SURGICAL PATHOLOGY OF THE AORTA

L. Maximilian Buja, M.D.
Professor of Pathology and Laboratory Medicine
Distinguished Teaching Professor

UTHealth®
The University of Texas
Health Science Center at Houston

McGovern
Medical School

Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association For European Cardiovascular Pathology: I. **Inflammatory degenerative diseases** — nomenclature and diagnostic criteria

James R. Stone, Patrick Bruneval, Annalisa Angelini, Giovanni Bartoloni, Cristina Basso, Lubov Batoroeva, L. Maximilian Buja, Jagdish Butany, Giulia d'Amati, John T. Fallon, Adriana C. Gittenberger-de Groot, Rosa H. Gouveia, Marc K. Halushka, Karen L. Kelly, Ivana Kholova, Ornella Leone, Silvio H. Litovsky, Joseph J. Maleszewski, Dylan V. Miller, Richard N. Mitchell, Stephen D. Preston, Angela Pucci, Stanley J. Radio, E. Rene Rodriguez, Mary N. Sheppard, S. Kim Suvarna, Carmela D. Tan, Gaetano Thiene, Allard C. van der Wal, John P. Veinot.

Cardiovasc Pathol 2015;24:267-278

Consensus statement on surgical pathology of the aorta from the Society for Cardiovascular Pathology and the Association For European Cardiovascular Pathology: II. **Non-inflammatory degenerative diseases** — nomenclature and diagnostic criteria

Marc K. Halushka, Annalisa Angelini, Giovanni Bartoloni, Cristina Basso, Lubov Batoroeva, Patrick Bruneval, L. Maximilian Buja, Jagdish Butany, Giulia d'Amati, John T. Fallon, Patrick J. Gallagher, Adriana C. Gittenberger-de Groot, Rosa H. Gouveia, Ivana Kholova, Karen L. Kelly, Ornella Leone, Silvio H. Litovsky, Joseph J. Maleszewski, Dylan V. Miller, Richard N. Mitchell, Stephen D. Preston, Angela Pucci, Stanley J. Radio, E. Rene Rodriguez, Mary N. Sheppard, James R. Stone, S. Kim Suvarna, Carmela D. Tan, Gaetano Thiene, John P. Veinot, Allard C. van der Wal. Cardiovasc Pathol 2016;25:247-257

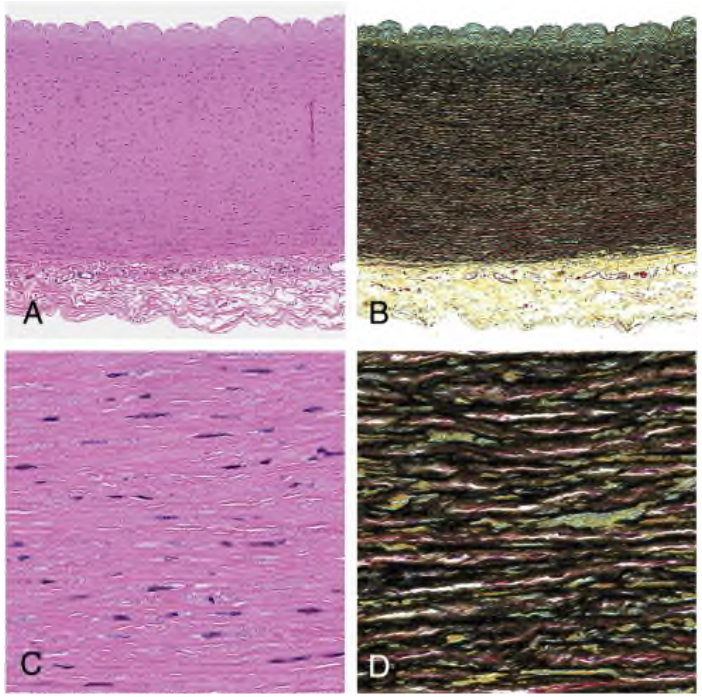


Fig. 1. Normal aorta, young adult. (A) Transverse section demonstrating all three aorta layers: intima at the luminal surface (top), media, and adventitia (50x, H&E). (B) On this stain highlighting elastic fibers, the intima is a distinctly paler layer tha...

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

Comparison of major diagnostic classes of inflammatory aortic diseases

Diagnostic class	Degree, location, and type of inflammation in relation to the degree of atherosclerosis present	Examples
Atherosclerosis	Routine for atherosclerosis	Atheroma, fibroatheroma, thin-cap fibroatheroma
Atherosclerosis with excessive inflammation	Uncommon for atherosclerosis but likely due to atherosclerosis	IAA, atherosclerosis with excessive neutrophilc inflammation
Aortitis/periaortitis	Cannot be accounted for by atherosclerosis.	Infectious aortitis/periaortitis, noninfectious aortitis/periaortitis

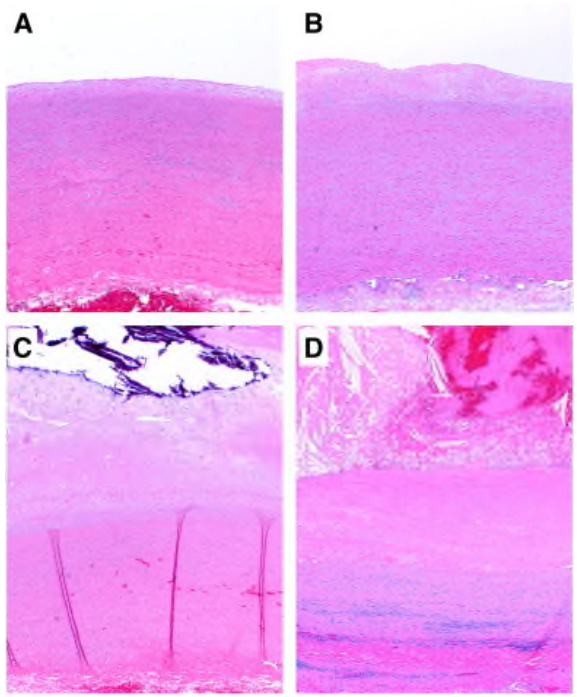


Fig. 1. Grades of Atherosclerosis. (A) No significant atherosclerosis. (B) Mild atherosclerosis. (C) Moderate calcific atherosclerosis. (D) Severe atherosclerosis with plaque disruption and surface thrombus.

