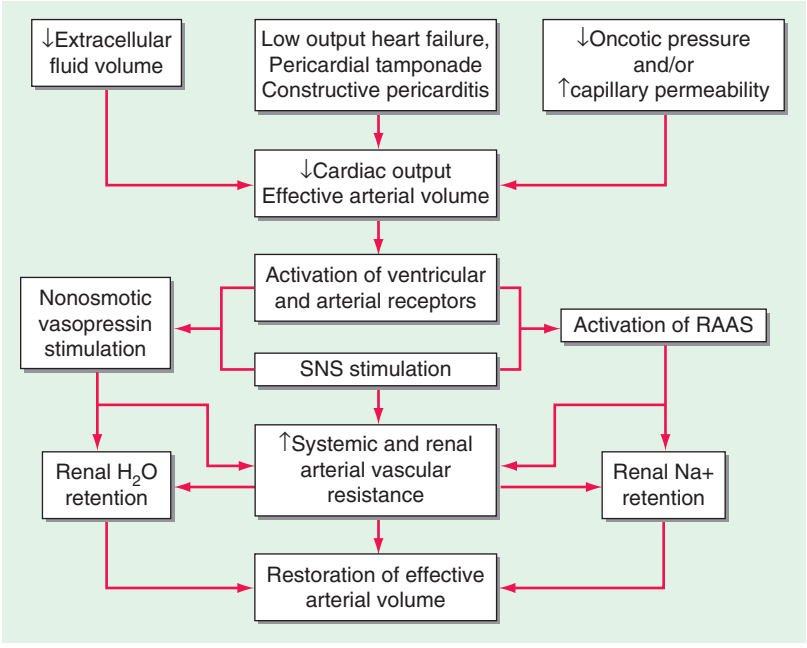
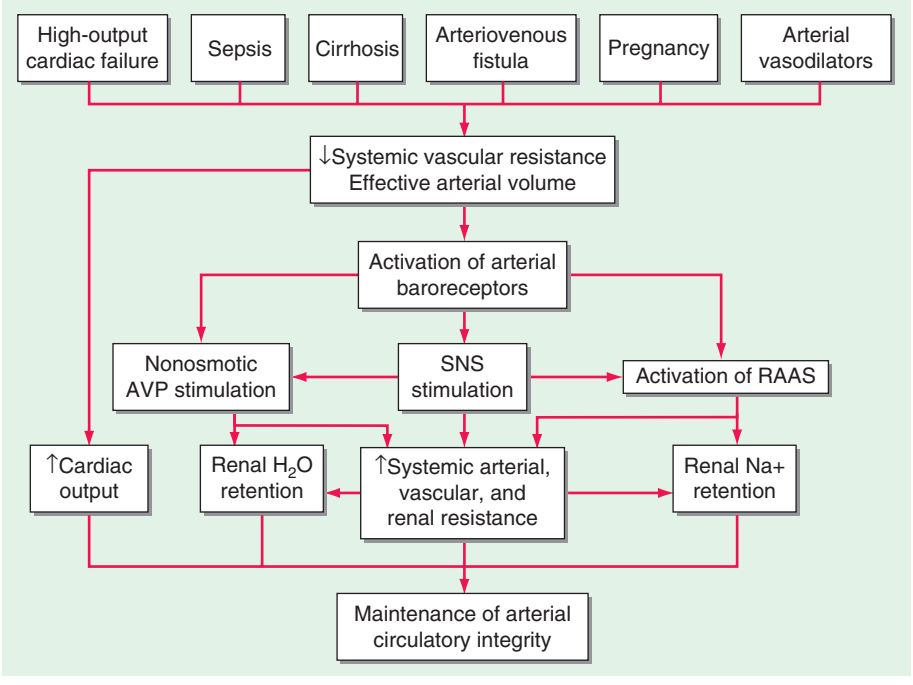


A



B

FIGURE 50-1 Clinical conditions in which a decrease in cardiac output (*A*) and systemic vascular resistance (*B*) cause arterial underfilling with resulting neurohumoral activation and renal sodium and water retention. In addition to activating the neurohumoral axis, adrenergic stimulation causes renal vasoconstriction and enhances sodium and fluid transport by the proximal tubule epithelium. RAAS, renin-angiotensin aldosterone system; SNS, sympathetic nervous system. *(Modified from RW Schrier: Ann Intern Med 113:155, 1990.)*

ENDOTHELIN-1

This potent peptide vasoconstrictor is released by endothelial cells. Its concentration in the plasma is elevated in patients with severe heart failure and contributes to renal vasoconstriction, sodium retention, and edema.

NATRIURETIC PEPTIDES

Atrial distention causes release into the circulation of atrial natriuretic peptide (ANP), a polypeptide; a high-molecular-weight precursor of ANP is stored in secretory granules within atrial myocytes. The closely related brain natriuretic peptide (pre-prohormone BNP) is stored primarily in ventricular myocytes and is released when ventricular diastolic pressure rises. Released ANP and BNP (which is derived from its precursor) bind to the natriuretic receptor-A, which causes: (1) excretion of sodium and water by augmenting glomerular filtration rate, inhibiting sodium reabsorption in the proximal tubule, and inhibiting release of renin and aldosterone; and (2) dilation of arterioles and venules by antagonizing the vasoconstrictor actions of AII, AVP, and sympathetic stimulation. Thus, elevated levels of natriuretic peptides have the capacity to oppose sodium retention in hypervolemic and edematous states.

Although circulating levels of ANP and BNP are elevated in heart failure and in cirrhosis with ascites, the natriuretic peptides are not sufficiently potent to prevent edema formation. Indeed, in edematous states, resistance to the actions of natriuretic peptides may be increased, further reducing their effectiveness.

Further discussion of the control of sodium and water balance is found in Chap. 64e.

CLINICAL CAUSES OF EDEMA

A weight gain of several kilograms usually precedes overt manifestations of generalized edema, and a similar weight loss from diuresis can be induced in a slightly edematous patient before "dry weight" is achieved. *Anasarca* refers to gross, generalized edema. *Ascites* (Chap. 59) and *hydrothorax* refer to accumulation of excess fluid in the peritoneal and pleural cavities, respectively, and are considered special forms of edema.

Edema is recognized by the persistence of an indentation of the skin after pressure; this is known as "pitting" edema. In its more subtle form, edema may be detected by noting that after the stethoscope is removed from the chest wall, the rim of the bell leaves an indentation on the skin of the chest for a few minutes. Edema may be present when the ring on a finger fits more snugly than in the past or when a patient complains of difficulty putting on shoes, particularly in the evening. Edema may also be recognized by puffiness of the face, which is most readily apparent in the periorbital areas.

GENERALIZED EDEMA

The differences among the major causes of generalized edema are shown in Table 50-1. Cardiac, renal, hepatic, or nutritional disorders are responsible for a majority of patients with generalized edema. Consequently, the differential diagnosis of generalized edema should be directed toward identifying or excluding these several conditions.

Heart Failure (See also Chap. 279) In heart failure, the impaired systolic emptying of the ventricle(s) and/or the impairment of ventricular relaxation promotes an accumulation of blood in the venous circulation at the expense of the effective arterial volume. In addition, the heightened tone of the sympathetic nervous system causes renal vasoconstriction and reduction of glomerular filtration. In mild heart failure, a small increment of total blood volume may repair the deficit of