OSMOMETRIC ANALYSIS OF THIRST IN MAN AND DOG

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A PREPONDERANCE of evidence favors the view that ordinary thirst is closely correlated with cellular dehydration and increased effective osmotic pressure of tissue fluids (1–6). In this view thirst is of ‘general origin’ although the consequences of such a cellular dehydration hypothesis would remain substantially intact if it were postulated that osmoreceptors of the Verney type (γ), rather than general body tissues, were the receptors in a thirst reflex. At the present time a cellular dehydration hypothesis has been blocked out only qualitatively.

This hypothesis has remained attractive to physiologists despite the fact that present experimental methods for determining cellular water are inadequate for assessing minute changes in its volume. The measurement of cellular water by difference of total and allegedly extracellular water is subject to errors in excess of the changes predicted by theory which would suffice to cause thirst. To estimate cellular water differences between normal and thirsting states is to compound experimental errors to a degree which precludes testing the theory by this means. If we assume that tissue cells behave enough like perfect osmometers to render osmometric calculations from concentration increments valid, the problem is somewhat less difficult. However, analytical methods would be called on to indicate critical differences smaller than one per cent. The attendant technical efforts which would be required to this end are not likely to engender the same interest in testing the hypothesis as if experimental methods were simple and well adapted to the task.

It is proposed here to show how osmometric analysis can be used to quantify the cellular dehydration hypothesis, to suggest crucial experimental tests of it, and actually to calculate degrees of hyperdipsia, hypodipsia, and antidipsia.

PROCEDURES

Dogs were taken from cages where they had easy access to water, were catheterized and were loosely confined to a stall as previously described (8). They were confronted with a dish of water which was in no case acceptable before the beginning of an intravenous infusion of sodium chloride. Infused solutions varied from 1.3 to 6.1 per cent and were administered at a rate of 4.11 cc/min. At a variable time following the onset of infusion a dog would begin to drink. In 5 experiments on 3 dogs, the infusion was stopped at that time, the dog was permitted access to water for 10 minutes, the volume drunk was recorded, and urine was collected at the end of drinking. In 6 experiments on 4 dogs, when drinking began, the water was removed, the urine collected, and the infusion of salt solution was continued for a variable time. At the end of an additional period, infusion was stopped,
the dog was allowed to slake its thirst as above, the volume of water drunk was recorded, and urine was collected at the end of drinking.

Young male medical students were also infused with salt solutions, at the same rate. Infusion was started about one hour after the subject's lunch and continued until the subject, who was alerted for the end point, stated an unequivocal desire to drink water. From the nature of this end point, the conditions of the experiment, and known equilibration times for salt load, it is believed that this thirst threshold is a maximal value in whatever may be the range of this physiological parameter. In 4 experiments on 4 men the urine was collected at this time, 28 cc. more of salt solution was infused, and then 52 per cent aqueous glucose solution was infused until the subject's desire to drink just disappeared. Urine was collected at the onset and disappearance of thirst. In 5 experiments on 4 men, at the onset of thirst, infusion was stopped, urine was collected and the subject was allowed to drink ad libitum for 15 minutes, whereupon a final urine collection was made.

All experiments on dog and man were performed in a room kept between 21° and 23°C. Measurements included quantities of fluid administered and urinated, and the concentration of sodium in these fluids. Insensible water loss was estimated at 0.4 cc/minute for the dog (10) and 0.7 cc/minute for man (11).

**CALCULATIONS**

*Symbols Used.*

- \( A \) = initial effective osmolal concentration of extracellular fluid for which is substituted a value of 150 mEq/l. Na;
- \( i \) = rate of infusion of fluid (cc/min.);
- \( I \) = concentration of salt in infusion fluid (mEq/l.), and, where indicated, retention concentration, \( L_{Na}/L_{H_2O} \);
- \( L \) = load of salt, specifically, \( L_{Na} \) (mEq.);
- \( L_{H_2O} \) = load of water (liters);
- \( Q_N \) = quantity of water required to restore hypertonic body fluids to isotonicity (liters);
- \( Q_T \) = quantity of water required to restore hypertonic body fluids to their concentration at the thirst threshold (liters);
- \( t \) = time (min.);
- \( \tau \) = relative cellular water deficit at the thirst threshold (= \( \Delta V_i/V_i \));
- \( u \) = rate of urine flow (cc/min.);
- \( U \) = concentration of solute in urine (mEq/l.);
- \( V_i \) and \( V'_i \) = initial and final extracellular fluid volumes, respectively (liters);
- \( V_i \) and \( V'_i \) = initial and final intracellular fluid volumes (liters);
- \( w \) = rate of extrarenal (insensible) water loss (cc/minute);
- \( W \) = initial total body water volume (liters).

