Distribution of this document is unlimited.

TRENDS IN SYSTOLIC BLOOD PRESSURE IN THE THOUSAND AVIATOR COHORT OVER A 24-YEAR PERIOD Albert Oberman, Norman E. Lane, William R. Harlan, Jr., Ashton Graybiel, and Robert E. Mitchell

Bureau of Medicine and Surgery MF022.03-02.5007.15

NASA Order R-136

Approved by<br>Released by<br>Ashton Graybiel, M. D. Director of Research<br>Captain H. C. Hunley, MC USN<br>Commanding Officer

25 April 1967

## ADMINISTRATIVE INFORMATION

This investigation was supported by the National Aeronautics and Space Administration Order R-136, a Fellowship 1-F3-HE-33, 537-01 from the National Heart Institute, National Institutes of Health to Dr. Oberman, by the United States Public Health Service, and the Bureau of Medicine and Surgery, U. S. Navy.

This paper was presented in part at a symposium, Host Factors in Cardiovascular Disease, in honor of Dr. Ashton Graybiel, Pensacola, Florida on June 22, 1966.

## ACKNOWLEDGMENT

We are indebted to Mrs. Margaret Duty for her assistance in compiling the data.

## THE PROBLEM

A cohort of 1056 normotensive, heal thy, young men initially examined in 1940 at the mean age of 24 years has been followed at three periodic intervals. The trends in systolic blood pressure in this "Thousand Aviator" group over a 24 -year period are reported.

## FINDINGS

The group demonstrated little change in mean systolic blood pressure beyond age 35. Frequency distributions of systolic blood pressure from age 40 to 54 at five-year intervals could be almost perfectly superimposed upon one another. Inherent bias and loss to follow-up would in no way preclude the fact that a segment of this cohort showed no appreciable rise of systolic blood pressure (S.B.P.) with age.

If the men are classified by quintile according to systolic blood pressure in 1940, those men in the upper quintile tend to stay in the fourth or fifth quintile for the remainder of the study, implying that a subgroup of the cohort maintains a given level in the distribution of systolic blood pressure at an early age. If the men are classified by blood pressure quintile in 1951, most of them maintain their relative position; over one half of the men in the lower quintile remain in the first or second quintile, and nearly two-thirds in the fifth quintile remain there or in the fourth quintile until 1963-64. The predictive utility of an S.B.P. may be a function of its actual level as well as the age of the individual.

At least two factors influenced the systolic blood pressure of this cohort, namely, parental longevity and weight gain independent of arm circumference. A segment of the cohort whose parents lived to old age showed less of an increment in systolic blood pressure with age than those whose parents died in middle age. There was a consistent difference in systolic blood pressure at every examination between these groups with different parental longevity, significantly so when an overall index of blood pressure for the entire 24 -year period, mean systolic score, was used. The significant effect of parental longevity on systolic blood pressure became less important relative to weight gain as time progressed, and after the age of 41 had an appreciable effect only on those men who had gained more than 20 pounds. Weight gain, obviously more important than parental longevity both by inspection and analysis, had a significant effect upon systolic blood pressure only after 1940, which became more pronounced as the cohort increased in age.

These results, though not directly applicable to a general population, suggest determinants of blood pressure in middle age which certainly have possible therapeutic implications.

## INTRODUCTION

Pickering (22) and Platt (23), questioning the division of blood pressure into normotension and hypertension have repeatedly stressed the need for longitudinal information. Previous studies of blood pressure have generally been retrospective without experimental control over the collection of data, or have been cross-sectional whereby inferences about the significance of blood pressure at various ages must be generated from measurements in altogether different groups of people.

Prospective investigations directed toward the description of population characteristics related to blood pressure, elucidation of its inheritance, and the change of mean blood pressure with age $(2,8,20,28)$ for the most part have been based on single measurements, either initial or most recent. Armitage and Rose (1) have enumerated the advantages and improvements in precision from taking multiple readings. These methodological difficulties have added to the conflicting interpretations of environmental influences, genetic factors, and longitudinal variation in blood pressure.

In the present study, an extension of the work previously reported by Harlan et al. (6), we have combined systolic readings from a cohort of naval aviators examined periodically from young to middle age. This cohort, homogeneous in background and environmental circumstances, obviously does not lend itself directly to generalization, but does provide an unusual opportunity for the longitudinal study of systolic blood pressure in a young group of men, with minimal extraneous sources of variability. We examined these data collected over a 24 -year span for the purpose of determining whether individuals maintain their rank in the distribution of systolic blood pressure through middle age, and the extent to which certain factors, especially parental longevity and weight gain, modify their position.

