Individual therapeutic decisions and the interpretation of data obtained in clinical trials designed to evaluate various interventions depend largely on an accurate appreciation of plaque morphogenesis and on valid interpretations of the corresponding images and hemodynamic measurements. Improvements in resolution of clinical imaging modalities, including capabilities for three-dimensional image reconstruction, permit increasingly detailed evaluation of the atherosclerotic process in the principal vascular locations at high risk. Tissue excised during surgical procedures, including endarterectomy and atherectomy, as well as vessels obtained at autopsy provide material for morphometric characterization of plaque organization and composition, and for histochemical, immunocytochemical, and molecular biologic studies of lesion cell function. These findings may then be correlated with antecedent angiographic, computed tomographic, magnetic resonance, intravascular ultrasonic, and angioscopic studies and with duplex imaging and hemodynamic studies in order to identify and document the morphologic features revealed by the various imaging procedures. Ideally, these correlations take into account associated local clinical manifestations, flow field features, and artery wall mechanical properties. The resulting data may be expected to provide a better understanding of the natural history of human plaques and of the differential effects of various modes of risk factor control and direct intervention.

Several specific areas of concern directly relevant to diagnosis and treatment are addressed in this chapter [1–8]. These include 1) detection of minimal, asymptomatic lesions; 2) changes in plaque size, composition, and organization; 3) features indicative of plaque stability or instability; and 4) morphologic and hemodynamic antecedents of restenosis following direct interventions. The clinicopathologic problems related to each of these critical clinical concerns are outlined below.

1. Detection of minimal, asymptomatic lesions. The detection of features that correspond to intimal lesion initiation or induction should permit evaluation of clinical risk factor interventions at
this presumably early stage of plaque development. The endpoints include identifiable features of lesion formation, plaque resolution or arrest of further growth of such lesions, and prevention of additional plaque formation.

Detection of minimal intimal thickening depends on measurements of artery wall thickness (intima plus media) and changes in mural mechanical properties and wall composition (matrix fibers, lipid core, cell content, and calcification). In view of the usually focal and eccentric location of plaques and the relationship of plaque location to geometric transitions, selection of the precise regions to be interrogated is critical.

2. Changes in plaque size, composition, and organization. On sequential studies, increased, diminished, or unchanged plaque and wall thickness, cross-sectional area, and lumen contour or diameter are likely to be indices of lesion progression, regression, or stabilization, permitting evaluation of treatment options in the presence of manifest plaques. It should be noted, however, that angiographic images of lumen diameter may yield information regarding comparative degrees of lumen narrowing but may not provide an accurate appraisal of lesion cross-sectional area or volume. This limitation is due to 1) the compensatory enlargement of arteries where plaques form; 2) changes in lumen size due to modification of plaque composition; 3) the occurrence of plaque disruptions and ulcerations; 4) erosions of the underlying media; and 5) the formation and organization of thrombi.

3. Features indicative of plaque stability or instability. These include characteristic modifications of lumen contour, lesion configuration, lesion composition, and lumen surface integrity. Lumen and plaque features that connote imminent, immediate, recent, or remote plaque disruption, fissuring, hemorrhage, and thrombus deposition are likely to be closely related to specific symptomatic manifestations of atherosclerosis. Problems of clinical interpretation arise in relation to artery and plaque modeling in response to alterations in flow and wall tension, to the rate and nature of component segregation and stratification during lesion induction, progression, or regression, and in relation to healing processes following plaque disruption, hemorrhage, or thrombosis. Foci of symptom-producing plaque disruption may be quite small, limiting detection by some current imaging methods. Predictions of plaque instability from images depend on detection, identification, and quantitative appraisal of these features.

4. Morphologic and hemodynamic antecedents of restenosis. Plaque disruption or partial excision by intravascular instrumentation or by intraoperative endarterectomy create marked changes in lumen and lesion configuration and, therefore, in the distribution of flow- and tension-related physical stresses. Subsequent changes in image appearances correspond both to the degree of lesion modification by the intervention and the subsequent healing-remodeling proliferative and differentiating processes initiated by the injury. Interpretation of these features in relation to clinical determinations of flow and progression of the atherosclerotic process may be expected to identify factors that could establish the bases for and the predictors of eventual long-term patency or the development of secondary obstruction (restenosis) at sites of intervention.

