

savouring a smaller amount of carbohydrate and to eat as much protein, fruit and vegetables as one likes. This method is nearly always successful with a co-operative patient. A doctor friend of mine has just recently instituted an overweight club. He proposes the members from his patients, who meet once a week. The health visitor weighs them, instructs them about suitable diets, and gives short talks on nutrition. The club is a great success; the spirit of competition helps to spectacular triumphs those who could not previously lose weight. This form of group therapy is well worth pursuing.

Now I want to end with a story. I have just returned from holiday, a sailing holiday on a 30-foot sailing sloop. Holiday is one's chance of relaxing from this overworrying I've been talking about, though unfortunately many people choose their holidays for the very wrong reasons, keeping up with the Jones's or going abroad for the cachet, even though the whole thing is a bit of a strain. My brother was recently on holiday in southern Ireland and was very annoyed with himself because he had forgotten to bring his camera to record some of the views. He went into a small general village store and asked the woman behind the counter if she had any postcards with local views. "No," she said, "we just have Killarney's lakes and the mountains of Mourne and Dublin's fair city. We used to stock the local views but they sold out so fast we did not order any more."

This is a quiet, relaxing note on which to finish my talk.

THE ORIGINS OF DEGENERATIVE DISEASE

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I have been asked to talk about the origins of degenerative changes which occur, or rather make themselves manifest for the first time, in middle age. It is a vast subject which any number of facets. I could for example consider the repercussions of the fact that the human brain loses roughly a 100,000 cells a day from the age of about 25 onwards: a solemn thought, although one can take a little

comfort from the fact that at this rate it would take 250 years before one became completely decerebrate! The subject is so large, however, that I must in twenty minutes confine myself to only one aspect of it and must even deal with that very superficially; I choose atherosclerosis, for it has been proved that man is as old as his arteries. If you have four good tubes going to the brain—two carotid arteries and two vertebrals, two good tubes going to the kidneys and some good coronary ones, you can be an active, intelligent, aggressive man at the age of 80, whereas if they are defective you can be an enfeebled old dotard at the age of 50.

Genetics, prosperity and calories

Atherosclerosis arises from a deposition of porridge-like material beneath the intima of the artery. This causes a reduction of its calibre and a weakening of its wall, which may result in aneurysmal dilatation. In either case a zone is created which favours the deposition of platelets and the formation of a thrombus with consequent infarction of the organ supplied and the danger of systemic embolization. The cause of atherosclerosis is quite unknown, although there are lots and lots of theories about it. There is of course not a shadow of doubt that the quality of the tubing with which we are endowed is a legacy from our parents, and that health and longevity depend more than anything else on family history. Were I in charge of a life insurance company, the age of the proposer's forebears would be the aspect to which I would pay most attention. Unfortunately, however, we cannot choose our parents, and it therefore becomes of interest to enquire: is there any other action we can take to prevent the development of atherosclerosis and add a cubit to the stature of our longevity?

Morbidity and mortality from atherosclerosis are not uniform throughout the world, and its incidence is undoubtedly very much greater in the so-called privileged countries. This is certainly not due to mere genetic differences, as is shown by the fact that immigrants from underdeveloped to more developed countries show a rise in the incidence of atherosclerosis in proportion to their increased prosperity in the new state: for example, Negroes and Japanese in California, and Ukrainian Jews and Yemenites in Israel have a far higher incidence of atherosclerosis in their new countries than they did in their original states. In the multiracial communities in Capetown there is a clear correlation between the incidence of atherosclerosis and the prosperity of the inhabitants, the incidence being much the lowest among the poorest Bantu, increasing steadily as the Bantu become more prosperous, higher still among the Cape coloured community, and highest in the white population. In Britain, the estimated caloric intake per person per day has increased

by 13 per cent since the beginning of the century, and this may be a factor in the modern increased incidence of atherosclerosis and myocardial infarction. There are of course some authorities who question the increase in atherosclerosis and who say that it has not really occurred, attributing the change entirely to more accurate diagnosis and to the greater longevity of the population. This must seem nonsense, however, to anyone who has had extensive experience of clinical medicine during the last 40 years. Do you really believe that skilled pathologists during the great era of morbid anatomy in the early part of this century were missing those atherosclerosis infarctions at autopsies which are so distressingly common nowadays?

