

CAN EXPECTATION OF LIFE IN WESTERN POPULATIONS BE INCREASED BY CHANGES IN DIET AND MANNER OF LIFE?

PART II

A. R. P. WALKER, D.Sc. (CAPE TOWN), CSIR/SAIMR Human Biochemistry Research Unit, South African Institute for Medical Research, Johannesburg

Recapitulating, the substance of Part I was as follows: Until the beginning of the 19th century, expectation of life was about 25-30 years. Now it is about 70 years, because of the near elimination of mortality from infectious diseases in the young. In the elderly, expectation has risen by only a few years. Only slight further reductions in deaths among the young appear feasible. In the elderly, a worth-while increase in expectation can result only from reducing or markedly delaying mortality from leading causes of death—coronary heart disease, cancer, and 'strokes'. To throw light on the possibility of increasing the expectation of life of adults, certain sequelae of ageing were discussed, namely, changes in growth rate, weight, blood pressure, atheroma, also serum lipids and glucose tolerance, in relation to (i) populations in the past, (ii) primitive or emerging populations, and (iii) present-day western populations. The conclusion was reached that, broadly, the deleterious changes in levels of these parameters are not physiological. The factors believed to be primarily responsible for degenerative changes in western populations, namely, alterations in diet, activity, smoking, stress, etc., were then examined as they obtained or now occur in the three types of population cited. It was concluded that the adverse changes prevailing are implicit and inherent in the mode of life pursued.

THE BEARING OF THE AGEING OF A POPULATION ON THE PREVALENCE OF STIGMATA OF DEGENERATION

Before entering into a detailed description and discussion of measures calculated to retard sequelae of ageing, the following question requires consideration: Is it not possible, despite the evidence given in Part I, that the enormous increases in mortality rates from degenerative diseases are due solely to the spectacular increases in life expectancy that have occurred in the younger age-groups? This question has been pointedly raised by some workers, particularly in relation to coronary heart disease. Thus, in 1963, Campbell¹³⁶ published a detailed analysis of the British Registrar General's figures from 1876 to 1960, and reached the conclusion that the increasing death rate due to heart disease could largely, if not wholly, be explained by alterations in the age structure of the population, and that, within this, the increases recorded for coronary heart disease are mainly due to changes in medical views and knowledge. He stated '... all this increase (from heart disease) is due to the older age of the population, which has resulted from the saving of younger lives forty years before ...'.

Campbell's hypothesis has been supported and enlarged upon in a robust manner by Robb-Smith,¹³⁷ who concluded, *inter alia*, '... for the middle aged individual it may be a consolation to feel that he has to face the possibility of a cardiovascular dysfunction which is not a consequence of some new technological advance, or way of living, save

in so far that social and medical advances over the last half century have allowed so many more of his or her contemporaries to survive to an age when this type of disease may manifest itself. It is probable if he or she would wish to postpone or protect themselves from its effects that they would be wiser to listen to the advice of Dr William Evans or Paul White than sit in their motor cars while eating an unpalatable diet enlivened by doses of rat poison and heparin ...'

On the one hand, Campbell and Robb-Smith are certainly to be commended for underlining the profound role of the ageing factor in determining crude mortality rates from cardiovascular and like diseases. On the other hand, unquestionably these protagonists have gone too far. Biorck¹³⁸ maintains that the hypothesis cannot explain the different mortality trends for men and women. In Australia, Reader and Wynn,¹³⁹ in studying the increased mortality from coronary heart disease in men from 1950 to 1962, concluded that '25 per cent was due to the older age structure of the population, and 75 per cent to an increase in the force of causal factors for the disease. For women, it is entirely due to the increased age structure.'

The hypothesis virtually ignores the differences in coronary heart disease mortality rates that exist among populations having approximately the same age structure, and more especially disregards the major differences in rates reported between rural and urban, and primitive and sophisticated populations, of the same ethnic group. In this respect, the experience of South African Indians may be cited and is particularly apposite.¹⁴⁰ With their rise in prosperity they have suffered very greatly increased mortalities from coronary heart disease, cerebral vascular disease, hypertensive heart disease, and diabetes; the increases are such that already the population has an expectation of life at middle age less than that in infection-ridden rural dwellers in India. Accordingly, for these reasons as well as on account of the evidence given in Part I, it is maintained that there is no doubt that the sequelae of ageing are modified by environmental factors.

WHAT RETARDING MEASURES ARE FEASIBLE?

Alterations in Total Environmental Context

What are the chances of a person seeking to extricate himself partially from the context or *milieu* of western life? In the first place, the possibilities that exist are likely to be decreased in the future. It has been stated previously that the more rapid development of the sequelae of ageing described are 'built in' to our current way of life. It is judged that the environmental conditions now prevailing and the trend of changes likely to develop in the future favour still more rapid deterioration.¹⁴¹ Thus, modern diets tend to greater palatability, with the likelihood of greater intakes of calories, fat, sugar, and animal protein. Foods high in bulk-forming capacity are becoming increasingly

unpopular. More and more people have the means of running cars. Even among the South African Bantu, a greater proportion own cars than is the case in certain European countries. For example, in Soweto, Johannesburg, there is now an average of one motor vehicle for every 6-7 families. National fitness campaigns seem to make little headway with pupils who have left school, and scarcely touch the middle-aged. Despite enlightened warnings, decreases in the practice of smoking are slight. Finally, present-day man is likely to become subjected to more, not less, vocational responsibility, competition, and national and international tension.

For individuals who seek to reorientate themselves, to what extent can changes be made? A White person does not become a Bantu just by lowering his intake of fat or his level of serum cholesterol,¹⁴² nor a Masai simply by markedly increasing his habitual activity.¹⁴³ Nor upon request or with intention does he become relaxed and lessen his competitive or anxious personality merely by resolving that it shall be so.

Consider for the moment some of the groups or communities who have low prevalences of coronary heart disease. There are the elderly but very active Swiss mountain farmworkers;¹⁴⁴ can the relevant protecting features, including presumably their regular and tranquil manner of life, really be adopted? In Norway,¹⁴⁵ as previously cited, there are certain farming communities, who, compared with the population of Oslo, have far lower mortalities from arteriosclerotic and degenerative heart disease, and also from cancer. But how can the sophisticated man of Oslo hope to take on the necessary protective feature or features of the rural farmworker's life? How can the elderly in Bucharest incline toward the life led by Danube Delta fishermen?¹⁴⁶ Then there are the Seventh Day Adventists;^{146,147} can the adoption only of their diet, of their non-smoking habits, etc., confer the lower prevalence of coronary heart disease that they enjoy? What of the role of their religion and philosophy?

To those who attach considerable aetiological importance to stress, consider first the medical profession. Bearing in mind the grading of doctors (in regard to coronary heart disease proneness) by Russek¹⁴⁸ and others,¹⁴⁹ at middle life, can the general practitioner change over and do the work of the more favourably placed consultant? Or the surgeon become pathologist or skin specialist? In the legal profession, can the advocate change to the more favourable work of the attorney? Can the director of companies reduce his responsibilities by directing one company instead of ten? Or can a president step down to vice-presidency or lower? Can the headmaster abdicate his heavy responsibilities for less onerous duties; or the mine-captain, or the works foreman; or, indeed, any man or woman who feels the burden of stressful employment or way of life, no matter how lowly the occupation or the duties that are undertaken? At the time when the individual may feel that his manner of life is more taxing than he would wish, it is virtually impossible for him to disentangle or withdraw himself; for he is tied for reasons of prestige, financial obligations, retirement pension, family relationships, and so forth. When a man reaches retirement he has a measure of choice of what to do; but what

proportion of persons at that age can constructively change or modify the type of life previously led?

