Papers and Originals

THE HEREDITARY FACTOR IN ARTERIAL BLOOD-PRESSURE

BY

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The current conflict of views about the nature of essential hypertension reflects our ignorance of arterial pressure in the general population. Though reliable apparatus for the indirect measurement of blood-pressure has been available for over half a century we still do not know how arterial pressure increases with age in the population at large; we know little of the influence of environmental factors and there is disagreement about the mode of inheritance of hypertension. Investigations of these questions cannot easily be initiated from hospital practice, and it seems highly probable that the long-term study of representative populations by the modern techniques of epidemiology will contribute much to the understanding of the factors affecting blood-pressure within the next decade.

Two such long-term epidemiological studies are in progress in South Wales, and this report summarizes the analyses of the genetic data derived from them. Other papers will deal with the influence of environmental and personal factors. The results reported here include data derived from the original "cross-sectional" surveys, and from the follow-up surveys which were undertaken four years later.

Some of these data have been published previously (Miall and Oldham, 1955, 1957, 1958; Miall, 1962), but we believe that their re-examination in the light of subsequent analyses helps to form a clearer picture of the pattern of inheritance which is emerging.

The Population Samples

These surveys arose from the obvious need to investigate quantitatively the pattern of inheritance of arterial pressure in families that were not selected, as they had hitherto been, on the basis of propositi with and without hypertension defined in terms of some threshold pressure determining the boundary between normal and abnormal. The propositi were randomly selected from subjects over the age of 5 years in two geographically defined populations in South Wales. The populations and the methods of selection of random samples from them have been described elsewhere (Miall and Oldham, 1958). In the Rhondda Fach, 250 randomly selected propositi and 978 of their first-degree relatives co-operated in our surveys; in the Vale of Glamorgan a total of 373 propositi and 1,267 first-degree relatives co-operated. Over 95% of both the propositi and relatives living within 25 miles were examined in each survey. The completeness of the follow-up of these populations is shown in Table I. In the follow-up surveys over 99% of the Rhondda subjects and over 98% of those in the Vale were re-examined.

Use of Age-adjusted Scores

The hypothesis that essential hypertension is one manifestation of the inheritance of a single gene needs more detailed specification before it can be explored using data such as those now being presented. In particular, the hypothesis must specify how essential hypertension is defined in relation to arterial pressure at different ages in the two sexes. So far the proponents of the single-gene hypothesis have not suggested how this should be done, but have searched in sets of data for examples of segregation into two or three distinct classes.

We have adopted the method of analysis used for arterial pressure by Hamilton and his colleagues (1954). This is based on age- and sex-adjusted scores, designed to allow direct comparison between relatives of different age and sex and are derived as follows: the deviation of an individual's pressure from the mean for his or her age and sex is given a positive or negative sign according to whether it is above or below the mean value. This deviation is then adjusted to a reference age to allow for the variation in the range of pressures with age of persons of the subject's sex by multiplying it by the ratio of the standard deviation at the reference age to that at the subject's age. The reference age is chosen to be one at which the standard deviation is the same or closely similar for the two sexes; in this way the scores adjust also for sex.

This system of scoring is exactly appropriate for investigating the hypothesis of multifactorial inheritance of arterial pressure in its simplest form. On this hypothesis any individual inherits an array of genes which determine his relative position on the nearly continuous distribution curve of arterial pressure, and only non-genetic factors (which will count as random errors in a genetic analysis) can cause him to change this relative position. He is fixed by his genes at a certain percentile point in the distribution, and it is this percentile point or its equivalent which is estimated by his age-adjusted score.

