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DECREASED BODY CLEARANCE OF DIFLUNISAL IN RENAL INSUFFICIENCY—AN ALTERNATIVE EXPLANATION

Verbeeck, Tjandramaga, Mullie, Verbesselt, Verberckmoes & de Schepper (1979) recently reported a striking decrease in the total body clearance of diflunisal, a salicylic acid derivative that is eliminated almost entirely by formation of ester and ether glucuronides (Tocco, Breault, Zacchei, Steelman & Perrier, 1975), in patients with renal insufficiency. Verbeeck *et al.* (1979) suggested that this was due to slowed biotransformation of diflunisal but they also recognized that other studies have shown no apparent effect of renal dysfunction on the glucuronidation of several drugs.

The glucuronides of diflunisal have a molecular weight above 400 and it is therefore reasonable to assume that they are excreted not only in the urine but also in the bile (Smith, 1971). Renal dysfunction would cause a larger fraction of these conjugates to be excreted in the bile, complete renal failure will probably result in the total excretion of diflunisal metabolites by the biliary route.

Hydrolysis of diflunisal glucuronides in the intestinal tract permits at least partial reabsorption of diflunisal. Such recycling results in an apparent increase in the biologic half-life of a drug and may cause overestimation of the apparent volume of distribution and underestimation of the body

clearance. Thus, the very important findings of Verbeeck *et al.* (1979) need not reflect decreased glucuronidation of diflunisal in patients with renal insufficiency.

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