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Sinusoidal Dilatation Occurring in Livers of Mice with a Transplanted
Testicular Tumor.* (18007)

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Growth of certain transplanted ovarian tumors in mice is associated with an increased blood volume and sinusoidal dilatation in the liver, spleen, and adrenal glands(1,2,3). This phenomenon is not related either to the hormonal activity of the tumor or to an associated viral infection(4). The changes that are seen occur consistently with certain granulosa-cell tumors that have been induced in this laboratory by the homologous transplantation of an ovary into the spleen(5).

Experimental. Hybrid mice (A x C₃H) that carried subcutaneous or intraperitoneal transplants of a testicular interstitial cell tumor (3AC₁SS)(6) that arose in a stilbestrol-treated hybrid mouse of similar parentage were used. The tumor had been trans-

planted for 20 "transfer" generations before the present observations began. Originally the tumor grew only in estrogen-treated mice but subsequently grows in both male and female mice. Although sinusoidal changes similar to those occurring in mice bearing granulosa cell tumors may have occurred prior to the twentieth "transfer" generation, adequate studies were not made.

Animals bearing subcutaneous transplants of the testicular tumor did not show as extensive dilatation of the hepatic sinusoids as was observed in animals bearing intramesenteric transplants of comparable size.

The livers of these animals developing sinusoidal dilatation were congested and heavier than those of the controls; their surfaces were mottled and bled easily when touched. Microscopically, the hepatic sinusoidal dilatation ranged from slight to extreme dilatation with sinusoids isolating individual cords of liver cells. The dilatation began in the peri-lobular portal areas and extended toward the central veins which remained intact until gradually the entire architecture of the liver was destroyed. There was no increase in the number of mitoses among the liver cells and there was no polymorphonuclear or round cell infiltration. There was a slight increase in the number of Kupfer cells; the small bile ducts were not dilated. The spleens of these animals were

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TABLE I.
Organ Weights and Degree of Sinusoidal Dilatation in Mice Bearing a Transplanted Interstitial-Cell Testicular Tumor.

Animal No.	Liver wt, g	Spleen wt, g	Tumor wt, g	Sinusoidal dilatation*	
				Liver	Adrenal
Subcutaneous tumors					
T ₂₂ -1 ♂	2.47	.26	2.24	++	0
T ₂₂ -2 ♂	2.12	.29	6.44	+++	0
T ₂₂ -3 ♂	2.17	.40	6.80	+++	0
18 ♀	2.39	.47	6.98	+	0
32 ♀	2.87	.77	7.58	+	0
D-1 ♂	2.87	.46	7.60	++	0
1 ♂	3.65	.54	8.80	+++	++
2 ♀	2.72	.75	10.40	+	0
Range	2.12-3.65	.26-.77	2.24-10.40		
(8) Avg wt	2.66	.49	7.11		
Intra-mesenteric tumors					
6 ♀	2.86	.52	3.71	+	0
3 ♂	1.74	.34	3.95	+	0
7 ♀	2.12	.37	5.27	+	++
4 ♀	2.40	.52	5.30	++	+
1 ♂	2.69	.41	5.66	+++	0
12 ♀	2.31	.27	5.70	++	0
15 ♂	2.06	.27	5.90	++++	++++
6 ♀	2.21	.44	6.67	+++	0
14 ♀	2.08	.30	6.79	++	0
11 ♂	2.32	.37	7.96	++++	+++
2 ♂	2.45	.46	8.92	+++	+
8 ♂	1.80	.56	9.17	+++	0
4 ♂	2.14	.67	9.88	+++	++++
16 ♂	2.00	.27	10.93	++++	++++
Range	1.74-2.86	.27-.67	3.71-10.93		
(14) Avg wt	2.23	.41	6.84		
Controls					
1 ♀	1.48	.12			
2 ♀	1.81	.20			
3 ♂	1.57	.18			
4 ♂	1.70	.17			
5 ♂	1.65	.19			
6 ♂	1.50	.16			
7 ♂	1.41	.20			
Range	1.41-1.81	.12-.20			
(7) Avg wt	1.58	.17			

* 0 to + Beginning sinusoidal dilatation.
+ to ++ Early sinusoidal dilatation.
++ to +++ Moderate sinusoidal dilatation.
+++ to ++++ Extreme sinusoidal dilatation.

likewise enlarged and congested. Microscopically, they showed marked congestion of the red pulp and no increase in hematopoiesis.

The changes in the adrenal glands were most striking. Grossly, the adrenal glands were enlarged several times and had a homogenous red-purple color. Histologically, the sinusoids at the cortico-medullary junction were dilated and distended into the cortex, disrupting the normal architecture of

the cortex until only scattered individual cortical cells remained. The cells of the medulla remained essentially intact.

Castrate animals did not reveal any hormonal activity of the tumor. There was no correlation between the sinusoidal dilatation and the amount of necrosis observed in the tumor; neither was there any correlation with the rate of growth nor with the sex of the animal. The most extensive sinusoidal

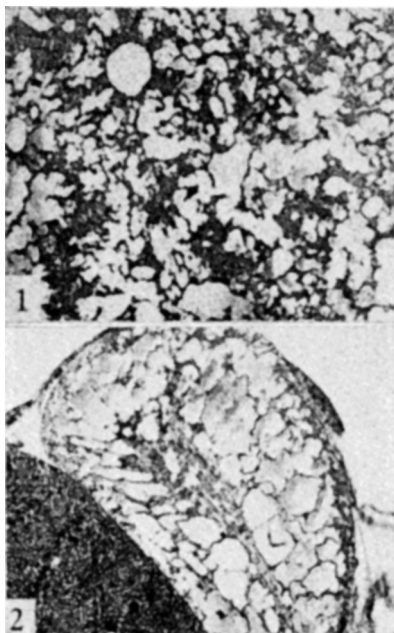


FIG. 1.

Section of liver of tumor bearing animal No. 15 ♂ AC₁, showing ++++ sinusoidal dilatation. Mag. 32 mm objective and 8x ocular.

FIG. 2.

Section of adrenal gland of tumor bearing animal No. 15 ♂ AC₁, showing ++++ sinusoidal dilatation. A small section of the kidney is included in the lower left corner. Mag. 32 mm objective and 8x ocular.

dilatation occurred in mice bearing intra-mesenteric transplants exceeding 5 g at about 4-6 weeks after transplantation.

Discussion. The pathogenesis of these changes remains to be described. Their occurrence with tumors that have no apparent hormonal activity tends to eliminate the possibility of the steroid hormones as the causative agent. They may be due to a hormonal imbalance as a hepatic perilobular sinusoidal dilatation has been described as occurring in the livers of hyperthyroid rats(7); however, histological examination of the thyroids of the animals in this experiment revealed normal histology. This tumor may be producing a specific protein factor or inducing a deficiency state yet to be recognized.

Summary. 1. Mice having a transplanted interstitial cell testicular tumor developed sinusoidal dilatation in the liver, spleen and adrenal glands. 2. These changes were more marked in animals with intra-mesenteric transplants than in animals with subcutaneous transplants. 3. This testicular tumor did not have any hormonal activity in castrate animals.

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Development of Hypertension in the Adrenalectomized Nephritic Rat Maintained on NaCl.* (18008)

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From reports in the literature, it is difficult to determine whether adrenal cortical hormones are essential for the development or maintenance of experimental renal hypertension.

In the dog, Goldblatt(1) has stated that

"bilateral adrenalectomy eliminates completely the response to constriction of the renal arteries." Page's(2) and Blalock's observations(3) are in accord with this statement. On the other hand, Rogoff *et al.*

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