a predisposition to have premature babies, and yet are quite capable of having normal babies. We have shown that this predisposition is made up of two components - a predisposition to have full-time babies of low birth weight, and a predisposition to have abnormally short pregnancies - both of which result in prematurity according to the birth weight definition. There is evidence, which has been quoted earlier (Baird,1945b; Baird and Illsley,1953), of a relationship between maternal height and the occurrence of prematurity, and there is also evidence (Drillien,1957) that this relationship is particularly associated with full-time 'prematurity'. Drillien showed that, if the mothers of 'premature' children were divided into two groups, those delivered prematurely and those delivered at term, the mothers of the full-time 'premature' babies were smaller than the mothers of babies delivered before term. If we consider this along with the evidence that there is an association/

association between maternal height and birth weight (Walton and Hammond,1938; Thomson,1951; Tanner,Healy,Lockhart,MacKenzie and Whitehouse,1956), and the evidence that there is a degree of likeness between the birth weights of siblings (Karn,Lang-Brown,MacKenzie and Penrose,1951), it seems probable that the predisposition to have full-time babies of low birth weight is largely due to small maternal stature. This small maternal stature may be due to poor nutrition in childhood, as Baird (1945b) suggested, or to genetic causes, a possibility which Martin (1954) thought could not be dismissed. However, the result of this small maternal stature seems to be that the average birth weight of the children of these mothers is reduced, so that a certain proportion of them are classified as premature.

The majority of the mothers of premature babies have a predisposition to have abnormally short pregnancies, and it is this important group which we must consider now. It has been shown that the prematurity in the families of these mothers occurs in apparently random fashion, so that the risk of prematurity to each child must be the same. This suggests that there is some form of control over the proportion of children in these families who will be premature, so that a certain proportion of the pregnancies of these mothers apparently cannot go to term. We are therefore faced with the problem of why, in a certain proportion of pregnancies, these mothers go into labour before the end of the normal gestation period.

The/

The way in which labour is initiated at the end of a normal pregnancy is not known, but it can be regarded as a reaction between the mother on the one hand and the products of conception on the other. Whatever the exact mechanism may be, it is presumably the products of conception which initiate the onset of labour, while the mother thereafter plays the active rôle. Now in the cases under consideration we have a group of mothers who go into labour prematurely in a proportion of their pregnancies, but we know that these same mothers are also capable of having pregnancies which go to term and result in babies of normal birth weight. It therefore seems unlikely that the explanation of the early onset of labour, when it occurs in these cases, is to be found in the mothers. In the first place, it is probably the function of the products of conception to initiate labour, and further, the mothers have demonstrated that they are capable of maintaining some of their pregnancies to term. It is more likely that the fault is to be found in those foetuses which are born prematurely. In other words, a certain proportion of the foetuses of these mothers must have some property or attribute which causes their mothers to go into labour prematurely, while the remainder of the foetuses of these mothers do not have this property.

There are two ways in which these foetuses could acquire such a property - as a result of environmental influences, or by inheritance. In this particular case it seems unlikely that/

that environmental influences are responsible. The foetus is peculiarly protected from external influences of this sort and in any case it is highly improbable that such influences would result in a random distribution of prematurity throughout these families. The other way in which such a property could be acquired is by inheritance. We have so far talked about the mothers having a predisposition to prematurity but although the mothers may exert some modifying influence it is really the matings of a particular man and woman which have resulted in the premature children, for with few exceptions we were dealing with ordinary family units. That certain of the foetuses from such matings should inherit some peculiar quality which causes their mothers to go into labour prematurely is perfectly feasible. We can only make very tentative suggestions about how this may actually be brought about, but no doubt some pathological train of events is involved. It has been shown (Walker and Turnbull,1953) that foetal anoxia is a feature common to prematurity and a number of complications of pregnancy, and it is not impossible that these are all manifestations of the same process. It might be that the appearance of these manifestations is influenced by modifying circumstances, but this does not invalidate the basic suggestion that the prematurity in these cases is due to a maternal-foetal reaction resulting from the genetic constitution of the foetus.

This/

This theory would be supported by any evidence which showed that prematurity occurred more frequently than would be expected among the relatives of the parents of premature children. Brander (1939) gave many instances of families in which prematurity had occurred in several branches of the family, or in several generations, but declined to conclude that there was a hereditary predisposition because in so many cases another possible cause was present. Such other causes, however, consisted of accidents, intercurrent illness, pyelitis and paternal alcoholism, and it is doubtful whether these should have been allowed to stand in the way of accepting the possible influence of heredity. Martin (1954), in comparing a large sample of primiparous mothers of premature children with a similar sample of mothers of full-time children, reported that 28.1% of the premature group claimed that either their mothers or their siblings, or both, had been premature, compared with 17.9% of the control group, and this difference was significant.

Our present material has yielded similar evidence, although it has been looked at from a different direction. In the course of the enquiry the mothers were asked whether they themselves or their husbands had been premature, or if they knew of any other children in their families who had been premature or had low birth weights, or of any in the families of their husbands. Only those cases in which the mother seemed reasonably/

reasonably sure of the facts were considered to have a positive family history of prematurity. It is recognised that information of this sort is not above suspicion, but it is hoped that the error, if any, will be that some cases with a positive family history have been excluded but that none without it have been included. In this way it was found that out of the total of 515 cases there was a positive family history in 111, or 21.6%. It was particularly interesting that of these 111 cases the history was on the father's side in 35 (31.5%). As the informant was nearly always the mother, who is likely to know less about her husband's family than about her own, it may be that a positive family history is as common on the father's side as on the mother's. There is no doubt that failure to elicit a family history of prematurity was often due to ignorance. It might be thought that older women with larger families would be better informed and would thus be more likely to give a positive family history if it existed. This, however, does not appear to be the case and Table 46 shows the proportion of women giving positive histories, according to the number of previous pregnancies which they had had at the time the premature child was born in 1950. Although there seems to be a slight gradient with increasing parity, this is not significant and this possibility of bias can be rejected.

Now if the genetic constitution of the foetus is related

to the occurrence of prematurity we would expect to find more prematurity among the children of parents with a family history of prematurity than among the children of parents without such a history. We have, however, divided the cases into aetiological groups, and these groups must be considered separately. It will be recalled that only 435 of the 515 mothers had any other single live-born children, and in 205 out of these 435 cases the occurrence of prematurity in 1950 was apparently not related to extraneous influences and the distribution of prematurity throughout these families did not differ significantly from the expected distribution on the assumption that the risk of prematurity to each child was the same. From this we have suggested that the prematurity in these 205 families, apart from the 'prematurity' due to low birth weight at term, was due ultimately to the genetic constitutions of the foetuses concerned, and, if this is so, the fact that a family history of prematurity was elicited ought not to make any difference to the incidence of prematurity in these families. Presumably the genetic mechanism is functioning in any case and whether or not we obtained a family history would depend on the chance distribution of prematurity among the relatives, the number of relatives, and how much the parents knew about them. This expectation is confirmed in Table 47 which shows that the incidence of prematurity among the other children of these 205 mothers is the same, whether there was a family history of prematurity or not.

The position regarding the remaining 230 mothers out of the/

the 435 who had other children is quite different. It was shown that in these cases there was reason to believe that some of the prematurity in 1950 was due to special circumstances which applied exclusively to that pregnancy and did not apply to the other pregnancies of these mothers. Although only some of the prematurity would be due to these special circumstances it was necessary to withdraw large groups of cases from the data because there was no means of identifying these special cases among them. These 230 cases therefore consist of two undifferentiated groups of cases, in one of which the prematurity in 1950 was due to special circumstances, while in the other it may have been due to the same predisposition which was apparently the cause of prematurity in the other 205 cases. Therefore in these 230 cases a family history of prematurity might indicate that the prematurity was due to the genetically determined predisposition, whereas the absence of a family history would indicate that the prematurity was due to causes peculiar to the pregnancy in 1950. If this is the case we would expect to find more prematurity among the other children in the families in which there was a family history of prematurity, since they would all be subject to an abnormal risk of prematurity. Table 48 shows that in this group of 230 mothers there actually was significantly more prematurity among the other children of those mothers who had given a family history of prematurity than among the other children of those who had/

had not. Not only so, but the incidence of prematurity among the other children of those mothers who gave a family history is curiously similar to the incidence among the other children of the 205 mothers who apparently showed a predisposition to prematurity, and this supports the contention that in these cases the same predisposition operated.

It might be objected that the mothers who had had premature children more than once would be likely to take a keener interest in the occurrence of prematurity among their relatives and for this reason would be more likely to give a positive family history when asked. It is impossible to refute this objection entirely, but if this was the case we ought to have found that the women in the group of 205 cases with a predisposition to prematurity who gave a family history were the ones who happened to have most prematurity among their own children. This was certainly not what was found (Table 47) and there is no reason to suppose that this objection would apply with any more force to the other 230 cases.

Therefore it can be concluded that in a mixed group of cases in which some of the prematurity may be due to a predisposition to prematurity and some not, the mothers who gave a family history of prematurity had more prematurity in their families than the mothers who did not, but in a homogeneous group in which all the prematurity is apparently due to a predisposition, a family history of prematurity is not associated with such a difference. This conclusion gives support to the suggestion that the predisposition to prematurity shown by certain

mothers is due to the genetic constitution of a proportion of their foetuses.

CONCLUSIONS.

The aim of this study was to examine the occurrence of prematurity against the background of the reproductive tendencies of the mothers of premature children, and to consider the possibility that certain mothers have a predisposition to premature delivery. It was suggested that we should regard the outcome of each individual pregnancy as the result of the action of two sets of forces - the mother's reproductive tendencies, and relevant modifying factors. It is possible that the action of either set of forces could result in prematurity - that is to say, either the mother has a tendency to premature delivery, or certain factors influenced the pregnancy concerned and resulted in premature delivery on that particular occasion. Now, it is known that premature delivery is more likely to occur in certain circumstances than in others, and hence it follows that the action of special factors in these circumstances must play some part in causing the prematurity. Thus, even if certain mothers have a fundamental tendency to have premature babies which may express itself during any pregnancy, all mothers are apparently liable to have premature babies on particular occasions if certain factors operate. Therefore, if we examine the reproductive histories of mothers of premature babies the underlying pattern which would result from a predisposition to premature delivery will be confused by/

by the inclusion of the reproductive histories of mothers who had premature babies because of special circumstances applying to particular pregnancies. Much of the present study was necessarily devoted to disentangling this confusion.

