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SPECIAL ARTICLE

2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides

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Introduction

The goals of the first International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides (CHCC1994) were to reach consensus on names for the most common forms of vasculitis and to construct a specific definition for each (1). An effort was made to adopt names and definitions that were already widely accepted. Because of advances in our understanding of vasculitis, another International Chapel Hill Consensus Conference (CHCC2012) was convened to improve the CHCC1994 nomenclature, change names and definitions as appropriate, and add important categories of vasculitis that were not included in CHCC1994. As in the original CHCC, the emphasis was on making changes only when justified. Herein we report the CHCC2012 revised nomenclature for vasculitides.

CHCC is a *nomenclature system* (nosology). It is neither a *classification system* that specifies what findings must be observed in a specific patient to classify that patient for clinical research nor a *diagnostic system* that directs clinical management (Table 1). A disease nomenclature system specifies the name that should be used for a specifically defined disease process. A nomenclature system is constructed based on the state of knowledge at the time it is developed, and specifies the name that

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Table 1. Explanation of terminology*

Term	Explanation	Example 1	Example 2
Diagnosis	The name of a disease	Acute myocardial infarction	Polyarteritis nodosa
Definition	Disease processes present in any patient that justify assignment of the diagnosis (name)	Ischemic coagulative necrosis of myocardial tissue	Necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules, and not associated with ANCA
Classification criteria	Observations that classify a specific patient into a standardized category for study	Any 2 of the following: symptoms of myocardial ischemia, rise/fall of cardiac troponin, EKG changes indicative of new ischemia, or imaging evidence of new loss of viable myocardium	Medium artery necrotizing arteritis seen on biopsy, negative ANCA, no MCLNS, and no evidence of glomerulonephritis
Diagnostic criteria	Observations that demonstrate or confidently predict the presence of the defining features of the disease in a specific patient	Any 2 of the following: symptoms of myocardial ischemia, rise/fall of cardiac troponin, EKG changes indicative of new ischemia, or imaging evidence of new loss of viable myocardium	Medium artery aneurysm seen on imaging or necrotizing arteritis seen on biopsy, negative ANCA, no MCLNS, and no evidence of glomerulonephritis

* The classification criteria and diagnostic criteria in the table are putative examples that are not derived from any validated study. Note that classification criteria and diagnostic criteria do not necessarily require microscopic confirmation of a pathologic process that is a defining feature of a disease (e.g., histologic confirmation of myocardial necrosis is not a required classification or diagnostic criterion for an actionable diagnosis of acute myocardial infarction). ANCA = antineutrophil cytoplasmic antibody; EKG = electrocardiography; MCLNS=mucocutaneous lymph node syndrome.

should be used when a patient fulfills a definition. A nomenclature system differs fundamentally from categorization systems that use identifiable classification criteria or diagnostic criteria to decide what disease definition is fulfilled by an actual patient. The name and definition of a disease are a given (i.e., specified in an accepted nomenclature system), whereas diagnostic criteria and classification criteria are features that can be observed in a patient so that the presence of the disease can be inferred from this evidence. CHCC2012 nomenclature and definitions do not provide diagnostic and classification criteria, but provide a framework for inferring and rigorously verifying such criteria.

The distinction between definitions and diagnostic or classification criteria must be clear in order to understand that histopathologic terms used in definitions do not mean that a diagnosis of the disease can be made only if the pathologic process is directly observed histologically in a tissue specimen (Table 1). For example, clinically apparent mononeuritis multiplex can be a diagnostic or classification criterion for vasculitis affecting peripheral nerves without the need for a nerve biopsy in which the vasculitis is observed histologically. Likewise, in the appropriate clinical context, cavitary lung lesions documented by imaging studies can be a sufficient surrogate criterion to conclude that a patient has necrotizing granulomatous pulmonary inflammation even if tissue has not been examined histologically.

As in many other settings, the use of eponyms is being phased out in the nomenclature of vasculitides. The use of each vasculitis eponym was carefully and vigorously deliberated to determine if a noneponymous replacement term was suitable. The participants took into account the fact that existing eponyms have value in the categorization of vasculitides and should not be replaced with nonspecific descriptive terms that lack pathophysiologic specificity. In general, eponyms were retained if there was inadequate understanding of the pathophysiology to propose an alternative name.

