VU Research Portal

Cigarette smoking and linoleic acid

Berns, M.A.M.; Katan, M.B.

published in

Lancet

1989

DOI (link to publisher)

[10.1016/S0140-6736\(89\)90459-5](https://doi.org/10.1016/S0140-6736(89)90459-5)

document version

Publisher's PDF, also known as Version of record

[Link to publication in VU Research Portal](#)

citation for published version (APA)

Berns, M. A. M., & Katan, M. B. (1989). Cigarette smoking and linoleic acid. *Lancet*, 334(8657), 275-276.
[https://doi.org/10.1016/S0140-6736\(89\)90459-5](https://doi.org/10.1016/S0140-6736(89)90459-5)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal ?

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

E-mail address:

vuresearchportal.ub@vu.nl

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.

This study was supported by the Deutsche Forschungsgemeinschaft. The DNA probes used were provided by Dr D. R. Higgs, Dr R. D. Nicholls, and Dr M. Breuning. We thank Dr Gilessen-Kaesbach, Essen, for referring family 3.

Institute of Pathology,
University of Heidelberg,
D-6900 Heidelberg, West Germany

RÜDIGER WALDHERR

Institute of Human Genetics,
University of Bonn

KLAUS ZERRES
ANDREAS GALL

Institute of Anthropology and Human Genetics,
University of Tübingen

HERBERT ENDERS

1. Reenders ST, Zerres K, Gal A, et al. Prenatal diagnosis of autosomal dominant polycystic kidney disease with a DNA probe. *Lancet* 1986; ii: 6-8.
2. Pretorius DH, Lee ME, Manco-Johnson ML, et al. Diagnosis of autosomal dominant polycystic kidney disease in utero and in the young infant. *J Ultrasound Med* 1987; 6: 249-55.
3. Sedman A, Bell P, Manco-Johnson M, et al. Autosomal dominant polycystic kidney disease in childhood: a longitudinal study. *Kidney Int* 1987; 31: 1000-05.
4. Gal A, Wirth B, Kaariainen H, et al. Childhood manifestation of autosomal dominant polycystic kidney disease: no evidence for genetic heterogeneity. *Clin Genet* 1989; 35: 13-19.

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.

Department of Human Nutrition,
Agricultural University,
6703 BC Wageningen, Netherlands

MONIQUE A. M. BERNIS
MARTIJN B. KATAN

1. Bernis 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 sucrose¹ 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

308 Cricklewood Lane,
London NW2 2PX

JEFFREY J. SEGALL

1. Temple NJ. Coronary heart disease dietary lipids or refined carbohydrates? *Med Hypotheses* 1983; 10: 425-35.
2. Segall JJ. Lactose. In: Freed DLJ, ed. Health hazards of milk. London: Baillière Tindall, 1984: 229-39.
3. Cuddenec Y, Delbruck H, Flatz G. Distribution of the adult lactase phenotypes—lactose absorber and malabsorber—in a group of 131 army recruits. *Gastroenterol Clin Biol* 1982; 6: 776-79.
4. Fujimoto N, Matsubayashi K, Miyahara T, et al. The risk factors for ischaemic heart disease in Tibetan highlanders. *Jpn Heart J* 1989; 30: 27-34.
5. Jackson RT, Latham MC. Lactose malabsorption among Masai children of East Africa. *Am J Clin Nutr* 1979; 32: 779-82.
6. Fox KM, Shapiro LM. Heart disease in Asians in Britain: commoner than in Europeans, but why? *Br Med J* 1988; 297: 311-12.
7. Keim NL, Marlett JA, Amundson CH. The cholesterolemic effect of skim milk in young men consuming controlled diets. *Nutr Res* 1981; 1: 429-42.
8. Kritchevsky D, Davidson LM, Kim HK, et al. Influence of type of carbohydrate on atherosclerosis in baboons fed semipurified diets plus 0.1% cholesterol. *Am J Clin Nutr* 1980; 33: 1869-87.