Obesity and atherosclerosis

Overeating is far the commonest nutritional disturbance in prosperous communities where men and particularly women dig their graves with their teeth, while on the other hand a greater or less degree of undernutrition is a cause of a different type of ill-health, not atherosclerosis, in the underdeveloped and underprivileged countries. The first thing that any poor person does when he gets a little more money is to go and buy some more food with it, and there would consequently seem to be a direct relationship between the level of nutrition and the incidence of atherosclerosis. This is further borne out by its very low incidence as revealed by autopsies conducted on persons who had lived, say, through the siege of Leningrad in 1942 or had died after years in European concentration camps. Lastly, the statistics of life insurance companies all show that mortality rates rise steadily in proportion to the extent to which people are overweight. It seems that a man 50 pounds overweight at the age of 45 has no better expectancy of life than the average expectancy for those suffering from all forms of valvular heart disease; for every fat person who reaches the age of 80 there are ten lean ones who do. I do not of course suggest that the decreased life expectancy of the obese is entirely attributable to atherosclerosis and ischaemic heart disease, for long-continued obesity has as its almost invariable concomitants more or less grave disturbances of all the systems of the body—flat foot, varicose veins, osteoarthritis of the knees and hips, ventral hernia, low backache, gall-bladder disease, bronchitis, and postoperative pulmonary complications are all far commoner, as well as atherosclerosis and ischaemic heart disease, in the obese than in the lean. Thus one of the major dangers for middle-aged people is the middle-aged spread and this is always avoidable, for the only cause of obesity is prolonged consumption of more food than is necessary for the repair of the body's tissues, and for supplying energy for its vital functions and physiological activities. This maxim is one which fat people find extremely difficult to believe. It's true that like motor cars some people run

15 and others 40 miles to the gallon, but obesity is always due to an excess of intake over output. Fat comes only off a plate, not out of the air; there were no fat persons when we entered Belsen concentration camp.

The question of fats

Though it is perfectly clear that obesity is an important factor in the morbidity and mortality of the middle-aged, we are on less sure grounds when we come to consider whether the actual constituents of the diet, apart from total calories, are of importance in the aetiology of atherosclerosis. Patients suffering from atherosclerosis and ischaemic heart disease often have a disturbance of the mechanism for lipid transport in their blood, characterized by high levels of plasma cholesterol and lipoprotein. It is also significant that diseases of which a high plasma cholesterol is a feature, such as uncontrolled diabetes, myxoedema, and hypercholesterolaemic xanthomatosis are associated with a high and early incidence of atherosclerosis and myocardial infarction. Where fats contribute 40 per cent or more of the total calorie intake, high plasma cholesterol levels and atherosclerosis are common, and such high fat diets are rare among the underprivileged. Though these observations support the view that dietary fat, plasma cholesterol levels and atherosclerosis are positively correlated, they cannot be accepted unreservedly, since they overlook the fact that many other possible factors, some of which we will consider, may be operative among underprivileged communities besides an intake of fat. There is some evidence, for example, that a reduction in dietary protein and choline leads to a reduction in the plasma cholesterol level in man. Further, there are some very difficult questions to answer before we accept the theory. Why, for instance is it that atherosclerosis and myocardial infarction seem to have increased just as much among the privileged as among the working classes in this country in this century, though the intake of animal fat among the former is less than it used to be? Some of you, like myself, will remember the Edwardian country house breakfast. No one was considered a man at all unless he ate porridge and cream, a couple of eggs and bacon, two herrings and lashings of toast and butter. Now he only has a few Rice Krispies! Yet myocardial infarction was rare among these eminent Edwardians though it is very common among their prototypes now. In addition there are some rural communities in Norway which have the highest intake per person of dairy products in the world, particularly milk, but where the incidence of myocardial infarction is low rather than high.

Until recently, animal and vegetable fats were believed to be interchangeable in their effect on the plasma cholesterol levels.

