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Diet and Arterial Diseases

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I am going to talk about arterial disease, primarily atherosclerois, which is an important cause of myocardial ischaemia; this is defined as a condition in which the blood supply to the myocardium is impaired. Myocardial ischaemia is becoming increasingly important; in fact it is *the* important cause of death in this country and in other civilized countries such as America, countries where the standard of living is very high, particularly with reference to the consumption of dairy produce and animal fats. There is no doubt at all about the relationship between coronary thrombosis and a high intake of dairy products, particularly in the Scandinavian countries. Myocardial ischaemia is due to coronary obstruction, and this can be due to at least two things, atheroma and thrombus.

Most of the normal coronary artery wall consists of muscle, which we call the media, and separating the media from the inside is a layer called the internal elastic lamina within which is the intima, and it is in the intima that we find the first cause of coronary occlusion, the condition called atheroma, a porridgy degeneration. This is a progressive accumulation at first of fibrous tissue and later of lipid and fibrous tissue, which may ultimately, particularly in small branches of the coronary arteries, block them completely. The second mechanism is that of thrombosis, which is an occlusion of the vessel by the progressive aggregation of layers of platelet cells and fibrin; this always occurs on the surface of an atheromatous plaque, and often in a vessel narrowed by atheroma.

Atherosclerosis in man starts off as a fibrous thickening of the intima. The earliest lesion which one sees in children about the age of two or three is a barely visible fibrous thickening of the intima. It is sometimes called a fatty streak, but the amount of fat is very little more than is found in the normal intima. This is an important point because it immediately makes us wonder about the significance of lipids as causative factors in the production of atherosclerosis. Later on in life, usually about the twenties, this lesion begins to change in character. It is still fibrous but more lipid appears in it. Later on much more lipid accumulates, and a porridgy mass remains which ultimately ulcerates to produce the so-called atheromatous ulcer. Finally, at the end of life (if the patient can survive this sort of thing going on in his coronary arteries) in the sixties and seventies,

he is often in the happy position of having widely dilated and calcified coronary arteries, severely diseased but widely patent, the atherosclerotic lesion being then often largely fibrous with little fat in it. The sequence of accumulation of fat in these lesions is a very important point. Cholesterol accumulates in any damaged tissue, and the arteries are no exception to this. Yet ever since Vogel described cholesterol in arterial lesions, people have always wondered whether or not cholesterol played any part in the inception of these lesions and made desperate attempts to reduce serum cholesterol levels in the vain hope, I need hardly say, of affecting these arterial lesions.

In man thrombosis occurs on atheromatous plaques, and it is not surprising therefore, that people have assumed that the cause of thrombosis is the presence of a plaque. Yet at the London Hospital Morris made a survey of post mortems carried out there over the first 50 years of the century. He found that there was, if anything, no change or even a slight reduction in the incidence of atherosclerosis of the coronary arteries found post mortem, yet the incidence of coronary thrombosis had increased some ten times. This suggests that atherosclerosis alone cannot be responsible for coronary thrombosis, since in the presence of the same amount of arterial disease in the coronary arteries the incidence of coronary thrombosis has increased.

This led A. N. Howard and myself to look into experimental studies of animals fed various diets, to see if we could dissociate thrombosis and atherosclerosis. First of all, we fed rats with three types of diet. One diet contains butter, together with other agents designed to raise the plasma cholesterol level (group I). The second group has arachis oil, a vegetable oil (group II). The third group is the control group. The important point is that butter contains much more saturated fatty acid than arachis oil, and the latter contains much more unsaturated fatty acid than does butter. Both groups (I and II) fed butter or arachis oil died about 100 days after the start of the experiment. Animals in the butter group developed thrombosis in the heart and in the aorta, and lots of lipid-laden cells (not atheromatous lesions) in many organs (lungs, spleen, liver) which also adhered to the arterial walls. Butter did not produce anything that looked like an atherosclerotic lesion. Six of the rats had cardiac infarction, while two others had renal infarcts, due to vascular blockage. The butter in these rats produced predominantly thrombosis, but little in the way of arterial lesions. Arachis oil, containing unsaturated fatty acid, produced lesions very similar to those seen in human early atherosclerotic streaks. So it does seem that we managed to dissociate thrombosis and atherosclerosis by means of diet.

