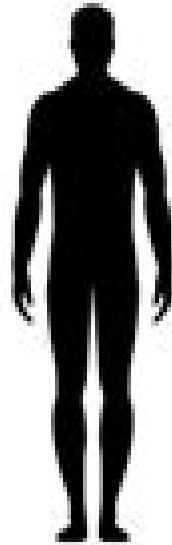
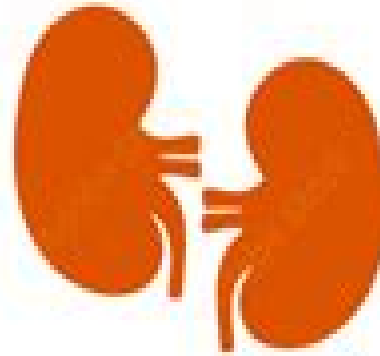


## Patient - related



## Kidney - related



## Drug-related



Old age ( $\geq 60$ -65 years)

Female sex

Altered pharmacogenetics  
- genetic variations in hepatic CYP450 system and kidney transporters

Comorbidities: cirrhosis, diabetes, hypertension, heart failure, sepsis, metabolic perturbations (hypokalemia, hypomagnesemia, hypercalcemia, urine pH disturbances), active cancers

Underlying kidney insufficiency with  $GFR < 60 \text{ mL/min/1.73m}^2$

True or effective volume depletion (kidney hypoperfusion)

Biotransformation of drugs to nephrotoxic metabolites and reactive oxygen species

High metabolic rate of tubular cells within a hypoxic environment

Proximal tubular uptake of drugs: apical via endocytosis or pinocytosis with drug accumulation or basolateral drug transport via hOATs or hOCTs

Use of high doses and prolonged dosing periods

Potent direct nephrotoxic drug effects

Exposure to multiple nephrotoxic agents

Pharmacokinetic and / or pharmacodynamic interactions between drugs that increase the free fraction, interfere with biotransformation or impair the excretion of drugs and their metabolites

# Renal Disposition And Nephrotoxicity Of Xenobiotics

**Lei Shi**



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