Most names for diseases are not sufficient literal descriptions but are idioms that require a deeper understanding of the meaning than is provided in the words alone. When descriptive terms are used in names, it is important to realize that these are convenient idiomatic expressions that refer to some distinctive feature of the disease, but the definition must be consulted for a detailed and specific description of the disease. For example, the term “giant cell arteritis,” if taken literally, could be applied to multiple different forms of vasculitis in which there are giant cells in the inflamed area; however, the definition of giant cell arteritis restricts the name to a single distinct category of vasculitis.

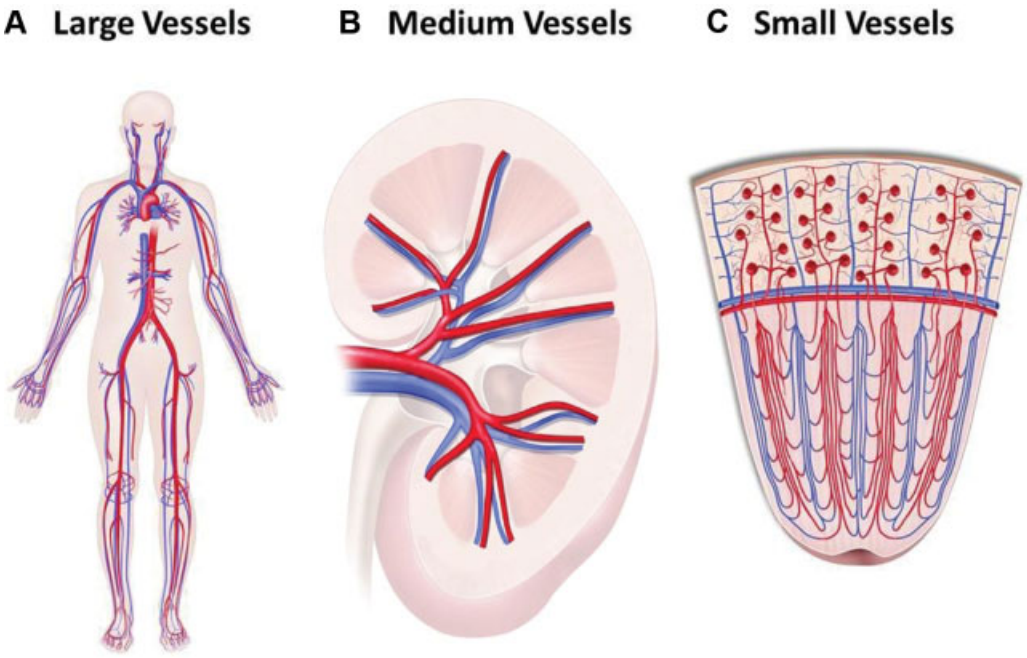

Figure 1. Types of vessels that are defined as large vessels (**A**), medium vessels (**B**), and small vessels (**C**) in the Chapel Hill Consensus Conference nomenclature system. The kidney is used to exemplify medium and small vessels. Large vessels are the aorta and its major branches and the analogous veins. Medium vessels are the main visceral arteries and veins and their initial branches. Small vessels are intraparenchymal arteries, arterioles, capillaries, venules, and veins.

Methods

A modified nominal group technique was used for CHCC2012, with one of the authors (JCJ) as moderator. The 28 participants from 12 countries had recognized expertise in vasculitis from multiple subspecialty perspectives including internal medicine, nephrology, otolaryngology, pathology, pulmonology, and rheumatology, with expertise in pediatric as well as adult disease represented. For 3 months prior to the May 2011 Chapel Hill meeting, ideas and proposals were deliberated in group e-mails received by all participants, and were discussed, clarified, and modified based on e-mail input from all participants. Priority was given to establishing definitions before coming to consensus on names. As the consensus evolved, each name and definition was voted on at least once by every member of the group. During the face-to-face meeting in Chapel Hill in May 2011, the group agreed that >80% consensus was needed to make a change in a CHCC1994 name or definition, or to add a new name or definition. The initial proposals considered in Chapel Hill were those for which there was >50% agreement in e-mail responses prior to the Chapel Hill meeting. The Chapel Hill meeting focused primarily on definitions rather than names, and all definitions that were adopted received >80% agreement by a show of hands. Decisions about the remaining definitions and names were made through online deliberations for 5 months after the meeting.