## PROCEDURE

This population consists of survivors of a cohort participating in an investigation termed the "Thousand Aviator Study," initiated in 1940 to determine important physiologic and psychologic measures for selection of pilots. The original 1056 members were drawn from the population of aviation cadets and flight instructors who were at the Pensacola Naval Air Station at that time. All of the men were preselected in that they entered the study at optimal weight, with supine blood pressure under $132 / 86 \mathrm{~mm} \mathrm{Hg}$, and had qualified for flight training by passing rigorous medical and flight proficiency exams. This cohort, then in their mid-twenties, was re-examined at each of the following times: 1951-52, 1957-58, 1963-64. Details of the composition of the group, selected characteristics, and various aspects of the examinations are described in previously published monographs $(17,18)$.

We present here the findings on blood pressure and related data obtained from these serial examinations at which, respectively, 703 ( $85 \%$ ), 785 ( $96 \%$ ), and 675 ( $85 \%$ ) of the surviving members were examined. Of the original cohort, 213 men died in the

Second World War. Of the survivors, 575 men had blood pressure data available from all four examinations; subjects on whom complete data were not available were excluded from some analyses.

The 1940 examination included a supine "casual" blood pressure and a "basal" blood pressure recorded as part of a cold pressor test performed in the manner of Hines and Brown (7). The blood pressures analyzed in this report are supine "casual" systolic pressures (S.B.P.) taken by the examiner midway through the physical examination. Although diastolic pressure is the preferred index of hypertension clinically, only the systolic pressure is used in the present analyses because of the statistical advantages of less error in the measurement, a wider range of values, and the more linear relationship with age. Moreover, systolic pressure correlates highly with diastolic pressure and is of equal or better value as a risk factor in coronary heart disease (9, 13, 29). In this study systolic pressure correlated well with diastolic in $1940(r=0.4), 1951(r=0.6)$, $1957(r=0.7)$, and $1963(r=0.7)$.

Because of differences in S.B.P. variation at each examination, individual values could not be compared across time directly. In order to facilitate such a comparison, S.B.P. measures for an individual were converted to $T$-scores for each of the four examinations:

$$
T=10\left(\frac{x-\bar{x}}{5}\right)+50
$$

where $x=$ systolic pressure at any given examination, $\bar{x}=$ mean systolic pressure of the cohort for that examination, and $s=$ standard deviation of the cohort for the examination. This conversion produces distributions with the same variance in each examination, and a subject's standing in one examination can be directly compared to his standing in each of the other examinations. The mean of these four $T$ values for an individual then indicate his over-all or "average" position in the S.B.P. distribution for the entire 24-year period of the study. We shall refer to this mean T-score as the mean systolic score (M.S.S.).

Measurement of height, weight, and somatotype (25) were available from the 1940 evaluation. We also used the 1951 weight and heart rate because these values were thought to be more representative in some ways than those recorded in 1940, a time at which all subjects were in optimal physical condition. Amount and duration of smoking, a social status index (11), and family history were culled from a detailed 1963 questionnaire.

## RESULTS

Harlan et al. (6) have reported for this cohort the frequency distribution curves of S.B.P. at $5-\mathrm{mm}$ intervals "smoothed" to correct for number bias for each five-year age interval from 15 to 44 years. The configuration of the frequency distribution for the 40- to 44-age group corresponds closely to the curves for the 45- to 49- and 50to 54 -age groups from the present study (Figure 1), the primary difference being the

FREQUENCY DISTRIBUTIONS OF SYSTOLIC BLOOD PRESSURE


Figure 1
few more extreme values at the upper end of the distribution with increased age. Systolic B.P. at all ages ran lower in the Thousand Aviator cohort than in either the National Health Survey (16) or the population of Hamilton and co-workers (5), but higher than the insurance population studied by Robinson and Brucer (24) (Figure 2). The slope of the curve from the Thousand Aviator Study is notably less steep after age 35 than prior to that age. Variance of S.B.P. increased with age as noted previously for this group (6) and for others (16).

