upon termination of care of the young. It is obvious that any episodic release is triggered to an external event and in this connection a very curious and interesting observation has been made in some ducks. The drake here assumes no responsibility for his offspring and, upon observing signs of broodiness in his mate, takes his departure. He now joins a group of his fellows and proceeds to molt into the eclipse plumage(10). The pituitary has long been implicated in this special molt(11); does not the sympathetic performance of the drake suggest that prolactin may be the specific secretion involved?

Summary. Adult capons were treated with prolactin (LTH), follicle stimulating hormone (FSH), luteinizing hormone (LH), singly or in combination with a constant progesterone (Pg) dosage. In addition, Pg was administered alone. Pg was effective in activating the castrate feather papilla, these findings confirming earlier responses obtained in both intact sexes of fowl by others. FSH and LH were both ineffective in stimulating capon feather regeneration; in combination with Pg, the reaction was similar to that toward Pg alone. LTH uniformly caused molt of the capon feathering whether given alone, in combination with Pg, or alone as a highly purified preparation. The positive performance of LTH in the male castrate feathering described here, together with the observed lack of response toward FSH and LH in this fowl, suggest that prolactin may be the immediately effective agent in stimulating the feather papilla to production of a new plumage.

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Physiological Disposition of Heparin.* (24147)

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The property of heparin as inhibitor of blood coagulation has been known for a number of years(1). Although the exact mechanism for this action is still unknown, indications are that heparin acts primarily in preventing conversion of fibrinogen to fibrin. The extreme rapidity of its action, after injection, makes it a valuable therapeutic agent when employed clinically in early cases of coronary thrombosis. On the other hand the pharmacological effect of heparin disappears comparatively rapidly, consequently provision must always be made for prolonging blood coagulation time by continued administration of an anticoagulant. The physiology and metabolism of heparin has been slightly elucidated. Its importance and potential use have never been fully appreciated, possibly because the quantity of heparin in tissues is minute and previous methods for measuring and distinguishing it from other mucopolysaccharides are very tedious and open to question. With the preparation of radioactive heparin labeled with sulfur-35(2) the possibility was opened for quantitative metabolic studies of this substance. We reported results on clear-

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TABLE I. % of Administered Radioactivity after Intravenous Injection of Heparin-S^{35}.*

	Hours after inj.			
	.25	2	24	48
Blood	82	23	0	0
Liver	4.4	22.6	28	0
Lung	3.3	12.5	14	0
Spleen	0	1.2	.8	0
Kidney	0	.5	.4	0
Heart	0	.11	.1	0
Urine			24	0

* Each figure is avg of results obtained from at least 3 experiments.

ance of heparin from the bloodstream(3). The present paper reports the distribution of heparin in tissues and its excretion from urine after intravenous injection.

Methods. The radioactive heparin-S^{35} used was prepared in our laboratory as described previously(2). This material, as the sodium salt, with specific activity of 1.3 X 10^4 cpm was dissolved in physiological saline to a concentration 1 mg/ml. Dogs weighing 5.4 to 6.6 kg were injected intravenously with 2 ml of radioactive heparin solution (2.6 X 10^4 cpm)/kilo body weight. In one series of experiments, the animals were sacrificed at various time intervals (Table I) and the desired organs extirpated for radioactivity assay. The organs were homogenized and duplicate aliquots were combusted and assayed as barium sulfate. A sample of the original heparin was also combusted and plated in similar manner so that a comparison between radioactivity of tissues and of heparin could be made. In another series, the injected animals were placed in metabolism cages 4 days and urine collected daily was assayed for radioactivity. All samples were counted with a gas flow counter and sufficient counts were taken to obtain an accuracy of $\pm$ 10%. The values obtained were converted to the number of cpm at infinite thinness.

Results. Following intravenous injection with a dose of 2 mg/kilo the heparin-S^{35} is rapidly cleared from the bloodstream. After 2 hours only 23% of radioactivity can be detected (Table I). A considerable portion of radioactivity accumulates in the liver so that after 24 hours, this organ accounts for 28% of the injected material. It might be noted, however, that after 48 hours, there is no measurable amount of radioactivity in the liver or any other organ, probably due to rapid turnover of heparin in the living organism, although the possibility that there is desulfation, whereby the label is lost, cannot be completely excluded. The presence of heparinase, as reported in rabbits by Jacques(4), could not be found in our dogs. However, other modes of degradation and desulfation are quite possible. In addition to liver, an appreciable amount of injected heparin accumulates in the lungs, while only minute quantities are found in spleen, kidney, or heart. On the other hand, if one considers comparative weights of organs and amounts of radioactivity/g of tissues, there is no preferential accumulation in any tissue. Excretion of radioactivity from urine is comparatively rapid so that 45-55% of the injected dose is excreted within the first 24 hours (Fig. 1). In one experiment, urine was obtained from animal 30 minutes after injection and 2% of radioactivity had already been excreted. Over 60% is excreted after 48 hours; 75-85 and 80-90% after 72 and 96 hours, respectively.

