CLINICAL SIGNS OF VOLUME EXPANSION

- Edema
- Pulmonary crackles
- Ascites
- Jugular venous distention
- Hepatojugular reflux
- Hypertension

FIGURE 2-22
Clinical signs of volume expansion.

CLINICAL SIGNS OF VOLUME DEPLETION

- Orthostatic decrease in blood pressure and increase in pulse rate
- Decreased pulse volume
- Decreased venous pressure
- Loss of axillary sweating
- Decreased skin turgor
- Dry mucous membranes

FIGURE 2-23
Clinical signs of volume depletion.

LABORATORY SIGNS OF VOLUME DEPLETION OR EXPANSION

- Hypernatremia
- Hyponatremia
- Acid-base disturbances
- Abnormal plasma potassium
- Decrease in glomerular filtration rate
- Elevated blood urea nitrogen–creatinine ratio
- Low functional excretion of sodium (FE_{Na})

FIGURE 2-24
Note that laboratory test results for volume expansion and contraction are similar. Serum sodium (Na) concentration may be increased or decreased in either volume expansion or contraction, depending on the cause and intake of free water (*see* Chapter 1). Acid-base disturbances, such as metabolic alkalosis, and hypokalemia are common in both conditions. The similarity of the laboratory test results of volume depletion and expansion results from the fact that the "effective" arterial volume is depleted in both states despite dramatic expansion of the extracellular fluid volume in one.

Unifying Hypothesis of Renal Sodium Excretion

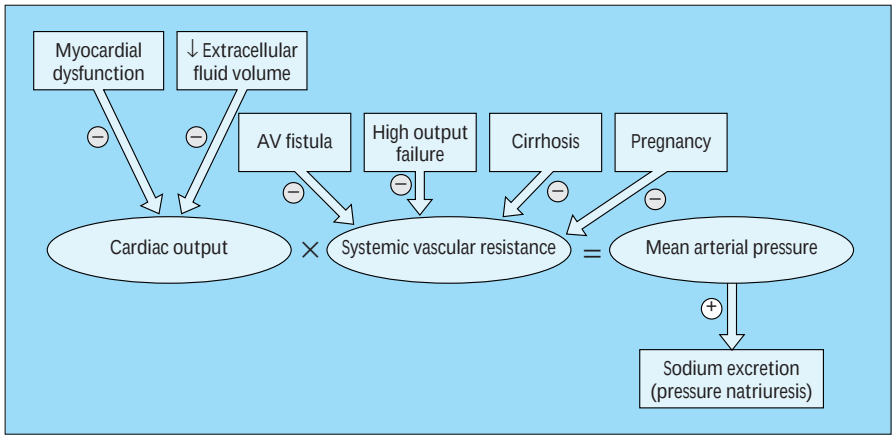

FIGURE 2-25
Summary of mechanisms of sodium (Na) retention in volume contraction and in depletion of the "effective" arterial volume. In secondary Na retention, Na retention results primarily from a reduction in mean arterial pressure (MAP). Some disorders decrease cardiac output, such as congestive heart failure owing to myocardial dysfunction; others decrease systemic vascular resistance, such as high-output cardiac failure, atriovenous fistulas, and cirrhosis. Because MAP is the product of systemic vascular resistance and cardiac output, all causes lead to the same result. As shown in Figures 2-3 and 2-4, small changes in MAP lead to large changes in urinary Na excretion. Although edematous disorders usually are characterized as resulting from contraction of the effective arterial volume, the MAP, as a determinant of renal perfusion pressure, may be the crucial variable (Figs. 2-26 and 2-28 provide supportive data). The mechanisms of edema in nephrotic syndrome are more complex and are discussed in Figures 2-36 to 2-39.