Cardiovascular Pathology, Volume 24, Issue 5, 2015, 267–278

http://dx.doi.org/10.1016/j.carpath.2015.05.001

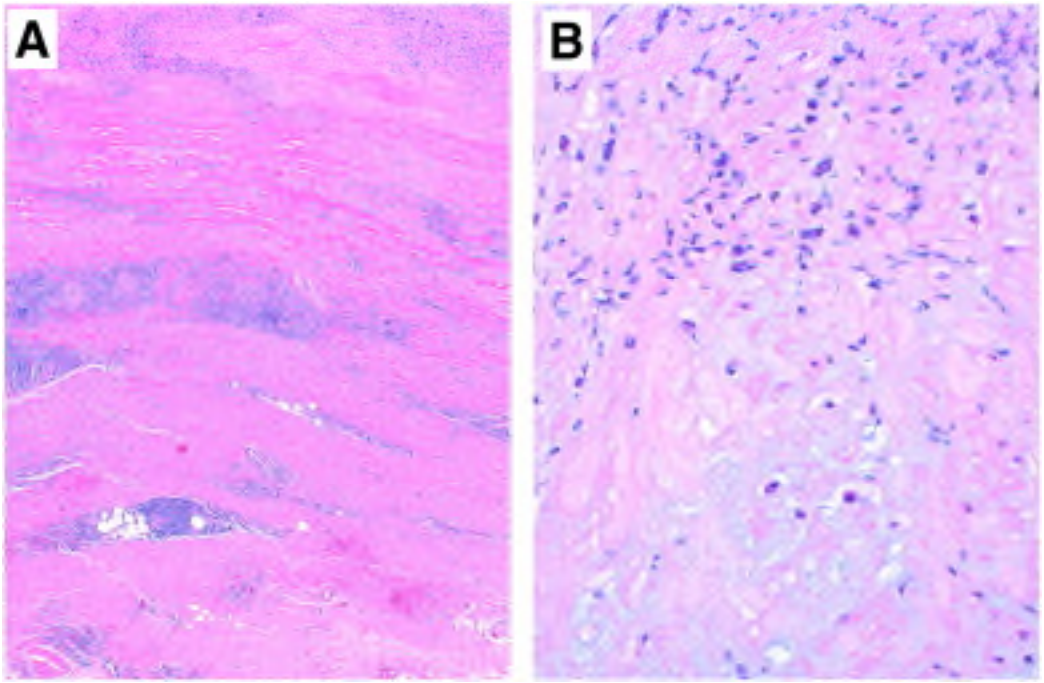


Fig. 2. Atherosclerosis with excessive inflammation. (A) IAA. (B) Atherosclerosis with excessive neutrophilic infiltrates.

Cardiovascular Pathology, Volume 24, Issue 5, 2015, 267–278

http://dx.doi.org/10.1016/j.carpath.2015.05.001

Inflammatory patterns in aortitis and periaortitis

Inflammatory pattern	Composition	Examples of specific systemic diseases
Granulomatous/giant cell pattern	Clusters of epithelioid macrophages with or without giant cells or compact/well-formed granulomas	Usually without compact/well-formed granulomas: GCA, GPA, EGPA Sometimes with compact/well-formed granulomas: Rheumatoid arthritis, Takayasu arteritis Usually with compact/well-formed granulomas: Sarcoidosis, mycobacterial and fungal infections
Lymphoplasmacytic pattern	Lymphocytes and plasma cells without a granulomatous component	IgG4-RD, lupus, AS, syphilitic aortitis, an undersampled granulomatous aortitis
Mixed inflammatory pattern	All/most inflammatory cell types without an overt granulomatous pattern	Cogan syndrome, Behçet's disease, relapsing polychondritis
Suppurative pattern	Neutrophilic abscesses with necrosis and cell debris	Staphylococcus, Streptococcus, Salmonella, Pseudomonas, and fungal infections

GCA-giant cell arteritis; GPA-granulomatosis with polyangitis (Wegener's granulomatosis) ;
EGPA- eosinophilic granulomatosis with polyangitis (Churg-Strauss)

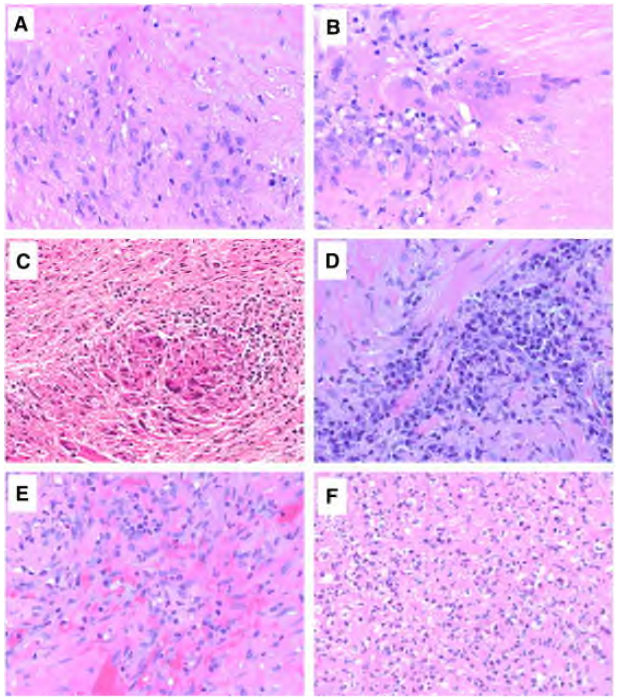


Figure. 3. Inflammatory patterns for aortitis and periaortitis. (A–C) The granulomatous/giant cell pattern is comprised of clusters of epithelioid macrophages (A), giant cells (B), and/or compact well-formed granulomas (C). (D) Lymphoplasmacytic pattern. (E) Mixed inflammatory pattern. (F) Suppurative pattern.