It is now proposed to discuss the bearing of changes of a number of single factors on certain sequelae of ageing—principally in relation to the possibility of decreasing the proneness to coronary heart disease. The factors to be considered, as in Part I, include diet, weight, blood pressure, physical activity, smoking and stress.

Alterations in Particular Factors

Diet: Involuntary Changes

It has already been indicated that the pattern of diet and manner of life pursued in western countries in the past when degenerative disease, particularly coronary heart disease, was rare, were similar in certain aspects to those now prevailing with some primitive and emerging populations. But this pattern also obtained to a varying degree in certain European countries during World War II, when the staple cereal was of less refined meal, consumptions of fat and sugar were reduced, and physical activity increased. A number of investigations revealed that in the populations affected, deaths from diabetes fell, the rate of development of atheroma decreased, and mortality from coronary heart disease became slightly reduced.¹⁴⁹⁻¹⁵¹ Admittedly, there are limitations in the relevant evidence, which have been pointed out and discussed by many workers, such as Keys.⁶² Notwithstanding, it may be accepted that certain of the effects of ageing were retarded. The changes, of course, were *involuntarily* entered into; they were imposed by war-time conditions for a limited period. The important point, however, is that soon after the end of the war, the ageing sequelae referred to reverted to peace-time levels; they then became more adverse than they were before.^{152,153} Thus, the lessons that could have been learnt from war-time experiences were either ignored or deemed too difficult or inexpedient to implement.¹⁵⁴

Under other conditions of compulsory privation and change, e.g. in prisons, there is some evidence that ageing effects are delayed. Locally, White long-term prisoners conform in measure to the dietary pattern and manner of life of Bantu. At Pretoria Gaol, Antonis and Bersohn¹⁵⁵ showed that by dietary manipulation the blood lipid picture of White prisoners can be changed in a few weeks to that of Bantu, and vice versa. Certain studies, both in the USA¹⁵⁶ and in South Africa,¹⁵¹ have shown that under prison conditions mortality from coronary heart disease is less than that in the general population. In South Africa, in the main prisons for White long-term offenders, during 1960-1965 among 2,450 persons who were 20 years old and upward, there was an annual average of 3 episodes of, and 1 death from, coronary heart disease. In an age-matched male population in Johannesburg, deaths were many times more common.

Diet: Voluntary Changes

Several long-term dietary studies have now been carried out on various groups of Whites. The motive, ultimately, has been to reduce or delay coronary events, whether new or re-infarctions. The immediate aims have been to reduce overweight, serum cholesterol level, and hyperten-

sion. Observations have been made on several classes of subjects:

1. Subjects free from overt coronary heart disease at the beginning of the period of observation, e.g. the Anti-Coronary Club study,¹⁵⁷ and the USA National Diet Heart Study.^{158, 159}
2. Random subjects in institutions, as in the investigation of Turpeinen *et al.*¹⁶⁰
3. Random subjects in everyday work, as in Natwig's investigations.¹⁶¹
4. Subjects at high risk, as in the Chicago study of Stamler *et al.*⁷⁰ and the study at Cleveland undertaken by Brown and Page.¹⁶²
5. Subjects who have already experienced a myocardial infarction. It is this type of population group that has been most frequently investigated, e.g. by Lyon *et al.*,¹⁶³ Morrison,¹⁶⁴ Rose *et al.*,¹⁶⁵ Ball *et al.*,¹⁶⁶ Leren,¹⁶⁷ Bierenbaum *et al.*,¹⁶⁸ and, more recently, by Morris and Ball.¹⁶⁹

This list of studies given is not exhaustive. Certain of the investigations will now be described.

*The Anti-Coronary Club investigation in New York.*¹⁵⁷ The Diet and Coronary Heart Disease Study Project of the Bureau of Nutrition of the Department of Health of the City of New York—the Anti-Coronary Club study—may be summarized as follows: The subjects participating, of 40-59 years, were observed from 1958 to 1967. The diet consumed previously was composed of approximately 18% protein, 42% carbohydrate, and 40% fat. The division of total fat was as follows: saturated fatty acids 46% of total fat, mono-unsaturated fatty acids 40%, and polyunsaturated fatty acids 14%. The experimental or Prudent Diet averaged 19% protein, 48% carbohydrate, and 33% of fat calories. The distribution of the fatty acids in terms of per cent of total fat was as follows: saturated fatty acids 33%, mono-unsaturated fatty acids 33%, and polyunsaturated fatty acids 34%. This diet (with appropriate directions for weight reduction when necessary) was found to result in a significant decrease in 3 of the acknowledged risk factors (obesity, level of serum cholesterol, and blood pressure), and a significant diminution in the incidence of clinical coronary heart disease in the experimental group when compared with the control group after 9 years of observation. The smoking habits and levels of activity of the experimental and control groups did not change. Briefly, in the experimental group of 814 actively participating men, there were 339 confirmed new coronary events per 100,000 person-years. In the control group of 463 men, the comparable figure was 980 per 100,000 person-years, or almost *three times* as many new events. Rinzler *et al.*¹⁵⁷ maintain that 'the nutritional adequacy of the Prudent Diet, its acceptance by free-living ambulatory subjects, its capacity to lower serum cholesterol and triglyceride levels, and most important, its apparent influence on the significant reduction of new clinical coronary artery disease events, make it, in the opinion of the authors, an important public health modality for primary prevention of coronary heart disease'.

The USA National Diet Heart Feasibility Study.^{158, 159} To determine the practicability of conducting a long-term and intensive national diet heart study, a feasibility investi-

gation was initiated in 1966 which included observations of 1,211 men of age 45-54 years, for 1 year. Participants, who were free from evidence of overt coronary heart disease, were randomly divided into 3 main groups, the diets of which had the following features: (i) 30% of calories derived from fat, and of low cholesterol content; (ii) 40% of calories from fat, and reduced cholesterol content; and (iii) a control diet comparable to the average American diet. The diets that were expected to reduce blood cholesterol levels were high in polyunsaturated fat and low in saturated fat and cholesterol. The diets were controlled through the use of special foods. The decreases in serum cholesterol in the two experimental groups were 25 and 28 mg./100 ml., respectively. In a group in a closed institutional centre, the mean fall was 36 mg./100 ml. There was also a fall in mean diastolic pressure and body-weight. The results were regarded as paving the way for the carrying out of a major definitive long-term study.

Investigations on high-risk subjects. One of the earliest serious attempts to combat overweight, hypertension and hypercholesterolaemia was made by Stamler *et al.*,⁷⁰ in Chicago in 1958. It was undertaken on high-risk men of 40-59 years. The over-all changes in daily nutrient and foodstuff intake involved less calories and reduced intakes chiefly of fat. As a result of the nutritional alterations, a highly significant over-all decline in serum cholesterol was induced in the order of 14.7%. Weight and blood pressure were significantly reduced. In a sizable number of men these falls resulted in their attaining levels of serum cholesterol, weight and blood pressure below those set as criteria for the high-risk designation.

