How fats and oils affect the heart

'Epidemic' is a word usually associated with transmitted diseases like 'flu or cholera. But this century has witnessed an epidemic of an illness not caused by either bacteria or viruses — coronary heart disease.

Known risk factors predisposing us to heart disease include poor diet and lack of exercise.

Coronary heart disease is a major problem in developed countries. The symptoms range from a short and fleeting chest pain — angina — to a more severe and prolonged pain, which can end in sudden death.

At the beginning of this decade, more than 56 000 people were dying of this disease each year in Australia. Heart attacks are costing the Australian economy almost $2000 million per year, or an estimated $5·46 million per day. About 40% of sufferers die in middle age from their first major heart attack and three-quarters of these deaths occur outside hospital. More than two-thirds of those who die from heart disease are men.

What has caused the epidemic? Research has shown that a number of 'risk' factors are implicated, including high blood cholesterol and fat levels, high blood pressure, and smoking.

Attention has been focused on the role of diet in the development of risk factors, particularly the Western diet's traditionally high levels of animal fat. The average Australian derives a little over one-third of his or her calories as fat, either in meat and dairy products or in vegetable oils and margarine. Interestingly, a noticeable drop in deaths from heart disease in Australia and the United States since the late 1960s has coincided with increased consumption of less saturated vegetable oils relative to more saturated animal fat.

Diet trials

The reasons why so many of our hearts become diseased and fail are still not clear. However, clues are emerging, some from studies at the CSIRO Division of Human Nutrition in Adelaide, that are providing evidence of what happens to the heart and blood vessels at the cellular level as a result of various diets.

The Division has sited the experimental program at its Glenthorne laboratories on the outskirts of Adelaide. For Professor John Charnock, who heads the program, the research is a continuation of his studies in Canada on hibernating animals. In the summer months there, 'hibernators' function at the normal mammalian body temperature of 37°C and with heart rates characteristic of small rodents. But in winter, their body temperatures drop dramatically to 5°C and below, and their hearts beat about once every 2 to 3 minutes. To the children who often dig into the earth to find them, the animals appear dead.

Hibernation remains a mystery. The American space agency, NASA, unsuccessfully spent large amounts of money trying to find out how to induce animals to hibernate, so that they could put astronauts into hibernation for long space journeys. Professor Charnock and his colleagues in Canada concentrated on identifying how seasonal changes caused the changes they had observed in the hibernators' heart tissue.

A bright-eyed and bushy-tailed ground squirrel family enjoying the Canadian summer...

One of the animals studied — a species of ground squirrel — surprised the researchers by emerging from its seasonal sleep in the laboratory and promptly devouring its neighbour. Looking more closely at

...and a ground squirrel assuming a hibernation-like state in the laboratory.

their diet in the wild, Professor Charnock found that the hibernators emerged from the winter as carnivores, then passed through an omnivorous stage to a final seed-eating diet rich in vegetable poly-unsaturated fats in autumn, before resuming hibernation.

The researchers in Canada had already established a link between changes in the way the heart functioned and seasonal changes in the lipids (or fats) that form a vital part of the membrane of mammalian heart muscle cells. The seasonal factor behind these lipid changes appeared to be diet. Before hibernation, the animals ate food high in polyunsaturated oils (seeds), and on emerging from their long sleep, they sought foods rich in saturated fats (meat).

Heart attacks cost Australia almost $2000 million per year.

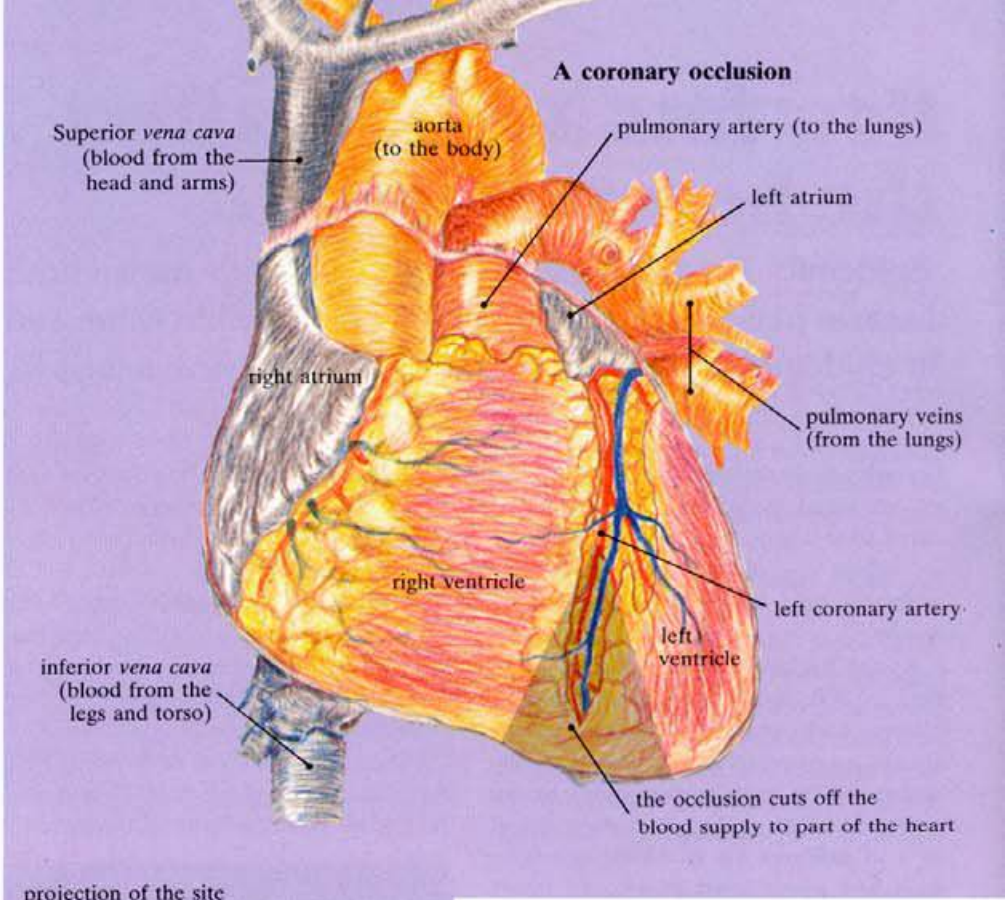
Identifying the link between lipid nutrition and heart structure and function is the aim of Professor Charnock's CSIRO program. Most overseas researchers who have looked at the effects of diet on heart tissue have restricted their studies to observing the effects of short-term cholesterol- or fat-loading experiments. Few have looked at how long-term low-dose feeding causes changes in cardiac and blood vessel tissue. Professor Charnock and his co-workers at Glenthorne — Dr Mahinda Abeywardena, Dr Ted McMurchie, Dr Peter McLennan, and Dr Graeme McIntosh — have adopted the latter approach, which more closely resembles the human situation.

