

for the release of the gene-dependent substances. Changes in genetic constitution occur in somatic tissues as the result of mutations or of chromosomal processes like segregation, non-disjunction, etc.; and in germ cells as the result of recombination of genes during the maturation divisions.

An analysis of the few cases in which genetically determined characters can be observed in single cells, in *Delphinium*, *Zea Mays*, the smut fungus *Ustilago* and *Chlamydomonas*, indicates that specific genes can interact with the cytoplasm during the resting state of the nucleus. These genes are concerned in the production of anthocyanes, of specific sexual reactions, and of different morphological characteristics. Further work undoubtedly will increase the number of known cases. It remains to be seen whether examples will be found in which gene-controlled substances exert visible effects after the breakdown of the membrane only, as is possible in some cases of pollen dimorphism.

A more complete discussion of the data will appear in the *American Naturalist*.

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Action of Pancreatic Extract on Fatty Liver

Kaplan and Chaikoff¹ have shown that the fatty infiltration of the liver in depancreatized insulin-treated dogs can be inhibited by the addition of raw pancreas to the usual diet. Dragstedt² and his co-workers then showed that the active factor can be extracted from pancreas by the aid of alcohol. In conjunction with these investigations, we sought to answer the following two questions: (1) whether in normal rats the fat content of the liver can be influenced by a diet of pancreas; and (2) whether a variation in the fat content of the liver is linked with a variation of the carbohydrate content.

Pancreatic extracts were prepared by a method almost identical with that of Dragstedt. Each rat received a quantity of extract per week corresponding to 100–150 gm. of fresh pancreatic tissue.

In normal fed rats (20 per cent casein, 70 per cent starch, 10 per cent fat), no definite differences in the fat content of the liver were evident when the pancreatic extract was added to the diet. When, however, a fatty liver had been produced by diet, an average decrease from 12.8 per cent liver fat content to 5.2 per cent was obtained by administration of pancreatic substance in fourteen experiments. The nutrition period lasted 6–14 days and in two cases 30 days. The diet was as follows: saccharose 45 per cent, butter fat 40 per cent, casein 5 per cent, marmite 5 per cent, salt mixture 5 per cent (Channon³).

Extracts of spleen, brain or liver prepared in exactly the same fashion and fed in the same manner were generally without effect or very much weaker (liver) than those of pancreas. No uniform differences in fat and sugar content of the blood or in the excretion of total acetone bodies were observed as between control rats and rats treated with extract. If the quantity of acetone bodies is assumed to be a measure of fatty acid oxidation, it must be concluded that the pancreatic extract under consideration is without effect on fat oxidation. This conclusion is supported by the fact that in the two experiments of longest duration, no less body fat was found in rats treated

with pancreatic substance than in the control animals. The weights in the treated animals were in general better maintained than in the controls.

As regards the second question, it can be stated that in conjunction with the decrease of fat content of the liver of treated animals no increase of glycogen content could be established in our brief experiments, so that for our conditions at all events the antagonism between fat and glycogen in the liver does not exist. Experiments in this connexion extending over longer periods will be reported later.

It is clear that the rat method possesses great advantages in the investigation of the pancreatic substance. This substance could not be demonstrated in the outer medium after extended dialysis through parchment membranes. Positive results could be obtained, however, after a brief period of dialysis through 'Cellophane' and cuprophane. A strongly positive effect is obtained with pancreas autolysate. It is not quite clear as yet, however, if this effect is absolutely specific. The question whether the active principle in pancreas is choline (Best) has to be clarified. The fact that the quantity of choline necessary according to Best could not have been contained in the quantities of extract fed by us is against this conclusion, as is also the ineffectiveness of extracts of the other organs mentioned. Moreover, choline is adsorbed by Lloyds reagent and can be eluted by barium hydroxide. These tests failed with the pancreatic substance under consideration.

After the experiments here reported had been concluded, a paper was published by Eaton M. MacKay⁴, in which the rat method for the demonstration of the action of pancreas on liver fat was used. His results are consistent with ours.

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¹ Kaplan, A., and Chaikoff, J. *Biol. Chem.*, **108**, 201 (1935); **119**, 435 (1937).

² Van Prohaska, I., Dragstedt, L. R., and Harms, H. P., *Amer. J. Physiol.*, **116**, 122 (1936); **117**, 166, 175 (1936).

³ Channon, H. J., and Wilkinson, H., *Biochem. J.*, **30**, 1033 (1936).

⁴ MacKay, E. M., *Amer. J. Physiol.*, **119**, 783 (1937).

Specific Action of Ferricyanide on Aerobic Glycolysis of Tumour Cells

It has been found¹ that ferricyanide (10^{-2} mol./litre) stops aerobic glycolysis of mammalian tumour cells, but it does not affect anaerobic glycolysis of any cell in mammals. In this respect, ferricyanide differs fundamentally from all other substances which have been found to check glycolysis (fluoride², monoiodoacetic acid³, glyceric aldehyde⁴).

Ferricyanide is reduced by tumour cells, probably combining with and inactivating some part of their glycolytic system. The action of ferricyanide outlasts the time of its application: tumour cells once deprived of their aerobic glycolysis by ferricyanide do not glycolyse aerobically for many hours if kept in a medium no longer containing ferricyanide.

In order to find out whether the action of ferricyanide would be restricted to glycolysis of tumour cells and thus be specific, experiments were done with medulla of kidney, which has been found^{5,6} to be the only normal mammalian tissue with aerobic glycolysis. Rat, cat and guinea pig kidneys were used. In no case did ferricyanide check the aerobic