Professor Basant K. Puri's Medical School Talk on Fatty Acids & Health – Part I

by **Albert Cilia-Vincenti** *MD FRCPath*

Basant Puri is a consultant psychiatrist holding a Personal Chair in the MRI Unit of the Medical Research Council's Clinical Sciences Centre at the Hammersmith Hospital, and is also Head of the Lipid Neuroscience Group at Imperial College, London.

Basant Puri was invited by our University departments of Family Medicine and of Psychiatry, and was duly introduced by Drs Philip Sciortino and David Cassar. Although his talk on 11th December was expected to focus on fatty acid research in depression, chronic fatigue syndrome/Myalgic Encephalomyelitis and attention deficit and hyperactivity disorder, he tackled a whole gamut of serious chronic diseases which might be ameliorated by dietary fatty acids and, in particular, by the omega-3 polyunsaturated fatty acid eicoapentaenoic acid (EPA).

He started off on cardiac health by going back to the Eskimo studies of the Oxford biochemist Dr Hugh Sinclair in 1944 and those of the Danish scientists Drs Hans Bang and Jorn Dyerberg in 1976. Sinclair had first noted a possible association between eating plenty of fish and virtually no heart attacks, psoriasis, asthma, diabetes, immune disorders, gallstones, diverticular disease or ulcerative colitis in Eskimos, although they did suffer from some cancers, peptic ulcers and cerebral haemorrhage. The reason for this different disease pattern from Westerners was not genetic, because Eskimos who had emigrated from Greenland to Canada, and adopted a Western lifestyle, suffered heart attacks and other Western disease patterns within a time span of a single generation.

Bang, Dyerberg and Sinclair found that Eskimos' bleeding time was about twice that of Europeans and, although they had similar average total cholesterol levels, Eskimos had higher high-density lipoprotein cholesterol (HDL-C) and far lower blood triglycerides. The blood lipid differences were not fully understood at the time, but the longer bleeding time due to diminished platelet aggregation in Eskimos was clear enough. In 1979 Sinclair put himself and other volunteers at Oxford on a 3-month fish and seafood-only diet. He found that although their total blood cholesterol was slightly higher, their HDL-C had risen, their triglycerides had fallen sharply, and their bleeding time had roughly doubled. This Eskimo pattern of blood findings was therefore not genetically determined, but was diet-related. Something in fish diminished platelet aggregation and was probably responsible, via this mechanism, for the rarity of coronary thrombosis in Eskimos.

"Good" Eicosanoids	"Bad" Eicosanoids
Prevent blood clots caused by platelet aggregation	Promote blood clots caused by platelet aggregation
Cause vasodilatation	Cause vasoconstriction
Reduce pain	Promote pain
Decrease cell division	Promote cell division
Enhance the immune system	Depress the immune system
Improve brain function	Depress brain function

Figure 1

In 1982 the Nobel Price for Medicine went to John Vane, Sune Bergstrom and Bengt Samuelsson for their work on eicosanoids and elucidation of how the 20th century wonder drug, acetylsalicylic acid (aspirin), worked. Eicosanoids are a large family of fast-acting, very short-lived autocrine hormones acting locally in all cell membranes, and not at distant sites via blood transport. They include *prostaglandins, thromboxanes, leukotrienes and lipoxins*. Although they control every physiological function, they are almost undetectable within blood and have largely remained mysterious to most members of the medical and pharmaceutical professions. Different eicosanoids have diametrically opposite physiological actions, and biological equilibrium is maintained by a balance of these opposing actions. For simplicity, eicosanoids can therefore be broadly divided into 'good' and 'bad' according to the physiological changes they encourage (Figure 1).

The author has included an eicosanoid pathophysiology outline to enhance understanding of Basant Puri's delivery on the omega-6 essential fatty acids metabolism cascade (Figure 2). The metabolism of arachidonic acid is controlled by the cyclo-oxygenase enzymes COX-1 and COX-2. Aspirin and other NSAIDs inhibit both COX-1 and COX-2. Aspirin's analgesic, anti-inflammatory, anti-thrombotic and tumour-inhibiting actions are delivered via this mechanism. When pharmaceutical companies thought they had developed drugs that selectively inhibited COX-2 for anti-inflammatory action only, they did not realise that some of these new drugs might eventually cause thrombotic complications due to encouragement of platelet-aggregating eicosanoids. The complicated biochemistry of eicosanoids is still poorly understood.

The omega-3 fatty acid EPA is thought to exert its various claimed beneficial functions, including anti-thrombotic and ant-inflammatory actions, by inhibiting the arachidonic acid pathway (Figure 2), thus encouraging the 'good eicosanoids'. Its anti-thrombotic action probably explains the Eskimo and Japanese cardiovascular disease patterns. Japanese ischaemic heart disease prevalence is low compared to Western countries, and Japan maintains the world's highest longevity figures. This is claimed to be largely due to their mainly vegetarian and fish diet with little or no animal-origin foods.