The main conclusion is that much of the prematurity which occurs is the result of a predisposition to premature delivery on the part of certain mothers. If we eliminate all the instances of prematurity which might possibly be accounted for by the action of extraneous influences, almost half the cases remain, and it was shown that the prematurity in these cases can reasonably be attributed to a predisposition on the part of the mothers. To some extent this predisposition is simply the tendency of certain mothers, probably of small stature, to have full-time babies of low birth weight, who are classified as premature if they happen to weigh $5\frac{1}{2}$ lbs. or less, but in the majority of cases there is a predisposition to have abnormally short pregnancies and a certain proportion of the pregnancies of these mothers fail to go to term. This failure is due, in the first instance, to the genetic constitution of the foetus, which has inherited some property which causes an abnormal maternal-foetal reaction resulting in premature delivery. It is suggested that such complications of pregnancy as may appear in these cases are generally/

generally further manifestations of this reaction, and are certainly not the cause of the prematurity. There is no fundamental aetiological difference between prematurity which occurs after uncomplicated pregnancies and prematurity which occurs in association with complications.

In order to demonstrate the existence of this predisposition to prematurity we eliminated those cases in which it was possible that the prematurity in 1950 was due to the action of influences peculiar to these particular pregnancies and not to a predisposition on the part of the mothers. From the figures obtained in this investigation, and from what was already known from previous work, it seems that prematurity can be caused by factors associated with first pregnancies, high parity, and pregnancies during the later child-bearing years. In slightly more than half the cases in this study the pregnancy in 1950 was a first one, or the mother had already had several pregnancies, or she was 35 years or older, and these special factors might have been responsible for the prematurity on that occasion. As it was not possible to identify precisely the cases in which these factors operated it was necessary to remove them all from the data and concentrate on the cases in which the reproductive histories of the mothers were not confused by the addition of the cases in which the prematurity in 1950 was due to special circumstances on that occasion. Nevertheless, the incidence of prematurity among the other children/

children in the families which were excluded in this way was still unduly high, and it is likely that the special circumstances accounted for the prematurity in 1950 in a minority of cases only, while in the majority of them it was probably due to the same fundamental predisposition to prematurity which apparently accounted for the prematurity in the other cases which did not have to be removed from the data.

Thus the majority of cases of prematurity are due to a predisposition on the part of the mother, either to have mature babies of low birth weight, or to have abnormally short pregnancies because of the occurrence during certain pregnancies of an abnormal maternal-foetal reaction of genetic origin. Most of the remaining cases are caused by factors associated with first pregnancies, high parity, and pregnancies in the later child-bearing years. Doubtless there are a few cases of prematurity due to various other causes such as systemic illness of the mother during pregnancy, but the number of such cases is very small.

One further conclusion has emerged. The mothers of the premature children in this investigation had an unduly high incidence of abortions among their pregnancies. This is especially so if we exclude the mothers of the heavier premature children, many of whom would be mature children of low birth weight./

weight. It therefore follows that the mothers who tend to have premature children because of interrupted pregnancies also tend to have abortions. It is, of course, a fundamental characteristic of both prematurity and abortion that the pregnancy is interrupted before term, and we have already quoted Crew (1949) to show that many abortions are probably due to the action of genes, an aetiology very similar to the one which we have advanced to account for so much prematurity. We have also referred to other observations of a tendency for abortions and prematurity and sometimes toxaemia to occur on several occasions during the reproductive careers of certain women. This evidence is not sufficient to justify an unqualified assertion that abortion, prematurity, and toxaemia have a common aetiology, but it is sufficient to allow us to conclude that the causes of these three abnormalities have something in common.

S U M M A R Y

1. The neo-natal death rate among premature babies is very much higher than that among mature babies, and as a result of the changing pattern in infant mortality in recent years prematurity has become relatively more important as a cause, or contributing cause, of infant deaths.

2. When surviving premature children are compared with surviving mature children it has been found that the premature children are at a disadvantage in various respects.

3. For these reasons it is important to attempt to reduce the incidence of prematurity, but this object is hampered by inadequate knowledge of the aetiology of prematurity.

4. A premature child is defined as a child who weighs 5½ lbs. (2500 G.) or less at birth, regardless of the length of gestation. In spite of its faults, this is the best definition available.

5. The aetiology of prematurity is not fully understood. In about half the cases of prematurity which occur no cause can be defined. In the remaining half the prematurity is associated with complications of pregnancy and it is generally assumed that these complications are the cause of the prematurity, but the way by which this/

this is brought about is not known. It is known that a large number of factors such as social class, maternal age, and parity influence the prematurity rate. It is also known that prematurity tends to be repeated and this tendency may be associated with a tendency to abort and show signs of toxaemia.

6. The aim of this study was to examine the occurrence of prematurity against the background of the reproductive tendencies of the mothers of premature children. In order to do this, we interviewed the mothers of 515 single-born premature children who had been born in Glasgow during the year 1950, and obtained the obstetric histories of these mothers. There does not appear to be any bias in the sample which would influence the conclusions which will be drawn.

7. The incidence of prematurity among the single-born siblings of these premature children was 26.4%. It was shown that in a number of cases the prematurity in 1950 might have been caused by factors associated with that particular pregnancy, but if these cases were excluded it would be reasonable to postulate that the prematurity in the remaining cases was due to a predisposition on the part of the mothers to have premature babies.

8. This predisposition to prematurity is made up of two tendencies - one to have mature babies of low birth weight

which/

which are by definition premature, and the other to have abnormally short pregnancies.

9. There is no fundamental difference between the reproductive histories of mothers who have premature babies after uncomplicated pregnancies and mothers who have premature babies after complicated pregnancies . Such differences as appear to exist are due to a tendency for the mothers who had complicated pregnancies to have still-births and abortions instead of premature live-births among their other pregnancies, and to the fact that most of the mature children of low birth weight who are classified as premature are born after uncomplicated pregnancies. There is an important relationship between prematurity and complications of pregnancy in that prematurity occurs more often in the presence of complications than in their absence, but the similarity in reproductive histories, and the absence of satisfactory evidence to the contrary, justifies the rejection of the view that prematurity is caused by complications of pregnancy.

10. The incidence of abortions among the other pregnancies of the mothers of these premature children was unduly high, especially when the birth weight of the premature child had been low. This and other evidence led to the conclusion that there is some common factor in the aetiologies of abortion, prematurity, and toxaemia.

11. The/

11. The main conclusion drawn from this study is that most cases of prematurity are due to a maternal predisposition to have premature babies. This may simply be a tendency for certain mothers, probably of small stature, to have full-time babies of low birth weight, but more often it is due to a tendency to have abnormally short pregnancies. These short pregnancies are caused by a maternal-foetal reaction due ultimately to the genetic constitution of the foetus. This conclusion is supported by the finding that there is a relationship between a history of prematurity in the family of either parent and the incidence of prematurity among their children. Most of the remaining cases of prematurity, which are not due to a maternal predisposition, are caused by the action of factors associated with first pregnancies, high parity, and pregnancies during the later child-bearing years. A small residue is due to various other causes.

A P P E N D I X.

Progress and Development of Premature Children.

The field work of this investigation involved visiting the mothers of the 515 single-born children who formed the material for the main part of the work at a time when the children were just over 5 years old and had recently entered school. Opportunity was therefore taken to ask the mothers for an account of the children's health up till that time, and to visit the schools which they were attending to scrutinise their medical records and obtain the findings of the first school medical examination.

When the records of the Medical Officer of Health were being examined to obtain the names of these premature children the names of all premature children were extracted regardless of whether they resulted from single or multiple pregnancies. Multiple births were excluded from the discussion of aetiology, but in fact the names of 225 premature twins born during the year 1950 were obtained and an attempt was made to trace and visit the mothers of these children. Like the singletons, these children were either stated on the Health Visitors' records to have had birth weights of $5\frac{1}{2}$ lbs. or less, or to have been born prematurely. No attempt was made to trace the mothers of children who had died, and these 225 children were known from the Health Visitors' records to have survived. The mother of one pair of twins refused to co-operate, but/

but of the remaining 223 individual children, 155 (69.5%) were ultimately traced and included in the survey. Of the 68 who were not traced, the birth weights of 16 had not been recorded by the Health Visitors and it is doubtful how many of them would have been premature by birth weight definition. Of the remaining 52 of known birth weight who were not traced, 25 had left the city, and 2 had been adopted. This left only 25 of whom no trace could be found. These figures are given in Table 49. It is probable that the 155 who were included in the survey are a reasonably unbiased sample. Fifty-five of these 155 children had lost their partners through still-birth or death, or else their partners had weighed more than 5½ lbs. at birth and were therefore not regarded as premature. The remaining 100 children were in pairs - i.e. 50 pairs.

In an earlier section evidence was quoted (Steiner and Pomerance,1950; Record,Gibson and McKeown,1952) to show that premature babies born of multiple births have lower mortality rates than single-born babies of similar birth weight, thus suggesting that they are more mature than their birth weights would indicate. Because of this it is worth examining the progress of these twin premature children and comparing them with the single-born ones as well as comparing both groups with suitable standards for all Glasgow children.

The birth weight distributions of the premature singletons and the premature twins differ (Table 50) and this must be borne/

borne in mind in making comparisons, but apart from this there are no apparent differences which are likely to influence the comparisons which will be made. The social class distributions of both groups are similar (Table 51).

Previous work on the progress and development of premature children has already been quoted (p.11 to p.18) and it has been shown that premature children have an excessive amount of illness in their early years, much of the excess being due to lower respiratory infection, that they have a higher incidence of congenital defects than mature children, that they lag behind mature children in physical development for at least some years, that they have a greater incidence of mental deficiency, epilepsy, and spastic paralysis than children of normal birth weight, and that their intelligence is slightly lower than the intelligence of comparable non-premature children.

The information which was obtained about the progress of the premature children in this investigation is in general agreement with previous findings, but some new points have emerged. It is proposed to present this information under a number of separate headings.

Hospital Care during First Five Years of Life.

The mothers were asked about all the admissions of their children to hospital up till the time when they went to school. The number of admissions, the duration of each spell in hospital, and the reasons given by the mothers for each admission were/

were all noted. From this information the total time spent in hospital by each child was calculated. The time spent in the maternity hospitals immediately after birth was, of course, omitted.

It was found that the total time spent in hospital by these premature children was related to birth weight. The numbers of single-born children in each birth weight group who had spent varying times in hospital are shown in Table 52. It will be seen that while the numbers of children who had never been in hospital, or who had spent short periods in hospital, do not vary appreciably with birth weight, it is clear that the proportion of children who spent over 3 months in hospital is much greater among the children of very low birth weight than among the children who had been heavier at birth. This variation with birth weight is significant.

This agrees with an earlier follow-up of premature children in Glasgow (Ferguson, Brown, and Ferguson,1952) when it was found that "... the proportion receiving hospital treatment was high among infants who had weighed not more than 4½ lbs. at birth". It also agrees with the findings of Douglas and Mogford (1953b) that the amount of hospital care required by premature children in their first 4½ years was excessive if the birth weight had been less than 5 lbs. These workers also found that the amount of hospital care required by males was greater than that required by females, but this is not supported by the present investigation. Of the 25 children who spent

over/

over 3 months in hospital only 11 out of a total of 229 (4.8%) were males while 14 out of a total of 286 (4.9%) were females.

