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Blood pressure studies in children

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WHO Study Group

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Geneva, 3–5 November 1983

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BLOOD PRESSURE STUDIES IN CHILDREN

Report of a WHO Study Group

INTRODUCTION

A WHO Study Group on Blood Pressure Studies in Children met in Geneva from 3 to 5 November 1983. The meeting was opened by Dr Lu Rushan, Assistant Director-General of WHO. He recalled that arterial hypertension is a major health risk in virtually all populations of the world. Although control of high blood pressure can be successfully achieved by medication, the ultimate goal, in general, and in WHO programmes specifically, is the primary prevention of hypertension. In 1958 the WHO Expert Committee on Cardiovascular Diseases and Hypertension provided the first international recommendations on epidemiological research into hypertension (*1*). That Committee also recommended criteria for hypertension and standards for blood pressure measurements. In 1961 and in 1978 two other WHO Expert Committees reviewed the existing recommendations concerning classification, methods, treatment, and prevention (*2, 3*). More recently, a Scientific Group on Primary Prevention of Hypertension met in Geneva in 1982 to define the research priorities in this field and to advise on research into the primary prevention of hypertension to be organized and/or coordinated by WHO (*4*). The Scientific Group recommended that blood pressure should be measured and recorded regularly, particularly in the children and families of hypertensive patients, and that populations at risk should be educated and encouraged to reduce excessive salt intake and obesity. The Scientific Group also mentioned that further research was required to define more precisely the factors causing a sustained elevation of blood pressure. Such research would necessarily include studies on blood pressure in childhood and adolescence.

During the 1970s, three WHO meetings were organized in Geneva on the study of the precursors of atherosclerosis in children. A WHO Protocol was drawn up and then offered to different research institutions in order to improve the comparability among studies in

the field and to promote international cooperation.[1] One substantial part of this Protocol deals with blood pressure.[2] Furthermore, numerous studies concentrating on blood pressure in children have been conducted in different countries.

1. BACKGROUND AND RATIONALE

Raised arterial blood pressure is a strong predictor of cardiovascular and renal disease. Indeed, high blood pressure or hypertension,[3] may be considered a major cause of death and morbidity in many populations. The causes of hypertension are generally unknown and high blood pressure of unknown origin is usually referred to as essential (or primary) hypertension. Most investigators consider high blood pressure to be a quantitative deviation from the norm, and this view has fostered the epidemiological approach to hypertension, in which the distribution, determinants, and development of blood pressure are investigated. This approach and others have led to the notion that essential hypertension in adults is the result of a process that starts early in life; investigation of blood pressure in children can therefore contribute to knowledge of the etiology of the condition. In addition, childhood studies have the important advantage that they may lead to the prevention of high blood pressure before its harmful sequelae can occur.

These considerations concerning the etiology and prevention of hypertension form the rationale for blood pressure studies in childhood, and thereby for this report.

The tasks of the present Study Group were thus:

(1) to review current knowledge related to blood pressure levels during childhood;
(2) to review factors that affect the levels of blood pressure in children;

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[1] *Study of the precursors of atherosclerosis. Protocol of a WHO collaborative project.* Unpublished WHO document CVD/78.1, Rev. 1 (1978).

[2] *Report of the meeting of investigators on epidemiological studies of atherosclerosis determinants and precursors.* Unpublished document WHO/CVD/84.2 (1984).

[3] For definitions of hypertension in adulthood and childhood, see references *3* and *12*. For definitions of primary and secondary prevention see reference *4*.

(3) to review the methods of blood pressure measurement in childhood;
(4) to define research priorities for the coming years;
(5) to discuss preventive measures that may be recommended immediately.

The aims of this report are to emphasize the need for further research on the etiology and prevention of hypertension, and to suggest preventive measures in childhood that are warranted in view of the available evidence. This report is made up of three main parts: the first deals with the types of blood pressure study carried out in childhood; in the second part the epidemiological evidence on blood pressure in childhood is reviewed; and in the third section the primary prevention of essential hypertension is discussed.

2. METHODS OF STUDYING BLOOD PRESSURE IN CHILDHOOD

There are several reasons why the methods used in blood pressure studies in childhood are important. Growth and development during the pre-adult years provide unique possibilities for the investigation of the determinants of blood pressure level and change. However, they also place restrictions on studies during this phase of life, and this may sometimes result in the use of study designs and measurement procedures that are different from those employed in adults. Nevertheless, the essential subject of blood pressure research is the course of blood pressure throughout life, from childhood to the adult years. The scientific questions in this context are numerous and they have a variety of implications for the design of studies. Blood pressure studies in children are the only way to obtain scientific evidence on factors that contribute to blood pressure elevation and on the ways to control or modify these factors.

The conduct of population studies of blood pressure is relatively simple (perhaps deceptively so) and together with the rapid growth of interest in the problem this has resulted in the large number of studies reported in the literature. However, the usefulness of some of this evidence is limited because of the large variation in investigation methods used, which seriously restricts any comparison of the studies and makes proper interpretation of the findings difficult. In addition, there are still conflicting opinions on a number of details of the procedures for the measurement of blood

pressure; if agreement can be reached on such matters, the differences between studies might be reduced and thereby the value of the research enhanced.

This is not to argue for uniformity in all studies, but to suggest that mere procedural differences ought to be minimized in the interest of advancing this entire area of research. With this in mind, the following topics will be discussed in this section. First, the available study designs are reviewed briefly. Second, the main points concerning blood pressure measurement are discussed, and finally, some recommendations are made with respect to recording, analysis, and reporting of data.

2.1 Study design

2.1.1 *Objectives*

Research on blood pressure in childhood has two main objectives: (*a*) to increase knowledge on the etiology of high blood pressure, and (*b*) to provide insight into the possibilities of preventing high blood pressure. Etiological studies, including those on the natural history of (high) blood pressure, concentrate on the factors that determine the level of, and changes in, blood pressure during childhood. Prevention (or intervention) studies are aimed at lowering blood pressure or preventing the rise of blood pressure with age.

These various objectives require different research designs. Without yet considering the material aspects of enquiries about blood pressure in childhood, a variety of possibilities to answer scientific questions will be reviewed. This will cover the use of existing data, observational studies, and intervention (experimental) studies.

2.1.2 *Use of existing data*

Many studies on blood pressure in children have already been performed, and it is important to exploit fully the data already available. This may be done in two ways: by using published material, and by carrying out new analyses of unpublished data.

(1) *Published reports.* Review of published reports can provide valuable insights into the epidemiology of blood pressure in children, because many studies are sufficiently well described to permit at least qualitative comparisons. For example, a review of

population surveys to compare in childhood the patterns of blood pressure change with age in different groups could provide data analogous to those of Epstein & Eckoff for adults (*5*). An important question to be studied in this way is whether the rate of change in systolic or diastolic pressure is constant with age. Furthermore, it may be possible to identify in this way populations already studied and of special interest for further research.

(2) *Data files.* In addition to the published material there are, in many instances, data files that could be used for further analysis. It is possible to perform specific analyses in a given data-set or to pool data from different data-sets. Some limitations of published reports, with respect to comparability of classification of subjects or lack of data on related measurements desirable for certain analyses, could be overcome in this way. Such exploitation of existing data might be undertaken by individual investigators pursuing a new line of research, either using their own data, or in some instances as part of a collaborative project. This approach has been shown to be fruitful in related areas (*6*) and it is strongly recommended. To anticipate the use of data from future studies, the establishment of data banks with full documentation of study design and procedures should be encouraged.

2.1.3 *Observational studies*

Observational, i.e., descriptive studies on blood pressure in children may use either a cross-sectional or a longitudinal study design. The objective of observational studies may be to compare blood pressure values or their determinants in children within one population or between populations. In observational studies, it is always important to describe the population to which the persons concerned belong, whether it is a "general" population or a specially selected group.

