Acute renal failure (ARF) is a syndrome characterized by an abrupt and reversible kidney dysfunction. The spectrum of inciting factors is broad: from ischemic and nephrotoxic agents to a variety of endotoxemic states and syndrome of multiple organ failure. The pathophysiology of ARF includes vascular, glomerular and tubular dysfunction which, depending on the actual offending stimulus, vary in the severity and time of appearance. Hemodynamic compromise prevails in cases when noxious stimuli are related to hypotension and septicemia, leading to renal hypoperfusion with secondary tubular changes (described in Chapter 13). Nephrotoxic offenders usually result in primary tubular epithelial cell injury, though endothelial cell dysfunction can also occur, leading to the eventual cessation of glomerular filtration. This latter effect is a consequence of the combined action of tubular obstruction and activation of tubuloglomerular feedback mechanism. In the following pages we shall review the existing concepts on the phenomenology of ARF including the mechanisms of decreased renal perfusion and failure of glomerular filtration, vasoconstriction of renal arterioles, how formed elements gain access to the renal parenchyma, and what the sequelae are of such an invasion by primed leukocytes.
14.2 Acute Renal Failure

Vasoactive Hormones

**FIGURE 14-1**
Pathophysiology of ischemic and toxic acute renal failure (ARF). The severe reduction in glomerular filtration rate (GFR) associated with established ischemic or toxic renal injury is due to the combined effects of alterations in intrarenal hemodynamics and tubular injury. The hemodynamic alterations associated with ARF include afferent arteriolar constriction and mesangial contraction, both of which directly reduce GFR. Tubular injury reduces GFR by causing tubular obstruction and by allowing backleak of glomerular filtrate. Abnormalities in tubular reabsorption of solute may contribute to intrarenal vasoconstriction by activating the tubuloglomerular (TG) feedback system. GPF—glomerular plasmaflow; P—glomerular pressure; Kf—glomerular ultrafiltration coefficient.

**FIGURE 14-2**
Vasoactive hormones that may be responsible for the hemodynamic abnormalities in acute tubule necrosis (ATN). A persistent reduction in renal blood flow has been demonstrated in both animal models of acute renal failure (ARF) and in humans with ATN. The mechanisms responsible for the hemodynamic alterations in ARF involve an increase in the intrarenal activity of vasoconstrictors and a deficiency of important vasodilators. A number of vasoconstrictors have been implicated in the reduction in renal blood flow in ARF. The importance of individual vasoconstrictor hormones in ARF probably varies to some extent with the cause of the renal injury. A deficiency of vasodilators such as endothelium-derived nitric oxide (EDNO) and/or prostaglandin I2 (PGI2) also contributes to the renal hypoperfusion associated with ARF. This imbalance in intrarenal vasoactive hormones favoring vasoconstriction causes persistent intrarenal hypoxia, thereby exacerbating tubular injury and protracting the course of ARF.
Pathophysiology of Ischemic Acute Renal Failure

**FIGURE 14-3**
The mesangium regulates single-nephron glomerular filtration rate (SN GFR) by altering the glomerular ultrafiltration coefficient ($K_f$). This schematic diagram demonstrates the anatomic relationship between glomerular capillary loops and the mesangium. The mesangium is surrounded by capillary loops. Mesangial cells (M) are specialized pericytes with contractile elements that can respond to vasoactive hormones. Contraction of mesangium can close and prevent perfusion of anatomically associated glomerular capillary loops. This decreases the surface area available for glomerular filtration and reduces the glomerular ultrafiltration coefficient.

**FIGURE 14-4**
A. The topography of juxtaglomerular apparatus (JGA), including macula densa cells (MD), extraglomerular mesangial cells (EM C), and afferent arteriolar smooth muscle cells (SM C). Insets schematically illustrate, B, the structure of JGA; C, the flow of information within the JGA; and D, the putative messengers of tubuloglomerular feedback responses. AA—afferent arteriole; PPC—peripolar cell; EA—efferent arteriole; GMC—glomerular mesangial cells. (Modified from Goligorsky et al. [1]; with permission.)