Increased Viscosity of Cells of Induced Tumors*

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In an earlier study (1) the authors found that tumor cells (carcinoma, sarcoma, adenofibroma, adenocarcinoma) of rats remained unstratified or stratified but feebly when centrifuged at extremely high speeds. In that series of experiments the tumor tissue was first transplanted to such organs as adrenal gland, kidney, pancreas, liver, spleen, stomach, and intestine. After growth was well established, bits of the transplant together with pieces of the host tissue were rotated in a Beams air-driven ultracentrifuge at a speed which produced a displacement pull of about 400,000 times that of gravity. Invariably the cells of the normal tissues became markedly stratified; those of the tumor tissue remained largely unchanged. It was inferred therefore that the protoplasm (both cytoplasm and karyoplasm) of the latter had become so viscous that the cellular contents were unable to move freely and take positions according to their respective densities.

In the present study advantage has been taken of the well-known tendency of butter yellow, p-dimethylaminoazobenzene, to induce cancer of the liver after prolonged feeding. The liver tissues used were from rats which had lived on a ration containing butter yellow for from 1 to 689 months. We are indebted to Van Rensselaer Potter of the McArdle Cancer Research Institute for liver tissue from the 24 rats used in this study. After treatment was begun the animals were killed, 3 at a time, at the end of 4, 6, 8, 10, 13, 18, 21, and 26 weeks respectively. The photomicrographs (Figs. 1 to 7), illustrating the cytological effects observed, were made from paraffin sections of tissue fixed in Bouin's fluid and stained with Harris' hematoxylin and eosin or acid fuchsin.

The purpose of our investigation was to find out if the cells of such induced tumors showed increased viscosity in comparison with adjoining normal cells centrifuged at the same time, and if so, what could be determined about the onset of the condition.

For purposes of general histological guidance and comparison we depended mainly on Orr's (2) recent careful study on the histology of the rat's liver during the course of carcinogenesis by butter yellow. Of 136 rats fed on a diet containing butter yellow and killed at intervals through a period of from 1 to 11 months, Orr found that 56 displayed tumors, of which 43 were definitely malignant. The tumors described by him were of three types: (a) bile duct carcinomas (cholangiomas); (b) bile duct cystadenomas; and (c) liver cell carcinomas (hepatomas). Any particular liver might contain all three kinds or any one or two.

Occurrence of excessive proliferation of ducts and the presence of cystic bile ducts were usually the first indication of a definitely affected liver. Almost invariably, in the vicinity of such proliferative centers, certain areas of the liver cells lose their characteristic corded arrangement and become more or less nodular in appearance, although nonneoplastic liver cells may remain scattered throughout the developing tumor. Within such disorganized masses of cells, tubules or cysts begin to appear—first with small lumina and thick walls of columnar cells. As the tubules become fully developed the cells of the walls become cuboidal and eventually flattened. Such cells in all stages of

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Fig. 1.—Photomicrograph of section of normal liver of the rat showing stratification of the component cells after centrifuging for 1 hour. The vacuoles below the nuclei represent regions originally occupied by glycogen which has been dissolved out by treatment with water. Mag. X 430, approx.

Fig. 2.—Photomicrograph of section of centrifuged normal liver stained for glycogen only. The glycogen has been displaced to the centrifugal side of the cell. Mag. X 430, approx.

Fig. 3.—Photomicrograph of section of a nodule of the liver of the rat showing effects of administration of butter yellow. Mag. X 430, approx.

Fig. 4.—Photomicrograph of section of tissue from a nodule in the same liver as that from which the section shown in Fig. 3 was taken. After an hour of severe centrifuging the cells remain unstratified. Mag. X 430, approx.

Fig. 5.—Photomicrograph of a representative area of centrifuged tissue from the liver of a rat after 6 months' treatment with butter yellow, showing proliferation of bile ducts, granulation, and pyknosis. Mag. X 100, approx.

Fig. 6.—Photomicrograph of section of the same liver as that from which the tissue shown in Fig. 5 was obtained. After an hour of severe centrifuging the cells of the ducts and cysts remain unstratified. Mag. X 430, approx.

Fig. 7.—Photomicrograph of a section from a carcinomatous nodule in the liver of a rat after six months' treatment with butter yellow. Mag. X 430, approx.
were fixed in alcohol and stained specifically for
appear to show two vacuoles, one on the centrifugal
cell. This was puzzling for a time until similar cells
stratification (Fig. 1). Some of the centrifuged cells
superabundant cysts and ducts (Figs. 5 and 6).
also true of the cells constituting the walls of the
remain unstratified after being centrifuged. This was
containing scattered large cells. Longer feeding of
the cells of which, like those of typical carcinomas,
butter yellow led to the occurrence of definite tumors
Whether or not this indicates the onset of malignancy
intensified staining indicating chemical change, and,
coming visible, (Fig. 3) the affected regions showed
perhaps indicated by the occasional occurrence of areas
2 months, where evidence of neoplasms was just be-
incipient tumor cells seen after some 2
viscosity apparently comes on fairly early since it is
evident in incipient tumor cells seen after some 2 months of feeding butter yellow. It is suggested that
the increasing lactic acid output of the abnormal cell may be the cause of its enhanced viscosity.

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