## LONGITUDINAL TRENDS

We divided the cohort into quintiles at each examination according to their S.B.P. so that an individual's rank at two different examinations might be comparable even though the distribution of S.B.P. might vary absolutely from one time to the next. Next

## THE RELATIONSHIP OF SYSTOLIC BLOOD PRESSURE tO AGE IN VARIOUS STUDIES



Figure 2
we traced separately each of the 1940 quintiles from 1951 to 1963 to determine the proportion of men falling into each quintile at subsequent examinations. For example (Table I and Figure 3), of those in the lowest quintile (I) in 1940, 16.5 per cent were in the lowest quintile in 1951; 19.8 per cent in the second quintile; 13.2 per cent in the third, et cetera. It is immediately apparent that the first four quintiles did not follow any definite pattern in succeeding evaluations, but those men in the fifth quintile, and, to some extent those in the fourth quintile, did maintain upper ranks throughout the study. If, however, the 1951 quintiles are used as the initial criteria for ranking (Table II and Figure 4), a more consistent pattern evolves; men in all quintiles tend to maintain their relative position as is evident from the distribution at each subsequent examination. More than one half of the men in the first quintile in 1951 were in either the first or second quintile in 1957 and 1963, and approximately two thirds of those in the fifth quintile in 1951 were in either the fourth or fifth quintile for the remainder of the period of follow-up. There was a striking tendency for those men in the fifth quintile in 1951 to remain there in 1957 and 1963.
Table I
Percentage Distribution of Initial Quintile（1940）

|  |  | 1951 Quintile |  |  |  |  | 1957 Quintile |  |  |  |  | 1963 Quintile |  |  |  |  | N |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | 1 | 11 | III | IV | V | 1 | 11 | III | IV | V | 1 | 11 | III | IV | V |  |
|  | 1 | 16.5 | 19.8 | 13.2 | 27.5 | 23.1 | 16.5 | 35.2 | 15.4 | 8.8 | 24.2 | 22.0 | 22.0 | 22.0 | 14.3 | 19.8 | 91 |
|  | 11 | 14.8 | 27.9 | 18.9 | 22.1 | 16.4 | 13.1 | 26.2 | 24.6 | 13.1 | 23.0 | 21.3 | 23.0 | 18.0 | 20.5 | 17.2 | 122 |
|  | III | 8.8 | 22.5 | 18.8 | 31.3 | 18.8 | 12.5 | 21.3 | 25.0 | 15.0 | 26.3 | 22.5 | 21.3 | 23.8 | 15.0 | 17.5 | 80 |
|  | IV | 6.3 | 18.8 | 17.4 | 30.6 | 27.1 | 10.4 | 19.4 | 27.8 | 14.6 | 27.8 | 9.7 | 21.5 | 23.6 | 19.4 | 25.7 | 144 |
|  | V | 10.9 | 19.6 | 15.9 | 22.5 | 31.2 | 4.3 | 16.7 | 26.1 | 15.9 | 37.0 | 8.0 | 14.5 | 15.9 | 29.0 | 32.6 | 138 |
|  | $N$ | 64 | 124 | 97 | 152 | 138 | 62 | 132 | 140 | 79 | 162 | 89 | 116 | 117 | 118 | 135 | 575 |


|  | Z |  |
| :---: | :---: | :---: |
|  |  | ふぃ○○ <br>  <br> －ぺック！ $\dot{O}-\dot{\sim} \infty \stackrel{\sim}{N} \underset{\sim}{\infty}$ <br> ソフォへの。 <br> ヘベホㄴํ <br> ๓Oㅇ․－ <br>  <br> － $\boldsymbol{J i n}^{\infty}$ ヘ <br> ジロー்ニか |
|  |  |  <br>  <br>  <br> － $0 \infty$ ○ <br> N্ল্M Ni <br>  $-=\equiv \geq>\mathbf{z}$ <br> ə！！！！ |

PERCENTAGE DISTRIBUTION OF
INITIAL QUINTILE (I95I) FOR
SUCCEEDING EXAMINATIONS



 PERCENTAGE DISTRIBUTION OF
INITIAL QUINTILE (I940) FOR SUCCEEDING EXAMINATIONS


Year of examination

371ININO - 70 39V1N3043d
$\mapsto$
三
曰
$\geqq$
$\lambda$
Figure 3

We also compared subjects in the upper quintiles (fourth and fifth) in 1963 to the remainder of men with regard to movement among quintiles during the span of the study. Nine per cent of the cohort in these upper quintiles remained in the same quintile for all four examinations, whereas only 2 per cent of the other quintiles did so. Only 8 per cent of the upper quintiles were in a different quintile for each examination compared with 15 per cent of those in the lower quintiles. A majority of both upper and lower quintiles transgressed three or four quintiles during the four examinations.

