the gravid uterus. This suggests that pregnancy in hamsters is a host factor which increases their susceptibility to infection with rat virus. The rapidly differentiating tissues of the placenta and the embryo as well as the striking metamorphic changes in the endometrial stroma during gestation might provide the proper milieu for viral propagation. RV produces no recognizable histological disease in either pregnant or fetal hamsters. A similar absence of histological change has been described in lung infections induced in newborn mice with polyoma virus(7). The main pathogenic effects of RV appear to be in young suckling hamsters in which it proliferates to high titers(6), inducing inclusion bodies for only a limited period at peak of the infection, a situation similar to that described in the Mastomys rat(8). Inclusion bodies were not observed in the infected adult hamsters.

Whether RV can induce tumors or has potentialities for inducing mongolism *in utero* remains unknown. It is becoming apparent from our continuing studies that RV actually represents a spectrum of strains, all interrelated but having differing properties, as has been recently discussed by Moore(9). The strain used in the present studies was highly hamster-adapted. It is conceivable that effects other than those obtained might have resulted from use of the strain in a still more hamster adapted form, or, at the opposite extreme, as the form originally isolated from rats. Both of these possibilities are being investigated.

Conclusions. 1. RV injected into pregnant hamsters during early stages of gestation has a predilection for tissues associated with the gravid uterus and embryo, reaching significantly higher titers in 4 days as compared to control tissues, then decreasing as maternal antibody levels begin to rise. 2. Direct intraembryonic injection of RV into fetal hamsters on the 12th or 13th day of gestation produces fetal death at, or soon after, parturition. 3. Following intravenous injection, RV causes no apparent ill-effect on either the maternal or embryonic tissues.

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ACTH Content of Dog Kidneys.* (28122)

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Richards and Sayers(1) have reported that in rats relatively large amounts of injected ACTH accumulate in the kidneys, and others have confirmed this observation(2,3). Since little if any of the ACTH appears in the urine, it has been suggested that ACTH might be returned to the blood stream from this extrapituitary storage site. In Richards and Sayers' study, there were small but detectable amounts of ACTH in the kidneys of stressed normal rats that had not been injected with exogenous ACTH(1). The present studies were undertaken to quantitate the amount of endogenous ACTH in the kidneys of surgically stressed normal dogs, and to determine whether ACTH was released from the kidney into renal venous blood following laparotomy and hemorrhage.

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Methods. Kidneys removed surgically from normal dogs under pentobarbital anesthesia and stored in the frozen state were subsequently weighed and extracted for ACTH according to the procedure described by Astwood(4). Pools of 4 to 8 kidneys were homogenized in cold acetone, and the homogenate filtered. The residue was dried, then taken up in acetone-glacial acetic acid, which was heated to 70°C, and filtered while warm (35-45°C). After repeated washing with acetone, the residue was discarded. 5M NaCl and acetone was added to the filtrate with vigorous stirring; a flocculent precipitate which appeared upon standing at 4°C was removed by filtration. Addition of ether to the clear filtrate produced a precipitate, portions of which were assayed for ACTH activity by the method of Nelson and Hume(5). In 2 of the assay dogs, the effect on aldosterone secretion of an amount of extract equal to one kidney was determined by measuring the aldosterone output in the adrenal vein before and 4-14 minutes after injection. To estimate losses of ACTH in the extraction procedure, a pool of kidneys was divided into 2 portions, and to one of these, 4.56 USP units of ACTH were added during homogenization. Both homogenates were then extracted as described and assayed for ACTH content. The amount of extract injected into assay dogs was equivalent to 0.002-1.0 kidney per injection.

