THE INFLUENCE OF WHEAT GERM OIL IN THE DIET ON THE INDUCTION OF TUMOURS IN MICE

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Considerable attention has always been paid to the possibility that tumour formation, either spontaneous or experimental, might be influenced by nutritional conditions in the host. In this connection special interest seemed attached to reports by Davidson (1934, 1935) that a diet rich in vitamin E inhibited the development of tar cancer in mice.

Two further observations may bear some relation to this problem. Evans (1928) described the high incidence of deciduomata during pseudopregnancy in rats maintained on a diet deficient in vitamin E. More recently Adamstone (1934) discussed a possible relationship of vitamin E to unrestricted cell division. In his experiments a deficient diet—freed from the vitamin by a modification of the Waddell-Steenbock method—was fed to chicks over a prolonged period. The treatment resulted in the development of characteristic visceral lesions represented by " foci of degeneration and destruction of normal tissues accompanied by replacement and invasion by new cell growths, ..." This Adamstone regarded as an example of uncontrolled cell growth simulating malignancy, and he suggested that vitamin E is so essential for the maintenance of the normal nuclear condition that it acts indirectly as a control over cell division.

In view of these suggestions it was decided to investigate the effect of a diet supplemented with wheat germ oil on the production of skin tumours in mice by means of 3:4-benzpyrene (Cook, Hewett and Hieger, 1933). It must be made clear that Davidson related the phenomenon he described simply to the addition of wheat germ oil and not necessarily to the content of the oil in vitamin E.

Experimental

Sixty young female albino mice were divided into two equal groups, A and B, and were kept in smaller groups of 2, 3, or 4 in each cage. Group A was fed on the ordinary laboratory diet consisting of dog biscuit and milk daily, with a small ration of cod-liver oil and green vegetable once a week. Group B received the same diet supplemented by the daily addition of 0.5 c.c. of wheat germ oil (" Fertilol " brand supplied by Vitamins Limited) and about

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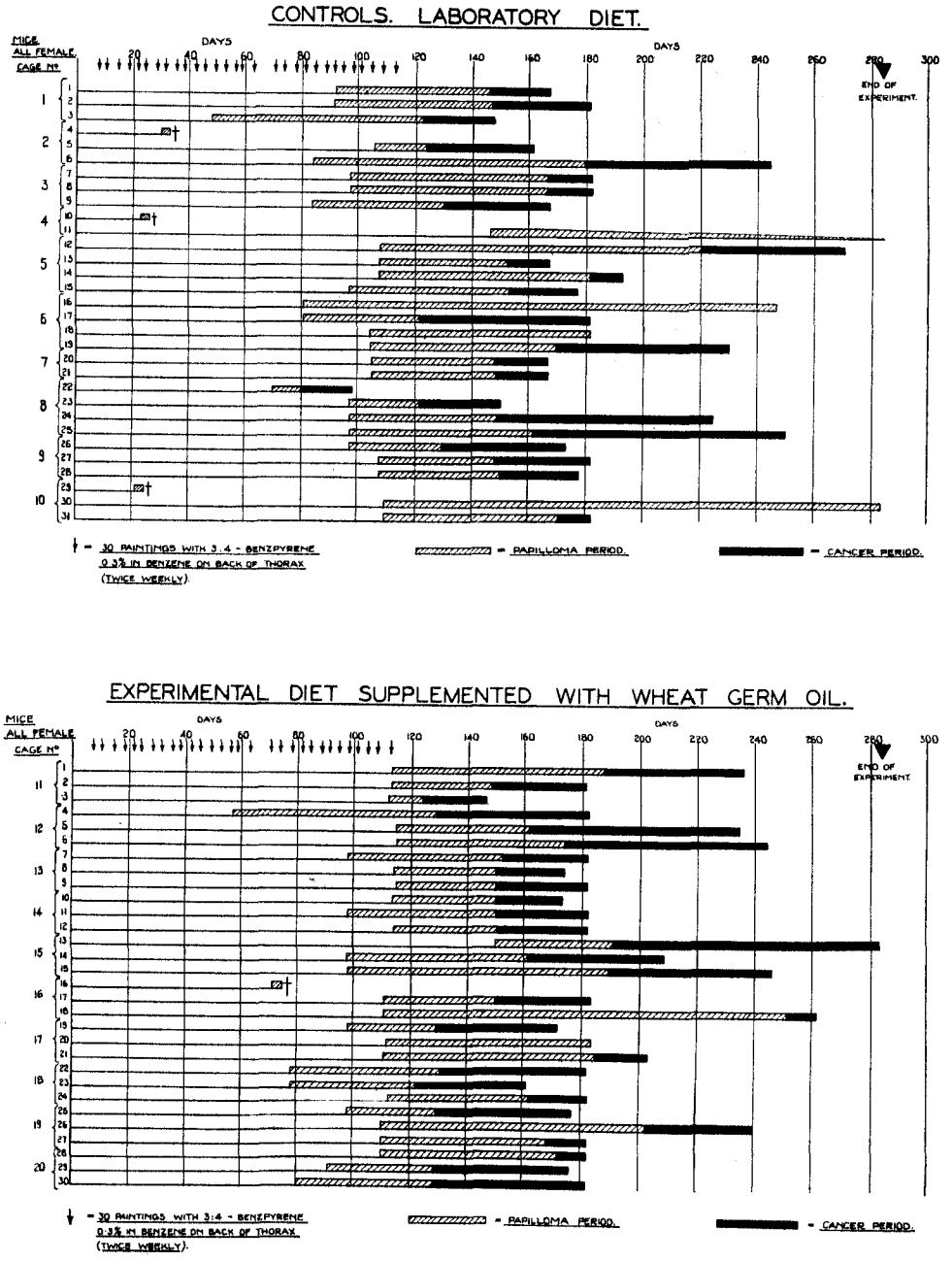