Of those 134 men who exceeded the arbitrary cut-off point of 140 mm Hg S.B.P. at any of the examinations, 2 per cent had done so in 1940, 50 per cent by 1951,78 per cent by the mean age of 42 years in 1957, and the remainder exceeded this level in 1963.

Additional information of S.B.P. trends across time is given by the correlation matrix in Table III. The correlations can in one sense be viewed as reliability coefficients, with varying intervals between retesting. From this standpoint, it is apparent that the prognostic value of a "casual" S.B.P. obtained early in adult life is limited. The S.B.P. in 1940 correlated poorly with that obtained 24 years later. Yet, it must be remembered that in 1940 the men were in optimal physical condition and had a narrow range of S.B.P. Better correlations between S.B.P. in 1940 and other examinations were obtained by using the "basal" S.B.P. (19).

## Table III

Correlation Matrix of Mean Systolic Pressure and Mean Systolic Score by Examination Year

| Systolic <br> Pressure | 1940 | 1951 | 1957 | 1963 | Mean Systolic <br> Score |
| :--- | :---: | :---: | :---: | :---: | :---: |
| 1940 | - | .10 | .19 | .15 | .52 |
| 1951 |  | - | .43 | .39 | .69 |
| 1957 |  |  | - | .58 | .79 |
| 1963 |  |  | - | .77 |  |

$N=444$
Two tailed significance values for correlation coefficients
$r(.05)=.09$
$r(.01)=.12$
$r(.001)=.16$

## HEREDITY

Morrison and Morris (14) suggested that the inheritance of blood pressure be studied by dividing subjects into two groups -- those persons, one or both of whose parents died at $40-64$ years, and those whose parents lived to age 65 . Hypertension, presumably an important factor in shortening life, should be more frequent in those parents dying in middle age. The Kolmogorov-Smirnov Test (26) has been used to test statistically the difference in the distribution curves of S.B.P. between the men with different histories of parental longevity (2). If the groups have cumulative distributions which diverge significantly at any point, the samples may have emanated from different populations, indicating a possible genetic influence.

Our analyses for the difference in parental longevity were carried out for each examination for S.B.P. and for the M.S.S. representing all examinations. Although the curves for S.B.P. were not different at the 0.05 significance level for any one examination, there was a definite approach to significance with age. The M.S.S., a better index of S.B.P. because it represents the mean of scores in relation to variance over a period of years, did show that those men whose parents lived to old age had a consistently lower cumulative percentage for each M.S.S., significant ( $p<0.02$ ) at the most divergent portions of the curves (Figure 5). Furthermore, men whose parents died in middle age had higher S.B.P. at all four examinations and greater increments with age for successive examinations (Table IV).

Table IV
Mean Systolic Blood Pressure and Mean Systolic Score by Parental Longevity Group

|  |  | Examination |  |  | Mean <br> Systolic <br> Score |
| :--- | ---: | ---: | ---: | ---: | ---: |
| Both parents <br> died $>64$ <br> Either parent <br> died 40-64 <br> Difference | $1940-1941$ | $1951-1952$ | $1957-1958$ | $1963-1964$ | 120.98 |

# CUMULATIVE PERCENTAGE DISTRIBUTION OF MEAN SYSTOLIC SCORES 

BY PARENTAL GROUPS


Figure 5
Significantly more men from quintile V in 1940 had short-lived parents compared to those in quintile I (Students $t$ test $p<0.05$ ). The men in these extreme quintiles did not differ significantly in any of the other variables measured in 1940. Yet, in 1951 heart rate and weight variables in quintile I were significantly different from those in quintile $V$, but the parental longevity groups showed no such differences.

Separation of groups by parental history of known vascular disease (hypertension, "heart" disease, or cerebrovascular "accident") before the age of 60 revealed no significant differences for S.B.P. or the M.S.S. This discrepancy between parental age at death and history of vascular disease as a discriminant for S.B.P. may perhaps be explained by the inaccuracy of more subtle differences in the family history.

