SHORT STATURE IN SCOTTISH SCHOOLCHILDREN:
A COMMUNITY STUDY WITH SPECIAL EMPHASIS
ON THE PREVALENCE OF
SEVERE GROWTH HORMONE DEFICIENCY

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The primary objective of this study has been to determine the prevalence of growth hormone deficiency among Scottish school children. To achieve this it was first essential to identify a large number of very small children in a defined population and it was proposed to study thereafter all those comprising the smallest 1% in the population.

Clearly, many children had factors other than growth hormone deficiency contributing to their short stature, and therefore the literature relating both to this and the influences of genetic, environmental and other biological factors upon growth has been reviewed.

The method originally proposed for identifying these children was based upon a central computer-based file of the heights of children at the school entrance medical inspection. Intractable difficulties inherent in this approach soon emerged and, as these would have prevented the identification of all short children within a defined population and made it impossible to accurately estimate the true prevalence of growth hormone deficiency, this method had to be discarded.

The revised method entailed personally screening the heights of 48,221 children attending all education authority schools and a selection of independent schools in Edinburgh, Glasgow and Aberdeen, and identifying from them all children who were -2.5 standard deviations or more below the mean height for their chronological age (N = 449).

Permission was sought from the parents of those found to be of small/
small stature to undertake studies of the medical and social background and where appropriate to gather auxological data. Where no definite cause for short stature was apparent, these children were screened for growth hormone deficiency wherever possible. Children who failed to produce adequate growth hormone levels on the screening test and/or those whose twelve month height velocities were below average (less than the 25th centile for chronological age) were then further investigated for growth hormone deficiency with an insulin tolerance test.

A group of control children from a similar social background but of average height for age was also selected in Edinburgh and Glasgow. Some of the social and medical data from this group has been compared to the group of children with short stature in an attempt to identify any significant differences. The study has confirmed the strong association of previously recognised environmental and genetic factors with short stature.

The results of the study also suggest that severe growth hormone deficiency is a more common cause of short stature than previously thought and that it frequently remains undiagnosed for longer than necessary.
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INTRODUCTION

One of the primary objectives of a health surveillance system for young children is to detect those with deviant growth or development. A child with extremely small stature in relation to his peers is stigmatised even in the absence of other physical abnormalities, and often subjected to a number of adverse sociocultural influences which may interfere with the development of his self image and later psychological adjustment, apart from its effect in limiting the range of occupational choices available to him.

The growth of many individuals with established short stature will not be helped by medical intervention. Sadly, the biblical question, "Which of you by taking thought can add one cubit to his stature?", applies only too often to all forms of intervention. There are however some conditions in which treatment is successful. Amongst these are the provision of improved nutrition or vitamins in states of chronic starvation or vitamin deficiency, the exclusion of gluten containing foods in coeliac disease, and the correction of several endocrinologic disorders characterised either by hormonal deficiency, such as growth hormone or thyroid deficiency, or hormonal excess - as in those with precocious puberty.

Effective treatment for growth hormone deficiency has been available since 1959 (Raben, 1959) but at present it is thought that many children with this condition remain undiagnosed for many years after short stature first becomes apparent (Tanner, 1975). It is clear that only a small proportion of short children are referred to hospital consultants, and referral depends upon the "anxiety and knowledge of parents as well as the concern and interest of family doctors"/
doctors" (Farquhar, 1974). Accordingly, it seems likely that some cases of growth hormone deficiency are missed completely. Because of this, the true prevalence of growth hormone deficiency has been unknown, although such knowledge would be helpful, as not only would it give indication of the extent to which delayed diagnosis is a problem in this condition, but also some estimate of the potential demand for therapeutic supplies of growth hormone, were all potential cases of growth hormone deficiency being effectively diagnosed.

The possibility of undertaking a study in Scotland to determine the prevalence of growth hormone deficiency arose when it was discovered that it might be possible to identify a cohort of children with short stature by means of a national records system based in Edinburgh, which contained details of the height of all children at the time of the school entrants' medical inspection. The concept of the study received strong support from the Medical Research Council's Human Growth Hormone Working Party, who for a number of years have been responsible for the MRC's clinical trial of Human Growth Hormone (HGH). An application for the necessary financial support for the study was made, and a special project grant was awarded by the MRC.

It was considered that as growth hormone deficiency (GHD) was unlikely to be a frequent cause of short stature, such a study would also enable one to place in perspective the contribution of other biological and social factors in the aetiology of short stature.

The following study firstly reviews the literature relating to the/
the various factors that influence normal growth, and the circumstances under which they may result in short stature. A comprehensive review of growth hormone pathophysiology is included.

The deficiencies of the originally proposed method of the study are outlined and the methodology subsequently adopted is described in some detail.

The demographic distribution of short stature and the social and biological variables found associated with it are described and discussed. Auxologic characteristics of the various diagnostic groups are delineated. The results of the endocrinologic studies are presented and their significance is discussed. Finally, the implications for case finding of the prevalence of growth hormone deficiency observed in this study are considered and the way in which the referral patterns noted may delay the diagnosis of growth hormone deficiency is discussed.
SHORT STATURE: THE PROBLEM IN PERSPECTIVE

"And there was a man named Zacchaeus .... And he sought to see who Jesus was, but could not on account of the crowd, because he was small of stature. So he .... climbed up into a sycamore tree to see him."

The difficulties confronting individuals with short stature have been recognised from antiquity. Indeed any person who is conspicuously endowed with a greater or lesser quantity of any of the common physical characteristics is naturally regarded as abnormal by others. Whilst in some cases such differences may be regarded as desirable, equally often they can handicap the individual in his relationships with other people. Dorner and Elton (1973) writing on the problems of children with short stature stated, "There is a pervasive social attitude which links tallness with all kinds of positive psychological attributes, and just as consistent a relation between smallness and such characteristics as inadequacy."

The phenomenon of human growth, and the factors linked with its extremes, both in similar and widely different communities has long been of scientific interest. The oldest longitudinal record in existence dates from the eighteenth century when Count Philibert de Mont Beillard recorded the height of his son from birth to the age of eighteen years (Tanner, 1962). Whilst it is true that there are numerous/
numerous medical conditions associated with short stature, it is
evident that these in themselves are not responsible for the differ-
ences in average height between different communities. Nor are they
necessarily the cause of short stature in those individuals whose
height is less than 97% or 99% of others in the community. Indeed
it is clear that factors other than these, such as genetic, racial,
and environmental influences are of great importance. For instance,
certain racial groups, e.g. the Mbaiki, Asians, including Chinese
and Japanese, in comparison with European norms, appear to have a
very high prevalence of short stature. Consequently, the definition
of what constitutes short stature for a particular community can
only be made when the normal range of height at each age for that
community is known from birth to maturity. For European populations,
the widely accepted standards of Tanner et al. (1966) are generally
applicable (Tanner, 1976), and any individual whose height is less
than the first percentile has a significant degree of short stature.

The study of growth and short stature in particular has two
important functions. Firstly it can lead to a greater understanding
of the relative importance of the various factors contributing to
short stature. At the same time children with a medical condition
contributing to their short stature can be found, and, where
necessary, as in the case of growth hormone deficiency, appropriate
treatment can be commenced. Whilst the growth of whole communities
of children has been frequently studied in either longitudinal or
cross-sectional surveys, there have been remarkably few attempts to
study populations with the objective of identifying individual
children/
children with short stature (Lacey and Parkin, 1974, a, b).

Secondly, "a well designed growth study is a powerful tool with which to monitor the health of the population, or to pinpoint some groups of a population whose share in economic and social benefits is less than it might be". (Eveleth and Tanner, 1976). In 1926, Paton and Findlay wrote that height was the best single index of the standard of growth and development, and fifty years later Eveleth and Tanner reiterate this view. "A child's growth rate reflects, better than any other single index, his state of health and nutrition. The average values of children's heights and weights reflect accurately the state of the nation's public health and the average nutritional status of its citizens. As the infant mortality rate goes down during a country's development, so the importance of monitoring the growth rate increases."

In the following sections, previous studies which have shown the influence of various genetic and environmental factors upon growth, and the way in which, if sufficiently adverse, these may interact to cause growth retardation and short stature will be reviewed. Subsequently the relationship between growth hormone deficiency and short stature will be reviewed in depth and brief mention made of other medical conditions usually associated with short stature.
GENETIC INFLUENCES UPON GROWTH

As with many other biological characteristics, there has been frequent debate about the relative importance of genetic and environmental influences upon the rate of growth. It is probably impossible to separate entirely their varying contributions. Whilst some characteristics affecting growth, such as race, are primarily genetic, others, such as poor nutrition and physical overcrowding are undoubtedly environmental. Further influences upon growth, such as birth weight, the effect of social class, and the rate of skeletal maturation, are themselves results of interactions between the genes and their environment. "Final size reflects a continuous interaction of hereditary and environmental forces during the whole period of growth ... and it is impossible to speak in general of the relative importance of heredity and environment in contributing to the variance of height. (Thus) two gene types which produce the same adult height under optimal environmental circumstances, may produce different heights under circumstances of privation. Two children who would be the same height in a well-off community may not only both be smaller under poor economic conditions, but one may be significantly smaller than the other." (Tanner, 1973; Eveleth and Tanner, 1976).

As living standards improve, it would appear that environmental influences upon stature are relatively less important than genetic factors. "The nearer the optimal the environment, the more the genes have a chance to show their influence." (Tanner, 1973). Evidence in support of this opinion is provided by a number of studies./
studies. Whilst it is true that there are, for example, marked differences between the heights of children subjected to contrasting environmental conditions, Habicht et al (1974) have shown that the variation in height between well-off, environmentally privileged children of different ethnic backgrounds from countries as disparate as Iran, Nigeria, Nepal, Columbia, Britain and the USA, is of the order of only 3%, which is in sharp contrast to the much larger differences of the order of 12% "between these children and those of a similar ethnic background living in the poorer urban and rural regions of developing countries". Similarly, Eveleth and Tanner (1976), noted that at four years of age the difference in mean heights between well-off urban children in Ibadan and tribal children in the Pangani Basin was about twelve centimetres.

In the presence of a uniformly favourable environment, such differences in stature that do persist between different racial groups, are primarily genetic. For instance the mean adult heights of Hong Kong Chinese from high socio-economic groups, Japanese immigrants living in California, as well as those remaining in Japan, are all less than those of similarly privileged European populations. In contrast black American women living in Washington D.C. have been shown to be taller than European women (Eveleth and Tanner, 1976). Other studies have repeatedly confirmed that black children living in either Africa or America are more mature skeletally than children of European descent and are thus likely to be taller at a given age than their European counterparts (Tanner, 1962) (see also page 42).

It is, nevertheless, probable that selective environmental pressures/
pressures have interacted with the underlying genotype to produce a characteristic phenotype. The lean, tall physique, and resulting large surface area, of the Nilotics of Northern Africa and Australian aborigines who have evolved in the arid Central Australian environment, undoubtedly confers upon them an ability to radiate heat, whilst Eskimos faced with the need to conserve heat, have developed a much more squat body habitus with a relatively lower surface area. (Eveleth and Tanner, 1976)

The differences in height that continue to exist between well-off children living in the same community are also arguably genetic in origin. In a survey of 3707 five year old singleton white Californian children, whose parents were all members of a prepaid health maintenance insurance organisation, Wingerd (1974) found that 88.6% of the variation in height could be accounted for by differences in the height of the parents, with the relatively small residual variation deriving mainly from environmental factors.

The relationship between the height of parents and that of their children is indeed a close one, although as Tanner, Goldstein and Whitehouse (1970) have shown, this effect does not become marked until the children are aged two years, when the effect of their own genes outstrips the effect of the uterine environment in which they developed. The correlation co-efficients for height between three and nine years are between 0.3 and 0.5 (Goldstein, 1971), similar to those found between singleton siblings for height, as well as other growth characteristics such as height velocity and skeletal maturity (Hewitt and Stewart 1957; Hewitt et al., 1958). Thus/
Thus although the range of expected height is 25 cms. in the general adult population, it diminishes to 17 cms. within a given family (Eveleth and Tanner, 1976). Until recently there has been some disagreement about whether the parent/child correlations in the same sex case, that is mother/daughter, and father/son, are higher than in the unlike sex case (Tanner, Goldstein and Whitehouse, 1970) but currently there is little evidence in support of this hypothesis.

So close and consistent are these relationships that Tanner, Goldstein and Whitehouse (1970) have used them to construct charts which take into account both parents' heights and the child's actual recorded height. From these, it is possible to estimate whether the height of any child, aged between two and nine years, who appears small for his age can be accounted for on a genetic basis. Using these charts in a community study of short stature in children in Newcastle-Upon-Tyne, Lacey and Parkin (1974) were able to show not only that the mid-parental height of 82 children less than the third centile was significantly less than the population mean, but that genetic factors alone were probably responsible for short stature in 67% of the children.

Twin studies have also furthered the understanding of genetic influences on growth. A number of these were recently reviewed by Eveleth and Tanner (1976). Monozygotic twins reared apart are more different in adult stature than those reared together, but are nevertheless more similar than dizygotic twins. The normal (+ 2 SD) range of height found amongst pairs of adult monozygotic twins is only 1.6 cms. (Osborne and De George, 1959), whereas the same range amongst a group of brothers averages 16 cms. (Howells, 1966).
Shields (1962) however, points to examples of monozygotic twins who have been reared apart, where one twin has been subjected to illness or neglect, and in which marked differences in height age occur in response to the over-riding effect of a poor environment.

GROWTH AND THE ENVIRONMENT

Some mention has already been made of studies which demonstrate the impact of the environment on growth. Further evidence of its influence, provided by numerous studies which confirm geographical differences in height attained amongst ethnically similar populations, will be discussed in this section. Some studies have suggested that an adverse environment slows the growth rate of males to a greater extent than in females (Tanner, 1962). Initially, however, it is important to outline a way by which the component parts of the environment can be more readily studied.

The environment can be considered in different ways. "The physical environment (includes) the air we breathe, the water we drink, (the food we eat), our housing, roads, sanitation, noise, climate and transportation .... The social environment includes the family and the community." (Hetzel, 1971). Thus socio-economic status and the adequacy of housing and nutritional intake, have all been used as indices of the quality of the environment, both at community and individual levels. Within families, birth order, family size and parental age are other important indicators, and parental cigarette smoking characteristics are an additional clue to the physical environment within the home.
There is considerable evidence that a deprived environment, "principally poor nutrition, mediated by an inadequate diet and worsened by the conditioning of repeated infections", interferes with an individual's genetic potential for growth, often resulting in permanent stunting (Jelliffe and Jelliffe, 1974). For instance Morley (1973) has shown that poorly nourished children may take from one to three months to recover the weight lost during an episode of measles.

A socially deprived environment may exist at two levels. The environment of a whole community, or large sections of it, may be deprived, and this manifests itself in generally low standards of living and its consequences - low income, substandard and overcrowded housing and poor nutrition which is associated with generally poor health. Adults in such communities may suffer from a variety of chronic illnesses, from parasitic infestation, anaemia and tuberculosis, to alcoholism and psychiatric disorders (Cawte, 1973). The children often suffer from recurrent respiratory and gastro-intestinal infections (Morley, 1973; Hetzel, 1974), malnutrition and retarded growth. Within such communities infant mortality is high (Moodie, 1969) and, perhaps as a consequence of a low life expectancy in preceding generations, parity remains high (Morley, 1973) even when living standards improve and death rates fall, resulting in an increased average family size.

Such conditions still prevail in many of the developing countries in Africa, Asia, South and Central America, but are by no means confined to them. Geographical and racial enclaves of relative/
relative deprivation are also found within many developed countries, including Australia (Hetzel, 1974), Great Britain (CIUD 6, 1975; Holtermann, 1975; Stanfield, 1977) and the USA (Haggerty, Roghmann and Fless, 1975).

Wedge and Prosser (1973) have studied the geographical distribution of disadvantaged children within Great Britain from information collected during the National Child Development Study. Their definition of disadvantage includes children who were in "either a one parent or large family (more than five children) and who were also badly housed (no running hot water or living at a density of more than 1.5 persons per room)." In addition, the family was on a low income and thus qualified for free school meals or was in receipt of a supplementary allowance. Although one in sixteen children in Britain as a whole were found to be disadvantaged, the proportion was much higher in Scotland (1 in 10), Wales and the north of England (1 in 12) than in the more prosperous south of England (1 in 47).

Holtermann (1975) has analysed the geographical distribution of urban census enumeration districts (CED's) that could be regarded as "deprived" at the time of the 1971 census. These CED's included those in which at least one of five indicators of social deprivation were present. Thus each district had to have at least 15.1% of males unemployed, or 10.1% of households living at a density in excess of 1.5 persons per room or 50.5% of households without exclusive use of a bath, or 38.2% of households without exclusive use of running water, or 57.0% without exclusive use of an inside toilet.
An excessively high proportion of deprived districts was found in Scotland compared with England and Wales, and within Scotland the worst affected area was the Clydeside conurbation consisting of Glasgow and its environs.

Although this study had only looked at the extent of deprivation in different urban districts, an earlier study in 1947 (SCRE, 1953) had noted that overcrowding was more common in cities than in rural areas; in the cities 55% of people lived at a density of more than two persons per room compared with 43.3% in rural districts - despite the fact that family size was smaller in the cities (3.59) than in the country (3.91).

Deprivation at a second level, that of an individual child's family, may also be found. Although understandably this is observed relatively more frequently when a whole community is disadvantaged, families may exist as islands of deprivation surrounded by a sea of affluence. Such families are characterised by marital disharmony or breakdown (Wolff, 1972), job instability, and chronic physical or psychological illness in the parents or children (Rutter, 1966; Rutter, Tizard and Whitmore, 1970). Recently attempts have been made to measure the quality of family functioning (Pless, Roghmann and Haggerty, 1972), knowledge of which is important, since amongst the children in such families a significantly increased incidence of what have been termed "diseases of the social environment" are found (Miller et al, 1960). As well as short stature (Lacey and Parkin, 1974 a, b; Whitten, 1969) which is sometimes but not invariably associated with apparent suppression of growth hormone production under/
under these circumstances (Powell et al, 1967) these include non-
accidental injury (Smith et al, 1975), sudden unexpected death in
infancy (Emery, 1976), accidental injury (Adelstein and White, 1976)
and educational subnormality (Wedge and Prosser, 1973).

Within a deprived community, factors clearly operate at an
individual family level which either potentiate or mitigate the
deleterious effects of the surrounding environmental circumstances.
For instance in Jamaica, Richardson (1974) has found that the
families of children who suffer from malnutrition and later short
stature differed in a number of respects from families whose
children grew normally and remained well-nourished. The mothers of
the malnourished group were of lower intelligence, had fewer years
of schooling, and were more isolated from friends and relatives than
the control group; their houses had fewer amenities and were more
overcrowded, and the mortality amongst the remaining siblings was
higher than in the control group.

Geographical Differences in Growth Patterns

It is not surprising, in view of the wide range of environ-
mental conditions that exist between and within different countries
that there are marked geographical variations in height. As previously
mentioned (page 7) most of this variation can indeed be attributed
to environmental factors, rather than differences in genetic con-
stitution. In reviewing a large number of recently undertaken
European growth studies, Eveleth and Tanner (1976) concluded that
the tallest European children were to be found in Oslo, Sweden,
Helsinki/
Helsinki, Hamburg and the Netherlands. At four years they were four centimetres, and at sixteen years, seven centimetres taller than the smallest, who were found in Brussels, Paris, Rumania and Carrara, Italy. Whilst genetic factors may be partly responsible, it is surely more than coincidental that the tallest children were found in those countries with a higher standard of living, and the shortest in countries which by comparison were relatively poor. Interestingly, these studies have also shown that the average height of Dutch children living abroad in places as widely scattered as Australia, New Zealand, South Africa, the West Indies and the USA, was several centimetres less than those who remained in the Netherlands.

Differences in the average heights of children in Britain have been shown to exist within cities (Elderton, 1914), between cities (Stein, 1951; Weir, 1952; Berry and Cowin, 1954), and between urban and rural districts (Paton and Findlay, 1926; SCRE, 1952).

Paton and Findlay (1926) reviewed a large number of the earlier studies, most of which had found that country children were generally taller than city children, but they emphasised that social class differences had not always been considered. They presented height data obtained from the reports of the various education authorities in Scotland, which showed a significant difference in height between children in the rural areas of Scotland and those in Glasgow. The growth curves of child populations in different rural areas of the country were very similar to each other. The study of the Scottish Council for Research in Education (SCRE, 1952) demonstrated in/
in 1947 that the eleven year old children in Scottish cities were on average 1.4 cms. shorter than those living in country districts. The authors considered the possibility that part of this difference may have been due to the migration of genetically shorter people to the cities from rural districts in previous generations. They observed however, that such migration as was occurring at the time of the study indicated that those moving into and out of the cities - predominantly the children of salaried and professional workers - were taller than those who did not migrate.

Differences also exist in the heights of adults dwelling in city and rural districts. Clements (1953) found that men from the Scottish Highlands were 1.8 cms. taller than those in Edinburgh, who themselves were 1.0 cms. taller than those from Glasgow and the surrounding industrial boroughs. He believed that these regional differences were mainly due to differences in social class distribution, although evidence that this was not the complete explanation was provided by the observation that regional differences in height persisted even when social class was taken into account. Men in social class IV and V in the Shetlands were about 2.5 cms. above the national mean for these social classes; in contrast social class V men in Glasgow were about 2.5 cms. less than the national average. Genetic factors could again be partly responsible for these differences, as people of Scandinavian extraction commonly found in Shetland are generally taller than those in the west of Scotland who tend to be of Celtic origin.

In contrast with these earlier findings, urban children today,
in developed countries, are thought in general to be taller than those in the surrounding countryside. Eveleth and Tanner (1976) have put forward the view that the secular trend in growth (see page 32) is in fact a consequence of urbanisation, which has resulted not only in an improved supply of goods, health and sanitation services, but also has provided better access to educational, recreational and welfare facilities. In Finland, for instance, Backström-Järvinen (1964) has found that eight year old boys in Helsinki were 2.4 cms. taller than boys in rural Finland. Studies in Australia (Jones et al., 1973) and the USA (Hammill et al., 1972) have however shown no height differences between city and country children. Children in smaller towns and non industrial cities are also taller than those living in large conurbations, but again this may be primarily an effect of differences in social class distribution. It has frequently been observed for instance, that Edinburgh children are taller than those living in Glasgow, although the evidence from school health data cited by Keddie (1956) indicated that for nine year old boys these gaps had narrowed from a difference of 3.6 cms. in 1913-14 to 0.8 cms. in 1953-54. Differences in mean height have also been noted between the children in different English cities. Berry and Cowin (1954) reported that fourteen year old boys living in Salford, an industrial town on the outskirts of Manchester, were 6 cms. shorter than those from Kingston-upon-Thames, a residential area on the outskirts of London; Bristol boys were even taller.

Numerous studies have confirmed that English children are taller than those in Scotland. Weir (1952) found that London children/
children had been consistently taller than those in Glasgow ever since height records were begun in 1905. In successive surveys of five year old boys, the differences had always been between 1.4 and 1.9 cms. Stein (1953) noted that children living in a working class ward in Edinburgh in 1951-52 were about 2.5 cms. shorter than London children of a corresponding age. In 1958 Douglas and Blomfield (1958) found that 4½ year old children in Scotland were on average 2 cms. shorter than those in England. The National Child Development Study, begun in 1958 (Davie, Butler and Goldstein, 1972), found that the height of English seven year olds averaged 0.5 cms. more than those in Wales, who in turn were 0.6 cms. taller than Scottish children. They concluded that the most likely explanation for these differences was that they reflected national differences in parents' heights and social class distribution, as when these were taken into account, national differences in children's height were eliminated.

A more recent study still in progress - the National Study of Health and Growth - (Irwig, 1976; Holland, 1977) reaches a different conclusion; even when social class factors were allowed for, seven year old Scottish children were still shorter than their English counterparts.

Social Class

Social class, as measured by the occupation of the father in the family (OPCS, HMSO, 1970) is the most frequently used indicator in Britain of socio-economic status. In spite of criticism, the Registrar General's classification has withstood the test of time.
As a generalisation, the level of income and the qualifications necessary to undertake particular occupations, rise as one progresses upwards from unskilled (social class V) to professional (social class I) occupations.

Moreover, it is a fact in this country, perhaps to a greater extent than others, notably Sweden, that extremes of social class are characterised, for whatever reason, by totally different attitudes and lifestyles (Davie, Butler and Goldstein, 1972). It is still true of Britain that "a man's occupation tends to be related to the way he lives outside his work situation". Social class is thus a convenient and useful indirect measure of many aspects of children's environment, which will to some extent shape the way they develop.

Indirectly, social class may be regarded as an indicator of groups within society most likely to suffer deprivation. Members of unskilled occupational groupings are more likely to have less disposable income than others, which may result in the families eating food of poorer quality, although not necessarily quantity (Cook et al, 1973). They are also more likely to live in housing with fewer amenities. In addition, they are at higher risk of becoming unemployed and remaining so for a longer time. Thus, "whereas social class V occupations account for only about 8% of economically active men, they account for nearly a quarter of the men who were out of employment" (OPCS, 1971).

The level of unemployment within a community is commonly regarded as a measure of social deprivation (CIUD 6, 1975; Holtermann, 1975) and its relationship with stature has recently received attention/
attention from several authors (Wedge and Prosser, 1973; Lacey and Parkin, 1974b). For instance, Lacey and Parkin (1974b), in a study previously referred to, found that about one third of the fathers of children with short stature had been unemployed for a significant length of time between birth and the time of the survey at the age of ten years.

Numerous studies of children's growth in this and the previous century have, almost without exception, demonstrated that children in the families of manual workers are shorter than those whose parents are engaged in professional or salaried occupations. The report of Wingerd and Schoen (1974) referred to earlier is the only one reviewed which fails to demonstrate any significant difference in height at the age of five between children whose fathers were engaged in professional and nonprofessional occupations. However, as was emphasised previously, the study was limited to a white middle class Californian population who gave a high priority to health.

As long ago as 1829, Villermé cited by Paton and Findlay (1926) stated that "stature is greater, and the growth sooner completed, all other things being equal, in proportion as the country is richer and the comforts of the inhabitants more general". Later in the report of the Anthropometric Committee of the British Association (1880), cited by Paton and Findlay (1926), the heights of boys at Marlborough Public School were on average 4.22 inches greater than those of factory boys. Among adults grouped into five social classes there was a difference of 3½ inches between the mean of the most favoured class/
class and that of the poorest town class.

By the mid twentieth century, the social class differences appear to have narrowed somewhat both in adults and children. In a study of Scottish men aged 18-41, Clements and Pickett (1952) noted that men from social class I were on average 1.4 inches taller than those in social class IV. Several years later Acheson and Hewitt (1954) found similar differences in Oxford where men in social classes I or II were 1.7 inches, and women 1.4 inches taller than those in social classes IV or V. A random survey of eleven year old Scottish children in 1947 (SCRE, 1953) found that the children of unskilled workers were 2.5 inches shorter than those of professional workers. It is at this age, however, as Tanner points out (1962), that the differences between social classes are likely to be at their most extreme, because of the effects of the earlier onset of the pubertal growth spurt in well-off children.

These social class differences may reflect differences in income. Quaas (1956), in a sample of 3771 Copenhagen children aged 6-16, noted a strong correlation between the children's height and the father's income which persisted even when the hereditary influence of father's height was considered, although Paton and Findlay (1926) had earlier been unable to demonstrate any association between height and income in either poor rural (children of unskilled agricultural workers) or urban children (slum dwellers in Dundee, Edinburgh and Glasgow).

Douglas and Blomfield (1958) in the National Survey of Child Health and Development begun in 1946, found an average difference of/
of 2.3 cms. at two years of age, and 3.4 cms. at 4\frac{1}{2} years of age between the children of professional and salaried workers and those of unskilled labourers. Acheson and Hewitt (1954) noted similar differences in height in Oxford children, and predicted that if the social class differences both in height and the rate of skeletal maturation found in preschool girls were to continue, the social class differential in the height of adult women would exceed those of men. In the Thousand Family Study in Newcastle-upon-Tyne, Miller et al (1960) reported a difference of 2.5 cms. between three year old children from the highest and lowest social classes. Regrettably though, these heights had been recorded by the parents.

The most recent studies suggest that the differences are still decreasing but have not yet disappeared. Goldstein (1971) reporting on data concerning seven year old children in the 1958 National Child Development Study, noted that children from social class V were on average 3.3 cms. shorter than those in social class I or II. When allowance was made for the contribution of other factors to the difference in height, the adjusted differences between the social classes was only 1.3 cms. Some of this residual difference could have been accounted for by other factors, such as father's height, which were not examined. Topp et al (1970) found a difference of 1.8 cms. between boys aged 5-8 in the lowest and highest social classes. In girls the difference was only 0.8 cms. This finding is consistent with the proposition that the growth process is better canalised in girls than boys (Tanner, 1962).

These studies have, with only one exception, all convincingly demonstrated/
demonstrated to a greater or lesser extent that children of the lower social classes tend to be shorter. It would not be surprising therefore to find that a much higher proportion of children with short stature come from the lower social classes. Several studies have confirmed that this is indeed the case. Within the total study group of 5386 children mentioned earlier, Douglas and Blomfield consistently (1958) identified a group of 61 who were more than 1 SD below the mean height between the ages of 2 and 4. Both later born children and children of manual workers were significantly overrepresented. In the recent community study of children below the third percentile in Newcastle, Lacey and Parkin (1974 b) found a much higher proportion of children without an organic cause for their short stature came from social class V compared with the social class distribution of the reference population from which the short children were drawn.

Overcrowding

As early as 1908, MacGregor (1908-9) comparing the physique of Glasgow children grouped according to the number of rooms in the home, had found for example, that five year old boys living in one room were 6.0 cms. shorter than those living in three rooms. Similar findings had been noted in the report of the Education Committee of the London County Council (1905); moreover the average height of children living at a density of more than five to the room was 9.1 cms. less than those living at a density of one or two persons per room. Paton and Findlay (1926), found that the effects of overcrowding were not apparent until after the first year of life, and/
and the size of the correlation did not in their opinion support the suggestion that it was a dominant factor influencing the nutrition and growth of the child. In 1945, Young (1945) found similar differences still existed in Glasgow to those found earlier and in the 1947 Scottish Mental Survey (SCRE, 1953) it was shown that the reduction in height with increasing overcrowding was markedly less in children within the families of professional and salaried workers than those whose parents were in manual occupations.

**Parity and Size of Sibship**

Numerous studies have confirmed that both increasing parity and family size are associated with a reduction in stature, which is to some extent independent of the degree of overcrowding. Later born children tend to be shorter than their elder siblings. As in the case of overcrowding, the fall off in height with increasing family size is more pronounced in social classes IV and V. For example, the 1947 Scottish Mental Survey (SCRE, 1953) found that the difference between families with one and five children in the height of eleven year old children was only 0.5 cms. in those whose parents were engaged in professional or salaried occupations; in contrast the height differences in the children of unskilled workers averaged 3.5 cms. Douglas and Simpson (1964) similarly noted that the 2.5 cms. difference between the height of seven year old boys from large (three or more sibling) families and those with no siblings, was almost halved when adjusted for the effect of social class. Surprisingly girls of the same age showed little reduction in the...
even greater (4.3 cm) height difference when social class was taken into account. These findings, showing a greater reduction in the height of girls compared with boys under adverse environmental circumstances are uncommon (see page 23).

Scott (1961) found a slightly different picture in eight year old London children, where the height differences between those from one child families and those containing five or more children was 4 cm in boys, and only 3.2 cm in girls. Goldstein (1971) in the National Child Development Study noted an average difference of 2.3 cm between the first and fourth or later born seven year olds. He also attempted to isolate the biological effects of parity and the number of children in the family who were younger than the index child, and found that first born children were 2.8 cm taller than fourth or later born children for a given number of younger siblings. At a given parity, those children with no younger siblings were 1.1 cm taller than those with two or more younger siblings. Hence the effects of being a later child and having younger siblings combined to decrease height.

Lacey and Parkin (1974 b) have convincingly demonstrated that these effects do indeed lead to short stature. They found that 55 of 82 children below the third centile came from families containing more than four children, which in the case of social class III and V was significantly more than expected.

Two possible explanations for these observed differences were offered by Tanner (1962). The first was the simple environmental explanation that with more mouths to feed and children to bother about/
about, both feeding and general care are handled less efficiently. Alternatively, genetically smaller and less able persons produce on average more children than genetically taller and more able ones.

**Maternal Age**

Few studies have looked at the association of maternal age with children's growth. Paton and Findlay (1926) found that infants of young and old mothers were shorter in the first six months of life than those of mothers of medium age, but by the end of the first year of life only the infants of the older mothers were still shorter. Goldstein (1971) noted that even when allowance had been made for other variables (social class, parity, birth weight, length of gestation, maternal height, maternal smoking habits during pregnancy, and number of younger siblings), the children of mothers aged less than 25 at the birth of the indexed child were on average 0.6 cms. shorter than children of mothers aged 25 or over.

**Smoking During Pregnancy**

Another influence that has been recognised to have an association with growth is cigarette smoking by the mother during pregnancy. Children born to mothers who smoke more than ten cigarettes per day were on average 170 gms. lighter at birth than children of nonsmokers (Butler and Alberman, 1969). Smoking also has an influence on the postnatal growth of children which is independent of its effect upon birth weight. Even when birth weight and a number of other variables were considered, seven year old children of women who had smoked more than ten cigarettes a day were on average 0.6 cms. shorter than those whose/
whose mothers had been nonsmokers (Goldstein, 1971). This residual
difference may indicate that cigarette smoking affects directly the
growth potential of the foetus, or it may reflect additional factors
which are associated with heavy smoking amongst mothers, including
perhaps a post natal environment which is unfavourable for physical
growth (Davie, Butler and Goldstein, 1972). Wingerd (1974) found
similar height differences to those described by British workers,
exist between five year old Californian children who had and had
not been exposed to cigarette smoking during foetal life.
Yerushalmy (1971) has maintained that the demonstrable differences
between the growth of children of smokers and nonsmokers are
primarily social class effects.

Growth and Nutrition

The effects of nutrition upon growth have been clearly demon¬
strated in animal experiments and from observations made in humans.
McCance (1960) and Widdowson and McCance (1963, 1975) have shown that
the timing of a nutritional insult in relation to the stage of
development is the critical factor in determining whether the
impairment in growth is likely to be permanent.

In rats, starvation between the three week period from birth
to weaning, which corresponds to later foetal development in man,
results in permanent stunting of growth, possibly through decreasing
cell division and reducing the number of cells in the organism at
maturity, and probably also through a permanent suppression of
appetite, acting through the hypothalamus, which at that time is
being/
being integrated with the size of the developing organism. "The plane of nutrition until this time, and consequently the size the animal has reached, determine what its final size will be, even though this may be smaller than its genetic legacy." (Widdowson and McCance, 1975). Starvation for a similar length of time at the later age of nine to twelve weeks in the rat is followed by a period of "catch up" growth in which the animal returns to the original growth curve along which it had been growing prior to starvation.

Extrapolating such evidence to the human situation would indicate that poor nutrition is only likely to cause permanent stunting if it has been present during the critical period of development either before or immediately after birth. Such extrapolation is possibly unwise; nevertheless it does indeed seem probable that the earlier the nutritional insult in the child's life, the more likely it is to have a permanent effect upon growth.

There is increasing evidence that amongst children with a low birth weight (see page 35) it is those who have suffered from intrauterine growth retardation as a result of poor utero-placental function, and who are thus born light for dates, who later have diminished growth. (Fitzhardinge, 1975)

On the other hand there is conflicting evidence as to the permanent effects on growth, of kwashiorkor and marasmus, during the first five years of life. In many developing countries today, the growth of many children is clearly affected by malnutrition towards the end of the first year of life, even in those communities in which it has had no effect upon the birth weight. Whilst malnutrition undoubtedly/
undoubtedly reduces the rate of growth and prolongs the growing period (Widdowson and McCance, 1975), adult height is not always reduced. Garrow and Pike (1967) found that most children reached equality of height with their well-nourished siblings before puberty, although others (Graham, 1972) believe they may suffer long term effects. Many of these studies have been handicapped by the unsatisfactory nature of the control populations studied (Eveleth and Tanner, 1976).

In the industrialised countries there have also been studies of the effects on subsequent growth of malnutrition resulting from surgical conditions in infancy. Valman (1974) has shown that the long-term growth of infants brought up in well-off homes who are subjected to such temporary malnutrition is not affected. Berglund and Rabo (1973), in a retrospective Swedish study of adults who had suffered from conservatively managed pyloric stenosis in infancy found no difference in adult height between those mildly affected (who regained their birth weight by five weeks of age) and controls. Those more severely affected who had taken fifteen weeks to recover their birth weight, however, had an adult mean height some 4 cm. less than the controls.

The effects of malnutrition upon the growth of older children have been clearly demonstrated in growth data collected from children in Stuttgart, Germany, during the first half of the century (Tanner, 1962). During both world wars, the height gain of children at all ages slowed, and was followed by a period of "catch-up" growth. Dietary supplementation of similarly malnourished children was shown by/
by Widdowson and McCance (1954) to be an effective means of promoting "catch-up" growth, during which not only height and weight, but skeletal maturity advanced at a greater than normal rate.

There is conflicting evidence of the extent to which poor nutrition is a major factor responsible for the difference in stature between different groups in Britain. Although clinical signs of malnutrition are rare, the effect on height of social deprivation in this country is at least in part mediated through generally poorer nutrition and health. Cook et al (1973) have suggested that in relatively prosperous countries the quality of the diet, as assessed by the nutrient intake per 1,000 Kcal, is a more important influence on growth than the total nutrient intake. They found the variation in intake of nutrients/1,000 Kcal between different social class and family size groups, paralleled the height differences. Children in lower social classes and large families had a lower intake of all nutrients/1,000 Kcal except carbohydrate and sugar, indicating their reliance on cheaper nutrients as a source of energy rather than relatively more expensive protein and fat.

Stanfield and Donnet (1976) have more recently shown that poor nutrition, recurrent gastro-intestinal infections and frequent hospitalisations are associated with short stature in infants in a socially deprived council estate in Glasgow. In a neighbouring working class area with fewer indices of social deprivation there was better nutrition and less ill health and no significant incidence of short stature. However, the mean height of the parents was significantly less in the deprived estate. Two explanations for this/
this are possible; either the parents themselves were shorter for genetic reasons or alternatively their growth had been permanently affected by adverse environmental circumstances in their own childhood.

Although earlier studies (Orr, 1923; Leighton and Clark, 1929) had demonstrated that supplementing the diet of Scottish school children with milk resulted in improved height gains (compared with unsupplemented controls), more recent studies by Cook et al (1975), have not demonstrated that school milk confers any benefit to school children in Kent with regard to gain in height. They did observe however that the shorter children had lower than recommended intakes of calcium and riboflavin, either because of a decreased appetite, or because being short, they have a lower requirement than taller children. The possibility of previous undernutrition causing the diminished stature was not excluded. As previously mentioned (page 14), there are important differences in the family characteristics that appear to determine which children become malnourished. Further evidence in this country (Lacey and Parkin, 1974b) suggests that poor parental care and poor living conditions are found significantly more often in children with short stature than those of a similar social class in the rest of the community.

Better nutrition, and the consequent reduction in the incidence of the severity of infectious diseases is also thought to underlie much of the secular trend towards earlier physical maturity. As a result of this trend, children's heights have increased on average by one to two centimetres per decade during this century, although in upper and/
and middle class American families it now appears to have stopped (Damon, 1968). The progressive reduction in the age of menarche over the last several centuries provides clear evidence of earlier maturation but similarly this trend now appears to be slowing down. The height of mature adults has also undergone an increase of about one centimetre per decade over the same period.

**Sex Differences in the Effects of an Adverse Environment**

Malnutrition and other adverse environmental conditions appear to retard the growth of boys to a greater extent than girls (Tanner, 1962), which is perhaps another example of the biological inferiority of the male as exemplified by the finding at all ages of a higher mortality in males compared with females. Tanner (1962) however, believes that it is the existence of better "canalisation" of growth in females (i.e. they show less tendency to be thrown off their growth curves) that is responsible, rather than their ability to better withstand adverse environmental circumstances, since improvement in the environment results in faster growth in males than females. For example, Harrison et al (1959) has demonstrated that male mice show a greater increase in tail length than females, when exposed to a hotter (i.e. more favourable) environment. On the other hand, Douglas and Simpson (1964) found that the growth of girls was more influenced by environmental factors. At each age they found that "a greater difference between the adjusted average heights of upper middle class and lower manual working class girls, than between the adjusted average heights of similar groups of boys".

Greulich/
Greulich, in two separate studies (Greulich, 1951; Greulich et al., 1953) demonstrated less growth retardation in the girls than the boys, who were survivors of the stresses of both conventional and atomic warfare. Widdowson and McCance (1954) noted that orphanage girls were less growth retarded prior to dietary supplementation, and exhibited more rapid catch up growth after the supplementary diet was begun.

The greater fall off in height noted in boys exposed to an adverse environment is perhaps caused in part by a greater reduction in the rate of skeletal maturation in boys compared to girls (Acheson and Hewitt, 1954). They concluded that retardation under these "pathological" circumstances, resulted in a relatively short final height - unlike the situation in physiologically slow maturers, whose rate of growth is slower than average, but in whom final height may be equal to or greater than physiologically fast maturers. Both sexes demonstrated a greater diminution in the rate of growth compared to the rate of skeletal maturation, but this disproportion was more noticeable in girls. They therefore argued that malnutrition and other adverse environmental influences would cause a greater reduction in final adult stature in women.

Conclusion

It is clear that there is a wide interaction between these different environmental measures. In adverse circumstances they all seem to contribute to the failure of children to reach their genetic growth potential. It seems that the timing of the adverse environmental/
environmental circumstances in relation to the child's age is important. "If a particular environmental stimulus is lacking at a 'sensitive period' then the child's development may be shunted, as it were, from one line to another" (Eveleth and Tanner, 1976). It is probably also true to say, as they did, that in the final analysis "most of the environmental influences upon growth rate depend upon the level of nutrition, acting in some areas in conjunction with infection" (Eveleth and Tanner, 1976). In a perfect world one could speculate that most of the variation in children's height would be due to genetic differences, but alas, such conditions are rarely, if ever, met.

LOW BIRTH WEIGHT AND SUBSEQUENT SHORT STATURE

It would seem only logical to expect that the size of an individual at birth would bear some relationship to later growth. As well as the obvious effect of the length of gestation, a number of other maternal and foetal influences are important determinants of birth weight and length, but they vary in their contribution to later growth. Thus, although the correlation between birth length and adult height is only about 0.3, by the age of two years the correlation between length and final height is approximately 0.8 (Tanner, 1973). One reason for this variation is that uterine factors which are major constraints upon birth weight and length (Smith et al., 1976) have less important effects upon later growth. When uterine space is almost fully occupied - usually at about 34-36 weeks of gestation in singletons, but obviously earlier in twins - foetal growth/
growth is slowed down and this mechanism therefore "allows a genetically large child developing in the uterus of a small mother to be successfully delivered" (Tanner, 1973). Smith et al (1976) in a recent study have confirmed that birth length related predominantly to maternal size, whereas by two years of age the length of the child correlated best to midparental height, reflecting the genetic growth factors of both parents. The possible influences of medical and environmental factors were reduced by only including in the study healthy well-nourished children of middle class parents. Hence it is not necessarily true, either that the largest babies will become the biggest children and tallest adults of the future, or that the smallest babies will become the most diminutive adults.

Much of the earlier literature (e.g. Drillien, 1958; Lubchenco et al, 1963) concerning the relationship between low birth weight and later growth is difficult to interpret because it considered en bloc all infants whose birth weight was less than 2500 gms. and failed to distinguish between those "preterm" infants who were born after an abnormally short gestation (usually less than 37 weeks) but were an appropriate size (AGA), and those who were small for dates (SFD) i.e. were more than 2 SDs below the mean birth weight for their postmenstrual age. Lubchenco for example, found that 41% of infants with birth weights less than 1500 gms. were below the 10th centile for height at ten or more years of age, but he does not differentiate between those who were preterm and those who were small for dates. Clearly such distinction can only be made accurately when the age from conception is known, and it is only with the recent/
recent development of clinical scoring systems (Dubowitz, 1970) and ultrasonic cephalometry (Campbell, 1974) that anything superior to the mother's ability to recall the date of onset of her last menstrual period has been available.

Foetal growth is more rapid than at any other time of life and is characterised by rapid cellular division. "As the foetus gets older the proportion of cells undergoing mitosis in any tissue becomes progressively less" and from about six months after conception growth in many tissues occurs principally by the development and enlargement of existing cells (Tanner, 1973). One would therefore expect the first six months following conception to be a particularly vulnerable period, since any damage done during this time would permanently reduce the final number of cells, and result in permanent stunting, a situation similar to that commented upon earlier in relation to laboratory animals (Widdowson and McCance, 1975) (see page 28). In a very significant recent study, Fancourt et al (1976) have shown that the time of onset of intra-uterine growth retardation is indeed a critical factor in determining the long term prognosis with respect to growth. He and his colleagues noted that a foetus with evidence of intra-uterine growth retardation (as measured by ultrasonic cephalometry) before 34 weeks gestation, was significantly more likely to have a height and weight less than the tenth centile at four years of age than those in whom growth retardation did not become apparent until later in pregnancy.

A number of genetic and environmental influences affect birth weight, but this is not an appropriate place to do more than summarise some/
some of them briefly.

Maternal factors found to be associated with low birth weight include low socio-economic status (Drillien, 1957; Baird, 1964; Bjerre and Värendh, 1975), short stature (Baird, 1964; Tanner and Thompson, 1970), cigarette smoking (Butler and Alberman, 1969; Miller et al, 1976), and the presence of certain pathological states such as severe pre-eclampsia (Butler and Alberman, 1969) and low maternal weight gain during pregnancy (Weiss et al, 1969), and more recently, chronic alcoholism (Hanson, 1976). Indeed Weiss and Jackson found that "among 32 factors affecting birth weight examined simultaneously in a multiple regression analysis to investigate the rank order of their importance, the amount of weight gained by the mother during pregnancy, and her prepregnant weight showed the strongest correlations with the weight of the infant at birth.

There is much evidence of the affect of maternal malnutrition upon foetal growth and development (Osofsky, 1975). Smith (1947), for example, noted that during the 1944-45 Dutch famine the birth weight declined markedly in those infants whose mothers had been exposed to severe malnutrition during the first half of pregnancy. Cameron and Graham (1944) found that with close dietary supervision in a group of 500 pregnant Glasgow women who were poorly nourished at conception, the incidence of LBW was significantly reduced compared with the control group in which no such intervention took place.

Primary foetal abnormalities also understandably affect birth weight. Intra-uterine viral infections such as rubella or chromosomal abnormalities/
abnormalities are often associated with low birth weight as also are a number of other conditions in which the aetiology is less clear (Smith, 1970). These include those children with the Silver-Russell syndrome (Tanner et al, 1975). There has been some recent discussion as to whether this condition, which is characterised by a typical triangular facial appearance, low set ears, down-turned corners of the mouth, relatively small mandible in relation to maxilla, short incurved fifth fingers, and frequent asymmetry "constitutes an entity separable from the general run of SFD infants with no obvious syndrome diagnosis". The finding of an almost universal absence of LBW in the sibs of these children would, these authors conclude, not be an expected finding if these children were merely those SFD infants who turned out smallest in childhood.

As already mentioned, a number of studies have shown that many LBW infants remain small throughout childhood, becoming the "LBW dwarfs" described by Black (1961) and Clayton et al (1967). Previously these children had been termed "primordial" dwarfs (Wilkins, 1965). Some writers confine this classification to infants less than 2.05 kg. (Black, 1961; Joss, 1975) whilst others (Lacey and Parkin, 1974) include only those who were SFD. More recent studies which differentiate between "preterm" and "small for dates" infants indicate that it is indeed the latter group who are most at risk of continuing short stature (Chamberlain and Davey, 1975). Fitzhardinge and Steven (1972) found that 35% of 96 SFD infants were below the 3rd centile for height and weight at four years. Bjerre (1975) also noted that SFD infants, particularly girls, were significantly shorter/
shorter than average at five years of age, but found only a few children had significant short stature (below -2 SD). Lacey and Parkin (1974) thought that low birth weight for gestational age was the sole factor responsible for short stature at age ten years in four of 82 children below the third centile. It also contributed in many of the remaining children who were small for genetic reasons or because of delayed development (see page 10). As well as being small these children are often underweight and have low skinfold thickness measurements, which may differentiate them from children with growth hormone deficiency (see page 65).