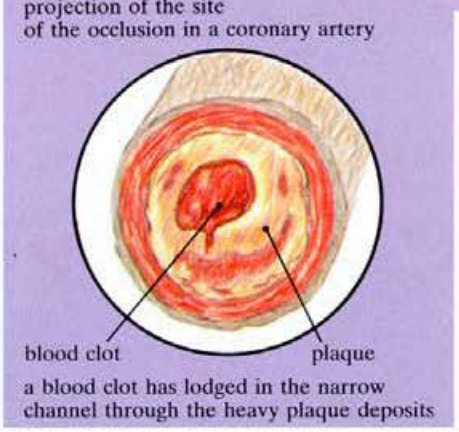
The CSIRO group set up long-term trials in which they supplemented animals' standard laboratory diets with either sheep fat or sunflower-seed oil — the extremes of the dietary spectrum here in Australia. Sheep fat is a typical example of the saturated fat found in meat, while sunflower-seed oil is one of the linoleic-acid-rich polyunsaturated vegetable oils used in the manufacture of table margarine. A third diet with mixed animal and vegetable oil supplements served as a control or reference diet.

Dr McIntosh looked at how different fats affected the levels of cholesterol circulating in the animals' blood. During the last 30 years, much of the research into fats and heart disease has centred on problems like atherosclerosis, caused by the build-up of cholesterol deposits along the inside of arteries. Dr McIntosh found that, in rats, a diet supplemented with sheep fat increased the levels of circulating cholesterol, as well as causing increases in weight and blood pressure.

In another animal, the marmoset, which has a physiology nearer to that of man, the results were similar. Within 4 weeks of beginning a high-sheep-fat diet, the animals developed 'hypercholesterolaemia', which led to a disorder of the blood vessels and blood cell membranes. Cholesterol and fatty acids tend to make the membranes more rigid, producing an effect something like bullets (in this case blood cells) ricocheting through a system of rigid pipes. Plasma cholesterol also increased with age in the animals fed the standard diet.

Experiments elsewhere had suggested that rats fed on diets high in linoleic acid — the main polyunsaturated fatty acid in many vegetable oils — showed an increased coronary blood flow rate, more regular heart muscle contraction, and an increased protection against heart damage. Vegetable oils high in linoleic acid include sunflower-seed oil and safflower oil, but not coconut or palm oil.





Blockage of a coronary artery deprives heart muscle beyond the occlusion of blood (shaded area), causing the ventricle to contract incompletely and irregularly.

Measuring contraction

Heart performance can be measured in a number of ways. One technique used by the Glenthorne researchers involved looking at the behaviour of a single isolated heart muscle called the papillary muscle. This connects the wall of the ventricle to the valves of the heart.

As well as assessing the effect of diet on heart performance, Dr McLennan and Professor Charnock were interested in finding out the effect of age.

They found that the muscles of aged rats fed a standard diet were slower to contract and relax than those of younger rats, but the force of contraction increased with age. They also found that the maximum pull or tension developed by the muscles from animals fed vegetable oil remained well below those of the saturated-fat and control groups. In fact, the scientists noted that such animals' muscle response pattern resembled the 'juvenile' response, while the heart muscles of animals fed an animal-fat diet displayed the characteristic aged response pattern.

The sunflower-seed-oil diet had also made the heart muscles less sensitive to the effects of adrenaline, a substance released

by the body during stress. Too much adrenaline can lead to irregularities in the heartbeat, known as arrhythmia.