Cardiovascular Pathology, Volume 24, Issue 5, 2015, 267–278

http://dx.doi.org/10.1016/j.carpath.2015.05.001

Comparison of GCA and Takayasu arteritis

	GCA	Takayasu arteritis
Age	Usually > 50 years	Usually <50 years
Most severely afflicted race	Northern European	Asian
Arteries involved	Aorta, proximal branches, cranial arteries	Aorta, proximal branches, pulmonary arteries
Aortic layers involved	Inner media > outer media and adventitia	Outer media and adventitia > inner media
Compact granulomas	Usually absent	May be present

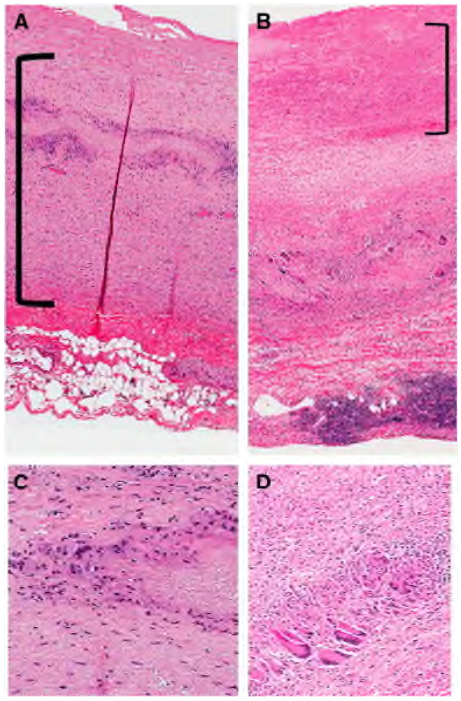


Fig. 4. Comparison of GCA with Takayasu Arteritis. The aortitis in GCA (A) tends to involve the inner half of the media most severely with less adventitial involvement and with usually no compact/well-formed granulomas. In contrast, the aortitis in Takayasu arteritis (B) tends to show more adventitial involvement and may contain compact/well-formed granulomas. At higher magnification, the aortitis in GCA contains epithelioid macrophages and often giant cells (C), while, in addition to these features, compact granulomas may also be present in Takayasu arteritis (D).

Cardiovascular Pathology, Volume 24, Issue 5, 2015, 267–278

http://dx.doi.org/10.1016/j.carpath.2015.05.001

Eponyms and historical nomenclature for selected histopathologic terms related to aortic medial degeneration

Current term	Historical term(s)
MEMA	Cystic medial degeneration, cystonecrosis, cystic medionecrosis, cystic medial necrosis, medial necrosis, mucoid degeneration, medionecrosis, medial degeneration
Elastic fiber fragmentation and/or loss	Elastin fragmentation
Smooth muscle cell nuclei loss	Medionecrosis, smooth muscle cell necrosis, laminar medial necrosis
Laminar medial collapse	Laminar medial necrosis, laminar necrosis

MEMA – mucoid extracellular matrix acculumulation

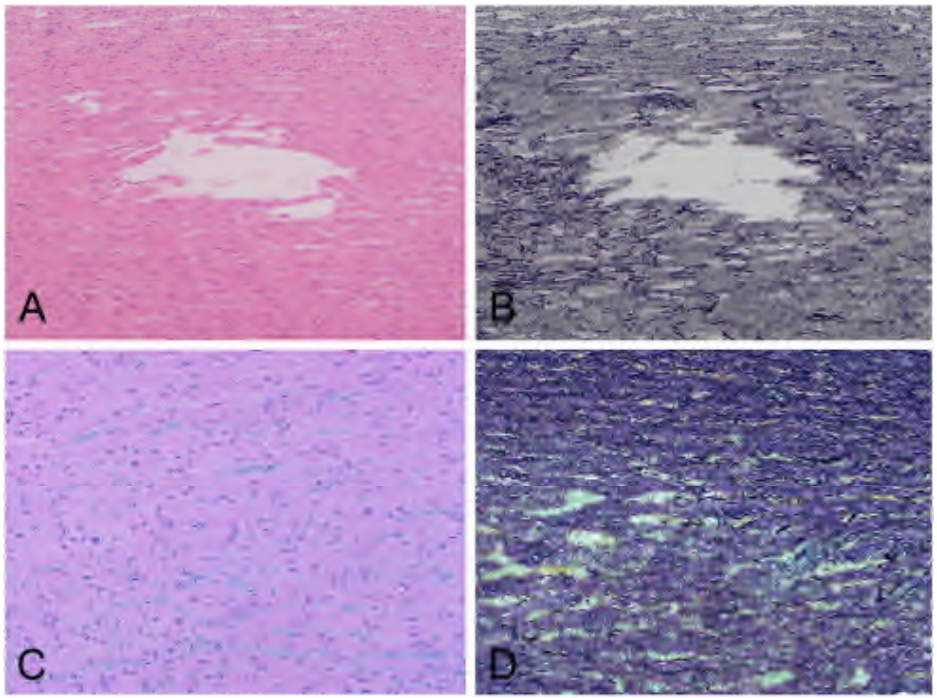


Fig. 2. MEMA. (A and B) Translamellar MEMA is a collection of mucoid material that breaks across lamellar units. (C and D) Intralamellar MEMA is an expansion of mucoid material that does not extend across the lamellar unit (H&E, Movat's pentachrome, 100x).

