against lethality of both homologous and heterologous endotoxins is afforded by passive transfer of serum of a tolerant animal of another species. The success with the *i.v.* route shortly before the *i.p.* challenge rules out direct neutralization of the endotoxin by residual serum, or inactivating factor, in the peritoneum. (It is known(1) that a mixture of endotoxin and antiserum retains the toxicity of the former.) Preliminary experiments indicate that the protective serum of tolerant donors stimulates the reticuloendothelial system of the recipient, as measured by carbon-clearance in the latter. Whether there is equivalent protection against homologous and heterologous challenge cannot be answered unequivocally; the data do not require an assumption of non-equivalence. While it is true that tolerance to, *e.g.*, pyrogenicity by treatment with one endotoxin confers tolerance to pyrogenicity of other endotoxins, whether there is quantitative equivalence of tolerance is far from proved.

Summary. Serum of rabbits rendered tolerant by a brief schedule of endotoxin administration protects mice against the lethality of homologous or heterologous endotoxin and this protective effect is not attributable to antibody content of the serum.

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Effects of Steroid Induced Potassium Depletion on Renal Control of Sodium.* (25297)

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Sodium retention is a common side effect of continuous therapy with corticoids. Another potential effect of prolonged dosage with cortical hormones is potassium depletion. Since potassium deficiency is known to produce significant alterations in renal function (1), we hypothesized that renal management of sodium during steroid treatment might be influenced by this known change in potassium balance. The present experiments compared renal responses of intact dogs to intravenous administration of sodium after they had received large repeated daily doses of nine-alpha-fluorohydrocortisone (FF) with and without potassium supplements.

Materials and method. The experiments were performed on 12 mongrel dogs weighing between 8.1 and 12.7 kg, divided according to weight into 1 control and 2 test groups, each containing 2 males and 2 females. They were housed individually in metabolism cages and offered a daily food ration of 280 g of Gaines meal wetted with 300 ml of distilled water. Their daily dietary intakes of sodium and potassium were 42 and 62 mEq respectively. Dogs in Group A were injected intramuscularly once daily for 3 weeks with FF alcohol (1 mg/kg), suspended in an aqueous vehicle. This regimen usually elicits a negative potassium balance, manifested by a drop in serum potassium and mild muscular weakness(2).

* The authors thank Dr. Josef Fried of Squibb Inst. for generous supply of nine-alpha-fluorohydrocortisone.

TABLE I. Renal Responses of Dogs to Intravenous Sodium Administration after Repeated Doses of Nine-Alpha-Fluorohydrocortisone (FF) Alone or with Potassium Supplements.*

Glomerular filtration rate	Urinary output	Sodium			
		Serum level,	Filtered†	Excreted	Reabsorbed,
ml/min.		meq/l	meq/min.		%
Group A (4 dogs): FF without potassium supplement					
31 ± 5 (<.02)	2.2 ±.6 (ns)	154 ± 1 (<.01)	4.77 ± .84 (<.05)	.16 ±.05 (<.01)	96.7 ±.8 (<.05)
Group B (4 dogs): FF with potassium supplement					
61 ± 9 (ns)	2.9 ±.4 (ns)	153 ± 3 (<.02)	9.33 ±1.24 (ns)	.41 ±.04 (ns)	95.6 ±.3 (<.05)
Group C (4 dogs): Controls					
51 ± 2	2.8 ±.4	143 ± 1	7.29 ± .25	.46 ±.03	93.7 ±.7

Avg values followed by stand. errors. Numbers in parentheses are P values of *t* tests *vs* control data; "ns" denotes not significant.

* Test dogs were given 1 mg FF/kg/day i.m. for 3 wk; supplemented dogs also received 0.15% KCl in their drinking water. Results tabulated here were obtained on the 21st day during the 3rd hour's infusion with 0.85% saline, 5 ml/min.

† No correction for Donnan effect.