TABLE I.—*Follow-up of Male and Female Populations, Rhondda Fach (1954–58) and Vale of Glamorgan (1956–60)*

	Males				Females				Total			
	Random Samples		First Degree Relatives		Random Samples		First Degree Relatives		Random Samples		First Degree Relatives	
	Rhondda	Vale	Rhondda	Vale	Rhondda	Vale	Rhondda	Vale	Rhondda	Vale	Rhondda	Vale
Followed up	120	161	404	576	103	161	487	554	223	322	891	1,130
Left area	9	11	28	23	6	15	23	39	15	26	51	62
Died	5	13	22	33	5	6	9	24	10	19	31	57
Refused follow-up	2	2	1	6	0	4	2	9	2	6	3	15
Original population	136	187	455	638	114	186	521	626	250	373	976	1,264

More complicated forms of the multifactorial hypothesis, such as one involving a variation of expressivity of the genes with age, would require a more complex scoring system. The need for this would be indicated, if sufficient data were available, by the appearance of particular patterns of heterogeneity in the scores. Some forms of the single-gene hypothesis—for example, one in which the same fraction of the upper end of the distribution of pressures was hypertensive, whatever the actual pressure or the age of the subjects—would also be satisfactorily explored by the use of age-adjusted scores. Other forms would not—for example, any in which a particular pressure was regarded as the boundary of normality. In this case segregation into classes with and without hypertension could be obliterated by the pooling of age-groups in which a varying proportion of subjects attained the critical pressure.

We make no apology for basing our exploration of the data on the multifactorial hypothesis in its simplest form. In the absence of an alternative hypothesis of sufficiently detailed specification it is the natural hypothesis to use with data appearing as continuously distributed measurements, and if it is wrong we believe this will be revealed by internal contradictions in the data.

Survey and Analysis Techniques

All the blood-pressure determinations were made by one observer, and the survey technique was designed to be as near identical in each study as it is possible to achieve. Casual blood-pressure measurements were made in the individual's home surroundings after a period of at least five minutes spent seated. We deliberately chose to record casual arterial pressure for four main reasons: first, because casual pressures have most ready application in clinical medicine—they are the measurements made and used by the vast majority of physicians and almost all general practitioners; second, because it is with these rather than with basal pressures that we live most of our waking lives; third, because we wanted our data to be comparable with those of other workers; and fourth, because in epidemiological work one must consider the demand made upon the population. Very frequent or prolonged investigations cannot be applied in the general population without seriously influencing the response rate, and we hoped to keep the co-operation of our populations over a period of years.

In deriving scores in the initial prevalence surveys we measured the deviations from the cubic regressions best fitting the data. After the follow-up surveys we were able to obtain a better estimate for mean arterial pressures than those based on the observations made at either survey by using data collected at both surveys. As the surveys were carried out at four-yearly intervals mean values were calculated in four-year age-groups; by so doing, adjacent age-groups are separated by the intersurvey interval and those forming a particular age-group at the first survey are still found as a group on the second occasion. The mean values in each age-group were derived from those subjects who were in that age-group at the first survey, from the second survey results of those who at the first survey were in the preceding age-group, and from the estimated second survey pressures of those who were in the preceding age-group at the first survey but were not followed up. These values were weighted according to their standard errors and the overall means calculated (Fig. 1). It was then found that we could obtain a better fit to these mean values by drawing freehand curves than by fitting a mathematical equation, and the latest scores are based on these curves. In deriving these scores we have used the mean of the pressures recorded on the two occasions and the mean age, and thus have roughly halved the random element in the error of the measurements.

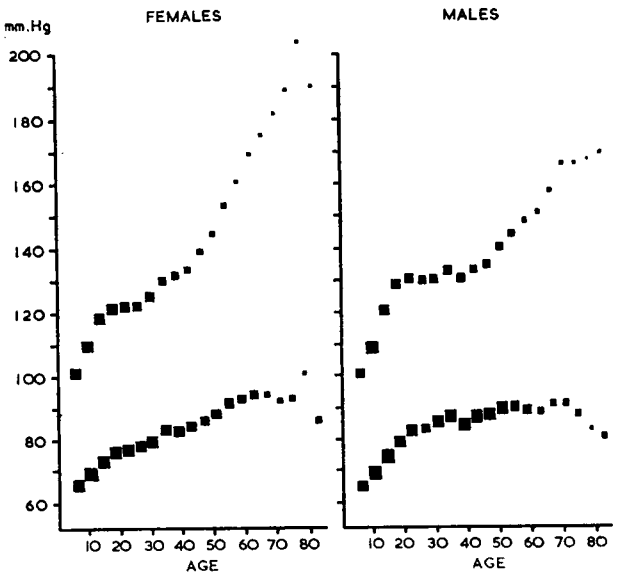

FIG. 1.—Mean systolic and diastolic pressures in the Rhondda Fach and Vale of Glamorgan populations, based on the findings in two surveys. The area of each square is inversely proportional to the standard error of the mean, and so indicates the weight to be attached to each mean.