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

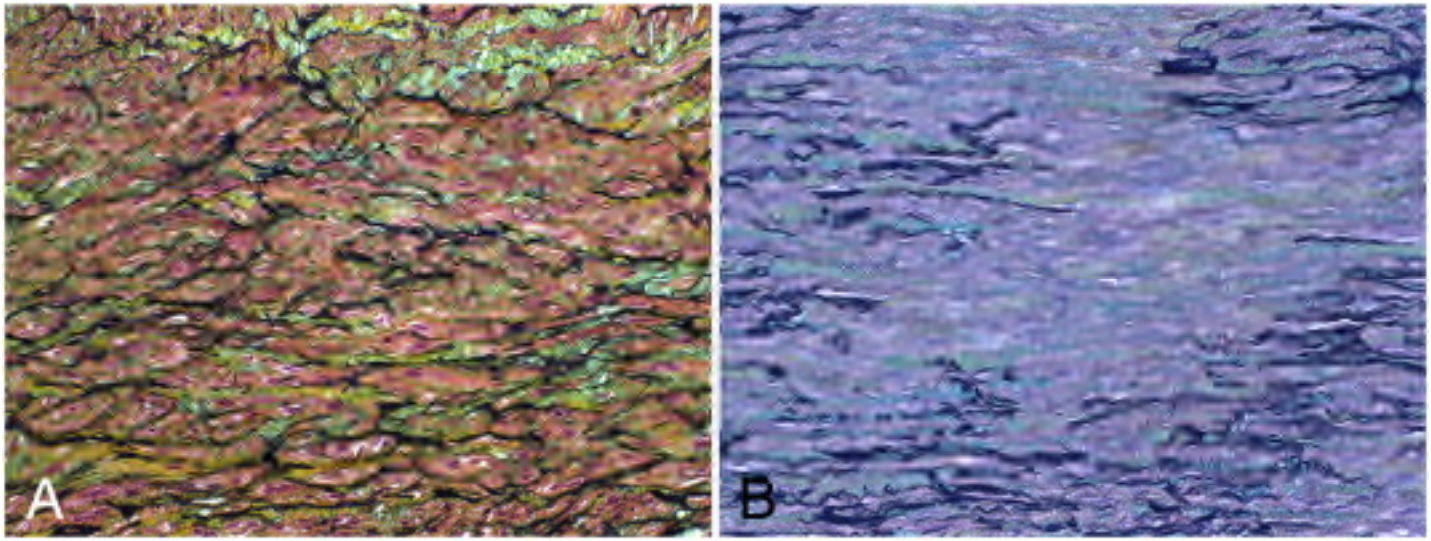


Fig. 3. Elastic fiber fragmentation and/or loss. (A) Fragmentation of the elastic fibers, where they no longer extend across the length of the image, is seen. (B) Complete loss of elastic fibers can occur (Movat's pentachrome, 400x).

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

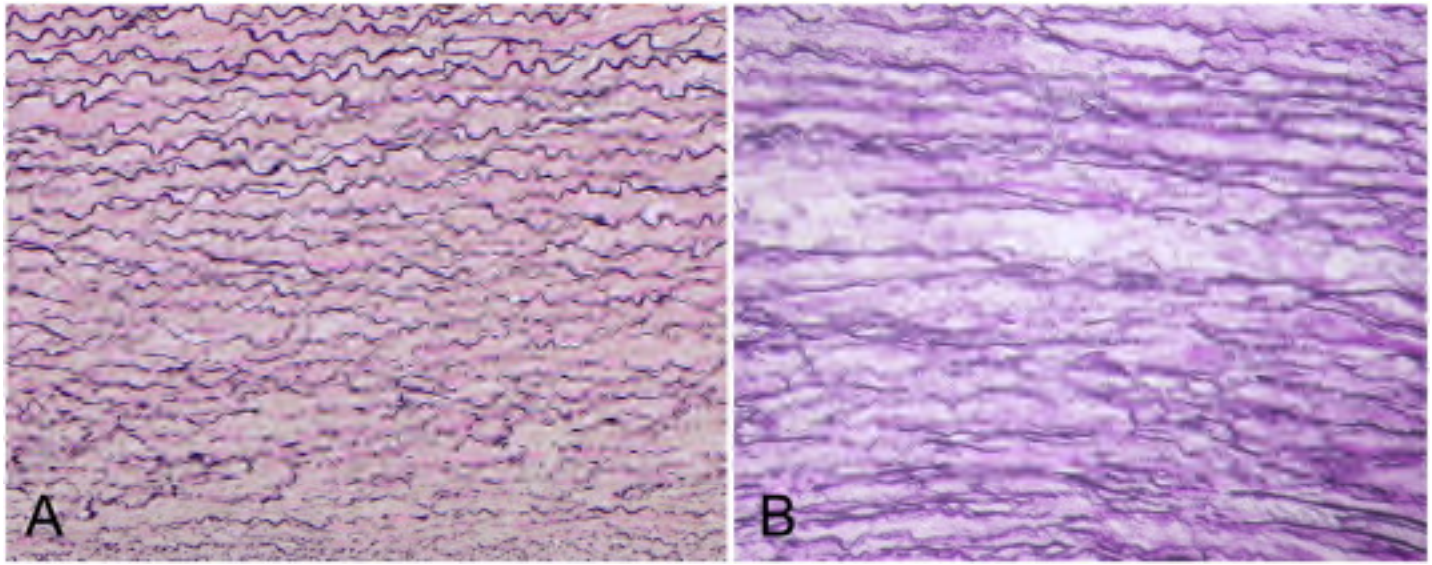


Fig. 4. Elastic fiber thinning. (A and B) In this entity, the elastic fibers are intact; however, they are thinned with a wide separation between them. This change would be seen in conjunction with an increase of extracellular matrix material (VVG, 20x).