The amount of hospital care required by the twins is shown in Table 53. Although the numbers are smaller the general distribution seems to be the same as in the case of the single-born children (Table 52) and the totals in the two groups differ very little.

Incidence of Lower Respiratory Infections.

It was decided to accept admission to hospital with a diagnosis of pneumonia or bronchitis as an indication that a child had had a lower respiratory infection. It is probable that nearly every child with such an infection resulting in more than a slight and transient illness would be admitted to hospital, particularly in view of the unsatisfactory housing conditions in which so many of them lived. The number of children admitted to hospital with a diagnosis of pneumonia or bronchitis will therefore give a fairly accurate estimate of the incidence of these infections.

The numbers of single-born children in each birth weight group who were admitted to hospital at least once with a lower respiratory infection are shown in Table 54. Although 12.0% of all the single-born children had been admitted at least once it is apparent that the incidence increases markedly with diminishing birth weight and this variation is significant.

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This agrees with previous findings. Drillien (1948) reported that in the first year of life the pneumonia rate in a group of premature children was six times the rate in a control group. Douglas and Mogford (1953b) confirmed this excess of respiratory infections in the first year of life and showed that it took the form of bronchitis and pneumonia and although it affected mainly the first year of life, some excess persisted into the second year.

The numbers of twins in each birth weight group who were admitted to hospital at least once with a lower respiratory infection are shown in Table 55. It will be seen that the total incidence was 10.3%, which is similar to the total incidence among the single-born children but there is no evidence of variation with birth weight.

Type of School Attended.

As part of the investigation the schools which the children were attending were visited and their medical records examined. The records of 489 (95.0%) of the 515 single-born children and of all the 155 twins were seen. Some of the 26 single-born children whose records were not seen were attending private schools and a few of them could not be traced at the schools which their mothers said they were attending.

It is of some interest to consider the numbers of children attending normal and special schools. Of the 489 single-born children, 12 (2.5%) were attending special schools and occupation centres. When the children were divided into birth weight groups/

groups it was found that 10 out of 190 (5.3%) with birth weights up to and including 4 lbs. 15 oz. were attending special schools and occupation centres, whereas only 2 of the 299 (0.7%) with birth weights over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz. were attending special schools and occupation centres. It is also interesting to note that only one of the 155 twins was attending a special school and this child was a female who had a birth weight of 4 lbs. and had deafness following tuberculous meningitis. Her partner was a normal male with a birth weight of 6 lbs.

These findings are in agreement with the work of Asher and Roberts (1949) who found an excess of children with low birth weights among educationally sub-normal children amd mental defectives.

Defects Found at School Medical Examination.

The children were examined by a school medical officer shortly after admission to school and their heights and weights and any defects found were noted on their medical record cards. Each child was then classified according to the defects found, the basis of the classification being the remediability of these defects. When the records were examined it was found that 485 of the single-born children and 154 of the twins had been classified in this way.

Of the 485 singletons, 231 (47.6%) were free from defects, and of the 154 twins, 78 (50.7%) were free from defects. If we/

we exclude the 13 children at special schools and occupation centres, we are left with a total of 309 out of 626 (49.4%) of the children attending ordinary schools free from defect. By contrast, 59.0% of all the children in this age group at ordinary schools in Glasgow during session 1955-56 were free from defect (Ewan,1957). It is therefore apparent that the incidence of defects among premature children at the first school medical examination is much higher than the general incidence. This was also found in the earlier follow-up of premature children in Glasgow to which reference has already been made (Ferguson, Brown, and Ferguson,1952). Although many different types of defect contribute to this excess among premature children, one defect in particular attracted attention during this investigation and appears to have received little notice in the past. This was the incidence of squints.

Prematurity and Squints.

According to the school medical records, 46 out of 486 (9.5%) premature singletons and 11 out of 154 (7.1%) premature twins had squints at the time of their first medical examination. This gives a total incidence among these children of 57 out of 640 (8.9%). In contrast to this, the incidence of squints among all Glasgow children in this age group during the session 1955-56, calculated from the figures given in the Annual Report of the School Health Service (Ewan,1957), was 4.69%, and this incidence has varied little in recent years.

It therefore appears that premature children have an abnormally high incidence of squints, and further, it appears that the incidence increases with diminishing birth weight (Table 56), although with the present numbers this variation is not significant.

There are two earlier findings which give some support to the conclusion that premature children are particularly liable to have squints. Heinonen (1947) in Copenhagen found that the incidence of prematurity among persons with squints was 8.8% whereas the general incidence was only 3.2%. This, however, was based on small numbers and was not conclusive. Centano, Walter, and Thelander (1956) reported on a follow-up of premature children in California to the age of 6 years, and while their losses were very heavy, they found that 15 out of 218 (7.1%) of the children had squints. It therefore seems fairly certain that the incidence of squints among premature children is greater than among mature children. The information at present available does not specify the types of squints found in these children and this calls for further investigation.

Physical Development and Growth Rates.

The school medical examinations of these children were carried out shortly after entry, and this meant that the ages of the children at the time of examination varied slightly. The majority of the single-born children were examined/

examined between the ages of 5 years 0 months and 5 years 9 months, and the majority of the twins between the ages of 5 years 0 months and 5 years 7 months, and it is therefore possible to examine the apparent rates of growth throughout these age ranges. These rates are, of course, based on cross-sectional evidence, but nevertheless they are probably worth examining.

The mean heights and weights of singletons and twins of each sex at each monthly age throughout the periods concerned are set out in Table 57. From the figures in this table graphs have been drawn showing the rates of increase in height and weight of singletons and twins of each sex. Each graph shows the actual mean value at each month of age, and also a moving average based on three values, which reduces the fluctuations and gives a clearer indication of the real rates of increase. For comparison the growth rate of all Glasgow children of the appropriate sex at this age has been inserted in these graphs. This is derived from the mean heights and weights at the standard age of 5 years and 4 months, and the average rates of increase per month of age which are used by the School Health Service to correct the heights and weights of Glasgow children to the standard age. These figures are published annually (Ewan,1957).

The increases in height and weight of male singletons are shown in Figure I. It is apparent that the mean heights

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and weights of these children are, as would be expected. a little below the means for all Glasgow male children, but their rate of growth is so similar to the general rate that they are neither gaining or losing ground. This agrees with the finding of Speirs (1956), which was also derived from Glasgow children, that there is no significant difference between the apparent rates of growth of mature and premature males.

The increases in height and weight of female singletons are shown in Figure II. Again it is apparent that the premature female children are shorter and lighter than all Glasgow female children in this age group. Their rate of increase in height appears to be similar to the rate of increase for all female children, but their rate of increase in weight is apparently less, and in fact their weight appears to have been almost stationary during this 9 month period. A similar finding was noted by Speirs (1956) - "For some reason which is not clear the mature females had an apparently greater growth rate in most of the features studied throughout the age range."

Obviously it would be important to know what the growth rates were over a much longer period than 9 months and it would be desirable to have information based on a longitudinal study, but it is clear that there is much more to be learned/

learned about the growth of premature children than will be revealed by comparing heights and weights at one or two ages with the heights and weights of comparable control groups.

The growth rates of the twins show differences from those of the single-born children even over the limited age ranges available for study. The increases in height and weight of the male twins are shown in Figure III. It is obvious that although these children start at the beginning of the period well below the means for all Glasgow children, their rate of growth is much greater, so that in the brief space of 7 months they have made up their deficiencies in both height and weight. In the case of the female twins (Figure IV) the difference in rate of growth is not so striking, but they appear to be increasing their height a little more rapidly than the Glasgow children in general,and their increase in weight also appears to be more rapid, and is in marked contrast to the change in weight of the single-born female premature children shown in Figure II. Thus, in general terms it can be said that the twins are growing more rapidly than the single-born children.

In seeking an explanation for this we must recall that these premature children have been classified as premature because/

because their birth weights were 5½ lbs. or less, and therefore we are in fact dealing with a group of children with the common characteristic of low birth weight. There are several reasons for this low birth weight. To take the single-born children first, we have already pointed out that a substantial proportion of these children are in fact full-time children of low birth weight and these children do not owe their small size at birth to an inadequate time in utero. On the other hand, the remaining single-born children were the products of abnormally short pregnancies and presumably would have reached a greater birth weight if they had remained in utero for the normal time. We have already discussed (p.33 - p.35) the relationship between maternal stature and birth weight and quoted evidence to show that there is a relationship between them and that it is to be expected that small mothers will have small babies. The converse must also be true, and if we take a sample of babies who were small at birth we would expect to find that their mothers were of less than average stature. In this investigation we have selected 515 children who were small at birth. Two hundred and thirty-five (45.6%) of them were born after pregnancies which were reputed to have lasted 38 weeks or more so that it would be reasonable to regard them as small mature babies and to expect that their mothers would be of less than average height. The remaining 280 children were born after abnormally short pregnancies and

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it is not reasonable to expect that their birth weights would in normal circumstances have been so low, and we cannot therefore make any assumptions about the heights of their mothers.

The important point for our present purposes is that the average height of the mothers of single-born premature children will be influenced by the inclusion of a large group of mothers who had full-time babies of low birth weight and who would themselves be of lower than average height. The effect of this on the later development of the children will be considered in a moment, but first the causes of low birth weight among the twins will be considered.

The causes of low birth weight among twins have been discussed fully on page 25-26, and here it is sufficient to say that McKeown and Record (1952) found that the mean birth weight of twins is 5.27 lbs., so that the majority of them are inevitably classified as premature. For our present purposes the important point is that the mean height of the mothers of premature twins will not be influenced by the presence of a group of mothers of lower than average height, as was the mean height of the mothers of single-born premature children, and there is no reason to suppose that the mean height of the mothers of premature twins would differ from the mean height of the mothers in general.

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This has some bearing on the apparently different growth rates of single-born and twin premature children. All these children started at birth with a deficiency of about 2 or 3 pounds compared with normal children. We can take it that this deficiency was not, in a direct sense, genetically determined. It was due either to interruption of pregnancy before term, to the influence of small maternal stature on the growth of the foetus in the later stages of pregnancy, or to the retardation of growth of multiple foetuses, also in the later stages of pregnancy. On the other hand, when the children were examined at school there is reason to believe that the height and weight then recorded would be largely genetically determined. Tanner, Healy, Lockhart, MacKenzie and Whitehouse (1956) state that "The inherent growth characteristics of the child assert themselves after birth, however, and the correlations of childhood measurements with adult measurements rise sharply..." It follows from their work that adult size can be predicted from about the age of 3 years onwards. We would therefore expect that the heights and weights of the premature children in the present investigation, which were recorded when they were just over 5 years old, would be related to their ultimate adult heights and weights. These are bound to be influenced, in the case of single-born children, by the fact that a large group of the mothers were probably below aver-

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average in height and therefore it is reasonable that their children should remain a little below average in height and weight. The fact that the curves showing the monthly increases in height and weight of the single-born male premature children are below but parallel to that of all male children is quite consistent with this view but the apparent relative loss of ground by the single-born premature females during the period 5 years 0 months to 5 years 9 months still remains unexplained.