(1) *Inter-population studies.* In studies in which different populations are compared, the emphasis is mostly on relating blood pressure distributions to differences in exposure to risk factors; for example, differences in sodium intake (*7, 8*). In some inter-population studies, longitudinal observations on the same individuals are included (e.g., in migration studies) (*9, 10*). These may be either "cross-cultural" studies, i.e., studies on children who

have moved from one culture to another, or studies where the culture of the population is in the process of transition but the children themselves do not move.

(2) *Intra-population studies.* Studies that concern the individuals within one population may be cross-sectional studies, i.e., relating blood pressure levels in children to a certain characteristic measured simultaneously. They may also be longitudinal studies, where, for example, the same children are observed for a given period of time, in an attempt to relate initial blood pressure levels to the rate of subsequent rise and to determine the factors associated with any rise in blood pressure. In retrospective studies, which are conceptually also longitudinal, an attempt may be made to select individuals within different blood pressure categories (e.g., quintiles) and see how they vary in terms of presumed risk factors for high blood pressure.

(3) *Family studies.* Families are the smallest units in which interactions between man and his environment take place. They are especially well suited for the investigation of the relative contributions of heredity and environmental influences, difficult though such studies are. The study design is usually cross-sectional, but could also with advantage be prospective. With particular reference to young ages, they may take several forms:

—studies of children with hyper- and normotensive parents;
—family studies of children in different blood pressure ranges;
—twin studies;
—studies of natural and adopted children.

2.1.4 *Intervention studies*

Intervention (experimental) studies are urgently needed, not only to investigate the role of a suspected risk factor for hypertension but also to study how strong the relationship appears to be under the conditions of the experiment. A prevention trial can give definitive answers only if quantitative differences between the experimental and comparison groups can be achieved. The investigators must decide whether the participants in the trial are chosen from the top range of the distribution or over the whole range of blood pressure levels.

(1) *Trials that attempt to lower blood pressure.* There are no firm guidelines as to the ideal length of trials of this kind. They may be relatively short-term, as in trials to assess the effect of dietary sodium restriction on blood pressure, or they may be designed to assess the longer-term effect of an intervention. In the latter case, a duration of 1–2 years may be appropriate. Even longer follow-up periods will be needed to assess the stability of any change in blood pressure level achieved.

(2) *Trials that attempt to prevent a rise of blood pressure with time.* In contrast to the previous design, an attempt to prevent or reduce a rise of blood pressure with time usually requires a follow-up of at least several years. Since the subjects who are destined to become hypertensive adults cannot (yet) be identified early in life, the true aim of preventive measures in the population must be to delay or abolish this rise in blood pressure with time, resulting in a shift to the left of the current distribution curve of blood pressure values at age 20 years and above. Trials in this age group deserve serious consideration.

(3) *Trials to prevent the development of hypertension.* This objective includes the specification of a certain level beyond which the blood pressure should not be allowed to increase. Such studies may be practical only in selected high-risk groups.

2.2 Measurements

Despite more than 75 years of experience with the non-invasive measurement of blood pressure, discussion continues concerning its reliability, its wide variation in individual subjects, and the uncertain validity of comparisons between persons or groups or over time. However, it should be emphasized that the limitations of blood pressure measurement are not as serious as these concerns might suggest. This is confirmed by the large body of knowledge that has accumulated on the prevalence and incidence of high blood pressure, on the risks associated with increased blood pressure, and on the effects of intervention upon high blood pressure levels. It is suggested that the continuing concern about the measurement of blood pressure is in part a consequence of new questions that require more accurate and more comparable measurements than were needed in some of the earlier studies. In this section, the areas of concern about

measurement of blood pressure etc. are reviewed in the specific context of studies in children and adolescents. For details of measurement procedures, such standard references as those published by the World Health Organization (*2, 3*), the American Heart Association (*11*), and others (*12*), should be consulted.

2.2.1 *Blood pressure*

The chief elements of a blood pressure measurement are of course the observer, the apparatus, the circumstances of the examination, and the overall protocol. Each of these aspects will be discussed briefly below.

(1) *The observer.* Much attention has been given to the role of the observer in blood pressure measurement, not only regarding the technical accuracy of the readings taken but also the interaction between the observer and the subject. The training, testing, and certification of observers have been frequently discussed over the past 10 years or more, and most recently in a report on the training and recertification procedures for observers in the US Hypertension Detection and Follow-Up Program (*13*). There is little disagreement that studies of high quality will make use of one or more of the training aids now available. The components of the training programme are of far greater importance than the prior experience or skill of the observer, since observers can become well trained in several hours of supervised and individual practice, during a few days of instruction. For any study extending over several months or longer, it is important to reinforce the initial training course with a retesting programme.

(2) *The apparatus.* There is no special blood pressure device available for children, although the cuff size deserves special attention (*11, 12*). This subject of apparatus has also received much attention. Devices have been developed that are intended to substitute for what is generally regarded as the "standard" device, i.e., the mercury sphygmomanometer, with manually inflated cuffs and with direct interpretation of the acoustic signals by the observer using a stethoscope. Devices that attempt to blind the observer to the actual pressure levels when the signals are interpreted, such as the Hawksley Random-Zero device (*14*), or the London School of Hygiene instrument (*15*), have had a generally positive reception

from epidemiologists. Others, that aim to remove the observer further from the procedure, have not been well received (*16*). The most widespread reaction has been to require strict evaluation, consistent with published guidelines for this purpose (*11–13, 16*), upon which to judge the acceptability of a proposed substitute for the standard apparatus. This attitude is sound and should be maintained. The potential advantages of a more automatic procedure are considerable from a theoretical point of view, but have not been attained in practice.

Blinding the observer is especially important when cut-off points of blood pressure are used for decisions about referral or management. This is also the case when the putative effect of a certain exposure on blood pressure is studied, and the observer can not be blinded against this exposure, e.g., in the comparison of areas differing in cadmium exposure or drinking-water sodium concentrations (*17*). Apart from these circumstances, however, there is good reason for confidence that properly trained observers can perform satisfactorily using the standard apparatus, with some safeguard in a concurrent assessment of data quality, as will be discussed below. The aneroid manometers should be mentioned for completeness but they are not generally favoured for use in epidemiological studies.

Because there may be systematic differences in blood pressure values observed with different devices it is important that all blood pressure values in a single study are measured using only one type of device. Furthermore, in relation to the apparatus, proper provision must be made for inspection, calibration, maintenance, and repair of any blood pressure measurement device. Study protocols should give thorough attention to this aspect.

There is general agreement that in the presence of a wide range of body sizes and arm dimensions, in children and adolescents especially, an appropriate set of cuffs should be employed so as to meet certain specifications of cuff dimensions relative to dimensions of the arm (*18*). For specific recommendations, the guidelines described for a WHO Collaborative Study[1], and by others (*19*), should be consulted.

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[1] *Study of the precursors of atherosclerosis. Protocol of a WHO collaborative project.* Unpublished WHO document CVD/78.1, Rev. 1 (1978).

(3) *Circumstances of examination.* Many aspects of the circumstances of examination have been considered in the epidemiological and clinical literature. These circumstances include features of the physical environment, the position of the subject, and external stimuli that affect the actual blood pressure of the subject thereby compromising both the repeatability of readings for the individual and the standardization of measurements between individuals or groups. Such aspects as the gender and skin colour of the observer vis-à-vis the subject, or location, whether school, medical facility, home or elsewhere, do not have clearcut effects. Recently, firm evidence has been provided on the effects of room temperature, time of day, and perhaps season, at least among 6–9-year-old subjects (*19*). As to position, Prineas et al. (*19*) adopted the supine position on the practical ground that arm-height (relative to the heart) is uniformly controlled in this way. This recommendation received serious consideration by the WHO Study Group, who concluded that continuity of methods in children with those in adults was the most important consideration, so that the sitting position should be retained.