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

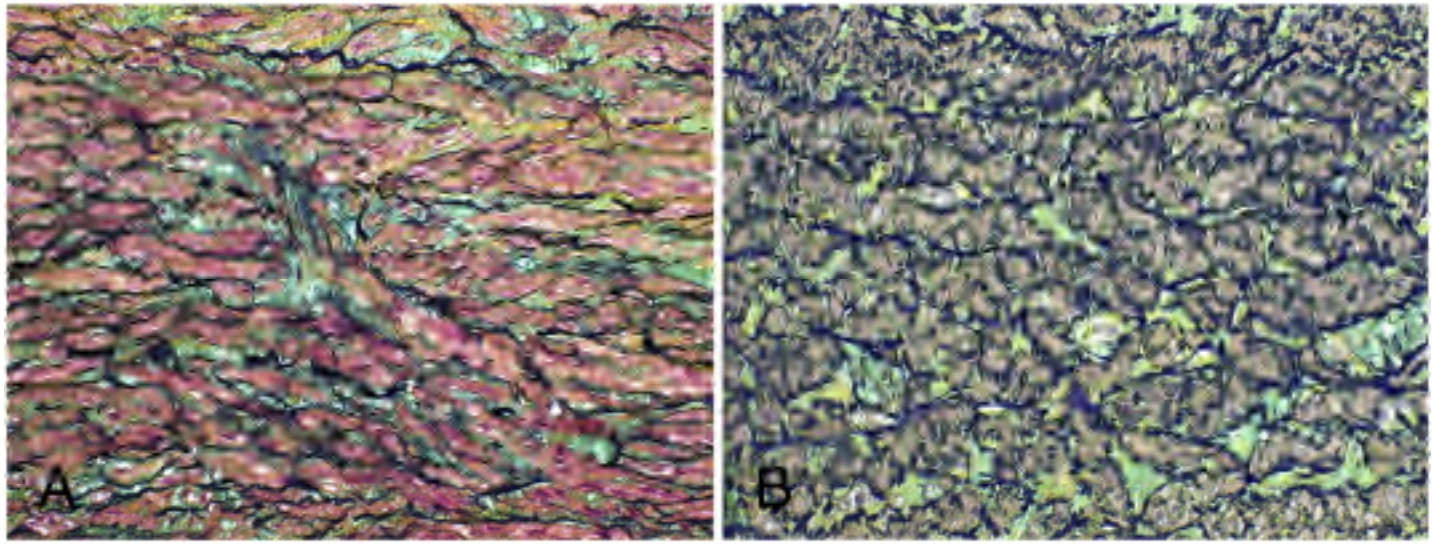


Fig. 5. Elastic fiber disorganization. At high power, there is a disruption in the organization of the wall, such that elastic fibers no longer adhere strictly to a circumferential course and can be oriented perpendicular to the lumen wall, which for these cases would be left to right. (A) Disorganization can be mild or (B) severe (Movat's pentachrome, 400x)

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

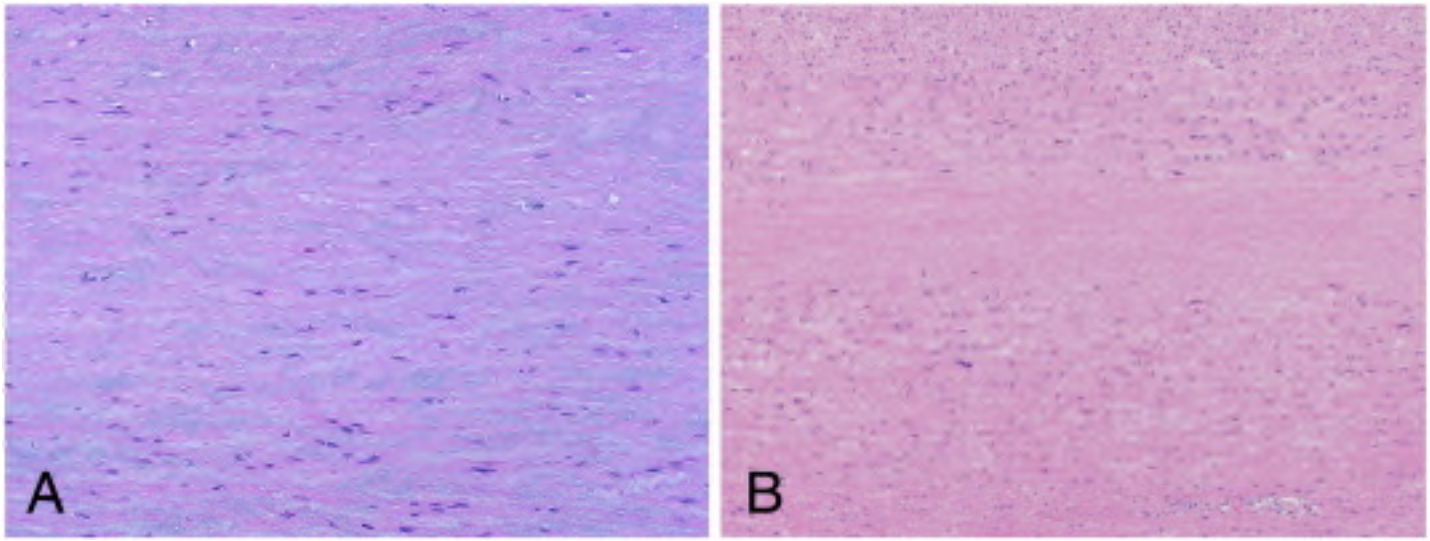


Fig. 6. Smooth muscle cell nuclei loss. Smooth muscle cells, as noted by their nuclei on an H&E stain, can be lost in a (A) patchy or (B) band-like fashion (H&E, 200 ×, 160 ×).

