sucrose with storage at —70°C appeared to be optimal for retention of RS virus infectivity. Virus was stored under these conditions for periods in excess of 2 years with no significant loss in infectivity. Storage at —20°C, even in the presence of hypertonic sucrose, was less satisfactory than at 4°C or at —70°C. Cotton swabs containing less than 10 $TCID_{50}$ retained viable virus in 44.5% sucrose at 4°C for a period of 7 days. The application of these observations in both the laboratory and clinic are discussed.

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Renin Secretion during Mannitol Diuresis and Ureteral Occlusion* (33055)

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A considerable body of evidence supports the concept that the macula densa is involved in the control of renin release (1). The present experiments were designed to distinguish between two of the hypotheses concerning the possible sensory signal to the macula densa: (i) It has been proposed that a decrease in total sodium load, independent of concentration, to the macula densa induces increased renin secretion (1); and (ii) in contrast, Thurau has proposed that an increased intratubular sodium concentration induces increased renin secretion (2).

Results of the only extensive micropuncture observations (3) in a situation known to increase renin secretion, namely reduction of renal arterial pressure, were consistent with both hypotheses, since early distal sodium load decreased whereas sodium concentration increased. Conversely, mannitol diuresis which has been shown to inhibit the renin release induced by pressure reduction (4), increased early distal sodium load and decreased sodium concentration (5–7).

In order to produce simultaneously a decrease in both early distal sodium load and sodium concentration, the present experiments employed complete ureteral occlusion during maximal mannitol diuresis. Stop-flow analysis has clearly demonstrated that, during the period of ureteral occlusion, the sodium concentration of the fluid within the loop of Henle and distal nephron either does not change or decreases (8), whereas the delivery of fluid (and, therefore, the total sodium load) to these nephron segments virtually ceases (9).

Methods. Experiments were performed on 9 mongrel dogs weighing 15–20 kg and maintained on standard dog chow (Friskies). The dogs were anesthetized with 30 mg/kg sodium pentobarbital intravenously with supplements given as required. The right ureter was catheterized, and a catheter (2.4 mm, o.d.) was manipulated, via a femoral vein and the vena cava, into the right renal vein. Arterial blood was obtained from a femoral artery catheter. Mean arterial pressure was monitored continuously using a Statham transducer and Grass polygraph. In 3 experiments total renal blood flow was monitored continuously using a Carolina square-wave electromagnetic flow meter and probe.

Experimental manipulations were not begun until at least 45 min after completion of all operative procedures. Control samples were then obtained following which the ani-

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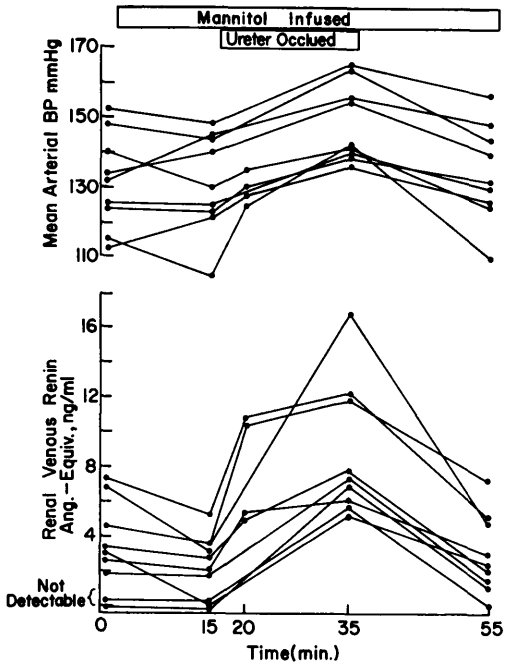

FIG. 1. Effects of mannitol diuresis and ureteral occlusion on renal venous renin activity and mean arterial blood pressure in 9 dogs.

mals were given intravenously 20% mannitol, 200 ml as prime and 10 ml/min as infusion. Fifteen min later the second samples were taken and the ureteral catheter occluded. Further samples were taken 5 and 20 min after the onset of occlusion following which the occlusion was released and final samples taken 20 min later.

The method used for determination of plasma renin activity has been described in detail previously (4). The results are expressed as nanograms of angiotensin-like activity (Ang.-Equiv.) produced/ml of plasma during *in vitro* incubation.