With the onset of thirst, or at the time the thirst threshold was just exceeded, the loads of salt and water were computed on the assumption that the subject initially had no load of either. Thus

\[
L_{Na} = 0.001(iU_{Na} - uU_{Na})t
\]

and

\[
L_{H_2O} = 0.001(i - u - w)t
\]

From the osmometric equation (12) the augmented extracellular volume was calculated as

\[
V'_i = \frac{(W + L_{H_2O})(V_iA + L_{Na})}{WA + L_{Na}}
\]

The cellular volume was obtained from

\[
V_i = W - V_e
\]

The diminished cellular volume was obtained from

\[
V'_i = W + L_{H_2O} - V'_i
\]

*All solute concentrations and loads are ideally to be given in effective osmolar units.*
The percentual diminution of the cellular compartment was obtained from

\[ \frac{100}{V_i} = \frac{100(V_i - V'_i)}{V_i} = \frac{100(\Delta V_i)}{V_i} \quad (6) \]

For example, for dog Q (table I), 24.4 kg., with \( L_{Na} = 57.4 \) mEq. and \( L_{H_2O} = 0.023 \) liters at the thirst threshold, we compute as follows, regarding the total water of the body to be 70 per cent (0.700) of the body weight, the extracellular volume to be 20 per cent (0.200) of the body weight, and the concentration of plasma sodium to be effectively 150 mEq/l.:

\[
\begin{align*}
W &= 0.700 \times 24.400 = 17.080 \text{ l.} \\
V_e &= 0.200 \times 24.400 = 4.880 \text{ l.} \\
W_A &= 17.080 \times 150 = 2562 \text{ mEq.} \\
V_e A &= 4.880 \times 150 = 732 \text{ mEq.} \\
V_i &= W - V_e = 17.080 - 4.880 = 12.200 \text{ l.} \\
V'_i &= (W + L_{H_2O})(V_e A + L_{Na}) \\
&= \frac{(17.080 + 0.023)(732 + 57.4)}{2562 + 57.4} = 5.154 \text{ l.} \\
\frac{100}{V_i} &= \frac{100(V_i - V'_i)}{V_i} = \frac{100(12.200 - 11.949)}{12.200} = 2.06 \text{ per cent}
\end{align*}
\]

RESULTS

Tables 1 and 2 show the decrements in cellular water content (\( \tau \)) which theoretically are sustained at the thirst threshold. Mean values (and average deviations) of \( 100 \tau \) for the dog were 2.91 ± 1.38 per cent; for man, 1.23 ± 0.48 per cent. Reasons are given below for doubting that the \( \tau \) values obtained for the dog are strictly comparable to those for man.

Figure 1 illustrates for a 20-kg. dog how the thirst threshold separates dipsic and adipsic areas on an osmometric diagram based on equation (3). The ‘isotonic line,’ \( I = 150 \), is the only retention concentration (10) greater than zero which can be plotted rectilinearly. When both coordinates are plotted to the same scale, the isotonic line passes through the origin at 45°. The thirst threshold, according to the assumption of this osmometric analysis, is a line parallel to the isotonic line, intersecting the ordinate at \( V'_e - V_e = \Delta V_i \). The value \( \Delta V_i \) is obtained from \( V'_i \) (in this particular graph, 0.0297 \times 10.000 = 0.297 liters), laid off in the ordinate, and a 45° line passed through it.

