

**Contrasting Inhibitory Effects of Probenecid on Tubular
Excretion of P-Aminohippurate and on the Active
Reabsorption of Urea in the Dogfish***

Roy P. Forster and Fredrik Berglund
Dartmouth College and Boston University

Urea has in common with uric acid the feature of being excreted against a concentration gradient by the renal tubules of certain vertebrates while being actively reabsorbed by the renal tubules of others. It is of interest to know what characteristics are shared by these cellular processes which transfer identical compounds in opposite directions.

Probenecid (p-dipropylsulfamyl-benzoic acid), at concentrations which do not affect either glomerular filtration rates or cellular oxidative processes, depresses tubular transport of uric acid in mammals, whether this transfer is in the direction from blood to urine as in the Dalmatian dog or in the reverse direction as in man and various other mammals (Beyer et al, '51). Similarly Probenecid blocks specifically the tubular excretion of urea in bullfrogs where the transfer process is an active one and characterized by a maximum rate (T_m) at high plasma concentrations (Forster, '54). Inasmuch as urea is actively reabsorbed by dogfish and other Elasmobranchii (Smith, '36 and Kempton, '53), where its high concentration in body fluids plays an important role in osmotic regulation, it was of interest to test whether Probenecid acts similarly to depress the tubular transport of urea in those forms where net movement is in the opposite direction to that in bullfrogs.

Doses of Probenecid sufficient to depress the tubular secretion of PAH and PAAH by more than 50 per cent were ineffective in altering the rate of urea reabsorption expressed at mM absorbed per unit volume of glomerular filtrate. The reabsorption of urea expressed in absolute amounts (mM/kg/day) showed a slight fall when there was a concomitant reduction in glomerular filtration rate after Probenecid. That the reabsorption of urea varied with the glomerular filtration rate is not surprising in view of the fact that 81 to 94 percent of the filtered urea was reabsorbed. When no change in glomerular filtration rate occurred after Probenecid administration, the rate of urea reabsorbed was unaffected, measured either as mM/day or as mM excreted per ml of glomerular filtrate. Simultaneously, the secretion of PAH plus PAAH was depressed by Probenecid to 30 per cent of control values.

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