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

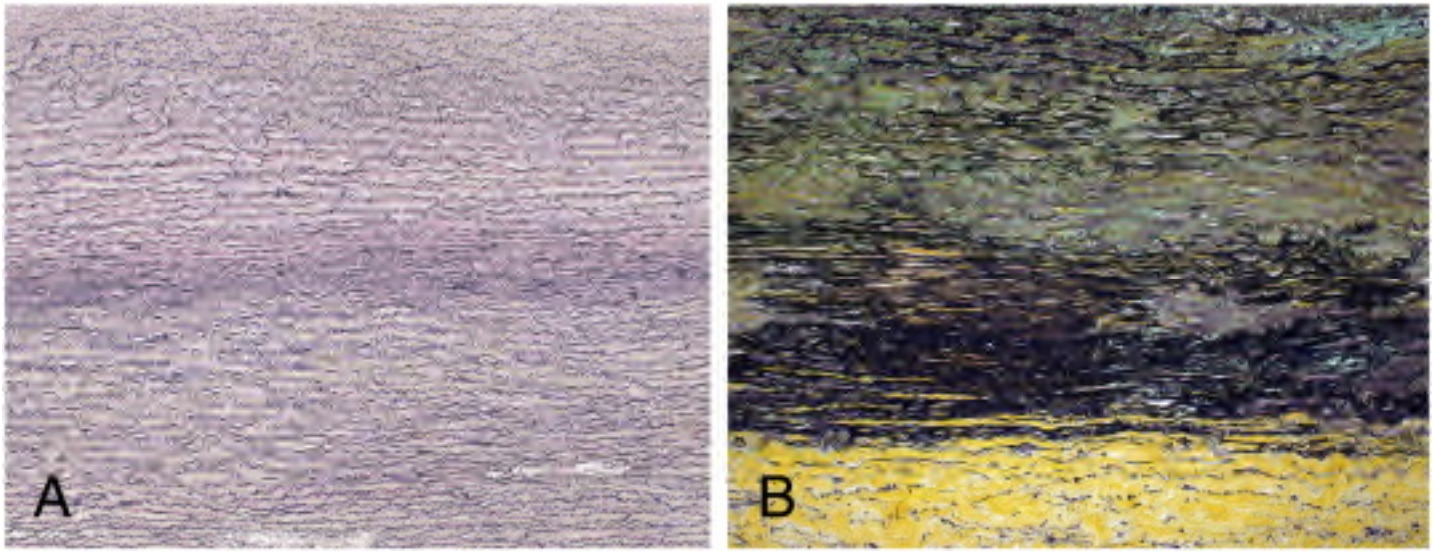


Fig. 7. Laminar medial collapse. In conjunction with a loss of smooth muscle cells in the lamellar units, the elastic fibers can collapse together. This banding pattern, only appreciated on an elastic stain, can be (A) thin or (B) dense (Movat's pentachrome, 100 ×, 40 ×)

,

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

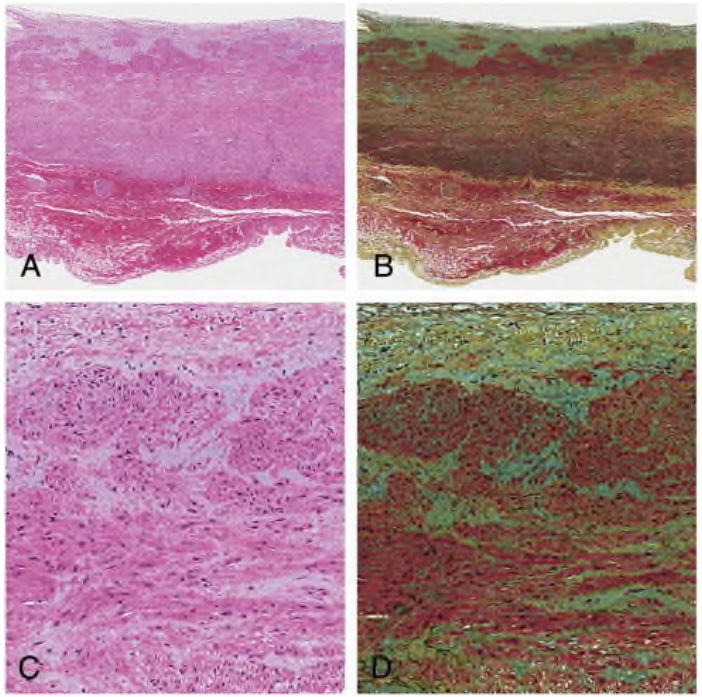


Fig. 8. Smooth muscle cell disorganization. (A) There is a conspicuous disarray of the bundles of smooth muscle cells throughout the media. (B) There is a slight thickening of the intima by mucopolysaccharide (blue-green ground substance)-rich extracellular matrix and small clusters of mucopolysaccharide accumulation in between the disorganized bundles of smooth muscle cells. Interstitial fibrosis (yellow) is also discernible at low magnification. There is a conspicuous decrease in the number of elastic lamellae. Organized lamellar units are practically absent. (C) At higher magnification, the disorganization of the smooth muscle cells is clearly shown. Note the orientation of the smooth muscle cells, ranging from transverse section of the smooth muscle cells to oblique to longitudinal orientation. Increased mucopolysaccharides (pale-blue areas) are present. (D) This high-power view shows disorganized smooth muscle cells, barely visible elastic laminae (black) as well as the abundant mucopolysaccharides in the interstitial space (H&E, Movat's pentachrome, 50 ×, 500 ×)

