CORRESPONDENCE

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Nature Conservation Council has publicly stated that such sites are "gems" (BBC Radio 4, 22 January). He is indeed correct, for, like jewels, they provide neither nourishment nor habitation nor protection (the three necessities of life). But they are worse than jewels for they cannot be traded in time of hardship and instead of representing riches they are a permanent impoverishment to their owners. The usual epithet for such items is "white elephants".

Let us have no more of this folly in the name of science. The value to science of any objects or phenomena lies not in themselves but in the information they yield to study. Once this information is recorded and published whatever value remains in the objects or phenomena is of no value to science, for unless the original study was incompetently executed nothing new will be learned by preservation. I do not in the least condone the wilful pursuit of rare organisms, or the careless or selfish pollution of the environment, and I admit the possible future benefits which may be derived by maintaining "gene banks" of rare forms of cultivated organisms, but all that is quite a different matter. Should there be a popular demand for the preservation of areas of wilderness then justice requires that the populace provide compensation to the owners, but let there be no mistaken idea that this cost, which will be measured in hundreds of thousands of pounds annually, is a deserving use of the funds made available to science, nor that compulsion is justified by the supposed advance of knowledge. If any individual or body of scientists presumes that it is only necessary to legislate or to spend enough money in order to halt not only natural selection but also the very evolution of the inaminate world, such presumption is an affront to reason and must bear the condemnation of responsible scientists for misleading those who know no better.

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Origin of cancer

SIR — Cairns's[1] article is a welcome breath of fresh air in trying to put the causes of cancer into a realistic perspective. However, he could have strengthened his case for genetic transposition as a major cause by considering the relevance of DNA double-strand breaks as a molecular mechanism. Over the last few years Leenhouts and Chadwick[2] have convincingly demonstrated that the biochemical basis of malignancy lies most probably in the generation of double-strand breaks–lesions which cannot be repaired but which may result in genetic transposition. The evidence comes from many sources including those quoted by Cairns as well as radiation damage effects and cell-fusion experiments. Since double-strand breaks are necessary for some mutations, chromosomal abnormalities and genetic transpositions, Occam's razor would suggest this as a suitable model on which to test Cairns's hypothesis.

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2. Leenhouts, M.P. & Chadwick, K.M. *Int. J. Radiat. Biol.* **33**, 357-370 (1978).

SIR — John Cairns's speculative article[1] on the origin of human cancer is open to criticism both for what it says and for what it leaves unsaid.

Garner and Hertzog[2] have already drawn attention to the tenuous nature of the evidence on which Cairns bases his suggestion that "Chemical mutagens (of the kind detected in the usual tests for mutagenicity) seem unlikely to be rate-limiting components in most human carcinogenesis" and that "large-scale changes in the genome (such as rearrangements and deletions) seem to be more hazardous than the local changes produced by conventional mutagens". They might have put their case even more strongly.

First, the fact that patients with xeroderma pigmentosum (XP) do not show a high incidence of cancer in tissues other than skin may imply only that cancer in these other tissues is not associated with the formation of "UV-like" lesions[3] because the essential anomaly in XP seems to be failure to recognize lesions of this kind rather than inability to excise and repair DNA lesions in general.

Second, the association of chromosomal abnormalities with a high incidence of leukaemias, lymphomas and carcinomas in patients with Bloom's syndrome tells us nothing about the aetiology of cancer in the vast majority of the population who do not have Bloom's syndrome. Similarly it seems unjustifiable to assume that most cancer cells have an abnormal karyotype simply because this is often the case with cells from leukaemias, lymphomas, meningiomas and gliomas. Moreover, even if this generalization were true, it is conceivable, as Cairns himself points out, that the observed chromosomal rearrangements could have resulted from "trivial secondary events that occur after all the rate-limiting steps of carcinogenesis have been completed".

Third, it is not clear how the phenomenon of carcinogenesis in experimental animals by implanted films of plastic (and other materials) supports Cairns's argument. The underlying mechanism is still far from clear but, contrary to what Cairns suggests, Karp *et al.*[4] (whose work he cites) concluded that the hypothesis that tumours develop because the cells have lost the restraining influence provided by contact with each other, was specifically excluded by their observations. It is also worth pointing out that this form of carcinogenesis does not seem to have been reported in man despite the fact that foreign material of various kinds, and sometimes in sheet form, has been used in human surgery for many years (for example, in hernia repair, orthopaedic surgery and vascular surgery).

Finally, even if large-scale changes in the genome were shown to occur in cells from most common human cancers, this would not exclude the possibility that environmental pollution by chemical mutagens of various kinds, including mutagens detectable by the Ames test, plays an important part in the aetiology of human cancer. Many such mutagens, as Garner and Hertzog point out, and as Cairns admits, can increase the frequency of sister chromatid exchange and cause other chromosomal interactions in mammalian cells. The extent to which such changes are "functionally equivalent to genetic transpositions" seems to be of secondary importance in comparison with the question of whether or not they are associated with a high incidence of cancer.

As regards what is left unsaid, Cairns seems to equate "the creation of a cancer cell" with the development of cancer. Thus, while he recognizes the possible role of DNA repair mechanisms in preventing the emergence of cancer cells, he ignores the possibility, which I have discussed at length elsewhere[5], that homeostatic mechanisms of another kind may operate to destroy transformed cells or prevent them from dividing, and thus prevent the development of overt cancer. It is clear from the work of Mondale and Heidelberger[6], and others, which Cairns cites, that there may be a long interval between the application of a mutagen to cells in tissue culture and the emergence on repeated subculture of cells with the hallmarks of malignant transformation. The mechanisms responsible have not been fully elucidated but there seems no reason to doubt that they also operate *in vivo* and play a part in delaying the development of tumours in response to exposure to chemical and physical carcinogens; this, however, does not exclude the possibility that, *in vivo,* other mechanisms are also involved.

The long interval, often of many years' duration, which can occur between the locally successful removal of a primary tumour and the appearance of metastases would seem to imply either that cancer cells can remain dormant, or that cell proliferation may be balanced by cell death, for a long time, and studies of tumour cell population kinetics in both animals and man confirm this conclusion[5]. It has, moreover, been observed that the period of apparent dormancy may be abruptly terminated by experimental[7] or therapeutic[8] procedures. If metastatic tumours can be held in check in this way, why not primary tumours? My colleagues and I have recently described a technique which makes it possible to investigate this question directly in an animal model[9,10].

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10. I thank Professor H.J. Evans for his helpful comments on this letter.