A Longitudinal Study of Blood Pressure

By William R. Harlan, M.D., Robert K. Osborne, M.D., and Ashton Graybiel, Capt. (MC) USN

Individual physiologic characteristics, and environmental and genetic factors have been implicated in the alteration of blood pressure and in the pathogenesis of essential hypertension. It is recognized that those factors which influence blood pressure can be identified and evaluated only through a prospective study of an initially healthy population. Thus far there have been no longitudinal studies of blood pressure within a single group, and the major part of our knowledge has been derived from retrospective analysis or cross-sectional studies of presumably normal populations. These limited observations have led to conflicting interpretations concerning the nature of hypertension and the importance of various factors in its pathogenesis.

Pickering has challenged the classical concept that essential hypertension is a specific disease entity by presenting evidence that in a general population blood pressure represents a continuous variable with the hypertensive and nonhypertensive segments defined by an arbitrary division line.1,2 His thesis is that the hypertensive segment displays no discrete difference from that of the remaining segment and that hypertension is attributable to a multifactorial genetic inheritance rather than to the influence of a single gene. In support of the classical concept are the findings of Platt3 and of Morrison and Morris4 demonstrating bimodality in frequency distribution curves of blood pressure. Starting with a general population whose blood pressures represented a continuous variable, they replotted the data after separating them into two groups, the people with parents who died prior to age 60 and, the second, those alive through age 60. These curves and those based on plots of hypertensive probands and their siblings showed a bimodal distribution. This was taken as evidence in support of the thesis that the segment of the population with elevated blood pressure differs qualitatively from the normal segment and that this difference lies in the inheritance of a single gene which determines the disease, hypertension.

The available data are susceptible to different interpretations, and McKusick5 has indicated the need for a prospective study that would allow evaluation of both environmental influences and hereditary factors. The present report describes the findings in a longitudinal study of a homogeneous group of white men followed over an 18-year period. The results support the concept that hypertension is a quantitative difference in blood pressure resulting from a multiplicity of factors, both genetic and environmental.

Materials and Methods

In 1940, a group of 1,056 healthy white men were evaluated by a team of investigators sponsored by the Harvard Fatigue Laboratory. This group was composed of men previously selected for Naval Flight Training partially on the basis of meeting physical standards, and subsequent to this selection no subject has been eliminated from the group. The mean age in 1940 was 23.6 years (± 3.6 years). Each subject entered the study at an optimal weight and with a supine blood pressure under 132/86 mm. Hg. A number of physiologic and psychologic studies were performed in an attempt to delineate factors of importance in pilot selection. A monograph describes in detail the composition of the group, the studies performed, and the group performance.6 Surviving members of the original group were re-examined in 1951-52, and several reports have described various aspects of this examination.7,8 In 1957-58, these men were re-evaluated. During this period 785 men were examined, and this represents over 96 per cent of the surviving men.

From the Departments of Medicine and Biochemistry, Duke University, Durham, North Carolina; the Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts; and the U. S. Naval School of Aviation Medicine, Pensacola, Florida.
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members. All deaths within the group have been verified, and in most cases the exact cause has been documented with hospital records or post-mortem reports. Only three members of the original group could not be located. The data presented are derived from the serial examinations.

Blood pressure measurements in 1940 included a "casual" blood pressure recorded in the supine position, and a "basal" blood pressure recorded in connection with a cold pressor test performed in the manner described by Hines and Brown. Measurement of height and weight, and an electrocardiogram were performed. Profile nude photography was accomplished with somatotyping of body characteristics under the direction of Dr. W. H. Sheldon.10

Subsequent examinations have included a medical history with special emphasis on family history and personal habits and a complete physical examination with special attention directed to the cardiovascular system. The examinations in 1957-58 were performed either in convenient government facilities or in the home of the subject. Laboratory evaluations in the present follow-up included 12-lead electrocardiograms with standard exercise test, chest x-ray, and measurement of serum cholesterol and lipoproteins.

The blood pressure measurements reported are "casual" blood pressures recorded in the supine position midway through the physical examination. Blood pressure was recorded with a standard 13-cm. cloth cuff and mercury manometer. Systolic pressure was read with the appearance of sounds and diastolic at the point of disappearance of Korotkoff sounds. In 1940 and in 1958, the scale was read to the nearest even number. An effort was made to minimize "number bias." During the 1952 examination, no special care was taken to avoid number bias, and this point receives further attention below. Only the first reading obtained in the supine position has been analyzed, but blood pressure was recorded in other positions and after a period of rest. Arm circumference was measured with a flexible tape in 200 subjects.

