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EFFECTS OF VARIOUS AMBIENT TEMPERATURES AND OF HEATING AND COOLING THE HYPOTHALAMUS AND CERVICAL SPINAL CORD ON ANTIDIURETIC HORMONE SECRETION AND URINARY OSMOLALITY IN PIGS

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SUMMARY

1. Plasma ADH concentration, urinary and plasma osmolality and haematocrit were measured in young pigs placed in cold, thermoneutral, warm and hot ambient temperatures. In some experiments a thermode placed in the hypothalamus or over the cervical spinal cord was heated or cooled at various ambient temperatures.

2. Plasma ADH concentration remained at a low level (0·5–5 μu. ml.$^{-1}$) over 2 hr or 3 hr periods when the pigs were in cold, thermoneutral or warm ambient temperatures. A hot environment, which caused a marked rise in the pigs' rectal temperature, was associated with a large rise in plasma ADH level.

3. The rise in plasma ADH level which occurred during an increase in body temperature was consistently and completely suppressed by simultaneous cooling of the thermode in the pre-optic region to 5 or 10° C. When the thermode was in the region of the supraoptic nucleus the rise in ADH was only partly suppressed, and when it was over the cervical cord it was only sometimes suppressed.

4. Cooling the thermodes in any position at a cold or thermoneutral ambient temperature, or heating them at a thermoneutral or warm ambient temperature, caused no consistent change in ADH.

5. A diuresis, with a urinary flow-rate of at most 1 ml. min^{-1} and minimal urinary osmolality of 53 m-osmole kg^{-1}, was observed on only three occasions, twice during cooling of a thermode in the hypothalamus and once after the end of a period when the thermode was heated. In each case, the plasma ADH was less than 2 μu. ml.$^{-1}$.

6. A slight rise of haematocrit in cold ambient conditions and a slight fall in the warm were observed. Otherwise changes in haematocrit were trivial, and a shift of water between vascular system and interstitium could not be invoked to account for changes in ADH levels. Observed variation of plasma osmolality was also slight.

INTRODUCTION

It is well-established that the output of antidiuretic hormone (ADH) from the posterior pituitary is modified by osmolality of the plasma as sensed by osmoreceptors (Verney, 1947). There is an increasing body of evidence suggesting that the secretion of ADH may also be changed by variation of the blood volume, particularly in the thoracic region (Baratz & Ingraham, 1960; Share, 1965; Dunn, Brennan, Nelson & Robertson 1973). The consequence of changes of hormonal output observed under these experimental conditions has been that animals show a diuresis when the plasma is hypotonic, or when its volume is raised isosmotically; and an antidiuresis in the converse conditions. If the same changes were to occur under physiological conditions, this could be a precise homoeostatic mechanism tending to maintain volume and osmolality of plasma within certain limits.

Exposure to a high ambient temperature decreases urinary flow and raises plasma ADH in men (Weiner, 1944; Segar & Moore, 1968) and increases the antidiuretic activity in the serum of rats (Itoh, 1954). Conversely, at cool ambient temperatures, some mammals show the phenomenon of 'cold diuresis' (Pabst & Thron, 1960; Bader, Eliot & Bass, 1952). It was recently observed (Szczepanska-Sadowska, 1974) that in dogs heating a thermode implanted in the pre-optic region of the hypothalamus, a region known to contain temperature-sensing neurones, caused an increase in plasma ADH level and urinary osmolality and a decrease in urinary volume, even when the dogs had been allowed to drink sufficient fluid to initiate a water diuresis, a condition calculated to suppress ADH secretion. As part of a wider study of the effect of environmental conditions on endocrine function in pigs, the aim of the present study was to find the effect on the plasma ADH of pigs, and on their urinary volume and osmolality, of changes in ambient temperature and of heating or cooling thermodes implanted in temperature-sensitive regions of the central nervous system.

A preliminary account of some of this work has already been published (Forsling, Ingram & Stanier, 1975).

METHODS

Animals. Thirty-four young female pigs of the Large White breed, and weighing between 13 and 23 kg were used. The animals were trained to wear a light leather harness and to stand or lie comfortably in a temperature-controlled room in a frame to which the harness was tied.

