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Biological mechanisms for link

EDITOR,—Frank DeStefano and colleagues report an increased risk of coronary heart disease and mortality in men with dental disease.[1]

There is evidence that immunocompetent cells have a role in initiating and accelerating the development of atherosclerosis and myocardial infarction. In particular, activated macrophages are considered to play a pivotal part. Increased serum concentrations of neopterin are found in patients with atherosclerosis,[2] and in a community based study neopterin was the best single predictor of atherosclerosis—even better than more classic variables like cholesterol, low density lipoprotein, and high density lipoprotein.[3] Large amounts of neopterin are released from human macrophages on stimulation with interferon γ. Increased serum neopterin concentrations have been found in patients with infectious syndromes, malignancies, and autoimmune diseases.[4] Interestingly, among blood donors a substantial proportion with a raised serum neopterin concentration presented with dental diseases.[5]

These data indicate that dental diseases may often lead to chronic activation of the immune system, which may render patients more susceptible to atherogenesis, thus increasing the risk of myocardial infarction. It would be interesting to learn from DeStefano and colleagues whether variables of immune activation are more commonly increased in their patients with dental disease and with increased risk of myocardial infarction.

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Roles of white cells and fibrinogen

EDITOR,—Frank DeStefano and colleagues report that dental disease is associated with increased risk of coronary heart disease and mortality.[1] They note that "the biological mechanism by which periodontal disease or poor oral hygiene could lead to coronary heart disease is not clearly established."

In a recent study of 50 consecutive patients with gingivitis or periodontitis, or both, colleagues and I observed significant increases in plasma fibrinogen concentration and blood leucocyte count compared with values in 50 age matched controls. Multivariate analysis controlling for the effects of age, smoking, social class, and case or control group showed significant correlations between fibrinogen concentration, leucocyte count, and three variables of dental disease (plaque index, gingival index, and the community periodontal index of treatment needs).[2] Both plasma fibrinogen concentration and leucocyte count have been shown to be strong, independent primary risk factors for coronary heart disease and death in several large prospective population studies.[3] The increases in fibrinogen concentration and leucocyte count that we observed in patients with dental disease[2] were consistent with a substantial increased risk of coronary heart disease and mortality according to these studies,[3] in keeping with that observed by DeStefano and colleagues.

I therefore suggest that (*a*) hyperfibrinogenaemia and leucocytosis may be plausible biological mechanisms by which dental disease may directly promote coronary heart disease and death[3]; (*b*) plasma fibrinogen concentration and leucocyte count should be measured in future studies of dental disease and cardiovascular disease to test this hypothesis; and (*c*) oral bacterial infection, which is common in populations at high risk of coronary heart disease, may be an important determinant of variability in plasma fibrinogen concentrations and leucocyte counts in the population, most of which is unexplained.[4,5]

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African drugs slur

EDITOR,—The authors of "Drug smuggler's delirium" consider, among other signs and symptoms, "recent travel in West Africa" as being of diagnostic significance.

West Africa is made up of 15 countries—Ghana, Nigeria, Ivory Coast, Mali, Liberia, Benin, Senegal, Upper Volta, Mauritania, Cameroon, Gambia, Gabon, Guinea, Sierra Leone, and Togo—with a total population of over 175 million. As far as I am aware (and I take a keen interest in these statistics) four Nigerians have died as a result of carrying drugs internally. Travel in West Africa, therefore, seems to be a dubious criterion when deciding whether a patient was suffering from drug delirium.

Articles in the *BMJ* which contain biased statements demean its international stature.

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Transgenic pigs under stress

EDITOR,—Claims that human transplants could be revolutionised by success in breeding pigs with "human" organs are inaccurate and misleading.[1] These are not pigs with "human hearts"; they are genetically engineered mutant pigs carrying human genes. There is no evidence that transplanting these unfortunate animals' organs into humans will actually save lives. There is, however, considerable evidence to show that attempts to produce genetically engineered "transgenic" animals of this type often produce physical and developmental abnormalities which inevitably cause pain and suffering to many animals. Transgenic pigs, carrying a human growth hormone gene, produced at the US government's Beltsville Research Station provide a well known example of the dangers of this type of research. The Beltsville pigs suffered from defective vision, arthritis, and muscular weakness and were impotent and very susceptible to stress.

All 35 attempts to transplant animal organs into humans have failed. This new approach using genetically altered animals remains highly experimental. Furthermore, it is clear that this approach cannot provide an answer to the chronic problems of organ rejection.

Only last month the government's advisory council on science and technology recommended the introduction of a new nationwide "opt out" donor scheme which, the committee said, would alleviate the "chronic shortfall" of donors in the United Kingdom. Rather than carrying out bizarre experiments on animals, this country should be investing in health education and taking simple administrative action to save human lives.

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Interferon first in chronic hepatitis C

EDITOR,—Two points warrant clarification in Johnson Y N Lau and Gary L Davis's editorial on chronic hepatitis C.[1] The subtitle of the editorial—"interferon beneficial where steroids fail"—takes out of context the author's statement referring only to patients who have coexisting hepatitis C and autoimmune markers. Even in this group the decision to defer or withhold potentially curative interferon treatment in a chronic infection that may progress to cirrhosis requires careful consideration.

Though there is no doubt that interferon may seriously exacerbate autoimmune hepatitis misdiagnosed as chronic hepatitis C by false positive results of first generation antibody tests, such mishaps are unlikely if a definite diagnosis of chronic hepatitis C is sought with second generation multiantigen tests and confirmatory polymerase chain reaction. Most reported exacerbations induced by interferon developed slowly over weeks and responded to its withdrawal with or without the addition of steroids.

Patients with well documented chronic hepatitis C, as with other forms of liver injury, may have circulating autoantibodies to a range of intracellular antigens, although whether these are merely markers of cell death or play a part in mediating tissue injury is unclear. Varying prevalences of 21% to 41% have been reported.[2] The strong association between chronic hepatitis C and antibodies to liver and kidney microsome type 1 (anti-LKM-1) has given rise to speculation that hepatitis C may precipitate type II autoimmune hepatitis, though recent evidence suggests that the LKM-1 antibodies in the two conditions recognise subtly different epitopes.[3]

Information is scarce concerning the influence of autoimmune markers on the course of chronic hepatitis C. In one study of 102 patients with the disease the 21 patients who had coexistent autoantibodies did not differ from those who were autoantibody negative in terms of age, sex, risk factors, histological findings, or response to interferon.[2] In another study, in which five patients with both chronic hepatitis C and autoimmune markers received interferon, three of the patients responded, one did not respond, and one suffered an exacerbation of the disease.[4]

Overall, the presence of autoimmune markers