THE EFFECTS OF CHRONIC HYPOKALAEMIA, HYponatraemIA, AND ACID–BASE ALTERATIONS ON ERYTHROCYTE SODIUM TRANSPORT

M. L. LEVIN,* F. C. RECTOR, JR AND D. W. SELDIN

Department of Internal Medicine, University of Texas, Southwestern Medical School, Dallas, Texas, U.S.A.

(Received 5 January 1972)

SUMMARY

1. Erythrocyte sodium concentration and fluxes were measured in patients with acid–base disturbances, hypokalaemia and hyponatraemia. Results were similar to those obtained with normal erythrocytes exposed to artificial in vitro alterations.

2. Erythrocyte sodium content and influx varied directly with extracellular bicarbonate which appeared to influence membrane permeability.

3. Hypokalaemia increased the erythrocyte sodium content by decreasing active transport initially. When a new high erythrocyte steady-state sodium concentration was reached, active transport returned to normal but efflux and influx were increased considerably by the appearance of a large component of exchange diffusion in the hypokalaemic environment.

4. Hyponatraemia induced a decrease in sodium influx secondary to the decreased transmembrane sodium concentration gradient. A decrease in erythrocyte sodium content then ensued.

5. The results are discussed in relation to the assessment of cell membrane function in disease states.

Key words: erythrocyte sodium transport, sodium, potassium, alkalosis, hypokalaemia, hyponatraemia.

Determination of electrolyte content and membrane transport characteristics of erythrocytes has been used in evaluating the effect of certain pathologic states on the membranes of body cells in general (Welt, Sachs & McManus, 1964; Welt, Smith, Dunn, Czerwinski, Proctor, Cole, Balfe & Gitelman, 1967; Smith & Samuel, 1970; Villamil, Rettori, Simpson & Kleeman, 1972).
Uraemia, for example, has been found to impair the active transport of sodium and potassium across the erythrocyte membrane and thus to elevate intracellular sodium concentration in 20–25% of cases (Welt et al., 1964). These abnormalities are not specific for uraemia since similar changes are found in the erythrocytes of patients with a variety of terminal illnesses (Welt et al., 1967).

It has been suggested that measurement of erythrocyte sodium may be a simple means of screening patients for defects in membrane transport. An elevated erythrocyte sodium content, however, may result from impaired active transport out of the cell as well as from an accelerated inward leak resulting from altered permeability. To distinguish between these possibilities it is necessary to measure either the influx or efflux of sodium, or both. Additionally, the conditions (e.g. uraemia, terminal illness, myocardial infarction) which may alter the transport and permeability properties of cell membranes are frequently associated with electrolyte and acid–base disturbances. These alterations in internal milieu might influence erythrocyte sodium concentration independent of any intrinsic abnormalities of the membrane.

The present study was performed to examine the effects of acute and chronic alterations in extracellular acid–base, sodium, and potassium content on erythrocyte sodium concentration and transport. Acute changes were induced by modifying the composition of the media in which normal erythrocytes were incubated. Chronic changes were evaluated by studying erythrocytes from patients with either chronic hypokalaemia or hyponatraemia.

**MATERIALS AND METHODS**

Human erythrocyte sodium concentration and fluxes of radioactive sodium were measured by a modification of the method of Tosteson & Hoffman (1960) as previously reported (Levin, Rector & Seldin, 1968). Cells used to investigate effects of alterations *in vitro* of pH, bicarbonate and external sodium concentration were obtained from healthy volunteers. Control fluxes were always determined using the indigenous plasma of the erythrocytes. Erythrocytes were also incubated in an artificial medium in which the composition of a given constituent could be varied. The basic medium contained 118 mM-NaCl, 25 mM-NaHCO₃, 1.65 mM-NaH₂PO₄, 9.35 mM-Na₂HPO₄, 5 mM-KCl. All fluxes were measured at 37°C after 2 h of preincubation in O₂ + CO₂ (95:5). Erythrocyte sodium concentration was expressed as mEq/l of cells.

The influence of acid–base composition on sodium flux was investigated in two ways. First, the pH of the medium was varied by replacing various amounts of NaHCO₃ with equimolar quantities of NaCl whilst maintaining Pco₂ at 40 mmHg. Secondly, the concentration of NaHCO₃ was varied by substitution with NaCl, but the pH was kept constant by changing Pco₂ proportionally.