In the case of the twins, however, the ultimate height and weight will not be influenced by the presence of a group of small mothers and there is no reason to suppose that their ultimate height and weight will differ from the general averages. As they started life with a handicap it is essential that they make it up at some stage in their growth; the alternative is to continue growing for a longer time than normal and this seems unlikely. It is consistent with this reasoning that the twins should grow faster at this particular age (5 years 0 months to 5 years 7 months) than the Glasgow children in general. What is particularly interesting is that this appears to be the stage at which the male twins eliminate their handicaps, whereas the female children apparently do not do so until some time later.

While these tentative conclusions appear to be consistent with the evidence from this and other investigations it would obviously be desirable to know more about the growth rates over a longer period of time.

TABLES 1 - 57 AND FIGURES I - IV.

TABLE 1.

Deaths at various ages under 1 year per 1000 births in Scotland during 5 year periods from 1931 until 1955.

MALE

Years.	Under 1 year.	Under 7 days.	*7-27 days.	*28 days & under 3 mths.	3 mths.& under 6 months.	6 mths.& under 12 mths.
1931-35	90.3	27.9	13.0	14.3	15.0	20.1
1936-40	85.2	28.5	13.0	14.3	14.2	15.3
1941-45	76.4	25.9	12.4	14.1	13.4	10.6
1946-50	53.2	22.3	7.0	9.2	8.3	6.4
1951-55	36.8	19.8	3.7	5.4	4.9	3.0

FEMALE

Years.	Under 1 year.	Under 7 days.	*7-27 days.	*28 days & under 3 mths.	3 mths.& under 6 months.	6 mths.& under 12 mths.
1931-35	70.8	21.6	11.0	10.2	11.4	16.6
1936-40	65.9	21.8	10.3	9.9	11.0	12.8
1941-45	58.5	19.2	9.9	10.0	10.2	9.2
1946-50	41.1	16.9	5.9	6.5	6.4	5.3
1951-55	28.8	14.9	2.9	4.3	3.9	2.9

*Prior to 1950 these numbers and rates relate to 1 week and under 1 month, and 1 month and under 3 months.

TABLE 2.

Numbers of premature live-births in England and Wales and prematurity rate per 100 live-births during years 1953-55.

	1953	1954	1955
No.of premature live-births notified.	45,472	46,042	46,137
Premature live-births per 100 live-births.	6.6	6.9	6.9

TABLE 3.

Proportion of neo-natal deaths in England and Wales during the years 1953-55 which occurred among premature babies.

	1953	1954	1955
Total neo-natal deaths.	12,088	11,946	11,516
Neo-natal deaths among premature babies.	7,043	6,996	6,882
Percentage of neo-natal deaths among premature babies.	58.3	58.6	59.8

TABLE 4.

Numbers of premature still-births in England and Wales and prematurity rate per 100 still-births during years 1953-55.

	1953	1954	1955
No. of premature still-births.	7,407	8,150	8,068
Premature still-births per 100 still-births.	48.0	51.7	52.3

TABLE 5.

Premature babies born in England and Wales during the years 1953-55. Deaths within 28 days per 100 live-births in each birth weight group.

Birth weight.	1953	1954	1955
Up to and incl.3 lbs.4 oz.	687	685	682
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	201	199	188
Over 4 lbs. 6 oz. up to and including 4 lbs. 15 oz.	79	81	81
Over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz.	41	44	39
All with B.W. up to and including 5 lbs. 8 oz.	155	152	149

TABLE 6.

Birth weight distributions of 659 cases in which birth weights were recorded by Health Visitors and 39 cases in which birth weights were not recorded.

Birth Weight.	Recorded.	Not recorded.
Up to and incl.3 lbs.4 oz.	22 (3.3%)	3 (7.7%)
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	107 (16.2%)	13 (33.3%)
Over 4 lbs.6 oz. up to and including 4 lbs. 15 oz.	112 (17.0%)	6 (15.4%)
Over 4 lbs. 15 oz. up to and including 5 lbs.8 oz.	418 (63.4%)	17 (43.6%)
Total	659 (100%)	39 (100%)

$\chi^2 = 10.57 \quad n = 3 \quad 0.02 > P > 0.01$

TABLE 7.

Reasons for failure to trace 176 cases.

Could not be found	74
Known to have left the city	95
Known to have been adopted	7
Total	176

TABLE 8.

Comparison between proportion of primigravid mothers among those traced and co-operating and among those not traced or not co-operating.

	Total mothers.	Primigravidae.	Percent. Prim.
Traced, etc.	476	172	36.1%
Not traced, etc.	183	86	47.0%

$\chi^2 = 6.10 \quad n = 1 \quad 0.02 > P > 0.01$

TABLE 9.

Birth weight distributions of the cases which were traced and co-operated and of the cases which were not traced or did not co-operate.

Birth weight.	Traced, etc.	Not traced, etc.
Up to and including 3 lbs. 4 oz.	15 (3.2%)	7 (3.8%)
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	78 (16.4%)	24 (15.8%)
Over 4 lbs. 6 oz. up to and including 4 lbs. 15 oz.	89 (18.7%)	23 (12.6%)
Over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz.	294 (61.8%)	124 (67.8%)
Total.	476 (100%)	183 (100%)

TABLE 10.

Birth weight distributions of the 515 cases in the survey, by sexes and together.

Birth weight.	Male.	Female.	Both sexes.
Up to and incl. 3 lbs. 4 oz.	7 (3.1%)	11 (3.8%)	18
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	43 (18.8%)	48 (16.8%)	91
Over 4 lbs.6 oz.up to and including 4 lbs. 15 oz.	38 (16.6%)	57 (19.9%)	95
Over 4 lbs.15 oz.up to and including 5 lbs. 8 oz.	141 (61.6%)	170 (59.4%)	311
Total.	229 (100%)	286 (100%)	515

TABLE 11.

Birth weight distributions of cases divided according to whether or not the pregnancy had been complicated.

Birth weight.	Uncomplicated.	Complicated.
Up to and incl.3 lbs.4 oz.	9 (2.8%)	9 (4.7%)
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	42 (13.0%)	49 (25.5%)
Over 4 lbs. 6 oz. up to and including 4 lbs. 15 oz.	62 (19.2%)	33 (17.2%)
Over 4 lbs. 15 oz. up to and including 5 lbs. 8 oz.	210 (65.0%)	101 (52.6%)
Total.	323 (100%)	192 (100%)

$\chi^2 = 15.59 \quad n = 3 \quad P < 0.01$

TABLE 12.

Birth weight distributions of cases according to the number of pregnancies which had preceded the birth of the premature child.

	Number of previous pregnancies.					
Birth weight.	0	1	2	3	4	5 or more.
Up to and including 3 lbs. 4 oz.	7	1	3	2	1	4
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	33	14	15	11	4	14
Over 4 lbs. 6 oz. up to and including 4 lbs. 15 oz.	31	22	17	8	5	12
Over 4 lbs. 15 oz.up to and including 5 lbs. 8 oz.	117	75	39	26	17	37
Total.	188	112	74	47	27	67

TABLE 13.

Distribution of uncomplicated and complicated cases according to the number of pregnancies which had preceded the birth of the premature child.

Pregnancy in 1950.	Total.	Number of previous pregnancies. 0	1	2	3	4	5 or more.
Uncomplicated	323	115	77	48	25	19	39
	100%	35.6%	23.8%	14.9%	7.7%	5.9%	12.1%
Complicated	192	73	35	26	22	8	28
	100%	38.0%	18.2%	13.5%	11.5%	3.2%	14.6%

$\chi^2 = 5.19 \quad n = 5 \quad 0.50 > P > 0.30$

TABLE 14.

Birth weight distributions of the children which were born at home, in hospitals, and in nursing homes.

Birth weight.	Place of Birth. Home.	Hospitals.	Nursing Homes.
Up to and incl. 3 lbs. 4 oz.	4 (2.6%)	14 (4.2%)	-
Over 3 lbs. 4 oz. up to and including 4 lbs. 6 oz.	25 (16.1%)	61 (18.2%)	5 (20.8%)
Over 4 lbs. 6 oz. up to and including 4 lbs. 15 oz.	23 (14.8%)	69 (20.5%)	3 (12.5%)
Over 4 lbs.15 oz. up to and including 5 lbs. 8 oz.	103 (66.5%)	192 (57.1%)	16 (66.7%)
Total.	155 (100%)	336 (100%)	24 (100%)

TABLE 15.

Comparison between state of crowding of the families into which the premature children were born (i.e.excluding the premature child from the reckoning) and the state of crowding of families in Glasgow as a whole at the time of the Census in 1951.

Persons per room.	Families in this survey.	All Glasgow.
Up to and including 1.	87 (16.9%)	48.8%
Over 1 up to and including 1½.	95 (18.4%)	19.2%
Over 1½ up to and including 2.	166 (32.2%)	16.1%
Over 2 up to and including 3.	97 (18.8%)	11.2%
Over 3.	70 (13.6%)	4.7%
Total.	515 (100%)	100%

TABLE 16.

Social Class distribution of all cases.

Social Class -	I	II	III	IV	V	Unknown	Total
	3	22	295	47	138	10	515
	0.6%	4.3%	57.3%	9.1%	26.8%	1.9%	100%

TABLE 17.

Social Class distributions of cases in each birth weight group. (Cases of unknown Social Class omitted).

Birth weight.	Social Class. I & II	III	IV & V	Total
Up to and incl.3 lbs. 4 oz.	1 5.6%	8 44.4%	9 50.0%	18 100%
Over 3 lbs. 4 oz. up to and incl. 4 lbs. 6 oz.	4 4.5%	52 59.1%	32 36.4%	88 100%
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	6 6.3%	55 57.9%	34 35.8%	95 100%
Over 4 lbs. 15 oz. up to and incl. 5 lbs. 8 oz.	13 4.3%	180 59.2%	111 36.5%	304 100%

TABLE 18.

Social Class distributions of uncomplicated and complicated cases. (Cases of unknown Social Class omitted.)

