CORRESPONDENCE

Alchemy in cancer

SIR — Your editorial (*Nature* 5 November, p.1) describing the attitude of the sponsors of cancer research in the United States towards those who perform the research was most timely. The relationship between sponsor and sponsored in research generally is presumably similar except that in cancer research the goal is more visible and unseemly at the failure to achieve it more acute.

Without wishing to push the analogy too far, there is an apparent similarity in the relationship between workers in cancer research and their sponsors on the one hand, and on the other, the alchemists pursuing the philosopher's stone at the behest of their princely masters. It is a sobering thought that many alchemists lost their heads for failing in their sphere of endeavour. Fortunately, nowadays, it is only our jobs that are at risk.

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Creationism

SIR — Our letter "American Creation" (*Nature* 2 July, p.95) appears to have resulted in two misunderstandings. The first, implied by the misleading title, is that it was primarily a critique of American Creationism. It clearly was not. The second, that we argue for a "God of gaps" by resorting to the supernatural to fill the gaps in current scientific knowledge, requires more serious consideration, since we agree with Sidney Fox (*Nature* 6 August, p.490) that such a view is a "copout" scientifically and theologically.

In common with most creationists, we acknowledge that faith is based on revelation and on personal knowledge of the Creator. The only empirical evidence to support the assertion that all nature, however adequately or inadequately explained, is God's handiwork, is the fact that all things exist, and show evidence of design and purpose which reflect the revealed nature of the Creator. Given belief in such a Creator we expect to find evidence consistent with his revelation of himself. No doubt an atheist will likewise expect to find evidence consistent with his philosophical position and is likely to leave discordant data to one side in the belief that future study will show it to be either erroneous or, given further data, assimilable to his present beliefs. In that sense it is indisputable that since scientific knowledge is incomplete, gaps exist in any account of the natural world.

Furthermore we would argue that the primary purpose of man's quest to understand origins is philosophical not scientific, and that in a society that will not tolerate a personal infinite God, the purpose of evolutionary theory is often the justification of atheism. In this context it is critical that scientific evidence be analysed within a completely objective framework, before presuppositions are imposed upon it.

Our position is that we believe that existing evidence does not disprove the existence of a Creator and further that the most probable explanation of his activity as Creator is one which does not accord with current evolutionary theory. In examining the factual evidence available in biology we consider that the correct objective approach to biological

systematics is to employ cladistics, a methodology which might usefully be applied also to protein and nucleic acid sequences. The interpretation of such an analysis is subjective, resting on philosophical presuppositions. So any evolutionary relationships that exist are properly deduced from cladistics.

So far as the origin of life is concerned we suggest that the most likely interpretation of scripture is that life did not evolve from a prebiotic soup. Thus we are not surprised that there are difficulties in proposing plausible chemical mechanisms to support the spontaneous generation position. For example, to take Fox's experimental model, we agree that while plausibility can be argued indefinitely, nonetheless the only basis on which the plausibility of such a model may be assessed, however subjectively, is by an examination of the experimental data. Although we do not think it appropriate here to enter into detailed technical comments, we find Fox's data (*Biosystems* 12, 55) singularly unconvincing.

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Malaria debated

SIR — I have read the paper by Chapin and Wasserstrom (*Nature* 17 September, p.181) with interest. I am disappointed with the presentation and discussion of the important subject of malaria resurgence and its relationship to agricultural production.

The authors give a garbled account of the very concept of malaria eradication and especially of the causes of the relative failure of this great endeavour. They imply that the main obstacle to the early achievement of the planned goal was resistance of *Anopheles* to insecticides. This is not so, even though the latter phenomenon played a significant part in technical problems that the World Health Organization (WHO) was facing during the late 1960s. The most comprehensive analysis of the multiple causes of the disappointing progress of malaria eradication in some parts of the tropical world was presented by WHO in 1969¹. It pointed out that administrative, social, economic and financial factors were largely responsible for the resurgence of malaria at the end of that decade, especially in India.

There is nothing "ironical" in the fact that agriculture in India and elsewhere expanded in regions where malaria incidence decreased spectacularly. It is precisely because of the improved health conditions, due to the use of residual insecticides against *Anopheles* vectors, that efficient agriculture became possible not only by rich landlords but also by small farmers. The astounding graph showing the positive association between the use of DDT in India and the striking increase of malaria in 1969–77 cannot be accepted in support of the authors' thesis of a causal relationship between the two factors.

