

DISTRIBUTIONS AND FAMILIAL STUDIES OF BLOOD PRESSURE AND SERUM CHOLESTEROL LEVELS IN A TOTAL COMMUNITY—TECUMSEH, MICHIGAN*

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THE question of the roles of heredity and environment is of prime importance to the understanding of the nature of chronic diseases. Genetic mechanisms must be known not only for a better understanding of pathogenesis but, to the extent to which genetic forces are operative, also to identify susceptible persons prior to the onset or full development of the pathological process. Knowledge of the way in which a genetic predisposition toward a chronic disease interacts with specific environmental forces may indicate the appropriate means for its control.

Many disease entities are difficult to study in this way, largely because the threshold for recognition is poorly defined and frequently corresponds to a relatively late stage of the pathogenetic spectrum. In situations which are identified by a measurement, such as blood pressure or cholesterol levels, the precise identification of the threshold of abnormality is not necessary. Study of the distributions of these measures in a population, and of the degree of resemblance within families and kindreds presents a good opportunity to evaluate these relationships. The study of a total, natural community which is being conducted in Tecumseh, Michigan, provided an excellent setting for such an analysis.

METHODS

Collection of data

The population in which these data were obtained has been previously described [1–4]. The total population at the time the study began, consisted of approximately 9800 persons of all ages; 88 per cent of these contributed an extensive medical history and received a comprehensive medical examination. The current analysis confines itself to data collected during the first round of examinations during 1959 and 1960; further information will be forthcoming as the community is re-examined at intervals.

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Blood pressures of the subjects were taken in the right arm in the sitting position by carefully instructed physicians. The present analysis is based on the first reading, which was obtained at the beginning of the physical examination. Almost all of the examining physicians had at least three years training in internal medicine or pediatrics and were on the faculty of the University of Michigan Medical School.

The present data on 8380 blood pressure readings were determined by a total of 49 examiners. Each of 11 examiners obtained 400 or more of these readings, 10 recorded 200–399 readings, 17 determined the pressures in 100–199 and 11 physicians each examined less than 100 persons.

Of the many sources of variability in blood pressure recording, one of the most difficult to quantitate is the difference in reading habit between examiners in a situation in which each person is observed by only one examiner. In order to determine whether a physician's readings were consistently high or low relative to other examiners, the mean of each observer's systolic pressure readings was compared, in each age–sex group, with the mean of all the examiners' readings in that specific group. By this comparison, the readings of three examiners were relatively high, while three other examiners more frequently read low. The magnitude of these deviations from the population means, calculated by a separate test, was generally quite small. By this test, however, four additional examiners, though not reading consistently higher or lower, varied significantly when compared with other examiners' mean readings across all of the age–sex groups. Since the performance of the readers has not usually been tested in other studies involving multiple examiners, it cannot be determined how the present performance compares with that of others.

Measurement error remains a great problem in epidemiological studies. Unconscious bias and digit preference in examiners' readings undoubtedly cause distortions of the distributions as well as difficulty in interpretation of individual readings. In an effort to minimize these effects in the second round of examinations now in progress in the community, an instrument designed by ROSE, HOLLAND and CROWLEY [5], with some modifications, is being used by a trained technician, in addition to the standard readings by the physician.

The cholesterol determinations were performed by the method of ABELL and co-workers [6] in a special research laboratory serving the Tecumseh Community Health Study. The technical error (standard deviation of blind replicates) of these tests, in this laboratory, was 5.2 mg/100 ml, comparing well with accepted standards of performance.

In the descriptions to follow, the population parameters are shown, persons with possible secondary hypertension or conditions associated with hypercholesterolemia are not removed, since it is felt that they contribute to the total population spectrum. Serum cholesterol determinations were performed for 6788 persons; no blood specimens were obtained from persons under 4 years of age.

Processing of data

The IBM 7090 at the University of Michigan Computing Center was used to perform the following:

1. Computation of age–sex adjusted scores for blood pressure and serum cholesterol values for each person, giving his relative position within his age and

sex distribution. The score was computed by subtracting from the value for a given person the sex-specific mean value in his five-year age group, and dividing by the standard deviation for his age-sex group. Other scoring methods have attempted to make allowance for an increasing variance with age by computing the score on the basis of a ratio of the standard deviation at a young adult age to the standard deviation at the person's present age [7-12]. Since this procedure would only multiply each score by a constant (the young adult standard deviation), the two methods are considered comparable. The score, then, represents the distance between a person's reading and his age and sex mean in standard deviation units. If the levels of all persons rise with age, and each person retains the same relative position in the distribution of his age-sex cohort, each person would keep the same score throughout life. These assumptions are not true for all persons, yet the use of scores is a simple method of adjusting for age and sex differences.