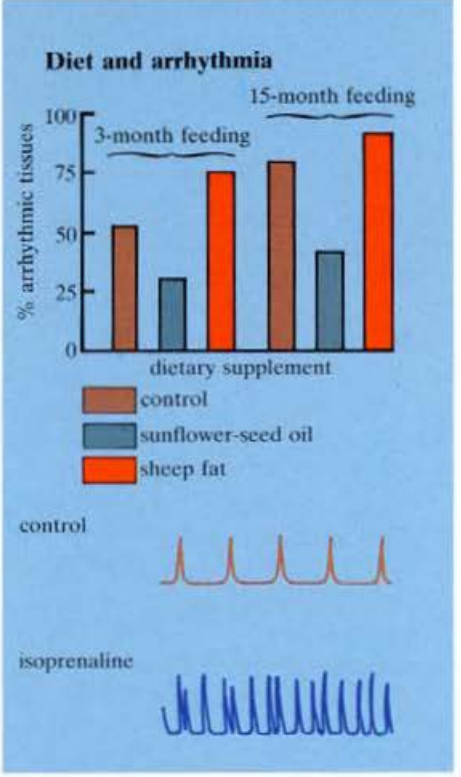
Using an analogue of adrenaline, isoprenaline, Dr McLennan and Professor Charnock observed that muscles from both the aged rats and those whose diets were supplemented with sheep fat succumbed to the arrhythmic effects of isoprenaline more easily than muscles in the juvenile state, including those from the sunflower-seed-oil-supplemented group.

What can research on twitching muscles tell us? A little-known fact is that about half of the Western world's deaths from coronary heart disease are, in fact, caused by uncontrolled ventricular fibrillation — heart muscles beating erratically and with little co-ordination, which prevents the heart from pumping blood to the rest of the body, leading to death.

Each beat of the normal heart represents the synchronized contraction of individual muscle cells. When a blockage occurs in a coronary artery supplying the main chambers of the heart (the ventricles), heart muscle beyond the block is deprived of blood (occluded), causing the ventricle to contract incompletely. Within a period of hours the muscle cells within the occluded region begin to die, reducing the pumping capacity of the heart. The remaining healthy heart muscle has to work harder and may not be able to cope with simple stresses such as those that result from climbing stairs.

Coronary artery occlusion also causes disruption of the regular electrical activity

Image of a marmoset heart obtained by radionuclide angiography. The left ventricle (left) is expanded.



When isoprenaline was used to induce arrhythmia in rat papillary muscle tissue, the proportion of tissue affected varied with the animal's diet. Tissue from sheep-fat-fed rats was the most affected. The electro-cardiograph (ECG) tracings below were produced by normal (top) and arrhythmic tissues.

of the ventricle, leading to arrhythmia. This occurs within minutes of the occlusion and can rapidly lead to ventricular fibrillation. Blood is no longer pumped, and blood pressure falls, leading to death. The risk is greatest within the first half-hour of having a 'heart attack'.

When the researchers induced myocardial infarction — death of heart tissue caused by blockage of the circulation — and cardiac arrhythmia in experimental rats by tying the coronary arteries of anaesthetized rats, their results confirmed their predictions. Rats fed a diet supplemented with sheep fat suffered more severe arrhythmias than animals fed a standard or sunflower-seed-oil supplement.

In fact, sunflower-seed oil seemed to provide protection against arrhythmia, as the animals fed extra linoleic acid experienced fewer and less severe arrhythmias than the control group. The area of heart muscle damaged following ligation was also smaller in this vegetable-oil group than in the others. And these effects became even more pronounced with longer-term dietary supplementation.

Dynamic assessment

The Glenthorne team has been anxious to find a relatively harmless yet sensitive method for monitoring heart function in animals. Dr McIntosh and Dr Charnock, together with Dr Leighton Barnden and Dr Ian Buttfield, from the Department of Nuclear Medicine at Adelaide's Queen Elizabeth Hospital, have begun using the technique of radionuclide angiography, already used for humans, to observe the function of rat and marmoset hearts.

The researchers inject the animals with a radioactive isotope — technicium 99, which has the very short half-life of only 6 hours — and this emits *gamma* radiation that is picked up by a special camera placed over the heart. The technique measures how fast and how effectively the heart is pumping blood.

Dr McIntosh and Dr McLennan used this method to assess differences between animals on oil or fat diets. Again, the marmosets fed sunflower-seed oil performed well — their hearts worked more efficiently than those of other groups. The hearts of mutton-fat-fed marmosets, on the other hand, worked harder.

Still, all of these results tell us only how diet affects heart performance, not why. Researchers agree that the cell membrane seems to be the key to this question because it regulates interactions between the inside and outside of cells. Furthermore, fatty acids are an integral part of membranes and any changes in the types present — for example, through diet — could change the functioning of the membrane. In heart muscles, the membrane plays a central role in keeping the heart pumping, and is also an important site of drug action.