Investigations on patients who have had myocardial infarction. The British studies on low fat intake, alone,¹⁶⁵ or supplemented with corn oil,¹⁶⁶ or soy-bean oil,¹⁶⁶ all yielded negative results, i.e. there was not a significant difference in re-infarction rate between the experimental and control groups. The USA studies of Morrison¹⁶⁴ and of Bierenbaum *et al.*,¹⁶⁸ based on low fat and low cholesterol regimens, revealed an advantage to the experimental groups by virtue of a lower frequency of re-infarctions. This also applied to the investigation of Leren,¹⁶⁷ perhaps the most widely quoted, which will now be described.

*The investigation at Oslo, Norway.*¹⁶⁷ In Oslo, from 1957 to 1962, Leren carried out a controlled clinical trial on the effect of a plasma-cholesterol-lowering diet in male survivors of myocardial infarction. The coronary heart disease relapse rate was studied over a 5-year period on a group of 206 infarction patients, and the results were compared with those of another 206 patients who continued on a conventional diet. The experimental diet, which was low in animal fat and cholesterol, and rich in vegetable oil, included *per diem*: 92 G protein, 104 G fat, 269 G carbohydrates, and 264 mg. cholesterol. The mean daily calorie intake was 2,387 calories. The fat, which supplied 39% of total calories, included soy-bean oil (72%), fish fat (11.6%), animal fat (8.8%), cereal fat (5%), and fat from other sources (2.6%). The mean change in serum cholesterol level in subjects under 60 years was from 273 to 252 mg./100 ml. In patients of 60 years or over, the corresponding figures were 310 and 280 mg./100 ml.

In the group consuming the experimental diet, 43 myocardial re-infarctions occurred in 34 patients, 10 of the re-infarctions being fatal. In the control group, 64 myocardial re-infarctions occurred in 34 patients, 23 of the re-infarctions being fatal. It was found that on subdividing patients into age-groups below and above 60 years, the difference in coronary heart disease relapse rate was statistically significant only in the patients below 60 years. It is interesting to note that body-weight, blood pressure and smoking habits did not influence the relapse rate. Regarding weight, the group on the experimental diet lost a mean of about 5 lb. within the first 3 months, but thereafter weight remained steady. There were no changes in smoking habits or blood pressure.

Before discussing the general reaction of workers to the findings in these studies, a summary will be given of certain official dietary recommendations.

Official Recommendations on Changes of Diet in Relation to Coronary Heart Disease

In 1961, an *ad hoc* committee of the American Heart Association published a report entitled 'Dietary fat and its relation to heart attacks and "strokes"',¹⁷⁰ in which a call was made for the reduction or control of fat consumption under medical supervision with reasonable substitution of polyunsaturated for saturated fats in the diet, especially in the vulnerable groups. In 1962, the Council on Foods and Nutrition of the American Medical Association published a report on 'The regulation of dietary fat',¹⁷¹ which discussed the kind and amount of fat in the American diet, and suggested to physicians certain indications, including hyperlipidaemias, which could justify modification of the kind and amount of dietary fat consumed. In 1965, a further statement from the same body appeared on 'Diet and the possible prevention of coronary atheroma',¹⁷² in which the 1962 recommendations were reiterated with special reference to the counselling of young men on the advisability of diet modifications.

In 1966, a report was published by the Food and Nutrition Board of the USA National Academy of Sciences, on *Dietary Fat and Human Health*.¹⁷³ It was stated that: 'Results of recent studies, while valuable and thought provoking, do not provide sufficient data for firm recommendations for radical dietary changes . . . Until we learn more about which fats are desirable nutritionally, the Board recommends that the American consumer should partake of the foods that make up a varied, adequate, and not overly rich diet and maintain a normal body-weight by judicious control of caloric intake and by daily physical exercise.' In 1968, in an Editorial in *Circulation*, Keys¹⁷⁴ wrote: 'Here in the United States many experts are increasingly insistent that such advice as now issued officially in Scandinavia should be urged on the general public. But our government agencies have stood aloof and our medical and health organizations have temporized by making it a responsibility of the individual physician to decide upon the dietary prescription for the individual patient. With a substantial fraction of the adult population at risk of premature coronary heart disease, this situation essentially prevents any effective public health action'. The following excerpts were given by Keys¹⁷⁴ of the Scandinavian recommendations:

'If we want to prevent the disease (coronary heart disease) by means of a special diet, it should be introduced at an early stage and the change of diet applied to the whole population. The prevention of illness resulting from overeating or faultily constituted diets calls for some changes in our eating habits.

'First and foremost this rearrangement should bring about a decrease in the consumption of foodstuffs containing a large quantity of fat and/or sugar. This would leave room for a higher consumption of foodstuffs rich in protein, mineral substances, and vitamins.

'The supply of calories in the diet should in many cases be reduced to prevent overweight.

'The total consumption of fat should be reduced from 40%—the present figure—to between 25% and 35% of the total calories.

'The use of saturated fat should be reduced and the consumption of polyunsaturated fats should be increased simultaneously.

'The consumption of vegetables, fruit, potatoes, skimmed milk, fish, beans, meat and cereal products should be increased.

'From the medical and nutritional standpoints the importance of taking regular exercise from an early age for all those who have mainly sedentary occupations should be emphasized.'

Comment on Results of Dietary Studies

When commenting on these studies, firstly, it remains to be seen, as Biorck¹⁷⁵ has stressed, whether the beneficial results will be of substantial or only of marginal value. On the sanguine side are views such as those expressed by Rinzler *et al.*¹⁷⁶ (already quoted) and also by Stamler *et al.*⁷⁰ The latter maintain that 'It has been unequivocally demonstrated that medicine has the means—nutritional, hygienic and pharmacologic—to correct and control the cardinal coronary risk factors in most persons harbouring them'. On the depressing side, however, are the negative findings, particularly in the British studies, and also the scepticism of authorities such as Marquis and Oliver¹⁷⁷ and of Gofman and co-workers.¹⁷⁸ The latter feel that blood lipid levels are of little prognostic value in already manifest coronary heart disease in persons over 50 years of age; they consider that moderate reductions in blood lipids will have no influence on life expectancy beyond 55 years of age. It is noteworthy that the National Heart Foundation of Australia,¹⁷⁷ from a meticulous and detailed examination of the studies enumerated, has concluded that no definite conclusion was warranted.

In a Leading Article in *The Lancet*¹⁷⁸ on the subject, it was stated: 'Many doctors and patients are confused about the value of special diets in the treatment of coronary heart disease. It has recently been stated: "There are two extremes: diet is nonsense; and diet is crucial. No-one has irrefutable evidence of either. Thus, human beings currently are presented the choice of following a daily special pattern of living, which is far from easy, or forgetting the whole thing. A great majority of people follow the latter choice."¹⁷⁹ Except for reduction of excess weight, the facts at present indicate that they may well be right.' Finally, probably all would agree with Biorck¹⁷⁵ that 'Diet

changes, in order to have effect, must begin early and be drastic. The lower the dividends become with age, the more imperative will it be to establish the predictive value of biological indices in young individuals and to act selectively on young candidates.

The results of changes in particular factors will now be described.

