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THE RESPONSE OF PUPPIES TO A LARGE DOSE OF WATER

By R. A. McCANCE and ELSIE M. WIDDOWSON

From the Medical Research Council Department of Experimental Medicine, University of Cambridge

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The capacity of puppies, 2 days old, to produce and sustain a diuresis in response to a dose of water was first investigated by Adolph (1943), and since that time little work has been done on the subject, although Dicker (1952) studied the diuresis brought about by the introduction of hypertonic solutions of osmotically active solutes into the puppy's circulation. Some work on human infants was carried out about 1920 (Aschenheim, 1919; Lasch, 1923), and since 1943 experiments have been made on the newborn rat (McCance & Wilkinson, 1947; Heller, 1947, 1951), the guinea-pig (Dicker & Heller, 1951; Heller, 1951) and the human infant (Barnett, Vesterdal, McNamara & Lauson, 1952; Ames, 1953; McCance, Naylor & Widdowson, 1954). The results of these investigations may be summarized by saying that no newborn animal has yet been found to excrete water so rapidly and completely as the corresponding adult, but that there are considerable differences between the newborn of one species and another in (1) the ability to produce a high rate of urine flow, (2) the dilution achieved at the peak of the flow, (3) the percentage of the test dose excreted within the time of observation, (4) the rate of maturation of these functions. Speaking generally, the rat has been found to be the least developed at birth and to mature slowly, whereas the guinea-pig and man are further advanced at birth, and certainly the human infant may respond as an adult does within a few weeks of birth (Ames, 1953). This period of time is a much smaller fraction of the total life span than that required by the newborn rat to reach the same degree of maturity. The subject has been discussed by McCance *et al.* (1954) and the experiments now to be described were undertaken to find out more about the response of puppies to large doses of water and to compare them in this respect with the young of other species.

MATERIAL AND METHODS

The experiments were made on four pure bred bull terrier bitches and on five of their litters. The puppies were studied when they were 48 hr old, or as near it as the time of their birth and the working day allowed. In all, sixteen puppies were used, and three of the bitches were studied twice. The dogs had been without food or water for about 16 hr before the experiments began, the puppies for about 2 hr. The dose of water was 5% of the body weight, or about 6% of the body water, and was given by stomach tube. The urine was collected at 15 min intervals from the dogs, but only at hourly intervals from the puppies. The puppies were lodged in separate compartments of a basket, and were kept comfortably warm by varying their distance from a source of radiant heat. Urine was obtained from them by stroking the perineal region with the edge of the small tube in which the urine was collected. The dogs had been trained to lie quietly on a table for long periods with a catheter in the bladder, and their urine was allowed to drip into a measuring cylinder. All urines were preserved under toluol. Losses by the skin and lungs were calculated from the weights of the puppies at the beginning and end of the experiments, the weights of water administered and the weights of the urines excreted. Blood was collected at the end of the experiment from a subcutaneous branch of the saphenous vein in the dogs, and by cardiac puncture from the puppies.

Urea was determined by Lee & Widdowson's (1937) method and total osmolar concentration was calculated from the depression of freezing-point measured in the apparatus described by Hervey (1955). Other chemical and physical methods were the same as those used and described by Cort & McCance (1954).

RESULTS

The curve in Fig. 1 was obtained by averaging the rates of urine flow (ml./kg/hr) obtained in the seven experiments on the four bitches over succeeding 15 min periods. It shows that the rate of urine formation was most rapid about 1 hr after the water had been given. A somewhat different picture was obtained when the hourly rates of flow were computed for comparison with those of the puppies. When this was done the second hour appeared to witness the highest rate of flow. The results for dogs and puppies are given in Fig. 2. The puppies raised their rate of urine flow less rapidly and to a smaller extent than the dogs, but they maintained it longer so that in the fourth hour they were still excreting urine at the rate of 6·4 ml./kg body weight/hr, whereas the dogs at that time had reduced their rate to 4·2 ml./kg/hr. It is improbable that this difference in the rate of excretion was due to a difference in the rate of absorption (Adolph, 1943; Heller, 1951).