2. Computation of correlation and regression coefficients for intra-family comparisons.

RESULTS

Population data

The basic population data for blood pressure and cholesterol levels are shown in Tables 1-3. The distributions by age and sex group, though not shown, were

TABLE 1. BLOOD PRESSURE OF MALES BY AGE, TECUMSEH 1960

Age	Systolic			Diastolic (muffling)		Diastolic (disappearance)	
	No.	Mean \pm S.D.	Median	No.	Mean \pm S.D.	No.	Mean \pm S.D.
0-2	262	107 \pm 16	106	124	71 \pm 12	198	67 \pm 11
3	106	104 \pm 13	102	72	69 \pm 11	89	68 \pm 11
4	127	106 \pm 11	105	94	72 \pm 11	110	67 \pm 11
5	120	109 \pm 13	106	77	74 \pm 10	104	71 \pm 9
6	109	109 \pm 12	106	84	74 \pm 12	89	68 \pm 10
7	119	110 \pm 12	108	86	75 \pm 12	107	69 \pm 10
8	126	111 \pm 12	110	91	77 \pm 10	122	69 \pm 10
9	108	113 \pm 13	110	84	77 \pm 12	102	72 \pm 11
10	98	115 \pm 13	112	74	76 \pm 13	89	69 \pm 9
11	120	116 \pm 10	116	94	77 \pm 11	113	70 \pm 11
12	120	120 \pm 12	120	99	79 \pm 11	108	71 \pm 10
13-14	180	124 \pm 14	122	154	77 \pm 10	165	69 \pm 12
15-16	149	129 \pm 16	126	126	78 \pm 11	139	70 \pm 11
17-19	137	130 \pm 14	126	123	82 \pm 12	127	74 \pm 12
20-24	181	132 \pm 13	130	169	84 \pm 12	180	77 \pm 12
25-29	274	133 \pm 15	132	247	86 \pm 13	274	79 \pm 12
30-34	332	134 \pm 16	132	311	89 \pm 14	332	82 \pm 12
35-39	346	134 \pm 16	132	330	89 \pm 13	345	83 \pm 12
40-44	242	136 \pm 18	133	226	91 \pm 14	243	85 \pm 13
45-49	224	141 \pm 22	136	207	94 \pm 14	224	88 \pm 14
50-54	170	148 \pm 21	142	152	95 \pm 18	170	88 \pm 13
55-59	162	141 \pm 20	140	154	92 \pm 13	162	87 \pm 12
60-64	97	148 \pm 28	143	90	90 \pm 14	95	87 \pm 14
65-69	80	145 \pm 22	142	72	91 \pm 16	80	85 \pm 14
70-74	65	147 \pm 26	140	54	90 \pm 12	65	85 \pm 12
75-79	35	149 \pm 25	140	31	91 \pm 14	34	84 \pm 13
80+	26	156 \pm 32	145	23	92 \pm 26	26	83 \pm 13

