Hypolactasia and protection against Plasmodium spp infection in Homo sapiens

Editor,—Anderson and Vullo’s hypothesis (Gut 1994; 35: 1487–9) is based on the contention that hypolactasia phenotype represents the normal state for Homo sapiens (and all other mammals), and that persistence of the enzyme into adult life in certain groups before ‘artificial’ mass population movements (for example, northern Europeans to the USA) affords humans a significant survival advantage against human Plasmodium spp infection. Available evidence (quoted by the authors) indicates, however, that such a deficiency exists only in those individuals whose diet has profoundly influenced on the metabolism of the malarial parasite.

The overwhelming consensus of current opinion is that the hypolactasia phenotype represents the normal state for Homo sapiens and all other mammals, and that persistence of the enzyme into adult life in certain groups before ‘artificial’ mass population movements (for example, northern Europeans to the USA) affords humans a significant survival advantage against human Plasmodium spp infection. Available evidence (quoted by the authors) indicates, however, that such a deficiency exists only in those individuals whose diet has profoundly influenced on the metabolism of the malarial parasite.

Plasmodium spp are extremely ancient organisms; before they infected the earliest mammals, they utilised more primitive organisms, including reptiles, birds, etc, as reservoir hosts. The Anderson and Vullo hypothesis therefore implies that the very widespread prevalence of the hypolactasia phenotype in the animal kingdom developed as an exceedingly early protective mechanism against Plasmodium spp, and persistence of the enzyme into adult life only developed very much later in areas where Plasmodium spp was not a major environmental hazard affecting survival. The Hamitic tribes of east, west, and central Africa (most adults possess persistence of the enzyme into adult life) presumably migrated into northern Africa comparatively recently (within the last few thousand years) — and were hence ‘unprotected’ against Plasmodium spp. How then, did some (or all) “malaria tribalists” survive Plasmodium falciparum infection? I know of no evidence that Hamites are, at the present day, more prone to P falciparum infection compared with Bantu with the exception that they lack certain major genetic diseases5,6 (see later) P vivax infection was certainly a problem in northern Europe until recent times; however, it never caused the widespread acute mortality associated with human P falciparum infection — which probably originated in Africa also comparatively recently.

The approximate parallel outlined in the hypothesis between the geographical areas incorporating the hypolactasia phenotype and those in which major haemoglobinopathies (which clearly possess a selective advantage against P falciparum infection) are comparatively common, is of interest.5,6 But even here the degree of protection is only partial; riboflavin deficiency has probably exerted a comparatively minimal, and certainly a lesser, effect in terms of selective Darwinian pressures.

Therefore, although this hypothesis seems superficially attractive, I have grave doubts that it explains the human lactase polymorphism more satisfactorily than several of the previous theories.1

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In vitro dissolution of cholesterol biliary stones

Editor,—We read with great interest the paper by Bergman et al (Gut 1994; 35: 1653–8) who reported on in vitro cholesterol gall stone dissolution with methyl-tert-butyl ether (MTBE) and ethyl propionate in the presence of bile with or without dimethyl-sulphoxide (DMSO). We would like to comment further on the important role of DMSO on stone dissolution.

We have experience with the clinical use of different solvents containing DMSO. Based on previous studies by Montet’s group in which it was shown that the addition of DMSO to MTBE improved the dissolution rate of cholesterol1 or biliary calculi2 we have recently studied the bile duct stone dissolving capacity of multicomponent solvents in humans.3 In these mixtures, DMSO was present both in solvent 1 (aqueous glycine-NAOH buffer solution of EDTA, sodium deoxycholate and 30% DMSO) and in solvent 2 (DMSO/MTBE 70/30). Solvent mixtures were infused continuously and alternately for 16–24 hours through a nasobiliary catheter placed into the common bile duct over the stone(s). In 20 of 22 patients with pigment or mixed biliary duct stone(s), or both, which were too large to be removed after endoscopic sphincterotomy, a stone free state of one or good disintegration of stones (11 of 22) was achieved with these solvents. Only mild toxic side effects were seen during treatment. These mixtures containing DMSO proved effective enough to dissolve not only cholesterol but also pigment or mixed stones, or all three.

Our recent in vitro investigation in the field of contact dissolution therapy of bile duct stones provides further evidence on the beneficial effect of DMSO.4

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