An epidemiological analysis of the resurgence of malaria in India, such as the one carried out by Akhtar and Learmonth², showed that the increase in the incidence of malaria in India from 350,000 cases in 1969 to nearly 2 million in 1973 and then to 5 million

in 1975 was due to other conditions with an adverse affect on the standard of anti-malaria operations in India and in other countries of the subcontinent. The military conflict with Pakistan, the sharp fall in the flow of American aid and the temporary food shortages due to bad harvests took place during that period. There were delays in the allocation of foreign exchange for insecticides and drugs and there was some loss of urgency of the malaria control campaign because of its good results and the emphasis on family planning.

The successful 1965–69 phase of malaria eradication in India left uncompleted four large areas from which the consequent resurgence spread. These were the Rann of Kutch in western India, Madhya Pradesh hill forests, Orissa hill forest tracts and the forested areas of Assam. Akhtar and Learmonth² indicated that densely populated areas, with extensive irrigation and high agricultural production, have shown less malaria than other areas during the period 1970–75. On the other hand, in spite of the continuous use of DDT for agricultural needs, the amount of malaria in India decreased sharply between 1977 and 1980, thanks to better implementation of control programmes.

A series of valuable studies by Indian experts^{3,4} and an Audit Report of the Agency for International Development⁵ attach much less importance to the problem of insecticide resistance and could be quoted as an argument against the thesis so eagerly adopted by Chapin and Wasserstrom.

The adverse effects of excessive use of residual insecticides in agriculture have been known and stressed by WHO for well over a decade. It is quite untrue that WHO did not urge all countries in the developing world to decrease as much as possible (without endangering their food and health programmes) the use of residual insecticides and to introduce alternative methods of pest control. The emphasis on this policy was clearly stated in the 16th Report of the WHO Expert Committee on Malaria⁶ and was repeated and emphasized in the 22nd Report of the WHO Expert Committee on Insecticides⁷ and in every other relevant WHO report.

The serious imputation that the Food and Agricultural Organization (FAO) policy is being influenced by large insecticide-producing companies will certainly be answered by those accused of irresponsibility or other more sinister intentions. The authors use with evident relish the impressive term "integrated control" although it is doubtful that they fully understand its practical implications. Integrated pest management means a combination of chemical, biological and environmental methods. The complexity of implementation of these methods is often difficult to fathom by non-specialists, who invoke the term with more heat than light and over-estimate its universal feasibility. Integrated control methods are certainly successful in some areas with important crops but they must be tailored to local conditions. Their use requires not only a constant assessment of the size of the pest population but also carries with it the uncertainty of

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results should the crops be attacked by more than one pest. Chemical pesticides are still the main component of most methods of integrated control and several progressive companies have now developed insecticides (chlorvinphos) that are particularly suitable for this purpose.

Integrated pest management is now accepted and promoted by WHO and FAO wherever scientific agriculture and progressive health programmes exist. No doubt wider use of this approach is desirable but this depends largely on the availability of well trained specialists and on the understanding by farmers of the need for restraint in the use of chemicals. In this respect the paper by Chapin and Wasserstrom is of some value, although its sensational presentation (with sub-titles such as "Deadly link") undermines the credibility of the authors involved.

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1. WHO Official Records of the WHO 176, 106-124 (1969).
2. Akhtar, R. & Learmonth, A. *Malaria* (Research Paper No.3, Science Faculty, Open University, 1979).
3. Ray, A.P. J. *Communicable Dis.* 9, 145-171 (1977).
4. Rao, T.R. *Sisir Kumar Mitra meml Lect.* (Indian National Science Academy, New Delhi, 1978).
5. Agency for International Development *Audit Report* 76-348, 37-40 (1976).
6. WHO tech. Rep. Ser. No.549 (1974).
7. WHO tech. Rep. Ser. No.585 (1976).

SIR — It is generally agreed among malariologists that agricultural insecticides have made a contribution to selection for insecticide resistance in mosquitoes and that such resistance has made a contribution to the resurgence of malaria in Central America and South Asia. It is also generally agreed that one should be very careful before inferring a causal relationship from the discovery of a correlation between two sets of measurements.

No such care was exercised by Chapin and Wasserstrom (*Nature* 17 September, p.181-185). They infer that in El Salvador

lines but no actual data points. Each graph has a correlation coefficient marked on it of 0.96 or 0.99, but, especially in the case of the curvilinear relationships, the reader has no means of assessing how these coefficients were calculated. Their Fig. 1 is entitled "Effect of DDT on rice production in India, 1970-77", as if the correlation between these two parameters were a simple causal one. In fact, however, it is well known that other independent factors, notably the introduction of high yielding varieties, have both boosted rice yield and allowed and/or required more insecticide usage.