TABLE 2. BLOOD PRESSURE OF FEMALES BY AGE, TECUMSEH 1960

Age	Systolic			Diastolic (muffling)		Diastolic (disappearance)	
	No.	Mean \pm S.D.	Median	No.	Mean \pm S.D.	No.	Mean \pm S.D.
0-2	227	106 \pm 15	105	112	71 \pm 12	163	67 \pm 10
3	113	108 \pm 14	108	73	72 \pm 12	97	69 \pm 10
4	124	106 \pm 14	104	67	71 \pm 11	103	68 \pm 10
5	114	108 \pm 13	106	77	75 \pm 11	99	69 \pm 9
6	101	107 \pm 13	106	72	73 \pm 12	87	67 \pm 10
7	110	112 \pm 15	110	77	76 \pm 10	97	72 \pm 10
8	113	112 \pm 13	110	82	74 \pm 12	98	69 \pm 11
9	118	114 \pm 12	112	89	77 \pm 10	110	70 \pm 10
10	93	116 \pm 11	115	77	76 \pm 9	83	69 \pm 9
11	110	119 \pm 13	118	86	77 \pm 10	102	70 \pm 10
12	109	120 \pm 12	118	93	79 \pm 9	100	72 \pm 10
13-14	173	125 \pm 12	122	139	79 \pm 11	158	74 \pm 11
15-16	155	124 \pm 13	122	134	81 \pm 11	140	74 \pm 11
17-19	161	123 \pm 13	120	137	79 \pm 11	143	73 \pm 11
20-24	257	122 \pm 14	120	235	80 \pm 12	257	74 \pm 10
25-29	328	123 \pm 12	122	297	91 \pm 11	327	75 \pm 10
30-34	364	126 \pm 14	124	335	84 \pm 17	363	78 \pm 10
35-39	339	129 \pm 18	125	313	85 \pm 12	339	80 \pm 11
40-44	262	134 \pm 20	130	238	88 \pm 15	260	82 \pm 12
45-49	212	140 \pm 22	138	182	91 \pm 15	210	86 \pm 13
50-54	167	149 \pm 25	148	152	96 \pm 16	167	91 \pm 13
55-59	157	152 \pm 26	150	145	96 \pm 15	157	90 \pm 14
60-64	94	161 \pm 34	156	82	96 \pm 18	94	92 \pm 17
65-69	102	160 \pm 29	154	90	94 \pm 16	102	88 \pm 12
70-74	75	164 \pm 25	160	67	94 \pm 14	75	88 \pm 14
75-79	44	171 \pm 33	156	43	93 \pm 16	43	89 \pm 15
80+	43	163 \pm 36	160	37	91 \pm 20	42	84 \pm 15

TABLE 3. SERUM CHOLESTEROL, BY AGE AND SEX, TECUMSEH 1960

Males			Females		
Age	No.	Mean \pm S.D.	Age	No.	Mean \pm S.D.
4-9	437	177 \pm 30	4-9	370	178 \pm 27
10-14	468	172 \pm 28	10-14	405	176 \pm 31
15-19	281	166 \pm 31	15-19	284	173 \pm 31
20-24	176	179 \pm 33	20-24	243	189 \pm 40
25-29	272	195 \pm 36	25-29	311	194 \pm 41
30-34	328	214 \pm 39	30-34	350	197 \pm 39
35-39	343	216 \pm 42	35-39	328	207 \pm 38
40-44	242	229 \pm 42	40-44	253	219 \pm 39
45-49	225	229 \pm 38	45-49	208	224 \pm 43
50-54	167	238 \pm 43	50-54	163	238 \pm 38
55-59	155	232 \pm 44	55-59	150	249 \pm 48
60-64	94	225 \pm 41	60-64	90	255 \pm 50
65-69	78	230 \pm 47	65-69	95	258 \pm 57
70-74	65	220 \pm 44	70-74	69	253 \pm 48
75-79	33	218 \pm 46	75-79	41	231 \pm 49
80+	25	208 \pm 37	80+	39	245 \pm 49

found to be unimodal, nearly symmetrically distributed in the young adult, with slightly increasing positive skewness as age progressed. The latter effect was more pronounced for blood pressure than for cholesterol. In general, the parameters for these variables differ in no major degree from other large studies [7, 13-16], but are unique in describing a large intact population of a community rather than a restricted sample.

The means by sex and age for these measures (Figs. 1 and 2) show similar crossover patterns; women in the child-bearing period have, on the average, lower

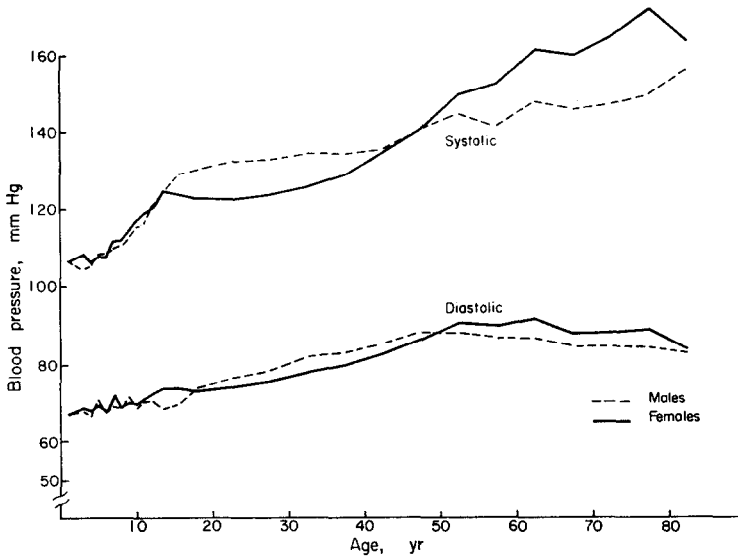


FIG. 1. Mean systolic and diastolic (V) blood pressures by sex and age, Tecumseh, Michigan, 1960.

