related to it both in antigenic composition and biological characteristics.

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GONADECTOMY AND ADRENAL NEOPLASMS

CARCINOMA of the adrenal cortex is a relatively rare type of tumor in both man and in experimental animals. In man these neoplasms have been of unusual interest because of sexual disorders which have been associated with them. In experimental animals, carcinomas of the adrenal cortex have appeared too infrequently for critical study. Observations in this laboratory, however, indicate that primary carcinomas of the adrenal cortex can be produced in a high percentage of the individuals of at least one strain of mice by means of gonad removal.

It has been found that when mice of the extreme dilution strain (ce) were gonadectomized at two days of age, carcinoma of the adrenal cortex occurred in a high percentage of cases. Table 1 shows the frequency of these in various age groups up to one year. No such tumors have so far been observed in normal male and female mice of the ce strain. Adrenals of these mice are being studied in more detail, however.

Present knowledge indicates that sex hormones have an influence in the formation of certain types of neoplasms in mice. Increasing or decreasing these hormones is effective. It has been shown that injections of estrogenic hormones have been instrumental in

TABLE 1

Sex	Mice of ce strain Age at autopsy: 4 months		6–7 months		8–10 months		11–12 months	
	No. of mice	Per cent with adrenal cancer	No. of mice	Per cent with adrenal cancer	No. of mice	Per cent with adrenal cancer	No. of mice	Per cent with adrenal cancer
Ovariectomized ♀♀ ...	4	0	9	88.9	3	100	6	100
Castrated ♂♂ .	4	0	7	28.6	7	85.7	5	100

producing interstitial cell tumors of the testes,[1] carcinomas of the cervices,[2] adenomas of the hypophyses[3] and mammary gland carcinomas[4] in mice. In the dba strain of mice gonad removal resulted in nodular hyperplasia of the adrenal cortex and carcinomatous changes of the mammary gland in both sexes.[5, 6] It seems likely that all these results may be explained by the theory that hormonal imbalance is at least one of the factors leading to these forms of cancer. A more detailed study is to be reported elsewhere.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

IMPROVED APPARATUS FOR LIVER PERFUSION

LIVER perfusion studies in which the R.Q. of the liver was found from the arterio-venous blood gas differences have resulted in extremely low R.Q.'s which have been interpreted as support for the theory that oxygen is being utilized by the liver in the formation of carbohydrate intermediates from fatty acid or fatty acid intermediates. The methods used in former studies did not control or measure the escape of CO_2 from the surface of the liver. It is conceivable that the amount of CO_2 passing from the liver into the surrounding air is considerable and would be related to the tension of the CO_2 in the perfusate and the production of CO_2 by the liver. If this loss of CO_2 from the liver could be measured exactly in terms of volumes per cent. of CO_2, the A.V. R.Q. could be corrected for the amount lost.

The escape of appreciable amounts of CO_2 is demonstrable by perfusing the liver in an air-tight tin box of known volume as shown in the accompanying diagram (Fig. 1). The box is washed out with warmed outside air at the start of the experiment. At the end of a given period of time the air in the box is sampled and analyzed for CO_2 and O_2. The CO_2 which enters the box from the surface of the liver is expressed in volumes per cent. from the total volume of perfusate passing through the liver during the period. The oxygen level in the box remains constant providing there are no leaks in the circulating system.

In Table 1 the average loss of CO_2 in volumes per

1 C. W. Hooker, W. U. Gardner and C. A. Pfeiffer, *Jour. Am. Med. Asn.*, 115: 443–445, 1940.
2 E. Allen and W. U. Gardner, *Cancer Research*, 1: 359–366, 1941.
3 W. Cramer and E. S. Horning, *Lancet*, 1: 247–249, 1936.
4 A. Lacassagne, *C. R. Acad. Sci.*, 195: 630, 1932.
5 Elizabeth Fekete, George Woolley and C. C. Little, *Jour. Exp. Med.*, 74: 1–8, 1941.
6 George Woolley, Elizabeth Fekete and C. C. Little, *Endocrinology*, 28: 341–343, 1941.