Each change or addition in a name or definition that arose from the group deliberations was posed to the group for a vote, followed by an additional 2-week online discussion period, and then another vote by all members. Votes were sent to the moderator and copied to all participants. Proposed changes or additions that received >80% agreement (i.e., 23 or more votes) were adopted. Proposed changes or additions that received <80% agreement were not adopted.

Major vasculitis categories

Vasculitis is inflammation of blood vessel walls. Inflammation of blood vessel walls at least at some time during the course of the disease is a shared defining feature of all categories of vasculitis. Some categories of vasculitis also have characteristic tissue injury unrelated to the vasculitis. Features that vary among different forms of vasculitis and can be used for categorization include etiology, pathogenesis, type of vessel affected,

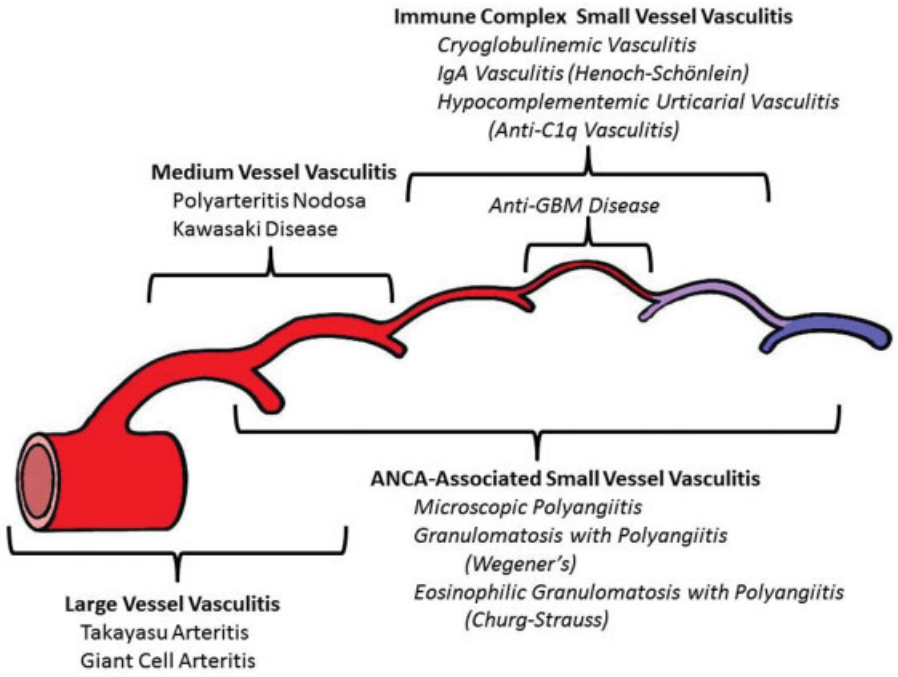

Figure 2. Distribution of vessel involvement by large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis. Note that there is substantial overlap with respect to arterial involvement, and an important concept is that all 3 major categories of vasculitis can affect any size artery. Large vessel vasculitis affects large arteries more often than other vasculitides. Medium vessel vasculitis predominantly affects medium arteries. Small vessel vasculitis predominantly affects small vessels, but medium arteries and veins may be affected, although immune complex small vessel vasculitis rarely affects arteries. Not shown is variable vessel vasculitis, which can affect any type of vessel, from aorta to veins. The diagram depicts (from left to right) aorta, large artery, medium artery, small artery/arteriole, capillary, venule, and vein. Anti-GBM = anti–glomerular basement membrane; ANCA = antineutrophil cytoplasmic antibody.

type of inflammation, favored organ distribution, clinical manifestations, genetic predispositions, and distinctive demographic characteristics (e.g., with respect to age, sex, race, ethnicity, and geographic distribution). Disease categorization based on etiology is often a preferred approach; however, this is not feasible for most vasculitides because the etiology is unknown. Thus, the CHCC nomenclature subdivides vasculitides based on combinations of features that separate different forms of vasculitis into definable categories.

