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## Renal Tubular Acidosis

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## Renal Tubular Acidosis

Stanley Goldfarb, MD, FACP

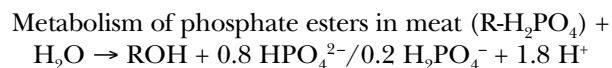
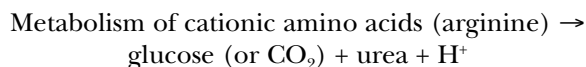
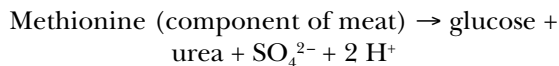
### INTRODUCTION

The kidney normally acts to regulate serum bicarbonate ( $\text{HCO}_3^-$ ), or the fixed, nonvolatile component of the acid-base status, at a level between 24 and 27 mEq/L.<sup>1</sup> Renal regulation of the acid-base balance involves both the reabsorption of  $\text{HCO}_3^-$  and the excretion of hydrogen ions ( $\text{H}^+$ ). In rare instances, defects in the renal mechanisms responsible for this regulatory system arise despite relatively normal rates of glomerular filtration; the clinical sequelae that result from these defects are termed *renal tubular acidosis* (RTA). This review presents an overview of the role of the kidney in regulating acid-base balance and discusses various forms of RTA with an emphasis on the underlying pathophysiology.

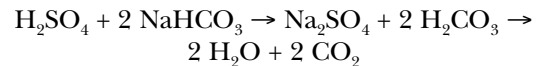
### RENAL REGULATION OF ACID-BASE BALANCE

The kidney normally must carry out 2 functions vis-à-vis acid-base metabolism. First, it must accomplish the reabsorption of filtered  $\text{HCO}_3^-$ , which occurs in the proximal convoluted tubule. Second, it must accomplish the excretion of fixed (nonvolatile) acids through the titration of urinary buffers and the excretion of ammonium with secreted protons, which takes place primarily in the distal nephron.<sup>2,3</sup> Reabsorption in the proximal tubule leads to the preservation of existing  $\text{HCO}_3^-$ , while the distal tubular process leads to the creation of new  $\text{HCO}_3^-$  to replace  $\text{HCO}_3^-$  lost in buffering the acid load of the normal diet and the incomplete metabolism of glucose and fat.

$\text{HCO}_3^-$  is used in the metabolism of components of the diet into end products that generate acid.<sup>4</sup> The following reactions illustrate this phenomenon:



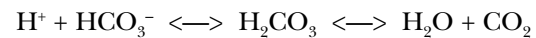
Thereafter, the metabolism of these acids consumes  $\text{HCO}_3^-$ :



Thus, any circulating  $\text{HCO}_3^-$  must be preserved, and because the normal diet generates  $\text{H}^+$  at a rate of approximately 1 mEq/kg of body weight daily, 50 to 100 mEq of  $\text{HCO}_3^-$  must be created daily to maintain acid-base balance in a typical person.<sup>1</sup>

### PROXIMAL TUBULE BICARBONATE REABSORPTION

Approximately 80% to 90% of filtered  $\text{HCO}_3^-$  is preserved through reabsorption in the proximal tubule. The mechanisms for proximal reabsorption involve  $\text{H}^+$  secretion at the luminal membrane of the proximal tubule via a protein termed the  $\text{Na}^+/\text{H}^+$  exchanger and secondary  $\text{HCO}_3^-$  transport at the basolateral membrane via a protein that couples sodium and  $\text{HCO}_3^-$  cotransport.<sup>5</sup> The sodium gradient across the luminal membrane drives sodium into the cell in exchange for  $\text{H}^+$  (Figure 1, site 1).<sup>6</sup> This gradient is created by the action of  $\text{Na}^+, \text{K}^+$ -ATPase located on the basolateral or blood side of the epithelial cell. As  $\text{H}^+$  are secreted in exchange for sodium ions delivered via glomerular filtration, the  $\text{H}^+$  combine with filtered  $\text{HCO}_3^-$  ions to produce the following reaction:



The carbon dioxide formed diffuses into the cell (Figure 1, site 2), where it combines with water to form carbonic acid ( $\text{H}_2\text{CO}_3$ ). An equilibrium is formed between  $\text{HCO}_3^-$  and  $\text{H}^+$  as illustrated in the equation. A key feature of this complex system is the presence of carbonic anhydrase, an enzyme located both at the luminal membrane and within the tubule cell.<sup>6</sup> Carbonic anhydrase allows the rapid dissociation of carbonic acid into water and carbon dioxide in the lumen and also the rapid formation of carbonic acid from carbon dioxide and water within the cell. The  $\text{HCO}_3^-$  that is formed enters the circulation via the  $\text{Na}^+/\text{HCO}_3^-$  cotransporter (Figure 1, site 3). Through the integrated set of transport systems and enzymatic reactions, the filtered  $\text{HCO}_3^-$  is returned to the body.<sup>7</sup> In addition,