Protection Against Cholera

Early Indian medical literature describes clinical features of patients with a disease similar to cholera (*1*). Since then, there have been many worldwide pandemics (involving Europe and North America) of cholera, most of them originating from the Indian subcontinent. However, the incidence of the cystic fibrosis (CF) gene among Asians is extraordinarily low (*2*), which does not appear to be compatible with the hypothesis that this gene has a protective effect against cholera (S. E. Gabriel *et al.*, Reports, 7 Oct., p. 107). Genetic traits that offer protection against infectious diseases have been shown to be high among populations where the disease is endemic. The prevalence of the sickle cell gene, for example, hypothesized to confer some immunity to falciparum malaria, parallels the geographic distribution of this disease.

Although the finding that mice which do not express the CF transmembrane conductance regulator protein were protected from the effects of cholera toxin is significant, it is not clear how that relates to the high incidence of the CF gene observed among Caucasians.

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References

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Response: Fontelo raises an interesting question. Although it is clear that cholera was and remains a major cause of mortality in the Indian subcontinent, it is also of historical importance in the Northern European population. We used cholera toxin in this study because it is the archetypal enterotoxin causing secretory diarrhea and the mechanism of action is well defined. However, we had also suggested that other bacterial toxins, including *Escherichia coli STa* and *LT*, which may have been more prevalent in the Caucasian population, could have had similar protective effects, because the rate-limiting step for secretion is the CF transmembrane conductance regulator (CFTR). Regretfully, this information was deleted because of an editorial decision to shorten the manuscript. Clearly any potential heterozygote advantage is only of importance in a population expressing the disorder at a high incidence. Therefore, correlation for a CF heterozygote is only relevant in the Caucasian population. Speculation regarding the absence of such a complex effect such as a balanced polymorphism (or selective heterozygote advantage) in one population versus another is considerably beyond the scope of our study. Differences between population CF frequencies may actually reflect more on the genetics of CF than on the ability of cholera to increase the population frequency. Most important, our data demonstrate the molecular and functional differences between CFTR(−/−), CFTR(+/−), and CFTR(+/+) mice in response to toxin. Resistance against cholera or other bacterial enterotoxins may have been a selective pressure for the high frequency of the human CF heterozygote, but a large human epidemiological study would be required to ultimately address that issue.

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Mo_nC_{4n} Cluster Synthesis: Clarification

In our report "Synthesis and characterization of molybdenum carbide clusters Mo_nC_{4n} (n = 1 to 4)" (7 Jan. 1994, p. 68) (*1*), we found negative ion mass spectral evidence for Mo_nC_{4n} species produced by XeCl laser photolysis of $Mo(CO)_6$. The molecular stoichiometry of this new molybdenum carbide was proposed on the basis of observations of negative ion masses and their corresponding isotope abundances, fragmentation information, ion-molecule reactions, and elemental analysis.

Previous work had indicated that the ultrafine particles generated by laser photolysis of $Mo(CO)_6$ consisted primarily of molybdenum and carbon (*2*). We examined the solid with glow discharge mass spectrometry, which yielded an elemental composition of 51.8% carbon, 46.1% molybdenum, 1.6% iron, and 0.29% oxygen and a molar stoichiometry similar to that of MoC_6. These data appeared to support the mass spectral measurements of Mo_nC_{4n} and indicated that the black solid was mainly molybdenum and carbon with only a trace of oxygen.

Subsequent to these studies, Kenneth Suslick and Taeghwan Hyeon (*3*) obtained very similar laser desorption negative ion mass spectra from a sample of Mo_2C (an observation that we had also made previously). D. Cox (*4*) has pointed out to us that most samples of Mo_2C contain a small amount of molybdenum oxide (as verified by Raman spectroscopy). Because molybdenum oxide has a relatively large electron