In contrast with these findings, short stature is an uncommon sequelae in those preterm infants whose birth weight is appropriate to gestational age. Fitzhardinge and Steven (1972) found that only four (12.5%) of 32 surviving infants with birth weights under 1251 gms. born between 1960 and 1966, who were appropriate for gestational age were less than the third centile at the age of five years. Of 67 appropriate for date infants born eight or nine weeks before term during 1970-72, none were of short stature at twelve months of age (Fitzhardinge, 1975). Indeed heights of both sexes did not differ significantly from either controls or accepted standards, findings similar to those also observed recently by Bjerre (1975).

DELAYED MATURATION AND SHORT STATURE

Children vary widely in the rate at which they progress towards their final adult height. At no time is this variation more apparent than during puberty when, for instance, at the same chronological age/
age, children show a wide range not only of pubertal development, but
in the proportion of their final adult height that they have
attained. Tanner (1973) has been quick to point out that similar
individual differences in the tempo of growth occur at all ages,
even though not as obvious as at adolescence.

This disparity between chronological age and development has
given rise to the concept of "developmental age" (Tanner, 1962).
Skeletal age is one of several important indices of developmental
age, and thus at any given chronological age it is a useful indicator
of the remaining potential for growth. It is "a measure of how far
the bones of an area have progressed towards maturity, not in size
but in shape and their relative positions to one another as seen on
the radiograph" (Tanner, 1973). Earlier, (1962) he wrote "each bone
begins as a primary centre of ossification", passes through the
stage of enlargement and shaping of the ossified area, acquires
perhaps one or more epiphyses, and finally reaches the adult form with
epiphyseal fusion. The sequence of events in each bone is essentially
the same in all individuals, irrespective of whether the bone is
advanced or retarded in relation to chronological age. Skeletal
maturity is judged, both on the number of centres present, and the
stage of development reached. Other measures of assessing develop¬
mental age, including dental age and shape age, will not be further
considered here. It appears that children tend to be consistently
advanced, or retarded in their maturity, during the whole of their
growing lives, and this is particularly so from the age of three.

Tanner (1973) has shown that skeletal age is much more closely
linked/
linked to the onset of adolescence than chronological age. "The range of chronological ages within which the menarche may normally fall is about 10-16, but the corresponding range of skeletal ages is only 12½-14½ years."

There are a number of methods of assessing skeletal maturity, but after one year of age the most widely accepted are based upon the radiological appearances of the hand and wrist. (Todd, 1937; Greulich and Pyle, 1959; Tanner, Whitehouse and Healey, 1961). The left hand and wrist are always studied following widely accepted convention (Tanner, 1962). The assessment of skeletal age can be made either by comparing the overall radiological appearances of any individual with a standard - which is the modal for each particular age (Todd, 1937; Greulich and Pyle, 1950, 1961) or individual bones in the X-ray are matched with a series of standard stages - each individually scored - through which each bone passes - giving an overall maturity score of the X-ray, which can be related either to a percentile status for chronological age, or converted to a skeletal age (Tanner, Whitehouse and Healey, 1961).

A number of factors influence skeletal maturation and these have been extensively reviewed by Tanner (1962, 1972). At any given chronological age, girls are further advanced towards maturity, and they increase their lead over boys from about two weeks at birth to two years at adolescence and this is taken into account when standards are constructed. Race is also important as blacks living in America, West or South Africa, are further advanced than children of European descent, and these differences cannot be explained/
explained purely on socio-economic grounds. Tanner proposes that they may be due to a greater preponderance of early developer genes in negroes, and perhaps also to "environmentally caused differences in intra-uterine development". In Asiatics, skeletal maturity is similar to European standards until adolescence, when it becomes comparatively advanced (Eveleth and Tanner, 1976). Mesomorphic individuals, as a group, are more advanced skeletally than relatively and linear eutrophic persons. They tend to enter puberty earlier, and to be shorter as adults.

Some reference has already been made to the effect of malnutrition upon skeletal development (see page 34). Improved nutrition or other environmental influences are thought to underlie the more rapid skeletal development of Japanese children living in California, compared with those remaining in Japan (Sutow, 1953; Greulich, 1957).

Skeletal maturity is also affected by endocrine factors. It is advanced when androgens are administered (Sobel et al, 1956) or in children with precocious puberty. Noran and Sanders (1969) have noted that skeletal development is retarded following the administration of either naturally occurring or synthetic ACTH or steroids. Growth hormone deficiency (Tanner et al., 1971) and thyroid deficiency are both associated with marked slowing in the rate of skeletal maturation.

The importance of taking skeletal maturity into account in children with short stature has been emphasized by many. Children with lower skeletal ages as a group tend to be shorter than those with more advanced skeletal development. It is not surprising therefore/
therefore to find that many children with short stature have a significantly retarded bone age. Lacey and Parkin (1974b) found that 34% of 82 children with heights below the third centile had more than one year's delay in skeletal age. The height of many was within the normal range when it was plotted against skeletal rather than chronological age. Although small, the bodily proportions of these children are normal. Tanner (1973) regards short stature arising in these circumstances as an example of "growth delay", which he arbitrarily subdivides into "normal" (that is the bone age is within two standard deviations of the mean), or "abnormal" (that is the bone age is beyond this limit). Many children with "growth delay" also have short parents, siblings or other relatives (Tanner, 1973), and many have had a low birth weight. Short stature arising in these circumstances has been classified by Tanner (1971) as "small-delay". Others refer to this condition as "constitutional short stature" (Wilkins, 1965; Kaplan et al, 1968; Rook et al, 1971; Joss, 1975). It is thought that most of these children will achieve their genetic potential for height, although the onset of puberty and its accompanying growth spurt will probably be late in occurring (Tanner, 1973). Because of this, psychological problems may arise. However, in some circumstances, if the delayed skeletal development has resulted from extremely adverse environmental circumstances such as malnutrition, the full genetic growth potential may not be achieved because the rate of growth will have been disproportionately more slow than the rate of maturation (Acheson and Hewitt, 1954).
PATHOLOGICAL CONDITIONS CAUSING SHORT STATURE

It is clear from the literature that short stature may result simply from the interaction of adverse environmental conditions and genetic factors. Short stature under these circumstances, affecting limbs and trunks proportionately, may have been present since birth, or developed later in childhood and be found associated with delayed skeletal maturation. Other members of the family may also be small. In their community study, Lacey and Parkin (1974b) found such "normal" short children accounted for 83% of children less than the third centile for height. Although free from organic disease their biological and social backgrounds were decidedly abnormal. "The parents of the children are short, and they tend to come from the lower social classes, to have large families, and rear their children in poor social conditions. There is a tendency for the children themselves to be of low birth weight, and to have slow physical growth as measured by skeletal development. In addition, they score poorly in tests of mental ability and attainment." Thus in these circumstances short stature may be rightly regarded as a "disease of the social environment".

The association between mental retardation, whatever the cause, and growth failure has been described frequently. The pathogenesis of the growth failure is in many instances unknown. Bailit and Whelan (1967) found that 44% of children categorised as "cultural-familial retardation" were -2 SD or more below the mean height of the general population. Although various experimental brain lesions, particularly those of the hypothalamus and amygdaloid regions have been/
been shown to be followed by growth retardation in animals, their possible role in the pathogenesis of short stature in mentally defective humans is uncertain. Presently recognised endocrine abnormalities, such as growth hormone deficiency, have not been observed (Frasier et al, 1970).

It is important however to distinguish children who have a pathological cause for their short stature from those regarded as "short normals". When other abnormalities are present, such distinction is relatively easy, as in these cases the short stature is often disproportionate. There are nevertheless, certain conditions, such as growth hormone deficiency, or exceptionally coeliac disease, where apart from short stature, other physical abnormalities may be minimal or even absent.

Smith (1967, 1972) has classified and given several excellent accounts of the many pathological causes of short stature which are briefly summarised below, using the classification of Tanner (1973). Most are the relatively infrequent causes of short stature in the general community (Lacey and Parkin, 1974a). Corrective treatment is ineffective in the majority, the few endocrine conditions, including growth hormone deficiency which is discussed subsequently, being an exception.

Because chronic alcoholism has a notoriously high prevalence in Scotland, it is therefore pertinent to briefly mention the Fetal Alcohol Syndrome which has recently been described by Lemoine et al (1968) and Jones et al (1973). This affects the offspring of mothers who are chronic alcoholics. In a recent review of 41 patients/
patients with features of the condition Hanson et al (1976) found that 97% had both prenatal and postnatal growth deficiency, 93% microcephaly, 92% short palpable fissures, 89% developmental delay or mental deficiency and 80% fine motor dysfunction. Other features noted have been midfacial hypoplasia, epicanthic folds, abnormal palmar creases, minor joint anomalies, cardiac defects, minor anomalies of the external genitalia, minor ear anomalies, and strawberry haemangiomas. Occasionally, the presence of these abnormalities in a child has resulted secondarily in the realization that the mother was a chronic alcoholic. The authors believe that cases with these features represent only those most severely affected. "At the milder end of the spectrum may be a larger number of less severely affected children of chronically alcoholic women who manifest only mild degrees of mental and growth deficiency, and whose few defects do not permit a definite clinical diagnosis." Hanson et al have suggested that the risk of alcoholism giving rise to a serious problem in the developing foetus is between 30% and 50%.

"Short normal"
- genetic short stature
- delayed development - 'normal'
- genetically short and delayed development ("Small-delay")
- non specific LBW short stature.

Chromosomal abnormality syndromes
- Trisomy 21
- Trisomy 18
- Turner’s syndrome (XO, or mosaic with deleted short arm of X).
Endocrine abnormalities
- Isolated growth hormone deficiency - partial or severe
- Panhypopituitarism with deficiency of growth hormone, ACTH, TSH, and gonadotrophins.
- Hypothyroidism
- Cortisol excess - e.g. adrenal tumour
- Steroid therapy for arthritis or asthma etc.
- Precocious puberty

Intra-uterine dwarfism
- LBW short stature - non specific
- Russell-Silver Syndrome (see page 39)
- Seckel's Syndrome
- Fetal Alcohol Syndrome

Malabsorption and Intestinal Disease
- Coeliac disease
- Cystic fibrosis

Renal disease
- chronic renal failure
- tubular dysfunction

Hepatic Disease
- glycogen storage disease

Anoxaemia
- Congenital heart disease - particularly if associated with right to left shunt.
- Chronic severe asthma
- Bronchiectasis
- Cystic /
- Cystic fibrosis
- Chronic anaemia (e.g. thalassemia major)

Mucopolysaccharidoses
- Hurler's Syndrome
- Morquio's Syndrome

Syndromes with Bone Dysplasia
- Achondroplasia
- Hypochondroplasia
- Spina Bifida
SHORT STATURE AND GROWTH HORMONE DEFICIENCY

It is essential to eliminate growth hormone deficiency (GHD) in any child with short stature, particularly those whose physical appearance is normal, as it is one of the relatively few instances in which short stature can be successfully overcome by therapeutic intervention. The administration of human growth hormone (HGH), which can be prepared by extraction from pituitaries removed at autopsy, increases the height velocity in most deficient children. The success of such treatment was first reported by Raben in 1958. Several comprehensive reviews have appeared recently covering many aspects of the current understanding of the role of growth hormone in health and disease (Tanner, 1972; Joss, 1975; Hunter, 1976).

Structure of Growth Hormone

HGH is a polypeptide (molecular weight 21,500) produced by the acidophil cells in the pituitary. Purified HGH was first prepared from human material by Li and Papkoff (1956) although bovine growth hormone had been isolated in a highly purified form a decade earlier (Li and Evans, 1944). Subsequent improvements in the techniques of isolation and purification were achieved by Raben (1959), Wilhelmi (1961) and Roos et al (1963). The molecular structure of HGH was first described by Li, Dixon and Liu (1969), but a modification of this was proposed by Niall (1971) in 1971 and is now generally accepted. Growth hormone is species specific (Knobil and Greep, 1959) and neither bovine nor porcine growth hormone are effective in man.
Measurement

Circulating levels of growth hormone are routinely measured by a radioimmunoassay first developed some fifteen years ago by Hunter and Greenwood (1962) and Glick et al (1963). Previously, rather unsatisfactory bio-assay methods had been used but none are still in common use (Hunter, 1976). The double antibody radioimmunoassay technique presently used has been described in detail by Hunter (1973, 1976).

Physiology

A better understanding of the role of HGH followed once it became possible to measure HGH levels in different physiological states. Hunter (1976) drew attention to the major problem that still exists when one tries to compare HGH levels reported in the literature because "a variety of standards have been in use and some authors have failed to identify the standards employed. Furthermore, laboratories using the same standards may not all obtain the same values because of differences in the specificity of antisera" (Hunter, 1976).

A large proportion of samples taken from adults in uncontrolled situations yield undetectable HGH levels (less than 1 µg/L) but a few have levels as high as 50 µg/L (Hunter, 1976). Roth et al (1963, 1964) reported that in normal adult subjects HGH secretion was stimulated by insulin induced hypoglycaemia, exercise, and although secretion was initially suppressed by oral glucose administration, a marked increase in plasma levels occurred during the early post absorptive phase. Section of the pituitary stalk abolished HGH secretion/
secretion and HGH response to insulin. Later Hunter and Rigal (1966) noted elevated HGH levels during sleep in adults, but first assumptions that these may have been simply the result of fasting were proved incorrect when it was found later that they coincided with deep sleep (stage III and IV) that occurs most frequently just after falling asleep (Takahashi, Kipnis and Daughaday, 1968). Normal children also show elevated sleep levels (Eastman and Lazarus, 1973). The HGH responses to fasting, exercise (Roth et al, 1963) and sleep (Quaabe and Helge, 1967) are blunted in obese subjects.

The ideal way of assessing HGH production is probably to measure it over a full 24 hour period (Joss, 1975). Measurements of growth hormone levels in serum samples collected over a full 24 hour period have shown that in normal subjects, individual bursts of secretion occur, causing transient elevations of HGH levels (Hunter, Rigal and Sukkar, 1968). These elevations have shown considerable individual variation in both frequency and magnitude, and the exact purpose or mechanism of them is not understood. Some have suggested that the stress of venepuncture is responsible (Hunter, 1976), and others that they are responses to an as yet unidentified feedback signal, possibly somatomedin (Tanner, 1972). Hunter (1976) postulated that the secretory burst may simply be the end product of an inherent neurogenic rhythmicity (Hunter, 1976).

There is however, considerable evidence that when energy is required HGH has a protein sparing effect by mobilising free fatty acids from adipose tissue. Persistently high levels which are not abolished by hyperglycaemia, have been noted in kwashiorkor (Pimstone et al/
et al., 1967) and in the former case they have only returned to normal after protein feeding. In normal subjects HGH levels rise following a protein meal - a rise which follows immediately upon the increased secretion of insulin provoked by the meal. Sukkar, Hunter and Passmore (1967, 1968) have postulated that the fat mobilising effect of HGH is a useful antagonist to some of the metabolic effects of insulin in this situation. If unopposed, insulin would cause a fall in free fatty acids, and, in the absence of endogenous carbohydrates, would also result in the utilisation of newly absorbed amino acids for fuel. Certainly, Fineberg, Horland and Merimee (1972) have found that the simultaneous administration of corn oil and heparin, which both raise free fatty acid levels, abolishes the HGH response to protein ingestion.

A marked rise in plasma HGH has also been noted to follow the administration of single amino acids. Merimee et al., (1965, 1967) noted that I.V. arginine (0.5 g/kg) administered over a 30 minute period produced a maximal HGH response in most subjects at about 60 minutes, and this was accompanied both by a rise in plasma insulin and a marked fall in free fatty acid levels. The rise in HGH is however not mediated by insulin provoked hypoglycaemia. Women usually responded better than men, although if given stilboestrol, men who had previously lacked a response now responded in a normal fashion (Merimee, Burgess and Rabinowitz, 1966). Similar responses have been observed to valine, phenylalanine, histidine, methionine and isoleucine (Hunter, 1976). It has been speculated that it is the amino acid content of "Bovril", a proprietary meat extract drink which/
which is responsible for HGH secretion which follows its administration, although Jackson, Grant and Clayton (1968) found no evidence of an accompanying rise in plasma insulin.

Other hormones have important effects on HGH secretion, and have accordingly been used in a number of the commonly employed diagnostic tests.

**Insulin**, when given intravenously in a dose of 0.1 unit - 0.2 unit/kg, causes hypoglycaemia, which in most normal fasting subjects is usually associated with marked elevation in HGH levels (Greenwood, Landon and Stamp, 1966), provided that at the time of the injection growth hormone levels are not already elevated. Under such circumstances, the stimulus provided by insulin induced hypoglycaemia may arrive immediately following the completion of a previous secretory episode, striking a refractory period in the system (Kaplan *et al.* 1963; Joss and Zuppinger, 1972; Hunter, 1976). Joss (1975) has recommended withdrawing two or more blood samples 15-30 minutes before insulin is administered to be sure of detecting such secretory bursts. It is also essential when this test is used to detect GHD, that the glucose level falls below 2.2 mmol/L or to less than 50% of the fasting value. Frantz and Rabkin (1964) have shown that therapeutically administered adrenal glucocorticoids blunt the HGH response to insulin. HGH secretion is also considerably depressed in idiopathic hypothyroidism (Iwatsubo *et al.*, 1967) and HGH response to insulin may be absent. Thyrotoxicosis also produces an impaired HGH response to insulin (Hunter, 1976). Hunter (1976) and others have emphasised the importance of a euthyroid state/
state before investigating HGH function. The enhanced GH response to arginine in women and men given oestrogens has already been mentioned. On the other hand, Simon et al (1967) have shown that large doses of medroxyprogesterone can suppress HGH response to insulin and possible arginine. In boys during early adolescence there is also evidence of diminished HGH responsiveness to both arginine and insulin (Martin, Clark and Connor, 1968) which returns to normal following the administration of testosterone or when they show evidence of rising endogenous androgen levels. In adults, following glucagon there is usually a well marked secondary rise in HGH with an average maximum at two hours (Hunter, 1976). Mitchell, Suvunrugsa and Sawin (1971) found that the simultaneous administration of propranolol augmented this response and produced a normal response in the small proportion of subjects who had failed to respond to glucagon alone. In children the response following glucagon is less clear. Weber, Helge and Ouabe (1970) have found elevated HGH levels 20 minutes following injection even in the presence of concurrent hyperglycaemia. Vasopressin has an inconsistent effect on HGH (Czarnye et al, 1968).

Somatomedin

It appears that many of the metabolic effects of HGH are mediated through somatomedin, a substance released from the liver and possibly the kidney (Tanner, 1972). Somatomedin was known originally as sulfation factor following the discovery by Salmon and Daughaday (1957) that it increased the uptake of radioactive sulphate by cartilage/
cartilage from immature hypophysectomised rats, even although HGH in vitro by itself had no such effect. Following the intravenous infusion of HGH in children with GH deficiency, Hall (1971) showed that somatomedin levels, normally low in such children, rose after about three hours and remained elevated for at least 24 hours. Hennemann (1971) demonstrated that the multiplication of cartilage cells, skeletal growth, and the synthesis of collagen, all actions of HGH were mediated by somatomedin. Rabinowitz, Klassen and Zierler (1965) has produced experimental evidence showing that HGH does nevertheless have some direct actions which are not mediated by somatomedin. They infused HGH directly into the brachial artery, and showed that the uptake of free fatty acids in the forearm muscle was enhanced. The method of the experiment excluded any possible intermediary effect of somatomedin produced by the liver or kidney.

Control of Growth Hormone Secretion

The secretion of other anterior pituitary hormones is known to be controlled by specific releasing hormones which are produced in the hypothalamus and travel to the anterior pituitary via the portal blood system.

At one point, Schally et al (1971) thought that they had identified a decapeptide with a specific action on HGH - a growth hormone releasing factor (GHRF), but in further tests they concluded (Schally, Arimura and Kastin, 1973) that their earlier findings were incorrect. At the moment there is no definite evidence of the existence of such a substance (Hunter, 1976).

The first evidence in support of a growth hormone release inhibiting/
inhibiting factor (GRIF) was produced by Krulich, Dhariwal and McCann (1968) and this tetradecapeptide was later isolated, synthesised and its activity confirmed (Burgus et al., 1973; Rivier et al., 1973). In humans it has been shown to inhibit the secretion of HGH following insulin (Copinschi et al., 1974) and sleep (Parker et al., 1974).

The normal stimuli for the release of GRIF and if it exists GRIF in man are unknown. 2-deoxy-D-glucose, which inhibits glucose utilisation, if injected directly into the lateral hypothalamic area near the ventro-medial nucleus in rhesus monkeys stimulates HGH secretion (Himsworth, Carmel and Frantz, 1972). Systemic administration of this substance in humans also has been found to stimulate HGH production (Wegienca and Copinschi, 1967).

It seems likely that a beta adrenergic pathway is involved in HGH release since infusion with propranolol (a beta blocker) augments HGH secretion in response to insulin (Imura et al., 1968). Oral administration of L-dopa, an agent used in the treatment of Parkinsonism, which crosses the blood-brain barrier and then converted to dopamine, has also been found to stimulate HGH release. This effect is not blocked by oral or intravenous glucose (Boyd, Lebovitz and Pfeiffer, 1970).

The Role of Growth Hormone in Growth Regulation

In spite of considerable understanding of the physiological actions of HGH, Hunter (1976) is still rather uncertain as to whether it has any physiological role in controlling normal growth, and if so, its mechanism of action. Nitrogen retention is known to occur during/
during therapeutic administration with HGH (Prader et al., 1964; Brown et al., 1967; Clayton, Tanner and Vince, 1971). It appears that as children with isolated growth hormone deficiency may be a normal size at birth (Trygstad, 1969), foetal growth is independent of the action of growth hormone. Joss (1975) has however reported two familial cases of GHD in which birth length was relatively low with respect to birth weight. Tanner (1972) believed earlier that the pubertal growth spurt was primarily a response to the influence of sex hormones, as it could occur in boys with isolated GHD (Merimee, 1974), but in more recent work Tanner et al. (1977) have suggested that the increased leg length and muscle bulk that occur during puberty are dependent to some extent upon growth hormone.

Hall and Olin (1972) showed that in children with growth hormone deficiency being treated with HGH, the initial velocity of "catch-up" growth was linearly related to the concentration of somatomedin. As the growth velocity fell in later years of treatment (see page 68) the level of somatomedin also fell even although the dose of administered HGH was unchanged. It thus seems possible that the GH - somatomedin mechanism may be involved in controlling the growth of normal children.

Tanner (1972) put forward the view that in general the normal long term stimulus to the secretion of growth hormone in children was a decrease of blood somatomedin, a theory which is supported by several experimental observations. Abrams, Grumbach and Kaplan (1971) showed that normal young men who had received six days of repeated HGH injections were unable to secrete growth hormone in response/
response to insulin hypoglycaemia for a period of about 12 hours after the last injection. Normal responses had returned by about 48 hours, and Tanner (1972) believes that these time relations would be consistent with a somatomedin-feedback situation. Similarly the children with Laron dwarfism (Laron, Fertzelan and Mannheimer, 1966; Laron, Fertzelan and Karp, 1968) who have an inherited inability to secrete somatomedin have high HGH levels. An alternative explanation is that the HGH itself has a direct inhibiting effect upon its own release by acting at the proposed hypothalmic GHRH centre (Sakuma and Knobil, 1970).

Growth Hormone Deficiency

"Pituitary dwarfism" as a cause of short stature has been recognised for many years but its exact relationship with growth hormone deficiency (GHD) was not elicited until accurate radioimmunoassay methods of measurement were developed. There is now indisputable evidence from many centres that children lacking measurable HGH usually respond significantly to treatment (e.g. Prader et al., 1964, 1967; Goodman, Grumbach and Kaplan, 1968; Trygstad, 1969; Tanner et al., 1971; Aceto et al., 1972; Joss, 1975).

GHD may be total, severe, or partial, the division between these categories being somewhat arbitrarily based upon HGH responses to provocative diagnostic tests, the most widely accepted of these being insulin hypoglycaemia. Auxological differences between severe and partial GHD are also described. Children with total GHD have undetectable HGH levels (less than 1 mU/L) and those with severe GHD/
GHD are generally recognised as having levels less than 7 mU/L (Tanner et al., 1971), although the Human Pituitary Advisory Committee of the Australian Government have placed the upper limit of severe GHD at 10 mU/L (Med. J. Aust., 1974). The upper limit of partial GHD has been set at 20 mU/L, although there are children who in a response to provocative tests have produced HGH levels higher than this and yet responded to therapeutically administered HGH (Tanner and Whitehouse, 1967; Eastman and Lazarus, 1973; Wise et al., 1975) whilst others with maximum levels less than 20 mU/L have clearly failed to respond to therapy. Those with total or severe GHD usually have a more severe degree of short stature and a lower height velocity than those with partial GHD. They also tend to be more obese, in terms of skinfold thickness measurements (Tanner et al., 1971). Some children whose short stature may have otherwise been accounted for by genetic factors or delayed skeletal retardation (i.e. "short/delay") may on provocative testing be found to have partial GHD (Tanner et al., 1971) raising the strong possibility that these categories merge together. Joss (1975) concluded that there is probably a continuous scale from total to different degrees of partial GHD.

Growth hormone deficiency may occur in an isolated form, or in association with other pituitary hormone deficiencies (e.g. TSH, ACTH, or gonadotrophins). At the moment the definition of isolated GHD includes cases who are subsequently shown to be gonadotrophin deficient also, as until puberty, or its failure to appear, it has not generally been possible to distinguish cases of isolated GHD from those with gonadotrophin deficiency. However, Hunter (1977) and others have/
have now developed an accurate assay technique for the measurement of gonadotrophins. About a third to a half of cases of "isolated" GHD are subsequently found to have multiple pituitary hormone deficiency (Tanner, 1972).

Panhypopituitarism may also be associated with other intracranial lesions, most frequently a craniopharyngioma, but also in association with septo optic-dysplasia (Harris and Haas, 1972). Multiple pituitary hormone deficiency may also follow cranial irradiation for cerebral tumours (Shalet et al., 1976) or leukaemia. In such cases, although provocative testing has demonstrated GHD, growth failure has not always been apparent (Finkelstein et al., 1972; Saenger et al., 1974; Shalet et al., 1976).

The exact aetiology of isolated GHD has until recently been uncertain. Tanner (1972) believed that "most cases are developmental in origin and probably represent lesions of the hypothalamus rather than the pituitary". In two series both of 35 patients reported by Tanner et al (1971) and Goodman, Grumbach and Kaplan (1968), pregnancy, birth and neonatal histories were reportedly normal, although in both series the proportion of breech deliveries was about 10%, which is somewhat higher than that usually found in the general population (Butler and Bonham, 1963). Joss (1975) reported abnormal birth histories in eight out of fifteen patients with idiopathic GHD, and of the six with multiple pituitary hormone deficiencies, five had been breech deliveries. In contrast the incidence of breech deliveries in children with constitutional short stature was normal.
In a very significant recent epidemiological study, Rona and Tanner (1977) have confirmed the previously reported association between idiopathic GHD and breech delivery, which they found had occurred in 13.7% of a total of 206 patients. They have also shown a higher incidence of early vaginal bleeding and forceps delivery, particularly in multipara. First born children were at a higher risk of developing GHD. They found that the frequency of either forceps or breech deliveries was 43% in those with multiple pituitary deficiencies and in isolated GHD it was 20%. This prompted them to make the suggestion that multiple pituitary deficiency was simply a more severe form of isolated GHD.

From extensive family studies they found that only 3% of sibships had more than one affected child, which is a much lower frequency than would be expected if an autosomal recessive pattern of inheritance was responsible. As only four fathers and perhaps three mothers had GHD, a dominant autosomal or sex linked recessive pattern of inheritance was also excluded. Individual family histories however, were consistent with various forms of single gene inheritance as reported previously by a number of authors. Rimoin, Merimee and McKusick (1966), and Seip, Van der Hagen and Trygstad (1968) have described families in which growth hormone deficiency appears to have been inherited as an autosomal recessive genetic defect. Sheikholisham and Stempfel (1972) and Poskitt and Rayner (1974) noted families with an apparently dominant pattern of inheritance. In view of these findings, Rona and Tanner (1977) have proposed that individual susceptibility to GHD is polygenically inherited/
inherited and this susceptibility is acted upon by 'exciting' factors such as birth trauma to produce the clinical disease. A similar model has been used by Carter (1976) to explain a number of other disorders and malformations such as pyloric stenosis, anencephaly and cleft lip and palate.

**Prevalence of GHD**

At the end of 1976, 435 children in Great Britain, or about one in 25,000 of the population aged under fifteen (OPCS, 1976) were being treated for growth hormone deficiency (MRC, 1977). Boys outnumbered girls by about 2.9 to one (Rona and Tanner, 1977) although in those with the less severe isolated GHD, up to 80% of those affected have been boys (Rona and Tanner, 1977; Tanner et al, 1971).

This prevalence rate agrees closely with the findings of a study in the Newcastle-upon-Tyne region (Parkin, 1974) which suggests an incidence of one in 30,000 births about half the cases being due to idiopathic deficiency and the remainder secondary to intracranial disease. Rona and Tanner (1977) have speculated that the incidence in males may be as high as one in 5,000.

The diagnosis of GHD in most cases has depended primarily upon parents and general practitioners initiating the referral of a child with short stature for diagnostic screening. On only one occasion, in the study of Lacey and Parkin (1974 a, b), have all short children within the population been screened for GHD. The total size of the population in which the short children had been identified was only 8,000. An accurate estimate of the prevalence of GHD has not therefore/
therefore been possible.

Tanner (1975) has drawn attention to the fact that at present many children with GHD remain undiagnosed for much longer than is necessary. The average age of children with idiopathic GHD at the time they are submitted to the MRC GH Working Party for consideration for treatment is 10.2 ± 1.1 years, and yet short stature is often obvious by two years. Merimee (1974) found that birth length ranged from 41-48 cms. in 35 deficient children and in nearly every instance growth failure was evident by six months of age.

Diagnosis

Although diagnosis of GHD depends primarily upon the demonstration of an inability to secrete normal amounts of HGH in response to a provocative test, many children with isolated GHD have common physical characteristics which help to distinguish them from those with short stature secondary to LBW, or constitutional short stature. These have been the subject of detailed reviews by Tanner et al (1971) and Joss (1975). The mean height SDS for chronological age in Tanner's series ranged from -2.6 to -7.3 with a mean of -4.7. The short stature tended therefore to be more extreme than in most children with a diagnosis of "short-delay". Joss (1975) stated that with increasing age the overlap of height SDS's between those with GHD and constitutional short stature diminished, and although he found no overlapping between the two groups after the age of twelve years, this is of limited practical use as in most children with short stature one would be seeking to make the diagnosis at a much younger age. Pretreatment height velocity was also low and SDS scores/
scores for chronological age range from -0.9 to -4.5, with a mean of
-2.8 ± 0.2 in Tanner's series of 20 patients. In a series of 67
patients (26 with severe GHD, 6 with partial GHD, 28 with constitu-
tional short stature and 7 with LBW short stature), Joss (1975)
stated that height velocity calculated in relation to bone age
rather than chronological age, differentiated between the groups
with severe GHD and constitutional or LBW short stature at all ages.
Children with GHD have usually been of normal birth weight (mean
birth weight + 0.2 SD ± 0.2) (Tanner et al, 1971) unlike some
"short normal" children. The height of the parents of children
with GHD was usually within normal limits, in contrast to many
parents of children with constitutional short stature. Body propor-
tions have been normal, but a tendency towards obesity has been
apparent, with an increased deposition of fat in the pectoral region,
the hips and the abdomen, giving a pudgy appearance (Goodman,
Grumbach and Kaplan, 1963). The apparent obesity has been confirmed
by finding increased triceps and subscapular skinfold thickness
measurements which range from an SDS score of -1 + 2.5 (Tanner et al,
1971). This finding is probably not surprising in view of the
known physiological actions of HGH in mobilising fat. Up to half
the boys (Tanner et al, 1971) have had an underdeveloped penis and
scrotum, and some have had unilaterally or bilaterally undescended
testes. Muscle bulk has also been reduced. Bone age has generally
been retarded and in Tanner's series varied from -0.8 to -5.7 SDS
below the mean, although children with apparent GHD following
cerebral irradiation may have a normal bone age (Schiliro, 1976;
Shalet et al, 1976). Joss (1975) reported that the bone age was
more/
more retarded in older children with severe GHD than in "short-normal" children. Although the differences between the groups were significant, he found a large degree of overlap. The mean bone age SDS of the patients with partial GHD was not significantly different from those with constitutional short stature.

Diagnostic Tests

These were extensively reviewed recently by Frasier (1974). Because HGH is only secreted intermittently, provocative testing is always necessary to establish the diagnosis of GHD. Most provocative tests involve multiple blood sampling (e.g. insulin hypoglycaemia (Frasier, 1967), arginine infusion (Raiti, Davis and Blizzard, 1967), extended glucose tolerance test (Hunter et al, 1967), Bovril (Jackson, Grant and Clayton, 1968)). L-dopa (Root and Russ, 1972; Weldon et al, 1973) has been generally discarded as it may be physically unpleasant and occasionally dangerous. Convulsions may occur during insulin hypoglycaemia particularly in children with panhypopituitarism, and for this reason the ability to produce normal amounts of other pituitary hormones should, in ideal circumstances have first been ascertained by less dangerous tests (Cameron, 1977) e.g. by carrying out a TRH test to demonstrate the ability or otherwise to produce normal amounts of TSH. One death has been recently reported following insulin hypoglycaemia (Hull, 1976). The cause was unclear and may have been the result of extreme hyperglycaemia.

Because of the difficulties of provocative testing, initial screening with a less unpleasant test has usually been recommended (Hunter/
Hunter, 1976). Buckler (1973) and Lacey, Hewison and Parkin (1973) have all found that in a single blood sample taken 25-30 minutes after the start of a ten minute period of intensive exercise, over 90% of normal children produce HGH levels in excess of 10 mU/L. Underwood et al. (1971) found that 72% of normal children produce HGH values of 10 mU/L or more in a single blood sample taken one hour after the onset of sleep, but this test is hardly useful on an outpatient basis. The extended oral glucose tolerance test (Hunter et al., 1967) is less satisfactory, as Stimmler et al. (1967) found that only 71% of children produced levels above 7 mU/L at three hours and moreover, because the timing of the peak is less certain, multiple samples are necessary from 3-5 hours after the ingestion of a dose of 1.4 g/kg of glucose.

None of the widely accepted definitive diagnostic tests are completely satisfactory as a number of normal children, or those with constitutional short stature, have failed on at least one occasion to produce acceptable growth hormone levels. Possible reasons for this have already been outlined. Raiti, Davis and Blizzard (1967) performed paired insulin sensitivity and arginine tests on 31 non GHD patients with short stature and found satisfactory responses in both tests in only 22 cases. Five patients responded to insulin but not to arginine, and four to arginine but not to insulin. Joss (1975) mentions eight children who in an initial ITT had HGH levels consistent with partial GHD, three of whom produced a normal response when the test was repeated and were accordingly regarded as examples of constitutional short stature.
Because of the difficulty in distinguishing between some children with constitutional short stature and partial GH deficiency on the basis of equivocal diagnostic tests, it has been suggested (Joss, 1975; Tanner and Preece, 1976) that where auxological findings are consistent with the latter diagnosis, a therapeutic trial may be undertaken in which the height velocity response to administered HGH is observed. The main danger of this is the risk of producing anti-HGH antibodies (see page 70) in children with constitutional short stature.

Treatment

No review of GHD would be complete without a brief mention of the effects of treatment. (Indeed some parents only agreed to co-operate in the present study when it was pointed out to them that if the diagnosis of GHD was confirmed in their child, effective treatment would be available.)

Raben (1958) was the first to demonstrate that purified HGH increased the growth velocity of a pituitary dwarf, and since then large numbers of patients have been treated. Because of the high cost and difficulty of extraction of HGH, its availability has been limited, and consequently in most countries, multicentre treatment has been co-ordinated on a national basis (Tanner et al., 1971; MJA, 1972; Aceto et al., 1972; Guyda et al., 1975; Preece et al., 1976). This has also enabled the comparative effectiveness of different dosage schedules to be studied (Preece et al., 1976) and the early detection of any significant complications, such as the formation of HGH antibodies.
The most obvious effect of repeated injections of HGH in children with proven deficiency has been increased height velocity. Initial acceleration in growth has been quite marked (Tanner et al., 1971) and similar to other examples of "catch up" growth which occurs, for example, following the treatment of severe malnutrition. Later, the rate of growth slows somewhat - a phenomenon termed regulatory deceleration by Tanner et al. (1971), but it usually remains in excess of pretreatment height velocity provided high affinity HGH antibodies have not appeared. Effective treatment is only possible if epiphyseal fusion has not occurred (Tanner, 1972). The response in cases of partial GHD is usually less than in severe GHD (Tanner et al., 1971) although Joss (1975) has reported three patients with what he calls partial GHD whose treatment height velocities were in the same range as those with severe GHD. As Joss sets the upper limit of severe deficiency at only 2 ng/ml, others would regard these children as examples of severe deficiency.

Other effects of treatment include an increase in bone age, (Tanner et al., 1971) although this is not accelerated to the same extent as longitudinal growth, an increase in the cortical width of the metacarpals (Joss, 1975), decreased skinfold measurements, and increased muscle width measurements (Tanner et al., 1971). The value of early diagnosis and treatment has been stressed by a number of authors, because it is clear that the earlier before puberty treatment is started, the greater the likelihood of attaining a normal adult height (Tanner, 1975). It has been thought advisable to continue treatment through puberty until growth has ceased, as recent work/
work (Tanner et al., 1977) has clearly demonstrated that HGH is responsible for about a half of the pubertal growth spurt.

The main complications of treatment have been the development of specific HGH antibodies. Different centres (Frader et al., 1967; Frasier et al., 1974; Chalkley and Tanner, 1971) have reported their appearance in a number of patients. For instance Frader et al. (1967) found that antibodies developed in eight of eighteen patients on treatment with the Raben HGH preparation. Chalkley and Tanner (1971) on the other hand, found only four of 42 children with isolated GHD had developed permanent growth retarding antibodies. Later experience in this country was even more satisfactory and Tanner was able to report in 1974 (Maclaren, Cornblath and Raiti, 1974) that none of the last 200 patients treated in the MRC (UK) Trial had developed growth inhibiting antibodies. More recent work suggests that the situation in Britain is less satisfactory as Preece (MRC, 1977) has recently indicated that some patients in the MRC (UK) Trial who have developed high affinity antibodies, have ceased growing in spite of continued HGH replacement therapy. Frasier et al. (1974) reported that changing the preparation of HGH used was often followed by a renewed growth response. Several authors (Illig, 1970; Underwood, Voina and Van Wyk, 1974) have suggested that the Roos preparation is the least antigenic of the commonly used preparations.

Most countries administer HGH on a two or three times a week injection schedule. Preece et al. (1976) have recently reported that a dose of 20 IU HGH per week is more effective than 10 IU and concluded/
concluded that children receiving the larger dose would be
approximately 10 cms. taller as adults than those on the smaller
dosage.

Other conditions associated with apparent growth hormone deficiency
Kaplan et al (1968), Day, Evans and Wharton (1973), and
Vanderschueren-Lodeweyckx et al (1973) have reported abnormal growth
hormone responses to insulin and Bovril in some children with
coeliac disease maintained on a gluten free diet. The mechanism has
not been clear. In neither of the latter two series were patients
treated with HGH and accordingly it is impossible to exclude GHD
with certainty.

Previous reports have also suggested that transient GHD may
exist. Moshang et al (1974) reported the case of a boy with
isolated GHD which appeared to develop following an acute pneumo-
nitic illness at the age of seven. Initially at the 75th centile
for height, progressive growth failure occurred so that by the age
of 11.2 years his height was at the third centile. He was treated
with HGH and androgens for several years with a successful outcome.
Subsequent provocative tests in puberty demonstrated normal HGH
secretion.

Psychosocial Short Stature
Transient GHD has also been reported in short children in whom
the growth failure has been attributed to emotional deprivation.
Reference has already been made to reports in the literature
describing/
describing the association between short stature and various sorts of deprivation (see page 11). Talbot et al (1947) was amongst the first to suggest that functional pituitary deficiency may have been the cause of short stature in a group of 51 very short children aged between two and fifteen years. Genetic reasons were excluded in all but a few children. All had been difficult feeders from an early age and 30% of the children were underweight which may have contributed to their short stature. Only one of seventeen children studied in depth had a normal psychosocial background. No studies of HGH secretion were possible at that time.

Patton and Gardner (1962) described a further six emotionally deprived children aged 13 months to 6½ years with short stature. Many of the older children were reported by their parents to have ravenous appetites. Silver and Finkelstein (1967) later elaborated the bizarre dietary habits which included food stealing and eating of garbage that were alleged to be present in many of the older children. Whitten, Pettit and Fischhoff (1969) later suggested that such behaviour may have been the result of underfeeding by the parents.

Powell, Brasel and Blizzard (1967) were the first to report biochemical evidence of HGH and ACTH deficiency in this condition, evidence it was thought of functional hypopituitarism. They described 13 children with clinical features of the syndrome. There were two sibling pairs. Marital disharmony and breakdown had occurred in most families, and the parents had all done poorly at school. In two instances the siblings of the index cases had been maltreated. Characteristic/
Characteristic of the syndrome were the rapid gains in height and weight and a dramatic improvement in behaviour which followed admission to hospital. Growth hormone levels were measured shortly after admission to hospital in eight of the thirteen children during insulin induced hypoglycaemia. Six had a value less than 5 mUg/ml, but in two the level was above 16mUg/ml. Another child was first tested after growth had improved and had a normal HGH response on two occasions. The child stopped growing after leaving hospital and when investigated at this stage, failed to secrete HGH. All children investigated had adequate GH responses when growing. The authors concluded that since two patients with the syndrome had normal HGH responses when first seen, evidence of GHD was not necessary for the diagnosis of psychosocial short stature.

Whitten, Pettit and Fischhoff (1969) later introduced new evidence suggesting that psychosocial short stature was primarily the result of underfeeding and/or undereating, and not because of a "psychologically induced defect in absorption or metabolism". Regrettably, none of the sixteen children studied had any endocrinological investigations, but as already indicated, abnormalities of HGH secretion had not been found universally in earlier cases. Eleven of thirteen deprived infants aged three months to two years gained weight when fed adequately in hospital, even although the windowless room in which they were confined for two weeks and the minimal amount of handling and stimulation they received was designed to simulate the home environment. After an initial control period half the group received "improved mothering" but this was not shown/
shown to increase the rate of weight gain. The two children who failed to gain weight had poor appetites and a retrospective history of forced feeding was obtained from the parents. After discharge home, only four of the ten infants continued to gain weight satisfactorily, although all were stated to have an adequate intake. A measured diet was then taken to the homes of four children by a nurse and given to the children in her presence, but no other advice or instructions were offered. All gained weight at a rate comparable to that previously noted in hospital. Three further infants in whom the condition was newly diagnosed were given a measured diet at home before the parents were informed of the diagnosis, and all grew satisfactorily. In none did the authors believe that the emotional climate within the home had been significantly altered although considering the help and social support they received, this conclusion seems unwarranted. This was an important study in many ways as it demonstrated that the reports of excessive food intake given by the parents could not be substantiated. The authors concluded that such claims by the parents were not deliberate attempts at deception, but rather reflected the fact that they themselves were so consumed by their own psychosocial problems that they tended to remember only the large occasional meal eaten by their children rather than the usual twenty-four hour intakes. They concluded that permanent stunting was likely in many of these children because of the timing and duration of the nutritional insult and also because many of the children had been of low birth weight.

Frasier and Rallison (1972) were the first to report the effect of/
of administering HGH to a 5½ year old girl with psychosocial short stature and apparent GHD. In the seventeen months before treatment her height velocity was only 1.8 cms. per year. When treated with a dosage of 30 units HGH per week for eighteen months her height velocity increased to 6.9 cms. per year, which was well below the average increase in height velocity of nine other GHD patients receiving therapy in the same clinic. At this stage emotional deprivation was first suspected. Treatment was ceased and her height velocity over the next eighteen months was only 0.4 cms. per year. She was then sent to live with her aunt, and although receiving no HGH she grew at 16.1 cms. per year over the next nine months. There are certain criticisms which can be levelled at the diagnostic work-up in this case which limit the conclusions which may be drawn from it. The initial diagnosis of GHD was based upon an insulin hypoglycaemia test in which adequate hypoglycaemia had not been achieved, and during the second pretreatment insulin hypoglycaemia test a high fasting GH level of 6 ng/ml had been present which possibly may have inhibited her response to hypoglycaemia. Also both HGH assays were done in different laboratories using different methods.

Tanner et al (1971) reported three well nourished patients with psychosocial short stature, and failed to observe any growth acceleration following treatment with HGH. However, all had normal HGH levels during an insulin hypoglycaemia test prior to growth acceleration. Apley (1973) has also reported children with clear evidence of psychosocial short stature, but normal GH levels. Tanner (1973) postulated that high cortisols found in some patients with/
with psychosocial short stature may inhibit the response of somatomedin to HGH.

Castells et al (1975) has recently described a very interesting fifteen year old boy with a history of maternal deprivation since the age of two years, who had severe growth retardation and panhypopituitarism. GHD was demonstrated by consistently abnormal HGH responses to insulin, arginine, and sleep. He was also noted to have a poor ACTH response to metapyrone and prepubertal concentrations of FSH. When he was reinvestigated a year later, having stayed in the meantime with his grandmother, these abnormalities were still present. Moreover he had not grown. This is the only case of psychosocial short stature in which a permanent impairment of pituitary function has been demonstrated. The authors propose that maternal deprivation was the cause of his panhypopituitarism, as growth failure had not been noted before the allegedly sudden onset of severe and prolonged maternal deprivation from the age of two years. It is nevertheless, possible that the association is fortuitous.

As already mentioned, some of the reports of GHD in psychosocial short stature have been based upon inadequate laboratory evidence. Sometimes only one test of growth hormone function has been carried out and in some of the insulin hypoglycaemia tests not only have high fasting HGH levels been present but inadequate hypoglycaemia has been achieved (Krieger and Mellinger, 1971; Frasier and Rallison, 1972). As already suggested (page 67), testing has clearly demonstrated that inconsistent results may be obtained in children with constitutional short stature (Joss, 1975) and/
and it seems possible that had more tests been repeated in the initial diagnostic work up of children with psychosocial short stature, growth hormone deficiency would have been eliminated in many if not all.
CHAPTER II

MATERIALS AND METHODS

The primary objective of this study has been to determine the prevalence of growth hormone deficiency (GHD). As GH is only of therapeutic benefit to children with GHD before the completion of epiphyseal fusion, early diagnosis is a distinct advantage as it prolongs the time available for replacement therapy. Although it is generally agreed that clinical evidence of GHD is present in many affected children during the first year of life (Goodman, Grumbach and Kaplan, 1968; Tanner et al, 1971), present evidence (MRC, 1977) suggests that diagnosis at this age is uncommon. Although 25% of children with idiopathic GHD for whom applications for treatment were made to the HGH Working Party of the Medical Research Council in 1977 were aged under five years, the average of these children was 10.1 ± 1.1 years.

Richards (1971) estimated that only 63% of Scottish children were ever taken to child health clinics during the first five years of life, and thus the earliest age at which the entire population can be effectively screened for GHD, is immediately following school entry between 4½ and 5½ years of age. Even if total population screening was feasible earlier, it is doubtful whether the presently available diagnostic tests for GHD would make it a practical proposition.

Although many have suggested that all children less than the third/
third centile in height are in need of further investigation, the
previous study in Newcastle-upon-Tyne (Lacey and Parkin, 1974a, b)
has suggested that only a minority of these children have an organic
basis for their short stature, and organic causes do not predominate
until children are -3 SD or more below the mean (Tanner, Whitehouse
and Takaishi, 1966). Accordingly, in this survey, it was arbitrarily
decided to restrict the screening for GHD to the smallest 1% of the
population.

INITIAL ATTEMPTS TO LOCATE CHILDREN WITH SHORT STATURE

The method originally proposed for identifying the cohort of
children with short stature to be included in the study was to have
been based upon school health records. All entrants to Education
Authority primary schools in Scotland, and many of those beginning
school at independent and grant-aided schools are medically inspected
in their first year at school when they are aged between 4½ and 6½
years. This examination is supposed to include measurement of the
child's stature with shoes removed. The data thus obtained is
coded and subsequently stored on a computer file in Edinburgh,
maintained by the Common Services Agency of the Scottish Home and
Health Department (SHHD, 1972; Heasman and Mitchell, 1974). This
scheme, unique to Scotland in the UK, made a national study of short
stature theoretically feasible and indeed this was originally
proposed.

