J. chron. Dis. 1966, Vol. 19, pp. 245–254. Pergamon Press Ltd. Printed in Great Britain

ARTERIOSCLEROTIC HEART DISEASE IN A FAVORED COMMUNITY*

ANCEL KEYS, Ph.D.

The Laboratory of Physiological Hygiene, School of Public Health, University of Minnesota, Minneapolis

(*Received* 21 *June* 1965)

THE interesting hypothesis that differences in the psycho-social characteristics of communities produce important differences in the frequency of myocardial infarction, and by implication coronary heart disease in general has been advocated by BRUHN [1] in attempting to explain the low incidence of the disease reported for the little town of Roseto, Pennsylvania, by investigators from the University of Oklahoma [2]. The hypothesis is particularly attractive when it is proposed that the happy life in a well-knit community, where mutual self-help is the rule and where "there is no crime" [2], may allow carefree indulgence in an abundant, rich diet without hazard to the arteries. But before drawing conclusions from the favored town of Roseto, it is necessary to examine the acutal data more critically.

The Oklahoma University team who discovered Roseto emphasized that among a population of 780 males (in the 1960 census), they could authenticate only five deaths ascribed to myocardial infarction in the records for the 7-year period 1955–1961 [2]. In four other considerably bigger towns nearby, the reported rate was much higher. A peculiarity is indeed indicated from their figures for deaths in which it was judged that myocardial infarction was involved, and for deaths from arteriosclerotic heart disease without mention of infarction. For the men of Roseto the ratio of 'infarct' to 'non-infarct' deaths from arteriosclerotic heart disease was 0.7; in the other towns the ratio ranged from 2.7 to 3.2. The corresponding ratios for women were 1.0 in Roseto, and 1.0 to 1.5 in the other towns.

But death from arteriosclerotic heart disease is not necessarily more desirable simply because the physician does not mention 'infarction'; with or without the label there is no reason to believe that the basic etiology is different. In the International Statistical Classification of Diseases, Injuries and Deaths there is no special classification for myocardial infarction; in all epidemiological analyses this condition is included in the general category No. 420, "Arteriosclerotic heart disease, including coronary disease."

DEATH RATES

The death rate from arteriosclerotic heart disease (List No. 420) is strongly related to age in all populations. Table 1 gives death rates from the Vital Statistics of the United States for 1958, the mid-year pf the period covered by the Oklahoma team in

*Aided by Grant No. HE-04997 from the National Heart Institute.

TABLE 1. DEATH RATES PER 100,000 FOR ARTERIOSCLEROTIC HEART DISEASE* IN WHITE RESIDENTS OF U.S.A. IN 1958, BY AGE AND SEX.

POPULATION OF ROSETO, BANGOR AND 3 OTHER TOWNS, BY AGE AND SEX, 1955–1961†

	Sex	<35	35–44	45–54	55–64	65+
Death rates, U.S.A., white	M	2.8	86.9	341.9	895.7	2682.5
,, ,, ,, ,,	F	0.7	12.7	63.2	272.3	1743.2
Population, Roseto	M	429	122	99	65	70
,, Bangor	M	1353	397	422	304	299
,, 3 other towns	M	5028	1229	1179	956	1022
Population, Roseto	F	438	147	133	63	72
,, Bangor	F	1370	485	445	348	392
,, 3 other towns	F	5274	1341	1306	1161	1372

*International List No. 420. "Arteriosclerotic heart disease, including coronary disease".
†Average estimated from U.S. census data for 1950 and 1960.

their examination of death data, for U.S. white residents. The very great rise in the death rate with advancing age means that in any attempt to compare populations it is essential to make careful allowance for age. Table 1 shows the estimated average age distributions in Roseto and the other towns for the years 1955–61.

In order to calculate death rates, STOUT *et al.* [2] obtained population values "by a linear estimation utilizing the 1950 and 1960 census data summarized by age, sex and town". We used a similar method to obtain the population numbers for 1955–61 in Table 1. Since the census data refer to April 1, 1950 and 1960, the death data for calendar years 1955–61 inclusive, extend back 5.25 years before and 1.75 years after the 1960 census figures. Hence if the 1960 census enumeration for a given age, sex and town is X and that in 1950 is $X+\Delta$, the calculation for the estimated average population during the calendar years 1955–61 inclusive, is $X+\frac{1}{2}(0.525\Delta-0.175\Delta)$ or $X+0.175\Delta$. The results of this calculation are also given in Table 1. This corrected estimate is still subject to error because the assumption of linear change cannot be validated.

