employed, the presence of antigen must be excluded, for in some weakly immunized animals antigen persists during long periods within the blood stream.

This reversed passive anaphylaxis suggests a simple explanation of the phenomena of anaphylaxis. Characteristic reactions occur whenever antigen and antibody meet within tissues, which are in consequence of their peculiar functions susceptible to stimulation or injury. This explanation does not exclude the possibility that changes resulting in symptoms may occur within the blood stream. An analogous series of events are observed when antigen is injected into the skin of sensitized animals; acute inflammation (Arthus phenomenon) follows. This tissue sensitization may be produced passively and, as pointed out above, the usual procedure may be reversed, acute inflammation being produced by intracutaneous injection of anti-serum into animals sensitized by antigen. In this experiment the reversible relation of antigen and antibody to the changes which occur in the tissues is more evident than in anaphylactic shock but in each instance antigen and antibody has caused a reaction, the character of which is determined by functional peculiarities of the affected tissue.

2888

Studies in adrenal insufficiency.

G. N. STEWART and J. M. ROGOFF.

[*From the H. K. Cushing Laboratory of Experimental Medicine, Western Reserve University, Cleveland, Ohio.*]

Duration of survival of pregnant dogs after adrenalectomy.— The period of survival has been seen to be greatly increased in pregnancy. Two examples will be given: one in which the second adrenal was removed soon (probably no more than a week) after impregnation, and another in which gestation was from half to two-thirds over when the second adrenalectomy was performed. One dog (1036), known to have been impregnated in the interval between removal of the first and second adrenal, lived 46 days 3

hours after the second operation. Even then the immediate cause of death was perforation of a duodenal ulcer (15 to 20 mm. in diameter). The fatal symptoms developed abruptly on the 46th day. The coma was temporarily relieved by intravenous injections of Ringer-dextrose solution and 3 pups were born, two of them dead. Three more were found at autopsy, which was performed immediately. The breasts did not seem to contain milk. The pups were probably within about a week of full term. As the only coition took place 5 to 8 days before removal of the second adrenal, impregnation could not have occurred more than 54 days before delivery. The average period of gestation in dogs is in the neighborhood of 60 days. It is a matter of speculation how much the survival period would have been lengthened but for the complication of the duodenal ulcer. All that can be said is that it would certainly have exceeded 46 days. In our experience ulcers (gastric and duodenal) are not very commonly encountered *post mortem* in dogs dying from adrenal deficiency (5 times in 31 autopsies carried out immediately after death). The case mentioned is the only one out of 60 animals in which death was due to perforation. It is evident that the survival period was far greater than in control animals (males or non-pregnant females), 7 times greater than the average. In fact the animal lived considerably longer than any of those referred to in a previous paper,[1] whose lives had been prolonged by regular injections of Ringer-dextrose solution.

In another bitch (1034), the second adrenal was removed 24 days before the birth of 5 pups, apparently at full term. Impregnation must have occurred about 4 weeks before removal of the first, and 5 weeks before removal of the second adrenal. In other words, when the acute adrenal insufficiency was produced in the mother the embryos had completed nearly two-thirds of their intra-uterine life. She remained in good health till the pups were born and for about 3 days thereafter. Lactation was normal and the pups were well nursed. At the end of this time, however, she was found in coma and died soon after. Lengthened survival has been seen under conditions which preclude any influence of the adrenals of the embryos. For instance, in a bitch parturition began one-half hour after removal of the second adrenal. She sur-

[1] Stewart, G. N., and Rogoff, J. M., PROC. SOC. EXP. BIOL. AND MED., 1925, xxii, 394.

vived 26 days, nursing 3 pups excellently. This is suggestive of a possible life-prolonging influence due to changed metabolism in the pregnant and lactating mother or to some more specific effect of certain maternal organs (uterus, *corpus luteum,* interstitial cells of ovary,?). Obviously pregnant animals must henceforth be excluded as controls.

Duration of survival of control animals.—Of 25 male control dogs, 2 survived the removal of the second adrenal for 2 1/2 days; 2 for 3 1/2 days; 1 for 4 days, 3 hours; 2 for 4 3/4 days; 1 for 5 days, 2 hours; 2 for 5 1/2 days; 2 for 5 3/4 days; 1 for 6 days, 7 hours; 1 for 6 2/3 days; 1 for 7 days; 1 for 7 days, 3 hours; 1 for 7 days, 4 hours; 1 for 7 3/4 days; 1 for 8 days; 1 for 8 1/2 days; 1 for 9 days; 3 for 9 1/2 days; and 1 for 10 days. Average 6.4 days.