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

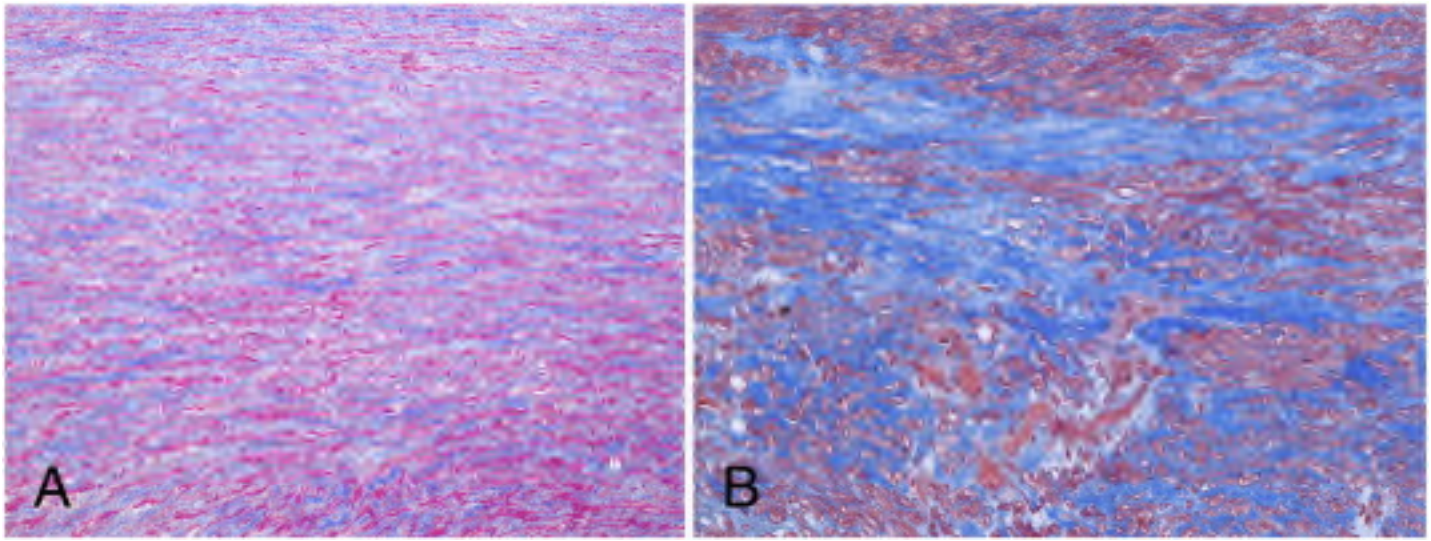


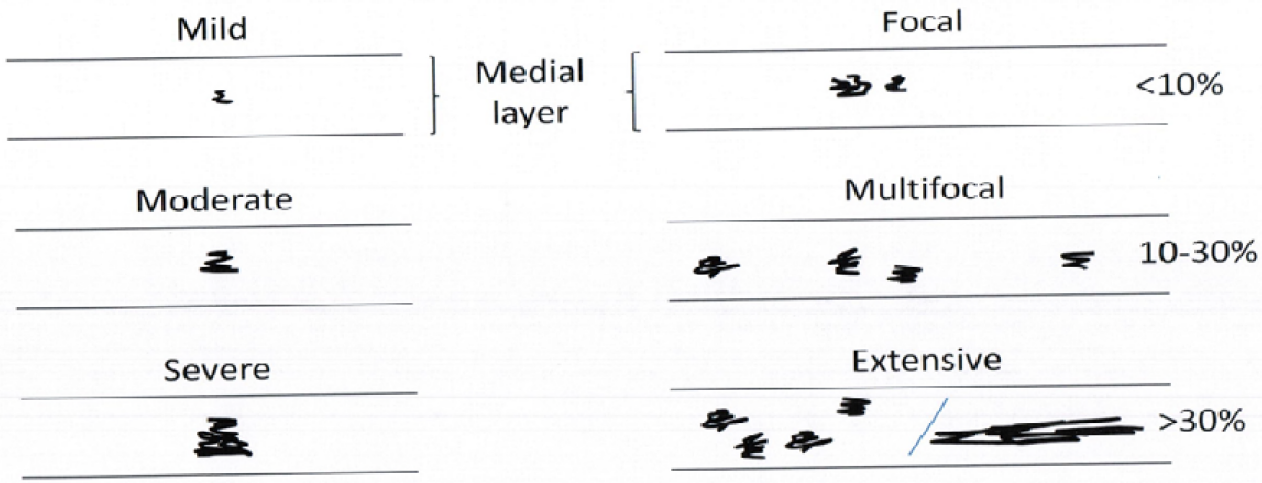
Fig. 9. Fig. 9. Medial fibrosis. Excess collagen can be noted in some specimens. (A) An intralamellar accumulation of collagen (royal blue) leaves the lamellar unit intact. (B) Translamellar fibrosis disrupts the lamellar unit and can be associated with smooth muscle cell disorganization (Masson's trichrome, 100 ×)

Cardiovascular Pathology, Volume 25, Issue 3, 2016, 247–257

http://dx.doi.org/10.1016/j.carpath.2016.03.002

Grading Scheme

Suppl. Fig. 8



Consensus grading scheme to evaluate aortic medial degeneration

MEMA-Intralamellar	MEMA-Translamellar	Elastic fiber fragmentation and/or loss	Smooth muscle cell nuclei loss	Laminar medial collapse	Overall Medial Degeneration
Absent	Absent	Absent	Absent	Absent	**NONE**
Mild Focal Multifocal		**Mild** Focal Multifocal	**Patchy** Rare	**Thin** Focal	**MILD**
Moderate Focal		**Moderate** Focal			
Mild Extensive	**Mild** Focal Multifocal Extensive	**Mild** Extensive	**Patchy** Frequent	**Thin** Multifocal Extensive	**MODERATE**
Mod. Multifocal	**Mod.** Focal Multifocal Extensive	**Mod.** Multifocal			
Sev. Focal	**Sev.** Focal	**Sev.** Focal	**Band-like** Frequent	**Dense** Focal	
Moderate Extensive	**Moderate** Extensive	**Moderate** Extensive	**Patchy** Extensive	**Dense** Multifocal Extensive	**SEVERE**
Severe Multifocal Extensive	**Severe** Multifocal Extensive	**Severe** Multifocal Extensive	**Band-like** Extensive		