## OTHER INFLUENCING FACTORS

We divided the cohort into five approximately equal groups on the basis of the M.S.S. to determine the possible influence of pertinent variables on S.B.P. over the years. The gradation of significant variables with the grouping of M.S.S. is demonstrated on Table V. Although heart rate in 1951 related to M.S.S., it is evident that
Table V
Mean Values of Selected Variables for Five Levels of Mean Systolic Score and
Correlation Coefficients Between Variables and Mean Systolic Score

|  | Mean Systolic Score |  |  |  |  |  |
| :--- | :---: | :---: | :---: | :---: | :---: | :---: |
| Variable | $34.4-44.2$ | $44.3-47.9$ | $48.0-50.8$ | $50.9-55.1$ | $55.2-80.6$ | Correlation Coefficient <br> Variables vs MSS |
|  | $\mathrm{N}=114$ | $\mathrm{~N}=114$ | $\mathrm{~N}=111$ | $\mathrm{~N}=116$ | $\mathrm{~N}=116$ | $\mathrm{~N}=484$ |

[^0]those factors associated with weight were the most important. This is more than an artifact of arm size. Removing the effect of weight of arm circumference statistically resulted in a partial correlation of $\mathbf{- 0 . 0 1}$, indicating that arm circumference itself did not bear on S.B.P. Smoking habits and social status in 1963 were not related to S.B.P. over the period of the study.

## INTERACTION OF HEREDITY AND ENVIRONMENT

The combined effect of more than 20 pounds weight gain and short-lived parents on S.B.P. and M.S.S. is shown in Figure 6. To test the significance of these differences, we did an analysis of variance (Table VI ) for the data at each examination and for the M.S.S., using the method of expected cell frequencies to adjust for nonproportional N's (15). In order to better evaluate the changes in the effects of the variables across time, we also estimated the variance components (ECV) (15) for each analysis. These components are really an estimate of the variance due to the independent effect of a particular variable; the larger the ECV, the greater the influence of that source of variance.

SYSTOLIC BLOOD PRESSURE AND MEAN SYSTOLIC SCORE BY WEIGHT GAIN AND PARENTAL LONGEVITY


Figure 6
Table VI

## The Significance of Parental Longevity and Weight Gain on Systolic <br> Analyzed by Variance and Estimation of the Components and Variance

| The Significance of Parental Longevity and Weight Gain on Systolic <br> Blood Pressure by Examination Year and Mean Systolic Score <br> Analyzed by Variance and Estimation of the Components and Variance |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Source $(N=541)$ | 1940 |  | 1951 Examination |  |  | 1957 | 1963 |  | Mean Systolic Score |  |
|  | $F^{\text {a }}$ | P | F | P | F | P | F | P | F | P |
| $p^{c}$ | 4.31 | $<0.05$ | 3.19 | $<0.10$ | 5.55 | $<0.025$ | 3.91 | $<0.050$ | 8.90 | $<0.005$ |
| W | 0.03 | N.s. ${ }^{\text {b }}$ | 7.09 | < 0.01 | 9.34 | $<0.005$ | 13.42 | $<0.001$ | 11.18 | < 0.001 |
| $\mathrm{P} \times \mathrm{W}$ | 0.59 | N.S. | 0.94 | N.S. | 4.55 | $<0.050$ | 5.01 | < 0.025 | 2.67 | N.S. |
| Estimated Components of Variance |  |  |  |  |  |  |  |  |  |  |
| P | 0.91 |  | 1.26 |  | 2.82 |  | 1.99 |  | $1.36{ }^{\text {d }}$ |  |
| W | 0.00 |  | 3.52 |  | 5.54 |  | 8.49 |  | $1.76{ }^{\text {d }}$ |  |
| P $\times$ W | 0.00 |  | 0.00 |  | 4.40 |  | 5.48 |  | $0.58{ }^{\text {d }}$ |  |
| a -- Sources of variance have one degree of freedom <br> b-- N.S. = Not significant <br> $c--P=$ Parental longevity $\quad W=$ Weight gain $P \times W=$ Interaction of $P$ and $W$ <br> d - - Not directly comparable to estimates of variance for years because of a different scale of values |  |  |  |  |  |  |  |  |  |  |

Estimated Components of Variance
p $89^{\circ} 0$
p $9 \cdot 1$
$p^{\circ} \varepsilon^{\circ} \cdot 1$
Table VI

