

variation from the conditions described by Robb in the large and small races of rabbits otherwise studied by Castle and Gregory. There the rate of post-natal growth was identical in the 2 races until after puberty; in pigeons the total size difference is attained before puberty. This difference, however, is in no way dissonant with the basic contribution of Castle and Gregory.

Summary. Data on relative growth-rates have been obtained for 2 small and 2 large races of common pigeons from the time of hatching to a period, 87 days later, at which their adult body weight is practically attained.

The weights of embryos of these 4 races at hatching demonstrate that racial size difference is only partially and very imperfectly expressed by size differences attained during embryonic life. A large part of racial size difference in pigeons is rapidly attained early in the post-hatching period by differential growth-rate, and practically all of adult size difference is attained before puberty.

These are marked variations from the time relations of differential growth in the large and small races of rabbits studied by Castle and Gregory, but such variations offer nothing adverse to their main conclusion. We consider it an open question, to be investigated within each species or group, whether and to what extent endocrine (pituitary) difference influences racial differences of growth-rate at a particular developmental stage; but wholly probable that such endocrine difference is an effective factor in the growth of higher animals at one or another stage.

6291

Glycosuria in Rabbits Following Injections of Saline Extract of Anterior Pituitary.

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A relation of the anterior pituitary to carbohydrate metabolism has often been suspected on the basis of the frequent occurrence of hyperglycemia and glycosuria in acromegaly, and of anatomical changes in the anterior pituitary in diabetes mellitus, but such a connection was not indicated experimentally until Houssay and Biasotti¹

¹ Houssay, B.-A., and Biasotti, A., *Comp. rend. de la Soc. biol.*, 1930, **104**, 407; 1930, **105**, 121.

showed that pancreatic diabetes could be prevented in toads by removal of the anterior pituitary. Subcutaneous implantation of anterior pituitary in such depancreatized toads re-established the diabetes. They were unable to show a similar relation in mammals either by gland implantation or by injections of anterior pituitary extracts, although depancreatized and hypophysectomized dogs survived longer and showed milder diabetes than did depancreatized controls². Evans, Meyer, Simpson, and Reichert³ reported observations in which they produced glycosuria and polyuria in 2 of 4 dogs by daily injections of the growth hormone fraction of anterior pituitary extracts for 8 or 9 months.

We have made somewhat similar observations in rabbits. Hyperglycemia, polyuria, glycosuria, and lipemia developed after injecting a saline extract of ox pituitary daily for 6 or more days, in some instances of surprisingly great intensity. It occurred in each of the 4 rabbits used, though varying in degree.

The extract was prepared twice weekly from fresh chilled glands, according to the method of Schockaert⁴ except for the measures used in sterilization. It produced typical reactions among which were rapid hypertrophy of the mammary glands with lactation, luteinization of the ovaries, hypertrophy of the thyroid and suprarenal cortex.

The rabbits were kept on our stock diet of alfalfa hay and oats. Two were injected with 2 cc. and 2 with 4 cc. daily, equivalent to one-half and one anterior pituitary respectively. The data are summarized in the following table:

Collection Period	2 cc. ext. daily				4 cc. ext. daily			
	R 1039		R 1073		R 1041		R 1097	
	Glucose	Amt. per day	Glucose	Amt. per day	Glucose	Amt. per day	Glucose	Amt. per day
days	%	gm.	%	gm.	%	gm.	%	gm.
6-7	5.0	8.1	0.5	0.4	0.4	0.5	0.4	0.4
8	5.1	10.2	0.6	0.6	6.9	16.7	0.6	0.7
9-10	4.8	6.6	1.6	1.1	10.4	15.7	1.4	1.4
11	5.3	10.2	1.0	1.1	14.5	34.9	3.9	5.8
12-13	5.1	8.3	1.3	1.2	9.0	18.6	5.6	7.6
14-15	0.4	0.7	0.6	0.5	9.1	15.7	1.2	1.3
16-17*		trace?		trace?	5.2	7.8	0.4	0.4
18-19		neg.		neg.		neg.		neg.

*Last injection on 17th day.

² Houssay, B. A., and Biasotti, A., *Pflüger's Arch.*, 1931, **227**, 664.

³ Evans, H. M., Meyer, K., Simpson, M. E., and Reichert, F. L., *Proc. Soc. Exp. Biol. and Med.*, 1931, **29**, 857.