Surgery. Thermodes were implanted into the hypothalamus under sterile conditions and general anaesthesia. The thermodes had already been used on pigs as reported in earlier studies (Baldwin & Ingram, 1967; Ingram & Legge, 1971). The position was checked radiographically during the operation using the techniques previously described and was not subsequently checked by histology. A sterile polyethylene cannula was placed in the jugular vein through an incision in the neck, and pushed into the right atrium. The other end of the tube was led out through the skin on the back. The tube was flushed with heparinized saline, plugged with a stainless steel stilette, and coiled into a roll which was fixed against the back with sticking-plaster. A Foley catheter was placed in the bladder and left to drain freely. The pig was allowed to recover from the operation for at least 2 days before being used for an experiment.

Experimental procedure. The animals were housed in holding pens at approximately 20° C. Before an experiment they were brought to the temperature-controlled room in a trolley and the Foley catheter was stoppered. The pig was then tethered in the frame, and in studies involving a thermode the necessary connexions were made. The thermodes were heated or cooled by circulating fluid and the temperatures monitored as previously described (Baldwin & Ingram, 1967; Ingram & Legge, 1971). Blood samples were taken via the implanted catheter with minimal disturbance to the pig. The respiratory frequency was determined by counting flank movements, and rectal temperatures were recorded from a probe inserted 100 mm deep to the anus. A note was also made of shivering or excessive salivation.

ADH assay. Blood samples were collected in polypropylene centrifuge tubes, lightly coated inside with powdered heparin. After removal of a small sample for determination of haematocrit, the blood was centrifuged, the plasma separated, and stored at − 20° C until the assay was performed. The plasma was extracted and ADH measured by bio-assay on water-loaded rats according to the method previously described (Forsling, Jones & Lee, 1968; Forsling, 1974). Pure synthetic lysine vasopressin, the porcine form of ADH, was used as standard. The procedure was checked by assay of samples of blood taken from a pig immediately after nicotine injection which revealed the predicted rise in ADH output, and by determination of the plasma concentration following infusion of exogenous hormone.

Other methods. Haematocrit was measured by centrifugation in the Hawkesley microhaematocrit centrifuge. Osmolality of plasma and urine samples was measured in a Fiske osmometer. Half-time, clearance and apparent volume of distribution of ADH were calculated according to the methods described by Fabian, Forsling, Jones & Lee (1969).

RESULTS

Exposure to thermally neutral conditions

Observations were made on three pigs at an ambient temperature of 20° C. Two blood samples were taken at an hour's interval before the pig was placed in the room, further hourly samples were taken over a period of 3 hr in the room and two more samples were taken 1 and 2 hr after the

pig was taken out. During the whole period the concentration of ADH was low, rarely as high as 5 μu. ml.$^{-1}$, fluctuating between this level and 0·5 μu. ml.$^{-1}$. This established the limits of 0·5–5 μu. ml.$^{-1}$ as the control or base line range of normal plasma ADH concentration in our pigs. Treatments might be considered to have an effect only if they consistently caused plasma ADH to depart from this range.

The haematocrit, which is normally in the range 28–32 % in pigs (though sometimes as low as 24 %), remained almost unaltered throughout the 6 hr period. The osmolality of urine collected at hourly intervals also remained within the normal range for pigs of 500–900 m-osmole kg^{-1}, and samples from any one experiment rarely varied by more than 200 m-osmole kg^{-1} (Fig. 1*A*).

Exposure to cold and warm conditions

Four pigs were exposed for a 3 hr period to cold conditions, two at 0° C and two at −5° C. On two occasions, once at 0° C and once at −5° C, plasma taken during cold exposure showed a concentration of ADH between 6 and 7 μu. ml.$^{-1}$ (the first of these is illustrated in Fig. 1*B*). All other samples taken during cold exposure showed levels below 2 μu. ml.$^{-1}$. Thus although on two occasions during treatment plasma ADH reached a level just outside the range which we have taken as normal, the effect was not reproducible and we could not claim that cold conditions affected ADH concentration.

Two pigs were exposed to an ambient temperature of 35° C, and two to 40° C and blood samples taken at hourly intervals as before. The plasma ADH level remained at about 3 μu. ml.$^{-1}$ throughout the duration of the exposure. Another pig was exposed to an ambient temperature of 32° C and blood samples were taken 15 and 30 min after the start of the exposure, in an attempt to detect any earlier transient rise of plasma ADH. No such change could be detected and plasma ADH was below 2 μu. ml.$^{-1}$ even during the initial stage of the exposure.

The haematocrit rose slightly during exposure to the cold environment from about 30 to 33 % but quickly regained its original value after termination of the cold exposure. The converse change of a fall from about 30 to 26 % occurred during exposure to warm environments. Similar slight and transient changes in relative plasma and cell volumes have been observed in other species during acclimatization to warm and cold conditions (Bazett, Sanderman, Doupe & Scott, 1940; Rodbard, Daiki, Malin & Young, 1951).