All data were coded and placed on IBM cards to facilitate analysis. The compiled data were used to construct a large matrix of Pearson correlation coefficients through use of an IBM 704 computer. This complete correlation matrix will be presented in a separate communication.

Results

A series of frequency distribution curves for systolic and diastolic blood pressure are plotted against age (fig. 1). These curves were plotted by grouping the recorded blood pressures at 5-mm. Hg intervals and the age at 5-year intervals. All curves are composed of serial blood pressure measurements on the same group. The number, mean, and standard deviation of the blood pressure have been noted for each group. The first pair of curves (the 15 to 19 year group) were derived from physical examinations recorded prior to the initiation of this study, but have been included for comparison. The abrupt cut in the upper limb of the diastolic curve represents the cut-off point for qualification in the flight program. In the 1952 examination there was no effort to avoid number bias. The exact plots of systolic and diastolic blood pressure recorded during this examination are presented in figure 2. This indicates the probable effect of unconscious "number avoidance" with a tendency of the examiners in 1952 to avoid 115 mm. Hg and 125 mm. Hg systolic and 75 mm. Hg diastolic. This phenomenon has been noted previously and suggested as a source of bimodality in curves presented from other studies. The curves for 30 to 34 years and 35 to 39 years have been altered by averaging data from either sides of these points. No alterations have been made in the other curves as plotted directly from the data.

It is apparent from figure 1 that with increasing age the mean systolic and diastolic blood pressures increase and the distribution curves change in configuration. The curves broaden and assume a positive skew with a greater spread from the mode to the upper ranges. The lower segment remains relatively unchanged. These frequency distribution curves have a striking similarity to the curves derived by Hamilton et al. through cross-sectional sampling of a smaller population. This is true of the absolute values for blood

*The authors are indebted to Drs. R. A. McFarland, A. Damon, and W. H. Sheldon for making available the original photographs and interpretation.

†Both examiners were cognizant of the tendency for observers to prefer or to avoid certain numbers while taking and recording blood pressures. With this knowledge and after some practice, it was possible to minimize although not completely eliminate "number bias."

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Figure 1
Frequency distribution curves for blood pressure in the same group plotted at 5-year intervals.

pressure and the configuration of the curves. These curves suggest that there is a single population with regard to blood pressure. With the qualification that blood pressures recorded in 1952 represent an unnatural result of bias in recording, there is no evidence of bimodal distribution and no indication of the separation of qualitatively different groups.

Data from the other physiologic measure-
ments were further analyzed to distinguish characteristics that influenced relative standing within the distribution curve and were important in altering blood pressure. A correlation matrix is presented in table 1. The mean, standard deviation, and number of observations are listed at the bottom of the table. Correlations above 0.10 are significant at the 0.005 level of confidence. The important factors will be considered individually and then in relation to their influence on the relative standing of subjects within the population sample.

Age and Weight

The close association of the factors of age and weight requires that they be evaluated together. In figure 3 the systolic and diastolic blood pressure are plotted against age. The solid line represents the mean, and the shaded area one standard deviation above and below the mean. The linear increase of 7.06 mm. Hg in diastolic pressure is significant (p < 0.001) and the over-all regression coefficient is 0.20. The curve for systolic blood pressure is flat and the increase of 2.31 mm. Hg is less significant (p < 0.01). The mean pulse pressure decreased from 48.9 (±9.27) to 45.3 (±9.87). These curves illustrate the increase in arterial pressure with age and the increasing variance of both systolic and diastolic blood pressure comparable to the skewing of the frequency distribution curves. The regression curve for mean diastolic pressure can be superimposed exactly on the plot presented by Hamilton et al.12 and agrees favorably also with data collected by Gover.13 The curve for systolic pressure begins to plateau in contrast to the results of Hamilton et al. (represented by the broken line). Our curve for systolic pressure resembles that plotted by Mail1 and Oldham14 for male subjects in the Welsh mining valley.

