UNIVERSITY OF SOUTHAMPTON

EARLY DETERMINANTS OF BLOOD PRESSURE AND RELATED DISEASE.

(SINGLE VOLUME)

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ABSTRACT
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EARLY DETERMINANTS OF BLOOD PRESSURE AND RELATED DISEASE.
By Adrian Richard Bull.

Two studies were designed to examine the relations between early growth and cardiovascular disease in adult life.

The first study was a survey of pelvimetry in 1,615 men and women aged 50 yrs or more living in 8 English towns. The mean diameters at the pelvic inlet were smaller in towns with higher SMR's for cardiovascular disease. In both sexes the pelvises of those aged 75 or more had a lower brim index than the pelvises of those who were younger.

The second study followed up 449 infants born in Preston during 1935-1943 who were still living in Lancashire. In both sexes systolic and diastolic pressures were strongly related to placental weight and birth weight. Mean systolic pressure rose by 15 mmHg as placental weight increased from 1lb or less to greater than 1.5lb, and fell by 11 mmHg as birth weight increased from 5.5lb or less to greater than 7.5lb. These relations were independent of each other, and of the observed effects of higher body mass index and alcohol consumption.

Analysis of subjects born after 38 weeks completed gestation showed that for those with placental weights of 1.25 lb or less, mean systolic pressure rose by 13 mmHg as ponderal index (w/l^3) at birth fell from greater than 14.75 to 12 or less, while for those with placental weights of greater than 1.25 lb , mean systolic pressure rose by 14 mmHg as head circumference/length increased from less than 0.65 to 0.7 or more.

Growth in early life, reflected in the size of the adult bony pelvis, is related to risk of cardiovascular disease. The intrauterine environment, through an effect on intrauterine growth, has an important effect on blood pressure in adult life. Two groups of babies, characterised by birth measurements, have been identified as being at increased risk of raised blood pressure in adult life.

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PREFACE.

Ischaemic Heart Disease (IHD) and Cerebrovascular disease (CVD) cause a considerable burden of mortality in England and Wales. In 1986 IHD (ICD code 410-414) was the underlying cause of 157,995 deaths, and CVD (ICD code 430-438) the cause of 71,328 deaths in England and Wales (27.3% and 12.3% of all deaths respectively) (1). Against a world standard population, the age standardised mortality for IHD in England and Wales in 1987 was 156 per 100,000 (range for 52 countries observed 16.8 - 190.2) and for CVD was 60.7 per 100,000 (range 17.5 - 153.5) (2).

This thesis examines two propositions - that under nutrition in early life is an important factor in the genesis of cardiovascular disease, and that fetal growth is related to blood pressure in adult life.

A literature review is reported that considers:
1. The relationship of cardiovascular disease in adulthood to conditions experienced in early life,
2. Blood pressure as a risk factor for IHD and CVD,
3. Blood pressure and its relationship to birthweight,
4. Maternal influence on birthweight,
5. Stature and pelvimetry.

Two epidemiological studies are reported. One is a comparison of pelvic anatomy in different parts of England. The other is a follow up after 50 years of 443 people born and still living in Preston, whose birth records have been preserved.

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AUTHOR'S CONTRIBUTION.

PELVIMETRY SURVEY. I designed the study, recruited the contributing hospitals, and supervised the collection of the data. Miss Vines (statistician) provided statistical assistance with the analysis of the data, supported by Dr Osmond (statistician). Professor Barker (my supervisor) assisted with the interpretation of the results and suggested certain refinements of the analysis. Drs Guyer and Herbetko read the X-ray films.

PRESTON COHORT STUDY. From the original clinical records I designed the study, taking advice on methods of tracing subjects. I led the collection of the data, management of the fieldwork, and tracking of elusive cases, supported by Mrs Simmonds (research assistant). First analysis and interpretation was shared between myself, Professor Barker and Dr Osmond. Dr K Godfrey (epidemiologist) contributed to subsequent analysis within different groups of intra uterine retardation.

INTRODUCTION.

I THE RELATIONSHIP OF CARDIOVASCULAR DISEASE IN ADULTHOOD TO CONDITIONS EXPERIENCED IN EARLY LIFE.

HISTORICAL AND GEOGRAPHICAL ASSOCIATIONS BETWEEN MATERNAL, INFANT AND ADULT HEALTH.

In 1964, Rose made (as one of three alternatives) the suggestion that 'ischaemic heart disease tends to occur in individuals who come from a constitutionally weaker stock, more liable to submit to a variety of disease' (3). This conclusion was drawn from a case control study, which compared 75 patients admitted for ischaemic heart disease with patients admitted for conditions not known to be associated with that condition. Controls were matched for age, sex, and whether manual or clerical workers. It was observed that amongst siblings of the index cases there had been a large excess mortality in infancy. Index cases themselves were more likely to have been admitted to hospital in the past, for conditions other than ischaemic heart disease. An excess of parental mortality from ischaemic heart disease had occurred amongst index cases, but for males only. Rose concluded that the evidence for familial aggregation of ischaemic heart disease did not preclude mechanisms that were environmental rather than genetic.

This association of infant mortality with subsequent ischaemic heart disease in the same generation was later demonstrated by a different epidemiological method (4). Standardised mortality rates were calculated for each local authority area in England and Wales, using all deaths in the period 1968-1978, and 1971 census data. A close geographical relationship was observed between current mortality rates for ischaemic

heart disease and past infant mortality rates. The correlations were consistent for both sexes and all age groups. Stroke (defined as cerebrovascular disease other than subarachnoid haemorrhage) was similarly correlated with infant mortality. Among the other common causes of death, only bronchitis, stomach cancer and chronic rheumatic heart disease had a close relationship to infant mortality. Bronchitis and chronic rheumatic heart disease mortality, however, were associated with post neonatal mortality, unlike stroke and ischaemic heart disease which were associated more closely with neonatal death. This suggests a different mechanism for the influence observed, since post neonatal mortality was related to overcrowding and family size, and thus exposure to respiratory infections, whereas stillbirth and neonatal mortality rates depended upon variations in maternal health and nutrition and thus the nature of the intra uterine environment (5,6).

As a consequence of the study described above, a detailed geographical comparison was made of maternal mortality (deaths attributable to pregnancy or childbirth) before and after the First World War, and standardised mortality ratios at ages 55-74 during 1968-1978 (7). The results showed a strong and consistent relationship between mortality from stroke and ischaemic heart disease in one generation and maternal mortality (from causes excluding puerperal fever) of the preceding generation.

The relationship between ischaemic heart disease in middle and late life, and infant mortality of the same generation cohort has been demonstrated in Norway, where it was observed that current geographical variations in mortality in middle age were correlated with the pattern of infant mortality that had existed for that generation (8). The

correlation was particularly evident for arteriosclerotic heart disease. The author suggested that 'the more fit survive and carry with them a life long vulnerability because of the poor living conditions in early years'. It was later suggested that the Norwegian correlations were explained by an effect on serum cholesterol of deprivation during childhood followed by later affluence (9). An association between poor socioeconomic circumstances during childhood and ischaemic heart disease in adult life was also shown in Finland by Kaplan and Salonen, who examined a population of 1513 men in the rural and urban communities of Kuopio (10). Socio economic conditions experienced during childhood were assessed by fathers' education and occupational prestige, mothers' occupational prestige, whether the family lived on a farm, and whether the family was perceived as being 'wealthy'. Current lifestyle and past medical history were fully assessed. Subjects who reported low socioeconomic status during childhood were significantly more likely to have cardiac ischaemia on exercise than those reporting high socioeconomic class during childhood. There was no effect on risk of ischaemic heart disease of any interaction between adult socioeconomic status and that of childhood, as had been proposed by Forsdahl (9).

Barker et al argued that the factor underlying these observations was maternal health and early growth rather than socioeconomic conditions experienced in childhood and in later life (4,5,7). A direct link between low birthweight, reduced infant growth and cardiovascular risk in individuals was shown in a follow up study of 5654 men born in Hertfordshire, England, during 1911-1930 (11). In that county, from 1911, every baby was weighed at birth, visited periodically through the first year, and weighed again at one year. The records have been preserved allowing men now aged about sixty to be traced.

The early development of these individuals could thus be related to later illness and death. Cause of death in this cohort was analyzed in relation to birthweight, weight at one year, and method of feeding. The relative risk of death from ischaemic heart disease was strongly related to both prenatal and postnatal growth. Standardised mortality ratios for ischaemic heart disease fell with increasing birthweight at one year, a trend not evident for deaths from non-circulatory causes. Mortality from Ischaemic heart disease also fell with increasing birthweight, although the trend did not reach statistical significance. When those who had been bottle fed were excluded (because of different associations of bottle feeding with Ischaemic heart disease), a simultaneous effect of birthweight and weight at one year was demonstrated, with men for whom both weights were lowest having the greatest risk of mortality from ischaemic heart disease. Stroke mortality showed similar trends. Among babies with above average birthweight the risk of ischaemic heart disease was found to be below average, irrespective of infant growth (12).

HEIGHT RELATED TO ISCHAEMIC HEART AND CEREBROVASCULAR DISEASE.

Adult height is influenced by the combination of genetic potential and environmental conditions during early growth, and reflects the conditions of early life (13-18). Adult height decreases with socioeconomic status - an effect which is still apparent among children in England and Wales (19-22).

An excess risk of mortality from ischaemic heart disease and cerebrovascular disease has

been demonstrated among people of low stature in Norway, Finland, Sweden, and Britain (19,23-25). The common conclusion drawn from these observations was that factors operative in early life that are associated with low adult stature are also associated with risk of cerebrovascular or ischaemic heart disease. It was suggested that these factors could be either hereditary or environmental. The regional variation in height of mothers and children in a British study has also been shown to have a negative correlation with standardised mortality ratios for cerebrovascular and ischaemic heart disease (26).

CONCLUDING REMARKS.

A number of authors have observed that ischaemic heart and cerebrovascular disease are related to conditions experienced in early life (8,10,23-25,27). Examination of maternal and early infant mortality point to fetal and infant growth as a major influence on cardiovascular disease (4,5,11,12).

II BLOOD PRESSURE CEREBROVASCULAR DISEASE AND ISCHAEMIC HEART DISEASE.

BLOOD PRESSURE AS A RISK FACTOR.

In 1959 Leishman suggested that, because of the profession's preoccupation with lowering blood pressure, it was already difficult to assess properly the natural history of the hypertensive condition (28). Leishman was able to report, however, a comparison of 211 untreated hypertensive patients (diastolic pressure >100 mmHg) first identified in 1946, with two further groups treated by sympathectomy and ganglion blocking drugs. The study demonstrated the link between hypertension and cerebrovascular and renal disease, and the advantage of hypotensive therapy.

In 1970 Kannel et al reported the findings of a prospective study which followed up more than 5,000 men and women for a period of 14 years - the Framingham cohort (29). A comprehensive programme meant that only 2% of the study population were completely lost to the project, although initial recruitment was only 68% of those identified for inclusion. A detailed examination of non-haemorrhagic stroke showed gradients of risk with blood pressure level that were similar for both diastolic and systolic measurements, after adjustment for age. The data showed that there was no threshold of risk - that the risk was proportional to the level of blood pressure, from lowest recorded to highest. The relationship of risk to blood pressure was apparent at all ages.

In 1978, the same cohort provided data for analysis which related to more than 2 decades follow up (30). Systolic blood pressure was confirmed as the most powerful predictor of risk for non-haemorrhagic stroke. The data also supported earlier findings that elevated blood pressure remained a risk factor for stroke in the older age groups. The authors stressed that the risks were related to blood pressure and not to arbitrarily designated hypertension.

Further examination of data from this cohort demonstrated that blood pressure lability did not lessen the association between blood pressure and risk of stroke - the mean, minimum and maximum of three blood pressures taken during an examination were equally predictive of cardiovascular disease (31).

These findings have been confirmed in other populations. A North American population of mixed race was sampled in 1960-1962; 2,350 people were re-examined seven to nine years later with careful analysis of medical history or death suggestive of stroke (32). Transient ischaemic attacks were not included in the analysis. The risk of stroke showed a clear gradient across three categories of blood pressure.

In Sweden, 789 men aged 54 at initial examination in 1967 were followed up until the end of 1985, with all strokes being determined from a stroke register, hospital activity data, mortality data, and clinical interview (33). Diastolic blood pressure predicted stroke independently of other risk factors - maternal history of stroke, abdominal obesity, plasma fibrinogen.

In 1972 over 9,000 men and women were examined in Eastern Finland, having been selected by random sampling from the population register (34). Follow up for strokes or transient ischaemic attacks was carried out through national hospital discharge and mortality data. The age adjusted risk of any stroke or brain infarction was observed to rise steadily with increasing baseline blood pressure. Other risk factors for stroke identified for men in a multiple logistic model were daily number of cigarettes and history of previous stroke. No threshold of blood pressure associated risk was observed. The authors pointed out that only 27 per cent of cases occurred among men with diastolic pressures of 95 mmHg or more and concluded that population measures to reduce blood pressure should be sought, since active intervention would have to include groups with only borderline hypertension.

A survey of 17,530 London civil servants aged 40 to 64 (the Whitehall study) showed that blood pressure was a risk factor for coronary heart disease, and linked both blood pressure and symptoms of disease to employment grade (19).

In 1986, results were reported from the Multiple Risk Factor Intervention Trial (MRFIT), in which 361,662 men aged 35-57 were screened in the years 1972-74 (35). In 1982, the mortality experience of this cohort was analyzed from death certificates obtained through state health departments. There were 2626 deaths from coronary heart disease. Mortality was analyzed against diastolic blood pressure and a gradual increase in risk was demonstrated over most levels, with an accentuation of risk at diastolic blood pressure greater than 94 mmHg (above the 85th centile), such that those in the top 15% of the population for blood pressure had a relative risk of death from ischaemic heart disease

of 2.5 compared with the bottom 25%.

Data from the same study (MRFIT) were used in an analysis of 325,384 white men who were originally screened, in which cohort 2,426 deaths occurred (36). The mortality rate from coronary heart disease was seen to increase progressively across the five quintiles of blood pressure. The risk associated with rising blood pressure was shown to be independent of that observed with serum cholesterol or smoking.

The role of blood pressure as a population risk factor for cardiovascular disease has been demonstrated by the British Regional Heart Study (37). The project examined the cardiovascular mortality of a number of towns. A clinical survey of middle aged men was then conducted in 25 of these towns (individuals being identified by general practice) to examine the relationship between distribution of cardiovascular risk factors and cardiovascular mortality rates. Cardiovascular mortality included cerebrovascular disease and ischaemic heart disease. The rates were associated with mean systolic blood pressure, prevalence of heavy cigarette smoking, and heavy alcohol consumption. The cohort was followed up over 8 years at which point a relative risk of having had a stroke was 12.1 in men who were smokers and had a systolic blood pressure of 160mmHg or more, compared with normotensive non smoking men (38).