The effect of hypo-osmotic hyponatraemic medium was examined by measuring erythrocyte sodium content and sodium influx in solutions with various NaCl concentrations. Other studies were performed in which osmolality was maintained constant by substituting equimolar amounts of choline chloride for NaCl.

The effect of chronic changes in sodium and potassium concentration were studied in blood from patients with either chronic, stable hyponatraemia or hypokalaemia. Fluxes were measured both in the patients’ own plasma and in the basic incubation medium. In three studies the effluxes were also measured in the patients’ own plasma after correcting the plasma potassium
concentration to normal by addition of appropriate quantities of KCl. In these experiments the cells were labelled with $^{22}\text{Na}$ by preincubation in plasma with an uncorrected potassium concentration.

All chemical and radioactive determinations were performed as described by Levin et al. (1968).

**RESULTS**

The effect of acid-base changes *in vitro* on erythrocyte sodium is summarized in Table 1. The mean erythrocyte sodium in the normal acid-base state ($P_{\text{CO}_2}$ 40 mmHg, HCO$_3^-$ 26 mEq/l, pH 7.4) was 9.7 (SD 0.5) mEq/l. The erythrocyte sodium concentration varied directly with bicarbonate concentration, falling to 7.8 mEq/l in the absence of bicarbonate and rising to 10.7 mEq/l at a bicarbonate concentration of 42 mEq/l. This effect was related to bicarbonate concentration and not pH, since identical erythrocyte sodium concentrations were obtained when pH was permitted to vary or was maintained constant by changing the $P_{\text{CO}_2}$.

The effects of acid-base changes on sodium influx are shown in Fig. 1. The ratio, sodium influx in artificial medium to influx in indigenous plasma, is plotted against external bicarbonate concentration. Since flux values vary from individual to individual, use of the ratio allows correction for these differences. Influx varied directly with bicarbonate concentration whether or not pH changed. Whether there is also a small additional effect of pH *per se* cannot be determined from these studies.

The effect on erythrocyte sodium concentration of a relatively acute (2 h) exposure to artificial media of various potassium concentrations can be seen in Fig. 2. The results and methods used were reported by Levin et al. (1968). Erythrocyte sodium concentration increased as the extracellular potassium concentration decreased below 3 mEq/l. External potassium had no effect above 4 mEq/l.

Clinical data, including the erythrocyte sodium content of seven hypokalaemic patients are presented in Table 2. The erythrocyte sodium concentrations of all but two of these patients were well above the value for normal subjects in our laboratory (8.8 ± 1.2 mEq/l of cells) (Levin et al., 1968). The relation between external potassium and the patients’ cell sodium
FIG. 1. Effect of bicarbonate and pH on erythrocyte sodium influx. The vertical axis represents the ratio of sodium influx measured in the various artificial media to that measured in the cells' indigenous plasma on the same day. The patients' plasma all had normal pH and bicarbonate values. O, Values at pH 7.4, $P_{CO_2}$ as indicated in parentheses, $n=2$, except at 26 mEq/l, where $n=7$; ▲, values at $P_{CO_2}$ 40 mmHg, pH as indicated in parentheses, $n=2$, except at 0 mEq/l, $n=7$. The bar indicates 1 SD.

FIG. 2. Effect of external potassium concentration on erythrocyte sodium concentration. O, Controls, $n=6$; ●, patients; the bar indicates 1 SD.
Erythrocyte sodium flux in electrolyte disorders

content is also shown in Fig. 2. Most of the patients' values for erythrocyte sodium were greater than those of normal erythrocytes incubated in artificial media of similar potassium concentration. Since the normal erythrocytes were exposed to a hypokalaemic environment for only 2 h, they may not have achieved a true steady state, and their sodium concentration may not have reached ultimate steady-state levels. The patients' erythrocytes, however, had been exposed to hypokalaemia for much longer periods in vivo, and had presumably achieved complete equilibrium with their surroundings.

