LETTERS TO THE EDITORS

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Effect of X-Rays on the Rate of Turnover of Phosphatides

IONIZING radiation produces chemical effects on the irradiated tissue which often lead, after a very appreciable lag, to extensive morphological changes. It is of interest to investigate which chemical processes are involved in the immediate effect of the ionizing radiation.

At an earlier date¹ it was found that the rate of turnover of desoxyribonucleic acid is diminished under the influence of X-rays. This was shown by using radiophosphorus as an indicator. From the ³²P content of the desoxyribonucleic acid and that of the inorganic phosphorus isolated from Jensen sarcoma of the rat, it was calculated that of a hundred desoxyribonucleic acid molecules extracted from the sarcoma 2 hours after administration of labelled phosphate, about two had been built up in the course of the experiment. If irradiation with several hundred r. units preceded the administration of labelled phosphate, the corresponding figure was decreased to a half to a third of the above value. The effect of X-rays on the rate of turnover is temporary, disappearing with time. The phenomenon of recovery of the nucleic acid cycle from the effect of X-rays is of importance for the understanding of the different sensitivities of growing and full-grown tissue to the effect of X-rays. In the latter case the average cell is very much further from the mitotic stage than in the growing tissue, and thus has time to recover its normal nucleic acid cycle before any appreciable change in the nuclear structure takes place. This is not the case in the growing tissue where, in the absence of a normal nucleic acid cycle, an anomalous nuclear development takes place with all its far-reaching consequences.

It is not only the rate of turnover of desoxyribonucleic acid that is diminished under the action of X-rays. A similar behaviour is also shown by the phosphatide turnover, as seen from the accompanying table.

EFFECT OF X-RAYS ON THE TURNOVER OF PHOSPHATIDES OF THE CELL NUCLEI AND ON THE TOTAL TISSUE OF THE JENSEN SARCOMA AND THE LIVER OF THE RAT. AVERAGE WEIGHT OF RATS, 150 GM.

Groups of 12 rats	Activity of 1 mgm. phosphatide phosphorus as a percentage of the activity of 1 mgm. inorganic tissue phosphorus			
	Sarcoma		Liver	
	Nuclei	Tissue	Nuclei	Tissue
Controls	2.86	3.75	10.34	20.44
Controls	2.33	2.37	8.15	11.25
Controls	2.75	2.67	11.33	14.25
Irradiated	2.56	2.32	3.29	12.30
Irradiated	1.02	1.52	4.08	8.91
Irradiated	1.44	1.41	4.83	8.20
Percentage decrease due to irradiation	37	38	59	36

To groups of twelve rats, after irradiation with 1,000 r., labelled phosphate is administered, and control groups are treated in a similar way. After the lapse of 2 hours, the sarcomata and livers are pooled separately. An aliquot is used in the determination of the specific activities of the inorganic and phosphatide phosphorus of the tissue, while from the bulk of the material cell nuclei are isolated by the method of Dounce². The specific activities of the corresponding phosphorus fractions of the nuclei are also determined.

As seen from the table, the rate of turnover of the phosphatides in the nuclei is markedly diminished under the effect of X-rays and that in the cytoplasm is also diminished (the greater part of the phosphatides of the tissue is present in the cytoplasm).

No appreciable difference is found between the rates of renewal of phosphatides present in the nuclei and in the cytoplasm of the sarcoma. In the nuclei of the liver, however, the rate of renewal of phosphatides lags behind the rapid turnover of these compounds in the cytoplasm. The question of a possible interchange between the phosphatide molecules of the nuclei and those of the cytoplasm is under investigation.

While irradiation of the sarcoma diminishes the rate of turnover of the total phosphorus of the tissue by 10 per cent only, the corresponding value for the sarcoma nuclei is reduced to a third of its normal value. This result is partly to be explained by the comparatively high content and rate of turnover of the desoxyribonucleic acid phosphorus and phosphatide phosphorus of the nuclei of the sarcoma.

I wish to express my thanks to Prof. H. von Euler for numerous facilities kindly placed at my disposal, to Prof. M. Siegbahn for the radiophosphorus used, and to Miss Marianne Andersen for very efficient assistance.

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¹ v. Euler, H., and Hevesy, G., *Kgl. Danske Vidensk. Selskab. Biol. Medd.*, **17**, 8 (1942); *K. Svenska Vetenskapsakad., Arkiv f. Kemi*, **17**, A, Nr. 30 (1944). Ahlstrom, L., v. Euler, H., and Hevesy, G., *l.c.*, **19**, A, Nr. 9 (1944). Hevesy, G., *Rev. Mod. Phys.*, **17**, 102 (1945). Cf. also Mitchell, T. S., *Brit. J. Radiol.*, **16**, 339 (1943).