Mechanisms of Extracellular Fluid Volume Expansion in Congestive Heart Failure

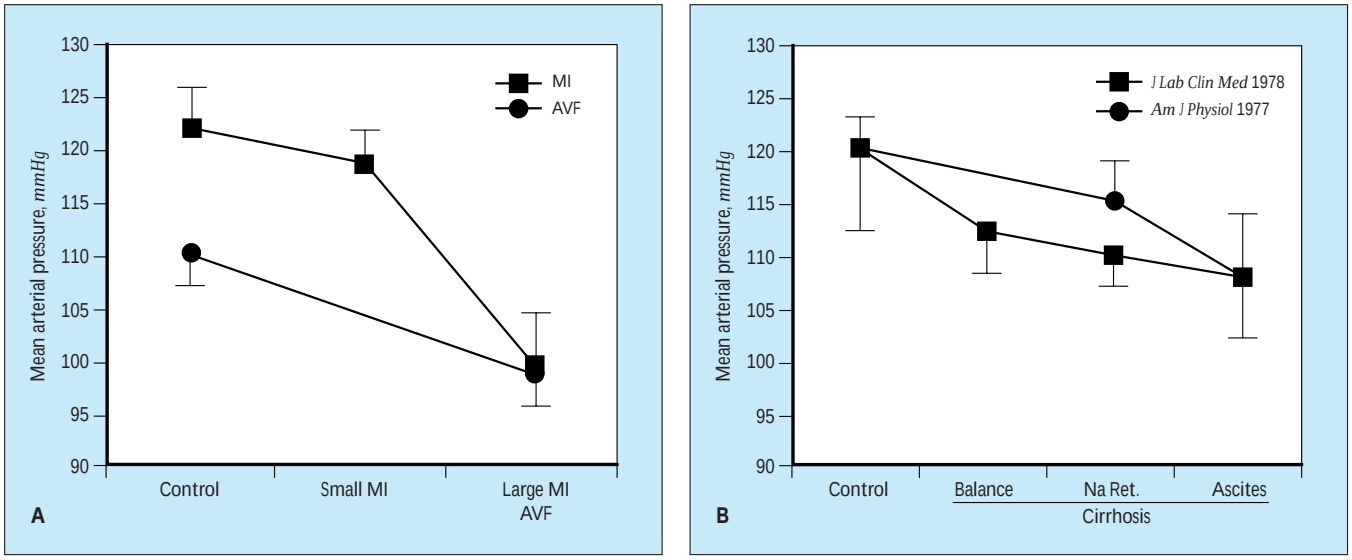

FIGURE 2-26

Role of renal perfusion pressure in sodium (Na) retention. **A**, Results from studies in rats that had undergone myocardial infarction (MI) or placement of an arteriovenous fistula (AVF) [54]. Rats with small and large MIs were identified. Both small and large MIs induced significant Na retention when challenged with Na loads. Renal Na retention occurred in the setting of mild hypotension. AVF also induced significant Na retention, which was associated with a decrease in mean arterial pressure (MAP) [55,56]. Figure 2-3 has shown that Na excretion decreases greatly for each mm Hg decrease in MAP. **B**, Results of two groups of experiments performed by Levy and Allotey [57,58] in which experimental cirrhosis was induced in dogs by sporadic feeding with dimethylnitrosamine. Three cirrhotic stages were identified based on the pattern of Na retention. In the first, dietary Na intake was balanced by Na excretion. In the second, renal Na retention began, but still without evidence of ascites or edema. In the last, ascites were detected. Because Na was retained before the appearance of ascites, "primary" renal Na retention was inferred. An alternative interpretation of these data suggests that the modest decrease in MAP is responsible for Na retention in this model. Note that in both heart failure and cirrhosis, Na retention correlates with a decline in MAP.

