swine-kidney monolayers because of the difficulty in keeping primary swine cultures for the long time needed for plaque production. However, work on this problem is being continued.

Summary. Plaque formation by infectious canine hepatitis virus was demonstrated on dog kidney monolayers with both dog and swine kidney grown virus. A plaque-derived virus clone was identified as ICH by stationary tube neutralization test as well as by plaque assay. Under conditions of the study, assay by plaque plates appears to be a more sensitive titration method than by stationary tissue culture tubes.

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Experimental Aminonucleoside Nephrosis (II): Effect of Adrenalectomy on Fluid Retention of Aminonucleoside Nephrosis.* (24713)

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In young immature rats, aminonucleoside nephrosis is characterized by proteinuria, hypoproteinemia, hypercholesterolemia, increased rate of secretion of aldosterone, and fluid retention of which 50% is in the form of ascites(1-3). To appraise the relationship of hyperaldosteronism to fluid retention, the ascites produced by aminonucleoside nephrosis was measured in adrenalectomized rats receiving maintenance doses of corticosterone and maintenance or increased doses of either desoxycorticosterone or aldosterone. The results strongly suggest that in aminonucleoside nephrosis an increased rate of production of aldosterone is one, but not necessarily the only, causative factor in gross fluid retention.

Methods. Immature rats of Long-Evans strain, weighing 90-100 g, were used and fed a diet of Purina Fox Chow. Following adrenalectomy the animals were maintained on 1% sodium chloride in drinking water. Four days after operation the saline solution was replaced by tap water and maintenance therapy with aldosterone and corticosterone was started. After 4-5 days of maintenance therapy, nephrosis was induced by single daily subcutaneous injections of 6-dimethyl-aminopurine 3-amino-d-ribose at dose of 1.75 mg in 0.2 ml of water/rat/day for 8 consecutive days. Six days following last injection of the nephrotoxic drug, the animals were killed by bleeding from inferior vena cava. Development of nephrosis was established on the basis

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TABLE I. Development of Aminonucleoside Nephrosis in Adrenalectomized Rats.

	Total serum proteins, g %	Serum albumin, g %	Serum cholesterol, mg %	Ascites, ml/kg of body wt
Intact controls (9)	5.4 ± .7*	3.4 ± .1	63 ± 9	0
Intact nephrotics (10)	3.7 ± .7	1.7 ± .6	394 ±107	69 ± 21
Adrenalectomized—Series A				
Controls (8)	5.2 ± .6	3.6 ± .7	51 ± 7	0
Nephrotics (10)	4.1 ±1.2	1.9 ± .6	200 ± 59	0
Adrenalectomized—Series B				
Controls (8)	4.8 ± .3	3.5 ± .3	85 ± 14	0
Nephrotics (11)	4.1 ± .7	1.9 ± .6	250 ± 43	60 ± 20
Adrenalectomized—Series C				
Controls (9)	5.2 ± .3	3.3 ± .2	57 ± 14	0
Nephrotics (5)	4.1 ± .5	1.9 ± .4	273 ± 32	62 ± 37

* Stand. dev. of mean.

Numbers in parentheses indicate No. of rats. Rats of Series A were maintained on aldosterone and corticosterone. Series B and C received high doses of desoxycorticosterone and of aldosterone respectively.

of hypoalbuminemia(4), hypercholesterolemia (5), and characteristic changes in electrophoretic pattern of plasma proteins. Just before exsanguination volume of ascites was carefully measured by withdrawal into a syringe.

Results. Six days after last of 8 injections of aminonucleoside, intact nephrotic animals, as compared to normal rats, present hypoproteinemia, mostly accounted for by decrease of serum albumin, a marked degree of hypercholesterolemia and mean volume of ascitic fluid of 69 ± 21 (S.D.) ml/kg of body weight (Table I).

Maintenance therapy for adrenalectomized rats consisted of aldosterone and corticosterone in daily doses of 1.5 γ and 220 γ/100 g of body weight, respectively. Although these values were established by taking into consideration secretion rate of these hormones in adrenal vein blood of normal rats(3), it is doubtful that they represent more than an approximation of daily output of aldosterone and corticosterone by adrenals of intact rats. The total serum proteins, albumin, and cholesterol of adrenalectomized control rats receiving this maintenance therapy did not differ from those of intact rats.