Table 1

<table>
<thead>
<tr>
<th>Correlation Matrix of Important Variables</th>
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</thead>
<tbody>
<tr>
<td>1940 Systolic mm. Hg</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>1940 Systolic mm. Hg</td>
</tr>
<tr>
<td>1940 Diastolic mm. Hg</td>
</tr>
<tr>
<td>1952 Systolic mm. Hg</td>
</tr>
<tr>
<td>1952 Diastolic mm. Hg</td>
</tr>
<tr>
<td>1958 Systolic mm. Hg</td>
</tr>
<tr>
<td>1958 Diastolic mm. Hg</td>
</tr>
<tr>
<td>Weight change 1940-58</td>
</tr>
<tr>
<td>Weight/height 1958</td>
</tr>
<tr>
<td>Endomorphy</td>
</tr>
<tr>
<td>Mesomorphy</td>
</tr>
<tr>
<td>Ectomorphy</td>
</tr>
</tbody>
</table>

Mean | 120.70 | 71.78 | 123.70 | 76.13 | 123.01 | 77.71 | 17.48 | 2.494 | 3.16 | 4.42 | 3.13 |
Standard deviation | ±8.59 | ±7.73 | ±13.43 | ±10.73 | ±13.51 | ±9.74 | ±14.21 | ±0.256 | ±0.92 | ±0.85 | ±1.07 |
Number | 755 | 755 | 695 | 695 | 744 | 744 | 770 | 771 | 659 | 659 | 659 |

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Maill and Oldham demonstrated a plateau in the 20 to 40 age group followed by a rising systolic pressure in succeeding decades. There is no ready explanation for this difference except the relatively short span of this study and the young age of the subjects.

It is difficult to determine the amount of blood pressure increase that is attributable solely to age. Other factors influence blood pressure change concomitantly. The mean weight change in this group of +17.5 pounds over the 18-year period indicates that increasing age was associated with a significant increase in weight. In a subgroup of 124 subjects, who remained within 5 pounds of their original weight, the mean increment for systolic pressure was 1.0 mm. Hg, and for diastolic 3.4 mm. Hg. The difference in the increment of blood pressure between this subgroup and the group gaining weight is significant with respect to diastolic pressure \( (p < 0.01) \). When the additional variable of positive family history of vascular disease was removed from this subgroup, the 78 remaining subjects had a change in diastolic of 2.5 mm. Hg. This change in diastolic pressure did not prove to be significant. Thus, after the elimination of other variables known to influence blood pressure, age alone did not appear to have a significant effect on blood pressure over the interval of study.

Correlations between 1958 blood pressure and the variables of weight in 1958, weight change from 1940 to 1958, and ponderal ratio (weight/height) demonstrated that weight has a significant relationship to blood pressure. These correlation coefficients range from 0.20 to 0.28. Not shown in table 1 are correlations between weight and weight/height in 1940 and diastolic blood pressure in 1940, which are 0.05 and 0.07 respectively. When the subjects were young and at optimal weight, there was no significant relation between weight and blood pressure. In 1958, a significant relationship was demonstrable between the ponderal ratio (weight/height) and systolic pressure (0.26) and diastolic pressure (0.28). Correlations with mean body radius (R) and per cent deviation from standard weight (Metropolitan Life Tables) had values approximating the weight/height correlation. As previously noted, subjects gaining weight had a significantly greater increment in systolic and diastolic blood pressure than subjects maintaining their weight within 5 pounds of their original weight, and this significant difference was maintained when the division between groups was moved to 10 pounds or to 15 pounds. There was a large degree of individual variability within the groupings for weight change. Within this variability modifying relationships could be demonstrated with the parameters of somatotyping and family history.

**Somatotyping**

The body characteristics of endomorphy, mesomorphy, and ectomorphy were scored as described by Sheldon et al. Data were available on 659 of the 785 men examined in 1958. The mean scores for the group are presented in table 1. The predominance of mesomorphic
rating probably represents a selection of this type of individual for flying. In addition to the three classifications, another grouping was made by addition of mesomorphic and endomorphic scores in an effort to include a group not having clear dominance of either component but a significant preponderance of a combination of these features.