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 al² 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 filterable³ and why cigarette smoking has a dose-related adverse effect on blood rheology,⁴ reversible by abstinence 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 $\times$ 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.

Department of Pathology,
Medical School,
University of Otago,
Dunedin, New Zealand

L. O. SIMPSON

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 acid⁴ 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 herring⁵ (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.

26 Gorse Road,
Blackburn, Lancashire

GEOFFREY P. WALSH

1. Sinclair H, Gale M. Eicosapentaenoic acid in fat. *Lancet* 1987; i: 1202.
2. Dehmer GJ, Popma JJ, et al. Reduction in the early rate of restenosis after coronary angioplasty by a diet supplemented with N-3 fatty acids. *N Engl J Med* 1988; 319: 733-40.
3. Barbir M, Vile D, Trayner I, Aber VR, Thompson GR. High prevalence of hypertriglyceridaemia and apolipoprotein abnormalities in coronary artery disease. *Br Heart J* 1988; 60: 397-403.
4. Sacks FM. Effect of dietary stearic acid on plasma cholesterol levels. *N Engl J Med* 1988; 319: 1093.
5. Walsh GP. The history of the herring and with its decline the significance to health. *Med Hypotheses* 1986; 20: 133-37.
6. Walsh GP. A GP's use of omega-3 lipids in coronary heart disease. *Br J Clin Pract* (2nd Maxepa conference) 1983; 2: 75-77.

FAMILIAL INTRACTABLE HICCUP RELIEVED BY BACLOFEN

SIR,—Intractable hiccups persist despite the usual home treatments. Williamson and Macintyre¹ 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 al² reported control of intractable hiccups by sodium valproate in 4 of 5 cases. Burke and White's³ 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

1. Kury PG, Ramwell PW, McConnell HM. The effects of prostaglandin E_1 and E_2 on the human erythrocyte as monitored by spin labels. *Biochem Biophys Res Comm* 1974; 56: 478-83.
2. Rasmussen H, Lake W, Allen JE. The effect of catecholamines and prostaglandins upon human and rat erythrocytes. *Biochim Biophys Acta* 1975; 411: 63-73.
3. Norton JN, Rand PW. Decreased deformability of erythrocytes from smokers. *Blood* 1981; 57: 671-74.
4. Ernst E, Matrai A, Schmolzl C, Magyarosy I. Dose-effect relationship between smoking and blood rheology. *Br J Haematol* 1987; 65: 485-87.
5. Ernst E, Matrai A. Abstinence from chronic cigarette smoking normalises blood rheology. *Atherosclerosis* 1987; 64: 75-77.
6. Kubota K, Yamaguchi T, Abe Y, Fujiwara T, Hatazawa J, Matsuzawa T. Effects of smoking on regional cerebral blood flow in neurologically normal subjects. *Stroke* 1983; 253: 720-24.
7. Rogers RL, Meyer JS, Shaw TG, Mortel KF, Hardenberg JP, Zaid RR. Cigarette smoking decreases cerebral blood flow suggesting increased risk for stroke. *JAMA* 1983; 250: 2796-807.
8. Rogers RL, Meyer JS, Judd BW, Mortel KF. Abstinence from cigarette smoking improves cerebral perfusion among elderly chronic smokers. *JAMA* 1985; 253: 2970-74.
9. Simpson LO, Olds RJ, Hunter JA. Changes in rheological properties of blood in cigarette smokers taking Efamol: a pilot study. *Proc Univ Otago Med Sch* 1984; 62: 122-23.
10. Simpson LO, Shand BI, Olds RJ. The effects of dietary supplementation with Efamol on the healing rate of intractable leg ulcers. *NZ Family Physician* 1986; 13: 68-70.

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 (ω 3 lipids, eicosapentaenoic acid [EPA]) cannot be measured accurately¹ 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