These data show that the pituitary gland of the anestrual ewe is comparable to that of the breeding-season ewe in having the ability to store gonadotrophic hormones in increased amounts following spaying. Thus the anestrual ewe has the ability to produce appreciable amounts of these hormones, and the suggestion is strong that this ability may be as great as in the breeding-season ewe. This latter point cannot be considered as proven, however, since the amount of hormone stored in the gland may reach an equilibrium in less than 90 days. The data provide no information on the rate of increase.

In view of the apparent ability of the anestrual ewe to produce gonadotrophic hormones, the current theory that anestrus is due to a lowered activity on the part of the pituitary gland may have to be modified. Quite possibly the immediate cause of the anestrual season is some changed physiological condition outside the pituitary gland which influences the ability of the ovary to respond to gonadotrophic hormones. Any attempt to discuss possible factors at this time would be mere speculation.

Summary. The gonadotrophic potency of pituitary glands from crossbred Lincoln × Rambouillet ewes was significantly higher than that of pituitaries from purebred Hampshire ewes. The gonadotrophic potency of glands from both breeds increased markedly during a 90-day period following spaying whether during the breeding season or during anestrus.

15661

Utilization of Glucose and Acetone Bodies by Gastrointestinal Tract in Fasting Normal and Diabetic Dogs.

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Although the method of arterio-venous differences has often been used to study the metabolism of muscle[1-5] and of brain[6,7] in both normal and diabetic animals and men, this procedure has apparently seldom been applied to the gastrointestinal tract. It is now generally recognized that the RQ of the brain is always close to unity, and that it continues to remove glucose from the blood and utilize this sugar as its chief, if not its only fuel, under a great variety of conditions including fasting and diabetes. In skeletal muscle, however, it has been found by all who have studied A-V differences in severe diabetes that either no glucose is removed or the amount removed is greatly reduced even after the administration of this sugar. Only Cavett and Seljeskog[4] report that as much glucose is removed in diabetic patients as in normal controls, but it seems improbable that they studied severe diabetes for only one of their 8 patients had a blood sugar level above 180 mg/ml. Others have also reported nearly normal values in mild diabetes,[1,3] but absent or reduced A-V differences in severely diabetic patients.

London[8] found that the portal blood of normal dogs contained 6 to 9 mg/100 ml

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less glucose than the arterial, and that lactic acid might be either removed or added. Cherry and Crandall,[9] in dogs fasted 18 hours, observed a difference of 2.9 mg of glucose and no significant change in lactic acid. In amytalized dogs fasted 28 hours, Wierzuchowski and Fiszel[10] report the removal of 1.9 mg of glucose and the addition of 3.1 mg of lactic acid.

In the course of determinations on hepatic glucose output and blood flow in normal[11] and diabetic[12] dogs, an opportunity was presented to obtain data on the retention or output of glucose, lactic acid and acetone bodies by the gastrointestinal tract.

Methods. London cannulae were applied to the portal (and hepatic) veins of normal dogs by the usual method. Other animals were similarly angiostomized and the pancreas completely removed at the second stage of the operation. Survival of the angiostomized-depancreatized dogs was promoted by postoperative treatment with sulfathiazole. Both normal and depancreatized animals were trained until they were not disturbed by the procedure of withdrawing blood. The diabetic dogs were kept on a diet of beef heart, raw pancreas, and milk with sufficient insulin (regular and protamine separately injected once daily) to reduce the urinary glucose loss to 1 or 2 g per day; these animals were not used until they had been stable on this regime for at least 2 weeks. The normal dogs were fasted 3 to 5 days. Blood samples were then taken from the femoral artery and portal vein at intervals of 1 or 2 hours until 3 or 4 pairs of samples had been removed. Similar pairs of samples were taken from the depancreatized dogs 3 to 7 days after withdrawal of food and insulin. All blood samples were analyzed for glucose by the method of Shaffer and Somogyi,[13] lactic acid by the method of Barker and Summerson,[14] and acetone bodies by the method of Crandall.[15]

Results. In Tables I and II we present the data on arterio-portal differences in normal dogs and in depancreatized dogs that have been without food and insulin for 3 or more days. Since blood sugar levels and urine glucose loss in the depancreatized dogs became stabilized on the third day, we consider that the latter animals were completely diabetic at this time.

It will be noted that the gastrointestinal tract of the normal dog removes significant amounts of glucose and acetone bodies from the arterial blood, but has no consistent effect upon the concentration of lactic acid. In more than half of all pairs of samples, there was no appreciable effect on lactic acid concentration, and although lactic acid was removed more often than it was added, the behavior of the gastrointestinal tract toward this substance is unpredictable. These statements apply equally to animals fasted 3 and 5 days.

There are suggestive differences with respect to glucose and acetone bodies between dogs fasted 3 days and those fasted 5 days as shown in Table III, although none of these differences is statistically significant.

The utilization of glucose, in terms of quantity per unit blood flow, is seen to be 1.6 mg/100 ml higher in the diabetic dogs than in normal animals. This is an increase of 90% over the normal value, but the difference only approaches statistical significance; $t = 2.1$, $P<0.05$. In the diabetic dog there is also an appreciable utilization of lactic acid, which is probably significant, and the utilization of acetone bodies is 1.4 mg/100 ml greater than in normal dogs. The "t" for the difference in acetone utilization between normal and diabetic dogs is 3.1, $P<0.001$. The average blood levels in

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TABLE I.
Normal Dogs.
Arterio-portal Differences of Glucose, Lactic Acid, and Acetone Bodies.