FIG. 1. EFFECT OF WHEAT GERM OIL IN THE DIET ON INDUCTION OF TUMOURS IN MICE

1.0 gm. wheat germ meal for each mouse. The wheat germ oil ration was reduced by half on the 122d day of the experiment, when it was noticed that the mean weight of the experimental group was slightly lower than that of the controls, possibly on account of the mild laxative action of the oil.

After a week on these diets the mice were painted twice weekly for fifteen weeks with a 0.3 per cent solution of 3:4-benzpyrene in benzene. In the course of the experiment note was made of the time of appearance of papillomata and of the date on which it was judged that a cancer had emerged. This information was supplemented by histological examination of the mice which died from time to time as the experiment proceeded. Sections of the tumours of 20 such mice were prepared in the laboratory of the Royal College of Physicians of Edinburgh, and it was reported that 19 of them had a squamous-cell cancer and that 3 showed metastases in the internal organs. The experiment was terminated on the 284th day, when only 3 mice remained alive.

Results

Since 24 of the control animals and 28 of the experimental group developed obvious cancers (Fig. 1), it was apparent that the diet had not influenced the numerical yield of tumours. The detailed data for each group were further analysed, however, under four headings: (*a*) the mean time till death from the commencement of painting: this estimate excluded three animals in group A and one in group B which were considered invalid on account of premature death; (*b*) the mean latent period in animals which developed papillomata, *i.e.*, all except those invalid in (*a*); (*c*) the mean duration of the papilloma stage; (*d*) the mean duration of the cancer stage. In each case the significance of the difference in the means (P) was assessed by the *t* method of Fisher (1932). The following table shows the mean duration of these periods and the values of P. It is evident that in no instance are the differences significant.

Period of Experiment	Mean Duration in Days		Value of P
	Group A (Control)	Group B (Experimental)	
(*a*) Interval till death	194.5	197.3	0.3–0.4
(*b*) Latent period	98.3	104.9	0.1–0.1
(*c*) Papilloma period	66.0	54.5	*c*0.2
(*d*) Cancer period	35.0	39.3	0.4–0.5

Discussion

In this experiment it appears that the liberal addition of wheat germ oil to the diet has no influence on the subsequent emergence of tumours induced by benzpyrene. In particular, no inhibitory influence was detected such as has been reported by Davidson (1935). On the other hand, Davidson's re-

sults seem undoubtedly significant, and it is probable that other factors are responsible for this discrepancy. The present experiment, while similar in plan, is almost certainly not strictly comparable; of many possible points of difference, the most likely is that of diet. It may also be that a nutritional effect of this kind, although demonstrable by the use of a carcinogenic tar of moderate activity, tends to be masked in the case of a highly potent hydrocarbon such as 3:4-benzpyrene.

Such work raises the whole question as to how far the process of carcinogenesis can be influenced by external and dietary conditions. Confirmation of Davidson's work would suggest that certain nutritional conditions maintain the stability of the body cells even in the presence of a carcinogenic agent. Conversely, Adamstone's work indicates that prolonged deprivation of vitamin E is followed by changes which point to cell instability.

A distinct but related question is the influence of environmental and particularly of dietetic factors on the occurrence of spontaneous tumours: this represents an even more complex problem but one which demands the closest attention. In the first place, instances have been described in which mice of a recognized cancerous stock, following their establishment in another laboratory, failed to develop their characteristic tumour rate (see, for example, Annual Report of the South African Institute for Medical Research, 1934, pp. 24–25). In the absence of any genetic explanation, it can only be concluded that environmental influences were responsible. In the second place it has been suggested by Strong (1932–33, 1934, 1935), on the basis of experiments in which various essential oils (gaultheria, thyme, and allspice) were added to the diets of cancer-susceptible mice, that such treatment reduces the rate of appearance and the total incidence of spontaneous tumours. It is obvious that much further work is necessary before real answers can be given to the questions of how far it is possible to affect the inherent stability of body cells in the presence of a carcinogenic agent and to what extent genetic susceptibility to tumour formation can be modified by environmental factors.

Summary

The addition of wheat germ oil to the diet of mice had no apparent influence on the development of tumours induced by painting the skin with 3:4-benzpyrene.

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