These average results cover up individual differences, which in puppies may be considerable even within the confines of a single litter. Fig. 3 shows the individual responses of three litter-mates. Puppy D1 had its highest rate of urine flow in the second hour, puppy D2 during the third hour, and puppy D4 excreted more and more with each succeeding hour of the experiment. As a matter of fact this last was an exceptional response and only occurred in two out of the sixteen puppies that were investigated. Apart from these rather unusual results, however, Adolph (1943) appears to have been quite correct in stating that in puppies the diuresis after the administration of water continued at a slow rate for a considerable time after the more rapid early flow had subsided. In this respect, therefore, puppies may differ from young guinea-pigs (Heller, 1951) and human infants (McCance *et al.* 1954), in whom the rate of flow may completely subside before all the water has been excreted.

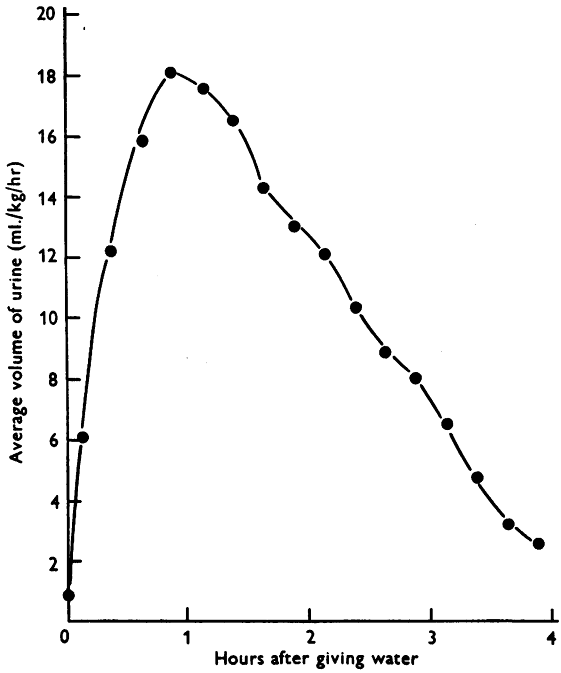

Fig. 1. Average urine volumes of dogs over succeeding 15 min periods.

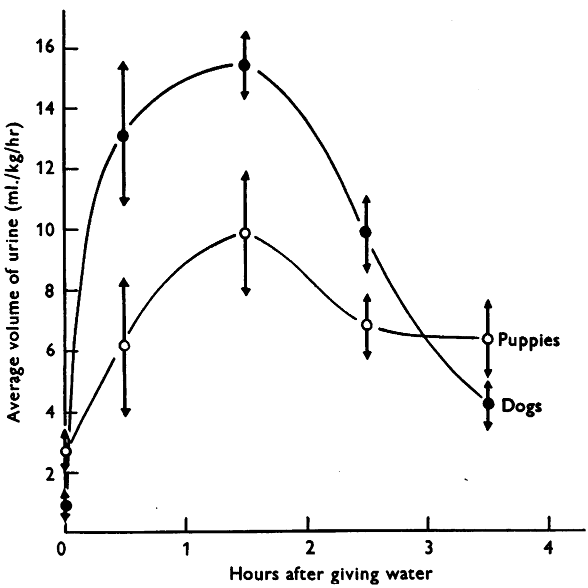

Fig. 2 Average urine volumes of dogs and puppies over hourly periods.

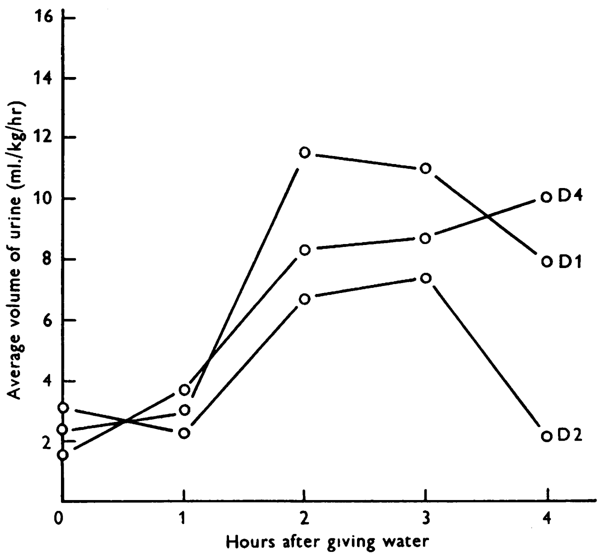

Fig. 3. Urine volumes of three puppies from one litter.

