Variations in the Insecticide Tolerance of Insects

Recent communications[1,2] on the variance of the dosage-mortality response of strains of housefly and mosquito susceptible and resistant to insecticide serve to emphasize that, although there is considerable information on the inheritance of resistance to insecticide in some insects, especially houseflies[3], *Drosophila*[4] and now mosquitoes[5], there has as yet been no direct estimate of how much of the unselected tolerance is genetically determined, how much is due to environmental effects. Beard[6], who first directed attention to the possibilities, considered the non-genetic variation might so predominate as to overwhelm the genetic components.

One would not wish to dispute the contention[1] that insect populations comprised of a single resistance-susceptibility genotype are likely to be less variable in their tolerances than are populations containing all possible resistance-susceptibility genotypes. But that fact is scarcely relevant to what Hewlett originally suggested[7], namely, that a portion of the tolerance variance is susceptible to manipulation without any change in gene frequency. That this interpretation was, at least in part, intended is shown by the example selected[8], the decrease in variance of the tolerance found with a DDT-resistant strain of housefly when increasing amounts of the insecticidally inert synergist DMC were added to the applied DDT. One point which strongly supports Hewlett's hypothesis, but has not been commented upon, is the very obvious increase in variance with the smallest amount of DMC compared with that found with DDT alone[8].

It is usual to assume that the genes for resistance are extremely rare in Nature, or, as stated by Wilson-Jones and Davidson[1], so infrequent that an average sample of wild insects is unlikely to contain resistant genes. This assumption has been made repeatedly in attempts to explain the often rather slow emergence of resistance in the field, but, as was recently pointed out[9], it is unlikely that this assumption of rarity is correct. Indeed, the only quantitative work as yet available on the frequency of resistant genes in wild populations showed that there may be as many as 12 per cent of dieldrin-resistant heterozygotes in the *Anopheles gambiae* populations of areas as yet untouched by dieldrin[10]. Finally, laboratory populations originate as samples from wild populations, most but not all attempts in the laboratory to induce insecticide resistance are successful, and sometimes resistance to a number of insecticides can be developed sequentially[11].

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Fluorescent Mast-Cell Reaction in Precancerous Skin of the Lizard *Lacerta agilis*

The mast-cell reaction of the mouse skin, painted with tar or carcinogenic hydrocarbons, has been known for a long time[1]. According to several authors, these cells show a golden-brown fluorescence when examined under the microscope in ultra-violet light[2], though other investigations give some evidence to the contrary[3].

Recently, it has been established that the mast cells of the mouse and the rat contain not only histamine but also 5-hydroxytryptamine[4]. This substance can be converted into a fluorescent β-carboline derivative by the action of formaldehyde, and in the mast cells of the precancerous mouse skin it reaches a concentration which is normally only achieved by the cells of the enterochromaffin system[5].

In the mastocytosis of the mouse skin after painting with 9,10-dimethyl-1,2-benzanthracene in acetone it could be demonstrated to direct assay and by paper chromatographic examination that the fluorescent substance of the mastocytes is the 5-hydroxytryptamine derivative β-carboline[2].

Continuing these investigations, we examined a cutaneous carcinoma of a lower vertebrate, namely, the squamous-cell carcinoma of the lizard *Lacerta agilis*. This tumour seemed pre-eminently suitable for this purpose, because a distinct precancerous phase occurs in its development[6,7]. At first we had seven tumour-bearing animals, but by extending the material we finally had 104 specimens at our disposal.

From these specimens the precancerous portions of the skin were excised. The examination of the mast cells was carried out with frozen sections (cut in a horizontal as well as in a vertical direction), free-hand sections and tissue spreads prepared from dermal scrapings. The skin material, fixed in 10 per cent formalin or otherwise, was examined under the microscope in ultra-violet light. Then the material was stained either with acetylated sudan black for phospholipids[8] or with toluidine blue for mast cells.

Just as in the mouse, the mast cells of the precancerous skin of the lizard gave a golden-brown fluorescence in ultra-violet light, but only after treatment with formalin. The fact that a non-fluorescent precursor substance can be extracted from the mast cells by prolonged treatment of the skin tissue with acetone suggests that the fluorescence is a consequence of the action of formaldehyde on the above-mentioned substance. Acetone treatment apparently did not affect the ability of the mast cell granules to stain with either acetylated sudan black or with toluidine blue.