The data usually takes several years to compile, and it is,
in practice, not available until children are well into their second
year/
year of school. At the end of 1974, data relating to 1972-3 school
entrants was available, and a printout of the numbers of children
with heights above and below 109 cms. for each month of age from
50-76 months at the time of measurement, was obtained separately for
each sex. The group below 109 cms. was further subdivided into
individual centimetre groupings. At each month of age a height was
selected for each sex, which was nearest to that, at or below which,
4% of the population were found. If the closest value to 4%
included less than 3% of the population, a height 1 cm. above this
was chosen even although this may have meant including 5% or more of
the population.

A further printout was then obtained listing in alphabetical
order, the surnames, initials, sex, dates of birth and medical
inspection of the 3,301 children in every education authority area,
whose height at school entrance fell into this category. It was
hoped that by including those comprising the smallest 4% at school
entrance it would be possible, by subsequently remeasuring them at
school with portable measuring equipment contained in a specially
constructed mobile clinic, to identify the smallest 1% of children
at the time of the survey.

A number of problems with the data soon emerged. Firstly, in
order to ensure an adequate sample size from which an accurate
estimate of the prevalence of GHD could be made, it was thought
desirable to screen two successive cohorts of school entrants. By
the time one was ready to commence field work, only the data
relating/
relating to 1972/3 entrants was available and that for 1973/4 would not, it was thought, have been available for another three to six months. Awaiting the delivery of this data would have caused an intolerable delay.

Secondly, details on each child were too imprecise to enable the present whereabouts of the child to be discovered. The only geographical information known for each child was the Education Authority area. Neither the child’s school nor home address were known. Both of the largest Education Authority areas in terms of population, Glasgow and Edinburgh, believed nevertheless that given the information available for each child, they would have been able to identify the child’s school at the time of medical inspection two or more years previously, from records maintained centrally in their offices. In Edinburgh, it was found that this information could be updated by the school attendance officers to list the child’s present school and home address (Priestley, 1974). In Glasgow (Sloan, 1974) no such updating was possible; the only way of finding the child’s present school and home address was by contacting the school attended at the time of medical inspection and tracing the movements of the child from that time. From 1966 and 1971 census data (Levine, 1975), and previous survey experience in Glasgow of others (Barclay, 1974), it was known that in some districts up to 20% of the population move within the local authority area each year, which would have made precise localisation extremely time consuming, if not impossible.

Personal investigation of the situation in most other Education Authority areas at the end of 1974, suggested that similar, if not greater/
greater difficulties were likely to occur, particularly as in some areas no central records were held, and the information required was only available in the schools.

Thirdly, independent research undertaken by Barclay (1974) suggested the data base probably contained significant errors. Barclay had used copies of the original 1972-3 school entrant's medical inspection forms in Glasgow, and painstakingly identified all Glasgow children with heights less than the third centile (Tanner, Whitehouse and Takaishi, 1966). One would have expected that the names of all these children would have been included amongst the 825 Glasgow children listed on the computer printout of the smallest 4% of 1972-3 entrants. However, he identified a further 54 children who fulfilled the criteria for inclusion, but whose names did not appear on the printout. A search of the computer file revealed that no data base existed for 52 of these children (Mitchell 1975). (Four of these children were eventually included in the final study.)

A search of the medical inspection forms of children rejected by Barclay because their heights were in excess of the third centile, identified a further 21 children whose names should have appeared in the printout, five of whom were included in the final study. These preliminary investigations suggested an omission rate in Glasgow of between five and ten per cent and subsequent checks by Mitchell (1975) have indeed confirmed that data is probably processed for only 90-95% of school entrants. The remaining children have presumably never had a medical inspection or their forms have not been forwarded/
forwarded for processing. The latter applies particularly to physically and mentally handicapped pupils enrolled at special schools and children who belong to highly mobile families or are frequently absent from school. Indeed a later check of 93 medical cards at one school in one of the deprived districts in Glasgow found that height had not been recorded in 11.8% of entrants. The data from some forms would also have been rejected during computer checks because of inaccuracies. This was a particular problem with the 1972-3 entrants' inspection which followed immediately after metricalation in the Glasgow School Health Service.

It was clearly impossible to ascertain whether the rest of the children in the population with a normal height had an equal chance of being omitted which would have made it impossible to accurately calculate either the prevalence of short stature or of GHD.

For these reasons it was decided to abandon the use of the central computer file as a means of identifying children with short stature, although it was used later to estimate the upper limit of height of the smallest 1% (see page 85).

Retrospective analysis of the final survey population has confirmed the wisdom of this decision. The computer lists of the smallest 4% of entrants in 1972-3 and 1973-4 contained the names of only 64.4% of the 449 children in the study. Whilst some of those omitted may have been recent immigrants (0.7%), or entered school in 1971-2 (7.4%) or have been enrolled at a special school (9.1%), no satisfactory explanation existed for the omission of 18.4% of the children studied. Presumably these children had been measured inaccurately/
inaccurately, never been measured, or were too large for inclusion within the smallest 4% at the time of medical inspection.

Subsequent observations of the measuring apparatus used by the schools has also revealed an unacceptable degree of inaccuracy. Occasionally, measuring equipment was unusable, and in other cases the height indicated was up to 5 cms. from the true value. Although it cannot be certain from this study, these errors may have been random. Had this been the case, they would have tended to cancel each other out, and thus had had little effect on any subsequent calculation on the mean height of school entrants in any Education Authority area. However, individual children whose true height placed them in the smallest 4% of entrants may have been excluded.

SURVEY METHOD

Following the decision not to use the computer based child health records it was evident that the only accurate way in which a cohort of short children could be found, was by personally screening the heights of all children in a defined population and selecting those comprising the smallest 1%.

It was decided to continue with the original proposal to investigate children in their second or third year of school, although it would have been possible, using the revised method, to study children in their first year. To have included these children would however have posed practical problems which would have considerably delayed the progress of the study. They have limited school hours, and because of age are less able to co-operate satisfactorily in the exercise/
exercise screening test that was used to exclude GHD. The revised method was more time consuming than that originally proposed, and the survey was therefore restricted to the cities of Edinburgh, Glasgow and Aberdeen. In Aberdeen, where height screening took place a year after the other two cities, children in the fourth year of school were also studied. Lack of time prevented the extension of the study as had originally been planned, to more sparsely populated rural areas.

IDENTIFICATION OF THE SMALLEST 1%

The next task was deciding upon the method to be used to select those comprising the smallest 1% of the population. As mentioned in the review of the literature, numerous studies have found that Scottish children are several centimetres shorter than those of the same age in England, and had one used cut-off heights derived from Tanner, Whitehouse and Takaishi's (1966) English data, which corresponded to the smallest 1% (i.e. -2.32 SD), considerably more than 1% of the Scottish population would have been included.

From the computerised data for 1972-3 school entrants which has already been described, the height corresponding to the first centile at age 5.5 years was calculated. The sample size was boosted by including all children measured within ± two months of 66 months. For the 18,122 boys, the first centile was 99 cms, and for the 17,152 girls it was 98 cms. This corresponded to a standard deviation score (SDS) of -2.53 for boys and -2.49 for girls in the data of Tanner, Whitehouse and Takaishi (1966). If one then made the/
the assumption that height velocity was the same in both Scottish and English children, the smallest 1% at any age between six and ten years would therefore comprise children at or below -2.5 SDS.

HEIGHT SCREENING

The survey was financially supported by the Medical Research Council and backed by the Scottish Home and Health Department. Permission was sought and obtained from Chief Area Medical Officers throughout Scotland for the survey to proceed within their jurisdiction (Appendix 1). The Scottish Home and Health Department also approached the Scottish Education Office, who in turn notified Directors of Education throughout Scotland, seeking their individual co-operation (Appendix 2). Agreement in principle was unanimously obtained. Contact was also made with the governing bodies of each of the independent and grant aided schools in Scotland (Appendix 3) and many responded favourably. The permission of parents for height screening was not thought necessary by either Health or Education Authorities as only removal of shoes and socks was required. At independent schools, because of the smaller numbers involved, parental consent was however first sought (Appendix 4). A mobile clinic was designed and constructed for the survey in which children could be measured and investigated (Figure 1). This contained a Harpenden wall-mounted stadiometer, a Watson MX 2 portable X-ray unit, chairs, an examination couch, storage space for notes and other equipment and washing facilities. If adequate space was not available in the school, parents could, if necessary, also be interviewed.
Figure 1.

The Mobile Clinic
interviewed in the clinic.

Education Authority schools were then visited by prior arrangement (Appendix 5) and children, having removed their shoes, had their height screened in their classrooms using a Harpenden portable anthropometer (Figure ii). The exception to this was in a few schools for the severely mentally or physically handicapped, where supine length was measured.

Initially, the age of/oldest child in each classroom was ascertained and any child whose height was less than that corresponding to a height just greater than \(-2.5\) SDS for boys at that age (derived by reference to the table shown in Appendix 6) was selected for more precise measurement in the mobile clinic. With further experience, the method was modified and teachers were asked to ensure beforehand that children knew their age in years, and at the time of screening, the children were divided into their appropriate age groupings, and any whose height was less than that corresponding to height just greater than \(-2.5\) SDS for boys at the beginning of the next year of age were selected for further measurement. An example will make this clear. The \(-2.5\) SDS for boys aged 8.0 years is 111.9 cms., and accordingly any child aged seven but not yet eight years, whose height was less than 113 cms. was selected for further measurement. The cut off heights used for six, seven, eight, and nine year old children were, respectively, 108 cms., 113 cms., and 123 cms. At the time of the school visit, personal details (birth date, home address, and where possible the name of the child's general practitioner) were obtained from the class registers for all children/
Figure 11

Harpenden Portable Anthropometer
children selected for further measurement, as well as the total number of boys and girls enrolled. Numbers of absentees were also recorded and the school was visited again to measure any absent children thought by their teachers to be either the smallest in the class, or as small as any of the children selected for further measurement.

Children selected for further measurement with the stadiometer in the mobile clinic, were measured using the technique previously described by Tanner et al. (1971). Slight upward pressure was applied to the angle of the jaw whilst ensuring that the head was kept in the Frankfurt plane by making sure that the lower border of the orbit, and the external auditory meatus were in the same horizontal plane. Simultaneously, children were encouraged to stretch upwards whilst another observer ensured that the feet were perfectly flat on the floor. Relaxation of the shoulders was achieved by asking the child to breathe in as deeply as possible and then letting their breath out. Using this technique, Tanner et al. (1971) has succeeded in getting 95% of repeat readings within 3 mm. The accuracy of the stadiometer was checked at each school, and the reliability of the measurements were checked on one occasion by measuring 28 children from one school on successive days, when 95% of repeat heights were within 4.5 mm. (Figure iii).

A standard deviation score (SDS) was calculated for each child according to the method described by Tanner et al. (1971)

\[ SDS = \frac{x - \bar{x}}{\sigma} \]

where \( x \) = actual height in centimetres
\( \bar{x} \) = mean height for that age and sex (cms.)
\( \sigma \) = SD corresponding to that age and sex.
Figure iii

Harpenden Stadiometer and Measuring Technique
with an SDS of -2.5 SD or less were included in the definitive study group. This group was only a relatively small proportion of all the children accurately measured in the clinic.

Children attending most independent schools in the sample were screened in the same way. In several schools, pupils' heights had been measured since beginning school, and any children below the fourth centile (Appendix 7) were remeasured after obtaining parental permission. The numbers currently enrolled at each school were again obtained from school registers.

THE DEFINITIVE STUDY OF THE SMALLEST 1%

With only a few exceptions, the parents of children with a height of -2.5 SDS or less were contacted by letter (Appendix 8). The exceptions were children in Aberdeen who were known to have a clear organic cause for their short stature. In the event of non-response, health visitors or school nurses, who had been informed of the reasons for the study, both by personal explanation and in writing (Appendix 9), tried to contact the parents. The purpose of this was to briefly explain the reasons for the study to parents and seek their co-operation. A further letter (Appendix 10) was written to those parents who failed to respond to either approach or who refused to co-operate, in which permission was sought to remeasure their child as close as possible to twelve months after the initial height screening, to enable the child's height velocity to be calculated (Tanner, Whitehouse and Takaishi, 1966). The parents of any child found at this point to have a height velocity less than the 25th centile for chronological age, were personally approached in an attempt/

1 Approval was sought and given from Area Ethical Committees.
attempt to encourage them to participate in the study or, failing this, to obtain where possible some information about the child's birth weight and the height of other members of the family. At the same time as the initial contact with parents, the child's general practitioner (GP) was contacted (Appendix 11) asking for his or her co-operation. In this letter, GPs were requested to supply details of any past major illnesses or relevant investigations, as well as any pertinent information about the social background of the family. Consultant paediatricians, who had previously been informed of the study (Appendix 12) were also contacted where it was known that children had previously been referred to them.

Subsequently, an appointment was made to meet the study children and parents who had agreed to co-operate. This was usually arranged at the child's school, but at the request of a few parents, it took place at home. In the former case the appointment was made at a time when it was known from head teachers that school medical rooms would be available. At this visit, the purpose of the study was again explained to the parents, and details of any previous major illnesses or investigations obtained by means of an interview schedule (see page 104). A physical and auxological examination was carried out on each study child and any abnormalities other than short stature were carefully noted. In the absence of previous investigations, or any evident organic basis for short stature, all children had a wrist X-ray and screening test for GHD (see page 95). The stature of one, and where possible both parents was also measured to the nearest centimetre using the Harpenden portable anthropometer.
anthropometer.

The following anthropometric measurements (to the nearest millimetre) were done on all study children investigated for GHD either during or prior to the study as well as some of those with other organic causes of short stature:— standing height, sitting height, left upper arm circumference, left triceps skinfold thickness, left subscapular skinfold thickness, head circumference. The recommended methods for performing these measurements had been carefully observed during several previous visits to the Department of Growth and Development at the Institute of Child Health, London.

Sitting height was measured, using the wall-mounted stadiometer to measure the child's height, whilst seated on a stool with the thighs supported, and the legs, bent at the knees, hanging unsupported over the edge, with the backs of the knees nearly touching the edge of the stool. The child's back was stretched up straight, and his head was kept in the Frankfurt plane.

Upper arm circumference was measured with a steel tape measure at a point midway between the tip of the acromion and the posterior border of the olecranon process, ensuring that the skin was not compressed.

Triceps skinfolds were measured with a Harpenden skinfold caliper according to the technique described by Tanner and Whitehouse (1975). This measurement of a double fold of skin and subcutaneous tissue picked up between thumb and forefinger and pulled away from the underlying muscle, was taken halfway between the tip of the acromion and the posterior border of the olecranon process in a line passing directly up the centre of the arm from the olecranon. Sub-

subscapular skinfolds/
skinfolds were measured using the same technique. The measurement was taken below the angle of the scapula, with the fold vertical, or slanting slightly downwards and outwards.

Head circumference was measured in the occipito-frontal diameter.

Weight was recorded in indoor clothes with shoes removed on school weighing machines, which were all of the lever balance type. Their accuracy was not checked, as for the purpose of this study, weight was not a particularly critical measurement.

In addition, the upper arm muscle circumference (UAMC) was calculated according to the method of Jelliffe (1966)^2.

An X-ray of the left wrist was taken using Kodirex autoprocess film which was later processed in Edinburgh. The hand was positioned according to the instructions of Tanner (1962) and his directions also followed for the distance between the X-ray tube and the film. Children were protected during this procedure by wearing a lead apron. The bone age was later calculated by the TW II method (Tanner, Whitehouse and Healey, 1961) by my wife and colleague, Dr. Anne Vimpani, who had satisfactorily completed a two week course of instruction in its use at the Institute of Child Health, London.

\[ UAMC = UAC - TII (TSF) \]

\[ UAC = \text{upper arm circumference (mm)} \]

\[ TSF = \text{triceps skinfold thickness (mm)} \]
Screening Test for GHD

As discussed earlier, exercise appears to be the most satisfactory method of screening for GHD in ambulatory subjects (page 67). An exercise bicycle (figure iv), fitted with a speedometer in which variable resistance could be applied to the wheel was used in all except several of the participants in the study who were exercised by being persuaded to run up and down stairs for fifteen minutes.

As GH levels are usually depressed for up to two hours following carbohydrate ingestion, the parents were asked to omit the child's breakfast or lunch, depending upon the time of day investigation was being performed. Parental compliance with this request is unknown.

Children were persuaded to cycle as hard as possible, and most became sweaty, breathless and tachycardic, by the end of two miles. (A reward was offered in the form of twenty "Smarties" which were given one at a time on completion of each 0.1 of a mile, although these were not consumed until after the blood was collected.) The importance both of the distance covered, and the appearance of these physical signs were stressed during discussions with a colleague (Parkin, 1974) with considerable experience of this investigation in slightly older children.

Some of the children investigated had blood sampled thirty minutes after the completion of the 10-20 minute period of exercise (the modified exercise test). In the great majority of children investigated however, blood was collected thirty minutes from the beginning/
Figure iv

Bicycle used for Exercise Test
beginning of exercise, as recommended by Buckler (1972).

Blood for GH analysis was placed in a clean glass tube and allowed to clot before being centrifuged. Separated serum was kept at 4°C until the evening when it was transferred to storage at -10°C. A number of other analyses were done on the remainder of the 20 mls. of blood collected after exercise but these will not be described further here.

**Growth Hormone Assay** (by Regional Hormone Laboratory, Edinburgh)

HGH determinations were carried out by an automated specific radioimmunoassay procedure using a second antibody separation stage, based upon the method of Hunter (1975). Batches were set up using a Dual Micro Model Compupet diluter-dispenser (General Diagnostics, William Warner & Co. Ltd., Eastleigh, Hampshire) and separated, counted and computed on a prototype 'Kemtech' instrument based upon equipment designed by Professor K. D. Bagshawe (Kemble Instrument Co. Ltd., Burgess Hill, Sussex). Computation involved the use of a four-parameter log/logit transform. The assay standard was IRP 66/217, and the lower limit of detection used was 0.56 mU/L ± 0.22 (n = 32), defined as that dose corresponding to a 20% fall in the binding of tracer observed in zero standards. The within-batch CV was 8.5% (n = 21) calculated from determinations on aliquots of four different pools measured at the beginning and the end of each batch run. The mean pool values were 3.3, 8.5, 31 and 134 mU/L respectively.

A between-assay CV of 12.5% (n = 21) was observed which was calculated by comparison of repeat analysis data, i.e. each new batch/
batch included three samples chosen randomly from previously analysed batches. The assay also consistently showed a between-batch CV of 10% in the UK inter-laboratory quality control scheme for HGH.

Other Screening Tests

In those cases where exercise was impossible, either because of breathlessness on exertion secondary to cardiorespiratory disease, or mental retardation, an extended glucose tolerance test or an insulin tolerance test was performed.

The extended glucose tolerance test was done according to the method recommended by Hunter et al (1967). Most children were admitted overnight to hospital to ensure they were in a fasting state. Blood was sampled half hourly from two to four hours after 1.4 g/Kg of glucose had been given orally.

Insulin Tolerance Test

Where a screening test had not satisfactorily eliminated GHD (GH less than 18 mU/L), and/or the height velocity was less than the 25th centile for chronological age, and where no other adequate explanation for short stature existed, children were admitted to hospital for an insulin tolerance test (ITT) with parental consent. Most children with GH levels less than 10 mU/L during screening had an ITT, even if the height velocity and other clinical findings suggested GHD to be an unlikely diagnosis. This was considered ethically justifiable, because severe biochemical GHD can exist in the presence of normal growth and further understanding of this phenomenon/
phenomenon is desirable. When this study was planned and this decision put into effect, the ITT had never been associated with any fatalities or other permanent sequelae.

The test was done according to the standard method first described by Roth et al (1963) and later Greenwood, Landon and Stamp, (1966). Children were fasted overnight and the following morning an I.V. line was established, and kept patent with normal or half normal saline. One or more base line samples of blood were withdrawn for blood sugar and GH analysis prior to soluble insulin in a dose of 0.12 units/Kg being injected intravenously. Blood samples were taken at 30, 60, 90, 120, and 150 minutes in all children for GH and blood sugar assays, and in some children an additional sample was collected at 15 minutes. All children showed some clinical evidence of hypoglycaemia (for example, drowsiness, tachycardia, sweating, feelings of hunger). The test was only regarded as valid if the minimum blood sugar level was 2.2 mmol/L or less. Occasionally severe hypoglycaemia was terminated with I.V. 50% dextrose. Only one child, subsequently found to have multiple pituitary hormone deficiency, convulsed because of severe hypoglycaemia, but she does not appear to have suffered any long term effects.

**Analysis of Results**

In every case the age of children was first converted to a decimal value (Tanner, 1973). The results of all anthropometric measurements and laboratory investigations were entered on standard forms and the information later transferred to 80 column punch cards.
A FORTRAN programme was then written (by Dr. Stuart Pocock of the Medical Computing Group, University of Edinburgh), converting the raw anthropometric data to standard deviation or percentile scores making use of established standards. In general, the published standards are for intervals of 0.5 of a year and interpolation has therefore been necessary to enable calculations to be made to the exact age of the child.

As all children were pre-adolescent, the standards used in the calculation of SDS for height attained were the cross sectional ones of Tanner (1973) (his tables 7:4 a, and 7:4 b). The height SDS of individual parents was calculated from the adult values given in these tables. The same source was used in the calculation of sitting height SDS (tables 7:10 a, and 7:10 b).

The SDS for midparental height was derived from the mean (166.9 cms.) and SD (6.16 cms.) for this value given by Tanner, Goldstein and Whitehouse (1970).

UAMC was calculated as a percentage of the mean given by Jelliffe (1966). No published British standards are thought to be available.

Triceps and subscapular skinfolds have been expressed both as a percentage of the mean, and as a percentile ranking, both having been derived from the revised charts of Tanner and Whitehouse (1975).

Upper arm circumference was calculated as a percentage of the mean. The standard used was that obtained during a 1975 London County Council study (Cameron, 1977).

Weight/
Weight has been expressed as a percentage of the mean and as a percentile ranking from the data given by Tanner (1973) (tables 7:5a; 7:5 b).

Height velocity has been calculated by dividing the increment in height (millimetres) by the age increment in years. To minimise seasonal influences on growth rate, only height velocities derived from measurement intervals in excess of 0.875 years have been included in the analysis. (In only 4% of cases was the interval between 0.875 and 1 year.) Because height velocity is not normally distributed over the whole age range of children in the study, it has not been possible to calculate a height velocity $SDS_{CA}$ for all children. Height velocity has thus been expressed as a percentile ranking in relation to the age midway between the two measurements (Tables VIIa and VIIib of Tanner, Whitehouse and Takaishi, 1966).

However, for those in whom bone age was known, height velocity has been expressed as an SDS in relation to it ($SDS_{BA}$). (The distribution of height velocity was Gaussian at the majority of bone ages of the children in this study.)

1. The interval in remaining analysed cases was between 10.15 years.
THE CONTROL STUDY

In the overall planning of the study it was thought unlikely that GHD and other organic conditions, including many of the congenital abnormality syndromes such as achondroplasia, would be very frequent causes of short stature. One anticipated that many of the children in the study would be free of organic illness - the "short normal" children described by Lacey and Parkin (1974 a, b). It was decided to study the extent to which the biological and social backgrounds of the "short normal" children differed from the community norm, by selecting a group of "control children" of average height, and then comparing the frequency with which a number of social and medical variables occurred in both groups. The growth hormone status of the "controls" was not studied.

Two methods of selecting controls were possible. The first would have involved a random selection of controls from within the screened population. In this case the frequency distribution of the selected variables would, allowing for sampling error, have been representative of the total screened population. Some of this information, such as social class, was already available in the 1971 census data (OPCS, 1973), and more could be gleaned from studies such as the National Child Development Study (Butler, Davie and Goldstein, 1973) and the 1970 British Births Survey (Chamberlain, 1974). Indeed, it was anticipated that the frequency distribution of these variables would be quite different in a group of "short normal" children from those in the general population (Lacey and Parkin, 1974 b) and there seemed therefore little point in confirming/
confirming the obvious.

Selecting matched controls seemed more logical. By doing this, the effect of certain variables, notably social class, could be eliminated, and it would then be possible to examine which, if any, variables within social class were associated with short stature.

An attempt was accordingly made to select two controls for each short normal child on the basis of the following criteria:

1. Average height (mean ± 2 SD).
2. Same social class.
3. Same school class.
4. Same sex.
5. If (1) to (4) were satisfied for more than two children, the two whose dates of birth were nearest to the short child were selected.

As the control study was supplementary to the main objective of the study, and since locating and interviewing controls was expected to be time consuming, it was not possible to select controls for every short normal child. An attempt was therefore made to select about one hundred controls, restricting this part of the investigation to Edinburgh and Glasgow.

The parents of the child whose date of birth was closest to that of the short child were then contacted by mail and asked to take part in the study (Appendix 13). If no reply was received an identical letter was sent to the parents of the alternate control. Lack of time prevented an intensive pursuit of non-responders. Ideally, non-responding controls should have been pursued with the same/
same intensity as the children with short stature (MacMahon and Pugh, 1970), but as this would have detracted from the main purpose of the study, it was not possible. At a later date, an appointment was made to visit the parents of those agreeing to take part, when an interview schedule was administered (see page 104). This was identical to the one used for the short children with the exception that questions specifically referring to short stature were omitted. Where possible, the heights of both parents were measured with the Harpenden portable anthropometer to the nearest centimetre. The heights of the control children were similarly recorded.

**Interview Schedule (Appendix 15)**

The schedule was administered to all parents participating in the study. The child's mother was the usual respondent. Clearly, both the interviewers, and those being interviewed, knew whether or not their child was of normal height. Indeed, the parents of the control children had been told initially the basis upon which their child had been included in the study (see Appendix 13). The interviewers were accordingly instructed to tell the interviewees that we were trying to obtain details of the medical and social backgrounds of all children in the study to see if they bore any relationships to growth. It was stressed that all information gathered would be treated as confidential.

The full interview schedule had three parts, the contents of which are summarised below. Only some of the large amount of information recorded during these interviews has been analysed for this particular/
particular study.

The first part - only relevant to short children - sought to discover if and when the parents had first become conscious of their child's short stature and what previous action they and their medical advisers had taken (Questions 24-30). This prevented unnecessarily repeating investigations, and also provided information about referral patterns in children with short stature.

The second section was concerned with the child's medical history. It would enable one to determine whether biological factors, such as low birth weight, familial short stature, or previous organic illness were present significantly more often in short children compared to controls. The questions focussed upon the child's past health, including details of pregnancy and birth (Questions 33-41, 44, 46), early child development (42, 43, 57-57, 62), immunisation history (58), clinic attendance record (59-60) and episodes of hospitalisation (22). A systematic symptom enquiry, which included specific questions about diet was pursued (5-21, 23, 61), but time did not permit a very detailed dietary analysis. Information was also sought about the details of the mother's previous pregnancies (47, 48), and the health of other members of the family (67, 68) including information about any siblings who had died (49, 50). (Many of these questions were modifications of those contained in the questionnaire administered during the second phase of the 1970 survey of British births, which were made available by courtesy of Professor Neville Butler.)

The third part of the schedule contained questions about social and family background/
background of the child. Information was requested about the number and relationship of the siblings (71) and parent figures (31, 32), their present age (66) and age on leaving school (82). Details about the educational and family background (79-83), the occupation of both parents (84, 86) and the employment status of father (87) were also obtained. Questions were also asked to determine whether the family was one of 'low income' (63, 88). The adequacy of housing (70-73, 75-78) and the mobility of the family were also assessed (65, 74, 79). The alleged smoking habits of both parents were also recorded (69). The extent of social isolation present in the family (89-93), the mother's intelligence and general appearance (94) were also assessed.

The original interview schedule was piloted on parents of a number of children admitted to wards of the Royal Hospital for Sick Children, Edinburgh, and the order of questions altered so that they followed more logically. The majority of interviews were undertaken by my wife or myself. About fifty were carried out by two health visitors, both of whom had had previous training and experience in interview techniques.

The interview responses were precoded, and the results were later transferred to 80 column punch cards for computer analysis using the Statistical Package for the Social Sciences (Nie et al., 1975).
Disadvantage Score

From information derived from the interview schedule, a disadvantage score was constructed for each child based on indicators of disadvantage that were previously described by Wedge and Prosser (1974). One point was given for each of the following social attributes, resulting in a maximum score of three and a minimum of zero:

(1) The family had at some stage been in receipt of a Supplementary Benefit, or the child was eligible for free school meals.
(2) The child's household was living at a density of more than 1.5 persons per room, or did not have exclusive use of hot water.
(3) There were five or more children in the family, or the child was a member of a one parent family.

STATISTICAL ANALYSIS

Several diagnostic groups have been defined in the cohort of short children (see page 13), and where the nature of the data has allowed it, means and SD's of the different variables studied have been calculated, and between-group comparisons then made using Student's t test. Occasionally, when small skewed samples were being compared, the use of this test was inappropriate and the Mann Whitney U test was used to test the differences between groups. (Siegel, 1956).

For many parameters, means and SD's were not available. It has often been possible however to group the data against a scale with an underlying numerical value (e.g. an ascending percentile rank/
rank) which thereby made it possible to compare groups using a test for trend in proportions (Cox, 1970). The test statistic (e) is normally distributed and its significance can be easily read from tables of the normal distribution.

When the variables being studied had only two possible outcomes (e.g., normal or abnormal pregnancy) comparisons between groups have been made using a $\chi^2$ test for two independent samples, making a correction for continuity wherever appropriate.

In the case-control study, comparisons have been made separately within each city and the information from the separate contingency tables combined (Cox, 1970). This increases the chances of detecting an overall significant difference between cases and controls, which may not otherwise have been apparent in the individual cities because of smaller sample size.
CHAPTER III

RESULTS OF THE STUDY

INTRODUCTION

The results of the study will be presented in eight major sections. The first (1) describes the demographic characteristics of the study population. The next section (2) outlines how the outcome of the GH investigations in the study population have been used to assign each child to an appropriate diagnostic group. Next (3) the auxological findings of children in each of the diagnostic groups have been summarised, and then (4) the frequency with which selected social and biological variables were present is described. In the following section (5) the GH responses following exercise during insulin hypoglycaemia are compared in greater detail. These results have enabled the prevalence of severe GHD to be calculated (6). Factors which were associated with the seeking of medical advice in children with short stature, and the reported action taken by medical advisers when their advice was sought is discussed in the next section (7). Finally (8), after the suitability of the selected controls has been discussed, the frequency with which some social and medical variables appeared in them and constitutionally short children is presented.

THE DEMOGRAPHIC CHARACTERISTICS OF CHILDREN WITH SHORT STATURE

The heights of all second and third year pupils attending all Education Authority primary and special schools in Edinburgh, Glasgow and/
and Aberdeen have been screened; in Aberdeen fourth year pupils were also screened. Children enrolled in the majority of independent and grant-aided schools in these cities have also been measured. The results are set out in Table 1.

In Edinburgh, height screening was done over a five week period in January-February 1975; in Glasgow it took twelve weeks (March-May 1975), and in Aberdeen, three weeks (May June, 1976). Some within-city migration probably occurred during each of these periods, particularly in Glasgow, and thus some children may have escaped measurement altogether, whilst others may have been measured and counted twice. An accurate assessment of the numbers involved is impossible, but these children would have comprised only a small proportion of the total population screened.

Not all children were present at the time of the first school visit, and details of the absentees are included in Table 2. Attempts were made on a later visit to the school to measure those thought by their teachers to be below average height. The proportion of short absentees actually measured is shown in Table 3, and it is clear that the proportion of absentees with short stature is similar to that found in children measured during the initial visit. If one assumes that short children were no more likely to be absent from school than children of average height, these results suggest that the teachers' estimates of heights were probably accurate. It was estimated that, at most, a further nine children with short stature would have been found if the remaining absentees had all been measured.

Four hundred and forty-nine children with a height less than $-2.5$ SDS/
### Table 1

**Children Enrolled by City, School Category**

<table>
<thead>
<tr>
<th>Schools</th>
<th>Edinburgh</th>
<th>Glasgow</th>
<th>Aberdeen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- boys</td>
<td>5,818</td>
<td>13,216</td>
<td>4,470</td>
<td>23,504</td>
</tr>
<tr>
<td>- girls</td>
<td>5,652</td>
<td>12,550</td>
<td>4,242</td>
<td>22,444</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11,470</td>
<td>25,766</td>
<td>8,712</td>
<td>45,948</td>
</tr>
<tr>
<td><strong>Special</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- boys</td>
<td>62</td>
<td>164</td>
<td>62</td>
<td>288</td>
</tr>
<tr>
<td>- girls</td>
<td>43</td>
<td>137</td>
<td>52</td>
<td>232</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>105</td>
<td>301</td>
<td>114</td>
<td>520</td>
</tr>
<tr>
<td><strong>Independent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- boys</td>
<td>1,615</td>
<td>180</td>
<td>83</td>
<td>878</td>
</tr>
<tr>
<td>- girls</td>
<td>429</td>
<td>332</td>
<td>114</td>
<td>875</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1,044</td>
<td>512</td>
<td>197</td>
<td>1,753</td>
</tr>
<tr>
<td><strong>All Schools</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- boys</td>
<td>6,495</td>
<td>13,560</td>
<td>4,613</td>
<td>24,670</td>
</tr>
<tr>
<td>- girls</td>
<td>6,124</td>
<td>13,019</td>
<td>4,408</td>
<td>23,551</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td>12,619</td>
<td>26,579</td>
<td>9,023</td>
<td>48,221</td>
</tr>
</tbody>
</table>
### Table 2

**Absentees - by School Category**

<table>
<thead>
<tr>
<th>Schools</th>
<th>Edinburgh</th>
<th>Glasgow</th>
<th>Aberdeen</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average height</td>
<td>532</td>
<td>1,756</td>
<td>261</td>
<td>2,549</td>
</tr>
<tr>
<td>&quot;Small&quot;</td>
<td>166</td>
<td>406</td>
<td>42</td>
<td>614</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>698</td>
<td>2,162</td>
<td>303</td>
<td>3,163</td>
</tr>
<tr>
<td>Absentees as percentage of enrolled population</td>
<td>6.8%</td>
<td>8.4%</td>
<td>3.5%</td>
<td>6.9%</td>
</tr>
<tr>
<td><strong>Special</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average height</td>
<td>6</td>
<td>17</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>&quot;Small&quot;</td>
<td>5</td>
<td>9</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11</td>
<td>26</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>Absentees as percentage of enrolled population</td>
<td>10.0%</td>
<td>8.6%</td>
<td>5.3%</td>
<td>8.3%</td>
</tr>
<tr>
<td><strong>Independent</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average height</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>&quot;Small&quot;</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td><strong>All Schools</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average height</td>
<td>542</td>
<td>1,774</td>
<td>269</td>
<td>2,585</td>
</tr>
<tr>
<td>&quot;Small&quot;</td>
<td>171</td>
<td>416</td>
<td>43</td>
<td>630</td>
</tr>
<tr>
<td><strong>Grand Total</strong></td>
<td>713</td>
<td>2,190</td>
<td>312</td>
<td>3,215</td>
</tr>
</tbody>
</table>
TABLE 3

SHORT STATURE PREVALENCE IN CHILDREN AT
SCHOOL ON FIRST VISIT & ABSENTEES

<table>
<thead>
<tr>
<th>Description</th>
<th>Present on First Visit</th>
<th>Absentees</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Number</td>
<td>45,006</td>
<td>3,215</td>
</tr>
<tr>
<td>(b) Number estimated short by teachers</td>
<td>-</td>
<td>630</td>
</tr>
<tr>
<td>(c) Number estimated short and remeasured</td>
<td>-</td>
<td>554</td>
</tr>
<tr>
<td>(d) Number of short children found</td>
<td>423</td>
<td>26</td>
</tr>
</tbody>
</table>

Prevalence of short stature

\[
\frac{1,000 \times 423}{45,006} = \frac{1,000 \times 26 \times 630}{554 \times 3,215}
\]

9.40\%  
9.20\%
-2.5 SDS (see page 90) were identified in the screened population of 48,221. The distribution of these children in each city by sex, and school category is shown in Table 4. The prevalence of short stature in each sub-group has been calculated as "cases" per one thousand enrolled population.

The following conclusions may be drawn from the foregoing tables:

**Sex Differences in Short Stature Prevalence**

Whilst there was no overall sex difference in the prevalence of short stature - boys 9.77 per 1,000, girls 8.83 per 1,000 ($X^2_1 = 1.05$, n.s.) - short stature was significantly more common in girls in Aberdeen - 8.39 per 1,000 - compared with boys - 4.77 per 1,000 ($X^2_1 = 4.02$, $p < 0.05$). A reverse trend was apparent in Glasgow where a higher proportion of boys - 13.6 per 1,000 - was of short stature compared to girls - 10.4 per 1,000 ($X^2_1 = 4.98$, $p < 0.05$).

**Between-City Differences**

A significantly higher proportion of all children in Glasgow were of small stature - 12.1 per 1,000 - compared with Edinburgh - 5.47 per 1,000 - and Aberdeen - 6.54 per 1,000 ($X^2_2 = 49.77$, $p < 0.001$).

The between-city differences in the prevalence of short stature in children attending ordinary primary schools are even more striking; such children are generally free of major physical and mental handicaps. The prevalence in Glasgow - 10.8 per 1,000 - was double that in either Edinburgh - 4.88 per 1,000 - or Aberdeen - 4.25 per 1,000 ($X^2_2 = 54.24$, $p < 0.001$).

The social class distribution and the proportion of the economically/
TABLE 4

SHORT STATURE - NUMBERS AND PREVALENCE RATES PER 1,000 (%)

BY CITY, SEX AND SCHOOL CATEGORY

<table>
<thead>
<tr>
<th>SCHOOLS</th>
<th>EDINBURGH</th>
<th>GLASGOW</th>
<th>ABERDEEN</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIMARY</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys - no.</td>
<td>26</td>
<td>159</td>
<td>13</td>
<td>198</td>
</tr>
<tr>
<td>- %</td>
<td>4.47</td>
<td>12.03</td>
<td>2.91</td>
<td>8.42</td>
</tr>
<tr>
<td>Girls - no.</td>
<td>30</td>
<td>119</td>
<td>24</td>
<td>173</td>
</tr>
<tr>
<td>- %</td>
<td>5.30</td>
<td>9.48</td>
<td>5.66</td>
<td>7.71</td>
</tr>
<tr>
<td>TOTAL</td>
<td>56</td>
<td>278</td>
<td>37</td>
<td>371</td>
</tr>
<tr>
<td>- %</td>
<td>4.88</td>
<td>10.8</td>
<td>4.25</td>
<td>8.07</td>
</tr>
<tr>
<td>SPECIAL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys - no.</td>
<td>8</td>
<td>26</td>
<td>9</td>
<td>43</td>
</tr>
<tr>
<td>- %</td>
<td>129</td>
<td>158.5</td>
<td>145.2</td>
<td>149.3</td>
</tr>
<tr>
<td>Girls - no.</td>
<td>5</td>
<td>16</td>
<td>12</td>
<td>33</td>
</tr>
<tr>
<td>- %</td>
<td>116.3</td>
<td>116.8</td>
<td>230.8</td>
<td>142.2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>42</td>
<td>21</td>
<td>76</td>
</tr>
<tr>
<td>- %</td>
<td>123.8</td>
<td>139.5</td>
<td>184.2</td>
<td>146.2</td>
</tr>
<tr>
<td>INDEPENDENT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys - no.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>- %</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Girls - no.</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>- %</td>
<td>-</td>
<td>3.01</td>
<td>8.77</td>
<td>2.29</td>
</tr>
<tr>
<td>TOTAL</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>- %</td>
<td>-</td>
<td>1.95</td>
<td>5.08</td>
<td>1.14</td>
</tr>
<tr>
<td>ALL SCHOOLS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys - no.</td>
<td>34</td>
<td>185</td>
<td>22</td>
<td>241</td>
</tr>
<tr>
<td>- %</td>
<td>5.23</td>
<td>13.6</td>
<td>4.77</td>
<td>9.77</td>
</tr>
<tr>
<td>Girls - no.</td>
<td>35</td>
<td>136</td>
<td>37</td>
<td>208</td>
</tr>
<tr>
<td>- %</td>
<td>5.72</td>
<td>10.4</td>
<td>8.39</td>
<td>8.83</td>
</tr>
<tr>
<td>GRAND TOTAL</td>
<td>69</td>
<td>321</td>
<td>59</td>
<td>449</td>
</tr>
<tr>
<td>- %</td>
<td>5.47</td>
<td>12.08</td>
<td>6.54</td>
<td>9.31</td>
</tr>
</tbody>
</table>
economically active population out of work at the time of the 1971 census in the three cities has been shown in Appendix Tables 1 and 2. It is clear that the ranking of the cities in descending order of prevalence of short stature in primary school children, is in marked contrast with their ranking in total population numbers, the proportion of the populations employed in industrial occupations within each city (that is social class III manual, IV and V) and the extent of male unemployment, which has been considered previously to be an indicator of social deprivation. (Appendix Table 2).

School Differences

Short stature was found seven times more frequently in children attending ordinary primary schools - 8.07 per 1,000 - than in those at independent schools - 1.14 per 1,000 \((X^2_1 = 9.59, p < 0.01)\) - reflecting well known differences in the social background of these sub-groups.

These differences were not as great as those observed between children attending primary and special schools. 14.6% of special school children were small, a rate over eighteen times higher than in children attending ordinary primary schools, mirroring the frequency with which congenital abnormalities and other medical conditions are usually found in this group of children. The differences between the prevalence of short stature in the three categories of special schools in Glasgow is shown in Table 5, from which it is also clear that the most severely mentally and often multiply handicapped children - in occupational centres - had the highest rates of short stature \((X^2_2 = 7.71, p < 0.05)\). Whilst only 0.56% of the Glasgow/
TABLE 5

SHORT STATURE BY SPECIAL SCHOOL CATEGORY

<table>
<thead>
<tr>
<th>School Category</th>
<th>Enrolled Population</th>
<th>Short Children</th>
<th>Short Stature Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational Centre (IQ &lt; 50)</td>
<td>66</td>
<td>15</td>
<td>22.7%</td>
</tr>
<tr>
<td>School for Physical Handicap</td>
<td>80</td>
<td>13</td>
<td>16.2%</td>
</tr>
<tr>
<td>E.S.N. School</td>
<td>155</td>
<td>14</td>
<td>9.03%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>301</strong></td>
<td><strong>42</strong></td>
<td><strong>14.0%</strong></td>
</tr>
</tbody>
</table>

Glasgow school population attended the ESN schools, such schools accounted for 4.4% of all short children at the time of height screening. During the course of the study a further fourteen children with short stature originally attending ordinary primary schools were transferred to these schools, so that eventually 9.6% of all "short-normal" children in Glasgow - i.e. excluding those at occupational centres or schools for the physically handicapped - had been classified as mentally subnormal by the education authorities, confirming the strong association between short stature and mental subnormality found previously by others (e.g. Lacey and Parkin, 1974 b).

*Within-City Variation in the Prevalence of Short Stature*

The clearly significant geographical variation between the three cities in the extent of short stature prompted an analysis of the differences within two of the cities, Edinburgh and Glasgow.

Geographical subdivision in both cities has been based on postal/
postal code districts, although one based upon municipal ward boundaries could also have been chosen. Indeed in Edinburgh, the latter method of subdivision may have been more useful, as short stature prevalence could than have been compared with triennial infant mortality rates which are available for each ward (Armand Smith, 1977) and other health data (Carstairs, 1977). In Glasgow however, the municipal ward boundaries were drawn before the relatively recent dispersal of the population, from the now largely demolished central tenements to the peripheral housing schemes; the largest ward now has a population nineteen times higher than the smallest. Consequently, large wards tend to contain very mixed populations. Each postal code district does however tend to be relatively homogeneous within itself.

Primary schools have thus been grouped according to postal code district, of which there are 28 in Glasgow and 17 in Edinburgh, and the number of children enrolled in the primary schools within each district calculated. In both cities the numbers of children enrolled in special schools within each district have been omitted as such schools are irregularly distributed throughout both cities. Short children attending special schools, have however been assigned to the postal code district of residence. The effect of this modification is to very slightly raise the calculated prevalence of short stature - e.g. in Glasgow, by omitting special school populations the overall prevalence is increased by 0.35 cases per 1,000.

Districts with a total enrolled population of less than 400 have been grouped with one or more neighbouring districts with an apparently/
apparently similar physical environment, in an attempt to reduce the standard error of district prevalence rates. Within one Glasgow district, the children attending the three schools serving a particularly deprived housing scheme, have been extracted and considered separately. As a result, Glasgow has been divided into twenty-two districts (Table 6) and Edinburgh fifteen (Table 7).

In Table 6, the Glasgow districts have been ranked according to the prevalence of short stature. The wide variation in the prevalence of short stature (mean 12.5 per 1,000; range 1.9 per 1,000 to 38.0 per 1,000) is immediately apparent.

It was evident from personal observation that districts ranked highly in the prevalence of short stature were characterised by poor quality private and municipal housing, as well as other features of urban decay and deprivation.

After discussion with Levein (1975) use was made of data derived from the 1971 census by him and others to look at the association of social deprivation with short stature, using a fairly crude epidemiological method. The association between short stature and social disadvantage has been considered in greater detail in the case-control study (see page 183).