Adrenalectomized rats receiving this therapy and injected with aminonucleoside presented a degree of hypoalbuminemia and hypercholesterolemia comparable to that found in intact nephrotic rats. There was however, a striking absence of ascites (Table I).

Two groups of adrenalectomized rats (Series B and C of Table I) were maintained on replacement doses of aldosterone and corticosterone for the period preceding injections of aminonucleoside. From this time until end of experiment, these 2 series of animals received respectively desoxycorticosterone acetate at dose of 400 γ and aldosterone at 16 γ/100 g body weight/rat/day. These dosages were chosen to simulate increased rate of production of aldosterone previously demonstrated in adrenal vein blood of nephrotic animals(3). The dose of corticosterone was unchanged. After injection of aminonucleoside, animals in both series presented a degree of hypoalbuminemia and hypercholesterolemia comparable both to that of intact nephrotic rats and to that of adrenalectomized nephrotic rats receiving maintenance doses of adrenal hormones; in contrast to the latter, a severe state of fluid retention was observed, as shown by volume of ascites virtually identical with that of intact nephrotic rats. Adrenalectomized, nonnephrotic rats, receiving same dosage of corticosterone and either desoxycorticosterone acetate or aldosterone as the nephrotic animals in Series B and C, presented levels of total serum proteins, serum albumin and cholesterol strictly comparable to those of intact controls and did not develop fluid retention.

Discussion. Singer(2) first demonstrated

that aminonucleoside nephrosis in rats is accompanied by increased rate of production of aldosterone. Further studies of this experimental syndrome have indicated that 4-androsten-3-one 17-spirolactone, an inhibitor of mineralocorticoids at kidney tubule level, promotes loss of ascites in aminonucleoside nephrotic rats without affecting their high rate of secretion of aldosterone (unpublished). By demonstrating that on maintenance doses of aldosterone, adrenalectomized nephrotic rats do not accumulate ascites whereas on higher doses of either aldosterone or desoxycorticosterone a state of fluid retention comparable to that observed in intact nephrotic rats is induced, the present data strongly suggest that hyperaldosteronism of aminonucleoside nephrosis is responsible for the presence of severe fluid retention. The same dosage of mineralocorticoids is without apparent noxious effects in adrenalectomized control rats.

Surtshin(6) reported severe fluid retention in adrenalectomized aminonucleoside nephrotic rats maintained on 1% NaCl in drinking water, but without any supportive therapy with adrenal hormones. We have confirmed this observation; this, together with results described above, suggests that fluid retention of aminonucleoside nephrosis is secondary to a decreased ability to excrete sodium. Hyperaldosteronism is one factor contributing to this disability.

Summary. Gross fluid retention and hyperaldosteronism are 2 characteristic features of aminonucleoside nephrosis in rats. Adrenalectomized aminonucleoside nephrotic rats receiving maintenance doses of aldosterone and corticosterone do not present fluid retention, whereas they do upon administration of aldosterone at doses equivalent to amount of this hormone secreted by adrenals of intact nephrotic animals.

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Cardiovascular and Respiratory Effects of Lethal Doses of Histamine and Compound 48/80 in Rabbits.* (24714)

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Compound 48/80 has been reported a potent liberator of endogenous histamine, capable of producing the main features of histamine and anaphylactic shock in several species(1,2). It is probable that 48/80 exerts pharmacologic and toxic effects which are unrelated to histamine released from tissues. Experiments have been made, using artificial respiration, to distinguish the effects of lethal doses of 48/80 and histamine on respiratory and cardiovascular systems of the rabbit, in which species 48/80 does not induce marked hypotension(2).

Methods. Albino rabbits of both sexes weighing from 3.0 to 4.6 kg were anesthetized with urethane (25% aqueous solution intravenously; 1.2 g/kg). The trachea was intubated with T-shaped glass cannula and respiration recorded semi-quantitatively on kymograph by connecting one of the outlets of the cannula to a recording bromoform manometer or to a rubber tambour. Femoral or carotid mean arterial pressure was recorded

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