Using biochemical analyses, Professor Charnock, Dr Abeywardena, and Dr McMurchie found that rats given the sunflower-seed-oil supplement had a higher proportion of arachidonic acid — a derivative of linoleic acid — in their tissues than

Fats and their molecular family

Fatty acids comprise one of the four major types of molecules found in living organisms; the others are sugars, amino acids, and nitrogenous bases (found in DNA). Each of the more than 100 known fatty acids is made up of a long chain of carbon and hydrogen atoms with a terminal acid group. The chains vary between 12 and 22 carbon atoms long; other differences concern whether the chain contains any carbon : carbon double bonds, and whereabouts in the chain these bonds occur.

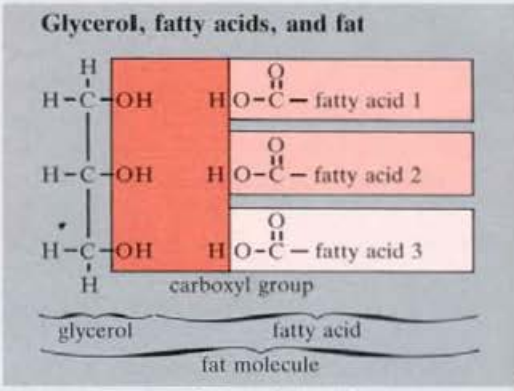
Lipids such as oils, fats, and waxes are largely made up of fatty acids. In the body, lipids serve as energy storage (as fats or oils) or structural components — for example, as phospholipids in the cell membrane, or as waxes. A defining characteristic of all lipids is that they don't dissolve in water.

The energy-rich bonds in the long carbon–hydrogen chain in fatty acids contain more chemical energy than carbohydrate molecules such as glucose. Also, because they are water-repellent, they can't be hydrated; as a result, fat can store more concentrated energy than the storage carbohydrate glycogen. Animals, such as migrating birds and camels, take advantage of this and store extra fats to tide them over long migrations or severe winters.

A fat molecule consists of three molecules of fatty acid joined to a single molecule of the alcohol, glycerol. A saturated fatty acid — like stearic acid, found in sheep fat — has no double bonds. It is called saturated because the bonding possibilities for all the carbon atoms in the chain have been taken.

An unsaturated fatty acid such as linoleic acid, on the other hand, contains some carbon atoms joined by double bonds. These carbon atoms are able to form up to six additional bonds with other atoms. Plants more commonly contain unsaturated fats — such as olive oil, peanut oil, or sunflower-seed oil — than animals. Many unsaturated fatty acids are 'polyunsaturated' — they contain more than one double bond.

The human body can synthesize saturated fatty acids from carbohydrate, but polyunsaturated fatty acids have to be obtained from the diet. Polyunsaturated fatty acids are commonly denoted by chemical shorthand. In this system, linoleic acid is written as C18:2(n-6); C18 refers to the number of carbon atoms in the chain, 2 to the number of unsaturated (or double) bonds, and (n-6) to the position of the first



Glycerol is one of the building blocks of fats — a fat molecule consists of three fatty acids joined to the glycerol molecule. Each glycerol–fatty acid bond forms when condensation removes a molecule of water (colour).

the group fed saturated fat. Arachidonic and linoleic acids belong to the n-6 family of fatty acids (see the box above). The rats fed the saturated-fat supplement tended to accumulate a fatty acid from another family altogether, the n-3 series.

Surprisingly, this one, docosahexaenoic acid (DHA), was not present in any of the diets administered. DHA is not a component of either sheep fat or sunflower-seed oil. The increase must have been due to the stepped-up conversion of another of the n-3 family, linolenic acid, usually present in food in small amounts. The researchers believe that the reduced availability of linoleic acid in the sheep-fat diet might have triggered off this conversion.

Results from the same experiments on marmosets were not identical. This made Professor Charnock's team more aware of the dangers of directly extending the findings of rat studies to humans. However, in both the rat and marmoset studies, manipulation of the intake of polyunsaturated and saturated fats caused a significant change in the ratio of n-6 to n-3 acids present in cardiac membranes.

Prostaglandins

The n-3 acids are known to be potent inhibitors of a key enzyme involved in the production of a group of substances called the prostaglandins. These recently discovered hormone-like chemicals were so named because they were first detected in seminal vesicles, and thought — wrongly, as it turned out — to be produced exclusively by the prostate gland. Now we know that a large series of these substances, all related structurally but with different and sometimes opposite effects, are generated by many different tissues of the body.

Dr Bengt Samuelsson and Dr Sune Bergstrom, of Sweden, together with Dr John Vane of England, received the Nobel Prize in Physiology–Medicine in 1982 for their work in isolating and characterizing prostaglandins.

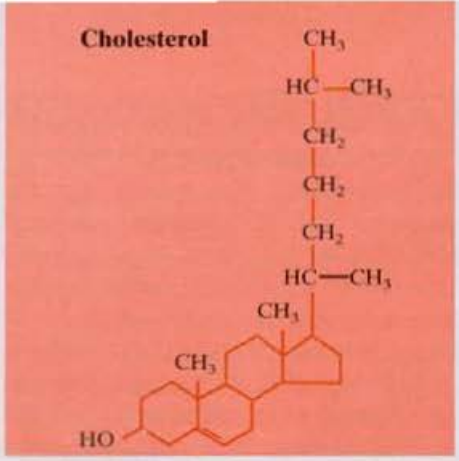
Prostaglandins differ from hormones in a number of ways. They are even more potent and so, not surprisingly, the body produces only tiny amounts of them, and enzyme systems rapidly break them down. After they form, prostaglandins are highly unstable — some of them have a half-life of only 30 seconds. Obviously, they need to be produced very near their target.

