RESPIRATORY ACIDOSIS AND HYPOCHLOREMIC ALKALOSIS: ORIGINS, DIFFERENTIATION, EFFECTS AND THERAPY

The combination of an increased serum total CO_2 content and lowered levels of serum chloride may result from a primary retention of CO_2 as in cardiopulmonary disease with a secondary lowering of the chloride level, referred to as respiratory acidosis, or it may represent one of the two forms of metabolic alkalosis, i.e., the hypochloremic type stemming from losses of extracellular chloride rather than the hypernatremic type resulting from increases in serum sodium concentrations above normal.

The origins of respiratory acidosis may lie in cardiac or pulmonary disease which interferes with transfers of CO_2 across the respiratory epithelium, but can also be produced by inhalation of high concentrations of CO_2 as in asphyxia. The hypochloremic form of metabolic alkalosis can result from losses of chloride via gastric lavage, in vomitus, or in other gastrointestinal secretions, may stem from excessive urinary excretion of chloride as in patients receiving mercurial diuretics, or it may reflect, as Heppel[1] first suggested, depletion of cellular potassium. Insofar as the last category is concerned, Darrow and others[2-6] have presented evidence that as potassium moves out of cells, sodium and hydrogen move in. This results in an intracellular acidosis and an extracellular alkalosis. Under these circumstances the lowering of chloride has been interpreted as originating from dilution of chloride space, from extracellular transfers or segregation of chloride, or most likely from losses in urine. The importance of continued renal losses of potassium in the production of deficiencies of this ion have been amply established,[7-10] even though in the unstressed animal potassium conservation can be marked during periods of deprivation.[11]

In his original report Darrow and others[2] cited unpublished studies which indicated that low potassium diets unaccompanied by extra intake of sodium and chloride did not produce the marked lowering of muscle potassium, the rises in cell sodium, nor the hypochloremic alkalosis. Since then other workers have shown that significant degrees of potassium depletion, i.e., 5 per cent of the body stores, may be induced without production of either hypochloremia or alkalosis.[12,13] Abstraction of chloride, sodium loading, or interference with sodium excretion following ACTH did. Data are too limited at present to assert that hypochloremic alkalosis associated with potassium losses always represents chloride deficiency or necessitates sodium loading.

The similar and the distinguishing biochemical features of these two entities are shown in figure 1. Comparable degrees of hypochloremia and increased serum total CO_2 content may be present in both, though extremely low chloride levels, i.e., below 70 mEq/L. under these circumstances usually indicate primary chloride losses in gastrointestinal secretions. The serum *p*H which is lowered in respiratory acidosis and increased in hypochloremic alkalosis readily distinguishes between the two and, together with the serum total CO_2 content, permits calculation or estimation of the PCO_2, i.e., the partial pressure of CO_2 in serum.[14] In respiratory acidosis this value is definitely above the usual range in health (35-48 mm. Hg) and is normal or slightly increased in hypochloremic alkalosis.

Clinical signs associated with respiratory acidosis include evidences of a chronic cardiopulmonary disease, if that is its etiology, with dyspnea and cyanosis and loss of consciousness with oxygen therapy, while metabolic alkalosis may result in tetany, weakness, mental confusion and a variable degree of hypoventilation. In respiratory acidosis the urine becomes more acid. In hypochloremic metabolic alkalosis the urine is usually alkaline but may be acid, especially in potassium deficiency, presumably because this ion is not available for competition with hydrogen in exchange for reabsorbed sodium.[14]

The chief importance of these two conditions lies in the fact that they are useful indicators of profound disturbances in body fluids which require corrective therapy. In respiratory acidosis this is limited to measures designed to improve ventilatory exchange and minimize production of H_2CO_3 by inhibition of carbonic anhydrase by agents such as Diamox.[R] In hypochloremic alkalosis interruption of etiologic factors such as vomiting, ACTH or steroid therapy and replacement of chloride deficits or of potassium deficits usually suffices. HCl and NH_4Cl have been used for this purpose but involve unnecessary risks and may prove fatal in patients thought to have hypochloremic alkalosis but really suffering from respiratory acidosis.

