Cigarette smoking and linoleic acid

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in a relevant proportion of cases, perhaps in most patients carrying the PKD1 mutation, ADPKD may start as early as the 12th week of gestation. This contrasts with the late appearance of clinical signs and symptoms which do not appear before the third to fifth decade in many individuals.

We believe that ADPKD starts in fetal life in a substantial number of cases, implicating the first functioning nephron generations. Our finding is of clinical importance since it offers the possibility of following patients at risk in infancy or childhood to prevent or delay progression to end-stage renal failure by influencing cyst growth and by modulating major risk factors—ie, hypertension, infection,and possibly, protein intake.

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CIGARETTE SMOKING AND LINOLEIC ACID

SIR,—Professor Oliver (June 3, p 1241) reports that smokers in Scotland consumed less linoleic acid than non-smokers. This led us to check relations between smoking and diet in a cohort of 315 Dutch men, aged 28 and 29 years.[1] 174 were non-smokers, 67 moderate smokers (1–14 cigarettes per day mean 8), and 74 heavy smokers (15–40, mean 21). Most had not changed their smoking habits over the past ten years. Diet was assessed by dietary history and cross-checked with a food frequency list. In our cohort linoleic acid intake was not related to smoking, and contributed 5·6% of daily energy intake in non-smokers, 5·5% in moderate smokers, and 5·5% in heavy smokers. Significant associations between diet and smoking were found only for total energy (13·2 MJ per day in non-smokers, 13·1 in moderate smokers, and 15·6 in heavy smokers), and alcohol (3·9% of energy for non-smokers and 6·5% for moderate and heavy smokers). The fatty acid plus cholesterol intake, when combined according to Keys' equation,[1] was significantly associated with the serum cholesterol level (regression coefficient 0·83 [SE 0·27], $n = 315$, $p < 0·05$); this suggests that our assessment of dietary fatty acid intake was reasonably precise. Thus we cannot confirm that smokers eat less linoleic acid. Perhaps the finding is limited to countries where foods rich in linoleic acid are less common than in the Netherlands.

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1. Berns MAM, de Vries JHM, Katan MB. Increase in body fatness as a major determinant of changes in serum total and HDL-cholesterol in young men over a 10-year period. *Am J Epidemiol* (in press).

SIR,—Professor Oliver makes a strong case for dietary linoleic and eicosapentaenoic acids as coronary protective factors. However, some of the sources he cited are at least as supportive of the hypothesis that the readily absorbed carbohydrates sucrose[1] or lactose (in lactose absorbers)[2] may be coronary risk factors.

Referring to the eating habits of healthy Scotsmen, Oliver states that "smokers ate substantially less polyunsaturated fat (mainly linoleic acid), less fibre, and less fish". The source data show that the lower consumption of fish in smokers was limited to the manual social group, whereas smokers in both the manual and non-manual classes consumed substantially more sugar, confectionery, and preserves than the non-smokers.

Referring to M. G. Marmot's 1985 study Oliver states that in the USA "the consumption of linoleic acid has steadily risen over the past twenty years". That study records a rise in the percentage of food energy from linoleic acid since 1909–13; in daily supply the increase was from 9 g per head in 1909–13 to 16 g in 1957–9 and 26 g in 1984. The increase in dietary linoleic acid thus occurred during the rise as well as the fall in the US coronary experience. The contribution from fish to the American intake of fat remained stationary and low at 2–3% during the whole period 1909–13 to 1984.[1] During this same period the saturated fat supply ranged from 52 to 59 g per head per day with only small fluctuations that show no trend up or down. On the other hand, milk consumption was rising until the late 1950s, and then fell before and during the decline in US coronary mortality:[2] the daily supply of total dairy products excluding butter decreased from 532·3 g in 1955–59 to 478·0 g in 1970, rising again to 492·6 g by 1973; from 1976 to 1984 daily total whole milk and fresh whole milk products excluding butter decreased from 371·4 to 338·9 g.

The lower coronary disease rates of the southern French, to which Oliver refers, are associated with a low supply in France of whole milk and fresh whole milk products, of which the intake can be assumed to be lower in the south where it is estimated about half the population have physiological lactose malabsorption.[3]

Oliver stresses the importance of an inverse relation between adipose linoleate and risk of coronary disease. However, dietary linoleic and eicosapentaenoic acids are unlikely to be the factors that protect the nomadic Tibetan highlanders from their high saturated fat diet, because their serum levels of these polyunsaturated fatty acids were significantly lower than those of Japanese control subjects.[4] Although the Tibetans have a high intake of milk, this is taken mainly lactose-fermented, as with the Masai, who, in addition, have a high prevalence of lactose malabsorbers.[5]

The liability to coronary disease of Asians in Britain, not mentioned in Oliver's article, cannot be attributed to a low intake of linoleic acid or a high intake of saturated fat.[6] However, north Indians and Pakistanis are predominantly lactose-absorbers and tend to take a lot of milk.

In a controlled metabolic study, consumption of skimmed milk was associated with significant increases in plasma cholesterol and low-density lipoprotein cholesterol and decrease in high-density lipoprotein cholesterol.[7] In baboons, lactose has been found to be atherogenic, considerably more so than fructose, sucrose, or starch.[8]

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SIR,—Professor Oliver draws attention to the low levels of adipose linoleate in patients with coronary heart disease and points out that cigarette smokers have abnormally low levels of linoleic acid in their diets. The possible consequences of low levels of dietary linoleic acid were discussed in terms of the effects on platelet aggregability and low-density lipoprotein (LDL) cholesterol. But

an inadequate intake of linoleic acid will adversely affect prostaglandin synthesis. In man linoleic acid is the first step in the metabolic pathway leading to prostaglandin E_1 (PGE_1) synthesis. PGE_1 seems to increase the fluidity of the lipid bilayer in red cell membranes, thus enhancing cell deformability, so PGE_1 may have a role in determining the flexibility of the erythrocyte membrane. Rasmussen et al[2] confirmed these findings by showing that PGE_1 increased the filterability of erythrocytes.