² Dounce, A. L., *J. Biol. Chem.*, **151**, 221 (1943).

Sensitization of Muscle to Choline and Acetylcholine, and the Supposed Existence of Choline Acetylase

NACHMANSOHN and his colleagues^{1,2} and Feldberg and Mann³ have suggested the enzymatic synthesis of acetylcholine from choline and acetate in the presence of adenosine triphosphate. The alleged enzyme has been named choline acetylase. The authors used the m. rectus abdominis of frogs to test the quantity of synthesized acetylcholine.

Repeating their experiments, we found that the contraction of m. rectus abdominis of frogs and of the dorsal muscle of leeches in response to choline, concentration $1:10^{-2}$ – $1:10^{-4}$, is greatly increased in the presence of adenosine triphosphate ($1:10^{-4}$ – $1:10^{-6}$), this increase depending on the concentration of adenosine triphosphate. In an earlier communication⁴ we described the same effect of adenosine triphosphate upon muscle contractions produced by acetylcholine.

Since this effect of adenosine triphosphate was not taken into consideration by the authors mentioned above^{1,2,3}, the increase of observed muscle contraction may possibly have been due not to the stimulation of acetylcholine synthesis by adenosine triphosphate, but to the sensitizing effect of this substance upon the test-muscles.

The sensitizing effect of adenosine triphosphate is also of interest in connexion with the observations of Binet and Minz⁵, Bergami⁶, Feldberg⁷, and others, concerning the sensitization of muscle to acetylcholine in the presence of extracts and emulsions of nerve tissue. It is possible that this sensitization is due to the adenosine triphosphate present in these extracts. Further data on this matter will be given in a separate communication.

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⁴ Babsky, E., Korenevsky, O., and Minajev, P., *Bull. Biol. et Med. Exper. de l'URSS.*, **20**, 34 (1945).

⁵ Binet, L., and Minz, B., *C.R. Soc. Biol.*, **116**, 107 (1934).

⁶ Bergami, G., *Physiol. J. USSR.*, **24**, 56 (1938).

⁷ Feldberg, W., *J. Physiol.*, **103**, 367 (1945).

The Pancreas and Alkaline Phosphatase

In various accounts of histochemical studies on the presence of alkaline phosphatase (substrate: sodium- β -glycerophosphate, pH 9) in homologous organs, correspondences (for example, in kidney and intestine) have usually been stressed rather than differences. It seems, however, appropriate to direct attention to the latter in order to place the value of experiments on animals in its proper perspective. If the pancreas is selected for discussion, it is because of the confusion which seems to exist in the literature concerning the phosphatase content of this organ. It is often stated in a general way that the enzyme occurs or has been shown to be present in pancreatic tissue^{1,2}. The fact is that Grosser and Husler³, who investigated the pancreas of cattle, sheep, cat and man biochemically, expressly emphasize the complete absence of the enzyme. Again, Takamatsu⁴, and Kabat and Furth⁵ failed to produce histochemical evidence for the presence of phosphatase in the pancreas of man. Gomori⁶ reported that only in the pancreas of the dog are the smallest ducts strongly outlined in black (phosphatase-positive). I found⁷, in histochemical tests, the epithelial cells, which are related to the duct system of the external secretion of the pancreas, entirely negative in the guinea pig and rat, but strongly positive in the dog (from the centro-acinar cells to the epithelium of large ducts; Fig. 1), thus confirming and extending Gomori's observation.

More recent studies on the rabbit showed that in this species, too, the duct system gives a definitely positive reaction, though somewhat less extensively than in the dog, the centro-acinar cells and smallest ducts being mainly affected (Fig. 2).

Fig. 1

Fig. 2

FIG. 1. FROM PANCREAS OF DOG. CENTRO-ACINAR CELLS, SMALL DUCTS AND A LARGER DUCT HEAVILY PHOSPHATASE-POSITIVE (BLACK). $\times 100$

FIG. 2. FROM PANCREAS OF RABBIT. MAINLY CENTRO-ACINAR CELLS POSITIVE. IN BOTTOM-LEFT CORNER IS PART OF A LARGER DUCT THE EPITHELIUM OF WHICH IS NEGATIVE. $\times 100$