Exposure to a cold or a warm environment produced no change in volume and osmolality of urine. Urine flow-rate was typically about 0·3 ml. min^{-1} and osmolality about 800 m-osmole kg^{-1}. In particular,

there was no evidence of a 'cold diuresis' such as is observed in man during mild cold exposure, and in dogs during exposure to an ambient temperature of about 0° C.

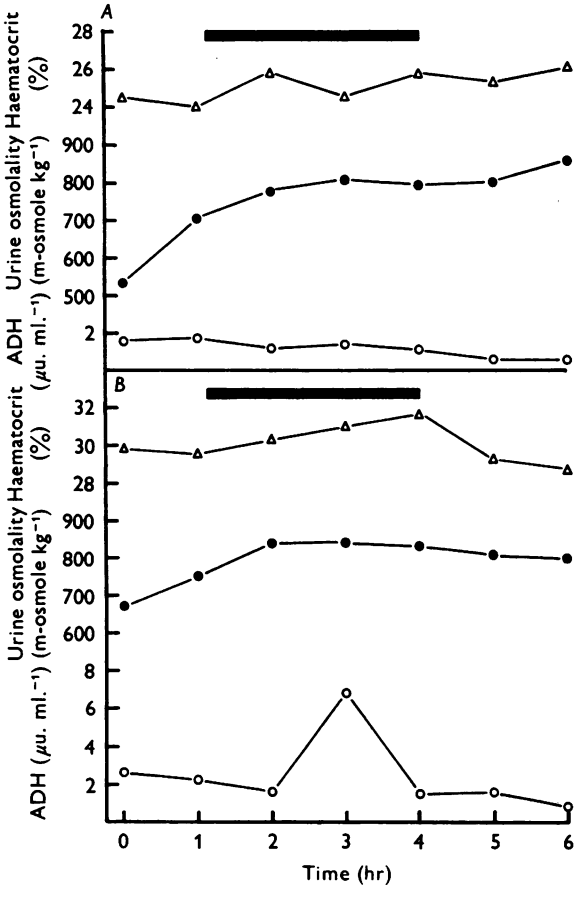

Fig. 1. *A*, the effect of a period of exposure to 20° C in a temperature controlled room (filled bar) on haematocrit, plasma ADH and urine osmolality. *B*, the effect of a period of exposure to 0° C in a temperature controlled room (filled bar). The rise in the level of ADH was the greatest recorded during exposure to cold.

Exposure to hot environments

Seven pigs were exposed to hot environments of 45° C in four experiments and 50° C in three experiments. The rectal temperature was continuously monitored and rose from 39 to 43° C in these conditions in about 60 min. The pig panted heavily and there was abundant salivation. Blood

samples were taken at intervals corresponding to each 1° C rise in rectal temperature. Urine samples were taken via Foley catheter whenever possible.

In contrast with the trivial changes in plasma ADH in the cold and warm environments, there was always an increase in plasma ADH in a hot environment. When the rectal temperature was between 41 and 42° C, the plasma ADH began to rise, reaching a peak which was usually about