The rapid removal of radioactivity from the bloodstream is a clear indication that disappearance of the pharmacological effect after a comparatively short interval is not due to deactivation or neutralization of the heparin but rather to actual loss of this substance from the circulatory system. In addition, results with other tissues demonstrate that heparin has a rather rapid turnover rate so that it is

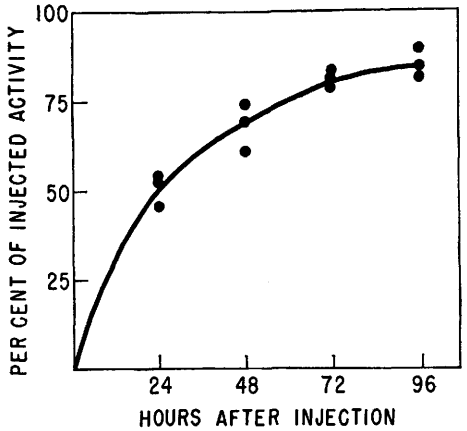

FIG. 1. Excretion of radioactivity in urine of dogs after inj. of Heparin-S^{35}. Dose was 2 mg (specific activity 2.6 $\times$ 10^4 cpm)/kg body wt.

almost completely excreted within a few days.

Summary. After intravenous administration of heparin-S^{35} to dogs, it is rapidly cleared from the bloodstream. The highest radioactivity is found in liver and lung. However, no measurable radioactivity is detected in any organ after 48 hours.

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Evidence for Conversion of Corticosterone to Aldosterone in Man.* (24148)

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Although corticosterone (compound B) might reasonably be considered a biosynthetic precursor of aldosterone (18-aldehydo-corticosterone), conversion of the former steroid to the latter has not previously been demonstrated in man. Moreover, studies using animal tissues have yielded conflicting results. Rosemberg and Dorfman(1) found only inconsequentially increased secretion of aldosterone-like material by calf adrenals perfused with corticosterone. Wettstein(2) reported actual suppression of aldosterone synthesis when beef adrenal homogenates were incubated with compound B. In contrast, upon incubating beef adrenal capsule strippings with corticosterone-4-C^{14}, Travis and Farrell recently isolated aldosterone having a molar specific activity 54% that of the labeled corticosterone(3). The present study revealed that prolonged, continuous infusion of corticosterone† to normal man simultaneously caused sharply increased urinary aldosterone and profound depression of 17-hydroxycorticosteroids. The alterations in steroid excretion were accompanied by marked shifts in urinary electrolytes, but no metabolic evidence of enhanced glucocorticoid activity.

Material and methods. Three male patients, 33 to 43 years of age, having no organic disease were studied. During a 3-day control period on hospital diet, daily sodium and potassium excretions remained essentially constant. On days 4 and 5 corticosterone was administered continuously by vein, patient A receiving 200 mg daily and patients B and C receiving 300 mg/24 hours. Daily steroid was infused in 2000 ml of 5% glucose in water, except that patient C inadvertently received his first 300 mg of compound B in 2000 ml of 0.9% NaCl. Aliquots of 24-hour collections of urine were analyzed by flame photometry for sodium and potassium, and by standard methods for glucose,‡ creatinine(4) and uric acid(5). Urinary aldosterone was assayed by the physico-chemical method of Neher and Wettstein(6), and 17-hydroxycorticosteroids by the Porter-Silber procedure(7).

Results. Qualitatively similar changes were shown by all 3 patients during and after perfusion with corticosterone (Table I). Excretion of aldosterone at least doubled during steroid administration, then fell to sub-baseline values in the recovery period before regaining normal levels. Mean daily aldosterone titers for the group were 8.6 μg in the control period, 20.0 μg at peak excretion during corticosterone infusion, and 6.1 μg on the second day of recovery. Simultaneous mineralocorticoid effects were evidenced by a sharp fall in Na/K ratio during the infusion period (from mean control value of 1.2 to minimum of 0.4), the decrease reflecting

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‡ "Glucostat," Worthington Biochemical Corp., Freehold, N. J.