The technique of analysis has been to score each subject's systolic and diastolic pressure, and to plot those of first-degree relatives against those of their propositi for the twelve different relations (male propositi, father, mother, brothers, sisters, sons and daughters, and similarly for female propositi), test for heterogeneity, and thence to calculate the regression of scores of all relatives on those of propositi of either sex, testing for significant deviation from a linear regression. On the basis of polygenic or graded inheritance it would be expected that the mean scores of relatives of propositi covering the whole range of pressure found in the population at large would fit this regression more and more closely as the numbers analysed increased and the errors were eliminated.

Results

In the analysis of the initial Rhondda Fach survey systolic-pressure scores only were investigated as it has been shown by Hamilton and his colleagues (1954) that the genetic factor was similarly manifested by either systolic or diastolic pressure. The values of the regression coefficients in the six different relationships of propositi of either sex satisfied a test of homogeneity based on an assumed Gaussian distribution, as did the average regressions of all relatives on male or on female propositi, so the separate relationships were pooled and the average regression coefficient was calculated. This overall regression had the value 0.239 ± 0.032, and the fit of the mean scores to this linear regression is shown in Fig. 2.

Though there appeared to be some divergence of those mean scores of relatives corresponding to the extremes of the range of scores of propositi, the numbers involved

in these groups were small, and the scatter was no greater than would be expected by chance.

Following the first survey in the Vale of Glamorgan we pooled the data from this and the earlier Rhondda Fach survey, which seemed justifiable in view of the close similarity in the relationship between pressure and age in the populations, and the inheritance factor was investigated in the 612 families of propositi aged 5 to 79 years. The regressions for the twelve different relationships were recalculated, and for systolic pressure

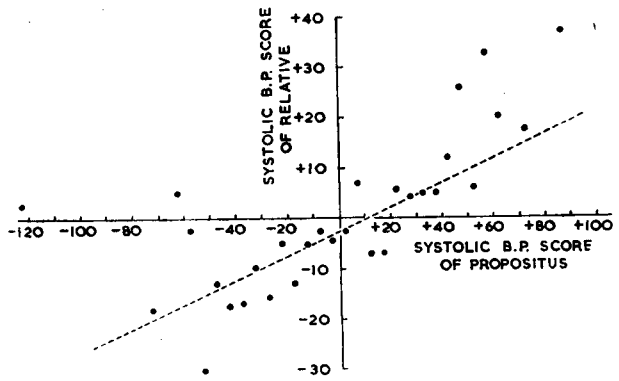

FIG. 2.—Relationship between the systolic-blood-pressure scores of propositi and the mean systolic scores of relatives. From the first Rhondda Fach survey.

showed no evidence of heterogeneity. The overall regression for all relatives on all propositi now had a value of 0.224 ($\pm$0.022) for systolic pressure, and the fit of the mean values to the linear regressions had clearly improved (Fig. 3). The separate regressions of relatives' diastolic scores on those of male propositi did not differ significantly; those on female propositi showed evidence of heterogeneity (again based on Gaussian distributions) inasmuch as the average regression of male relatives on female propositi (0.146) did not adequately represent the regressions of fathers' scores (0.012) or brothers' scores (0.267) on these female propositi; nor did the regression of female relatives' scores on female propositi (0.045) adequately represent those of mothers on female propositi (0.064). These apparent differences among the regressions do not form any reasonable pattern, and it may be that too rigorous a test of homogeneity has been applied, or that the differences are due to the interplay of environmental