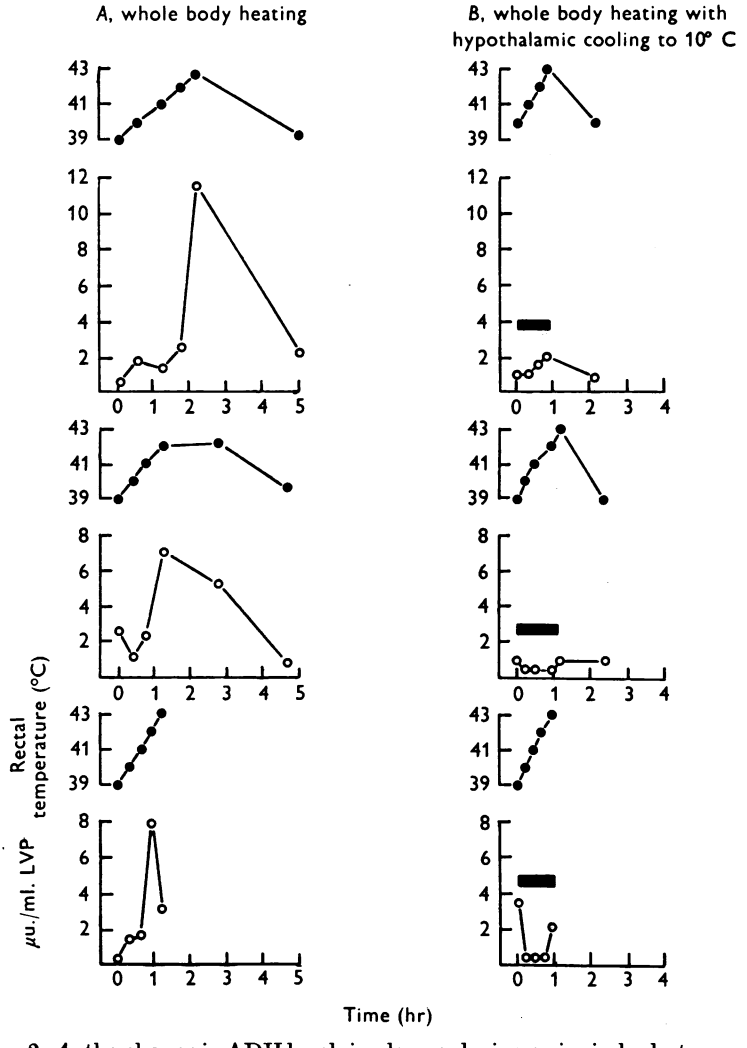

Fig. 2. *A*, the change in ADH levels in plasma during a rise in body temperature consequent on exposure to a hot environment (whole body heating); *B*, the effect on ADH levels in the plasma of cooling a thermode in the hypothalamus during whole body heating in a hot environment.

10 μu. ml.$^{-1}$ but occasionally over 20 μu. ml.$^{-1}$. During this process, urinary flow-rate decreased; in one case from 1·2 to 0·2 ml. min^{-1}, in another from 0·6 to 0·2 ml. min^{-1}. Changes in urinary osmolality were slight and no urine specimens more concentrated than 850 m-osmole kg^{-1} were obtained during heating. When rectal temperature reached 43° C, the room heating was switched off, the door opened, and ambient temperature allowed to fall. In most cases the plasma ADH level dropped quickly thereafter, even before the pig's rectal temperature had fallen very far (Fig. 2*A*).

Cooling thermodes in the hypothalamus or over the spinal cord

Twenty-eight experiments were carried out on twenty pigs in which a thermode placed in the hypothalamus (pre-optic region, or supraoptic nuclei, or at an intermediate point between these two regions), or on the cervical spine, was cooled to a temperature of 5 or 10° C or (in three cases) to 20° C. Various ambient temperatures were used. The cooling was continued for 2 or 3 hr. In earlier experiments blood samples were taken at hourly intervals from the start of cooling, and in a control period at the appropriate ambient temperature before and after cooling. In later experiments, samples were taken at $\frac{1}{4}$ and $\frac{1}{2}$ hr from the start of cooling, in order to increase the chance of observing any possible early transient change in ADH secretion.

Table 1 shows the number of experiments performed at various ambient

TABLE 1. Effect on the plasma ADH levels of pigs of cooling thermode in hypothalamus or cervical cord at various ambient temperatures. (Normal range of plasma ADH in thermoneutral conditions, 0·5–5 μu./ml.$^{-1}$)

No. of experiments	Ambient temperature °C	Temperature of thermode °C	Position of thermode	Results: numbers refer to concn. plasma ADH (μu. ml.$^{-1}$)
3	Thermoneutral 20	5 or 10	Cervical	Below 3 throughout
3	Thermoneutral 20	5 or 10	Pre-optic	1 sample 3·7, all other samples < 2
7	Cold 10	5 or 10	Pre-optic	Below 3 throughout
1	Cold 10	20	Pre-optic	6·2 at 3rd hr, all other samples < 3
4	Hot 40, 45, 50 (2)	5 or 10	Pre-optic	Below 4 throughout
2	Hot 40, 45	20	Pre-optic	Below 4 throughout
1	Hot 45	10	Supraoptic	Low until final sample, 22·5
1	Hot 40	10	Intermediate	Below 4 throughout
6	Hot 45	10	Cervical	In two experiments, maximum levels 9·4, 5·7; all other samples < 4

temperatures and the effect of thermode cooling on plasma ADH level. Cooling of temperature-sensitive regions of the central nervous system did not appear to lower the ADH secretion at thermoneutral or cold ambient temperature, though of course the normal level of circulating ADH in the pigs was so low that a fall might be undetectable. The significant finding was that cooling of the pre-optic or intermediate region of the hypothalamus at ambient temperatures of 45 or 50° C (temperatures which would normally have produced a large increase in ADH secretion) had the effect of suppressing this increase, so that the circulating ADH remained at the low level of less than 4 μu. ml.$^{-1}$ (Fig. 2*B*). Cooling of the supraoptic region also maintained a low level of ADH, until, at a rectal temperature of 43° C, there was a sudden increase. Cooling the temperature-sensitive part of the cervical region in the hot ambient temperature suppressed the expected rise of ADH secretion completely in two experiments, partially in two and not at all in one.