MEMA – mucoid extracellular matrix accumulation


UTHealth
The University of Texas
Health Science Center at Houston
McGovern
Medical School

Eponyms and historical nomenclature for selected inflammatory aortic diseases

Disease	Eponyms and historical nomenclature
GCA	Horton's disease, cranial arteritis, giant cell aortitis, granulomatous arteritis, polymyalgia arteritis, temporal arteritis
Takayasu arteritis	Aortic arch syndrome, idiopathic arteritis, Martorell syndrome, nonspecific aortoarteritis, obliterative brachiocephalic arteritis, occlusive thromboaortopathy, panaortitis or aortitis syndrome, pulseless disease, reversed coarctation, Takayasu's disease, Takayasu syndrome, young female arteritis
GPA	Wegener's granulomatosis, pathergic granulomatosis, ANCA-associated granulomatous vasculitis
EGPA	Churg Strauss syndrome, allergic granulomatous vasculitis
Behçet's disease	Adamantiades–Behçet's disease, Behçet's syndrome, Silk Road disease

GCA-giant cell arteritis; GPA-granulomatosis with polyangitis (Wegener's granulomatosis) ; EGPA-eosinophilic granulomatosis with polyangitis (Churg-Strauss)

Grading atherosclerosis in surgically resected segments of aorta

Grade/qualifier	Gross	Histology
No significant atherosclerosis	Normal or fatty streaks	Intimal thickening/hyperplasia Scattered intimal foam cells and lymphocytes
Mild atherosclerosis	Raised plaques	Extracellular lipid deposition without fibrosis (AHA grade III/IV [8,9]) Minimal to no destruction or loss of media
Moderate atherosclerosis	Raised or confluent plaques	Extracellular lipid deposition with fibrosis (AHA grade V and above [9]) Destruction or loss of less than 1/3 of the media thickness
Severe atherosclerosis	Raised or confluent plaques	Extracellular lipid deposition with fibrosis (AHA grade V and above [9]) Destruction or loss of 1/3 or more of the media thickness
Atherosclerosis with plaque disruption and surface thrombus	Ulcerated plaque with surface thrombus	Atherosclerotic plaque (AHA grade III and above [8,9]) with surface disruption and surface thrombus
Calcific atherosclerosis	Firm calcified plaque	Atherosclerotic plaque (AHA grade III and above [8,9]) with calcification.

Risk factors and histologic changes seen in ascending aortic aneurysms in the aged

Process	Associated risk factors	Associated histologic findings*
Aging	Smoking, hypertension, hypercholesterolemia, history of other aneurysms	MD++, MEMA-T+, SMCL+++, LMC++, EFF+, EFD+

Key: *: “+” denotes frequency of description in the literature. MD: Medial degeneration; MEMA-T: Translamellar MEMA; SMCL: Smooth muscle cell nuclei loss; LMC: Laminar medial collapse; EFF: Elastic fiber fragmentation and loss; EFD: Elastic fiber disorganization.

Syndromic forms of ascending aortic aneurysm

Syndrome or disorder	Mutated gene	Associated phenotype	Associated histologic findings**
MFS	FBN1	Pectus excavatum, arachnodactyly, tall stature, lens ectopia, mitral valve prolapse	MD+++, MEMA-T+++, SMCL+, EFF+++
Vascular Ehlers-Danlos (vEDS/EDS-IV)	COL3A1	Thin skin with visible veins, easy bruising, visceral rupture, thin pinched nose, thin lips, prominent ears	MD+, MEMA-T+
LDS	TGFBR1 TGFBR2TGFB2SMAD3	Hypertelorism, wide/bifid uvula, cleft palate, craniosynostosis, visceral rupture, easy bruising	MD+++, MEMA-I+++, MEMA-T+, EFF+++, EFD+
Turner syndrome (TS)	Monosomy X	Female sex, webbed-neck, short stature, lymphedema	MD++, MEMA-T+++
Arterial tortuosity syndrome (ATS)	SLC2A10	Extreme vascular tortuosity, dolicocephaly, malar hypoplasia, joint laxity	MD++, EFF+++
Shprintzen-Goldberg (SG)	SKI	Features of MFS, LDS+mental retardation, severe hypotonia	
Autosomal dominant polycystic kidney disease (ADPKD)	PKD1	Renal cysts, renal failure, saccular intracranial aneurysms	MEMA+
FTAAD	MYH11†	Patent ductus arteriosus	MD++, EFF++
	ACTA2†	Moyamoya, livido reticularis	

MD: Medial degeneration; T: translamellar, I: intralamellar; EFF: Elastic fiber fragmentation and/or loss; EFD: Elastic fiber disorganization; SMCL: Smooth muscle cell nuclei loss; LMC: Laminar medial collapse

Syndromic forms of ascending aortic aneurysm

- Key: **: “+” to “+++” represents frequency of description in the literature.
- FBN1: Fibrillin 1; COL3A1: Collagen 3A1; TGFBR1: Transforming growth factor beta receptor 1; TGFBR2: Transforming growth factor beta receptor 2; TGFB2: Transforming growth factor beta 2; SMAD3: Mothers against DPP homolog 3; SLC2A10: Glucose transporter 10; SKI: SKI protooncogene; PKD1: Polycystic kidney disease 1; MYH11: Myosin heavy chain 11; ACTA2: Actin, alpha 2, smooth muscle; MD: Medial degeneration; T: translamellar, I: intralamellar; EFF: Elastic fiber fragmentation and/or loss; EFD: Elastic fiber disorganization; SMCL: Smooth muscle cell nuclei loss; LMC: Laminar medial collapse; “†” represents a minority of involved individuals.