Vasculitides can be broadly dichotomized into infectious vasculitis, known to be caused by direct invasion and proliferation of pathogens in vessel walls with resultant inflammation, versus noninfectious vasculitis, not known to be caused by direct vessel wall invasion by pathogens. Examples of infectious vasculitis include rickettsial vasculitis, syphilitic aortitis, and *Aspergillus* arteritis. CHCC addresses only vasculitis that is not known to be caused by invasion of vessel walls by pathogens; however, infection is indirectly involved in the pathogenesis of some of the vasculitides addressed. One of many examples is cryoglobulinemic vasculitis caused by an autoimmune response initiated by hepatitis C virus infection.

CHCC categorizes noninfectious vasculitis by integrating knowledge about etiology, pathogenesis, pathology, demographics, and clinical manifestations. The first categorization level is based on the predominant type of vessels involved, i.e., large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis (Figures 1 and 2, and Tables 2 and 3). These terms refer to vessels that differ not only in size, but also in structural and functional attributes. Differences among these categories of vessels correlate with function and susceptibility to specific variants of vasculitis. There are further distinctions within each vessel type, for example, capillaries in different organs (e.g., in brain, kidney, and lung) and different segments of the aorta (e.g., arch, thoracic, abdominal) have different biochemical and functional properties that make them vulnerable to different pathogenic mechanisms. Large vessel vasculitis affects large arteries more often than medium or small vessel vasculitis, medium vessel vasculitis affects predominantly medium arteries, and small vessel vasculitis

Table 2. Names for vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides

Large vessel vasculitis (LVV)
Takayasu arteritis (TAK)
Giant cell arteritis (GCA)
Medium vessel vasculitis (MVV)
Polyarteritis nodosa (PAN)
Kawasaki disease (KD)
Small vessel vasculitis (SVV)
Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV)
Microscopic polyangiitis (MPA)
Granulomatosis with polyangiitis (Wegener's) (GPA)
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)
Immune complex SVV
Anti–glomerular basement membrane (anti-GBM) disease
Cryoglobulinemic vasculitis (CV)
IgA vasculitis (Henoch-Schönlein) (IgAV)
Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)
Variable vessel vasculitis (VVV)
Behçet's disease (BD)
Cogan's syndrome (CS)
Single-organ vasculitis (SOV)
Cutaneous leukocytoclastic angiitis
Cutaneous arteritis
Primary central nervous system vasculitis
Isolated aortitis
Others
Vasculitis associated with systemic disease
Lupus vasculitis
Rheumatoid vasculitis
Sarcoid vasculitis
Others
Vasculitis associated with probable etiology
Hepatitis C virus–associated cryoglobulinemic vasculitis
Hepatitis B virus–associated vasculitis
Syphilis-associated aortitis
Drug-associated immune complex vasculitis
Drug-associated ANCA-associated vasculitis
Cancer-associated vasculitis
Others

affects predominantly small arteries and other small vessels, but a key concept is that vasculitis of all 3 major categories can affect any size artery. It is very important to realize that medium vessel vasculitis and even large vessel vasculitis can affect small arteries.

Large vessel vasculitis (LVV). LVV is vasculitis that affects large arteries more often than do other vasculitides. Takayasu arteritis and giant cell arteritis are the 2 major variants.

By the CHCC2012 definitions, all of the vessels shown in Figure 1A are large vessels except the most distal branches, which are medium vessels. All vessels not shown in Figure 1A are medium vessels or small vessels (not large vessels). No "large vessels" are inside organs including muscles, nerves, kidney, and skin.

Even though LVV affects large arteries much more often than does vasculitis of any other category, in a specific patient large arteries may not be the predominant type of vessel affected, because for every large artery that is affected there may be many smaller branches affected (especially medium arteries). How often this is the case is not known. For example, imaging and fluorescein angiography studies have shown that ocular involvement in giant cell arteritis may affect not only ophthalmic arteries, but also retinal arteries and multiple ciliary arteries (medium arteries), and even smaller branches of the ciliary and retinal arteries (small arteries) (2). Large artery injury may not be the cause of the most significant morbidity, as when blindness is due to injury to smaller branches of the ophthalmic arteries.

The histopathologic features of Takayasu arteritis and giant cell arteritis are indistinguishable. Both Takayasu arteritis and giant cell arteritis occur predominantly in females. The age at onset has been used by many but not all investigators to distinguish between giant cell arteritis and Takayasu arteritis. Some have suggested that they are the same disease. This remains unsettled, and CHCC2012 participants did not seek to resolve this important question. Lacking definitive evidence of shared causality, we have retained prior guidelines that consider Takayasu arteritis to be a disease predominantly of younger individuals and giant cell arteritis to be a disease predominantly of older individuals (3–5).