No significant correlations were present between blood pressure in 1940 and body configuration; for 1958, however, significant correlations were noted. With diastolic pressure, endomorphy had a positive correlation of 0.17 and ectomorphy a negative 0.17 relationship. The correlation with mesomorphy was not significant, but mesomorphy-endo- morphy had a value of 0.19. Slightly smaller coefficients with the same relative strength were present for change in systolic and diastolic blood pressure from 1940 to 1958. Somatotype had an insignificant correlation with weight change during the interval of study, but body habitus did have a significant relationship with the ponderal ratio. The latter had correlation coefficients of 0.35 (endomorphy), 0.12 (mesomorphy), −0.33 (ectomorphy), and 0.24 (endomorphy-meso- morphy). The relationship between somatotype and blood pressure might be explained by a propensity of one body type to gain excessive weight, a specific effect of somatotype on blood pressure regardless of weight change, or a modifying influence of somatotype on the change induced by weight gain.

In table 2, the influence of weight and somatotype on increments of systolic and diastolic blood pressure have been analyzed. The significant difference in the blood pressure increment between the group maintaining constant weight and the group gaining weight has been mentioned. The subjects are grouped in table 2 on the basis of their predominant body characteristics. The total score for the three body features in a single subject is about 10.5, and each group is composed of subjects with a score of 4.5 or more for a single component. The group with ectomorphic characteristics had significantly less increase in diastolic pressure with weight gain (4.4 mm. Hg) than groups with mesomorphy (7.6 mm. Hg), endomorphy (11.1 mm. Hg), or mesomorphy-endomorphy (8.7 mm. Hg). All differences are significant (p < 0.01 or greater). In comparing groups with constant weight, the mean change in diastolic pressure was less in the ectomorphic group, but this change was not significant (p < 0.1). The endomorphic group had a significantly greater increment in diastolic pressure with weight gain. In each classification weight gain is accompanied by an increased increment of blood pressure, but this difference is most marked in the endomorphic and ectomorphic groups.

From these data, it would appear that differences in blood pressure increment are associated with external body characteristics. These differences in blood pressure increment probability.
with somatotype are influenced by weight gain. There is the possibility that these differences are artifactitious and related to spurious recording of arterial pressure due to varying arm size. Arm circumference was measured in 200 of the subjects and there was no direct relationship between blood pressure and an arm size between 26 and 33 cm. Above this range larger arms were associated with higher pressures. Unfortunately, there were no serial measurements of arm size available.

Family History

The information used for the analysis of family history was that obtained on the most recent evaluation in 1958. At this time the average age of the subjects was 41.2 years (±2.3 years) and it would be anticipated that their parents would be over 60 years and have symptomatic complications or be cognizant of vascular disease. The data were analyzed by separation into a group with no known family history of vascular disease and several groups with a positive family history. These latter groups were: family history of vascular disease with death prior to 60, history of vascular disease with death after age 60, and history of vascular disease alive after 60 years. No significant correlations were derived between these classifications and the variables of blood pressure, weight, ponderal ratio, and somatotype. Investigation of a subgroup giving a family history of known hypertension yielded no significant difference in the mean blood pressure in either 1940 or 1958.

The change in blood pressure from 1940 to 1958 was investigated after dividing the subjects into two groups: those with no family history of vascular disease and those with a positive family history (hypertension, atherosclerotic heart disease, and cerebrovascular accident). With this classification there was a difference in the mean diastolic increment over the 18-year interval. In the group with a positive history this increment was 7.4 mm Hg and in the group with a negative family history, 5.1 mm Hg. This difference was significant (p < 0.005). A further classification into categories of no gain in weight and gain of over 5 pounds is presented in table 3. The influence of a positive family history was not dependent upon weight gain, but gain in weight did influence the degree of change in diastolic blood pressure. The difference in the increase in blood pressure in these two groups was present throughout the entire range of blood pressure and not confined to a particular segment of the group.

Characteristics within the Distribution Curves

From the results of the entire group, the characteristics of groupings within the frequency distribution curves were investigated. The distribution curve for diastolic blood pressure for the three examinations was divided arbitrarily at the mean and roughly one standard deviation above and below the mean. The first consideration was whether there was a tendency for each individual to maintain his relative standing within the frequency distribution curves throughout the period of study. A chi-square analysis for consistency of ranking in the four groups on serial examination indicated that the probability was small—that the ranking of an individual was on a random basis (p < 0.001). This is consistent with the significant correlations for systolic and diastolic blood pressure.

