Bourquin[4] has shown that experimental *diabetes insipidus* in dogs is an irritation rather than a deficiency phenomenon. Slight cauterization of the floor of the third ventricle produces the diabetes but deeper cautery destroys it. She further concludes that "the diuresis must be due to a substance produced at the site of the causative disturbance" for the *diabetes insipidus* "runs its typical course after trans-section of the spinal cord at the level of the eighth cervical vertebra, double vagotomy below the diaphragm, and paralysis of the parasympathetic nervous system with atropin."

If the cause of experimental *diabetes insipidus* is to be ascribed to the irritative production of a hormone in the floor of the third ventricle, it is no less reasonable to suppose that the hormone is derived from the *pars tuberalis,* which is distinctly a glandular structure, than that it is produced by brain tissue.

The participation of the *pars tuberalis* in the causation of *diabetes insipidus* has not been ruled out by those who injure the floor of the brain between the optic chiasm and the mammillary bodies. In this connection the action of *pars tuberalis* extracts on urine secretion is of interest.

This is a preliminary report.

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Influence of Pituitrin on Diuresis Variously Induced.

F. P. KNOWLTON, A. N. CURTIS AND A. C. SILVERMAN.

From the Physiological Laboratory, College of Medicine, Syracuse University.

The diuretic action of extracts of the pituitary body was first described by Magnus and Schafer.[1] Their finding has been confirmed repeatedly. Von den Velden[2] showed that pituitrin may exert an opposite or antidiuretic effect. Reasoning that the polyuria of *diabetes insipidus* was caused by pituitary deficiency, he further used pituitary extracts successfully in the control of the polyuria. Recent papers by Smith and McClosky,[3] Fromherz,[4] and Stehle[5] give a review of the literature. As yet there is no general agreement as to the explanation of the apparently contradictory results.

TABLE I. *Influence of Pituitrin on diuresis variously induced.*

Exp. No.	Form of Diuresis and Injection Rate cc. Ringer per min.	Pituitary Extract	Period Before Pituitrin		Injection of Pituitrin		Period After Pituitrin		Remarks.
			Length of Period Min.	Urine Drops per 5 Min.	Length of Period Min.	Urine Drops per 5 Min.	Urine Drops per 5 Min.		
							First hr.	Sec'd hr.	
1.	1.47	Infundin, 1-100 R.* Iv.	90	89	80	255	130		
2.	1.72	Infundin, 1 cc. Im.	110	35	60	116	25		
3.	1.73	Infundin, 1 cc. Im.	150	102	60	198	79		
4.	1.77	Pituitrin, 1 cc. Im.	120	26	60	133	40		
5.	1.72	Pituitrin, 2 cc. Im.	95	49	60	167	93		
6.	2.19	Pituitrin, 1-50 R. Iv.	185	35	35	261	147	89	
7.	2.54	Pituitrin, 1-400 R. Iv.	90	19	100	170	81	74	
8.	2.53	Pituitrin, 1-1000 R. Iv.	115	88	115	179	99	152	
10.	2.54	Pituitrin, 1-5000 R. Iv.	45	25	60	110	107		
11.	2.55	Pituitrin, 1-10000 R. Iv.	25	46	30	120	59		
12.	2.48	Pituitrin, .25 cc. Iv.	10	32	60	309	207	178	Atropine, gr. 1/90
13.	Urea 5% in 0.52	Pituitrin, 1-200 5% urea Iv.	65	81	40	131	85		
15.	Urea 5% in 0.55	Pituitrin 1-100 5% urea Iv.	70	11	35	142	23	48	
16.	Urea 10% in 0.55	Pituitrin 1-100 10% urea Iv.	45	82	15	254	98	81	
17.	Urea 10% in 0.55	Pituitrin, .43 cc. Im.	55	39	60	114	110		
18.	NaCl 5%, 0.40	Pituitrin, 1-100 5% NaCl Iv.	45	68	75	134	44	45	Constantly falling blood pressure
19.	Theocin 0.5%, 0.40	Pituitrin, 1-100 5% Theocin Iv.	40	121	45	122	10		Constantly falling blood pressure
20.	Ringer. 2.5 cc	Pituitrin, 1-1000 R. Iv.	15	36	15	227	123		

* R means Ringer, Iv intravenously, Im Intramuscularly.

TABLE II. *Influence of Pituitrin. Injections repeated at intervals.*

Exp. No.	Initial Period		First Pituitrin Period		Interval		Second Pituitrin Period		Interval		Third Pituitrin Period		Interval		Fourth Pituitrin Period		Remarks.
	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	Length of Period Min.	Drops per 5 Min.	
1.	20	66	15	88	—	—	15	86	—	—	15	84	—	—	15	120	Ringer Diuresis. Pituitrin 0.5 cc. hypodermically. Rate of urine flow increased for an hour after last injection.
2.	20	20	10	112	20	52	10	80	20	34	10	71	20	57	10	70	Ringer Diuresis. 1-1000 pituitrin intravenously.
3.	20	43	10	226	20	150	10	221	20	127	10	219	20	142	10	230	Ringer Diuresis. 1-1000 pituitrin intravenously.
4.	30	161	30	319	40	167	60	231	—	—	—	—	—	—	—	—	Ringer Diuresis. 1-100 pituitrin intravenously.
5.	60	17	60	218	35	55	20	232	—	—	—	—	—	—	—	—	Ringer Diuresis. 1-100 pituitrin intravenousy.
6.	60	37	60	133	60	37	60	96	—	—	—	—	—	—	—	—	Ringer Diuresis. Blood pressure low. 1 cc. pituitrin intramuscularly.
7.	30	16	35	145	30	57	30	100	30	67	—	—	—	—	—	—	5% Urea Diuresis. 1-100 pituitrin intravenously.
8.	30	18	30	136	30	87	15	130	15	73	15	129	—	—	—	—	Ringer Diuresis. 1-200 pituitrin intravenously