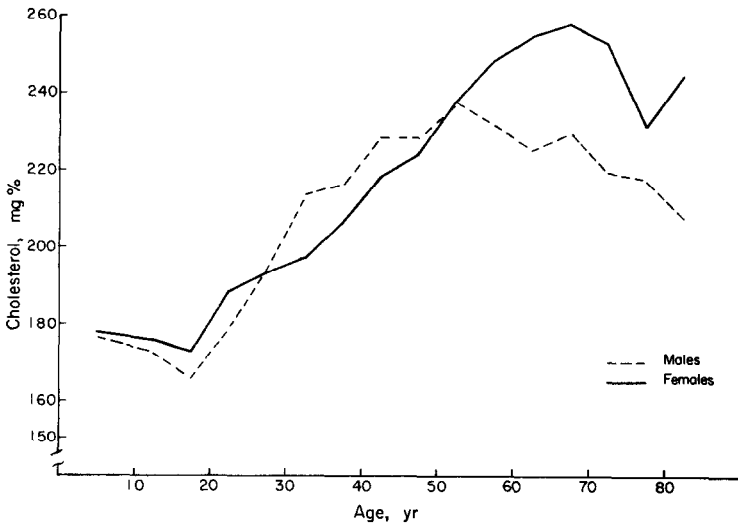


FIG. 2. Mean cholesterol by age and sex, Tecumseh, Michigan, 1960.

TABLE 4. CORRELATION BETWEEN PARENTS AND CHILDREN, SYSTOLIC BLOOD PRESSURE, TECUMSEH 1960

Parent	Age of parent	Age of son						Age of daughter					
		0-4	5-9	10-14	15-19	20-29	30-39	0-4	5-9	10-14	15-19	20-29	30-39
Father	30-39	<i>0.12</i>	<i>0.14*</i>	<i>0.23*</i>	-0.06				<i>0.15*</i>	<i>0.17*</i>	0.17		
	40-49	0.05	<i>0.26*</i>	<i>0.28*</i>	<i>0.07</i>	-0.02		<i>0.30*</i>	<i>0.22*</i>	<i>0.42*</i>	0.11		
	50-59		0.12	0.40*	-0.23*	0.27			0.19	<i>0.31*</i>	<i>0.19</i>		
Mother	30-39	<i>0.08</i>	<i>0.11*</i>	<i>0.12*</i>	<i>0.19</i>			<i>0.20*</i>	<i>0.09</i>	<i>0.08</i>	0.20		
	40-49		<i>0.34*</i>	<i>0.05</i>	<i>0.04</i>	<i>0.23*</i>		-0.01	<i>0.21*</i>	<i>0.27*</i>	<i>0.17</i>		
	50-59		0.30	0.30	0.16	<i>0.28*</i>			-0.20	<i>0.29*</i>	-0.03		

Italic values are based on 50 or more observations. No coefficients listed for $n < 30$.

*Significantly different from zero at 5 per cent level.

TABLE 5. CORRELATION BETWEEN PARENTS AND CHILDREN, SERUM CHOLESTEROL, TECUMSEH 1960

Parent	Age of parent	Age of son						Age of daughter					
		4-9	10-14	15-19	20-29	30-39	4-9	10-14	15-19	20-29	30-39		
Father	30-39	<i>0.25*</i>	<i>0.35*</i>	0.20			<i>0.29*</i>	<i>0.29*</i>	0.29				
	40-49	<i>0.33*</i>	<i>0.10</i>	<i>0.33*</i>	0.25		<i>0.31*</i>	<i>0.25*</i>	<i>0.26*</i>	0.08			
	50-59		0.27	0.26	<i>0.35*</i>		0.04	0.03	0.14				
Mother	30-39	<i>0.29*</i>	<i>0.23*</i>	<i>0.39*</i>			<i>0.28*</i>	<i>0.40*</i>	<i>0.26*</i>				
	40-49	0.15	<i>0.42*</i>	<i>0.41*</i>	<i>0.26*</i>		0.25	<i>0.25*</i>	<i>0.16</i>	<i>0.28*</i>			
	50-59		0.24	0.24	<i>0.33*</i>	<i>0.17</i>		<i>0.36*</i>	<i>0.11</i>	<i>0.14</i>			

Italic values are based on 50 or more observations. No coefficients listed for $n < 30$.