Table 3

<table>
<thead>
<tr>
<th>Family History</th>
<th>Less than 5 lbs.</th>
<th>More than 5 lbs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative family history</td>
<td>(N) (402) 5.1 mm Hg</td>
<td>(N) (34) 2.5 mm Hg</td>
</tr>
<tr>
<td>Positive family history</td>
<td>(N) (291) 7.4 mm Hg</td>
<td>(N) (324) 5.8 mm Hg</td>
</tr>
</tbody>
</table>

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pressure on the three examinations. The characteristics of the upper and lower groups (greater than one standard deviation from mean) are listed in table 4 and are compared with findings for the entire group.

Review of the findings in 1940 indicates no difference between the characteristics of the groups at the ends of the distribution range. The distribution of the group with regard to blood pressure occurred independently of any of the measured variables.

In 1952 and 1958 significant differences were present in the characteristics of the upper and lower groups. The lower group was recruited from individuals with pressures below the mean in 1940. In addition, these individuals had gained less weight and had a smaller ponderal ratio (weight/height). The upper group in 1952 and 1958 was derived from the group with blood pressures above the mean in 1940. They had a significantly greater weight gain and ponderal ratio and had strong endomorphic characteristics with a paucity of ectomorphic features. All differences between the upper and lower groups in 1952 and 1958 are significant (p < 0.01 for all features). Ranking according to blood pressure in 1940 was not determined by any of the parameters measured although factors that influenced this standing may not have been prominent enough to alter the means. There was a tendency for this relative ranking to be maintained during the period of study, rather than a random alteration. However, a significant modification of this distribution occurred as the result of genetic and environmental factors. Thus, the final ranking may be stated as being the resultant of two determinants: one influencing the standing of an individual in a population and not associated with any of the variables measured, and a second composed of genetic and environmental factors that were expressed during the period of study.

The upper groups in 1952 and 1958 deserve further scrutiny because of the close clinical association between elevated blood pressure and vascular disease. Members of this group

<table>
<thead>
<tr>
<th>Characteristics of Upper and Lower Groups within the Distribution Curve</th>
<th>1940</th>
<th>1958</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>Pressure (mm Hg)</td>
<td>132/76</td>
<td>123.7/78</td>
</tr>
<tr>
<td>+ 2.3/4.0</td>
<td>+ 2.4/4.5</td>
<td></td>
</tr>
<tr>
<td>Below 80</td>
<td>120/79</td>
<td>120/81</td>
</tr>
<tr>
<td>+ 1.1/3.6</td>
<td>+ 1.1/3.6</td>
<td></td>
</tr>
<tr>
<td>Above 80</td>
<td>133/85</td>
<td>133/74</td>
</tr>
<tr>
<td>+ 1.1/3.6</td>
<td>- 4.4/3.1</td>
<td></td>
</tr>
</tbody>
</table>

Table 4

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were investigated individually in an effort to assign a possible mechanism for their appearance within this group. It is recognized that this involves circuitous reasoning, as our assumptions of the importance of various factors arise from study of a group containing some of these individuals. An analysis was made of these various influences after elimination of this upper group and found not to be greatly different from the entire group. As mentioned previously, the majority of this group was derived from the segment above the mean in 1940. This meant that a smaller increment of blood pressure over the 18-year period was necessary for inclusion in the upper group. It should be noted that the mean blood pressure increase over the period of study was greater for the group below the mean in 1940 than for the group above the mean. Thus, the mechanism responsible for the relative ranking of the group on the first examination did not appear to regulate the change in blood pressure during the period of study.

Of the 117 subjects in the upper group in 1958, 10 had blood pressures greater than one standard deviation above the mean in 1940. Six of these subjects had a weight increase of 16 pounds or more. The mean change in blood pressure in these subjects was 11/11 mm. Hg, which is less than the change noted in the remainder of the upper group. Fifty-six members of the upper group had a positive family history, and in 45 of these this was associated with excessive weight gain. Eleven subjects had no weight gain and only a family history of vascular disease. There were 34 subjects with a negative family history of vascular disease but a weight increase of over 16 pounds. The majority of these subjects had a preponderance of mesomorphic or endomorphic characteristics and only three had a preponderance of ectomorphy. In 17 of the 117 subjects, none of the above mechanisms could be invoked to explain their elevated blood pressures. No attempt was made to rule out other etiologies of hypertension in this group, but presumably there are instances of secondary hypertension or labile elevations of blood pressure within this group. It is of interest that selecting a cut-off point at 95 mm. diastolic does not alter significantly the composition or characteristics of the “hypertensive” group. The physical and laboratory findings of this group were reviewed. The incidence of abnormalities in retinal vascular pattern, electrocardiogram, and heart size was the same within this group regardless of the proposed “mechanism” for the elevation of blood pressure.