(4) *Protocol.* The protocol, or design, of the actual examination requires careful consideration of all the foregoing issues. Furthermore, the timing of the blood pressure measurement in the overall flow of the examination is a potential source of error in the readings for some subjects. It is desirable to plan a sequence that is not likely to influence adversely the accuracy of readings for any subject, and then to standardize the sequence so that exceptions do not occur. This includes the number of readings and the waiting or rest periods before and between readings, but the relation to other procedures, such as venepuncture or physical exercise of some kind, must be considered also.

2.2.2 *Other variables*

Certain other measurements are so clearly required for meaningful observation and interpretation of blood pressure readings as to require little discussion. They are mentioned only for completeness and include the arm length and circumference, in order to select the correct cuff; height and weight, without which blood pressure values in growing children and adolescents cannot be properly interpreted; and pulse or heart rate, which should be

included both because of its relation to blood pressure levels and also because it is an easily measured index of cardiovascular function whose relation to blood pressure patterns by age is far from clear. An argument can be made for the inclusion of the triceps skinfold thickness as part of the minimum data-set, to add insight into body composition and the configuration of the arm on which the cuff is placed, but at this point many would object that proper measurement is difficult and time-consuming relative to the other procedures and would be only a part of a more extensive anthropometric examination if this were the objective of a particular study. A similar argument could be made regarding the assessment of sexual maturation, with its important insights but added practical difficulties in some settings. On balance, the WHO Study Group concluded that the skinfold measurement should be included, but that the assessment of sexual maturation should be considered more appropriately as a strongly desirable adjunct.

2.2.3 *Measurements in longitudinal studies*

The foregoing considerations are applicable to the simplest of study designs, the cross-sectional population survey with a single examination for each participant. Such studies are very much needed and they can provide valuable information on population similarities and differences regarding the changes in blood pressure during childhood, adolescence, and early adulthood. Additional questions of great importance, however, require repeated measurements made on the same subjects. Questions such as the timing of blood pressure changes in relation to biological maturation require studies with a predetermined number and frequency of examinations, and with the age and developmental state of the subjects taken into account. Such matters are mentioned here only to indicate that the longitudinal dimension of such studies confirms the importance of all the aspects discussed above and raises some additional ones as well.

2.3 Data-recording, analysis, and reporting

To facilitate collaborative studies of blood pressure levels among children in various populations it would be important to reach agreement upon a simple and uniform recording format for the

measurement of blood pressure and other characteristics. The Study Group recommends the formation of a small WHO Working Party to develop detailed guidelines concerning the design, conduct, recording, and analysis of studies of blood pressure in childhood.

Studies of blood pressure must have a provision for quality control, for descriptive presentation of raw data and summary statistics, and for the further analyses. Quality control should, as far as possible, be concurrent with data collection. It should include analysis of blood pressure data in relation to the observer and also to any other factor suspected of introducing systematic error (*19*). Frequency distributions by observer, end-digit frequencies, etc. should be planned and monitored frequently to detect possible measurement problems. Instrument problems could also be detected in this way.

The statistical analysis of blood pressure investigations largely depends, of course, on the scientific question under study. It seems that the analysis of cross-sectional studies in general poses few problems. In contrast, longitudinal studies with repeated blood pressure measurements are more complicated analytically, as has been shown in much of the recent literature on the subject (*20–24*); this seems to be particularly true for blood pressure studies in childhood (*22, 23*). The analytical problems are, in general, related to the large intra-individual variability of blood pressure and to the random error of the measurement. In particular, analysis of the stability of blood pressure rank, of the predictive value of a certain level of blood pressure, and of the relationship between level and subsequent change of blood pressure is severely hampered. Guidelines concerning the analysis of blood pressure studies will need to emphasize these aspects.

The information given in published reports on blood pressure studies is often incomplete (*25*). Narrative descriptions of procedures, including training and performance testing of observers, and of the study population with respect to demographic characteristics, relevant personal history items, and other factors particularly relevant to the study, should be included in every report. Omission of these items of information compromises the use of the results for comparative purposes. The Study Group recommends the development of minimum guidelines for the reporting of blood pressure data, and that these should be added to detailed guidelines for the design, conduct, and analysis of studies of blood pressure in childhood.

2.4 Ethical considerations

The Study Group emphasizes that studies in children raise special ethical considerations that should be borne in mind in the design and conduct of any study. This is especially important if any invasive examination procedure is contemplated (*26–28*).

3. EPIDEMIOLOGY OF BLOOD PRESSURE IN CHILDHOOD

This section deals with the results of epidemiological studies of blood pressure in infants, children, and adolescents. It reflects the two main objectives of epidemiological research, i.e., an understanding of both the early etiology and the prevention of hypertension. The level of blood pressure and its determinants, the determinants of change in blood pressure, the stability of blood pressure rank, and the prediction of future hypertension will each be discussed, with emphasis on the needs for further research.

3.1 Level of blood pressure during childhood

As early as the first decades of this century, blood pressure was investigated in children and young adults (*29, 30*). In these earliest studies, it was observed that the average level of blood pressure in childhood increases markedly with age. Since then, virtually all studies of blood pressure in childhood, performed in a variety of populations, have shown a rise of blood pressure with age (reviewed in references *31–33*). This rise is particularly marked for the systolic pressure. Both boys and girls show an average increase in systolic blood pressure. However, in adolescence the rise is steeper in boys than in girls. This is the reason for the difference in systolic blood pressure between males and females at the age of 20 years. The average annual increase in systolic pressure from birth until the age of 20 is about 0.26 kPa (2.0 mmHg) in boys and about 0.13 kPa (1.0 mmHg) in girls. Between the ages of 10 and 14 years, however, the average increase is greater. For diastolic blood pressure also, most studies have shown an increase in average levels with age

during childhood. However, the rise in diastolic pressure is less marked than the increase in systolic pressure, and there does not seem to be a major difference between boys and girls. The average annual increase in diastolic pressure throughout childhood and adolescence for both boys and girls is about 0.07–0.13 kPa (0.5–1.0 mmHg).

3.2 Determinants of blood pressure level

The level of arterial blood pressure is determined by cardiac output and systemic vascular resistance. Many factors influence cardiac output and total peripheral resistance and some of these are considered here. It has not yet been determined whether the increase in blood pressure that occurs early in life is due mainly to an increase in cardiac output or to an increase in peripheral resistance (*34*). In children, some studies, in particular those with invasive measurement of cardiac output, have suggested that a high cardiac output sometimes referred to as a hyperkinetic circulation plays a part in the early pathogenesis of hypertension (*35–38*). Other studies, mainly those involving the non-invasive measurement of cardiac output (*39–43*), have produced results that support the hypothesis of a gradual increase of peripheral vascular resistance with age. Further research to resolve this issue needs to be undertaken in order to decide whether epidemiological studies should focus mainly on putative determinants of vascular resistance or of cardiac output in childhood. In this context, the further development and application in epidemiological studies of non-invasive methods of measuring cardiac output are important.

3.2.1 *Genetic factors*

(1) *Evidence.* The evidence on the role of heredity in determining the level of blood pressure and the occurrence of hypertension in man is considerable and will be reviewed briefly below.

(*a*) *Twin studies.* Most studies on the variability of blood pressure between monozygotic and dizygotic twins have focused on adults. Typical values for the intra-class correlation in these circumstances are 0.55 for monozygotic twins, and 0.25 for dizygotic twins (*44–45*). Correlations in juvenile twins tend to be even higher (*46*). Levine et

al. (*47, 48*) have followed cohorts of monozygotic and dizygotic twins from birth to 1 year of age. The overall estimates of heritability were lower than those cited for adults, but one has to bear in mind that this was based on data pooled from different ethnic groups.

