THE MITOCHONDRIA OF THE HEPATIC CELL DURING
CHOLAGOGIC STIMULATION. 1

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My previous studies on the mitochondria of the liver of animals that
had received whole bile to stimulate additional hepatic secretion disclosed
no modification of these elements from the normal condition. It was con-
cluded that there was a slight tendency for the chondriosomes to become
more clumped in the experimental than in the control specimens, but that
they were unaltered in shape and size. Seven species, the cat, rabbit,
chicken, pigeon, guinea pig, white mouse and white rat, were employed
in the work (KATER 1933). Despite the relatively extensive material
some question has arisen in my own mind as to the validity of the con-
clusion. This doubt came from two sources. First, although whole bile
was given the experimental animals, administered orally or by subcu-
taneous injection, no measurement of the bile secretion was made. So
the conclusion rested upon the assumption that the bile had exerted
cholagogic effect. Second, in the extensive studies of NOËL (1923) the
numerous alterations of mitochondrial morphology that accompany
digestive processes were interpreted as probable expressions of activity
in the secretion of bile rather than in response to the other functions of
the liver. This contradiction suggested the desirability of testing the
experimental studies on one of the animals formerly used to determine
whether or not the methods were accurate. Some investigations that
purport to deal with this problem, such as merely tying the bile duct
and bathing excised bits of liver in bile salts, need not be considered in
relations to this work, since they could not possibly relate to the central
question involved.

Material and Methods.

The rabbit was selected because of its size and ease of handling, a
relatively large laboratory animal being necessary to keep any error in
the measurement of bile secretion at a minimum. This report is based
upon the study of twenty-four specimens; the relatively great number
was used in order to have enough readings to clearly establish the con-
clusion, and avoid the former lack of definiteness.

1 A portion of the specific expenditure required for this work was supplied by
the Grants-in-Aid Committee of the National Research Council.
As the determination of the quantity of bile secreted required surgery it was obviously desirable to find an anaesthetic which would not disrupt the control element. It is known that both chloroform and ether distinctly modify the cytology of the liver (Kater 1931); so sodium amytal was tested and found to be satisfactory (Kater 1935). Therefore the term "control" as used in the present report signifies a rabbit that had received its last meal of grain and greens twenty-four hours previously and had been anaesthetized with sodium amytal, 1 grain per kilogram body weight generally being sufficient.

The experimentals, of course, were taken under the same conditions, with bile in addition. A relatively impure sodium taurocholate (Digestive Ferments Co.) was given orally in gelatin capsules, one gram per kilogram of body weight, or by the much simpler and preferable method of dissolving the salt and injecting directly into the stomach through the left side.

The rate of bile secretion was determined in two ways. For half of the rabbits only relative measurements were made; for the others the amount of bile secreted was determined quantitatively. In the former the body cavity was opened, the cystic duct tied off, the common bile duct severed at the point of connection with the duodenum, clamped with a haemostat and then drained as rapidly as it filled. For the quantitative measurements the cystic duct was ligated and a cannula inserted in the common bile duct at the duodenal end. To avoid back pressure, resulting from the small bore of the tube, a hypodermic needle was slipped into the cannula and the bile withdrawn with a syringe. By using a calibrated syringe the bile was measured as it was extracted.

The different specimens were kept on the operating table for periods varying from one-half to two hours, the minimum being the most frequent time. Experimental material was taken in periods ranging from three to twenty-four hours after administration of sodium taurocholate.

The mitochondrial preparations were made according to Regaud's method.

Observations and Discussion.

The rate of secretion of bile is extremely variable in control rabbits. In fact, it is much more irregular in the controls than in those that have received artificial stimulation. In those whose bile was measured relatively, the lowest required five minutes to fill the common bile duct, while the highest consumed only two minutes. This is a greater variation than that encountered in the rabbits on which quantitative measurements were made, the amount ranging from 0.2 cc. to 0.35 cc. per minute.

For three hours after receiving the sodium taurocholate there is no change from the controls, but beginning at that time there is a sudden and rapid increase in the flow of bile. The peak is reached in four and one-half to five hours, and is maintained for a period of one-half hour