chimpanzees and cynomologous monkeys, though showing no apparent illness which could be ascribed to the virus, readily became carriers and developed neutralizing antibodies. Kaplan and Melnick(6) have also shown that newborn mice are susceptible to oral infection with 5 different strains (4 immunologic types) of C virus, though not all of the mice became infected. Adult lactating females could not be infected with the High Point strain by feeding. The authors say that they have "observed many adult female mice who cannibalized their infected young without effect on the mothers." Whether this included mothers of sucklings infected with the Conn.-5 strain is not stated.

Since it has been shown that the mothers may become spontaneously infected with the Conn.-5 strain of Coxsackie virus and since those that survive may develop neutralizing antibodies which, by placental transmission or through lactation might protect their offspring, it is obvious that subsequent litters would be unsuitable for experiments with this strain. That this might also apply to other strains of Coxsackie virus is suggested by the recent finding that the Powers(7) and DeMole(8) strains are also capable of producing pancreatitis in adult mice(9).

Summary. Mothers of suckling mice may spontaneously become infected with Conn.-5 strain of Coxsackie virus, following inoculation and infection of their young with this virus. They develop pancreatic lesions and, in some cases, hepatic lesions identical with those produced after intraperitoneal injection of virus. This condition can be reproduced experimentally in adult mice of either sex by feeding them with the carcasses of infected suckling mice.

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Influence of Glomerular Filtration Rate upon the Renal Tubular Reabsorption of Sodium.*† (19421)

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In a recent study(1), the administration of hypertonic saline to dogs resulted in an increased rate of sodium reabsorption in every case. Since the rise in plasma sodium concentration was accompanied by a variable, but consistently present, elevation of glomerular filtration rate in each experiment, it was not possible to determine the factor which was responsible for the altered rate of sodium reabsorption. Other investigators also have observed changes in glomerular filtration rate subsequent to hypertonic saline infusions, the usual effect being an augmentation(2-3), although reduced filtration rates have occurred in some cases(4).

In the present series of experiments the administration of hypertonic saline exerted only a negligible effect upon the rate of glomerular filtration in six out of eight experi-

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ments. This made it possible to distinguish the acute effects of elevated plasma sodium levels from those due to changes in filtration rate upon the rate of renal tubular reabsorption of sodium.

Methods. Eight acute experiments were performed upon male dogs anesthetized with sodium pentobarbital, 30 mg/kg. Urine was collected by means of plastic catheters inserted directly into the ureters through a suprapubic incision. After a pair of control clearance periods the plasma sodium level was progressively elevated by means of a continuous intravenous infusion of 3% saline. Eight successive clearance periods were then obtained beginning soon after the hypertonic saline infusion had been started. The rate of saline administration was gradually augmented after every 2 periods. Plasma sodium levels were elevated for a total of only one hour or less in each experiment. Glucose Tm was determined in 5 of these experiments, and PAH Tm in the other 3, in an attempt to evaluate the effects of hypertonic saline upon renal tubular function. The clearance of creatinine was used to measure the glomerular filtration rate in all experiments. Creatinine was determined in plasma filtrates and urine by the method of Folin and Wu(5); PAH by the method of Smith *et al.*(6); and glucose by the method of Benedict(7). The sodium content of all urine and plasma samples was determined with a Perkin-Elmer flame photometer employing an internal lithium standard. No corrections were made in our calculations for the Donnan effect.

Results. Fig. 1 illustrates the changes which occurred in glomerular filtration rate (C_{Cr}), the rate of sodium reabsorption (T_{Na}), and the maximum secretory capacity for PAH (Tm_{PAH}) in 3 experiments following the administration of hypertonic saline. It is evident from the figure that only slight changes in C_{Cr} and T_{Na} are manifest in 2 of these experiments, represented by the squares and triangles. In both of these experiments, C_{Cr} remained within $\pm$ 4 cc/min of the mean value for that experiment, and T_{Na} did not vary by more than $\pm$ 0.6 mEq/min from the mean rate of sodium reabsorption, despite wide variations in the plasma sodium concentration (P_{Na}). This relatively constant rate of sodium reabsorption in the face of significant increases in sodium load resulted in tremendous increases in the rate of sodium excretion.