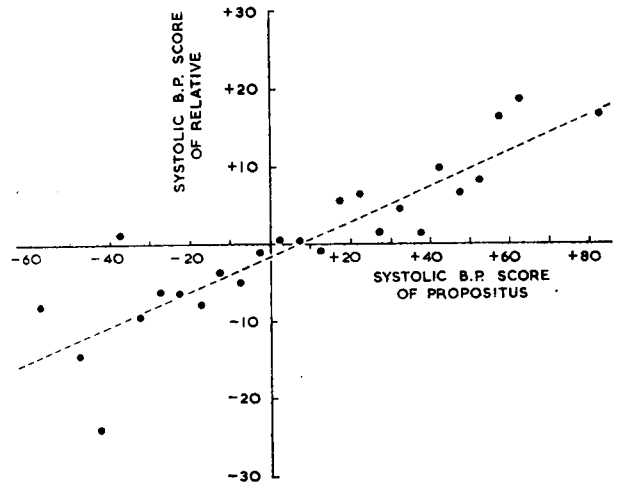

FIG. 3.—Relationship in Fig. 2 when the results of the first Vale of Glamorgan survey are added.

factors. Bearing other possibilities in mind, we may summarize them by a single overall regression of value (0.178 ± 0.024) which, with the mean scores of relatives, is illustrated in Fig. 4.

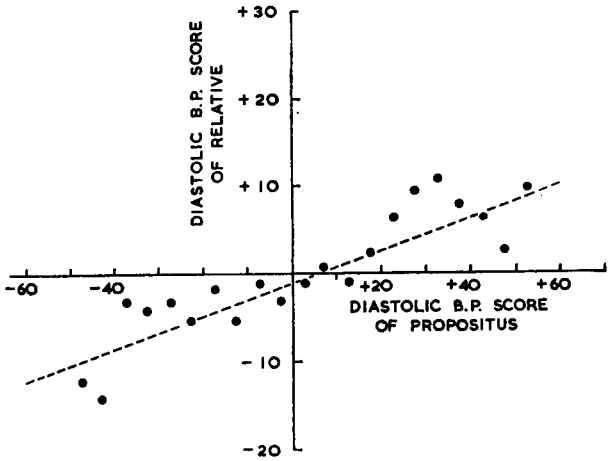

FIG. 4.—As for Fig. 3, but for diastolic-blood-pressure scores.

Having followed up both these populations, as already indicated, we have used new scores based on the mean of two readings and mean age, and have again calculated the regressions. These and the values derived previously are shown in Tables II, III, and IV. The twelve regression coefficients involving the six different relationships and male propositi have increased in value in ten cases and diminished slightly in two (systolic scores of sons and diastolic scores of daughters on male propositi). Those involving female propositi have increased in value in eight cases and diminished somewhat in four (systolic scores of daughters, diastolic scores of brothers, sisters, and daughters).

TABLE II.—*Regression Coefficients of Relatives on Male Propositi, as Derived from a Single Measurement* (1958) *and the Mean of Two Measurements* (1961)

	Systolic		Diastolic	
	1958	1961	1958	1961
Fathers	0·122	0·211	0·007	0·146
Mothers	0·258	0·287	0·265	0·396
Brothers	0·239	0·321	0·152	0·232
Sisters	0·182	0·272	0·209	0·297
Sons	0·188	0·159	0·171	0·202
Daughters ..	0·195	0·248	0·121	0·109
All relatives ..	0·209	0·267	0·163	0·246

TABLE III.—*Regression Coefficients of Relatives on Female Propositi, as Derived from a Single Measurement* (1958) *and the Mean of the Two Measurements* (1961)

	Systolic		Diastolic	
	1958	1961	1958	1961
Fathers	0·175	0·271	−0·012	0·154
Mothers	0·166	0·235	−0·064	0·112
Brothers	0·168	0·261	0·267	0·205
Sisters	0·328	0·452	0·350	0·338
Sons	0·205	0·225	0·052	0·085
Daughters ..	0·271	0·247	0·286	0·231
All relatives ..	0·233	0·302	0·196	0·209