(*b*) *Family studies.* Family studies are of two types. First, there are those studies where the families are selected because of the presence of hypertension. Bianchi et al. (*49*) estimated that the children of two normotensive parents have a 3% probability of developing hypertension, whereas this possibility is 45% in children of two hypertensive parents. Second, there are studies in which the families are selected because they possess some attribute other than the one under scrutiny; for example, because of the presence of twins or of adopted children. Nance et al. (*50, 51, 53*) noted that studies of sibships of identical twins can differentiate between maternal and environmental effects (*52*). Studies of families with both natural and adopted children contribute to a better quantification of the sources of variation (*54–56*). These have shown that the correlation between foster parent and adopted child is consistently smaller than the correlation between the parent and natural child. Similarly, the correlation between natural siblings is greater than that between children both of whom are adopted or between a natural child and an adopted child.

(*c*) *Population studies.* The distribution of blood pressure levels and the prevalence of hypertension varies in different ethnic groups. Studies between unmixed populations and groups from the same population mixed with other ethnic groups help to define the influence of genetic factors on blood pressure. Studies in offspring of interracial marriages may be useful in order to determine the penetrance of a possible high-risk genotype.

(*d*) *The search for genetic markers.* A variety of biochemical markers determining blood pressure and hypertension are being studied. Evidence of the role of sodium transport, urinary kallikrein, and the catecholamines in the determination of blood pressure are under investigation.

(2) *Further research.* Even though there is considerable evidence that genetic factors play an important role in determining the level of blood pressure, further research should show how many genes and loci are involved and what their mode of inheritance is. Furthermore, the study of biochemical markers of the genes involved in hypertension should be pursued.

3.2.2 *Maturation*

(1) *Evidence.* In all studies of systolic blood pressure in infants and children, a rise in level with age has been observed. At puberty an acceleration of the rate of systolic pressure rise has been observed in both sexes. Whether this is the result of pubescent acceleration of maturation generally, a specific direct effect of a particular aspect of hormonal change, a response to structural changes concomitant with growth, or other influences, is not clear (*33, 57*).

(2) *Further research.* There is a need for further study of the relationship between biological maturation and blood pressure rise. In particular, investigations of various indices of growth (e.g., body size, sexual and skeletal maturation, hormonal changes) could yield more insight into the separate and joint effects of nature and nurture on the course of blood pressure change. This could lead to a more precise assessment of the potential of prevention of hypertension by altering environmental influences early in life. To this effect, various methods of assessing maturation may be applied in epidemiological studies. The use of indices for sexual maturation (*58*), the radiographic assessment of bone age for skeletal maturation (*59*), and change in height may be considered as measures of maturation for population studies.

3.2.3 *Body size*

(1) *Evidence.* Most cross-sectional studies in children have shown a strong positive relationship between blood pressure and height, weight, and various indices for body mass (*60–69*). Body weight is also a predictor of elevated blood pressure in follow-up studies in children (*70–72*). In addition, it has been reported that body weight predicts the rise of systolic blood pressure in childhood (*73*). The mechanisms by which body weight is related to blood pressure have not yet been determined (*74*) and it is not clear to what extent the association of body weight with level and change of blood pressure is due to maturation (see section 3.2.2). In adults there is evidence that a reduction in energy intake leading to weight loss may lower blood pressure (*75, 76*). In children the evidence of a similar effect is limited.

(2) *Further research.* Two types of further study of body size and blood pressure are suggested. First, investigation of the mechanism

of the association between body weight and blood pressure early in life are important, and in particular the effect of maturation might be studied in this context. Second, although the mechanism is as yet unknown, the potential of weight reduction in children for lowering blood pressure and for preventing the rise of blood pressure with age needs to be studied. In addition, effective means of maintaining long-term weight loss need to be developed.

3.2.4 *Endocrine and renal factors*

(1) *Evidence.* Many endocrine and renal factors have been implicated in the regulation of blood pressure in adults, but there is only little information on the role of these factors in childhood. Kallikrein (*77*) has been studied in adolescents. Virtually all studies on blood pressure and catecholamine levels in young people revealed significantly higher noradrenalin levels in hypertensives than in normotensives (*78, 79*). This supports the contention that overactivity of the sympathetic nervous system in childhood may play a part in the early pathogenesis of hypertension.

(2) *Further research.* In general, the role of the endocrine or renal determinants of blood pressure level in adults may also be studied in childhood to elucidate their role in the early pathogenesis of hypertension. In particular, it seems promising to investigate the relationship between the levels of growth hormone and sex hormones and the changes in blood pressure in childhood and adolescence.

3.2.5 *Dietary factors, in particular sodium intake*

(1) *Evidence.* The view that high sodium intake is implicated in the etiology of high blood pressure was advanced many years ago (*80*). This hypothesis has been strongly supported by some scientists (*81, 82*), whereas others have been less enthusiastic (*83–85*). Animal experiments in which salt-sensitive and salt-resistant rat strains have been developed have supported the association (*86*). Data available from populations differing in sodium intake have revealed a higher proportion of subjects with high blood pressure in populations with a high average sodium intake than in those with a low sodium intake (*7, 8, 81, 82*). Studies of the effect of high sodium concentrations in drinking-water on blood pressure in children have produced

conflicting results (*17*). A randomized trial in newborn infants has suggested that sodium intake may be etiologically related to blood pressure very early in life (*87*). An important question is whether sodium restriction would lower blood pressure. There is growing evidence that sodium restriction lowers blood pressure in some adult hypertensive patients (*88–91*). However, it is not yet possible to identify individuals who are sodium-susceptible. As yet, there is only little evidence to support the view that sodium-restriction may be beneficial in young people with relatively high blood pressure (*92, 93*). As far as the whole population is concerned, very little information is available, and therefore the benefits of lowering sodium intake are as yet uncertain. Other cations, e.g., potassium, calcium, and magnesium, have also been suggested as determinants of blood pressure level (*82, 94–96*). In children, no evidence of this has been reported. Dietary factors such as protein, fibre, saturated fats, and alcohol intake have also been implicated in the etiology of hypertension. Again, in childhood, no evidence is available on these putative determinants.

(2) *Further research.* Intervention studies concerning the effect of sodium restriction or increased potassium intake on blood pressure in young people with relatively high blood pressure are much needed. The effects of a reduction in the intake of saturated fats on blood pressure also needs investigation. The same applies to the possible relationships between alcohol and coffee consumption on blood pressure in childhood.

3.2.6 *Physical activity*

There is some evidence to suggest that vigorous physical activity in children may lower high blood pressure levels (*97*). This is potentially important and there is a need for intervention studies to investigate the effect of vigorous activity upon the blood pressure levels of children.

3.2.7 *Other factors*

A number of other factors have been suggested as being related to blood pressure level in children. These include environmental cadmium exposure (*98*), oral contraceptives, noise (*99*), and

psychological and social influences (*100*). The role of any of these factors upon the level and change of blood pressure during childhood and adolescence has still to be determined.

3.3 Determinants of blood pressure change

(1) *Evidence.* The determinants of change in blood pressure during childhood have not been studied as extensively as the determinants of blood pressure level. It has been observed that blood pressure change during childhood is associated with parental blood pressure, as well as with body weight and height, and serum levels of uric acid (*73*). To what extent the rise in blood pressure with age is determined by genetic factors and to what extent by environmental influences is not yet known. The contention that people with the highest levels of blood pressure have the largest subsequent rise in blood pressure ("horse racing"), has not been supported in studies of children and young adults (*73, 101–104*). Very little is known about the effects of some determinants of blood pressure level in adults (and children) on blood pressure change, i.e., use of oral contraceptives, dietary fats, fibre, coffee, cigarette smoking, alcohol intake, and physical activity.

