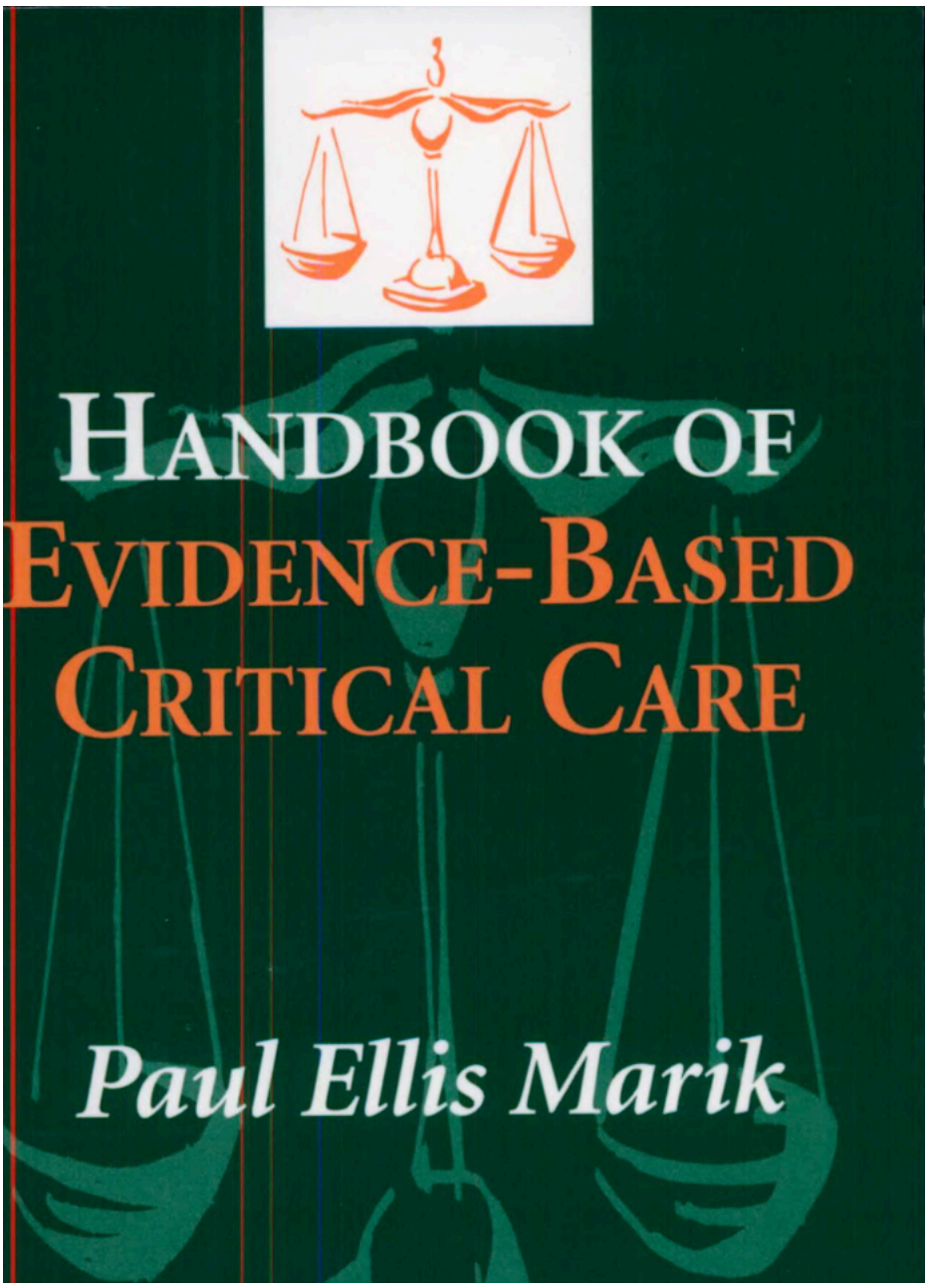
HANDBOOK OF
EVIDENCE-BASED
CRITICAL CARE
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A reduction in intravascular volume results in a fall in stroke volume, which is initially compensated for by an increase in heart rate, thereby maintaining cardiac output. However, with further volume depletion, cardiac output and then blood pressure fall. This is associated with a reduction in organ perfusion. At the organ level, local autoregulatory mechanisms come into play in an attempt to maintain tissue perfusion. A reduction in renal perfusion normally results in dilatation of the glomerular afferent arteriole and constriction of the glomerular efferent arteriole so that glomerular capillary hydrostatic pressure and glomerular filtration rate (GFR) remain constant. However, a decrease in *renal perfusion pressure* below the autoregulatory range (*mean arterial pressure* $< 80\,mm\,Hg$) leads to an abrupt fall in GFR and urine output (oliguria). In the elderly and in patients with diseases affecting the integrity of the afferent arterioles, lesser degrees of hypotension may cause a decline in renal function and oliguria. While primary renal diseases and urinary tract obstruction may lead to oliguria, intravascular volume depletion with renal hypoperfusion is the most common cause of oliguria in clinical practice. The management of oliguria due to intravascular volume depletion is ***aggressive***