Of 16 non-pregnant females, one lived after removal of the second adrenal for 2 days, 7 hours; 1 for 3 days, 10 hours; 1 for 3 1/2 days; 1 for 4 1/2 days; 1 for 4 2/3 days; 1 for 5 days, 4 hours; 1 for 5 1/2 days; 1 for 7 days; 1 for 7 days, 5 hours; 1 for 7 days, 8 hours; 1 for 7 1/2 days; 1 for 8 3/4 days; 1 for 9 days, 4 hours; 1 for 9 1/2 days; 1 for 10 days; 1 for 10 days, 9 hours. Average 6.6 days.

Autopsy findings.—While the hemorrhagic congestion in the gastro-intestinal mucosa, with blood in the lumen, is very common in greater or less degree, there are animals, whose death cannot be attributed to anything else than adrenal deficiency, in which one or both of these conditions may be absent. Thus, in 5 out of 52 adrenalectomized dogs (about 10 per cent) there was no congestion or hemorrhage of any part of the mucosa, or at least nothing more than may sometimes be seen in dogs not deprived of their adrenals and not known to be suffering from any disease. Adopting a necessarily arbitrary scale, with + signs to indicate the severity of the changes, we classify somewhat less than half of the adrenalectomized animals as showing severe and extensive congestion of the mucosa, often from stomach to rectum. In a second group, comprising about one-fifth of the cases, the condition was well marked, though less severe and less extensive. In a third group, comprising about a quarter of the cases, the condition was less marked, although recognizable, and generally it was more localized. Microscopically it is seen that the distribution of the congestion varies also in depth in the different

cases, sometimes involving the whole depth of the mucosa, in other cases only a zone next the lumen.

Congestion of the pancreas is even more common than congestion of the gastro-intestinal mucosa. In only 2, possibly 3, cases out of 53 has it been missed and in the great majority of cases it is well marked as compared with normal animals. Microscopically the islets have been found well injected but the greatest distension is in the veins in the tuberculæ. In 20 control dogs used for various purposes but not adrenalectomized, and killed with chloroform, or in other ways, only twice was a mild degree of congestion of the pancreas observed.

Presence of blood or blood pigment in the gastro-intestinal contents.—The amount of blood varied greatly but was often very considerable. In the great majority of cases it was mixed with more or less bile. Frequently blood clots were present on the mucosa. Blood pigment in the contents was often in the form of hematin. Only in 4 adrenalectomized dogs, out of 54, was no blood or blood pigment found. In 3 of these animals no congestion and no hemorrhagic condition were noted in any part of the gastro-intestinal mucosa; in the remaining dog, congestion was noted, but it was mild and not extensive. Animals dying of adrenal deficiency do not eat for a while before death, and there is no reason to suppose that blood pigment found in the gut could have come from the food.

Blood examinations.—In 20 of the dogs blood examinations were made, including estimation of sugar (Folin-Wu), of hemoglobin (comparative, with Haldane's standard); erythrocyte and leucocyte counts; conductivity of blood and serum with calculation of the number of cc. of serum in 100 cc. of blood; and often sp. gr. of blood and serum. Specimens of the results are given in the table. Dogs 1035 and 1037 were males, the rest females. It was common to find towards the end of the survival period, perhaps only on the day before death or the day of death, that the relative volume of serum dropped sharply. This was not infrequently accompanied by a diminution in the conductivity of the serum. The conductivity of serum tends to remain so constant under ordinary conditions that more weight can be given to relatively small variations. Occasionally we have thought that "concentration", with a concomitant diminution in the conductivity of the serum, could be observed beginning in the period of good

