*IFCC/EWGISE Proceedings (ISBN 87 88138-10-0) 1986; 7: 285-91*

# Clinical interpretation of the plasma sodium concentration: a volume-tonicity chart

OLE SIGGAARD-ANDERSEN, NIELS FOGH-ANDERSEN AND PETER D. WIMBERLEY

Department of Clinical Chemistry, Herlev Hospital, University of Copenhagen, Herlev, Denmark

Changes in the plasma sodium-ion concentration may be due to changes in either the amount of sodium or the amount of water in the extracellular fluid (or both). Interpretation of the sodium concentration therefore depends on a careful evaluation of the extracellular hydration. The extracellular sodium and water status directly influences the intracellular potassium and water status because the extracellular and intracellular osmolality must be identical. We have illustrated these relationships by means of a chart showing the extracellular sodium/water status as well as the intracellular potassium/water status. The chart is a useful teaching aid, illustrating important relationships between sodium, potassium and water in the organism.

Key words: Sodium, potassium, extracellular fluid, intracellular fluid, electrolyte balance, graphical interpretation, bivariate analysis.

Clinical chemical quantities are always related to a reference interval and a special clinical terminology is employed, e.g. hypernatremia or hyponatremia for an increased or a decreased plasma sodium-ion concentration. When two quantities are interdependent a graphical interpretation may be helpful. We then get a reference area for healthy individuals and reference areas for typical pathophysiological disturbances (1,2). A diagram with the extracellular fluid volume on the abscissa and sodium-ion concentration on the ordinate illustrates clinical conditions such as hypotonic, isotonic, and hypertonic dehydration, or hypo-, normo-, and hypervolemic hyponatremia. The "extracellular" diagram may be expanded with an "intracellular" diagram, illustrating the intracellular hydration (abscissa) and intracellular tonicity (ordinate).

## DESCRIPTION OF THE VOLUME-TONICITY CHART

1. *The plasma sodium-ion concentration*, $c\text{Na}^+\text{P}$, is indicated on the ordinate with a logarithmic scale, that is, the ordinate linearly represents log $c\text{Na}^+\text{P}$. The reference interval is 136 to 146 mmol/L. The plasma sodium concentration is representative of the mean extracellular sodium concentration defined as the amount of extracellular sodium ($n\text{Na}^+$) divided by the extracellular volume ($V$):