Weight: Dublin and Marks,¹⁹⁰ from an examination of data presented in the Metropolitan Life study, and also obtained in the Build and Blood Pressure Study undertaken in 1959, concluded that reduction of weight by overweight individuals conferred on them more favourable mortality rates, much the same as that of standard risks. It is not known with certainty whether the effect of reduction by individuals of 'average' weight to 'ideal' weight confers on them the lower risks associated with habitually underweight individuals. Seltzer,¹⁹¹ however, has criticized the 'ideal' weights that have been put forward as unrealistic. 'Persons using the Metropolitan Life Insurance Company tables of average weights for height should recognize that they are not representative of current weights of the adult population; they are considerably lower. Those using the tables of desirable weights for men and women, while recognizing that weight control is indicated for some persons for reasons of health, should be aware of the severity and often unrealistic requirements of these tables and the marked extent to which they are below the known average weights of Americans, including young adults.'

Blood pressure: In the dietary treatment of hypertension, as Ungerleider⁹⁰ has emphasized, the two chief aspects that lend themselves to change are weight and salt intake. The association of overweight and hypertension, and vice versa, has already been discussed. Although vigorous restriction of salt intake, involving lowering sodium intake to 200 mg. or less daily, has been very successful as a sole measure in controlling hypertension, such restriction is not very suitable for long-term practice. Patients may fare very well during long periods of drastic sodium restriction while living in an institution, but the results are far less satisfactory on returning home. Nevertheless, with appropriate discipline, it can be done. As already noted, a reduction in the prevalence of hypertension occurred in certain of the dietary studies described. A reduction can occur with sustained increase in exercise; in one investigation a mean fall from 155/95 to 133/85 was reported.¹⁹²

Blackburn and Parlin¹⁹³ have stated: 'The most pertinent question concerning the effect of modern antihypertensive therapy on mortality is of considerable interest to the insurance industry as well as to the general public health. There are no insurance mortality data available which permit investigation of this question.' While this paper is not concerned with ageing changes modified by drugs, it must be pointed out that evidence indicates that modern antihypertensive treatment has prolonged life in persons with cerebral vascular disease and hypertensive heart disease. Thus, in the USA from 1950 to 1960, the death rate per 100,000 for 'strokes' fell from 182.2 to 139.0 in males of 55-64 years; the changes for females were 156.9 to 103.0.¹⁹⁴

Physical activity: Knowledge is lacking of the beneficial effects of increased activity in the middle-aged. In a recent

review by Katz,¹⁹⁵ in which the bearing of increasing exercise on proneness to coronary heart disease was examined, the available evidence was considered inconclusive. Frank *et al.*,¹⁹⁶ in their study of survival after myocardial infarction in relation to changes in activity and smoking habits, concluded that: 'One cannot judge from the data presented whether the relatively inactive adult male who moderately increases his customary level of physical activity thereby acquires the advantage of the lower mortality from first infarction shown by the other (active) men. Nor is it possible to predict how soon such a postulated advantage might appear. The importance of obtaining answers to these questions is evident. Favourable answers would project the exciting possibility that moderate increases in the physical activities of the least active members of an adult male population without prior myocardial infarction might significantly reduce the incidence of and the morbidity from this manifestation.'

Cumming,¹⁹⁷ in a contribution on physical fitness and cardiovascular health, has made similar comments. He says that answers to the questions: 'Does physical fitness delay the development of coronary heart disease or prolong life? What is the optimum level of fitness? What facets of fitness are most desirable for health and longevity? How is this fitness best achieved?—are likely years away . . . Discussion of the value, or lack of value, of physical fitness will go on for many years. Even if it can be shown that a high level of physical fitness reduces significantly the incidence and mortality from coronary heart disease, a major problem confronting public health officials is to motivate people to want fitness badly enough to do something about it.'

Cigarette smoking: Although heavy cigarette smokers have a death rate 2-3 times that of non-smokers, on reform this is stated to be reduced to normal, or at least 1.5 times the normal risk.^{198,199} In a study on stress, tobacco and coronary disease in North American professional groups, Russek²⁰⁰ found that cigarette smoking was statistically correlated with the reported frequency of ischaemic heart disease in the groups studied; an unexpected finding was that the prevalence of the disease in ex-smokers became reduced to a level below that for non-smokers. This obviously requires confirmation. Unfortunately, certain considerations tend to dampen the elation engendered by the foregoing. In the first place, a new evaluation of the effect of smoking on coronary heart disease has been published by Seltzer.¹⁹⁸ He has concluded that 'in some respects the epidemiological evidence is less clear now than at the time of the 1964 Report (see below). It is, therefore, difficult to see from the new epidemiological data how valid causal inferences can be drawn that cigarette smoking is linked to excess coronary heart disease deaths or that the excess coronary heart disease deaths are "caused by" cigarette smoking. We do not know whether or not there is a causal connection between cigarette smoking and increased deaths from coronary heart disease. The present state of our knowledge still suggests (as the Surgeon General's Advisory Committee's Report on Smoking and Health stated in 1964) that "male cigarette smokers have a higher death rate from coronary artery disease than non-smoking males, but it is not clear that

the association has causal significance". Next, in relation to the more practical aspects, attention is drawn to a recent Leading Article¹⁵⁹ in the *British Medical Journal* on 'Prevention of coronary heart disease'. Regarding smoking it was regretted that 'Six months after a serious warning about the dangers of smoking, they (Mausner *et al.*)¹⁶⁰ found that only one-third of the patients had reduced their consumption by at least 10 cigarettes a day. Moreover, when a lead is given by the medical profession themselves, as in the case of smoking in relation to lung cancer, this is unlikely to be followed by the general public.'

Stress: In contrast to previous changes described which are deemed feasible and advocated, it is not believed that in the great majority of people affected, the amelioration of stressful contexts is practicable. At middle age, the changing of a person's occupation, or a migration from a big city to a small town or village, is considered to be almost out of the question.

DISCUSSION

It will, of course, be apparent that the subject at issue merits far more intensive treatment than has been found possible in this contribution. Some aspects, particularly that of nutrition, have been dealt with in some detail. Others have been scarcely mentioned, or discussed superficially. Repeatedly, the central problem is what can be done to control coronary heart disease; for were a measure of prevention or retardation achieved, there would undoubtedly be reductions in other causes of death, and associated increases in life expectancy. This concentration of attention requires no apology.

A major question is—apart from uncertainties over chances of improvement—are we really fitted to enjoy a delay in ageing, and to enjoy more years of life? Over half a century ago, Osler¹⁶¹ expressed, in a remarkable valedictory address, the uselessness of men above 60 years and comfortable ways of getting rid of them. More recently, Dunlop,¹⁶² in 'Personal View' in the *British Medical Journal*, wrote with grim humour that 'There are lots of men who become mentally enfeebled old dotards at the age of 50 with characters set into a cast like plaster, never to soften again; creatures who move in determinate grooves, the iron yoke of conformity on their necks, current slogans in their mouths, and the pain of a new idea agonizing to their brains'.

Another foreboding has been expressed by Björck.¹⁶³ In referring to the possibility of a major increase in life expectancy, he has stressed the enormous 'impact on the society caring for the tremendous, aged population that would result from it—a society with four or even five generations living side by side—at a time when automation reduces the need for human labour in our societies and "the population explosion" in other parts of the world is considered to be humanity's greatest peril'. An increase in expectation would be of value only if, as Paul White¹⁶⁴ says, we are enabled to add life to years, not just years to life.