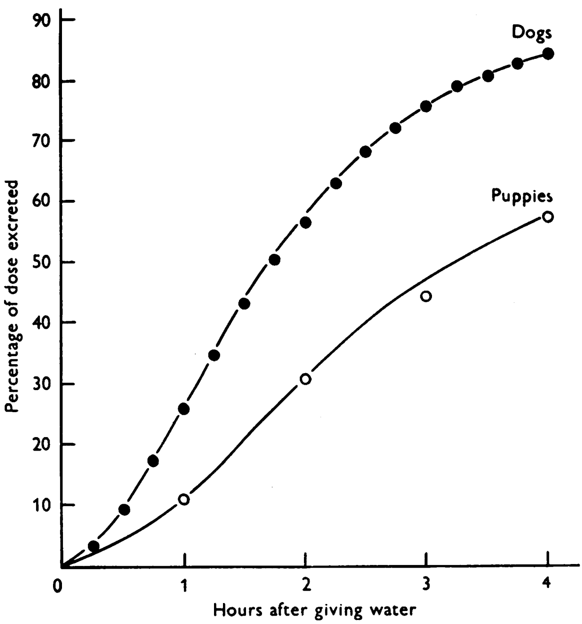

Fig. 4. Percentage of the administered water excreted by dogs and puppies.

Fig. 4 shows the percentage of the administered water excreted by the end of each hour by the dogs and puppies. The curves for the first 3 hr are similar to those given by Dicker & Heller (1951) for guinea-pigs, and differ only in that the curve for the puppies does not flatten out in the fourth hour. McCance *et al.* (1954), however, found that human infants aged 6–18 days might excrete quite as large a percentage of the administered water as adults within the first 2 hr although they subsequently excreted much less and never the whole of it within 4 hr.

TABLE 1. Puppies' water losses by the skin and lungs

Puppy no.	Weight (g) Initial	Weight (g) Final	Water given (g)	Urine excreted (g)	Water lost by skin and lungs (g)
B1	365	366	19	13·4	4·6
B2	365	367	19	12·0	5·0
B3	348	353	17	8·8	3·2
B4	383	389	19	9·7	3·3
C1	270	270	13·5	9·3	4·2
C2	227	229	11·4	5·3	4·1
D1	380	381	19	12·9	5·1
D2	430	439	21·5	8·1	4·4
D3	371	375	18·5	9·5	5·0
D4	312	314	15·6	10·4	3·2
Average	345	348	17·3	9·9	4·4

TABLE 2. Average volume and composition of the urine at the height of the diuresis

	Puppies	Dogs
Volume (ml./kg/hr)	10·7	15·6
Total osmolar concentration (m-osmole/l.)	156	78
Urea (m-osmole/l.)	85·8	36·8
Cl (m-equiv/l.)	12·2	3·3
Na (m-equiv/l.)	5·8	2·6
K (m-equiv/l.)	17·4	2·9

Table 1 shows the amount of water lost by puppies through the skin and lungs during these experiments. If the losses by these channels are added to those in the urine the puppies eliminated in 4 hr 80% of the water administered to them. In this time the dogs excreted 85% of the water by the kidney alone and if the losses by their skin and lungs had been measured the total output of water would probably have been found to be as great as the amount administered.

Table 2 gives information about the average volume of urine passed during the second hour after the water had been administered to the dogs, and about the volume during the hour of greatest urine flow in the puppies. The total osmolar concentration of these urines and the concentrations of some of the major urinary constituents are also given. There were important differences between the dogs and puppies, for the puppies were excreting volumes of urine smaller by about a third than the dogs, whereas the average osmolar concentrations were twice as high, and the amounts of some of the osmolar constituents excreted/hr were considerably greater. In this respect puppies would appear to differ from human infants aged 6–18 days, for these were found by McCance *et al.* (1954) to excrete a urine at the height of a water diuresis containing no more sodium, chloride or potassium than that of an adult correspondingly hydrated.

Table 3 shows that the puppies'excretion of osmolar material was considerably greater than that of the dogs at low as well as at high rates of urine flow.

