goal of eradication of neonatal or puerperal tetanus will not be complete by the end of present century.

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The Manchester seaman

SIR—Hooper and Hamilton (Nov 16, p 1363)[1] confirm that the Manchester seaman who allegedly died of AIDS in 1959 was not infected with HIV as previously thought. It should be noted that rational investigation into the origin of AIDS contributed to this correction of the scientific record.[2,3]

Hooper and Hamilton propose the diagnoses of Wegener's granulomatosis or idiopathic CD4 lymphopenia to explain why the Manchester seaman developed infection with two opportunistic agents, cytomegalovirus and *Pneumocystis carinii*, in the absence of HIV disease. A more logical diagnosis is iatrogenic immunosuppression. According to the original *Lancet* report,[4] the patient in question had an undiagnosed skin disorder that was treated with topical and systemic corticosteroids, as well as localised radiation. Corticosteroid-induced immunosuppression may therefore have contributed to his infectious complications and clinical demise. In support of this hypothesis, a study of *P carinii* pneumonia in HIV-negative patients has implicated corticosteroid therapy in 92% of the infections and in 100% of the patients who died.[5]

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1 Hooper E, Hamilton WD. 1959 Manchester case of syndrome resembling AIDS. *Lancet* 1996; **348:** 1363–65.
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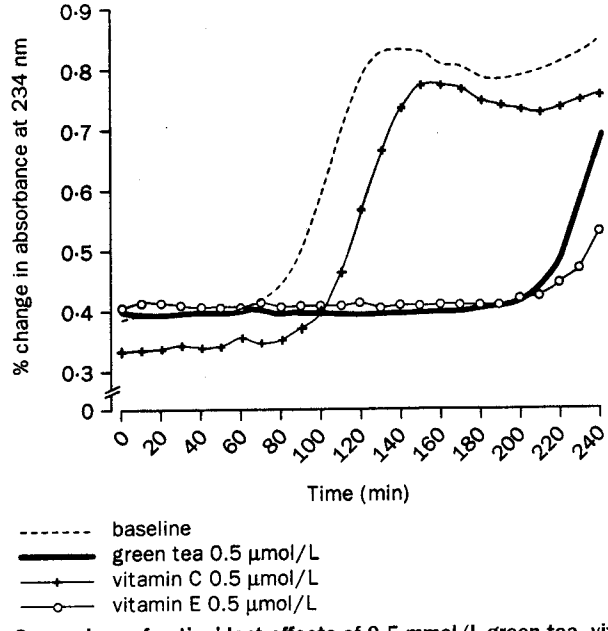
Inhibition of LDL oxidation by green tea extract

SIR—Low-density lipoprotein (LDL) oxidation, which plays an important part in the development of atherosclerosis, can be effectively inhibited by drug(s) and nutients. Kondo and colleages (Nov 30, p1514)[1] report the inhibition of LDL oxidation by cocoa. However, concerns about side-effects such as high-density lipoprotein (HDL) lowering effect by probucol[2] and long-term safety of high-dose nutrient supplementation have been raised.[3] Green tea contains antioxidant polyphenolic derivatives consisting of various flavan-3-ols. We have assessed the antioxidant effect of green tea and compared it with equimolar concentrations of vitamins C and E by the in-vitro LDL oxidation method.[4] A classic metal chelator edetic acid (EDTA) was used to elucidate the possibility of antioxidisability of green tea polyphenols by metal chelation.

A good dose-dependent antioxidant effect of green tea was recorded (data not shown). At 0·5 μmol/L concentration, green tea increased lag time from 79 min to 211 min, vitamin C to 95 min, and vitamin E to 213 min (figure). In a competitive experiment, proportional metal chelation of EDTA caused its oxidation curve to overlap with that of the baseline (without addtion), but this was not the case for green tea. The lag times by equimolar concentrations of green tea polyphenols were greatly increased.

Our results clearly demonstrate the antioxidant power of green tea extract standardised for polyphenolic content (the minimum concentration of green tea extract used was 0·25 μmol/L). The antioxidant effect of green tea was greater than vitamin C, but equivalent to vitamin E on a molar basis, and the antioxidant effect of green tea was not attributable to metal chelation. These findings are relevant to antioxidant usage and safety since green tea is a natural antioxidant that has been used in the most enduring of food cultures—Chinese and Japanese teas—and to the safety concerns about nutrient supplements such as vitamin C, vitamin E, and β-carotene.[3] Although these concerns still exist, consumption of naturally derived antioxidants such as green tea beverages and extracts may be a safer alternative and effective means of increasing the dietary intake of antioxidants, since each cup of green tea (100 mL) is reported to contain 50–100 mg of polyphenols,[5] equal to 1·6–3·2 mmol/L, which would be 6300–12 600 times higher than the dose used in this in-vitro LDL oxidation study. Therefore, if completely absorbed, as little as one cup of green tea per day may provide



Comparison of antioxidant effects of 0·5 mmol/L green tea, vitamin C, and vitamin E on in-vitro LDL oxidation

an adequate intake of antioxidant polyphenols.

