Liver Weight Changes During Distant Growth of Transplanted Tumor[1] (34952)

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Enlargement of the tumor-free liver in the tumor-bearing animal has been reported with a variety of spontaneous and experimental tumors (1–6). Hepatomegaly in the absence of hepatic metastases has been described in humans with cancer of the gastrointestinal tract and hypernephroma (7, 8). Although the liver of the tumor-bearing animal has a higher water content than the control (1, 9–11) the increased weight of this organ cannot be attributed only to water retention because both the dry weight and the total nitrogen of the tumor-free liver of the host have been found elevated (12–14).

The purpose of the present study was to follow the dry liver weight changes during the tumor growth and to correlate these changes to the tumor weight and to the carcass weight.

Materials and Methods. C3H (Bittner Zb) mice of both sexes, 5–6 weeks old, were used to receive the tumor transplant. Two different transplantable tumors were used. The first was a spontaneous mammary cancer that arose in an old female C3H (Bittner Z) mouse. This tumor when transplanted subcutaneously kills the majority of the animals by the ninth week. The second tumor was a transplantable ascites tumor 6C3HED, originally a lymphosarcoma (15). This tumor can grow as a rich ascites tumor when injected intraperitoneally or as a solid tumor when transplanted subcutaneously. The solid phase when minced and injected intraperitoneally can convert to the ascitic phase immediately (16). When transplanted subcutaneously this tumor kills most of the animals by the sixth week.

[1] This work was supported by Grants CA-05158, CA-08832, and CA-08101 from the National Cancer Institute.

Animals were matched in pairs of the same age and sex and similar weight within 0.4 g of weight difference at most. One partner in each pair received the tumor and the other served as its control.

The mammary tumor was minced and suspended in normal saline, and 0.2 ml of this suspension was injected subcutaneously on the back of the recipient. The control animal received a suspension of thigh muscle from the tumor donor. For the second series of experiments, the lymphosarcoma tumor in the ascites form from several donors was pooled together and 0.2 ml of the pooled ascites was injected subcutaneously on the back of the recipient. The controls received normal saline injection.

The animals were fed Purine Laboratory Chow and water *ad libitum* and were kept under standardized environmental conditions. Eight to ten pairs of animals were sacrificed every week starting with the second week after transplantation. The weight of the total animal, and after dissection, the wet weight of the liver, the tumor of the tumor-bearing (experimental), and the carcass (body minus liver and minus tumor in the experimental animal) were determined. All specimens were then dried for 24 hr at 110° and the dry weight of the liver, tumor, and carcass were determined again (to 0.0001 g).

The carcass weights include the gastrointestinal tract contents. These contents might be somewhat higher in the control than in the tumor-bearing animals because of the anorexia and lower food consumption of the experimental mice.

In the last week of the experiments, necrosis and hemorrhage were present in most mammary and lymphosarcoma tumors.

The tumors used grow locally and do not

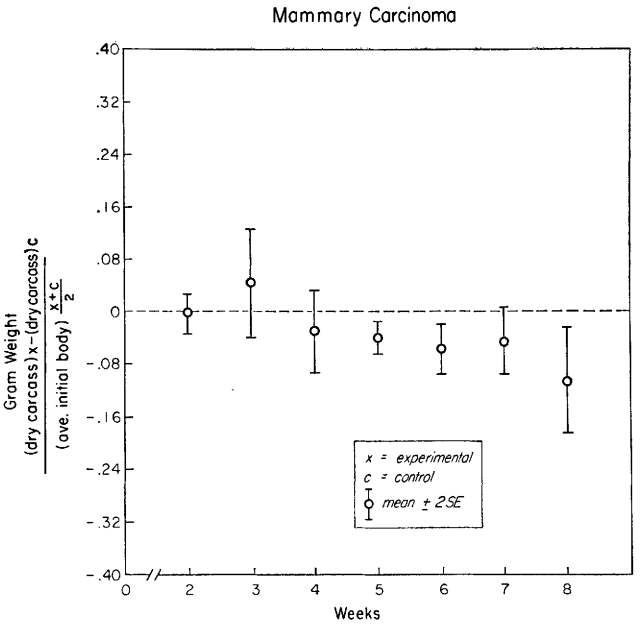

FIG. 1. Dry carcass weight changes in mice during the growth of transplanted mammary carcinoma.

metastasize. The liver of the host has been shown to be free of tumor throughout the study period, both on histologic sections and with transplantation experiments in which liver of the tumor-bearing animal was transplanted subcutaneously or intraperitoneally and no growth was observed in the recipients.

Results. During the growth of the mammary carcinoma the dry weight of the carcass of the experimental animal progressively decreased (Fig. 1). The ratio of the dry weight of the liver over total animal (carcass + liver + tumor) kept increasing as the tumor grew (Fig. 2). To determine whether this increase of the ratio of dry liver over dry total animal is not due to the mere loss of weight by the carcass, the carcass weight loss of the experimental animal was taken into consideration. The same ratio was determined as in Fig. 2 substituting the carcass weight of the experimental by the carcass weight of its control partner. Significant increase in the dry liver weight was observed (Fig. 3) and, therefore, the increase in the dry liver weight was absolute and not relative resulting from the decrease in carcass weight of the host. A direct relationship between liver weight gain and tumor weight increase was found (Fig. 4).