TABLE 3. The rate of excretion of total osmolar material and its major constituents at low and high rates of urine flow

	Puppies		Dogs	
Urine flow (ml./kg/hr)	2·42	10·7	1·32	15·6
Total osmolar material (m-osmole/kg/hr)	1·27	1·67	0·58	1·22
Urea (m-osmole/kg/hr)	0·70	0·92	0·32	0·57
Cl (m-equiv/kg/hr)	0·116	0·131	0·018	0·052
Na (m-equiv/kg/hr)	0·050	0·062	0·026	0·041
K (m-equiv/kg/hr)	0·139	0·186	0·027	0·045

The puppies tended to have higher concentrations of urea in their blood than the dogs (puppies average 31·2, range 18·0–41·6; dogs average 20·1, range 14·3–33·3 mg/100 ml.) and this probably partly accounts for their higher rates of excretion of urea. Differences in serum concentration cannot, however, be held to account for the differences in excretion of Cl, Na and K. The puppies, therefore, had more concentrated urines at the height of the diuresis for two reasons (1) they were excreting more osmolar material, particularly K, per min than the dogs and (2) they were excreting less water.

DISCUSSION

The analysis of the dog's renal response to water which has recently been carried out by Sellwood & Verney (1955) shows that the mechanism is a complicated one, involving far more than the antidiuretic hormone. Nevertheless, the response of the adult kidney to a large dose of water can be regarded as having three characteristics (McCance *et al.* 1954). These are (1) a great increase in urine flow, (2) an extensive fall in the osmolar concentration of the urine, (3) the excretion within a few hours and before the flow of urine subsides of a volume which is roughly equal to that of the water administered. The present experiments on the dogs illustrate all three effects, although the total volume excreted was not so great as the amount administered. This is not unusual (Adolph, 1943). Puppies responded differently in all three respects, as the results have shown. Thus (1) they did not increase the rate of urine flow to the same extent. (2) The osmolar concentration of the puppies' urine did not fall to such a low level as that of the dogs'. This was partly because less water was excreted, but mainly because they had been excreting more osmolar material per kg per hr before the diuresis began, and continued to do so without much change after the water had been administered. (3) Puppies did not excrete so much of the water administered.

The young rat does not increase its urine flow appreciably after the ingestion of water, and consequently there is no dilution of the osmolar material in it. The experiments which have been carried out, however (McCance & Wilkinson, 1947), indicate that the newborn rat differs in other ways from the puppy aged 2 days because its rate of excretion of osmolar material per kg of body weight is only half that of the adult.

The reasons why the very young animal excretes a standardized dose of water less rapidly and less completely than an adult has not been fully explained. The glomerular filtration rate/unit of body water is often lower in the very young animal and this would help to account for a lower rate of excretion. Failure to excrete a standardized dose so rapidly might also be due to incomplete destruction of the circulating antidiuretic hormone after the absorption of water had inhibited further release. Heller (1951), however, has shown that the young rat is insensitive to the action of the hormone and other newborn animals seem to be relatively so. The problem can only be solved by further work.

Broadly speaking, however, it would appear that the puppy's renal response to a large dose of water is less mature at 2 days of age than that of the human infant 6–18 days old, and more mature than that of the young rat for the first 2 weeks or more of its life. The puppy at 2 days may approximate in development most closely to the newborn guinea-pig, but its renal function seems to have certain characteristics which distinguish it.

SUMMARY

1. After being given 5% of their own weight of water, puppies differed from adult dogs in that: (i) Their rate of urine flow averaged only 10·7 ml./kg/hr during the hour of maximum flow: the rate in adult dogs was 15·6 ml./kg/hr. (ii) The osmolar concentration of the urine passed during the hour of greatest flow was higher than in dogs. This was partly due to the flow of urine being smaller, but also to the larger quantities of osmolar material excreted by the puppies whatever the rate of flow. (iii) A volume of urine corresponding to only 56% of the test dose was excreted within 4 hr, whereas adult dogs excreted 85%.

2. These findings suggest that, so far as the excretion of water is concerned, the renal function of the puppy at 2 days of age is further developed than that of the rat until the latter is at least 2 weeks old but less developed than that of the human infant aged 6–18 days.

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