A further question is, should mortality from, say, coronary disease, be reduced by the application of one or more of the measures indicated, would the total death rate fall correspondingly, or would the people 'protected' merely

die from other causes? Blomqvist and Björck¹⁶⁵ aver that mortality from coronary heart disease shows a fair correlation to mortality from all causes. It is interesting to note in this connection that Japanese males in California,¹⁶⁶ aged 55-64 years, whose death rate from the disease in 1960 was 254.6, had a death rate from all causes of 1,111 per 100,000. The corresponding figures for USA males were 901.3 and 2,225.2. Thus, while Japanese males had less than a quarter of the coronary mortality of USA males, their death rate, although not proportionately lower, was still much below that of USA males.

On the other hand, looking elsewhere, there are anomalies.¹⁶⁷ Thus in 1964, for subjects aged 45-64 years, in Australia and Belgium total death rates per 100,000 were much the same, 1,082 and 1,110; but death rates from heart disease were quite different, 431 and 252. Again, in West Germany and Sweden, mortalities from heart disease were much the same, 259 and 233; yet mortalities from all causes were markedly different, 1,075 and 764. Clearly, in countries embarking on preventive or remedial programmes, a satisfactory picture regarding falls in age-specific mortality rates and gains in expectation of life will emerge only from long-term observations. Within the limitations of the available information it would be unwise to make unduly optimistic predictions.

Returning to the burden of this paper, there is no doubt that the bulk of middle-aged western populations (in Australia, Hickie¹⁶⁸ mentions 40% of males over 40 years) would benefit by favourable alterations in the factors discussed. For weight could be reduced, blood pressure decreased in measure, the development of atheroma retarded, and biochemical components such as blood lipids and glucose tolerance changed to the good. The situations regarding coronary heart disease and also diabetes could be improved; the same applies to 'strokes' and to hypertensive heart disease. On the other hand, benefits in respect of malignant growths, excluding cancers affected by cigarette smoking, may not be claimed.

Quantitatively, what improvement is reasonably attainable? Hickie¹⁶⁹ has compiled figures indicating predicted coronary morbidity after a preventive programme. Expressing expected coronary morbidity as 100 units, he considers that appropriate and severe changes in diet could reduce the index to 50; stopping smoking could have the same effect. An increase in exercise could reduce the figure from 100 to 70; reduction in weight, 100 to 85, and reduction in blood pressure, 100 to 75. The chances of the preventive measures just mentioned being implemented on a national scale are regarded as virtually nil. Public health authorities and other medical or health workers may be expected to go to great lengths to encourage people to eat frugally of diets of lesser sophistication, to stop smoking, and to take more exercise in their leisure time. But, to repeat *ad nauseam*, who will heed? It is reiterated that the young regard the perils of middle-age as too far away to concern them, and that the middle-aged and over have minimal capacity for altering habits of a lifetime; moreover, many, with defeatism, accept that it is too late to change. 'It would seem to be inescapable that most people prefer to continue to pursue their habitual way of life, which at least has not the physical rigour of the past, and

to accept the risks of degenerative disease which are implicit in the manner of life prevailing, risks which may well be increased by every milestone of socio-cultural-economic advancement—the rapid growth of the middle class, the "Affluent Society", the "New Frontier", the "Great Society".¹⁴¹

The frame of mind prevailing is such that it cannot be frightened or stamped into making radical changes. It is believed that a widespread alteration in diet and manner of life would be feasible *only* were a measure of compulsion exerted. Even Hickie,¹⁹⁶ in his detailed and enthusiastic contribution on the prevention of coronary heart disease, reluctantly concludes that for a programme to be really effective 'coercion' will be needed. Biorck¹⁸⁸ maintains that changes 'must begin early and be drastic'. But it would be wholly wrong to say that beneficial changes *cannot* be made. Cassius said to Brutus, 'The fault, dear Brutus, is not in our stars, but in ourselves that we are underlings'. In a Leading Article in the *British Medical Journal*¹⁹⁷ on 'The inheritance of diabetes', it was stated, 'It is gluttony more than genes which causes us to degenerate'.

SUMMARY

Only slight further reductions in deaths among the young appear feasible. In the middle-aged and elderly, a worth-while increase in expectation of life cannot be accomplished apart from substantially reducing or markedly delaying mortalities from leading causes of death—coronary heart disease, cancer, and 'strokes'.

A number of the sequelae of ageing have been discussed, namely, changes in growth rate, weight, blood pressure, atheroma, and also serum lipids and glucose tolerance, in relation to (a) populations in the past, (b) primitive or emerging populations, and (c) present-day western populations. In virtually all the respects enumerated, the deleterious changes in levels of these health parameters which occur from adulthood onwards are not physiological.

The factors primarily responsible for the adverse changes in western populations are alterations in diet, activity, smoking, and stress. The adverse changes that have occurred are implicit and inherent in the mode of life prevailing, and they are far from being due solely to the ageing of populations.

In the middle-aged or elderly among whom stigmata of ageing are already very evident, the changes that must be made by those who are determined to promote an increase in expectation of life are described. Several of the recent relevant studies have been discussed.

The benefits of improved regimens in terms of falls in mortality, or the delaying of death, relate primarily to coronary heart disease. But they also apply in measure to 'strokes', hypertensive heart disease and diabetes. Improvements in respect of cancer (excluding lung and similarly affected cancers) are not claimed.