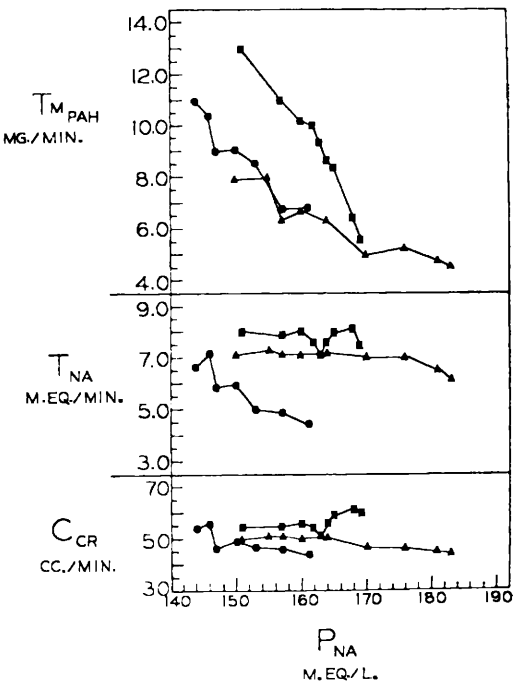

FIG. 1. Effects of hypertonic saline upon PAH Tm, sodium reabsorption (T_{Na}), and glomerular filtration rate (C_{Cr}).

In the third experiment, represented by the circles in Fig. 1, C_{Cr} dropped from a value of 54 cc/min at a P_{Na} of 144 mEq/l to 44 cc/min when P_{Na} was elevated to 161 mEq/l. Under these conditions the T_{Na} fell from 6.7 to 4.4 mEq/min, a decrease which is relatively greater than the decline in C_{Cr}. In all 3 animals the elevation of P_{Na} obviously exerted a marked depressant effect upon the Tm_{PAH}. The Tm values at elevated plasma sodium levels were 43, 58, and 62% of control.

Five similar experiments were performed in which the glucose Tm (Tm_G) was determined instead of the PAH Tm, and these experiments are illustrated in Fig. 2. In this figure, the greatest alteration in glomerular filtration rate is manifest in the experiment represented by the open circles. There was a rise in this experiment from 54 cc/min at a P_{Na} of 144 mEq/l to a rate of 73 cc/min

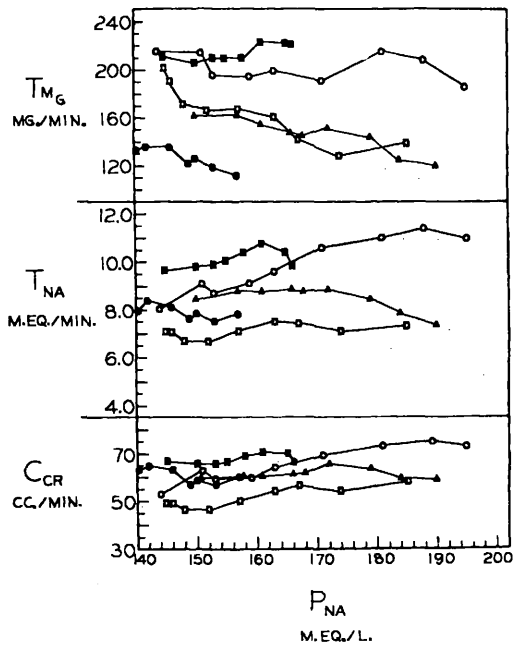

FIG. 2. Effects of hypertonic saline upon glucose Tm, sodium reabsorption, and glomerular filtration rate.

when the P_{Na} was 195 mEq/l. Under these conditions the rate of sodium reabsorption increased from 8.0 to 10.9 mEq/min, tending to parallel the change in C_{Cr}. The results of this experiment closely simulate those of the previous studies reported by Selkurt and Post(1).

In the other 4 experiments included in Fig. 2, the C_{Cr} changed to a much lesser extent, and the T_{Na} also remained relatively constant over a wide range of plasma sodium concentrations. In these 4 experiments the greatest change in C_{Cr} was $\pm$ 7 cc/min from the mean value for that experiment (open squares), and the variation was significantly less in the remaining experiments of this group. The greatest deviation in T_{Na} was $\pm$ 0.75 mEq/min from the mean (solid triangles). In all experiments the rate of sodium excretion increased markedly as P_{Na} rose.