Takayasu arteritis (TAK). TAK is arteritis, often granulomatous, predominantly affecting the aorta and/or its major branches. Onset usually occurs before the age of 50 years, which is a major distinction from giant cell arteritis, whose onset usually occurs after age 50. As with all eponyms, there was considerable deliberation about whether to retain the eponym "Takayasu" or replace it with a noneponymous term such as "early-onset granulomatous aortitis/arteritis." The consensus was that, for now, this eponym is more effective than any alternative that was proposed.

Giant cell arteritis (GCA). GCA is arteritis, often granulomatous and usually affecting the aorta and/or its major branches, with a predilection for the branches of the carotid and vertebral arteries. Giant cells are frequently but not always observed in biopsy specimens from patients with active GCA. The term "temporal arteritis" is not a suitable alternative for GCA because not all patients have temporal artery involvement, and other categories of vasculitis can affect the temporal arteries.

Medium vessel vasculitis (MVV). MVV is vasculitis predominantly affecting medium arteries, defined as the main visceral arteries and their branches. Any size

Table 3. Definitions for vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides (CHCC2012)

CHCC2012 name	CHCC2012 definition
Large vessel vasculitis (LVV)	Vasculitis affecting large arteries more often than other vasculitides. Large arteries are the aorta and its major branches. Any size artery may be affected.
Takayasu arteritis (TAK)	Arteritis, often granulomatous, predominantly affecting the aorta and/or its major branches. Onset usually in patients younger than 50 years.
Giant cell arteritis (GCA)	Arteritis, often granulomatous, usually affecting the aorta and/or its major branches, with a predilection for the branches of the carotid and vertebral arteries. Often involves the temporal artery. Onset usually in patients older than 50 years and often associated with polymyalgia rheumatica.
Medium vessel vasculitis (MVV)	Vasculitis predominantly affecting medium arteries defined as the main visceral arteries and their branches. Any size artery may be affected. Inflammatory aneurysms and stenoses are common.
Polyarteritis nodosa (PAN)	Necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules, and not associated with antineutrophil cytoplasmic antibodies (ANCAs).
Kawasaki disease (KD)	Arteritis associated with the mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries. Coronary arteries are often involved. Aorta and large arteries may be involved. Usually occurs in infants and young children.
Small vessel vasculitis (SVV)	Vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries, and venules. Medium arteries and veins may be affected.
ANCA-associated vasculitis (AAV)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) ANCA or proteinase 3 (PR3) ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, e.g., MPO-ANCA, PR3-ANCA, ANCA-negative.
Microscopic polyangiitis (MPA)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.
Granulomatosis with polyangiitis (Wegener's) (GPA)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries and veins). Necrotizing glomerulonephritis is common.
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when glomerulonephritis is present.
Immune complex vasculitis	Vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries). Glomerulonephritis is frequent.
Anti–glomerular basement membrane (anti-GBM) disease	Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with GBM deposition of anti-GBM autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents.
Cryoglobulinemic vasculitis (CV)	Vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with serum cryoglobulins. Skin, glomeruli, and peripheral nerves are often involved.
IgA vasculitis (Henoch-Schönlein) (IgAV)	Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gastrointestinal tract, and frequently causes arthritis. Glomerulonephritis indistinguishable from IgA nephropathy may occur.
Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)	Vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (i.e., capillaries, venules, or arterioles), and associated with anti-C1q antibodies. Glomerulonephritis, arthritis, obstructive pulmonary disease, and ocular inflammation are common.
Variable vessel vasculitis (VVV)	Vasculitis with no predominant type of vessel involved that can affect vessels of any size (small, medium, and large) and type (arteries, veins, and capillaries).
Behçet's disease (BD)	Vasculitis occurring in patients with Behçet's disease that can affect arteries or veins. Behçet's disease is characterized by recurrent oral and/or genital aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal, and/or central nervous system inflammatory lesions. Small vessel vasculitis, thromboangiitis, thrombosis, arteritis, and arterial aneurysms may occur.
Cogan's syndrome (CS)	Vasculitis occurring in patients with Cogan's syndrome. Cogan's syndrome characterized by ocular inflammatory lesions, including interstitial keratitis, uveitis, and episcleritis, and inner ear disease, including sensorineural hearing loss and vestibular dysfunction. Vasculitic manifestations may include arteritis (affecting small, medium, or large arteries), aortitis, aortic aneurysms, and aortic and mitral valvulitis.