TABLE IV.—*Regression Coefficients of All Relatives on All Propositi, as Derived from a Single Measurement* (1958) *and the Mean of Two Measurements* (1961)

	All Propositi—All Relatives	
	Systolic	Diastolic
1958	0·224	0·178
1961	0·287	0·224

The average systolic regression of all the relatives on male propositi has increased from 0.209 to 0.267, that for diastolic scores has increased from 0.163 to 0.246 (Table II). The comparable regression coefficients involving female propositi have increased from 0.233 to 0.302 and from 0.196 to 0.209 (Table III). The overall regressions for relatives of any kind on propositi of either sex have increased from 0.224 (±0.022) to 0.287 (±0.024) for systolic scores, and from 0.178 (±0.024) to 0.224 (±0.023) for diastolic scores (Table IV).

The intra-class correlation coefficients E given in Hamilton *et al.* (1954) and in Miall and Oldham (1955) have also been recalculated from the pooled data. These reflect any resemblance among sets of sibs or children of the same propositus; in fact, the variance of pressure within families is compared with that between families. This measure is independent of the regression of relatives on propositi. For systolic pressure, E is 0.248, for diastolic 0.203. The previous value for systolic pressure (based on the Rhondda survey only) was 0.190 (0.206 among sibs, 0.156 among children).

The scatter about the regression lines continues to diminish (Figs. 5 and 6) and shows no tendency to segregate into different patterns for those with high and those with low pressure. There is no significant residual variation left between relatives of propositi with different scores when the linear regression has been removed. Within the general population the relationship in arterial pressure between close relatives appears to be independent of the range of pressure considered.

By considering the means of pairs of observations derived from the two surveys we must approximately have halved the variance due to the random or observational element present in each, which can be thought of as additional to that variance between subjects which reflects real differences in pressure. In fact if c is the co-variance due to the resemblance of relatives, σ^2 the true variance of pressure, and s^2 the additional error variance (both σ^2 and s^2 being similar in the two surveys), the regression of relatives on propositi b_1 observed in the first survey will be

$$c/(\sigma^2+s^2),$$

while the regression b_2 observed in the two surveys pooled will be

$$c/(\sigma^2+\tfrac{1}{2}s^2).$$

It is therefore possible to estimate the value of b, equal to

$$c/\sigma^2,$$

that would be found if there were no error variance. In fact, it can be shown that

$$c/\sigma^2=b_1\,b_2/(2b_1-b_2),$$

and substituting the values 0.224 for b_1, 0.287 for b_2, we find an estimate of the true regression of the systolic pressures of first-degree relatives on the propositi to be 0.399. Similarly, substituting 0.178 for b_1 and 0.224 for b_2, the estimate of the true diastolic regression is 0.302.

The accuracy of these estimates is low, and not much weight should be attached to them. Moreover, similarities of environmental factors acting within families may be inflating the co-variance observed between first-degree relatives, and we can make no attempt to estimate this effect. It is thus unwise to remove non-genetic variance from the denominator of the ratio giving the regression while leaving the numerator unchanged. The uncorrected regression coefficients may be the more reliable.

If arterial pressure were completely determined genetically, by multiple genes without dominance, the regression of first-degree relatives on propositi would be the same as the proportion of genes they have in common—that is, 0.5. If there were dominance the degree of resemblance would be less than the proportion of genes in common, and, as was pointed out by Oldham *et al.* (1960), cannot be calculated but must be estimated from the data, as we have done. Whatever pattern of dominance is present, provided the frequency of the dominant allele is the same in each gene pair involved, the deviation of the regression of sibs from 0.5 must always be half that of the deviation of the regression of parents on children (see Roberts, 1959, p. 208).

Table V shows the average regressions of sibs and of parents and children in our pooled data. The deviation from 0.5 is indeed smaller in sibs than in parents and children but not significantly so, and not to the extent that dominance would cause. The regressions for both relationships do not differ significantly from each other, but the hypothesis that the difference is due to dominance is not excluded by these figures.