Results. All data for renal venous renin activity and mean arterial pressure are given in Fig. 1. The induction of mannitol diuresis caused a consistent, although small, decrease in renal venous renin activity; the decrease for the entire group was 1.2 ± 0.5 ng/ml (mean ± SE), $p<.05$ by paired samples analysis. Mean arterial pressure was not significantly changed. In every dog, complete ureteral occlusion produced an increase in both renal venous renin activity and mean arterial blood pressure, the changes being evident within 5 min. For the entire group, at 20 min, the renin increase was 6.8 ± 0.9 ($p<.001$) and the blood pressure increase was 17.2 ± 2.7 ($p<.001$). These increases were reversed in every dog within 20 min after release of occlusion.

Figure 2 presents the data for the three dogs in which total renal blood flow and arterial and renal venous renin activities were measured, and total renin secretory rates were calculated according to the following formula: Renin secretion = (TRPF)—V_{Urine}) ($Renin_{Renal\ Venous}$) — (TRPF) ($Renin_{Art}$). The pattern for total renin secretion was identical to that observed for renal venous renin; secretion was decreased by the mannitol and increased markedly by ureteral occlusion. Renal plasma flow was increased by the mannitol and then decreased by the ureteral occlusion; however, it is important to note that, despite the decrease induced by ureteral occlusion, the total renal plasma flow was the same as or greater in every case than the premannitol control value.

Discussion. In a previous study (4), it was demonstrated that mannitol infusions prevent or reverse the increase in renin secretion

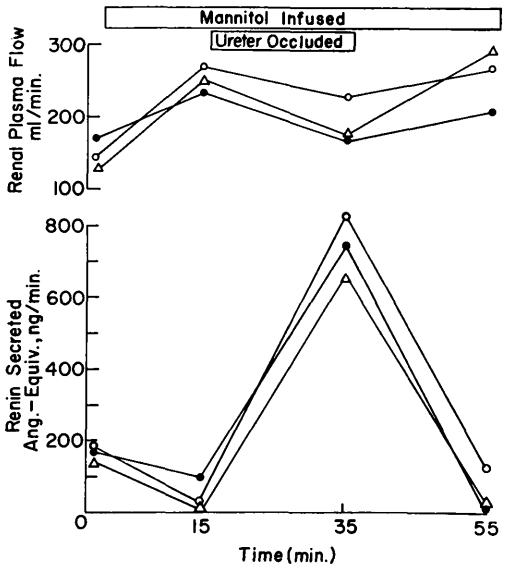

FIG. 2. Effects of mannitol diuresis and ureteral occlusion on renin secretion and renal plasma flow in 3 dogs. All data are for the right kidney only.

induced by reduction of renal arterial pressure. Although there was also generally a decrease in renal venous renin activity when mannitol was given to dogs in whom the arterial pressure had not been lowered, the change for the entire group was not statistically significant. The present study extends these findings and demonstrates a consistent and statistically significant decrease in renin secretion in normotensive animals.

In contrast to mannitol diuresis, alone, the superimposition of complete ureteral occlusion produced a marked rise in renin secretion. These data constitute evidence against the theory that renin secretion is increased as a result of increased intratubular macula densa sodium concentration, since early distal sodium concentration is, if anything, further decreased during ureteral occlusion (8) from the already low values of free-flow mannitol diuresis (6, 7). In contrast, as described in the introduction, the changes in renin secretion observed during both free-flow diuresis and stop-flow are consistent with (although, of course, do not prove) the hypothesis that renin secretion is inversely related to the total load (rather than concentration) of sodium entering the distal tubule per unit time. A possible mechanism by which changes in sodium load might be detected by the macula densa cells has been described previously (1).

These data also provide additional evidence that neither a decrease in renal blood flow nor in arterial blood pressure is a prerequisite for increased renin secretion; indeed, the increased secretion was associated with an increased blood pressure (probably secondary to increased plasma angiotensin) and renal plasma flow. The changes in renal blood flow are similar to those reported by several other investigators for similar conditions (see Circulation Res., Supp. I to Vols. 14 and 15, 1964).

Summary. Renin secretion was decreased during mannitol diuresis, alone, but was increased by the superimposition of ureteral occlusion. The data are consistent with the "sodium load" hypothesis for control of renin secretion but not with the "sodium concentration" hypothesis.

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Antinuclear Antibodies—Attempts at Ultrastructural Localization* (33056)

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Considerable interest has evolved over the last 10 years concerning the *raison d'être* as well as the pathogenic significance of antinuclear antibodies among human disease states. The elution from isolated lupus glomeruli of antibodies showing distinct anti-DNA or anti-

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