Cells, rather than glands, produce them in most of the body's organs, and they often exert their effects on the tissue that produced them. Prostaglandins often work in antagonistic pairs. Derived from long-chain fatty acids, prostaglandins (like hormones) can be 'good' or 'bad' for the body in question. The bad prostaglandins can, among other things, cause vascular spasm in blood vessels and trigger the clumping of blood platelets, increasing the risk of clotting. They can also induce cardiac arrhythmias.

The precursor of many prostaglandins is arachidonic acid, the n-6 fatty acid found in greater quantity in the cardiac membranes of rats fed the linoleic-acid-rich sunflower-seed-oil supplement than in those of the linoleic-acid-poor sheep-fat-supplemented rats. Professor Charnock's group believe that the changes in the fatty acids of the heart muscle of trial animals might have led to changes in production of prostaglandins.

Prostaglandins have been implicated in many inflammatory and immune responses, such as rheumatoid arthritis and asthma, and their discovery solved the long-standing question of how the common pain-reliever aspirin worked. Now medical researchers know that it inhibits the synthesis of prostaglandins, producing its well-known soothing effects in inflammation and fever.

Dr Vane, who is the Director of Research at the Wellcome Research Laboratories in Beckenham, England, has studied a similar drug called indomethacin for human use. Indomethacin is a potent inhibitor of prostaglandin synthesis. This 'super aspirin' provides an alternative to the large doses of aspirin often needed to combat inflammation, thus reducing the unpleasant side



A cholesterol molecule comprises four carbon rings and a hydrocarbon chain.

double bond, counting from the non-acid end.

The two families of essential polyunsaturated fatty acids are the (n-6) family — linoleic acid and its metabolic derivatives — and the (n-3) family, derived from *alpha*-linolenic acid, C18:3(n-3). Oilseeds (like sunflower seed) provide us with most of our linoleic acid and green-leaf lipids with most of our linolenic acids.

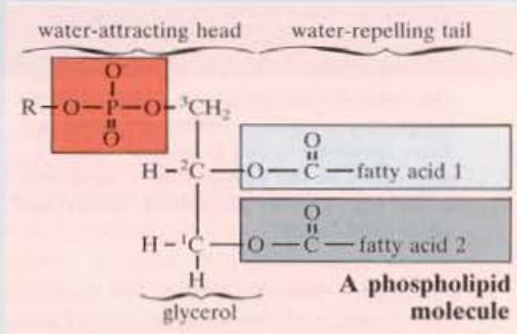
Conversion of these to longer-chain polyunsaturated acids (like arachidonic acid, C20) depends on the activity of enzymes that preside over the conversion. Ready-made C20 and C22 polyunsaturated fatty acids do occur naturally, however, in meat and fish.

The traditional food of Eskimos is flesh and blubber from whales and seals, as well as fish and wildfowl. The fat in this diet is rich in C20:5(n-3) and C22:6(n-3), respectively known as eicosapentaenoic and docosahexaenoic acids. The source of these two substances is phytoplankton, back at the beginning of the marine food chain. Docosahexaenoic acid (DHA) occurs to a large extent in the oils of fish caught in Australian waters. Vegetarian diets, while adequate in 18:2 and 18:3 polyunsaturated fatty acids, provide few of the longer-chain acids found in meat and fish.

Another fat-like substance is cholesterol. This belongs to a group of compounds known as steroids. Although they don't resemble lipids structurally, steroids are also insoluble in water. All of them have four linked carbon rings, and many have the hydroxide group found in alcohols.

Along with fatty acids, cholesterol occurs in cell membranes: it constitutes about one-quarter of the membrane of red blood cells. With age, the body can sometimes accumulate enough cholesterol on the inside of blood vessels to restrict flow sufficiently to cause a stroke or heart attack. Diet is not the only source of cholesterol — many of the cells of the human body can make their own.

Phospholipids are the most important structural lipids. Like fats, they consist of fatty-acid chains attached to a glycerol backbone. But, unlike fats, they have one of the carbons in the glycerol molecule bonded to a phosphate group instead of a fatty acid. As a result, the phosphate end of the molecule is water-attracting. These 'heads' extend into the inside or the outside of the cell. Phospholipids are important components of cell membranes.



A phospholipid molecule

The orange indicates the phosphate group, and 'R' represents an additional chemical group.

effects such as gastric bleeding and nausea that accompany anti-inflammatory action.

The Glenthorne team applied this knowledge to the heart muscle contraction studies. After they administered indomethacin, Dr McLennan and his colleagues found that isolated muscles showing an initial aged response — due to either age alone or a saturated-fat diet — soon assumed the 'juvenile' pattern. In the isolated papillary muscles the indomethacin treatment had obliterated diet-induced changes in tension that had taken 6 to 12 months to induce.

Members of the team are collaborating closely with scientists in Europe on identification of the prostaglandins involved. Two groups, one led by Professor Gerard Hornstra at the University of Limburg in Holland and the other led by Dr Sven Fischer at the University of Munich, are using the Glenthorne work to guide them in their search for a chemical model to identify the unknown prostaglandins produced by the hearts of the animals fed the different diets.