The basis of Chapin and Wasserstrom's curves (Figs 2 and 3) purporting to relate malaria incidence in India during 1969-77 to DDT usage and rice production, is unclear. In the figure (see below) I have plotted the data on malaria incidence issued by the Indian National Malaria Eradication Programme (NMEP) against the data shown by Chapin and Wasserstrom (Fig.4) for DDT usage. Certainly both quantities tended to rise over those years but so did other probably relevant factors such as irrigation. My graph shows a much less startling relationship than Chapin and Wasserstrom's because, according to the NMEP data, the minimum number of cases was higher, the maximum was lower and the malaria resurgence peaked in 1976 (and is reported to have continued to fall in subsequent years). No doubt the NMEP figures greatly under-report the true incidence of the disease, but there seems no reason to suppose that this under-reporting was greater

in the later years than in the earlier: Chapin and Wasserstrom give no information about any "correction factors" which they may have applied to the available data. I conclude that Chapin and Wasserstrom's graphs give a grossly misleading impression that there is a simple causal relationship between agricultural insecticides and malaria.

That the relationship is actually more complex is indicated by the following facts:

(1) Spraying of cotton crops has the, at least short term, beneficial side effect of suppressing mosquito populations.

(2) The large tonnage of insecticides used in anti-malaria spraying has certainly contributed to the selection for insecticide resistance in mosquitoes, as shown by the fact that withdrawal of this spraying has been found to lead to a levelling out or decline in the frequency of resistance genes.

(3) In the Gezira area of intensive agriculture in Sudan, resistance in *Anopheles arabiensis* is to malathion which is used in anti-malaria spraying and not to the other organophosphates used for spraying the cotton crop.

(4) Sri Lanka has very wisely banned the use of DDT and malathion in agriculture and reserved them for the anti-malaria campaign but has still had a hard struggle to contain and reverse its resurgence malaria problem.

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A reply —

SIR — We are sorry that Professor Bruce-Chwatt disagrees so radically with our interpretation of the facts surrounding malaria resurgence in India. In our own defence, however, we would suggest that the military conflict with Pakistan, the sharp fall in the flow of American aid, the temporary food shortages that took place there between 1973 and 1975, etc., do not explain the abundant entomological reports of *Anopheles* resistance which we cited in our article — even from such prosperous agricultural regions as Maharashtra and Gujarat. These reports, together with official accounts of the deliberations within WHO and FAO, constitute the major source of evidence upon which we have based our analysis.

Finally, like Professor Bruce-Chwatt, we appreciate the difficulties of implementing effective systems of integrated pest management in tropical areas. It was during the successful development of one such system in southern Mexico that the idea of writing this article first occurred to us.

In reply to Dr Curtis, it is unfortunate that in the process of reproducing our illustrations, many of the data points have become difficult to discern. Disregarding for the moment the 1979 figure on malaria incidence in India, however, Dr Curtis's information suggests an even higher correlation between DDT usage and the spread of disease than we have calculated. As for the question of decreased transmission, it may well be true that malaria in India peaked in 1976, but the 1977 figure he cites has been questioned by numerous specialists and in any case does not contradict

our argument about pesticide abuse.

As for the four points raised in his letter, we offer the following response:

(1) It is precisely the short-term beneficial effect of insecticides that encourages cotton growers and public health officials to apply them. What we have argued, however, is that the disadvantages of insect resistance soon come to outweigh these rather ephemeral benefits.

(2) It is difficult to separate the effects of insecticides used for malaria control and those used in agriculture. What is clear, however, is that the decline in resistance after anti-malaria programmes are discontinued is a limited and unfortunately rare phenomenon.

(3) Although it may be true that *Anopheles* mosquitoes in Sudan are not resistant to the organophosphates used on cotton, most countries have not been so lucky. How does Dr Curtis explain the almost complete and apparently irreversible resistance among malaria vectors in India, South-East Asia and Central America?

(4) As the case of Sri Lanka indicates, restricting the use of a particular chemical does not guarantee that mosquitoes will remain susceptible to it: application of related (and even unrelated) compounds is often sufficient to stimulate resistance. Moreover, if initial success in combating malaria leads to the reduction of screening and treatment procedures (as commonly occurs), epidemic resurgence will indeed be exceedingly difficult to control.

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"each kilo of insecticide added to the environment will generate 105 new cases of malaria". Taken literally and from their own data this would imply 168 million cases of the disease in a country with a population of 4.3 million.

Chapin and Wasserstrom present three figures with apparently calculated points and