Holterman (1975) and Levein and McKenzie (1973) had previously selected five indicators of deprivation and studied their geographical distribution in Great Britain. These indicators were:

(1) Households without exclusive use of hot water.
(2) Households without exclusive use of a fixed bath or shower.
(3) Households without exclusive use of an inside WC.
(4) Persons or private households living at a density greater than 1.5/
### Table 6

**Numbers Enrolled, Short Stature "Cases" and Prevalence of Short Stature, and Census Indicators of Urban Deprivation**

By Postal Code Districts - Glasgow

<table>
<thead>
<tr>
<th>District</th>
<th>Enrolled Population</th>
<th>Children &lt; -2.5 SDS</th>
<th>Prevalence of Short Stature/1000 Enrolled Population</th>
<th>Rank</th>
<th>%age of Total Indicators in Worst 5% for Britain</th>
<th>Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>474</td>
<td>18</td>
<td>38.0</td>
<td>1</td>
<td>33.3</td>
<td>6</td>
</tr>
<tr>
<td>B</td>
<td>782</td>
<td>18</td>
<td>23.0</td>
<td>2</td>
<td>57.8</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>1,602</td>
<td>30</td>
<td>18.7</td>
<td>3</td>
<td>40.0</td>
<td>3.5</td>
</tr>
<tr>
<td>D</td>
<td>665</td>
<td>11</td>
<td>16.5</td>
<td>4</td>
<td>25.0</td>
<td>8</td>
</tr>
<tr>
<td>E</td>
<td>620</td>
<td>10</td>
<td>16.1</td>
<td>5</td>
<td>40.0</td>
<td>3.5</td>
</tr>
<tr>
<td>F</td>
<td>1,267</td>
<td>20</td>
<td>15.79</td>
<td>6</td>
<td>34.3</td>
<td>5</td>
</tr>
<tr>
<td>G</td>
<td>825</td>
<td>13</td>
<td>15.75</td>
<td>7</td>
<td>6.7</td>
<td>19</td>
</tr>
<tr>
<td>H</td>
<td>1,463</td>
<td>23</td>
<td>15.70</td>
<td>8</td>
<td>13.3</td>
<td>14.5</td>
</tr>
<tr>
<td>I</td>
<td>2,344</td>
<td>35</td>
<td>14.9</td>
<td>9</td>
<td>14.3</td>
<td>12</td>
</tr>
<tr>
<td>J</td>
<td>1,352</td>
<td>20</td>
<td>14.8</td>
<td>10</td>
<td>20.0</td>
<td>10.5</td>
</tr>
<tr>
<td>K</td>
<td>445</td>
<td>6</td>
<td>13.5</td>
<td>11</td>
<td>13.3</td>
<td>14.5</td>
</tr>
<tr>
<td>L</td>
<td>1,423</td>
<td>17</td>
<td>11.9</td>
<td>12</td>
<td>23.3</td>
<td>9</td>
</tr>
<tr>
<td>M</td>
<td>1,977</td>
<td>23</td>
<td>11.6</td>
<td>13</td>
<td>31.1</td>
<td>7</td>
</tr>
<tr>
<td>N</td>
<td>1,103</td>
<td>12</td>
<td>10.9</td>
<td>14</td>
<td>44.4</td>
<td>2</td>
</tr>
<tr>
<td>O</td>
<td>603</td>
<td>6</td>
<td>10.0</td>
<td>15</td>
<td>20.0</td>
<td>10.5</td>
</tr>
<tr>
<td>P</td>
<td>1,418</td>
<td>14</td>
<td>9.9</td>
<td>16</td>
<td>13.3</td>
<td>14.5</td>
</tr>
<tr>
<td>Q</td>
<td>1,884</td>
<td>17</td>
<td>9.0</td>
<td>17</td>
<td>13.3</td>
<td>14.5</td>
</tr>
<tr>
<td>R</td>
<td>1,453</td>
<td>13</td>
<td>8.9</td>
<td>18</td>
<td>10.8</td>
<td>17</td>
</tr>
<tr>
<td>S</td>
<td>789</td>
<td>4</td>
<td>5.1</td>
<td>19</td>
<td>10.0</td>
<td>18</td>
</tr>
<tr>
<td>T</td>
<td>961</td>
<td>4</td>
<td>4.2</td>
<td>20</td>
<td>3.3</td>
<td>21</td>
</tr>
<tr>
<td>U</td>
<td>1,248</td>
<td>5</td>
<td>4.0</td>
<td>21</td>
<td>5.7</td>
<td>20</td>
</tr>
<tr>
<td>V</td>
<td>1,068</td>
<td>2</td>
<td>1.9</td>
<td>22</td>
<td>0</td>
<td>22</td>
</tr>
</tbody>
</table>

**Total** | 25,766               | 321                 | 12.5                                                |      |                                               |      |
### Table 7

NUMBERS ENROLLED, SHORT STATURE "CASES" AND PREVALENCE OF SHORT STATURE, AND CENSUS INDICATORS OF URBAN DEPRIVATION BY POSTAL CODE DISTRICTS - EDINBURGH

<table>
<thead>
<tr>
<th>DISTRICT</th>
<th>ENROLLED POPULATION</th>
<th>CHILDREN &lt; -2.5 SDS</th>
<th>PREVALENCE OF SHORT STATURE / 1000 ENROLLED POPULATION</th>
<th>RANK</th>
<th>%AGE OF TOTAL INDICATORS IN WORST 5% FOR BRITAIN</th>
<th>RANK</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>640</td>
<td>12</td>
<td>18.8</td>
<td>1</td>
<td>66.7</td>
<td>1</td>
</tr>
<tr>
<td>B</td>
<td>851</td>
<td>9</td>
<td>10.6</td>
<td>2</td>
<td>6.7</td>
<td>10.5</td>
</tr>
<tr>
<td>C</td>
<td>630</td>
<td>6</td>
<td>9.52</td>
<td>3</td>
<td>16.6</td>
<td>6</td>
</tr>
<tr>
<td>D</td>
<td>874</td>
<td>7</td>
<td>8.01</td>
<td>4</td>
<td>33.3</td>
<td>2</td>
</tr>
<tr>
<td>E</td>
<td>663</td>
<td>5</td>
<td>7.54</td>
<td>5</td>
<td>6.7</td>
<td>10.5</td>
</tr>
<tr>
<td>F</td>
<td>802</td>
<td>5</td>
<td>6.23</td>
<td>6</td>
<td>25.0</td>
<td>3</td>
</tr>
<tr>
<td>G</td>
<td>614</td>
<td>3</td>
<td>4.89</td>
<td>7</td>
<td>22.2</td>
<td>4</td>
</tr>
<tr>
<td>H</td>
<td>440</td>
<td>2</td>
<td>4.55</td>
<td>8</td>
<td>0</td>
<td>14.5</td>
</tr>
<tr>
<td>I</td>
<td>1,376</td>
<td>6</td>
<td>4.36</td>
<td>9</td>
<td>14.3</td>
<td>7.5</td>
</tr>
<tr>
<td>J</td>
<td>848</td>
<td>3</td>
<td>3.54</td>
<td>10</td>
<td>2.6</td>
<td>13</td>
</tr>
<tr>
<td>K</td>
<td>891</td>
<td>3</td>
<td>3.37</td>
<td>11</td>
<td>0</td>
<td>14.5</td>
</tr>
<tr>
<td>L</td>
<td>960</td>
<td>2</td>
<td>2.08</td>
<td>12</td>
<td>11.1</td>
<td>9</td>
</tr>
<tr>
<td>M</td>
<td>551</td>
<td>1</td>
<td>1.81</td>
<td>13</td>
<td>14.3</td>
<td>7.5</td>
</tr>
<tr>
<td>N</td>
<td>596</td>
<td>1</td>
<td>1.68</td>
<td>14</td>
<td>20.0</td>
<td>5</td>
</tr>
<tr>
<td>O</td>
<td>734</td>
<td>1</td>
<td>1.36</td>
<td>15</td>
<td>3.7</td>
<td>12</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>11,470</strong></td>
<td><strong>66</strong></td>
<td><strong>5.75</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*3 children attending special schools lived outside city boundary.*
1.5 persons per room.

(5) Economically active males who were unemployed but seeking a job or temporarily sick, at the time of the Census.

Any person or household in which one or more of these had been present was regarded as deprived for the purpose of their analyses. Holterman (1975) then calculated the proportion of deprived persons or households in every census enumeration district (CED) in Great Britain (that is those in whom each indicator was present).

The frequency distribution for each indicator was then derived for the 87,578 urban CED's, and the means, standard deviations and selected percentiles then calculated for each. Thus the 5% cut-off value of an indicator was defined as the value of that indicator exceeded or equalled by only the most deprived 5% of the total CED's.

The 5% values for each of the above indicators was as follows:

(1) 38.2% of households,
(2) 58.8% of households,
(3) 50.5% of households,
(4) 18.5% of persons or 10.1% of households,
(5) 15.1% of males.

Thus any CED in which the proportion of economically active males who had been unemployed (but seeking work or temporarily sick at the time of the 1971 census), was greater than 15.1% was deprived. Clearly some CED's were deprived for more than one indicator and therefore regarded as multiply deprived.

In Edinburgh and Glasgow, Levein and McKenzie (1973) grouped CED's on a geographical basis to form a number of common "Census Areas" (54 in Edinburgh and 117 in Glasgow) which are distributed throughout/
throughout the various postal code districts. Maps were drawn by
them showing the proportions of households in which each indicator
was present in each of these common areas. (In Edinburgh, maps have
only been drawn for indicators 2, 4 and 5, as no area was significantly
deprived for indicators 1 and 3).

In the present study, all common areas have been allocated to
their respective postal code district. The boundaries of areas and
districts are not always contiguous, and hence a single common area
may be distributed between three postal code districts. Under these
circumstances, areas overlapping district boundaries have been
allocated to each of the districts to which they contributed, and
have therefore been counted more than once. This applies to twenty-
three census areas in Glasgow and eighteen in Edinburgh. The extent
of deprivation in each postal code district was then calculated as
the percentage of total indicators within it that were in the most
deprived 5%

The proportion of indicators in each Glasgow district that
were in the most deprived 5% has been shown in Table 6, and these
proportions have been ranked in descending order. The correlation
coefficient (Spearman) between the districts ranked according to the
prevalence of short stature, and their ranking according to the
proportion of deprived indicators, was highly significant ($R_s = 0.73$;
p < 0.01) confirming a close association between short stature and
these measures of deprivation.

1 A postal code district may have contained five common areas,
each with five indicators. If four indicators were in the
deprived range, the extent of deprivation was calculated as
\[
\frac{4 \times 100}{25} = 16\%
\]
In Edinburgh - Table 7 - the correlation between the prevalence of short stature and the extent of deprivation was not statistically significant ($R^2 = 0.41, p < 0.1$). As will be indicated later however, organic causes of short stature - which are not generally related to deprivation - were present to a much greater extent in Edinburgh than Glasgow where "constitutional short stature" clearly predominated.

It has not been possible to undertake a similar analysis in the Aberdeen subsample, as the city is only divided into two postal code districts. One would also expect that analyses based upon the municipal wards would be unsatisfactory, as a number of small pockets of deprivation are scattered throughout the whole city.

SCREENING FOR GROWTH HORMONE DEFICIENCY - DEFINITION OF DIAGNOSTIC GROUPS.

Once the cohort of children with short stature had been identified, the next objective was to screen individual children for the presence of GHD. Clearly, not every child required investigation; some had previously been investigated, and others had obvious organic reasons causing their short stature. Moreover the parents of some children refused to allow their child to be investigated. The outcome of the survey has therefore been summarised in Flow Charts I-IX, Table 8, and Appendix Tables 3-6.

The parents of nineteen children were not contacted (Flow Chart I); enough information was available from school medical cards to indicate that an organic basis was responsible for the child's/
TOTAL POPULATION SCREENED
48,221

HEIGHT SDS
\( \leq -2.5 \)
449

PARENTS CONTACTED
430

ORGANIC AETIOLOGY
49
(Appendix table 3)

INITIAL RESPONDERS
335

INITIAL NON-RESPONDERS
(i.e. refused, emigrated)
95

FLOW CHART II

FLOW CHART III
TABLE 8
SUCCESSFUL CONTACTS

TOTAL 335

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Replied to first letter (Appendix 8)</td>
<td>198</td>
</tr>
<tr>
<td>Replied to second letter</td>
<td>11</td>
</tr>
<tr>
<td>Home visit by health visitor or school nurse</td>
<td>115</td>
</tr>
<tr>
<td>Home visit by G.V.V. after remeasuring</td>
<td>9</td>
</tr>
<tr>
<td>Home visit by G.V.V.</td>
<td>2</td>
</tr>
</tbody>
</table>

child's short stature. The diagnoses of these children are contained in Appendix Table 3.

The parents of 335 children agreed to co-operate (Flow Chart II) - an overall response rate amongst those approached of 77.9%. A variety of methods had to be used to obtain a response (Table 8). It is worth noting that but for the assistance of health visitors and school nurses, the response rate would have been extremely low (51.2%). Some parents were only persuaded to participate after remeasurement had indicated that their child was growing slowly (height velocity less than 25th centile).

Seven of the initial responders were never seen because of persistent defaulting; five had an organic basis for their short stature, and the others had normal twelve month height velocities. Two hundred and eighty of the children whose parents agreed to co-operate/
FLOW CHART II

INITIAL RESPONDERS
335

PERSISTENT DEFAULTERS - 7
- organic aetiology 5
  (see Appendix table 5)
- height velocity > 25th percentile

FLOW CHART III

INTERVIEW AND EXAMINATION
328

INVESTIGATED
280

PREVIOUS INVESTIGATIONS - 6
- Normal 5
- ? partial GHD 4

FLOW CHART IV

ORGANIC 42
- GHD 4
- non GHD 38
  (see Appendix Table 4)
co-operate were screened for GHD; the remaining children had either been previously investigated (6) or had an organic cause for their short stature (42), including four with previously diagnosed GHD. (See Appendix Table 4). Partial GHD has not been completely excluded in one of the children previously investigated (he has been included in the diagnostic group with possible GHD - see page 138).

The final responders (N = 102) comprised 23.7% of those asked to participate (Flow Chart III). Seven of these children emigrated from the survey area. GHD seemed unlikely in any of the seventeen children who had a probable organic basis for their short stature (Appendix Table 5). With the exception of nine children in Aberdeen, the remaining non-responders have all been remeasured; of those with a normal height velocity, six had a probable organic basis for their short stature (Appendix Table 5). Remeasured children with a low height velocity were visited at home, and from information supplied by the parents it appeared that most had either a genetic or organic reason other than GHD as a cause for their short stature. No satisfactory explanation was obtained for twelve children. GHD must therefore remain a possible diagnosis in 22 of the children of non-responding parents (indicated by an asterisk in Flow Chart III). This comprises 4.0% of all those in the study. The auxological findings (see page 139) suggested that at least one girl in this group probably had an organic basis for her short stature.

Two hundred and twenty-seven of the children were screened using the standard exercise test, 44 using the modified exercise test and nine with miscellaneous tests (Flow Charts IV-IX).
FLOW CHART III

INITIAL NON-RESPONDERS
95

PERSISTENT DEFAULTERS
7
(from Flow Chart II)

FINAL NON-RESPONDERS
102

ORGANIC 17
(see Appendix Table 5)

EMIGRATED
7

REMEASURED
69

NOT REMEASURED 9
- Genetic/LBW 5
- Chinese 1
- PH malnutrition 1*
- Hereditary deafness 1*
- Unknown 1*

HEIGHT VELOCITY NORMAL
(>25th centile)
42
- organic 6
(see Appendix Table 5)

HEIGHT VELOCITY LOW
(<25th %ile)
27

"EXPLANATION" 15
- LBW/genetic 13
- organic 2
(see Appendix Table 5)

NO EXPLANATION 12

* See text for explanation
FLOW CHART IV

INVESTIGATED
280

MODIFIED EXERCISE TEST
44

EXERCISE TEST
227

MISCELLANEOUS SCREENING TESTS
9

FLOW CHART VII

GH < 9.9 mU/L
43

FLOW CHART V

GH 10-17.9 mU/L
67

FLOW CHART VI

GH 18-19.9 mU/L
13

FLOW CHART VII

GH > 20 mU/L
104

NON GHD
FLOW CHART V

EXERCISE TEST
GH < 9 mU/L)
43

ACUTE LEUKEMIA θ
- died
1

PREVIOUS ITT
- normal
1

HEIGHT VELOCITY
> 25th percentile
2

PARENTS REFUSED ITT
7
(1 PH rickets) θ

ITT ARRANGED
39

ITT PERFORMED
32

SEVERE BIOCHEMICAL
GHD
(GH < 9.9 mU/L)
6

PARTIAL BIOCHEMICAL
GHD
(GH 10-15.9 mU/L)
8

NON GH DEFICIENT
(GH > 16 mU/L)
18

θ see text for explanation
FLOW CHART VI

EXERCISE TEST
GH 10-17.9 mU/L
67

HEIGHT VELOCITY
> 25th percentile
20

OTHER EXPLANATION 3
- scoliosis 1 ø
- glycogen storage disease 1 ø
- Turner's mosaic 1 ø

ITT ARRANGED
44

PARENTS REFUSEDITT
4
(IEW 2)

ITT PERFORMED
40

PARTIAL BIOCHEMICAL DEFICIENCY
(GH < 15.9 mU/L)
13

NON-GH DEFICIENT
(>16 mU/L)
27

ø see text for explanation

NON GHD
FLOW CHART VII

EXERCISE TEST
GH 18-19.9 mU/L

13

GH > 19.6 mU/L

OTHER EXPLANATION
- genetic/LEW
  - short stature
  - growth delay

NON
GH/D

HEIGHT VELOCITY
>25th centile

3
FLOW CHART VIII

MODIFIED EXERCISE TEST

GH < 17.9 μU/L
40

GH 18 μU/L
4

HEIGHT VELOCITY
> 25th centile
6

EMIGRATED
1

OTHER EXPLANATION
- genetic
1
(GH 17.8 μU/L)

ITT ARRANGED
32

PARENTS REFUSED ITT
1

ITT PERFORMED
31

SEVERE BIOCHEMICAL GHD
(GH < 9.9 μU/L)
3

PARTIAL BIOCHEMICAL GHD
(GH 10–16 μU/L)
3

NON-GHD
GH > 16 μU/L
25

NON GHD
FLOW CHART IX

MISCELLANEOUS SCREENING TESTS

EXTENDED GLUCOSE TOLERANCE TEST

I.T.T.

GH < 17.9 \text{ mU/L}

ITT PERFORMED

PARTIAL BIOCHEMICAL GHD

HEIGHT VELOCITY > 25th centile

NON GHD

(GH > 18 \text{ mU/L})
Insulin tolerance tests were done on 104 of the children with inadequate GH levels during the initial test.

Children have been regarded as having normal GH secretion if any of the following criteria were satisfied:

(i) GH level exceeded 17.9 mU/L on screening test (128 children).
(ii) GH level less than 17.9 mU/L on screening test but greater than 15.9 mU/L during ITT (71).
(iii) GH level less than 17.9 mU/L on screening, but height velocity greater than 25th centile (29).

These criteria were met by a total of 228 children in the study and they have been clearly indicated in the flow charts. Twenty-one of these children also had an organic condition which probably partly contributed to their short stature; nevertheless at the time, it did not seem an adequate enough explanation to make screening for GHD unwarranted. Details of these children have been included in Appendix Table 6.

Nine children were regarded as having severe biochemical GHD as their GH levels were consistently less than 9.9 mU/L (Flow Charts V, VIII).

1 These criteria were decided upon during discussions with Drs. W. Hunter and M. Preece. The lower limit of the normal range was set slightly higher for the screening test (18 mU/L) as Hunter (1976) has suggested that the GH level may be falsely elevated immediately after a large bolus has been secreted into the blood stream and before tissue redistribution has taken place. Flow chart VII clearly indicates that a satisfactory explanation existed for short stature in the group of 13 children with GH levels between 18 and 19.9 mU/L following exercise. It is possible that a few children with partial biological GHD may have been excluded by selecting 16 mU/L as the value for the end point of the lower range of normal on the definitive test. Inspection of the auxological data of the 21 children with maximum GH responses between 16 and 19.9 mU/L during an ITT, suggested that this was unlikely - their mean height SDS was the same as that of children with GH levels exceeding 20 mU/L.
V. VIII). One of these children has had a consistently normal height velocity and therefore cannot be regarded as having severe biological GHD (see page 14). 

Twenty-five children have been considered to have partial biochemical GHD; their maximum GH responses never exceeded 15.9 mU/L. Five had a normal height velocity, auxological findings which were inconsistent with a diagnosis of partial biological GHD (see page 14). 

Major organic pathology was present in five of the remaining 18 children found to have low GH levels during screening. The former children have been indicated in the flow charts by a © and also included in Appendix Table 6. The child with acute lymphatic leukemia had a GH level of 4.8 mU/L after exercise; he relapsed and died before investigations could be arranged. One girl was found during the survey to be a Turner mosaic, which was probably an adequate explanation for her short stature, as her GH (10.4 mU/L following exercise) had been high enough to exclude severe GHD. One child had suffered a non-accidental injury and nutritional rickets as an infant and had a low height velocity; her maximum GH level was only 9.6 mU/L and GHD cannot be excluded with certainty, although there was no evidence that she was currently suffering from psychosocial deprivation. A boy with a moderate scoliosis had a GH level of 15.2 mU/L following exercise; he moved to another part of Scotland before a definitive test could be arranged. The final subject, a boy with glycogen storage disease, was screened for GHD before the underlying diagnosis was clear.

Of the other thirteen children with low GH levels during screening/
screening, one emigrated to the USA, and another with a GH level of 17.8 mU/l probably had genetic short stature. The parents of the other eleven children refused permission for an ITT. Seven of these children had small parents and hence a possible diagnosis of simple genetic short stature. One had been small-for-dates at birth. This group of 13 children, along with the other child already mentioned whose previous investigations had not excluded partial GHD (page 128) have been regarded as having a diagnosis of "possible GHD".

Seven diagnostic groups have thus been defined:

(I) Non-responders without an organic basis for short stature (77).
(II) Organic short stature (excluding GHD) (82).
(III) Severe biochemical GHD (13).
(IV) Partial biochemical GHD (25).
(V) Possible GHD (14).
(VI) Constitutional short stature (212)
(VII) ?Organic short stature (26)

Group I (Flow Chart III) includes the 16 children who were never remeasured (7 emigrated, 9 in Aberdeen) and 61 who were, but in whom organic pathology was absent. Group II includes all children whose diagnoses have been tabulated in Appendix Tables 3 and 5, and all except the four with severe GHD listed in Appendix Table 4.

The children with constitutional short stature (Group VI) also include the six children who had previously been investigated for GHD and found to be normal, but exclude the 21 in whom organic factors may have contributed to their short stature (see page 136). These/
These children and the five other children with organic pathology who had low GH levels during the screening test have been allocated to Group VII. It is also possible to extract from Group VI 34 whose reported birth weights for gestational age and maternal height (Tanner and Thomson, 1970) were less than the fifth centile (Group VI B).

AUXOLOGICAL CHARACTERISTICS OF VARIOUS DIAGNOSTIC GROUPS

The detailed auxological findings are contained in Appendix Tables 7 to 22 (pages 262-279). Whilst extensive information is available for children in diagnostic Groups III to VII, less is known about those in Group I and II.

It should be noted that sitting heights have not been examined in detail in this analysis. None of the constitutionally short children, or those with GHD, had abnormal sitting height/stature ratios.

Group I - Non-Responders without an Organic Basis for Short Stature

The mean height SDS of this group (-2.73 ± 0.33 SD) was similar to that of children with constitutional short stature (Appendix Tables 7 - 8). 86% had a height greater than -3 SDS, which was in sharp contrast to the children with organic short stature and GHD. Only one child had a height less than -4 SDS: her height velocity was normal (excluding biological GHD) but her height SDS suggests that she could well have had other organic pathology.

The height velocity (chronological age based) of the non-responding group (Appendix Table 10) was significantly higher than that/
that of the group with constitutional short stature (test for trend; $c = 2.95$, $p = 0.003$). One could perhaps speculate that one of the reasons parents declined to participate in the study, was that they were conscious of the fact that although their child was small, he had been growing normally.

**Group II - Organic Short Stature**

This group, not surprisingly, had the lowest mean height SDS of any in the study (mean $-3.50 \pm 0.89$) (Appendix Tables 7, 8). 62% were more than 3 SDS below the mean height for their age compared with only 16% of children with constitutional short stature.

A variety of abnormalities was found. The diagnoses of all children with probable organic short stature (excluding those with GHD, but including those in diagnostic Group VII) have been listed in Appendix Table 22. From this it is clear that the most common organic condition associated with short stature in the study was Down's Syndrome, which was present in 3.3% of all children. Spina Bifida was almost as common.

**Group III - Severe Biochemical GHD**

**Stature** (Appendix Tables 7, 8). The thirteen children with maximum GH levels under 10 mU/L are particularly interesting. Considered as a group, their mean height SDS ($-3.39 \pm 0.78$) was significantly less than that of children with constitutional short stature ($'t' = 5.76$, d.f. = 189, $p < 0.001$). Although 54% were less than $-3$ SDS, there was nevertheless considerable overlap between them and children with constitutional short stature. Indeed, the girls/
girls with severe GHD were no smaller (mean height SDS -2.69 ± 0.16) than those with either constitutional short stature (-2.81 ± 0.33) or LBW short stature (-2.77 ± 0.35). The girls with severe GHD were significantly taller than the boys (mean -3.83 ± 0.68) (Mann Whitney U test, p = 0.001). None were more than 3 SDS below the mean, a finding with potentially important implications.

Height SDS has also been calculated in relation to bone age (SDS_{BA}), where this was available. The height SDS_{BA} of children in the two groups was again significantly different ('t' = -2.11, d.f. = 184, p < 0.05), but it should be noted that this measurement was unavailable for three of the children with severe GHD. The difference may have been accentuated if it had been available.

**Height Velocity** (Appendix Tables 10, 11). Both measurements were available for only nine children in the group - four of them girls. It is nevertheless clear that height velocities were skewed markedly downwards in the severely deficient children. One girl had a height velocity in excess of the 25th centile, which was inconsistent with a diagnosis of biological GHD. Nevertheless, she has failed to produce GH levels greater than 9 mU/L on three separate occasions. Eight - 89% - had a height velocity in relation to chronological age of less than the 25th centile, compared to only 61% of those with constitutional or LBW short stature (test for trend; c = -3.25, p = 0.004). Similar differences in the height velocity SDS for bone age also existed between the two groups (test for trend; c = 4.29, p < 0.001). There were no clear cut sex differences in height velocity, whether this was based upon chronological or bone age. Sixty-two children/
children with constitutional short stature have been excluded from
this comparative analysis either because the interval between
measurements was less than 0.875 years (47) or because height
velocity was not distributed normally at their bone age (15).

**Bone Age** (Appendix Table 12). This was only available on ten
of the severely deficient children (mean -1.87 SDS + 0.95). Although
six (60%) had a bone age SDS of less than -2, the bone ages of 41%
of children with constitutional short stature were retarded to the
same extent (mean -1.75 + 1.00). (test for trend; c = -0.24, n.s.).

**Triceps Skinfold Thickness** (Appendix Table 13). The skinfold
thickness measurements of children with severe GHD were significantly
higher than children who were constitutionally short (test for trend;
c = 2.55, p = 0.01). 85% were above the 25th centile, compared to
only 54% of children with constitutional short stature.

Subscapular skinfold measurements have not been analysed.

**Upper Arm Circumference** (Appendix Table 14). No significant
differences were found between children with severe GHD and those
with constitutional short stature. 85% of children in both groups
had a value less than the mean.

**Upper Arm Muscle Circumference** (Appendix Table 15). Upper
arm muscle circumference measurements were significantly less in
children with severe GHD compared to those with constitutional short
stature (test for trend; c = 2.44, p = 0.015). Indeed, 69% of
children with severe GHD had an upper arm muscle circumference which
was less than 90% of the mean, compared to only 30% of children with
constitutional or Lbw short stature.

Head/
Head Circumference (Appendix Table 16). The mean head circumference of the twelve children in whom it was recorded (-0.60 SDS ± 0.96) was marginally higher than in children with constitutional short stature ('t' = 1.75, d.f. = 188, 0.05 < p < 0.1); it was significantly higher than the mean (-1.29 ± 0.86) in children with LBW short stature ('t' = -2.32, d.f. = 43, p < 0.05).

Mothers' Heights (Appendix Table 17). The height of 89% of the mothers of all children in the study were measured. The mean height SDS (-1.44 ± 1.54) of the mothers of the severely deficient children was greater than the children with constitutional or LBW short stature (-1.83 ± 0.85), but the differences failed to reach significance ('t' = -1.51, d.f. = 214, 0.1 < p < 0.2). This is not altogether unexpected as the mother of one of the deficient boys probably had GHD herself (height 133 cms. - GH undetectable on an extended GTT).

Fathers' Heights (Appendix Table 18). The heights of 74% of the fathers in the survey were estimated by mothers, and accordingly they should be treated with some suspicion. The fathers of the severely GHD children were the tallest (mean SDS -1.25 ± 1.26) of any in the study, but the difference between them and children in Group VI did not reach statistical significance ('t' = -1.17, d.f. = 177, n.s.).

Midparent Heights (Appendix Table 19). These results should likewise be regarded with some suspicion. The estimated midparent heights of the severely GHD children (mean SDS -1.23 ± 1.26) were not significantly greater than the children with constitutional or LBW short/
short stature (mean SDS -1.52 ± 0.78) ('t' = 1.24, d.f. = 207, n.s.).

When midparent height was allowed for (Appendix Table 20) the stature of seven (54%) severely deficient children was more than 3 SD below the mean height - a much greater proportion than the 6% of children in Group VI (test for trend; c = 4.85, p < 0.001).

The auxological characteristics of children with severe GHD and constitutional or LBW short stature have been summarised in Table 9 (see page 145).

**Group IV - Partial GHD**

Twenty-five children (17 boys) had biochemical evidence consistent with a diagnosis of partial GHD. Auxologically they occupied a position midway between children with severe GHD and those with constitutional short stature. In some cases they were indistinguishable from the latter group of children.

Their mean height SDS<sub>AUX</sub> (-2.95 ± 0.36) (Appendix Table 8) was significantly less ('t' = 2.52, d.f. = 201, p < 0.02) than the group with the constitutional short stature (-2.77 ± 0.33). Height SDS<sub>Ba</sub> (Appendix Table 9) was however significantly higher than that of children with constitutional short stature ('t' = 2.00, d.f. = 196, p < 0.05).

After parents' height has been allowed for (Appendix Table 20) the partially deficient children were significantly taller than those with severe deficiency (test for trend; c = 2.69, p = 0.007), and comparable to the constitutionally short and LBW children (test for trend; c = 1.15, n.s.).

The height velocity percentile distribution (chronological age based)/
<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>SEVERE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>SIGNIFICANCE LEVEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height SDS&lt;sub&gt;AUX&lt;/sub&gt;</td>
<td>-3.39 ± 0.78</td>
<td>-2.77 ± 0.33</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>&quot; boys</td>
<td>-3.83 ± 0.68</td>
<td>-2.73 ± 0.32</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>&quot; girls</td>
<td>-2.69 ± 0.46</td>
<td>-2.81 ± 0.33</td>
<td>n.s.</td>
</tr>
<tr>
<td>Height SDS&lt;sub&gt;BA&lt;/sub&gt;</td>
<td>-1.51 ± 1.30</td>
<td>-1.02 ± 1.08</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Height SDS&lt;sub&gt;AUX&lt;/sub&gt; corrected for parents' height &lt; -3 SDS</td>
<td>54%</td>
<td>8%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Height velocity SDS&lt;sub&gt;BA&lt;/sub&gt; &lt; -2</td>
<td>67%</td>
<td>15%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Bone Age SDS &lt; -2</td>
<td>60%</td>
<td>41%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Triceps skinfold thickness &gt; 25th centile</td>
<td>85%</td>
<td>54%</td>
<td>p = 0.01</td>
</tr>
<tr>
<td>Upper arm muscle circumference ≤ 90% of mean</td>
<td>69%</td>
<td>30%</td>
<td>p = 0.015</td>
</tr>
<tr>
<td>Head circumference SDS</td>
<td>-0.60 ± 0.96</td>
<td>-1.17 ± 1.10</td>
<td>0.05 &lt; p &lt; 0.1</td>
</tr>
<tr>
<td>Mothers' height SDS</td>
<td>-1.44 ± 1.54</td>
<td>-1.83 ± 0.85</td>
<td>n.s.</td>
</tr>
<tr>
<td>&quot;Fathers' height&quot; SDS</td>
<td>-1.25 ± 1.23</td>
<td>-1.65 ± 1.26</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
based) of the partially deficient group was markedly skewed towards the lower end of the range and did not differ significantly from those with severe GHD (test for trend; c = 0.82, n.s.), although it was considerably different from those with constitutional or LBW short stature (test for trend; c = -3.38, p = 0.0009).

Height velocity based on bone age (Appendix Table 11) was also not significantly different from children with severe deficiency (test for trend; c = 1.50, p = 0.13). The height velocity of both groups combined was significantly less than children in Group VI (test for trend; c = 4.88, p < 0.0001).

The bone ages of those with partial GHD (Appendix Table 12) were significantly more retarded than children with constitutional short stature (p<0.05) although there was clearly a considerable overlap between the two groups. Again, there was no significant difference between the severe and partially deficient groups (test for trend; c = 0.88, n.s.).

Triceps skinfold thickness measurements (Appendix Table 13) tended to be lower in those with partial GHD than in those with severe deficiency (test for trend; c = 1.78, p = 0.07) and did not differ significantly from those with constitutional short stature (test for trend; c = 0.13, n.s.).

Their upper arm muscle circumference measurements (Appendix Table 15) tended to be midway between those with severe GHD (test for trend; c = 1.34, n.s.) and constitutional short stature (test for trend; c = 1.15, n.s.).

There was no statistically significant difference between them and/
and those with constitutional or LBW short stature in the distribution of upper arm circumference (Appendix Table 14), head circumference (Appendix Table 16), maternal, paternal or midparent heights (Appendix Table 17 - 19).

**Group V - Possible GHD**

These children were virtually indistinguishable from those with constitutional or LBW short stature. They did have a lower height velocity which was only to be expected, since all children with a normal height velocity had by definition been excluded from this group and included in Group VI. There was a suggestion that the parents may have been a little taller, but not significantly so (Appendix Table 17).

**Group VI - Constitutional Short Stature**

Thirty-four of the 212 children in this group (Group VI B) had birth weights, as recalled by their parents, of less than the fifth centile when maternal height and gestational age were taken into consideration (Tanner and Thomson, 1970). In spite of this the children in Groups VI A and VI B, with one exception, did not differ significantly from each other. The one exception noted was a significantly higher proportion of boys with low birth weight - sex ratio 2.4 (Binomial test; p = 0.02).

The triceps skinfold measurements of the LBW group (Appendix Table 13) tended to be lower than those with constitutional short stature, although the differences failed to reach significance (test for trend; c = 1.59, p = 0.11). These measurements also differed significantly with increasing degrees of social disadvantage - as measured/
measured by the disadvantage score (Appendix Table 21). Only 34% of those with a score of 0 had skinfold thickness measurements of less than the 25th centile compared with 55% of those with a score of 3 (test for trend; \( c = 2.15, p = 0.03 \)).

Other auxological characteristics of these two groups of children have been extensively covered in earlier sections, and the differences that were present between them and children with severe GHD were summarised in Table 9. All except 11 of the children with constitutional short stature (Group VI A) could be regarded as examples of what Tanner has termed "short/delay" (Table 10).

<table>
<thead>
<tr>
<th>TABLE 10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FEATURES OF CHILDREN WITH CONSTITUTIONAL AND LOW BIRTH WEIGHT SHORT STATURE</strong></td>
</tr>
<tr>
<td><strong>Height with normal range when parents' height allowed for:</strong></td>
</tr>
<tr>
<td>&quot;Genetic&quot; short stature.</td>
</tr>
<tr>
<td><strong>Growth delay - normal</strong></td>
</tr>
<tr>
<td>(bone age retarded 1-2 years)</td>
</tr>
<tr>
<td><strong>Growth delay - abnormal</strong></td>
</tr>
<tr>
<td>(bone age retarded more than 2 years)</td>
</tr>
<tr>
<td><strong>Low birth weight</strong></td>
</tr>
<tr>
<td><strong>None of the above</strong></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
</tr>
</tbody>
</table>

**Group VII - Organic Short Stature**

The auxological findings in these 26 children, 18 of whom were boys, warrants their being considered separately from other children who were investigated in the study and in whom GHD was excluded.

Their/
Their mean height $SDS_{AUX} (-3.15 \pm 0.75)$ (Appendix Table 8) was significantly less than the children with constitutional short stature ($t^* = 4.46$, d.f. = 282, $p < 0.001$). Indeed, 50% were less than $-3$ SDS (Appendix Table 7). The sex ratio in the group (2.25) was also different from the children in Group VI A, and similar to that observed in children with low birth weight, (Binomial test; $p = 0.05$). Their mean height SDS in relation to bone age was midway between children with severe GHD and constitutional short stature (Appendix Table 9). When height SDS was corrected for mid-parental height (Appendix Table 20), a significantly higher proportion - 31% - were below $-3$ SDS compared with the constitutionally short group - 8% - (test for trend; $c = 3.56$, $p = 0.0005$).

The height velocity percentile distribution (Appendix Table 10) also differed significantly from children with constitutional short stature (test for trend; $c = 2.28$, $p = 0.02$) as did height velocity in relation to bone age (Appendix Table 11) (test for trend; $c = 2.31$, $p = 0.02$). In both instances, the children in whom organic illness was present were growing more slowly. It should however be noted that twelve month height velocities were not available for 46% of the children in this group.

Other auxological findings were similar to those of children in Group VI.
BIOLOGICAL AND SOCIAL CHARACTERISTICS OF CHILDREN IN DIFFERENT DIAGNOSTIC GROUPS

None of this information was available for the children of parents who were not interviewed, and hence no details are available for any of the children in diagnostic Group I. In addition, only 45% of the parents of children with organic short stature (Group II) were interviewed. Only six parents in the remaining five groups have not completed the interview - all of them being in Group VI. The main objective of this section has been to draw attention to the ways in which children with severe GHD (Group III) differ from those with constitutional or LBW short stature (Group VI). Some comments have also been made about the features found in the other four groups (II, IV, V and VII).

Age Distribution. The age distribution was similar in all diagnostic groups, and ranged from 6.03 to 9.36 years at the time of the initial height screening.

Pregnancy Number (Appendix Table 23). Children with severe GHD were born significantly earlier in the birth order than those with constitutional short stature (test for trend; c = 2.54, p = 0.01). Indeed, 38% of the former group were the outcome of the first pregnancy compared to only 16% of children with constitutional short stature. Those whose short stature was secondary to other organic pathology also tended to be the outcome of earlier pregnancies compared to those with constitutional or LBW short stature (test for trend; c = 1.80, p = 0.07). The characteristics of the children with partial GHD were similar to those with constitutional and LBW short/
short stature.

**Age of Mother at Birth of First Child** (Appendix Table 24). The age distribution of mothers at the birth of their first child was similar in the group of children with severe GHD to those with constitutional short stature (test for trend; $c = 0.13$, n.s.). Mothers of children with organic or probable organic short stature (Groups II and VII) were significantly older than the latter group (test for trend; $c = 2.94$, $p = 0.003$).

**Age of Mother at Birth of Index Child** (Appendix Table 25). The mothers of children with severe GHD were significantly younger at the birth of the index child compared to mothers of children with constitutional or LBW short stature (test for trend; $c = 2.97$, $p = 0.003$). Two thirds were aged under twenty - only 21% of the mothers of constitutionally short children were as young as this. The mothers of those with organic short stature were the oldest in the study; 21% were aged over 36 at the birth of their affected child - twice as many as the mothers of the constitutionally short children (test for trend; $c = 2.41$, $p = 0.02$).

**Smoking in Pregnancy** (Appendix Table 26). The mothers of the children with possible GHD were more likely to have smoked during pregnancy than those whose children had severe GHD (Fisher's exact test; $p = 0.03$). Apart from reflecting the different social characteristics of the two groups this seems unlikely to have any other significance. Although a slightly lower percentage of the mothers (42%) of the group with severe GHD hadn't smoked during pregnancy, the proportion was not significantly different ($x^2 = 1.04$, n.s.) from/
from that found - 61% - in the constitutionally short group.

Complications in Pregnancy (Appendix Table 27). Over twice as many mothers (69%) of the severely GHD children had an abnormal pregnancy compared to those whose children were constitutionally short - 32% ($X^2 = 5.88, p < 0.02$). The proportions in the mothers of those with partial or possible GHD were comparable to the constitutionally short group, as were those with an organic condition associated with their short stature.

Birth (Appendix Tables 28, 29). Abnormal deliveries had been more common in children with severe GHD - 42% - compared with the constitutionally short children - 15% ($X^2 = 3.97, p < 0.05$). Some interviewees (e.g. fathers or guardians) were unable to supply information about the circumstances of the child's birth; had their responses been distributed unfavourably, the differences between the groups would have fallen just short of statistical significance ($X^2 = 2.87, p < 0.1$). The group of children with a clear organic cause for their short stature (Group II) had, not unexpectedly, a much higher proportion of abnormal births than any other group (54%). Those with possible organic short stature (in whom the underlying pathology often developed sometime after birth) had a birth history comparable to the children with constitutional or LBW short stature. The proportions of breech or other abnormally presenting births (Appendix Table 29) did not differ significantly in any of the diagnostic groups.

Gestational Age (Appendix Table 30). The gestational age of children with severe GHD did not differ significantly from those with
with constitutional short stature. When considered together, however, children with severe and partial GHD appear to have had a significantly higher incidence of postmaturity, as reported by their parents - 29% - than the latter group - 11% ($x^2 = 6.65, p < 0.01$). Although there was a tendency for children with organic short stature to be born prematurely - 27% were born before 39 weeks gestation - this was not significantly different from either the group with constitutional-LBW short stature - 17% (test for trend; $c = 1.80$, $p = 0.07$), or severe GHD - 15%.

**Birth Weight** (Appendix Table 31). No less than 25% of children in the study, whose parents were interviewed, weighed less than 2.5 kg at birth (Figures v and vi). The mean birth weight ($3,238 \pm 613$ gms) of those with severe GHD was significantly higher than those with constitutional short stature ($2,861 \pm 518$ gms) ($t' = 2.51$, d.f. = 209, $p = 0.02$).

**Neonatal Morbidity** (Appendix Tables 32-34). 54% of the children with GHD were reported to have been kept in the nursery for longer than 24 hours after birth compared to only 30% of those who were constitutionally short (Appendix Table 32). This difference nevertheless failed to reach significance ($x^2 = 2.11, p < 0.2$). As one would have expected, over three quarters of the children with organic short stature (Group II) had a prolonged stay in the neonatal nursery.

As one would have expected, 72% of the mothers of children with organic short stature had been worried about their children in infancy (Appendix Table 33) - a much higher proportion than in any other/
Figure v

Birth Weight corrected for Maternal Height (Boys)

- Severe biochemical GHD
- Partial biochemical GHD
- Possible GHD
- Possible GHD (low birth weight)
- Constitutional short stature
- LBW short stature
- Organic short stature
Figure vi

Birth Weight Corrected for Maternal Height (girls)

(See Figure v for key to symbols)
other group ($x^2 = 25.34, p<0.001$).

Feeding difficulties in infancy (Appendix Table 34) were reported twice as often in children with severe GHD - 46% - as in those with constitutional short stature - 21% - although these differences fell short of statistical significance ($x^2 = 3.26, p<0.4$).

Social Characteristics

Family Size (Appendix Table 35). None of the children with severe GHD came from families containing more than five children, whereas 28% of those who were constitutionally short came from families containing six or more children (test for trend; $c = 2.67, p = 0.007$). Children with organic short stature also tended to belong to smaller families than children in the latter group (test for trend; $c = 3.19, p = 0.001$).

Social Class (Appendix Table 36). The social class distribution of the organic group again differed from those with constitutional short stature, as it included significantly fewer unemployed parents at the time of the study (test for trend; $c = 2.82, p = 0.005$).

Supplementary Benefit (Appendix Table 37). Although not as many parents of children with severe GHD had received Supplementary Benefit - 38% - as the parents of the constitutionally short not children - 59% - the difference was statistically significant.

Overcrowding (Appendix Table 38). Children with severe GHD lived in much less overcrowded circumstances than those with constitutional short stature. Indeed, 62% lived at a density of less than/
than one person per room, compared with only 16% of children in the latter group (test for trend; \( c = 3.57, p = 0.0005 \)). Similar differences also existed between the latter group and those with organic short stature (test for trend; \( c = 3.10, p = 0.002 \)).

**Social Disadvantage Score** (Appendix Table 39). A number of separate measures of social disadvantage have been combined (see page 107) to produce a disadvantage score. Those with organic short stature were significantly less disadvantaged than those who were constitutionally short (test for trend; \( c = 3.35, p = 0.0005 \)). 30% of the organic groups (Groups II and VII) had no stigmata of disadvantage compared with only 16% of those with constitutional or LBW short stature. Children with severe GHD were also significantly less disadvantaged than the latter group (test for trend; \( c = 1.93, p = 0.05 \)). Those with partial GHD were indistinguishable from the constitutionally short children.

**Subjective Assessment of Interviewee's Intelligence** (Appendix Table 40). The subjective assessment of the interviewee's intelligence - usually the mother - did not discriminate between different diagnostic groups. Although the proportions of low scoring parents (that is seemingly of low intelligence), in the groups with constitutional short stature, partial and possible GHD (25%, 24% and 21% respectively) were higher than in other groups, the difference was not statistically significant.

Table 11 summarises the biological and social differences between children with severe GHD and constitutional short stature.

It/
### TABLE 11

**Biological and Social Characteristics of Children With Severe GHD and Constitutional Short Stature**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Severe GHD</th>
<th>Constitutional Short Stature</th>
<th>Significance Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>First pregnancy</td>
<td>39%</td>
<td>16%</td>
<td>( p = 0.01 )</td>
</tr>
<tr>
<td>Age &lt; 20 at birth of first child</td>
<td>67%</td>
<td>56%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Age &lt; 20 at birth of index child</td>
<td>67%</td>
<td>21%</td>
<td>( p = 0.093 )</td>
</tr>
<tr>
<td>Smoked in pregnancy</td>
<td>42%</td>
<td>61%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Abnormal pregnancy</td>
<td>69%</td>
<td>32%</td>
<td>( p &lt; 0.02 )</td>
</tr>
<tr>
<td>Abnormal delivery</td>
<td>42%</td>
<td>15%</td>
<td>( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Postmature (&lt; 42 weeks)</td>
<td>31%</td>
<td>11%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean birth weight</td>
<td>3238 ± 613gm</td>
<td>2861 ± 518gm</td>
<td>( p = 0.02 )</td>
</tr>
<tr>
<td>Kept in nursery &gt; 24 hours after birth</td>
<td>54%</td>
<td>30%</td>
<td>( p &lt; 0.2 )</td>
</tr>
<tr>
<td>&quot;Worried&quot; about index child in infancy</td>
<td>38%</td>
<td>27%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Early feeding difficulties</td>
<td>46%</td>
<td>21%</td>
<td>( p &lt; 0.1 )</td>
</tr>
<tr>
<td>Mean family size</td>
<td>3.23 ± 1.48</td>
<td>4.67 ± 1.98</td>
<td>( p = 0.007 )</td>
</tr>
<tr>
<td>Unemployed</td>
<td>23%</td>
<td>32%</td>
<td>n.s.</td>
</tr>
<tr>
<td>No father figure</td>
<td>23%</td>
<td>15%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Less than one person per room</td>
<td>62%</td>
<td>16%</td>
<td>( p = 0.0005 )</td>
</tr>
<tr>
<td>Not disadvantaged</td>
<td>38%</td>
<td>16%</td>
<td>( p = 0.05 )</td>
</tr>
</tbody>
</table>
It is evident that the social and biological characteristics of children with partial biochemical GHD were virtually indistinguishable from those with constitutional or LBW short stature. In contrast, those with organic short stature, whether this was a result of GHD or other organic causes, tended to differ both biologically and socially. The time of birth was surrounded by more complications in both groups and social disadvantage was not present to anywhere near the same extent as in children with constitutional and LBW short stature.

GROWTH HORMONE INVESTIGATIONS

The broad outline of the GH results has already been sketched (see page 124), but a few other details not mentioned at that time remain to be added. Only one child (with hypothyroidism) was not euthyroid when investigations were done (Appendix Table 6), and her GH response to exercise was normal.

Exercise Test

It is evident (Figure vii) that the timing of blood sampling in relation to the start of exercise was a crucial factor in determining its effectiveness as a screening test for GHD. Only two (4.5%) of 44 children had normal GH levels when blood was collected 30 minutes from the end of exercise, compared with 55.5% when blood was sampled 30 minutes from its start. In the latter case the actual duration of exercise does not appear to have been critical (Appendix Table 41). The responses were similar in boys and girls (Appendix Table 42) and at the various ages of children in the study (Appendix Table 43).

Comparison/
GH RESPONSE FOLLOWING EXERCISE □ and MODIFIED EXERCISE ■

Figure vii
Comparison of GH Responses Following Exercise and During ITT

The comparison of the GH responses following exercise and during ITT has been illustrated in Figure viii. Although some children clearly had a better GH response following exercise than during an ITT, exercise was nevertheless far from perfect as a screening test for severe GHD (Table 12). Although the exercise

<table>
<thead>
<tr>
<th>GH RESPONSE</th>
<th>NUMBER</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise GH &gt; 10 mU/L</td>
<td>184</td>
<td>81.1%</td>
</tr>
<tr>
<td>Exercise GH &lt; 10 mU/L and ITT GH &gt; 16 mU/L</td>
<td>19</td>
<td>8.4%</td>
</tr>
<tr>
<td>Exercise GH &lt; 10 mU/L and ITT GH &lt; 16 mU/L</td>
<td>8</td>
<td>3.5%</td>
</tr>
<tr>
<td>Exercise GH &lt; 10 mU/L and height velocity normal</td>
<td>2</td>
<td>0.9%</td>
</tr>
<tr>
<td>Exercise GH &lt; 10 mU/L and ITT GH &lt; 10 mU/L</td>
<td>6</td>
<td>2.6%</td>
</tr>
<tr>
<td>Exercise GH &lt; 10 mU/L but final status uncertain</td>
<td>8</td>
<td>(3.5%)</td>
</tr>
</tbody>
</table>

response excluded severe GHD in 184 (81.1%) of 227 subjects tested, GHD was subsequently excluded in a further 21 of the 43 subjects in whom the GH level on exercise was less than 10 mU/L, by either a normal height velocity or a normal GH response during an ITT.
Figure viii

(See figure v for key to symbols)

(Severe GHD shown here by ●)
As a screening test for partial GHD, exercise was far less satisfactory (Table 13). Although it excluded partial GHD in 51.5% of the subjects tested, no less than 61.8% of those with an exercise GH response of less than 18 mU/L had either a normal height velocity or a normal GH response (greater than 16 mU/L) during insulin hypoglycaemia.