Figure 2 illustrates the thirst threshold for man on an osmometric diagram which omits most retention concentration curves and salt load lines. Hyperdipsic, hypodipsic, and adipsic areas are distinguished.

\[^3\] The equation of the thirst threshold is \( V'_i - V_e = L_{H_2O} + \Delta V_i \). Where \( L_{H_2O} = 0 \) at the ordinate, the increment in extracellular volume can come only from intracellular decrement.
### Table 1. Relative Cellular Water Deficits ($\Delta V_i/V_i$) in Dogs of Body Weight (B.W.)

Symbols heading columns are defined in text under 'Calculations'.

<table>
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<tr>
<th>EXPER. NO.</th>
<th>SUBJECT</th>
<th>1</th>
<th>B.W.</th>
<th>WA</th>
<th>$V_e$</th>
<th>$V_e$/WA</th>
<th>$V_e$/B.W.</th>
<th>$V_e$/LNa</th>
<th>$V_i$</th>
<th>$V_i$/V_i</th>
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1 is concentration (mEq/l.) of Na in infused fluid. Letters $r$, $H$, and $E$ alongside values in $\Delta V_i/V_i$ column signify, respectively, the thirst threshold, hyperdipsia, and the state at the end of the experiment. Excluding exper. 13, the mean value of 100 $r$ averages 2.78 $\pm$ 1.32%. Excluding also the results on dog D (exper. 2 and 14), 100 $r$ averages 2.15 $\pm$ 0.64%.

1 When $L_{Na}/L_{H_2O} < 150$ mEq/l., $\Delta V_i/V_i$ is negative.

2 Hypodipsia. Thirst threshold was not attained after 5 hours of infusion.
DISCUSSION

Nature of Assumptions in Osmometric Analysis of Thirst. Two important assumptions should be noted. One is that the osmometric equation permits an estimation of changes in body compartmental volumes sufficiently accurate that the results derived from it may be applied with an acceptable degree of validity. The other is that the

<table>
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<th>SUBJECT</th>
<th>I. B.W.</th>
<th>W</th>
<th>WA</th>
<th>( V_v )</th>
<th>( V_vA )</th>
<th>( I_{Na} )</th>
<th>( I_{H2O} )</th>
<th>( V_e )</th>
<th>( V_i )</th>
<th>( \Delta V'_i )</th>
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\( I \) is concentration (mEq/l.) of Na in infused fluid. Letters \( \tau \), \( H \) and \( E \) alongside values in \( \Delta V'_i/V'_i \) column signify, respectively, the thirst threshold, hyperdipsia, and state at end of experiment. Average value for \( 100 \, \tau \) was 1.23 ± 0.45 per cent.

thirst threshold, and the degree of thirst, is directly related to the magnitude of cellular dehydration, or to the effective osmotic pressure of the body fluids at large.

With reference to the first assumption, it is not especially significant to recount those instances in which body compartments appear to behave as the chambers of a perfect osmometer (12-17), or not (18). In these studies the view is taken that the calculations from loads of water and from loads of solute substantially confined to
the extracellular space, permit determinations of volume changes which cannot be made by any direct, accurate, experimental method at present. If percentually large deviations between calculated and 'actual' changes are ultimately discovered, that will not alter the fact that the osmometric equation is a tool which can serve to reify

[Diagram of Osmometric Thirst Diagram]

Fig. 1—Osmometric Thirst Diagram based on a 20-kg. dog containing 14 liters of total body water and 4 liters of extracellular fluid. Ordinate: change in extracellular volume in liters ($V'_o - V_o$). Abscissa: load of water in liters ($L_{H_2O}$). The interrupted lines passing through the origin represent retention concentrations in mEq/l. of administered or withdrawn NaCl solutions ($I = L_{Na}/L_{H_2O}$). Each of the almost parallel salt load lines ($L$) crossing the coordinates represents a given load of NaCl in mEq. The line separating the stippled from unstippled areas is a thirst threshold (see fig. 2) representing a $\tau$ value of 0.0207, somewhat higher than average. Where retention concentration lines intersect the thirst threshold the projection on the abscissa measures the volume of retained solution which will just provoke thirst.

