Intravascular volume depletion
Activation of the renin-angiotensin axis
Angiotensin II–mediated vasoconstriction
Pressure-induced natriuresis and diuresis
Abrupt increase in blood pressure
Malignant hypertension

FIGURE 8-20
Role of diuretics in the treatment of malignant hypertension. Traditionally, it had been taught that patients with malignant hypertension require potent parenteral diuretics in conjunction with potent vasodilator therapy during the initial phase of management of malignant hypertension. However, evidence now exists to suggest that parenteral diuretic therapy during the acute management phase actually may be deleterious. In experimental animals, spontaneous natriuresis appears to be the initiating event in the transition from benign to malignant hypertension, and treatment with volume expansion leads to resolution of the malignant phase [24]. Rapid weight loss often occurs in patients with malignant hypertension, which is consistent with a pressure-induced natriuresis. In analgesic nephropathy, profound volume depletion often accompanies malignant hypertension, perhaps owing to tubular dysfunction with salt-wasting [5]. In this setting, restoration of normal volume status actually lowers blood pressure and leads to resolution of the malignant phase. Thus, some patients with malignant hypertension may benefit from a cautious trial of volume expansion. Volume depletion should be suspected when there is exquisite sensitivity to vasodilator therapy with a precipitous decrease in blood pressure at relatively low infusion rates. Even patients with malignant hypertension complicated by pulmonary edema may not be total-body salt and water overloaded. Pulmonary congestion in this setting may result from acute hypertensive heart failure caused by an acute decrease in left ventricular (LV) compliance precipitated by severe hypertension. In this setting, pulmonary edema occurs owing to a high LV end-diastolic pressure with normal LV end-diastolic volume (Fig. 8-24). Thus, the need for diuretic therapy during the initial phases of management of malignant hypertension depends on a careful assessment of volume status. Unless obvious fluid overload is present, diuretics should not be given initially. Overdiuresis may result in deterioration of renal function owing to superimposed volume depletion. Moreover, volume depletion may further activate the renin-angiotensin system and other pressor hormone systems. Although vasodilator therapy will eventually result in salt and water retention by the kidneys, an increase in total body sodium content cannot occur unless the patient is given sodium. Eventually, during long-term treatment with oral vasodilators, the use of diuretics becomes imperative to prevent fluid retention and adequately control blood pressure.
Hypertensive encephalopathy

Pathogenesis and treatment of hypertensive encephalopathy

Malignant hypertension (hypertensive neuroretinopathy present) → Sudden or severe nonmalignant hypertension (hypertensive neuroretinopathy absent)

Sudden onset or severe hypertension → Failure of autoregulation of cerebral blood flow (breakthrough of autoregulation)

Forced vasodilation of cerebral arterioles

Endothelial damage (increased permeability to plasma proteins) → Cerebral hyperperfusion (increased capillary hydrostatic pressure)

Cerebral edema

Hypertensive encephalopathy (headache, vomiting, altered mental status, seizures) → Prompt blood pressure reduction with nitroprusside

New or progressive focal findings (suspect primary central nervous system process) → Dramatic clinical improvement (diagnostic of hypertensive encephalopathy)