The cholesterol levels in these animals is interesting; it is much raised in the butter group. It is also raised in the arachis oil group as compared to the normal group III. However, plasma cholesterol levels were raised very much in the butter group. Tissue cholesterol levels in the spleen and the liver were also raised in both groups, but were higher in the arachis oil group than in the butter group, so one cannot infer the degree of tissue deposition of cholesterol from the plasma level. This then is the next important point.

The next two steps which we took in our experiments were, first of all to study other plasma lipids in these animals to see how abnormal they were (we had already studied the cholesterol levels) and secondly to study the clotting mechanism. When we studied the plasma lipid levels, we found that the plasma phospholipid levels were raised in the two experimental groups (very much so in the butter group) but the most significant elevation was of the triglyceride level, which was very high indeed in the butter group as compared with the control and arachis oil groups. This is important, because triglycerides, put into tissues in experimental animals, are potent injurious agents. It has also been shown that there is a close association between the incidence of coronary thrombosis and plasma triglyceride levels in man.

The next step was to study the clotting mechanism. Why did the butter-fed animals have thrombosis and the arachis-oil-fed animals have none? In collaboration with Dr E. Davidson in the Department of Medicine, who did most of this work, Dr A. N. Howard and I investigated the clotting machinery, and we found to our astonishment that in both the arachis oil group and in the butter group (groups I and II) values for all clotting factors were elevated; this was disappointing because we had hoped to find them elevated in the butter group and not in the arachis oil group. The platelet count was also greatly raised. We then fed these diets together with phenindione and found that we were able to reduce the incidence of thrombosis in the butter group, and of atherosclerosis in the arachis-oil-fed group, but when we came to look at the coagulation factors, we found them still as high as they were before we had given phenindione, so we were altering something which we were not measuring. Perhaps it was some platelet factor (platelets are very difficult things to investigate). Perhaps it was the fibrinolytic activity of the blood which had altered, but measurement of fibrinolysis is, at the moment, notoriously difficult.

Atherosclerosis in other animals is uncommon. It is seen in old cats and dogs, in old pigs, and in parrots in the zoo (the latter are particularly severely affected). It occurs naturally in the baboon, and we are investigating this at the moment. All these conditions

are rarely associated with thrombosis; this is the important point in which animals differ from man.

Turkeys suffer from an interesting condition which is rupture and dissection of the posterior aorta. This is an important disease, because it tends to pick off the biggest and best birds, which are usually the males, and often males that may be needed for breeding purposes. Indeed this was one of the reasons why people turned to artificial insemination in breeding these birds. At the site of the tear there is an atherosclerotic plaque, and the turkey plaque resembles the human plaque closely. It may be that the atherosclerosis is responsible for the rupture in the turkey aorta, but turkeys are also peculiar in that they have a high blood pressure compared with other birds, and this may also be a reason for aortic rupture, particularly in the weakened zone.

We fed turkeys on a variety of diets containing a variety of fats, and we found that they all produced plaques, no matter what type of diet we fed them. However, if they are fed a synthetic diet without fat, they also produce plaques, and rabbits fed a synthetic diet without fats do this too. So perhaps atherosclerosis has nothing to do with fat at all; perhaps it is some deficiency such as pyridoxine, which is known to produce arterial lesions in certain animals, conditioned by dietary lipid.

Lastly, there is no doubt at all that lipids are not the only factor involved. For example, the aorta of young persons with renal hypertension may show atherosclerotic plaques most of whose contents are fibrous in quality. Here the hypertension is undoubtedly the main factor, and any accumulation of lipid purely secondary. Atherosclerosis is then a multifactorial entity. Many factors come into play; one of them is diet but this is far from being the only factor. The lesson to be learned from these experiments is moderation in diet rather than violent change as a possible preventative of ischaemic heart disease.

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What Can Be Done

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When I qualified in medicine in 1948, the word " cholesterol " meant very little to me. I knew that the blood cholesterol level was raised in myxoedema and lowered in thyrotoxicosis. I knew that