for hematocrit values to remain low after sympathectomy but suggested that the change might be more apparent than real. They believe that sympathectomy, by altering the caliber of the smaller vessels, may cause redistribution of the red cell mass in the vascular system. This in turn would change the cell-plasma ratio in the larger vessels from which sampling is accomplished. Although this possibility cannot be excluded, it can hardly be of the magnitude and persistence required to explain our observations. In addition, any significant changes resulting from sympathectomy involve arterioles rather than capillaries and should not necessarily result in the shifting of large portions of the blood volume. The absence of any significant increase in blood volume after sympathectomy raises the question as to whether any widespread dilatation has actually occurred. A similar pronounced reduction in hematocrit was observed by Green[8] after surgical removal of a pheochromocytoma. The explanation of these observations is as yet obscure.

Although our series is admittedly small, it seems probable that patients with low red cell masses preoperatively can expect little from sympathectomy whereas if the red cell mass is elevated the prognosis is considerably better. Whether this is simply another way of saying that patients operated on early in the course of the disease do better postoperatively cannot be determined from these data.

Summary. Blood volume studies on 20 patients with hypertensive vascular disease before and after sympathectomy revealed no consistent long-term postoperative changes other than immediate decrease in the red cell mass with tendency toward delayed recovery. There was no consistent deviation from "normal" in the preoperative determination. Patients with low red cell masses preoperatively showed poor postoperative response and there was a general tendency for patients with long-term vascular disease to have low blood volume.

[8] Green, D. M., *J. A. M. A.*, 1946, **131**, 1260.

16410 P

Production of Alloxan Diabetes in the Dog.

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The discovery that a diabetic state could be induced in experimental animals by a single injection of alloxan opened a new field for the investigation of problems relating to the control of sugar metabolism. This technique has been applied and found successful in most of the ordinary species of laboratory animals. However, the results are not nearly so satisfactory in one of the more valuable experimental animals, the dog. Ordinarily, a satisfactory diabetic dog is obtained in only one out of 7 or 8 attempts. Doses of alloxan greater than 100 mg per kilo are frequently fatal, and smaller doses usually do not produce an appreciable and sustained elevation of the blood sugar. Failures in these larger laboratory animals is expensive and time consuming and makes a more effective method desirable.

The alloxan in varying dosages was injected directly into the abdominal aorta, and the hepatic, gastro-duodenal, and pancreatic arteries in an attempt to obtain a higher concentration of the drug in the pancreas with a smaller amount of the drug in the general circulation, thereby avoiding toxic effects on other organs. These attempts failed: only one in 8 dogs developed a moderate hyperglycemia and this effect did not persist longer than 2 weeks.

Kass and Waisbren[1] increased the per-

[1] Kass, E. H., and Waisbren, B. A., PROC. SOC. EXP. BIOL. AND MED., 1945, **60**, 303.

TABLE I.
Fasting Blood Sugars.

Animal No.	Control	Days after alloxan administration* 1	2	3	6	7	8	10	11	12	13	14	15	19	Hyperglycemia
1	125	179		337				435	Insulin started				150	155	Sustained
2	126	250		362				421	Insulin started				210	320	"
3	78	325		127		178									Transitory
4†	181					262				152		166			"
5†	160					323	Insulin started			287		215			Sustained
6†	188					181				122		112			Transitory
7	140	600	died												Severe
8	140	583	"												"
9	100	750	"												"
10	120	370	Insulin started		190						175				Sustained

* Each dog received 75 mg per kilo of alloxan intravenously.
† These animals received part of dose subcutaneously, consequently did not develop severe or sustained diabetes.

centage of alloxan diabetes in rats by starving the animals for 48-60 hours before injecting the alloxan. A similar procedure has been applied to the dog and found to be successful.

Method. After maintaining the animals for three days on water only, 75 mg per kilo of body weight of alloxan in 5% solution was given intravenously as a single dose. Immediately following injection the animals were fed. If food was withheld for as long as 6 hours after receiving the drug, the animals would not ordinarily survive. Control blood sugars were taken at intervals thereafter. Specimens for blood sugar determinations were taken with the animals in a fasting state, food having been withheld for 12 hours. After diabetes had become established, it could be controlled with insulin.