The changes in haematocrit were small, but there was, as before, a slight rise during exposure to the cold ambient temperature.

The changes in volume and composition of urine were also small. A diuresis was observed only twice. In these experiments, a large volume of urine was produced throughout the cooling period and the osmolality was low (450–500 m-osmole kg^{-1}). In each case the pre-optic region of the hypothalamus was being cooled, in one case at ambient temperature of 10° C in the other at 45° C. In each case the circulating level of ADH was very low, less than 1 μu. ml.$^{-1}$ throughout.

Warming thermodes in the hypothalamus and over the spinal cord

Twenty-seven experiments were carried out on fifteen pigs in which a thermode implanted in the hypothalamus or on the temperature-sensitive region of the cervical cord was heated to 43° C. Again various ambient temperatures were used. In the earlier experiments blood was sampled at hourly intervals before, during and after 3 hr of heating the thermode. In later experiments, the samples were taken $\frac{1}{4}$, $\frac{1}{2}$ and 2 hr from the start of a 2 hr period of heating the thermode.

Table 2 shows the results of these experiments. The table is arranged in order of increasing ambient temperatures at which the thermode was heated. The level of plasma ADH sometimes increased slightly but seemed in the main to be unaffected by heating the thermode whatever the ambient temperature (Fig. 3). At the ambient temperature of 45° C which was sufficiently hot to cause of itself a rise of deep-body temperature and ADH, heating the thermode to 43° C would increase the temperature of the central nervous system over the general body temperature by a relatively small amount. The observed ADH rise, given in the last line of Table 2,

probably occurred as a result of the rise in deep-body temperature rather than as a result of local heating of the central nervous system. The only exception to the set of negative findings occurred on one occasion when a thermode in the supraoptic nucleus was heated at an ambient temperature of 43° C. Within 20 min the circulating level of ADH reached 29 μu. ml.$^{-1}$. However, the same experiment carried out on the same pig the previous

TABLE 2. Effect on plasma ADH levels of pigs of warming thermode in hypothalamus or cervical cord at various ambient temperatures. (Normal range of plasma ADH in thermoneutral conditions, 0·5–5 μu. ml.$^{-1}$)

No. of experiments	Ambient temperature (° C)	Temperature of thermode (° C)	Position of thermode	Results: numbers refer to concn. plasma ADH (μu. ml.$^{-1}$)
6	Thermoneutral 20	43	Pre-optic	Below 4 throughout
2	Thermoneutral 20	40, 43	Cervical	Below 3 throughout
11	Warm 30–36	42–43	Pre-optic	2 samples, 5, all other samples < 3
2	Warm 25, 34	43	Intermediate	< 2
2	Warm 34	43	Supraoptic	One < 3 throughout, one rise to 29
3	Warm 35	43	Cervical	Below 3 throughout
1	Hot 50	40	Pre-optic	Rise to 9·4

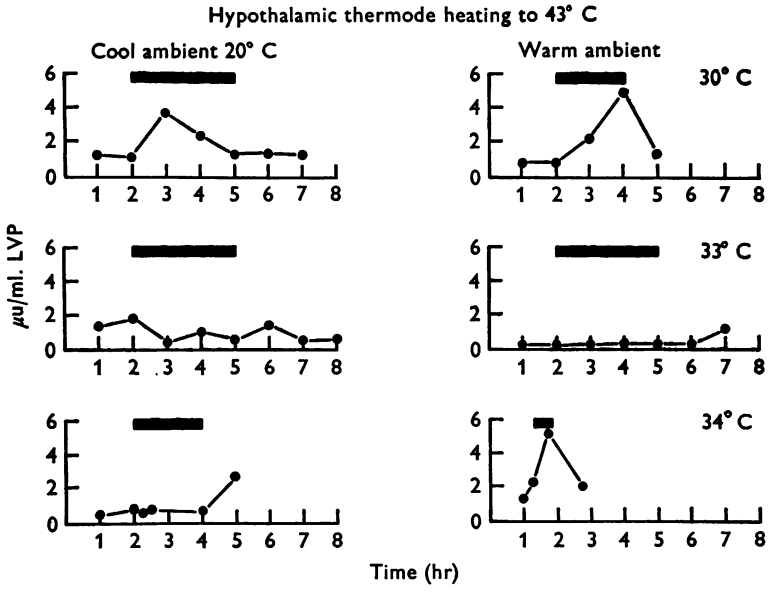

Fig. 3. Changes in ADH levels in the plasma during heating of a thermode in the hypothalamus to 43° C (filled bar) at various ambient temperatures.

day had produced no such rise; the ADH remained below 3 μu. ml^{-1} (Fig. 4).

