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Countercurrent Multiplication in the Kidney: Is it Real?

A fundamental function of the mammalian kidney, when blood plasma osmolality is too high, is to produce a urine that is more concentrated than blood plasma and thereby reduce blood plasma osmolality to a normal level. Urine is concentrated in the renal medulla by means of a concentration gradient that promotes osmotic water withdrawal from the kidney's collecting ducts. It has become widely accepted that the osmolality gradient along the cortico-medullary axis of the mammalian outer medulla is generated and sustained by a process of countercurrent multiplication: active NaCl absorption from thick ascending limbs is coupled with a counter-flow configuration of the descending and ascending limbs of the loops of Henle to generate the axial gradient. However, aspects of anatomic structure (e.g., the physical separation of the descending limbs of short loops of Henle from contiguous ascending limbs), recent physiologic experiments (e.g., those which suggest that the thin descending limbs of short loops of Henle have a low water permeability), and mathematical modeling studies (e.g., those which predict that water-permeable descending limbs of short loops are not required for the generation of an axial osmolality gradient) suggest that countercurrent multiplication may be an incomplete, or perhaps even erroneous, explanation. We propose an alternative explanation for the axial osmolality gradient: we regard the thick limbs as NaCl sources for the surrounding interstitium, and we hypothesize that the increasing axial osmolality gradient along the outer medulla is primarily sustained by an increasing ratio, as a function of medullary depth, of NaCl absorption from thick ascending limbs to water absorption from thin descending limbs of long loops of Henle and from collecting ducts.