When Fig. 2 is compared to the preceding figure, it is obvious that Tm_{PAH} was much more severely depressed than was Tm_G for equivalent increases in P_{Na}. The glucose Tm varied from 32% below control to 5% above control following the administration of hypertonic saline, with an average depression to 16% below control for the 5 experiments.

Discussion. When the plasma sodium concentration was progressively elevated without incurring any significant alterations of glomerular filtration rate, the rate of sodium reabsorption remained remarkably constant, and the excess sodium was eliminated in the urine. In those experiments in which an increase or decrease in filtration rate did occur, T_{Na} changed concordantly. In the studies of Selkurt and Post(1), C_{Cr} and T_{Na} increased in every case, but the greatest rises in T_{Na} were observed in those experiments where C_{Cr} was augmented the most. Thus, it appears that the rate of sodium reabsorption is independent of acute changes in plasma sodium concentration, but is very sensitive to changes in filtration rate. In these respects the mechanism of sodium reabsorption appears to be similar to that for bicarbonate(8) and chloride (9).

The depressant effect of elevated P_{Na} levels upon the glucose and PAH transport mechanisms is undoubtedly nonspecific in nature. Hypertonic saline has a similar action upon the rates of reabsorption of bicarbonate(8), sulfate(10), and ascorbic acid(11). It was shown by Selkurt and Houck(11) that the effect of hypertonic saline upon the ascorbic acid Tm was not due to the resultant diuresis, for equivalent increases in urine flow produced by mannitol did not affect the rate of ascorbic acid reabsorption. Contrary to our demonstration of the marked depression of Tm_{PAH} by hypertonic saline, Stamler(12) demonstrated that saturation of the tubular secretory mechanism for PAH does not alter the rate of sodium transport. Therefore the depressant effect of elevated P_{Na} upon the Tm_{PAH} is not a true competitive phenomenon, and its exact nature remains obscure. It is evident, however, that neither Tm_{PAH} nor Tm_G should be used to assay effective tubular mass under conditions where significant alterations in P_{Na} are produced.

This very appreciable effect upon the transport mechanisms for glucose and PAH leads us to suspect that tubular function in general might be depressed by hypertonic saline. With respect to the renal tubular reabsorption of

sodium in particular, two alternative possibilities should be considered. First, it may be assumed that all aspects of tubular function actually are impaired. In this event the renal tubular cells might tend to reabsorb additional quantities of sodium as the load is increased, but would be prevented from doing so because of the impairment of function. The resultant effect would be the constant T_{Na} which was observed. The second possibility is that only certain discrete enzyme systems are inhibited and that the sodium reabsorptive mechanism is spared, thereby allowing T_{Na} to remain constant, while Tm_{PAH} or Tm_G are significantly reduced. Credence is lent to this possibility by the fact that Tm_{PAH} appears to be much more markedly affected than is Tm_G, indicating that the various transport systems are not all altered to the same extent. At present, we cannot say which of these alternatives is the correct one.

Summary. 1. When the plasma sodium concentration is progressively elevated in dogs by the administration of hypertonic saline, the rate of renal tubular reabsorption of sodium remains constant in those experiments where the glomerular filtration rate is not significantly affected. If the filtration rate increases or decreases in response to the hypertonic saline, the rate of sodium transport deviates in the same direction. Therefore, in experiments where the sodium level is elevated for a period of one hour or less, any alteration in the rate of sodium transport is dependent upon the concomitant change in filtration rate. 2. Hypertonic saline exerts a profoundly depressant effect upon the PAH Tm, and a significant but less marked influence upon the glucose Tm. This depression is believed to be nonspecific in nature and contra-indicates the use of these determinations as an index of effective tubular mass in experiments in which variations in sodium concentration are involved.

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A Protective Role of Pyridoxin Against the Toxic Effects of P^{32}.* (19422)

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In a continuation of our study on the effects of internal radiation by P^{32} as related to various dietary factors(1,2), the role of pyridoxin has now been investigated. After

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