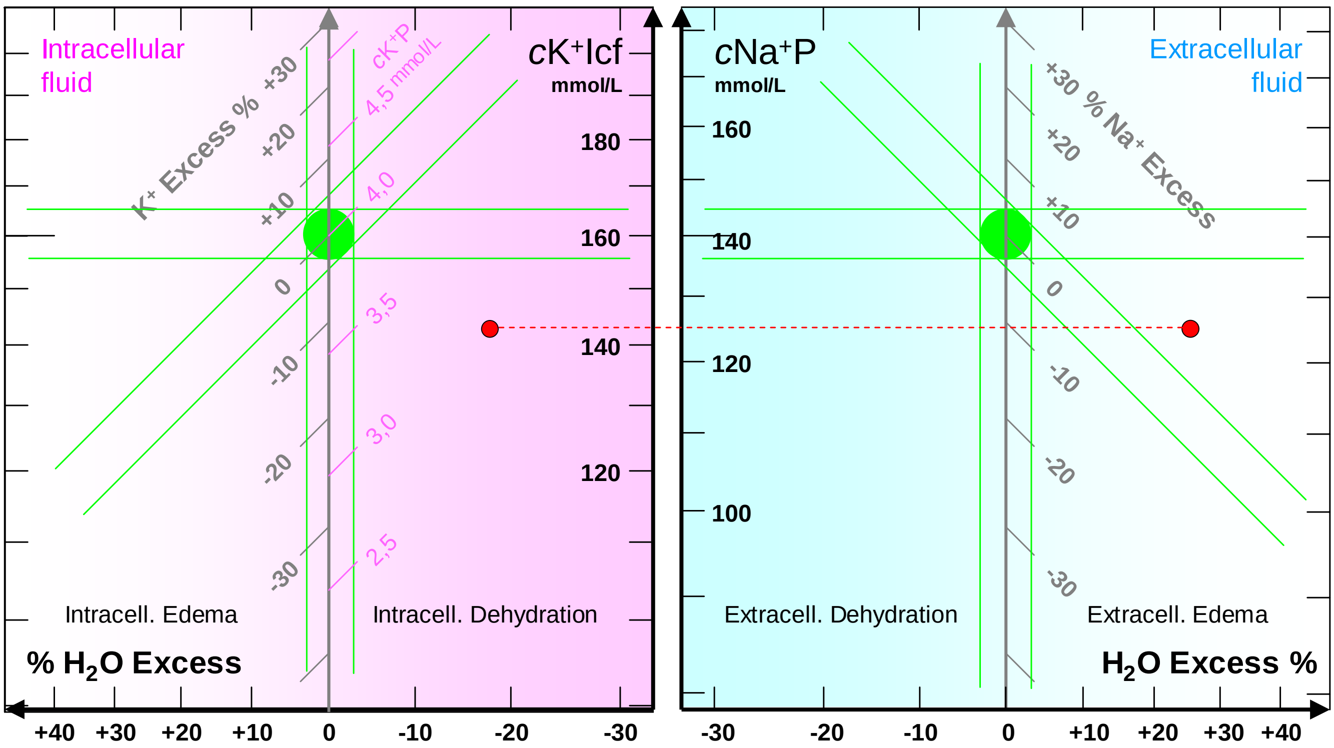
$$c\text{Na}^+ = n\text{Na}^+ / V.$$

Hence changes in the extracellular sodium concentration may be due to changes in $n\text{Na}^+$ (extracellular sodium excess or deficit) or to a change in $V$ (excess or deficit of extracellular water).

The extracellular sodium concentration is the main determinant of the extracellular tonicity. It may be useful to distinguish between osmolality, related to the concentration of total osmolutes (including glucose and carbamide) and tonicity, related to the concentration of osmolutes that pass the cell membranes with difficulty, such as $\text{Na}^+$ and $\text{K}^+$.

Any value below the reference interval indicates hyponatremia or extracellular hypotonicity, any value above the reference interval indicates hypernatremia or hypertonicity.

It should be emphasized that in cases of severe hyperlipidemia or hyperproteinemia, the sodium concentration should be corrected to a normal lipid and protein concentration to avoid a diagnosis of "spurious" hyponatremia. Measurement by direct potentiometry (ISE) with whole blood or undiluted plasma or serum automatically provides corrected values.




Legend to Figure. Volume/tonicity chart illustrating the extracellular and intracellular water-electrolyte balance. As an example the points are plotted for a patient with a hyponatremia (125 mmol/L) and hypokalemia (3.0 mmol/L). The patient has en uncompensated cardiac failure with edema and the extra-cellular overhydration was estimated to be +25 %. According to the chart the extracellular sodium excess is then +10 %. An extracellular sodium concentration of 125 mmol/L indicates an intracellular potassium concentration of 142 mmol/L (normal: 160 mmol/L). A plasma potassium concentration of 3.0 mmol/L indicates 25 % potassium depletion. This together with the intracellular potassium concentration of 142 mmol/L indicates an intracellular dehydration with a water deficit of 17 %. This illustrates a complex situation with hyponatremia in spite of a sodium retention and with extracellular edema but intracellular dehydration.

2. *Volume of the extracellular fluid* is indicated on the abscissa in terms of the relative excess or deficit, relative to the normal mean value for the patient. Mathematically the abscissa linearly represents log(*V*Ecf/*V*Ecf°), where *V*Ecf° is the standard extracellular volume for the patient. The scale is drawn to show 100 · (*V*Ecf – *V*Ecf°)/ *V*Ecf°. The total volume is almost identical with the water volume and hence the label on the abscissa is water excess or deficit, a negative value indicating a deficit. The reference interval is taken to be ±5 %.