Discussion

Within this group of men, blood pressure represented a continuous variable with quantitative differences subject to both genetic and environmental influences. Frequency distribution curves of blood pressure plotted against age for the same group over an 18-year interval demonstrated movement of a significant portion of the distribution toward higher values with little change in the lower segment. Inspection of the curves from this study revealed no natural point of segmentation and no indication that a separate group was emerging. A basic tenet of the thesis advanced by Platt is that bimodality would be expected to develop in the distribution curve of a population followed over a period of years. This second curve (or antemode) would be composed of a group with a single qualitative difference, the dominant gene for the disease, hypertension. Pickering and others have championed the view that elevated blood pressure represents a quantitative difference in a continuous variable, and no single, specific qualitative difference exists. With this concept, “hypertensive” would be a term applied to individuals exceeding an arbitrarily selected level and would not constitute a discrete entity. The etiology of the elevated blood pressure would be multiple and perhaps represent a quantitative difference in those factors normally causing an increase in blood pressure. Genetic influence would be multifactorial, also, rather than dependent on the expression of a single gene. Prior to this study the data presented were derived from cross-sectional studies or retrospective analy-
sis of blood pressure data not originally collected for this purpose.

The problem of unconscious observer bias in recording blood pressure was well illustrated in the data from the 1952 examination. Frequency distribution curves of blood pressure from this examination would appear to divide the population into several groups. Subsequent distribution curves did not display this segmentation and it would seem to be an artifact and not the result of a natural process. It has been noted previously that there is an unconscious avoidance of 5's in recording blood pressure.\textsuperscript{11} Retrospective plots of blood pressure from the study of Morrison and Morris\textsuperscript{4} have demonstrated bimodality and have been cited as evidence in favor of the emergence of a separate population. These conclusions have been criticized from the standpoint of observer bias, and the data from the present study serve to emphasize this as a possible source of error in the collection of data and confusion in its interpretation.

The longitudinal nature of this study permitted evaluation of physiologic and environmental factors that influence the change in blood pressure. Significant correlations were demonstrated between weight, change in weight, ponderal ratio (weight/height), and the blood pressure on follow-up examinations. Although operative throughout the entire range of blood pressure, the effect of weight was most impressive when the extremes of blood pressure distribution were examined. At the initial "ideal" weight (necessary for admission to the flight program) there was no relationship between weight or ponderal index and blood pressure. As the group assumed a less Spartan and more typically American life, however, with increasing weight and decreasing activity, differences were noted in the upper and lower segments of distribution. The upper group, composed of subjects with diastolic pressure of 88 mm. Hg and over, had a significantly greater gain in weight and increase in ponderal index. By contrast, the lower segment was composed of individuals with less weight gain, significantly lower ponderal index, and a decrease in blood pressure. At the extremes of blood pressure distribution the influence of weight change and of body mass was most marked.

There was considerable individual variation in the effect of increasing weight on blood pressure increment. Some of this variability was related to external body characteristics. Somatotyping had been performed when the subjects were young, near ideal weight, and structural attributes less obscured by environmental factors. Classification at this time would reflect genetic influence better than studies accomplished later in life.\textsuperscript{10} No significant correlation was present between body habitus and the distribution of blood pressure on the first examination. On subsequent examinations a significant relationship was present with endomorphy (+0.17) and ectomorphy (−0.17). Analysis of subjects grouped according to the predominant somatotype indicated that the change in blood pressure in the endomorphic group was significantly less than in the endomorphic or mesomorphic groups. This difference was present in a subgroup with no change in weight (±5 pounds), but was most prominent in the subgroup with an increase in weight. The endomorphic group gaining weight had a significantly greater increase in blood pressure than the other groups. The effect of weight gain on blood pressure was a function of somatotype. However, the influence of somatotype on the change in blood pressure was not limited to individuals gaining weight.