⁴ Schockaert, J. A., *Anat. Record*, 1931, **50**, 381.

Analyses were made on the urine in the collection bottles combined with the washings from the metabolism cages. The values in the table are not strictly 24 hour ones, but the total amount for the entire period is complete. Periods of one or 2 days were used as indicated; the amount excreted is calculated per day. The percent of sugar is lower than that of the urine as excreted due to dilution of the urine with cage washings. In one of the rabbits there was a very high percentage of sugar in the urine, as secreted, amounting to 18% on the 11th day.

The exact date of the onset of glycosuria unfortunately is not known. We did not suspect the presence of sugar in the urine until the sixth day when our attention was drawn to the large volume of urine excreted and the intense heat generated on the addition of chromic acid. In rabbit 1039 glycosuria was marked on this day, while in the other rabbits there was only 0.4-0.5% of sugar in the urine. In these 3 it is probable that glycosuria did not appear before the fifth day, while in rabbit 1039 the onset may have occurred on the third day. The intensity of the glycosuria was somewhat independent of the amount of extract injected, probably due to variations in susceptibility.

After 11 daily injections the morning blood sugar levels on rabbits 1039, 1041, 1073, and 1097 were 475, 348, 240, and 122 mg.% respectively (by the method of Folin⁵). The sera of these bloods were very milky. Ten days after the last injection the blood sugars of 1073 and 1097 were 92 and 93 mg.% respectively and the sera were clear. In this connection it should be remembered that the blood lipids of rabbits are quite low.

Since saline extracts are unstable they may have deteriorated during the 4 days they were kept. The extract used for the injections on the 14-17th days may have been inactive because the glycosuria decreased beginning on the 14th day. The possibility that the animals became resistant to the effects of pituitary extract must be considered. Injections were discontinued on the 17th day; 2 or 3 days after injections were stopped, glycosuria disappeared completely.

That the reducing substance in the urine was glucose was shown by making the phenylosazone. Its crystalline form and melting point corresponded to that of glucososazone. Clarified urine was strongly dextrorotatory.

Infection was not a factor in these findings.

In spite of large losses of sugar in 2 instances (50 gm. and 120

⁵ Folin, O., *J. Biol. Chem.*, 1929, **82**, 83.

gm. in 6 days), there were no significant changes in body weight. The pH of the urine varied between 8.5 and 9.5, usual for rabbits on our stock diet.

We have also tested in 4 rabbits the effect of "phyone"[†] which according to Van Dyke⁶ contains the pituitary growth hormone. Rabbit 1060, male, after injections of 1 cc. of phyone for 3 days had 0.5% sugar in its urine. The daily injections were continued and on the 4th day 5.6 gm. of sugar was excreted and on the 5th and 6th days 8.9 and 10.4 gm. respectively. Injections were stopped and the sugar output dropped to 4.8 gm., then to 2.6 gm., and 3 days after cessation of phyone administration no sugar was excreted. Five days later the blood sugar was 106 mg.%. Rabbit 1068 after injections of 1 cc. for 5 days and 2 cc. for 10 days showed no glycosuria. After the last injection the morning blood sugar was 100 mg.%. Rabbit 1063 had a trace of sugar in its urine after a single injection of 1 cc. of phyone but this did not increase although it received 10 cc. during the next 8 days. The blood sugar was 129 mg.%. Rabbit 1071 received 11 cc. of phyone during a period of 8 days. On 2 occasions a questionable test for sugar was obtained in the urine and on the last day its morning blood sugar was 121 mg.%.

Our results with phyone are similar to those of Evans, Meyer, Simpson and Reichert in that only one of the four rabbits developed a severe glycosuria. Since a much more regular and definite response was obtained with saline extracts, one is led to infer either that a material loss in activity must have occurred in the preparation of the growth hormone fraction (equivalent amounts in terms of anterior pituitary of both phyone and saline extract were used), or that the hyperglycemia and glycosuria are caused by something distinct from the growth hormone.

Respiratory quotients have been determined in 2 rabbits rendered hyperglycemic and glycosuric by the Schockaert saline emulsion but the results so far are doubtful and quotients varying between 78 and 85 have been obtained, indicating that the animals were utilizing sugar.

[†]Kindly supplied to us by Wilson and Co. through the courtesy of Dr. David Klein.

⁶ Van Dyke, H. B., and Wallen-Lawrence, Z., *J. Pharm. and Exp. Therap.*, 1930, **40**, 413.