Fluid resuscitation

The effective circulating volume refers to that part of the intravascular volume that is in the arterial tree (normally about 700 mL in a 70-kg man) and is effectively perfusing the tissues.[1] Physiologically, the effective circulating volume is the *pressure perfusing the arterial baroreceptors* in the carotid sinus and glomerular afferent arterioles, since it is changes in pressure (or stretch) rather than volume or flow that is sensed. The effective circulating volume usually varies directly with the ECF volume. However, in some settings the effective circulating volume may be independent of the ECF volume, the plasma volume, or even cardiac output. In congestive heart failure, the effective circulating volume is reduced because a primary decrease in cardiac output lowers the pressure at the baroreceptors. This decline in pressure and flow induces compensatory fluid retention by the kidney, leading to expansion of the ECF. The net result is effective intravascular volume depletion in association with increases in both the plasma and total ECF volumes. The increase in volume in this setting is appropriate because the associated rise in intracardiac filling pressure can, by increasing cardiac stretch, improve cardiac contractility and raise cardiac output and systemic blood pressure toward normal (Frank-Starling mechanism). Sodium and water retention is therefore an appropriate compensation in that it restores tissue perfusion, even though it also augments the degree of edema. In patients with cirrhosis, the

ECF volume is expanded, the plasma volume is increased, and the cardiac output is increased because of systemic vasodilation. Yet, in these patients the effective intravascular volume is reduced

due to decreased systemic perfusion pressure and intense renal vasoconstriction.

Diuresis with loop diuretics in patients with normal or reduced effective intravascular volume is invariably associated with a fall in intravascular volume, a fall in plasma volume, a fall in GFR, and a rise in serum urea nitrogen (BUN). The fall in GFR has been correlated with the fall in intravascular volume. Contraction of the intravascular volume and fall in GFR may occur in the absence of a fall in cardiac output. Volume depletion is associated with a greater rise in the BUN than in the plasma creatinine due to increased passive reabsorption of urea that follows the hypovolemia-induced increase in sodium and water resorption in the kidney. An increasing BUN/creatinine ratio in a patient receiving a diuretic is a reliable sign of intravascular volume depletion and should prompt the immediate discontinuation of these agents.

Contrary to popular belief, the GFR falls (rather than rises) with loop diuretics. In the mammalian kidney, there is close coordination between the processes of glomerular filtration and tubular reabsorption. Coordination between the glomerulus and tubule is mediated by a system of tubuloglomerular feedback that operates within the juxtaglomerular apparatus of each nephron. Microperfusion experiments have demonstrated that an increase in flow rate of tubule fluid through the loop of Henle following the use of a loop diuretic is followed by a reduction in single-nephron GFR. This has been shown to be mediated via feedback control by the macula densa, which is the flow-dependent distal-sensing site. When the tubular glomerular feedback pathway is interrupted with a loop diuretic, there is an attenuation of the pressure-induced afferent arteriolar dilatation with impairment in blood flow autoregulation. In patients with extracellular volume depletion, this effect is exaggerated with a dramatic fall in GFR.