otherwise nebulous concepts. We can accurately assess increments in actual osmotic pressure but not in effective osmotic pressure; in parallel, we can accurately assess 'perfect' osmometric volume changes but not actual volume changes. To calculate merely that the increment of osmotic pressure just bringing a man to the thirst threshold is $\Delta\tau/(1 - \tau)$ is not so instructive as a fuller volumetric analysis of thirst.
Of unique interest is the fact that 1007 has a value essentially the same as the approximation made by Verney (7) of 1.2 per cent for the osmotic increment required to

Fig. 2—OSMOMETRIC THIRST DIAGRAM based on a 70-kg. man containing 49 liters of total body water and 14 liters of extracellular fluid. Ordinate: change in extracellular volume in liters ($V_t - V_s$). Abscissa: load of water in liters ($L_{H_2O}$). The retention concentration lines (I, of fig. 1) and most of the salt load lines (L) have been omitted for clarity. The thirst threshold, separating the hyperdipsic area (densely stippled) from the hypodipsic area (sparsely stippled) is the heavy line, parallel to the isotonic line, which intersects the ordinate at $\Delta V_i$. The value for $\Delta V_i$ was obtained by using the average $r$ value (0.0123) found in human experiments. Thus, where the cellular water in a 70-kg. man is 35 liters, $\Delta V_i = 0.0123 \times 35.000 = 0.431$ liters.

An isodip is a line (e.g. $AB$) which is the locus of all points ($L_{Na}, L_{H_2O}$) of equal thirst. For a hyperdipsic point, $A$, one measures the degree of thirst by passing a salt load line (in this case, $L = 300$) from $A$ to the thirst threshold at $C$ or to the isotonic line at $D$. The projections $EF$ and $EG$ measure, respectively, the volume of water required to move from the given hyperdipsia to hypodipsia, and from the given hyperdipsia to adipsia. Quantities of water required to relieve hyperdipsia may be determined directly from the Equations of Thirst. (See text.)

From the intersection of the thirst threshold and the salt load line $L = O$, at $H$, the perpendicular to $J$ may be erected. The abscissal distance from $J$ to the origin represents the absolute water deficit, with no salt loss, which should just provoke thirst, according to the cellular dehydration hypothesis. The value obtained here, viz. $-0.60$ liters, represents a deficit of 0.86% of the body weight. Algebraically, this latter value is equal to $\gamma r$ (total body water as percentage of body weight, multiplied by 0.0123).
stimulate osmoreceptors of the ‘water conservation’ reflex, in which the posterior pituitary is an effector. It is not an untenable hypothesis that the same or similar osmoreceptors lie on the afferent side of a ‘thirst reflex.’

The second assumption is, in a sense, tested in these experiments. Nothing in the present findings can be construed to argue seriously against the cellular dehydration hypothesis of the origin of thirst. (However, see section below.) The data on hand support it although at the present time it is meaningless to suppose a primacy of either cellular dehydration or of increased effective osmotic pressure in body fluids.

Use of Osmometric Thirst Diagram. In figures 1 and 2 the ‘isotonic line,’ I = 153, separates the osmometric diagram into 2 areas. Above and to the left lies a hypertonic region of salt-water loads which favor cellular dehydration. Below and to the right lies a hypotonic region of loads favoring cellular hydration. The line representing the thirst threshold is, theoretically, the locus of all points of salt and water loads (LNa, LH2O) at which a critical cellular water deficit exists, which evokes thirst. Points lying above and to the left of the thirst threshold represent varying degrees of hyperdipsia, measured roughly by their perpendicular distances from the thirst threshold. The quantity of water required to restore an individual from a given hyperdipsic state to the thirst threshold is obtained graphically by passing a salt-load line from the hyperdipsic point to the thirst threshold. In figure 2 perpendicularly dropped from the hyperdipsic point (A) and from the point of intersection of the salt-load line and the thirst threshold (C), mark off on the abscissa the required water load, EF. However, drinking usually goes beyond restoration of the thirst threshold, causing the final point (LNa, LH2O) to lie nearer the isotonic line, and most often (particularly when glucose is given intravenously) to lie in the hypodipsic area between the thirst threshold and the isotonic line.