Once again, the haematocrit varied only slightly during the course of the experiment. Changes in urine volume and in urinary plasma osmolality were also very small. In one case, a large volume of dilute urine was excreted during the 2 hr after the end of a period of warming the hypothalamus, at ambient temperature 20° C. During the warming, urinary flow had been about 0·2 ml. min^{-1} and osmolality 864 m-osmole kg^{-1}. Afterwards, the flow-rate reached 1·8 ml. min^{-1} and osmolality fell to 53 m-osmole kg^{-1}. The plasma ADH had been less than 2 μu. ml.$^{-1}$ in samples taken at hourly intervals throughout the 5 hr period of observation.

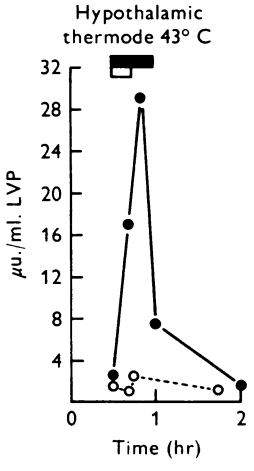

Fig. 4. Two effects in the same pig of heating a thermode in the hypothalamus to 43° C at the same ambient temperature, 34° C. The open bar represents the shorter period of heating associated with the first experiment (13 November) where ADH is represented by open circles. The rise in ADH in the second experiment (14 November) was the greatest recorded during heating of the hypothalamus.

Validity of ADH assay

As a check on the validity of the method for the assay of ADH (lysine vasopressin) as applied to pig plasma, one 18 kg pig was injected with 4 mg nicotine, a substance which is a powerful stimulant for ADH release. Blood samples were taken before injection and again 1, 3 and 15 min afterwards. The assay revealed levels of 1·6 μu. ml.$^{-1}$ before injection and 37, 29·2 and 10·8 μu. ml.$^{-1}$ afterwards. The predicted release of ADH therefore occurred and was readily detected by the assay. The relatively short half-life of the hormone in blood was also demonstrated.

The interpretation of a rise in plasma ADH at high body temperature as due to an increased rate of secretion rather than as a delay in its breakdown was investigated in two animals. On one day the pig was exposed to a thermally neutral environment and a constant infusion of a solution of lysine-vasopressin (Sigma) was made via an indwelling catheter over a period of 40 min. The infusion was then stopped and blood samples taken via a separate catheter at frequent intervals up to 30 min from stopping the infusion. On another day the procedure was repeated in a hot environment which was adjusted so that the pig's rectal temperature remained close to 42° C. The rate of decline in the plasma ADH was similar under both conditions as shown in Table 3 which records the clearance rate and biological half-life of ADH found in these experiments.

TABLE 3. Half-time, clearance and apparent volume of distribution of lysine-vasopressin in two pigs, each of which was studied at two ambient temperatures

Animal no.	Temperature (° C)	Half-time (min)	Clearance (ml./kg per min)	Volume (ml./kg)
1967	25	5·0	17·8	128·6
1967	45–50	6·0	20·9	181·0
2141	25	4·3	19·8	123·0
2141	45–50	4·9	22·5	158·0

DISCUSSION

One conclusion to be drawn from this work is that, for pigs, changes in ambient temperature in the range −5 to 35° C, or heating or cooling thermodes in temperature-sensitive regions of the central nervous system, gave no consistent or readily-reproducible changes in plasma ADH level, or in plasma or urinary osmolality or urine flow. However, placing the pig in an environment sufficiently hot to raise its deep-body temperature to 42° C (from the normal 39° C) invariably caused a large rise in plasma ADH; this rise could be prevented by simultaneous cooling of temperature-sensitive regions of the central nervous system. That this rise of plasma ADH was owing to increased secretion rather than to slower removal was made clear by the finding that a rise of deep-body temperature had little effect on the biological half-life of infused ADH.