**TABLE 13**

**Exercise as a Screening Test for Partial GHD**

N = 227

<table>
<thead>
<tr>
<th>GH Response</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise GH ≥ 18 mU/L</td>
<td>117</td>
<td>51.5%</td>
</tr>
<tr>
<td>Exercise GH &lt; 17.9 mU/L and ITT GH ≥ 16 mU/L</td>
<td>46</td>
<td>20.3%</td>
</tr>
<tr>
<td>Exercise GH &lt; 17.9 mU/L and ITT GH &lt; 15.9 mU/L</td>
<td>27</td>
<td>11.9%</td>
</tr>
<tr>
<td>Exercise GH &lt; 17.9 mU/L and height velocity normal</td>
<td>22</td>
<td>9.7%</td>
</tr>
<tr>
<td>Exercise GH &lt; 17.9 mU/L and final status uncertain</td>
<td>15</td>
<td>6.6%</td>
</tr>
</tbody>
</table>

**Relationship Between Maximum GH Response During ITT and Height Velocity**

As has been noted previously (Tanner et al, 1971), there was a significant association between height velocity and maximum GH response during a satisfactorily performed ITT. (Appendix Table 44). The mean maximum GH during an ITT of children with a height velocity of less than the third centile (13.9 ± 8.5 mU/L) was significantly lower/
lower than that of those with a normal (i.e. greater than 25th
centile) height velocity \((21.2 \pm 10.1 \text{ mU/L})\). \((t' = 2.12, \text{ d.f.} = 27,\p = 0.05)\).

**Reproducibility of GH Response During ITT**

Insulin tolerance tests were repeated in ten children (Figure ix) after an interval of six to nine months. All except one were
moderately or severely disadvantaged by the criteria used in the
study. In all, the initial responses had been at the upper end of the
severely deficient range or consistent with a diagnosis of partial
GHD. In seven, a high fasting GH level (greater than 2 mU/L) had
been present during the initial ITT. No less than six of the repeat
tests were normal - these children henceforth being regarded as
examples of constitutional short stature - in spite of the fact
that in four, high fasting GH levels were also present on the
second occasion. Both tests were done in an identical manner, and
on no occasion had any measure been taken to improve the child's
home environment. Others (e.g. Joss, 1975) have also noted that
some children with constitutional short stature may respond differ¬
ently to repeated insulin tolerance tests, and have suggested that
the presence of high fasting serum GH levels when insulin is
injected, has been partly responsible (see page 67). The results
of this study (Appendix Table 45) have confirmed that there is a
much greater likelihood of achieving a normal GH response during
insulin hypoglycaemia when fasting GH levels are less than 2 mU/L
\((X^2_1 = 6.35, \ p < 0.02)\).
CORRELATION BETWEEN REPEATED I.T.T.'s

Figure ix

(See Figure v for key to symbols)

(Severe GHD shown here by •)
PREVALENCE OF SEVERE GH DEFICIENCY

Thirteen children, including four previously diagnosed cases, have been found in the study with severe biochemical GHD (Vimpani et al, 1977). A summary of the auxological and biochemical findings in individual children is contained in Appendix Table 46, but that for the group as a whole has been presented earlier. Three children (024, 211, 234) had short stature which could have been accounted for on genetic grounds, since their heights fell within the normal range when midparental height was taken into account; one (211) also had a sibling in the study (Appendix Table 47) who was originally thought to have also had severe GHD, but in whom a repeat ITT was normal. Another child (234) had a normal bone age, and another (024) a normal height velocity, and has not therefore been considered as having severe biological GHD. Only one child (426) had a poor ACTH response to insulin hypoglycaemia and therefore probably has multiple pituitary deficiency. There was no evidence that any of the other cases had multiple deficiency or intracranial disease, although skull X-rays have not yet been done in all. All children were therefore probably examples of "idiopathic" GHD.

Deprivation may have been partially responsible for the depressed GH responses in several children. Although only one child was severely disadvantaged, there was a significant correlation within the severely deficient group (Spearman Rₜ = 0.62, p < 0.05) between the maximum GH response and the degree of disadvantage (Appendix Table 46) - those with the higher GH levels being more disadvantaged than those with more severe degree of deficiency. Some/
Some of the more disadvantaged children were indeed those (024, 211, 234) in whom an explanation other than GHD may have accounted for their short stature. There is no reason however to suppose that GHD cannot co-exist with social disadvantage, and the response to a therapeutic trial with GH would seem to be the only satisfactory way of confirming the diagnosis of severe biological GHD in those with severe biochemical deficiency who are growing poorly.

As centres disagree about the maximum GH levels consistent with the diagnosis of severe GHD, the prevalence of severe deficiency has been calculated for various maximum GH levels of between 6 and 10 mU/L (Table 14). In this population the prevalence of severe biochemical GHD was between 14.5 and 27.0 cases per 100,000. If the three children whose short stature may have been genetic in origin are excluded from the calculation, the prevalence is between 14.5 and 20.7 per 100,000 (95% confidence limits for the latter being 9.9 to 38.1 per 100,000) i.e. between one/6,890 and one/4,822 individuals.

The final diagnosis of the 25 children with partial biochemical GHD is still uncertain. All come from Glasgow, and were as socially disadvantaged as children in that city with a diagnosis of constitutional short stature (Appendix Table 39). Several were growing normally, and doubt about the reproducibility of the GH responses during insulin hypoglycaemia in some of those who have had two ITT's (see page 164) seems adequate justification for the present intention to repeat ITT's in all whose height velocities continue to be below normal. In addition, two have constitutionally short siblings in the study (Appendix Table 47) which inevitably has cast some/
TABLE 14
PREVALENCE OF SEVERE GH DEFICIENCY

<table>
<thead>
<tr>
<th>MAXIMUM GH (mU/L)</th>
<th>TOTAL</th>
<th>SEX RATIO</th>
<th>MALE PREVALENCE</th>
<th>FEMALE PREVALENCE</th>
<th>TOTAL PREVALENCE PER 100,000</th>
<th>95% CONFIDENCE LIMITS FOR PREVALENCE PER 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;6</td>
<td>7</td>
<td>1.3</td>
<td>1/6168</td>
<td>1/7850</td>
<td>14.5</td>
<td>5.8 - 29.9</td>
</tr>
<tr>
<td>&lt;7</td>
<td>8</td>
<td>1.0</td>
<td>1/6168</td>
<td>1/5888</td>
<td>16.6</td>
<td>7.2 - 32.7</td>
</tr>
<tr>
<td>&lt;8</td>
<td>10</td>
<td>1.5</td>
<td>1/4112</td>
<td>1/5888</td>
<td>20.7</td>
<td>9.9 - 38.1</td>
</tr>
<tr>
<td>&lt;9</td>
<td>13*</td>
<td>1.6</td>
<td>1/3084</td>
<td>1/4710</td>
<td>27.0</td>
<td>14.4 - 46.2</td>
</tr>
</tbody>
</table>

* 1 normal height velocity

some suspicion upon their own diagnosis. Because of this, it is not yet possible to include cases with GH levels between 10 and 16 mU/L in an overall estimate of the prevalence of both severe and partial GHD.

REFERRAL PATTERNS OF CHILDREN WITH SHORT STATURE

Only four of the children found to have severe biological GHD had been previously diagnosed, as has already been noted. Of the six newly diagnosed cases in whom a genetic explanation for short stature could be excluded, the parents of five had consulted their general practitioners at some stage before this study, but none had been referred for further investigations. Indeed, the parents of two of the previously diagnosed cases reported that they had had to exert/
exert considerable pressure on their family doctors before a further opinion had been sought (Appendix Table 73). The parents of only one child had not been concerned about their child's short stature.

Questions 24-30 of the interview schedule were designed to explore this topic in more detail. Because this study has involved screening the whole of a geographically defined population of very short children, it has been possible to ascertain how widespread similar patterns of referral behaviour have been amongst the parents and general practitioners of short children, and to examine what other factors have been associated with them. This analysis has been restricted to children in diagnostic Groups III to VII.

Parental Concern About Study Child's Growth and Development
(Appendix Tables 48-61)

Only 44% of parents in diagnostic Groups III to VII had been concerned about their child's short stature (Appendix Table 48). Although the proportion of boys' parents who were concerned was slightly higher (45% cf. 40%), it was not significantly different from that in the girls. It was of some interest to find that the parents of children with severe and partial GHD (Appendix Table 49) admitted to being concerned significantly more often (61% cf. 40%) than the parents of children with constitutional or LBW short stature ($x^2 = 4.45, p < 0.05$). (The parents of children with organic short stature were also more concerned than those in the latter group.)

A number of other social and biological variables have been examined to see which, if any, were associated with parental concern. Firstly/
Firstly, there were no significant social class differences (Appendix Table 50). Secondly, although an apparent trend existed suggesting that there was an increased likelihood of concern with an increasing degree of short stature (Appendix Table 51), it was not significant (test for trend; c = 1.18, n.s.).

The parents were asked if they could remember their height as children (question 28). It is clear that a much higher proportion (77%) of the mothers of children with severe GHD (Appendix Table 52) considered that their heights had not been smaller than average as children, compared with the mothers of constitutionally short children (29%). It should be noted that even if the replies of the parents of the constitutionally short children who responded "Don't know" to this question (21) were distributed in the most unfavourable way (i.e. all as "no's") the differences would still have been statistically significant ($X^2 = 7.68, p < 0.01$).

It is evident (Appendix Table 53) that the mothers who considered themselves to have been of average height as children were concerned significantly more often - 55% of 37% - about their child's growth than the mothers who thought that they had been smaller than average as a child ($X^2 = 7.00, d.f. = 1, p < 0.01$). It is also clear (Appendix Table 54) that the mothers whose present height was normal (> -2 SDS) were concerned twice as often as abnormally small mothers ($X^2 = 21.6, p < 0.001$).

A slightly different picture was found in the case of fathers' heights. In any event some caution should be exercised in interpreting these results as two possible sources of error were present. Firstly, the/
the children's fathers were not often seen in the study, and the question about the father's height as a child was generally put to the mother; not surprisingly, a quarter of the mothers were unable to answer the question. Secondly, most of the fathers' present heights have been estimated by the mothers and not measured. Although a significantly higher proportion of the fathers of the children with organic short stature (excluding GHD) were not thought to have been small as children (76%) there was no significant difference between the fathers of children with GHD and those with constitutional or LBW short stature (Appendix Table 55). Where the interviewees were were able to offer an opinion (Appendix Table 56) about the father's height as a child, parental concern was expressed significantly less often when fathers were thought to have been small ($X^2 = 5.72, p < 0.02$). As previously noted with regard to the mothers, concern was also present significantly more often (test for trend; $c = 2.28, p = 0.02$) when the fathers' present heights were normal or allegedly normal (Appendix Table 57).

74% of all parents considered that the study child was smaller than other siblings (Appendix Table 58). Such parents were more likely to have been concerned (49% cf. 22%) about the child's growth (Appendix Table 59) than those who considered other children in the family to have been as small as the index child ($X^2 = 15.19, p < 0.001$).

Other variables such as the age of the mother at the time of the study (Appendix Table 60) and the child's preschool immunisation history (Appendix Table 61) were also examined, but there were no significant differences in the proportions of concerned parents in younger/
younger and older mothers, or in those who had or had not had their child immunised before starting school.

General Practitioner Consultations About Short Stature
(Appendix Tables 62-72)

Less than half of the parents in the study had been concerned about the index child's short stature. Only 20% had sought any medical advice (Appendix Table 62). The parents of children with severe GHD were more likely (69% cf. 18%) to have consulted their general practitioners than the parents of constitutional or LBW short stature ($X^2 = 14.16, p < 0.001$). There were small but insignificant sex (Appendix Table 63) and social class differences (Appendix Table 64) similar to those noted in the earlier question. The results in Appendix Table 65 suggest that there was no statistical evidence to support the hypothesis that the parents of the smallest children were more likely to have consulted their doctors than parents of relatively taller children in the study (test for trend; $c = 0.95$, n.s.).

Parental height was also an important factor linked with GP consultations. Mothers who considered themselves to have been small as children (Appendix Table 66) were far less likely to have consulted their doctors (17% cf. 29%) than those who did not think that they had been small ($X^2 = 5.00, p < 0.05$). In view of this, it was somewhat surprising to find that the mothers whose heights were normal at the time of the study (Appendix Table 67) had not consulted their GP's more frequently than the mothers who were abnormally small/
small \( (X^2 = 2.42, \ p < 0.1) \).

Bearing in mind the earlier caution (see page 170) about the interpretation of data based on fathers' heights, it was again clear on the available evidence, that there were significant differences between allegedly small and average-sized fathers. When fathers were considered to have been children of average height (Appendix Table 68) the family doctor had been consulted twice as frequently as when they were thought to have been small \( (X^2 = 9.74, \ p < 0.01) \). Similar differences existed between fathers who were reported to be of average or above average height as adults (Appendix Table 69) and those who were reportedly small (test for trend; \( c = 2.68, \ p = 0.007 \)).

General practitioners were three times more likely to have been consulted when the index child was the smallest in the family (Appendix Table 70) \( (X^2 = 7.66, \ p < 0.01) \).

The immunisation history of the child (Appendix Table 71) was not associated with significantly higher GP consultation rates, but the proportion of mothers aged less than 30 who had consulted their GP's was 29% - was almost twice as common as the proportion of mothers aged over 30 - 16% (Appendix Table 72) \( (X^2 = 5.78, \ p < 0.02) \).

**Reported Action Taken by General Practitioners** (Appendix Table 73)

The information about action taken by general practitioners was supplied by the parents, and it should perhaps be interpreted with some caution. Nevertheless, only a few general practitioners replied to the original letter sent to them in connection with the survey (Appendix 11), and one thus suspects that these reports were substantially/
substantially correct. Less than 30% of general practitioners approached by parents were said to have done more than offer reassurance. The action taken for children in each diagnostic group appears to have been similar, but the numbers were too small to allow adequate comparison. It is nevertheless clear that the experience of the parents of children with severe GHD was not substantially different from that of parents in other diagnostic groups.

**Age When Short Stature First Noted** (Appendix Table 74)

Only two thirds of the parents of the children with severe GHD had noticed that their child was small before starting school. Although this proportion was higher than amongst the parents of the constitutionally short children, it nevertheless does mean that in some cases the school entrance medical examination is vital for the early diagnosis of severe GHD.

Finally, it is also interesting to note that according to parental reports, children with GHD were perhaps more likely to be self conscious about their short stature than those with constitutional short stature (Appendix Table 75) who more often came from families where other members were of below average height. These differences however were not conclusive ($X^2 = 2.51, p < 0.2$).

**BIOLOGICAL AND SOCIAL CHARACTERISTICS OF CONSTITUTIONALLY SHORT CHILDREN AND CONTROLS IN EDINBURGH AND GLASGOW**

In this section, the results of the attempt to select controls will be described and after their age, sex and social class distribution has been compared with the study children who were regarded as/
as having constitutional or LBW short stature, selected biological and social characteristics will be compared between the various groups.

Matching

**Edinburgh.** An attempt was made to select controls for 42 short children. Matching was not possible in four, as children of an equivalent social class were not available (see page 103). All except six of the 38 controls selected agreed to participate in the study. Sixteen of the controls were boys. Subsequently twelve of the short children for whom controls were originally selected, were found to have an organic condition which probably contributed to their short stature, and they have accordingly been withdrawn from the study group. This, and the refusal of some of the controls to participate has lead to some mismatching of the short children (hereinafter referred to as "cases") and controls on a basis of sex (Table 15). Nevertheless the social class characteristics of the 30 cases and 32 controls were similar (Table 16). The parents of 28 of the Edinburgh cases had agreed to participate after receiving the original letter (Appendix 9) but two only agreed after receiving a home visit from a Health Visitor. All Edinburgh cases have been combined for the "case-control" comparisons.

**Glasgow.** Matching was only attempted for the first 147 constitutionally short children seen during the second phase of the study (see page 103). Matching was unsuccessful in 31: school medical cards were unavailable in 15 and no controls of the corresponding social class were available for another 16 - usually because the/
TABLE 15
SEX RATIO OF 'CASES' WITH CONSTITUTIONAL SHORT STATURE AND CONTROLS

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th></th>
<th>Edinburgh Cases</th>
<th>Edinburgh Controls</th>
<th>Glasgow Cases Group I</th>
<th>Glasgow Cases Group II</th>
<th>Total Glasgow Cases</th>
<th>Glasgow Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOYS</td>
<td>11</td>
<td>16</td>
<td>51</td>
<td>46</td>
<td>97</td>
<td>40</td>
</tr>
<tr>
<td>GIRLS</td>
<td>19</td>
<td>16</td>
<td>30</td>
<td>31</td>
<td>61</td>
<td>23</td>
</tr>
<tr>
<td>SEX RATIO</td>
<td>0.58</td>
<td>1.0</td>
<td>1.70</td>
<td>1.48</td>
<td>1.59</td>
<td>1.74</td>
</tr>
</tbody>
</table>

The short child was the only person in the class from a one-parent family, or a family where the father was unemployed. 116 "control" parents were therefore invited to participate - eight refused and 45 did not reply to the letter. Despite this unfortunately large drop out (see page 103), the sex and social class composition of the Glasgow controls (Tables 15, 16) did not differ to any great extent from that present in either the total number of Glasgow cases, or those who have been classified as Group I cases (see below). There were slight excesses of both unemployed and one-parent families amongst the cases, and slightly fewer cases in social class IV.

Nearly half the Glasgow cases were visited by a school nurse before the parents were persuaded to participate in the study. Cases in Glasgow have therefore been subdivided into two groups: 81
<table>
<thead>
<tr>
<th>SOCIAL CLASS</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1 (3%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>-</td>
<td>2 (6)</td>
<td>-</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>-</td>
</tr>
<tr>
<td>III non-manual</td>
<td>-</td>
<td>-</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
<td>3 (2%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>III manual</td>
<td>10 (33%)</td>
<td>18 (56%)</td>
<td>24 (30%)</td>
<td>19 (25%)</td>
<td>43 (27%)</td>
<td>19 (30%)</td>
</tr>
<tr>
<td>IV</td>
<td>9 (30%)</td>
<td>4 (13%)</td>
<td>13 (16%)</td>
<td>13 (17%)</td>
<td>26 (16%)</td>
<td>17 (27%)</td>
</tr>
<tr>
<td>V</td>
<td>3 (10%)</td>
<td>2 (6%)</td>
<td>7 (9%)</td>
<td>4 (5%)</td>
<td>11 (7%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>UNEMPLOYED (Not classified)</td>
<td>5 (17%)</td>
<td>3 (9%)</td>
<td>24 (30%)</td>
<td>21 (27%)</td>
<td>45 (28%)</td>
<td>16 (25%)</td>
</tr>
<tr>
<td>NO FATHER FIGURE</td>
<td>2 (7%)</td>
<td>3 (9%)</td>
<td>12 (15%)</td>
<td>17 (22%)</td>
<td>29 (18%)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
<tr>
<td>CLASSIFIED BUT UNEMPLOYED</td>
<td>-</td>
<td>2 (6%)</td>
<td>6 (7%)</td>
<td>2 (3%)</td>
<td>8 (5%)</td>
<td>2 (3%)</td>
</tr>
</tbody>
</table>
in Group I whose parents agreed to participate after receiving the original letter (Appendix 9) and 77 in Group II whose parents had first required a home visit from the school nurse. Only the first group has been considered in the case-control comparisons unless otherwise specified, as the method used to contact them was identical to that in the controls. Cases and controls have been grouped for the following analyses, as the alternative method of considering individual case-control pairs would have lost substantially more information.

Case-Control Analysis

The mean height SDS of cases and controls has been tabulated in Table 17. Although the mean height of the controls was clearly less than the national mean (Tanner, Whitehouse and Takaiishi, 1966) this was not unexpected considering their social class distribution. The controls had also been born slightly later, but by the time of the interview their mean age was a little older than the cases. Age was not of critical importance in the analysis however, as few of the variables studied would have altered over a period of six to nine months.

Table 17

<table>
<thead>
<tr>
<th>Number</th>
<th>Mean Ht. SDS</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>Controls</td>
<td></td>
</tr>
<tr>
<td>Edinburgh</td>
<td>Glasgow</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>-2.74</td>
<td>+0.23</td>
</tr>
<tr>
<td>32</td>
<td>-0.17</td>
<td>+0.80</td>
</tr>
<tr>
<td>81</td>
<td>-2.72</td>
<td>+0.32</td>
</tr>
<tr>
<td>77</td>
<td>-2.77</td>
<td>+0.32</td>
</tr>
<tr>
<td>158</td>
<td>-2.74</td>
<td>+0.32</td>
</tr>
<tr>
<td>63</td>
<td>-0.23</td>
<td>+0.87</td>
</tr>
</tbody>
</table>

Cf: Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>Cases</td>
</tr>
<tr>
<td>30</td>
<td>77</td>
</tr>
<tr>
<td>32</td>
<td>77</td>
</tr>
<tr>
<td>81</td>
<td>158</td>
</tr>
<tr>
<td>77</td>
<td>63</td>
</tr>
</tbody>
</table>
Parents' Heights (Appendix Table 76). As one would have expected, the parents of the controls were significantly taller than the parents of the cases. In Edinburgh the mean difference in height of the mothers was approximately 9 cm. compared with 6.6 cm. in Glasgow; for the children's fathers the differences were approximately 7.2 cm. in Edinburgh and 6.1 cm. in Glasgow, although as mentioned earlier, the latter results should be viewed with some suspicion as the heights of most of the fathers of both cases and controls, were estimated by mothers, rather than actually measured. There were similar differences in midparent heights. It is also of some interest to note that the mothers of cases in Edinburgh (mean height SDS -2.01 ± 0.81) were approximately 2 cm. shorter than those in Glasgow Group I (mean height SDS -1.66 ± 0.98). These differences were of marginal significance ('t' = 1.74, d.f. = 108, p < 0.1) and they could lead one to speculate that the genetic contribution to constitutional short stature was greater in Edinburgh than in Glasgow.

Age of Mother at Birth of First Child (Appendix Table 77). A tendency was present in both cities, but particularly in Glasgow, for the mothers of cases to have had their first child at a slightly younger age than the mothers of the controls. If the information from both places is pooled (see page 108) the difference is significant (combined test for trend; c = 2.13, p = 0.03).

Age of Mother at Birth of Index Child (Appendix Table 78). No significant differences were noted between the cases and controls in either city.

Pregnancy Number (Appendix Table 79). This study has not demonstrated/
demonstrated any significant differences between cases and controls in relation to the position of the index child in the family, whether the cases and controls from Glasgow and Edinburgh are combined (test for trend; \( c = 1.51, p = 0.13 \)) or considered separately for each city.

**Length of Gestation and Birth Weight** (Appendix Tables 80, 81). Although there was no significant difference in the incidence of premature delivery between cases and controls in either city (Appendix Table 80) birth weights were clearly different (Figures v, vi, x, xi). Over a quarter of the cases weighed under 2.5 kg compared with only 9% of controls. The mean birth weight (Appendix Table 81) of the 95 controls was 434 gms higher than the combined 107 Edinburgh and Glasgow Group I cases \( (p < 0.005) \). In this study, these differences do not appear to have been linked with maternal smoking habits during pregnancy (Appendix Table 82) as similar proportions of mothers smoked in all groups. Although the mean birth weight did not differ noticeably between cases in Edinburgh and Group I in Glasgow, a significantly higher proportion of the Glasgow mothers \( (70\% \text{ cf. } 43\%) \) admitted to smoking during the index pregnancy \( (X^2 = 4.98, p < 0.05) \).

**Family Size** (Appendix Table 83). The mean family size for both cases and controls was larger in Glasgow than Edinburgh. The average family size of the controls was about 0.5 less than the cases in both Edinburgh and Glasgow \( (\text{combined test for trend; } c = 2.38, p = 0.02) \). In view of this, it is not surprising that the households of both the cases and controls were more overcrowded in Glasgow than in Edinburgh (Appendix Table 84). The overall differences between/
Figure x

Birth Weight Corrected for Maternal Height (boys)

Controls
Figure xi

Birth Weight Corrected for Maternal Height (girls)

Controls
between cases and controls were also significant (combined test for
trend; \( c = 2.25, p = 0.03 \)). Glasgow children were also more likely
to have shared a bed (Appendix Table 85) with another member of the
family than children in Edinburgh. Although these between-city
differences were significant for controls \( (X^2 = 4.05, p < 0.05) \),
they were not for cases \( (X^2 = 1.92, \text{n.s.}) \).

The families of the cases in both cities were more likely to
have received supplementary benefit at some stage compared to the
controls (Appendix Table 86) \( (c = 1.95, p = 0.07) \). They were also
more likely to have been eligible for free school meals (Appendix
Table 87) (eligibility is based upon both income and family size).

55% of the cases in Edinburgh and Glasgow did not have to pay for
school meals compared to only 39% of controls \( (c = 2.12, p = 0.03) \).
These differences undoubtedly partly reflect the fact that in a
small proportion of cases (see page 175) low income controls had not
been available for matching. Clearly however, this supports rather
than detracts from the argument that those children with constituc-
tional or LBW short stature, in general, came from poorer homes than
children of average height.

**Disadvantage Score** (Appendix Table 88). Some of the individu-
al variables used in calculating the score have already been
mentioned. Overall, the cases were significantly more disadvantaged
than the controls (test for trend; \( c = 2.72, p = 0.007 \)). It is also
evident that Edinburgh cases were decidedly less disadvantaged than
the Group I cases in Glasgow (test for trend; \( c = 3.27, p < 0.001 \)).

Some degree of disadvantage was present in no less than 86% of the
cases/
cases, and 78% of the controls in Glasgow, whereas in contrast none of the Edinburgh cases or controls was severely disadvantaged.

**Pre-school Immunisation History** (Appendix Table 89). Although a seemingly higher proportion of cases had not been immunised compared to the controls in Glasgow, the differences failed to reach significance \( (X^2 = 3.21, p < 0.1) \) although the trend that was present does suggest that the parents of the cases may have been less orientated towards the prevention of disease.

**Maternal Characteristics** (Appendix Tables 90-93). Differences between the mothers of cases and controls were found in education, social involvement, and apparent intelligence. The mothers of the controls in both cities were twice as likely to have had further educational training after leaving school (Appendix Table 90) as the mothers of the cases \( (b = 2.19, p = 0.03) \).

**Social Involvement** (Appendix Tables 91, 92). In Glasgow, but not in Edinburgh, twice as many control mothers considered that they had been a source of help of advice to others \( (X^2 = 17.29, \text{ d.f.} = 1, p < 0.001) \). Moreover, 42% of the mothers of Edinburgh controls stated that they belonged to a group or society compared to only 17% of cases. The difference however fell just short of statistical significance \( (X^2 = 3.25, 0.05 < p < 0.1) \).

**Mother's Intelligence** (Appendix Table 93). The subjective rating of the intelligence of those being interviewed was done immediately following the interview. Although there were significant differences between cases and controls in the proportion of seemingly low intelligence interviewees \( (25\% \text{ cf. } 10\%; b = 2.72, p = 0.007) \), the/
the presence of some degree of observer bias could not be eradicated. Interviewers knew at the time which parents were cases and which were controls. Moreover, all of the controls, but only a few of the cases, were interviewed in the familiar surroundings of their own home, which may have enabled control parents to relate and perform better during the interview.

It is clear from the preceding analyses that the cases differ from the controls in a number of biological and social variables confirming the importance of both genetic and environmental factors in the causation of short stature. In general, it is quite clear that the social circumstances of children in Glasgow — whether they were cases or controls — were considerably more depressed than in Edinburgh.
This has probably been the largest community study of children with short stature yet undertaken, and because it has eliminated the effect of bias which is inevitably present in hospital populations, it has been able to seek answers to several questions that were previously unanswered. As a result of the study, new questions have been raised suggesting several areas where further research is necessary.

The Prevalence of Severe GHD

In this study, children with GH levels less than 10 mU/L have been considered to have severe GHD. As stated previously, the selection of a GH level discriminating between severe and partial GHD is somewhat arbitrary, and the level chosen varies from centre to centre. In general, children with lower maximum levels tend to have more exaggerated clinical features of GHD.

It is immediately evident from the auxological, biological and social data that the thirteen study children with GH levels under 10 mU/L did indeed comprise a distinctive population which was different in many ways from children with constitutional or LBW short stature and even from those with partial GHD. (Table 9). As a group they were smaller (although there were noticeable sex differences which are discussed later), and were growing more slowly. They also had a significantly higher mean head circumference and thicker triceps/
triceps skinfolds than the groups with constitutional short stature or partial GHD. They also tended to have a lower upper arm muscle circumference than children with constitutional or LBW short stature. Somewhat surprisingly, the individual and midparental heights of the children didn't differ significantly from those found in constitutionally short children. However, when their height SDS was corrected for midparental height they were significantly smaller than those with partial GHD of constitutional/LBW short stature.

There were also significant differences in a number of biological and social variables between them and those with either partial GHD or constitutional short stature. The differences have all been similar to those reported in the recent epidemiological study of Rona and Tanner (1977). Biased reporting of symptoms by the parents of the severely GHD children was unlikely to account for these differences, as, with the exception of the four previously diagnosed cases, the diagnosis in individual children was unknown by either interviewers or parents at the time the information was obtained.

Children with severe GHD were less disadvantaged socially than those with constitutional short stature. The proportion with severe disadvantage (8%) was indeed no different from the 10% found in the general Scottish population at the time of the eleven year old follow up of the National Child Development Study (Wedge and Prosser, 1973). Whilst there is no reason to suppose that GHD originating from a combination of genetic factors and triggering environmental insults around the time of birth, could not co-exist with social disadvantage, the possibility nevertheless does remain that disadvantage/
disadvantage itself can precipitate GHD, albeit temporary, as suggested by others (Powell, Brasel and Blizzard, 1967). One could perhaps speculate that the 13 children with severe biochemical GHD consisted of reality of two subgroups: the first being a group with severe biological GHD secondary to genetic/organic factors, all of whom had GH levels of less than 6 mU/L (Appendix Table 46), and the second a group with less severe deficiency (GH 7–9 mU/L) in whom social disadvantage was present, and in whom conceivably it could have been an aetiological factor. Further work is clearly necessary to see whether these subgroups can be distinguished biologically, auxologically or in their response to therapeutic HGH.

Whilst the scoring system used in the study to assess social disadvantage has the merit both of having been used previously and of being objective, it does not have the facility of detecting the far more subtle psychological deprivation that may affect children living in homes that have no material disadvantages. Deprivation of this nature may be of equal importance as a cause of growth failure with or without associated GHD.

The sex ratio of the children in the study with severe biochemical GHD was 1.6 (boys/girls). If the two girls and one boy, about whom there is some remaining doubt as to the final diagnosis, are excluded from consideration, the ratio is 2.3, more comparable with that previously reported by Rona and Tanner (1977). The girls found during the study were significantly taller than the boys and even if the three doubtful subjects were excluded, the differences were still highly significant (Mann Whitney U test, $p=0.008$). In spite/
spite of the auxological differences, there was no evidence that
girls had a measurably less severe degree of GHD, as their GH levels
did not differ significantly from the boys (Mann Whitney U test, \( p = 0.33 \)). Similar differences have not been reported by others which
inevitably raises the question as to whether this has been a chance
finding in this study, or, alternatively, whether it is possible that
girls with severe GHD are protected to a certain extent, by a mechanism
as yet unknown, from the severe growth retardation that usually exists
with GHD, and which is clearly apparent in the boys in the study.
This is clearly an area for further study which can only be properly
investigated in further community studies. These findings do suggest
however that by restricting the search for severe GHD to children
with heights of less than -3 SDS, many cases in girls may be missed
until very late in childhood.

The prevalence of severe biological GHD found in the study was
between 1/4000 and 1/6900, somewhat higher than previous evidence
has suggested. Present referral patterns are probably responsible
for a number of undiagnosed cases at the moment (see page 168 ). Of
the 13 subjects in whom severe biochemical GHD was found, three came
from Edinburgh, three from Aberdeen, and seven in Glasgow. One of
the 13 children with a maximum GH response of less than 10 mU/L
probably does not have biological GHD. As mentioned earlier, (see
page 61 ) occasional reports have been made (e.g. Kaplan et al, 1968) of normal growth occurring in children of normal height,
despite inadequate GH responses during provocative testing. It
could also be argued justifiably, that two of the remaining children
who/
who had short parents and less retarded bone ages, may not have had genuine biological GHD, but simply have responded inadequately, despite repeated provocative testing. It will only be possible to determine their true biological status by observing their response to therapy. Clearly treatment is not indicated at this stage in the child whose height velocity was normal, although continued observation of her growth is mandatory. Despite the small risk of producing anti-GH antibodies, a therapeutic trial is probably indicated in the child whose father's height was -3.6 SDS and who, on this basis, could himself have GHD. In the remaining subject about whom there is still doubt, further provocative testing and observation is warranted, particularly in the light of experience with her constitutionally short brother (see Appendix Table 47) who was also in the study cohort.

Partial GHD

The biological status of the 25 children with biochemical evidence of partial GHD is as yet unresolved. Auxologically they tended to occupy a position midway between the severely deficient children and those with constitutional short stature as has been found by others (Tanner et al, 1971). They were smaller, and on average were growing more slowly than children with constitutional short stature. Their bone ages were also more retarded. Upper arm muscle circumference measurements tended to be midway between those with severe GHD and constitutional short stature, but their other auxological findings were indistinguishable from the latter group of children. The medical and social backgrounds were also similar to those/
those with constitutional short stature. This lack of comparability in past medical history to the children with severe GHD does suggest the possibility that the aetiology in the partially deficient children in this study was different. One could speculate that the depressed GH levels were secondary not to a genetic tendency and neonatal trauma, but to deprivation, as may have also been the case with some of those with severe GHD. In support of this is the fact that all those found in the study with partial GHD came from Glasgow, which, as has been amply confirmed in this study, is a significantly more disadvantaged community than either of the other two cities. There was no evidence to suggest however, that children with partial GHD were more disadvantaged than those with constitutional short stature.

The presence of deprivation could perhaps explain why some children who had two ITTs (see figure ix) produced normal amounts of GH on the second occasion, even although no attempts had been made between tests to improve the social conditions in the child's home. The very size of the survey has made it physically impossible to measure children as frequently as one would have liked - in particular, to see whether an increase in height velocity accompanied the improved GH response in these children. It could equally well be argued that the discrepancy in results may have been merely because high fasting GH levels during the initial ITT test, inhibited a maximum GH response following the injection of insulin. Although, as has already been mentioned, the ITT seems less satisfactory as a provocative test if insulin is given immediately following a natural/
natural burst of GH secretion, the change in GH response in those children who had repeated tests, did not show any consistent relationship to a decrease in the fasting GH level. Indeed, several the children whose GH response during/repeated ITT was normal, actually had higher fasting GH levels on that occasion than they had formerly.

Five of the children with partial deficiency had other pathology which could have contributed to their short stature; one had asthma, one had features of the Russell-Silver syndrome and another had physical features suggestive of the fetal alcohol syndrome, although as far as was known by the child’s GP, his mother was not a known alcoholic. Another two had coeliac disease which has been reported by others to be associated with an abnormal GH response (Vanderschueren-Lodeweyckx, 1973). It is difficult to see how co-existent GHD can be excluded in these children in the absence of a therapeutic trial.

The children in this group are being kept under continued observation, and further tests of GH status are planned where height velocities remain below average.

**Constitutional Short Stature**

The study has confirmed the major role of genetic and environmental factors in the causation of short stature. The term "constitutional short stature" has been preferred to describe this group of children to that used by Lacey and Parkin (1974 a, b) who have described these children as "short-normals". As they themselves pointed out, the social backgrounds of such children are decidedly abnormal. The high prevalence of short stature in the disadvantaged districts of Glasgow, and to a lesser extent in Edinburgh, confirmed the/
the association between the prevalence of constitutional short stature and deprivation. Most of the children in the study fell within this diagnostic group. Not surprisingly, 75% of the constitutionally short children came from Glasgow, where no fewer than 52% of all those in the study cohort were in this diagnostic category. In Edinburgh, the proportion was only 43%, and in Aberdeen, it was an even lower 34%.

Major differences in social and biological backgrounds distinguished constitutionally short children from those of normal height, even when the effect of social class was reduced to a minimum. Their parents were shorter, and the children themselves tended to have lower birth weights. Constitutionally short children also tended to come from more overcrowded homes, containing larger families, and in general were more disadvantaged than children of normal height. Within the group of constitutionally short children, there was evidence suggesting the presence of poorer nutrition (as measured by triceps skinfold thickness measurements) with increasing poverty. No significant differences were found between cases and controls in recalled smoking habits during pregnancy of the index child, a finding at variance with the earlier work of Goldstein (1970) but consistent with the more recent report of Alvear and Brooke (1977). Similar differences have also been noted between the mothers of the constitutionally short children and the controls, to those previously observed between the mothers of malnourished children and controls (Richardson, 1974). The mothers of the constitutionally short children tended to start their families at a younger age, were less well educated, and more socially isolated.

Subjectively/
Subjectively, they appeared less intelligent, but this impression was undoubtedly biased by circumstances.

The case-control studies also highlighted important regional differences in social conditions which undoubtedly accounted to some extent for the high prevalence of constitutional short stature in Glasgow. It was particularly interesting to note that the mothers of the constitutionally short children were shorter in Edinburgh than Glasgow, and one could speculate that as a result of the better environmental conditions present in Edinburgh, and probably Aberdeen as well, children of slightly taller parents grew more rapidly than in Glasgow, and became too tall for inclusion in the study population. In Glasgow the added weight of environmental disadvantage meant that "genes causing short stature" did not have to penetrate to the same extent to produce short stature.

The study has also provided some support for the concept of sex differences in the canalisation of growth. This hypothesis (see page 33) proposes that the growth of males is affected by the extremes of environment to a greater extent than in females. The sex ratio of the constitutionally short children whose parents were interviewed in Edinburgh, Aberdeen and Glasgow was respectively 0.58, 0.36, and 1.59, which does in fact suggest that constitutional short stature was more common in boys when circumstances were poor, and relatively more common in girls, in the presence of a more favourable environment.

The LBW children were generally indistinguishable from other children with constitutional short stature on auxological, biological or/
or social grounds. Only three of the LBW group had clinical features consistent with the Russell-Silver syndrome.

These findings have two important implications. Firstly, the genetic component in GHD may be of greater importance than is presently realised. If, as the study has suggested, the prevalence of GHD is higher than previously thought, then those cases that are likely to be missed at the moment are, as the study of referral patterns has indicated, those in whom one or other of the parents themselves are small. Thus, cases presently being diagnosed are likely to be those in whom the genetic component is least.

Secondly, it confirms the crucial role of the School Health Service in case finding (Tanner, 1975). Ideally, departures from normal growth should be detected during the preschool years, but few child-health clinics have satisfactory measuring equipment available (e.g. infant stadiometers). This situation is somewhat inferior to that in Scandinavia where measurement of length as well as weight, is a routine part of all preschool examinations. This study has clearly shown that GHD must be excluded, either by a normal height velocity, or a screening test for GHD, in all apparently normal short children whose height SDS is less than -2.5 in the case of girls, or less than -3.0 in the case of boys. Such children are unlikely to be found with any regularity in routine health checks, until height and weight percentile charts are regularly used for all children. Unfortunately, the perfect screening test for GHD does not exist. This is particularly so for preschool children. Exercise is probably the best test available for children of school age.
age. All cases of severe GHD in the present study had GH levels on exercise of less than 10 mU/L, whereas only 17% of children found subsequently not to have severe GHD, had levels as low as this. If large scale screening using exercise were to be undertaken in the School Health Service for the above groups of children, it may well be preferable to definitively investigate - with an ITT - only those whose maximum GH levels were less than 10 mU/L. Whilst some cases of partial GHD would be missed, hospital facilities would be able to cope with the demand. Clearly such screening would need to supplement rather than replace present methods of case finding, which are likely to remain of major importance in the preschool age group for some time.

Growth hormone deficiency is indeed one of the commoner forms of short stature. In a non-disadvantaged community, it may be present in up to 5% of all short children (including those with organic disease), or in 10% of those who, apart from short stature, appear to be healthy. As treatment is so rewarding for the child and his parents, and adequate GH supplies are currently available, a more intensive search for those suffering from the condition than is presently being undertaken, is clearly warranted.
ACKNOWLEDGEMENTS

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My other supervisor, Dr. Una MacLean, of the Department of Community Medicine, has also offered constructive advice and criticism based upon her own knowledge and experience of community studies.

Dr. Stuart Pocock, of the Medical Computing Group, made a number of helpful suggestions about the conduct of the study, as well as providing valuable statistical assistance. Mrs. Frances Stent ably undertook most of the card punching and computer programming for the data analysis. Dr. M. Heasman and Mr. G. Mitchell of the Common Services Agency, also offered statistical advice.

Dr. P. Levein, of the Scottish Development Department, willingly provided information about patterns of social deprivation in Scottish cities.

Drs. J. Mok and N. Falaki carried out most of the hospital investigations that were necessary in the Edinburgh subsample.

Drs. Euan Cameron and Graham Lidgard, ably supported by Mrs. P. B. Sanger and Mr. K. S. Nicol, of the Regional Hormone Laboratory, Edinburgh, undertook all the GH and TSH assays done in the study.

Although/
Although they have not been presented in any detail in this thesis, other laboratory investigations have been performed by Dr. W. Hunter (gonadotrophins), Dr. J. Seth (serum thyroxine), Mrs. E. Grace (cytogenetics), Dr. E. Innes (Haematology) and Mrs. R. Steven (25-hydroxycholecalciferol, urea, serum and urine osmolality).

Mrs. D. Morris, and Miss E.M. Wilkinson helped with the field work and interviewing, often at very short notice.

The Department of Medical Illustration meticulously reproduced and mounted the illustrations.

Professors J. O. Forfar, J. Hutchison, and A. Campbell, Drs. W. Hamilton and M. Fyfe, have all readily co-operated, making hospital beds and facilities available wherever necessary. In addition, Dr. W. Hamilton has kindly consented to assist in the follow up of those children with partial GHD.

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All the members of the Working Party of the Medical Research Council's clinical trial of HGH have supported the study with their helpful advice and interest. Dr. M. Parkin gave helpful advice about the conduct of the exercise test.

The Scottish Home and Health Department, and the Scottish Education Department, provided help at the outset of the study and the administrative staff of the local education authorities in Edinburgh, Glasgow and Aberdeen, have provided continuing assistance throughout.

Drs./
Drs. P. Ludlam, M. Menzies, and C. Robb, Community Medicine Specialists in Child Health in each of the three cities, also provided help enabling minor local difficulties to be overcome.

Thanks are also due to the teachers and head teachers of each of the schools visited during the study, for their cheerful co-operation and intelligent understanding.

The study would not have been possible without the co-operation of those parents and children who agreed to participate.

Finally, sincere thanks are due to two people without whose help the study would have foundered. My secretary, Miss Rosemary Lamb, as well as undertaking routing secretarial duties, was responsible for the smooth day by day organisation of the field work. She has also been responsible for typing this thesis. No words of thanks can adequately express my appreciation and admiration for my wife, Anne, who has helped so unselfishly throughout with the field work. As well as doing most of the interviewing, she was responsible for estimating the bone ages of all children in the study and undertaking most of the insulin tolerance tests in Glasgow and Aberdeen. Through her patience, understanding and encouragement, she has been a major source of help in the preparation of this thesis.
PRESENTATIONS AND PUBLICATIONS

Over the past fifteen months, some of the material included in this thesis has been presented at scientific meetings in Edinburgh, Glasgow, Aberdeen, London, York and Inverness. One scientific paper ("The Prevalence of Severe GHD") has been accepted for publication by the British Medical Journal.
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APPENDICES
Dear

National Study of Short Stature at Five Years with Special Reference to Growth Hormone Deficiency

The Medical Research Council wishes to know the prevalence of growth hormone deficiency dwarfism in the United Kingdom with a view to advising the Department of Health and Social Security, the Scottish Home and Health Department and the Ministry of Health and Social Security, Northern Ireland, on the amount of human growth hormone (prepared from cadaver pituitaries) needed for therapy. The Council has awarded me a special project grant of about £30,000 for the above study in order to obtain this information which is not currently available.

In brief* the school entrance height for cohorts of children examined at 1972-74 are being computer-scanned by the Information Services Division of the Common Services Agency. It is then proposed that a comfortable and well equipped mobile clinic will visit schools, remeasure the small children listed and note those below the current Scottish first centile for height. Sanation of parents and medical practitioners for further investigation will then be sought. Parents will be interviewed, children will be examined and their bone age determined. A simple exercise test (in the form of a game) will then be used to provoke growth hormone secretion and a blood specimen will be taken and will be assayed by the MRC Radioimmunoassay Team in Edinburgh. In the small proportion which fails to raise the acceptable growth hormone level the child, again with parental sanction, will be admitted for 24-hours to a suitable local unit for a hypoglycaemia test of growth hormone response. Proved cases will be offered treatment which is known to be effective in most cases. Children whose dwarfism is proved not to be due to human growth hormone deficiency will be discussed with the family doctor. The parents will be reassured (parents of such tiny children are usually anxious and will welcome this) when appropriate or the child will be transferred to local colleagues for systematic investigation when abnormality (eg coeliac disease) is suspected.

The/

* Further information may be available later in the "Health Bulletin".
The project has already been discussed informally with members of the Scottish Committee of the British Paediatric Association (consisting of the four Professors of Child Health, and Dr. Patrick MacArthur in Inverness) and with paediatricians representing all other parts of the country. They accept the project on these terms and the cooperation of other colleagues is expected.

The MRC research fellows appointed to work with me and who will staff the mobile clinic are an Australian husband and wife team from Adelaide. The husband, Dr. Graham Vimpani, has already completed a year in the United Kingdom to which he came as a Heinz Fellow of the British Paediatric Association for special study relating to social paediatrics. His wife has worked during the past year in obstetrics and they are well qualified not just in medical training and experience alone but in personality for this project. They are, of course, registered with the General Medical Council and insured for Medical Defence. Dr. Graham Vimpani, the senior fellow, hopes to call on CAMOs personally to answer such questions as may arise and for the duration of the project is on the staff of the University of Edinburgh.

We know that this year of change is a difficult one in which to start such a study and are sorry to suggest even the possibility of further work. The method however has been prepared to cause little or no inconvenience to medical or education administration or to parents and children. Should local help happen to be available then it will of course be welcomed. The project is based, with the full support of Professor J.O. Forfar, on this Department but Professor J.H. Hutchison has kindly provided desk space in his Department in Glasgow since a good deal of the Vimpanis' work will take place in the West.

The Scottish Education Department has already circulated Directors of Education to inform them of the project and to enlist the cooperation of head teachers in primary and special schools.

Yours sincerely,

J.W. Farquhar MD FRCPE
Reader in Child Life and Health
Consultant Physician, Royal Hospital for Sick Children, Edinburgh
Consultant Paediatrician, Royal Infirmary, Edinburgh
To: The Director of Education

Please reply to The Secretary
Your reference

Our reference CS 194/22
Date 20 September 1974

Dear Director

HUMAN GROWTH HORMONE RESEARCH

We understand that the Medical Research Council has commissioned a research project which aims to ascertain the prevalence of human growth hormone (HGH) deficiency in children. The research can only be conveniently carried out in Scotland as it is only here that data on the height of school children shortly after they enter school is regularly collected. This information is held by the Scottish Home and Health Department. HGH deficiency is one of the causes of short stature in children and once identified can be remedied by treatment with doses of the hormone. The research is to be directed by Dr. J.V. Farquhar, Reader in Child Life and Health at the University of Edinburgh, and Consultant Paediatrician at the Royal Hospital for Sick Children, Edinburgh. It will be carried out by Dr. Graham Vimpani of the same Department.

The proposal is that children who are unusually small (say the smallest three per cent) at school entrance medical inspection in the sessions 1972-73 and 1973-74 will be re-measured during the next two to three years by the research team. Those found to be very small (say the smallest one per cent) will then be re-examined and investigated. Parental and family doctor consent will be sought. Hormone deficient children will be recommended for treatment which is known to be very effective in most cases. Other causes of very short stature may be recognised and suitable action can then be taken. In order to minimise interference with schooling and to reduce inconvenience to parents and children both preliminary and further investigations will be carried out at the pupil's own school in a specially equipped van. This comfortable mobile clinic requires a connection to an electric power outlet point. Most schools visited by mobile dental caravans will already have an outdoor point but the van will carry special lengths of cable for indoor connections.

The research team will give advance warning to the head teacher of any school where a visit is proposed (no visits are likely before the beginning of 1975 and the team will probably deal first with schools in the industrial lowlands).

The lists of children held by the Scottish Home and Health Department do not give the schools which the children are currently attending and identification of the schools will be the research team's first task. The team intends preparing separate alphabetical lists of the smallest boys and girls in each education authority area and will include initials and date of birth. Enough copies will be supplied to provide each school with one and it should take only a few minutes for teachers to recognise a child in their class and mark the name accordingly. Where records are held centrally rather than at schools this task may be undertaken by an office clerk and the team has budgeted for payment.
We would very much hope for your cooperation in this project and if you foresee any problems about the proposed arrangements in your own area we should be pleased to discuss them with you. Otherwise I should be grateful if you could convey the information in this letter to the head teachers of all primary and special schools within your area.