By erecting a perpendicular from the point of intersection (H) of the thirst threshold and the salt-load line, L = O, to the abscissa (J), we locate theoretically the deficit of total body water (JO), which should just provoke thirst in an individual who, starting with no water or salt loads, has become dehydrated chiefly by pulmonary water loss. There are for man, few data in the literature bearing closely on this matter but these enable us to approximate it as less than one per cent of the body weight (τ, 19). From figure 2 we may infer a probable average value (maximal rather than minimal) for this deficit as 0.86 per cent of the body weight (100 X -0.60/70 = - 0.86). Algebraically this value is found directly in the product 70τ, i.e. 70 X 0.0123 = 0.86.

In the dog more extensive data of Robinson and Adolph (20) are available and their deficit of 0.5 per cent of the body weight (equivalent to τ = 0.0071) does not agree with the maximal threshold value found here (fig. 1, table I) of 1.51 per cent of the body weight (70 X τ = 70 X 0.0215 = 1.51). It is believed that the Robinson-Adolph figures more properly indicate the thirst threshold in the dog than do those

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4 It is interesting to note Verney’s record of ‘lip-smacking’ resulting from injection of hypertonic solutions into the internal carotid artery of dogs.

5 ‘Hyperdipsia’ is used here to indicate sensible thirst which is relatively temporary as opposed to ‘polydipsia’ which is relatively sustained. ‘Hypodipsia’ denotes an insensible or twilight thirst. It is a condition of hypertonicity of body fluids insufficient to initiate drinking but sufficient to sustain drinking once initiated.
obtained here for 3 reasons. 1) 'Psychological' factors probably operate in dogs un-
trained for the present experiments, to prevent some from taking water at the
onset of 'thirst.' In one instance a dog (not used to obtain any data recorded here)
was infused with a load of salt and water which by comparison with loads given to
other dogs should have caused severe hyperdipsia. This dog showed no apparent
interest in drinking even when water was urged upon it. When the infusion of salt
solution was stopped and the dog returned to its cage, it immediately began to
drink from its accustomed trough. 2) The Robinson-Adolph threshold implies a \( \tau \)
value more in line with the data from the better controlled human experiments.
3) Individual values of \( \tau \) varied from 0.0002 to 0.0615 in the dog compared with
0.00407 to 0.0225 in man, showing considerable overlap in the 2 species. Table 1
shows how Dog D6 repeatedly evidenced an unusually high thirst threshold.

The data from which the actual value of the thirst threshold was obtained in
this study are derived from salt-water loads in the 1st quadrant of the osmometric
diagram. Supporting evidence is found from the data in the literature which concerns
loads in the 3rd quadrant (point \( H \), fig. 2). It remains to be learned if data from
loads in the 4th quadrant and from different loads in the 3rd quadrant will also be
consistent with the cellular dehydration hypothesis.

Note that the \( I \) values in the Osmometric Thirst Diagram are not concentrations
of infused fluid, except ideally, at zero time after the beginning of infusion. For the
Diagram, \( I = \frac{L_{Na}}{L_{H_2O}} \) and is defined as a retention concentration (10). The retention
concentration is the virtual concentration of the loaded fluid any time after infusion
begins and after some renal excretion has modified the retained load. Thus, while a
solution of 200 mEq Na per liter might, in large enough load, cause the thirst
threshold to be reached, such a solution infused slowly, would probably never reach
the thirst threshold because the urine formed under these conditions is more con-
centrated than the infused fluid and the retention concentration would tend to become
lower the longer the infusion continued. Experiment 13 (table 1) is a case in point,
where 5 hours of infusion did not provoke drinking.

