



Atomisers used in insecticidal work

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The recent invasion of the Amazon area by non-immune people is creating serious health problems. Ten years ago the situation regarding malaria was much more satisfactory. I travelled extensively in the Amazon around that time, and the ministry campaign against malaria (SUCAM) had it fairly well controlled. Brazil was fortunate in that the major anophelene vector, *Anopheles darlingi*, had not developed genetic resistance to dichlorodiphenyltrichlorophane (DDT). The fleet of small boats in Manaus would go up the multitude of rivers spraying the houses: people live mainly on the banks of a river as it is the only route of cheap transport. Naturally eradication was not

possible but the level of control was high. At that time *P falciparum* resistant to chloroquine had been reported but was still uncommon; now it is the rule. Also *A darlingi* has developed so called behavioural resistance; it is no longer resting on the sprayed walls but bites its hosts around dwellings. Therefore the malaria problem grows. Also a large part of this population influx is speculators mining mainly for gold or diamonds or cattle rearing. The miners are the worst because they are virtually impossible to control, flying into remote areas, often secretly, because of the lure of what is beneath the ground. Nobody knows how many mining concerns there are in this region but it must be hundreds. The ministry struggles with the problem of controlling malaria among them as well as the transmission of AIDS. It is a herculean task.

Development of antimalarial drugs has been related to wars and the availability of quinine. After the second world war six groups of antimalarials were available but *P falciparum* has a remarkable capacity to develop resistance. The Vietnam war highlighted the problem for the American army, which set up an admirable drug screening programme at the Walter Reed Army Institute of Medical Research in Washington. To date this programme has screened 300 000 compounds for antimalarial activity. Mefloquine is the result of this programme, but because it is another quinoline (like quinine) resistance has already been reported, though it is still unknown in Brazil. Such powerful, effective schizonticides must be rigorously controlled otherwise indiscriminate use will result in resistance as occurred with chloroquine. Today the situation for treating severe falciparum malaria in Brazil is better than it has been for some years, as apart from mefloquine there are other new schizonticides to which resistance is still unknown.

Scientifically Speaking

Growing catalogue of fraud

Bernard Dixon

"Why does this book fail? Primarily because the authors took reports of scientific fraud and strung them together, claiming that their analysis would reveal something profound about science. It doesn't. From fraud, one only learns about fraud."

Thus the distinguished molecular biologist Norton Zinder of Rockefeller University, New York, writing in *Science* 83 (January/February 1983, p 94). His target was William Broad and Nicholas Wade's *Betrayers of the Truth*, published by Simon and Schuster some months earlier. In private, as I know from talking to Zinder around that time, he was rather more intemperate in his criticisms of a book which had for the first time painted a synoptic view of cheating and data fabrication in science. Despite the existence of such classics as the Piltdown forgery (an undoubted contrivance) and Gregor Mendel's too perfect breeding data (tidied up by an over zealous assistant?), most scientists fiercely resisted the notion that dishonesty was an endemic part of the scientific enterprise. Peer review, at the heart of research evaluation, rendered the very idea absurd.

We now know otherwise. Month by month throughout the 1980s the catalogue of fraud has grown. Retractions, corrections, and warnings in scientific journals have become if not commonplace then

certainly no longer rare and conspicuous exceptions to the passing parade of "normal science." Even within the scientific community there has been a gradual, grudging acceptance that numbers of biologists and physicists, chemists and psychologists *do* sometimes depart from the conventionally rigorous standards of their profession—and that the temptation to do so has been aggravated by the financial and other pressures of modern, highly professionalised and politicised science.

Political interference

Unfortunately, however, we are now reaping ill rewards from scientists' own haughty rejection of suggestions of dishonesty at the beginning of the decade. Indeed, politicians in the United States have latched on to the cheating phenomenon with such zeal that conventional scientific intercourse is itself now in serious danger of being distorted and corrupted by political interference.

Consider the following (true) story. In April 1986 two collaborating laboratories published a paper in *Cell*, describing the way in which a foreign gene inserted to make transgenic mice affected antibody production by existing genes. The principal authors

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were David Baltimore, who is director of the Whitehead Institute for Biomedical Research and professor of biology at Massachusetts Institute of Technology, and Thereza Imanishi-Kari of the nearby cancer centre of the institute.

One of Imanishi-Kari's postdoctoral students, Margot O'Toole, had reviewed a draft of the paper and made helpful suggestions. Soon after publication, however, Dr O'Toole alleged that some of Imanishi-Kari's findings did not support its conclusions. She complained not to the authors or even to the institute, but to Tufts University, which was considering whether to appoint Imanishi-Kari to its faculty. A review panel was assembled and soon concluded that the central thrust of the paper was not at issue and that its conclusions were sound. Imanishi-Kari was given her tenured appointment.