*Significantly different from zero at 5 per cent level.

systolic and diastolic pressures, and except for the period of 15–24 years, lower cholesterol levels as well.

By contrast, in the period from early childhood to adult age, blood pressures, particularly systolic, show a rather rapid increase, while cholesterol values are relatively stable, and actually decline slightly. These data are, of course, cross-sectional and cannot be interpreted as longitudinal or cohort data.

Parent-child comparisons

Allowance for age and sex difference was made by comparing within age-specific groups, and also by using the scoring system previously described. The age-sex specific data for systolic blood pressures of parents and children are shown in Table 4. Most correlations are positive, although the coefficients are generally quite small. Similar computations for cholesterol values in parents and children (Table 5) demonstrate that the correlations in almost all age groups are considerably higher than those for systolic blood pressure.

Fig. 3 is a single graphic example of the parent-child relationship for cholesterol values in specific age groups. Each group in Tables 4 and 5 was directly visualized by such plots drawn directly by the computer.

Within each age-sex group, an attempt was made to determine more specifically the relationship of the child's reading to his parents' readings. The least squares second degree polynomial was obtained for each age-sex group. Out of the 52 such regressions computed for systolic blood pressure, only 3 showed a quadratic component of variance significant at the 0.05 level. For cholesterol the corresponding numbers were 4 out of 41. Hence, no evidence was found for any consistent non-linear component of these regressions. Linearity in these regressions would suggest that the degree of similarity between parents and children is essentially the same whether the parent is high, intermediate or low in blood pressure or cholesterol. Thus, parents with higher levels tend to have children with relatively higher levels while lower levels in parents are likewise reflected in lower levels in their offspring. It is further observed (Tables 4 and 5), on comparing parents of the same age with children within different age ranges, that there is no consistent trend for the correlations to change with age. A test was made for heterogeneity of the correlation coefficients in each of the four sets of parent-child coefficients for each variable. None of the four tests for the cholesterol coefficients gave significant results. The father-son set of coefficients for blood pressure was the only set found to be significantly heterogeneous and then only at the 0.05 level.

Utilization of age-sex adjusted scores permits comparisons to be made across much larger groups. The current blood pressure data for parents over age 30 and their children are compared (Table 6) with those of MIALL, OLDHAM and their co-workers [8–11]. Their data were derived from population samples in Wales and in Jamaica. The scoring system used by them was similar to that used in the present study. The data from Wales and Jamaica actually represent regression coefficients for scores, but because the method employed for score computation gives equal age-sex specific standard deviations, it is presumed that regression and correlation coefficients for scores should be nearly equal. MIALL and OLDHAM's original data from Wales (1958) were based upon a single casual reading, whereas the subsequent

TABLE 6. CORRELATIONS BETWEEN PARENTS AND CHILDREN FOR BLOOD PRESSURE SCORES IN SEVERAL STUDIES

	Father-Son	Father-Daughter	Mother-Son	Mother-Daughter
Systolic pressure				
Tecumseh	0.142	0.184	0.119	0.133
Wales (1958) [9]	0.122	0.175	0.258	0.166
Wales (1958-61 mean) [11]	0.159	0.248	0.225	0.247
Jamaica [10]	0.078	0.285	0.221	0.075
Diastolic pressure				
Tecumseh (5th phase)	0.095	0.073	0.015	0.095
Tecumseh (4th phase)	0.073	0.075	0.032	0.118
Wales (1958)	0.007	0.012	0.265	0.064
Wales (1958-61 mean)	0.202	0.109	0.085	0.231
Jamaica	-0.016	0.256	0.189	0.168

data were calculated from the mean of the 1959 reading and a second reading taken in 1961, using the mean age for score computation.

In all of these studies, correlations are almost always slightly larger for systolic than for diastolic readings. For all of the various parent-child relationships, the correlations are rather low, but increase markedly in the second Welsh study using the mean of two readings. The Tecumseh correlations tend to be more uniform and consistent than those in the other studies.