Some of the properties of the Osmometric Thirst Diagram may be summarized
as follows: 1) Every point on the graph represents a given salt-water load \( (L_{Na},
L_{H_2O}) \). 2) The coordinates for every point on the graph indicate the prevailing incre-
ments in extracellular volume and in water load. 3) Salt-load lines are straight lines,
crossing the coordinates. They originate from a common point where \( L = -V' A,
L_{H_2O} = -W \), and where \( V'_e - V_e = -V_e \). 4) Retention concentration lines \( I \)
passing through the origin are all curvilinear with the exception of \( I = 150 \) and
\( I = 0 \). The latter line is the same as the line \( L = 0 \). 5) Isodips of the \( Q_N \) type are
curves asymptotic with the isotonic line at extremely high \( L_{H_2O} \) values. All points
on a given isodip are points of equal degrees of thirst in the objective sense that
almost equal quantities of water are required to bring the individual from any of
these hyperdipsic points to the thirst threshold; and equal (but greater) quantities
of water are required to bring the individual from these points to isotonicity. Thus
the degree of hyperdipsia is measured by the \( Q_o \) or the \( Q_N \) value. The thirst threshold
itself is not strictly an isodip of the \( Q_N \) type since at different salt loads, different

\* An old dog, inured to laboratory insult.
quantities of water are required to restore isotonicity. The equation of an isodip of the $Q_N$ type is

$$V'_e - V_e = \frac{(W + L_{H_2O})(V + Q_N + L_{H_2O})}{W + Q_N + L_{H_2O}} - V_e \quad (7)$$

6) In the case of hyperdipsic points, passing an isodipsic line (practically a straight line in the range of salt-water loads considered here) through any given one until it intersects the ordinate lays off a distance between this point of intersection and the origin which measures the absolute water deficit of the original hyperdipsic state.

*Equations of Thirst.* More suitable in general than the graphic method of determining the quantity of water required to bring a hyperdipsic individual to the thirst threshold ($Q_T$), or to restore his body fluids from dipsogenic hypertonicity to isotonicity ($Q_N$), is the use of what we may call the Equations of Thirst, the derivations of which will be given elsewhere (22). These are

$$Q_N = \frac{L_{Na}}{A} - L_{H_2O} = \frac{L_{Na}}{150} - L_{H_2O} \quad (8)$$

and

$$Q_T = \frac{(1 - \tau)(WA + L_{Na})}{A} - (W + L_{H_2O}) \quad (9)$$

### Table 3. Comparison of actual quantity of water ($Q_A$) drunk by dogs with the quantity theoretically required ($Q_N$) to restore their body fluids to isotonicity

<table>
<thead>
<tr>
<th>Exper. No.</th>
<th>Dog</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>D</td>
</tr>
<tr>
<td>4</td>
<td>K</td>
</tr>
<tr>
<td>5</td>
<td>Q</td>
</tr>
<tr>
<td>6</td>
<td>O</td>
</tr>
<tr>
<td>7</td>
<td>Q</td>
</tr>
<tr>
<td>10</td>
<td>R</td>
</tr>
<tr>
<td>12</td>
<td>O</td>
</tr>
<tr>
<td>13</td>
<td>K</td>
</tr>
<tr>
<td>14</td>
<td>D</td>
</tr>
<tr>
<td>15</td>
<td>Q</td>
</tr>
<tr>
<td>16</td>
<td>O</td>
</tr>
</tbody>
</table>

Average $^{1}$: .................................................................................. .598 .342

$^{1}$ No drinking. Exper. 13 not included in averages.

In tables 3 and 4 is presented evidence that, under the conditions of these experiments, the quantity of water actually taken to alleviate thirst generally brings the organism to the hypodipsic state, i.e. below the thirst threshold but not quite to isotonicity. It is interesting to note that in man thirst passes off when glucose solution is taken in amounts which only bring the individual slightly below the thirst threshold. Drinking *ad libitum*, however, restores him practically to isotonicity. There
was some evidence that men receiving intravenous glucose, rather than drinkers, became uncommonly thirsty several hours after conclusion of the experiment. The role of initial salt-water imbalances, and possible 'adaptation' factors in thirst (r) are beyond the scope of this study.