Cases.	I & II	III	IV & V	Total
Uncomplicated	15 4.7%	175 55.0%	128 40.3%	318 100%
Complicated	9 4.8%	120 64.2%	58 31.0%	187 100%

$\chi^2 = 4.31$ $n = 1$ $0.05 > P > 0.02$

(Classes I,II & III taken together)

TABLE 19.

Comparison between the incidence of prematurity among the other children of those mothers who were having a first pregnancy in 1950 and those who were having a later pregnancy.

Pregnancy in 1950.	No.of mothers.	No.of other children of known B.W.	No. which were prem.	Percentage which were prem.
First	121	198	34	17.2%
Not first.	314	1021	288	28.2%
Total	435	1219	322	26.4%

$\chi^2 = 10.39$ n = 1 $P < 0.01$.

TABLE 20.

The non-primigravid mothers have been divided according to the number of single live-born children which they had had up to the time of interview in 1955-56. This table shows, for families of varying sizes, the incidence of prematurity among the siblings of the children born in 1950 according to whether these siblings were born before or after 1950. (Siblings of unknown B.W. are omitted.)

No.of sibs in family.	No.of such families.	Time of birth relative to 1950.	No.of sibs.	No.of prem. sibs.	Percentage of prem. sibs.
1	58	Before	53	21	39.6%
		After	-	-	-
		Total	53	21	39.6%
2	83	Before	110	33	30.0%
		After	54	15	27.8%
		Total	164	48	29.3%
3	50	Before	99	27	27.3%
		After	44	12	27.3%
		Total	143	39	27.3%
4	46	Before	111	36	32.4%
		After	67	21	31.3%
		Total	178	57	32.0%
5	23	Before	83	23	27.7%
		After	32	7	21.9%
		Total	115	30	26.1%
6	20	Before	83	15	18.0%
		After	30	9	30.0%
		Total	113	24	21.2%
7	13	Before	63	22	34.9%
		After	18	8	44.4%
		Total	81	30	37.0%
8	11	Before	67	18	26.9%
		After	13	9	69.2%
		Total	80	27	33.8%
9 or more	10	Before	80	11	13.8%
		After	14	1	7.1%
		Total	94	12	12.8%
Grand Total	314		1021	288	28.2%

TABLE 21.

Comparison between the proportion of children born before 1950 which were premature and proportion after 1950, when the total number of children in each family does not exceed 6 (i.e. the premature born in 1950 and 5 others). Children of unknown B.W. are omitted.

Time of birth.	No.of children.	No. which were premature.	Percentage which were premature.
Before 1950	456	140	30.7%
After 1950	197	55	27.9%

$\chi^2 = 0.50 \quad n = 1 \quad 0.50 > P > 0.30$

TABLE 22.

Comparison between the proportion of children born before 1950 which were premature and proportion after 1950, when the total number of children in each family exceeds 6 (i.e. the premature born in 1950 and 5 others). Children of unknown B.W. are omitted.

Time of birth.	No.of children.	No. which were premature.	Percentage which were premature.
Before 1950	293	66	22.5%
After 1950	75	27	36.0%

$\chi^2 = 5.74 \quad n = 1 \quad 0.02 > P > 0.01$

TABLE 23.

The mothers have been divided according to their ages at the time of the birth of the premature child in 1950 and this table shows the incidence of prematurity among their other children according to whether these other children were born before or after 1950. Other children of unknown B.W. are omitted.

Mothers' ages in 1950.	No. of cases.	Time of birth relative to 1950.	No. of other children.	No. which were premature.	Percentage which were premature.
Under 20	1	Before	1	1	100.0%
		After	1	0	0.0%
		Total	2	1	50.0%
20 - 24	63	Before	76	25	32.9%
		After	81	28	34.6%
		Total	157	53	33.8%
25 - 29	78	Before	115	39	33.9%
		After	74	17	23.0%
		Total	189	56	29.6%
30 - 34	63	Before	130	42	32.3%
		After	36	11	30.6%
		Total	166	53	31.9%
35 or older	58	Before	127	29	22.8%
		After	12	3	25.0%
		Total	139	32	23.0%
Grand total.	263		653	195	29.8%

TABLE 24.

Comparison between the incidence of prematurity among the other children of those mothers who were less than 35 years old at the time of birth of the premature child in 1950 and the other children of those mothers who were 35 or older.

Mothers' ages in 1950.	No. of other children of known B.W.	No. which were premature.	Percentage which were premature.
Under 35	514	163	31.7%
35 or older	139	32	23.0%

$\chi^2 = 3.95 \quad n = 1 \quad 0.05 > P > 0.02$

TABLE 25.

Comparison between the incidence of prematurity among the other children of those mothers who had an artificially induced labour in 1950 and those mothers who had a spontaneous onset of labour.

Labour in 1950.	No.of cases.	No.of other children of known B.W.	No.which were prem.	Percentage which were premature.
Induced	12	28	6	21.4%
Spontaneous	193	486	157	32.3%

$\chi^2 = 0.99 \quad n = 1 \quad 0.50 > P > 0.30$

TABLE 26.

Comparison between the incidence of prematurity among the other children of those mothers who were delivered by Caesarean Section in 1950 and those mothers who were not.

Delivery in 1950.	No.of cases.	No.of other children of known B.W.	No.which were prem.	Percentage which were premature.
Caesarean Section.	10	26	6	23.1%
Not C.S.	195	488	157	32.2%

$\chi^2 = 0.57 \quad n = 1 \quad 0.50 > P > 0.30$

TABLE 27.

Comparison between the incidence of prematurity among the other children of those mothers who had an artificially induced labour or were delivered by Caesarean Section in 1950, and the remaining mothers.

Birth in 1950.	No.of cases.	No.of other children of known B.W.	No.which were prem.	Percentage which were premature.
Induction or C.S.	22	54	12	22.2%
Remainder	183	460	151	32.8%

$\chi^2 = 2.51 \quad n = 1 \quad 0.20 > P > 0.10$

TABLE 28.

Comparison between the incidence of prematurity among the other children of mothers who had "fair" health during the pregnancy in 1950 and the other children of the remaining mothers.

Health in 1950.	No.of cases.	No.of other children of known B.W.	No. which were prem.	Percentage which were premature.
"Fair"	33	77	20	26.0%
Otherwise	172	437	143	32.7%

$\chi^2 = 1.38 \quad n = 1 \quad 0.30 > P > 0.20$

TABLE 29.

Comparison between the incidence of prematurity among the other children of mothers who had "bad" health during the pregnancy in 1950 and the other children of the remaining mothers.

Health in 1950.	No.of cases.	No.of other children of known B.W.	No. which were prem.	Percentage which were premature.
"Bad"	11	24	6	25.0%
Otherwise	194	490	157	32.0%

$\chi^2 = 0.25 \quad n = 1 \quad 0.70 > P > 0.50$

TABLE 30.

Comparison between the incidence of prematurity among the other children of mothers who had "fair" or "bad" health during the pregnancy in 1950 and the other children of the remaining mothers.

Health in 1950.	No.of cases.	No.of other children of known B.W.	No. which were prem.	Percentage which were premature.
"Fair"or "Bad"	44	101	26	25.7%
Otherwise	161	413	137	33.2%

$\chi^2 = 2.07 \quad n = 1 \quad 0.20 > P > 0.10$

TABLE 31.

Distribution of prematurity throughout the families of the 205 mothers who remained after the exclusion of various special groups. The families have been divided according to the number of children which they contained in addition to the premature one born in 1950. The families have then been arranged to show how many families of each size contained each possible number of premature children. Immediately below this the expected number is shown, calculated on the assumption that the probability that each of these children would be premature is 0.317, and the significances of the differences between each of these sets of figures is shown separately below.

No.of additional children per family.	No.of such families.	No. of such families which contained the undernoted numbers of premature children.					
		0	1	2	3	4	5
1	44	28	16				
		30.1	13.9				
2	70	38	22	10			
		32.6	30.3	7.0			
3	39	17	17	3	2		
		12.4	17.3	8.0	1.2		
4	36	10	10	8	4	4	
		7.8	14.5	10.1	3.1	0.4	
5	16	7	2	4	1	1	1
		2.4	5.5	5.1	2.4	0.5	0.0

Significances of differences between observed and expected values:-

Line.	χ^2	n	P
1	0.47	1	0.50 - 0.30
2	4.46	2	0.20 - 0.10
3	3.63	2	0.20 - 0.10
4	2.45	2	0.30 - 0.20
5	0.28	1	0.70 - 0.50
Total	11.29	8	0.20 - 0.10

TABLE 32.

The relationship between the estimated duration of pregnancy and the birth weight of the 205 children whose mothers apparently had a predisposition to prematurity.

Birth weight.	Duration of Pregnancy. Not known	30-31 weeks	32-33 weeks	34-35 weeks	36-37 weeks	38 weeks or more	Total
Up to and incl.3 lbs. 4 oz.		3		1	2	1	7
Over 3 lbs. 4 oz. up to and incl.4 lbs.6 oz.		13	2	2	10	7	34
Over 4 lbs.6 oz. up to and incl. 4 lbs. 15 oz.	2	3	5	3	20	9	42
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.		2		6	43	71	122
Total	2	21	7	12	75	88	205

TABLE 33.

The relationship between the incidence of prematurity among the siblings of the premature children born in 1950 and the birth weights of these children.

B.W. of child born in 1950.	No.of cases.	Sibs. of known B.W.	Premature siblings.	Percentage of premature siblings.
Up to and incl. 3 lbs. 4 oz.	7	22	5	22.7%
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	34	90	42	46.7%
		112	47	42.0%
Over 4 lbs.6 oz. up to and incl. 4 lbs.15 oz.	42	92	27	29.3%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	122	310	89	28.7%
		402	116	28.9%
Total	205	514	163	31.7%

$\chi^2 = 6.94 \quad n = 1 \quad P < 0.01$

(Comparison has been made between the lower two birth weight groups and the upper two).

TABLE 34.

The relationship between the proportion of non-premature siblings which had birth weights of 7 lbs. or more and the birth weights of the premature children born in 1950.

B.W.of child born in 1950.	No.of cases.	Non-prem. sibs. of known B.W.		No.with B.W. of 7 lbs. or more.		Percentage with B.W.of 7 lbs.or more.	
Up to and incl. 3 lbs. 4 oz.	7	17	130	12	86	70.6%	66.2%
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	34	48		33		68.8%	
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	42	65		41		63.1%	
Over 4 lbs. 15 oz. up to and incl.5 lbs.8 oz.	112	221		98		44.3%	
Total	205	351		184		52.4%	

$\chi'^2 = 15.61 \quad n = 1 \quad P < 0.01$

(Comparison has been made between the lower three birth weight groups and the upper one.)

TABLE 35.

This table shows how the proportion of siblings which were either premature or had birth weights of 7 lbs. or more varies with the birth weight of the child born in 1950. In the 4th column the first figure is the number of premature siblings, the second figure is the number with birth weights of 7 lbs. or more, and the third figure gives the total.