Results. Of the 10 dogs injected, 7 developed a sustained or severe hyperglycemia and 3 developed a transitory hyperglycemia, as shown in Table I. Animals 11, 12, and 13 received part of their doses subcutaneously and this alteration of treatment is assumed to account for the less severe and transitory hyperglycemia observed. Animals 14, 15, and 16 received no food for 6 hours following injection, and they died on the second day after the administration of the drug. The greatly elevated blood sugar levels occurring in these 3 animals on the day following injection indicate that the islet cells were severely damaged with a resultant, sustained hyperglycemia had the animal survived. The diabetic animals were sacrificed for post-mortem examination after 45 days.

Discussion. The reasons for the effectiveness of the simple procedure are not entirely clear. Kass and Waisbren reported that the action of alloxan could be prevented by the injection of adrenalin just preceding or along with the alloxan, or by intravenous glucose administration 6 hours before the injection of alloxan. If the glucose were given one hour before the alloxan it would not prevent the development of the diabetic state. These data, together with the fact that starvation enhances the diabetogenic action of alloxan suggest that its action may in some way be related to the functional state of the glucose regulating mechanism. Lazarow[2] found that the hyperglycemic effect of alloxan could be prevented by the administration of glutathione and cysteine and he proposed that alloxan may act by inhibition of the sulfhydryl enzymatic system. He suggested that normally this system may be relatively deficient in the beta cells of the pancreatic islets. Starvation may further lower the sulfhydryl enzymatic system, and enhance the action of

2 Lazarow, Arnold, PROC. SOC. EXP. BIOL. AND MED., 1946, **61**, 441.

alloxan. These speculations require further investigation.

Conclusion. Alloxan diabetes can be produced in a high percentage of dogs by the simple expedient of starving the animals for 3 days prior to the injection of alloxan.

16411

Effect of Liver Extract on Growth of Rabbits.*

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The increasing use of rabbits in biochemical and nutritional investigations has led to further study in preparation of simplified diets for these animals. Wooley and Sebrell[1] described a purified diet supplemented only with pure vitamin preparations. Nearly normal growth was obtained for a limited period of time when this diet was fed.

In the present investigation we have studied the adequacy of diets for rabbits in which the vitamins were supplied in a purified form and also the effect of the addition of a 1:20 liver concentrate powder† to this diet.

Experimental. Rabbits of the New Zealand White breed were used in all experiments. The rabbits were weaned at 5 to 6 weeks of age at a weight of about 950 g and placed on the experimental diets. The change from the stock diet to the simplified diets was effected gradually over a period of three days after which time the new diet was accepted by all animals.

Preliminary observations were obtained with several diets to determine the best diet to use as a basis for comparison in a series of investigations on the nutritional requirements of rabbits. Results obtained with 3 of these diets, 2 of which contained 4% of the liver concentrate (rations 11 and 12), indicated that when liver concentrate was added to the diet an improved growth response was obtained. The average rate of growth of the rabbits which received the liver concentrate was significantly higher as determined by "analysis of variance" than for the rabbits fed ration 1, without the liver concentrate (P equals 0.02). The average rate of growth, during a 6 week experimental period, of the animals fed ration 1 was 175 g per week, while the average gains of those fed rations 11 and 12 containing liver concentrate were 226 and 209 g per week for the respective diets.

Rations 11 and 12 differed essentially only in the cellulose content. Variation in rate of growth was not as great on the 6% level of cellulose (ration 11) as on the 12% level (ration 12). The average gains, however, were not significantly different and in the statistical analysis the data obtained from rabbits on theses diets were treated as a single group.

To extend these observations weanling rabbits were fed a purified basal diet (ration 14) which was composed of casein 22%, peanut oil 8%, cerelose 53.5%, cellulose 12%, Salts IV[2] 4%, Vitamin A and D Concentrate (Nopco XX) 0.5%, mixed tocopherols 50 mg, choline 200 mg, niacin 20 mg, inositol 10 mg, pyridoxine 0.7 mg, thiamine 0.7 mg, riboflavin 0.7 mg, calcium pantothenate 1.5

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1 Wooley, J. G., and Sebrell, W. H., *J. Nutrition*, 1945, **29**, 191.

† Generously supplied by the Wilson Laboratories, Wilson and Co., Inc., Chicago, Ill.

2 Phillips, P. H., and Hart, E. B., *J. Biol. Chem.*, 1935, **109**, 657.