If we confine the analysis to the middle-aged siblings of middle-aged propositi (we took ages 40–59 at the time of the first survey for this purpose) and examine the relationship between propositi and relatives we find a regression of 0.27 for systolic pressure and 0.31 for diastolic pressure. The diastolic data are shown in Fig. 7; these are based on only 183 individuals in the appropriate age range and the scatter about the regression

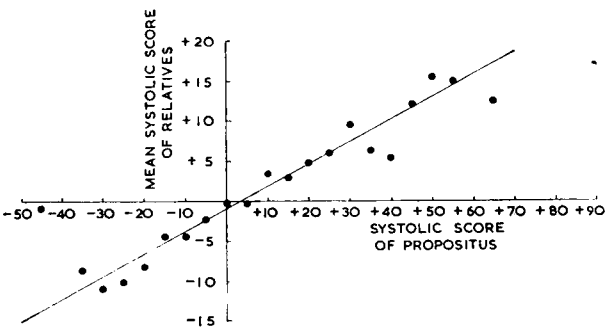

FIG. 5.—Relationship between the systolic-blood-pressure scores of propositi and the mean systolic scores of relatives, from the combined Rhondda and Vale initial and follow-up surveys.

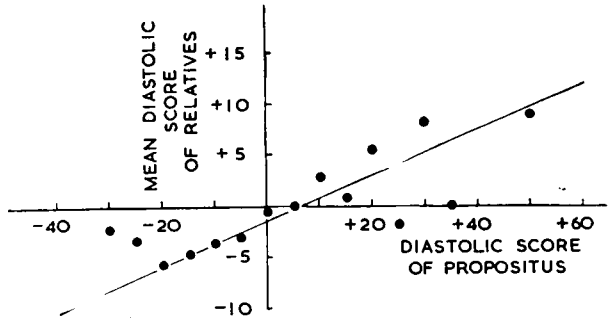

FIG. 6.—As Fig. 5, but for diastolic-blood-pressure scores.

TABLE V.—*Average Regression Coefficients Among Siblings and Among Parents and Children as Derived from the Mean of Two Measurements*

	Systolic	Diastolic
Siblings	0·333	0·265
Parents and children	0·237	0·183

line is greater. There is a suggestion that the pattern of inheritance of diastolic pressure in the families with propositi having scores of +10 and over may be different from those with lower values, but no similar pattern was found in the corresponding analysis of systolic scores. The deviations from the linear regression

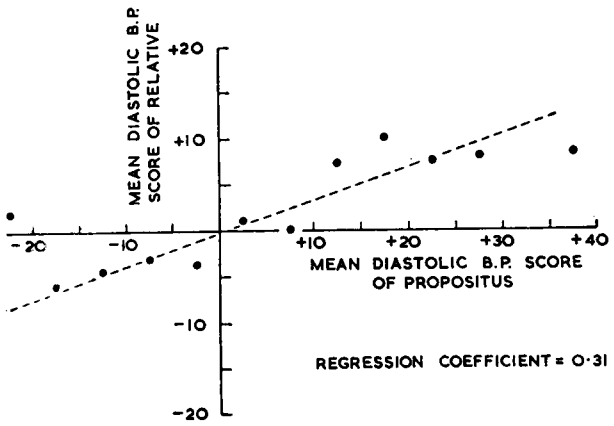

FIG. 7.—As Fig. 6, but for propositi and relatives aged 40-59 at the time of the first surveys.

again are not statistically significant, and this is the only suggestion of such a result which we have been able to find.

The proportion of the total variance of blood-pressure accounted for by inheritance is of interest in comparison with the amount that must be attributed to environment. If a characteristic were entirely inherited multifactorially, 50% of its variance would be accounted for by a knowledge of all the parental genes. The remainder reflects the fundamental uncertainty of which allele of each gene-pair of a parent was handed on. Our estimate of the systolic regression coefficient, 0.287, is also an estimate of the correlation between first-degree relatives. Its square, 0.082, estimates the proportion of variance accounted for by one parent, and an equal amount can be attributed to the other. Since at most 50% of the variance is accounted for in this way, when hereditary determination is complete, 16.4% corresponds to 32.8% hereditary determination. The complementary fraction, 67%, of the variance may be environmentally determined. The corresponding figure for diastolic pressure is 79.9%. The 95% fiducial limits are for systolic pressure 55.6% and 76.7%, for diastolic pressure 70.9% and 87.2%.