INTERVENTION STUDIES.

A number of studies have demonstrated that blood pressure is a remediable cause of ischaemic heart and cerebrovascular disease. In 1967, results were published of a

randomised control trial of hypotensive therapy for people with diastolic pressures averaging between 115 and 129 mmHg (39). A beneficial effect on both mortality and morbidity was reported. A randomised controlled trial of people with mild hypertension was conducted by a Medical Research Council working party. It demonstrated a reduced risk of stroke and some effect on ischaemic heart disease with lowered blood pressure (40). A similar effect has been shown in American and Australian populations (41,42).

In 1989 a working party reviewed the evidence of such trials and concluded that pharmacological treatment of hypertension is indicated for diastolic blood pressures which are consistently over 100 mmHg (43).

A CONTINUUM OF RISK.

In many of these prospective studies, the relative risk of cardiovascular disease is shown to be related to blood pressure, even in what is considered to be the normal range. Elevation of blood pressure across the full range in a population is as important to the incidence of blood pressure related disease as the proportion of individuals within the population who have the highest levels (44). This is discussed by Kannel et al (36), who calculated that an average reduction in diastolic pressure of 8 mmHg in the North American population would produce a 20.6% reduction in Coronary Heart Disease deaths for men aged 35 - 57, which is similar to the calculated effect of eliminating diastolic hypertension (>90 mmHg). By pooling the results of nine controlled trials of treatment of hypertension, McMahon has calculated that an overall reduction of diastolic pressure

of 5.7 mmHg would result in a 38% reduction of non fatal stroke (45).

CONCLUDING REMARKS

Raised blood pressure is a risk factor for both cerebrovascular and ischaemic heart disease, independent of other risk factors, whether one considers individuals within a population or compares different populations. Nevertheless, coronary heart disease has a different epidemiology from that of stroke (46). Low rates of coronary heart disease may occur in countries with a high prevalence of stroke and hypertension (47). Hypertension, unlike coronary heart disease, is not uncommon in third world countries (48). These differences in epidemiology, however, may be explained by differences in risk factors other than hypertension (49 -51).

III TRACKING OF BLOOD PRESSURE FROM CHILDHOOD AND ITS RELATION TO BIRTH WEIGHT.

The level of blood pressure at one examination is the most powerful predictor of blood pressure at follow up (51,53). Furthermore, a relatively high initial blood pressure is associated with a relatively fast subsequent increase of blood pressure (54-56). The question arises, at what age does an irreversible trend towards hypertension begin? In 1977 a National (American) Task Force on Hypertension accepted that hypertension could be predicted from measurements of blood pressure in childhood, and even suggested that active therapy should be considered at that stage (57), although in an extensive review it was concluded that there was insufficient long term data to support such action (58).

Tracking is the term used to describe the persistence of rank order for the blood pressure of an individual relative to others in a population of similar age.

TRACKING OF BLOOD PRESSURE IN ADULT LIFE.

In 1975 data from the Framingham study showed that over 20 years' follow up of subjects, a high correlation was maintained between blood pressures of individuals from one medical examination to the next irrespective of the variability of three blood pressure readings taken at one examination (31).

A cohort of 3983 men declared fit for pilot training prior to World War II, 90% of whom

were aged 20-39, was followed up over 30 years (59). Initial blood pressures of the subjects were read from the medical records of World War survivors (and so were not taken in a standardised manner). Subsequent examinations were made at 5 yearly intervals. Analysis considered the relative position within the overall distribution on each occasion. There was a significant correlation between the single casual measurement of blood pressure at entry, and subsequent follow up levels, for all ages and all periods of follow up. The relationship was seen for both diastolic and systolic readings. The correlation between sequential measurements was observed to be greater as the cohort grew older, and to decrease as the interval between measurements increased. Those whose blood pressure was in the upper part of the distribution at early examinations tended to retain that position at later examinations.

In another cohort of pilots, which was followed up over 24 years, the initial blood pressure measurements were taken in a more standardised fashion and body weight (as well as parental longevity) was taken into account in the analysis (60). Blood pressure was not shown to increase with age in every individual, although it did so for the cohort as a whole. One sub group was identified that experienced a steady rise in blood pressure. This group was further characterised by greater increase in weight and by reduced parental longevity. Throughout the study, those men in the top quintile for blood pressure in 1940 (when the men were in their early twenties) retained their position in the range of blood pressure.

In a study of college students, conducted retrospectively over 22-31 years, both systolic and diastolic blood pressure at initial examination were associated with the incidence of

doctor-diagnosed high blood pressure (as reported by questionnaire response) at follow up (61). The risk of hypertension for those in the top quartile of blood pressure at College was over twice that of the remainder on univariate analysis. Ponderal Index (weight/height^3) at College was also associated with subsequent risk, although cross tabulation showed that early systolic blood pressure levels were predictive of later hypertension independent of obesity.

Taking yet another group of aviators, Froom et al calculated that the sensitivity of elevated blood pressure at entry medical (obtained retrospectively) as a test for raised blood pressure 12-15 years later was 32.4%, with a specificity of 86.7% and a positive predictive value of 10.8% (62). No allowance was made for change in other factors that affect blood pressure. The authors concluded that these figures were broadly in line with those estimated from other studies of adults and that this would suggest there is limited predictive value of casual blood pressure measurement in early adulthood. Szklo has pointed out the important differences between regression and correlation (53) observing that average associations, but not individual associations, are strong between initial and subsequent blood pressures.

In Wales, a follow up study was conducted over 17 years, in which the subjects were initially aged between 5 and 74 (63). Tracking correlations were found to occur for all age groups, for both systolic and diastolic readings, but to increase with initial age and to decrease with longer intervals between measurements. Most of the increase in correlation occurred before an initial age of 20, at which point analysis of variance suggested a discrete rise. Other factors (such as body mass) were not taken into account.

TRACKING OF BLOOD PRESSURE IN CHILDHOOD.

To examine the tracking phenomenon in children, a Dutch group followed up 386 individuals aged 5 - 19 over four to five years, measuring blood pressures annually (64). Tracking coefficients (age-standardized regression coefficients of rank in blood pressure distribution over time) were observed of 0.4-0.6 for systolic blood pressure, and 0.2-0.5 for diastolic. The coefficients were largest in older children. Using a different method of analysis, 60% of those children whose systolic blood pressure was in the upper third of the distribution at initial examination retained their position at four years. For diastolic blood pressure the figure was 52%. Coefficients were similar in obese and non obese children, and in children whose parents had high blood pressure compared with those whose parents did not. There was no analysis which controlled for changes in other factors (such as obesity) which are known to affect blood pressure.

The Bogalusa Heart Study examined 3524 children aged 2-14 yrs, using a particularly strict and careful study protocol (65). Careful analysis of blood pressure at one year showed a high consistency of ranking in the top decile of blood pressure. A multiple regression test for determinants of blood pressure at one year showed that initial systolic blood pressure had a partial regression coefficient of 0.61-0.66, and initial diastolic pressure a coefficient of 0.36-0.52, independent of age, race and obesity. The authors concluded that their observations contributed to the probability that primary hypertension begins early in life. The cohort of children was followed up for a period of eight years, at which time analysis was made of sensitivity and specificity of initial blood pressure levels as a screening test (66). Positive predictive values were shown that were

equivalent to those of other studies in older children, and higher than those using equivalent age groups. The authors concluded that the basal blood pressure measurements which they had measured showed a greater tendency to track with age than the casual blood pressure measurements made by other workers.

In New Zealand, a cohort of 361 Polynesian children aged 5-14 years was examined and followed up over 1.5-3.7 years (67). Using a technique which adjusted for age, a strong correlation was shown between initial and follow up systolic blood pressure. Partial regression analysis, controlling for Quetelet (Body Mass) Index, and for length of follow up showed that the predictive effect of initial blood pressure was independent of these factors.

A much larger group of 4,313 children, again aged 5-14 at the start, was followed up over ten years (68). Analysis of the rank order of blood pressure and other parameters at interval examinations during the study showed that changes in the blood pressure rank of individuals were associated with differences in the rate of growth of height and weight of that child. The study clearly identified groups of children who remained at a consistently high rank for blood pressure, or who showed a consistently increasing (or decreasing) rank order. The authors suggested that final rank order of blood pressure may not be established until growth ceases. This would accord with those studies described above that demonstrate higher tracking coefficients in mature adults than in younger individuals. That these observations made in study populations may be extrapolated to the general US population was demonstrated by results of a large national survey (69), which used a national probability sample chosen to be representative of the

US population. 2,618 children aged 6 - 11 years were followed up over 6 years. The results confirmed the relationship between successive measurements of blood pressure and the authors suggested that risk of adult hypertension could be estimated from childhood blood pressure.

Tracking of blood pressure in childhood has been shown from earlier ages. A small study of 28 children whose blood pressures were relatively elevated at 5 years showed that the elevation was still present at 11-12 years (70). A study of 1,797 infants, whose blood pressure was first measured at an age of four days, demonstrated weak (though significant) correlations for systolic blood pressure under one year, with the strength of the correlations increasing with age up to four years (71). Analysis corrected for weight of infant and state of wakefulness. The authors suggested that tracking of blood pressure starts at about 1 year. A study of 730 infants aged 5 days to 2 years, however, showed that blood pressures taken earlier than 6 months after birth were not consistently predictive of later levels, but that both systolic and diastolic pressures at 6 and 12 months were significantly correlated with blood pressure at later ages (72). The same researchers followed up an older cohort for eight years, when 484 children were finally examined (73). Simple regression and Chi squared analysis showed a highly significant correlation between blood pressure order at initial examination and eight years later. For both systolic and diastolic pressures, the tracking coefficients increased with age group.

The evidence for lifelong tracking of blood pressure depends upon a number of follow up studies covering different stages of life. Some of the adult studies depend upon retrospective determination of blood pressure taken during routine examination and none

make sufficient allowance for change in other correlates of blood pressure such as body mass and alcohol consumption. These inadequacies would however tend to diminish the ability of the studies to detect the tracking phenomenon, so that an underlying perseverance of blood pressure ranking may in fact be greater than has so far been demonstrated.

BLOOD PRESSURE AND BIRTHWEIGHT.

In 1985, data from a national birth cohort which had reached 36 years of age were analyzed (74). Birth weight was shown to be inversely associated with adult levels of systolic pressure in men and women. Stepwise multiple regression analysis showed that birth weight was significantly related to adult systolic blood pressure, independently of adult body mass, smoking habit, social class, and family history of hypertensive or ischaemic heart disease. A second national birth cohort was examined at the age of ten years (75). Systolic blood pressure was again shown to be inversely related to birth weight, independently of current weight, and this relationship persisted after adjustment for mothers' blood pressure. The observations were similar at all gestational periods, suggesting that the effect of birth weight was not a result of shortened gestation. A follow up study of 468 men with a mean age of 64 years showed that blood pressure in adult life was inversely related to birth weight (12).

A case control study of low birthweight babies showed that at 10 years of age the cases had higher systolic and diastolic blood pressures than the controls, who were matched for maternal height, social class, smoking habit of mother, sex of child, and ordinal position

of birth (76). At seven years of age, systolic pressure in 692 children in New Zealand was shown to be inversely related to birth weight (77). A study of 692 children at the same age showed a similar inverse relationship between blood pressure and birthweight (78) and this has been confirmed in other studies (79-81). A small, retrospective study of Swedish conscripts showed that the risk of increased diastolic blood pressure in early adult life was significantly higher in those whose birth weight was small for gestational age (82).

Low birthweight is associated with raised blood pressure in later life, and this effect is independent of duration of gestation. Further study is required to examine the relations of duration of gestation, different measurements of the baby at birth, and level of blood pressure in adult life.

IV PATTERNS AND INFLUENCES IN INTRA UTERINE GROWTH.

MATERNAL INFLUENCE ON BIRTH WEIGHT.

In 1965, Ounsted showed that the most significant difference between a group of growth retarded infants and controls (who were similar in respect of maternal age, parity, ill health and raised BP) was in sibling birth weights, the siblings of the growth retarded infants being significantly smaller than the siblings of the controls. A deficiency of tall mothers and social class I and II was observed in the low birth weight group, and an excess of smokers, but these differences were small compared with the 'gross and significant' differences in birth weight of live-born siblings. In a development of the study, a small group of infants delivered early was studied and no tendency to repeat short gestation was detected in the mothers. The author concluded that growth retardation was a result of some maternal factor which did not appear to be genetically determined, and that within the amorphous group of 'premature' infants were two distinct entities - truly premature and growth retarded (83). Prematurity due to early onset of labour showed no tendency to recur in an individual mother.

In the following year it was again observed that certain mothers have a 'predisposition ... to produce malnourished infants repeatedly ' although analysis did not adequately consider other factors such as habitual smoking (84). Bakketeig et al, in a study of 454,358 single births in Norway, supported the observation that intrinsic maternal factors, the nature of which remains uncertain, give rise to a marked tendency to produce infants

of similar gestational age and weight (85). Calculations showed that the relative risk of low birth weight for gestational age in a second delivery, given that the first birth was also small for gestational age, is 3.4. If a mother had either one or two previous low birth weight babies, then the relative risk of a low weight third birth was 5.8. The effect persisted after controlling for medical complications, onset of labour and length of interpregnancy interval, although not for habits such as smoking.

In a study of births used for the 1958 British Perinatal Mortality Survey, low birth weight at term showed a striking association with a history of previous low birth weight live births to that mother. Other associations also shown were with low social class, smoking, previous stillbirth or neonatal death, maternal employment, primiparity, and (negatively) maternal height and prepregnant weight. Again, analysis was univariate for each factor (86).

In separate reviews, Snow and Roberts concluded that, with the limited knowledge of intrauterine growth available, the contribution to birth size of a fetus' genes is very small in comparison with the (largely environmental) influence of the mother, and that this environmental influence is exerted only in late gestation - from about 28 weeks (87,88). Furthermore, it has been proposed that maternal influence over fetal growth is a function of the constraint imposed upon a mother when she herself was a fetus (89).

Other observations support the predominance of the in utero environmental influence over that of the fetal genotype. In 1956 follow up measurements were carried out on young adults who had previously been measured at birth and in early childhood. The

observation that measurements of length at birth showed considerably less correlation with later height than did length at one year led to the conclusion that the major determinant of newborn size is the nature of the prenatal environment, and that the inherent growth characteristics do not assert themselves until after birth (13). In a small series of middle class suburban infants, the correlation between length at birth and length at one and two years was poor, although there was good correlation between length at 1 and 2. Similarly, there was no correlation between birth length and parental size (except some correlation between baby girls and maternal height), but demonstrable correlation between height at one and two years and parental height. The authors took these results as evidence that birth length is a function of the maternal environment, with parental genetic influence manifesting itself subsequent to and not before birth (90).