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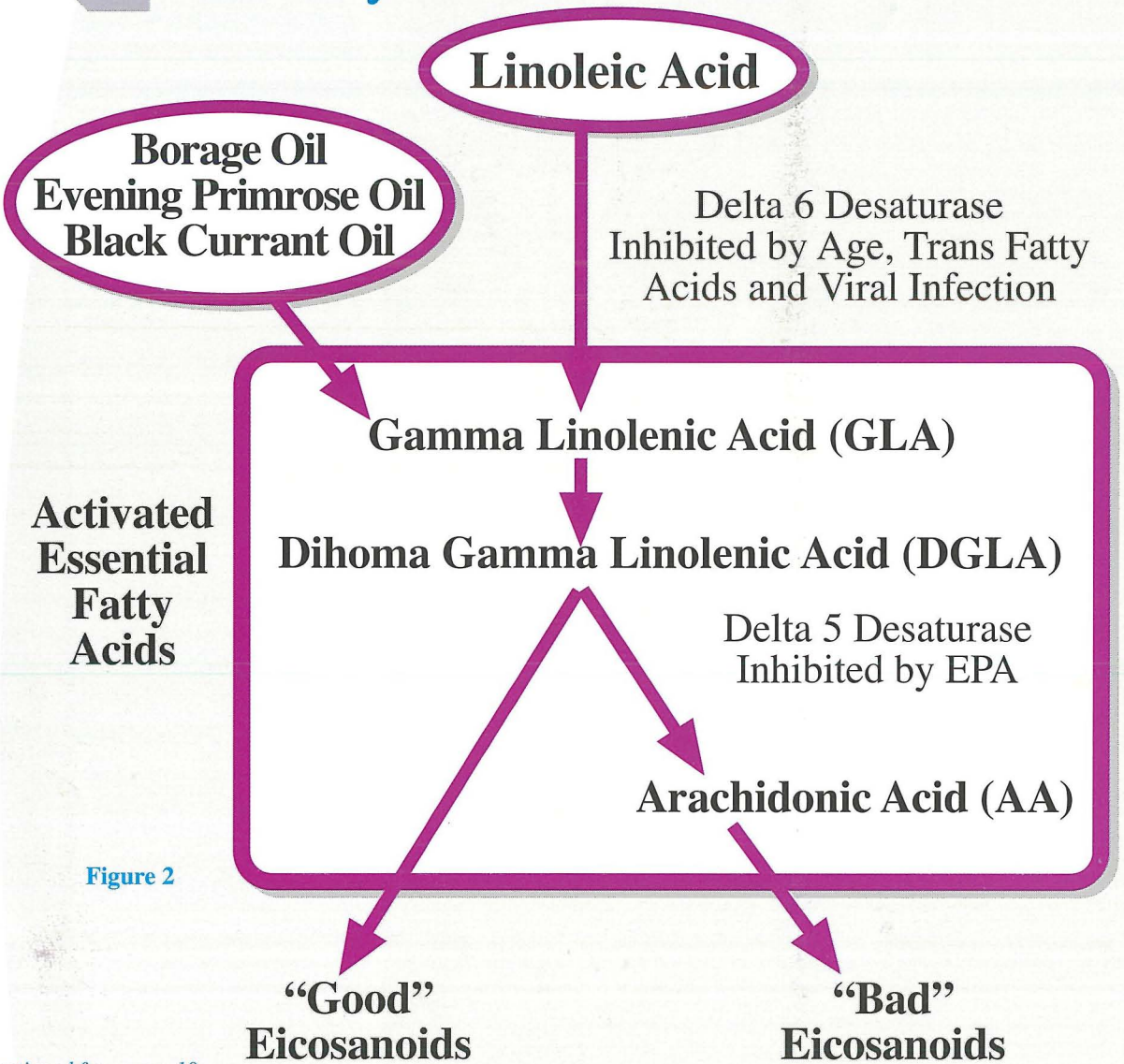

Figure 2

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Furthermore, a recently published Japan EPA lipid intervention study (JELIS) demonstrates that addition of EPA to statins has beneficial effects on lipid profiles of patients with mixed type hypercholesterolaemia and reduces further their major coronary events.[1] Purified EPA is already approved by Japan's Ministry of Health, Labour and Welfare as a treatment for hyperlipidaemia and peripheral artery disease.

The JELIS study also focused on risk factors for coronary disease other than low-density lipoprotein cholesterol (LDL-C).[2] In the higher risk group with high triglyceride and low HDL C, commonly seen in the metabolic syndrome, pure EPA suppressed the risk of coronary artery disease by 53%, suggesting that EPA is particularly beneficial in this group of patients.

Furthermore, *The Lancet* comment on a recently published Italian study3 states, "supplementation with omega-3 fatty acids should join the short list of evidence-based life-prolonging therapies for heart failure".

A further article on the part of Basant Puri's talk dealing with EPA and brain function will appear in the next issue.

References

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