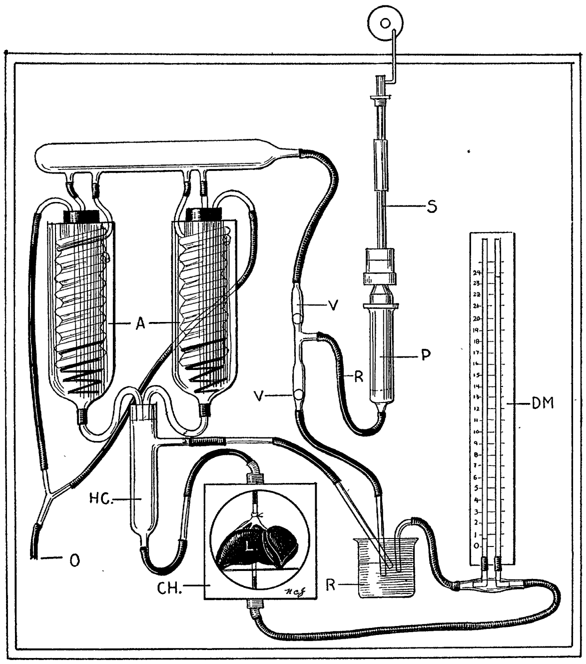

FIG. 1

cent. is 0.25 vol. per cent. This loss of CO_2 from the surface of the liver is sufficient to explain many of the R.Q.'s (arteriovenous) below the level found for the whole organism during starvation, reported in the literature (*e.g.,* Blixenkrone-Møller.[1]).

TABLE I

Arterial Vol. % CO_2	Venous Vol. % CO_2	Vol. % Diff.	A.V. R.Q.	Venous return cc/min gm of liver	ml CO_2 lost min gm of liver	Vol. % correction	Corrected R.Q.
11.01	11.56	0.55	.42	1.8	.0073	.26	.610
9.57	10.37	0.80	.73	1.8	.0055	.26	.965
7.71	9.87	1.87	.57	0.8	.0041	.48	.880
5.5	6.35	.85	.43	2.6	.0039	.19	.530
11.10	12.05	.95	.74	1.8	.0038	.21	.907
6.38	6.85	.47	.66	2.5	.0035	.13	.840

The apparatus shown (Fig. 1) is designed to eliminate several other sources of error as well in the perfusion technic, such as the loss of fluid by evaporation, wide fluctuation in CO_2 and O_2 levels of the perfusate, edema of the liver, turgence and discoloration caused by excessive hydrostatic pressure. Pressure can be kept constant and absolutely controlled within limits found for the portal vein of the cat. The volume of flow through the liver can be held constant and controlled.

The venous return can be estimated for a given period of time by means of the differential manometer (d.m.). A master curve is prepared by plotting the difference in height (h) between the two manometers when various volumes of perfusate are passing through the system (V) per minute. When V is plotted against $\sqrt{h}$ a linear relation is found between the values 80 cc/min and 250 cc/min for V. An extrapolation of this line intercepts the $\sqrt{h}$ axis at a distance (C) from zero. *K* is calculated in the formula $V = K\ (\sqrt{h} - C)$ and is constant between the above limits. Therefore, during an experimental run the differential reading (h) is taken at three levels of (V) venous return and *K* for this experiment is calculated. When *K* for a particular experiment differs from *K* for the master curve described above, h for the experiment is accordingly corrected and the venous return for any particular time can be estimated to within 1 per cent. error from the manometer reading by finding the V value on the straight line, *V* plotted against $\sqrt{h}$.

[1] *Zeit. f. Physiol. Chemie,* 252: 117, 1938.

The sequence of flow through the apparatus shown below is as follows: blood passes from the reservoir (R) through the lower valve (V) to the pump (P), then through the upper valve (V) to the oxygenator (O) and to the hydrostatic column (H.C.), thence to the liver in the box (CH, closed by a friction lid) by way of the portal vein and leaves the liver by the hepatic vein passing the differential manometer (d.m.) and returns to the reservoir.

Oxygen bubbles through warm water and passes downward through the center of the spiral cylinder, then upward around the outside spirals. Perfusate passes down both the outside and inside spirals. There appears to be no loss of fluid by evaporation and the oxygen level in the perfusate remains reasonably constant in a given experiment, which in itself is indicative of a constant volume. The perfusate always to be preferred is one which most closely approaches the O_2 and CO_2-carrying capacity of whole blood and to which a compatible anticoagulant is added.

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