It is to be noted that the rise in the serum total CO_2 content and the degree of hypochloremia can be identical in those two conditions. Measurements of the *p*H and an estimate of the PCO_2 as derived from nomograms[14] serve to differentiate them.

In respiratory acidosis the retention of CO_2 increases PCO_2 and hence the H_2CO_3 and H^+ of the body fluids.

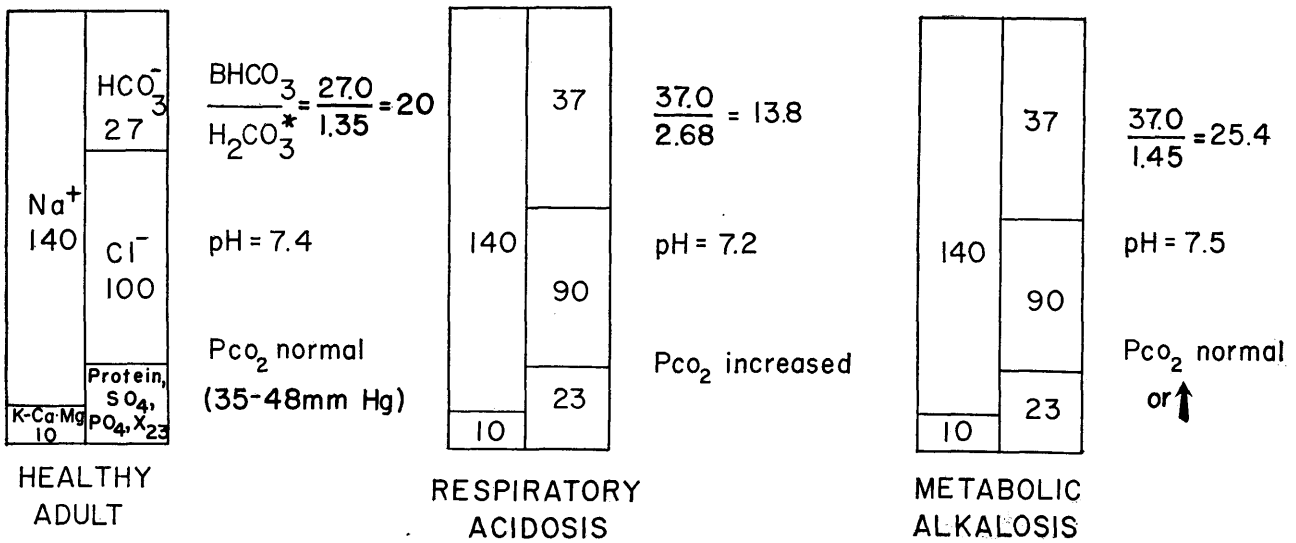

FIG. 1. Cation-anion pattern in healthy adults and in patients with respiratory acidosis or hypochloremic (metabolic) alkalosis.
By accepted and convenient convention $H_2CO_3 = K_0 Pco_2$ · K_0 = solubility coefficient of carbon dioxide = 0.03mM per L (plasma) per mm (mercury) Pco_2; t = 38°C. Strictly speaking, $K_0 Pco_3 = CO_2$ (unhydrated) + H_2CO_3 (hydrated or true carbonic acid).

$$Pco_2 + H_2O \overset{\text{carbonic anhydrase}}{\leftrightarrows} H_2CO_3 + H_2O \leftrightarrows HCO_3^- + H_3O^+$$

The secondary lowering of serum chloride values permits an increase in the serum bicarbonate associated with cations which exerts a common ion effect upon the bicarbonate derived from H_2CO_3, driving the above reaction to the left. This is not sufficient, however, to restore *p*H values to normal and an acidosis persists.

In hypochloremic (metabolic) alkalosis the decrease in chloride permits an expansion in the bicarbonate associated with cations and, by the common ion effect, diminishes the ionization of H_2CO_3. The *p*H is therefore raised. The secondary hypopnea which may increase the Pco_2 slightly above normal usually does not cancel the change in *p*H.

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