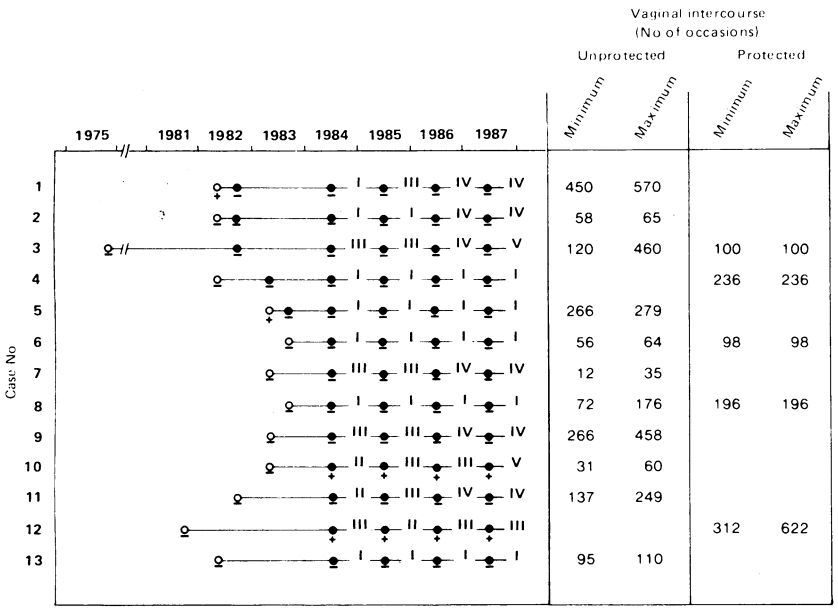

Patients' history from date of last serum sample that was negative for HIV antibody (○) and estimated total number of times that patients subsequently had unprotected or protected vaginal intercourse.
●=Serum sample positive for HIV antibody. +=Sample positive for HIV antigen. —=Sample negative for HIV antigen. I-V=Walter Reed classification of disease (see text for details)

positive for HIV antibody, and four patients (cases 3, 4, 6, 8) started to use condoms after being told that they were positive. At the time of the last negative sample 12 of the patients were sexually active with their present partner. We calculated that in 11 couples unprotected vaginal intercourse occurred a maximum of 2520 times (minimum 1563) without transmission of HIV; for protected vaginal intercourse the figures were 1252 and 942 respectively (figure).

According to the Walter Reed classification, seven patients had progressive disease. Six patients (cases 3, 5, 9-12) developed thrombocytopenia or leucopenia, or both. Two patients had sustained antigenaemia (figure). One partner had unexplained lymphadenopathy during the three years of the study; results of serological tests for Epstein-Barr virus, cytomegalovirus, toxoplasma, hepatitis B virus, and HIV were negative. All other partners were generally healthy, and none developed laboratory evidence of infection with HIV. None of the patients or their partners had serological evidence of active infection with cytomegalovirus or Epstein-Barr virus.

Comment

The prevalence of HIV infection in female partners of haemophiliacs positive for HIV antibody has been reported to be 6·8-8·0%. [3 4] The studies gave no information on risk factors, sexual habits, or disease related to HIV. Our patients had had different stages of HIV infection, including AIDS, for three to five years, and two had had continuous antigenaemia; we calculate that the rate of transmission of HIV by unprotected and protected intercourse was <0·04-0·06% and <0·08-0·1% respectively.[1] In this calculation we assumed that the one partner with lymphadenopathy was not infected, though possibly she will become positive for HIV antibody or will develop antigenaemia during longer follow up.

We suggest that in the absence of other risk factors transmission of HIV from men to women by vaginal intercourse is infrequent.

This study was supported by the Preventie Fonds, The Netherlands. Part of it was reported at the second international conference on AIDS, Paris, June 1986.