Similar calculation, using the estimated error-free regressions of 0.399 for systolic and 0.302 for diastolic pressure, would leave 36.3% of the systolic variance and 63.5% of the diastolic variance attributable to non-familial environmental factors.

Discussion

The kind of analysis which we have presented has been criticized in the past on two main grounds. The first concerns the use of scores, the second the use of the general population (Morrison and Morris, 1960: Platt, 1961).

We have already given our reasons for basing our analysis on transformations of the measured arterial pressures. Such scores have been criticized for several reasons. First, because they are a manipulation of the raw data. This is true: they are deviations from average of pressures multiplied by a ratio (the ratio of two standard deviations). The distributions of scores in any age-group, when compared with the distributions of pressure, are either compressed or expanded, depending on the age-group, but they are not distorted. If bimodality occurs in the distributions of pressures it will be found in the distributions of scores. Second, scores are criticized because they are used for comparing subjects of very different age, though it has been shown by Hamilton and his colleagues that the relatives of subjects with essential hypertension showed higher pressures at all ages which they studied—that is, in all relatives over the age of 10 years.

Platt criticizes the practice of grouping relatives and examining only their mean pressures (or mean scores) because in so doing the distributions among these relatives are concealed (Platt, 1961). This is also true. We have failed to find evidence which suggests single-gene inheritance to us, but our data will be made available to others who wish to search for it. We have not seen any convincing evidence that the distributions of relatives' pressure are anything but unimodal in the general population, and so have investigated what is to us the more probable hypothesis of multifactorial inheritance—that is, the extent to which relatives, *on average*, resemble each other. It is still too soon for these scores to have been validated adequately in terms of stability in follow-up surveys in the general population or in terms of morbidity and mortality, a criticism which also applies to pressure measurements.

The second ground for criticism is more difficult to follow. It is being conceded that there is strong evidence in favour of multifactorial genetic and environmental determination of blood-pressure in the general population, but it is said that by studying random samples of the general population we are determining the factors influencing normal blood-pressure but are hardly concerned with the problem of essential hypertension (Morrison and Morris, 1960; Platt, 1960). There is a paradox here which is perhaps only a further manifestation of the arbitrary nature of the diagnosis; if essential hypertension is a disease with a gene frequency of 19–30%, as Platt (1959) believed, or of 30–40%, as Søbye (1948) believed, then we should be seeing it well represented in our populations. If, on the other hand, it is characterized by subjects with mean pressures of 240/142 mm. Hg, as were the propositi in Platt's (1961) recent genetic analysis, then it is a very rare disease in the general population. Studies based on hospital populations in which such propositi may be found may have little relevance to the aetiology of the hypertension which is common in the general population and which has been found in our samples to be a frequent cause of morbidity and excess mortality (Miall, 1962).

It is possible that several different kinds of single-gene inheritance play an important part in determining the arterial pressure of a very small section of the community. It is true that studies of the general population such as those we are reporting are unlikely to detect such cases. We claim only that in that large fraction of the population which has high blood-pressure, and in which the ill effects of high blood-pressure can be seen to be arising, a multifactorial pattern of inheritance identical with that shown by persons with average pressures appears to fit the facts adequately.

Summary

This report summarizes the genetic analysis of arterial-blood-pressure measurements obtained in the

first four years of an epidemiological study of 612 families randomly selected from two populations in South Wales.

No evidence is found in our data to suggest that arterial pressure is not a continuously variable characteristic, and in the absence of a sufficiently precise definition of essential hypertension to allow its genetic investigation in the general population we have used the appropriate system of quantitative analysis to investigate the simpler concept of multifactorial inheritance.