*V*Ecf may be measured, for example as the chloride, bromide, sulphate or inulin space. *V*Ecf° may be estimated on the basis of lean body mass, age and sex of the patient. However, for routine clinical purposes the extracellular water excess or deficit is estimated clinically (edema, skin turgor, moisture of the mucous membranes, venous filling, pulse, blood pressure, diuresis, change in body mass).

Plasma protein and albumin and hematocrit are employed as indicators of the extracellular hydration. If $a$ is the relative increase in plasma protein or albumin concentration then the relative increase in plasma volume is

$$b = -\,a\,/\,(1 + a),$$

provided the amount of protein or albumin is unchanged. If $g$ is the relative increase in hematocrit (relative to the normal value $h°$) then the relative increase in plasma volume is

$b = -g / ((1 + g) \cdot (1 - h°))$,

provided the erythrocyte volume is unchanged. This shows that the hematocrit is much less sensitive as an indicator of hemodilution or hemoconcentration than the plasma protein or albumin concentration. All three parameters reflect changes in plasma volume. In most clinical situations (e.g. extracellular edema) relative changes in plasma volume are less than the relative changes in total extracellular volume.

In conclusion, estimation of the value of the abscissa is very difficult in most clinical situations, yet it is very important in order to classify the water-electrolyte disturbance correctly. Any value to the right of the reference interval indicates extracellular edema or overhydration, any point to the left indicates extracellular dehydration.

3. *The relative excess of extracellular sodium* is indicated on a vertical axis in the middle of the chart. The divisions on the scale give $(n\mathrm{Na}^+ - n\mathrm{Na}^{+\circ}) / n\mathrm{Na}^{+\circ}$, where $n\mathrm{Na}^+$ is the total amount of $Na^+$ in the extracellular space and $n\mathrm{Na}^{+\circ}$ is the normal mean value for the individual.
The reference interval is taken to be ± 5 %.

The amount of $Na^+$ in the extracellular fluid is equal to the product of the sodium concentration and the extracellular fluid volume. Hence with logarithmic scales for sodium concentration and volume of extracellular fluid the isopleths for amount of $Na^+$ are straight lines with slope -1. Therefore projections to the scale should be made at an angle of 45°.

It should be added that an excess or deficit of $Na^+$ is always associated with an excess or deficit of an accompanying anion, usually chloride although other anions (e.g. bicarbonate) may also be involved or the excess or deficit of $Na^+$ is associated with a deficit or excess of another cation.

4. *The normal area* is the circular area in the middle of the chart. The oval shape indicates a slight negative correlation between the plasma $Na^+$ concentration and the extracellular hydration.

5. *There are twelve pathological areas* starting at 12 a'clock and going clock wise: 1) sodium excess with normal extracellular volume, 2) combined extracellular $Na^+$ and $H_2O$ excess with hypernatremia, 3) isotonic overhydration, 4) hypotonic $Na^+$ excess (a paradox encountered in patients with cardiac insufficiency and edemas treated with diuretics), 5) pure $H_2O$ excess or pure dilutional hyponatremia, 6) combined $Na^+$ depletion and $H_2O$ excess or combined dilutional and depletional hyponatremia, 7) normovolumic hyponatremia, 8) dehydration with Na-depletion, 9) isotonic dehydration, 10) hypertonic dehydration with $Na^+$ depletion, 11) pure $H_2O$ deficit or concentrational hypernatremia, 12) combined $Na^+$ excess and $H_2O$ deficit.

6. *The intracellular tonicity* is mainly determined by the intracellular potassium-ion concentration as indicated on the ordinate of the "intracellular" chart to the left. The tonicity of the intra- and extracellular fluid must be the same due to the free movement of water and because no pressure difference can exist. Osmolality is defined as:

$$osmolality = -\ln aH_2O / MH_2O,$$

where $aH_2O$ is the activity of water and $MH_2O$ is the molar mass of water (0.018 kg/mol). If the water activities are equal in the two phases, then the osmolalities (tonicities) are also equal.

Therefore measurement of the extracellular $Na^+$ concentration gives an estimate of the average intracellular $K^+$ concentration, or in other words, the ordinate must be the same for the intracellular and the extracellular fluid. The intracellular $K^+$ concentration is slightly higher (≈ 15 %) than the extracellular $Na^+$ concentration because there are fewer small intracellular anions to contribute to the tonicity. The reference interval is 153 to 167 mmol/L.