These considerations indicate that data obtained from quantitative clinicopathologic correlative studies of human atherosclerotic plaques are not likely to be replaced by those obtained by cell culture or by studies of animal models of atherogenesis. Specific questions of cell and molecular biology, usually best addressed in experimental model systems, may be identified and better focussed on the basis of information derived from the human findings. The morphologic features of plaque evolution relevant to each of the above-noted categories are illustrated in this chapter.
The vessels at highest risk for plaque formation are the carotid bifurcation, the coronary arteries, the abdominal segment of the aorta, and the vessels of the lower extremities. The precise localization of detectable intimal thickening is often closely associated with flow conditions in these regions, most notably at geometric transitions. The zones of selective involvement are those where flow separation occurs and where wall shear stress is low and tends to reverse in direction during the cardiac cycle. These regions are also often zones of tensile stress concentration.

These effects are well illustrated by the usual location of lesions about the carotid bifurcation. A, Angiogram of a human carotid bifurcation obtained at autopsy. B, Cross-sections taken at the levels indicated on the angiogram include the common carotid artery immediately proximal to the bifurcation (A), at the proximal internal carotid level (B), at the midportion of the sinus (C), and at the internal carotid artery level distal to the sinus (D). Plaque formation is most prominent opposite the flow divider in the proximal internal carotid artery and in the mid-sinus. The arteries are largely spared in the region of the flow divider and in the sections distal to the sinus and proximal to the bifurcation. Arrows mark corresponding positions on the angiogram and on the cross-sections. When plaques are advanced and stenosis is clinically significant, the lesion may extend both proximally and distally and eventually involve the entire circumference. (Adapted from Zarins and coworkers [9]; with permission.)
Figure 2-3. Similar geometric conditions prevail at the division of the left main coronary artery (LM) into its anterior descending (LAD) and circumflex (LCX) branches. A, In a study of plaque localization in this region in a series of axially opened human specimens, usual lesion distribution, outlined in this diagram by perimeter contours [11], is predominantly opposite the flow divider (arrow). B, In a study of lesion location on cross-sections taken in this region, a similar distribution is apparent [1]. C, The aortic orifices of the celiac and superior mesenteric arteries are shown. The plaques (arrows) develop initially and principally at the inflow side of the orifices where flow separation and relatively low wall shear stress prevails. (Part A adapted from Stary [1], with permission.)
Although the distal common carotid artery (C), the sinus, and the proximal internal carotid artery (I) are often regions of prominent plaque formation, local and regional variations and departures from the predominant pattern of flow would be expected to modify lesion localization. Plaque distribution is therefore likely to correspond to individual geometric variations. Thus, a single direction of ultrasound interrogation for early detection may not yield information concerning maximum lesion thickness, particularly for minimal or moderately advanced asymptomatic lesions. Interrogation of a region at risk, such as the proximal carotid bifurcation, should therefore be examined over a range of adjacent incident angles whenever possible. In a study of sequential levels of carotid bifurcation obtained at autopsy of patients without cerebrovascular symptoms, the distribution of foci of maximum intimal thickness followed a somewhat helical distribution [2].

A, Location of the section levels. II-5 are sequential sections of the internal carotid branch, whereas C1-4 are sequential sections through the common carotid artery. B, The circumferential location of maximum intimal thickening for each axial level of section about the carotid bifurcation is shown by dots (top) [12], and a diagrammatic representation of the axial distribution of usual early maximum intimal thickening is also shown (bottom). The distribution tends to be helical in keeping with the configuration of the flow field, which may differ on the right versus the left.

Although the extent to which atherosclerosis can be detected or quantified on the basis of calcification in this or other sites remains to be defined, dystrophic calcium deposits occur regularly in plaques that have not necessarily resulted in stenosis or undergone disruption. The extent to which atherosclerosis in a location at high risk may serve as a surrogate for appraisal of plaques in another site also awaits further investigation. Accruing evidence suggests that abdominal aortic and coronary atherosclerosis may precede the formation of thoracic aortic disease or cerebrovascular disease. However, metabolic abnormalities such as diabetes mellitus or other major risk factors appear to be linked to certain patterns of preferential involvement and lesion composition and complication. (Adapted from Masawa and coworkers [2]; with permission.)
CHANGES IN PLAQUE SIZE, COMPOSITION, AND ORGANIZATION