In analysis of a smaller group of middle class infants, Little related infant birthweight to that of both parents, controlling for a number of potentially confounding variables which included cigarette smoking and alcohol consumption (91). In this population, genetic factors were seen to influence birth weight. The authors acknowledged that their results were consistent with a mechanism that allows genetic influences to operate at larger birthweights, but that is overridden by phenotypic maternal constraints at lower birthweights, a theory clearly expounded by the Ounsteds (92).

That the in utero environment is a growth restraining factor is further supported by the observation that from thirty weeks' gestation, twins experience a progressive deficit of weight and, to a lesser extent, length which is not apparent in their singleton equivalents

(93,94). Tanner has observed (as have others) that 'babies having genes for large size but born to small mothers move upwards through the (growth) centiles to catch up their proper growth once the maternal restraint is removed' (93,95,96), although any such catch up growth may itself be constrained by the socio-economic conditions in which the child might find itself (15,17,18).

The nature of the restraint imposed upon the fetus relates to what might be termed the reproductive efficiency of the mother, which is considered to be a result of adequate growth and development of the mother through her own formative years. The maternal influence over the growth of her child in utero appears to be one of restraint (95) such that, in ideal circumstances, circumstances in which the mother herself was properly nurtured and nourished, such restraint may not occur and genetic determinants of birthweight are allowed to express themselves (91,92). Intra uterine growth restraint appears to be due to characteristics of the mother that are not genetically but environmentally determined (87-89).

In a carefully cross tabulated analysis of age, social class, parity, and year of birth of mothers, Baird showed that the incidence of low birth weight was associated with low height and (subordinately to height) estimated level of health and physique of the mothers. Low birth weight incidence was also associated with maternal social class (independent of age and parity but not of height) and, across all social classes, showed a fluctuating pattern that could be explained by variations in the socio-economic circumstances in which the maternal generation was born and raised (97).

In a study of 'prematures' (infants of low birth weight), all such infants were enrolled from the 1946 national birth cohort, and controls were selected that were matched for sex, ordinal position of birth, locality of residence, maternal age, and social class. It was seen that the mothers of the cases were shorter and lighter than the mothers of the controls (98). A different analysis of data from the same cohort showed an association between social class and low birth weight, although it was observed that increasing maternal age tended to reduce the association, which is to be expected since maternal age itself has an influence on reproductive efficiency (99).

A more modern analysis was carried out on a series of 20,698 singleton births which occurred in Greater Dublin in 1978/1979 (100). The author examined birthweight, classified into 'low' (<2,500g), 'suboptimal' (2,55-3,000g) and 'optimal (3,000-4,499g) groups, as related to birth order and social class. It was observed that social class had a dominant effect, independent of birth order, that was calculated to explain 93% of the variation of optimal birthweight and 76% of the variation of suboptimal birthweight. There was a linear relationship between the birthweight classes and social group. Smoking habit, maternal health, and other factors were not analyzed separately but were assumed to be a part of the socio-economic influence.

The relationships between social class, maternal height, and perinatal mortality (stillbirths plus neonatal mortality) were studied by Baird in the 1940's (101). In a comparison of women attending a public hospital (social classes III-IV) and women attending a private nursing home (classes I & II), a clear association with low social class was shown for reduced height, increased perinatal mortality (after allowing for age differences at

delivery) and increased 'prematurity' rates. These effects were attributed to the poor diet, poor physique, and contracted pelves of the working class women. Subsequent work confirmed the relationship of low height to social class, and further suggested that tall women were, on the whole, healthier than small women (102). An excess of perinatal mortality in short women was observed, as was an excessive rate of Caesarian section. Analysis of the Caesarian sections showed that contracted pelvis was a cause for the operation only in small women. Later work by Baird continued to show the relationship of low birth weight with low social class, from which the author concluded that a social policy was required that would raise standards of health and physique (103).

THE NATURE OF INTRA UTERINE GROWTH RETARDATION.

The retardation of growth in utero has more than one pattern or mechanism. In 1966, charts of intrauterine growth were constructed from observations on 4,700 babies. An increase in weight:length ratio between 30-38 weeks was noted (104). Thus retardation of growth at different stages of gestation would have different effects on the neonate's physical proportions. In 1971, four patterns of abnormal intrauterine growth were described from observations on another series of newborn babies: i)infants with abnormally short body length for dates, ii) infants showing disproportionate growth between body length and head circumference, iii) infants who were malnourished according to variation of soft tissue mass (determined by Rohrer's ponderal index w/l^3), iv) infants who were overweight (105). The authors concluded that reduced skeletal growth was determined by crown to heel length and reflected in an increased ratio of head circumference to length at birth. Birth weight by itself was not a valid measure of

skeletal or soft tissue mass growth. In 1977, the distinction between symmetrically and asymmetrically retarded intrauterine growth was examined using ultrasound measurement of fetal head and abdomen circumference (106). The authors distinguished a 'low growth profile' group of prolonged, symmetrical retardation, from a group suffering a 'late flattening growth retardation pattern' which was associated with a normal serial cephalometry curve. This was reflected by Meire who observed that the rate of head growth was slowest after 32 weeks (107).

The different timing of various aspects of fetal growth was described in 1982 when it was observed that peak velocity of length growth was in the 2nd trimester, and of weight gain was in the third trimester (108). The authors described three clinical types of intra uterine growth retardation. Type 1 was described as chronic or proportionate IUGR due to malnutrition of the fetus from the first trimester, Type 2 was named subacute or disproportionate IUGR and was said to be due to adverse effects from the start of the third trimester, and Type 3 or acute IUGR was due to adverse effects in the last two or three weeks of gestation. The distinction between the three groups was made by anthropometry of the new born infant, in particular the Ponderal Index (PI) which is calculated as weight/length^3 x100. Type 1 IUGR was characterised by a normal PI but reduced weight, length and biparietal head diameter. Type 2 IUGR showed low values of Ponderal Index with moderate reduction in length and more severe reduction in weight. Type 3 was characterised by a very low ponderal index, with normal length and only slightly retarded biparietal diameter, classic examples of which are babies born to mothers with severe, acute preeclampsia.

Similar observations were made by other authors. Villar, Smeriglio and others differentiated IUGR with a low Ponderal Index (insult late in pregnancy) from IUGR affecting length and head growth (109). Kliegman and Kins described growth impairment due to placental insufficiency or malnutrition occurring at an earlier point resulting in a normal ponderal index but high head circumference to length ratio, and at a later time resulting in low ponderal index (110). Much of this had been anticipated by Gruenwald in 1963 who differentiated chronic fetal distress (which caused retardation in skeletal growth) from subacute fetal distress (which caused wasting) (111). Chronic fetal distress affected body length but not head size due to mechanisms which preserved brain growth, so that affected babies had relatively large heads for their body size. Subacute fetal distress caused no reduction in longitudinal growth so that the babies were thin for their length.

V MATERNAL HEIGHT AND PELVIC SIZE & SHAPE.

The shape of the inlet to the bony pelvis varies from flat (a transverse oval) to heart shaped (android). The pelvic shape is one aspect of maternal physique to be linked to obstetric complications, with the anthropoid (long oval) and gynaecoid (round) pelvises being obstetrically safest (112-115).

The relationship of a woman's height to the physical characteristics of her pelvis was examined in a series of 500 women attending a London antenatal clinic. X Rays were taken using lateral and pelvic inlet views. Analysis demonstrated that height was correlated with conjugate diameter (symphysis pubis to sacrum) at the brim and, to a lesser extent, with transverse diameter at the brim. A correlation between height and pelvic brim index (conjugate diameter/transverse diameter x 100) suggested a significant tendency of short women to have flat (transverse oval) as opposed to round pelvic inlets. There was no evidence that other characteristics of body type related to parameters of pelvic shape and size (112).

In 1938, a comparison of pelvic proportions was made between 600 primigravid women of lower social class, and 100 nulliparous nursing students who came from a more privileged background. The study adopted a classification system which described four types of pelvis: 1) Dolichopellic; conjugate diameter > transverse diameter (long oval), 2) Mesatipellic; transverse diameter equals conjugate or exceeds it by no more than 1cm (round), 3) Brachypellic; transverse diameter exceeds conjugate by 1.1-2.9cm, 4)

Platypellic; transverse diameter exceeds conjugate by 3cm or more (flat). Despite the common perception at the time that brachypellic and platypellic pelves were the normal type, it was seen that there were no platypellic pelves among the nursing students and a greater proportion of dolichopellic or mesatipellic types than among the primiparous women. A series of young girls aged 5-15, of similar social class to the primiparous women, also showed a higher proportion of dolichopellic pelves, although this proportion decreased with age. The authors suggested that antero posterior flattening of the pelves results from inadequate nutrition during growth (116). In subsequent analysis of the results, the authors showed a correlation between greater height and the dolichopellic or mesatipellic pelvic types (long oval or round), although other bodily dimensions showed no such association (117).

In Aberdeen pelvic anatomy was further examined by comparing 100 short women (under 5 ft) with 100 tall women (over 5ft 5ins). All were primiparous and under 30 years of age. Radiography showed a considerably greater proportion of flat pelves among the shorter women, and the incidence of one in three observed in this group was confirmed by X Rays of a further 200 women. There was a significant difference in both mean brim area and mean conjugate diameter between the two groups. Examination of the womens' background showed that a greater proportion of small than of tall women had grown up in families of lower income and larger size. A similar comparison was made of radiographic pelvic dimensions in males from differing socio-economic backgrounds and of differing heights, and a similar pattern was observed of pelvic flattening related to reduced height and impoverished background. The author concluded that pelvic

flattening is caused by a poor environment during growth (118). Maclennan observed that 'contracted pelvises existed chiefly in the industrial centres in Scotland where the standard of living was low... whereas the incidence of contracted pelvis in agricultural areas was so small as to pose no practical problem', showing that the incidence of contracted pelvis varied with the incidence of rickets (115). Maclennan concluded that the problem of contracted pelves was '...the problem of rachitic contraction' which, he argued, occurs in early childhood and has already affected bony growth by the time children reach school age.

Another series was compiled of 350 women who presented to the maternity ward of Moreton District Hospital in Gloucestershire. Radiography of the pelvic brim used a stereometric technique which minimised errors of measurement. A lack of correlation between transverse and conjugate diameters was shown, but an association between pelvic index (Conjugate diameter/transverse diameter) and pubic angle was demonstrated and attributed to a common mechanism of defective (rachitic) nutrition in childhood (119,120). An extension of the series was studied in terms of the transverse and conjugate diameters as they fluctuated from women presenting in one year to women presenting in the next. The conjugate diameter showed significant variation while the transverse diameter did not. The correlation of conjugate diameter to height and the apparent association of flattened pelves with exposure at a sensitive age to the malnutrition of World War I, were taken as evidence for the dependence of pelvic shape on adequate nutrition in early life (121).

In 1981 radiological pelvimetry was carried out on 242 males and 314 females at the

Royal Victoria Hospital in Belfast. Height was found to be positively correlated with year of birth, with conjugate and transverse diameters, and with brim index (among women only; among men $r=0.12$ $p=.059$). By cross tabulation, the brim index was seen to increase with year of birth for standardized height, while the conjugate diameter was more clearly associated with height for standardized year of birth. The authors concluded that changes in pelvic size and shape were observed which were most probably explained by environmental factors such as nutrition. They went on to suggest that geographical differences in pelvic size may explain the differences in perinatal mortality through obstetric complications that occur from one area of the country to another (122).

Earlier this century the common perception was that a flattened pelvis was the norm amongst Caucasian women - even that there was a biological advantage in such a shape; 'With the evolution of the races one finds a tendency in the development of the pelvis from the long oval through the round to the transverse oval. Among European women generally the pelvis is transverse oval in shape.' (123).

In a paper mixed of anecdote, review, and observation of highly selected samples, Vaughan concluded that a round (or dolichopellic) pelvis is common among women who live in open air surroundings and have adequate nutrition, but that the flattened pelvis is more commonly seen among women who live in conditions of confinement or poverty. Flattening of the pelvis, the author says, is caused by rickets and disuse of the sacroiliac joints before 14 years of age (124).

In a more scientifically argued paper, Thoms considered the possibility of mild rickets as a cause of pelvic flattening by studying the relative lengths of the sacral, iliac, and pubic parts of the pelvis in the plane of the ileo-pectineal line, using radiographs of fifty females. The author showed that the iliac portion was shortened in flattened pelves, a sign that he accepted as strongly indicative that mild rachitis during childhood caused flattening of the pelvis (125).

Thoms observed that the pelvis is normally dolichopellic throughout childhood for both sexes (126). In general, the growth of the pelvis is thought to keep pace with growth of the lower limbs, with the characteristic sexual differences in shape becoming manifest at puberty, when females have rapid growth of their pelvises while males have rapid growth of their shoulders (127). The size and shape of the pelvis is affected by nourishment throughout childhood (128). The shape of the pelvis continues to be affected by nutrition during adolescence when there are differential rates of transverse and conjugate growth, especially in girls (120,126-128).

Because of the different effects of nutritional standards on pelvic size and shape during different stages of growth, it was thought that an examination of pelvic size and shape in relation to cardiovascular mortality may give some insight into the period during which undernutrition has the greatest effect on later risk of cardiovascular disease.

VI CONCLUSIONS FROM THE ABOVE REVIEW.

Blood pressure is an important risk factor for cardiovascular disease. Many factors influence the level of blood pressure, including obesity and alcohol consumption (37,129-131). These factors, which come to operate increasingly in later life, would tend to distort the patterns established earlier on, and so it is not surprising that studies of the tracking phenomenon should demonstrate a decreasing correlation with length of interval between measurements. Rather it is remarkable that tracking is observed at all by analyses which do not fully control for other, independent variables.

The influence on blood pressure of factors operating in early life is an important one. Those factors may be responsible for the different patterns of blood pressure with age seen in certain subgroups of the population (60,68). Conditions of early life may have affected the blood pressure levels of generations on a wide scale. The impact of a small change in risk affecting the whole population is considerable, and may be much greater than the impact of a large change affecting a small proportion of the population (36,44).

The association of raised blood pressure with low birth weight has been demonstrated, but this association requires further examination in order to identify which subgroups of low birth weight are particularly affected. The relationship of low birth weight in general to raised blood pressure will be weaker than the relationship that will be observed between raised blood pressure and the relevant subgroups of low birth weight.