In another series of experiments, 4 normal dogs previously subjected to left nephrectomy were anesthetized with pentobarbital and the remaining right kidney exposed through a flank incision. A plastic cannula was inserted in the femoral vein and guided into the renal vein. A plastic choker was placed around the renal vein at its junction with the vena cava. When this choker was tightened, all renal venous blood flowed out the cannula. Cannulae were also inserted in the femoral artery, carotid artery and jugular vein. Blood pressure was monitored continuously using a Statham strain gauge and Grass Model 5 polygraph. Simultaneous 200 ml collections of renal venous and peripheral arterial blood were made in iced heparinized tubes, collecting the blood intermittently and slowly. The blood collected was replaced by simultaneous infusion of bank blood from hypophysectomized donor dogs. In 2 additional normal dogs, a cannula was inserted into the vena cava through the femoral vein and adjusted so that its tip was at the level of the renal veins. The aorta and vena cava were tied below the renal vessels. A choker was placed around the vena cava above the orifices of the renal veins. When this choker was tightened, all the renal venous blood flowed out the cannula. These animals were bled 15 ml/kg of body weight from the femoral artery, and 6 minutes following the start of hemorrhage, 200 ml renal venous and peripheral arterial samples were collected simultaneously while reinfusing the dog's own blood and bank blood. All specimens were centrifuged promptly in the cold and the plasma frozen. Subsequently, these were thawed, centrifuged, and the supernatant injected intravenously into nephrectomized, hypophysectomized dogs. Adrenal venous blood specimens were collected from assay dogs before and starting 4 minutes following injection. The interval between injections was at least 1 hour. All but one dog also received 1 IU of ACTH at the end of the assay. Adrenal venous plasma 17-hydroxycorticoids were determined by the method of Silber and Porter(6), and aldosterone by the double isotope derivative technic of Kliman and Peterson(7).

Results. The data on ACTH content of kidney extracts are summarized in Table I. Lot A contained about 4 mU/kidney, and Lot B contained none. The calculated ACTH content of the portion of Lot B to which 4.56 USP units of ACTH had been added during homogenization was 4.56 mU/mg of extract. Since it was found to contain an average of 3.3 mU/mg, recovery of added ACTH by the extraction procedure employed was 72%.

An amount of extract equivalent to one kidney (550 mg) produced a rise of 1 mμg/min in aldosterone secretion when injected into one hypophysectomized assay dog, and a rise of 7 mμg/min in another assay dog. None of these extracts had any effect on blood pressure.

Renal venous and arterial plasma from surgically stressed dogs had similar effects upon

TABLE I. ACTH Content of Kidney Extracts.

Kidney extract	Assay dog	Mg of extract injected	Whole kidney equivalent (%)	ACTH content mU/injection	
Lot A	1	1	0.2	0	
		25	5	0	
		50	9	0	
	2	550	100	8	
	3	550	100	3	
	4	550	100	3	
Lot B	5	175	100	0	
Lot B	6	.5	.3	2.0	4.0 mU/mg
plus 4.56		2.0	1.1	6.0	3.0 "
mU ACTH/mg		5.0	2.9	>10.0	—
of extract					
	7	.5	.3	1.5	3.0 "
		1.0	.6	4.0	4.0 "
		3.0	1.8	>10.0	—
	8	2.0	1.1	5.0	2.5 "
		10.0	5.9	>10.0	—

mean 3.3 mU/mg

adrenal venous Porter-Silber chromogens when injected into nephrectomized-hypophysectomized recipients (Table II). Peripheral blood from the 2 hemorrhaged dogs caused somewhat greater adrenocortical stimulation than renal venous blood. Since these samples were injected in dogs not given graded doses of the ACTH standard, the results cannot be quantitated in terms of units of ACTH. However, on the basis of the ACTH standard curves obtained in dogs receiving kidney extracts as well as the magnitude of response to 1 IU of ACTH, the blood ACTH levels in the stressed dogs can be estimated to have been in the range of 2-4 mU/100 ml of plasma.