REFERENCES

1. Roche, A. F. (1964): *Med. J. Aust.*, **2**, 11.
2. Jacklin, H. (1967): *Ann. Life Insur. Med. (Berl.)*, **2**, 1.
3. Helley, E. in Weister, H. (1962): *Ibid.*, **1**, 3.
4. Gale, A. H. (1959): *Epidemic Diseases*. Baltimore: Penguin Books.
5. Studies on Medical and Population Subjects (1966): *Regional and Social Factors in Infant Mortality*. Study No. 19. London: H.M.S.O.
6. Gonin, H. T. (1966): *S. Afr. J. Sci.*, **62**, 141.
7. Bureau of Census and Statistics (1960): *South African Life Tables*, vol. VIII. UG/49. Pretoria: Government Printer.
8. Thomas, W. A. in James, T. N. and Keys, J. W., eds. (1963): *The Etiology of Myocardial Infarction*, p. 30. Boston, Mass.: Little John & Co.
9. Mortality Statistics (1967): *Epidemiol. Vital Statist. Reps.*, **20**, 401 and 535.
10. Oliver, M. F. and Stuart-Harris, C. H. (1965): *Brit. Med. J.*, **2**, 1203.
11. Walker, A. R. P. (1967): *Bull. Int. Acad. Path.*, **8**, 71.
12. Walker, A. R. P., Calderwood, M. J. and Walker, B. F. (1968): *J. Trop. Pediat.*, **14**, 205.
13. Roderuck, C. E. (1963): *Amer. J. Clin. Nutr.*, **13**, 173.
14. Garrow, J. S. (1967): *Lancet*, **1**, 278.
15. Ciba Foundation (1955): *Colloquia on Ageing*, vol. I. London: Ciba Foundation.
16. Bureau of Census and Statistics (1958): *Population Census*, vol. 5. UG/42. Pretoria: Government Printer.
17. Tanner, J. M. and Whitehouse, R. H. (1962): *Brit. Med. J.*, **1**, 446.
18. Hodges, R. E. and Krehl, W. A. (1965): *Amer. J. Clin. Nutr.*, **17**, 200.
19. Walker, A. R. P. (1965): *Nutr. Revs.*, **23**, 321.
20. Cathcart, E. P. (1940): *Lancet*, **1**, 533.
21. Padmavati, S. and Gupta, S. (1959): *Circulation*, **19**, 395.
22. Shaper, A. G., Williams, A. W. and Spenser, P. (1961): *E. Afr. Med. J.*, **38**, 569.
23. Kammer, B. and Lutz, W. P. (1960): *Circulation*, **22**, 289.
24. Walker, A. R. P. (1964): *Amer. Heart J.*, **68**, 581.
25. *Idem* (1966): *S. Afr. Med. J.*, **40**, 814.
26. Abrahamson, J. H., Gampel, B., Slome, C. and Scotch, N. (1961): *Amer. J. Clin. Nutr.*, **9**, 217.
27. Valiente, S., Arteaga, A. and Santa-Maria, J., in Mills, C. F. and Passmore, R., eds. (1964): *Proceedings of the 6th International Congress on Nutrition*, Edinburgh, Edinburgh: E. & S. Livingstone.
28. Khosla, T. and Lowe, C. R. (1968): *Lancet*, **1**, 742.
29. National Centre for Health Statistics (1966): *Weight, Height and Selected Body Dimensions, United States: 1960-1962*, Series 11, No. 8. Washington, DC: U.S. Department of Health, Education and Welfare.
30. Stamler, J. (1961): *The Early Detection of Heart Disease*, p. 57. Education Series No. 97. Michigan: University of Michigan School of Public Health.
31. Hutchinson, J. J. (1961): *Ann. Intern. Med.*, **54**, 90.
32. Keys, A., Brozek, J., Henschel, A. and Taylor, H. L. (1950): *The Biology of Human Starvation*. Minneapolis: University of Minnesota Press.
33. Shakespeare, W.: King Henry IV, Part II, Act V, Scene V.
34. Srikanthia, S. G., Jagganatham, S. N. and Gopalan, C. (1961): *Indian J. Med. Res.*, **49**, 99.
35. Whyte, H. M. (1958): *Aust. Ann. Med.*, **7**, 36.
36. Lowenstein, F. W. (1961): *Lancet*, **1**, 389.
37. Maddocks, J. and Lovell, R. R. H. (1962): *Brit. Med. J.*, **1**, 436.
38. Ordman, B. (1948): *Clin. Proc.*, **7**, 183.
39. Abrahams, D. G., Alele, C. A. and Barnard, B. G. (1960): *W. Afr. Med. J.*, **9**, 45.
40. Moser, M. (1960): *Ann. N. Y. Acad. Sci.*, **84**, 989.
41. Cruz-Coke, R., Etcheverry, R. and Nagel, R. (1964): *Lancet*, **1**, 697.
42. Prior, I. A. M., Rose, B. S. and Davidson, F., in Mills, C. F. and Passmore, R., eds. (1964): *6th International Congress on Nutrition*, Edinburgh, p. 618. Edinburgh: E. & S. Livingstone.
43. Maisnikov, A. L. (1960): *Amer. J. Cardiol.*, **5**, 692.
44. National Centre for Health Statistics (1966): *Blood Pressure of Adults by Race and Area, United States, 1960-1962*, Series 11, No. 5. Washington, DC: Department of Health, Education and Welfare.
45. Lygonis, C. (1967): *Dan. Med. Bull.*, **14**, 82.
46. Tsai, H. C., Cheng, J. T., Wang, L. T., Hsieh, Y. Y., Wu, T. L. and Chen, J. S. (1967): *Amer. J. Epidemiol.*, **86**, 253.
47. Master, A. M., Garfield, C. L. and Walters, M. B. (1952): *Normal Blood Pressure and Hypertension*. London: Kimpton.
48. Clark, V. A., Chapman, J. M. and Coulson, A. (1967): *J. Chron. Dis.*, **20**, 571.
49. Page, I. H. (1962): *Circulation*, **25**, 433.
50. Ungerleider, H. E. (1964): *Ann. Life Insur. Med. (Berl.)*, **2**, 122.
51. Gill, A. (1963): *N. Y. Med. J.*, **63**, 1718.
52. Chicago Society of Actuaries (1959): *Build and Blood Pressure Study*.
53. Morris, J. N. and Crawford, M. D. (1958): *Brit. Med. J.*, **2**, 1485.
54. Stamler, J., Lindberg, H. J., Berkson, D. M., Shaffer, A., Miller, W., Poindexter, A., Colwell, M. and Hall, Y. (1960): *J. Chron. Dis.*, **11**, 405.
55. Dawber, T. R., Kannel, W. B. and McNamara, P. M. (1963): *Trans. Ass. Life Insur. Med. Dir. Amer.*, **47**, 70.
56. Keys, A. and Blackburn, H. (1963): *Progr. Cardiovasc. Dis.*, **6**, 14.
57. Morris, J. N., Kagan, A., Pattison, D. C., Gardner, M. J. and Raffle, P. A. B. (1966): *Lancet*, **2**, 553.
58. Enos, W. F., Beyer, J. C. and Holmes, R. H. (1955): *J. Amer. Med. Assoc.*, **158**, 912.
59. McGill, H. C., Geer, J. C. and Strong, J. P. (1963): *Natural History of Human Atherosclerotic Lesions*, p. 39. New York: Academic Press.
60. Anderson, M., Walker, A. R. P., Higginson, J. and Lutz, W. (1959): *Arch. Path.*, **68**, 380.
61. Hirst, E. A., Piyartin, P. and Gore, I. A. (1962): *Amer. J. Publ. Hlth.*, **38**, 162.
62. Bernstein, D. S., Sadowsky, N., Hegsted, D. M., Guri, C. D. and Stare, F. J. (1966): *J. Amer. Med. Assoc.*, **198**, 499.
63. Keys, A. in Sandler, M. and Bourne, G. H., eds. (1963): *Atherosclerosis and its Origin*, p. 263. New York: Academic Press.
64. National Centre for Health Statistics (1966): *Serum Cholesterol Levels of Adults, United States, 1960-1962*, Series 11, No. 23. Washington, DC: Department of Health, Education and Welfare.
65. Keys, A., Kimura, N., Kusukawa, A., Bronte-Stewart, B., Larsen, N. and Keys, M. H. (1958): *Ann. Intern. Med.*, **48**, 83.
66. Walker, A. R. P. and Arvidsson, U. B. (1954): *J. Clin. Invest.*, **33**, 1358.
67. Bersohn, I. and Wayburne, S. (1956): *Amer. J. Clin. Nutr.*, **4**, 117.