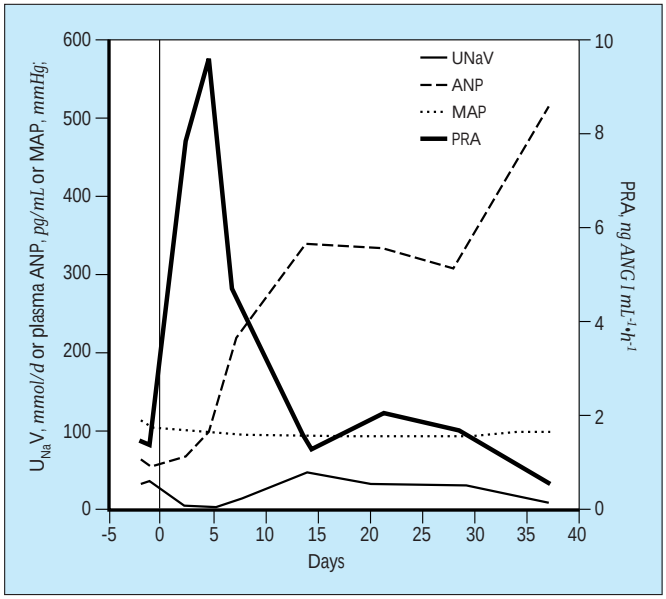

FIGURE 2-27

Mechanism of sodium (Na) retention in high-output cardiac failure. Effects of high-output heart failure induced in dogs by arteriovenous (AV) fistula [59]. After induction of an AV fistula (day 0), plasma renin activity (PRA; thick solid line) increased greatly, correlating temporally with a reduction in urinary Na excretion ($U_{Na}V$; thin solid line). During this period, mean arterial pressure (MAP; dotted line) declined modestly. After day 5, the plasma atrial natriuretic peptide concentration (ANP; dashed line) increased because of volume expansion, returning urinary Na excretion to baseline levels. Thus, Na retention, mediated in part by the renin-angiotensin-aldosterone system, led to volume expansion. The volume expansion suppressed the renin-angiotensin-aldosterone system and stimulated ANP secretion, thereby returning Na excretion to normal. These experiments suggest that ANP secretion plays an important role in maintaining Na excretion in compensated congestive heart failure. This effect of ANP has been confirmed directly in experiments using anti-ANP antibodies [60]. AI—angiotensin I.

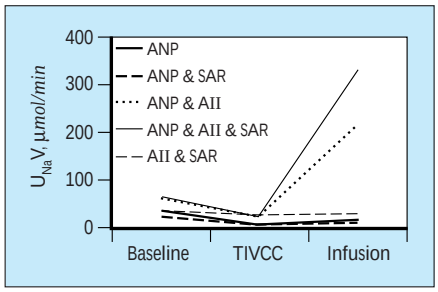

FIGURE 2-28

Mechanism of renal resistance to atrial natriuretic peptide (ANP) in experimental low-output heart failure. Low-output heart failure was induced in dogs by thoracic inferior vena caval constriction (TIVCC), which also led to a significant decrease in renal perfusion pressure (RPP) (from 127 to 120 mm Hg). ANP infusion into dogs with TIVCC did not increase urinary sodium (Na) excretion ($U_{Na}V$, ANP group). In contrast, when the RPP was returned to baseline by infusing angiotensin II (AII), urinary Na excretion increased greatly (ANP + AII). To exclude a direct effect of AII on urinary Na excretion, intrarenal saralasin (SAR) was infused to block renal AII receptors. SAR did not significantly affect the natriuresis induced by ANP plus AII. An independent effect of SAR on urinary Na excretion was excluded by infusing ANP plus SAR and AII plus SAR. These treatments were without effect. These results were interpreted as indicating that the *predominant* cause of resistance to ANP in dogs with low-output congestive heart failure is a reduction in RPP. (*Data from* Redfield and coworkers [61].)

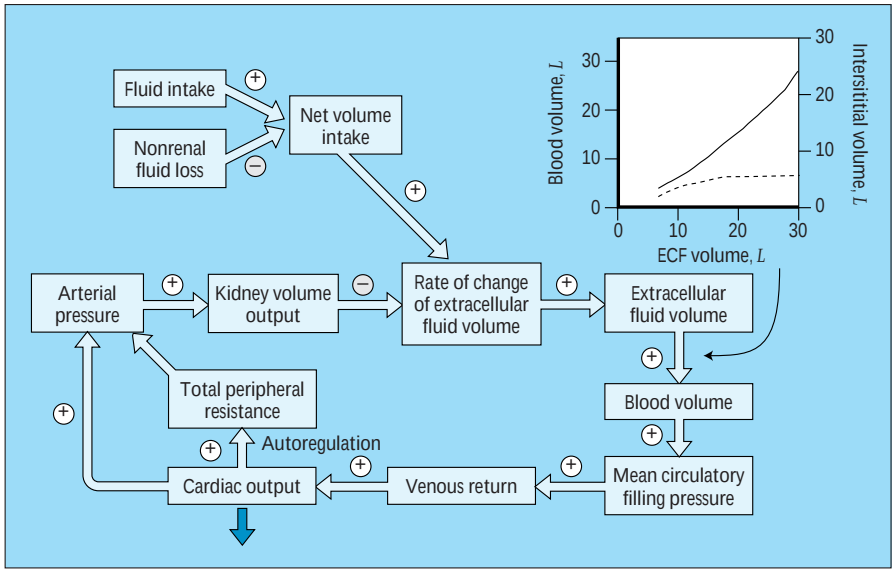

FIGURE 2-29

Mechanism of extracellular fluid (ECF) volume expansion in congestive heart failure. A primary decrease in cardiac output (indicated by dark blue arrow) leads to a decrease in arterial pressure, which decreases pressure natriuresis and volume excretion. These decreases expand the ECF volume. The inset graph shows that the ratio of interstitial volume (solid line) to plasma volume (dotted line) increases as the ECF volume expands because the interstitial compliance increases [62]. Thus, although expansion of the ECF volume increases blood volume and venous return, thereby restoring cardiac output toward normal, this occurs at the expense of a *disproportionate* expansion of interstitial volume, often manifested as edema.