



### Drug distribution

Headward fluid shift / increased natriuresis and diuresis, decreased thirst, and increased evaporation through the lungs and the skin  
 Fluid redistribution (from plasma to extracellular volume; from extracellular to intracellular volume)  
 Decreased plasma volume  
 Reduced volume of drug distribution  
 Higher drug plasma concentrations  
 Altered plasma protein binding  
 Endothelial dysfunction



### Drug absorption and metabolism

Delayed gastric emptying: increased drug degradation  
 Accelerated intestinal transit: reduced drug absorption  
 Fluid shift/tissue oedema: reduced drug absorption  
 Changes in the expression of GI enzymes and transporters: modification of drug absorption  
 Changes in gut microbiota  
 Food interactions  
 Changes in hepatic blood flow velocity and first-pass metabolism



### Drug elimination

Changes in hepatic metabolism  
 Decreased urinary excretion

**Figure 1**