Low birth weight is associated with poor maternal condition. Maternal factors are seen to influence the incidence of intra uterine growth retardation, but not of preterm delivery (83). Differences in low birth weight incidence are determined by variation in the intrauterine growth retardation rate rather than by the incidence of preterm delivery (132). Since blood pressure varies with incidence of low birth weight, and since low birth weight incidence variations are caused by changes in the rate of intrauterine growth retardation, it is inferred that raised blood pressure is associated with restrained intrauterine growth - and so with poor maternal condition.

This inference is supported by the close epidemiological relationship of cardiovascular disease to maternal mortality of the previous generation (7) and to the socioeconomic conditions of the family of origin (8).

Pelvic size and shape are determined by nutritional factors during growth periods in early life (120,126-128). Populations suffering high levels of cardiovascular disease appear to be characterised by poor standards of nutrition in early life (4,8,10,11).

Two studies are reported:

1) A survey of pelvic size and shape among men and women aged 50 years or more, currently living in 6 towns across England. This study tests the relation between nutrition in early life (as indicated by pelvic growth) and later experience of cardiovascular disease.

2) A follow up study from birth records of men and women currently aged 46 - 54 to test the relation between current levels of blood pressure and intra uterine growth.

METHODS.

1. PELVIMETRY SURVEY.

Eleven towns with a range of mortality rates from cerebrovascular and ischaemic heart disease were selected across England. The Radiological department of the central hospital in each of these towns was approached and invited to take part in the study. Nine towns agreed to do so and ethical permission was obtained in each place.

Patients aged 50 and above presenting for non-urgent lumbo-sacral spine X-ray, Intra venous pyelography, or other abdominal radiographs were invited to consent to a further single antero posterior X-ray of the pelvis. The method of invitation varied from town to town according to local ethical stipulations. In most towns, an oral explanation and consent were accepted. The date of birth, name, sex, and town of birth was recorded for each patient. In order to adjust for the effect of magnification, the distances from table top to symphysis pubis and from table top to film were recorded. The distance from source to film was standardised at 100cm.

A standard sitting AP pelvic inlet X-ray was taken, with the patient reclining to an angle which brought the posterior superior iliac spines level with the symphysis pubis. This allowed accurate measurement of both sagittal and coronal inlet diameters, in addition to the interspinous distance. From these diameters, the brim index (conjugate diameter/widest transverse diameter), sagittal index (posterior sagittal diameter/conjugate

diameter) and posterior sagittal transverse index (posterior sagittal diameter/widest transverse diameter) could be calculated (figure 1).

On receipt the films were made anonymous and allocated a random number. The films were read blind by two radiologists and measurements were taken of the true conjugate, widest transverse, posterior sagittal and interspinous diameters from those films on which the pelvic inlet rim could be clearly identified. A magnification factor was derived from film to source and symphysis pubis to source distances and this was used to adjust for the effect of magnification. A test for inter observer differences showed no significant variation.

Mortality and census data were obtained for the towns for the years 1980-1988, the latest period for which they were available. Standardised mortality ratios for cerebrovascular and ischaemic heart disease (ICD codes 430-438, 410-414) were calculated using national rates for England and Wales as the standard.

2.PRESTON COHORT STUDY.

An historian was employed to search out hospitals in which detailed obstetric records had been preserved. At Sharoe Green Hospital in Preston, which is an industrial city in Northern England, labour and post natal records had been preserved of all deliveries that occurred during 1935-1943. Records had been made by completing standard forms so that, except for incompleteness, the same information was available for every case. The data included personal details and residential address, date of admission, birth and discharge, date of last menstrual period, obstetric history, placental weight and nature, mother's pulse and pelvic measurements, neonate's weight, length and head measurements, daily weight of child until discharge, and method of feeding.

The data was extracted from the records and a sample taken on the basis of completeness: a minimum data set was specified (table 1) and only those records which satisfied the specification were selected.

Of those measurements which had been made of the mothers' pelves, the interspinal, intercristal, and external conjugate and true conjugate (estimated) diameters were used. The prescribed methods by which these diameters should have been measured were:

"Interspinal; This measurement is taken by placing one point of the pelvimeter on the outside of one anterior superior iliac spine, and the other point on the outside of the opposite anterior superior iliac spine.

Intercristal; ... is taken by placing one point of the pelvimeter on the outer margin of

one crest of the ilium, and the other point on the outer margin of the opposite crest of the ilium.

Ext Conjugate; ... one point of (the pelvimeter) is placed on the spine of the last lumbar vertebra, and the other on the front of the pubes. The measurement is taken either when the patient is sitting or is in the left lateral position."

(These definitions taken from Berkely C. Pictorial midwifery. 4th ed. Bailliere Tindall Cox. London 1941).

Weights were measured in pounds and pelvic diameters, infant lengths and head circumferences in inches. Measurements had often been rounded and the original units were thus preserved.

In all, 1298 cases were notified to the National Health Service Central Register at Southport, ethical approval for the project having been obtained. The mothers' names and addresses and the sex and dates of birth of the babies were sufficient to allow identification of the infant from 1939 census data. For those born subsequently Christian names were obtained from birth registration certificates. From NHSCR records, it was then ascertained whether or not the individual was currently registered with the Lancashire Family Practitioner Committee.

Lists of those currently registered with the Lancashire FPC were submitted to the FPC office which identified the address and General Practitioner of each case. Letters were sent to the GP's of each individual, asking that addresses be checked against practice

records, and seeking the GP's agreement that their patients be included in the study. Individuals were then invited by letter to participate in the project.

Of 1298 notified to the NHSCR, 1122 (86%) were traced. 503 were found to be living in Lancashire at addresses known to the FPC or General Practitioner and were asked to take part in the study. 449 (89%) agreed to do so. An initial study sample of 259 adults was examined. A second sample of 190 subjects was taken to test observations made on the first. The two samples were similar (table 2) and so were treated as one study population for further analysis.

Each subject was visited in their home by one of four field workers. The field workers had not seen the obstetric data recorded for the subjects. After initial introductions, measurements were taken of height (using a standardised portable stadiometer), weight (using standard Seca spring scales), abdominal girth (at the umbilicus) and hip girth (at the Trochanteric prominence). The first blood pressure and pulse readings were then taken using an automated Dinamap machine. A second reading of pulse and blood pressure was taken after administration of the questionnaire during which the subject remained seated. All readings were taken on the left arm using a cuff which covered at least two thirds of the upper arm. The mean of the two readings was used in the analysis. Room temperatures were measured.

A questionnaire was used to explore past medical history, parental history of ischaemic heart disease, cerebrovascular disease or raised blood pressure, Obstetric history, current medication, and smoking habit. Alcohol consumption was derived from the frequency

with which people were accustomed to drink, and the amount they would drink on a typical occasion. Consumption was converted to the total number of grams consumed per week and categorised as low (up to 168 g), moderate (up to 280 g) and high. The corresponding figures for women were 112 g and 168 g. Father's occupation was used to define social class of the subject at birth (OPCS 1980). Current social class was derived from the subject's occupation or, in the case of housewives, that of the husband.

The fieldworkers were trained to record measurements and to apply the questionnaire in a standard fashion. The techniques of the field workers were compared at intervals throughout the survey on small groups of individuals who were not a part of the main study, and the results showed no significant inter observer variation.

RESULTS

I PELVIMETRY SURVEY.

Nine towns submitted 1652 X-Rays. The twenty six x-rays from one town (Bath) could not be used due to missing information necessary to calculate a magnification factor. Eight x-rays were unusable due to distortions of the pelvis by disease, three because subjects were under 50, which left 1615 x-rays from eight towns available for analysis.

The mean age of the men was 66 yrs and of the women 67 yrs. Women had pelvises that were larger in all dimensions than those of the men (table 3). There was no regular progression of pelvic size or shape across all age groups. There was, however, a significant difference between those aged 75 years or more and those younger than 75, the effect being apparent in each sex. In females, the conjugate diameter and brim index were significantly larger in those aged less than 75 years than in those aged 75 years or more (table 4). The mean transverse diameter was larger in the older age group, but not significantly so. In men, the conjugate diameter was larger in those aged less than 75, but this was not statistically significant. The brim index was larger in the younger group by a degree that was marginally significant ($p=.056$). The mean transverse diameter was larger in men aged 75 or more, but this failed to reach significance ($p=.086$). The remaining measures of pelvic size and shape were all larger in the younger age group in both sexes. Because the differences between the two age groups were similar for males and females (although to a different degree), the two sexes were combined for further analysis, with an allowance made for the effect of sex. In the combined group, it was

seen that those aged 75 or more had smaller conjugate and posterior sagittal diameters, but a larger mean widest transverse diameter, so that the brim index was 2.8 less in the older age group than in the younger (95%CL 1.79 - 3.81) (table 5). Further analysis used pelvic measurements adjusted for the effects of both age and sex.

The mean values for conjugate diameter, widest transverse diameter, and brim index are shown by town and SMR in table 6.

Mean pelvic size in all planes decreased as SMR for cardiovascular disease increased. Correlation coefficients of rank were calculated. For the whole study population, negative correlations were observed between SMR and conjugate diameter ($p < .02$) and between SMR and posterior sagittal diameter ($p < .01$). Correlations for SMR and diameters in the coronal plane (widest transverse and interspinous) were not significant at the 5% level (table 7).

Pelvic shape also varied with SMR, the three pelvic indices showing negative correlations that did not, however, reach statistical significance (tabe 7).

Separate analysis for the two sexes showed the correlations of SMR with pelvic size and shape to be stronger in women than in men (table 7).

II PRESTON COHORT STUDY.

1. DESCRIPTION OF STUDY POPULATION

The study population of 449 subjects comprised 236 men and 213 women, aged between 46 and 54 years at interview, with a mean age of 50 years. The mean birthweight of the cohort was 6.98 lbs, the mean placental weight 20.81 ozs, and the mean systolic blood pressure 150 mmHg. Placental weight and birthweight were strongly correlated (r=0.52). The total study population was collected as two samples, as described in the method. The mean systolic pressure of the men was 154 mm Hg (SD = 20) and of the women 146 mmHg (SD=23). Systolic pressure rose by 1.3 mmHg per year of age and diastolic rose by 1.0 mmHg. For further analysis, all pressures were adjusted to age 50 yrs.

2.EFFECT OF ADULT PARAMETERS ON BLOOD PRESSURE

In the combined group of men and women, mean systolic pressure rose with increasing body mass index (kg/m^2) (table 8) from 145 mmHg in those in the lowest quartile (24 kg/m2 or less) to 156 mmHg in those in the highest quartile (>28 kg/m2) (p=0.0001). The effect was the same in both sexes.

78 individuals fell into the category of moderate or high alcohol intake, and their mean systolic pressure was 4 mmHg higher (95%CL -1 - 10) than that of the rest. For men, the difference was 5.1 mmHg (95%CL -0.3 - 10.5) (table 8).

Blood pressure was not consistently related to smoking nor to room temperature.

For analysis of blood pressure associations with birth parameters, mean systolic and diastolic pressure were adjusted for body mass index and alcohol intake.

3.BIRTH PARAMETERS AND BLOOD PRESSURE IN ADULT LIFE

Placental and birth weights

Systolic and diastolic blood pressure were related to placental weight and birthweight. Systolic pressure fell with increasing birth weight, from 154mmHg in babies weighing up to 5.5 lbs, to 149 in babies weighing over 7.5 lbs. Systolic pressure rose, however, with increasing placental weight, from 147 mmHg in those with a placenta 16 ozs or less to 157 mmHg in those with a placenta over 24 ozs (table 10). The associations of blood pressure with birthweight and placental weight were independent of the other. At each birthweight systolic pressure was seen to rise across the range of rising placental weight. At each placental weight systolic pressure was seen to fall consistently with increasing birthweight. Multiple regression analysis showed a fall of 11 mmHg (95%CL 3 - 19) from birthweights of 5.5 lb or less to birthweights above 7.5 lbs. The same analysis showed a rise of 15 mmHg (95%CL 8 - 23) in individuals who had had placental weights

of one pound or less to those who had had weights above 1.5 lb. At each category of birthweight, systolic pressure was considerably higher in those whose placenta had weighed more than 1.5 lb (table 10). For the two sexes combined, the difference in blood pressure between those whose placentas weighed 1.5 lbs or less, and those whose placentas weighed more than 1.5 lbs was 9 mmHg (95%CL 4 - 14).

The variation of blood pressure with birth and placental weights was similar for diastolic pressure and for men and women when analysed separately (tables 11,12). Multiple regression analysis for diastolic pressure showed a fall of 2 mmHg (95%CL -2 - 7) from subjects who had had birthweights of 5.5 lb or less to those who had weighed more than 7.5 lb, and a rise of 6 mmHg (95%CL 2 - 10) from subjects who had had placental weights of 1 lb or less to those who had had placental weights greater than 1.5 lb.

The combined effect of birth and placental weights on blood pressure was such that the highest blood pressures were to be found in those adults who had been small babies with large placenta, and the lowest in those who had been large babies with small placenta.

The effect of a discordance between placental weight and birth weight was further examined by considering the placental weight as a proportion of the total weight of the feto placental unit. There was a progressive increase of average systolic blood pressure with the size of this proportion independently of sex, such that those with a proportion above the 80th centile (0.181) had an average systolic of 154.9 mmHg compared with

those for whom the proportion fell below the 20th centile of 147.2 mmHg, a difference of 7 mmHg (95%CL 1.4-14).

36 of the subjects (21 men and 15 women) were being treated for hypertension. The relative risk of falling into this group increased to 3.0 across rising placental weight ($p<.001$). There was no trend of risk with birthweight. 124 subjects (75 men and 49 women) had a systolic pressure greater than 160 mmHg. The relative risk of falling into this group showed a similar trend with placental weight up to 2.5 ($p<0.01$) (table 13). The relative risk of hypertension declined with increasing birthweight (to 0.7 in those weighing over 7.5 lb) but this was not significant at the 5% level.

The simultaneous trends in systolic pressure with placental weight, birth weight, body mass index, intake of alcohol and sex were calculated by multiple regression. Table 14 shows that the size of the trends in systolic pressure with placental and birth weight are only slightly changed by adjustment for the three other variables.

Duration of gestation.

Duration of gestation could be estimated for 370 subjects for whose mothers the date of onset of the last menstrual period had been recorded. Placental and birth weight increased with gestation such that those born after a gestation of less than 38 weeks had a mean birthweight of 95.4 ozs and mean placental weight of 19.9 ozs compared with 113.6 ozs and 21.6 ozs respectively for gestation of more than 38 weeks. Length of gestation showed no relationship to blood pressure. Including gestation as an independent

variable in multiple regression analysis had little effect on the trends in systolic pressure with birthweight and placental weight (table 15). Findings for diastolic pressure were similar.

Parity.

