SCHOENINGER AND DENIRO REPLY—Sullivan and Krueger raise three points that require discussion. First, they indicate that they have reservations about the method we used to remove normal (non-apatite) carbonates from bone. As we indicated[1], X-ray diffraction analysis demonstrated that calcium carbonate present in fossil bones was removed by our method.

Second, Sullivan and Krueger present ^{14}C data from which they conclude that 'isotopic exchange of carbonate with bone apatite is limited to a few per cent'. This conclusion is based on calculations which depend on the assumption that fossil bone apatite undergoes exchange only with modern carbonate (carbonate with a ^{14}C activity of 1.000) in groundwater. This assumption is not reasonable. After an animal dies and its bones are buried, the bone apatite could begin to exchange immediately with contemporaneous groundwater carbonate. The exchange process could continue up until the time the bone was excavated or might stop sometime earlier, due to changes in the depositional environment (for example, inundation of the sediment with oil) or in the accessibility of the apatite to groundwater (for example, sealing off the bone with secondary calcium carbonate or other mineral deposits). The ^{14}C activity of the groundwater carbonate with which fossil bone apatite exchanged could range from 0 (for old bones in which the exchange process stopped long before excavation) to 1.000 (for bones in which the exchange process continued until excavation). This value cannot be estimated from the ^{14}C activity of secondary carbonates deposited on the bones because these deposits may be contaminants of recent origin[2]. Thus the amount of carbon isotope exchange that has occurred in fossil bone apatite cannot be calculated according to the method Sullivan and Krueger have used.

Finally, Sullivan and Krueger now indicate that their original model[3] is applicable only to herbivores. We cannot comment on the models they are developing to explain the isotopic relationships between bone collagen and apatite for carnivores and omnivores. However, we cannot conceive of any model that could explain our observation[1] of an 8.3‰ range in the $\delta^{13}C$ values of bone apatite from eight individuals who lived during the Venta Salada phase of the Tehuacan Valley occupation, for whom the archeological as well as the bone collagen carbon and nitrogen isotopic evidence all indicate the same diet.

We therefore stand by our original conclusion[1] that the $^{13}C/^{12}C$ ratios of fossil bone apatite cannot be used for dietary reconstruction until a method is developed to identify those specimens in which the apatite has not been subjected to postmortem exchange. One critical test of such a method would be its application to bones from a group of individuals of a single species for which the archaeological or palaeontological data indicate the same diet. The $^{13}C/^{12}C$ ratios of diet reconstructed from the bone apatite carbon isotope ratios of such a group should have a small range and agree with the diet $^{13}C/^{12}C$ ratios as reconstructed from the bone collagen isotopic composition.

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1. Schoeninger, M. J. & DeNiro, M. J. *Nature* **297**, 577–578 (1982).
2. Haas, H. & Banewicz, J. *Radiocarbon* **22**, 537–544 (1980).
3. Sullivan, C. H. & Krueger, H. W. *Nature* **292**, 333–335 (1981).

Mycoplasma pneumoniae and a dual aetiology for Spanish oil syndrome

RECENTLY, Pestaña and Muñoz suggested[1] that Spanish oil syndrome was caused by a cytotoxic reaction to anilides based on a free radical pathology. The symptoms of this disease do not, however, correspond[2,3] to toxicity due to aniline or to any of the other known components of the oil (for example, erucic acid, quinoline, toluene, benzene, glucosinates and short-chain hydrocarbons). No laboratory has found clinical toxicity due to aniline at levels comparable to that found in the oil[1,4–7].

Pestaña and Muñoz have suggested that the anilides are somehow "activated by free radicals in the oil". However, Garcia-Gancedo *et al.*[1] found that vitamin E, a free radical scavenger, is ineffective in clinical trials: "there are no clinical data in support of free radical pathology". Thus, the available data support neither anilides as the prime toxic substance nor a free radical pathology. Indeed, denatured oils have been marketed in Spain for years without known adverse affects. Pestaña and Muñoz, without any data, assert that earlier oils must therefore have been "devoid of anilines". Other researchers alternatively conclude[8] that "the incriminated oil is not *per se* the cause of the epidemic. Rather (the cause) is a combination of factors, some of which remain to be explained".