The question arises whether this increased ADH output during severe heating was a direct or an indirect effect of the change in deep-body temperature. An indirect effect might be mediated through a change in blood osmolality, or volume, or even through a redistribution of blood such that the volume in the thoracic region decreased. The panting and salivation of the pig at 42° C might be expected to cause some dehydration

but, in fact, it was not sufficient to produce a measurable change in plasma osmolality and, after heating, the plasma ADH always started to fall before the animal was allowed to drink and thus to replace any water loss incurred during heating. Furthermore, the slight changes in haematocrit occurring during the heating negated the idea that a large drop in plasma volume (caused, say, by the removal of plasma water to the interstitium) could be the initial stimulus to the ADH output. However, nothing in the present work would be contrary to the suggestion (similar to that made by Wyndham, Benade, Williams, Strydom, Goldin & Heyns, 1968), that the immediate stimulus to ADH secretion might be the redistribution of blood from the centre to the periphery of the animal's body, perhaps by massive dilatation of the skin vessels. The consequent alteration of the tone of volume-receptors in the heart or main veins (Johnson, Moore & Segar, 1969) might elicit the secretion. The fact that heating of the skin or central nervous system causes an increase in peripheral blood-flow of pigs, and cooling a decrease (Ingram & Legge, 1971) would be in line with this suggestion, and this hypothesis is now being tested further. The outcome of the present work is that the ADH secretion, however caused, can be suppressed by simultaneous cooling of several parts of the central nervous system (even in the cervical region remote from the neurohypophysis) known to contain temperature-sensing neurones. This suggests at least some connexion between neurones responsive to temperature and those concerned with releasing ADH from the neurohypophysis.

Hayward & Baker (1968) cooled thermodes implanted in the hypothalamus of monkeys and in two animals out of the nine studied they obtained a diuresis. They did not measure circulating ADH levels but found that the diuretic response was abolished if exogenous ADH had been injected before the cooling. In our pigs a diuresis was observed on two occasions, out of seventeen trials at various ambient temperatures, during cooling of a thermode in the pre-optic region of the hypothalamus, and on one occasion after the end of a period of heating such a thermode. On all these occasions the circulating level of ADH was low. However, in the pig, normal circulating level in thermoneutral conditions is low, and any possible decrease resulting from an experimental manoeuvre might be unmeasurable by the ADH bio-assay method. Szczepanska-Sadowska (1974) heated thermodes in the hypothalamic region of five dogs in a thermoneutral environment and found, in all five animals, a rise in plasma ADH and in urinary osmolality and a fall in urinary flow-rate; whereas in our pigs thermode heating in thermoneutral or warm conditions produced no consistent changes in urinary flow or osmolality and on only one occasion out of twenty-six trials was there any marked elevation of plasma ADH during heating (Table 2 and Fig. 4). This discrepancy between our

results on pigs and Szczepanska-Sadowska's dogs might be explained by a difference of response of either osmoreceptors or of possible 'volume receptors'. The dogs were panting heavily during the thermode heating, and perhaps the panting was severe enough to cause fluid loss and consequent rise of plasma osmolality sufficient to stimulate osmoreceptors and thus to elicit ADH secretion by the mechanism described by Verney (1947). Our pigs also panted during thermode heating though not as heavily as during whole-body heating and certainly not enough to produce a detectable change in plasma osmolality. Again, it has been shown in pigs that the combined effects of thermode heating with heating of the skin caused a greater increase in peripheral blood flow than heating the thermode alone (Ingram & Legge, 1971). Possibly in the dogs local heating of the pre-optic region was able to cause the same amount of redistribution of blood volume towards the periphery as could be achieved in pigs only by whole-body heating.

Though our concern was mainly with the effect of temperature changes on endocrine function rather than on renal function, we took the opportunity of observing any possible renal effects of the temperature changes and ADH levels. It was not perhaps surprising that a cold environment never elicited a 'cold diuresis' in our pigs as this appears to be a somewhat variable and inconsistent phenomenon in other species (Pabst & Thron, 1960; Bader *et al.* 1952). We might have expected to see some increase in urinary osmolality accompanying the very high plasma ADH levels seen during whole-body heating but these high ADH levels were so transient that any renal effects were difficult to observe. In any case, a poor correlation has been found in dogs between plasma ADH and urinary osmolality (Forsling & Ullmann, 1974), and there is little reason to suppose that the correlation would be better in any other species.