Dog	Date	Blood Sugar	Hb	Erythrocytes	K x 104 at 25° C. Blood	K x 104 at 25° C. Serum	Serum Per cent	Remarks.
1020	May 13	0.10						
	May 14			6,320,000				2nd adrenal out after blood got.
	May 16	0.095		6,240,000	58.8	126.2	63.9	
	May 18	0.077	90	6,440,000	53.7	120.0	62.4	
	May 20	0.085						
	May 23	0.074	90	6,250,000	52.5	119.5	61.0	Sp. gr. 1,058. Blood got day before death.
1025	June 4	0.10	100	7,740,000	55.3	132.0	58.8	2nd adrenal out June 5.
	June 8	0.108	99	7,100,000	43.1	127.2	49.6	
	June 10	0.105	120	9,100,000	30.3	120.0	38.6	
	June 12	0.118	122	8,500,000	30.6	120.0	38.1	
	June 14	0.083	128	9,100,000	26.8	117.8	35.2	Serum sp. gr. 1,026. Dead in night.
1028	May 21			6,550,000				
	May 22	0.108	94	6,250,000				Sp. gr. 1,056. 2nd adrenal out after blood got.
	May 25	0.082	116	8,100,000	34.4	115.0	44.7	
	May 26	0.095	96	7,700,000	38.7	115.5	49.0	
	May 28	0.093	114	8,500,000	31.0	115.0	40.9	
	May 29	0.069	120	9,350,000	25.9	108.8	36.7	Died in night.
1034	May 28	0.087	94	6,450,000	55.5	131.7	59.2	
	June 1	0.093	88	6,000,000				1st adrenal out after blood got.
	June 8	0.094	74	5,480,000	64.2	127.8	67.3	2nd adrenal out June 9.
	June 13	0.121	84	6,200,000	68.0	125.6	71.2	
	June 19	0.118	66	4,200,000	76.0	129.6	74.9	
	June 23	0.045	66	4,700,000	70.8	142.4	66.9	
	June 26	0.11	50	3,950,000	75.3	133.8	77.5	5 pups born July 2 to 3.
	July 7	0.051	102	12,000,000	37.7	128.4	45.3	Blood got just before death.
1035	May 28	0.09	98	5,600,000	54.2	132.4	57.7	
	June 1	0.082	92	5,700,000				1st adrenal out after blood got.
	June 8	0.10	82	6,400,000	57.9	124.9	63.5	2nd adrenal out June 9. Has "snuffles."
	June 10	0.066	92	6,000,000	45.6	120.9	54.1	Died during the night.
1036	June 2	0.088	88	5,900,000	47.6	130.6	52.7	1st adrenal out June 3.
	June 11	0.074	104	8,500,000	41.6	128.9	47.7	2nd adrenal out June 12.
	June 15	0.08	110	7,250,000	35.4	124.3	42.8	Sp. gr. blood 1,0697; serum 1,0246.
	June 19	0.91	102	6,200,000	39.5	123.7	47.2	
	June 23	0.08	102	7,850,000	45.3	142.4	47.1	
	June 26	0.09	102	8,500,000	43.5	133.8	47.9	
	July 9	0.093	100	8,500,000	38.2	131.7	43.5	Died July 28.
1037	June 2	0.084	110	7,800,000	41.6	128.8	47.6	1st adrenal out June 3.
	June 11	0.091	108	8,800,000	42.1	128.2	48.3	2nd adrenal out June 12.
	June 15	0.085	118	8,000,000	34.1	124.9	41.3	Sp. gr. blood 1,0644; serum 1,0239.
	June 19	0.074	126	9,700,000	23.2		29.4	Died night June 21 to 22.
1038	June 2	0.09	108	7,200,000	46.5	132.4	51.1	1st adrenal out June 3.
	June 10	0.09	106	6,400,000	45.9	132.5	50.6	2nd adrenal out after blood got.
	June 13	0.091	130	10,200,000	30.5	123.7	37.9	
	June 16	0.085	116	8,200,000	25.7	116.0	34.4	Sp. gr. blood 1,0702; serum 1,0252.
	June 18	0.058	128	8,500,000	21.3	116.6	29.1	Sp. gr. blood 1,071; serum 1,0233.
	June 19	0.07	122	8,250,000	17.1		23.7	Died 2 hours after blood got.

health before the animal began to refuse food, and presaging the fatal change. But too much stress ought not to be laid on this or on the terminal "concentration" of the blood. The latter is seen in dog 1035, which is for this reason included in the table, although in all probability it did not die of adrenal deficiency. In dog 1034, instead of a concentration, there is some dilution of the blood after removal of the second adrenal, although the terminal concentration is seen. In this animal during the period of good health there was one apparent relapse, when the blood sugar sank to 0.045 per cent., and it looked as if the animal was going to die. She recovered, however, and lived a fortnight longer.

2889

Starch grains of wheat considered as partially dehydrated amylose.

H. L. VAN DE SANDE BAKHUYZEN. (Introduced by C. L. Alsberg).

[*From the Food Research Institute, Stanford University, Calif.*]

Alsberg and Perry[1] have shown that about 60 per cent of the starch grains is soluble in cold water if it is ground for several days in a pebble mill. This fact will be used in this paper as a basis for an explanation of the properties and structure of wheat starch grains. The assumption that amylose occurs in starch grains in different stages of dehydration proved to be the most satisfactory working hypothesis. We will assume the grains to be built up of alternate layers of more hydrated amylose (less refractive rings) and of less hydrated amylose (refractive rings, to which belongs the surface ring). If we follow the terminology of Meyer, without accepting his theory in detail, the former, β-amylose, is not only soluble in hot water, but also in cold water; the latter, α-amylose, is not soluble in boiling water at 100° C. Of the α-amylose rings, the surface ring is the denser and the more dehydrated. It has a low swelling capacity at room temperature. Though the inner layers, being less dehydrated, tend to have a higher water content and to elongate their circumfer-

[1] Alsberg, C. L., and Perry, E. E., PROC. SOC. EXP. BIOL. AND MED., 1924, xxii, 60-61.