We considered dogs in this group to be deficient in potassium, and therefore suitable for testing, only if they exhibited both of these effects. Dogs in Group B received similar doses of FF but, in addition, were given 0.15% KCl in their drinking water. Ferrebee *et al.*(3) found this procedure effective in counteracting signs of steroid induced potassium depletion. Control dogs (Group C) received injections of the aqueous vehicle alone. Effects of different treatments on renal responses to intravenous sodium administration were assessed by clearance technics at the end of the 3-weeks' dosing period. The dogs were anesthetized with intravenous pentobarbital (30 mg/kg), then given an intravenous priming dose of creatinine (60 mg/kg) followed by an infusion (5 ml/min.) of 0.85% saline containing sufficient creatinine (0.06%) for measurement of filtration rate. Renal functions were compared during the 3rd hour of infusion when urinary excretion rates of the 3 groups were roughly comparable. Four 15-minute clearance tests were made during the hour; urinary samples were obtained through an indwelling catheter and arterial blood samples were withdrawn from the femoral artery at the mid-point of each collection period. Sodium and potassium were analyzed by internal standard (Li) flame photometry and creatinine by a modification of the Bonsnes and Taussky technic(4). The significance of the differences between the mean effects produced by the test and control treatments was calculated by the *t* test for small samples(5). A probability of ≤ 0.05 was considered significant.

Results. During the 3-weeks' dosing period the dogs in both test groups showed equal losses in body weight (avg 10%) and developed polydipsia and polyuria. Dogs given FF without supplemental potassium exhibited signs of potassium depletion as evidenced by mild muscular weakness and hypokalemia (avg ± S.E., 2.64 ± 0.15 mEq/l); in contrast, dogs given FF and additional potassium showed no muscular dysfunction and had serum potassium levels (4.85 ± 0.26 mEq/l) comparable to those of the controls (4.86 ± 0.11 mEq/l).

The apparent disparity in potassium economy between the 2 groups of dogs given FF was reflected by differences in their renal responses to intravenous sodium administration (Table I). Although the animals in both groups had significantly higher concentrations of serum sodium and reabsorbed greater percentages of filtered sodium than the controls, urinary excretion of sodium in the deficient dogs was significantly lower than in the controls but in the supplemented animals it was similar to that of the controls. The difference in sodium output between the 2 test groups was caused by differences in their filtered fractions of sodium as determined by glomerular filtration: in the deficient dogs glomerular filtration was reduced but in the supplemented animals this function, although not significantly different from that of the controls, showed a tendency to be augmented.

It is evident from these studies that FF may have different effects on sodium excretion, depending upon degree of potassium depletion. It is also apparent that erroneous conclusions may be drawn from experiments in which urinary excretion of sodium is used as the sole criterion for determining the sodium retaining properties of corticoids. We believe that studies of potassium balance such as those previously reported from our laboratories(2) and of glomerular-tubular functions as reported here are also needed to elucidate the potential long range effects of new adrenal steroids on sodium excretion.

Summary. The loss of potassium attending repeated administration of large doses of nine-alpha-fluorohydrocortisone (FF) to dogs depressed their glomerular filtration rate. In contrast, glomerular function showed a tendency to be augmented in a group of dogs that received supplemental potassium with the steroid. The ability of FF to increase renal tubular reabsorption of sodium was observed under conditions of both potassium depletion and repletion. In the former case sodium retention was enhanced by the reduction in filtration rate but in the latter case no significant retention of sodium occurred, despite its augmented tubular reabsorption.

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Multiplication and Cytopathogenicity of Herpes Simplex Virus in Cultures of Feline Renal Cells.* (25298)

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Virus of herpes simplex has been reported to propagate in many tissue culture hosts(1-12); a search of the literature, however, yielded no reference to its growth in feline renal cells. A strain of herpes simplex virus was isolated in our laboratory and its identity confirmed by complement fixation. The purpose of this work was to determine whether the virus would propagate in these cells and to study the cytopathology. This paper describes the cytopathology of herpes simplex virus in cultures of feline renal cells, its behavior in 20 serial passages, and several conditions that influence the type of cell response to this strain of virus.

Materials and methods. Tissue cultures were prepared in 15 × 155 mm tubes and on 11 × 22 mm coverslips in Leighton tubes. Cell cultures of feline renal cells were prepared by the method of Madin(13). Second and third subcultures of human kidney were prepared by trypsin and versene digestion. The nutrient medium was 0.5% lactalbumin in modified Hank's salt solution containing 0.01 M tris (hydroxymethyl aminomethane), adjusted to pH 7.4 and 20% human serum. Prior to inoculation the cultures were rinsed 3 times with Hank's salt solution. The fluid was replaced with 0.5% lactalbumin hydrolysate containing 5% lamb serum. Human amnion cells (FL)(14) were grown in Eagle's medium containing 20% human serum. At the time of inoculation, maintenance medium, consisting of Eagle's basal medium plus 3% horse serum, was placed on the cultures. Streptomycin (0.5 mg/ml) and penicillin (500 u/ml) were incorporated in all media.

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