Both parental longevity (P) and weight gain (W) had significant effects on S.B.P., but the importance of these effects changed with the year of examination. In 1940 parental longevity was significant, weight gain was not, and there was no interaction between these variables. After 1940 the estimated component of variance for weight gain (ECV ${ }_{W}$ ) increased from 0 to 8.49 and exceeded the estimated component of variance for parental longevity ( $E C V_{p}$ ) at each examination. In 1957 and 1963 there was significant PW interaction; ECV ${ }_{P W}$ exceeded $E C V_{p}$, indicating that the effect of parental longevity might not exist independently of the interaction of P and W . The effect of parental longevity on S.B.P. was dependent upon which level of weight gain was being considered. While parental longevity had a significant effect in the analysis of variance beyond 1940, it was primarily with those men gaining more than 20 pounds; the mean S.B.P.'s in 1963 were identical for those gaining less than 20 pounds with dissimilar parental longevity ( 122.8 versus 122.8 ). It is apparent both by analysis and by inspection that weight gain was more important than parental longevity as a determinant of S.B.P. From 1951 to 1963 a weight gain of more than 20 pounds superseded the influence of short-lived parents on S.B.P. The men with the highest M.S.S. had short lived parents and weight gain over 20 pounds, whereas at the opposite end of scale, although separated from the remainder of the cohort to a lesser extent, were those men with long-lived parents and weight gain not exceeding 20 pounds.

## DISCUSSION

We hoped to obviate many of the shortcomings of the cross-sectional study by maintaining a cohort composition constant over time, and using blood pressure singly and in combination from four intervals over a span of 24 years. Moreover, our investigation began when the subjects were in their early twenties, rather than at a chance point in time, enabling direct observations to be made of secular trends and the interplay of heredity and environment.

Efforts were made to reduce error in measurements so that a more precise representation of trends could be made. With rare exception, blood pressures were obtained in a nonclinical setting familiar to the aviator. A variety of environmental and somatic stimuli may still, of course, influence these isolated recordings, but the assumption that the biologic variation will be random and not bias the estimate of the population mean is a reasonable one (4). To eliminate variability among evaluations, T -scores and quintiles, as previously described, were employed. A distinct problem exists, though, with loss of subjects to follow-up whether by death or otherwise; available data indicated a slightly higher mean S.B.P. in this group.

The minimal increase of S.B.P., especially in the fourth decade of the cohort, might be attributed in some part to loss to follow-up of the hypertensives, but no doubt in greater part to the initial selection procedure for these men. Addition of lost hypertensives to this population could raise the mean S.B.P. with age, especially since the range of blood pressure was limited at the onset of the study, but would in no way preclude the fact that a segment of this cohort shows no appreciable rise of S.B.P. with age. It is also conceivable that hypertension may become manifest at a later age in
such a preselected cohort; these men may just now be entering this critical period. Recent studies (16) have shown S.B.P. to change with age exponentially. On the other hand, Paul and Ostfeld (21) have pointed out the fallacy of assuming blood pressure to be a function of age. Stamler (28) reported that approximately 30 per cent of utility company employees with 20- to 30-years follow-up demonstrated little or no rise of blood pressure with age. The S.B.P. of insurance applicants studied by Robinson and Brucer (24) remained stable until after age 40.

For 24 years the men of our study comprising the upper quintile in 1940 maintained their rank; this trend was discernable despite regression to the mean S.B.P. which undoubtedly occurred. Others did not have a "fixed" rank until 1951 at which time they were still for the most part in their mid-thirties. These data suggest that a part of the cohort at the upper end of the S.B.P. distribution in 1940 have their pressure determined at an early age, perhaps due to some autoregulatory mechanism such as setting of baroreceptors at a higher level.

This predisposition, if representing autonomic balance, is not manifest by significant differences between the extreme quintiles in 1940 in heart rate, weight, or somatotype. Parental longevity does differ between quintiles I and V. Those at the lower end of the S.B.P. distribution do not manifest consistent systolic levels until 1951 after which everyone in the cohort maintains his relative rank in the S.B.P. distribution, especially those in the first and fifth quintiles. Responsibility for this difference in age at attainment of a "fixed" rank between the upper and other quintiles might be attributed to an interplay of environmental and genetic factors shortly after the special circumstances in 1940 when all subjects at optimal physical condition and in a common environment exhibited more uniform systolic pressures. Delayed expression of genetic influences is another possibility.