As the atherosclerotic process proceeds, both plaque and artery wall are modeled and remodeled in relation to atherogenic metabolic factors and in relation to the mechanical forces associated with the circulation. The major physical forces that ordinarily determine vessel dimensions and composition are represented diagrammatically; these include wall shear stress (A) and mural tensile stress (B) [12]. Individual differences in the frequency and amplitude of the cyclic variations of these stresses may also play a major role. For any given flow rate, wall shear stress ($\tau_w$) varies inversely with the cube of the radius. A small change in radius may therefore have a marked effect on $\tau_w$. d—wall thickness; $\mu$—fluid viscosity; P—pressure; Q—volume flow rate; r—vessel radius; S—wall tensile stress; T—total tangential wall tension. (Adapted from Glagov and coworkers [12]; with permission.)

Figure 2-5. As the atherosclerotic process proceeds, both plaque and artery wall are modeled and remodeled in relation to atherogenic metabolic factors and in relation to the mechanical forces associated with the circulation. The major physical forces that ordinarily determine vessel dimensions and composition are represented diagrammatically; these include wall shear stress (A) and mural tensile stress (B) [12]. Individual differences in the frequency and amplitude of the cyclic variations of these stresses may also play a major role. For any given flow rate, wall shear stress ($\tau_w$) varies inversely with the cube of the radius. A small change in radius may therefore have a marked effect on $\tau_w$. d—wall thickness; $\mu$—fluid viscosity; P—pressure; Q—volume flow rate; r—vessel radius; S—wall tensile stress; T—total tangential wall tension. (Adapted from Glagov and coworkers [12]; with permission.)

Figure 2-6. In the absence of atherosclerosis, increased flow results in vessel diameter enlargement, which stabilizes when wall shear stress is restored to mean normal baseline levels of approximately 15 dynes/cm². Restriction of flow, however, may result in artery lumen narrowing to maintain baseline wall shear stress. Tensile stress varies directly with pressure and radius and inversely with wall thickness. Changes in wall tension induce modifications of wall thickness and wall composition. Although artery wall architecture varies considerably for different levels and locations in the arterial tree, homologous arteries in mammals tend to have similar structure [13].

A. Unilateral dilation of an otherwise normal right iliac (RI) artery proximal to an experimental arteriovenous fistula (arrow) had stabilized at 6 months [14] when wall shear stress reached the same baseline mean value as was computed for the unoperated control left iliac (LI) artery. Flow meters (FM) were placed in an experimental animal on the RI and LI arteries at the conclusion of the experiment. B. Differences between the vessels are considerable for flow and diameter but wall shear stress is the same for both sides at the time of stabilization because of the increase in diameter on the side with the fistula. (Adapted from Zarins and coworkers [14]; with permission.)

### B. RI ARTERIOVENOUS FISTULA IN CYCLOMOLGUS MONKEYS (n=6)

<table>
<thead>
<tr>
<th>ARTERY</th>
<th>VOLUME FLOW (ml/min)</th>
<th>FLOW VELOCITY (cm/s)</th>
<th>LUMEN DIAMETER (mm)</th>
<th>SHEAR STRESS (dynes/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RI</td>
<td>420±95</td>
<td>31±6</td>
<td>5.4±0.4</td>
<td>16±4</td>
</tr>
<tr>
<td>LI</td>
<td>44±9</td>
<td>12±1</td>
<td>2.6±0.3</td>
<td>15±2</td>
</tr>
</tbody>
</table>
As arteries adapt to changes in pressure and flow, the intima may participate in the corresponding modeling reactions, even in the absence of atherosclerosis. Nevertheless, these adaptations occur also in the presence of atherosclerosis [3]. During plaque morphogenesis, lipid initially accumulates interstitially and within macrophages in a focal eccentric widening of the intima often in association to an associated intimal fibrocellular thickening containing smooth muscle cells. As the plaque progresses, reactions may be noted in the underlying media (M). Although erosion of the media may be noted, as in this section of the common carotid artery at the bifurcation (A), the intimal reaction immediately adjacent to the media is often characterized also by fibrosis (arrows), as in this section of a human coronary artery (B). Both collagen and elastin fibers are usually prominent in this reaction. In both A and B, the lumen (L) is occupied by a gelatin-carbon mass introduced under conditions of controlled pressure fixation in an attempt to restore in vivo dimensions. Note that in the absence of plaque ulceration or thrombosis, the plaque does not form a bulge into the lumen and the plaque lumen surface maintains a concave configuration [4].

