

# DEVELOPMENTAL CHANGES IN THE REFLEX CONTROL OF OSMOTIC PRESSURE

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Of the research on the osmoregulatory reflex, the least work has been done on its afferent portion. Verney [5] first describes specific osmoreceptors in the hypothalamic region lying along the course of the internal carotid artery. He thought that only this area was sensitive to changes in blood osmotic pressure. However it was found later that osmoreceptors are by no means confined to the hypothalamic region, but that they are widely distributed throughout the body [1]. A marked reduction in diuresis occurs when hypertonic solutions are injected not only into the carotid artery but also into other vessels, particularly those of the liver.

The object of the present investigation was to study hepatic regulation of osmotic pressure during the early postnatal period: This work included determining the time at which the reflex was formed, studying it in detail, and finding the relation between it and sensitivity to the antidiuretic hormone.

## METHOD

The experiments were performed on puppies aged from one day to two months.

A urinary fistula was established under ether anesthesia. Hypertonic solutions were introduced into the splenic vein through a polyethylene canula inserted into it. To do this, the abdominal cavity was opened on the left side, and the spleen removed after tying off all the vessels to it; the canula was now inserted into the splenic vein, and the abdominal cavity sewn up. The canula was taken to the outside, and attached to the skin. The solution introduced through the canula passed effectively directly into the portal vein. Pituitrin was injected into the jugular vein through a second canula.

In puppies up to 10 days old, both operations were performed at the same time, and the experiment begun four hours later. In older animals, the urinary fistula was established first, and the venous canuli introduced after the animal had recovered completely. The experiment was performed one day after the last operation.

The osmotic pressure of the urine was measured cryoscopically using a thermistor. The freezing point was determined to an accuracy of 0.005°.

The puppies were hyperhydrated by injecting 3 to 8% of the body weight of water through the canula. Diuresis was measured at 5 minute intervals and expressed as the amount per square meter of surface area per minute. The hypertonic saline was given in concentrations from 1.5 to 7%. The puppies received 0.25 to 2.5 ml according to age. From 1.5 to 2 l. U. of pituitrin per kilogram weight were given.

## RESULTS

A hypertonic solution was injected into the portal vein in 42 puppies aged from 1 to 60 days. The results obtained are shown in the table; from which it can be seen that the number of cases in which there was a reduction in diuresis increased with the age of the puppy.

Whereas in the first three days, no result was obtained in any of the experiments, from the 11th day onwards there was a reduced diuresis in almost all cases.

Besides the antidiuretic action there is also an increased urinary osmotic pressure. It can be seen therefore that the oliguria is not caused by a reduction in filtration but by an increased facultative reabsorption leading to an increase in the concentration of the osmotically active substances in the urine.

The absence of any reaction in the early postnatal period may indicate that the afferent and efferent portions of the osmoregulatory reflex are not yet developed. Evidence on this point is afforded by the reaction obtained from one animal to injections of both hypertonic saline and pituitrin.

It is well known that in the early postnatal period there is practically no response to the antidiuretic hormone [3, 4]. It is also known [3], that pituitrin given in doses even exceeding ten times that which produces a maximal effect in an adult may produce no antidiuretic action in puppies up to ten days old.

In our experiments the reaction to hypertonic saline injections into the portal vein were the same as those obtained with injections of pituitrin. In experiments where a reduced diuresis followed raising the osmotic pressure in the liver, it could be confidently expected that an oliguria would be obtained on injecting pituitrin; also when no oliguria followed saline injections there was no reaction to pituitrin either (Figs. 1 and 2).

In some cases, however, the responses to osmotic stimulation and to the injection of pituitrin were not identical. In two puppies aged  $1\frac{1}{2}$  days the saline injection caused no reduction in diuresis, while the pituitrin injection caused a marked though short lasting oliguria.

Measurement of the freezing point of the urine showed that the urinary osmotic pressure was not increased, i.e., that the urine had not become more concentrated. It follows that the oliguria did not result from any specific action of the antidiuretic hormone on the kidney tubules, but was a vascular effect caused by the pituitrin reducing glomerular filtration.