Discussion. The material recovered from dog kidneys which stimulated adrenal cortical secretion was probably ACTH. Large doses of renin also stimulate 17-hydroxycorticoid secretion(8), but renin is destroyed at temperatures above 56°C(9), and in the course of the extraction presently employed, kidney homogenates were heated to 70°C. The likelihood that this treatment inactivated renin was borne out by the fact that none of the extracts influenced blood pressure, even when amounts of extract equivalent to one whole kidney were injected.

TABLE II. Adrenocortical Response to Plasma from Stressed Dogs Given to Hypophysectomized Nephrectomized Recipient Dogs.

Donor dog	Renal vein plasma (100 ml)	Femoral artery plasma (100 ml)	ACTH (1 IU I.V.)
A*	1.4	.5	—
B*	0	.4	3.3
C*	1.2	1.3	4.6
D*	1.0	1.1	7.0
Mean	.9	.8	5.0
E†	1.8	6.3	5.7
F†	.3	2.5	11.2
Mean	1.1	4.4	8.5

Values are 17-hydroxycorticoid outputs (μg/min).

* Surgical stress; unilaterally nephrectomized.

† Surgical stress plus hemorrhage.

The data indicate that the maximum amount of ACTH that can be extracted from the kidneys of surgically stressed dogs is less than 4 mU/kidney. Even if this value were doubled and corrected for the 28% loss incurred during extraction, the maximum amount of ACTH in 2 kidneys would be no more than 11 mU, an amount sufficient to produce only a transient maximal corticosteroid output in hypophysectomized dogs(5, 8). In studies previously reported from this laboratory, doses of ACTH as large as 50 mU failed to produce any appreciable or consistent increase in aldosterone secretion. The slight change in aldosterone secretion produced by kidney extract in this study is in the same range as that obtained with 2-50 mU doses of commercial ACTH in the previous study(8).

Comparison of the adrenal stimulating activity of renal venous and peripheral arterial blood failed to indicate that detectable quan-

tities of ACTH were released from the kidney of the stressed dog. In fact, in 5 of 6 dogs, there was more activity in arterial than in renal venous blood. It therefore seems unlikely that any significant renal release of ACTH occurred following surgical stress or hemorrhage.

Summary. The amount of ACTH that could be extracted from kidneys of surgically stressed normal dogs was 0 and 4 mU/kidney in 2 lots tested. Seventy-two percent of the ACTH added to half of one batch of kidneys was recovered by the extraction technic used. On injection into hypophysectomized dogs, renal venous plasma from surgically stressed or hemorrhaged dogs had no more adrenal cortical stimulating activity than peripheral arterial plasma collected at the same time. These findings do not support the hypothesis that significant amounts of ACTH are released from the kidneys into the circulation during surgical stress or hemorrhage.

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Response of Rats with Gastric Fistulas to Injection of Gastrin.* (28123)

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This study was done to determine whether rats with gastric fistulas would secrete acid in response to injection of extracts containing gastrin. It was found that they did respond and a comparison was made between gastrin and histamine as secretory stimulants.

Methods. Gastrin free of histamine was prepared from the mucosa of the pyloric gland area of the stomachs of hogs by a method previously described(1). Doses of gastrin are expressed as grams of mucosa from which the extract was derived. The protein plus polypeptide content of the gastrin extract was 1.1 mg per gram wet weight of mucosa. A single pooled sample of gastrin was used for all the studies reported here.

Ampules containing 1 mg histamine phosphate per ml were used. Doses of histamine are expressed as mg of this salt.

Injections of gastrin or histamine were given subcutaneously.

Gastric fistulas were prepared by the method of Lane *et al.*(2) in 8 male rats of the Long-Evans strain weighing between 336 and 452 g. Rats were first used for testing 1 week after surgery.

Before each test the rats were fasted for 18 hours by placing them in a restraining cage (3). Water was allowed during this period but was removed during testing. The rats remained in the restraining cages during the tests. Hypodermic needles (22 gauge) were inserted under the skin at the beginning of the test and were left in place until injections had been given. The cannulas were opened; the stomach was flushed repeatedly with water

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