From the data given by STOUT *et al.* [2] it is possible to find the actual numbers of deaths ascribed to arteriosclerotic heart disease (with or without evidence of infarction) in the several towns in 1955–61. These reported numbers are given in Table 2. And from the data in Table 1 it is possible to calculate the deaths expected, if the arteriosclerotic heart disease death rates of the people in these towns were no different from those for the whole U.S. white population in the mid-year, 1958, of the period covered by their data. The results of these calculations, using the best estimates of average population exposure in 1955–61, are also given in Table 2.

Table 2 indicates that the deaths reported from arteriosclerotic heart disease in Roseto were below expectations from data on all U.S. whites; in the other towns there was a trend in the reverse direction. However, the differences in Roseto from U.S. expectation are not statistically significant; $P=0.07$ for men and $P=0.30$ for women. In next-door Bangor, the men were very close to U.S. expectations but the women had a large excess mortality. The men, but not the women, in the other three towns had a significantly higher death rate than U.S. expected, with $P>0.005$. On the other hand, the male death rate from arteriosclerotic heart disease in Roseto is

TABLE 2. REPORTED AND EXPECTED DEATHS FROM ARTERIOSCLEROTIC HEART DISEASE (IL No. 420)

Town	Sex	Deaths		P‡
		Reported*	Expected†	
Roseto	M	12	20.4	0.07
,,	F	8	10.7	0.50
Bangor	M	97	87.9	0.35
,,	F	86	56.9	<0.001
3 other towns	M	337	288.6	<0.005
,, ,, ,,	F	191	196.8	0.70

*Reported by STOUT *et al.* [2]
†Expected from U.S. white death rates in Table 1 applied to the population estimated for 1958 for each age, sex and town.
‡P is probability of finding a difference between reported and expected as large as that observed (calculated by chi-square with Yates' correction).

significantly less than expected from the reported experience of the four other Pennsylvania towns combined, though the difference in the death rates of the women is not significant.

But two questions remain. Does the difference in the male death rates reflect low death rates in Roseto or high death rates in the other towns? The second question concerns the extent to which the reported death rates truly represent the towns concerned. This question arises when the attempt is made to account for the changes in the age distributions of the populations from 1950 to 1960.

POPULATION CHANGES FROM 1950 TO 1960

Valid comparisons of these towns in regard to death rates ascribed to arteriosclerotic heart disease require assurance that the population bases were stable and not subject to selection that might lead to bias. But how stable were these populations?

In each town the persons who were 45–54 in 1960 must comprise those who were in that town in 1950 and then aged 35–44, less losses from and plus additions to the town, after 1950, of persons of the same age. Accordingly, any difference between the numbers aged 35–44 in 1950 from those aged 45–54 in 1960 must be accounted for by deaths and the net effect of migration. Similarly, the numbers aged 55–64 in 1960 must be accounted for on the basis of persons aged 45–54 in 1950.

Table 3 gives the relevant data. Between 1950 and 1960 in this region there were losses from the adult population that could not be accounted for by deaths unless the death rates were very much higher than for U.S. white people generally. But the loss from Roseto was almost twice that of the other towns. Unfortunately, the census data for Roseto are inadequate to calculate the change in the population of those aged 55 and older in 1960.

The data indicate a substantial net migration away from Roseto in the years 1950–60. The fact that the discrepancy between 1950 and 1960 populations is much less for the other towns does not necessarily mean that their populations were more stable in residence; it could be merely that migration away from these towns was more nearly

TABLE 3. CHANGES IN THE POPULATIONS FROM 1950 TO 1960

Town	Age 1950	Sex	% population loss by 1960	
			Total	Net*
Roseto	35–44	M	18.4	16.2
	,,	F	12.1	10.9
	45–54	M	16.9	11.4
	,,	F	20.3	17.4
	35–54	Both	16.2	13.6
4 other towns	35–44	M	9.0	6.8
	,,	F	8.2	6.9
	45–54	M	17.7	12.3
	,,	F	8.1	5.1
	35–54	Both	10.3	7.4

*'Net loss' is the loss not accounted for by deaths estimated from U.S. vital statistics for all deaths among white residents.

balanced by migration into them. Nothing is known about the health and disease experience of any of these migrants, of course, but it is a common experience that emigrants are seldom a fair sample, in regard to health, of the population they leave behind. If only a few cases of arteriosclerotic heart disease were included among the Rosetans who moved away, the picture would be entirely different. Speculation is idle but it is easily possible that the data in Table 2 were biased by emigration.