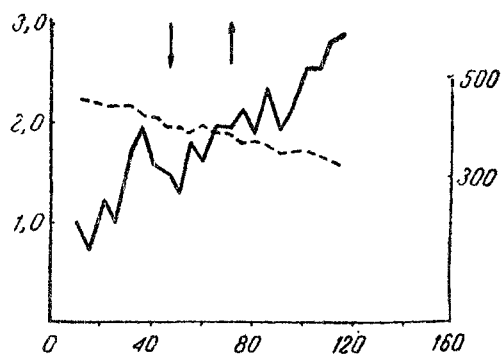


Fig. 1. No reaction to injection of saline (↓) and pituitrin (↑) in a 4-day old puppy. Left ordinate) diuresis in milliliters per square meter per minute; Right ordinate) osmotic pressure of urine in milliosmoles per liter; abscissa) time in minutes; — change in diuresis; --- change in the urinary osmotic pressure.

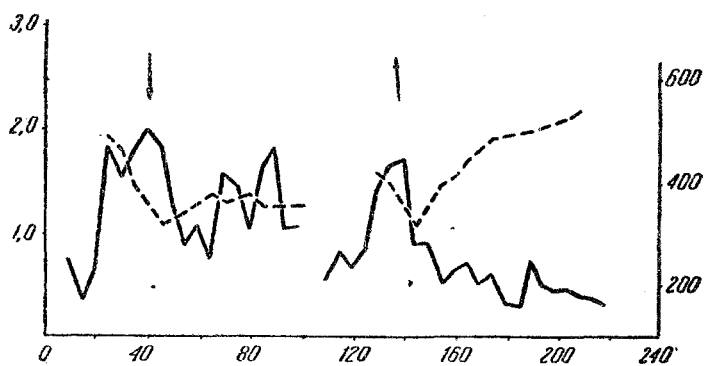


Fig. 2. Oliguria following injection of saline (↓) and pituitrin (↑) in an 8-day puppy. Indications as in Fig. 1.

#### Effect of Osmotic Stimulus to Liver on Diuresis

Age (in days)	Number of experiments	Response to injected saline	
		oliguria	no effect
1—3	4	0	4
4—7	7	3	4
7—10	10	7	3
10—30	21	20	1
30—60	17	17	0

In five experiments there was a marked response to the injection of hypertonic saline although pituitrin had no effect. Freezing point determination showed that in these cases the osmotic pressure of the urine was increased (Fig. 3).

Since in these animals the kidney did not respond to pituitrin, it must be supposed that the osmoreceptor reflex of the liver influenced the kidneys via the efferent renal nerves and that they were stimulated to reabsorb water [2].

If this was so, it is still not clear why the nervous mechanism does not effect an oliguric response in all cases, when hypertonic saline is given to an animal whose kidney is not yet sensitive to the antidiuretic hormone.

On the basis of the above argument we concluded that the antidiuretic response to hypertonic saline injected into the portal vein develops simultaneously with the sensitivity to pituitrin. The coincidence of both effects shows that the response studied is brought about by the antidiuretic hormone whose liberation stimulates the hepatic osmoreceptor reflex. In most newborn animals whose kidneys are not sensitive to the hormone, there is no antidiuretic response. In a few cases the reflex is brought about without the participation of the hormones, in all probability through the efferent renal nerves.

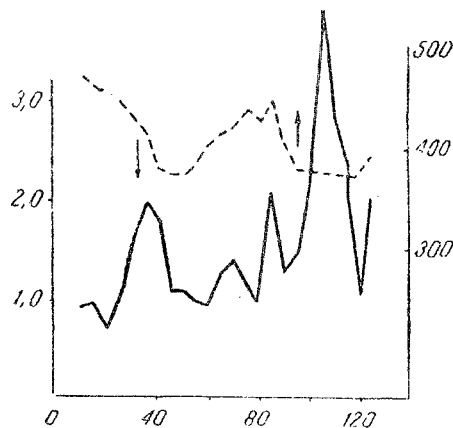


Fig. 3. Response to the injection of saline (↓) and pituitrin (↑) in a 6-day puppy. Indications as in Fig. 1.

The afferent portion of the osmoregulatory reflex becomes established earlier than does its main efferent pathway which is the humoral link in the reflex.

#### SUMMARY

Experiments on puppies aged from 1 to 60 days showed that the oliguric response to the administration of hypertonic sodium chloride solution into the portal vein occurs at the same time that sensitivity to pituitrin develops. Evidently the reaction is brought about by the antidiuretic hormone whose liberation is stimulated by the hepatic osmoreceptor reflex. In certain cases the reflex is developed without the participation of the hormone, apparently through the action of the efferent renal nerves.

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\* Original Russian pagination. See C. B. Translation.

\*\* See English translation