

between deoxyribonucleic acid and protein, as suggested by Kirby<sup>4</sup>, or by a higher concentration of deoxypolynucleotides in the thymus. As the increase of deoxypolynucleotides has been observed only for a short period after irradiation<sup>2</sup>, whereas the increased yield of deoxyribonucleic acid remains constant for a longer period, the first assumption seems more likely. To obtain further evidence on this point, nucleohistone was extracted from the thymus with 1 M sodium chloride, precipitated by dilution to 0.14 M sodium chloride and used for further treatment with phenol-trichloroacetic acid. As will be published later in detail, a similar irradiation effect can be observed as in the whole organ. From thymus-nucleohistone, prepared from animals 6 hr. after 800 r., 50 per cent of the deoxyribonucleic acid is extracted in 0.5 per cent trichloroacetic acid, whereas from nucleohistone of normal animals, only 10 per cent deoxyribonucleic acid can be obtained in 0.5 per cent trichloroacetic acid. This indicates a labilization of the deoxyribonucleic acid from the protein, probably due to a break in bivalent metal linkages.

This labilization occurs in an early post-irradiation period, that is, 1-6 hr. after irradiation. Histological observations demonstrate death of some cells at this time, although the weight of the organ and the deoxyribonucleic acid content per gm. of tissue begin to decrease later, namely, 6-10 hr. after irradiation. It seems probable that the labilization of deoxyribonucleic acid from protein occurs prior to histologically observable death of a cell. The distinct lag period of 1 hr. before labilization begins, however, suggests that some other processes in the nucleus are involved with it or responsible for it. In particular, the possibility must be investigated of a preliminary degradation of the deoxyribonucleic acid chain.

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### Localization of a Halogenated Porphyrin in Mouse Tumours

Schwartz *et al.* observed that certain commercially obtainable haematoporphyrin preparations were contaminated by a porphyrin capable of becoming localized in experimental tumours<sup>1,2</sup>, and that pure haematoporphyrin was unable to do so. These findings gave the impetus to the present work on halogenoporphyrins. The premise on the basis of which halogenoporphyrins were chosen was the assumption that the aforementioned impurity represents an intermediate formed in the course of the synthesis of haematoporphyrin from haemin. One such intermediate could be *bis*-(2-bromo-ethyl)deuteroporphyrin. Since iodine-131 is a more convenient isotope for the purpose of labelling than isotopes of bromine, the iodine 131-labelled analogue was synthesized.

When given parenterally, *bis*-(2-iodoethyl-<sup>131</sup>I) deuteroporphyrin became localized selectively in transplanted adenocarcinomata of *Dba1* mice and in spontaneous mammary adenocarcinomata of *C3H* mice. This conclusion is based on the following experimental findings. All tumours when examined 6 hr. after injection or later exhibited the red fluorescence characteristic of porphyrins; the fluorescence was non-uniformly distributed within these tumours. In contrast, none of the other tissues exhibited this phenomenon. Although extracts of organs from mice injected with *bis*-(2-iodoethyl-<sup>131</sup>I)deuteroporphyrin contained no porphyrins, radioactivity, probably due to products of porphyrin catabolism, was found to be present. When tumours or other tissues were extracted with a mixture of ethyl acetate/acetic acid (4:1, v/v), only the extracts of tumours contained detectable amounts of a single porphyrin. This porphyrin was identical with *bis*-(2-iodoethyl-<sup>131</sup>I)deuteroporphyrin with respect to its specific radioactivity. Furthermore, when the aforementioned tumour-extracts were chromatographed on paper strips and the developed chromatograms scanned for radioactivity, the radioactivity of the porphyrin-containing spot accounted for all the activity initially placed on the strip.

When sections prepared from a transplantable mammary carcinoma were examined after fixation in formaldehyde and after removal of paraffin with benzene, fluorescence typical of porphyrin was observed within the tumour cells. In the limited number of observations made, fluorescence was found to be present only in intact tumour cells.

The mechanism underlying the selective accumulation of *bis*-(2-iodoethyl-<sup>131</sup>I)deuteroporphyrin in the tumours studied remains to be established and is now being investigated.

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### Synthesis of Diphosphopyridine Nucleotide in Irradiated Rats

WHEN suspensions of nuclei from thymus or spleen are incubated *in vitro*, adenosine monophosphate in the nuclei is phosphorylated to the triphosphate<sup>1</sup>. This phosphorylation appears to be abolished following low doses of X- or  $\gamma$ -radiation, given either *in vitro* or *in vivo*<sup>2</sup>. However, the net synthesis of diphosphopyridine nucleotide *in vivo* following intraperitoneal injection of 0.5 gm. nicotinamide/kgm. (ref. 3) was not abolished when rats were exposed to X-radiation in doses up to 1,500 r. 3-60 min. before nicotinamide injection (Table 1); in these experiments, the pyridine nucleotide content of the tissue extracts was measured by the alcohol dehydrogenase method<sup>4</sup>. Since the synthesis of this nucleotide is restricted to the nucleus of the cell<sup>5</sup> and