(and other) indices were measured in several hundred people and then subsequent coronary or cerebrovascular events recorded. In the Northwick Park Heart Study of 1511 white men aged 40 to 64 at recruitment both high factor VII activity and high plasma fibrinogen concentrations were strongly associated with ischaemic heart disease.^{3,4} In both cases the association was particularly strong for the subgroup of men who developed heart disease within five years of their blood being examined. The findings are intriguing in that the associations with coagulation factors seem stronger than that between cholesterol concentrations and heart disease. Fibrinogen concentration has also been identified as a risk marker in a smaller prospective study of coronary disease⁵ and in a prospective study of myocardial infarction and stroke.⁶ In other investigations a high white cell count has also proved to be a risk marker for myocardial infarction and stroke.^{7,8}

In general the incidence of thrombotic disease in black people is lower than that in whites, and findings that blood from healthy whites is "hypercoagulable" or displays a lower fibrinolytic activity, or both, when compared with blood from healthy blacks^{9,10} support the concept that blood composition may contribute to developing thrombosis. Until recently, reports of coagulation and fibrinolytic studies in different ethnic groups have been limited to subjects in one geographic locality because haematological indices can be compared only if methods are standardised. Standardisation is often difficult between adjacent laboratories, never mind countries, but, using continuous external quality control of the laboratory measurements, the World Health Organisation has started a study to compare the effects of different oral contraceptives on coagulation, fibrinolysis, and platelet "function" in women from diverse geographical locations. A recent article records the baseline data from clinical centres in Dublin, Salvador (Brazil), Santiago (Chile), and Singapore.¹¹ The women in the study are to be given oral contraceptives, which makes the decision to study these particular centres surprising given the Catholic influence in some of them, and women recruited in, for example, Dublin are unlikely to be a completely random sample.

Data were provided for just under 200 women at each centre. Not all of it stood up to the external quality control, but the information was sufficient for some clear patterns to emerge. The most interesting data came from Dublin (where all the women were white) and from Salvador (where the women were predominantly black or mulatto). Blood from the Dublin women turned out to be "hypercoagulable" (short prothrombin time, short activated partial thromboplastin time, increased factor X activity, and increased concentration of antiplasmin) while that from the Salvador women turned out to be "hypocoagulable" (prolonged prothrombin time, prolonged activated partial thromboplastin time, lower factor VII activity, increased plasminogen activator activity, and decreased concentrations of antiplasmin). In contrast, the Dublin women had higher concentrations of antifactor Xa and antithrombin III (which may, the authors suggest, protect against the hypercoagulability), and the Salvador women had lower concentrations of these antiproteases. Unfortunately information on white cell counts was incomplete and the platelet studies were not fully standardised.

The authors of the report consider the data in terms of "the clinical impression that the 'epidemic' of thromboembolism... in Western countries has not been shared by the developing parts of the globe where clinical evidence of thromboembolism is relatively rare." A critical study of

venous thrombosis in Nigerians questioned, however, the previous largely clinical impression of a lower incidence of the disease in this population.¹² The WHO investigators must now copy Meade *et al.* and follow up the patients to determine the actual rates of thrombosis. Some information may be obtained as a byproduct of giving oral contraceptives—provided that the group studied is large enough and the procedures adopted to detect thrombosis well standardised.

Prospective and large scale comparative studies (particularly in diverse geographical locations) are expensive and require much organisation and energy, huge resources, and good quality control. Nevertheless, this type of study will tell us most about the aetiology of thrombosis—information of fundamental importance if the disease is to be controlled.

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Coffee, cholesterol, and colon cancer: is there a link?