Table 2. Erythrocyte sodium concentration and clinical data of hypokalaemic patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical diagnosis</th>
<th>Plasma concentration (mEq/l)</th>
<th>Whole blood pH during incubation</th>
<th>Erythrocyte sodium concentration (mEq/l of cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Potassium</td>
<td>Sodium</td>
<td>Bicarbonate during incubation</td>
</tr>
<tr>
<td>1 Cirrhosis, diuretic therapy</td>
<td>2.2</td>
<td>140</td>
<td>31</td>
<td>7.48</td>
</tr>
<tr>
<td>2 Chronic catharsis</td>
<td>2.5</td>
<td>142</td>
<td>23</td>
<td>7.31</td>
</tr>
<tr>
<td>3 ? Juxtaglomerular cell hyperplasia</td>
<td>2.4</td>
<td>141</td>
<td>26</td>
<td>7.41</td>
</tr>
<tr>
<td>4 Alcoholism and diarrhoea</td>
<td>1.6</td>
<td>145</td>
<td>35</td>
<td>7.52</td>
</tr>
<tr>
<td>5 Thiazide therapy of cyclic oedema</td>
<td>2.6</td>
<td>143</td>
<td>27</td>
<td>7.42</td>
</tr>
<tr>
<td>6 Diarrhoea and vomiting</td>
<td>1.8</td>
<td>140</td>
<td>22</td>
<td>—</td>
</tr>
<tr>
<td>7A Chronic vomiting</td>
<td>2.4</td>
<td>145</td>
<td>35</td>
<td>7.50</td>
</tr>
<tr>
<td>B 1 week post correction</td>
<td>4.6</td>
<td>142</td>
<td>25</td>
<td>—</td>
</tr>
</tbody>
</table>

Sodium fluxes were determined in the erythrocytes of patients 1–5, and the results are presented in Table 3. Because of the volume of blood necessary, all studies were not carried out in each patient. Included are results obtained from normokalaemic volunteers (Levin et al., 1968). With the exception of patient 2, influxes determined in indigenous plasma were greater than in normals and were greater than in the patients' erythrocytes incubated in artificial medium. This reversal of the usual medium/plasma influx ratio of 1.08±0.04 was never observed in control normokalaemic studies.

Both total and ouabain-inhibitible effluxes were also elevated above control values, but the ouabain-inhibitible efflux rate-constant was depressed in two of the three patients studied. However, when these measurements were made in normokalaemic media (either in the artificial medium or plasma with added potassium), the already high efflux values underwent a further increase. Under these conditions the rate constant increased to normal values or above (patient 2) and the erythrocyte sodium concentrations always fell.

Since patients with hypokalaemia frequently have concomitant acid–base disturbances, fluxes measured in the patients' plasma were corrected for abnormalities in bicarbonate
TABLE 3. Sodium flux data for hypokalaemic patients. Values are expressed as mean±SD with the number of measurements in parentheses.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Erythrocyte sodium (mEq/l of cells)</th>
<th>Sodium influx (mEq h⁻¹ l of cells⁻¹)</th>
<th>Total sodium efflux (mEq h⁻¹ l of cells⁻¹)</th>
<th>Ouabain-inhibitible sodium efflux (mEq h⁻¹ l of cells⁻¹)</th>
<th>Ouabain-inhibitible sodium efflux rate constant (h⁻¹)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Plasma</td>
<td>Medium</td>
<td>Plasma</td>
<td>Medium</td>
</tr>
<tr>
<td>Controls</td>
<td>8.8±1.2 (22)</td>
<td>3.26±0.38</td>
<td>3.52±0.35 (7)</td>
<td>3.31±0.33 (9)</td>
<td>3.57±0.30 (7)</td>
</tr>
<tr>
<td>1</td>
<td>16.3 Corrected for pH, HCO₃⁻</td>
<td>4.76</td>
<td>3.97</td>
<td>4.32</td>
<td>5.03</td>
</tr>
<tr>
<td>2</td>
<td>9.1 Corrected for pH, HCO₃⁻</td>
<td>3.49</td>
<td>3.83</td>
<td>3.52</td>
<td>4.31</td>
</tr>
<tr>
<td>3</td>
<td>12.1 Corrected for pH, HCO₃⁻</td>
<td>5.05</td>
<td>3.97</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>16.5 Corrected for pH, HCO₃⁻</td>
<td>8.11</td>
<td>9.08</td>
<td>9.28</td>
<td>4.64</td>
</tr>
<tr>
<td>5</td>
<td>12.0 Corrected for pH, HCO₃⁻</td>
<td>4.35</td>
<td>3.83</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Ouabain-inhibitible efflux/erythrocyte sodium content.
concentration. Using the data in Fig. 1, all measured influxes were corrected to the value expected at a plasma bicarbonate concentration of 26 mEq/l. With this correction, results obtained in the erythrocytes of patient 2 became similar to those of the other patients (Table 3). Since influx and total efflux must be equal in the steady state, similar bicarbonate corrections were applied to efflux values when necessary. Additionally, changes in erythrocyte sodium concentration associated with alterations in bicarbonate concentration (Table 1) would also influence active efflux (ouabain-inhibitible sodium efflux). Therefore, a similar bicarbonate correction was applied to the ouabain-inhibitible sodium effluxes in Table 3.
### Table 4. Erythrocyte sodium concentrations and clinical data of hyponatraemic patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Plasma sodium (mEq/l)</th>
<th>Plasma osmolality (mosm/l)</th>
<th>Plasma potassium (mEq/l)</th>
<th>Plasma bicarbonate during incubation (mEq/l)</th>
<th>Plasma pH during incubation</th>
<th>Erythrocyte sodium concentration (mEq/l of cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Congestive heart failure (off digitalis), mild azotaemia</td>
<td>128</td>
<td>287</td>
<td>5·1</td>
<td>19·4</td>
<td>7·27</td>
<td>6·4</td>
</tr>
<tr>
<td>2</td>
<td>Cirrhosis</td>
<td>130</td>
<td>263</td>
<td>4·2</td>
<td>26</td>
<td>7·40</td>
<td>7·6</td>
</tr>
<tr>
<td>3</td>
<td>Diarrhoea, salt depletion</td>
<td>126</td>
<td>255</td>
<td>4·1</td>
<td>25</td>
<td>7·41</td>
<td>5·8</td>
</tr>
<tr>
<td>4</td>
<td>Congestive heart failure (off digitalis)</td>
<td>122</td>
<td>256</td>
<td>3·5</td>
<td>25</td>
<td>7·39</td>
<td>8·9</td>
</tr>
</tbody>
</table>