Ratios

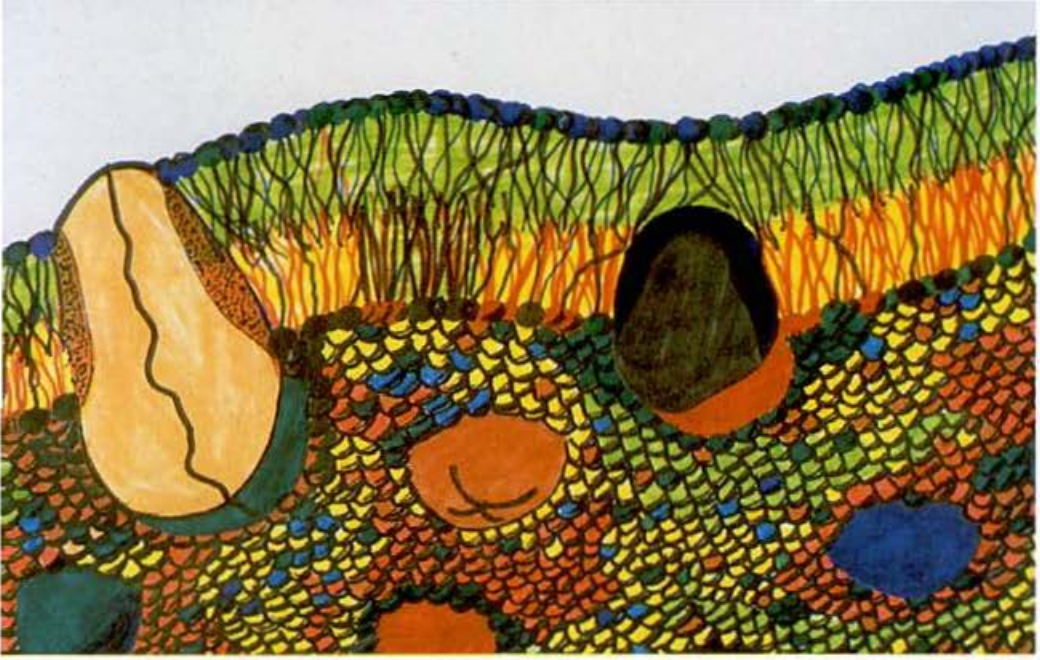
At the Division itself, Dr Abeywardena is studying the way changes in fatty-acid composition affect prostaglandin production in the heart and major blood vessels. Their short life makes them difficult to isolate and store, let alone study. But scientists elsewhere have developed bioassay techniques to study vascular prostaglandins from blood vessel walls, and Dr Abeywardena chose to study these before beginning work on cardiac prostaglandins themselves.

Because prostaglandins, arachidonic acid, and linoleic acid are different versions of the same molecular skeleton, Dr Abeywardena looked at the ratios between the three to determine how their relationship changes with diet. After a 12-month feeding trial, the results from studies using two different animals showed a complex picture.

While rats maintained constant levels of arachidonic acid in their vascular tissue, the levels in marmosets dropped following feeding with both types of supplement, and while the level of linoleic acid in rats fed sunflower-seed-oil supplement increased only slightly, the level in marmosets doubled. Further, rats fed a sheep-fat diet developed an increased capacity to generate prostacyclin — a 'good' anti-clotting prostaglandin — while their primate counterparts did not.

Puzzling indeed. Dr Abeywardena deduced that the high-saturated-fat diet, which tends to promote blood clotting, turns on a compensatory switch in the rat to produce the anti-platelet-aggregating prostacyclin. Apparently this response does not occur in marmosets. Once again, the difference in response between species

Eskimos have a low incidence of aging disease, including heart disease.



The lipid bilayer model of a cell membrane. Large active protein molecules, such as those involved in ion transport, are embedded in the phospholipid 'sandwich', consisting of outer phosphate 'heads' and inner lipid 'tails'.

provided a reminder for caution in simple extrapolation of the results of animal trials to human beings.

Fish oils

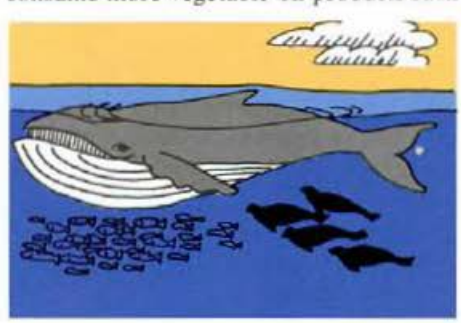
Fish oils provide another piece of the heart attack jigsaw puzzle. Researchers have known for some time that fish oils — rich in n-3 polyunsaturated acids — are potential antithrombotic agents. Studies of Eskimo populations and fishing communities in Japan have shown that heart disease is rare or non-existent among those peoples. They also have a low incidence of the aging diseases — diabetes, arthritis, etc. Their diet is rich in fish oils, and whale and seal blubber, which appear to be even more effective than linoleic-acid-rich vegetable oils in reducing the heart disease epidemic.