If arterial pressure is determined by graded polygenic inheritance it would be expected that the relationship in pressure between relatives and propositi would be similar at all ranges of pressure, and that the data would fit a linear regression more and more closely as the errors were eliminated. This is what we have found. On the basis of Mendelian inheritance of a specific gene for essential hypertension it would be reasonable to expect that the accumulation of more data, and more reliable data, would reveal internal inconsistencies in such an analysis and would segregate the population into at least two groups in which the relationship in pressure between relatives and propositi was different. We found no evidence of these.

It is possible that single-gene inheritance plays an important part in determining the arterial pressure of a very small fraction of the community, but our analyses suggest that in a representative sample of a general population which is experiencing what we take to be the usual morbidity and mortality associated with high blood-pressure this fraction is too small to be detected. For the majority of the population it appears that a regression of 0.287 for systolic pressures, and 0.224 for diastolic best summarizes the genetic resemblance of first-degree relatives, leaving between 55% and 77% of the systolic variance, and between 70% and 87% of the diastolic variance, for environmental factors to explain.

We gratefully acknowledge the continued co-operation of the families who are taking part in these studies, and the help of members of the survey team of the M.R.C. Epidemiological Research Unit who have assisted in the collection and analysis of the findings.

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"The Air Force Surgeon General's office [U.S.A.] has ordered Air Force hospitals and clinics to stop distributing free cigarettes to patients. A similar prohibition has been ordered on the inclusion of cigarettes in the packaged lunches that are prepared for service personnel on long flights. Major-General R. L. Bohannon, the Deputy Surgeon General, said in a strongly worded directive that the 'ever-increasing evidence' of a link between cigarette smoking and cancer and certain other diseases 'no longer can be ignored.'" *New York Times*, October 8.

BRONCHIECTASIS IN CHILDHOOD

BY

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Bronchiectasis, while not a very common disease in childhood, is by no means rare, often passes unrecognized for many years, and is responsible for a sum-total of chronic and recurrent ill-health quite out of proportion to the actual number of its victims. The natural history of this disease, as of most chronic conditions, is not easy to study, and our knowledge thereof is incomplete and based more upon impressions than objective observations.

So far as I know, only two comprehensive surveys of bronchiectasis in childhood have been published from this country in recent years (Field, 1949; Strang, 1956). While both contain much useful information, neither is based on a completely unselected series of cases. Field's cases were collected at the Hospital for Sick Children, Great Ormond Street, and at University College Hospital, London. Neither of these hospitals draws all the cases from any defined population group and both probably tend to attract the difficult or unusual case. Strang's report is based on the results of a follow-up of children admitted to Newcastle Regional Thoracic Surgery Centre: such a series is likely to be deficient both in cases with disease too extensive for surgery and in cases with few symptoms or symptoms well controlled by medical treatment.

The survey here reported was undertaken in the hope of building up a comprehensive picture of bronchiectasis in childhood and of assessing the end-results of treatment in an unselected series of cases.

Material

This survey covers all children aged 0 to 11 years inclusive in whom a diagnosis of irreversible bronchiectasis was first established in the Royal Aberdeen Hospital for Sick Children during the 10-year period 1946–55. This is the only children's hospital in the North-eastern Hospital Region of Scotland, an area which includes the City and County of Aberdeen and the Counties of Kincardine, Banff, Moray, Orkney, and Shetland. It is certain that during this period no children have been admitted for bronchography direct to the Regional Thoracic Surgical centre or to any other hospital in the Region. The regional boundaries are well defined and it can be claimed with some confidence that few, if any, cases living in this region have been investigated in adjacent regions. Indeed, our figures include a number of cases transferred from the Northern Hospital Region as possible candidates for thoracic surgery. This series therefore includes all cases of bronchiectasis confirmed in children from the North-eastern Hospital Region during a 10-year period. I have personally examined all these children and have taken part in their supervision throughout the whole period covered by the survey.

I have excluded from further consideration three cases of bronchiectasis due to mucoviscidosis (fibrocystic disease) and one case of congenital cystic disease of the lung presenting with tension cysts in the neonatal period (Clark *et al.*, 1956). No other case has been excluded as "congenital cystic disease."