Parity had been recorded for all but nine mothers. The relationships of systolic and diastolic pressure to birthweight were similar in children of primiparous and multiparous women. The difference in systolic pressures associated with placental weight greater than 1.5 lb compared with placental weights 1.5 lb or less was, however, greater in children of multiparous women (table 16).

5.SOCIAL CLASS AND BLOOD PRESSURE

The social class of 310 of the mothers could be classified from the father's occupation. The blood pressure of subjects in social classes I II and III(N-M) was 1.8 mmHg (95%CL -2.6 - 6.3) lower than the rest when social class was defined at birth, and 4.8 mmHg (95%CL 0.9 - 8.7) lower when defined currently. The relationship of systolic pressure to decreasing birthweight on the one hand, and rising placental weight on the other was similar for each social class, whether defined currently or at birth.

When social class was defined currently, those in classes I II and III(N_M) had a birth weight 3.8 ozs heavier than the remainder (95%CL 0.4 - 7.2). The distribution of

placental weight varied with social class. Fewer subjects in social classes I and II had placental weights at extreme values, either low or high. Of 254 individuals whose mothers were in social classes III IV and V, 62 (24%) had placentas weighing more than 1.5 lb, compared with only 4 (7%) of 56 individuals whose mothers were in social classes I or II. The relative risk of a baby having a placenta weighing more than 1.5 lbs was 4.2 (95%CL 1.5 - 12.1) in social classes III - V compared with 1.0 in social classes I and II.

6.FAMILY HISTORY

A history of high blood pressure in the mother was given by 94 subjects whose mean systolic pressure was 8 mmHg higher than that of the remainder (95%CL 3-13). The mean placental weight for this group was the same as that of the rest at 1.3 lb. A history of high blood pressure in the father was given by 58 subjects, whose mean blood pressure was 1 mmHg lower than that of the remainder (95%CL -7 - 5).

7.BABIES' BODY MEASUREMENTS AND PLACENTAL WEIGHTS

Further analysis was carried out to examine the separate relations of weight, length, and head circumference of the babies at birth. Because the proportionate relations of head circumference, length, and birthweight vary with length of gestation, this analysis was restricted to 327 men and women known to have been born after 38 weeks completed gestation, according to reported date of last menstrual period. The mean birthweight of this group was 7.1 lb, mean placental weight 1.3 lb, mean length 20.5 ins, and mean

head circumference 13.7 ins. Birthweight, length, and head circumference were strongly positively associated with placental weight. The subjects were accordingly divided into approximately equal groups of placental weight, one group with placentas 1.25 lbs or less, the other with placental weight greater than 1.25 lbs.

EFFECT ON BLOOD PRESSURE OF LENGTH AND HEAD CIRCUMFERENCE.

At placental wight of 1.25 lbs or less, systolic pressure fell with increasing head circumference, from 149 mmHg at Head circumference of 13.25 ins or less to 144 at head circumference of more than 14 ins, although the trend did not reach statistical significance ($p=0.2$). At placental weight greater than 1.25 lbs, there was no relationship of blood pressure to head circumference.

There were, however, significant trends of blood pressure with length at birth in both placental weight groups (table 17). At placental weights of 1.25 lbs or less, systolic blood pressure rose as length increased ($p=.06$). At placental weights above 1.25 lbs, systolic pressure fell as length increased ($p=.06$).

EFFECTS ON BLOOD PRESSURE OF RATIO OF WEIGHT/LENGTH^3 (PONDERAL INDEX).

The ponderal index was used to examine the trends of systolic pressure with length in relation to birthweight.

Placental weight 1.25 lbs or less.

At placental weights of 1.25 lbs or less, systolic pressure fell as ponderal index rose, from 154 mmHg at an index of 12 or less to 141 mmHg at an index greater than 14.75 ($p=.0001$) (table 18). This reflects the combined effect of systolic blood pressure falling with increasing birth weight and with decreasing birth length. Simultaneous regression analysis showed an inverse association of systolic pressure with birth weight ($p=.0006$) and a direct association with birth length ($p=.0006$).

Defining hypertension as a systolic pressure above 160 mmHg, the relative risk of hypertension at placental weights 1.25 lbs or less fell from 2.1 (95%CL 0.6 - 7.1) at a ponderal index of 12 or less, to 1.0 at a ponderal index greater than 14.75.

Placental weight over 1.25 lbs.

At placental weights greater than 1.25 lbs, just as the trend of blood pressure with birth length in this group was in the opposite direction to that for lower placental weight, systolic blood pressure increased with ponderal index as opposed to the decrease seen at lower placental weights, although the trend did not reach statistical significance ($p=.11$).

EFFECTS ON BLOOD PRESSURE OF RATIO OF HEAD CIRCUMFERENCE TO LENGTH.

Placental weight 1.25 lbs or less.

At placental weights up to 1.25 lbs there was no statistically significant relationship between systolic pressure and the ratio of head circumference to length.

Placental weight over 1.25 lbs.

At placental weights greater than 1.25 lbs, there was a significant association of adult systolic pressure with ratio of head circumference to length at birth ($p<.02$), with systolic pressure rising from 145 mmHg at head circumference/length (hc/l) less than 0.65, to 153 mmHg at hc/l 0.7 or more (table 19).

Defining hypertension as systolic blood pressure of 160 mmHg, the relative risk of hypertension among people born with placental weight over 1.25 lbs rose from 1 at a ratio of head circumference to length of less than 0.65 to 2.3 (95%CL 0.8-6.4) at a ratio of 0.7 or more.

FURTHER ANALYSIS OF EFFECTS OF LOW PONDERAL INDEX AND HIGH HEAD CIRCUMFERENCE/LENGTH RATIO.

The relationship of measurements at birth to adult blood pressure therefore differed with placental weight. At placental weights of 1.25 lb or less a low ponderal index predicted high adult blood pressure. At placental weights above 1.25 lbs, a high ratio of head circumference to length predicted high blood pressure. These relations were similarly strong in men and women, and in first born and later born children. They were also independent of placental weight within each placental weight group. The trends in

diastolic pressure were similar to those of systolic pressure but smaller.

Birth length, head circumference, birth weight, and placental weight are all closely related. In order further to explore the implications of low ponderal index and high hc/l, an analysis considered the study population in the two groups of placental weight by all four birth parameters.

Babies of low ponderal index at placental weight 1.25 lbs or less.

In order to characterise those babies with low ponderal index at low placental weight, the subjects in this group were divided into four approximately equal groups according to ponderal index (table 20). Simple regression analysis showed that the trends with ponderal index demonstrated in the table were significant for each measurement except placental weight. Babies in the lowest group for ponderal index (value 12 or less) had a mean adjusted systolic pressure 10mmHg higher than the remainder of the group (95%CL 4-16), a mean birth length 0.78 ins above the remainder (95%CL 0.51-1.05), a mean head circumference 0.2 ins less that the rest (95%CL 0-0.4) and a mean birth weight 11 ozs less (95%CL 6.7-15). In other words, the babies in the lowest ponderal index group had the highest blood pressure and were of slightly above average length with smaller heads but considerably reduced weight. There was no trend in placental weight across divisions of ponderal index.

Effects of high head circumference/length at placental weight over 1.25 lbs.

At placental weights over 1.25 lbs, systolic blood pressure increased with ratio of head circumference to birth length. In order to characterise those babies with high hc/l, the subjects were divided into four approximately equal groups according to ratio of head circumference to length (table 21). Those individuals whose ration of head circumference to length at birth was above 0.7 had a higher mean birthweight than the remainder of the group at 7.3 lbs, a higher mean head circumference of 14.5 compared with 13.8 (difference of 0.7, 95%CL .53-.87), and a birth length of 20.1 compared with 20.9 (difference of .8, 95%CL .53-1.1). Babies with the highest hc/l ratio in this group had the highest mean systolic pressure, were shorter and heavier with larger heads but had a similar placental weight to the remainder of the group.

8.INFLUENCES ON SIZE AND SHAPE OF BABIES

In order to gain some insight into factors affecting the size and shape of the babies, further analysis was carried out on the overall study population (n=447).

Placental Weight

Head circumference and crown heel length at birth both increased with birthweight. At any birthweight, head circumference tended to increase with placental weight, while length decreased. Thus, the ratio of head circumference to length at birth was related to placental weight, such that at constant birth weight a half pound increase in placental weight was associated with an increase in head circumference/length of 0.23 standard

deviations ($p < .01$).

External conjugate diameter of the mother's pelvis.

Birthweight increased progressively with the external conjugate diameter of the mother's pelvis such that an increase in conjugate externa of 1" was associated with an increase in birthweight of 9 ozs. Children born to mothers with conjugates of 7.25 inches or less had a mean birthweight of 6.6 lb, whereas those born to mothers with a conjugate of 8.25 inches or more weighed 7.5 lb, a difference of 0.9 lb ($p < .0001$) (table 22).

Head circumference also increased progressively with the conjugate external diameter ($p < .001$) such that an increase in conjugate externa of 1" was associated with an increase in head circumference of 0.25". Children born to mothers with a conjugate of 8.25" or more had a mean head circumference of 13.76, compared with a mean head circumference of 13.36 for those born to mothers with conjugate externas of 7.25 or less, a difference of 0.5" ($p < .001$).

Length at birth increased with conjugate externa ($p = .001$) such that an increase in conjugate externa of 1" was associated with an increase in length of 0.35". Children born to mothers with a conjugate of 8.25" or more had a mean length of 20.6" compared with a mean of 20.3" for those born to mothers with conjugate externa of less than 8.25" ($p < .05$).

Although placental weight increased with conjugate externa on simple regression analysis,

multiple regression showed no relationship independent of birthweight.

Regression analysis showed that ponderal index increased with conjugate externa ($p < .05$) with individuals born to mothers with a conjugate externa of 7.25" or less having a mean ponderal index of 12.9, whereas those born to mothers with a conjugate externa greater than 8" had a mean ponderal index of 13.7 ($p < .007$). Head circumference/length showed no relationship to pelvic size.

9. EFFECTS OF BIRTH PARAMETERS ON ADULT SHAPE

Adult height.

Adult height (allowing for the difference between the two sexes) increased with length at birth and birth weight independently ($p < .05$, $p < .0001$ respectively) such that an increase in birth length of 1 inch gave rise to an increase in adult height of 0.74 ins (95%CL .05 - 1.43), and an increase in birth weight of 8 ozs led to a rise in adult height of 0.73 ins (95%CL 0.33 - 1.14). Adult height was related neither to placental weight nor to head circumference independently of other birth parameters.

A strong relationship was observed between maternal conjugate externa and adult height of offspring ($p < .0001$) so that mean height for males and females of mothers with conjugates greater than 8 ins was 173 cm and 162 cm respectively, compared with heights from mothers with conjugates 7.25 ins or less of 170 cm and 156 cm

respectively. Simultaneous regression analysis showed that the relation of adult height to maternal conjugate diameter was independent of its relation to birth weight.

Adult body mass index.

Body Mass Index in adult life showed a relationship of borderline significance to placental weight, with a mean BMI of 26.2 in individuals with placental weights up to 1.25 lb, and a mean BMI of 27 for individuals with placental weights greater than 1.25 lb (difference 0.8, 95%CL -0.06 - 1.58). This effect was more pronounced for subjects who weighed 7.5 lb or less at birth. For this group, mean body mass index was 26.1 when placental weight was 1.25 lb or less compared with a mean of 27.1 for placenta heavier than 1.25 lb (a difference of 1, 95%CL .04 - 2.02). No significant relationship was observed for body mass index with ponderal index or head circumference over length.

COMPARISON OF ADULT AND BABY SIZES.

When comparing the ranked heights of subjects in adulthood with ranked length at birth, it was observed that the highest blood pressure (155 mmHg) was to be found in those who had been less than 20 ins at birth but were relatively tall as adults, and those who had been more than 20 ins at birth but were relatively short as adults (table 23). The mean systolic pressure for people falling into these categories was 153.5 mmHg compared with 147.8 mmHg for other people, a difference of 5.7 mmHg (95%CL 1.61 -

9.73). A similar difference was noted for Body Mass Index, those 20 ins or less at birth but in the tallest group as adults and those over 20 ins at birth but not in the tallest group as adults having a BMI of 27.2, compared with 26.2 for the remainder, a difference of 1 (95%CL .13 - 1.79).

DISCUSSION

I PELVIMETRY SURVEY.

The pelvis was larger at the brim in all dimensions in those towns with the lowest rates of cardiovascular mortality. Since pelvic size is correlated with adult height (112,116,118,121) this observation is consistent with the relation of adult height to cardiovascular mortality reported by Barker et al (26,75). The diameter in the sagittal plane showed the greatest difference so that the pelvis appeared to be less flat in shape for the populations of those towns, although this correlation was not statistically significant.

The method of selection of patients for the study was not consistent across all towns, although all were working to the same protocol. The practicalities of busy departments precluded the use of consecutive patients. Selection within each town was made by a number of radiographers, all of whom were unaware of their town's position in the study. It seems unlikely that a systematic sampling bias could have produced the results. For similar reasons, it is unlikely that any bias was introduced by different habits of referral for X-ray examination in the different towns.

Because the study is not confined to people who have always lived in the town in which they were X-rayed, the subjects cannot be taken as a sample of the adults who were brought up and continued to live in the towns. The standardised adult mortality ratios

were based on data from the years 1980-1988. The mean age of the study population in 1989/90 was 67 yrs. Thus the study sample does represent the population which gave rise to the recorded cardiovascular mortality rates for the towns, so that the association of those mortality rates with growth during childhood as reflected by pelvic size is not an artefact of migration.

Women aged 75 or more were found to have smaller pelvic diameters in the sagittal plane, and men in this age group to have larger transverse diameters, compared with those under 75. Both these relations were significant in analysis of the combined group when adjustments had been made for sex. In each sex, the pelvises were flatter among those aged 75 or more than among the younger age group. These observations are similar to those of Holland et al who reported a negative correlation of transverse diameter with year of birth (in women) and a positive correlation of conjugate diameter with year of birth (in both sexes) for people born between 1909 and 1950 (122).

A number of studies have demonstrated that pelvic growth was impaired in shorter women who suffered poor socioeconomic environments in childhood (116,118). Both the size and shape of the pelvis is affected by nourishment during childhood (121,128). The shape continues to be affected by nutrition during adolescence (especially in girls, for whom this is a period of maximum growth) (120,126-128). Rickets has been associated with flattening of the pelvis in both individuals and populations (115,117,120,133). It is important to note that the prevalence of dietary deficiency earlier this century was such that in the late 1920's, a survey found that 88% of 5 year old children in London had signs of rickets (134).