There is now, of course, no question that saturated fats—butter, cream, lard, beef dripping, and so on—are the factors which elevate it, whereas unsaturated fats—corn oil, sunflower seed oil, peanut oil and olive oil—decrease it. Hydrogenated vegetable fats such as margarine, the consumption of which has gone up enormously in the last 40 years, behave like animal fats since hydrogenation produces saturated fats from unsaturated fatty acids.

Besides dieting or the consumption of vegetable unsaturated fats, there are many medicinal agents which lower the plasma cholesterol level in man: sitosterol by decreasing the absorption of fat from the gut, large doses of nicotinic acid, oestrogens, and so forth. Recently there have been very favourable reports of an I.C.I. product, which lowers elevated serum lipid levels without the side-effects like baldness and cataracts, which somewhat similar agents have had in the past. It is by no means certain, however, that a lowering of elevated plasma cholesterol by dietary or medicinal means, in patients who have had a myocardial infarction prevents the development of further incidents. Studies claiming this have either been inadequately controlled, have covered too short a period of time, or have involved insufficient numbers of patients, while other reports have not suggested that morbidity and mortality rates are favourably influenced by these measures. It would indeed be very surprising if they could make much difference to a sclerosed, fibrotic, and often calcified arterial wall. To be effective, prophylactic measures would have to be started early in life and continued indefinitely. To my mind, the evidence is so far quite insufficient to justify the radical alteration of the food habits of the population and I feel that if convincing evidence materializes, the answer will be along medicinal rather than along dietary prophylactic lines, apart from the avoidance of obesity.

Physical activity

The influence of reduced physical activity must be taken into account in studying the epidemiology of atherosclerosis and the racial differences which occur in its incidence. Modern civilized man, particularly in the middle-aged group, has practically lost the use of his legs. I live in a house in the hills in Scotland where I sometimes have American and British doctors to visit me. After dinner if it is not raining, which it usually is, I sometimes take them out for a little stroll on the hills to see the grouse and the heather and the sunset, and when they come back you would think from their usual account that they had walked to the North Pole, proving conclusively that their previous exercise had been limited for many years to walking along half a block. The remarkable rise in the incidence of atherosclerosis and myocardial infarction in the last

40 years can just as well be correlated with the increased use of the internal combustion engine, automobiles, tractors, bulldozers, and mechanical labour-saving devices which affect all classes of the community as they can with the increased use of animal fats.

There is indeed some convincing evidence to show that men in physically active jobs have a lower incidence of atherosclerosis than in sedentary occupations. The eminent Edwardians who ate so much animal fat and who seemed not to have anything like the modern incidence of myocardial infarction took a great deal of exercise; they rode horses and pushbikes, plunged into cold baths and walked miles in pursuit of things to kill. Against this, it must be recorded that Canadian and Norwegian lumberjacks, whose labour is perhaps more strenuous than that of almost anyone else, have a relatively high incidence of myocardial infarction. Incidentally, they get a large part of their enormous intake of total calories from fat bacon.

Hormonal factors

Women live longer than men, and certainly up till the time of the menopause atherosclerosis is much less pronounced among women than amongst men. Premenopausal myocardial infarction is rare among women unless they are diabetics or myxoedematous, but after the menopause its incidence is similar in both sexes. Dr M. F. Oliver has been particularly interested in this intriguing aspect of the problem, and as he works in the wards next door to mine I have had some opportunity of observing his work. He has shown quite conclusively that oestrogens and certain thyroid analogues lower blood cholesterol levels, whereas androgens raise them. Unfortunately, there is as yet no convincing evidence that converting men who have had a myocardial infarction into, as far as possible, women, has any effect in reducing further incidents. He has followed up over many years a large group of relatively young, middle-aged men who have had an infarction and compared them with a similar group treated with oestrogens to the extent of diminishing their potency and causing gynaecomastia, but without noting any significant statistical difference between the two groups in the further incidence of infarction, in spite of the lower blood cholesterol levels in the treated groups.