Dr Abeywardena looked at four different groups of rats on diets supplemented with Australian tuna-fish oil, sunflower-seed oil, sheep fat, or the standard mixed diet. All animals, with the exception of those given tuna-fish oil, had unchanged levels of arachidonic acid in the lipids of one of their major blood vessels. In addition to a 50% reduction in arachidonic acid — the major precursor of prostaglandins — the fish-oil-fed rats also had high levels of DHA, which is reported to inhibit prostaglandin synthesis. So this group had the lowest capacity to produce prostaglandins, while the high-saturated-fat group had the highest. Interestingly, a good relationship between the ratio of membrane linoleic acid to arachidonic acid and prostaglandin synthesis was apparent for all dietary groups, confirming the role of these two n-6 unsaturated fatty acids in prostaglandin biosynthesis.

Dr McIntosh focused on another aspect — the tendency for certain diets to increase blood coagulation. He found that bleeding and clotting times doubled for the fish-oil-fed group relative to the controls. The diet rich in saturated fats also increased the likelihood of thrombosis, while a fish-oil diet reduced this tendency.

In fact, the ability of fish oils to prevent clotting is so effective that Eskimos bleed very easily, and face the prospect of bleeding to death from what we would regard as minor injuries. The polyunsaturated oils from fish block the production of thromboxane, the prostaglandin involved in platelet aggregation. Obviously, an optimum diet is one that produces enough thromboxane to prevent excessive bleeding, but enough prostacyclin to prevent clotting.

Professor S. Renaud of the Inserm research institute in Lyon, France, carried out a study of Scottish farmers to compare how the different life styles on the east and west coasts affect their health patterns. The traditional diet of the west coast communities — meat and dairy products — led to an increased tendency to develop blood clots, which in turn led to the development of atherosclerosis. This showed in the higher incidence of heart disease in these farmers. On the east coast, where farmers consume more vegetable-oil products such as margarine in place of animal products, the incidence of heart disease was lower.



In his experiments with marmosets, Dr McIntosh found that animals fed the sunflower-seed-oil supplement produced less thromboxane than those receiving saturated fat supplements. And, to amplify their problem, animals fed on sheep fat produced less prostacyclin than the others. This proved that the balance between thromboxane and prostacyclin is important in blood clotting. Some researchers have speculated that the effect of sunflower-seed oil may be enhanced by its high content of vitamin E, which may tip the balance in favour of increased prostacyclin production.

Viscosity

Where does the structure of cell membranes come in? Heartbeat — the contractions of heart muscle — results from electrical excitation of cell membranes. This results from a momentary reversal in electrical potential as ions are pumped in and out of the membrane via carrier or transport systems.

A number of these transport mechanisms are lipid-dependent. Not only is the presence of lipid essential for their activity, but various properties of phospholipid molecules — due, for example, to their phosphate 'head' and fatty acid 'tail' — can affect their function. Any changes in the fatty-acid composition of heart muscle membrane induced by dietary fats may influence the properties of these lipid-dependent transport mechanisms.

Dr McMurchie, Dr Abeywardena, and Professor Charnock initially studied the effects of different fats on the behaviour of two enzymes involved with either calcium transport or sodium and potassium transport across membranes. Changes in the properties of these so-called 'ion pumps' could conceivably alter the ionic distribution in the cell and so affect heart muscle contraction.

While the results showed that the heart muscle membrane in animals fed saturated fats was less fluid than that of the sunflower-seed-oil group, the differences in diet did not affect the two ion-transporting enzymes. These transport systems, which span the width of the cell membrane, seem to be protected from diet-induced changes in the lipid composition of the surrounding membrane.

These findings generated a new idea that only 'mobile' enzymes and molecules are likely to be affected by changes in the lipid composition, and hence the viscosity, of the cell membrane. The so-called *beta*-recep-

Membranes: more than a double line

Living cells continually exchange material with their environment. The membrane surrounding a cell keeps certain things in and lets others out.

It is so fine — about 0·000008 mm thick — that it evades the resolution capacity of a light microscope. After being stained by special reagents under the electron microscope, it appears as a continuous thin double line.

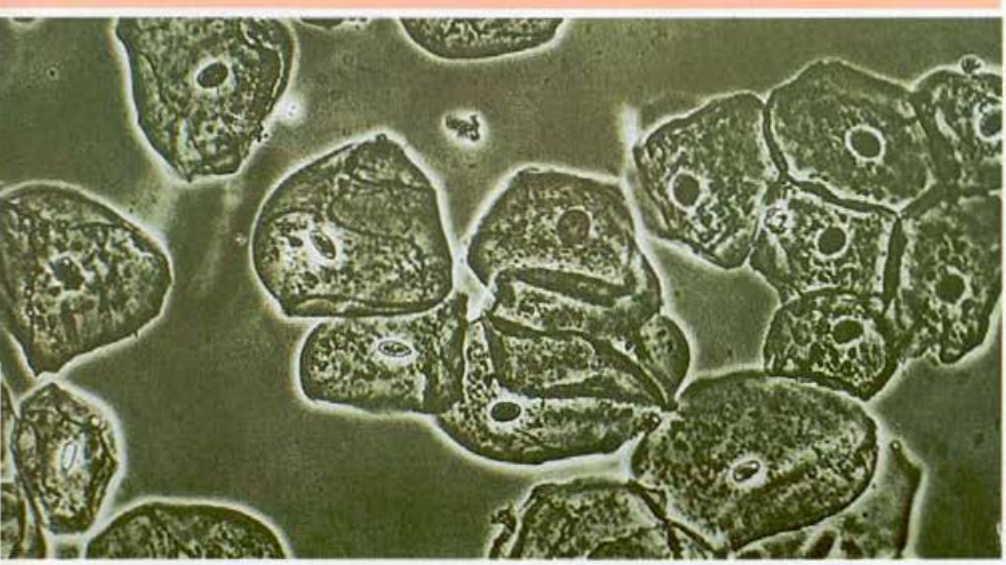
Scientists believe that this double line consists of phospholipid and cholesterol molecules arranged so that their water-repelling (hydrophobic) 'tails' are clustered inwards. Globular proteins embed themselves in this molecular sandwich. Most membranes are about 40% lipid and 60% protein.