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(Accepted 29 June 1988)

Coffee and cholesterol: Is it all in the brewing? The Tromsø study

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We previously reported a strong relation between consumption of coffee and serum cholesterol concentrations.[1] In the third health survey in Tromsø we explored the possibility that the method of brewing might be important to this relation, as has been suggested.[1-3]

Subjects, methods, and results

During 1986-7, 21 826 people in the municipality of Tromsø (81·3% of the eligible population) were screened. The present analysis is restricted to men and menstruating women aged 20-59 (n=18 012). We asked them how many cups of coffee and what type of coffee they usually drank each day. Total cholesterol concentration was measured by an enzymatic method with a commercial kit (cholesterol oxidase/peroxidase-amidopyrine, Boehringer Mannheim) and a Hitachi automatic analyser 737 (Boehringer Mannheim) in the division of clinical chemistry of the university teaching hospital.

Boiled coffee was the most commonly drunk brew (68% of both sexes). Filtered coffee was the next most popular (23% of the men and 20% of the women); only 2% drank instant coffee. Only 7% of the men and 9% of the women did not drink coffee at all. A small minority drank decaffeinated coffee.

The table shows the mean serum cholesterol concentrations for each sex according to consumption of coffee and method of brewing adjusted for the influence of age, body mass index, cigarette smoking, physical activity in leisure time, and salt and fat intakes. The concentration in the men who drank nine or more cups of coffee a day (all types of brew) was 0·52 mmol/l (10%) higher than that in the men who did not drink coffee at all. The corresponding figure in women was 0·40 mmol/l (8%). For those who drank mainly boiled coffee the increase in serum cholesterol concentration between people who drank less than one and those who drank nine or more cups of coffee was 0·61 mmol/l (11%) in men and 0·40 mmol/l in women. No statistical trend was observed for the other methods of brewing. There was also no correlation between consumption of coffee and serum concentrations of high density lipoprotein cholesterol and triglyceride.

Comment

Except for age coffee was the most important determinant of serum cholesterol concentration in this study. This finding confirms our previous observation that there is an association between coffee and serum cholesterol concentration in this population[1] and supports the suggestion that coffee causes the concentrations to increase.

Mean (1·96 SE) serum cholesterol concentrations in people in Tromsø aged 20-59 correlated with consumption of coffee and method of brewing

Cups of coffee each day	Men				Women (menstruating)			
	Boiled (n=6807)	Filter (n=2228)	Instant (n=224)	All (n=10 030)*	Boiled (n=5417)	Filter (n=1620)	Instant (n=168)	All (n=7982)†
None				5·38 (0·08)				5·07 (0·07)
<1	5·44 (0·19)	5·47 (0·24)	5·55 (0·59)	5·38 (0·14)	5·18 (0·15)	5·24 (0·21)	5·52 (0·50)	5·14 (0·11)
1-4	5·73 (0·05)	5·57 (0·06)	5·87 (0·19)	5·61 (0·04)	5·32 (0·04)	5·16 (0·06)	5·41 (0·16)	5·22 (0·03)
5-8	5·95 (0·04)	5·68 (0·06)	5·78 (0·22)	5·82 (0·03)	5·44 (0·04)	5·28 (0·07)	5·53 (0·29)	5·36 (0·03)
≥9	6·05 (0·06)	5·61 (0·12)	6·11 (0·44)	5·90 (0·05)	5·58 (0·08)	5·26 (0·15)	4·93 (0·52)	5·47 (0·07)
	Test for equality							
p Value‡	<0·00001	0·082	0·456	<0·00001	<0·00001	0·123	0·302	<0·00001
	Test for linear trend§ (with cups of coffee as covariate)							
Regression coefficient	0·18	0·05	0·08	0·15	0·13	0·06	−0·09	0·10
t	9·28	1·63	0·78	13·05	6·47	1·66	−0·84	9·19
p	<0·00001	0·103	0·437	<0·00001	<0·00001	0·098	0·404	<0·00001

*Including 27 who drank decaffeinated coffee.
†Including 40 who drank decaffeinated coffee.
‡Adjusted for age, body mass index, number of cigarettes smoked a day, salt and fat intakes, and physical activity in leisure time. (One way analysis of covariance.)
§Adjusted for age, body mass index, number of cigarettes smoked a day, salt and fat intakes, and physical activity in leisure time. (Multiple regression analysis.)