**FIGURE 2-7.** As arteries adapt to changes in pressure and flow, the intima may participate in the corresponding modeling reactions, even in the absence of atherosclerosis. Nevertheless, these adaptations occur also in the presence of atherosclerosis [3]. During plaque morphogenesis, lipid initially accumulates interstitially and within macrophages in a focal eccentric widening of the intima often in association to an associated intimal fibrocellular thickening containing smooth muscle cells. As the plaque progresses, reactions may be noted in the underlying media (M).

**FIGURE 2-8.** As the plaque progresses, a fibrocellular reaction is evident at the luminal or subendothelial side of the intima, such that the lipid core (LC) and the associated products of tissue generation and necrosis are segregated to a mid-intimal zone by deep (DF) and superficial (SF) fibrocellular reactions (A). The superficial zone often differentiates into a more compact distinct cellular structure, the fibrous cap (FC) (B). This structure may be similar in both thickness and architecture to the underlying media (M) or to the media of the opposite uninvolved portion of the artery. It is likely that the structural differentiation of the FC is a response to the circumferential stress concentration and its cyclic variation in this plaque region. Experimental studies have established close associations between tensile stimuli and smooth muscle biosynthetic matrix response [15,16]. (continued)
Although there is evidence that plaques may stabilize at any stage of development or revert to some extent to a previous stage, new lesions may develop on an apparently previously stabilized plaque (C) [7].

With advancing disease, circumferential extension and encroachment of the lumen from the initial focus of involvement proceed, although the distribution of intimal lesion thickness tends to remain eccentric. The modeling processes and the metabolic processes associated with continuing atherogenesis, particularly the relative effects of the erosion of the media and the deep and superficial fibrous reaction, determine lesion architecture and composition, and the plaque tends to be sequestered effectively from the lumen. In the absence of plaque complication by disruption, fissuring, hemorrhage, or thrombosis, the lumen surface remains smooth, the cross-sectional lumen contour remains more or less circular or oval, and the subendothelial fibrocellular zone or FC persists, isolating the lipid core from the lumen [4]. This effect is evident in all of the sections shown here. I—primary plaque; II—secondary plaque.

(Figures adapted from Stary [17]; with permission.)

**Figure 2-8** (continued)  
**Figure 2-9.** A, Fibrosis and calcification (CA) progress as plaque formation continues and tend to become increasingly prominent with increases in lesion size and with eventual narrowing of the lumen (L). Thus, large lesions tend to be complex. Lesion size may or may not correspond to the degree of stenosis, because erosion of the media or plaque disruption or disorganization may result in increased vessel lumen diameter or even ectasia or aneurysm formation in relation to the atherogenic process. B, A section of a coronary artery with a large fibrocalcific plaque (PL) and a large lumen. FC—fibrous cap; LC—lipid core.
FIGURE 2-10. In relation to the modeling and remodeling processes described, arteries appear to enlarge initially as plaques form, tending to preserve a lumen of adequate cross-section even in the presence of relatively large intimal plaques [18,19]. A. Postmortem sections of the left anterior descending coronary artery taken at the same level in two individuals. The lumen cross-sectional area (L) is approximately the same for each individual, although the lesion area is vastly different.

If the artery on the left had not enlarged to compensate for the large plaque that formed, the lumen would have been totally occluded. That artery enlargement is a consequence of plaque formation is indicated by the fact that in any given artery segment lumen cross-sectional area is often similar for involved and uninvolved segments. Enlargement usually occurs only where plaques are forming.

B. Diagram of artery enlargement with plaque formation based on a study of the human left main coronary artery [18]. Although plaque formation may be arrested at any stage, lumen stenosis appears to be evident on the average when 40% or more of the potential lumen area (as defined by the area encompassed by internal elastic lamina), is occupied by plaque. Plaque enlargement is mainly associated with outward bulging of the artery wall beneath the lesion. (Adapted from Glagov and coworkers [18]; with permission.)

