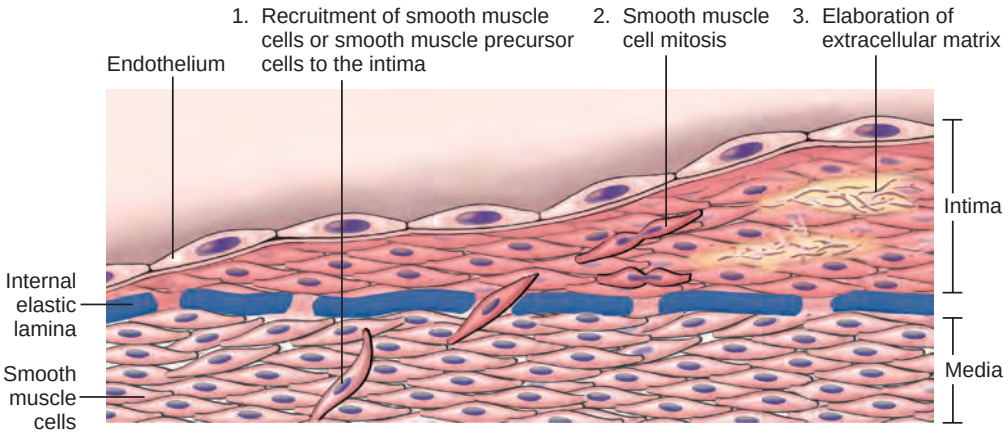

Figure 11-3 Stereotypical response to vascular injury. Schematic diagram of intimal thickening, emphasizing intimal smooth muscle cell migration and proliferation associated with extracellular matrix synthesis. The new intimal cells are shown in a different color to emphasize that they have a proliferative, synthetic, and noncontractile phenotype distinct from medial smooth muscle cells.

KEY CONCEPTS

Response of Vascular Wall Cells to Injury

- All vessels are lined by endothelium; although all endothelial cells share certain homeostatic properties, endothelial cells in specific vascular beds have special features that allow for tissue-specific functions (e.g., fenestrated endothelial cells in renal glomeruli).
- Endothelial cell function is tightly regulated in both the basal and activated states. Various physiologic and pathophysiologic stimuli induce endothelial activation and dysfunction that alter the endothelial cell phenotype (e.g., procoagulative vs. anticoagulative, proinflammatory vs. antiinflammatory, and nonadhesive vs. adhesive).
- Injury (of almost any type) to the vessel wall results in a stereotyped healing response involving smooth muscle cell proliferation, extracellular matrice deposition, and intimal expansion.
- The recruitment and activation of the smooth muscle cell involves signals from cells (e.g., endothelial cells, platelets, and macrophages), as well as mediators derived from coagulation and complement cascades.
- Excessive thickening of the intima may result in luminal stenosis and vascular obstruction.

Hypertensive Vascular Disease

Systemic and local tissue blood pressures must be maintained within a narrow range to prevent untoward consequences. Low blood pressure *(hypotension)* results in inadequate organ perfusion and can lead to tissue dysfunction or death. Conversely, high blood pressure *(hypertension)* can cause end-organ damage and is one of the major risk factors for atherosclerosis (see later).

Like height and weight, blood pressure is a continuously distributed variable, and detrimental effects of elevated blood pressure increase continuously as blood pressure rises—no rigidly defined threshold level of blood pressure identifies those who are at risk for cardiovascular disease. Both the systolic and diastolic blood pressure are important in determining risk; specifically, sustained diastolic pressures above 89 mm Hg or sustained systolic pressure above 139 mm Hg are associated with increased risk of atherosclerotic disease, and are thus considered clinically significant. Approximately 29% of individuals in the general population are hypertensive based on these criteria. However, such cutoffs do not reliably assess risk in all patients; for example, when other risk factors such as diabetes are present, lower thresholds are applicable.

Table 11-1 lists the major causes of hypertension. A small number of patients (approximately 5%) are said to have *secondary hypertension* resulting from an underlying renal or adrenal disease (e.g., primary aldosteronism, Cushing syndrome, or pheochromocytoma), renal artery stenosis, or other identifiable cause. *However, approximately 90% to 95% of hypertension is idiopathic—so-called essential hypertension.* Although the molecular pathways that regulate normal blood pressure are reasonably well understood, the causes of hypertension in most individuals remain unknown. It seems likely that hypertension is a multifactorial disorder, resulting from the cumulative effects of multiple genetic polymorphisms and interacting environmental factors.

The prevalence and vulnerability to complications of hypertension increase with age and are higher among African Americans. Besides increasing atherosclerotic risk, hypertension can cause cardiac hypertrophy and heart failure (*hypertensive heart disease*, Chapter 12), multi-infarct dementia (Chapter 28), aortic dissection (discussed later in this chapter), and renal failure (Chapter 20). Unfortunately, hypertension typically remains asymptomatic until late in its course and even severely elevated pressures can be clinically silent for years. Left untreated, roughly half of hypertensive patients die of ischemic heart disease (IHD) or congestive heart failure, and another third die of stroke. Treatment with blood pressure lowering drugs dramatically reduces the incidence and death rates attributable to all forms of hypertension-related pathology.

A small percentage of hypertensive persons (as much as 5%) show a rapidly rising blood pressure that, if untreated, leads to death within 1 to 2 years. This form of hypetension, called *malignant hypertension*, is characterized by severe hypertension (i.e., systolic pressure more than 200 mm Hg, diastolic pressure more than 120 mm Hg),