FIGURE 8-21

Pathogenesis and treatment of hypertensive encephalopathy. Hypertensive encephalopathy is a hypertensive crisis in which acute cerebral dysfunction is attributed to sudden or severe elevation of blood pressure [25–27]. Hypertensive encephalopathy is one of the most serious complications of malignant hypertension. However, malignant hypertension (hypertensive neuroretinopathy) need not be present for hypertensive encephalopathy to develop. Hypertensive encephalopathy also can occur in the setting of severe or sudden hypertension of any cause, especially if an acute elevation of blood pressure occurs in a previously normotensive person, eg, from postinfectious glomerulonephritis, catecholamine excess states, or eclampsia. Under normal circumstances, autoregulation of the cerebral microcirculation occurs, and therefore, cerebral blood flow remains constant over a wide range of perfusion pressures. However, in the setting of sudden severe hypertension, autoregulatory vasoregulation fails and there is forced vasodilation of cerebral arterioles with endothelial damage, extravasation of plasma proteins, and cerebral hyperperfusion with the development of cerebral edema. This breakthrough of cerebral autoregulation underlies the development of hypertensive encephalopathy. In patients with chronic hypertension, structural changes occur in the cerebral arterioles that lead to a shift in the autoregulation curve such that much higher blood pressures can be tolerated without breakthrough. This phenomenon may explain the clinical observation that hypertensive encephalopathy occurs at much lower blood pressure in previously normotensive persons than it does in those with chronic hypertension. Clinical features of hypertensive encephalopathy include severe headache, blurred vision or occipital blindness, nausea, vomiting, and altered mental status. Focal neurologic findings can sometimes occur. If aggressive blood pressure reduction is not initiated, stupor, convulsions, and death can occur within hours. The sine qua non of hypertensive encephalopathy is the prompt and dramatic clinical improvement in response to antihypertensive drug therapy. When a diagnosis of hypertensive encephalopathy seems likely, antihypertensive therapy should be initiated promptly without waiting for the results of time-consuming radiographic examinations. The goal of therapy, especially in previously normotensive patients, should be reduction of blood pressure to normal or near-normal levels as quickly as possible. Theoretically, cerebral blood flow could be jeopardized by rapid reduction of blood pressure in patients with chronic hypertension in whom the lower limit of cerebral blood flow autoregulation is shifted to a higher blood pressure. However, clinical experience has shown that prompt blood pressure reduction with the avoidance of frank hypotension is beneficial in patients with hypertensive encephalopathy [25]. Of the conditions in the differential diagnosis of hypertension with acute cerebral dysfunction, only cerebral infarction might be adversely affected by the abrupt reduction of blood pressure. Pharmacologic agents that have rapid onset and short duration of action such as sodium nitroprusside should be used so that the blood pressure can be titrated carefully, with close monitoring of the patient’s neurologic status. A prompt improvement in mental status with blood pressure reduction confirms the diagnosis of hypertensive encephalopathy. Conversely, when blood pressure reduction is associated with new or progressive focal neurologic deficits, the presence of a primary central nervous system event, such as cerebral infarction, should be considered.
Hypertensive encephalopathy can complicate malignant hypertension of any cause. However, not all patients with hypertensive encephalopathy have hypertensive neuroretinopathy, indicating the presence of malignant hypertension. In fact, hypertensive encephalopathy most commonly occurs in previously normotensive persons who experience a sudden onset or worsening of hypertension. In acute postinfectious glomerulonephritis, the abrupt onset of even moderate hypertension may cause breakdown of autoregulation of cerebral blood flow, resulting in hypertensive encephalopathy. Eclampsia can be viewed as a variant of hypertensive encephalopathy that complicates preeclampsia. Moreover, hypertensive encephalopathy is a common complication of catecholamine-induced hypertensive crises such as pheochromocytoma, monoamine oxidase inhibitor-tyramine interactions, clonidine withdrawal, phencyclidine (PCP) poisoning, and phenylpropanolamine overdose. Cocaine use also can induce a sudden increase in blood pressure accompanied by hypertensive encephalopathy. In children, acute lead poisoning, high-dose cyclosporine for bone marrow transplantation, femoral lengthening procedures, and scorpion envenomation may be accompanied by the sudden onset of hypertension with encephalopathy. A acute renal artery occlusion resulting from thrombosis or embolism can induce hypertensive encephalopathy. Likewise, atheroembolic renal disease (cholesterol embolization) can cause a sudden increase in blood pressure complicated by encephalopathy. Recombinant erythropoietin therapy occasionally results in encephalopathy and seizures. This complication is unrelated to the extent or rate of increase in hematocrit; however, it is associated with a rapid increase in blood pressure, especially if the patient was normotensive previously. Transplantation renal artery stenosis or acute renal allograft rejection may cause sudden severe hypertension with encephalopathy. Hypertensive encephalopathy may complicate acute or chronic spinal cord injury. Sudden elevation of blood pressure occurs owing to autonomic stimulation by bowel or bladder distention or noxious stimulation in a dermatome below the level of the injury. Hypertensive encephalopathy also may complicate the rebound hypertension that follows coronary artery bypass procedures or carotid endarterectomy.

CAUSES OF HYPERTENSION ENCEPHALOPATHY

- Malignant hypertension of any cause
- Acute glomerulonephritis, especially postinfectious
- Eclampsia
- Catecholamine-induced hypertensive crises
  - Pheochromocytoma
  - Monoamine oxidase inhibitor-tyramine interactions
  - Abrupt withdrawal of centrally acting \( \alpha_2 \)-agonists
  - Phenylpropanolamine overdose
- Cocaine-hydrochloride or alkaloid (crack cocaine) intoxication
- Phencyclidine (PCP) poisoning
- Acute lead poisoning in children
- High-dose cyclosporine for bone marrow transplantation in children
- Femoral lengthening procedures
- Scorpion envenomation in children
- Acute renal artery occlusion from thrombosis or embolism
- Atheroembolic renal disease (cholesterol embolization)
- Recombinant erythropoietin therapy
- Transplantation renal artery stenosis
- Acute renal allograft rejection
- Paroxysmal hypertension in acute or chronic spinal cord injuries
- Post-coronary artery bypass or post-carotid endarterectomy hypertension