68. Joubert, F. J., Van Bergen, A., Bersohn, I., Walker, A. R. P. and Lutz, W. (1962): *S. Afr. J. Lab. Clin. Med.*, **8**, 10.
69. Chapman, J. M. and Massay, F. J. (1964): *J. Chron. Dis.*, **17**, 933.
70. Stamler, J., Berkson, D. M., Lindberg, H. A., Hall, Y., Miller, W., Majonnier, L., Levinson, M., Cohen, D. B. and Young, Q. D. (1966): *Med. Clin. N. Amer.*, **50**, 229.
71. National Centre for Health Statistics (1966): *Glucose Tolerance of Adults, United States, 1960 - 1962*, Series 11, No. 2. Washington, DC: Department of Health, Education and Welfare.
72. Keen, H. (1964): *Proc. Roy. Soc. Med.*, **57**, 200.
73. Scott, E. M. and Griffith, I. V. (1957): *Metabolism*, **6**, 320.
74. Campbell, C. H. (1963): *Aust. Ann. Med.*, **2**, 607.
75. Prior, I. A., Rose, B. S., Harvey, H. P. and Davidson, F. (1966): *Lancet*, **1**, 333.
76. Poon-King, T., Henry, M. V. and Rampersad, F. (1968): *Ibid.*, **1**, 155.
77. Charters, A. D. and Arya, B. P. (1961): *Brit. Med. J.*, **1**, 773.
78. Campbell, G. D. (1963): *S. Afr. Med. J.*, **37**, 1195.
79. Walker, A. R. P., Richardson, B. D. and Mistry, S. D. (1964): *Brit. Med. J.*, **2**, 1394.
80. Richardson, B. D., Walker, A. R. P. and Walker, B. F. (1965): *Lancet*, **2**, 594.
81. Epstein, F. H., Ostrander, B. D., Johnston, B. C., Payne, M. W., Hayner, N. S., Keller, J. B. and Francis, J. (1965): *Ann. Intern. Med.*, **62**, 1170.
82. Ostrander, L. D., Francis, T., Hayner, N. S., Kjeldberg, M. O. and Epstein, F. H. (1965): *Ibid.*, **62**, 1188.
83. Walker, A. R. P. (1947): *S. Afr. Med. J.*, **21**, 590.
84. Leading Article (1937): *Brit. Med. J.*, **2**, 752.
85. Smith, E. (1871): *Ibid.*, **2**, 222.
86. National Food Survey Committee. Annual Report (1963): *Domestic Food Consumption and Expenditure, 1961*. London: H.M.S.O.
87. Orr, J. B. (1936): *Food, Health and Income*. London: Macmillan.
88. Drummond, J. and Wilbraham, A. (1939): *The Englishman's Food*. London: Jonathan Cape.
89. Yudkin, J. (1963): *Nature (Lond.)*, **200**, 728.
90. Dahl, L. K., Heine, M. and Tassinari, L. (1963): *Ibid.*, **198**, 1204.
91. Walker, A. R. P. (1961): *S. Afr. Med. J.*, **35**, 114.
92. Brunton, T. L. (1896): *Lancet*, **1**, 1483.
93. McEwen, W. (1904): *Brit. Med. J.*, **2**, 873.
94. Annotation (1929): *Lancet*, **1**, 1368.
95. Alvarez, W. C. (1924): *Physiol. Revs.*, **4**, 352.
96. Carlson, A. J. and Hoelzel, F. (1950): *Fed. Proc.*, **9**, 354.
97. Coleman, D. L. and Baumann, C. A. (1957): *Arch. Biochem. Biophys.*, **66**, 226.
98. Moore, J. H. (1967): *Brit. J. Nutr.*, **21**, 207.
99. Antonis, A. and Bersohn, I. (1962): *Amer. J. Clin. Nutr.*, **11**, 142.
100. Walker, A. R. P. (1959): *Nature (Lond.)*, **164**, 825.
101. Malhotra, S. L. (1967): *Brit. Heart J.*, **29**, 777.
102. *Idem* (1967): *Amer. J. Clin. Nutr.*, **20**, 462.
103. Wynder, E. L. and Shigematsu, T. (1967): *Cancer (Philad.)*, **20**, 1520.
104. Annotation (1968): *Lancet*, **1**, 628.
105. Oettle, A. G. (1964): *J. Nat. Cancer Inst.*, **33**, 383.
106. Botha, T. F., Clark, D. and Jokl, E. (1945): *S. Afr. Med. J.*, **19**, 381.
107. Jokl, E. (1963): *Ann. N. Y. Acad. Sci.*, **110**, 778.
108. Le Riche, H., Riordon, D., Best, P., Kinnear, A. A. and Walker, A. R. P. (1952): *S. Afr. Med. J.*, **26**, 207 and 233.
109. Rhoadh, K., Astrand, P. O., Birkhead, N. C., Hettinger, T., Issekutz, B., Jones, D. M. and Weaver, R. (1961): *Arch. Environm. Hlth*, **2**, 499.
110. Reindell, H., Koning, K., Rosskamp, H. and Keul, J. (1959): *Ärztl. Fortbild.*, **4**, 1.
111. Wyncham, C. H. (1966): Paper read at symposium on bilharzia, S.A. Institute for Medical Research.
112. Sloan, A. C. (1966): *S. Afr. J. Lab. Clin. Med.*, **12**, 46 and 52.
113. Astrand, P. O. (1952): *Experimental Studies of Physical Working Capacity in Relation to Sex and Age*. Copenhagen: Ejner Munksgaard Forlag.
114. Covell, B., El Din Nasr and Passmore, R. (1965): *Lancet*, **1**, 727.
115. Cureton, T. K. (1947): *Physical Fitness Workbook*. St. Louis: Mosby.
116. Passmore, R. (1966): *Amer. Heart J.*, **71**, 579.
117. Brunner, D. in James, T. N. and Keyes, J. W. eds. (1963): *The Etiology of Myocardial Infarction*. Boston: Little, Brown Co.
118. Frank, C. W., Weinblatt, E., Shapiro, A. and Sager, R. V. (1966): *Circulation*, **34**, 1022.
119. Hammond, E. C. and Horn, D. (1958): *J. Amer. Med. Assoc.*, **166**, 1159.
120. Doll, R. and Hill, A. B. (1964): *Brit. Med. J.*, **1**, 1461.
121. Auerbach, O., Hammond, E. C. and Garfinkel, L. (1966): *New Engl. J. Med.*, **273**, 755.
122. Sackett, D. L. and Winkelstein, W. (1967): *Amer. J. Epidemiol.*, **86**, 264.
123. Higginson, J. and Oettle, A. G. (1960): *J. Nat. Cancer Inst.*, **24**, 589.
124. Advisory Committee to the Surgeon-General of the Public Health Service (1964): *Smoking and Health*. Washington, DC: Department of Health, Education and Welfare.
125. Friedman, G. D. (1967): *J. Chron. Dis.*, **20**, 769.
126. Hay, D. R. (1967): *N. Z. Med. J.*, **66**, 362.
127. Scotch, N. A. (1960): *Ann. N. Y. Acad. Sci.*, **84**, 1000.
128. Howe, G. M. (1963): *National Atlas of Disease Mortality in the United Kingdom*. London: Nelson.
129. Berkson, D. M., Stamler, J., Lindberg, H. A. and Hall, Y. (1960): *Ann. N. Y. Acad. Sci.*, **84**, 835.
130. Enterline, P. E., Rikli, A. E., Sauer, H. I. and Hyman, M. (1960): *Publ. Hlth Rep. (Wash.)*, **75**, 759.