(2) *Further research.* Investigations into the relationship between the initial level of blood pressure and its subsequent change can be performed using existing data-sets. They may provide clues to possible early disfunction in the regulation of blood pressure level. Supporting background information is needed, especially regarding the effects of high blood pressure in childhood on early athero- and thrombogenesis.

3.4 Stability of blood pressure rank

(1) *Evidence.* It has been observed in many cross-sectional studies of blood pressure in children that there is a continuous rise in level from infancy through adolescence and that at any given age there is a wide distribution of blood pressure level (*31–33*). If blood pressure levels of individuals were to remain in rank order from early childhood into adult life, then those whose pressures were observed initially to be in the upper part of the distribution would be destined to have high blood pressure as adults. The persistence

of rank order of blood pressure has been referred to as "tracking" (*105–107*).

Longitudinal data from diverse populations and obtained by blood pressure measurements at various levels of rest in different body positions, and by variously trained observers, have shown different degrees of "tracking". All were based on the examination of the same population of children on two occasions. These data confirm that there is indeed some consistency of rank order of blood pressure during childhood, but many children do not maintain their rank during the period of observation (*108–116*). However, other consistent trends in blood pressure are seen in children. There are subjects who consistently increase or decrease their rank order of blood pressure as they grow older. This results in a decrease in the overall correlation coefficient of rank order of blood pressure from one time period to the next (*117*).

(2) *Further research.* It is particularly important to study further those subjects who show consistent rank order of blood pressure, or consistent trends in their rank order during childhood. From longitudinal studies of children it is possible to identify groups who appear to be destined to have high blood pressure in the future. These groups may be defined in terms of their level, trend, and variability of blood pressure rank order over a period of years. These subjects should be investigated regarding physiological, genetic, environmental, and nutritional factors in order to observe whether public health measures or individual medical care practices can influence the adult level of blood pressure.

3.5 Predictive value of blood pressure level

(1) *Evidence.* Although the actual blood pressure level is the best predictor of the future blood pressure level, the predictive value of a relatively high blood pressure for future hypertension is rather low (*116, 118*). This implies that it is not yet possible to detect future hypertensives early in life by measuring blood pressure.

(2) *Further research.* There are indications that adult hypertension may be determined during childhood, but the precise factors occurring during childhood that predict adult hypertension are not well defined. As reviewed earlier in this section, genetic factors, body size, sodium intake, and possibly recurrent

psychological and social stress have all been considered as determinants of hypertension. There is thus a need for studies that clarify the role of these factors during childhood.

4. PRIMARY PREVENTION OF HYPERTENSION

The prevention of high blood pressure in childhood and adolescence is, above all, aimed at the prevention of hypertension later in life. Preventive measures begun in adulthood are also a part of the strategy of prevention, but the chances are that the earlier prevention starts, the more likely it is to be effective. Moreover, the habits that are related to an undue rise in blood pressure with age are formed early and become increasingly difficult to change later in life. The preventive measures to be considered are discussed below.

In connection with prevention, the terms "high-risk strategy" and "community (mass) strategy" have become established (*119, 120*). These are not alternative, but complementary approaches. The high-risk approach is aimed at persons with elevated levels of possible risk factors. In children and adolescents, in contrast to adults, the definition of "high risk" is difficult because it is impossible to identify with precision those individuals who will become hypertensive later in life (see section 3.5). Therefore, for the present report, the term "individual approach" has been chosen. The "community approach", on the other hand, clearly means altering the life-style of persons of all ages and also some environmental factors in order to reduce the levels of those determinants that might contribute to the underlying causes of high blood pressure. Indeed, since children belong to the community, community programmes must include them for a variety of reasons, one being to protect them against the disorders of later life.

With reference to blood pressure, the community approach must be concerned with all members of the population and involve the introduction of measures that will result in a shift of the distribution of blood pressure towards lower levels. Individual preventive care is largely the responsibility of the practising physicians and affiliated health workers. The community approach requires the establishment of more broadly based networks of community organization, as described below.

While the emphasis of this report is on the needs for further research, much knowledge has been acquired already and awaits evaluation. This knowledge is partly based on studies in children and partly on reasonable extrapolations from investigations made in adults.

4.1 Preventive measures

The rise of blood pressure with age in childhood and the development of hypertension is the result of interaction between genetic and environmental factors. Among the environmental factors that have been identified as determinants of blood pressure level and change, the following could be of potential use for the primary prevention of blood pressure rise and hypertension in childhood: body weight, sodium intake, alcohol consumption, physical activity, and perhaps psychological and social factors. A major problem in assessing the potential for the primary prevention of essential hypertension beginning in children is that it is still unknown to what extent the marked rise in blood pressure during the first decades of life is a matter of biological maturation. Nevertheless, it is likely that the mentioned environmental factors account for a considerable proportion of the adult patients with hypertension. Alteration of these factors during childhood may therefore have a large impact on the occurrence of essential hypertension. These factors are closely related not only to the life-style of the individuals, but also to the life-style of the whole community.

4.1.1 *Community approach*

Although much has still to be learned about the factors that might lower blood pressure or prevent a rise in blood pressure with age, and although in particular the efficiency and effectiveness of the proposed preventive measures still have to be assessed, the present Study Group noted that there is, at the present time, enough evidence to recommend moderate dietary reductions in sodium and alcohol intake, early prevention of obesity, as well as increased physical activity in some populations. None of these measures involves any risk of adverse effects, and all may be beneficial. More precise recommendations have to await further study of the efficiency and effectiveness of these and other factors. The fact that

the recommended preventive measures in children are similar to those for the primary prevention of essential hypertension in adults (*4*) is very much intended. The Study Group took the view that the community approach to primary prevention of essential hypertension should not be fragmented according to age-category, or developmental stage. The intervention should be comprehensive and be based on information from both the public and health professionals about the possibilities of preventing hypertension through the modification of personal life-style and the environment. Among the measures to be employed, action via legislation—for instance the reduction of the sodium content of baby food—deserves special attention. Legislative action should be promoted when adequate information has been obtained through scientific research on the subject. Obviously, individuals other than health professionals are involved in the community approach to prevent hypertension. An important role can be played by teachers and other professionals who work with children.

4.1.2 *Individual approach*

A very small number of children have established hypertension, i.e., extremely high levels of blood pressure, possibly with symptoms and/or target organ damage. Generally, these are the result of underlying renal, endocrinological, or cardiovascular disorders. The clinical treatment of these children has been considered by another group and reference is made to their report (*12*). After considerable discussion, the present Study Group noted that pharmacological intervention for high blood pressure in children is the responsibility of the individual physician. When drugs are used for the care of children with severely elevated blood pressure, the possible side-effects of this therapy should be carefully monitored, so that any long-term effects on growth and development may be evaluated.

The question of therapeutic measures for preventing hypertension later in life is more difficult. This is so, particularly, because it is difficult to predict with any accuracy which children will be hypertensive in the future and for whom preventive treatment can be considered mandatory (see section 3.5). Nevertheless, children who have blood pressure that is permanently in the high end of the range over several years must be considered for intervention, especially if there is a family history of hypertension, obesity, or an unusually high intake of salt.

Intervention should consist primarily of alerting the subject and the parents to the need to follow the community-wide health recommendations.

4.2 Proposed action for prevention

Before preventive measures to lower blood pressure and to prevent the rise of blood pressure in children can be implemented at the community level, many issues should be considered and the problem areas identified. Such a community analysis should provide the basis for setting priorities and selecting the appropriate methods of intervention. Answers are needed to at least the following questions:

(1) which factors might be important in a particular community?
(2) to what extent do the preventive measures need to be aimed specifically at children, to what extent towards their families, and to what extent towards the entire community?
(3) what knowledge is available about the planned intervention measures?
(4) are the population and the various organizations in the community willing to cooperate?