PREVALENCE DATA

In 1963 the Oklahoma team made an electrocardiographic survey of volunteers among persons of Italian ancestry in Roseto and in nearby towns and the results have been offered in confirmation of the conclusion, from mortality data, about the relative immunity of the people of Roseto [1]. There is no evidence that these are random samples; only 49 per cent of the adult males and 51 per cent of the adult females in Roseto responded to the call for volunteers. Though no data are available on the response rate in the other towns, there is no indication that it was better than at Roseto. But the data, such as they are, can be analyzed; the results are summarized in Table 4.

The 'expected' cases of 'infarction' in Table 4 were calculated on the assumption that the incidence in Roseto and in the other towns is identical so that, for given age and sex, the proportion of all infarcts expected in Roseto is simply the proportion of the examined population of that age and sex represented by Rosetans. The sum of these expectations for the several age groups covering ages 35–64 is given in Table 4. There is no evidence that the age distribution in the open-ended category of 65 or older was the same in Roseto as in the other towns but inclusion of that group does not change the conclusion; in 1963 the Rosetans did not differ from the other people in prevalence of myocardial infarction.

It is difficult to reconcile these prevalence data with the report from the previous mortality study. But if both sets of data are valid, the indication is that the situation in 1963 must have been very different from that in 1955–61 and that the 7-year

TABLE 4. ECG 'INFARCTS' IN ROSETO AND OTHER TOWNS AMONG PERSONS AGED 35–64, INCLUSIVE

Town	Sex	Number examined	Mean age	'Infarcts' Obs.*	'Infarcts' Exp.†
Roseto	M	142	49.1	9	8.5
Bangor	M	133	48.5	7	7.8
Other	M	61	48.2	4	3.7
Total	M	336	48.7	20	20.0
Roseto	F	192	49.3	4	2.9
Bangor	F	143	47.9	2	2.2
Other	F	63	46.8	0	0.9
Total	F	398	48.4	6	6.0

*Observed numbers are from BRUHN [1].
†Expected numbers are based on the hypothesis that the prevalence rates are the same in all of the populations.

'myocardial infarct' mortality will be far greater in 1963–69 than in 1955–61. This follows from consideration of the prognosis of myocardial infarction and the relationship between prevalence of infarction in a population and subsequent incidence of new cases of infarction when that population is followed.

On prognosis, there is rather good agreement in the literature, as will be noted in another section, below. In the acute phase of the first month after the attack, the mortality is about one out of three when the sudden deaths, not admitted to hospital, are included. Thereafter, the annual death rate is of the order of 7–8 per cent per year. Among survivors of the acute phase, some live many years but a conservative estimate is that half are dead in 7 years.

Moreover, the incidence rate of new cases in a population must be related to the prevalence of infarctions in a population. In the Framingham study, at least in the early years of follow-up, the annual rate of new cases of infarction and sudden deaths was of the order of 25–30 per cent of the prevalence rate found in the first survey at the start of the follow-up [3]. With this experience and the prognosis data, it is possible to make a rough estimate as to what to expect in the follow-up of a population of men in which, as at Roseto, infarct prevalence at the outset is known.

If X is the prevalence rate, cases of infarction per thousand, those cases of infarction at the outset should contribute about $0.5X$ deaths in 7 years. But in the population of men who showed no evidence of infarction at the outset, about $7(0.25X)=1.75X$ infarcts would be expected in 7 years. The acute phase mortality of these new cases should contribute about $0.3(1.75X)=0.525X$ deaths in the 7 years. The survivors among these new cases of infarction amount to $0.70(1.75X)=1.225X$ and, at a death rate of 7 per cent per year, the sum of their contribution to the mortality would be $0.28(1.225X)=0.343X$. The total of all these expected deaths is $1.368X$.

The 1963 prevalence study reported 87 infarcts per 1000 men aged 45–64 in Roseto as well as elsewhere. So, during the 7-year period 1963–69, among men aged 45–64 in 1963, the expectation from myocardial infarction would be about $1.368\times 87=119$ deaths per thousand. This is vastly different from the figure of about 15.4 deaths reported for Roseto in 1955–61 and is also far more than the reports from the other towns.

The question of criteria obviously must be considered, Neither the criteria used in the 1955–61 mortality study nor those for ECG 'infarct' were given in sufficient detail for proper evaluation. But it is interesting to compare the prevalence of 'infarcts' reported [1] for Roseto and the other towns, with the findings in other surveys with more precisely specified criteria.