7. *The relative intracellular water excess or deficit* is indicated on the abscissa on a scale analogous to the scale for extracellular water excess or deficit. Intracellular water may be

measured as the difference between total body water and extracellular water. Total body water my be determined as the $D_2O$ (heavy water) space or the antipyrin space. For practical clinical purposes estimation of an intracellular dehydration or edema is very difficult (evaluation of the turgor of the thigh muscles has been suggested) and it is usually necessary to take anamnestic information into consideration (for example water intake or loss through skin, gastrointestinal tract, or kidneys).

8. *The relative excess or deficit of intracellular potassium* is indicated on the vertical scale in the middle of the chart. Projections to the scale should be made at an angle of 45°.

For practical clinical purposes the plasma potassium concentration is used as an indicator of potassium depletion of excess. As a very rough rule of thumb the relative change in plasma potassium may be assumed to equal the relative change in amount of intracellular potassium. However, it is necessary to take into account that changes in the plasma potassium concentration may be due to a redistribution of $K^+$ between cells and extracellular fluid, for example with acute pH changes $cK^+P$ changes as $\Delta cK^+P = -6 \cdot \Delta pH$. Often anamnestic information must be taken into consideration, e.g. prolonged treatment with diuretics with or without potassium supplementation.

## APPLICATION OF THE CHART

The chart is primarily a teaching aid, illustrating the various types of water and electrolyte disturbances. For example, what are the effects of a pure $K^+$ (and phosphate) depletion of 30 %? The point in the intracellular diagram would tend to slide down vertically to the –30 mark. With an unchanged intracellular water volume (zero excess or deficit), the intracellular potassium concentration would fall to 112 mmol/L. Extracellular tonicity is then higher than the intracellular tonicity and water would pass from the intracellular to the extracellular space. The intracellular point would slide upwards along the oblique –30 % $K^+$ deficit line, while the extracellular point would slide downwards from the normal area along the oblique 0 % $Na^+$ excess line. We would reach equilibrium when the intracellular dehydration is about –12.5 % and the extracellular overhydration is about + 25 %, which would represent equal volumes. The intracellular potassium concentration would be about 127 mmol/L and the extracellular sodium concentration about 113 mmol/L. The extracellular potassium concentration would probably be about 2.8 mmol/L.

A pure $Na^+$ ($Cl^-$) depletion of 30 % would similarly result in a situation with an extracellular dehydration of –22 %, an intracellular overhydration of +11 %, an extracellular sodium concentration of about 126 mmol/L and an intracellular potassium concentration of about 143 mmol/L.

Notice that the hyponatremia is more pronounced with a pure 30 % $K^+$ depletion that with a pure 30 % $Na^+$ depletion, at first a surprising result, which illustrates the complexity of the clinical interpretation of the plasma sodium concentration.

The effects of the regulatory hormones may also be illustrated. Mineralocorticoids cause a $Na^+$ retention, extracellular edema, a moderate $K^+$ depletion, an intracellular dehydration with a moderate rise in plasma sodium concentration and intracellular potassium concentration. Antidiuretic hormone causes a retention of $H_2O$ in the extracellular as well as intracellular phase with a corresponding fall in tonicity.

In summary the two points representing the extracellular $Na^+/H_2O$ status and intracellular $K^+/H_2O$ status always have the same ordinate because the tonicity must be the same in the two fluids. The horizontal distance between the two points reflects total body water: if total body water remains constant the distance between the two points should remain (almost) constant. $Na^+/H_2O$ disturbances fall in twelve classes and each class may be further sub-classified according to the intracellular $K^+/H_2O$ status.

## REFERENCES


1. Siggaard-Andersen O. An acid-base chart for arterial blood with normal and pathophysiological reference areas. Scand J Clin Lab Invest 1968; 21: 289-92.
2. Siggaard-Andersen O. Determination and presentation of acid-base data. Contr Nephrol (Karger, Basel) 1980; 21: 128-36.