	Mean A-P differences and standard errors		
	Glucose*	Lactic acid*	Acetone bodies*
Total No. of samples	57	38	37
Mean value, mg/100 ml	+1.8 ± 0.3	—0.1 ± 0.22	+0.38 ± 0.11
G-I removal: No. samples†	30	6	14
Range‡	+2 to +6	+0.6 to +5.4	+0.6 to +1.8
No change: No. samples†	23	20	21
Range‡	+1 to —1	+0.5 to —0.5	+0.5 to —0.5
G-I additions: No. samples†	4	13	2
Range‡	—2 to —5	—0.6 to —2.5	—0.6 to —0.9

* + indicates removal by gastrointestinal tract, — addition to blood.
† No. samples indicates the number of times that an amount of substance beyond the limits of error of the chemical method was removed or added, all others considered as "no change."
‡ "Range" indicates the range of value taken as indicating removal, no change, or addition, respectively.

TABLE II.
Diabetic Dogs.
Arterio-portal Differences of Glucose, Lactic Acid, and Acetone Bodies.

	Mean A-P differences and standard errors.		
	Glucose*	Lactic acid*	Acetone bodies*
Total No. of samples	33	33	33
Mean value, mg/100 ml	+3.2 ± 0.6	—0.37 ± 0.16	+1.8 ± 0.45
G-I removal: No. samples†	21	4	25
Range‡	+2 to +10	+0.6 to +2.5	+1.1 to +7.8
No change: No. samples†	8	15	5
Range‡	+1 to —1	+0.5 to —0.5	+1.0 to —1.0
G-I additions: No. samples†	4	14	3
Range‡	—2 to —3	—0.6 to —2.5	—1.1 to —5.3

*, †, ‡ as in Table I. Note that the range considered to be within the limits of error of the acetone body method is 1.0 mg/100 ml in diabetic dogs as compared with +0.5 in normal dogs; the higher range for the depancreatized animals is due to their higher blood acetone body level.

TABLE III.
Comparison of Arterial Blood Levels and Arterio-portal Differences in Dogs Fasted 3 and 5 Days.
(None of these changes is statistically significant.)

	Glucose		Lactic acid		Acetone bodies	
	Arterial blood conc.	A-P diff.	Arterial blood conc.	A-P diff.	Arterial blood conc.	A.P. diff.
3 day fasted	69	1.9	8.3	+0.2	2.9	0.23
5 " "	72	1.3	8.5	—0.35	5.6	0.53

the diabetic dogs were: glucose, —336, lactic acid, —13.4, and acetone bodies —67.9. The blood sugar and lactate levels showed a tendency to increase somewhat on the fifth, sixth, and seventh days after withdrawal of food and insulin, although no statistically valid correlation can be made. The acetone body concentration averaged 37.6 on the third day and 86.3 on the fourth or later days, the highest value attained being

210 mg/100 ml in one dog on the fourth day.

Discussion. From the data presented above we may conclude that the gastrointestinal tract of the fasting normal dog utilizes glucose and acetone bodies, but has no consistent effect on the concentration of lactic acid. It should be noted that removal of appreciable quantities of acetone bodies could not be expected to occur until the animal had been without food for at least 24 hours, for in the postabsorptive state these substances are not being manufactured by the liver and their concentration in the blood is insignificant.[16] We may also conclude that the gastrointestinal tract of the depancreatized dog from which food and insulin have been withheld for at least 3 days: (1) removes glucose possibly at a greater rate than the G-I tract of the normal animal, (2) adds lactic acid to the blood, and (3) removes acetone bodies at a more rapid rate than is true of the normal dog, the difference being in line with the higher blood acetone body concentration of this preparation.

Our present observations on normal dogs confirm the removal of glucose and inconsistent effect on lactic acid previously noted in normal unanesthetized dogs,[8,9] although the quantity of glucose taken up is less than reported by London.[8] The uptake of lactic acid reported by Wierzuschowski and Fiszel[10] may be attributed to their use of amytal anesthesia, since it has been shown that anesthetics may alter metabolic processes.[17] Utilization of acetone bodies by the normal gastrointestinal tract and the A-P differences in depancreatized dogs do not appear to have been reported previously. The structures drained by the portal vein may now be ranked with skeletal muscle in their ability to use acetone bodies, and brain remains the only tissue which has been shown not to remove them.[18]

Of particular interest is the continued utilization of glucose by the gastrointestinal tract in the diabetic dog. Assuming that the portal blood flow is 1.5 liters/kg/hour, our value would indicate the removal of 48 mg of glucose/kg/hour. Of this quantity some 11.6% is returned to the blood as lactic acid, leaving about 42 mg/kg/hour unaccounted for and presumably oxidized. This quantity would yield nearly 4 calories per kg per day. It has been shown that brain utilizes little, if any, other fuel than glucose in diabetes and accounts for about 10% of the total resting metabolism.[7] If then the utilization of glucose by the gastrointestinal tract accounts for another 8%, approximately 18% of the heat production of the resting diabetic dogs could be accounted for by the oxidation of glucose.

This inference, that 88% of the glucose removed by the gastrointestinal tract is oxidized, must of course be regarded as tentative, pending the demonstration of the actual fate of this sugar. However, it is difficult for us to conceive of any other explanation for its disappearance.

Summary. In the normal dog fasted 3 or 5 days, the organs drained by the portal vein remove significant amounts of glucose and acetone bodies, but have no consistent effect upon the blood lactic acid. In the depancreatized dog, 3 to 7 days after the withdrawal of food and insulin, these organs continue to remove statistically significant quantities of glucose and increase their removal of acetone bodies. Under these conditions they add lactic acid to the blood. If the glucose removed by the gastrointestinal tract of the depancreatized dog and not returned to the blood as lactate is oxidized, it will account for approximately 8% of the animal's resting metabolism.

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