With the more rapidly growing lymphosarcoma, the carcass had lost already significant weight by the second week (Fig. 5) and its weight remained unchanged after the third week despite further tumor growth. The liver, too, had gained significant weight by the second week (Fig. 6). As with the mammary carcinoma, the carcass weight loss contributed but could not account for the total increase of the ratio of dry liver over dry carcass, liver, and tumor of the experimental animal, but there was actual absolute dry liver weight gain. There was again a correlation between liver weight gain and tumor weight increase but the correlation was not as good as with the slower growing mammary carcinoma.

Discussion. This increase of the dry liver weight of the tumor-free liver in the tumor-bearing animal represents one of the remote effects of cancer on distant organs and tissues. The liver weight gain has been attributed to work hypertrophy concomitant with the synthesis of neoplastic tissue (3) comparable to what occurs during pregnancy (17). In-

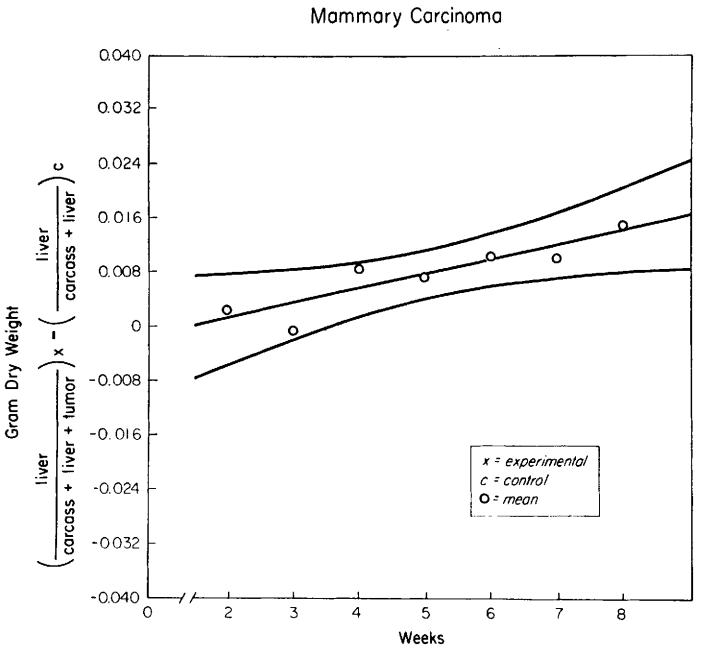

FIG. 2. Changes in the ratio of dry liver weight to total body weight in mice during the growth of transplanted mammary carcinoma. Least-squares line with 95% confidence bands.

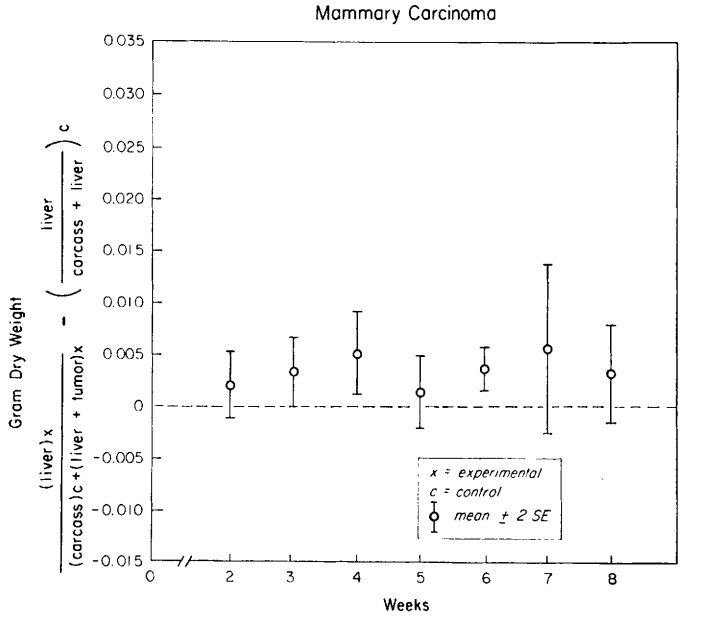

FIG. 3. Changes in the ratio of dry liver weight to total body weight in mice during the growth of transplanted mammary carcinoma. The carcass weight loss of the experimental animal was taken into consideration by substituting carcass C for X. After the second week the difference of the means from zero is significant at the less than 5% level.

creased turn-over rates of various metabolic components and increased mitotic activity in the liver of the host have been described in both the resting liver and the regenerating liver after partial hepatectomy (18, 19). However, the mechanism by which the tumor