It is difficult to promote acceptance of a combination of a low sodium diet, a low energy diet, and a low alcohol intake in modern societies. A strong commitment of the whole community will be needed in order to be able to initiate an effective programme, and this will require cooperation between sectors such as education, food production, industry, and marketing, as well as the health care providers and health educators.

The most effective and efficient use of health personnel will be in community participation rather than in discussions with individual children. Health professionals should take a leading role in organizing comprehensive community-based health promotion in childhood. It is not known which community methods are the most effective in organizing preventive programmes for hypertension in children and, therefore, further research is needed in developing community programmes.

One promising approach is to introduce at the same time several procedures that have the potential to prevent hypertension (see section 4.1.1). The reasons for this are that obesity, excess salt intake, and diminished exercise often occur simultaneously and that their

effect on blood pressure elevation may be additive or synergistic. Furthermore, small changes in several factors may have as large a preventive effect as that of a marked change in one factor, and those small changes will be easier to obtain.

Pending further study and more evidence, the Study Group believes that it is now prudent for communities to recommend a reduced dietary sodium intake, and alcohol intake, as well as to encourage physical activity, where these factors appear to be important health problems.

5. CONCLUSIONS AND RECOMMENDATIONS

(1) Studies of blood pressure in childhood may provide further clues to the etiology, prevention, and treatment of subsequent hypertension in adulthood.

(2) To facilitate collaborative studies of blood pressure levels among children in various populations, detailed guidelines should be developed by an international group regarding the design, conduct, and analysis of such studies.

(3) The study of blood pressure in childhood would benefit greatly from further development and application of methods for:

(*i*) measurement of growth velocity and acceleration;
(*ii*) non-invasive measurements of the structure and function of the circulatory system;
(*iii*) continuous blood pressure measurement.

(4) The search for genetic markers of hypertension should be actively continued.

(5) The stability of blood pressure rank over time, the predictive value of blood pressure in childhood for future blood pressure, and the relationship between the level and subsequent change of blood pressure need further investigation.

(6) The effect of biological maturation on the level and change of blood pressure and its interaction with environmental influences needs further study.

(7) Further research is required to elucidate the early pathogenesis of hypertension. In particular, there is a need to study haemodynamic and biochemical correlates of blood pressure level and change in early life.

(8) The possible effects of level and change of blood pressure in childhood on early athero- and thrombogenesis should be investigated.

(9) The relationships between blood pressure and the following dietary elements need more extensive investigation:

(*i*) dietary electrolytes (sodium, potassium, calcium);
(*ii*) dietary proteins, lipids, and fibre;
(*iii*) alcohol;
(*iv*) total energy.

(10) Further research is needed to evaluate the effects on the level and evolution of blood pressure in children of alterations in the following variables:

(*i*) dietary intake of electrolytes, proteins, lipids, alcohol;
(*ii*) body weight;
(*iii*) physical activity;
(*iv*) smoking habits.

(11) The potential value of preventing hypertension needs to be assessed by observational studies of naturally occurring blood pressure changes in the population as well as by intervention studies to lower blood pressure and to prevent the rise of blood pressure with age.

(12) Preventive activities in childhood should be consistent with those employed in adults; they should focus primarily on the population as a whole rather than on isolated children with high blood pressure detected through special screening programmes.

(13) As a prudent measure, it is recommended that community programmes are implemented to encourage moderate intakes of total energy, sodium, and alcohol, as well as to stimulate physical activity in the young in populations where adult hypertension is a major health problem.

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REFERENCES

1. WHO Technical Report Series, No. 168, 1959 (*Hypertension and coronary heart disease: classification and criteria for epidemiological studies:* first report of the Expert Committee on Cardiovascular Diseases and Hypertension).
2. WHO Technical Report Series, No. 231, 1962 (*Arterial hypertension and ischaemic heart disease: preventive aspects:* report of a WHO Expert Committee).
3. WHO Technical Report Series, No. 628, 1978 (*Arterial hypertension:* report of a WHO Expert Committee).
4. WHO Technical Report Series, No. 686, 1983 (*Primary prevention of essential hypertension:* report of a WHO Scientific Group).
5. EPSTEIN, F.H. & ECKOFF, R.D. The epidemiology of high blood pressure – geographic distributions and etiological factors. In: Stamler, J. & Stamler, R., ed. *The epidemiology of hypertension.* New York, Grune & Stratton, 1967, pp. 155–166.
6. Pooling project research group. Relationship of blood pressure, serum cholesterol, smoking habit, relative weight and ECG abnormalities to incidence of major coronary events. *Journal of chronic diseases,* **31**: 210–306 (1978).
7. PRIOR, I.A.M. ET AL. Sodium intake and blood pressure in two Polynesian populations. *New England journal of medicine,* **279**: 515–520 (1968).
8. PAGE, L.B. ET AL. Antecedents of cardiovascular disease in six Solomon Islands societies. *Circulation,* **49**: 1132–1146 (1974).
9. PRIOR, I.A.M. ET AL. The Tokelau Island migrant study. *International journal of epidemiology,* **3**: 225–232 (1974).
10. BEAGLEHOLE, R. ET AL. Blood pressure in Tokelauan children in two contrasting environments. *American journal of epidemiology,* **108**: 283–288 (1978).
11. Report of a subcommittee of the postgraduate education committee, American Heart Association. Recommendations for human blood pressure determination by sphygmomanometers. *Circulation,* **64**: 510A–519A (1981).
12. Report of the Task Force on blood pressure control in children, US National Heart, Lung and Blood Institute. *Pediatrics,* **59** (suppl.): 797–820 (1977).
13. CURB, J.D. ET AL. Training and certification of blood pressure observers. *Hypertension,* **5**: 610–614 (1983).
14. WRIGHT, B.M. & DORE, C.F. A random-zero sphygmomanometer. *Lancet,* **1**: 337–338 (1970).
15. ROSE, G.A. ET AL. A sphygmomanometer for epidemiologists. *Lancet,* **1**: 296–300 (1964).
16. LABARTHE, D.R. ET AL. Evaluation of performance of selected devices for measuring blood pressure. *American journal of cardiology,* **32**: 546–553 (1973).
17. FOLSON, A.R. & PRINEAS, R.J. Drinking water composition and blood pressure: a review of the epidemiology. *American journal of epidemiology,* **115**: 818–832 (1982).
18. ARNTZENIUS, A.C. ET AL. Measurement of blood pressure. In: Kesteloot, H. & Joossens, J.V., ed. *Epidemiology of arterial blood pressure.* The Hague, Martinus Nijhoff, 1981, pp. 3–28.
19. PRINEAS, R.J. ET AL. The Minneapolis children's blood pressure study. Part 1. Standards of measurement for children's blood pressure. *Hypertension,* **2** (suppl. I): 118–124 (1980).