FIGURE 2-11. The features of compensatory modeling of an artery during plaque development. When plaques are not complicated by ulceration or thrombosis, lumen contour remains regular and round or slightly oval, tending to preserve flow stability. The lesion tends to be sequestered to the "outside" of the artery by the fibrous cap on the lumen side and by the outward bulge because of erosion of the media and reactive fibrosis beneath the plaque. Finally, enlargement during atherogenesis tends to preserve lumen cross-sectional area. Although erosion of the media beneath the plaque appears to be the principal basis for the outward bulge and the preservation of lumen cross-sectional area and near-circular lumen contour, it is also possible that episodic narrowing of the lumen with plaque formation increases flow velocity and wall shear stress such that the intact artery wall opposite the plaque reacts by extension, as in the example shown in Fig. 2-10 and as described in Fig. 2-6 in association with the effect of high flow resulting from an arteriovenous fistula. This effect may contribute to the compensatory enlargement response. The two possible bases for enlargement are not mutually exclusive but the erosion-outward bulging effect appears to be the predominant determinant.

A. LIKELY ATEROGENIC (METABOLIC) DETERMINANTS OF PLAQUE MODELING

- Episodic progression, regression, disruption, healing, and compensatory reactions
- Age of onset; individual susceptibility
- Changes in lifestyle (diet, smoking, exercise)
- Superimposition of hypertension, diabetes mellitus

B. LIKELY HEMODYNAMIC (MECHANICAL) DETERMINANTS OF PLAQUE MODELING

- Local differences in hemodynamic risk
- Individual differences in hemodynamic risk
- Individual differences in tissue responses to physical stresses
- Changing mechanical properties of plaque
- Changing hemodynamics as plaques enlarge
FIGURE 2-13. At the histologic level, the features of acute or subacute disruption of plaque organization, which indicates underlying plaque instability include: 1) erosion of the fibrous cap (FC) with or without an associated inflammatory cellular infiltrate or thrombus deposition; 2) the presence of fissuring or ulceration with or without thrombus deposition; 3) the presence of manifest hemorrhage or hematoma within the plaque, due principally to dissection of blood into the plaque by a focal surface disruption (the presence of clusters of siderophages within the plaque suggests a previous hemorrhage); 4) secondary lesion formation on an older stratified plaque as indicated by foam cell and lipid core (LC) accumulations (see Fig. 2-14A) or focal inflammatory cell clusters within an underlying apparently stable plaque; and 5) the juxtaposition of regions of presumably different composition and elastic modulus associated with the above features and including the proximity of the LC and possibly of calcification to the lumen (L) surface. These findings often correspond to foci of plaque disruption.

Shown are sections of advanced plaques with complicating foci of fissuring and disruption obtained from endarterectomy specimens removed at surgery. A, Section from the sinus region of a carotid bifurcation. B, Section from the anterior descending coronary artery; arrows indicate the disruption or fissure in each case. In both sections the FC is thinned, eroded, and disrupted in close association with an erupting LC. C, The FC of a carotid endarterectomy specimen is focally eroded in association with a marked inflammatory exudate (IE). (Part A adapted from Glagov and coworkers [6]; parts B and C adapted from Glagov and coworkers [5]; with permission.)

FIGURE 2-14. A, Section of a carotid endarterectomy specimen in which blood and fibrin are noted in the interstices of a disrupted calcific deposit (asterisks) located immediately below the disrupted fibrous cap (FC) under the interrupted endothelial surface [6]; arrow indicates disruption. (continued)
is characteristic of well-organized thrombi. A fine fibrous cap-like intimal limiting structure has formed at the lumen surface (arrows), indicating the degree to which thrombi may be incorporated into the plaque and modeled in keeping with general features of plaque architecture. (Part A adapted from Glagov and coworkers [6]; parts B and C adapted from Glagov and coworkers [5]; with permission.)

**FIGURE 2-15.** Suggested clarification of the terms "complex" and "complicated" as applied to atherosclerotic plaques. Although complex plaques tend to become complicated it is useful to distinguish between complexity and complication.

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**CLARIFICATION OF COMPLEX AND COMPLICATED PLAQUES**

**Complex**
- Variety of morphologies
- Fibrosis, calcification
- Necrotic center, fibrous cap
- Cellular diversity
- Multiphasic architecture

**Complicated**
- Evidence of disruption
- Ulceration, thrombosis, hemorrhage, inflammation

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**What determines the outcome?**

**Cell biology**
- Macrophages
- Proteolysis
- "Soft" plaque
- Dilation
- Stabilize

**Smooth muscle cells**
- Fibrogenesis
- "Hard" plaque
- Compensation
- Stabilize
- Stenosis
C. MORPHOLOGIC CORRELATES OF PLAQUE INTEGRITY: FEATURES IMPLYING RESISTANCE TO DISRUPTION

Uniform plaque fibrosis on cross-section
Circular, regular lumen contour
Demarcated fibrous cap of uniform thickness:
absence of focal erosions or inflammation

FIGURE 2-16. (continued) Also shown are the morphologic correlates of plaque integrity for resistance to disruption (C) and for features associated with disruption (D).