Yours sincerely

Geo G McHaffie

G G McHaffie
HUMAN GROWTH HORMONE RESEARCH

I refer to Circular letter CS194/22 which I sent to you on 20 September 1974 seeking your help, and that of the headteachers of Primary and special schools, in a Medical Research Council project to identify children of abnormally small stature who entered school during sessions 1972/73 and 1973/74.

Preliminary work by the research team has revealed discrepancies between the lists of small children recorded in the Health Service Statistics Computer file and lists prepared by a hand sort of Medical Record Cards relating to individual schools. The error is in part the result of migration and in part due to the fact that a proportion of school entrants are not examined during the year of school entry because of absence or medical staffing problems. If a child is examined late details of the examination are not accepted by the computer because the child is over-age for the purpose of statistical analyses. An error in the region of 5% has been found in this preliminary work.

Dr Farquhar, the Director of the Research, and the Research Fellow, Dr Vimpani in discussion with a number of community medicine specialists responsible for child health services have come to the conclusion that the most satisfactory way of overcoming this problem will be to re-measure all children currently in Primary 2 and Primary 3 classes. This would take no longer than half-an-hour in any individual school provided that Primary 2 and Primary 3 class registers are made available at the time of the visit by the research team.

I would be grateful if you could inform headteachers of this change in procedure and ask for their co-operation in making class registers available to the secretary of the research team when they visit. Headteachers will of course be given advance notice of visits by the research team.

A copy of this letter is to be sent to the Chief Administrative Medical Officers of Health Boards for information.

Yours sincerely

G G McHAFFIE
Dear

Medical Research Council - Scottish Survey of Short Stature
with Particular Reference to Growth Hormone Deficiency

General Introduction

We are engaged in a survey of children who were particularly small at school entry medical inspection in 1972-73-74 (ie age 5-6 years). As a Medical Research Council project it has the backing of the appropriate Government Departments. Directors of Education as well as Chief Area Medical Officers are being informed.

We are doing it for three reasons:
(a) Some such children, while asymptomatic, can now be treated.
(b) Human Growth Hormone (HGH) is extremely expensive to make and the Medical Research Council hopes by means of our study to estimate the amount of it required for the United Kingdom.
(c) Only in Scotland are such heights recorded.

We have access to the heights of children who attend local authority schools but not at all to those of children at private and semi-private schools. We hope that you will be able to help us by granting us access to records and children, only of course with parental consent. We are willing to prepare letters to parents subject to you approving their content, and also to pay for the small amount of clerical help that might be needed. Should the school's governing body agree to the study we would want also to consult with the school doctor.

Further Information

Human Growth Hormone (HGH) Deficiency

HGH is a pituitary gland hormone which has been measurable now for ten years. Children who cannot produce enough of it grow only very slowly and remain short to the point of handicap all their lives (less than 5 feet, possibly closer to 4½ feet)

HGH is now available and is effective in enabling such children to grow. It is produced by the Medical Research Council from human pituitary glands at considerable cost. Treatment is very strictly controlled in order to conserve supplies. It has been given free of charge on a research basis but the National Health Service may take over hormone production and treatment soon.

Treatment is ultimately effective in the young (say from 5 to 8 or 9 years) and is progressively less so as the child ages. It is useless after sexual maturity has been reached.

No-one anywhere in the world knows with accuracy the prevalence of such deficiency. The Department of Health and Social Security therefore is uncertain about the amount of HGH it should produce. That is the point which we hope to settle in this study.

Nature of the Study/
Nature of the Study

We need only to remeasure the height of those children who were below a certain figure when examined for school entry. On national statistics this will be about 3 per cent of the intake of 1972-73 and 1973-74. In private and semi-private schools we would expect even fewer children to be below the 3rd centile line since on average they come from better environments.

We shall reduce inconvenience to the bare minimum by bringing an attractive and comfortable mobile consulting room, housed in a Bedford van, to the primary school concerned. It will be equipped with a special measuring instrument which is in fact no more than a sophisticated variation of measuring a child against the kitchen door.

Roughly two out of every three children examined will be dropped from the survey at this point and their parents can be reassured about them unless there is some unusual feature or unless the parents specifically asked for further investigation and the family doctor agreed. The smallest children however (1 per cent or less of your annual intake of 5-year-olds) will be further investigated very simply if the parents and family doctor agree.

Growth hormone deficient children can then be treated and we, if we can cover a sufficiently large population, can advise the DHSS and the Scottish Home and Health Department about the national need of HGH.

We hope to have our mobile clinic by January 1 and to begin work in Edinburgh where such a high proportion of children are at private and semi-private schools. We very badly need access to such schools if our determination of prevalence is to be valid.

Our Team

While the administration of the project is my responsibility the mobile clinic will be operated by a husband and wife team from Adelaide, Australia. Dr. Graham and Dr. Anne Vimpani have completed their first year in the United Kingdom to which Dr. Graham Vimpani (a Lecturer in the Department of Child Health, Adelaide) came on a Fellowship of the British Paediatric Association. They relate very well to both adults and children and will be happy to call on you and/or your school medical officer to answer such questions as you may have. He would hope in any case to speak to the school doctor.

I do hope that you can help us in a study which has a very practical application to a handicapping physical problem.

Yours sincerely,

J.W. Farquhar MD FRCPED
Reader in Child Life and Health
Consultant Physician, Royal Hospital for Sick Children
Consultant Paediatrician, Royal Infirmary, Edinburgh
Dear Mr. & Mrs.

The University of Edinburgh, Department of Child Life & Health, is carrying out a survey for the Medical Research Council which firstly aims to identify the smallest 1% of school entrants in 1972 and 1973. In most cases these children are being identified through the records of the School Health Service, or in the case of private schools, with their own medical examinations from perusal of these. Neither of these methods are available to enable identification of the smallest children in the school your child attends, and we are therefore asking your permission to measure your child's height at the school. The Headmistress has agreed to this, providing you have no objections. If she does not hear anything to the contrary from you we will take it that you are quite happy about us doing this. I would emphasize that all we will be doing is measuring your child's height. You would, of course, be contacted again, should your child fall into the smallest 1% in Scotland.

Yours faithfully,

Dr. Graham Vimpani,
Research Fellow.
Dear Head Teacher,

Medical Research Council - Scottish Survey of Short Stature

This letter supplements the one sent out by Dr. Maud Menzies of the School Health Division of the Greater Glasgow Health Board at the end of January 1975. Following our experiences screening the heights of Primary two and three children in Edinburgh, we believe this additional information may be helpful.

Firstly, in addition to the information Dr. Menzies requested you make available for us, could we please have access to the class registers.

Secondly, we have found that it is quicker and causes less disruption if we measure children in their classrooms. To do this we take a fairly sophisticated steel rod into each classroom and select all children falling below a specified height; these children are then taken to our mobile clinic and measured accurately on precise equipment. The number of children so selected in any class varies between about nought and five. This screening takes about three minutes per class. Difficulties may occasionally arise where vertical grouping is practiced.

Thirdly, we would point out that we hope to visit about six to eight schools per day; we have found our visit to most schools can be completed in under half hour. Clearly, unforeseen difficulties do crop up, delaying our arrival at subsequent schools, and thus other than the first schools we visit in the morning or the afternoon, our E.T.A.'s for individual schools are only approximate. For your information, we enclose a list of the other schools on our itinerary on the same day as your school.

Fourthly, we have found many teachers are interested in the reasons for the survey, and would probably value some prior explanation of it for their own interest. For this reason we have prepared and enclosed a short description of the aims of the project, which could be circulated amongst Primary two and Primary three teachers.

Finally, thank you for agreeing to help us.

Yours faithfully,

Dr. G. V. Vimpani, Research Fellow, and
Dr. A. F. Vimpani, Research Associate.

Encs.
APPENDIX 6

ESTIMATED FIRST CENTILE FOR HEIGHT

(Based on Tanner's mean - 2.5 SD)

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Dear Medical Research Council - Scottish Growth Study

The Department of Child Life and Health, in the University of Edinburgh, is engaged in carrying out this survey with the support of the Medical Research Council. Its aim is firstly to identify a group of children whose height is well below the average for age, and secondly to ascertain where possible the reasons for this. We want to include children who attend schools in both the private and public sector; only by including both will we get a complete picture of the problem in the community as a whole.

One of the principle reasons for the study is to find out what proportion of very small children have a deficiency of "Growth Hormone". Growth Hormone is a chemical substance produced by the pituitary gland, and its most important function is to stimulate growth. Without it children don't grow at a normal rate and remain shorter than average all their lives. Apart from being very short, such children may be otherwise quite healthy. Our interest is prompted by the fact that recent technical advances have enabled growth hormone to be prepared in the laboratory and it can thus be used to treat those very short children who are found after special tests to be unable to make enough of it for themselves. This treatment is given over a period of years and helps such children to catch up and grow at a normal rate. It is probably quite obvious, but should nevertheless be emphasized, that by no means all short children have growth hormone deficiency, and many other causes are known.

As the initial step in this project, we are checking the heights of all primary two and three children in Education Authority schools and where possible in independent schools. With the co-operation of the headteacher and school doctor at your child's school, we have found that your child's height was below average when last measured. With your permission, we would like to re-measure at the school using very accurate, but portable, measuring equipment. This would be all that is involved at this stage. We would contact you again and let you know the results of this and whether we would like to see you with a view to including him/her in the next phase of the survey. This will involve only those children comprising the smallest 1% of the population. If we do not hear from you by we will assume you have no objection to what we have proposed.

Yours sincerely,

Dr. Graham Vialpindi,
Research Fellow.
Dear Mr. & Mrs.

Medical Research Council - Scottish Growth Study

All the Primary two and three children in Glasgow have recently been measured at school as part of a survey of growth and development. My wife and I, both of us Australian doctors, have measured your child and found that is quite small for his/her age. We are hoping to meet the parents of all the small children we have found to try to find out why they are short.

We would like to meet either or both of you at your child's school, or at home if that is not convenient, to ask you some questions about past and present health and development and to carry out a careful medical examination of your child. After this, and a more detailed explanation of our aims, we would then like to carry out some tests if you were in agreement. These would help us to understand why is so small, and we could then see if something could be done to help his/her growth. We have a specially built mobile clinic which is set up like a doctors consulting room, in which we will be able to do all of this.

Would you be agreeable to meet us and talk it over? If so, could you please sign and return the slip in the reply paid envelope enclosed, as soon as possible. We will not be sending you an appointment until after the summer holidays, but we would like to know whether you are agreeable to take part, as soon as possible. Even if you are already seeing your own doctor about this we would still like to meet you; in many cases we have already been in touch with him.

We do hope you will agree to help in our survey as we hope that its findings will benefit many other children.

Yours sincerely,

Drs. Graham and Anne Vimpani, and

Dr. James W. Farquhar.
Information for School Nurses

Over the past two school terms, both of us, Australians attached to the Department of Child Life and Health of the University of Edinburgh, have been screening the height of children in Primary two and Primary three, and children of a similar age range in Special Schools and Occupational Centres in Glasgow. The aim of this has been to identify the smallest 1% of children within this population. About 320 children have thus been identified, out of a school population of approximately 25,000. (This is slightly more than 1% of the Glasgow population, because the standards we are using for height have been produced from data available on the whole of Scotland. The average height for children in the whole of Scotland is slightly above that in Glasgow and hence there is a higher proportion of very short children in Glasgow - 1.4% not 1%)

As this screening has involved every child in Education Authority schools in Glasgow and is being carried out with the co-operation of the School Health Service, parental consent for measurement was not thought necessary by those concerned.

The Next Task

Now that the very short children have been identified, the next part of the project will involve an approach to the parents to seek their further co-operation. The project has been funded by the Medical Research Council to find out the prevalence of growth hormone deficiency. Growth Hormone is the substance that is primarily responsible for growth of children up until puberty. If it is not produced in normal amounts, growth failure occurs. A number of people are immediately alarmed by the word "hormone" because they associate it in their minds with lurid stories in the press about sex, the "Pill", and beefy Russian woman athletes, but not with substances like insulin - a hormone that everyone accepts as being essential to health. There is not just one hormone but a variety of hormones each of which have specific functions. Growth Hormone thus ought to be regarded in the same way as insulin and is best thought of as the principal natural chemical substance by the body enabling normal growth to occur, produced.

The parents of all the short children have been written to at the beginning of July asking whether they would be willing to co-operate in this study. Those who failed to reply to this letter may need further explanation about this survey and some gentle persuasion by people known to them. Miss Cowan has very kindly offered the assistance of school nurses in this task. At the beginning of August a list of names of the defaulters will be made available to Miss Cowan and distributed to school nurses working in the appropriate areas.

Further Information for Parents

Please emphasize that this is a survey of growth and development of children, that is being undertaken in various parts of Scotland. They have been written to by the survey team because their child is particularly small and this may be caused by a deficiency in the growth factor responsible for normal growth. In some cases it is probable that the children have already been receiving medical attention either because of their short stature or because of another physical condition which is accompanied in their particular growth disturbance, but even in these cases the project team would like to meet the parents and find out from them details of their child's past health and development and what has been done in the way of medical investigation and treatment.

Please/
APPENDIX 9:2

Please point out that the growth factor deficiency we are looking for can only be discovered with certain special tests which we are planning to carry out in the survey ourselves, if they have not already been done by family doctors or consultant paediatricians. The survey team have a specially equipped mobile clinic which all the investigations necessary to exclude the presence of growth factor deficiency can be carried out. This will be visiting schools and in some cases the homes of children at dates and times to be arranged later. One of the tests to be carried out will require the child to have been fasted. Thus for children with appointments in the morning they should go without breakfast and for those with appointments in the afternoon they should go without lunch. Please explain to the parents that details about this would be sent to them along with the appointment at a later stage.

The only painful thing likely to happen to the children during the whole procedure is the collection of one blood specimen but the reasons for this would be fully explained to the parents beforehand by the survey team. Try to persuade them not to refuse permission because of the thought of one blood test as there is much more besides this that we hope to discover at the interview which would be most valuable in trying to decide the cause of short stature, even if after further explanation they decline to allow to have their child fasted. The main thing at this stage is to persuade them that we haven't got two horns and a pitch fork, and that if they will only agree to meet us we can explain in more detail what we are about and they will then be quite free to continue or withdraw.

Possible Objections

"But we are all wee, doctor"

It is quite possible that the parents or other relations of the child are small also. Although genetic factors are therefore probably partly responsible, one can never be sure as growth hormone deficiency has been reported - and two such cases exist in Edinburgh - in a parent and child. One of the other aims of the survey is to find out just how commonly genetic factors are responsible for children being as short as those in the survey. Only by such parents co-operating will we be in a position to answer this very important question.

"What's in it for me?"

The possibility of being able to help the child grow. The chance to talk to someone who is very interested in the growth and development of their child and who may be able to get help for their child that has not been possible previously.

"Our doctor already knows all about it"

The survey team do not want to interfere in any way with the management of children whose growth is already being investigated and the cause for their growth failure found. However, it is important in a community survey of this sort that we discover all the information that is available about each child whether diagnosed or undiagnosed. The parents are the best ones to be able to give this.

You will probably be asked other questions by the parents but there should be enough information in this circular to answer them. If there are still areas which have not been covered could you contact us at the above telephone number.

We anticipate that the interview and tests would be completed within two hours at the most.

DR. ANNE F. VIMPANI

DR. GRAHAM V. VIMPANI
Dear MRC-Scottish Growth Study

You will remember we have been in touch with you several times before about this survey of children who are well below the average height for their age. We are doing a blood test on children whose parents have agreed to take part in the survey to make sure they don't have a condition called growth hormone deficiency. The reason we are looking for it is that treatment is available for children with this problem. You may have seen a television programme about it earlier in the year on "Pebble Mill At One".

Last time I wrote, I asked if you would mind if we remeasured John so that we could find out how much she had grown in the last year. Our measurements show that his rate of growth has been below average over this period. Although the survey is not yet complete, we have already found several children in a similar condition who have got growth hormone deficiency.

I know that when we first wrote, you decided that you did not want John to take part in the survey. I wondered if in view of what we now know about John's rate of growth, I could call on you sometime in June to have a brief talk about the survey with you? Afterwards, you may decide to change your mind - although of course this would be entirely up to you. John may already have had the test we are talking about carried out by your own doctor, or a specialist, or you may know another reason why he is short, e.g. low birth weight, a family history of shortness, or another illness currently being treated. It would be very helpful to us if we could find out.

If you don't want me to call, could you write and tell me.

Yours sincerely,

Dr. Graham Vimpani,
Research Fellow.
Dear

Medical Research Council - Scottish Survey of Short Stature

The Medical Research Council has commissioned this study, under the direction of Dr. J.W. Farquhar, Reader in Department of Child Life and Health, Edinburgh University, and it has the support of the Scottish Home and Health Department, Area Health Boards, and Paediatricians throughout Scotland, primarily to determine the prevalence of Growth Hormone Deficiency amongst short children. Advance notice of the survey has recently appeared in the "Health Bulletin". The Research Team has been screening the height of all Primary two and Primary three children in Glasgow, and have thus identified all children whose height is more than 2.5 standard deviations below the mean height for age. I understand that

is one of your patients and he/she is in this group. With your permission, we would now like to interview the parents, and check their height, and then examine the child. Before doing this, we wanted to contact you to see whether you have any information of either a medical or social nature of which you feel we should be aware before proceeding further. We think this is particularly important as it is clear that some of these children come from unfavourable homes and we wanted to reassure you in particular that we hope to avoid any conflict of opinion concerning the diagnosis that could aggravate relationships that may in some cases be difficult.

Because this child is so short, it is possible that he/she has already been brought to your attention by the parents, and may have in fact been referred by you to a Consultant Paediatrician or Endocrinologist for an opinion. If this is so, we would be very pleased if you would let us have any information bearing upon this, in particular the name of the hospital and consultant.

We propose carrying out the interview with the parents and the examination using a mobile clinic which has been specially built, and with which we will be visiting the child's school. The Education authorities are quite happy for us to work on their premises. After the situation has been explained to the parents and their informed consent obtained we propose, where indicated, to do a number of investigations. These will necessitate taking only one blood sample from the child. We hope in this way to detect all those with Growth Hormone Deficiency and, if possible, to determine the aetiology of short stature in other cases. It is fundamental to our study to realise that Growth Hormone Deficiency may cause no symptoms other than short stature and that this often serious disability can be corrected by Human Growth Hormone Treatment, which as far as we know has no harmful side effects, and that this preferably be commenced well before puberty. Small children in families where both parents are
small does not necessarily indicate that the reason is "hereditary short stature" with normal Growth Hormone production, as in Edinburgh we have at least one case of a Growth Hormone deficient child being born to a very short mother, who is also Growth Hormone Deficient.

It is possible that after the initial series of tests the children may need admission to hospital for more investigations, and in each situation this would be done in consultation with the General Practitioner and local hospital medical staff. Once the children have been investigated they will be referred back to you, and/or the Consultant Paediatrician for continuing management as this survey is for diagnostic purposes only. If we do not hear from you to the contrary by we will assume that you have no objection to this study, and our next move will be to contact the parents. If you are uncertain about any points in the letter and would like clarification you could contact me at the above address. We will be in touch with you again after we have seen the child and his parents to let you know the outcome.

Yours sincerely,

[Signature]

Dr. Graham V. Vimpani, MB, BS, FRACP, RESEARCH FELLOW.
Dear

Medical Research Council - Scottish Survey of Short Stature
with Particular Reference to Growth Hormone Deficiency

Now that Human Growth Hormone replacement therapy is known to be effective, information about the prevalence of total and partial deficiency is necessary to guide production of the hormone for therapeutic purposes. Since only Scotland records children's height at school entry medical inspection and since this information can be readily recalled, the study will be made in Scotland on as large a population as can be examined. The Medical Research Council has accepted a suggested plan and has granted me £30,000 to carry it through.

Dr. Graham and Dr. Anne Vimpani of Adelaide have been appointed research fellows for a period of 2-3 years. They will operate from this Department but Professor Hutchison has kindly arranged for desk space to be available to the Vimpanis when they are operating in the Glasgow area since the number of children there clearly dominates the picture.

Our plan is to study the children in such a way as to cause the least possible inconvenience to them, to their parents and to their school teachers. Sanction for each step will be obtained from parents, from family doctors and (where they have been involved with individual children) from hospital consultants. We shall have lists of children who were below the 3rd centile at school medical inspection and will know the school which each child attends. We hope to have an attractive and comfortable mobile clinic (housed in a Bedford van) which will visit the schools. The Vimpanis will then identify and remeasure the children using Harpenden equipment. Those below the 1st centile for Scottish children will form the population to be studied. Permission to proceed will then be sought.

At the second visit a history will be taken, the child will be carefully examined and a simple screening test for HGH will be carried out (probably an exercise test). A number of groups will then emerge:

(a) Asymptomatic normal small children with a normal HGH response (parents to be reassured).

(b) Asymptomatic small children with a poor HGH response (to have further HGH tests at hospital).

(c) Small children from environments suggesting psycho-social deprivation and with or without a limited HGH response (to have further HGH tests at hospital and further investigation of background).

(a)
APPENDIX 12:2

(d) Symptomatic abnormal children with a normal HGH response (to have further investigation at hospital for the cause of growth retardation.

(e) Possibly one or two cases of craniopharyngioma with HGH deficiency.

It is at this stage that we hope for help from paediatric colleagues:

(1) To admit to their beds for 24 hours cases of possible HGH deficiency for an insulin hypoglycaemia test. The MRC Working Party (of which I am a member) has shown this test to have an excellent record for effectiveness and safety. The numbers should be small and experience may show that the Vimpani's will have time to assist in conducting the tests.

(2) To admit for study (to specialised units if necessary) children suspected to be in some other way abnormal.

We very much hope that the study has been designed in such a way as to avoid giving any colleague more than a very little extra work over a very short period of time and indeed the pilot study (starting in Edinburgh about 1/1/75) may show that we cannot cover all Scotland in the time allowed. Graham Vimpani who is a Lecturer in the Department of Paediatrics in Adelaide is already known (as a Heinz B Fellow) to many Scottish colleagues and he will be delighted to discuss the study personally with you if it should take him to your area or ahead of time if there are points you would like to clear with him. The study has been discussed with those concerned at the Scottish Home and Health Department and explanatory letters are being sent from there to Chief Area Medical Officers and from the Department of Education to Directors of Education. The children concerned were medically inspected for school admission in 1972-73-74 and should be from 6-8 years old when re-examined.

We hope very much for the co-operation of all concerned in a study which may uncover some interesting children in need of local investigation and help. Those with total HGH deficiency will be notified to the Working Party for HGH therapy. Those with partial deficiency will be followed up and HGH will be supplied if there is no recovery of function under good conditions.

Yours sincerely,

J.W. Farquhar MD FRCPed
Reader
Medical Research Council - Scottish Growth Study

We are studying the growth and development of all children who were in Primary two and Primary three in Scottish schools earlier this year.

Most children develop normally, but some children are very small for their age. Amongst these very small children there will be a few who can be helped to grow more normally with medical treatment. Our plan is to find these children so that they can be treated. We are also studying the effect of growth on children's general development and school progress. For this reason for every small child we see we are also seeing a child who is of normal height for his/her age. Your child has been chosen for the survey because his/her birthday is nearest to that of a small child in our study.

We would like to meet either or both of you at home to ask you some questions about your child's past and present health and development, if you are agreeable to take part in this study. This is all that is involved apart from measuring your child's height. Please let us know on the enclosed slip whether you are agreeable to take part and whether you are happy to see us at your home and whether you would prefer us to call in the morning or afternoon. We will then write and send you an appointment.

We do hope you will agree to help in our survey as we hope that its findings will benefit many other children.

Yours sincerely,

Dr. Graham V. Vimpani,
Dr. Anne F. Vimpani, and
Dr. James W. Farquhar.
MEDICAL AND SOCIAL QUESTIONNAIRE

(Coding boxes have been omitted)

1. Date of interview.

2. A. Surname
   B. First names

3. Date of birth

4. Sex 1. Male, 2. Female

Start interview by checking above information.
Introductory comments and explanation.
THANK PARENTS for participating.

5. A. Are you worried about N's health at the moment?
   1. No, 2. Yes, specify

   B. Does N have any symptoms at the moment as far as you know?
   Would you mind telling me what they are?
   What is N's appetite like? Describe diet.

"I am now going to ask you some specific questions about N's health".

6. A. Have you had any problems with N's eating in the last month or so?
   1. No
   2. Yes
   9. Don't know or uncertain

   B. IF YES
   1. Does he pick at his food or not eat enough?
   2. Does he eat too much - or is always hungry?
   3. Other - please describe.
   4. Not applicable.

7. A. Has N Been sick (Vomited) in the last year?
   1. No
   2. Once or twice
   3. More than twice in the year but less than once a week
   4. More than once a week
   5. Every day

   B. IF YES ask, does N ever vomit up blood?
   1. No
   2. Yes - specify
   9. Don't know
   0. Not applicable
APPENDIX 15:2

8. Has N had diarrhoea or loose bowel motions in the last year? If so, was there any blood present?
   1. No
   2. Yes - specify - frequency - appearance

9. Does N ever get pains in his/her tummy?
   1. No
   2. Yes
   9. Don't know

If yes, specify - site
   - frequency
   - duration
   - character

10. A. How many throat or ear infections has N had in the past year?
    1. Less than three
    2. More than three
    9. Don't know

B. Does N get frequent earaches or discharging ears?
   1. No
   2. Yes
   9. Don't know

C. Does N have any trouble with his/her hearing?
   1. No
   2. Yes - please specify

D. Has N had his/her tonsils out?
   1. Yes
   2. No
   9. Don't know

11. Has N ever had
A. ASTHMA
    1. No, 2. Yes, 9. Don't know
    Specify - age of onset
    - no. of attacks
    - frequency

B. BRONCHITIS, with or without wheezing
    1. No, 2. Yes, 9. Don't know
    Specify - age of onset
    - No. of attacks
    - frequency

C. Any other infection in the chest or lungs?
    1. No, 2. Yes, 9. Don't know
    Specify - diagnosis
    - no. of episodes
    - frequency
12. A. Has N ever had rheumatic fever?
   1. No, 2. Yes, 9. Don't know
      Please specify

   B. Has N ever had any other heart disease or suspected heart disease?
      1. No, 2. Yes, 9. Don't know
      Please specify

13. A. Has N ever complained of burning or discomfort when passing water (urine)?
      1. No, 2. Yes, 9. Don't know
      Please specify

   B. Has N ever had any treatment for a water (urine) infection, or infection of the bladder or kidney?
      1. No, 2. Yes, 9. Don't know
      Please specify

   C. Has N ever passed blood in the urine?
      1. No, 2. Yes, 9. Don't know
      Please specify

14. A. Has N ever broken any bones?
      1. No, 2. Yes, 9. Don't know
      Please specify

   B. Has N ever had any other bone, joint or spinal problem? e.g. CDH, TEV
      1. No, 2. Yes, 9. Don't know
      Please specify

15. A. Has N got any bad scars?
      1. No, 2. Yes, 9. Don't know
      Please specify

   B. Has N got any birth marks?
      1. No, 2. Yes, 9. Don't know
      Please specify

   C. Has N got any other possible disfiguring condition?
      1. No, 2. Yes, 9. Don't know
      Please specify

16. A. Has N had any eye trouble?
      1. No, 2. Yes, 9. Don't know
      Please specify

   B. Does N wear glasses?
      1. No, 2. Yes
17. Has N had any trouble with his speech now or in the past?
   1. No, 2. Yes, 9. Don't know
      Specify

18. Has N ever had a fit, convulsion, or fainting attack?
   1. No, 2. Yes, 9. Don't know
      Specify - age of onset
      - frequency
      - duration
      - nature
      - investigations
      - treatment

19. Does N ever get headaches or migraine?
   1. No, 2. Yes, 9. Don't know
      Specify

20. Has N ever been difficult to wake up in the morning?
   1. No, 2. Yes, 9. Don't know
      Specify - hours of sleep

21. Has N had any other illnesses or operations besides those we have mentioned already?
    (See questions 57 and 58 first)

22. A. Has N ever been admitted to hospital over night?
    1. No, 2. Yes, 9. Don't know
    B. If yes, please state number of admissions.
    C. PLEASE complete details for every hospital admission, giving names and addresses of all hospitals to which child has been admitted accurately enough to contact them by letter. Tell parents we may wish to approach the hospital(s) to get further medical details.

23. Is N currently taking any medicines or tablets, or having injections?
    1. No, 2. Yes - specify

24. A. Have you been concerned about N's growth or development?
    1. No, 2. Yes, 9. Don't know
    B. If yes, in what way?

25. How old was N when you first noticed that he/she was smaller than most children the same age?
    Enter age in years in box
    For birth enter 0
    1 = 2, enter 1
    2 = 3, enter 2 etc.
    Not applicable, enter 9
26. A. Have you been to see your family doctor specifically because of concern about N's growth?
   1. No, 2. Yes, 9. Uncertain

B. How old was N when you first saw your general practitioner about it?
   Enter age in years
   For birth enter 0
   1 - 2, enter 1
   If not applicable enter 9

C. What action did your GP take?
   1. None except reassurance
   2. Other illness present - no further action
   3. Blood tests and/or X-rays
   4. Referral to out-patients or special clinic
   5. 3 + 4
   9. Don't know
   0. Not applicable

27. Is N smaller than any of his brothers/sisters were at the same age?
   1. No
   2. Yes - specify which ones
   9. Don't know
   0. Not applicable

28. Were either you or N's father much smaller than average height when you were children?
   1. No, 2. Yes, 9. Don't know

29. A. How tall are you now? _feet _inches

B. How tall is N's father? _feet _inches

30. Do you think that N is self conscious or feels different in any way from other children because of his/her height?
   1. No, 2. Yes, 9. Don't know
   Specify

I would now like to ask some questions about N's birth.

31. A. Firstly, what is your relationship to N?
   1. Own or natural mother
   2. Mother by legal adoption
   3. Stepmother
   4. Foster mother
   5. Grandmother
   6. Co-habitee
   7. No mother figure - please specify
APPENDIX 15:6

31. B. If you are not the child's natural or legal adoptive mother, can you please tell me the reasons for this if possible?

1. Natural mother deceased
2. Natural mother separated
3. Natural mother divorced
4. Natural mother ill or disabled
5. Child in care of Local Authority
6. Other, please specify
7. Don't know
8. Not applicable

32. A. Is your present husband the child's natural father?

1. Natural father
2. Father by legal adoption
3. Stepfather
4. Foster father
5. Grandfather
6. Co-habitee - common law husband
7. No husband or father figure at the moment - please specify

B. If N is not living with his natural father at the moment, can you please tell me the reason for this if possible?

1. Natural father deceased
2. Natural father separated
3. Natural father divorced
4. Natural father ill or disabled
5. Child in care
6. Don't know
7. Not applicable

C. If you have no husband or N has no father figure at the moment, how long have you been living by yourself?

1. 0 - 1 years
2. 1 - 2 years
3. etc.
8. Not applicable

33. Were you well during your pregnancy with N? If not, what sorts of problems did you have?

1. Normal
2. Swelling or high blood pressure
3. Bleeding
4. Baby not growing well
5. Severe vomiting
6. Other complication requiring investigation and/or admission to hospital apart from in labour and/or induction.
7. Iron injections during pregnancy
8. Blood transfusion during pregnancy
9. Don't know
10. Not applicable
APPENDIX 15:7

34. How soon after you were pregnant did you first see a doctor about it?
   1. Less than three months
   2. Three to six months
   3. Six to nine months
   4. Never before birth
   9. Don't know
   0. Not applicable

35. Was N born around the due date? If not, how early or late was he/she?
   Enter gestational age in box

36. Was N born in hospital or at home? If N was born at home, who helped with the delivery?
   1. Hospital
   2. Home, no-one present
   3. Home, untrained person present
   4. Home, midwife or doctor present
   9. Don't know

37. Did you have any problems with the birth itself?
   1. Spontaneous delivery
   2. Assisted delivery
   3. Caesarian section
   4. Other - including prolonged labour, over 24 hours, preterm labour resulting in delivery at 36 weeks or earlier
   9. Don't know
   0. Not applicable

38. Was N born in the normal position?
   1. Vertex
   2. Breech
   3. Other
   9. Don't know


40. Do you know what length N was at birth?
   Enter length in centimetres in boxes
   If not known, enter 99

41. Did you nurse N straight after birth, or was he/she kept in the nursery for a time?
   1. Nursed straight away
   2. Kept in nursery for more than 12 hours
   9. Not applicable

42. How did you feel for the first few weeks after N was born?
   1. Alright
   2. Tired or worn out
   3. Sick
   9. Don't know
   0. Not applicable
APPENDIX 15:8

43. Did you have any worries with N at all when he/she was a baby?
   1. No
   2. Yes - please specify
   3. Don't know
   4. Not applicable

44. How old were you when you had your first baby?
Enter age in years.

45. A. How many children have you had during your present marriage?
Enter total no. of children in box

Can you tell me their dates of birth and whether they were boys or girls?

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Date of birth</th>
</tr>
</thead>
</table>

Enter total no. of boys in box

B. How many children have you had as a result of any previous marriage or relationship? Can you remember their dates of birth and whether they are boys or girls?

<table>
<thead>
<tr>
<th>Name</th>
<th>Sex</th>
<th>Date of birth</th>
</tr>
</thead>
</table>

Enter total number of children in box
Enter number of boys in box

46. From the above answers
   A. What is the pregnancy number of N?
   B. What is the interval between N and the older child?

Enter interval in months in box
Not applicable, enter 00
Don't know, enter 99
APPENDIX 5:2

46. C. What is the interval between N and the younger child?

Enter interval in months in box
Not applicable, enter 00
Don't know, enter 99

D. What is the overall average interval?

Enter interval average in months
Not applicable, enter 00
Don't know, enter 99

47. Did you have any trouble with any of your other pregnancies?

1: No trouble or only normal discomforts
2. Swelling or high blood pressure or excessive weight gain
3. Bleeding
4. Small baby or growing slowly
5. Severe vomiting
6. Other
9. Don't know
0. Not applicable

48. Have you had any trouble with any of your other births?

1. No
2. Yes – please specify
9. Don't know
0. Not applicable

49. A. Have you lost any children during a pregnancy before six months?

If yes, enter number in box, otherwise enter 0

B. Have you had any stillbirths?

If yes, enter no. in box, otherwise enter 0

50. Have you had any children who were born alive and have since died?

For none enter 0
If yes, enter no. in box
Specify reasons

51. A. Was N breast fed at all?

1. No
2. Yes
9. Don't know
0. Not applicable

B. If yes, for how many months?

If not breast fed at all enter 0
If breast fed less than one month enter 1
One to two months enter 2
Two to three months enter 3 etc.
If breast fed for eight or more months enter 9
52. A. Was N difficult to feed as an infant?
   1. No
   2. Yes - mild difficulty, same or less than other children
   3. Yes - very difficult, worse than other children
   9. Don't know

B. Did you consult a doctor about this?
   1. No
   2. Yes
   9. Don't know
   0. Not applicable

53. How old was N when he/she first walked alone?
   Specify age in months.

54. How old was N when he/she first started talking?
   (i.e. put two or more words together with meaning)
   If less than 2 years enter 01
   If more than 2 years enter no. of months

55. Does N wet the bed? If so, how often? If not, when was N regularly dry at night?
   1. Dry at nights before age 5
   2. Wets infrequently, once a month or less
   3. Wets more than once a month but not every week
   4. Wets more than once a week
   5. Wets nearly every night

56. Does N ever soil his/her pants?
   1. No
   2. Yes - specify

57. Has N ever had any of these infectious diseases?
   A. Measles
      1. No, 2. Yes, 9. Don't know
   B. Whooping cough
   C. Chicken pox
   D. Mumps
   E. German measles
   F. Meningitis
   G. Hepatitis
   H. T.B.

58. Was N immunised against any of the following diseases before he started school?
   A. Diphtheria
      1. No, 2. Yes, 9. Don't know
   B. Whooping cough
      1. " " "

58. C. Tetanus  1. No, 2. Yes, 9. Don’t know
      D. Polio  
      E. Measles  
      F. Smallpox  
      G. Any other disease  

59. Has N ever been to an infant welfare clinic?
    1. No, 2. Yes, 9. Don’t know

60. Have you or N ever been visited at home by a health visitor?
    1. No, 2. Yes, 9. Don’t know

61. Has N had any problems with his teeth?
Has N ever been to the dentist?
    1. No, 2. Yes, 9. Don’t know

62. A. Has N ever been looked after by someone other than you?
(excluding the newborn period)
How long was this for?

<table>
<thead>
<tr>
<th>First Placement</th>
<th>Second Placement</th>
<th>Third Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal caretaker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Place</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration</td>
<td></td>
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</tr>
<tr>
<td>Reason for change in placement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present father figure present during separation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child’s reaction to separation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B. Please list details if N has been looked after by someone other than present mother figure for more than one month in the past, excluding hospital admissions. Write details below, if insufficient space, attach list.
I would now like to ask you a few questions about N's schooling?

63. A. Does N have school dinners?
   1. No, 2. Yes

B. Do you have to pay for it?
   1. No, 2. Yes, 0. Not applicable

64. Does N miss much school?
   1. No, 2. Yes - away once a week or more often.
      Specify reasons.

65. How many different schools has N been to since starting school?
    Enter no. of schools in box.

Can you tell me a little bit about the rest of the family?

66. A. How old is mother?
    B. How old is father?

67. If there any family history of:-
   A. Bowel or digestive disturbances including coeliac disease or
      cystic fibrosis, or any stomach trouble?
      1. No, 2. Yes, 9. Don't know
   B. T.B., Asthma, or Bronchitis?
      1. No, 2. Yes, 9. Don't know
   C. Diabetes?
      1. No
   D. Heart Disease?
      1. No
   E. Growth problems?
      1. No

68. A. Has N ever lived in the same house as anyone suffering from
   any long standing illness or disability.
   e.g. chronic bronchitis, asthma, arthritis or any nervous or
   mental illness.
   1. No
   2. Yes - still living the same house
   3. Yes - not still living in the same house
      9. Don't know

B. If yes, which members of the family were affected?
   1. Mother or mother figure
   2. Father or father figure
   3. Other child
   4. Other adult
   5. More than one person
   0. Not applicable
APPENDIX 15:13

68. C. How severely affected were they by the illness?
    Enter grade of disability in box.

69. A. Do either you or the child's father smoke?
    1. Never smoked
    2. Used to smoke but not any longer
    3. Smokes now

B. If non-smoker, but previously smoked, how many years non-smoker?
    1. Less than 12 months
    2. One to two years
    3. Two to three years etc.
    4. Eight or more years
    0. Not applicable

C. How many cigarettes per day do you and N's father smoke?
    Enter 00 if non-smoker
    Enter 88 if pipe smoker only
    Enter 99 if cigar smoker only
    Enter 98 if unknown number

D. NB This question only applies if N's mother figure is his/her natural mother.
Did you smoke in your pregnancy with N?
    1. No
    2. Yes
    3. Can't remember
    0. Not applicable

70. How many people normally stay at your house with you?
    Include the child in the Scottish Growth Study, parent or people who act as parents, other adults, if any, e.g. relatives or lodgers who are members of the household, any other children, children of relatives or lodgers.
    Exclude anybody who is only at home for short periods e.g. children home from boarding school during holidays, servicemen on leave, relatives or friends who only stay occasionally.

71. What is the relationship of everybody staying with you to N?
    Below is a list of possible relationships. Please enter in the box the number of people in the household who bear that relationship to N. If there are two parents at home enter two in the box alongside of parents, if no one staying in the household has that relationship please enter 0 in box.
    1. Parent(s) or parent figure(s)
    2. Grandparent(s)
    3. Siblings
    4. Stepbrother(s) and/or stepsister(s)
    5. Other relative(s)
    6. Lodger(s) and children of lodger(s)
    7. Children of relatives

Please check that the total sum of the nos. in boxes is one less than no. in household.
72. A. What sort of accommodation do you have where you stay?
1. Rooms in non-self-contained flat
2. Flat/maisonette - self-contained
3. Whole terraced house including end of terrace
4. Whole semi-detached house or bungalow
5. Whole detached house or bungalow
6. Condemned housing awaiting demolition
7. Other, please specify

B. If rooms or flat, what floor are they on?
If higher than 9th floor, enter 9
If on ground or basement, enter 0
If answer to part A is 3 - 5 enter 0

73. A. Is the accommodation
1. Rented (including tied to employment)
2. Owned
3. Other (including squatting) specify

B. If rented, is it
1. Council
2. Private
3. Tied to occupation
0. Not applicable

C. If owned, is it
1. Mortgaged
2. Owned outright
0. Not applicable

74. A. How long have you stayed there?
Enter no. of years in box
0 - 1 enter 0
1 - 2 enter 1 etc.
If more than 9 years, enter 9

B. How many different places have you lived in since N was born?
If always at present address put 1 in box

75. How many rooms do you have?
Exclude bathroom, scullery, kitchen - unless used as living room
i.e. kitchen dinette = 1 room
Include living rooms, bedrooms, rooms used by lodgers or relatives who are members of the household

76. Where do you usually eat your meals?
Do you usually sit round a table?
1. No
2. Yes, but only at weekends or holidays
3. Yes, most meals
4. Other
9. Don't know
APPENDIX 15:15

77. A. Does N have his/her own bedroom?
   1. No
   2. Yes

B. Does N share a bed with anyone?
   1. No
   2. Yes - how many others

78. Does your household have

   1. Sole use
   2. Shared use
   3. No use - not available

of the following facilities?
A. Bathroom
B. Indoor lavatory
C. Outdoor lavatory
D. Hot water supply
E. Cooking facilities
F. Telephone (sole use = private, shared use = coin box on premises)
G. Refrigerator
H. TV - colour/b&w
I. Washing machine

I would now like to ask you some questions about yourself.

79. Where were you and N's father born?

   1. Glasgow or environs - specify
   2. Other large Scottish town or city
   3. Elsewhere in Scotland
   4. Elsewhere in UK large town or city
   5. Elsewhere in UK rural area
   6. Ireland
   7. Africa or West Indies
   8. Asia
   9. Elsewhere overseas
   0. Not applicable e.g. don't know, adopted mother etc.

80. A. How many brother and sisters stayed with you when you were growing up?
   Enter no. on box

   B. Was your father staying with you when you were at school?
   1. No
   2. Yes

   C. If not, who was the head of the household?

81. A. If your father lived with you when you were growing up, what was his job?
   Please specify
   Enter R.G. occupation in box
APPENDIX 15:16

81. B. If your father was not the head of the household but other male was named, what was his job when you were at school?
   Please specify
   Enter R.G. occupation in box

C. If no male was present, but female was head of household, what was her job?
   Please specify
   Enter R.G. occupation in box

82. A. How old were you (N's mother) when you left school?
B. How old was N's father when he left school? (or father figure)

83. A. How good were you at school work?
   1. Above the middle of the class (top 25%)
   2. Average (middle 50%)
   3. Below the middle of the class (bottom 25%)
   9. Don't know

B. Have you had any further educational training since you left school? (including night school, college, or university)
   1. No
   2. Yes - please describe

84. A. Did you work at all before you had your own children?
   1. No
   2. Yes, please describe job
   9. Don't know

B. How are you occupied now?
   1. Employed full time
   2. Employed part time, less than 10 hours weekly
   3. Employed part time, 10 to 30 hours weekly
   4. Not employed, or works at home
   5. Other, please specify

C. Which of the following best describes the mother's working hours?
   1. Standard hours - any time between 7.30 am and 6.30 pm
   2. Non-standard hours, early mornings, evenings or overnight
   3. Some days standard hours, other days non-standard
   4. Other situation
   5. Housewife
APPENDIX 15:17

84. D. Has the mother ever lost pay through taking time off for N to attend the following?
   (a) Immunisations or checkups at Child Welfare Clinics
   (b) Specialist clinics, outpatients, child guidance, speech therapy
   (c) Dental clinics
   (d) Emergency visits to your family doctor
   (e) Visiting child in hospital

   1. No
   2. Yes
   0. Not applicable

85. We have been hearing a lot lately about adults who are very embarrassed because, through no fault of their own, they find it very difficult to read. Do you have any problems with reading?

   1. No
   2. Yes
   9. Don't know

86. A. Can you tell me what sort of work N's father does?
   If the study child has no father, or father figure, please give details of the occupation of the male head of the household. If there is no male head, enter 000 in box. Full and precise details of the occupation are required. If a person's job in the trade or industry is known by a special name, write down that name. Additionally, please describe the industry or business the father is engaged in. Note: Vague terms such as scientist, engineer, machinist, fitter, foreman, checker, are not enough by themselves. Neither are general terms such as manufacturers, merchants, agents, brokers, dealers. If the father is a civil servant, please write in rank or grade. If the father is a miner, please state whether he has worked above ground or on the face.

   OCCUPATION:

   B. Is the father self employed?

   1. No, 2. Yes, 0. Not applicable

   C. Is the father an employee?

   1. No, 2. Yes, 0. Not applicable

   D. Is the father unemployed?

   1. No, 2. Yes, 0. Not applicable

   E. Is the father retired?

   1. No, 2. Yes, 0. Not applicable

87. Has N's father, or the male head of the household if no father, been off work in the past twelve months through illness, or unemployment?
87. A. Illness
   1. No, 2. Yes, 0. Not applicable
   How many weeks lost? 00. " "

B. Unemployment
   1. No, 2. Yes, 0. Not applicable
   How many weeks lost? 00. " "

88. Has the family ever been in receipt of a supplementary allowance or family income supplement?
   A. Supplementary allowance
      1. No, 2. Yes, 9. Don't know
   B. Family income supplement
      1. No, 2. Yes, 9. Don't know

89. Are there any groups or societies you belong to or attend, or do you do any church work?
   1. No, 2. Yes.

B. Do you or your husband have relatives who come to visit you or who you go to visit?
   1. No
   2. Yes - visitors belong only to the same generation as study child
   3. Yes - visitors belong only to parents' generation or older
   4. Yes - visitors include relatives of more than one generation.

90. Which of your relatives do you feel closest to?
    Who would you go to if you were in trouble?
   1. No one, or husband or own child only
   2. One of the following: grandparent, parent, parent-in-law
      step-parent, aunt, uncle, brother, sister, brother-in-law,
      niece, nephew, cousin.

91. Who do you go to for advice with problems?
   1. No one
   2. One or two people named above, or friends
   3. Names three or more people above, or friends
   4. Professional helpers only

92. Do you have friends and neighbours who call in to see you, or whom you call in on? If yes, how often?
   1. No one
   2. Frequency of less than once a month
   3. Frequency of at least once a month
   4. Frequency of at least once a week

93. Are there people who come to see you sometimes and ask for your help or advice? If yes, what for?
   1. No one comes
   2. People come for one of the following reasons:
      - help with housework, to borrow money or food
   3. People come for advice, for help with children or sickness, or for more than one reason.
A. Rate subjective impression of mother on a scale from 0-9.

(a) Depressed 0 - happy 9
(b) Untidy 0 - tidy 9
(c) Dirty 0 - clean 9
(d) Inadequate 0 - capable 9
(e) Uncooperative 0 - cooperative 9

A. How well did mother understand the questions in the interview?

B. How well did she respond to the questions?

C. How would you rate her intelligence?

D. Did she have any difficulty in thinking in terms of ideas?

1. Rated as having difficulty in understanding and difficulty in responding and below average intelligence compared with other mothers interviewed and only able to deal with concrete matter of fact things, ie poor performance in all four questions.