The experiments reported in this paper were limited to a study of the action of pituitrin superimposed on a diuresis variously induced, and to a comparison of the effect of variation in dosage and method of administration. It was hoped that such experiments might throw some light on the question of the mechanisms responsible for the antagonistic actions reported. Rabbits anesthetized with morphine and urethane were used throughout the experiments. Cannulae were inserted in the ureters and urine flow recorded by a drop counter. Blood pressure from the carotid was recorded simultaneously. By means of a Woodyatt injecting pump, solutions warmed to body temperature were injected at a uniform rate. In this way diuresis was induced and the effect of pituitrin upon this existing diuresis was studied. When injection is continued in this way at a rate varying from 2.5 cc. per minute to .5 cc. per minute, depending on the solution employed, the diuresis usually begins gradually and mounts slowly to a plateau like level which often may be maintained for some hours, provided blood pressure remains uniform. In a few instances among the controls, the slow rise continued until the end of the experiment. Such instances were

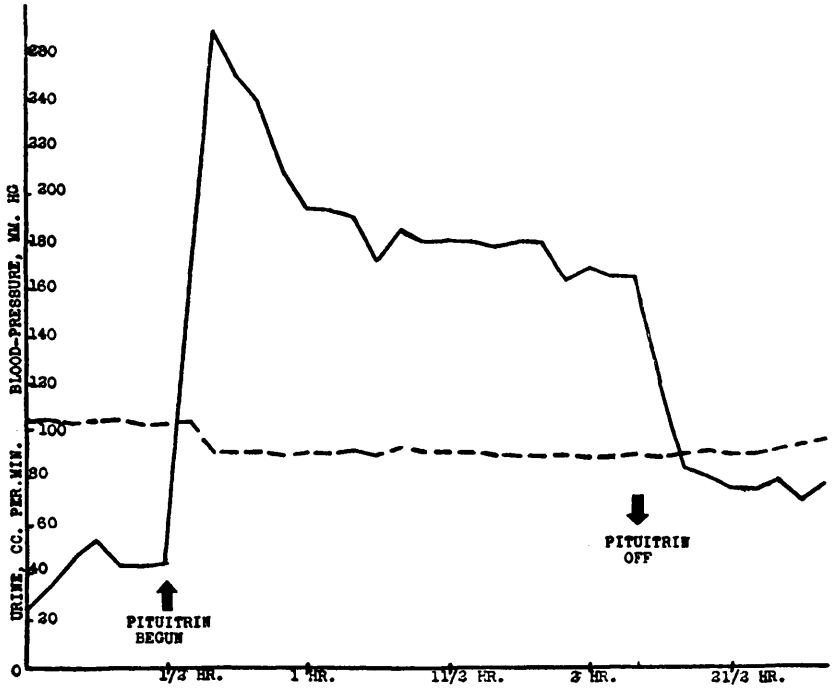

FIG. 1.

Ringer diuresis, injection rate 2.5 cc. per min.
Pituitrin, 1 cc. in 400 Ringer solution.

associated with gradual rise of blood pressure. Change to the solution with pituitrin added was made when the plateau was reached and had been maintained for from 15 to 30 minutes. Ringer solution, 5 per cent sodium chloride, 5 per cent and 10 per cent urea, and 0.5 per cent theocin solutions were used as the diuretic agents. With Ringer and sodium chloride solutions the urine flow was considerably less than the injection rate. With urea solutions the urine flow exceeded the injection rate, the animal being thus progressively dehydrated. The pituitrin was varied as to solution strength, duration of injection, and method of administration. Table I gives the results with pituitrin variously given. Table II gives the effects of repeat injections of pituitrin. Fig. 1 gives the detail of a typical experiment.

In all experiments without exception the addition of pituitrin to the solution injected increased the rate of urine flow. Effect of subcutaneous injection was not essentially different from the effect of intravenous administration (except that absorption time delayed the onset). There was no qualitative difference with dilution. Effects on urea and theocin diuresis were similar to effects on Ringer and 5 per cent sodium chloride solution. In nearly all instances the pituitrin effect had an immediate abrupt onset, rapidly rising to a maximum and slowly diminishing but remaining definitely above the previous level even though the pituitary injection was continued for an hour. On changing from the pituitrin solution to the original solution the rate of urine flow falls off although it usually maintains an average above that of the initial period. We have not been able to determine that it represents a definite antidiuretic period. (In this respect our results have differed from some of those previously reported.)

Summary. When diuresis is induced in anesthetized rabbits by the method of continuous intravenous injection pituitrin acts to augment such diuresis. The effects are similar with various diuretics and with varying dosage and administration of the pituitrin.

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