D. MORPHOLOGIC CORRELATES OF PLAQUE INTEGRITY: FEATURES ASSOCIATED WITH DISRUPTION

Large plaque with marked stenosis
Juxtaposed regions of contrasting composition:
Calcification, lipid pools, fibrosis,
cellularity, hematomas
Lumen irregularities and asymmetries:
Thromboses, cavitations
Focal fibrous cap thinning or defects:
Erosions and inflammation; neoformation of atherosclerosis within, upon, or beneath fibrous caps or at lumen surface
Close proximity to fibrous cap or lumen surface of lipid pools and/or calcification

MORPHOLOGIC PREDICTORS OF RESTENOSIS

FIGURE 2-17. Direct interventions on occlusive stenosing plaques, by means of such procedures as angioplasty or atherectomy, result in plaque disruption, fragmentation, hemorrhage, and thrombus formation. A, Typical plaque disruptions associated with angioplasty [20]. The sections were taken from a superficial femoral artery in which a stenotic lesion was dilated 1 month earlier. In the proximal region of the plaque (left), a thrombus (T) occludes the lumen. The plaque is fractured and separated from the wall in one sector (arrow). An adaptive intimal proliferative reaction (IT) is noted. A distal region of the plaque (right) shows multiple fracture disruptions as well as separation from the media (arrows). Enlargement of the effective lumen cross-sectional area is frequently achieved initially only to eventuate in reocclusion or restenosis after a few months in 30% to 50% of patients. B, The restenosing intimal hyperplasia (IH) [7] consists largely of smooth muscle cells in an abundant matrix with little distinct evidence of structural organization such as cell orientation or the layered presence of prominent collagen or elastin matrix fibers; arrows indicate fractured plaque remnant. Attempts to inhibit or control this obliterative intimal hyperplastic reaction by agents that have been shown in animal models of vessel injury or cell culture to control smooth muscle cells migration or proliferation have not altered the incidence of the restenotic reaction to date [21]. (Part A adapted from Zarins and Glagov [20]; part B adapted from Waller and coworkers [7]; with permission.)
Differences in histologic appearance between vessels that have become obstructed by intimal hyperplasia and those that have remained patent are under investigation. In contrast to vessels that re-occlude, the intimas of arteries that have undergone angioplasty but have not re-occluded contain intimal thickenings consisting of smooth muscle cells that are usually oriented in a common direction and are associated with less abundant matrix in relation to cell content, but often with well-formed layered collagen and elastin fibers. On morphologic grounds, the intimal reaction in arteries in which treated lesions have not restenosed appears to have differentiated into nonatherosclerotic intimal fibrocellular hyperplasia, a compact layered tissue resembling artery wall, whereas the intimal hyperplasia reaction that proceeds to occlusion has few if any of the microanatomic features that connote artery wall differentiation. It would thus appear that the modeling responses that induce adaptive intimal proliferation have not been able to re-establish baseline values of wall shear or tensile stress and, therefore, continue to occlusion of the lumen [8]. In the event that baseline values of the relevant mechanical stresses are re-established before total occlusion, the intimal reaction would be expected to stabilize and the lumen to remain patent. Waller et al. [7] studied samples of post-angioplasty arteries at postmortem examination.

A, Site of restenosis by intimal hyperplasia (IH) in a coronary artery of a patient 3 months after angioplasty (top). The occlusive intimal reaction is characteristic of restenosing IH. The arrowheads mark the remnants of the underlying plaque. Coronary artery section at an angioplasty site of another patient in whom restenosis did not occur over a similar time interval (bottom). The intimal deposit consists of well-differentiated intimal fibrocellular hypertrophic tissue (IFH) and the lumen (L) is entirely patent. B, Higher magnification views of the characteristic appearances of IH (described above), the proliferative cellular reactive phase without definite cellular or matrix fiber orientation (top), and IFH, the differentiated stabilized reaction in which both cells and formed matrix fibers are oriented (bottom) [8]. (Part A adapted from Waller and coworkers [7]; part B adapted from Glagov [8], with permission.)
REFERENCES


