On the Mechanism of HCO_3^- Permeation across the Peritubular Cell Membrane of Proximal Tubular Kidney Cells

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A major transport function of mammalian proximal tubules is the absorption of bicarbonate. We know today that HCO_3^- is taken up into the cells through secretion of H^+ into the tubular lumen (mostly in electroneutral exchange for Na^+ ions). H^+ ions react in the tubular lumen with HCO_3^- to form CO_2 and H_2O. The CO_2 diffuses into the cells and combines with the remaining OH^- ions to HCO_3^-. These reactions are catalyzed by carbonic anhydrase (CAH). The mechanism of HCO_3^- exit across the peritubular cell membrane, however, is not yet established. Previous electrophysiological experiments (1) had suggested that the peritubular cell membrane is highly permeable to HCO_3^- buffer, which was inferred from a strong dependence of the peritubular cell membrane potential (Pd) on the peritubular HCO_3^- concentration. Since partial HCO_3^- substitutions are necessarily associated with changes in CO_2 and/or pH, we have now studied the relations between individual buffer components and Pd systematically and have further investigated the nature of the inhibitory effect of CAH inhibitors on the bicarbonate dependence of the Pd. The cell membrane potential was measured in proximal tubular cells of rat kidney in vivo and the effect of rapid changes of the peritubular fluid composition on the Pd was recorded during perfusion of the peritubular blood capillaries with different artificial solutions. At constant pH the instantaneous ($\leq$1s) Pd response was 22.2±3.4 mV (n=4) per tenfold change in HCO_3^- concentration; at constant HCO_3^- the Pd response was 5.4±2.2 mV (n=5) per pH unit. In addition a similar pH dependence was observed in HCO_3^- and CO_2 free perfusates. These observations support the previously reached interpretation that OH^- (or H^+ in opposite direction) is the permeating ion species. The greater Pd change in HCO_3^- solutions is most likely due to the continuing supply of OH^- ions from HCO_3^- in the unstirred layer at the membrane surface which is catalyzed by the membrane bound CAH (2). In agreement with this view the Pd response declines after inhibition of the CAH with acetazolamide. The latter appears to be a specific CAH effect. Secondary effects resulting from a concomitant rise of the cell Pd or of the cytoplasmic pH can be excluded. This conclusion is also supported by the inhibition kinetics of acetazolamide.

1. Frömter, E. and Sato, K. (1976) In: Kasbekar, D.K., Sachs, G., Rehm, W.S. (eds) Gastric hydrogen ion secretion. Dekker New York, pp 382 - 403.
2. Wistrand, P.J., and Kinne, R. (1977) Pflügers Arch. 370, 121 - 126.