The correlation between parents over age 30 and their children for cholesterol levels based upon scores are shown in Table 7. The correlations based on scores are again considerably higher than those for blood pressure. The data by SCHAEFER, ADLERSBERG and STEINBERG [19], however, indicated a significantly higher correlation for mother-child than for father-child comparisons, though no evidence of sex-linkage was found. The present data point in the same direction but the differences are less marked.

TABLE 7. CORRELATIONS BETWEEN PARENTS AND CHILDREN FOR CHOLESTEROL SCORES, TECUMSEH 1960, AND A POPULATION GROUP IN NEW YORK CITY*

	Tecumseh		New York	
	n (pairs)	r	n (pairs)	r
Father-Son	1194	0.255	181	0.156
Father-Daughter	1066	0.222	192	0.262
Mother-Son	1288	0.277	181	0.340
Mother-Daughter	1175	0.258	192	0.390

*SCHAEFER *et al.* [19].

Sibship comparisons

The degree of sibship similarity was estimated by the determination of intraclass correlation (Table 8). An intraclass analysis was done to eliminate the necessity

TABLE 8. SIBSHIP INTRAClass CORRELATION COEFFICIENTS FOR BLOOD PRESSURE AND CHOLESTEROL, TECUMSEH 1960

Variable	Total number of sibships*	Intraclass correlation coefficient
Systolic pressure	1622	0.17
Diastolic (muffling)	1232	0.10
Diastolic (disappearance)	1464	0.12
Cholesterol	1153	0.35

*Sibships with 2-6 examined siblings. Numbers of sibships are not identical because both phases of diastolic pressure were not always recorded.

of choosing one sibling as a *propositus* against whom each of the others is compared. The data were first analyzed by groups of the same number of examined siblings, from sibships of two persons to sibships of six persons. Since the fluctuations in the coefficients were found to be quite small within these groups, the data were considered sufficiently homogeneous to be combined for computation of pooled intraclass coefficients. The difference in the method of computation does not permit precise comparisons with the magnitude of interclass correlations between parent and children described earlier. Nonetheless, it is observed that the coefficients for sibship comparisons are slightly higher than those for the parent-child comparisons for both blood pressure and, to a lesser extent, for cholesterol. Again, the correlation is noted to be rather higher for systolic than for diastolic pressure and much higher for cholesterol than for blood pressure.

Spouse comparisons

Similarities between blood relatives are presumably the resultant of both heredity and environment. The study of spouses provides a convenient way to compare persons with largely similar environmental influences and a minimum of similarity in genetic structure if, as in this population, consanguinity is not a significant factor. The extent and effect of associative mating is difficult to evaluate in any such study.

Preliminary analysis of all husband-wife pairs indicated no significantly positive correlations for either blood pressure or cholesterol, when viewed across all age groups. Since a real effect might be masked by the relatively great number of younger couples, in whom the common environment has been shared for only a short time, it would be desirable to analyze the data by length of marriage, or the relative 'exposure time' to the environment. The age of the wife was used as an approximation of the length of marriage. If environmental influences were to exert a cumulative effect over time, an increasing gradient of similarity would be expected. Such a gradient is not discernible, either in regard to blood pressure or cholesterol, although most of the coefficients are positive (Table 9). In the absence of a gradient, the solitary significant correlation for blood pressure in the age group 50-59 is difficult to interpret. Since some significant correlations are inevitable when many are tested, this apparent significant correlation may be spurious. Conceivably, the endocrine changes coincident with menopause could in some way bring about a greater similarity between spouses, perhaps by permitting a greater relative role to be played by environmental influences. However, since this period is one of rapid

TABLE 9. SPOUSE COMPARISONS FOR BLOOD PRESSURE AND SERUM CHOLESTEROL BY AGE OF WIFE, TECUMSEH 1960

Age of wife	No. of couples	Correlation coefficients		
		Systolic	Diastolic V	Cholesterol
20-29	488	0.01	-0.04	0.03
30-39	625	0.06	0.04	0.10
40-49	401	0.01	0.06	0.07
50-59	233	0.27*	0.21*	0.06
60+	161	0.10	-0.05	0.07

*Significantly different from zero at 5 per cent level.

change in blood pressure for many women (Fig. 1) causing temporary alterations in relative position in the distribution, the resultant effect may have been a closer similarity with their spouses, but this effect was not seen after 60 years of age.