Drinking coffee may raise serum cholesterol concentrations. The association was first observed by Bjelke in Norway in 1974¹ and has since been confirmed in three much larger Norwegian studies, one of which has been published in detail.² The association has also been observed in some, but not all, studies from other countries.³⁻⁷ That coffee (at least coffee brewed in the north Norwegian way) may actually cause the rise in cholesterol concentration has been suggested by two small experiments.^{8,9}

Coffee drinking may also be associated with a reduced risk of developing cancer of the colon. Bjelke found this to be so in his case-control studies with 162 cases in Norway and 259 cases in Minnesota,¹⁰ and similar findings have been reported from two other case-control studies.^{11,12} But no association was seen in two other case-control studies,^{13,14} and in a third "a significant but small excess risk" of colon cancer was associated with high coffee consumption.¹⁵

In a follow up in Norway of 16 555 people (mostly men)¹⁶ coffee drinking was negatively associated with the incidence of colon cancer. There was, however, a linear interaction with age, the lowest relative risk being in the youngest. For those under 65 at the start of 11½ years' follow up a strong statistically significant negative relation was seen, whereas a non-significant positive association was seen in older individuals. A positive association between coffee drinking and death from colon cancer has been reported from an Adventist cohort,¹⁷ whereas no association was seen between coffee consumption and risk of colon cancer in Japanese men in Hawaii.¹⁸ The coffee consumption in both of these cohorts was considerably lower than that in the Norwegian cohort. Another explanation for the finding in Adventists may be that coffee consumption shows poor adherence to the lifestyle recommended by the church. Furthermore, the positive association was limited to the last 11 of 21 years' follow up.

How can these associations be explained? Our proposal, which is in line with what Bjelke suggested 12 years ago,¹ is that coffee contains substances that reduce the excretion of bile acids or neutral sterols, or both, thereby reducing the risk of colon cancer but increasing the serum cholesterol concentration. Bile acids, particularly secondary bile acids, are potent promoters of colon carcinogens in animals. Furthermore, groups with diets associated with a high risk of colon cancer have an increased excretion of sterol metabolites, and higher faecal bile acid concentrations have been found in patients with colorectal cancer than in controls.¹⁹ Lowenfels has proposed that in some of those who consume a high cholesterol, high fat diet a lower serum cholesterol concentration indicates increased cholesterol excretion²⁰—thereby explaining the inverse relation between serum cholesterol and the risk of colon cancer,²¹ an association which still is under debate.²² The mechanism we propose linking coffee consumption with increased cholesterol concentration but reduced risk of colon cancer may operate only in groups with a high fat intake. This could explain the positive (or absent) association between coffee drinking and risk of colon cancer seen in Adventists¹⁷ and the Japanese in Hawaii.¹⁸

We know of no data on the effect of coffee consumption on bile acid and neutral sterol excretion from the liver in man. A significant physiological effect of coffee on liver metabolism is, however, suggested by Arnesen *et al.*, who have shown an inverse relation between coffee drinking and γ -glutamyltransferase activity in the Tromsø population—even after adjustment for other variables, including alcohol consumption.²³

We believe that the repeated findings of a positive relation between coffee consumption and serum total cholesterol concentration and a reduced risk for cancer of the colon, at least in the Norwegian population, make it reasonable to examine in man the interrelation between coffee (brewed in different ways), bile excretion, and cholesterol metabolism.

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HIV and sexual lifestyle

Human immunodeficiency virus (HIV) is predominantly sexually transmitted, and fears are widespread that Britain may be on the brink of a major heterosexual epidemic similar to that in Africa. Authorities agree that there will be a spread into the heterosexual population, but they disagree about the likely extent.

In Western societies HIV is still virtually confined to specific risk groups: homosexual and bisexual men, past recipients of blood and blood products, and intravenous drug abusers and their sexual partners and offspring. Further spread depends on the amount of sexual contact between those from high risk groups and the rest of the population. Bisexual men and heterosexual intravenous drug abusers, especially those who work as prostitutes to pay for their habit, are an obvious risk to the general population. In the United States 13 of 49 men with the acquired immune deficiency syndrome (AIDS) and no recognised risk factors admitted to sexual contact with prostitutes.¹

Homosexual practices seem to be the most efficient way of transmitting HIV and anal intercourse the most dangerous activity; the passive (anoreceptive) partner is much more at risk than the active partner. A recent study found no correlation between the presence of antibodies to HIV and either oral or rimming (oroanal sex), but the authors showed that fisting (brachioproctal intercourse) was a risk factor for the insertive partner.² The virus can enter the body through breaches in the mucosa and is present in semen, so that these statistical indications do not exclude reliably the risk of HIV