### Table 5. Sodium flux data for hyponatraemic patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Erythrocyte sodium concn. (mEq/l of cells)</th>
<th>Sodium influx (mEq h⁻¹ of cells⁻¹)</th>
<th>Total sodium efflux (mEq h⁻¹ 1 of cells⁻¹)</th>
<th>Ouabain-inhibitable sodium efflux (mEq h⁻¹ 1 of cells⁻¹)</th>
<th>Ouabain-inhibitable efflux rate constant (h⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Plasma</td>
<td>Medium</td>
<td>Plasma</td>
<td>Medium</td>
<td>Plasmal Medium</td>
</tr>
<tr>
<td>1</td>
<td>6·4</td>
<td>7·6</td>
<td>2·72</td>
<td>3·84</td>
<td>2·00</td>
</tr>
<tr>
<td></td>
<td>Corrected for pH, HCO₃⁻</td>
<td></td>
<td>3·24</td>
<td>3·84</td>
<td>2·39</td>
</tr>
<tr>
<td>2</td>
<td>7·6</td>
<td>9·6</td>
<td>2·90</td>
<td>3·37</td>
<td>1·66</td>
</tr>
<tr>
<td>3</td>
<td>5·8</td>
<td>7·5</td>
<td>2·98</td>
<td>3·48</td>
<td>1·94</td>
</tr>
<tr>
<td>4</td>
<td>8·9</td>
<td>11·0</td>
<td>3·35</td>
<td>4·64</td>
<td>1·69</td>
</tr>
</tbody>
</table>

M. L. Levin, F. C. Rector, Jr and D. W. Seldin
Correction of all flux values for bicarbonate alterations makes it possible to determine the effects of hypokalaemia.

The effect of extracellular potassium on sodium influx in normal cells is illustrated in Fig. 3. The ratio of sodium influx obtained in hypokalaemic media to influx obtained in the same

![Graph showing the effect of extracellular sodium concentration on erythrocyte sodium influx.](image)

**FIG. 5.** Effect of external sodium concentration on erythrocyte sodium influx. For details see the text and Fig. 1. O, Iso-osmotic; △, non-isosmotic. The bar indicates 1 SEM.

![Graph showing sodium influxes in patients compared with controls.](image)

**FIG. 6.** Sodium influxes in patients compared with controls. For details see the text and Fig. 1. ○, Patients; the shaded area indicates the limits of values in Fig. 5.

cells in normal plasma is plotted against external potassium concentration. The data have been reported by Levin et al. (1968). Sodium influx increases when the potassium concentration is less than 3 mEq/l. The bicarbonate-corrected influx data represent the ratio of influx in the
patients’ hypokalaemic plasma to influx when the cells were incubated in normokalaemic medium (Fig. 3). These points cluster about the curve formed by hypokalaemic flux data obtained in vitro.