Miscellaneous Observations. An observation which may be added to many others indicating dissociation between thirst and dryness of mouth is that human subjects receiving salt injections invariably report a drying of the mouth (21) considerably before any clear desire to drink. Conversely, with glucose injections in hyperdipsic men, the mouth moistened considerably before the desire to drink abated. Another observation, which may bear on the 'general' or perhaps the central nervous system origin of thirst, is that subjects made sufficiently hyperdipsic beyond the thirst

<table>
<thead>
<tr>
<th>EXPER. NO.</th>
<th>SUBJECT</th>
<th>L&lt;sub&gt;Na&lt;/sub&gt;</th>
<th>L&lt;sub&gt;H2O&lt;/sub&gt;</th>
<th>Q&lt;sub&gt;N&lt;/sub&gt;</th>
<th>Q&lt;sub&gt;A&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>W. H.</td>
<td>130</td>
<td>0.058</td>
<td>0.742</td>
<td>0.065</td>
</tr>
<tr>
<td>2</td>
<td>W. H.</td>
<td>175</td>
<td>0.088</td>
<td>1.029</td>
<td>0.281</td>
</tr>
<tr>
<td>3</td>
<td>J. B.</td>
<td>72</td>
<td>0.054</td>
<td>0.426</td>
<td>0.082</td>
</tr>
<tr>
<td>4</td>
<td>S. D.</td>
<td>130</td>
<td>0.058</td>
<td>0.809</td>
<td>0.340</td>
</tr>
<tr>
<td>5</td>
<td>S. D.</td>
<td>150</td>
<td>0.108</td>
<td>0.892</td>
<td>0.338</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.790</strong></td>
<td><strong>0.221</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EXPER. NO.</th>
<th>SUBJECT</th>
<th>L&lt;sub&gt;Na&lt;/sub&gt;</th>
<th>L&lt;sub&gt;H2O&lt;/sub&gt;</th>
<th>Q&lt;sub&gt;N&lt;/sub&gt;</th>
<th>Q&lt;sub&gt;A&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>W. H.</td>
<td>255</td>
<td>0.372</td>
<td>1.328</td>
<td>0.645</td>
</tr>
<tr>
<td>7</td>
<td>J. W.</td>
<td>92</td>
<td>0.079</td>
<td>0.534</td>
<td>0.360</td>
</tr>
<tr>
<td>8</td>
<td>L. P.</td>
<td>132</td>
<td>0.096</td>
<td>0.784</td>
<td>0.560</td>
</tr>
<tr>
<td>9</td>
<td>W. B.</td>
<td>51</td>
<td>0.094</td>
<td>0.246</td>
<td>0.747</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>0.723</strong></td>
<td><strong>0.628</strong></td>
</tr>
</tbody>
</table>

Q<sub>N</sub> is the quantity of water theoretically required to restore their body fluids to isotonicity.

Threshold report a severe burning sensation in the throat. One subject reported this sensation first in the arm above the site of salt injection, then in the throat, back and perineum, in that order. Glucose solution rapidly alleviated these paresthesias.

A quantitative description of the physiological antagonism between the dipsogenic factor of the insensible water loss and the antidiipsic factor of the maximum urinary concentration will be published shortly (22).

SUMMARY AND CONCLUSIONS

By means of intravenous salt-water infusions, various degrees of hypertonicity of body fluids and of thirst, were produced in dog and man. A thirst threshold was measured under these conditions in terms of a calculated relative decrease in the cellular water content, this value being called r. The value 100r is theoretically the percentual decrement in cellular water content at the thirst threshold. Calculations
based on the osmometric equation are considered at present the most satisfactory means for investigating the cellular dehydration hypothesis of thirst. In the dog, an average for 100 of 2.15±0.64 per cent is believed to be in excess of the ‘true’ thirst threshold. In man, 100 averaged 1.23±0.48 per cent which is thought to represent an upper limit of the ‘true’ thirst threshold. With reference to an Osmometric Thirst Diagram, graphic and algebraic interpretations of problems in thirst are presented. These make use of equations of thirst and of isodipsic parameters. Hyperdipsic, hypodipsic and adipsic states are distinguished. While no primacy can be given to increased effective osmotic pressure of body fluids or to decreased cellular water content in initiating thirst, it is believed that either or both when present to sufficient degree, can excite thirst. The cellular dehydration hypothesis is considered preferable to the ‘dry mouth’ hypothesis and it is suggested that particular osmo-receptors, probably in the central nervous system, and similar to or the same as those postulated by Verney, lie on the afferent side of a thirst reflex.

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