In the beginning of the Framingham study, the prevalence of myocardial infarction, including cases with only ECG evidence, was 26.6 cases per 1000 men aged 45–62 [3]. Among men over 40 in the garment industry in New York, the prevalence was much lower [4]. In Finland, where coronary heart disease frequency is of the same order as in the U.S., we totally sampled all men aged 40–59 in two defined areas and found a rate of 13 per 1000 with criteria to include 'possible' as well as more clear-cut cases; using the conservative criterion of Code No. I, 1, in the Minnesota classification [5], the rate was 8.6 per thousand [6].

Obviously the criteria used by the Oklahoma team were different from those more commonly applied. But they used the same criteria with all their volunteers so presumably the comparison of Rosetans with the other people examined by them is valid.

THE CHRONOLOGY OF ARTERIOSCLEROTIC HEART DISEASE

STOUT *et al.* [2] attempted to relate the contemporary characteristics of the mode of life of populations to the previous death rate, ascribed to arteriosclerotic heart diseaes in those populations. Elsewhere [7], it was pointed out that comparison of current dietary data for a population with death rates in that population years before is only justifiable if there is assurance that the current diet, or any other variable being evaluated in regard to a possible role in etiology, accurately reflects the situation over the period before death when the disease was developing.

It is necessary to ask when was the disease developing among the men who died in 1955–61. In this connection it is desirable to distinguish between myocardial infarction and other manifestations of arteriosclerotic heart disease.

For the largest series of patients with angina pectoris reported, BLOCK *et al.* [8] found 58 per cent still alive after 5 years. SIGLER [9] reported an average survival of 5.1 years among 1700 patients with angina pectoris. RICHARDS *et al.* [10] reported an average survival of 9.7 years in 456 angina patients followed for 25 years.

The prognosis of myocardial infarction is much worse and something like 30–35 per cent of these patients die within the first 4–6 weeks if account is taken of those who die before being hospitalized and 'sudden death' is counted as 'infarction' [11]. But among patients who have infarcts and survive 1–2 months, the 5-year survival rate was 66 per cent in SMITH's series [12], 40 per cent in the series of RICHARDS *et al.* [13], 67 per cent in the series of COLE *et al.* [14] and 66 per cent in the series of BJÖRCK *et al.* [15]. Ten-year survival after infarction is reported at 20–50 per cent in the above-quoted studies, the general average being about 35 per cent.

All the evidence indicates that in most arteriosclerotic heart disease deaths, there is a history of 5–10 years of well-established clinical disease before death.

In the case of the mortality in 1955–61, this means that it is necessary to consider the characteristics of these populations as early as 1950–1955 simply to reach the time when most of those who were to die had already developed clinical arteriosclerotic

heart disease. But even this is not enough when it is realized that the appearance of clinical arteriosclerotic heart disease is certainly preceded in almost all cases by many years of silent development of the basic disease of the coronary arteries.

THE DIET

In regard to the diet in Roseto, STOUT *et al* [2] state that "in the sample studied total fat consumption is at least equal to that of the average U.S. citizen." From this they conclude that the diet does not account for the "relatively salubrious condition" and "relative freedom of Rosetans from death from myocardial infarction" [2]. The foregoing analysis of the death and ECG survey data indicate that it is highly questionable whether Rosetans *were* specially protected from coronary heart disease in 1955–61 and therefore there might seem to be little reason to discuss the meager dietary data reported for 1963. But it is desirable to clarify the dietary problem.

STOUT *et al.* [2] discredit the hypothesis that dietary fat is important in atherogenesis and its clinical complication in the form of coronary heart disease. Actually, the hypothesis that most proponents offer is not as simple as they indicate. One statement of the hypothesis is: "Atherogenesis in the coronary arteries is promoted by increasing concentration of cholesterol in the β-lipoprotein in the blood plasma and this cholesterol concentration is raised by increasing the proportion of dietary calories supplied by saturated fatty acid, the poly-unsaturated fatty acids having a weaker opposing influence" [16].

STOUT *et al.* [2] said nothing about the diets in the other towns and offered no information on the fatty acids in the diet in Roseto. But they estimated, from dietary interviews, that the men of Roseto average 38 per cent of total calories from fats. For men, at least, this average is actually considerably lower than most recent estimates of diets of white adults in the U.S. made with similar interview methods. TRULSON [17] reported averages of 41 per cent fat calories for male factory workers and 45 per cent for college professors. The Framingham study reported 45 per cent of calories from fats for adult men [18]. STAMLER [19], reported an average of 42 per cent fat calories for the men in his prevention program before they were placed on dietary restriction. The U.S. Department of Agriculture Household Surveys [20] reported U.S. averages as 43 and 45 per cent fat calories in rural and urban diets, respectively, the average for the Northeastern States being 44.6 per cent in the Spring of 1955.

