

## **The role of transport in chemical nephrotoxicity.**

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Various physiologic factors play a role in determining the extent of chemical-induced nephrotoxicity. One such factor relates to the transport systems that exist in the kidney. Several examples can be given of organic substances that are nephrotoxic only after being transported into renal tubular cells. Some of the cephalosporin antibiotics have been shown to produce proximal tubular necrosis after transport into those cells. Blockade of transport by competitors eliminates or reduces the nephrotoxic response. Citrinin, a secondary product of fungal metabolism, also produces proximal tubular necrosis, but only after transport into proximal tubular cells. Both the cephalosporins and citrinin utilize the organic anion transporter for entry into the cells, a transporter present in adult animals of all species and probably important physiologically for moving metabolic substrates into cells. Various glutathione conjugates (e.g., S-(1,2-dichlorovinyl) glutathione [DCVG]) also are transported into proximal tubular cells with a resulting nephrotoxicity. DCVG utilizes the sodium-dependent transport process that moves glutathione into proximal tubular cells, a process that is inhibited by probenecid. Finally, certain heavy metals also are transported into renal tubular cells. For example, mercuric ion enters proximal cells both from the luminal and peritubular sides and sulfhydryl compounds modify the transport. Movement of mercury from the peritubular side of the cell may be modified by certain organic anions. The characteristics of these mechanisms are less well understood than the mechanisms for the organic compounds.