An inadequate linoleic-acid-related deficiency of PGE_1 could explain why smokers' blood is poorly filterable[3] and why cigarette smoking has a dose-related adverse effect on blood rheology,[4] reversible by abstention from smoking.[5] A functional consequence of smoking is reduced cerebral blood flow related to the level of cigarette consumption[6,7] but significant gains in cerebral blood flow were recorded within a year of abstaining from smoking.[8]

After dietary supplementation with linoleic and γ-linolenic acids (four × 500 mg capsules daily of 'Efamol' oil of evening primrose for 2 weeks) we found that blood filterability was improved in healthy subjects. Cigarette smokers taking the same quantity of efamol for the same length of time also had improved blood filterability,[9] and blood viscosity was lowered in elderly subjects with leg ulcers who took eight capsules of efamol daily for 6 weeks.[10] Since increased intakes of linoleic acid in both smokers and non-smokers improved blood rheology, it is unlikely that the effect was due simply to the restoration of linoleic acid levels to normal. It is more likely to be a consequence of increased PGE_1 synthesis.

Thus there are good haemorheological reasons for supporting Oliver's proposal that those who cannot refrain from smoking could reduce the risk of CHD by increasing polyunsaturated fat intake. Such advice could be of importance to cigarette-smoking pregnant women.

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SIR,—Professor Oliver favours an increase in dietary linoleic acid in which the Americans have successfully indulged. Your June 24 editorial suggests that only smoking and cholesterol reduction have been "shown to reduce coronary risk". In fact linoleic acid levels can be more prognostic than low-density lipoprotein (LDL) cholesterol levels because they both reduce LDL cholesterol and arterial thrombosis and spasm.

Linoleic acid's ability to reduce coronary risk was established in the Edinburgh-Stockholm study by the consistent demonstration that risks increase with reduced linoleic acid levels in adipose tissue (which are reliable in showing a patient's diet a year previous to a heart attack). Adipose tissue levels of fish oils (ω3 lipids, eicosapentaenoic acid [EPA]) cannot be measured accurately[1] but there is little doubt that they can reduce coronary risk, perhaps by their antithrombotic activity combined with an ability to raise high-density lipoprotein (HDL) cholesterol which may thus cause atheroma to regress. Their rheological advantages reduce angina and increase exercise tolerance, helping a sense of wellbeing. Moreover, when added to aspirin and dipyridamole, EPA more than halves these drugs' previous reduction of restenosis following angioplasty,[2] with little increase in bleeding.

EPA, like beta blockers, has the unfortunate tendency to raise apolipoprotein cholesterol levels,[3] which could at least make it neutral in the undecided low serum cholesterol/cancer question. Linoleic acid found in modern margarines and shortenings reduces levels of both LDL and HDL cholesterol whereas dietary stearic acid[4] and expensive olive oil gain by maintaining HDL cholesterol. EPA's ability to raise HDL cholesterol thus makes it a good partner for linoleic acid in the dietary control of CHD.

White fish were rare 100 years ago, before the coming of steam drifters and trawlers, and the main catch worldwide would be of surface fish such as the herring[5] (which is high in EPA content). Fishing bans have re-established the herring but not yet its popularity and the Russian North Sea fleets take much. However, one or two tablespoonsful of fish liver oil (cod)[6] would still be a valuable source of EPA.

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FAMILIAL INTRACTABLE HICCUP RELIEVED BY BACLOFEN

SIR,—Intractable hiccups persist despite the usual home treatments. Williamson and Macintyre[1] concluded that chlorpromazine and metoclopramide were the most effective drugs and that phrenic nerve injection and crush should be considered if these fail. Jacobson et al[2] reported control of intractable hiccups by sodium valproate in 4 of 5 cases. Burke and White's[3] findings that two patients showed rapid and sustained improvement with baclofen prompted us to use this drug in a patient with a history of intractable hiccup.

A man aged 70 years had had bouts of hiccup lasting 4–14 days, with only 4–8 days between each episode, since he was 40. On occasions, a rapid burst of hiccups led to the sensation of his diaphragm seizing up or locking which was relieved by swallowing, vomiting, or by firm pressure over his lower rib cage. The attacks often began after eating but were not precipitated by laughter or other emotion. If he refrained from eating for 24 hours he could remain free from hiccups for 6–10 days. He could relieve the episodes temporarily by drinking 1 can (about 300 ml) of lemonade quickly then lying down. He only stayed free of symptoms after drinking by lying on his back. His sleep was habitually interrupted because of the need to drink and urinate. The attacks of hiccups were associated with belching and passing flatus, attributed to air swallowing while drinking. After a bout of hiccups for some days, flat white lesions on the lips and gums developed which resolved when the episode subsided. His grandfather, father, father's brother and sister, and his own sister and two brothers have all had attacks of hiccups lasting 6–8 days.

When examined, he was hiccuping 27 times a minute, with indrawing of the suprasternal notch and supraclavicular fossae accompanying each hiccup. Blood pressure was 190/115 mm Hg but examination of the nervous and other systems was otherwise normal. His condition improved temporarily (hiccups milder and recurred less often) while he was taking sodium valproate 400 mg four times daily and chlorpromazine 50 mg three times daily. He could not tolerate higher doses of sodium valproate and did not