Coffee drinking and cancer of the pancreas

A recent American study showing an association between coffee drinking and cancer of the pancreas caused sufficient alarm to merit an editorial in the New York Times. MacMahon and colleagues1 had interviewed 369 patients with histologically proved pancreatic carcinoma and 644 controls drawn from other patients in the same hospitals (in Boston and Rhode Island). The intention of the study was to re-evaluate the relation of the disease to smoking and alcohol, already the subject of many publications—but the interviewers also asked how many cups of tea and coffee were consumed in a typical day before the current illness had become evident. Not unexpectedly, they found an association with cigarette smoking, the relative risk of the disease among smokers being 1-4 times that in non-smokers. Surprisingly, they found a stronger association with coffee drinking, with relative risks of 1-8 among those drinking up to two cups of coffee daily (in comparison with non-drinkers of coffee) and of 2-7 among those drinking three or more cups. These risks were calculated after adjustment for the cigarette smoking of the coffee drinkers. The increasing risk associated with increasing consumption reflected a dose-response relation which was found only in women. No association was found with the use of cigars, pipe tobacco, alcohol, or tea. These results may be important. Even though the relative risks are small coffee drinking is so widespread that many (the authors calculate perhaps half) of all cases of pancreatic cancer could be attributed to it. Such a gloomy conclusion presupposes, however, that the association shown by this study is both real and causal.

The case-control study is a fallible method of investigation. Sources of bias are numerous and often difficult to detect. When, as in this instance, the results of a study are unexpected then confirmatory data from other studies are essential. The correspondence which followed publication of the study suggested several possible biases. Some of these the authors could discount, but, as often happens, doubts were raised about the selection of controls. Because the study was designed to explore associations with smoking and alcohol potential control patients with diseases known to be associated with smoking or alcohol (cardiovascular disease, diabetes mellitus, respiratory or bladder cancer, and peptic ulcers) were excluded. Since smoking and coffee drinking are correlated this exclusion may have removed heavy coffee drinkers from the control group. The authors concede this, but make the questionable claim that heavy coffee drinkers will have been removed "only in so far as they were overrepresented in the first place."
Half the patients with fluorescent antinuclear antibodies had DNA antibodies and one-third had precipitins to extractable nuclear antigens. Two of these cases fulfilled the criteria for systemic lupus erythematosus. Antinuclear antibodies are not commonly found in other types of seronegative polyarthritis.

Patients who have fluorescent antinuclear antibodies may, indeed, be suffering from the mild form of systemic lupus erythematosus described from America, though the American patients frequently had multisystem disease with clinical and serological features of systemic lupus erythematosus. Some of the British patients may be examples of mild unisystem disease with serological evidence of systemic lupus erythematosus. Four of the Bath patients positive for fluorescent antinuclear antibodies had precipitins to extractable nuclear antigens, raising the possibility of mixed connective tissue disease, in which a non-deforming arthropathy has been well defined.

In the Leeds study 80 patients with rheumatoid arthritis, only 56 of whom had circulating rheumatoid factor, were compared with 31 patients with ankylosing spondylitis. The three groups had distinctive biochemical profiles. The serum concentrations of sulphhydril and haemoglobin were particularly good discriminators between ankylosing spondylitis and rheumatoid arthritis. Higher concentrations of IgA and IgM among the seropositive patients with rheumatoid disease indicated greater immunological activity, possibly associated with rheumatoid factor. By contrast, no difference was seen in the concentration of IgG. The low serum concentration of histidine in the seropositive group may have contributed to the formation of rheumatoid factor. The clinical activity of the disease in the seropositive and seronegative patients was similar, as were the reduced concentrations of sulphhydril and haemoglobin, but acute phase reactants and liver function tests showed greater abnormalities in the seropositive group.

One explanation for these findings could be that acute phase reactants reflect increased systemic activity not mirrored by clinical symptoms while the lower values for sulphhydril and haemoglobin may be a direct consequence of the disease. Some patients with seronegative chronic polyarthritis follow a pattern like that of rheumatoid arthritis, but the group is unlikely to be homogeneous.

The clinical tests in use are of little use in classifying seronegative patients. A battery of serological tests may be of some value in differentiating a group of “negative” patients, but even so these probably represent a variety of conditions. Biochemical diagnostic criteria may also be used to complement existing guidelines for the diagnosis of rheumatoid arthritis. With careful analysis, such studies enhance diagnostic accuracy, give insight into pathogenesis, and help clinicians choose from among the treatments available.

Shipyard eye

Now known by the more accurate, if less memorable, name of epidemic keratoconjunctivitis, shipyard eye infection remains a problem to both virologists and ophthalmologists.

Epidemic keratoconjunctivitis is a follicular conjunctivitis which presents with reddening, a feeling of grittiness or of a foreign body in the eye, non-purulent exudate, and enlargement of the preauricular lymph nodes. Corneal lesions develop seven to 10 days after onset with the characteristic subepithelial punctate keratitis that is the hallmark of the disease. The corneal infiltrates are slow to clear; indeed, opacities may persist for months or even years. Nevertheless, complete recovery is usual. Most of the patients are adults, and the disease may affect both eyes or only one. Over 20 years ago Jawetz wrote a classic description of shipyard eye in the BMJ. The disease is an iatrogenic infection with adenovirus type 8 with an unusual mode of transmission in that it is spread by contaminated instruments or hands during eye examinations at ophthalmology clinics. Two epidemiological features are of great interest. Firstly, the adenovirus responsible is unusual, for type 8 is not one of the common adenoviruses which are endemic in most communities. Secondly, despite its mode of spread and the means of prevention being known, outbreaks of the disease continue. Part of the explanation may