choroid tissue. Comparable data on the mitochondrion are collated from various authors. The values given are extreme ranges found for several determinations. Melanin granule data are corrected for the presence of contaminating sand.

Not accounted for in the above analysis was some 15 per cent of the granule. This fraction appeared to have a nitrogen content of 15–20 per cent. It contained an acid-soluble red-brown pigment and, possibly, difficultly hydrolysable protein. The high nitrogen content suggests that the fraction not accounted for contained little lipid. It would appear that all or most of the lipid of the granule had been estimated by the initial extraction procedure.

For every constituent, there is a great difference between the compositions of the melanin granule and the mitochondrion. Especially significant is the low lipid and content of ribonucleic acid of the melanin granule in contrast to the high content of these constituents in the mitochondrion. The high copper, zinc and iron content of the melanin granule is particularly noteworthy. Most of, if not all, these mineral constituents appear to be localized in the melanin granule.

The above results do not support the view that the mitochondrion is converted into a melanin granule by a simple process of 'melanization'. If a conversion does occur it would appear to involve a drastic reorganization of the cell contents. It seems desirable to regard the melanocyte as a whole as being involved in the formation of the melanin granule, rather than the granule in isolation.

A further report of the above findings and their bearing on the problem of melanogenesis will, it is hoped, be published elsewhere.

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Production of Cancer of the Bile Ducts with Thioacetamide

During the past ten months, I have been feeding rats on thioacetamide with the object of studying chronic intoxication induced by that compound. 1 gm. of thioacetamide was dissolved in 60 ml. absolute alcohol, thoroughly mixed with 3,125 gm. of M.R.C. powdered rat cubes, and the alcohol evaporated off. One hundred and fifty rats received unlimited amounts of this mixture; fifty had the control diet consisting of powdered cubes mixed with absolute alcohol in the same ratio as in the experimental mixture. Groups of animals were killed at regular intervals from each batch for a careful study of the liver pathology.

The earliest changes of necrosis and monocellular infiltration soon gave place to proliferation of the bile ducts and regeneration of the liver cells. After feeding for eleven weeks with thioacetamide, localized areas of cholangiofibrosis—a term used by Opie[1] in his study of butter yellow (*p*-dimethylaminoazobenzene) tumour formation—appeared and increased progressively until at nineteen weeks they formed large nodules indistinguishable from cancer of the bile duct. Less frequently, collections of cystic bile ducts also developed, but neither hepatomas nor metastases have so far been encountered. These pathological changes recall those met with in rats fed with butter yellow[2], and they likewise develop in the same sequence. Of the 150 rats exposed to thioacetamide, about fifty died before the ninth week from destruction of the liver; of the thirty-six animals killed between nine and twenty-three weeks, twenty-two showed cholangiofibrosis, eighteen bile duct cancers and five cystic dilatation of bile ducts. Several conditions are, of course, not infrequently found in the same animal. Feeding is still going on in the remaining sixty rats. No such changes were found in the control rats. Under these conditions, therefore, it appears that thioacetamide is a powerful cause of bile duct proliferation which culminates frequently in cancer.

Fitzhugh and Nelson[3] described liver cirrhosis in rats fed with thioacetamide and mentioned tumours in two of fifty rats, one said to be a liver cell adenoma, the other a "histologically malignant tumour originating from liver cells". A more detailed study by Rather and his co-workers[4] emphasizes gradually developing diffuse fibrosis, nodularity of the liver and increase in weight of that organ. Apparently no tumours were discovered. Taki *et al.*[5] describe experiments in which groups of rats were fed butter yellow alone, thioacetamide for six to eight weeks followed by butter yellow, and thioacetamide and butter yellow together. No tumours developed; but the duration of these experiments was rather short and details presented are scanty.

Thioacetamide was introduced by Childs and Siegler[6] in 1945 as a medium for the control of orange decays. It is known to penetrate to the juice of the orange, and must therefore be considered as a possible risk to consumers of oranges. I must emphasize that the carcinogenic effects in rats have been obtained only after prolonged feeding, although the quantity of thioacetamide consumed by a rat each day cannot have been more than a few milligrams.

The investigation, which was suggested by Prof. G. R. Cameron, is still going on and full details will be published in due course.

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