Prediction of future S.B.P. measured by correlation coefficients, though poor using the 1940 S.B.P., improved as the cohort grew older. The findings with quintiles indicate that the predictive utility of a S.B.P. may be a function of its actual level as well as of the age of the individual.

Lability of blood pressure has been considered a prehypertensive state or early phase of hypertension (3), yet the men in the upper portion of the S.B.P. distribution in 1963 had been slightly more stable than the remainder of the cohort. Frequent recordings of blood pressure by Sokolow et al. (27) demonstrated little relationship between variability and mean level of pressure.

The concept of two populations, one with a definite rise in blood pressure during middle age, and another with little or no rise, has been championed by Platt (23). A bimodal frequency distribution of blood pressure according to parental longevity would support this single gene hypothesis. On this basis Morrison and Morris (14) in their study claimed the rise in mean blood pressure in middle age was caused by a minority of busmen from hypertensive families. These data have been subject to criticism because
of small numbers (10). The findings could not be duplicated in Western Electric employees (20), longshoremen (2), or employees of an engineering firm (10).

Systolic B. P. was consistently higher for those men in our study with short-lived parents. Furthermore, the difference became more marked with time and reached significance when the M.S.S., the over-all index of S.B.P., was used to classify the cohort, implying the possibility of bimodality of distribution.

Concerning bimodality of blood pressure, McKusick (12) stated, "A study performed in a population as homogeneous as possible in racial background and environmental circumstances and designed to reduce extraneous sources of variability to a minimum might be ideal." Armitage and Rose (1) have further stated that bimodality might be obscured on the basis of a single blood pressure reading. A higher rate of increase of S.B.P. over the duration of the study in those men with short-lived parents further suggests a real dichotomy in this cohort.

Age of parental death appeared to be operative in 1940 with minimal dependence on weight gain, whereas weight gain was of greater significance from 1951 to 1963. As stated previously, it is not surprising that weight gain was unimportant in 1940 because the men were at that time in optimal physical condition with little excess weight; it is remarkable that the influence of parental longevity on S.B.P. can be shown in such a young group with a limited range of blood pressure. Those men with a large weight gain are more likely to have high S.B.P. if their parents died in middle age, but for those with 20 pounds or less weight gain, parental longevity is relatively immaterial. The combined effect of weight gain, and parental longevity to a lesser extent, is clearly evident in the M.S.S.

The main findings of this investigation, namely, S.B.P. does not necessarily rise with age; individuals at the extremes of the S.B.P. distribution tend to maintain their relative position; and both weight gain and parental longevity, separately and combined, have an early influence on S.B.P., have many possible therapeutic implications. Of further significance is the question of a perceptible difference in "target organ" damage between those who have attained a given level of S.B.P. by weight gain alone as opposed to those with short-lived parents and weight gain. Tantamount to this latter problem, is the duration of elevated S.B.P. more critical than the age at onset? Early classification of subjects likely to sustain cardiovascular injury by mild elevation of blood pressure appears requisite before guides for therapy of mild hypertension can be structured.