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HIV vaccines

SIR—Anderson and Garnett (Oct 12, p 1010)[1] neglect a critical parameter in their assessment via mathematical modelling of the potential of low-efficacy HIV vaccines to reduce the prevalence of HIV. That parameter is the relative extent of exposure to HIV in vaccinated and unvaccinated individuals. For HIV, individual behaviour is the dominant factor determining risk of transmission. It requires no stretch of the imagination to speculate that individuals at risk for HIV who receive a vaccine of limited efficacy may, by dint of feeling protected, increase their frequency of high-risk activities—sex with multiple partners, sex without condoms, needle sharing, &c. Such increased exposure to the virus could diminish or eliminate any reduction in risk attributable to the protective effect of the vaccine; it could even result in increased transmission rates.

Although Anderson and Garnett acknowledge the potential effect of behaviour change on the overall impact of a low efficacy vaccine, they have not explored this issue with their present model. Blower and McLean,[2] whom they cite, have attempted to model the effects of behavioural change, but use a model that makes the perhaps overly simplistic assumption of a linear relation between frequency of high-risk behaviour and risk of infection. High-risk behaviour is complex, involving not only several partners but choice of partners and types of sexual acts. It is likely that the most informative models would result from increased collaboration between mathematical modellers and other scientists. In addition to the needed input of behavioural scientists, involvement of vaccine scientists can assure consideration of other important factors such as the possible boosting of immune responses in vaccinees after natural exposure that might prolong the period of conferred immunity. The potential impact of low efficacy HIV vaccines on the dynamics of the epidemic will be better understood once models incorporating more of the relevant factors are developed.

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1 Anderson RM, Garnett GP. Low-efficacy HIV vaccines: potential for community-based intervention programmes. *Lancet* 1996; **348:** 1010–13.
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Author's reply

SIR—The point Ellenberg and Rida raise is important, was mentioned in our article, and covered in various reports referenced (particularly, the paper by Blower and McLean and a much earlier one in *Nature*[1]). We have explored the issue of low efficacy vaccines incouraging increased risky behaviour, and the conclusions are those expected intuitively. Current empirical studies of the possible effect of candidate HIV vaccines on sexual behaviour have been reviewed in a recent National Institutes of Health document arising from a meeting in Washington, USA, in 1996. The results are inconclusive. All agree, however, that if such vaccines were to be used they must be accompanied by careful counselling to try to ensure that the individuals vaccinated appreciate that they may not be fully protected against infection and should therefore continue safer sex practices. It would be perverse, in our view, if this concern hindered the development of a prophylactic tool.

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1 Anderson RM, May RM, Gupta S. Potential of community-wide chemotherapy or immunotherapy to control spread of HIV-1. *Nature* 1991; **350:** 356–59.

Low frequency of autoimmune disease in tropical Africa

SIR—Clark and colleagues (Nov 30, p 1492),[1] seeking to explain the low frequency of autoimmune disease, including systemic lupus erythematosus (SLE), in tropical Africa, argue that nitric oxide has a central immunosuppressive role, because of its upregulation during the establishment and maintenance of tolerance to malaria. A more convincing hypothesis—which accepts that immunosuppression occurs as protection against malaria[2]—suggests a central role for tumour necrosis factor (TNF).[3,4]

Much of the pathology associated with malaria is due to production of TNF. Mice that are poor producers of TNF and with a genetic predisposition to lupus nephritis can be protected by injections of TNF. There is also evidence from studies in man that TNF production is impaired in mononuclear cells from SLE patients (bearing DR2, DQW1 haplotypes). Variable regulation of TNF production as a result of genetic polymorphism may affect either central (thymic) or peripheral deletion of autoreactive T cells, leading to the development of SLE and its different subtypes.

In brief, the alternative hypothesis is that the TNF-α allele may be responsible for the lower occurrence of SLE in Africans as a result of endemic malaria, while absence of this stimulant of TNF production allows for the increased frequency of SLE in Afro-Americans.[3,4] Both this hypothesis and that of Clark and colleagues[1] may not be mutually exclusive. Habib and colleagues[5] postulate that locally produced TNF might contribute to the pathogenesis and complications of dilated cardiomyopathy by inducing nitric oxide synthase, which in turn produces nitric oxide. Whether a similar mechanism occurs in autoimmune diseases such as SLE is not known

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