The question whether a rise of ambient or deep-body temperature *per se* causes ADH secretion is still unanswered. It may do so but there is no reason, either from our results or from those of previous workers, to suppose that it does. The fact that in pigs no consistent change in plasma ADH could be observed within the range of ambient temperatures which this animal would be likely to meet in the field makes it improbable that, in this species at any rate, the ADH mechanism is involved in any thermally-induced changes in water requirement or osmolar homoeostasis.

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REFERENCES

BADER, R. A., ELIOT, J. W. & BASS, D. E. (1952). Hormonal and renal mechanisms of cold diuresis. *J. appl. Physiol.* **4**, 649–658.

BALDWIN, B. A. & INGRAM, D. L. (1967). The effect of heating and cooling the hypothalamus on behavioural thermoregulation in the pig. *J. Physiol.* **191**, 375–392.

BARATZ, R. A. & INGRAHAM, R. C. (1960). Renal hemodynamics and antidiuretic hormone release associated with volume regulation. *Am. J. Physiol.* **198**, 565–570.

BAZETT, H. C., SANDERMAN, F. W., DOUPE, J. & SCOTT, J. C. (1940). Climatic effects in the volume and composition of blood in man. *Am. J. Physiol.* **129**, 69–83.

DUNN, F. L., BRENNAN, T. J., NELSON, A. L. & ROBERTSON, G. L. (1973). The role of blood osmolality and volume in regulating vasopressin secretion in the rat. *J. clin. Invest.* **52**, 3212–3219.

FABIAN, M., FORSLING, M. L., JONES, J. J. & LEE, J. (1969). The release, clearance and plasma protein binding of oxytocin in the anaesthetized rat. *J. Endocr.* **43**, 175–189.

FORSLING, M. L. (1974). Extraction of neurohypophysial hormones for bio-assay. *J. Physiol.* **241**, 3–5*P*.

FORSLING, M. L., INGRAM, D. L. & STANIER, M. W. (1975). Effect of changes in hypothalamic temperature on ADH secretion in pigs. *J. Physiol.* **247**, 49*P*.

FORSLING, M. L., JONES, J. J. & LEE, J. (1968). Factors influencing the sensitivity of the rat to vasopressin. *J. Physiol.* **196**, 495–505.

FORSLING, M. L. & ULLMANN, E. (1974). Plasma vasopressin and renal concentrating ability in the anaesthetized dog. *J. Endocr.* **63**, 41–42.

HAYWARD, J. N. & BAKER, M. A. (1968). Diuretic and thermoregulatory responses to preoptic cooling in the monkey. *Am. J. Physiol.* **214**, 843–850.

INGRAM, D. L. & LEGGE, K. F. (1971). The influence of deep-body and skin temperature on peripheral blood flow in pigs. *J. Physiol.* **215**, 693–707.

ITOH, S. (1954). The release of antidiuretic hormone from the posterior pituitary body on exposure to heat. *Jap. J. Physiol.* **4**, 186–190.

JOHNSON, J. A., MOORE, W. W. & SEGAR, W. E. (1969). Small changes in left atrial pressure and plasma antidiuretic titres in dogs. *Am. J. Physiol.* **217**, 210–214.

PABST, K. & THRON, H. L. (1960). Kältediurese beim unnarkotisierten Hund. *Pflügers Arch. ges. Physiol.* **270**, 585–606.

RODBARD, S., DAIKI, J., MALIN, A. & YOUNG, C. (1951). Significance of changes in plasma and extracellular volumes during induced hyperthermia and hypothermia. *Am. J. Physiol.* **167**, 485–498.

SEGAR, W. E. & MOORE, W. W. (1968). The regulation of antidiuretic hormone release in man. *J. clin. Invest.* **47**, 2143–2151.

SHARE, L. (1965). Effects of carotid occlusion and left atrial distension on plasma vasopressin titre. *Am. J. Physiol.* **208**, 219–223.

SZCZEPANSKA-SADOWSKA, E. (1974). Plasma ADH increase and thirst suppression elicited by preoptic heating in the dog. *Am. J. Physiol.* **226**, 155–161.

VERNEY, E. B. (1947). The antidiuretic hormone and the factors which determine its release. *Proc. R. Soc.* B. **135**, 25–105.

WEINER, J. S. (1944). The diuretic response of men working in hot and humid conditions. *J. Physiol.* **103**, 36–37*P*.

WYNDHAM, C. H., BENADE, A. J. A., WILLIAMS, C. G., STRYDOM, N. B., GOLDIN, A. & HEYNS, A. J. A. (1968). Changes in central circulation and body fluid spaces during acclimatization to heat. *J. appl. Physiol.* **25**, 586–593.