A concern has been that different studies of this association have yielded differing results.[4] It was previously suggested that methods of brewing coffee might have a role.[1] This was later supported by two trials,[2,3] and the present study shows that consumption of boiled coffee was the main explanation for the strong association previously reported.[1] The association was not significant for the other methods of brewing. The numbers of people who drank instant or decaffeinated coffee were too small to give good estimates of possible effects.

We suggest that coffee contains one or more substances that affect the metabolism of cholesterol and that the length of time that the coffee grounds are in hot water determines the extent of the effect.

The coffee-cholesterol association may be mainly a Nordic problem because of the high consumption of coffee and the methods of brewing coffee in this part of the world. It is interesting, therefore, that part of the decline in serum total cholesterol concentrations in Finns has been ascribed to the changes in methods of brewing coffee that have taken place since the late 1960s.[5] Even if the effect of coffee in raising cholesterol concentrations seems small from a clinical point of view, a reduction of the mean cholesterol concentration of the population by 5-7% would reduce the incidence of coronary heart disease by 10-15%. Thus encouraging people to reduce their consumption of coffee and to change their methods of brewing it may represent a new tool in preventive cardiology.

This study was supported by the Norwegian Council on Cardiovascular Disease, the Norwegian Research Council for Science and Humanities, and the Aakre Foundation.

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(Accepted 11 July 1988)

Immunoglobulin heavy chain phenotypes and background retinopathy in non-insulin dependent diabetics

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Immunological factors may play a part in diabetic microangiopathy.[1] An association of HLA-B8, HLA-B15, and HLA-DR4 with retinopathy has been described in insulin dependent diabetes but has not been confirmed.[1] An association between the HLA-B3 allotype of the C4 component of complement and retinopathy has also been reported.[1] As this component is also encoded within the HLA region and is important in the humoral response immunoglobulin genes have also been studied. The allotype markers on human IgG, the Gm markers, are located within the constant regions of the heavy chain and encoded on chromosome 14. Retinopathy and the Gm (zaf;n;bg) phenotype are associated in insulin dependent diabetics.[2] As development of microangiopathy is probably similar in non-insulin dependent and insulin dependent diabetes we have studied the relation between retinopathy and Gm phenotypes in non-insulin dependent diabetics.

Patients, methods, and results

The patients comprised 110 patients who had been recruited to the Oxford prospective study of non-insulin dependent diabetes during 1973-6 who had been followed up from entry and in whom colour photographs of the retina were taken in 1982 and 1985, seven and 10 years after diagnosis respectively. The patients were of European white origin.

Samples of plasma were collected into edetic acid and frozen at −20°C for subsequent identification of the Gm phenotype on standard haemagglutination inhibition assay.[2] Heavy chain markers typed were: G1m (z), G1m (a), G1m (x), and G1m (f) in IgG subclass 1; G2m (n) in subclass 2; and G3m (bl) and G3m (g) in subclass 3. This permitted identification of the common haplotypes of European white people Gm (za;g), Gm (zax;g), Gm (f;b), and Gm (f;n;b). The typing was performed after analysis of the retinal photographs.

Statistical analysis was performed with the statistical package for the social sciences (SPSS). The differences in the frequencies of the Gm phenotypes between patients with and without retinopathy were analysed

Number (percentage) of patients with and without retinopathy seven and 10 years after diagnosis of non-insulin dependent diabetes, according to Gm phenotype

Gm phenotype*	Seven years after diagnosis		Ten years after diagnosis	
	Without retinopathy (n=67)	With retinopathy (n=43)	Without retinopathy (n=22)	With retinopathy (n=88)
f;n;b	22 (33)	12 (28)	12 (55)	22 (25)
zax;g	5 (7)	1 (2)	1 (5)	5 (6)
zafx;n;bg	4 (6)	16 (37)†		20 (23)
zaf;n;bg	15 (22)	5 (12)	3 (14)	17 (19)
zaf;bg	6 (9)	7 (16)	1 (5)	12 (14)
zafx;bg	3 (4)	1 (2)		4 (5)
f;b	6 (9)		4 (18)	2 (2)
za;g	2 (3)			2 (2)

*Additional phenotypes zaf;b, za;n;bg, zf;n;b, fx;n;b, and zax;n;g (each identified in only one patient) were not shown.
†χ^2=17·2, corrected p<0·01.