Finally, fluxes were determined in four hyponatraemic individuals whose clinical data and flux determinations are presented in Tables 4 and 5. Absolute flux values and cell sodium concentrations are lower in this group than in control fluxes measured in plasma containing normal amounts of sodium, and are in agreement with reports of the effects of alterations in extracellular sodium in vitro (Harris & Maizels, 1951; Solomon, 1952; Glynn, 1956). However, previous results were obtained under conditions of constant osmotic strength by addition of non-permeant solutes to the various hyponatraemic media. Although iso-osmotic hyponatraemia occurs under certain clinical conditions, hypo-osmotic hyponatraemia is more common. Therefore, the effect of osmotic strength upon erythrocyte sodium concentrations and sodium influx was examined.

Results are presented in Figs. 4 and 5 for non-iso-osmotic and iso-osmotic studies. The osmolarity (verified by osmometer) was achieved by addition of appropriate amounts of choline chloride to keep it iso-osmotic with the medium containing 165 mEq of sodium. Both erythrocyte sodium content and sodium influx vary directly with external sodium concentration, and the osmolarity has no special role. The ratio of sodium content of patients’ erythrocytes incubated in hyponatraemic plasma to the content of patients’ erythrocytes incubated in the 165 mEq sodium medium is plotted against the plasma sodium concentration (Fig. 4). The erythrocyte sodium concentration increased on exposure to a higher sodium concentration. The relationship between the external sodium concentration and the sodium influx ratio (flux in hyponatraemic plasma: flux in artificial medium) of patient’s erythrocytes is shown in Fig. 6. Sodium influx into the patients’ erythrocytes varied directly with extracellular sodium concentration.

DISCUSSION

It has been suggested that the measurement of erythrocyte sodium concentration be used as a rough index of the functional integrity of cell membranes in general. The current studies demonstrate that, in addition to altered membrane function in certain pathologic states such as intrinsic erythrocyte disease (Tosteson, Carlsen & Dunham, 1955), uraemia (Welt et al., 1964, 1967) and impending death (Welt et al., 1967), chronic alterations of the internal milieu influence sodium transport across the erythrocyte membrane and thus change the steady-state intracellular sodium concentration. Hypokalaemia and high bicarbonate concentrations each independently tend to raise erythrocyte sodium content, while hyponatraemia and low plasma bicarbonate concentrations tend to lower it.

The direct relationship between extracellular bicarbonate and both erythrocyte sodium concentrations (Table 1) and sodium influx (Fig. 1) leads to the conclusion that the prime effect of bicarbonate ion is to increase cellular permeability to sodium. Others have come to similar conclusions while examining a much wider, non-physiological range of bicarbonate concentrations (Wieth & Funder, 1965; Funder & Wieth, 1967).

This membrane action of bicarbonate offers a possible explanation for the mechanism by which bicarbonate infusion results in clinical correction of hyperkalaemia. By increasing sodium entry into cells, bicarbonate increases intracellular sodium content which in turn
Erythrocyte sodium flux in electrolyte disorders

activates heightened sodium–potassium linked active transport. Increased rates of potassium influx result with a secondary decrease in extracellular potassium.

The effects of potassium differ from those of bicarbonate. In previous studies, acute (2 h) exposure to hypokalaemic environment caused the erythrocyte sodium concentration to vary inversely with the extracellular potassium concentration (Levin et al., 1968). Sodium influx increased in a hypokalaemic environment, but this increase could be completely inhibited by ouabain. Total sodium efflux and ouabain-inhibitable efflux were both at normal values in the previous study, but the ouabain-inhibitable efflux rate constant was depressed in hypokalaemic media. This constellation of results led to the conclusion that lowering external potassium below 3 mEq/l decreased the active sodium efflux and produced a large component of exchange diffusion which probably proceeded through the same molecular pathway as active transport. Several others have published similar results and conclusions (Garrahan & Glynn, 1967a, b; Villamil & Kleeman, 1969; Sachs, 1970). Because of the initial decrease in active efflux in hypokalaemia, erythrocyte sodium content rises, resulting in stimulation of active efflux back toward normal values and a new steady state if some potassium is present. Increased exchange diffusion still occurs, however, and accounts for the high influxes.

