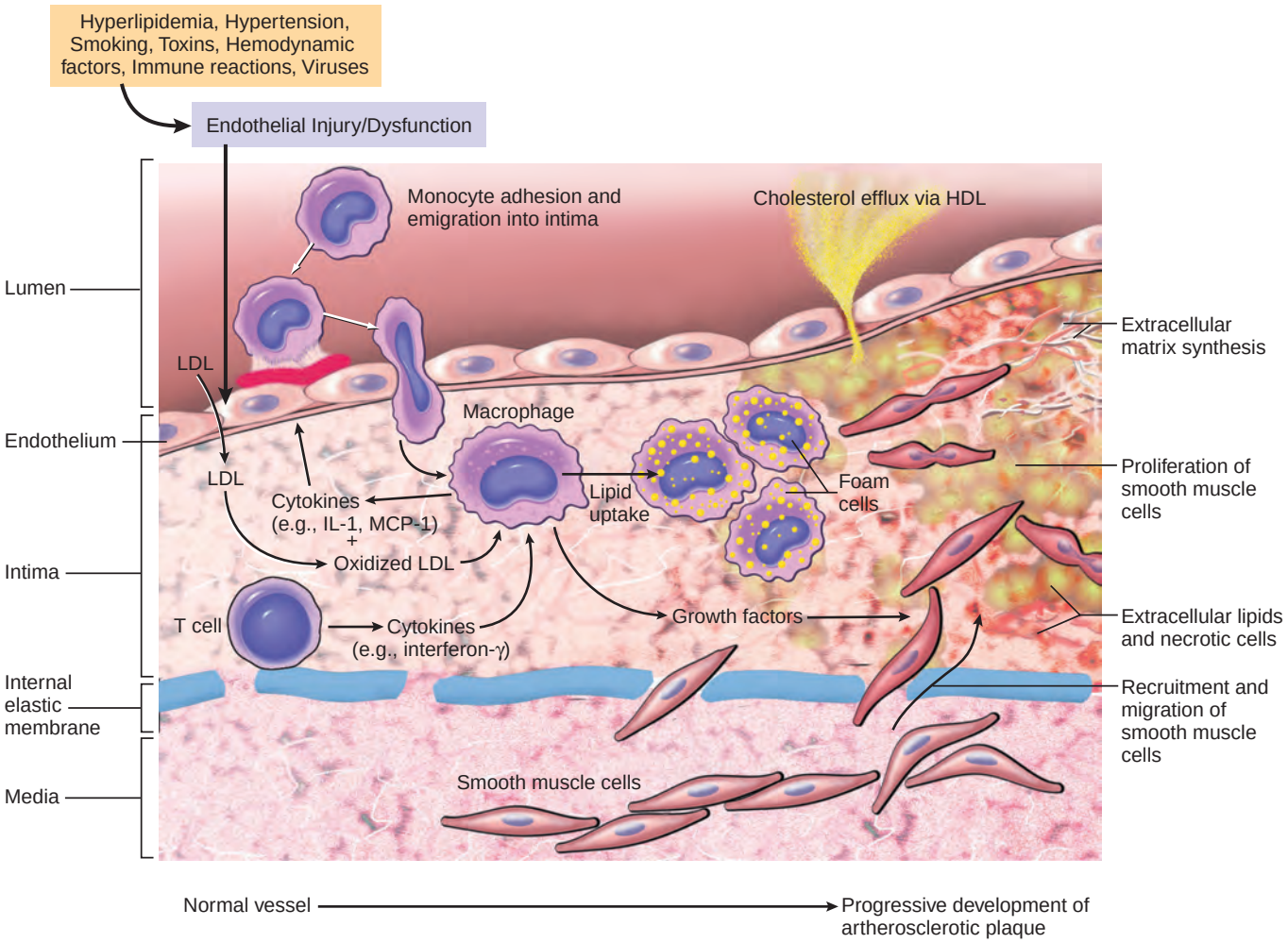

Figure 11-11 Sequence of cellular interactions in atherosclerosis. Hyperlipidemia, hyperglycemia, hypertension, and other influences cause endothelial dysfunction. This results in platelet adhesion and recruitment of circulating monocytes and T cells, with subsequent cytokine and growth factor release from inflammatory cells leading to smooth muscle cell migration and proliferation as well as further macrophage activation. Foam cells in atheromatous plaques derive from macrophages and smooth muscle cells that have accumulated modified lipids (e.g., oxidized and aggregated low density lipoprotein [LDL]) via scavenger and LDL-receptor-related proteins. Extracellular lipid is derived from insudation from the vessel lumen, particularly in the presence of hypercholesterolemia, as well as from degenerating foam cells. Cholesterol accumulation in the plaque reflects an imbalance between influx and efflux; high-density lipoprotein (HDL) likely helps clear cholesterol from these accumulations. In response to the elaborated cytokines and chemokines, smooth muscle cells migrate to the intima, proliferate, and produce extracellular matrix, including collagen and proteoglycans. IL-1, interleukin-1; MCP-1, monocyte chemoattractant protein-1.

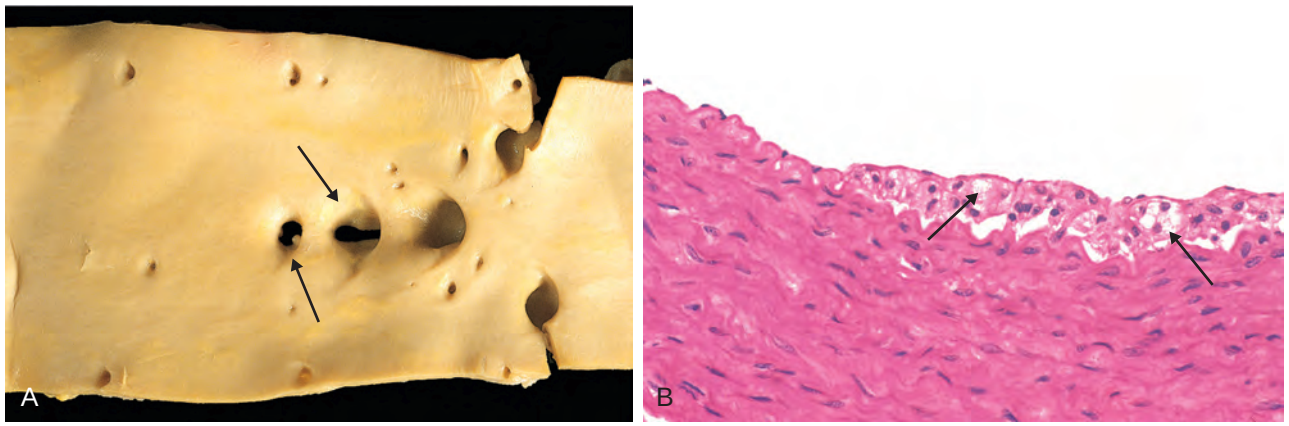

Figure 11-12 Fatty streak, a collection of foamy macrophages in the intima. **A,** Aorta with fatty streaks *(arrows),* associated largely with the ostia of branch vessels. **B,** Photomicrograph of fatty streak in an experimental hypercholesterolemic rabbit, demonstrating intimal, macrophage-derived foam cells *(arrows).* (**B**, Courtesy Myron I. Cybulsky, MD, University of Toronto, Canada.)