So it seems probable that at the time of the study the men in Roseto had a diet significantly lower in percentage of calories from fats than do U.S. men in general. And, unless the Rosetans have completely abandoned the Italian cuisine, the fat in their diet must be less saturated than that in the usual U.S. diet.

But these estimates pertain to 1963, and it is necessary to ask about the dietary history of the 1955–61 population. As indicated earlier, in the majority of cases clinical coronary heart disease is established quite a few years before death from that cause, so the relevant dietary story for the people in Roseto should go back to before 1950 simply to antedate frank morbidity. Further, it is widely agreed that the clinical picture is a late result of atherogenesis progressing over many years, at least back to early adulthood. So in considering deaths from arteriosclerotic heart disease in 1955–1961 the dietary history of Roseto from 1900 to 1950 would be much more relevant than the dietary practice in 1963.

These people came from a part of Italy where the diet was, and is, decidedly low in total fats and remarkably low in saturated fatty acids, almost all of the dietary fat being provided by olive oil; we have verified the official Italian statistics by repeated careful dietary surveys in southern Italy in which all foods consumed in 7 days were actually measured and the foods analyzed chemically. And certainly, like other immigrants to the U.S. from southern Italy, especially those who remain in a national origin enclave, they must have only slowly changed their dietary customs to those of the U.S. in general. The Rosetans and their way of life were long identified as Italian, not American, and on this account they were considered to be outsiders until "overt discrimination subsided in the 1930s" [1]. In the early 1960s there were still 12 per cent of the population who were born in Italy; these are undoubtedly concentrated in the older groups of the community—the ages of greatest risk from coronary heart disease.

This line of reasoning inevitably leads to the suggestion that during much of their lives prior to 1955–61, most of the older Rosetans must have had diets lower in fats, especially saturated fats, than the average of the diets surveyed in 1963. From the diet fat–coronary hypothesis, it would be expected that the death rate from arteriosclerotic heart disease in Roseto in 1955–61 should be lower than the U.S. average. The mortality data of STOUT *et al.* [2] suggest that this was the case but, as noted above, the population is too small to prove a significant difference. The upshot is that the data of STOUT *et al.* [2] do not prove that the Rosetans were protected from coronary heart disease but, if they really were protected, the hypothesis about the effect of fats in the diet would provide adequate explanation.

COMMENT

Differences between Roseto and contiguous Bangor in regard to diagnostic customs and criteria of the physicians who reported deaths were discounted by STOUT *et al.* [2] because "substantially the same physicians cared for the populations of both towns". The American Medical Directory lists eight physicians in Bangor (none in Roseto), two of whom have typical Italian names, the other six having typical British or German names. Since it is most unlikely that the strong clannishness of the Italo-Americans in Roseto does not extend to the choice of physicians, it is virtually certain that the Rosetans tended to be cared for by the physicians of their own national origin than by the doctors with a very different cultural background. Obviously, bias from differences in diagnostic predilections cannot be excluded.

If it is true that in years past the people of Roseto were less prone to die of arteriosclerotic heart disease than most Americans, it is possible that, besides their diet, lack of 'stress' and a comforting psycho-social atmosphere of the community also contributed to their protection. But before any positive conclusion is warranted about emotional influence, there are formidable, probably unsurmountable, requirements to be met:

1. Evidence is needed that the death data were really not biased by diagnostic customs of the physicians involved.
2. Evidence is needed that the death data do not reflect a bias from differential migration.
3. To discount the dietary factor, it must be shown that for many years prior to

1955–61 the diets of Roseto and the other towns were substantially identical in percentage of calories from saturated fatty acids.

It is perhaps gratuitous to add that it would be necessary to provide objective evidence that over the years previous, there was really a difference in 'stress' between the towns.

SUMMARY

A report on deaths in 1955–61 indicated that the incidence of arteriosclerotic heart disease is unusually low in the small town of Roseto, Pennsylvania, and an ECG survey in 1963 was offered in support. It was concluded that this singularity was not attributable to a low-fat diet but may be due to a favourable psycho-social environment.

Analysis of the death data for arteriosclerotic heart disease in Roseto shows no significant difference from U.S. averages, though the men in other nearby towns may have unusually high death rates. Possible bias from population movements and physician selection cannot be excluded. The 1963 ECG data actually indicate a high prevalence of myocardial infarction in Roseto which is identical with that in the other towns.

Consideration of the dietary information suggests that if the Rosetans were, indeed, protected from arteriosclerotic heart disease in 1955–61, this would be explicable from the diet over the years of development of the disease.

Acknowledgment—I am grateful to Mr. R. WILLIS PARLIN for statistical help.

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