These proteins, known as integral proteins, commonly span the membrane and protrude beyond its surfaces. The part embedded in the membrane bilayer repels water, whereas the protruding ends attract it. Some researchers believe that ion-carrying channels run through some of the integral proteins.

The two layers of the bilayer have different concentrations of specific types of lipid molecules. The integral proteins themselves have a definite orientation within the bilayer. The proteins vary from membrane to membrane, depending on the function of the cell. Some are enzymes, while others are carriers that transport molecules across the membrane.

The structure of the bilayer is quite fluid, so the lipid molecules and some of the protein molecules can move laterally within it. The carriers ferry back and forth molecules that could not readily cross the membrane by diffusion, because of their size or polarity.

One of the most thoroughly documented transport systems is the sodium–potassium pump. Most cells use energy to maintain a concentration gradient of sodium and potassium ions across the membrane. Sodium is kept at low levels inside the cell, and potassium at a high concentration. The carrier protein in the membrane has two configurations — one to take in potassium and the other to export sodium.



Human cheek cells under a microscope. They enable scientists to quickly assess the effects of different diets.

tors in the cell membrane that are involved in the action of adrenaline provide an example. This aspect is now being studied by Dr McMurchie and his laboratory team.

Cheek cells

Studies on human volunteers have confirmed the link between diet and the fatty-acid composition of body cells. The Glenthorne researchers are studying cheek cells, obtained by a simple and harmless method. Subjects simply 'swish' water in their mouths and spit out what has now become a dilute suspension of cheek cells.

Dr McMurchie has analysed the fatty-acid content of membrane phospholipids from cheek cells among vegetarian and non-vegetarian groups of people. He found that the proportion of saturated fatty acids was 12% lower in cheek cell lipids from the vegetarian group than from the non-vegetarian group.

In another study, Dr McMurchie asked two groups of volunteers from staff at the Royal Perth Hospital to adopt different diets. One group ate a diet high in polyunsaturated fats for 6 weeks followed by a low one for the following 6 weeks. The other group consumed meals relatively high in saturated fats for 6 weeks, then switched to a high-polyunsaturated-fat diet.

Following the change from the low- to high-polyunsaturated-fat diet, the proportion of linoleic acid in the volunteers' cheek cells and in their plasma lipids rose. But for the other group and the standard group, no apparent reductions in linoleic acid in the cheek cells occurred. Dr McMurchie did note, however, that a reduction occurred in the plasma lipids.

What both these studies show is that the fatty-acid profile of human cheek cells is a good indicator of short- and long-term changes in diet. Dr McMurchie is currently studying the lipids of school-children using samples of their cheek cells.

Through their co-ordinated efforts, the researchers in Professor Charnock's team at Glenthorne have laid the foundations for nutritional studies of humans. The differences between results for rats and marmosets indicate that great care will be necessary in translating the findings to humans. Nevertheless, their results are highly suggestive, and the human cheek lipid studies will provide further clues to how much extrapolation is possible.

Mary Lou Considine

More about the topic

Changes in fatty acid composition of the cardiac phospholipids of the cotton-eared marmoset (*Callithrix jacchus*) after feeding different lipid supplements. J.S. Charnock, G.H. McIntosh, M.Y. Abeywardena, and G.R. Russell. *Annals of Nutrition and Metabolism*, 1985, **29**, 83–94.

Diet and cardiac arrhythmia: effects of lipids on age-related changes in myocardial function in the rat. J.S. Charnock, P.L. McLennan, M.Y. Abeywardena, and W.F. Dryden. *Annals of Nutrition and Metabolism*, 1985, **29**, 306–18.

Dietary-induced changes in the fatty acid composition of human cheek cell phospholipids: correlation with changes in the dietary polyunsaturated/saturated fat ratio. E.J. McMurchie, B.M. Margetts, L.J. Beilin, K.D. Croft, R. Vandongen, and B.K. Armstrong. *The American Journal of Clinical Nutrition*, 1984, **39**, 975–80.

'Eating, Working, Living and Health' is a readable, profusely illustrated 68-page booklet about CSIRO's work in human nutrition, food safety, and occupational health. It is part of the *CSIRO Research for Australia* series (see the panel on page 31).