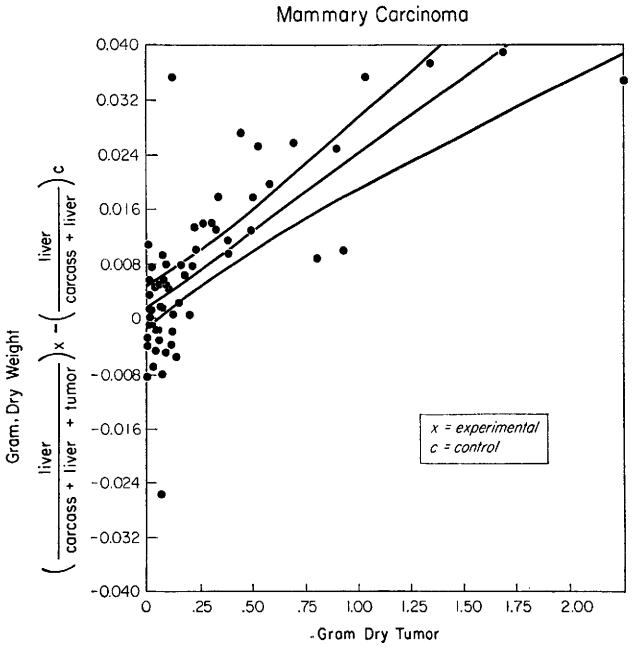

FIG. 4. There in a direct relationship between the ratio of dry weight of liver to whole animal and the dry tumor weight in mice bearing transplanted mammary carcinoma. Least-squares line with 95% confidence bands.

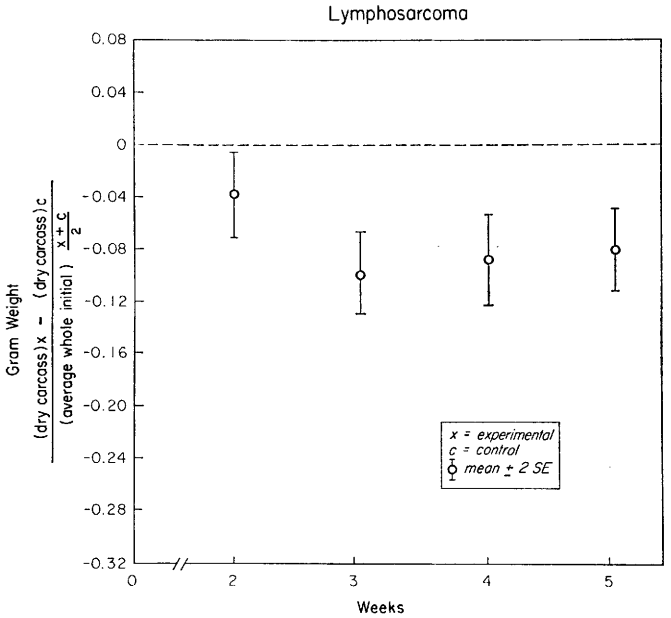

FIG. 5. Dry carcass weight changes in mice during the growth of transplanted lymphosarcoma.

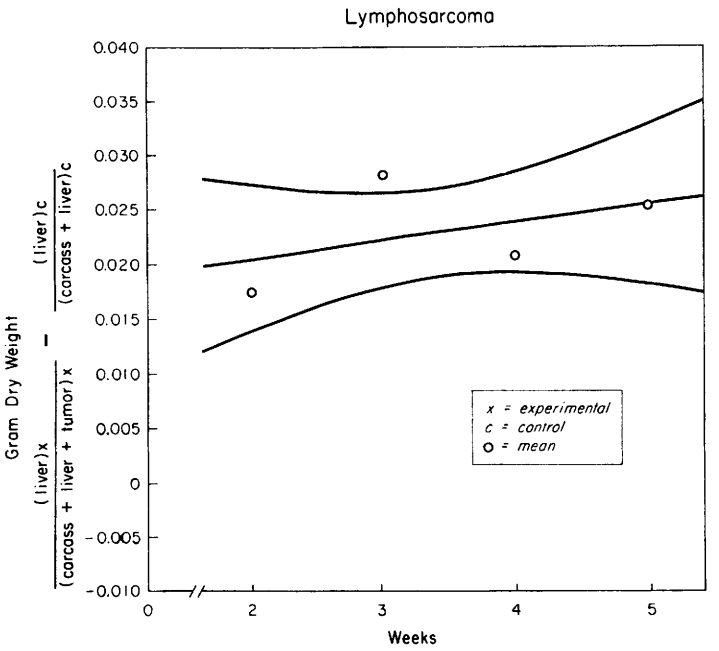

FIG. 6. Changes in the ratio of dry liver weight to total body weight in mice during the growth of transplanted lymphosarcoma. Least-squares line with 95% confidence bands.

exerts these remote effects remains obscure.

Summary. During the growth of subcutaneously transplanted mammary carcinomas or lymphosarcomas in mice the dry weight of the host carcass progressively decreases while the dry weight of the tumor-free liver of the host progressively increases. This dry liver weight gain is proportional to the dry tumor weight increase.

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Received Mar. 13, 1970. P.S.E.B.M., 1970, Vol. 134.