fers a means of detecting MAO inhibition directly, and when used in conjunction with other technics, serves to enlarge the pharmacology of various drugs.

Summary. A method for measuring activity of monoamine oxidase inhibitors as a function of suppression of 5-hydroxy-indoleacetic acid (5-HIAA) excretion is described. Increased excretion of 5-HIAA after 5-hydroxytyramine (5-HT) is effectively blocked by orally administered iproniazid, JB-516, and several harmala alkaloids. Correlation of these results with increased brain 5-HT is presented. Instances of non-correlation such as lack of effect of oral harmine on brain 5-HT with concomitant suppression of 5-HIAA excretion are discussed.

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Induction of Plasma-Cell Neoplasms and Fibrosarcomas in BALB/c Mice Carrying Diffusion Chambers. (24970)

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Plasma-cell neoplasms are rare in mice (1,2). Rask-Nielsen(2) increased the incidence of these tumors in mice of 2 strains by injecting a carcinogen into the thymus. The findings reported here suggest that a new method of inducing plasma-cell tumors has been found. Seven plasma-cell tumors arose in mice in 2 experiments which were set up by Dr. Algire for another purpose. The tumors arose in BALB/c mice, a strain in which plasma-cell tumors have not been found previously. These induced tumors are of particular interest because at least 4 are transplantable and synthesize abnormal proteins. Six spindle-cell sarcomas also arose but similar tumors have been found in other experiments in association with diffusion chambers. Experiments are now in progress to obtain more information about induction of plasma-cell tumors, but since it will require a year or more to complete them, preliminary findings are reported now.

Procedure. Diffusion chambers were of the cell-impenetrable type described by Algire(3). The chambers were made of lucite rings and Millipore membranes which had pores averaging 0.10, 0.05 or 0.01 μ diameter. Tissue for placement in the chambers was obtained from spontaneous mammary tumors that arose in C3H mice carrying the milk agent. Two tumors were used, one in each experiment. A piece of tumor tissue about 0.5 mm diameter moistened with balanced saline containing tris buffer, horse serum, penicillin and streptomycin(3), was sealed into each chamber. The chamber was inserted into peritoneal cavity of agent-free BALB/c female mouse 5 or 6 weeks

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of age. A 5 mg pellet of 5 or 10% diethylstilbestrol in cholesterol was placed subcutaneously when mouse was 2 to 4 months of age. Additional mice in each experiment received intraperitoneal injection of balanced saline containing 0.04 ml of a tissue mince of the mammary tumor tissue. These mice also received stilbestrol.

Results. Forty-six mice carrying diffusion chambers survived 6 months or longer. By 17 months, 7 had developed plasma-cell tumors and 6 had developed sarcomas (Table I). The 7 tumors identified histologically as plasma-cell tumors were inoculated into BALB/c mice. Two have not yet grown at 4 and 22 weeks respectively. Another grew on transfer for one generation but was not transferred again. Four have been successfully transplanted for 2 or more generations. In the first generation at least one tumor in each line grew at site of inoculation within 4 to 11 weeks. One tumor that grew in BALB/c mice, was inoculated at the same time into C3H mice where it failed to grow. Two of 6 sarcomas were transferred to both C3H and BALB/c mice but they grew only in strain BALB/c. A small fibrosarcomatous growth was found on connective tissue coating removed from one diffusion chamber. This chamber was placed in a second host and 2 months later a fibrosarcoma with areas of ossification was found in the abdominal cavity. One or 2 mice in each cage died for reason other than growth of plasma-cell tumors or sarcomas. Three had ascites but no abnormal growths were found. Twenty-one mice are still living. Neither plasma-cell tumors nor sarcomas developed in any of the 38 mice that survived over 6 months after receiving an intraperitoneal injection containing mammary tumor tissue.

TABLE I. Incidence of Plasma Cell Tumors and Sarcomas in Strain BALB/c Mice 6 to 17 Months after Intraperitoneal Implantation of Diffusion Chambers Containing C3H Spontaneous Mammary Tumor Tissue.

Diffusion chamber, avg pore size (μ)	Incidence: Mice with tumors / No. with chambers — Exp. I: Plasma-cell tumors	Exp. I: Sarcomas	Exp. II: Plasma-cell tumors	Exp. II: Sarcomas
.10	1/9	1/9	0/6	1/6
.05	1/8	0/8	1/7	3/7
.01	4/8	1/8	0/6	0/6