To establish the chemical identity of the fluorescing substance we prepared an extract of the precancerous lizard skin. For this purpose the dermal scrapings of the skins were homogenized in acetone, after which the extract was concentrated *in vacuo*. After the fats had been removed with petroleum ether the extract was treated with formaldehyde and could then be examined in ultra-violet light. The extract treated with formaldehyde exhibits the same golden-brown fluorescence as was found with the extract of mouse skin prepared in the same way[2]. A further extraction of the skin fragments with fat solvents failed to yield additional fluorescent material.

Like the mast cells of the precancerous mouse skin, the mast cells of the precancerous skin of the lizard probably contain a relatively large quantity of histamine and 5-hydroxytryptamine.

The source of 5-hydroxytryptamine is unknown; it may be either the inside or the outside of the precancerous epidermis. Possibly this substance plays an important part in the development of the squamous-cell carcinoma of the skin.

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Undergraduate Academic Record of Fellows of the Royal Society

The communication by Gross and Hudson in *Nature* of September 20, p. 787, shows an interesting difference between academic records of Fellows of the Royal Society who were respectively at Cambridge and at Oxford. Of those at Cambridge only about 77–78·5 per cent achieved a first, and in fact only about 55 per cent achieved a first in both parts of a tripos. The Fellows of the Royal Society who were at Oxford, on the other hand, graduated with first-class honours in about 97 per cent of cases.

The authors suggest that these interesting results are open to at least two interpretations: (1) that the Oxford examination is a more valid index of potential research ability; and (2) that the standards of the Oxford examinations are relatively lower than those of Cambridge. There is surely a very important third possible interpretation, namely, extra-curricular activities are far more interesting at Cambridge than at Oxford, and that in the widest sense the Cambridge education is therefore better.

The authors, strangely, make no comment on the fact that it seems to be three times as common for a Cambridge graduate to become a Fellow of the Royal Society, neither do they comment on the obvious fallacy of the whole investigation, namely, the opportunities for research offered to a young man at the beginning of his career. If these are, for example, only offered to those with a first-class degree, it is obvious that selection for the fellowship of the Royal Society in later years will be almost restricted to those who had first-class degrees. The method will fail to show whether there is a number of potentially good investigators among those with second-class degrees who have never been given the opportunities for a career in research.

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We certainly agree with Prof. Platt that the difference between the Oxford and Cambridge results is open to the third possible interpretation that he suggests, and we would welcome from him any suggestion as to how we could measure the "more interesting" nature of the "extra-curricular activities" at Cambridge.

We find nothing strange in "the fact that it seems to be three times as common for a Cambridge graduate to become a Fellow of the Royal Society" since there are almost three times as many science graduates from Cambridge as there are from Oxford.

During the period 1920–39, approximately 4,700 natural scientists, 1,400 mathematicians and 1,800 engineers graduated from Cambridge, while only 2,600 natural scientists (including engineers) and 400 mathematicians graduated from Oxford.

If we understand Prof. Platt's last paragraph correctly, we consider it to be true but irrelevant to our study and to the general problem under consideration. Obviously, as he points out, if only students with first-class degrees are given opportunities for research, the Fellows of the Royal Society will be drawn largely from this group. Our point is that, whatever selection procedures were used in the past, a considerable minority of the scientists elected to the Royal Society did not receive first-class degrees. From this we conclude that it may be unwise to use class of degree as the primary criterion for the award of research grants.

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Cancer and Smoking

In a letter published in *Nature* of August 30, p. 596, Sir Ronald Fisher quoted figures confirming previous observations that smoking habits are more similar in identical than in fraternal pairs of twins even when the identical pairs are reared apart. The result can be interpreted as showing that, like almost every trait, mental or physical, previously tested by the twin method, smoking habits are, to a greater or lesser degree, dependent upon genetical constitution. It is, however, difficult to appreciate the relevance of this demonstration to the problem as to whether or not cigarette smoking causes lung cancer.

The association between epithelioma and the occupation of sweeping chimneys has been well known in the past. Not improbably it could have been proved that identical twins were more often both chimney sweeps than would have been expected by chance. Such a finding would not have influenced the case for assuming a strong causal connexion between soot irritation and epithelioma.

Nevertheless, there are perhaps hitherto unexplored ways in which twin data might be usefully employed in the study of the effects of tobacco on the lungs. Pairs of identical twins, whose smoking habits were discordant, could be followed up with special reference to possible development of lung disorders in one or both members.

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