The relation of pelvic size to standardised mortality ratios is evidence of a link between nutrition in early life and later risk of cardiovascular disease. Pelvic size was more closely related to SMR's for cardiovascular disease than was pelvic shape, which suggests that growth during early childhood is of greater relevance to cardiovascular disease than growth during adolescence. It may also indicate that the period of growth that is most important to blood pressure related disease is that which occurs in babyhood, before weight bearing, since the effects of nutritional deficiency on pelvic shape are said to occur once weight bearing begins (115,120,121,125).

The predominant influence on intrauterine growth is the in utero environment provided by the mother (87,88). Genetic factors do not make a major contribution to birthweight (87-90,131). Low birthweight has been shown in the results from the preston cohort study described in this thesis to be associated with high blood pressure in later life, an association which has previously been reported (75). Low birth weight has been specifically related to low social class, small stature and poor physical health of the mother (103,97,98). Pelvic size and shape, indicating a poor maternal environment which limits intra uterine growth and thus the health of the fetus, may be an important predictor of the blood pressure and risk of blood pressure related disease in the succeeding generation.

2. PRESTON COHORT

The results of this follow up study show that the blood pressure and risk of hypertension in men and women aged 48-52 are strongly predicted by placental weight and birthweight. Whilst placental weight and birthweight are themselves closely related, the effects of each on blood pressure are independent and opposite; a fall of 11 mmHg occurred with increasing birthweight and a rise of 15 mmHg occurred with increasing placental weight. These relations were not dependent on length of gestation. Raised blood pressure was also associated with increased body mass index and alcohol consumption, in agreement with other studies (37,137-139). The relations of placental and birth weight to blood pressure were independent of and stronger than these effects (table 14).

BODY MASS INDEX AND ALCOHOL CONSUMPTION.

Factors operating in adult life were linked with increased blood pressure. For both sexes combined, mean systolic pressure was 10 mmHg (95%CL 4-15) higher in those with a body mass index over 28 kg/m2 than in those with a BMI of less than 24 kg/m2, an effect independent of alcohol consumption, birthweight and placental weight. This is consistent with other studies. The Caerphilly study of middle aged men showed a difference of 11 mmHg between those with a BMI of less than 24 kg/m2 and those with a BMI of >27 kg/m2 (129), and a similar difference was shown for middle aged men in England (37). That this relationship is partly one of cause and effect has been

demonstrated both by long term follow up studies which have linked a change in weight to a change in blood pressure (54,60), and by therapeutic trials which have demonstrated the beneficial effects of reducing weight in patients with mild or moderate hypertension (137-139).

In this study, 78 individuals reported a rate of alcohol consumption that was moderate or high. Their mean systolic pressure was 5 mmHg higher than that of the others (95%CI -2 - 12). The effect of alcohol on blood pressure has been demonstrated previously. In the British Regional Heart Study, men in the highest consumption group (consuming more than 6 drinks daily) had a mean systolic pressure 6-7mmHg higher than in the lowest consumption groups (37). In 1977 the results of a study based on the Kaiser-Permanente Medical Care Programme showed a mean difference of 10.86 mmHg for white men between non drinkers and those taking 6 or more drinks per day, and a difference of 5.39 mmHg between similar groups of white women (131). Again, the relationship was shown to be one of cause and effect by studies which followed the course of blood pressure during periods of altered drinking habit (138,140).

SOCIAL CLASS.

The mean blood pressure of those in social classes I-IIInon manual when defined currently was lower than that of the remainder. The different experience of the social classes with respect to ischaemic heart and cerebrovascular disease has previously been examined and trends demonstrated that are consistent with those observed in this study. In the United States a follow up study of 239 000 Bell company employees showed that

the incidence of coronary heart disease was 30% lower for those from a 'white collar' background than it was for those from 'blue collar' backgrounds (141). The author, expecting to see an adverse effect of promotion from blue to white collar circumstances because of altered lifestyle, found no such adverse effect. A sub sample of the workers showed that those from white collar origins were taller, slimmer, and more likely to have low blood pressure that their counterparts. The author concluded that '...the origins of coronary heart disease and efforts to prevent it must begin in early life'.

In Sweden, a retrospective analysis of data from the Gothenburg primary prevention study showed an independent association between occupational class and incidence of coronary heart disease after 10-13 years follow up (20). In Finland, SMR's were calculated for all ischaemic heart disease deaths among 25-84 year olds during 1969-1971 (142). Among 25-54 year olds, the data showed that, for other than divorced people, there was a greater risk of ischaemic heart disease mortality among the less educated of either blue collar or white collar occupations. The differences were smaller but still statistically significant for those aged 55-84. Analysis of risk factors associated with social class was not a part of the study, although the authors quoted unpublished data to the effect that there is a gradient from high to low occupational groups in the Finnish population of increasing blood pressure.

In Britain, results from the British Regional Heart Study were published of six years follow up of 7735 middle aged men (143). Major ischaemic heart disease events were shown to be more frequent among men in the lower social classes. Similar differences in blood pressure levels were also demonstrated.

POTENTIAL BIAS.

The results are not based on a random sample of the overall population. Sharoe Green Hospital (chosen for the study because of the ready availability of comprehensive individual records) was not the only hospital serving Preston. Of all those whose records were complete and available (1298), 86% were traced, but only 38% were still living in Lancashire at a valid address. During the period in which the subjects were born, hospitalisation for labour was not universal and most babies born in hospital were first born children. Correspondence attached to the maternity records showed that many hospital deliveries had been planned at an early stage, and that medical problems were not an important reason for hospital delivery. It is unlikely that the reasons for hospitalisation during labour would have introduced a bias which led to a difference in the nature of the relationship of blood pressure to placental and birth weight among people born inside hospital compared with those born outside. One feature of the study population was a high proportion of first births (79%) among the study population. Within the study, however, the relationships observed are similar for first and later-born children which suggests that birth order would not have given rise to a difference between those born inside and those born outside hospital.

Similarly, it is unlikely that these effects would have been artificially introduced by the success or otherwise of tracing individuals and including only those still resident in Lancashire. The birth measurements of those who were visited as adults are similar to those who were not (table 2).

Migration according to socio economic class is another possible selective factor for this study population. It has been argued that the apparently greater importance to blood pressure level of current residential address than of residential address at birth for migrants is evidence against an early influence on blood pressure (139). This argument was based on observations made on a relatively small number of subjects in a study which divided the country only into three areas. Selective migration according to socioeconomic class may have contributed to the conclusions drawn from that study, since the higher classes may be more mobile than others and would tend to move to areas of greater prosperity. In this study, the relationship between blood pressure and placental and birthweight is seen in each social class, whether defined currently or at birth, which suggests that selective migration could not have produced the observed relationships as artefacts.

No observer bias could have influenced the results since the fieldworkers were unaware of the birth measurements when they visited the subjects. Measurements made routinely at birth, especially of placental weight, are prone to error. The data available showed the anticipated evidence of rounding of these figures. Such errors would tend to reduce rather than exaggerate any relationship of those measurements with later blood pressure.

A small proportion of the subjects were on medication which would lower blood pressure, whether for specific hypotensive therapy or for other reasons such as angina. No adjustment was made for this, which would have tended to conceal rather than enhance the effects observed.

The strength, nature, and gradation of the relationship between blood pressure, placental weight and birthweight are such that the effect is unlikely to have been produced by an unknown confounding variable. The fact that placental and birth weights are correlated but that the effect on blood pressure is produced by disparity between these two parameters makes a confounding factor even more improbable. The strength of the effect of birth parameters, which remains unaffected when factors operative in adult life are taken into account, is such that environmental factors operative in utero cannot be discounted as a major influence on later blood pressure levels.

THE EFFECTS OF BIRTHWEIGHT AND PLACENTAL WEIGHT ON BLOOD PRESSURE.

An inverse relationship of birthweight to blood pressure was not unexpected. Several reports have been made of such a relationship in childhood (75,76,78-80). One small retrospective study of 77 conscripts at 28 years of age, using a case control study design, showed an increased odds ratio of diastolic (but not systolic) hypertension for low birth weight (82).

Only one cohort has previously been examined for a relationship between birthweight and blood pressure in adult life (74,75) but this provided no data on placental weight. This comprised a sample of 5,362 births occurring in one week of March, 1946. At 36 years of age, the blood pressure, height and weight of 3,259 men and women among that cohort were measured. Systolic but not diastolic pressure was inversely related to birthweight independently of adult body weight, so that among men mean systolic

pressure fell by 2.57 mmHg from the lowest to the highest birthweight group (95% CL 0.98-4.16) and among women by 1.83 mmHg (75). The results presented here, when no account is taken of placental weight, show a fall in systolic blood pressure of 2 mmHg for men and 4 mmHg for women from those who weighed over 7.5 lbs at birth to those who weighed less than 6.5 lbs (table 12). Birthweight was more strongly related to adult blood pressure in 785 men born and still resident in Hertfordshire, England, at an average age of 64 (145). Records of their birthweight had been preserved. Systolic blood pressure was inversely related to birthweight, falling from a mean of 169 mmHg in those weighing 5.5 lb or less at birth, to 162 mmHg in those weighing more than 9.5 lbs. This relationship was independent of body mass index.

Only when the previously unreported effect of placental weight is taken into account are the large, independent and opposing associations revealed in this study, of a fall of 11 mmHg with increasing birthweight, and a rise of 15 mmHg with increasing placental weight. The close relationship of placental and birth weights has disguised these important, independent effects in all previous studies. The effect of discordance between placental and birth weight is demonstrated by a consideration of the placental weight as a proportion of the feto placental unit. There is a strong relationship between that proportion and average systolic blood pressure in later life, with a difference of 7.7 mmHg between those above the 80th centile and those below the 20th.

PLACENTAL SIZE

The size of the placenta was an important and unexpected factor in later blood pressure

levels. Factors which determine the size of the placenta have not been fully explored.

A study of 8,684 consecutive births in Oxford during 1987-1988 showed that higher mothers' blood pressure at first antenatal attendance was not associated with higher placental weight, but that large placental weight was associated with low maternal haemoglobin and falls in maternal mean cell volume during pregnancy (146). In that study, the highest ratio of placental weight to birthweight was found in women with the lowest haemoglobins and largest falls in mean cell volume. An association of large placenta with low maternal haemoglobin was also described in 1970 (147). Gruenwald found an association between both very large and very small placenta and infant mortality, although he did not ascertain causes of placental hypertrophy, (111). He questioned whether the inadequacy of large placenta was due to infarction or detachment from the uterine wall. The data from the study reported here contained no information on maternal smoking which has, however, been shown to have no association with increased placental weight (148).

FAMILY HISTORY.

Mother's blood pressures are related to those of their children and it could be argued that placental weight is linked to adult blood pressure through a maternal mechanism which determines both blood pressure and placental weight. However, although people who reported that their mothers had high blood pressure had higher blood pressure themselves, the placental weight was no greater for births to mothers reported to have hypertension than it was for births to other mothers, which suggests that a direct influence of maternal

blood pressure is not operating through an effect on the intra uterine environment or on the placenta. People who reported that their fathers had high blood pressure did not themselves have raised blood pressure.

A number of studies have shown familial aggregation of blood pressure levels (61,73,149-151) and have postulated a genetic mechanism. As Szklo points out, however, it is difficult in such analyses to distinguish between shared genetic and shared environmental influences, especially if those environmental influences are operative in utero (53).

Studies which have reported family history of hypertension or hypertensive disease as predictive of hypertension have not always disaggregated maternal and paternal history (151). Those which have disaggregated these histories have shown a closer relationship of raised blood pressure to maternal family history than to paternal family history. In examining blood pressure of parents and offspring among the Framingham cohort, Havlick et al (150) found that maternal systolic blood pressure was significantly related to systolic blood pressure of the offspring after taking other blood pressure correlates into account, but that the relationship of paternal systolic blood pressure to that of male offspring was of borderline significance ($p=0.05$) and paternal to female offspring of no significance. In a follow up study over 18.5 years of 789 men, a maternal history of stoke correlated significantly with the incidence of stroke in the subjects, but there was no such effect for paternal history of stroke (33). Similar differences between the relationship of paternal and maternal blood pressure to that of their offspring have been

shown by other researchers (72,152,153).

The findings reported here are consistent with other studies and suggest that, since the pattern of blood pressure levels among siblings is not consistent with an X-linked genetic mechanism (150), familial aggregation of raised blood pressure is due to environmental rather than genetic factors, a conclusion consistent with the observations of other reviewers (3,53,58). Those environmental factors may operate in utero through an effect on placental and birth weights. A further possibility is that higher blood pressure in a mother reflects her own earlier growth, which influences the intrauterine environment she provides for her children.

INTRA UTERINE GROWTH.

The weight of an infant at birth is a crude guide to the growth experienced in utero. Low birth weight can result from an unduly short gestational term, intrauterine growth retardation (IUGR), or a combination of the two. Earlier this century, international convention was to describe as 'immature' or 'premature' any baby weighing 5.5 lbs or less (99,111), so that such distinctions were not made. It is likely, however, that changes in birth prevalence of low birth weight in Britain are principally due to variations in IUGR, with the birth prevalence of preterm babies varying to a lesser degree (132). In this study, duration of gestation was not related to later blood pressure levels, which suggests that the relationship of blood pressure in adult life to birth weight is due to variations in intrauterine growth retardation rather than prematurity. No analysis was made of maternal smoking, which has been shown to be associated with a proportionate

reduction in birthweight and length (154).

As described in the introduction, intrauterine growth retardation may occur a) throughout pregnancy, causing proportionately small babies, b) later in pregnancy resulting in failure of skeletal growth reflected in a high head circumference/length ratio, or c) in the very late stages of pregnancy leading to wasting and a low ponderal index (w/l^3).

An analysis was made of the relation of blood pressure to weight, length, and head circumference within two groups of placental weight, the analysis being restricted to those 327 subjects born after 38 weeks completed gestation. In those whose placental weights were 1.25 lb or less, mean systolic pressure and the risk of hypertension rose as ponderal index fell (table 18). In those whose placental weight was more than 1.25 lb, mean blood pressure and the risk of hypertension rose as the ratio of head circumference to length increased (table 19). An inverse relationship of systolic pressure to ponderal index has also been observed in 4 year old children studied in Salisbury (150). In that study, the effect was observed at all placental weights.

Placental weight 1.25 lb or less.

In the group of babies born with placental weights less than 1.25 lbs, there was a clear association of low ponderal index with increased blood pressure. The relationship was such that for a given weight, blood pressure increased with birth length, and for a given birth length, blood pressure decreased with birth weight. The babies with lowest

ponderal index were characterised by a small but significant reduction in head circumference, a small but significant increase in birth length, and a considerable decrease (by 10%) in birth weight compared with the others (table 20).

Placental weight over 1.25 lb.

In the group of babies born with placental weight 1.25 lbs or more, there was a clear association of increase in head circumference to length ratio with an increase in adult blood pressure. The vulnerable babies in this group were characterised by reduced length and increased head circumference, but were not significantly lighter that the rest (table 21).