## REFERENCES

1. Armitage, P., and Rose, G. A. , The variability of measurements of casual blood pressure. 1. A laboratory study. Clin. Sci., 30:325-335, 1966.
2. Borhani, N. O., and Hechter, H. H., The application of statistical methods in the analysis of blood pressure distribution curves. Ann. N. Y. Acad., Sci., 126:758-766, 1965.
3. Geiger, H. J., and Scotch, N. A., The epidemiology of essential hypertension. 1. Biologic mechanisms and descriptive epidemiology. J. chron. Dis., 1.6: 1151-1182, 1963.
4. Gerende, L. J., Some methodological problems in the study of the natural history of blood pressure: An examination of the Framingham Study data. Doctoral Thesis, Ann Arbor, Michigan, 1962.
5. Hamilton, M., Pickering, G. W., Roberts, J. A. F., and Sowry, G. S. C., The aetiology of essential hypertension. I. The arterial pressure in the general population. Clin. Sci., 13:11-35, 1954.
6. Harlan, W. R., Osborne, R. K., and Graybiel, A., A longitudinal study of blood pressure. Circulation, 26:530-543, 1962.
7. Hines, E. A., Jr., and Brown, G. E., Standard stimulus for measuring vasomotor reactions: Its application in the study of hypertension. Proc. Staff Meet. Mayo Clin., 7:332-335, 1932.
8. Johnson, B. C., Epstein, F. H., and Kjelsberg, M. O., Distributions and familial studies of blood pressure and serum cholesterol levels in a total community-Tecumseh, Michigan. J. chron. Dis., 18:147-160, 1965.
9. Kagan, A., Kannel, W. B., Dawber, T. R., and Revotskie, N., The coronary profile. Ann. N. Y. Acad. Sci., 97:883-894, 1963.
10. Lowe, C. R., and McKeown, J., Some sources of irregularity in the distribution of arterial pressure. In: Pemberton, J. (Ed.), Epidemiology, Reports on Research and Teaching. London, 1963 Chapt. 12.
11. McGuire, C., and White, G. P., The measurement of social status. Report No. 3. Austin, Texas: University of Texas Department of Educational Psychology, 1955.
12. McKusick, V. A., Genetics and the nature of essential hypertension. Circulation, 22:857-863, 1960.
13. Morris, J. N., Kagan, A. , Pattison, D. C., Gardner, M. J., and Raffle, P. A. B., Incidence and prediction of ischemic heart-disease in London busmen. Lancet, 2:553-559, 1966.
14. Morrison, S. L., and Morris, J. N., Epidemiological observations on high blood pressure without evident cause. Lancet, 2:864-870, 1959.
15. Myers, J. L., Fundamentals of Experimental Design. Boston: Allyn \& Bacon, 1966.
16. National Center for Health Statistics, Blood Pressures of Adults by Age and Sex. Vital and Health Statistics. Publication No. 1000 Series 11 - No. 5. Washington, D. C.: U. S. Public Health Service, 1964.
17. Oberman, A., Mitchell, R. E., and Graybiel, A., Thousand Aviator Study: Methodology. NSAM Monograph 11. Pensacola, Fla.: Naval School of Aviation Medicine, 1965.
18. Oberman, A., Lane, N. E., Mitchell, R. E., and Graybiel, A., Thousand Aviator Study: Distributions and Intercorrelations of Selected Variables. NAMI Monograph 12. Pensacola, Fla.: Naval Aerospace Medical Institute, 1965.
19. Oberman, A., Harlan, W. R., Jr., Graybiel, A., and Mitchell, R. E., Unpublished data.
20. Ostfeld, A. M., and Paul, O., The inheritance of hypertension. Lancet, 1: 575-579, 1963.
21. Paul, O., and Ostfeld, A. M., Epidemiology of hypertension. Prog. Cardiovasc. Dis. , 8:106-116, 1965.
22. Pickering, G., Hyperpiesis: High blood pressure without evident cause: Essential hypertension. Brit. med. J., 5469:1021-1026, 1965.
23. Platt, R., The nature of essential hypertension. Lancet, 2:55-57, 1959.
24. Robinson, S. C., and Brucer, M., Range of normal blood pressure: Statistical and clinical study of 11,383 persons. Arch. int. Med. , 64:409-444, 1939.
25. Sheldon, W. H., Dupertius, C. W., and McDermott, E., Atlas of Men. New York: Harper and Bros., 1954.
26. Siegel, S. Nonparametric Statistics for the Behavioral Sciences. New York: McGraw Hill, 1956.
27. Sokolow, M., Werdegar, D., Kain, H. K., and Hinman, A. T., Relationship between blood pressure measured casually and by portable recorders and severity of complications in essential hypertension. Circulation, 34:279-298, 1966.
28. Stamler, J., On the natural history of hypertension and hypertensive disease. In: Cort, J. H., French, V., Heil, Z., and Jirka, J. (Eds.), The Pathogenesis of Essential Hypertension. The Prague, 1961. P.67.
29. Westlund, K., and Nicolaysen, R., Serum cholesterol and the risk of mortality and morbidity. A three-year follow-up of 6,886 men. Scand. J. Clin. Lab. Invest., 18: suppl. 87, 1-19, 1966.


Unclassified
Security Classification



[^0]:    Two tailed significance values for correlation coefficients
    $r(.05=.09 \quad r(.01)=.12 \quad r(.001)=.16$
    $\mathrm{HT} / \mathrm{WT}$ represents 10 times the ratio of height in inches to weight in pounds