We suggest that one key factor has been overlooked. Spanish oil syndrome was first diagnosed as a form of atypical pneumonia. The Ministerio de Sanidad y Consumo published figures showing that *Mycoplasma pneumoniae* or other *Mycoplasma* were isolated from one-third of the cases studied[10]. Recent studies of *M. pneumoniae* indicate that it is very difficult to isolate and can only be diagnosed with certainty using antibody tests[11], and only 1 in 30 cases of *M. pneumoniae* infection are manifested as pneumonia[9]. Thus, the actual rate of *M. pneumoniae* infection is almost certainly higher than that reported by the Ministry. The normal incidence of *M. pneumoniae* is 0.6–3.1 per thousand per yr[12], yet an incidence of >300 per thousand per yr was seen among syndrome cases.

We have hypothesized that Spanish oil syndrome is a hyperacute form of *M. pneumonia* infection in which the ingested oil acts as an adjuvant[13]. We draw an analogy to hyperacute experimental allergic encephalomyelitis (EAE) which is 100 times more active than ordinary EAE. Several lines of evidence support our hypothesis. First, many neurological and vascular symptoms of the syndrome have been reported as unusual complications of *M. pneumoniae* pneumonia[14,16]. An oil adjuvant could have the effect of making these rare complications the norm, as in EAE. Second, the eosinophilia and perivascular cuffing associated with the syndrome are characteristic of chronic, allergic autoimmune diseases such as EAE. Third, a dual antigen aetiology would explain the observation that not all those people who ingested the oil became ill. The oil would be necessary but not sufficient alone to cause the disease. Finally, the ingestion of oil used in frying is not associated with the syndrome[15]. This observation argues against a free radical pathology as heat would create more free radicals. Alternatively, it is possible that some chemical constituent of the oil breaks down under heat to produce either nontoxic products or an inactive adjuvant. It is also possible that some of the oil was contaminated with *M. pneumoniae* introduced by unsanitary processing—an outbreak of pneumonia due to *M. pneumoniae* occurred just before the recognition of the syndrome[2].

Thus, we believe that our dual aetiology hypothesis deserves serious consideration as the most parsimonious explanation of all the available data.

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1. Pestaña, A. & Muñoz, E. *Nature* **298**, 608 (1982).
2. Ministerio de Sanidad y Consumo (Spain). *Syndrome Tox. Documentation Clinica*, May–December (1981).
3. Center for Disease Control. *MMWR* **30**, 436–438 (1981).
4. Fauci, A. S. *et al. Toxic-Allergic Syndrome Associated with Consumption of Contaminated Rape Seed Oil* (WHO, Copenhagen; 1981).
5. Gordon, R. S. *Lancet* **ii**, 1171–1172 (1981).
6. Kemper, F. H., Leupke, N.-P., Renhof, M. & Weiss, U. *Lancet* **i**, 98–99 (1982).
7. Tena, G. *Lancet* **i**, 98 (1982).
8. *Epidem. Bull.* **3**, 3–4 (1982).
9. Clyde, W. A. *Archs Neurol.* **37**, 65–66 (1980).
10. Ministerio de Sanidad y Seguridad Social (Spain). *Bol. Epidem. Sem.* **1485**, 153–155 (1981).
11. Roach, E. B. *et al. Pathology* **12**, 519–524 (1980).
12. Foy, A. M. & Allan, I. D. *Lancet* **i**, 392 (1982).
13. Root-Bernstein, R. S. & Westall, F. C. *Lancet* **i**, 969–970 (1982).
14. Biberfeld, G. *Clin. exp. Immun.* **8**, 319–333 (1971).
15. Valenciano, L. *Morbidity Mortaliity Wkly Rep.* **30**, 436–437 (1981).
16. Rothstein, T. L. & Kenny, G. E. *Arch. Neurol.* **36**, 476–477 (1979).