

**An active pathway for serotonin synthesis by renal proximal tubules.**

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Serotonin (5HT) has significant effects on renal metabolism and glomerular function and is a potent renal vasoconstrictor. In this study we describe and localize a highly active biosynthetic pathway for serotonin in the kidney. Rat kidneys were dissected into cortical and medullary fractions; in some experiments the cortex was also separated into subfractions enriched with glomeruli or proximal tubules. Serotonin and tryptophan hydroxylase (TyOH) were measured by radioenzymatic techniques. (table; see text) Renal denervation did not alter tryptophan hydroxylase activity. In kidneys from human cadaveric donors, cortical tryptophan hydroxylase ( $4.13 \pm 0.68$  nM/30 min/g) exceeded that in the medulla ( $1.96 \pm 0.86$  nM/30 min/g). Aromatic L-amino acid decarboxylase, the remaining enzyme for serotonin synthesis, is present in both rat renal cortex and medulla; however, we found 15-fold greater decarboxylase activity in proximal tubular ( $2070$  nM/30 min/g) as compared to glomerular ( $131$  nM/30 min/g) subfractions. We were able to demonstrate that under physiological conditions, **free urine serotonin reflects actual biosynthesis by the kidney**. Thus, although serotonin stores retained by the kidney appear small and relatively localized to the medulla, the enzymatic activity for the synthesis of serotonin in the kidney is comparable to that in the brain, with the complete pathway localized to renal cortical proximal tubules. These data suggest that further studies of renal serotonin metabolism may contribute to our understanding of renal function in health and disease.