20. FEINLEIB, M. ET AL. Relationship between blood pressure and age: regression analysis of longitudinal data. *Presented at the 97th annual meeting of the American Public Health Association, Philadelphia, 1969.*
21. ROSNER, B. The analysis of longitudinal data in epidemiologic studies. *Journal of chronic diseases,* **32**: 163–173 (1979).
22. DARBY, S. & FEAR, T. The Chatham blood pressure study. An application of Bayesian growth curve models to a longitudinal study of blood pressure in children. *International journal of epidemiology,* **8**: 15–21 (1979).
23. VOORS, A.W. ET AL. Time course studies of blood pressure in children – The Bogalusa Heart Study. *American journal of epidemiology,* **109**: 320–334 (1979).
24. LAIRD, N.M. & WARE, J.H. Random-effects models for longitudinal data. *Biometrics,* **38**: 963–974 (1982).
25. LEHANE, A. ET AL. Reporting of blood pressure data in medical journals. *British medical journal,* **2**: 1603–1604 (1980).
26. JONSEN, A.R. Research involving children: recommendations of the national commission for the protection of human subjects of biomedical and behavioural research. *Pediatrics,* **62**: 131–136 (1978).
27. Research involving children – ethics, the law, and the climate of opinion. (Editorial). *Archives of diseases in childhood,* **53**: 441–442 (1978).
28. DWORKIN, G. Legality of consent to nontherapeutic medical research on infants and young children. *Archives of diseases in childhood,* **53**: 443–446 (1978).
29. JUDSON, C.F. & NICHOLSON, P. Blood pressure in normal children. *American journal of diseases of children,* **8**: 257–278 (1914).
30. STOCKS, P. Blood pressure in early life. A statistical study. London, Cambridge University Press, 1924.
31. SZKLO, M. Epidemiologic patterns of blood pressure in children. *Epidemiological review,* **1**: 143–169 (1979).
32. LABARTHE, D.R. Blood pressure studies in children throughout the world. In: Gross, F. & Strasser, T., ed. *Mild hypertension.* New York, Raven Press, 1983, pp. 85–96.
33. KOTCHEN, J.M. ET AL. Blood pressure trends with age. *Hypertension,* **4** (suppl. III): 128–134 (1982).
34. FROHLICH, E.D. ET AL. Re-examination of the hemodynamics of hypertension. *American journal of medicine,* **257**: 9–23 (1969).
35. WIDIMSKY, J. ET AL. Changes of cardiac output in hypertensive disease. *Cardiologia,* **31**: 381–389 (1957).
36. LUND-JOHANSON, P. *Hemodynamics in early essential hypertension.* PhD thesis, University of Bergen, Bergen, 1967.
37. TARAZI, R.C. & DUSTAN, H.P. The hemodynamics of labile hypertension. In: Strauss, J., ed. *Pediatric cardiology.* New York, Plenus Press, 1976, pp. 96–108.
38. FOUAD, F.M. ET AL. Hemodynamics of essential hypertension in young subjects. *American heart journal,* **96**: 646–654 (1978).
39. GOLDRING, D. ET AL. Blood pressure in a high school population. II. Clinical profile of the juvenile hypertensive. *Journal of pediatrics,* **95**: 298–304 (1979).
40. HOFMAN, A. ET AL. Hemodynamics, plasma noradrenaline and plasma renin in hypertensive and normotensive teenagers. *Clinical Science,* **61**: 169–174 (1981).
41. HOFMAN, A. ET AL. Blood pressure and hemodynamics in teenagers. *British heart journal,* **48**: 377–380 (1982).
42. SCHIEKEN, R.M. ET AL. Left ventricular hypertrophy in children in the upper quintile of the blood pressure distribution. *Hypertension,* **3**: 669–674 (1981).

43. SCHIEKEN, R.M. ET AL. The cardiovascular responses to exercise in children across the blood pressure distribution. *Hypertension,* **5**: 71–78 (1983).
44. FEINLEIB, M. ET AL. Environmental and genetic factors affecting the distribution of blood pressure in children. In: Lauer, R.M. & Shekelle, R.B., ed. *Childhood prevention of atherosclerosis and hypertension.* New York, Raven Press, 1980, pp. 271–279.
45. MCINHANY, M.L. ET AL. The heritability of blood pressure: an investigation of 200 twin pairs using the cold pressor test. *Johns Hopkins medical journal,* **136**: 57–64 (1975).
46. HAVLIK, R.J. ET AL. Blood pressure aggregation in families. *American journal of epidemiology,* **109**: 512–516 (1979).
47. LEVINE, R.S. ET AL. Blood pressure in infant twins: birth to six months of age. *Hypertension,* **2** (suppl.): 29–33 (1980).
48. LEVINE, R.S. ET AL. Genetic variance of blood pressure levels in infant twins. *American journal of epidemiology,* **116**: 759–764 (1982).
49. BIANCHI, G. ET AL. A renal abnormality as a possible cause of "essential" hypertension. *Lancet,* **1**: 173–177 (1979).
50. NANCE, W.E. & COREY, L.A. Genetic models for the analysis of data from families of identical twins. *Genetics,* **83**: 811–826 (1976).
51. NANCE, W.E. The role of twin studies in human quantitative genetics. *Progress in medical genetics* (New series) **3**: 73–109 (1979).
52. ROSE, R.J. ET AL. Aggregation of blood pressure in families of identical twins. *American journal of epidemiology,* **109**: 503–511 (1979).
53. NANCE, W.E. ET AL. Monozygotic twin kinship: a new design for genetic epidemiologic research. In: Morton, N.E. & Chung, C.S., ed. *Genetic epidemiology.* New York, Academic Press, 1978, pp. 87–132.
54. ANNEST, J.L. ET AL. Familial aggregation of blood pressure and weight in adoptive families. I. Comparisons of blood pressure and weight statistics among families with adopted, natural, or both natural and adopted children. *American journal of epidemiology,* **110**: 479–491 (1979).
55. ANNEST, J.L. ET AL. Familial aggregation of blood pressure and weight in adoptive families. II. Estimation of the relative contributions of genetic and common environmental factors to blood pressure correlations between family members. *American journal of epidemiology,* **110**: 492–503 (1979).
56. BIRON, P. ET AL. Familial aggregation of blood pressure in adopted and natural children. In: Paul, O., ed. *Epidemiology and control of hypertension.* Chicago, Yearbook Medical Publishers, 1975, pp. 397–405.
57. TELL, G.S. Blood pressure related to growth and development in children and adolescents: a review (in press).
58. TANNER, J.M. *Growth at adolescence.* Oxford, Blackwell, 1962.
59. TANNER, J.M. ET AL. *Assessment of skeletal maturity and prediction of adult height (TW2 Method).* London, Academic Press, 1975.
60. RICHEY, H.G. The blood pressure in boys and girls before and after puberty. *American journal of diseases of children,* **42**: 1281–1330 (1931).
61. BERESFORD, A.A. & HOLLAND, W.W. Levels of blood pressure in children: a family study. *Proceedings of the Royal Society of Medicine,* **66**: 1009–1012 (1973).
62. KOTCHEN, J.M. ET AL. Blood pressure distribution of urban adolescents. *American journal of epidemiology,* **99**: 315–324 (1974).
63. LONDE, S. ET AL. Blood pressure and puberty. *Journal of pediatrics,* **87**: 896–900 (1975).