Several considerations are important in relating weight and body habitus to change in blood pressure. The possibility cannot be excluded that the changes in blood pressure recorded by indirect methods are not real and are related to changes in arm size. Ragan and Bordley\textsuperscript{15} have demonstrated the factitial elevation in indirect readings resulting from the use of a standard cuff on a large arm. More recently, a more comprehensive study by Birliner et al.\textsuperscript{16} indicated that "discrepancies between the direct and indirect methods were usually minor among the lean and moderately obese subjects and went in both

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directions.' In reviewing the ponderal indices of our group, there were none in the extreme categories listed by Birliner as having large discrepancies in the indirect readings. Measurement of arm circumference was performed in 200 subjects, and there appeared to be no systematic variation with blood pressure in the range between 26 and 33 cm. Outside of this range larger arms were associated with higher pressures and smaller arms with lower pressures. Whyte in an analysis of factors influencing blood pressure thought that arm size was of minor importance after the factors of age, weight, and body fatness had been excluded. It would appear that the relationship between weight and blood pressure is real. This is in agreement with the results reported by Fletcher on weight reduction in obese women and the studies by Keys, Henschel, and Taylor during controlled starvation. It is of interest that this is the first longitudinal study to document an increase in blood pressure related to weight gain.

The mechanism by which weight might affect arterial pressure is unknown. The fact that estimates of body mass have stronger correlations than weight or weight gain suggest that mass or surface area may be the more important determinants. This is consistent with the data on body configuration and pressure changes, since comparable weight gain in an ectomorphic individual should result in less change in body mass than in an endomorphic or mesomorphic individual. Whyte offers the intriguing suggestion that the increased bulk demands an increased cardiac output, and this forced into a vascular system that has not increased commensurately in volume. This suggestion perhaps represents an oversimplification and bypasses the buffering and regulatory properties of the autonomic nervous system. Another unexplored possibility is that external body features might reflect quantitative differences in electrolyte or renin-angiotensin metabolism. These differences would assume greater significance with weight gain and alterations in renal blood flow.

Clinical experience and studies of families leave little doubt that first-degree relatives tend to resemble each other in levels of blood pressure and that essential hypertension is genetically related. Determination of the strength of genetic factors and the mechanism is most profitably approached through recording of blood pressures in propositi and their relatives. Even in an intelligent group, the family history must be considered incomplete and perhaps inaccurate. Asymptomatic parental hypertension will often be unknown, whereas a history of symptomatic complications of vascular disease will be more readily obtained. With these considerations, it was not surprising that no strong relationship could be demonstrated between a family history of known hypertension and the development of elevated blood pressure. However, when the broad category of vascular disease (including hypertension and arteriosclerotic complications) was utilized as a point of division, there were significant differences in the increment of blood pressure during the period of study. These differences were influenced by gain in weight but were not dependent upon weight change for expression. The problem of equating arteriosclerotic complications with hypertensive vascular disease is evident, and the probable error in this approach has been documented. A significant relationship could be shown between the rise in blood pressure and a positive family history of vascular disease, and this factor was distinct from the other factors shown to influence blood pressure. This increased increment of blood pressure was present at all levels of blood pressure and not confined to a particular segment of the blood pressure distribution. In the group with elevated blood pressure the difference was quantitatively more impressive but presumably due to the same mechanism. There was no evidence that a positive family history separated a particular segment of the population or that the group with elevated blood pressure had a striking incidence of positive family history. These findings would be anticipated if hypertension were the expression of a single gene.
The genetically related factors of family history and somatotype were operative throughout the range of blood pressure with only quantitative differences being apparent.

It should be emphasized that these observations are compatible with the proposed participation of an angiotensin or angiotensin-aldosterone system in the pathogenesis of hypertension. Participation of this mechanism might occur as a primary factor active at the inception of elevated blood pressure or act in the propagation or perpetuation of elevated pressures initiated by other mechanisms. In the first instance, a proposed renal mechanism could be expressed either through inheritance or distribution of enzymatic activity coincident with the unexplained distribution of the group with regard to blood pressure on the initial examination. The preliminary observations of Wood\(^{21}\) tend to connect hereditary observations with a specific enzymatic mechanism. An alternate role for a humoral system might be in the perpetuation of elevated blood pressure initiated by other mechanisms such as obesity. The decrease in renal blood flow accompanying obesity may activate an angiotensin-aldosterone response as postulated by Genest and associates.\(^{22}\) The initial elevation of pressure would then be maintained through the action of this system. Although this study does not permit any conclusions as to the mechanisms involved in essential hypertension, the multifactorial nature of the pathogenesis of elevated blood pressure should be remembered. This may explain the variability observed when a single function is measured in hypertensive and in normal subjects. It would appear that there are several mechanisms operative in elevating blood pressure and many unknown interrelationships between these mechanisms.