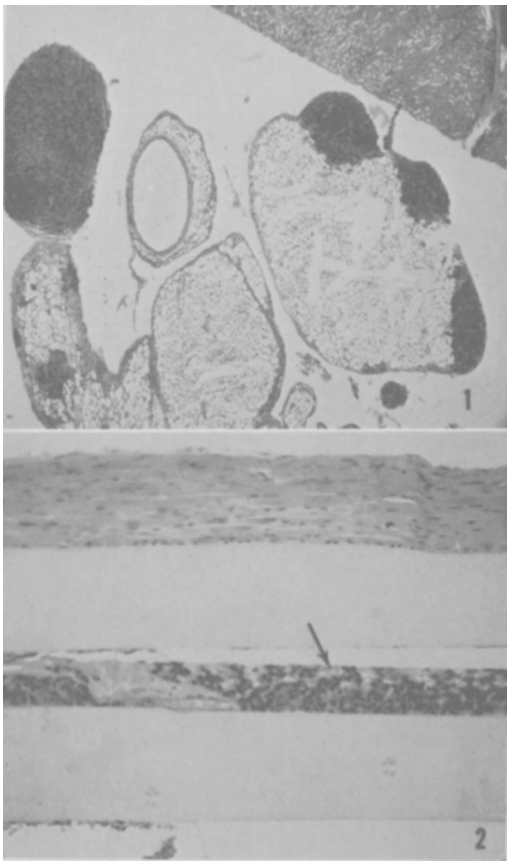

FIG. 1. Four nodules composed of neoplastic plasma cells attached to peritoneal surface where peritoneum covers adipose tissue of mesentery. Hematoxylin and eosin. × 25.

FIG. 2. Portion of cross section of diffusion chamber showing mammary tumor tissue (arrow) between 2 millipore membranes and showing layer of host fibrous tissue on outside surface of one of the membranes. Hematoxylin and eosin. × 105.

Pathology. The 7 mice with plasma-cell tumors had detectable ascites from less than 2 weeks to over 3 weeks at time of autopsy. In 5 of the 7 mice, the ascites was bloody. One side of diffusion chamber was close against the liver in most mice and the other side was coated with thick layer of connective tissue. Small nodules of tissue were distributed over entire peritoneal surface (Fig. 1). Larger nodules of various sizes were found in 5 mice but none were attached to tissue around the chamber. In contrast, in all mice

with sarcomas the largest and in some cases the only tumor mass was attached to connective tissue coating around the chamber.

Microscopically the plasma-cell neoplasms were composed of large cells with plasma-cell characteristics. Metastases were frequent. They were found in ovary, pituitary, spleen and lymph nodes. One tumor line caused a myeloma type change in kidney and another line produced osteolytic lesions.

Either whole mounts or sections were made of the porous membrane with adjacent cell layers from some diffusion chambers (Fig. 2). Viable appearing mammary tumor tissue was found in 4 of 5 chambers from mice that developed plasma-cell tumors. Histologically recognizable mammary tumor tissue was present in 3 of the 4 chambers taken from mice with sarcomas. The cells appeared necrotic in one chamber but the tissue surrounding the chamber was also necrotic.

Discussion. Induction of plasma-cell tumors was an unexpected result of these experiments originally set up to study passage of mammary tumor agent through pores of various sizes. The findings on mammary tumors will be published separately.

Unpublished observations show that rings, each with 1 membrane attached, induce sarcomas when implanted subcutaneously, but further experiments are needed to elucidate the role of diffusion chamber parts, the tissue inside the chamber and the stilbestrol in induction of plasma cell tumors.

Summary. Seven plasma-cell neoplasms and 6 fibrosarcomas developed in strain BALB/c mice that carried diffusion chambers in the peritoneal cavity. The diffusion chambers contained mammary tumor tissue obtained from strain C3H mice with the milk agent. Five plasma-cell tumors and all sarcomas were successfully transplanted to strain BALB/c mice. The 2 plasma-cell tumors and the 2 sarcomas transplanted to C3H mice failed to grow.

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Regulation of Cholesterol Oxidation by Liver *in vitro*.*† (24971)

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Careful balance studies of absorption and excretion of bile acids and cholesterol in rats (1) indicated that administration of bile acids in the diet depresses mobilization of liver cholesterol. Further analysis of this phenomenon in both rats(2,3) and mice(4) has shown that both rates of synthesis and mobilization of liver and adrenal cholesterol are reduced upon feeding bile acids. Bile acids are major products of cholesterol catabolism in the liver (5). Daily production of bile acids in the rat is greatly enhanced when enterohepatic circulation of acids is interrupted by cannulation of bile duct(6,7). Bergstrom and Danielsson(8) showed that it is the concentration of bile acid conjugates in portal blood which actually influences rate of further synthesis of bile acids in the liver. These findings indicate that *in vivo*, the level of recirculating bile salts controls cholesterol catabolism in liver and further production of bile acids. We have now observed this "feedback effect" in an *in vitro* system prepared from rat liver, which oxidizes cholesterol to CO_2 and bile acids (5,9).

Methods. Cholesterol-27-C^{14} was synthesized from 3β-hydroxy-5-norcholestene-25-one(10-11) and purified *via* the digitonide

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