Smoking and stress

Smoking has long been thought to play some part in the development of peripheral vascular disease. Indeed its deleterious effect on thromboangitis obliterans is quite certain. The inhaling of cigarette smoke will sometimes induce an attack of angina pectoris or intermittent claudication in some patients. These adverse

effects are usually attributed to the vasoconstrictor action of nicotine, though there are in addition other mechanisms through which smoking might be detrimental to the cardiovascular system; further studies are clearly necessary, but to deny that smoking is harmful to it, is to carry scepticism to an absurdity almost as absurd as to deny that it is a very important aetiological factor in bronchial cancer and bronchitis. Cigarette smoking, as opposed to pipe smoking, only became really general in the first world war. It has steadily increased since then *pari passu* with the rise of myocardial infarction to its modern epidemic proportions. There is surely no question at all that smoking is a dangerous habit and a most undesirable one for young people to acquire, though its most serious repercussions seldom occur before middle age. Those of us who are so hopelessly addicted that we cannot give up smoking should at least attempt to transfer the addiction to pipes and cigars which are much less deleterious, or better still to snuff, which besides being less detrimental is a great deal cheaper.

Lastly, there are those who say that the increased incidence of atherosclerosis is due to the increased stress and strains of modern life with its rush, bustle and atomic bombs. I wonder if in our modern welfare state with its 40 hour week we really work harder or whether there are more strains than in the old days when so many people knew not from whence their clothing, housing or next meal was coming, when the fear of death from disease and lack of drugs was constantly present and the fear of suffering from lack of surgery and anaesthetics was universal, and appalling wars decimated the population. It is common for doctors continually to advise middle-aged persons to rest more and to take things easier, but I doubt if that is usually wise. Routine, hard work is a great therapeutic agent and most people nowadays do not work hard enough. Like Mr Pickwick's cabhorse we tend to fall down when we are taken out of the shafts. It takes an exceptionally civilized man to be able to idle gracefully.

The problem of atherosclerosis is thus extremely complicated; there seem to be arguments pro and con almost all the theories that have been advanced to account for it. I do not suppose for a minute that there is a single aetiological factor responsible. Obesity, increased consumption of animal fat, sedentary habits, hormonal effects, and smoking may all play their part to a greater or less extent in individual patients. It's a pretty poor prospect, isn't it? It seems that from an early age we must eschew the pleasures of the table, especially the pleasures of dairy products and fat meats (and after all there are no other pleasures one can enjoy throughout life three times a day and take half an hour over each time), that we must exchange our automobiles for pushbikes, throw away our

cigarettes and take measures to become eunuchs! Well, thank God, no one has ever suggested that lashings of Scotch whisky are bad for atherosclerosis. In fact there is some evidence to suggest that whisky is good for it, though I can hardly claim that it has the same beneficial effects on the liver and the brain.

THE FORTIES: REORIENTATION ♀

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I am no longer a general practitioner and I wouldn't dare to call myself a physiologist, though I have a part-time appointment in the physiology department of the University of Edinburgh, where I endeavour to fit clinical spectacles on to the noses of the very knowledgeable young scientists in the five terms preceding the second professional examination. With this background, I may approach my subject with academic freedom.

On starting this study of middle-aged women, the disturbing discovery was made that there seemed to be a lack of serious investigation into the changes of middle-age. Hazards seemed a presupposition, as the 'pains' of labour. Many discussions have ensued with contemporaries and doctors, scientists, marriage guiders, office workers, psychiatric helpers, charladies and mums, some very postmenopausal subjects, and quite a few children with middle-aged relatives, and I have come to the conclusion that a great deal of useful female time is being wasted through lack of understanding, misinformation, and disbelief. Chambers' defines middle age as "between youth and old age, variously reckoned to suit the reckoner". The physiologist, dispassionately looking at the peak efficiency of cellular metabolism, reckons that it commences on the eve of one's twenty-first birthday. Is the official mind ahead of us when it directs us to give a specific age unless over 21? It would be pleasant to consider a timeless, gradual summer afternoon between adolescence and senescence, ideally quintessence, which is "the most essential part or embodiment of anything" (Chambers'). The female aspect of the problem is becoming confused; with this in mind, I will mention the comparative levels of nuisance and disease, accident and death in the age range 35—60 in general, and the changes of the