B.W. of child born in 1950.	No.of cases.	Sibs. of known B.W.	No. of prems. or with B.W. 7 lbs. or more.	Percentage of prems.or with B.W. 7 lbs.or more
Up to and incl. 3 lbs. 4 oz.	7	22	5 + 12 = 17	77.3%
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	34	90	42 + 33 = 75	83.3%
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	42	92	27 + 41 = 68	73.9%
Over 4 lbs. 15 oz. up to and incl.5 lbs. 8 oz.	122	310	89 + 98 =187	60.3%
Total	205	514	163 +184 =347	67.5%

$\chi^2 = 20.42$ $n = 3$ $P < 0.001$

TABLE 36.

This table shows how the birth weights of the premature siblings tended to be similar to the birth weights of the premature children born in 1950.

B.W.of child born in 1950.	Total prem. sibs.	Prem.sibs.with B.W. up to and incl. 4 lbs.15 oz.	Percentage of prem. sibs. with B.W. up to and incl.4 lbs. 15 oz.
Up to and incl.4 lbs. 15 oz.	74	44	59.5%
Over 4 lbs. 15 oz. up to and incl. 5 lbs.8 oz.	89	36	40.4%
Total	163	80	49.1%

$\chi^2 = 5.85 \quad n = 1 \quad 0.02 > P > 0.01$

TABLE 37.

Comparison between the incidence of prematurity among the other children of mothers who had uncomplicated and complicated pregnancies in 1950. Children of unknown B.W.are omitted.

Pregnancy in 1950.	No.of cases.	No.of other children.	No. which were prem.	Percentage which were premature.
Uncomplicated.	138	344	120	34.9%
Complicated.	67	170	43	25.3%

$\chi^2 = 4.83 \quad n = 1 \quad 0.05 > P > 0.02$

TABLE 38.

Comparison between the numbers of non-premature children with birth weights of 7 lbs. or more among the other children of mothers who had uncomplicated and complicated pregnancies in 1950. Children of unknown B.W.are omitted.

Pregnancy in 1950.	No. of cases.	No.of other children not premature.	No. which had B.W. of 7 lbs. or more.	Percentage which had B.W. of 7 lbs. or more.
Uncomplicated.	138	224	101	45.1%
Complicated.	67	127	83	65.4%

$\chi^2 = 13.35 \quad n = 1 \quad P < 0.01$

TABLE 39.

Cases in which the pregnancy in 1950 was UNCOMPLICATED - the relationship between the incidence of prematurity among the siblings of the premature children born in 1950 and the birth weights of these children.

B.W.of child born in 1950.	No.of cases.	Sibs. of known B.W.		Premature siblings.		Percentage of premature siblings.	
Up to and incl. 3 lbs. 4 oz.	3	12	59	4	27	33.3%	45.8%
Over 3 lbs. 4 oz.up to and incl.4 lbs.6 oz.	20	47		23		48.9%	
Over 4 lbs. 6 oz. up to and incl.4 lbs.15 oz.	28	60	285	22	93	36.7%	32.6%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	87	225		71		31.6%	
Total	138	344		120		34.9%	

$\chi^2 = 3.71 \quad n = 1 \quad 0.10 > P > 0.05$

(Comparison has been made between the lower two birth weight groups and the upper two.)

TABLE 40.

Cases in which the pregnancy in 1950 was COMPLICATED - the relationship between the incidence of prematurity among the siblings of the premature children born in 1950 and the birth weights of these children.

B.W.of child born in 1950.	No. of cases.	Sibs. of known B.W.	Premature siblings.	Percentage of premature siblings.
Up to and incl.3 lbs. 4 oz.	4	10	1	10.0%
		53	20	37.7%
Over 3 lbs. 4 oz. up to and incl. 4 lbs.6 oz.	14	43	19	44.2%
Over 4 lbs. 6 oz.up to and incl.4 lbs.15 oz.	14	32	5	15.6%
		117	23	19.7%
Over 4 lbs.15 oz. up to and incl. 5 lbs.8 oz.	35	85	18	21.2%
Total	67	170	43	25.3%

$\chi^2 = 6.30$ n = 1 $0.02 > P > 0.01$.

TABLE 41.

Cases in which the pregnancy in 1950 was UNCOMPLICATED - the relationship between the proportion of non-premature siblings which had birth weights of 7 lbs. or more and the birth weights of the premature children born in 1950.

B.W. of child born in 1950.	No.of cases.	Non-prem. sibs. of known B.W.		No. with B.W. of 7 lbs. or more.		Percentage with B.W. of 7 lbs.or more.	
Up to and incl. 3 lbs. 4 oz.	3	8	32	3	20	37.5%	62.5%
Over 3 lbs. 4 oz. up to and incl.4 lbs.6 oz.	20	24		17		70.8%	
Over 4 lbs.6 oz. up to and incl. 4 lbs. 15 oz.	28	38	192	20	81	52.6%	42.2%
Over 4 lbs.15 oz up to and incl.5 lbs.8 oz.	87	154		61		39.6%	
Total	138	224		101		45.0%	

$\chi^2 = 4.57 \quad n = 1 \quad 0.05 > P > 0.02$

(Comparison has been made between the lower two birth weight groups and the upper two.)

TABLE 42.

Cases in which the pregnancy in 1950 was COMPLICATED - the relationship between the proportion of non-premature siblings which had birth weights of 7 lbs. or more and the birth weights of the premature children born in 1950.

B.W. of child born in 1950.	No.of cases.	Non-prem. sibs.of known B.W.		No.with B.W.of 7 lbs.or more.		Percentage with B.W. of 7 lbs. or more.	
Up to and incl. 3 lbs. 4 oz.	4	9		9		100.0%	
Over 3 lbs. 4 oz.up to and incl.4 lbs. 6 oz.	14	24	60	16	46	66.7%	76.7%
Over 4 lbs.6 oz.up to and incl.4 lbs.15 oz.	14	27		21		77.8%	
Over 4 lbs.15 oz.up to and incl.5 lbs.8 oz.	35	67		37		55.2%	
Total	67	127		83		65.4%	

$\chi^2 = 6.43$ n = 1 $0.02 > P > 0.01$

(Comparison has been made between the lower three birth weight groups and the upper one.)

TABLE 43.

The incidence of still-births and abortions among the additional pregnancies of the 205 mothers, related to the birth weights of the children born in 1950.

B.W. of child born in 1950.	No.of additional pregnancies.		No.of S.B.	Percent. of S.B.	No.of abort.	Percent of abort.	
Up to and incl. 3 lbs. 4 oz.	30	152	3	10.0%	5	16.7%	21.7%
Over 3 lbs.4 oz. up to and incl.4 lbs.6 oz.	122		3	2.5%	28	23.0%	
Over 4 lbs.6 oz. up to and incl. 4 lbs.15 oz.	119	502	5	4.2%	15	12.6%	12.4%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	383		12	3.1%	47	12.3%	
Total	654		23	3.5%	95	14.5%	

Significance of difference in incidence of abortions, with lower two birth weight groups and upper two taken together:-

$\chi^2 = 8.24 \quad n = 1 \quad P < 0.01$

TABLE 44.

Comparison between the incidence of still-births and abortions according to whether the pregnancy in 1950 was uncomplicated or complicated.

Pregnancy in 1950.	No. of additional pregnancies.	No. of S.B.	No.of abort.	Total S.B.& abort.	Percentage S.B. and abort.
Uncomplicated	426	11	55	66	15.5%
Complicated	228	12	40	52	22.8%

$\chi^2 = 5.38$ n = 1 $0.05 > P > 0.02$

TABLE 45.

Comparison between the total incidence of premature births, still-births, and abortions, according to whether the pregnancy in 1950 was uncomplicated or complicated.

Pregnancy in 1950.	No. of additional pregnancies.	No.of prems.	No.of S.B.	No.of abort.	Total prems. S.B.& abort.	Percentage of prems. S.B.& abortions.
Uncomplicated	426	120	11	55	186	43.7%
Complicated	228	43	12	40	95	41.7%

TABLE 46.

The proportions of mothers who gave a positive family history of prematurity, according to the number of pregnancies which they had had before 1950.

	No.of pregnancies before 1950.						
	0	1	2	3	4	5 or more.	Total
Number of cases.	188	112	74	47	27	67	515
No.with family history of prematurity.	38	19	19	11	6	18	111
Percentage with family history of prematurity.	20.2%	17.0%	25.7%	23.4%	22.2%	26.9%	21.6%

$\chi^2 = 3.56 \quad n = 5 \quad 0.70 > P > 0.50$

TABLE 47.

205 cases in which prematurity was apparently due to maternal predisposition:-

Comparison between the incidence of prematurity among the other children of mothers who gave a family history of prematurity and the other children of mothers who did not.

	No.of mothers.	Other children of known B.W.	No.of prems.	Percentage of prematures.
With family history	47	128	41	32.0%
No family history	158	386	122	31.6%

TABLE 48.

230 cases in which prematurity could not have been due to maternal predisposition in every case:-

Comparison between the incidence of prematurity among the other children of mothers who gave a family history of prematurity and the other children of mothers who did not.

	No.of mothers.	Other children of known B.W.	No.of prems.	Percentage of prematures.
With family history	55	171	51	29.8%
No family history	175	534	108	20.2%

$\chi^2 = 6.83$ n = 1 P < 0.01

TABLE 49.

Reasons for failure to trace 52 premature twins of known birth weight:-

Could not be found	- 25
Known to have left the city	- 25
Known to have been adopted	- 2
Total	- 52

TABLE 50.

Comparison between the birth weight distributions of the premature singletons and premature twins.

	Singletons.		Twins.	
Birth Weight	No.	Percentage.	No.	Percentage.
Up to and incl. 3 lbs. 4 oz.	18	3.5%	7	4.5%
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	91	17.7%	40	25.8%
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	95	18.4%	34	21.9%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	311	60.4%	74	47.7%
Total	515	100%	155	100%

TABLE 51.

Comparison between Social Class Distributions of premature singletons and premature twins.

	Social Class.						
	I	II	III	IV	V	Unknown	Total
Singletons	3	22	295	47	138	10	515
	0.6%	4.3%	57.3%	9.1%	26.8%	1.9%	100%
Twins	2	3	94	21	34	1	155
	1.3%	1.9%	60.6%	13.5%	21.9%	0.6%	100%

TABLE 52.

The numbers of single-born children who spent various periods in hospital, according to birth weight.