64. LAUER, R.M. ET AL. Coronary heart disease risk factors in school children: The Muscatine study. *Journal of pediatrics*, **86**: 697–706 (1975).
65. VOORS, A.W. ET AL. Studies of blood pressure in children, ages 5–14 years, in a total biracial community. *Circulation*, **54**: 319–327 (1976).
66. VOORS, A.W. ET AL. Blood pressure of children, ages 2½–5½ years, in a total community – The Bogalusa Heart Study. *American journal of epidemiology*, **107**: 403–411 (1978).
67. CORNONI-HUNTLEY, J. ET AL. Blood pressure in adolescence – The United States Health Examination Survey. *Hypertension*, **1**: 566–571 (1979).
68. VOORS, A.W. ET AL. Relation of blood pressure to stature in healthy young adults. *American journal of epidemiology*, **115**: 833–840 (1982).
69. CHIANG, B.N. ET AL. Overweight and hypertension – a review. *Circulation*, **39**: 403–421 (1969).
70. HEYDEN, S. ET AL. Elevated blood pressure levels in adolescents, Evans County, Georgia. *Journal of the American Medical Association*, **2**: 1683–1689 (1969).
71. PAFFENBARGER, R.S. ET AL. Chronic disease in former college students. VIII. Characteristics in youth predisposing to hypertension in later years. *American journal of epidemiology*, **88**: 25–32 (1968).
72. FALKNER, B. ET AL. Cardiovascular characteristics in adolescents who develop essential hypertension. *Hypertension*, **3**: 521–527 (1981).
73. HOFMAN, A. & VALKENBURG, H.A. Determinants of change in blood pressure during childhood. *American journal of epidemiology*, **117**: 735–743 (1983).
74. LANGFORD, H.G. Symposium on obesity and hypertension. *Journal of chronic diseases*, **35**: 875–876 (1982).
75. HEYDEN, S. Diet treatment of obese hypertensives. *Clinical science*, **45**: 209s–212s (1973).
76. REISIN, E. ET AL. Effects of weight loss without salt restriction on the reduction of blood pressure in overweight hypertensive patients. *New England journal of medicine*, **298**: 1–6 (1978).
77. ZINNER, S.H. ET AL. Stability of rank and urinary kallikrein concentration in childhood. *Circulation*, **58**: 908–915 (1978).
78. GOLDSTEIN, D.S. Plasma norepinephrine in essential hypertension. A study of studies. *Hypertension*, **3**: 48–52 (1981).
79. GOLDSTEIN, D.S. Plasma catecholamines and essential hypertension. An analytical review. *Hypertension*, **5**: 86–99 (1983).
80. AMBARD, L. & BEAUJARD, E. Causes de l'hypertension artérielle. *Archives générales de médecine*, **1**: 520–533 (1904).
81. FREIS, E.D. Salt, volume and the prevention of hypertension. *Circulation*, **53**: 589–595 (1976).
82. MENEELY, G.R. & BATTARBEE, H.D. High sodium–low potassium environment and hypertension. *American journal of cardiology*, **38**: 768–785 (1976).
83. SIMPSON, F.O. Salt and hypertension: a sceptical review of the evidence. *Clinical science*, **57** (suppl. 5): 463–479 (1979).
84. SWALES, J.D. Dietary salt and hypertension. *Lancet*, **2**: 1177–1179 (1980).
85. PICKERING, G. Dietary sodium and human hypertension. In: Laragh, J.H. et al., ed. *Frontiers in hypertension research*. New York, Springer, 1981, pp. 37–42.
86. DAHL, L.K. ET AL. Effects of chronic salt ingestion. *Journal of experimental medicine*, **115**: 1173–1190 (1962).
87. HOFMAN, A. ET AL. A randomized trial of sodium intake and blood pressure in newborn infants. *Journal of the American Medical Association*, **250**: 370–373 (1983).

88. PARIJS, J. ET AL. Moderate sodium restriction and diuretics in the treatment of hypertension. *American heart journal,* **85**: 22–34 (1973).
89. MORGAN, T. ET AL. Hypertension treated by salt restriction. *Lancet,* **1**: 227–230 (1978).
90. HOLLY, J.M.P. ET AL. Re-analysis of data in two Lancet papers on the effect of dietary potassium on blood pressure. *Lancet,* **2**: 1384–1387 (1981).
91. MACGREGOR, G.A. ET AL. Double-blind randomised cross-over trial of moderate sodium restriction in essential hypertension. *Lancet,* **1**: 351–355 (1982).
92. COOPER, R. ET AL. Urinary sodium excretion and blood pressure in children: absence of a reproducible association. *Hypertension,* **5**: 135–139 (1983).
93. COSTA, F.V. ET AL. Effects of a low-salt diet and of acute salt loading on blood pressure and intralymphocytic sodium concentration in young subjects with borderline hypertension. *Clinical science,* **61**: 21s–23s (1981).
94. MCCARRON, D.A. Calcium and magnesium in human hypertension. *Annals of internal medicine,* **98**: 800–805 (1983).
95. RESNICK, R.M. ET AL. Divalent cations in essential hypertension. *New England journal of medicine,* **309**: 888–891 (1983).
96. DYCKNER, T. & WESTER, P.O. Effect of magnesium on blood pressure. *British medical journal,* **286**: 1847–1849 (1983).
97. DWYER, T. ET AL. An investigation of the effects of daily physical activity on the health of primary school students in South Australia. *International journal of epidemiology,* **12**: 308–313 (1983).
98. SCHROEDER, H.A. The role of trace elements in cardiovascular diseases. *Medical clinics of North America,* **58**: 381–386 (1974).
99. COHEN, S. ET AL. Physiological, motivational and cognitive effects of aircraft noise on children. *American psychologist,* **35**: 231–243 (1980).
100. CASSEL, J. Studies of hypertension in migrants. In: Paul, O., ed. *Epidemiology and control of hypertension.* New York, Grune & Stratton, 1975, pp. 41–58.
101. PETO, R. The horse-racing effect (letter). *Lancet,* **2**: 467–468 (1981).
102. SVARDSUDD, K. & TIBBLIN, G. A longitudinal blood pressure study. Change of blood pressure during 10 years in relation to initial values. *Journal of chronic diseases,* **33**: 627–639 (1980).
103. WU, M. ET AL. On the relation between blood pressure change and initial value. *Journal of chronic diseases,* **33**: 637–644 (1980).
104. JENSS, R.M. Age variations of systolic blood pressure in United States Army officers. *American journal of hygiene,* **20**: 574–603 (1934).
105. WARE, J.H. & WU, M.C. Tracking: prediction of future values from serial measurements. *Biometrics,* **37**: 427–438 (1981).
106. FOULKES, M.A. & DAVIS, C.E. An index of tracking for longitudinal data. *Biometrics,* **37**: 439–446 (1981).
107. MCMAHAN, C.A. An index of tracking. *Biometrics,* **37**: 447–455 (1981).
108. ZINNER, S.H. ET AL. A longitudinal study of blood pressure in childhood. *American journal of epidemiology,* **100**: 437–442 (1975).
109. DESWIET, M. ET AL. Blood pressure survey in a population of newborn infants. *British medical journal,* **2**: 9–11 (1976).
110. BEAGLEHOLE, R. ET AL. A longitudinal study of blood pressure in Polynesian children. *American journal of epidemiology,* **105**: 87–89 (1977).
111. ROSNER, B. ET AL. Age specific correlation analysis of longitudinal blood pressure data. *American journal of epidemiology,* **106**: 306–313 (1977).

112. CLARKE, W.R. ET AL. Tracking of blood lipids and blood pressure in children. *Circulation,* **58**: 626–634 (1978).
113. LEVINE, R.S. ET AL. Tracking correlations of blood pressure levels in infancy. *Pediatrics,* **61**: 121–125 (1978).
114. VOORS, A.W. ET AL. Time course studies of blood pressure in children – The Bogalusa Heart Study. *American journal of epidemiology,* **109**: 320–334 (1979).
115. HIAT, H.I. ET AL. A longitudinal study of blood pressure in a national survey of children. *American journal of public health,* **172**: 1285–1287 (1982).
116. HOFMAN, A. ET AL. The natural history of blood pressure in childhood. *International journal of epidemiology,* **13**: 416–422 (1984).
117. LAUER, R.M. ET AL. Levels, trend and variability. *Circulation,* **69**: 242–249 (1984).
118. FIXLER, D.E. & LAIRD, W.P. Validity of mass blood pressure screening in children. *Pediatrics,* **72**: 459–461 (1983).
119. ROSE, G. Strategy of prevention: lessons from cardiovascular disease. *British medical journal,* **1**: 1847–1851 (1981).
120. WHO Technical Report Series, No. 678, 1982 (*Prevention of coronary heart disease:* report of a WHO Expert Committee).