Although others investigators [20] have been in accord with the lack of spouse correlation, CHAZAN and WINKELSTEIN [21] have reported a positive relationship between spouses' blood pressures. Further clarification is needed.

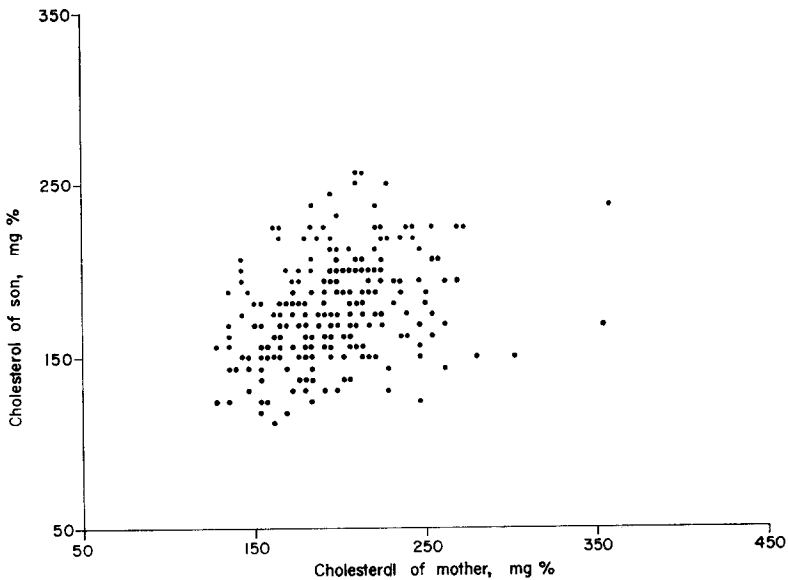


FIG. 3. Relationship between serum cholesterol values for mothers aged 30-39 and their sons aged 4-9. Slope=0.242; $r=0.294$.

DISCUSSION

The purpose of this report has been to describe distributions of blood pressure levels and cholesterol values in a complete, intact community. Against this background, each person may be viewed as an individual, as a part of a family or kindred group, or as a member of a specific environmental subgroup.

The overall study is concerned with the problem of identification of persons susceptible to any of the major chronic illnesses. Attributes which are measurable or definable such as physiological variables, present and past diseases, symptoms, family history, socio-economic factors, are all considered to be pieces of the puzzle from which susceptibility may be determined. Against this background, distributions of blood pressure and serum cholesterol levels have been analyzed revealing several interesting parallels.

The similarity in the pattern of increase of mean blood pressure and cholesterol with age is intriguing, and without satisfactory explanation. For both variables, women during most of the reproductive years have lower values, but after these years have considerably higher levels on the average than do men. The distributions themselves are similar, being unimodal, generally symmetrical, but progressively more skewed with age.

The establishment of 'normal' and 'abnormal' levels by a specific range or cut-off point has proved equally difficult for each. Whether high values in these distributions represent a truly qualitative disease state or merely the positive tail of the distribution has been discussed at length as regards blood pressure and less extensively for serum cholesterol. The role of inheritance in blood pressure levels in relatives has been studied by HAMILTON, PICKERING and associates [7, 12, 22], MIALL, OLDHAM and co-workers [8-11], PLATT [23], MORRISON and MORRIS [24] and others [25-28], and as it affects cholesterol levels by SCHAEFER *et al.* [17-19] and EPSTEIN *et al.* [29]. Two squarely opposed genetic mechanisms, the qualitative (single gene) hypothesis, and the quantitative or multifactorial hypothesis have been proposed to explain, in part, observed similarities between relatives. Symmetrical unimodality of the distributions favors the quantitative view. As stated by ROBERTS [30], "a reasonably Gaussian distribution is not proof of multiple causation and polygenic inheritance, but it is a necessary concomitant and an argument in its favor."

SHOPE [31] was the first to note familial similarities in inbred guinea pig strains with regard to serum cholesterol levels. The definition of the mode of inheritance of serum cholesterol levels has been reviewed by SCHAEFER *et al.* [19] and EPSTEIN *et al.* [29]. The tendency has been for earlier investigators to favor a single gene hypothesis and dominance but with restricted penetrance. However, fitting of any specific genetic model has been difficult. Recent work in mice [32] has pointed again toward the concept of a polygenic view, suggesting that inheritance of cholesterol levels in this species is neither dominant nor recessive, but intermediate and additive. Cholesterol values of offspring correlated well with the average of the values of their parents. In this case, environmental factors were the same for all animals, a situation impossible for human studies.