MECHANISMS FOR THESE EFFECTS.

Two groups of babies can be described who developed higher mean blood pressure as adults. The first group had placental weights of 1.25 lb or less, were thin (low ponderal index) with below average birthweight and head circumference, but above average length. The second group had placental weights over 1.25 lb, were short in relation to head size (high head circumference/length), with above average birthweight and head circumference but below average length.

Babies born at term with a low ponderal index have been described as suffering sub-acute fetal malnutrition (111), or fetal malnutrition (105), occurring at a stage in pregnancy too late to affect skeletal growth (and so birth length). Maternal influences known to be

associated with this form of growth retardation are calorie restriction and low weight gain in pregnancy (156). Babies born after the Dutch Hunger Winter of 1944-45 had a disproportionate reduction in birthweight in relation to length (157). A small placenta in itself, if giving rise to inadequate functional reserve, may result in fetal distress in the last weeks of pregnancy (107), and so to a low ponderal index.

In this study it was observed that the external conjugate diameter of the mother was associated with both birth length and birth weight. Babies in the low placental weight group vulnerable to later increased blood pressure were seen to be longer than the others. It is possible that babies able to grow to a full length in large mothers were more vulnerable to weight loss when exposed to inadequate nutrition in the latter stages of pregnancy, whether through mother's calorie restriction or the inadequate functioning reserve of an undersized placenta.

Large placental weight was associated with a higher head circumference to length ratio, and with raised systolic pressure. Maternal anaemia during pregnancy has been associated with increased placental weight (136,146). A recent study of four year olds in Salisbury showed that those whose mothers had been anaemic during pregnancy had higher mean blood pressure than those whose mothers had not been anaemic (155). A survey of children living in a rural community in the Gambia also found a relation between maternal nutrition, weight gain in the third trimester of pregnancy, and subsequent blood pressure in the offspring (158).

In the Preston cohort, placental weight tended to be higher in families with lower social

class (4 out of 56 (7%) of babies born at term to mothers in social class I or II had placentas heavier than 1.5 lb compared with 62 out of 254 (24%) for mothers in lower social classes: mean placental weight for father's social class being IV or V was 21.68 ozs compared with 20.57 ozs for social class I or II, p=0.16). The link between low social class and large placental weight is probably the standard of maternal nutrition.

Thus two mechanisms may operate to cause intra uterine growth retardation:

i) Relative under perfusion of a disadvantaged fetus may occur due to the presence of a large placenta,

ii) Inadequate nutrition of a fetus in the last stages of pregnancy may occur due to an inadequate (small) placenta.

The timing of these different insults would result in the different characteristics of the two groups of babies described as being at risk. Relative under perfusion because of a large placenta would occur throughout the last trimester, resulting in impaired length growth. Inadequate nutrition of a well grown (long) baby in the late stages of pregnancy would result in failure to put on weight and thus a low ponderal index (110).

A possible mechanism linking intra uterine growth retardation with late raised blood pressure is an effect of fetal hypoxia on the patterns of blood flow. In 1967, observations were made on the circulations of mature fetal sheep in a study of the regional controls of systemic vasomotor tone (159). Asphyxia, induced in the fetus by occlusion of the umbilical cord prior to artificial pulmonary ventilation, resulted in a fourfold increase in blood flow through the coronary and cerebral circulations, with a reduced flow through the femoral and renal arteries. Observation of the artero venous pressure differences

across the brain provided evidence that the altered flow patterns were due to active vasodilation in that area, with vasoconstriction occurring in the renal vascular beds. In 1983, results were reported of further studies on mature fetal sheep which replicated the observation that a reduced umbilical blood flow led to a moderate increase in flow to the myocardium and to the brain (160). Furthermore, an analysis of the flow patterns in the fetal circulation showed that blood with the highest oxygen concentrations was directed to the heart and brain, a phenomenon which was enhanced during episodes of fetal hypoxia. These effects could have a long term influence on renal function, since factors operating during fetal growth are known to program the physiology of adult life (161).

There is evidence from both animal and human studies that blood flow patterns in early life can alter arterial structure. In rats made hypertensive 4 weeks after birth, the wall of the aorta was shown to thicken rapidly, an effect that could be partly reversed by relieving the hypertension (162). In young children born with a single umbilical artery the common iliac on that side, through which blood flowed from the placenta, was seen to be elastic as opposed to the common iliac on the other side which was thin walled and muscular (163). The differences in structure of the arteries is reflected in differences in their compliance, as measured by ultrasound techniques (164). An arterial structure of thin, muscular vessel walls of poor compliance would predispose to raised blood pressure levels in later life. These mechanisms may operate in any fetus which is suffering subacute or chronic distress, even if that distress occurs too late in pregnancy to affect skeletal growth but leads instead to wasting.

MATERNAL STATURE, PLACENTAL WEIGHT, FETAL GROWTH, AND BLOOD PRESSURE.

This study shows that the external conjugate diameter of the mother's pelvis is related to birthweight and birth length of her offspring (table 22). A woman's physique depends partly upon her nutrition in childhood (as discussed earlier). Poor nutrition of the mother both in younger life and during pregnancy would thus predispose her offspring to higher blood pressure in adult life.

Maternal physique and intrauterine growth.

The results of this study provide some explanation of the links which have been observed between maternal stature, low birth weight, adult height, and risk of cerebrovascular or ischaemic heart disease (18,23,75,165). Birth size was strongly related to the external conjugate diameter of the mother's bony pelvis. Such an effect would be consistent with the separate conclusions of Snow, Roberts, and Ounsted (83,87,88) that intrauterine growth is predominantly a function of the intrauterine environment rather than of genetic make-up. The external measurement used in this study is only an approximation of the true conjugate diameter of the pelvis and was subject to the errors of all such routine measurements, both of which factors would tend to reduce its importance in the relationship observed with infant size.

Maternal height was not recorded at Sharoe Green hospital. A relationship between

maternal height and conjugate diameter has been observed (112,117,118,122) as has a relationship between maternal height and birthweight (165). The results reported here confirm the relationship of a woman's physique to the birthweight of her offspring.

A woman's physique depends upon the circumstances of her life during growth (18,101). That physique, through its influence on birthweight, is indirectly shown here to be a factor in the levels of blood pressure of her offspring. The high labour complication and Caesarian section rates observed in short women (102), and the increased perinatal mortality for that group (101), are consistent with the inference that an observed geographical relationship between maternal mortality among one generation and perinatal and cerebrovascular mortality among the next, is partly due to an influence of maternal physique on intra uterine growth and thus on the blood pressure of the offspring.

EFFECT OF BIRTH PARAMETERS ON ADULT SHAPE.

The adult height of the subjects was predicted by birth length and birth weight independently of each other, with birthweight having the greatest effect. Such a relationship would be blurred by catch up growth which, if conditions allow, is known to occur following intrauterine growth restriction (15,17,18,93,95,96). In view of the strength of the relationship of maternal physique to birthweight, it is apparent that limited growth during gestation due to an inadequate intra uterine environment does result in reduced adult height. The importance of intrauterine growth to adult height is further demonstrated by the inverse relationship of adult height to infant head circumference/length ratio. The trend, albeit of borderline significance at $p=.07$, that

exists for this relationship independently of birth weight suggests that a limitation of intra uterine trunk and limb growth leads to a reduction in adult height. Although no relationship was observed in this study between adult height and blood pressure levels, this effect of compromised fetal growth on adult height is consistent with the increased risk shown in considerably larger populations of cerebrovascular and ischaemic heart disease mortality among people of short stature (8,19,23,27).

Body Mass Index in adult life tended to increase with increased placental weight at birth, especially in smaller babies. An important effect of familial environmental factors in early life (as opposed to genetic factors) on adult body fatness has been shown in a study of 4643 non-familial adoptees (166). Thus part of the association between body mass index and blood pressure may be explained by common causation of the two by intra uterine growth retardation.

It was also observed that both those who were short at birth but subsequently caught up to be tall in adult life, and those who were fully grown at birth but who ended up being short in adult life, had higher blood pressure than the remainder, as well as a greater body mass index. This suggests that serious growth retardation both before and after birth could lead to increased adult body fatness and raised blood pressure, a hypothesis consistent with observations made of children up to 1 year born in Hertfordshire (11) where it was shown that there was a strong and graded relationship between the weight at one year and death from ischaemic heart disease in later life.

POPULATION EFFECT

The relations of placental and birth weight to blood pressure levels and risk of hypertension were independent of the effects of adult body mass index and alcohol consumption and were stronger than them (table 14). Routine measurements made at birth would appear to be better predictors of blood pressure than current factors, so much so that adjustment of the results to allow for alcohol consumption and obesity made negligible difference to the effects of birth measurements.

This study did not attempt an analysis of salt consumption. Early suggestions of a link between salt ingestion and blood pressure arose from observations of populations divided by migration (167-169). Observation of mildly hypertensive patients on salt restricted diets with subsequent reintroduction of slow sodium and placebo tablets in a double blind trial, suggested that salt restriction could have an effect for patients with elevated blood pressure levels (170), while others have concluded that altered sodium intake does not affect blood pressure in normotensive subjects (171). A recent cross cultural study in 52 centres concluded that reducing daily sodium intake from 170 mmol per day to 70 mmol would cause a reduction of 2mmHg in systolic blood pressure (172). A follow up study of 233 children found no significant association between sodium excretion and change in blood pressure over time, but an inverse relationship of systolic blood pressure with potassium intake and a positive association of Systolic blood pressure with sodium:potassium ratio (173). An analysis of 45 trials of salt intake concluded that reducing daily consumption by 50 mmol resulted in a fall in systolic blood pressure of

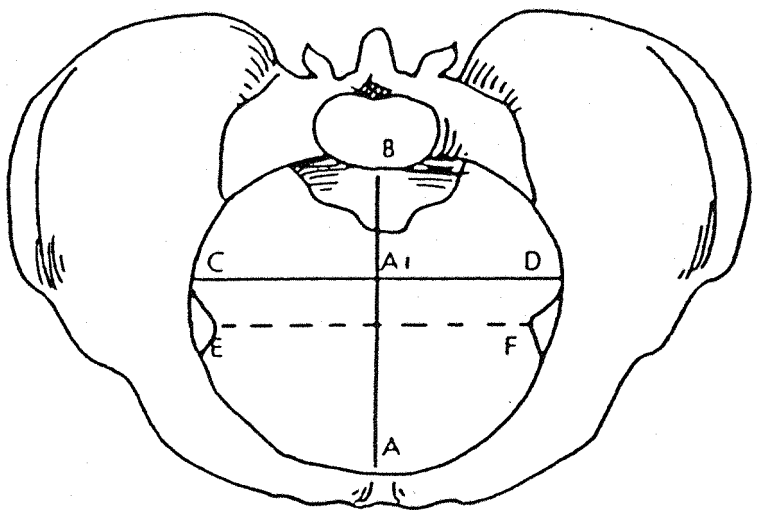
5 -7 mmHg depending on baseline blood pressure (174). At age 60-69, systolic blood pressure was reduced by a mean of 10 mmHG with a reduction in salt consumption of 100 mmol/24 hours. The effect was such that the group with the highest potassium intake had an annual change in systolic blood pressure 1 mmHg less than the group with the lowest potassium intake. These effects are small when compared to those associated with placental and birth weight, which range over 25 mmHg.

The combined effects of placental and birth weight on blood pressure in the adult are as large as 25 mmHg (table 14). Applied to a population such an effect would lead to a considerable excess of cerebrovascular and cardiovascular mortality. Various estimates of population attributable risk have been made to assess the broad effect of raised blood pressure. In calculations made from observations on an American population it was estimated that a reduction in diastolic pressure of 8 mmHg across the population would reduce coronary heart disease mortality by 20.6% and all cause mortality by 14.1% (36). Estimates on a British population are that a reduction of 10 mmHg in the blood pressure distribution would reduce total attributable mortality by 30% (44). More recently, Macmahon et al have estimated that a prolonged reduction of diastolic blood pressure by 5, 7.5 and 10 mmHg were respectively associated with a minimum of 34%,46% and 56% less stroke, and 21%,29% and 37% less coronary heart disease (175).

CONCLUSION.

Blood pressure in adult life, and risk of cardiovascular disease, are adversely affected by impaired growth during early life. This includes growth in the womb, which depends on the environment offered by the mother. The maternal environment and nature of any impairment of intra uterine growth is reflected by placental weight and the size and shape of the newborn baby. A sustained improvement in nutrition throughout growth and during pregnancy will make an important contribution to improved levels of blood pressure and associated morbidity in both the current and subsequent generations.

Figure 1: Inlet view of the pelvis indicating anatomical measurements



AB. true conjugate diameter; CD, widest transverse diameter; A_1B. posterior sagittal diameter and EF. the interspinous diameter.
Brim index = AB/CD x 100; Sagittal index = A_1B/AB x 100; Posterior sagittal transverse index = A_1B/CD x 100.

ıBLE 1.

NIMUM DATA SET FOR CASE SELECTION (FOR PRESTON COHORT).

For Tracing: Name of Mother
Address at time of birth
Date of birth
Sex of infant.

For Study: Mother's pelvimetry: Interspinous, Intercristal
Placental Weight
Length of baby
Birthweight
Weight when Baby > 3days old.
Head circumference.

ıo having the following characteristics: Married Mother
Live at discharge
Singleton birth.

BLE 2.

)MPARISON OF BIRTH PARAMETERS FOR SAMPLES AND TOTAL BIRTH POPULATION FROM HICH COHORT SELECTED, MEAN VALUES (sd). PRESTON COHORT.

	Sample 1	Sample 2	Combined (n=449)
Veight	110.2 (18)	113.6 (18)	111.7 (18)
lac wt	21.2 (4.7)	21.5 (5.4)	21.5 (5)
lead circ	13.7 (0>6)	13.6 (0.8)	13.6 (0.7)
ength	20.5 (1.1)	20.2 (1.1)	20.4 (1.1)
onjugate xterna	7.7 (0.5)	7.8 (0.5)	7.8 (0.5)
ystolic bp	150.2 (22.2)	149.8 (19.3)	
dult height	165.9 (9.7)	165.5 (9.1)	
dult weight	74.2 (14.4)	71.9 (15)	

.BLE 3.

LVIC MEASUREMENTS IN PELVIMETRY STUDY POPULATION BY SEX (SD).