131. Jervell, A., Meyer, K. and Westlund, K. (1965): *Acta med. scand.*, **177**, 13.
132. Walker, A. R. P. (1965): *Brit. Med. J.*, **2**, 361.
133. Russek, H. I. (1962): *Amer. J. Med. Sci.*, **243**, 716.
134. Rosenman, R. H., Friedman, M., Strauss, R., Wrum, M., Kositckek, R., Hahn, W. S. and Werthessen, N. T. (1964): *J. Amer. Med. Assoc.*, **189**, 15.
135. Syme, S. L., Borhani, N. O. and Beuchley, R. W. (1965): *Amer. J. Epidemiol.*, **82**, 209.
136. Campbell, M. (1964): *Amer. Heart J.*, **68**, 1.
137. Robb-Smith, A. H. T. (1967): *The Enigma of Coronary Heart Disease*. London: Lloyd-Luke.
138. Biorck, G. (1968): *Circulation*, **37**, 1071.
139. Reader, R. and Wynn, A. (1966): *Med. J. Aust.*, **2**, 740.
140. Walker, A. R. P. (1968): *Circulation*, **37**, 126.
141. *Idem* (1966): *Amer. Heart J.*, **72**, 721.
142. *Idem* (1964): *Circulation*, **29**, 1.
143. Mann, G. V., Shaffer, R. S., Anderson, R. S. and Sandstead, H. H. (1964): *J. Atheroscler. Res.*, **4**, 289.
144. Gsell, D. and Mayer, J. (1962): *Amer. J. Clin. Nutr.*, **10**, 471.
145. Steinbach, M. (1964): *Lancet*, **2**, 1116.
146. Wynder, E. L., Lemon, F. L. and Bross, I. J. (1959): *Cancer (Philad.)*, **12**, 1016.
147. Walden, R. T., Schaefer, L. E., Lemon, F. R., Sunshine, A. and Wynder, E. L. (1964): *Amer. J. Med.*, **36**, 269.
148. Morris, J. N., Heady, J. A. and Barley, R. G. (1952): *Brit. Med. J.*, **1**, 503.
149. Himsworth, H. P. (1949): *Proc. Roy. Soc. Med.*, **42**, 323.
150. Pezold, F. A. (1959): In *Atherosclerosis and Nutrition*, p. 246. Darmstadt: Verlag Dr Dietrich Steinkopff. Reviewed in *Amer. J. Clin. Nutr.*, **8**, 384 (1960).
151. Strom, A. and Jensen, A. R. (1951): *Lancet*, **1**, 126.
152. Cleave, T. F. and Campbell, G. D. (1965): *The Saccharin Diseases*. Bristol: John Wright.
153. Begg, T. B. (1964): *Abstr. Wild Med.*, **36**, 225.
154. Walker, A. R. P. (1947): *S. Afr. Med. J.*, **23**, 210.
155. Antonis, A. and Bersohn, I. (1963): *Ibid.*, **37**, 440.
156. Sprague, H. B. (1966): *Amer. Heart J.*, **33**, 676.
157. Rinzler, S. H., Archer, M. and Chritakis, G. J. (1967): *Ibid.*, **73**, 287.
158. Page, I. H. and Brown, H. B. (1968): *Circulation*, **37**, 313.
159. National Diet Heart Study (1968): *Ibid.*, **37** and **38** and Suppl. 1.
160. Turpeinen, O., Miettinen, M., Karvonen, M. J., Roine, P., Pekkarinen, M., Lehtosuo, E. and Alivirta, P. (1968): *Amer. J. Clin. Nutr.*, **21**, 255.
161. Natwig, H. (1967): *Tidsskr. norske Laegeforen.*, **87**, 1033.
162. Brown, H. B. and Page, I. H. (1958): *J. Amer. Med. Assoc.*, **168**, 1989.
163. Lyon, T. P., Yankley, A., Gofman, J. W. and Strisower, B. (1956): *Calif. Med.*, **84**, 325.
164. Morrison, L. M. (1960): *J. Amer. Med. Assoc.*, **173**, 884.
165. Rose, G. A., Thomson, W. B. and Williams, R. T. (1965): *Brit. Med. J.*, **1**, 1531.
166. Ball, K. P., Hannington, E., McAllen, P. M., Pilkington, J. R. E., Richards, J. M., Shaland, D. E. and Sowry, G. S. C. (1965): *Lancet*, **2**, 501.
167. Leren, P. (1966): *Acta med. scand.*, suppl. 466.
168. Bierenbaum, M. L., Green, D. P., Florin, A., Fleischmann, A. I. and Caldwell, A. B. (1967): *J. Amer. Med. Assoc.*, **202**, 1119.
169. Morris, J. N. and Ball, K. P. (1968): *Lancet*, **2**, 693.
170. Central Committee for Medical and Community Program of the American Heart Association (1961): *Circulation*, **23**, 133.
171. Council on Foods and Nutrition (1962): *J. Amer. Med. Assoc.*, **181**, 411.
172. *Idem* (1965): *Ibid.*, **194**, 1149.
173. National Research Council (1966): *Dietary Fat and Human Health*. Publ. No. 1147. Washington, DC: National Academy of Sciences.
174. Keys, A. (1968): *Circulation*, **38**, 227.
175. Marquis, R. M. and Oliver, M. F. (1964): *Brit. Med. J.*, **2**, 851.
176. Gofman, J. W., Young, W. and Tandy, R. (1966): *Circulation*, **34**, 679.
177. National Heart Foundation of Australia (1967): *Med. J. Aust.*, **1**, 309.
178. Leading Article (1968): *Lancet*, **2**, 901.
179. Page, I. H. and Stamler, J. (1968): *Mod. Conc. Cardio. Dis.*, **37**, 119 and 125.
180. Dublin, L. I. and Marks, H. H. (1941): *Trans. Ass. Life Insur. Med. Dir. Amer.*, **35**, 235.
181. Seltzer, C. C. (1965): *New Engl. Med. J.*, **272**, 1132.
182. Judd, J. L. and Day, W. C. (1967): *American Geriatric Society*, **15**, 373.
183. Blackburn, H. W. and Parlin, R. W. (1967): *Ann. Life Insur. Med. (Berl.)*, **3**, 33.
184. Gordon, T. (1967): *Publ. Hlth Rep. (Wash.)*, **82**, 973.
185. Katz, L. H. (1967): *Circulation*, **35**, 405.
186. Cumming, G. R. (1968): *Ibid.*, **37**, 4.
187. Russek, H. I. (1965): *J. Amer. Med. Assoc.*, **192**, 189.
188. Seltzer, C. C. (1968): *Ibid.*, **203**, 127.
189. Leading Article (1968): *Brit. Med. J.*, **3**, 689.
190. Mausner, J. S., Mausner, B. and Rial, W. Y. (1968): *Amer. J. Publ. Hlth*, **58**, 46.
191. Osier, W. (1904): In *Acquamitas and Other Addresses*, 'The fixed period'. London: Lewis.
192. Dunlop, D. (1968): *Brit. Med. J.*, **1**, 573.
193. White, P. D. (1964): *Fitness for the Whole Family*. New York: Doubleday.
194. Blomqvist, G. and Biorck, G. (1963): *Acta med. scand.*, **173**, 229.
195. Causes of Death (1967): *Epidem. Vital Statist. Rep.*, **20**, 80.
196. Hickie, J. B. (1968): *Med. J. Aust.*, **1**, 159.
197. Leading Article (1965): *Brit. Med. J.*, **1**, 940.