deoxypentose, hexosamine, and 5 other sugars were present in all of these matrices. The carbohydrate composition was similar in all stones with the exception of uric acid calculi, in which glucose appears to be absent.

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Metabolism of Steroids II. Half-Life of Various Steroids in Dogs.* (23162)

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Concentrations of free adrenal steroids in peripheral circulation are governed by a number of unknown factors, including rates of production by the adrenal cortex, of conjugation with other compounds, of excretion by the kidney and of *metabolism* in tissue. It has been established(1-3) that the disappearance of exogenous steroids from peripheral circulation is a first order reaction, *i.e.* rate of disappearance is proportional to plasma concentration. Accordingly, when logarithms of steroid concentration are plotted against time, a straight line results. From the equation for this regression line, the half-life of the steroid can be calculated. In human subjects the half-life of cortisol varies with age (4) and is influenced by certain diseases (1,2). Also, different steroids have different half-life values, but maintain a fairly consistent relationship to one another when studied in the same human subject(2,5). In the present study the rates of disappearance from the peripheral circulation of several different steroids have been measured in the dog.

Materials and methods. The animals used were trained, unanesthetized adult mongrel dogs, each weighing approximately 20 kg. Each animal was rested for at least one week and occasionally for several weeks between successive experiments. Thus, although each dog was used for many experiments during a 2-year period, and although blood loss per experiment approximated 200 ml, no animals developed anemia and the hematocrit values remained constant throughout an experiment. The steroids employed were cortisol (Compound F), cortisone (Compound E), corticosterone (Compound B), and Δ^1-cortisol (Δ^1-F). These compounds were prepared for intravenous administration by dissolving the free steroid in 50% ethanol.§ This solution was diluted in each case 15-20 fold with 5% dextrose in water and administered by intravenous drip during a 10 minute period. The amount of steroid given in each experiment was 2 mg/kg body weight. The moment the infusion was completed, was re-

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TABLE I. Half-Life of Various Steroids in 5 Dogs.

	Half-life (min.)				
	Cortisol (F)				
No. determinations	Mean & S.E.	Range	Cortisone (E)	Corticosterone (B)	Δ^1-cortisol (Δ^1-F)
25	51 ± 2.2	28-72	51	57, 30, 28	65, 56
26	49 ± 2.3	30-88	41	30	48, 56, 64
23	55 ± 1.8	44-81	38, 48	38	62, 73
6	64 ± 3.6	50-76		26, 35	114
4	51 ± 5.7	43-68		29	67
All dogs					
No. determinations	84		4	8	9
Mean ± S.E.	52 ± 1.2		45 ± 3.0	34 ± 3.5	67 ± 6.3
Range	28–88		38–51	26–57	48–114
	F		E	B	Δ^1-F
p *vs* F			<.50 >.10	<.01	<.01
vs E				<.10 >.05	.05
vs B					<.01

corded as zero time. Heparinized blood samples were obtained at intervals thereafter and the precise time of obtaining each sample was recorded; at least 5 samples were taken at 15 to 30 minute intervals. These samples were centrifuged after collection, and the plasma was separated and frozen until used for determination of steroid concentration. The concentration of Compound B was determined by modification of the fluorometric method of Sweat(6,7). Compounds F, E and Δ^1-F were determined as 17-hydroxycorticosteroids (17-OHCS) according to the method of Nelson and Samuels(8) as modified by Eik-Nes (9). Studies reported from this laboratory (10) have shown that this method can be used to determine Δ^1-F. In calculating the half-life for each of these steroids the logarithms of plasma steroid concentrations were plotted against time and the straight line of best fit was calculated according to the method of least squares. From the equation for this regression line the half-life of the steroid was calculated. Although evidence has been presented(11,12) that administration of cortisol and related steroids inhibits the release of endogenous ACTH, the duration of this action is not known. Hence, to minimize the influence of endogenous ACTH-induced corticosteroid secretion, plasma samples containing steroid concentrations less than 10 μg% were excluded from calculations of half-life. Physiological levels in dogs are well below this value(13).

Results. Our data are presented in Table I. The mean half-life for cortisol observed in 84 determinations in 5 dogs was 52 ± 1.2 minutes, with a range of 28 to 88 minutes. As shown in the column captioned "range," considerable half-life variation occurred among serial studies in each animal. Despite this, analysis of variance indicates that the probability of differences among these mean values being due to chance is less than 2%. Therefore, it appears that although unknown factors may influence this rate from day to day, the individual animal tends to remove free, exogenous cortisol from circulation at a characteristic rate and that this rate differs among different animals.

In the Table the half-life values for cortisone, corticosterone and Δ^1-cortisol in the same animals are compared with those for cortisol. The mean half-life for cortisone observed in 4 determinations was 45 minutes. This is essentially no different from that for cortisol. The value for corticosterone is much shorter than that for cortisol, with a mean of 34 minutes resulting from 8 determinations. The rate of removal from circulation of the synthetic steroid, Δ^1-cortisol, is definitely slower than those for compounds B, E, or F: the mean Δ^1-F half-life observed in 9 determinations was 67 minutes. In the 3 dogs in which more than one Δ^1-F half-life study was done not much variation was found, even though the range for the entire group was considerable (48-114 minutes).

Although the number of these Δ^1-F studies is too small to permit a definite conclusion, it appears that there is a tendency for the cortisol and Δ^1-cortisol half-lives to run parallel in the individual dogs: those animals which have a longer mean cortisol half-life also have a longer Δ^1-cortisol half-life.

Discussion. In these dogs the order for the rate of removal of exogenously administered steroid was Δ^1-cortisol$<$cortisol $\cong$ cortisone $<$ corticosterone. This same order has been found in human subjects, but the 2 species differ with regard to the absolute half-life values for these steroids. Considering the 4 steroids in the order listed, the mean half-life values for dogs were 67, 52, 45 and 34 minutes, respectively; compared with these are half-life values reported for human subjects of 192(10), 106-115(1,2), 94(14) and 39 (14) minutes, respectively.

Proportionate rates for disappearance of exogenous steroids also are different in the 2 species. Thus, the ratio for the mean half-life of each steroid in man to that observed in these dogs is roughly: for Δ^1-cortisol, 3; for cortisol, 2; for cortisone, 2; and for corticosterone, 1. For each steroid except corticosterone the half-life in the dog is much shorter than that in man. This may explain partially why the dog has a much lower plasma 17-hydroxycorticosteroid concentration than man(13) even though in both species cortisol is the major corticosteroid secreted by the adrenal cortex.

The relationship of Δ^1-cortisol half-life to cortisol half-life has been discussed elsewhere (10,15). In the metabolism of Δ^1-cortisol it first is converted to cortisol by reduction of the C^1 double bond before further saturation of ring A at C^4, and subsequent hydrolysis of the C^3Ketone(16,17). On the basis of the smaller Δ^1-cortisol/cortisol half-life ratio in dogs (1.3) than in man (1.8), there is indication that C^1 reduction occurs more rapidly in the dog.

Summary. Data concerning the half-life of exogenous cortisol, cortisone, corticosterone and Δ^1-cortisol in dogs were presented. Cortisone half-life was similar to that for cortisol. In contrast, Δ^1-cortisol half-life was considerably longer and corticosterone half-life considerably shorter. The relationship between these findings in dogs and those in human subjects was discussed.

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