

Renal Injury Due To Environmental Toxins, Drugs, and Contrast Agents

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The kidneys are susceptible to toxic or ischemic injury for several reasons. Thus, it is not surprising that an impressive list of exogenous drugs and chemicals can cause clinical acute renal failure (ARF) [1]. On the contrary, the contribution of environmental toxins to ARF is rather limited. In this chapter, some of the most common drugs and exogenous toxins encountered by the nephrologist in clinical practice are discussed in detail.

The clinical expression of the nephrotoxicity of drugs and chemicals is highly variable and is influenced by several factors. Among these is the direct toxic effect of drugs and chemicals on a particular type of nephron cell, the pharmacologic activity of some substances and their effects on renal function, the high metabolic activity (*ie*, vulnerability) of particular segments of the nephron, the multiple transport systems, which can result in intracellular accumulation of drugs and chemicals, and the high intratubule concentrations with possible precipitation and crystallization of particular drugs.

CHAPTER

11

General Nephrotoxic Factors

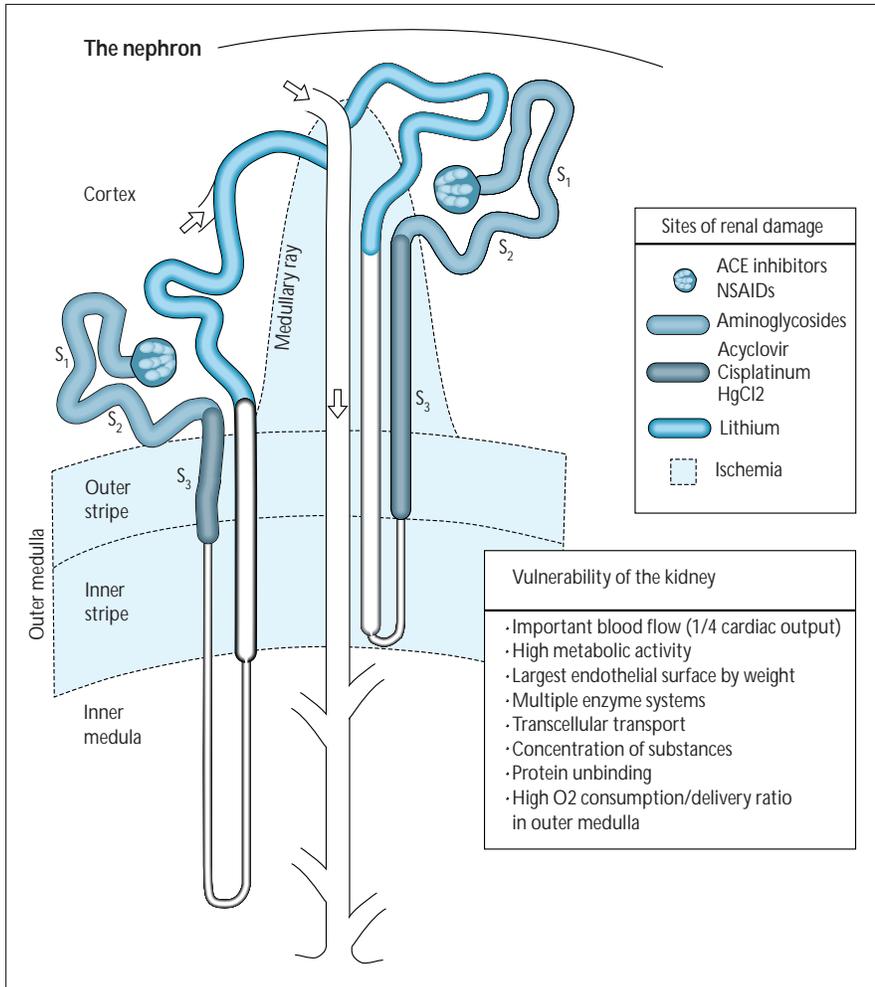


FIGURE 11-1

Sites of renal damage, including factors that contribute to the kidney's susceptibility to damage. ACE—angiotensin-converting enzyme; NSAID—nonsteroidal anti-inflammatory drugs; HgCl₂—mercuric chloride.

DRUGS AND CHEMICALS ASSOCIATED WITH ACUTE RENAL FAILURE

Mechanisms

M1 Reduction in renal perfusion through alteration of intrarenal hemodynamics

M2 Direct tubular toxicity

M3 Heme pigment–induced toxicity (rhabdomyolysis)

M4 Intratubular obstruction by precipitation of the agents or its metabolites or byproducts

M5 Allergic interstitial nephritis

M6 Hemolytic-uremic syndrome

M1	M2	M3	M4	M5*	M6	Drugs
✓	✓				✓	Cyclosporine, tacrolimus
✓	✓					Amphotericin B, radiocontrast agents
✓				✓		Nonsteroidal anti-inflammatory drugs
✓						Angiotensin-converting enzyme inhibitors, interleukin-2†
✓	✓		✓			Methotrexate§
	✓					Aminoglycosides, cisplatin, foscarnet, heavy metals, intravenous immunoglobulin¶, organic solvents, pentamidine
		✓			✓	Cocaine
		✓				Ethanol, lovastatin**
			✓	✓		Sulfonamides
			✓			Acyclovir, Indinavir, chemotherapeutic agents, ethylene glycol***
				✓		Allopurinol, cephalosporins, cimetidine, ciprofloxacin, furosemide, penicillins, phenytoin, rifampin, thiazide diuretics
					✓	Conjugated estrogens, mitomycin, quinine

* Many other drugs in addition to the ones listed can cause renal failure by this mechanism.

† Interleukin-2 produces a capillary leak syndrome with volume contractions.

§ Uric acid crystals form as a result of tumor lysis.

¶ The mechanism of this agent is unclear but may be due to additives.

** Acute renal failure is most likely to occur when lovastatin is given in combination with cyclosporine.

*** Ethylene glycol–induced toxicity can cause calcium oxalate crystals.

FIGURE 11-2

Drugs and chemicals associated with acute renal failure. (Adapted from Thadhani, *et al.* [2].)