The elevated erythrocyte sodium concentrations and influx values in these chronically hypokalaemic patients substantiate the previous observations in vitro. In addition, patient 7 illustrated that clinical correction of hypokalaemia results in correction of the high erythrocyte sodium concentration. The studies on patients support the hypothesis regarding exchange diffusion since the high effluxes were still accompanied by a diminished ouabain-inhibitable efflux rate constant. The discrepancy between the normal efflux rates in the acute (2 h) hypokalaemia studies and the elevated rates found in chronically hypokalaemic cells probably results from the fact that the erythrocyte sodium concentration in the acute studies had not yet reached equilibrium values. Therefore, active transport was not proceeding optimally (even for a hypokalaemic environment) and could not attain the values observed in the chronic state.

If the ouabain-inhibitable effluxes were composed entirely of active transport, the rate constant would be expected to be normal at these erythrocyte sodium concentrations since the sodium $K_m$ for active transport is about 20 mEq/l of cells (Post, Merritt, Kinsolving & Albright, 1960). The high measured fluxes result, then, from the combination of a normal rate of active transport plus exchange diffusion. The rate constant for exchange diffusion is much lower than that of active transport and is responsible for the overall decrease in the ouabain-inhibitable rate constant. Exposure to a normokalaemic environment results in increased active transport. Thus, effluxes and the rate constant both increase, and the erythrocytes lose sodium (Table 3, patients 1, 2 and 4).

The effect of hyponatraemia differs from either mechanism described above. In the studies in vitro, potassium and acid–base parameters were kept constant, and sodium influx decreased as the external sodium concentration was decreased (Fig. 5). Erythrocyte sodium concentration also decreased since the initial active efflux remained at a normal value. The efflux decreased to a new steady state only because the initial imbalance of fluxes caused erythrocyte sodium concentrations to decrease. The results in the hyponatraemic patients are in agreement with the those obtained in vitro. Confirmatory evidence that the low effluxes were obtained in response to the lowered erythrocyte sodium concentrations can be found in the normal ouabain-inhibitable rate constant in hyponatraemic erythrocytes. The rate constant remained stable
<table>
<thead>
<tr>
<th>Electrolyte disorder</th>
<th>Effect on erythrocyte sodium concn.</th>
<th>Primary effect(s) on membrane function</th>
<th>Effect on sodium influx</th>
<th>Effect on total sodium efflux</th>
<th>Effect on active sodium efflux</th>
<th>Effect on ouabain-inhibitable efflux constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>High bicarbonate</td>
<td>Increased</td>
<td>Increased permeability to sodium</td>
<td>Increased</td>
<td>Increased</td>
<td>Increased</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Low bicarbonate</td>
<td>Decreased</td>
<td>Decreased permeability to sodium</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Hypokalaemia</td>
<td>Increased</td>
<td>Initial decrease in active sodium efflux; increased exchange diffusion</td>
<td>Increased (normal leak plus increased exchange diffusion)</td>
<td>Increased (normal efflux in steady state plus increased exchange diffusion)</td>
<td>Initial decrease. Return to normal with new steady state</td>
<td>Decreased (combination of normal active transport constant and low exchange diffusion constant)</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>Unchanged</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Hyponatraemia</td>
<td>Decreased</td>
<td>Decreased trans-membrane sodium gradient resulting in decreased influx</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Hypermotraemia</td>
<td>Increased</td>
<td>Increased trans-membrane sodium gradient resulting in increased influx</td>
<td>Increased</td>
<td>Increased</td>
<td>Increased</td>
<td>Unchanged</td>
</tr>
</tbody>
</table>
when the erythrocytes were exposed to higher sodium concentrations and gained sodium (Table 5). The various effects of the acid–base and electrolyte disorders studied are summarized in Table 6.

Whether the results and conclusions of the current study can be extended to other cells is impossible to ascertain. The erythrocyte is quite simple compared with other cells and generalizations may be completely erroneous. However, since the erythrocyte has been used quite extensively in the investigation of disordered membrane function, this information should prove helpful. Nonetheless, alterations in acid–base and electrolyte parameters must be given careful consideration before conclusions can be drawn regarding changes in membrane function in disease states.

ACKNOWLEDGMENT

This work was supported by U.S. Public Health Service Grant 1 PO1 HE11662 and U.S. Public Health Service Grant 5 TO1 HE05469.

REFERENCES