Several considerations bear on the validity of these observations and the ability to extrapolate the results to a general population or individual instance. This study group does not represent a sample of the general population but a selected, homogeneous group. The subjects of this study were selected according to rigorous standards. Certainly within the rejected group there were a number of individuals with high blood pressure or labile blood pressure elevation. In spite of this selection, the incidence of hypertension (regardless of the line of division) in this group is approximately the same as that noted in studies of other, less selected populations.\(^{23, 24}\)

Another point of reference is the similar incidence of positive family history of vascular disease in this group and in the group of medical students studied by Thomas.\(^{25}\) Analysis of the group from the standpoint of flying revealed no difference in blood pressure between the flying and non-flying groups.

The validity of a single casual blood pressure measurement may be questioned. Although a single determination of a parameter with wide spontaneous variation cannot be used to characterize an individual, we do think that this determination may serve to place him within a certain relative grouping. The tendency for individuals to maintain their relative ranking within the same group on serial examinations confirms this concept. The relative importance of blood pressure variability on a casual determination may be gathered from the significantly greater correlation between basal blood pressure in 1940 and blood pressure in 1958 (0.28) compared with the correlation of casual blood pressure in 1940 and blood pressure in 1958 (0.12).

**Summary**

A longitudinal study of blood pressure in a homogeneous group of young men followed over an 18-year period has been presented. Seven hundred and eighty-five (96 per cent) of the surviving members have been re-evaluated, and the mean age at the time of re-examination was 42 years.

Frequency distribution curves of blood pressure yielded a unimodal distribution and indicated that blood pressure is a graded continuous variable. There was no evidence of natural bimodal distribution to suggest emergence of a qualitatively different population. Each individual tended to maintain his relative position within the distribution.
curve over the period of study, but this was modified by genetic and environmental factors.

Significant correlations were found between the variables of weight and somatotype. A significantly greater increase in blood pressure was noted in association with increasing weight. Subjects with a predominance of ectomorphic characteristics had a smaller increment of blood pressure over the period of study. Endomorphic subjects had a greater increment of blood pressure. The changes in blood pressure related to somatotype were modified by weight, but not dependent upon an increase in weight.

A family history of vascular disease was associated with a significantly greater increase in blood pressure. The greater increment in blood pressure associated with a positive family history was not dependent upon weight gain for its influence. There was no evidence that a positive family history separated a portion of the population ranked according to blood pressure.

Analysis of the upper and lower segments of the distribution curves revealed significant differences between the characteristics of each group. These differences followed the same pattern as the entire group but were quantitatively different.

These results are discussed with regard to the concept that hypertension represents a quantitative difference in blood pressure resulting from a multiplicity of factors, both genetic and environmental.

Acknowledgment

The authors wish to express their appreciation to each individual in the study group for his continuing interest and cooperation, which have been responsible for the success of this study. To our faithful and tireless corpsmen, C. W. Padgett, HM1 and W. J. Moates, HM2, we owe a debt of gratitude. We would also like to thank Mrs. Kay Kasparek for her continuing help with the study and editorial assistance.

References


Circulation, Volume XXVI, October 1962

The University and The Hospital

After all, it is a great laboratory in which we collect for rectification the experiments which nature makes upon us. The study of disease is just as much a part of university work as is the study of mathematics, and a close affiliation of the two institutions is the best guarantee of that combination of science with practice which it is the right of people at the present day to demand.—Sir William Osler. Aphorisms From His Bedside Teachings and Writings. Edited by William Bennett Bean, M.D. New York, Henry Schuman, Inc., 1950, p. 46.
A Longitudinal Study of Blood Pressure
WILLIAM R. HARLAN, ROBERT K. OSBORNE and ASHTON GRAYBIEL, Capt. (MC) USN

Circulation. 1962;26:530-543
doi: 10.1161/01.CIR.26.4.530

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