Birth Weight.	Total cases.	Never in hospital.	Up to 2 weeks.	2 weeks to 4 weeks.	4 weeks to 3 months.	Over 3 months.
Up to and incl. 3 lbs. 4 oz.	18	10	3	1	1	3
	100%	55.6%	16.7%	5.7%	5.7%	16.7%
Over 3 lbs. 4 oz. up to and incl. 4 lbs. 6 oz.	91	45	17	8	11	10
	100%	49.5%	18.7%	8.8%	12.1%	11.0%
Over 4 lbs.6 oz. up to and incl. 4 lbs. 15 oz.	95	50	20	9	10	6
	100%	52.6%	21.1%	9.5%	10.5%	6.3%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	311	173	70	21	41	6
	100%	55.6%	22.5%	6.8%	13.2%	1.9%
Total	515	278	110	39	63	25
	100%	54.0%	21.4%	7.6%	12.2%	4.9%

Significance of variation in number of children spending over 3 months in hospital (the lower two birth weight groups have been combined):-

$$\chi^2 = 18.01 \quad n = 2 \quad P = <0.01$$

TABLE 53.

The numbers of twins who spent various periods in hospital, according to birth weight.

Birth Weight.	Total cases.	Never in hospital.	Up to 2 weeks.	2 weeks to 4 weeks	4 weeks to 3 months	Over 3 months.
Up to and incl. 3 lbs. 4 oz.	7 100%	5 71.4%	-	2 28.6%	-	-
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	40 100%	20 50.0%	13 32.5%	2 5.0%	1 2.5%	4 10.0%
Over 4 lbs.6 oz. up to and incl. 4 lbs. 15 oz.	34 100%	21 61.8%	7 20.6%	1 2.9%	5 14.7%	-
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	74 100%	38 51.4%	19 25.7%	5 6.8%	8 10.8%	4 5.4%
Total	155 100%	84 54.2%	39 25.2%	10 6.5%	14 9.0%	8 5.2%

TABLE 54.

Number of single-born children in each birth weight group who were admitted to hospital at least once with lower respiratory infection.

Birth Weight.	Total children.	No.admitted.	Percentage admitted.
Up to and incl. 3 lbs. 4 oz.	18	6	33.3%
Over 3 lbs. 4 oz. up to and incl. 4 lbs. 6 oz.	91	20	22.0%
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	95	12	12.6%
Over 4 lbs.15 oz. up to and incl. 5 lbs. 8 oz.	311	24	7.7%
Total	515	62	12.0%

$\chi^2 = 19.92$ $n = 2$ $P < 0.01$
(Lower two birth weight groups combined)

TABLE 55.

Number of twins in each birth weight group who were admitted to hospital at least once with lower respiratory infection.

Birth Weight.	Total children.	No. admitted	Percentage admitted.
Up to and incl. 3 lbs. 4 oz.	7	1	14.3%
Over 3 lbs.4 oz. up to and incl. 4 lbs. 6 oz.	40	2	5.0%
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	34	4	11.8%
Over 4 lbs. 15 oz. up to and incl. 5 lbs. 8 oz.	74	9	12.2%
Total	155	16	10.3%

TABLE 56.

Incidence of squints among all premature children (singletons and twins) in each birth weight group.

Birth Weight.	Total cases.		No. with squints.		Percentage with squints.	
Up to and incl. 3 lbs. 4 oz.	24	269	2	29	8.3%	10.8%
Over 3 lbs. 4 oz. up to and incl. 4 lbs. 6 oz.	122		10		8.2%	
Over 4 lbs. 6 oz. up to and incl. 4 lbs. 15 oz.	123		17		13.8%	
Over 4 lbs. 15 oz. up to and incl. 5 lbs. 8 oz.	371		28		7.5%	
Total	640		57		8.9%	

TABLE 57.

Mean heights and weights of single-born premature children at monthly ages from 5 years 0 months to 5 years 9 months.

Age.	Male.			Female.		
	No.of cases.	Mn.Ht. (in.)	Mn.Wt. (lb.)	No.of cases.	Mn.Ht. (in.)	Mn. Wt. (lb.)
5 yr.0 mth.	15	41.1	39.1	12	39.9	37.7
5 yr.1 mth.	16	41.7	41.0	27	41.0	38.3
5 yr.2 mth.	26	40.4	37.5	23	40.4	36.8
5 yr.3 mth.	38	41.3	39.0	46	40.7	38.0
5 yr.4 mth.	32	41.6	39.9	43	41.2	38.0
5 yr.5 mth.	22	41.4	39.7	44	40.7	37.1
5 yr.6 mth.	26	41.2	39.4	23	42.0	38.9
5 yr.7 mth.	17	42.0	39.7	19	40.9	37.0
5 yr.8 mth.	8	42.5	41.5	6	41.6	39.9
5 yr.9 mth.	8	43.5	42.1	3	42.2	36.6

Mean heights and weights of premature twins at monthly ages from 5 years 0 months to 5 years 7 months.

Age.	Male.			Female.		
	No.of cases.	Mn.Ht. (in.)	Mn.Wt.	No.of cases.	Mn.Ht. (in.)	Mn.Wt. (lb.)
5 yr.0 mth.	6	40.7	38.3	6	40.5	36.7
5 yr.1 mth.	9	38.9	35.7	2	40.2	36.0
5 yr.2 mth.	14	40.6	38.0	7	40.8	37.1
5 yr.3 mth.	11	41.5	39.3	10	40.7	37.7
5 yr.4 mth.	9	42.9	41.4	15	41.8	38.6
5 yr.5 mth.	12	42.0	40.9	11	41.1	38.2
5 yr.6 mth.	6	43.1	41.4	13	41.2	39.6
5 yr.7 mth.	10	43.6	44.3	3	43.0	41.5

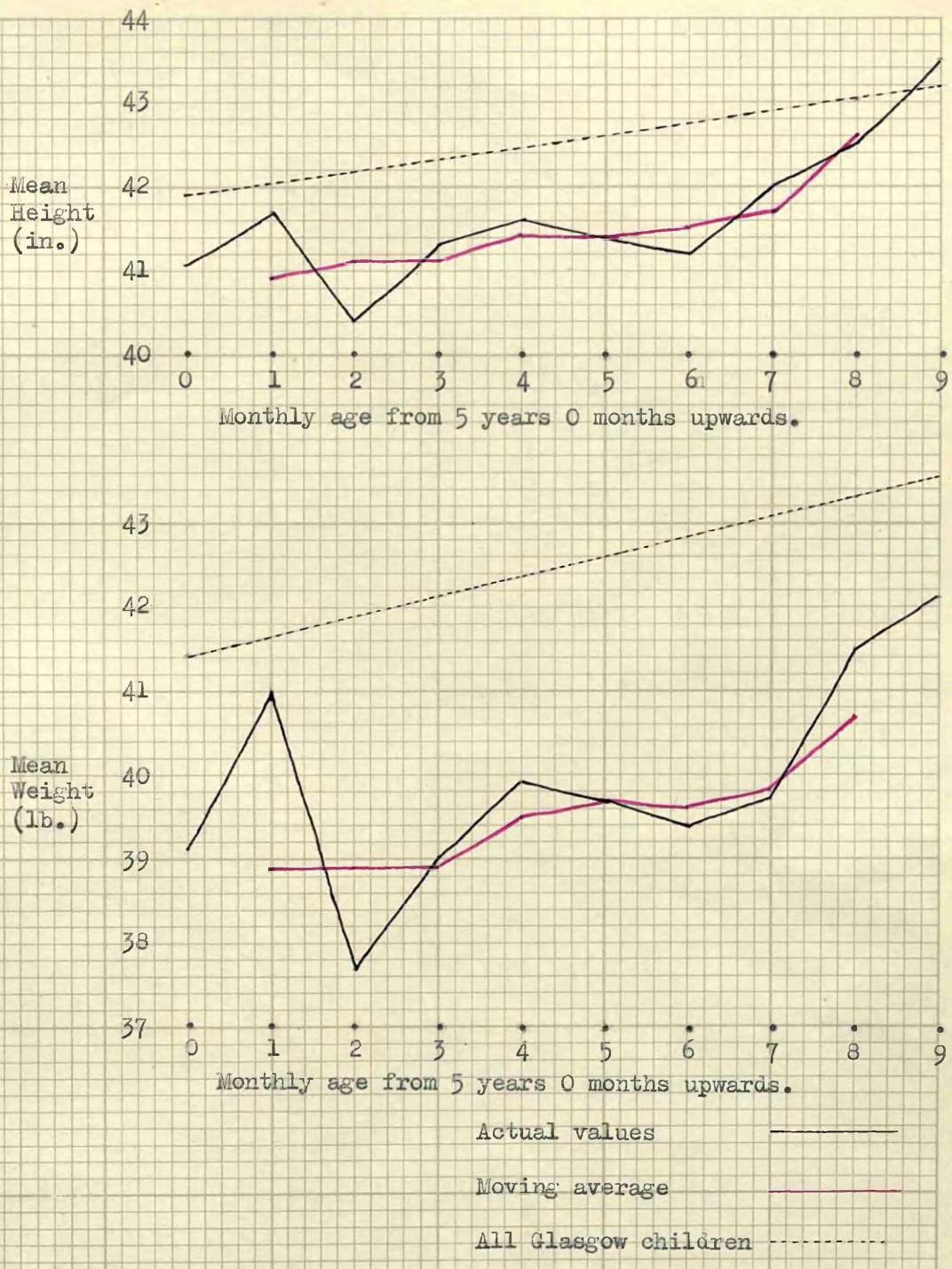


Figure I. Increases in height and weight of single-born male premature children.

