clusively by either fluorescent antibody microscopy or mouse inoculation that these bodies are due to infection with rabies virus *per se*.

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Glomerulosclerosis in Mice with Myeloid Leukemia. (29008)

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Although aging RF mice spontaneously develop sclerotic changes in renal glomeruli (1,2) such lesions were also observed in young mice of this strain with passaged myeloid leukemia. This report describes these changes and their induction by leukemic filtrates, ultracentrifugates, and cells.

Methods. The mice used were derived from a non-inbred production stock of the RF/Up strain. The passaged myeloid leukemia originated in an irradiated RF male and had been serially transmitted through more than 25 passage generations in mice of the same strain (3,4). It was transmitted by intravenous inoculation of leukemic spleen cells, ultracentrifugates, ultrafiltrates, and plasma ultracentrifugates. The spleen cells were prepared for injection by mincing the spleen of a freshly killed donor in cold Tyrode's solution, to give a suspension of 100-150 $\times$ 10^6 nucleated cells/ml. Ultracentrifugates of the spleen cell suspension were prepared by centrifugation in the cold at 1800 $\times$ g for 20 minutes, followed by further centrifugation of the supernatant fluid at 30,000 $\times$ g for 1 hour. The ultracentrifugates were prepared by filtration of the 1800 $\times$ g supernatant fluid through a Selas 03 filter under negative pressure, with simultaneous filtration of added *Escherichia coli* to check the integrity of the filter. The plasma ultracentrifugates were prepared from heparinized whole blood by the same procedure as that used for preparation of the spleen cell ultracentrifugate.

* Operated by Union Carbide Corp. for U. S. Atomic Energy Commission.

TABLE I. Glomerular Lesions in Relation to Type of Leukemic Passage Materials Inoculated and Resulting Leukemia.

Passage material injected	No. of mice	Age at death (mo)	Leukemia	Severity of glomerular change*				
				Neg	±	+	++	+++
None (control)	52	1-5	Absent	33	11	8	0	0
Leukemia cells	12	2-5	"	5	5	2		
Leukemia ultracentrifugate	11	5-6	"	4	1	4	2	
Leukemia cells	12	2-4	Present		1	4	6	1
Leukemia ultracentrifugate	27	1-6	"		2	7	13	5
Leukemia filtrate	11	1-6	"		2	6	3	
Plasma ultracentrifugate	7	1-4	"			1	4	2

* Figures denote numbers of mice showing various degrees of glomerular change, as scored by the histologic criteria described earlier(1); *i.e.*, (Neg denotes no abnormality; ±, a borderline change; +, a definite but mild lesion; ++, a lesion of moderate severity; +++, a far-advanced lesion).

Adult (8 to 10 weeks old) recipients were injected by tail vein (0.5 ml/mouse), and newborn recipients (<1 day old) were injected by anterior facial vein (0.05 ml/mouse). Further details of the method of leukemia transmission are given elsewhere (4). After injection, the mice were observed until death or until clinical manifestations of leukemia were observed, at which time they were killed. Animals without leukemia were killed for comparison. At autopsy, specimens of liver, spleen, kidney, and bone marrow were fixed in Zenker's fluid, embedded in paraffin, sectioned, and stained with hematoxylin and eosin for microscopic study. Histologic changes in the glomerulus were scored on the basis of a grading system described previously(1,2).

Results. In contrast to the absence of severe renal changes in the non-leukemic mice, the leukemic animals generally showed moderate to severe intercapillary glomerulosclerosis (Table I). Such changes were evident even in mice developing leukemia within 12 days after inoculation of leukemic cells. No significant differences in frequency or severity of changes were apparent in relation either to the type of passage material injected or age and sex of the recipient. The glomerular lesions appeared indistinguishable histologically from the intercapillary glomerulosclerosis developing spontaneously in older mice of the same strain(2).

Discussion. The high frequency and severity of glomerular lesions associated with the leukemia remain to be explained. It is noteworthy that in mice with rapidly developing leukemia such changes occurred within less than a fortnight after inoculation. Similar lesions have also been noted in 4-6-week-old RF mice developing reticulum cell sarcoma 4-6 weeks after inoculation with the Rauscher virus.† The rapid onset of glomerulosclerosis under these conditions contrasts sharply with its more gradual development after irradiation(6,7) and in aging(1,8).

The usual absence of glomerulosclerosis in mice failing to develop leukemia suggests that the occurrence of the renal lesions was dependent on the presence of leukemia rather than on inoculation of leukemic passage materials *per se* (the 2 non-leukemic mice with glomerular lesions of moderate severity may have been in an incipient stage of leukemia too early to be detected). Alternatively, it is conceivable that the characteristic failure of the non-leukemic, injected mice to show glomerulosclerosis is attributable to their resistance to both glomerulosclerosis and to leukemia independently, and that the two diseases were caused by different agents in the passage materials.

The histochemical and ultrastructural peculiarities of the glomerulosclerosis are yet to be analyzed in detail. In hematoxylin and eosin-stained sections, however, the disease is indistinguishable from that observed in non-leukemic aging RF mice(1,2) and in

† We are grateful to Frank J. Rauscher for kindly supplying the virus used in this work. The isolation and properties of the virus are described elsewhere.(5).

those of other strains(8). Similar lesions have been reported to occur in response to irradiation as well as to a variety of other agents (see 6). Hence, the specificity of the disease is highly uncertain, at least without more refined study. The possibility that it may denote an autoimmune lesion deserves consideration (see 9). The role of virus in the etiology of the lesion is being explored in view of its induction by leukemia virus preparations of diverse types and origins.

Summary. Intercapillary glomerulosclerosis was found in mice of the RF strain bearing passaged myeloid leukemia whether these mice developed the leukemia from inoculation with leukemic cells or subcellular materials. The glomerular lesions occurred as early as 2 weeks after inoculation in mice with rapidly developing leukemia. The glomerulosclerosis was indistinguishable histologically from that induced by irradiation or that developing spontaneously in aging control animals.

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Prevention of Salicylate Teratogenicity in Immobilized Rats by Certain Central Nervous System Depressants.* (29009)

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Congenital malformations have been produced in the offspring of pregnant rats by single injections of large doses of sodium salicylate on the 10th day of gestation(1). An investigation of the teratogenic role of the known metabolic consequences of salicylate poisoning has suggested that this agent is dysembryogenic more through the systemic responses of maternal central nervous system poisoning than through its direct embryonic cytotoxicity(2). The teratogenicity of salicylate has been shown to be enhanced quantitatively by maternal immobilization so that anomalies are caused by otherwise non-toxic, non-teratogenic doses of salicylate ("immobilization effect")(3). Either immobilization (4) or salicylate poisoning(5,6,7,8) produces systemic responses characteristically seen following environmental stress, *i.e.,* weight loss, eosinopenia, stimulation of respiration, hormone release, and changes in size of adrenals, thymus and lymph glands. In salicylate poisoning, these responses have been shown to be mediated through the central nervous system(7,8). Therefore, immobilization may enhance salicylate teratogenicity by augmentative effects on the maternal central nervous system. In the present report, this hypothesis was tested by determining whether the "immobilization effect" can be prevented by the central nervous system depressants, sodium pentobarbital and chlorpromazine.

Materials and methods. Virgin Sprague-Dawley females of the Charles River Caesarian derived albino rat colonies 8 to 9

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