	MEN	WOMEN	ALL
CONJUGATE DIAMETER	10.27 (1.04)	11.12 (1.00)	10.79 (1.10)
VIDEST TRANSVERSE DIAMETER	11.98 (0.84)	12.64 (0.84)	12.38 (0.90)
NTERSPINOUS DIAMETER	7.86 (0.77)	9.38 (0.85)	8.79 (1.11)
OSTERIOR AGITTAL DIAMETER	3.24 (0.55)	4.05 (0.68)	3.74 (0.74)
RIM INDEX	85.9 (8.23)	88.2 (8.67)	87.4 (8.65)
AGITTAL NDEX	31.5 (3.86)	36.3 (4.21)	34.4 (4.69)
OSTERIOR AGITTAL NDEX	27.1 (4.63)	32.1 (5.54)	30.2 (5.76)

.BLE 4.

AMETERS (cm) AND RATIOS AT THE PELVIC BRIM FOR EACH SEX BY AGE GROUP.
ELVIMETRY SURVEY).

	< 74 yrs	75+ yrs	Difference (95%CL)
Males			
Conjugate diam	10.29	10.22	.07 (NS se = .11)
Transverse diam	11.94	12.08	-.14 (-.3 - .02)
Posterior Sagittal Diam	3.26	3.17	.09 (-.02 - .2)
Brim Index	86.3	84.7	1.6 (0 - 3.2)
Sagittal Index	31.65	30.93	.72 (-.04 - 1.48)
Posterior Sagittal Index	27.4	26.98	1.12 (0.22 - 2.02)
Females			
Conjugate diam	11.21	10.86	.35 (.2 - .5)
Transverse diam	12.62	12.71	-.09 (NS se = .06)
Posterior sagittal Diam	4.13	3.82	.31 (.21 - .41)
Brim Index	89.14	85.65	3.49 (2.2 - 4.78)
Sagittal Index	36.69	35.1	1.59 (0.96 - 2.22)
Posterior sagittal Index	32.82	30.23	2.59 (1.77 - 3.4)

ABLE 5.

ELVIC DIMENSIONS BY AGE GROUP ADJUSTED FOR SEX, PELVIMETRY SURVEY.

	-74 YEARS	75+ YEARS	DIFFERENCE (95%CL)
CONJUGATE DIAMETER	10.86	10.61	0.25 (0.13,0.37)
WIDEST TRANSVERSE	12.35	12.46	-0.11 (-0.21,-0.01)
INTERSPINOUS DIAMETER	8.82	8.72	0.10 (0.005,0.20)
POSTERIOR SAGITTAL	3.79	3.57	0.23 (0.15,0.30)
BRIM INDEX	88.1	85.3	2.80 (1.79,3.81)
SAGITTAL INDEX	34.7	33.5	1.27 (0.79,1.75)
POST SAGITTAL INDEX	30.7	28.7	2.04 (1.43,2.66)

\BLE 6.

EAN CONJUGATE DIAMETER (sd), WIDEST TRANSVERSE DIAMETER (sd), BRIM INDEX (sd), ND SMR FOR CARDIOVASCULAR DISEASE (1980-1988) FOR EACH TOWN. (n = number of x-ys available for analysis, Pelvic measurements adjusted for age and sex, diameters in cm).

TOWN	n	SMR	CONJ DIAM	TRANS DIAM	BRIM INDX
Hertford	138	93	11.21 (0.89)	12.65 (0.74)	88.78 (7.71)
Shrewsbury	124	108	11.70 (1.14)	13.28 (0.78)	88.36 (9.06)
Preston	23	117	10.86 (0.87)	12.44 (0.66)	87.30 (6.65)
Carlisle	254	117	10.80 (0.95)	12.38 (0.82)	87.51 (8.05)
Burnley	273	123	10.59 (0.90)	12.26 (0.77)	86.64 (8.4)
Dewsbury	240	127	10.67 (1.08)	12.41 (0.75)	86.12 (8.52)
Wigan	105	133	10.75 (1.03)	12.41 (0.73)	86.84 (9.01)
Hartlepool	293	133	10.49)0.82)	11.96 (0.76)	88.06 (8.6)

ABLE 7.

ON PARAMETRIC CORRELATION COEFFICIENTS (FOR RANK) BETWEEN THE MEAN PELVIC EASUREMENTS AND STANDARDISED MORTALITY RATIO FOR EACH TOWN. ELVIMETRY SURVEY.

	Overall	Men	Women
Conjugate Diameter	-0.843 (.02 > p > .01)	-.530 (.2 > p > .1)	-0.868 (.02 > p > .01)
Widest Transverse Diam	-0.723 (.1 > p > .05)	-0.470 (p > .2)	-0.759 (.05> p > .02)
nterspinous Diameter	-0.687 (.1 > p > .05)	-0.554 (.2 > p > .1)	-0.783 (.05 > p > .02)
Post Sagittal Diameter	-0.94 (.01 > p > .002)	-0.494 (p > .2)	-0.904 (.01 > p > .002)
Brim Index	-0.603 (.2 > p > .1)	-0.289 (p > .2)	-0.470 (p > .2)
Sagittal Index	-0.470 (p > .2)	-.084 (p > .2)	-0.687 (.1 > p > .05)
Posterior Sag ndex	-0.518 (p > .2)	-0.319 (p > .2)	-0.783 (.05 > p > .02)

ABLE 8.

EAN SYSTOLIC BLOOD PRESSURE BY BODY MASS (PRESTON COHORT).

BMI -24	145 mmHg
BMI -26	149 mmHg
BMI -28	149 mmHg
BMI -30	156 mmHg

ABLE 9.

EAN SYSTOLIC PRESSURE FOR ALCOHOL INTAKE (N,SD). (PRESTON COHORT)

	Men	Women
Light drinkers	152.4 (171,18.7)	145.6 (200,22.8)
Moderate drinkers	158.2 (33,22.5)	141.8 (7,13.8)
Heavy drinkers	156.9 (32,14.6)	157.5 (6,16.1)

.BLE 10.

EAN SYSTOLIC PRESSURE ACCORDING TO PLACENTAL AND BIRTH WEIGHTS (n).
RESTON COHORT).

		Placental weight (lbs)			
Birth Weight	-1.0	-1.25	-1.5	>1.5	All
5.5	152 (26)	154 (13)	153 (5)	206 (1)	154 (45)
6.5	147 (16)	151 (54)	150 (28)	166 (8)	151 (106)
7.5	144 (20)	148 (77)	145 (45)	160 (27)	149 (169)
>7.5	133 (6)	148 (27)	147 (42)	154 (54)	149 (29)
All	147 (68)	149 (171)	147 (120)	157 (90)	150 (149)

ABLE 11.

EAN DIASTOLIC PRESSURE BY PLACENTAL AND BIRTH WEIGHTS (PRESTON COHORT).

		Placental weight (lbs)			
Birth Weight	-1.0	-1.25	-1.5	>1.5	All
5.5	84	87	87	97	86
6.5	84	88	85	93	87
7.5	84	84	84	90	85
>7.5	78	85	85	88	86
All	84	86	85	89	86

ABLE 12.

EAN SYSTOLIC PRESSURE BY SEX, PLACENTAL WEIGHT, AND BIRTH WEIGHT (n). RESTON COHORT).

	PLACENTAL WEIGHT (lbs)				
BIRTH WEIGHT MEN	-1.0	-1.25	-1.5	>1.5	ALL
-6.5	150	159	152	161	155 (79)
-7.5	152	154	147	164	154 (85)
>7.5	132	149	153	154	153 (72)
ALL	149 (26)	155 (88)	151 (66)	158 (56)	154 (236)
WOMEN					
-6.5	150	143	149	191	149 (72)
-7.5	141	141	143	155	144 (84)
>7.5	133	148	139	152	145 (57)
ALL	146 (42)	143 (83)	143 (54)	157 (34)	146 (213)

ABLE 13.

ELATIVE RISK OF BEING TREATED FOR HYPERTENSION OR HAVING A SYSTOLIC BLOOD ESSURE ABOVE 160 mmHg, ACCORDING TO PLACENTAL WEIGHT (95% CONFIDENCE MITS). (PRESTON COHORT).

	PLACENTAL WEIGHT (lbs)			
	-1.0	-1.25	-1.5	>1.5
TREATED HYPER-TENSION	1.0	1.3 (0.4,5.0)	2.4 (0.7,8.9)	3.0 (0.8,7.3)
SYSTOLIC >160 mmHg	1.0	1.1 (0.6,2.2)	1.2 (0.6,2.5)	2.5 (1.2,5.0)

ABLE 14.

EAN CHANGE (95% CONFIDENCE INTERVAL) IN SYSTOLIC PRESSURE ASSOCIATED WITH ACENTAL WEIGHT BIRTH WEIGHT, BODY MASS INDEX, ALCOHOL CONSUMPTION AND X. (PRESTON COHORT).

PLACENTAL WEIGHT (lb)	CHANGE IN SYSTOLIC PRESSURE
< = 1	0
- 1.25	4 (-2 to 10)
- 1.5	1 (-5 to 8)
> 1.5	12 (5 to 20)
BIRTH WEIGHT (lb)	
< = 5.5	0
- 6.5	-5 (-12 to 3)
- 7.5	-8 (-15 to -1)
> 7.5	-10 (-18 to -2)
BODY MASS INDEX (kg/m^2)	
< = 24	0
- 26	3 (-2 to 8)
- 28	3 (-3 to 8)
> 28	10 (4 to 15)
SEX	
Men	0
Women	-6 (-10 to -2)
ALCOHOL CONSUMPTION	
low	0
moderate	5 (-2 to 12)
high	5 (-2 to 12)

ABLE 15.

EAN CHANGE (95% CL) IN SYSTOLIC PRESSURE ASSOCIATED WITH PLACENTAL WEIGHT, RTH WEIGHT, LENGTH OF GESTATION AND SEX (PRESTON COHORT).

Placental weight (lbs)	Systolic pressure (mmHg)
<=1.	0
-1.25	4 (-2 to 10)
-1.5	3 ((-4 to 9)
>1.5	13 (6 to 21)
Birth Weight (lbs)	
<= 5.5	0
-6.5	-4 (-11 to 4)
-7.5	-7 (-15 to 0)
>7.5	-10 (-18 to -2)
Length of gestation (weeks)	
-37	0
38	-2 (-9 to 5)
39	-2 (-8 to 3)
40	-3 (-9 to 20)
41	1 (-6 to 7)
>= 42	-1 (-8 to 6)
Sex	
Men	0
Women	-7 (-11 to -3)

\BLE 16.

EAN SYSTOLIC PRESSURE (mmHg) BY PARITY (n). (PRESTON COHORT)

	Placental Weight (lbs).		
	-1.5	>1.5	All
Multiparous	146 (65)	162 (22)	150 (87)
Primiparous	149 (289)	156 (64)	150 (353)

ABLE 17.

YSTOLIC PRESSURE (ADJUSTED FOR AGE AND SEX) BY LENGTH AND PLACENTAL WEIGHT). GESTATION 38 WEEKS OR MORE. (PRESTON COHORT).

		LENGTH AT BIRTH (ins)			
PLACENTAL WEIGHT	<20	20	-21	>21	ALL
-1.25 lbs	142 (33)	146 (72)	150 (46)	153 (23)	147 (174)
>1.25 lbs	159 (11)	153 (77)	149 (38)	147 (26)	152 (152)
ALL	146 (44)	150 (149)	149 (84)	150 (49)	149 (326)

ABLE 18.

STOLIC PRESSURE (ADJUSTED FOR AGE AND SEX) IN THOSE BORN WITH MINIMUM RIOD OF GESTATION 38 WEEKS (n). (PRESTON COHORT).

	Ponderal Index				
Plac wt.	-12	-13.25	-14.75	> 14.75	All
1.25 lbs	154 (53)	147 (54)	142 (42)	141 (25)	147(174)
> 1.25 lbs	148 (27)	149 (27)	152 (48)	154 (50)	152(152)
All	152 (80)	148 (81)	147 (90)	150 (75)	149(326)

.BLE 19.

)JUSTED SYSTOLIC PRESSURE IN THOSE BORN WITH A MINIMUM OF 38 WEEKS :STATION ACCORDING TO PLACENTAL WEIGHT AND RATIO OF HEAD CIRCUMFERENCE) BIRTH LENGTH (n). (PRESTON COHORT).

		HC/L			
'LACENTAL VEIGHT	-0.65	-0.675	-0.7	0.7+	ALL
1.25 lbs	150 (66)	154 (40)	142 (52)	139 (16)	147 (174)
> 1.25 lbs	145 (38)	150 (40)	157 (46)	153 (28)	152 (152)

ABLE 20.

RTH PARAMETERS OF INFANTS BORN AFTER A MINIMUM 38 WEEKS GESTATION WITH ACENTAL WEIGHT 1.25 lbs OR LESS, CLASSIFIED ACCORDING TO PONDERAL INDEX. RESTON COHORT).

		PONDERAL INDEX.			
	-12	-13.25	-14.75	>14.75	SIGNIFICANCE OF TREND.
n=	53	54	42	25	
LENGTH (ins)	20.9	20.3	20	19.9	
WEIGHT (lbs)	6.3	6.6	7.0	7.8	
H CIRC (ins)	13.4	13.5	13.5	14	$p<.05$
ADJ SYS	154	147	142	141	$p<.05$
PLAC WT (lbs)	1.11	1.12	1.15	1.14	NS

ABLE 21.

RTH PARAMETERS OF INFANTS BORN AFTER A MINIMUM 38 WEEKS GESTATION WITH LACENTAL WEIGHT GREATER THAN 1.25 lbs CLASSIFIED ACCORDING TO HEAD RCUMFERENCE/LENGTH. (PRESTON COHORT).

		HC/L			
	-0.65	-0.675	-0.7	>0.7	SIGNIFICANCE OF TREND
n=	38	40	46	28	
LENGTH (ins)	21.2	20.6	20.2	19.9	
H CIRC (ins)	13.3	13.8	14.1	14.5	
WEIGHT (lbs)	7.5	7.6	7.4	7.3	NS
ADJ SYS	145	150	157	153	$p<.05$
PLAC WT (lbs)	1.61	1.58	1.61	1.61	NS

ABLE 22.

ELATIONSHIP OF MATERNAL CONJUGATE EXTERNA TO BIRTH PARAMETERS (n). RESTON COHORT).

	Conjugate Externa.			
	-7.25 ins	-7.75 ins	-8.0ins	>8.0 ins
Birthweight (lbs)	6.6 (82)	6.9 (165)	7.1 (127)	7.5 (66)
Head Circ (ins)	13.36	13.66	13.72	13.76
Birth length	20.1	20.23	20.58	20.62

ıBLE 23.

'STOLIC BLOOD PRESSURE ACCORDING TO INFANT AND ADULT SIZE (n=449). (PRESTON)HORT).

	Adult Height.		
ìirth Length	women -155cm men -169cm	women -162cm men -175 cm	women >162 cm men >175 cm
< = 20 ins	148	149	155
>20 ins	154	151	146

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