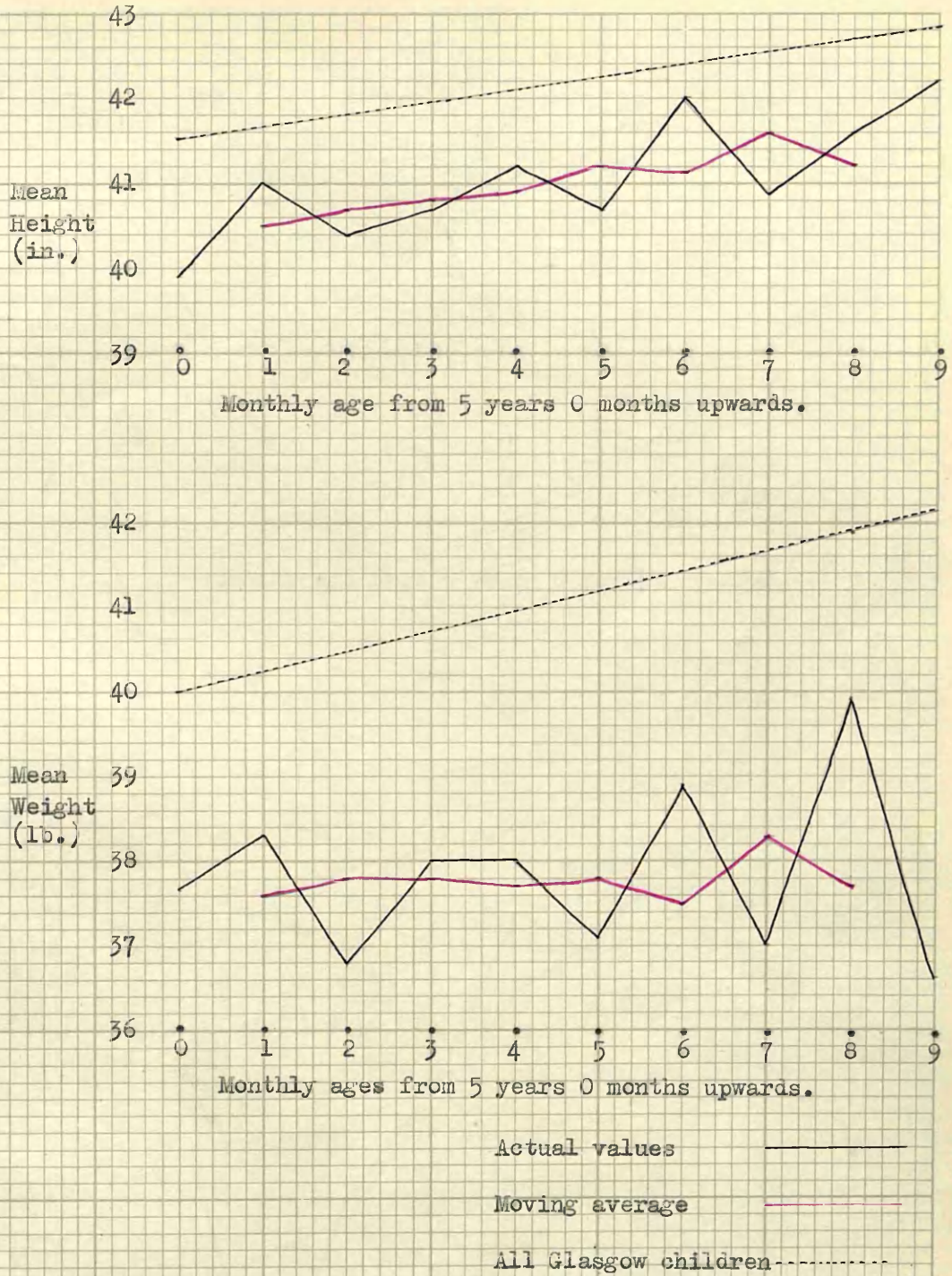
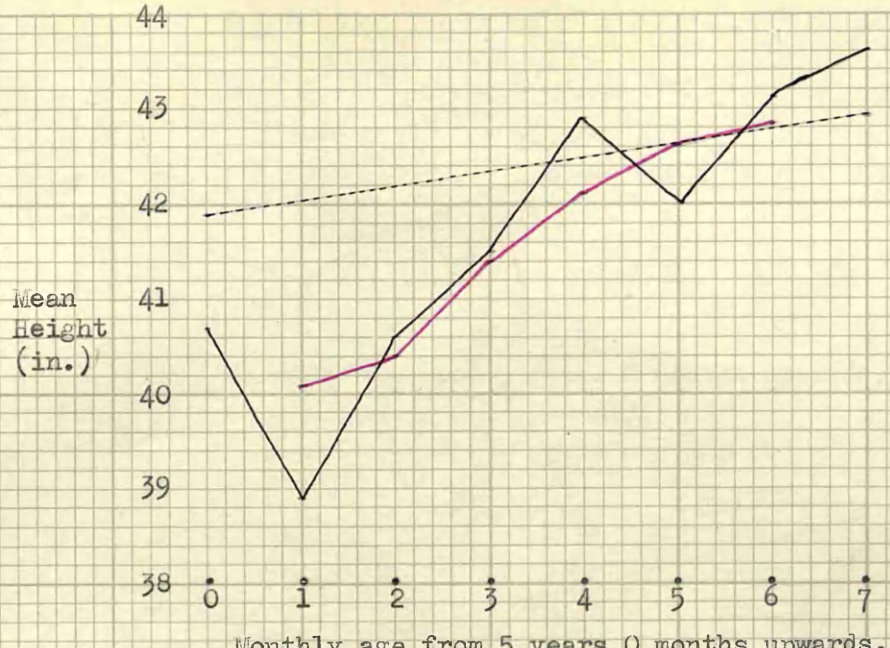


Figure II. Increases in height and weight of single-born female premature children.



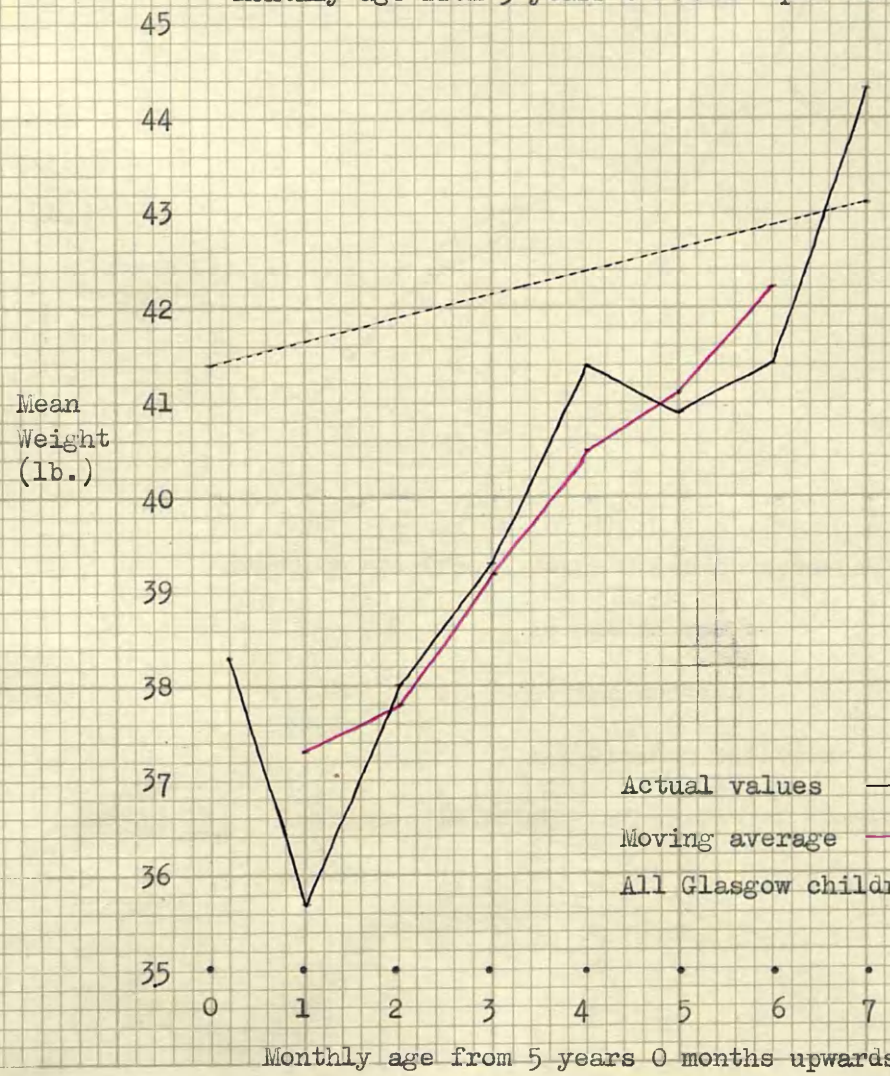
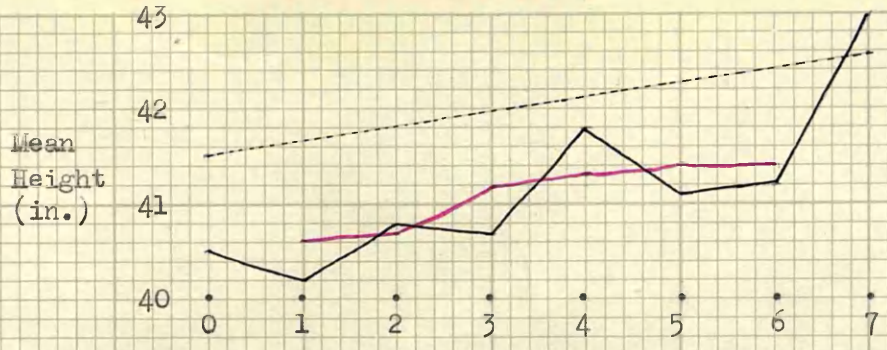


Figure III. Increases in height and weight of male twins.



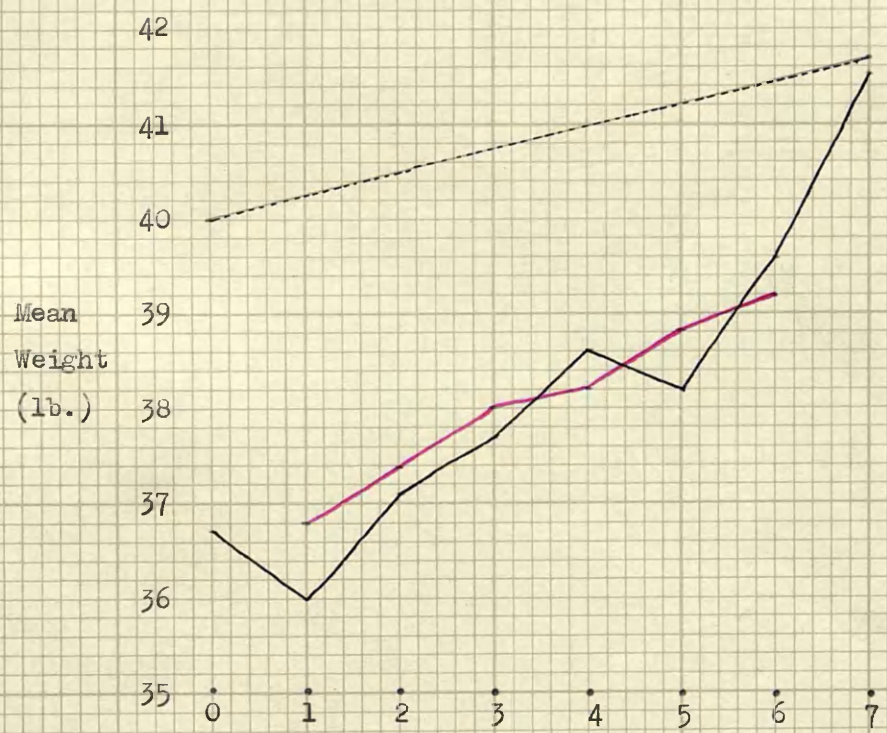


Figure IV. Increases in height and weight of female twins.

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