Some years ago, this journal published three Scientific Statements, in which the American Heart Association’s (AHA’s) Committee on Vascular Lesions had compiled much of what is known about the composition and structure of human atherosclerotic lesions and about arterial sites at which they develop. The known facts about the composition and structure of human atherosclerotic lesions and about arterial sites at which they develop.1–3 The Committee on Vascular Lesions had compiled much of what is available in clinical practice.

A priority, not least because of the urgent need for histological data, the Committee felt obligated to recommend use of a standard numerical nomenclature of precisely defined lesion types to replace a variety of duplicate and vague terms. The provision of an up-to-date histological classification of lesions was perceived as a priority, not least because of the urgent need for histological “templates” for images of lesions that were being obtained with a state-of-the-art histological methods and with the use of a standard numerical nomenclature of precisely defined lesion types to replace a variety of duplicate and vague terms. The provision of an up-to-date histological classification of lesions was thought to be timely and appropriate. Several autopsy studies in which state-of-the-art histological methods were used had just thrown new light on the compositions of lesions and on the diversity of mechanisms whereby they developed. After reviewing the new data, the Committee felt obligated to recommend use of a standard numerical nomenclature of precisely defined lesion types to replace a variety of duplicate and vague terms. The provision of an up-to-date histological classification of lesions was perceived as a priority, not least because of the urgent need for histological “templates” for images of lesions that were being obtained with a variety of invasive and noninvasive techniques that had become available in clinical practice.

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The AHA-recommended classification had been originally developed and used to convey the results of an inquiry into the compositions of atherosclerotic lesions as they silently develop over much of a lifetime in a population. In the accompanying article in this issue, Virmani and colleagues suggest terms for lesions that, in their studies of sudden death, they found preferable to a numerical classification.

In this Commentary, some issues that regard the numerical classification are addressed and, it is hoped, clarified. The issues include the relation between specific numbered lesion types and the development of clinical manifestations, the nature of the difference between lesion types IV and V, and the existence of more than one sequence in lesion progression and provision for this in the numerical classification.

Except for lesion types I through III, which are always small and clinically silent, there is no certain correlation between a lesion’s composition and size on one hand and the degree of lumen obstruction and clinical manifestations on the other. Thus, either of lesion types IV through VI may obstruct the lumen of a medium-size artery to the point of producing a clinical event, even a fatal one, or lesions of the same histologies may exist without significantly obstructing the lumen.

Numerous pathological studies indicate that clinical manifestations and fatal outcomes are most often associated with processes included under the type VI lesion (although even these processes may remain silent). The criteria for the type VI histology include one or more of surface defect, hematoma, and thrombosis. The three processes are often interrelated, although sometimes only one or two are present. For example, a fissure may produce hematoma but little or no superimposed thrombus; occlusive thrombi may form on a surface lacking an apparent defect; ulcerated lesions without much of either hematoma or thrombus may be present.

Clinical manifestations may emerge and fatal outcomes occur in the presence of lesions of type IV or V when these reach a size that is sufficiently obstructive. Lesions at the type IV or type V stage contain a lipid core, but they differ from each other in the derivation and thus, the nature of the fibromuscular layer that faces the lumen above the lipid core (the “cap” of the lesion).

In type IV lesions, the cap still constitutes only preexisting intima, which at highly susceptible artery sites is relatively thick (adaptive intimal thickening). Thus, depending on location in the vascular tree, the thickness of the cap of type IV lesions varies somewhat. However, cap composition is like that of normal intima. Because in type IV lesions the lesion cap represents the thickness of the intima at the affected intimal site, it is primarily the amount of lipid that is segregated at the core that determines the degree to which the lumen will be narrowed at this stage of development. In most people, a type IV lesion will not obstruct the lumen much, in part because of the vessel wall’s ability, at this stage, for outward expansion. However, when blood lipid levels are very high and a large amount of lipid accumulates quickly, this lesion type, too, may narrow a lumen.

Type V lesions, on the other hand, are defined as those in which major parts of the fibromuscular cap represent replacement of tissue disrupted by accumulated lipid and hematoma or organized thrombotic deposits. Cap portions or layers generated by disease and added to the preexisting part have a greater proportion of rough endoplasmic reticulum–rich smooth muscle cells. These cells do not follow the alignments usual of the normal intima (including adap-
lesion's position within the vascular tree and thus, the mechanical forces and the nature of the vessel wall at that point, determine, in large part, how a lesion is constituted. The characteristics of early lesions at highly susceptible sites lie in their greater content of lipid and macrophages and in the greater thickness of the intima at these sites. In the Figure, the type II changes are not subdivided into a and b types. Instead, the influence of highly versus moderately susceptible arterial sites is emphasized, and the propensity to development and progression is differentiated with the use of either thick or thin arrows.

Atherosclerotic lesions result from a variety of pathogenetic processes, including macrophage foam cell formation and death, accumulation of extracellular lipid, displacement and reduction of structural intercellular matrix and smooth muscle cells, generation of mineral deposits, chronic inflammation, neovascularization, disruptions of the lesion surface, and formation and transformation of hematoma and thrombus to fibromuscular tissue. One or the other process may dominate (or be lacking) in lesion development and progression. Some may continue for the duration of the disease while others are added at various stages. At later stages of lesion progression, many of the processes may run synchronously. But despite lesion diversity, the framework of principal morphologies and sequences shown in the Figure has been documented.

In the AHA-recommended classification including the updated form shown in the Figure, the preferred temporal sequence of typical histological morphologies is denoted with roman numerals. Steps in the development and progression of a disease are normally designated with numerals in medical writing. The AHA Committee had agreed that numerals that stood for strictly defined lesion types were preferable to the continued use of the large variety of traditional terms. To facilitate transition from existing gross pathological nomenclatures to the numerical one, frequently used terms that, though imprecise, seemed closest were appended to the precisely defined roman numerals.

Because preferred sequences do exist, the use of consecutive numerals is not only justified but, indeed, mandated. The arrows in the Figure indicate that after type IV has developed, the pathways to clinical disease vary. For example, a type IV lesion may develop type VI changes without first gaining much fibromuscular tissue (thus, not passing first through a type V stage), or a type IV or type V lesion may calcify (ie, become a type VII lesion) without first (or ever) developing type VI changes. Should additional developmental sequences be revealed, for example as the resolution of clinical imaging is perfected, a numerical scaffold would allow for additions and rearrangement.

### References


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