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Diabetes in Rats and its Alleviation with Sodium Chloride.*

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The occurrence of "diabetes" as indicated by a low tolerance to glucose in approximately 60% of adult rats of the "Yale" strain, whereas Wistar rats showed a normal tolerance, has been reported[1]. The incidence of the low glucose tolerance became progressively less in younger animals, all rats 50 days of age or less showing a normal tolerance. Some dysfunction of the anterior pituitary was suggested as a possible cause of the impaired carbohydrate metabolism.[2]

Similar observations have been made in this laboratory and the work has been extended in the following way.

Adult male and female albino rats of the "Yale" strain, (Connecticut Agricultural Experiment Station strain) were fasted 16 to 18 hours and were then administered intraperitoneally 350 mg glucose per 100 g body weight, as a sterile 8.75% solution. At the intervals shown in the table, blood was drawn from a tail vein and its sugar content was promptly determined by the Somogyi micro-modification of the Shaffer-Hartmann method.[3] The tolerance to glucose was likewise determined on a group of partially pancreatectomized adult rats.

The results, summarized in Table I, demonstrate clearly that approximately 40% of the intact animals had a low tolerance† to glucose, similar to that shown by the partially pancreatectomized rats. The blood sugar level rose to excessively high values and remained high during the 5-hour period of observation. It should be pointed out, however, that the response of an individual intact rat was not invariably the same. As was also observed by Cole and Harned[1], changes in the type of tolerance curve from diabetic to normal and vice versa on repeated tests were not uncommon. In a few studies, the data of which are not included in this paper, rats of the Wistar

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1 Cole, V. V., and Harned, B. K., *Endocrinology*, 1938, **23**, 318 .

2 Harned, B. K., and Cole, V. V., *J. Biol. Chem.*, 1939, **128**, xxxix.

3 Shaffer, P. A., and Somogyi, M., *J. Biol. Chem.*, 1933, **100**, 695.

† Some investigators[1] have arbitrarily designated a blood sugar value of 180 mg % at the end of the 5-hour period as the upper limit for a "normal tolerance." This value has also been adopted in the present study.

strain and 50-day-old rats of the Yale strain invariably showed normal tolerances to glucose.

The data obtained on the "low-tolerance" group of intact rats reveals an interesting trend in the blood sugar values. Usually, there was a sharp rise at the 30-minute interval, followed by a decrease at the 60- and 90-minute periods, then a second rise, frequently exceeding the first even at the end of the 5-hour period of observation. Since it is known that the injection of a hypertonic solution of glucose into the peritoneal cavity causes a migration of sodium and chloride ions into the peritoneal fluid[4], it appeared possible that a reduction of plasma sodium, or perhaps an altered ratio of plasma sodium to potassium, might be involved in the second rise in the blood sugar values and thus in the low tolerance. Support for such a possibility is found in the observations that sodium chloride administration increases the deposition of glucose in the liver as glycogen[5] and improves the utilization of glucose by human diabetics,[6] and that the administration of potassium salts to rats produces an hyperglycemia[7].

For these reasons, the effect of the intraperitoneal injection of glucose solution containing sodium chloride was studied in the rats previously used. A 1.58% concentration of sodium chloride, isotonic to the 8.75% glucose solution, was employed.

It is evident from a comparison of these data (Table I,B) with

TABLE I.

Average Blood Sugar Values of Intact and Pancreatectomized Rats Administered Glucose* with and without Sodium Chloride by Intraperitoneal Injection.

Group	No. of rats	"True" Blood Sugar—Mg %					
		Fasting	Minutes after glucose administration				
			30	60	90	120	180	300
A. Glucose Alone.								
1. Normal tolerance, intact rats	17	79	211	202	184	158	158	127
2. Low tolerance, intact rats	10	75	268	243	231	224	257	295
3. Partially pancreatectomized rats	8	88	309	318	322	320	337	307
B. Glucose with Sodium Chloride.								
1. Normal tolerance, intact rats	5	83	251	214	162	150	128	100
2. Low tolerance, intact rats	6	74	276	248	220	194	154	119
3. Partially pancreatectomized rats	4	90	319	240	176	155	121	104

* 350 mg C. P. Glucose per 100 g body weight.

4 Darrow, D. C., and Yannet, H., *J. Clin. Invest.*, 1935, **14**, 266.

5 Crabtree, D. G., and Longwell, B. B., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 705.

6 McQuarrie, I., Thompson, W. H., and Anderson, J. A., *J. Nutrition*, 1936, **11**, 77.

7 Silvette, H., Britton, S. W., and Kline, R., *Am. J. Physiol.*, 1938, **122**, 524.

those obtained on the rats given glucose alone that the response of the normal tolerance intact rats to injected glucose was not significantly altered by sodium chloride. On the other hand, the administration of *sodium chloride with glucose* to the "low tolerance" rats resulted in a normal utilization of glucose in all instances. The partially pancreatectomized rats likewise showed a normal tolerance to injected glucose solution containing sodium chloride.

As yet, no explanation of the favorable effect of sodium chloride on the utilization of intraperitoneally administered glucose by the intact diabetic rat and the partially pancreatectomized rat can be advanced. Further studies on this problem are in progress.

Summary. The report that approximately one-half of adult rats of the "Yale" strain show a diabetic tendency, as indicated by a low tolerance to glucose administered intraperitoneally, has been confirmed. This tendency is more marked in older rats than in younger ones. The administration of sodium chloride isotonic with the injected glucose results in a normal tolerance to glucose, both in intact rats showing the diabetic trait and in partially pancreatectomized rats.

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Ultrafiltration of the Virus of Infectious Avian Encephalomyelitis.

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The causal agent of the recently described[1-3] infectious avian encephalomyelitis or "epidemic tremor of young chickens" has been shown to pass through Berkefeld V and N, and Seitz 1- and 2-pad filters.[1-3] The present paper concerns experiments on ultrafiltration of the virus through gradocol membranes; thus a more precise measurement of its size might be acquired.

The membranes employed had an effective filtration-area of 5 cm^2 and were prepared after the method of Elford,[4] as modified in certain

1 Jones, E. E., *J. Exp. Med.*, 1934, **59**, 781.

2 Van Roekel, H., Bullis, K. L., and Clarke, M. K., *J. Am. Vet. Med. Assn.*, 1938, **93** (N.S. **46**), 372.

3 Olitsky, P. K., *J. Exp. Med.*, 1939, **70**, in press.

4 Elford, W. J., The sizes of viruses and bacteriophages, and methods for their determination, in *Handbuch der Virusforschung*, edited by Doerr, R., and Hallauer, C., Vienna, Julius Springer, 1938, Vol. 1, pp. 126-181.