2. Rated fairly well or better on one out of the four questions above.

3. Rated fairly well or better on two out of the four questions above.

4. Rated fairly well or better on three out of the four questions above.

5. Rated fairly well or better on all four questions.

Ascertain from the child's teacher the number of days absent from school in the last three completed terms where possible.
## APPENDIX TABLE 1

**SOCIAL CLASS DISTRIBUTION - EDINBURGH, GLASGOW, ABERDEEN**

<table>
<thead>
<tr>
<th>SOCIAL CLASS</th>
<th>EDINBURGH</th>
<th>GLASGOW</th>
<th>ABERDEEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>8.25</td>
<td>3.21</td>
<td>4.51</td>
</tr>
<tr>
<td>II</td>
<td>16.5</td>
<td>9.67</td>
<td>13.4</td>
</tr>
<tr>
<td>III Non-manual</td>
<td>13.8</td>
<td>10.5</td>
<td>10.9</td>
</tr>
<tr>
<td>III Manual</td>
<td>34.2</td>
<td>41.4</td>
<td>36.5</td>
</tr>
<tr>
<td>IV</td>
<td>15.8</td>
<td>18.7</td>
<td>21.1</td>
</tr>
<tr>
<td>V</td>
<td>8.3</td>
<td>13.8</td>
<td>11.6</td>
</tr>
<tr>
<td>Other</td>
<td>3.17</td>
<td>2.72</td>
<td>1.96</td>
</tr>
</tbody>
</table>

**SOURCE.** 10% Sample Census, Scotland, 1971. Table 4.

## APPENDIX TABLE 2

**NUMBERS AND PERCENTAGES OF ECONOMICALLY ACTIVE POPULATION OUT OF WORK - EDINBURGH, GLASGOW, ABERDEEN**

<table>
<thead>
<tr>
<th>Economically Active Population</th>
<th>Out of Work</th>
<th>% Out of Work</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDINBURGH 12,568</td>
<td>1,010</td>
<td>8.04</td>
</tr>
<tr>
<td>GLASGOW 25,268</td>
<td>3,474</td>
<td>13.7</td>
</tr>
<tr>
<td>ABERDEEN 4,905</td>
<td>345</td>
<td>7.03</td>
</tr>
</tbody>
</table>

**SOURCE.** 10% Sample Census, Scotland, 1971. Table 1.
### ORGANIC CONDITIONS PRESENT IN CHILDREN WHOSE PARENTS WERE NOT CONTACTED

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21 and congenital heart disease</td>
<td>5</td>
</tr>
<tr>
<td>Cerebral palsy with mental retardation</td>
<td>4</td>
</tr>
<tr>
<td>Epilepsy and mental retardation</td>
<td>2</td>
</tr>
<tr>
<td>Sacral tumour and other abnormalities</td>
<td>2</td>
</tr>
<tr>
<td>Achondroplasia and spina bifida occulta</td>
<td>1</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>1</td>
</tr>
<tr>
<td>Hirschsprung's disease and malabsorption: recent diagnosis and surgery</td>
<td>1</td>
</tr>
<tr>
<td>Cystic fibrosis (normal height velocity)</td>
<td>1</td>
</tr>
<tr>
<td>&quot;Trisomy 18&quot; syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Hurler's disease</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total = 19**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone deficiency</td>
<td>4</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>9</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>8</td>
</tr>
<tr>
<td>Cerebral palsy and mental retardation</td>
<td>5</td>
</tr>
<tr>
<td>Microcephaly and mental retardation</td>
<td>2</td>
</tr>
<tr>
<td>Achondroplasia</td>
<td>2</td>
</tr>
<tr>
<td>Ataxia telangiectasia</td>
<td>1</td>
</tr>
<tr>
<td>Coeliac disease (normal height velocity)</td>
<td>1</td>
</tr>
<tr>
<td>Congenital spinal malformation</td>
<td>1</td>
</tr>
<tr>
<td>Kyphoscoliosis (normal height velocity)</td>
<td>1</td>
</tr>
<tr>
<td>Idiopathic thrombocytopenic purpura</td>
<td>1</td>
</tr>
<tr>
<td>(normal height velocity)</td>
<td></td>
</tr>
<tr>
<td>Progeria</td>
<td>1</td>
</tr>
<tr>
<td>Asthma (normal height velocity)</td>
<td>1</td>
</tr>
<tr>
<td>Hypochondroplasia</td>
<td>1</td>
</tr>
<tr>
<td>Non-specific storage disease</td>
<td>1</td>
</tr>
<tr>
<td>Morquios</td>
<td>1</td>
</tr>
<tr>
<td>Gonadal hypoplasia</td>
<td>1</td>
</tr>
<tr>
<td>Intersex with congenital heart disease</td>
<td>1</td>
</tr>
</tbody>
</table>

**Total = 42**
APPENDIX TABLE 5

FINAL NON-RESPONDERS WITH ORGANIC BASIS FOR SHORT STATURE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spina bifida</td>
<td>5</td>
</tr>
<tr>
<td>C.P. + epilepsy + LBW</td>
<td>4</td>
</tr>
<tr>
<td>Asthma + eczema</td>
<td>2</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>2</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>2</td>
</tr>
<tr>
<td>Severely retarded</td>
<td>2</td>
</tr>
<tr>
<td>Achondroplasia</td>
<td>1</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>1</td>
</tr>
<tr>
<td>Imperforate anus and other congenital abnormalities</td>
<td>1</td>
</tr>
<tr>
<td>Klippel-Fiel syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>1</td>
</tr>
<tr>
<td>?Russell-Silver syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Renal hypoplasia</td>
<td>1</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>1</td>
</tr>
</tbody>
</table>

Total = 25

Numbers in parentheses indicate children with normal height velocity.
### APPENDIX TABLE 6

**CHILDREN WITH ORGANIC CONDITIONS SCREENED FOR GHD**

*Total = 26*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital heart disease (PS 2, VSD1)</td>
<td>3</td>
</tr>
<tr>
<td>Asthma</td>
<td>2</td>
</tr>
<tr>
<td>&quot;Chronic bronchitis&quot;</td>
<td>2 (1*)</td>
</tr>
<tr>
<td>Perthe's disease</td>
<td>2</td>
</tr>
<tr>
<td>Arrested hydrocephalus</td>
<td>2</td>
</tr>
<tr>
<td>Acute lymphoblastic leukaemia</td>
<td>1</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>1</td>
</tr>
<tr>
<td>Glycogen storage disease</td>
<td>1</td>
</tr>
<tr>
<td>Tracheo-oesophageal fistula, LBW, and &quot;surgical malnutrition&quot;</td>
<td>1</td>
</tr>
<tr>
<td>Metaphyseal dysostosis</td>
<td>1</td>
</tr>
<tr>
<td>FH rickets</td>
<td>1</td>
</tr>
<tr>
<td>Scoliosis</td>
<td>1</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>1</td>
</tr>
<tr>
<td>FH Meningitis and nerve deafness</td>
<td>1</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>1 *</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>1 *</td>
</tr>
<tr>
<td>Recurrent urinary tract infections</td>
<td>1</td>
</tr>
<tr>
<td>Russell-Silver syndrome</td>
<td>1 *</td>
</tr>
<tr>
<td>Turner's mosaic (45, X0/46, X i(Xq))</td>
<td>1 *</td>
</tr>
<tr>
<td>'Runt' twin</td>
<td>1</td>
</tr>
</tbody>
</table>

*(Diagnosis in survey)*

---

* PS - Persistent
* VSD1 - Ventricular septal defect
* LBW - Low Birth Weight
* FH - Familial

------

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**APPENDIX TABLE 7**

**HEIGHT SDS* BY DIAGNOSTIC GROUP**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>SDS</th>
<th>NON-ORGANIC NON-RESPONDERS</th>
<th>ORGANIC SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE EXCLUDING LBW</th>
<th>LBW SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 &gt; -2.5</td>
<td>21</td>
<td>5</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>36</td>
<td>6</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>-2.5 &gt; -3.0</td>
<td>45 (86%)</td>
<td>26 (38%)</td>
<td>12 (50%)</td>
<td>5 (46%)</td>
<td>18 (72%)</td>
<td>11 (86%)</td>
<td>111 (83%)</td>
<td>25 (86%)</td>
<td>253 (72%)</td>
</tr>
<tr>
<td>-3.0 &gt; -3.5</td>
<td>10</td>
<td>19</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>24</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>-3.5 &gt; -4.0</td>
<td>-</td>
<td>9</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>7</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>-4.0 &gt; -4.5</td>
<td>1</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td>-4.5 &gt; -5.0</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>&lt; -5.0</td>
<td>-</td>
<td>8</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9</td>
</tr>
<tr>
<td>TOTAL</td>
<td>77</td>
<td>82</td>
<td>26</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>449</td>
</tr>
</tbody>
</table>

* SDS* = Height SDS at chronological age when screened for GHD or when last seen (Group I and II).
### APPENDIX TABLE 8

*HEIGHT SDS* (MEANS, SD, & RANGES) BY SEX AND DIAGNOSTIC GROUP

<table>
<thead>
<tr>
<th></th>
<th>I NON-ORGANIC NON-RESPONDERS</th>
<th>II ORGANIC SHORT STATURE</th>
<th>VII ?ORGANIC SHORT STATURE</th>
<th>III SEVERE GHD</th>
<th>IV PARTIAL GHD</th>
<th>V POSSIBLE GHD</th>
<th>VI A CONSTITUTIONAL SHORT STATURE EXCLUDING LBW</th>
<th>VI B LBW SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOTH SEXES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>77</td>
<td>82</td>
<td>26</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>449</td>
</tr>
<tr>
<td>Mean</td>
<td>-2.73</td>
<td>-3.50</td>
<td>-3.15</td>
<td>-3.39</td>
<td>-2.95</td>
<td>-2.70</td>
<td>-2.77</td>
<td>-2.70</td>
<td>-2.94</td>
</tr>
<tr>
<td>SD</td>
<td>0.33</td>
<td>0.89</td>
<td>0.75</td>
<td>0.78</td>
<td>0.36</td>
<td>0.18</td>
<td>0.33</td>
<td>0.30</td>
<td>0.60</td>
</tr>
<tr>
<td>Range</td>
<td>-2.18 to -4.47</td>
<td>-2.20 to -6.31</td>
<td>-2.50 to -6.31</td>
<td>-2.55 to -4.84</td>
<td>-2.41 to -3.12</td>
<td>-3.88</td>
<td>-2.10 to -3.63</td>
<td>-2.07 to -6.31</td>
<td></td>
</tr>
<tr>
<td>BOYS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>32</td>
<td>43</td>
<td>18</td>
<td>8</td>
<td>17</td>
<td>8</td>
<td>90</td>
<td>24</td>
<td>240</td>
</tr>
<tr>
<td>SD</td>
<td>0.23</td>
<td>0.81</td>
<td>0.38</td>
<td>0.68</td>
<td>0.24</td>
<td>0.11</td>
<td>0.32</td>
<td>0.27</td>
<td>0.54</td>
</tr>
<tr>
<td>Range</td>
<td>-2.25 to -3.22</td>
<td>-2.46 to -5.34</td>
<td>-2.50 to -3.72</td>
<td>-2.55 to -4.84</td>
<td>-2.41 to -3.79</td>
<td>-3.88</td>
<td>-2.10 to -3.42</td>
<td>-2.07 to -5.60</td>
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<tr>
<td>GIRLS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>45</td>
<td>39</td>
<td>8</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>88</td>
<td>10</td>
<td>209</td>
</tr>
<tr>
<td>Mean</td>
<td>-2.76</td>
<td>-3.54</td>
<td>-3.57</td>
<td>-2.69</td>
<td>-2.96</td>
<td>-2.80</td>
<td>-2.81</td>
<td>-2.77</td>
<td>-2.97</td>
</tr>
<tr>
<td>SD</td>
<td>0.39</td>
<td>0.99</td>
<td>1.17</td>
<td>0.16</td>
<td>0.56</td>
<td>0.20</td>
<td>0.33</td>
<td>0.35</td>
<td>0.66</td>
</tr>
<tr>
<td>Range</td>
<td>-2.18 to -4.47</td>
<td>-2.20 to -6.31</td>
<td>-2.62 to -6.31</td>
<td>-2.57 to -2.91</td>
<td>-2.61 to -3.12</td>
<td>-3.64</td>
<td>-2.19 to -3.63</td>
<td>-2.41 to -6.31</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX TABLE 9

HEIGHT SDS<sub>BA</sub> BY DIAGNOSTIC GROUP

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>SDS&lt;sub&gt;BA&lt;/sub&gt;</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>0 &lt; 1</td>
<td>-</td>
<td>4</td>
<td>2</td>
<td>18</td>
<td>3</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>-1 &lt; 0</td>
<td>4</td>
<td>11</td>
<td>4</td>
<td>49</td>
<td>8</td>
<td>6</td>
<td>82</td>
</tr>
<tr>
<td>-2 &lt; -1</td>
<td>2 (60%)</td>
<td>3 (84%)</td>
<td>3 (92%)</td>
<td>71 (84%)</td>
<td>14 (82%)</td>
<td>8 (64%)</td>
<td>101 (82%)</td>
</tr>
<tr>
<td>-3 &lt; -2</td>
<td>3</td>
<td>4</td>
<td>-</td>
<td>23</td>
<td>4</td>
<td>9</td>
<td>43</td>
</tr>
<tr>
<td>&lt; -3</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>TOTAL</td>
<td>10</td>
<td>25</td>
<td>13</td>
<td>173</td>
<td>34</td>
<td>25</td>
<td>280</td>
</tr>
</tbody>
</table>

MEAN ± SD

<table>
<thead>
<tr>
<th></th>
<th>-1.51±1.30</th>
<th>-0.55±1.21</th>
<th>-0.34±1.56</th>
<th>-1.02±1.08</th>
<th>-0.83±1.29</th>
<th>-1.27±0.31</th>
</tr>
</thead>
</table>

UNKNOWN: 10
### APPENDIX TABLE 10

**HEIGHT VELOCITY PERCENTILES BY DIAGNOSTIC GROUP**

(CHRONOLOGICAL AGE BASED)

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PERCENTILES</th>
<th>NON-ORGANIC NON-RESPONDERS</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3rd</td>
<td>3</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>11</td>
<td>1</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>3 &lt; 10th</td>
<td>11</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>31</td>
<td>4</td>
<td>4</td>
<td>63</td>
</tr>
<tr>
<td>10th &lt; 25th</td>
<td>13 (44%)</td>
<td>1 (89%)</td>
<td>6 (80%)</td>
<td>7 (100%)</td>
<td>42 (61%)</td>
<td>11 (59%)</td>
<td>3 (79%)</td>
<td>83 (62%)</td>
</tr>
<tr>
<td>25th &lt; 50th</td>
<td>19</td>
<td>1</td>
<td>5</td>
<td>-</td>
<td>38</td>
<td>9</td>
<td>2</td>
<td>74</td>
</tr>
<tr>
<td>50th &lt; 75th</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>12</td>
<td>2</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>75th &lt; 90th</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>11</td>
</tr>
<tr>
<td>90th &lt; 97th</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>&gt; 97</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>SUB TOTAL</td>
<td>61</td>
<td>9</td>
<td>25</td>
<td>13</td>
<td>138</td>
<td>27</td>
<td>14</td>
<td>287</td>
</tr>
<tr>
<td>NOT KNOWN</td>
<td>16</td>
<td>4 *</td>
<td>-</td>
<td>1</td>
<td>40</td>
<td>7</td>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>TOTAL</td>
<td>77</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>26</td>
<td>367</td>
</tr>
</tbody>
</table>

* 3 children previously diagnosed: 2 on treatment
* 1 - investigations done less than 9 months ago

(GH < 1 mu/L)
APPENDIX TABLE 11

HEIGHT VELOCITY SDS BA BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>HEIGHT VELOCITY SDS BA</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR. LEW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>-1 &lt; 0</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>45</td>
<td>1</td>
<td>49</td>
</tr>
<tr>
<td>-2 &lt; -1</td>
<td>3 (33%)</td>
<td>13 (56%)</td>
<td>8 (82%)</td>
<td>78 (85%)</td>
<td>5 (50%)</td>
<td>107 (77%)</td>
</tr>
<tr>
<td>-3 &lt; -2</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>23</td>
<td>5</td>
<td>42</td>
</tr>
<tr>
<td>&lt; -3</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>9</td>
<td>25</td>
<td>11</td>
<td>150</td>
<td>14</td>
<td>209</td>
</tr>
<tr>
<td>Missing values</td>
<td>4</td>
<td>-</td>
<td>3</td>
<td>62</td>
<td>12</td>
<td>81</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>212</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
## Appendix Table 12

Bone Age SDS by Diagnostic Group

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>SDS</th>
<th>Mean ± SD</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional Short Stature</th>
<th>LBW Short Stature</th>
<th>Organic Investigated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN ± SD</td>
<td>-1.87±0.95</td>
<td>-2.29±1.06</td>
<td>-2.25±1.37</td>
<td>-1.75±1.00</td>
<td>-1.83±1.11</td>
<td>-1.87±0.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;0</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>6</td>
<td>1</td>
<td>-</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>-1 &lt; 0</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>27</td>
<td>6</td>
<td>5</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>-2 &lt; -1</td>
<td>2 (40%)</td>
<td>5 (36%)</td>
<td>3 (38%)</td>
<td>72 (61%)</td>
<td>11 (53%)</td>
<td>10 (60%)</td>
<td>103 (56%)</td>
<td>103</td>
</tr>
<tr>
<td>-3 &lt; -2</td>
<td>6</td>
<td>10</td>
<td>3</td>
<td>48</td>
<td>12</td>
<td>8</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>&lt; -3</td>
<td>-</td>
<td>6</td>
<td>5</td>
<td>20</td>
<td>4</td>
<td>2</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>Subtotal</td>
<td>10</td>
<td>25</td>
<td>13</td>
<td>173</td>
<td>34</td>
<td>25</td>
<td>280</td>
<td>280</td>
</tr>
<tr>
<td>Not Known</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>5</td>
<td>-</td>
<td>1</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>26</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>
## APPENDIX TABLE 13

### TRICEPS SKINFOLD THICKNESS (PERCENTILES) BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>TST %ILE</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 3rd</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>3 &lt; 10</td>
<td>-</td>
<td>5</td>
<td>2</td>
<td>24</td>
<td>6</td>
<td>4</td>
<td>41</td>
</tr>
<tr>
<td>10 &lt; 25</td>
<td>2 (15%)</td>
<td>4 (40%)</td>
<td>4 (50%)</td>
<td>47 (44%)</td>
<td>10 (56%)</td>
<td>2 (35%)</td>
<td>69 (43%)</td>
</tr>
<tr>
<td>25 &lt; 50</td>
<td>6</td>
<td>9</td>
<td>3</td>
<td>68</td>
<td>11</td>
<td>8</td>
<td>105</td>
</tr>
<tr>
<td>50 &lt; 75</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>22</td>
<td>3</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>75 &lt; 90</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>8</td>
<td>1</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>90 &lt; 97</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 14

UPPER ARM CIRCUMFERENCE (%AGE OF MEAN) BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PERCENTAGE OF MEAN</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LOW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80%</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>80% &lt; 90%</td>
<td>6 (46%)</td>
<td>9 (40%)</td>
<td>6 (43%)</td>
<td>50 (25%)</td>
<td>7 (31%)</td>
<td>78 (29%)</td>
</tr>
<tr>
<td>90% &lt; 100%</td>
<td>5</td>
<td>14</td>
<td>4</td>
<td>127</td>
<td>12</td>
<td>162</td>
</tr>
<tr>
<td>100% &lt; 110%</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>30</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>&gt; 110%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>212</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 15

UPPER ARM MUSCLE CIRCUMFERENCE (PERCENTAGE OF MEAN) BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>%AGE OF MEAN</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>LEW SHORT STATURE</th>
<th>NON ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80.0</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>80 &lt; 90</td>
<td>9 (69%)</td>
<td>9 (40%)</td>
<td>6 (43%)</td>
<td>52 (30%)</td>
<td>10 (29%)</td>
<td>9 (38%)</td>
<td>95 (34%)</td>
</tr>
<tr>
<td>90 &lt; 100</td>
<td>3</td>
<td>13</td>
<td>6</td>
<td>102</td>
<td>19</td>
<td>12</td>
<td>155</td>
</tr>
<tr>
<td>100 &lt; 110</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>23</td>
<td>5</td>
<td>4</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>34</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 16**

**HEAD CIRCUMFERENCE (SDS) BY DIAGNOSTIC GROUP (MEANS & SDS)**

*(Cumulative column percentages in brackets)*

<table>
<thead>
<tr>
<th>SDS</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL SHORT STATURE</th>
<th>LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>-1 &lt; -2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>7</td>
</tr>
<tr>
<td>0 &lt; 1</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>26</td>
<td>1</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td>-1 &lt; 0</td>
<td>5 (67%)</td>
<td>4 (32%)</td>
<td>5 (50%)</td>
<td>49 (45%)</td>
<td>11 (36%)</td>
<td>3 (38%)</td>
<td>77 (43%)</td>
</tr>
<tr>
<td>-2 &lt; -1</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>62</td>
<td>16</td>
<td>9</td>
<td>101</td>
</tr>
<tr>
<td>&lt; -2</td>
<td>2</td>
<td>7</td>
<td>5</td>
<td>36</td>
<td>5</td>
<td>7</td>
<td>62</td>
</tr>
<tr>
<td>TOTAL</td>
<td>12</td>
<td>25</td>
<td>14</td>
<td>178</td>
<td>33</td>
<td>26</td>
<td>288</td>
</tr>
</tbody>
</table>

**MEAN ± SD**

-0.6±0.96  -1.21±1.24  -1.29±1.15  -1.17±1.10  -1.29±0.86  -1.09±1.60

**NOT KNOWN:** 2
#### APPENDIX TABLE 17

**MATERNAL HEIGHT SDS BY DIAGNOSTIC GROUP (MEANS & SDS)**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>MATERNAL HEIGHT SDS</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LOW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -4.5</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>-3.5 &lt; -2.5</td>
<td>-</td>
<td>3</td>
<td>4</td>
<td>48</td>
<td>7</td>
<td>62</td>
</tr>
<tr>
<td>-2.5 &lt; -1.5</td>
<td>3 (38%)</td>
<td>13 (64%)</td>
<td>6 (77%)</td>
<td>85 (67%)</td>
<td>7 (58%)</td>
<td>114   (65%)</td>
</tr>
<tr>
<td>-1.5 &lt; -0.5</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>59</td>
<td>6</td>
<td>79</td>
</tr>
<tr>
<td>-0.5 &lt; 0.5</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td>&gt; 0.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>13</td>
<td>203</td>
<td>26</td>
<td>280</td>
</tr>
</tbody>
</table>

**MEAN ± SD**

<table>
<thead>
<tr>
<th></th>
<th>-1.44±1.54</th>
<th>-1.75±0.76</th>
<th>-2.10±0.80</th>
<th>-1.83±0.85</th>
<th>-1.74±1.24</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT KNOWN</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>212</td>
<td>26</td>
</tr>
</tbody>
</table>

(11.1% of heights were estimated, not measured)
APPENDIX TABLE 18

PATERNAL HEIGHT SDS* BY DIAGNOSTIC GROUP (MEANS & SDS)

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PATERNAL HEIGHT SDS</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -3.5</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>7</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>-3.5 &lt; -2.5</td>
<td>2</td>
<td>7</td>
<td>4</td>
<td>46</td>
<td>4</td>
<td>63</td>
</tr>
<tr>
<td>-2.5 &lt; -1.5</td>
<td>2 (38%)</td>
<td>7 (56%)</td>
<td>4 (62%)</td>
<td>66 (60%)</td>
<td>9 (50%)</td>
<td>88 (57%)</td>
</tr>
<tr>
<td>-1.5 &lt; -0.5</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>50</td>
<td>6</td>
<td>68</td>
</tr>
<tr>
<td>-0.5 &lt; 0.5</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>21</td>
<td>5</td>
<td>37</td>
</tr>
<tr>
<td>0.5 &lt; 1.5</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>9</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>&gt; 1.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>13</td>
<td>200</td>
<td>26</td>
<td>277</td>
</tr>
</tbody>
</table>

| MEAN ± SD          | -1.59±1.23 | -1.77±1.12 | -1.65±1.26   | -1.32±1.12                           |
| NOT KNOWN          | -          | -          | 1            | 12                                   | -                     | 13    |
| TOTAL              | 13         | 25         | 14           | 212                                  | 26                    | 290   |

* 73.6% of heights were estimated, not measured.
### MIDPARENT HEIGHT SDS BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>Parents' Height SDS</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional and LBW Short Stature</th>
<th>Organic Short Stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -4.5</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>-3.5 &lt; -2.5</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>17</td>
<td>3</td>
<td>23</td>
</tr>
<tr>
<td>-2.5 &lt; -1.5</td>
<td>2 (31%)</td>
<td>10 (48%)</td>
<td>9 (75%)</td>
<td>85 (52%)</td>
<td>7 (36%)</td>
<td>113 (50%)</td>
</tr>
<tr>
<td>-1.5 &lt; -0.5</td>
<td>5</td>
<td>9</td>
<td>2</td>
<td>77</td>
<td>11</td>
<td>104</td>
</tr>
<tr>
<td>-0.5 &lt; 0.5</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>15</td>
<td>4</td>
<td>27</td>
</tr>
<tr>
<td>0.5 &lt; 1.5</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Subtotal</td>
<td>13</td>
<td>25</td>
<td>12</td>
<td>196</td>
<td>26</td>
<td>272</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>(-1.23±1.26)</td>
<td>(-1.46±0.72)</td>
<td>(-1.73±0.77)</td>
<td>(-1.52±0.78)</td>
<td>(-1.31±1.03)</td>
<td></td>
</tr>
<tr>
<td>Not Known</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>16</td>
<td>-</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>212</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 20

HEIGHT $sds_{aux}$ (CORRECTED FOR PARENTS' HEIGHT) BY DIAGNOSTIC GROUP

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>CORRECTED $sds_{aux}$</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LOW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>-2 &lt; -1</td>
<td>3 (23%)</td>
<td>8 (32%)</td>
<td>8 (67%)</td>
<td>89 (46%)</td>
<td>4 (19%)</td>
<td>112 (42%)</td>
</tr>
<tr>
<td>-3 &lt; -2</td>
<td>3</td>
<td>15</td>
<td>4</td>
<td>90</td>
<td>13</td>
<td>125</td>
</tr>
<tr>
<td>-4 &lt; -3</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>15</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>&lt; -4</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>12</td>
<td>196</td>
<td>26</td>
<td>272</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>16</td>
<td>-</td>
<td>18</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>212</td>
<td>26</td>
<td>290</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE 21

**TRICEPS SKINFOLD THICKNESS BY DISADVANTAGE SCORE**

**CONSTITUTIONAL SHORT STATURE**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>SKINFOLD THICKNESS</th>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>3&lt;10</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>10&lt;25</td>
<td>2</td>
<td>7</td>
<td>15(42%)</td>
<td>13(42%)</td>
<td>45(48%)</td>
</tr>
<tr>
<td>25&lt;50</td>
<td>3</td>
<td>6</td>
<td>20</td>
<td>25</td>
<td>51</td>
</tr>
<tr>
<td>50&lt;75</td>
<td>4</td>
<td>6</td>
<td>7</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>75&lt;90</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>90&lt;97</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>32</td>
<td>53</td>
<td>57</td>
<td>62</td>
<td>204</td>
</tr>
</tbody>
</table>

Unknown: 2
APPENDIX TABLE 22

ORGANIC SHORT STATURE - EXCEPT GHD
(Mean height SDS, and range in brackets.)

<table>
<thead>
<tr>
<th>TOTAL - 108</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEUROLOGICAL ABNORMALITIES</td>
</tr>
<tr>
<td>Spina bifida (-3.7; -2.5 through -5.6)</td>
</tr>
<tr>
<td>Cerebral palsy (-3.2; -2.5 through -5.1)</td>
</tr>
<tr>
<td>Microcephaly (-3.0, -3.2, -4.0)</td>
</tr>
<tr>
<td>Arrested hydrocephalus (-2.6, -2.7)</td>
</tr>
<tr>
<td>Epilepsy and severe mental retardation (-3.4, -4.6)</td>
</tr>
<tr>
<td>Hemiplegia (-2.5)</td>
</tr>
<tr>
<td>Neurofibromatosis (-3.3)</td>
</tr>
<tr>
<td>PH Meningitis and nerve deafness (-2.7)</td>
</tr>
<tr>
<td>Mental retardation (-3.0, -3.2)</td>
</tr>
</tbody>
</table>

| SKELETAL ABNORMALITIES |
| Scoliosis (-2.8; -2.5 through -3.1) | 4 |
| Achondroplasia (-4.8, -4.3, -5.5) | 3 |
| Achondroplasia and SB occulta (-5.2) | 1 |
| Hypochondroplasia (-4.5) | 1 |
| Sacral tumour (-5.3, -4.8) | 2 |
| Perthes' disease (-3.2, -2.6) | 2 |
| Klippel Feil abnormality (-3.1) | 1 |
| Metaphyseal dysostosis (-3.3) | 1 |
| PH Rickets (-3.7) | 1 |
| Spinal deformity (-2.8) | 1 |
## APPENDIX TABLE 22 (cont.)

### CHROMOSOMAL ABNORMALITIES

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down's syndrome (-3.2; -2.5 through -4.2)</td>
<td>15</td>
</tr>
<tr>
<td>&quot;Trisomy 18&quot; (-4.0)</td>
<td>1</td>
</tr>
<tr>
<td>Turner's mosaic (45, X0/46, Xi(Xq))</td>
<td>1</td>
</tr>
</tbody>
</table>

### RESPIRATORY DISORDERS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma (-2.7; -2.5 through -3.4)</td>
<td>5</td>
</tr>
<tr>
<td>&quot;Chronic bronchitis&quot; (-2.7, -3.3)</td>
<td>2</td>
</tr>
<tr>
<td>Cystic fibrosis (-2.5)</td>
<td>1</td>
</tr>
<tr>
<td>(Partial GHD and asthma (-2.6) - 1)</td>
<td></td>
</tr>
</tbody>
</table>

### CARDIOVASCULAR DISORDERS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary stenosis (-3.1, -2.6, -2.8)</td>
<td>3</td>
</tr>
<tr>
<td>Ventricular septal defect (-3.7)</td>
<td>1</td>
</tr>
<tr>
<td>Patent ductus arteriosus (-3.2)</td>
<td>1</td>
</tr>
<tr>
<td>Intersex and CHD (-4.3)</td>
<td>1</td>
</tr>
</tbody>
</table>

### GASTROINTESTINAL ABNORMALITIES

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coeliac disease (-3.1, -3.2, -2.6)</td>
<td>3</td>
</tr>
<tr>
<td>Hirschsprung's disease (-3.7)</td>
<td>1</td>
</tr>
<tr>
<td>Imperforate anus and mental retardation (-3.2)</td>
<td>1</td>
</tr>
<tr>
<td>Tracheo-oesophageal fistula (-6.3)</td>
<td>1</td>
</tr>
<tr>
<td>(Partial GHD and coeliac disease (-3.1, -2.8) - 2)</td>
<td></td>
</tr>
</tbody>
</table>

### METABOLIC AND STORAGE DISORDERS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycogen storage disease (-2.9)</td>
<td>1</td>
</tr>
<tr>
<td>Hurler's syndrome (-5.6)</td>
<td>1</td>
</tr>
<tr>
<td>Morquio's syndrome (-4.8)</td>
<td>1</td>
</tr>
<tr>
<td>Non-specific storage disorder (-3.2)</td>
<td>1</td>
</tr>
<tr>
<td>Category</td>
<td>Condition</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td><strong>HAEMATOLOGICAL DISORDERS</strong></td>
<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>(-2.9)</td>
</tr>
<tr>
<td>Chronic idiopathic thrombocytopenic purpura</td>
<td>(-2.2)</td>
</tr>
<tr>
<td><strong>RENAL DISORDERS</strong></td>
<td></td>
</tr>
<tr>
<td>Renal hypoplasia</td>
<td>(-5.1)</td>
</tr>
<tr>
<td>Severe recurrent urinary tract infections</td>
<td>(-3.5)</td>
</tr>
<tr>
<td><strong>ENDOCRINE ABNORMALITIES</strong></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>(-2.6)</td>
</tr>
<tr>
<td>Gonadal hypoplasia</td>
<td>(-3.2)</td>
</tr>
<tr>
<td>(Intersex and CHD (-4.3) - 1)</td>
<td></td>
</tr>
<tr>
<td><strong>MISCELLANEOUS</strong></td>
<td></td>
</tr>
<tr>
<td>Russell-Silver syndrome</td>
<td>(-3.5, -4.0)</td>
</tr>
<tr>
<td>Ataxia telangiectasia</td>
<td>(-2.4)</td>
</tr>
<tr>
<td>Progeria</td>
<td>(-4.7)</td>
</tr>
<tr>
<td>&quot;Runt&quot; twin</td>
<td>(-3.7)</td>
</tr>
<tr>
<td>(Partial GHD and Russell-Silver syndrome (-2.9) - 1)</td>
<td></td>
</tr>
</tbody>
</table>
QUESTION: WHAT IS THE PREGNANCY NUMBER OF N?

(includes stillbirths and abortions)

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PREGNANCY NUMBER</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 (38%)</td>
<td>2 (8%)</td>
<td>4 (29%)</td>
<td>33 (16%)</td>
<td>8 (32%)</td>
<td>64 (20%)</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>6</td>
<td>2</td>
<td>41</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>8</td>
<td>1</td>
<td>39</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>33</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>5 or more</td>
<td>-</td>
<td>5</td>
<td>6</td>
<td>59</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>13</strong></td>
<td><strong>25</strong></td>
<td><strong>14</strong></td>
<td><strong>206</strong></td>
<td><strong>26</strong></td>
<td><strong>321</strong></td>
</tr>
</tbody>
</table>

**SUBTOTAL**

**UNKNOWN**

**TOTAL**
# Appendix Table 24

## Age at Birth of First Child

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>Age</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional and Low Short Stature</th>
<th>Organic Short Stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>21</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18-20</td>
<td>7 (67%)</td>
<td>12 (48%)</td>
<td>6 (43%)</td>
<td>95 (56%)</td>
<td>8 (31%)</td>
<td>9 (32%)</td>
</tr>
<tr>
<td>21-25</td>
<td>3</td>
<td>11</td>
<td>7</td>
<td>69</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>26-30</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>15</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>31-35</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>6</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>36</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>12</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
</tr>
</tbody>
</table>

*Note: The data represents the age at birth of the first child for different categories of GHD and other conditions.*
**APPENDIX TABLE 25**

**AGE AT BIRTH OF INDEX CHILD**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>AGE</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>5</td>
<td>-</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>18-20</td>
<td>6 (67%)</td>
<td>3 (12%)</td>
<td>2 (21%)</td>
<td>38 (21%)</td>
<td>3 (12%)</td>
<td>4 (17%)</td>
<td>56 (21%)</td>
</tr>
<tr>
<td>21-25</td>
<td>2</td>
<td>13</td>
<td>2</td>
<td>68</td>
<td>11</td>
<td>7</td>
<td>103</td>
</tr>
<tr>
<td>26-30</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>48</td>
<td>5</td>
<td>10</td>
<td>74</td>
</tr>
<tr>
<td>31-35</td>
<td>1</td>
<td>-</td>
<td>4</td>
<td>26</td>
<td>2</td>
<td>5</td>
<td>38</td>
</tr>
<tr>
<td>36+</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>21</td>
<td>5</td>
<td>8</td>
<td>38</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>12</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>36</td>
<td>319</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 26

QUESTION: DID YOU SMOKE DURING YOUR PREGNANCY WITH N?

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>HABIT</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEVER SMOKED</td>
<td>7</td>
<td>8</td>
<td>2</td>
<td>80</td>
<td>9</td>
<td>17</td>
<td>123</td>
</tr>
<tr>
<td>YES</td>
<td>5 (42%)</td>
<td>17 (68%)</td>
<td>11 (8%)</td>
<td>125 (61%)</td>
<td>16 (64%)</td>
<td>19 (53%)</td>
<td>193 (60%)</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>12</td>
<td>25</td>
<td>13</td>
<td>205</td>
<td>25</td>
<td>36</td>
<td>316</td>
</tr>
<tr>
<td>DON'T KNOW</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
QUESTION: WERE YOU WELL DURING YOUR PREGNANCY WITH N?
IF NOT WHAT SORTS OF PROBLEMS DID YOU HAVE?

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>COURSE</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LOW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Normal</td>
<td>4 (31%)</td>
<td>17 (68%)</td>
<td>10 (71%)</td>
<td>137 (68%)</td>
<td>19 (76%)</td>
<td>21 (57%)</td>
<td>208 (66%)</td>
</tr>
<tr>
<td>2. Swelling/PET.</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>13</td>
<td>1</td>
<td>2</td>
<td>21</td>
</tr>
<tr>
<td>3. Bleeding</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>10</td>
<td>-</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>4. Baby not growing well</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>5. Severe vomiting</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>6. Other complications</td>
<td>1</td>
<td>4</td>
<td>-</td>
<td>36</td>
<td>3</td>
<td>8</td>
<td>52</td>
</tr>
<tr>
<td>7.8. Parenteral iron or blood</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL ABNORMAL</td>
<td>9 (69%)</td>
<td>8 (32%)</td>
<td>4 (29%)</td>
<td>65 (32%)</td>
<td>6 (24%)</td>
<td>15 (42%)</td>
<td>107 (34%)</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>202</td>
<td>25</td>
<td>36</td>
<td>315</td>
</tr>
<tr>
<td>DON'T KNOW</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 28**

**QUESTION:** DID YOU HAVE ANY PROBLEMS WITH THE BIRTH ITSELF?

(Column percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional and Low Short Stature</th>
<th>Organic Short Stature</th>
<th>Total Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPONTANEOUS DELIVERY</strong></td>
<td>7 (58%)</td>
<td>20 (80%)</td>
<td>9 (69%)</td>
<td>173 (85%)</td>
<td>19 (73%)</td>
<td>245 (77%)</td>
</tr>
<tr>
<td><strong>ASSISTED DELIVERY</strong></td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>11</td>
<td>2</td>
<td>28</td>
</tr>
<tr>
<td><strong>LSGS</strong></td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td><strong>OTHER (prolonged labour)</strong></td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td><strong>SUBTOTAL</strong></td>
<td>12</td>
<td>25</td>
<td>13</td>
<td>204</td>
<td>26</td>
<td>317</td>
</tr>
<tr>
<td><strong>DON'T KNOW</strong></td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>321</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE 29

**POSITION AT BIRTH OR DURING LABOUR**

(Column percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VERTEX</strong></td>
<td>10 (83%)</td>
<td>25 (100%)</td>
<td>12 (86%)</td>
<td>193 (96%)</td>
<td>24 (92%)</td>
<td>32 (89%)</td>
<td>29 (95%)</td>
</tr>
<tr>
<td><strong>BREECH</strong></td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>7</td>
<td>2</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td><strong>OTHER</strong></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td><strong>SUBTOTAL</strong></td>
<td>12</td>
<td>25</td>
<td>14</td>
<td>200</td>
<td>26</td>
<td>36</td>
<td>313</td>
</tr>
<tr>
<td><strong>DON'T KNOW</strong></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>6</td>
<td>-</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 30**

**GESTATIONAL AGE**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>WEEKS</th>
<th>SEvere GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 28</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>29 - 32</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>33 - 36</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>13</td>
<td>3</td>
<td>3</td>
<td>26</td>
</tr>
<tr>
<td>37 - 38</td>
<td>1 (15%)</td>
<td>1 (20%)</td>
<td>4 (43%)</td>
<td>18 (17%)</td>
<td>3 (23%)</td>
<td>6 (30%)</td>
<td>32 (20%)</td>
</tr>
<tr>
<td>39 - 41</td>
<td>7</td>
<td>13</td>
<td>6</td>
<td>144</td>
<td>18</td>
<td>24</td>
<td>213</td>
</tr>
<tr>
<td>42 +</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>23</td>
<td>2</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>201</td>
<td>26</td>
<td>37</td>
<td>316</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE 31

#### BIRTH WEIGHT (gms.)

(Column percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LEW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1500 gms.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>1501 -</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>7</td>
<td>3</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>2001 -</td>
<td>1 (8%)</td>
<td>4 (17%)</td>
<td>6 (50%)</td>
<td>42 (26%)</td>
<td>4 (31%)</td>
<td>3 (22%)</td>
<td>60 (25%)</td>
</tr>
<tr>
<td>2501 -</td>
<td>5</td>
<td>12</td>
<td>1</td>
<td>67</td>
<td>9</td>
<td>12</td>
<td>106</td>
</tr>
<tr>
<td>3001 -</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>62</td>
<td>5</td>
<td>9</td>
<td>86</td>
</tr>
<tr>
<td>3501</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>15</td>
<td>3</td>
<td>5</td>
<td>33</td>
</tr>
<tr>
<td>4001 -</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>24</td>
<td>14</td>
<td>198</td>
<td>26</td>
<td>36</td>
<td>311</td>
</tr>
<tr>
<td>MEAN ± SD</td>
<td>3238 ± 613</td>
<td>2865 ± 482</td>
<td>2722 ± 518</td>
<td>2861 ± 518</td>
<td>2774 ± 664</td>
<td>2891 ± 303</td>
<td>2867 ± 583</td>
</tr>
<tr>
<td>UNKNOWN</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>8</td>
<td>-</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 32.**

**QUESTION:** WAS N KEPT IN NURSERY MORE THAN 24 HOURS AFTER BIRTH?

<table>
<thead>
<tr>
<th>No or born at home</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional or Low Short Stature</th>
<th>Organic Short Stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>6</td>
<td>17</td>
<td>9</td>
<td>142</td>
<td>17</td>
<td>199</td>
</tr>
<tr>
<td>YES</td>
<td>7 (54%)</td>
<td>5 (36%)</td>
<td>62 (30%)</td>
<td>9 (35%)</td>
<td>29 (78%)</td>
<td>119 (37%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>24</td>
<td>14</td>
<td>204</td>
<td>26</td>
<td>318</td>
</tr>
</tbody>
</table>

**DONT KNOW:** 3
QUESTION: DID YOU HAVE ANY WORRIES WITH N WHEN HE WAS A BABY?

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>8</td>
<td>15</td>
<td>10</td>
<td>149</td>
<td>18</td>
<td>10</td>
<td>210</td>
</tr>
<tr>
<td>YES</td>
<td>5 (38%)</td>
<td>10 (40%)</td>
<td>4 (29%)</td>
<td>54 (27%)</td>
<td>7 (28%)</td>
<td>26 (72%)</td>
<td>106   (34%)</td>
</tr>
<tr>
<td>SUBTOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>203</td>
<td>25</td>
<td>36</td>
<td>316</td>
</tr>
<tr>
<td>DON'T KNOW</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 34**

**QUESTION:** WAS IT DIFFICULT TO FEED AS AN INFANT?

<table>
<thead>
<tr>
<th></th>
<th>SEvere GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional OR LBW Short Stature</th>
<th>Organic Short Stature</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NO</strong></td>
<td>7 (46%)</td>
<td>18</td>
<td>12</td>
<td>162</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td>6 (28%)</td>
<td>7 (28%)</td>
<td>2 (14%)</td>
<td>43 (21%)</td>
<td>4 (16%)</td>
<td>19 (51%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>205</td>
<td>24</td>
<td>37</td>
</tr>
</tbody>
</table>

**DON'T KNOW:** 3
## APPENDIX TABLE 35

**Total Number of Children in Family and Mean Family Size**

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>NUMBER</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LOW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN ± SD</td>
<td>3.23 ± 1.48</td>
<td>4.92 ± 1.85</td>
<td>5.21 ± 2.19</td>
<td>4.67 ± 1.98</td>
<td>4.08 ± 1.83</td>
<td>3.68 ± 2.12</td>
<td>4.49 ± 2.0</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>20</td>
<td>4</td>
<td>6</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>8</td>
<td>2</td>
<td>45</td>
<td>6</td>
<td>13</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>50</td>
<td>6</td>
<td>2</td>
<td>64</td>
</tr>
<tr>
<td>5</td>
<td>4 (100%)</td>
<td>4 (64%)</td>
<td>2 (50%)</td>
<td>33 (72%)</td>
<td>4 (81%)</td>
<td>2 (76%)</td>
<td>49 (73%)</td>
</tr>
<tr>
<td>6 +</td>
<td>-</td>
<td>9</td>
<td>7</td>
<td>57</td>
<td>5</td>
<td>9</td>
<td>87</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
## APPENDIX TABLE 36

### SOCIAL CLASS

**Registrar General's Classification**

(Based on father's occupation)

Column percentages in brackets.

<table>
<thead>
<tr>
<th>Social Class</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional or LBw Short Stature</th>
<th>Organic Short Stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>2 (8%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>II</td>
<td>1 (8%)</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1 (4%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>III Non-manual</td>
<td>1 (8%)</td>
<td>-</td>
<td>-</td>
<td>3 (1%)</td>
<td>1 (4%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>III Manual</td>
<td>2 (15%)</td>
<td>9 (36%)</td>
<td>6 (43%)</td>
<td>62 (30%)</td>
<td>10 (38%)</td>
<td>105 (33%)</td>
</tr>
<tr>
<td>IV</td>
<td>2 (15%)</td>
<td>3 (12%)</td>
<td>2 (14%)</td>
<td>40 (19%)</td>
<td>-</td>
<td>51 (16%)</td>
</tr>
<tr>
<td>V</td>
<td>1 (8%)</td>
<td>2 (8%)</td>
<td>-</td>
<td>15 (7%)</td>
<td>3 (12%)</td>
<td>24 (7%)</td>
</tr>
<tr>
<td>Student</td>
<td>1 (8%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>UNEMPLOYED (Not classified)</td>
<td>2 (15%)</td>
<td>6 (24%)</td>
<td>3 (21%)</td>
<td>53 (26%)</td>
<td>6 (23%)</td>
<td>74 (23%)</td>
</tr>
<tr>
<td>NO FATHER FIGURE</td>
<td>3 (23%)</td>
<td>5 (20%)</td>
<td>3 (21%)</td>
<td>31 (15%)</td>
<td>3 (12%)</td>
<td>50 (16%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>321</td>
</tr>
<tr>
<td>Classified I-V but unemployed</td>
<td>1 (8%)</td>
<td>2 (8%)</td>
<td>2 (14%)</td>
<td>12 (6%)</td>
<td>-</td>
<td>19 (6%)</td>
</tr>
</tbody>
</table>

The table above provides a breakdown of the number of cases in each social class category, categorized by various classifications such as GHD, constitutional or LBw short stature, and organic short stature. The percentages in brackets indicate the proportion of the total cases within each category.
APPENDIX TABLE 37

QUESTION: HAVE YOU EVER RECEIVED SUPPLEMENTARY BENEFIT?