O'Toole next reported the matter to the institute. A second review confirmed the verdict of the first and concluded that minor errors in the paper did not require formal correction. So far, the disagreement was crucially about scientific interpretation. Now, however, it attracted the attention of Walter Stewart and Ned Feder, two National Institutes of Health scientists who had become famed for their investigations into laboratory cheats. Based on material received from O'Toole, they produced a manuscript charging that the paper had been consciously misleading. Several journals rejected the report by Stewart and Feder, who began instead to lobby scientists and to speak on the matter at universities and scientific meetings. Gradually, Baltimore and his coauthors found their names being linked with those of proved fraudsters.

The stage was set for the third episode in the saga. Early last year a newspaper reporter told Baltimore that Stewart and Feder were about to ventilate the affair before two congressional committees then looking into misconduct in science. One of these, the Oversight and Investigations Subcommittee of the House Energy and Commerce Committee, chaired by Democrat congressman John Dingell, has since assumed considerable importance for its extraordinary

and incongruous efforts to adjudicate over a matter of science. Although the inquiry fizzled out some months ago without reaching any clear conclusion, its work has done much to harm the public (but not the scientific) reputation of David Baltimore.

Laboratory notebooks subpoenaed

As a highly conspicuous scientist Baltimore became the principal target for Stewart and Feder's campaign. He also thought that he should take the premier place in defending research which took place in a collaborating laboratory. What he did not reckon with, at the outset, was the enormously emotive effect of, for example, Stewart and Feder's request that the secret service should examine laboratory notebooks subpoenaed from the authors. As he now reflects in *Issues in Science and Technology* (Summer 1989, pp 48-54), "the mere mention of the words 'Secret Service' had terrifying import, and carried the implication that we must have done something awful to warrant its involvement." As the hearings showed the secret service discovered no secrets or even surprises, but the damage was done.

"If the sad history of this investigation demonstrates nothing else, it shows that uninformed or malinformed outsiders cannot effectively review the progress of scientific activity," Baltimore writes. The affair has certainly shown that politicians, who may have a burning interest in righting wrongs, are generally not able to distinguish minor unconscious errors in a highly technical manuscript from serious, conscious fraud. The way in which the present case mutated from legitimate scientific criticism (although oddly prosecuted by Dr O'Toole) into an apparent scandal of national dimensions is an awful warning for the scientific community to put its own house in order. The Whitehead Institute is now doing this, creating machinery that allows whistleblowers to demand reviews, whose findings are publicised if fraud or serious error is found. But such mechanisms are far from universal. For many scientists the Dingell affair is as rare an aberration as is full blooded cheating.

ANY QUESTIONS

What might be the cause of slightly swollen breasts in a single woman in her mid-50s? A recent mammography showed no malignancy.

If a woman complains of swollen breasts it is important to identify whether the abnormality is confined to one side or is symmetric in both breasts. If the latter the patient may present with a complaint that the breasts feel tight within her bra, which may be the first indication of increasing obesity in a middle aged woman. In the mid-50s most of the parenchymal tissue of the breast is naturally replaced by adipose tissue and this may also be the site for excessive fatty deposits as part of generalised obesity. A second but rare cause for symmetric swelling of the breasts would be dependent oedema in the pendulous breasts of a woman suffering with congestive cardiac failure. It is extremely rare to have symmetric infiltration of the regional lymphatics by a chronic inflammatory or neoplastic process.

If the swelling is asymmetric this should immediately alert the clinician to a sinister diagnosis even though a mass may not be felt and a mammogram shows no evidence of malignancy. It is possible that she has developed a diffuse malignant process or an inflammatory carcinoma. Furthermore, unilateral breast engorgement may result from massive axillary node disease with either a lymphoma or metastatic breast cancer from an occult primary. Periductal mastitis is an unlikely diagnosis; it seldom affects the whole breast and usually resolves spontaneously within a week or two. —MICHAEL BAUM, *professor of surgery, London*

What is the place of cerebrospinal fluid examination in diagnosing and monitoring treatment in a patient with neurosyphilis?

Examination of the cerebrospinal fluid is still an essential part of the diagnosis and management of neurosyphilis. The cell count is the best guide to activity of the disease, and a rise in it or a positive result of a Venereal Disease Research Laboratory test is an indication for treatment. The optimal dose of penicillin is not known. Conventional doses of procaine penicillin, such as 600 000 units daily intramuscularly, do not lead to treponemical concentrations in blood and should be continued for three weeks. A higher dosage is sometimes combined with probenecid.¹

The spinal fluid should be examined after a few weeks and then every six months for two years. This is because late relapse sometimes occurs after conventional treatment and it is not yet established that the higher dosage eliminates relapse.² After adequate treatment the cell count and titre found with the Venereal Disease Research Laboratory test fall progressively. If the cell count is normal and the titre low (1/4 or less) after two years further follow up is unnecessary. —BRYAN ASHWORTH, *consultant neurologist, Edinburgh*

1 Reik L Jr. Spirochaetal infections of the nervous system. In: Kennedy PGE, Johnson RT, eds. *Infections of the nervous system*. London: Butterworth, 1987.

2 Hooshmand H, Escobar MR, Kopf SW. Neurosyphilis, a study of 241 patients. *JAMA* 1972;219:726-9.