Aside from academic interest, what practical value can result from the elucidation of the genetic pattern? If a qualitative factor is determined by dominant inheritance, the carrier of the gene may be identified by secondary or ancillary characteristics under the influence of the same gene. These in turn may possibly be useful as indicators of susceptible persons prior to the expression of the major effect, the disease itself. In polygenic inheritance, predictors of later abnormality may possibly be detected in the parents and relatives of index cases by the effects of closely associated genes, if these are identified.

Whatever the mode of inheritance, the interaction of environmental factors upon genetically susceptible persons is unquestionably important. These host and environmental variables are numerous and complex, some undoubtedly additive in the production observed effect, and others compensatory. Some environmental factors of etiological importance may be so universally distributed that a differentiating effect is lost. For example, diet is indisputably related to cholesterol levels, yet no correlation was found between spouses, regardless of the length of time during which they have shared the same table.

Much further work is necessary to clarify environmental interactions. External influences which may affect blood pressure or cholesterol may be detected by study of intrafamily similarities in differing environmental situations, if the force of heredity is considered nearly uniform. These environmental factors could produce a greater conformity within families or in differing geographical areas. Comparative study may aid in identification of these influences. Whatever role is played by inheritance, the correlations between relatives as reported in studies from various parts of the world seem to be quite similar in spite of seemingly widely divergent environmental factors. Identification of these factors in terms of significance must be pursued.

Perhaps the greatest need is the ability to judge which young person will show progressive elevations of blood pressure or cholesterol with advancing years and which will remain stable. This 'rise potential' may well also be a graded characteristic which may be identified by the proper tests. OLDHAM *et al.* [12] suggest that the observed evidence indicates that the tendency to rise with age is not the factor which is inherited, but rather the rate of rise be considered relatively uniform and the inherited factor is already manifest in the young person since both he and his parent occupy similar positions in their respective distributions. HARLAN *et al.* [34] have also shown that healthy young men tended to retain the same general blood pressure ranking in the study population when re-examined after 18 years. However, considering the fact of increasing skewness of the distributions with age, as well as the observations [35] indicating that a substantial portion of the population does not show a rise with age, it seems more probable that differing rates of rise exist, and may be in part inherited. The concept of differing rates is central to the qualitative hypothesis, but it does not seem incompatible with the quantitative hypothesis, and may actually account in part for the relatively low correlations seen.

In total, the evidence to date seems to lean heavily toward the quantitative hypothesis for both blood pressure and cholesterol. However, as stated by McKUSICK [33], this "does not preclude the desirability of searching for a unitary, genetically determined biochemical defect, the expression of which is modified by environmental or other genetic factors." Further longitudinal study of these factors within families and kindreds as planned in Tecumseh is necessary for better understanding of these conditions.

SUMMARY

The medical examination of the population of a complete natural community, Tecumseh, Michigan, has provided a basis for investigation of factors possibly relating to predisposition to chronic disease.

The following are reported :

1. Parameters for distributions of blood pressure and cholesterol values for the entire population, including young children.
2. Correlations between parents and children within specific age groups and by age-sex adjusted scores; these are relatively low, but consistently positive, being considerably greater for cholesterol than for blood pressure. Thus, there was a distinct resemblance in values between parents and children but the force of similarity was essentially equal over the entire range of distributions of blood pressure and cholesterol. Children resembled mothers and fathers equally in regard to blood pressure, but had some tendency to be more like their mothers in their cholesterol values.
3. Correlations between siblings, while somewhat greater, were found to be within the same general range of magnitude as the parent-child comparisons.
4. Spouse comparisons, as noted by most other investigators, showed a lack of significant correlations for either variable when all couples are viewed in the aggregate. No gradient of increasing conformity between spouses was demonstrable for either blood pressure or cholesterol when viewed by length of marriage, a rough index of the number of years of a shared environment.
5. Comparisons with other studies were presented and types of possible genetic control and environmental interaction was discussed. The present findings are compatible with the concept of a multifactorial genetic and environmental interplay for both blood pressure and cholesterol.

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