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LEW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>8</td>
<td>11</td>
<td>6</td>
<td>84</td>
<td>15</td>
<td>22</td>
<td>146</td>
</tr>
<tr>
<td></td>
<td>5 (38%)</td>
<td>14 (56%)</td>
<td>7 (54%)</td>
<td>122 (59%)</td>
<td>11 (42%)</td>
<td>15 (41%)</td>
<td>174</td>
</tr>
<tr>
<td>YES</td>
<td>13</td>
<td>25</td>
<td>13</td>
<td>20</td>
<td>26</td>
<td>37</td>
<td>320</td>
</tr>
</tbody>
</table>

DON'T KNOW: 1
APPENDIX TABLE 38

PERSONS PER ROOM IN HOUSEHOLD

(cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PERSONS PER ROOM</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>34 (54%)</td>
<td>6 (48%)</td>
<td>17 (48%)</td>
<td>72</td>
</tr>
<tr>
<td>1 &lt; 1.5</td>
<td>3 (85%)</td>
<td>5 (32%)</td>
<td>2 (36%)</td>
<td>64 (48%)</td>
<td>14 (77%)</td>
<td>8 (68%)</td>
<td>93 (51%)</td>
</tr>
<tr>
<td>1.5 &lt; 2.5</td>
<td>2</td>
<td>13</td>
<td>5</td>
<td>88 (54%)</td>
<td>6 (48%)</td>
<td>9 (68%)</td>
<td>124</td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>-</td>
<td>4</td>
<td>4</td>
<td>20 (54%)</td>
<td>- (48%)</td>
<td>3 (68%)</td>
<td>31</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
<td>321</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 39**

**DISADVANTAGE SCORE BY DIAGNOSTIC GROUP**

(Column percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5 (38%)</td>
<td>4 (17%)</td>
<td>2 (17%)</td>
<td>32 (16%)</td>
<td>9 (35%)</td>
<td>15 (41%)</td>
<td>67 (21%)</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>4</td>
<td>53</td>
<td>5</td>
<td>6</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>4 (8%)</td>
<td>8</td>
<td>2</td>
<td>57</td>
<td>9</td>
<td>12</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>8 (33%)</td>
<td>8 (33%)</td>
<td>4 (33%)</td>
<td>62 (30%)</td>
<td>3 (12%)</td>
<td>4 (11%)</td>
<td>82 (26%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>24</td>
<td>12</td>
<td>204</td>
<td>26</td>
<td>37</td>
<td>315</td>
</tr>
</tbody>
</table>

Not known: 2 possible GHD
1 Partial GHD
2 constitutional GHD
## APPENDIX TABLE 4.0

### SUBJECTIVE IMPRESSION OF INTERVIEWEE'S INTELLIGENCE (QUESTION 95)

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>SCORE</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL AND LEW-SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 3</td>
<td>1 (8%)</td>
<td>6 (24%)</td>
<td>3 (21%)</td>
<td>51 (25%)</td>
<td>4 (15%)</td>
<td>6 (16%)</td>
<td>71 (22%)</td>
</tr>
<tr>
<td>4 - 5</td>
<td>12</td>
<td>19</td>
<td>11</td>
<td>152</td>
<td>22</td>
<td>31</td>
<td>247</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>203</td>
<td>26</td>
<td>37</td>
<td>318</td>
</tr>
</tbody>
</table>

**UNKNOWN:** 3
APPENDIX TABLE 41

DURATION OF EXERCISE (MINUTES) BY GROWTH HORMONE LEVEL FOLLOWING EXERCISE (N = 227)

(Excludes 42 subjects: 21 in whom duration was unrecorded, and 21 with GH levels < 16 mU/L during an ITT)

<table>
<thead>
<tr>
<th>DURATION (minutes)</th>
<th>NUMBER</th>
<th>MEAN GH (mU/L) ± SD</th>
<th>RANGE OF GH LEVELS</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 - 12</td>
<td>6</td>
<td>18.6 ± 13.0</td>
<td>10.8 - 44.9</td>
</tr>
<tr>
<td>13 - 14</td>
<td>15</td>
<td>25.0 ± 18.4</td>
<td>6.3 - 78.4</td>
</tr>
<tr>
<td>15 - 16</td>
<td>35</td>
<td>22.2 ± 12.9</td>
<td>7.1 - 58.5</td>
</tr>
<tr>
<td>17 - 18</td>
<td>44</td>
<td>25.3 ± 15.3</td>
<td>4.8 - 54.9</td>
</tr>
<tr>
<td>19 - 20</td>
<td>49</td>
<td>20.6 ± 10.5</td>
<td>6.1 - 38.8</td>
</tr>
<tr>
<td>21 - 22</td>
<td>15</td>
<td>25.9 ± 14.0</td>
<td>3.7 - 46.0</td>
</tr>
<tr>
<td>23 - 24</td>
<td>8</td>
<td>17.5 ± 9.7</td>
<td>4.8 - 37.7</td>
</tr>
<tr>
<td>25 - 26</td>
<td>13</td>
<td>23.7 ± 14.2</td>
<td>6.5 - 47.7</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE 42

**EXERCISE TEST**  
**GH RESPONSE BY SEX**

<table>
<thead>
<tr>
<th>Sex</th>
<th>No.</th>
<th>Mean $\pm$ SD (mU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>129</td>
<td>22.2 ± 13.3</td>
</tr>
<tr>
<td>Girls</td>
<td>98</td>
<td>20.6 ± 13.3</td>
</tr>
<tr>
<td>Total</td>
<td>227</td>
<td>21.5 ± 13.7</td>
</tr>
</tbody>
</table>

### APPENDIX TABLE 43

**EXERCISE TEST**  
**GH RESPONSE BY AGE**

<table>
<thead>
<tr>
<th>Age</th>
<th>No.</th>
<th>Mean $\pm$ SD (mU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>81</td>
<td>21.0 ± 12.8</td>
</tr>
<tr>
<td>7</td>
<td>105</td>
<td>21.8 ± 12.9</td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>21.7 ± 16.1</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>21.4 ± 10.9</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 44

HEIGHT VELOCITY PERCENTILE RANK BY MAXIMUM GH RESPONSE FOLLOWING EXERCISE

<table>
<thead>
<tr>
<th>Height velocity percentile</th>
<th>No.</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>17</td>
<td>13.9 ± 8.5</td>
</tr>
<tr>
<td>3 &lt; 10</td>
<td>22</td>
<td>16.4 ± 7.7</td>
</tr>
<tr>
<td>10 &lt; 25</td>
<td>27</td>
<td>22.0 ± 10.7</td>
</tr>
<tr>
<td>25 +</td>
<td>12</td>
<td>21.2 ± 10.1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>78</td>
<td>18.5 ± 9.8</td>
</tr>
</tbody>
</table>

APPENDIX TABLE 45

MAXIMUM GH RESPONSE DURING ITT COMPARED WITH FASTING GH LEVEL (Excluding 'cases' of severe GHD.)
Row percentages in brackets.

<table>
<thead>
<tr>
<th>FASTING</th>
<th>GH RESPONSE</th>
<th>&lt; 20 mU/L</th>
<th>&gt; 20 mU/L</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 mU/L</td>
<td>10</td>
<td>19 (66%)</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>≥ 2 mU/L</td>
<td>44</td>
<td>24 (35%)</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>54</td>
<td>43 (44%)</td>
<td>97</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>SEX</td>
<td>AGE (yrs)</td>
<td>MAXIMUM GH (mU/L) ON ITT OR EXERCISE</td>
<td>HEIGHT SDS AUX</td>
</tr>
<tr>
<td>-----</td>
<td>-----</td>
<td>-----------</td>
<td>--------------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>014*</td>
<td>M</td>
<td>7.15</td>
<td>&lt; 1</td>
<td>&lt; 3rd ●</td>
</tr>
<tr>
<td>426*</td>
<td>F</td>
<td>8.09</td>
<td>1.1</td>
<td>- ●</td>
</tr>
<tr>
<td>239*</td>
<td>M</td>
<td>7.18</td>
<td>2.5</td>
<td>&gt; 97th ●</td>
</tr>
<tr>
<td>278*</td>
<td>M</td>
<td>8.02</td>
<td>3.0</td>
<td>&lt; 3rd ●</td>
</tr>
<tr>
<td>543</td>
<td>F</td>
<td>9.52</td>
<td>3.4</td>
<td>3-10th</td>
</tr>
<tr>
<td>536</td>
<td>M</td>
<td>9.38</td>
<td>5.7</td>
<td>3-10th</td>
</tr>
<tr>
<td>259</td>
<td>F</td>
<td>7.33</td>
<td>6.2</td>
<td>3-10th</td>
</tr>
<tr>
<td>211</td>
<td>F</td>
<td>7.41</td>
<td>7.6</td>
<td>10-25</td>
</tr>
<tr>
<td>213*</td>
<td>M</td>
<td>7.71</td>
<td>8.4</td>
<td>&lt; 3rd ●</td>
</tr>
<tr>
<td>234</td>
<td>M</td>
<td>7.61</td>
<td>8.4</td>
<td>&lt; 3rd ●</td>
</tr>
<tr>
<td>024</td>
<td>F</td>
<td>8.57</td>
<td>9.0</td>
<td>25-50</td>
</tr>
<tr>
<td>131*</td>
<td>M</td>
<td>8.42</td>
<td>9.3</td>
<td>&lt; 3rd ●</td>
</tr>
<tr>
<td>533</td>
<td>M</td>
<td>8.34</td>
<td>9.5</td>
<td>&lt; 3rd ●</td>
</tr>
</tbody>
</table>

* 4 previously diagnosed - 3 by Regional Hormone Laboratory, Glasgow; 1 by RHL in Edinburgh.
+ Mother of 014 extremely small - probable GHD (GH 1 mU/L on screening test)
● Multiple pituitary hormone deficiency.
Receiving HGH.
Interval between height measurements < 12 months.
**APPENDIX TABLE 47**

**Sibling Pairs**

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>SDSaux</th>
<th>SDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>024</td>
<td>F</td>
<td>Severe biochemical GHD</td>
<td></td>
<td>-2.50</td>
</tr>
<tr>
<td>023</td>
<td>M</td>
<td>Constitutional short stature</td>
<td></td>
<td>-2.99</td>
</tr>
<tr>
<td>061</td>
<td>F</td>
<td>Non-organic refusal</td>
<td></td>
<td>-2.28</td>
</tr>
<tr>
<td>062</td>
<td>M</td>
<td>Non-organic refusal</td>
<td></td>
<td>-2.48</td>
</tr>
<tr>
<td>*109</td>
<td>F</td>
<td>Constitutional short stature</td>
<td></td>
<td>-2.44</td>
</tr>
<tr>
<td>*110</td>
<td>F</td>
<td></td>
<td></td>
<td>-2.49</td>
</tr>
<tr>
<td>*152</td>
<td>F</td>
<td></td>
<td></td>
<td>-2.75</td>
</tr>
<tr>
<td>*154</td>
<td>M</td>
<td></td>
<td></td>
<td>-2.81</td>
</tr>
<tr>
<td>184</td>
<td>M</td>
<td></td>
<td></td>
<td>-3.42</td>
</tr>
<tr>
<td>183</td>
<td>M</td>
<td>Partial biochemical GHD</td>
<td></td>
<td>-2.99</td>
</tr>
<tr>
<td>210</td>
<td>M</td>
<td>Constitutional short stature</td>
<td></td>
<td>-3.09</td>
</tr>
<tr>
<td>211</td>
<td>F</td>
<td>Severe biochemical GHD</td>
<td></td>
<td>-2.74</td>
</tr>
<tr>
<td>238</td>
<td>M</td>
<td>Non-organic refusal</td>
<td></td>
<td>-3.22</td>
</tr>
<tr>
<td>237</td>
<td>F</td>
<td></td>
<td></td>
<td>-3.05</td>
</tr>
<tr>
<td>260</td>
<td>F</td>
<td>Partial GHD</td>
<td></td>
<td>-4.11</td>
</tr>
<tr>
<td>261</td>
<td>M</td>
<td>Constitutional short stature</td>
<td></td>
<td>-3.64</td>
</tr>
<tr>
<td>*263</td>
<td>F</td>
<td>Constitutional short stature</td>
<td></td>
<td>-3.48</td>
</tr>
<tr>
<td>*264</td>
<td>F</td>
<td></td>
<td></td>
<td>-3.33</td>
</tr>
<tr>
<td>307</td>
<td>M</td>
<td></td>
<td></td>
<td>-3.26</td>
</tr>
<tr>
<td>306</td>
<td>M</td>
<td></td>
<td></td>
<td>-2.93</td>
</tr>
<tr>
<td>*349</td>
<td>F</td>
<td>Non-organic refusal</td>
<td></td>
<td>-3.19</td>
</tr>
<tr>
<td>*350</td>
<td>F</td>
<td></td>
<td></td>
<td>-3.07</td>
</tr>
<tr>
<td>353</td>
<td>M</td>
<td>LBW</td>
<td></td>
<td>-2.89</td>
</tr>
<tr>
<td>354</td>
<td>F</td>
<td>Constitutional short stature</td>
<td></td>
<td>-2.47</td>
</tr>
<tr>
<td>403</td>
<td>F</td>
<td>LBW</td>
<td></td>
<td>-2.55</td>
</tr>
<tr>
<td>402</td>
<td>M</td>
<td>Constitutional short stature</td>
<td></td>
<td>-2.92</td>
</tr>
<tr>
<td>522</td>
<td>M</td>
<td></td>
<td></td>
<td>-3.88</td>
</tr>
<tr>
<td>524</td>
<td>F</td>
<td></td>
<td></td>
<td>-3.64</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 48

QUESTION: HAVE YOU BEEN CONCERNED ABOUT N'S GROWTH OR DEVELOPMENT? (Diagnostic groups 3-7).

(Row percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Yes (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>87</td>
<td>72 (45%)</td>
<td>159</td>
</tr>
<tr>
<td>Girls</td>
<td>72</td>
<td>48 (40%)</td>
<td>120</td>
</tr>
<tr>
<td>TOTAL</td>
<td>159</td>
<td>120 (43%)</td>
<td>279</td>
</tr>
</tbody>
</table>
### Appendix Table 49

**Parental Concern by Diagnostic Group**

(Column percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional or LBW Short Stature</th>
<th>Organic Short Stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not Concerned</strong></td>
<td>4</td>
<td>11</td>
<td>12</td>
<td>122</td>
<td>13</td>
<td>176</td>
</tr>
<tr>
<td><strong>Concerned</strong></td>
<td>9 (69%)</td>
<td>14 (56%)</td>
<td>2 (14%)</td>
<td>83 (40%)</td>
<td>13 (50%)</td>
<td>144 (45%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>205</td>
<td>26</td>
<td>320</td>
</tr>
</tbody>
</table>

Don't know: 1
### VARIATION IN PARENTAL CONCERN ABOUT GROWTH AND DEVELOPMENT BY SOCIAL CLASS

(Diagnostic groups 3 - 7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>Category</th>
<th>NOT CONCERNED</th>
<th>CONCERNED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>I - III non-manual</td>
<td>5</td>
<td>6 (54%)</td>
<td>11</td>
</tr>
<tr>
<td>III manual</td>
<td>50</td>
<td>39 (44%)</td>
<td>89</td>
</tr>
<tr>
<td>IV</td>
<td>31</td>
<td>17 (35%)</td>
<td>48</td>
</tr>
<tr>
<td>V</td>
<td>12</td>
<td>7 (37%)</td>
<td>19</td>
</tr>
<tr>
<td>Students</td>
<td>-</td>
<td>1 (100%)</td>
<td>1</td>
</tr>
<tr>
<td>Unemployed - not classified</td>
<td>37</td>
<td>30 (44%)</td>
<td>67</td>
</tr>
<tr>
<td>Single parent families</td>
<td>24</td>
<td>20 (45%)</td>
<td>44</td>
</tr>
<tr>
<td>Unknown 7</td>
<td></td>
<td></td>
<td>279</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 51

PARENTAL CONCERN ABOUT GROWTH
BY SUBJECT'S HEIGHT SDS\textsubscript{AUX}

(Diagnostic groups 3 - 7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>HEIGHT SDS\textsubscript{AUX}</th>
<th>NOT CONCERNED</th>
<th>CONCERNED (% in brackets)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2.0 &gt; -2.5</td>
<td>28</td>
<td>20 (42%)</td>
<td>48</td>
</tr>
<tr>
<td>-2.5 &gt; -3.0</td>
<td>104</td>
<td>70 (40%)</td>
<td>174</td>
</tr>
<tr>
<td>-3.0 &gt; -3.5</td>
<td>21</td>
<td>21 (50%)</td>
<td>42</td>
</tr>
<tr>
<td>\leq -3.5</td>
<td>10</td>
<td>11 (52%)</td>
<td>21</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>163</strong></td>
<td><strong>122 (43%)</strong></td>
<td><strong>285</strong></td>
</tr>
</tbody>
</table>

Missing value 1.
APPENDIX TABLE 52

QUESTION: WAS MOTHER MUCH SMALLER THAN AVERAGE HEIGHT AS A CHILD?

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>10 (77%)</td>
<td>8 (32%)</td>
<td>4 (31%)</td>
<td>50 (27%)</td>
<td>12 (50%)</td>
<td>21 (58%)</td>
<td>105 (35%)</td>
</tr>
<tr>
<td>YES</td>
<td>3</td>
<td>17</td>
<td>9</td>
<td>135</td>
<td>12</td>
<td>15</td>
<td>191</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>13</td>
<td>185</td>
<td>24</td>
<td>36</td>
<td>296</td>
</tr>
</tbody>
</table>

DON'T KNOW: 21 constitutional
3 organic short stature
1 possible GHD
APPENDIX TABLE 53

PARENTAL CONCERN ABOUT GROWTH BY MOTHER'S HEIGHT AS CHILD

(Diagnostic groups 3-7)

Row percentages in brackets

QUESTION: HAVE YOU BEEN CONCERNED ABOUT N'S GROWTH OR DEVELOPMENT?

<table>
<thead>
<tr>
<th>Question: Was mother smaller than average as a child?</th>
<th>NO</th>
<th>YES (Row%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>38</td>
<td>46 (55%)</td>
<td>84</td>
</tr>
<tr>
<td>YES</td>
<td>109</td>
<td>65 (37%)</td>
<td>174</td>
</tr>
<tr>
<td>TOTAL</td>
<td>147</td>
<td>111 (43%)</td>
<td>258</td>
</tr>
</tbody>
</table>

Unknown or missing: 28

APPENDIX TABLE 54

PARENTAL CONCERN ABOUT GROWTH BY MOTHER'S HEIGHT SDS

(Diagnostic groups 3-7)

Row percentages in brackets

<table>
<thead>
<tr>
<th>MOTHER'S HEIGHT (SDS)</th>
<th>NOT CONCERNED</th>
<th>CONCERNED (Row%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -2</td>
<td>106</td>
<td>46 (30%)</td>
<td>152</td>
</tr>
<tr>
<td>&gt; -2</td>
<td>51</td>
<td>73 (59%)</td>
<td>124</td>
</tr>
<tr>
<td>TOTAL</td>
<td>157</td>
<td>119 (43%)</td>
<td>276</td>
</tr>
</tbody>
</table>

Unknown or missing values: 10
QUESTION: WAS FATHER SMALLER THAN AVERAGE HEIGHT AS A CHILD?

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LOW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>7 (54%)</td>
<td>12 (57%)</td>
<td>6 (60%)</td>
<td>74 (47%)</td>
<td>9 (56%)</td>
<td>28 (82%)</td>
<td>136 (54%)</td>
</tr>
<tr>
<td>YES</td>
<td>6</td>
<td>9</td>
<td>4</td>
<td>84</td>
<td>7</td>
<td>6</td>
<td>116</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>21</td>
<td>10</td>
<td>158</td>
<td>16</td>
<td>34</td>
<td>252</td>
</tr>
</tbody>
</table>

DON'T KNOW: 48 constitutional short stature
13 organic short stature
4 possible GHD
4 partial GHD
### APPENDIX TABLE 56

**PARENTAL CONCERN ABOUT GROWTH BY FATHER’S HEIGHT AS CHILD**

(Diagnostic groups 3-7)

(Row percentages in brackets)

**QUESTION:** HAVE YOU BEEN CONCERNED ABOUT N’S GROWTH OR DEVELOPMENT?

<table>
<thead>
<tr>
<th>Question: Was father smaller than average as a child?</th>
<th>NO</th>
<th>YES</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>55</td>
<td>55 (50%)</td>
<td>110</td>
</tr>
<tr>
<td>YES</td>
<td>71</td>
<td>35 (33%)</td>
<td>106</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>126</td>
<td>90 (42%)</td>
<td>216</td>
</tr>
</tbody>
</table>

Unknown or missing values: 70

### APPENDIX TABLE 57

**PARENTAL CONCERN ABOUT GROWTH BY FATHER’S HEIGHT SDS.**

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>FATHER’S HEIGHT SDS</th>
<th>NOT CONCERNED</th>
<th>CONCERNED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -2</td>
<td>94</td>
<td>58 (38%)</td>
<td>152</td>
</tr>
<tr>
<td>-2 &lt; 0</td>
<td>48</td>
<td>47 (49%)</td>
<td>95</td>
</tr>
<tr>
<td>&gt; 0</td>
<td>10</td>
<td>14 (58%)</td>
<td>24</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>152</td>
<td>119 (44%)</td>
<td>271</td>
</tr>
</tbody>
</table>

Missing or unknown: 15
**APPENDIX TABLE 58**

**QUESTION:** IS N SMALLER THAN BROTHERS AND SISTERS WERE AT SAME AGE?

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>63</td>
<td>2</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>9 (82%)</td>
<td>19 (76%)</td>
<td>11 (79%)</td>
<td>135 (68%)</td>
<td>22 (92%)</td>
<td>28 (88%)</td>
<td>22 (74%)</td>
</tr>
<tr>
<td>YES</td>
<td>14</td>
<td>25</td>
<td>14</td>
<td>198</td>
<td>24</td>
<td>32</td>
<td>304</td>
</tr>
<tr>
<td>TOTAL</td>
<td>11</td>
<td>25</td>
<td>14</td>
<td>198</td>
<td>24</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

DON'T KNOW: 4 constitutional short stature

NO SIBLINGS: 13
APPENDIX TABLE 59

PARENTAL CONCERN ABOUT GROWTH
BY HEIGHT OF CHILD IN COMPARISON WITH SIBLINGS
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>QUESTION:</th>
<th>NOT CONCERNED</th>
<th>CONCERNED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is N smaller than any</td>
<td>NO</td>
<td>57</td>
<td>16 (22%)</td>
</tr>
<tr>
<td>of his brothers or</td>
<td>YES</td>
<td>99</td>
<td>96 (49%)</td>
</tr>
<tr>
<td>sisters were at the</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>same age?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>156</td>
<td>112 (42%)</td>
<td>268</td>
</tr>
</tbody>
</table>

No. siblings: 8
Missing values: 10

APPENDIX TABLE 60

PARENTAL CONCERN ABOUT GROWTH
BY MOTHER'S AGE
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>MOTHER'S AGE</th>
<th>NOT CONCERNED</th>
<th>CONCERNED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>46</td>
<td>43 (48%)</td>
<td>89</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>113</td>
<td>76 (40%)</td>
<td>189</td>
</tr>
<tr>
<td>TOTAL</td>
<td>159</td>
<td>119 (43%)</td>
<td>278</td>
</tr>
</tbody>
</table>

Missing values: 8
**APPENDIX TABLE 61**

**PARENTAL CONCERN ABOUT GROWTH**

**BY PRESCHOOL IMMUNISATION HISTORY**

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>NOT CONCERNED</th>
<th>CONCERNED (%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT IMMUNISED</td>
<td>40</td>
<td>19 (32%)</td>
<td>59</td>
</tr>
<tr>
<td>IMMUNISED</td>
<td>117</td>
<td>97 (45%)</td>
<td>214</td>
</tr>
<tr>
<td>TOTAL</td>
<td>157</td>
<td>116</td>
<td>273</td>
</tr>
</tbody>
</table>

*Missing values: 13*
**APPENDIX TABLE 62**

**QUESTION:** HAVE YOU SEEN YOUR FAMILY DOCTOR SPECIFICALLY BECAUSE OF CONCERN ABOUT N'S GROWTH?

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>?ORGANIC SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>4</td>
<td>18</td>
<td>13</td>
<td>167</td>
<td>20</td>
<td>33</td>
<td>255</td>
</tr>
<tr>
<td>YES</td>
<td>9 (69%)</td>
<td>7 (28%)</td>
<td>1 (7%)</td>
<td>37 (18%)</td>
<td>5 (20%)</td>
<td>4 (11%)</td>
<td>63 (20%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>204</td>
<td>25</td>
<td>37</td>
<td>319</td>
</tr>
</tbody>
</table>

**UNKNOWN 3:** 2 constitutional short stature
1 ?organic short stature
QUESTION: HAVE YOU BEEN TO SEE YOUR FAMILY DOCTOR SPECIFICALLY BECAUSE OF CONCERN ABOUT N’S GROWTH?

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOYS</td>
<td>123</td>
<td>35 (22%)</td>
<td>158</td>
</tr>
<tr>
<td>GIRLS</td>
<td>98</td>
<td>22 (18%)</td>
<td>120</td>
</tr>
<tr>
<td>TOTAL</td>
<td>221</td>
<td>57 (21%)</td>
<td>278</td>
</tr>
</tbody>
</table>

Missing values or unknown: 8

APPENDIX TABLE 64

GP CONSULTATION ABOUT CHILD’S SHORT STATURE
BY SOCIAL CLASS
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>CLASS</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>I – III non-manual</td>
<td>8</td>
<td>3 (27%)</td>
<td>11</td>
</tr>
<tr>
<td>III manual</td>
<td>69</td>
<td>20 (22%)</td>
<td>89</td>
</tr>
<tr>
<td>IV</td>
<td>37</td>
<td>11 (23%)</td>
<td>48</td>
</tr>
<tr>
<td>V</td>
<td>13</td>
<td>6 (32%)</td>
<td>19</td>
</tr>
<tr>
<td>Students</td>
<td>–</td>
<td>1 (100%)</td>
<td>1</td>
</tr>
<tr>
<td>Unemployed - not classified</td>
<td>59</td>
<td>7 (11%)</td>
<td>66</td>
</tr>
<tr>
<td>Single parent families</td>
<td>35</td>
<td>9 (20%)</td>
<td>44</td>
</tr>
</tbody>
</table>

TOTAL: 278

Unknown: 8
APPENDIX TABLE 65

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY SUBJECT'S HEIGHT SDSaux

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>HEIGHT SDSaux</th>
<th>NOT CONSULTED</th>
<th>CONSULTED (%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2 &gt; -2.5</td>
<td>50</td>
<td>12 (19%)</td>
<td>62</td>
</tr>
<tr>
<td>-2.5 &gt; -3.0</td>
<td>124</td>
<td>38 (23%)</td>
<td>162</td>
</tr>
<tr>
<td>-3.0 &gt; -3.5</td>
<td>31</td>
<td>9 (23%)</td>
<td>40</td>
</tr>
<tr>
<td>&lt; -3.5</td>
<td>13</td>
<td>6 (32%)</td>
<td>19</td>
</tr>
<tr>
<td>TOTAL</td>
<td>218</td>
<td>65 (23%)</td>
<td>283</td>
</tr>
</tbody>
</table>

APPENDIX TABLE 66

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY MOTHER'S HEIGHT AS A CHILD.

(Diagnostic groups 3-7)

(Row percentages in brackets)

QUESTION:
Was mother smaller than average as a child?

<table>
<thead>
<tr>
<th></th>
<th>NOT CONSULTED</th>
<th>CONSULTED (%)</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>59</td>
<td>25 (30%)</td>
<td>84</td>
</tr>
<tr>
<td>YES</td>
<td>144</td>
<td>29 (17%)</td>
<td>173</td>
</tr>
<tr>
<td>TOTAL</td>
<td>203</td>
<td>54 (21%)</td>
<td>257</td>
</tr>
</tbody>
</table>

Missing values: 29
APPENDIX TABLE 67

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY MOTHER'S HEIGHT SDS
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>MOTHER'S HEIGHT SDS</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; -2</td>
<td>104</td>
<td>20 (16%)</td>
<td>124</td>
</tr>
<tr>
<td>&gt; -2</td>
<td>114</td>
<td>37 (25%)</td>
<td>151</td>
</tr>
<tr>
<td>TOTAL</td>
<td>218</td>
<td>57 (21%)</td>
<td>275</td>
</tr>
</tbody>
</table>

Unknown or missing values: 11

APPENDIX TABLE 68

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY FATHER'S HEIGHT AS A CHILD
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>QUESTION: Was father smaller than average as a child?</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>76</td>
<td>34 (31%)</td>
<td>110</td>
</tr>
<tr>
<td>YES</td>
<td>92</td>
<td>13 (12%)</td>
<td>105</td>
</tr>
<tr>
<td>TOTAL</td>
<td>168</td>
<td>47 (22%)</td>
<td>215</td>
</tr>
</tbody>
</table>

Unknown or missing values: 71
### APPENDIX TABLE 69

GP CONSULTATION ABOUT CHILD’S SHORT STATURE

BY FATHER’S HEIGHT SDS

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>FATHER’S HEIGHT SDS</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ -2</td>
<td>93</td>
<td>14 (13%)</td>
<td>107</td>
</tr>
<tr>
<td>-2 &lt; 0</td>
<td>106</td>
<td>34 (24%)</td>
<td>140</td>
</tr>
<tr>
<td>&gt; 0</td>
<td>16</td>
<td>6 (33%)</td>
<td>24</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>215</strong></td>
<td><strong>56 (21%)</strong></td>
<td><strong>271</strong></td>
</tr>
</tbody>
</table>

Missing or unknown values: 15

### APPENDIX TABLE 70

GP CONSULTATION ABOUT CHILD’S SHORT STATURE

BY CHILD’S HEIGHT COMPARED WITH SIBLINGS

(Diagnostic groups 3-7)

(Row percentages in brackets)

<table>
<thead>
<tr>
<th>QUESTION: Is N smaller than any of his brothers and sisters were at the same age?</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>66</td>
<td>6 (8%)</td>
<td>72</td>
</tr>
<tr>
<td>YES</td>
<td>147</td>
<td>48 (25%)</td>
<td>195</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>213</strong></td>
<td><strong>54 (20%)</strong></td>
<td><strong>267</strong></td>
</tr>
</tbody>
</table>

No siblings: 8

Missing values: 11
**APPENDIX TABLE 71**

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY IMMUNISATION HISTORY
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th></th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT IMMUNISED</td>
<td>50 (8%)</td>
<td>8 (14%)</td>
<td>58</td>
</tr>
<tr>
<td>IMMUNISED</td>
<td>165</td>
<td>49 (23%)</td>
<td>214</td>
</tr>
<tr>
<td>TOTAL</td>
<td>215</td>
<td>57 (21%)</td>
<td>272</td>
</tr>
</tbody>
</table>

Missing values or unknown: 14

**APPENDIX TABLE 72**

GP CONSULTATION ABOUT CHILD'S SHORT STATURE
BY MOTHER'S AGE
(Diagnostic groups 3-7)
(Row percentages in brackets)

<table>
<thead>
<tr>
<th>Mother's age</th>
<th>NOT CONSULTED</th>
<th>CONSULTED</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>63</td>
<td>26 (29%)</td>
<td>89</td>
</tr>
<tr>
<td>&gt;30</td>
<td>158</td>
<td>30 (16%)</td>
<td>188</td>
</tr>
<tr>
<td>TOTAL</td>
<td>221</td>
<td>56 (20%)</td>
<td>277</td>
</tr>
</tbody>
</table>

Missing values: 9
APPENDIX TABLE 73

QUESTION: WHAT ACTION DID YOUR GP TAKE?

<table>
<thead>
<tr>
<th>Action</th>
<th>Severe GHD</th>
<th>Partial GHD</th>
<th>Possible GHD</th>
<th>Constitutional or low short stature</th>
<th>Organic short stature</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reassurance</td>
<td>5 (56%)</td>
<td>7 (100%)</td>
<td>-</td>
<td>25 (68%)</td>
<td>3 (60%)</td>
<td>40 (63%)</td>
</tr>
<tr>
<td>Other illness NFA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (50%)</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Blood tests etc.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (3%)</td>
<td>-</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Referred to consultant</td>
<td>4* (44%)</td>
<td>-</td>
<td>1 (100%)</td>
<td>8 (22%)</td>
<td>2 (40%)</td>
<td>17 (27%)</td>
</tr>
<tr>
<td>Blood tests + referral</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (3%)</td>
<td>-</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Don't know</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2 (5%)</td>
<td>-</td>
<td>2 (3%)</td>
</tr>
<tr>
<td><strong>TOTAL CONSULTED</strong></td>
<td><strong>9</strong></td>
<td><strong>7</strong></td>
<td><strong>1</strong></td>
<td><strong>37</strong></td>
<td><strong>5</strong></td>
<td><strong>63</strong></td>
</tr>
</tbody>
</table>

Not consulted: 255

* 2 under pressure
QUESTION: How old was N when you first noticed he was smaller than most children the same age?

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>AGE (years)</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 1</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>39</td>
<td>6</td>
<td>22</td>
</tr>
<tr>
<td>1 +</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>25</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2 +</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>13</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3 +</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>6</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>4 +</td>
<td>1 (62%)</td>
<td>1 (48%)</td>
<td>- (43%)</td>
<td>16 (48%)</td>
<td>3 (65%)</td>
<td>- (78%)</td>
</tr>
<tr>
<td>5 +</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>47</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>6 +</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7 +</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8 +</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Not noticed</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>47 (22.8)</td>
<td>3 (11.5)</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>13</td>
<td>25</td>
<td>14</td>
<td>206</td>
<td>26</td>
<td>37</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 75**

**QUESTION:** DO YOU THINK N IS SELF CONSCIOUS .... BECAUSE OF HIS HEIGHT?

<table>
<thead>
<tr>
<th>REPLY</th>
<th>SEVERE GHD</th>
<th>PARTIAL GHD</th>
<th>POSSIBLE GHD</th>
<th>CONSTITUTIONAL OR LBW SHORT STATURE</th>
<th>?ORGANIC ORGANIC SHORT STATURE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>5</td>
<td>17</td>
<td>10</td>
<td>136 (66%)</td>
<td>17</td>
<td>28</td>
</tr>
<tr>
<td>YES</td>
<td>7 (58%)</td>
<td>8 (32%)</td>
<td>4 (29%)</td>
<td>63 (32%)</td>
<td>9 (35%)</td>
<td>8 (22%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>12</td>
<td>25</td>
<td>14</td>
<td>199</td>
<td>26</td>
<td>36</td>
</tr>
</tbody>
</table>

DON'T KNOW 9: 7 constitutional short stature
1 organic short stature
1 severe GHD
**APPENDIX TABLE 76**

**PARENTS' HEIGHTS (SDS) - MEANS & SD'S**

Cases with Constitutional Short Stature and Controls

**Edinburgh & Glasgow**

<table>
<thead>
<tr>
<th></th>
<th>Edinburgh Cases</th>
<th>Edinburgh Controls</th>
<th>Glasgow Cases Group I</th>
<th>Glasgow Cases Group II</th>
<th>Total Glasgow Cases</th>
<th>Glasgow Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mother</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>30</td>
<td>29</td>
<td>80</td>
<td>74</td>
<td>154</td>
<td>62</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-2.01 ± 0.81</td>
<td>-0.51 ± 0.82</td>
<td>-1.66 ± 0.98</td>
<td>-1.84 ± 0.73</td>
<td>-1.75 ± 0.70</td>
<td>-0.56 ± 1.09</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td><strong>Father</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>30</td>
<td>29</td>
<td>79</td>
<td>72</td>
<td>151</td>
<td>59</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-1.52 ± 1.23</td>
<td>-0.44 ± 1.12</td>
<td>-1.50 ± 1.13</td>
<td>-1.89 ± 1.26</td>
<td>-1.68 ± 1.20</td>
<td>-0.59 ± 1.04</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td><strong>Midparent height</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>30</td>
<td>29</td>
<td>78</td>
<td>69</td>
<td>147</td>
<td>59</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>-1.54 ± 0.73</td>
<td>-0.23 ± 0.77</td>
<td>-1.37 ± 0.77</td>
<td>-1.63 ± 0.84</td>
<td>-1.49 ± 0.89</td>
<td>-0.35 ± 0.88</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>8</td>
<td>11</td>
<td>4</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 77

AGE OF MOTHER AT BIRTH OF FIRST CHILD

CASES WITH CONSTITUTIONAL SHORT STATURE AND CONTROLS

(Cumulative percentages in brackets)

<table>
<thead>
<tr>
<th>AGE</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 17</td>
<td>2</td>
<td>3</td>
<td>10</td>
<td>6</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>17 - 20</td>
<td>17 (63%)</td>
<td>10 (41%)</td>
<td>36 (57%)</td>
<td>35 (53%)</td>
<td>71 (55%)</td>
<td>28 (46%)</td>
</tr>
<tr>
<td>21 - 25</td>
<td>10</td>
<td>13</td>
<td>27</td>
<td>27</td>
<td>54</td>
<td>24</td>
</tr>
<tr>
<td>26 - 30</td>
<td>1</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>31 - 35</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>36 +</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 78

MOTHER'S AGE AT BIRTH OF INDEX CHILD

CASES WITH CONSTITUTIONAL SHORT STATURE AND CONTROLS

(Column percentages in brackets)

<table>
<thead>
<tr>
<th>AGE</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>TOTAL GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>18 - 20</td>
<td>7 (27%)</td>
<td>3 (16%)</td>
<td>14 (21%)</td>
<td>12 (17%)</td>
<td>26 (19%)</td>
<td>12 (19%)</td>
</tr>
<tr>
<td>21 - 25</td>
<td>9</td>
<td>11</td>
<td>32</td>
<td>20</td>
<td>52</td>
<td>21</td>
</tr>
<tr>
<td>26 - 30</td>
<td>8</td>
<td>9</td>
<td>14</td>
<td>20</td>
<td>34</td>
<td>19</td>
</tr>
<tr>
<td>31 - 35</td>
<td>2</td>
<td>3</td>
<td>10</td>
<td>13</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>36 +</td>
<td>3</td>
<td>3</td>
<td>8</td>
<td>11</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>31</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>

Missing: 1 control
APPENDIX TABLE 79

PREGNANCY NUMBER

CASES WITH CONSTITUTIONAL SHORT STATURE AND CONTROLS

Edinburgh & Glasgow

(Column percentages in brackets.)

<table>
<thead>
<tr>
<th>NO.</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>7</td>
<td>15</td>
<td>10</td>
<td>25</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>10</td>
<td>16</td>
<td>13</td>
<td>29</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>10</td>
<td>17</td>
<td>14</td>
<td>31</td>
<td>11</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>3</td>
<td>14</td>
<td>10</td>
<td>24</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>1 (23%)</td>
<td>-</td>
<td>8 (23%)</td>
<td>6 (39%)</td>
<td>14 (49%)</td>
<td>1 (19%)</td>
</tr>
<tr>
<td>6 or more</td>
<td>6 (3%)</td>
<td>2 (6%)</td>
<td>11 (23%)</td>
<td>2 (4%)</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE 80

**LENGTH OF GESTATION**

<table>
<thead>
<tr>
<th>WEEKS OF GESTATION</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES</th>
<th>GLASGOW GROUP I CASES</th>
<th>GLASGOW GROUP II CASES</th>
<th>TOTAL GLASGOW CASES</th>
<th>TOTAL GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 - 32</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>33 - 36</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td>11</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>37 - 38</td>
<td>1 (10%)</td>
<td>2 (6.5%)</td>
<td>10 (21%)</td>
<td>3 (12%)</td>
<td>13 (17%)</td>
<td>13</td>
<td>25 (25%)</td>
</tr>
<tr>
<td>39 - 41</td>
<td>19</td>
<td>62</td>
<td>20</td>
<td>12</td>
<td>3</td>
<td>113</td>
<td>154</td>
</tr>
<tr>
<td>42 +</td>
<td>8</td>
<td>9</td>
<td>12</td>
<td>3</td>
<td>15</td>
<td>13</td>
<td>60</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>30</strong></td>
<td><strong>31</strong></td>
<td><strong>80</strong></td>
<td><strong>74</strong></td>
<td><strong>154</strong></td>
<td><strong>154</strong></td>
<td><strong>214</strong></td>
</tr>
</tbody>
</table>

**Missing:** 4 cases

4 controls
APPENDIX TABLE 81

BIRTH WEIGHT DISTRIBUTION, MEANS ± SD IN CASES WITH
CONSTITUTIONALLY SHORT STATURE AND CONTROLS
(Cumulative column percentages in brackets)

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>BIRTH WEIGHT (gms.)</th>
<th>EDINBURGH &amp; GLASGOW GROUP I CASES</th>
<th>GLASGOW GROUP II CASES</th>
<th>TOTAL</th>
<th>ALL CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>2821 ± 505</td>
<td>2953 ± 492</td>
<td>2874 ± 502</td>
<td>3255 ± 552</td>
</tr>
<tr>
<td>&lt; 1500</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>1501 - 2000</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>2001 - 2500</td>
<td>29 (31%)</td>
<td>10 (18%)</td>
<td>39 (26%)</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>2501 - 3000</td>
<td>34</td>
<td>29</td>
<td>63</td>
<td>16</td>
</tr>
<tr>
<td>3001 - 3500</td>
<td>33</td>
<td>22</td>
<td>55</td>
<td>37</td>
</tr>
<tr>
<td>3501 - 4000</td>
<td>5</td>
<td>7</td>
<td>12</td>
<td>29</td>
</tr>
<tr>
<td>4001 +</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>TOTAL</td>
<td>107</td>
<td>73</td>
<td>180</td>
<td>95</td>
</tr>
</tbody>
</table>

Unknown: 8 cases
**QUESTION:** DID YOU SMOKE DURING YOUR PREGNANCY WITH N?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>TOTAL GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>17</td>
<td>15</td>
<td>24</td>
<td>29</td>
<td>53</td>
<td>20</td>
</tr>
<tr>
<td>YES</td>
<td>13 (43%)</td>
<td>17 (53%)</td>
<td>56 (70%)</td>
<td>48 (62%)</td>
<td>104 (66%)</td>
<td>42 (68%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>80</td>
<td>77</td>
<td>157</td>
<td>62</td>
</tr>
</tbody>
</table>

DON'T KNOW 3: 2 cases

1 control
### APPENDIX TABLE 83

**SIZE OF FAMILY**

**CASES WITH CONSTITUTIONAL SHORT STATURE AND CONTROLS**

**Edinburgh & Glasgow**

<table>
<thead>
<tr>
<th>NO. OF CHILDREN</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES</th>
<th>GLASGOW GROUP I</th>
<th>GLASGOW GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>TOTAL GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>10</td>
<td>6</td>
<td>6</td>
<td>12</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>9</td>
<td>17</td>
<td>14</td>
<td>31</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>7</td>
<td>22</td>
<td>16</td>
<td>38</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>6 (30%)</td>
<td>2 (19%)</td>
<td>15 (42%)</td>
<td>11 (53%)</td>
<td>26 (49%)</td>
<td>8 (30%)</td>
<td>11 (30%)</td>
</tr>
<tr>
<td>6 +</td>
<td>3 (30%)</td>
<td>4 (19%)</td>
<td>19 (42%)</td>
<td>30 (53%)</td>
<td>49 (49%)</td>
<td>11 (30%)</td>
<td>11 (30%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td><strong>MEAN ± SD</strong></td>
<td>3.97 ± 1.54</td>
<td>3.44 ± 1.41</td>
<td>4.51 ± 1.85</td>
<td>4.99 ± 2.76</td>
<td>4.85 ± 2.10</td>
<td>4.03 ± 1.88</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX TABLE 84

PERSONS PER ROOM IN HOUSEHOLD - MEAN ± SD AND DISTRIBUTION

CONTROLS AND CASES WITH CONSTITUTIONAL SHORT STATURE

(Cumulative column percentages in brackets)

<table>
<thead>
<tr>
<th>PERSONS PER ROOM</th>
<th>EDINBURGH SHORT CHILDREN</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW SHORT CHILDREN GROUP I</th>
<th>GLASGOW SHORT CHILDREN GROUP II</th>
<th>TOTAL CASES GLASGOW</th>
<th>CONTROLS GLASGOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>7</td>
<td>16</td>
<td>8</td>
<td>11</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>1 - 1.44</td>
<td>16 (79%)</td>
<td>12 (88%)</td>
<td>28 (44%)</td>
<td>16 (35%)</td>
<td>44 (40%)</td>
<td>25 (56%)</td>
</tr>
<tr>
<td>1.45 - 2.5</td>
<td>6</td>
<td>4</td>
<td>40</td>
<td>35</td>
<td>75</td>
<td>23</td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>15</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>

MEAN

<table>
<thead>
<tr>
<th></th>
<th>MEAN</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>1.25</td>
<td>± 0.20</td>
</tr>
<tr>
<td>1 - 1.44</td>
<td>1.17</td>
<td>± 0.38</td>
</tr>
<tr>
<td>1.45 - 2.5</td>
<td>1.66</td>
<td>± 0.54</td>
</tr>
<tr>
<td>&gt; 2.5</td>
<td>1.96</td>
<td>± 1.0</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1.80</td>
<td>± 0.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td>± 0.56</td>
</tr>
</tbody>
</table>
APPENDIX TABLE 85

QUESTION: DOES N SHARE A BED WITH ANYONE?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>21</td>
<td>27</td>
<td>43</td>
<td>27</td>
<td>70</td>
<td>39</td>
</tr>
<tr>
<td>YES</td>
<td>9 (30%)</td>
<td>5 (16%)</td>
<td>38 (47%)</td>
<td>50 (65%)</td>
<td>88 (56%)</td>
<td>24 (38%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 86**

**QUESTION:** HAVE YOU EVER RECEIVED A SUPPLEMENTARY BENEFIT?

Cases with Constitutional Short Stature and Controls

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>16</td>
<td>21</td>
<td>31</td>
<td>29</td>
<td>60</td>
<td>33</td>
</tr>
<tr>
<td>YES</td>
<td>14 (47%)</td>
<td>11 (34%)</td>
<td>50 (62%)</td>
<td>48 (62%)</td>
<td>98 (62%)</td>
<td>30 (48%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>
QUESTION: DO YOU HAVE TO PAY FOR SCHOOL MEALS?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>Edinburgh Cases</th>
<th>Edinburgh Controls</th>
<th>Glasgow Cases Group I</th>
<th>Glasgow Cases Group II</th>
<th>Total Glasgow Cases</th>
<th>Glasgow Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>12</td>
<td>8</td>
<td>49</td>
<td>42</td>
<td>91</td>
<td>29</td>
</tr>
<tr>
<td>Yes or not applicable</td>
<td>18 (60%)</td>
<td>24 (75%)</td>
<td>32 (40%)</td>
<td>35 (45%)</td>
<td>67 (42%)</td>
<td>34 (54%)</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>77</td>
<td>158</td>
<td>63</td>
</tr>
</tbody>
</table>
**APPENDIX TABLE 88**

"DISADVANTAGE" SCORE

CONTROLS AND CASES WITH CONSTITUTIONAL SHORT STATURE

<table>
<thead>
<tr>
<th>SCORE</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>8 (28%)</td>
<td>12 (38%)</td>
<td>11 (14%)</td>
<td>8 (11%)</td>
<td>19 (12%)</td>
<td>14 (22%)</td>
</tr>
<tr>
<td>1</td>
<td>11</td>
<td>12</td>
<td>19</td>
<td>19</td>
<td>38</td>
<td>19</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>8</td>
<td>24</td>
<td>19</td>
<td>43</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>-</td>
<td>27 (33%)</td>
<td>30 (39%)</td>
<td>57 (36%)</td>
<td>8 (13%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>32</td>
<td>81</td>
<td>76</td>
<td>157</td>
<td>63</td>
</tr>
</tbody>
</table>

Missing: 2 cases
**APPENDIX TABLE 89**

**QUESTION:** WAS N IMMUNISED AGAINST DIPHTHERIA BEFORE STARTING SCHOOL?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>2</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td>45</td>
<td>8</td>
</tr>
<tr>
<td>YES</td>
<td>26 (93%)</td>
<td>29 (91%)</td>
<td>59 (74%)</td>
<td>50 (68%)</td>
<td>109 (71%)</td>
<td>55 (87%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>28</td>
<td>32</td>
<td>80</td>
<td>74</td>
<td>154</td>
<td>63</td>
</tr>
</tbody>
</table>

UNKNOWN: 5 cases
QUESTION: HAVE YOU HAD ANY FURTHER EDUCATIONAL TRAINING AFTER LEAVING SCHOOL?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>25</td>
<td>19</td>
<td>69</td>
<td>71</td>
<td>140</td>
<td>50</td>
</tr>
<tr>
<td>YES</td>
<td>4 (14%)</td>
<td>12 (39%)</td>
<td>11 (14%)</td>
<td>1 (1%)</td>
<td>12 (8%)</td>
<td>13 (21%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>31</td>
<td>80</td>
<td>72</td>
<td>152</td>
<td>63</td>
</tr>
</tbody>
</table>

NOT KNOWN: 8 cases
QUESTION: ARE THERE PEOPLE WHO COME TO SEE YOU SOMETIMES AND ASK FOR YOUR HELP OR ADVICE?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>TOTAL GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No one comes</td>
<td>9</td>
<td>10</td>
<td>52</td>
<td>42</td>
<td>94</td>
<td>18</td>
</tr>
<tr>
<td>People come</td>
<td>20 (69%)</td>
<td>21 (68%)</td>
<td>28 (35%)</td>
<td>29 (41%)</td>
<td>57 (38%)</td>
<td>45 (71%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>31</td>
<td>80</td>
<td>71</td>
<td>151</td>
<td>63</td>
</tr>
</tbody>
</table>

UNKNOWN: 8 cases
1 control
**APPENDIX TABLE 92**

**QUESTION:** ARE THERE ANY GROUPS OR SOCIETIES YOU BELONG TO, OR ATTEND, OR DO YOU DO ANY CHURCH WORK?

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>REPLY</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>24</td>
<td>18</td>
<td>64</td>
<td>62</td>
<td>126</td>
<td>49</td>
</tr>
<tr>
<td>YES</td>
<td>5 (17%)</td>
<td>13 (42%)</td>
<td>16 (20%)</td>
<td>13 (17%)</td>
<td>29 (19%)</td>
<td>14 (22%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>31</td>
<td>80</td>
<td>75</td>
<td>155</td>
<td>63</td>
</tr>
</tbody>
</table>

**UNKNOWN:** 5 cases
**APPENDIX TABLE 93**

SUBJECTIVE RATING OF INTERVIEWEE'S INTELLIGENCE

Cases with Constitutional Short Stature and Controls.

Edinburgh & Glasgow

<table>
<thead>
<tr>
<th>POINTS</th>
<th>EDINBURGH CASES</th>
<th>EDINBURGH CONTROLS</th>
<th>GLASGOW CASES GROUP I</th>
<th>GLASGOW CASES GROUP II</th>
<th>TOTAL GLASGOW CASES</th>
<th>GLASGOW CONTROLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 3 (i.e. less intelligent)</td>
<td>9 (30%)</td>
<td>3 (9%)</td>
<td>19 (23%)</td>
<td>23 (30%)</td>
<td>42 (27%)</td>
<td>7 (11%)</td>
</tr>
<tr>
<td>4 - 5 (i.e. more intelligent)</td>
<td>21</td>
<td>29</td>
<td>62</td>
<td>53</td>
<td>115</td>
<td>56</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
<td>32</td>
<td>81</td>
<td>76</td>
<td>157</td>
<td>63</td>
</tr>
</tbody>
</table>

UNKNOWN: 1 case