Table 3. *(Cont'd)*

CHCC2012 name	CHCC2012 definition	CHCC2012 name	CHCC2012 definition
Single-organ vasculitis (SOV)	Vasculitis in arteries or veins of any size in a single organ that has no features that indicate that it is a limited expression of a systemic vasculitis. The involved organ and vessel type should be included in the name (e.g., cutaneous small vessel vasculitis, testicular arteritis, central nervous system vasculitis). Vasculitis distribution may be unifocal or multifocal (diffuse) within an organ. Some patients originally diagnosed as having SOV will develop additional disease manifestations that warrant redefining the case as one of the systemic vasculitides (e.g., cutaneous arteritis later becoming systemic polyarteritis nodosa, etc.).	**Vasculitis associated with systemic disease**	Vasculitis that is associated with and may be secondary to (caused by) a systemic disease. The name (diagnosis) should have a prefix term specifying the systemic disease (e.g., rheumatoid vasculitis, lupus vasculitis, etc.).
		Vasculitis associated with probable etiology	Vasculitis that is associated with a probable specific etiology. The name (diagnosis) should have a prefix term specifying the association (e.g., hydralazine-associated microscopic polyangiitis, hepatitis B virus–associated vasculitis, hepatitis C virus–associated cryoglobulinemic vasculitis, etc.).

artery may be affected. Polyarteritis nodosa and Kawasaki disease are the major variants. The onset of inflammation in MVV is more acute and necrotizing than the onset of inflammation in LVV.

Polyarteritis nodosa (PAN). PAN is necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules, and not associated with antineutrophil cytoplasmic antibodies (ANCAs). In CHCC2012, the specification that ANCAs are not associated with PAN and the addition of a category for ANCA-associated vasculitis reflect advances in knowledge about ANCA since CHCC1994 (6,7). Although the role of ANCA in the pathogenesis of vasculitis has not been fully elucidated, many studies have confirmed that ANCA is a reliable marker for a clinically and pathologically distinct category of small vessel vasculitis (6), and that it is typically absent in patients with PAN (7). This is a useful discriminator, because PAN and ANCA-associated vasculitis can exhibit clinically and pathologically indistinguishable necrotizing arteritis of medium and small arteries.

Kawasaki disease (KD). KD is arteritis associated with the mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries. Coronary arteries are often involved; aorta and large arteries may be involved. KD usually occurs in infants and young children. As with TAK, the consensus was that, for now, the eponym "Kawasaki" is more effective than any alternative that was proposed, such as mucocutaneous lymph node syndrome arteritis.

Small vessel vasculitis (SVV). SVV is vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries, and venules. Medium arteries and veins may be affected. In essence, all intraparenchymal vessels are small vessels, with the exception of the initial penetrating branches of medium arteries (Figure 1B). Small biopsy specimens usually contain only small vessels, thus even the largest arteries in such specimens are small arteries. The 2 categories of SVV are characterized by a paucity of vessel wall immunoglobulin in one, and a prominence of vessel wall immunoglobulin in the other.

ANCA-associated vasculitis (AAV). AAV is necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries), associated with ANCA specific for myeloperoxidase (MPO-ANCA) or proteinase 3 (PR3-ANCA). A prefix should be added to the name to indicate ANCA reactivity, i.e., MPO-ANCA, PR3-ANCA, or ANCA-negative. Additional prefixes might become appropriate in the future if new clinically important ANCA specificities are discovered. ANCA-negative AAV is analogous to seronegative lupus or seronegative rheumatoid arthritis, and is used if the patient otherwise fulfills the definition for an AAV but has negative results on serologic testing for ANCA. Patients with ANCA-negative AAV may have ANCA that cannot be detected with current methods or may have ANCA of as-yet-undiscovered specificity, or pathogenic mechanisms that do not involve ANCA at all may be occurring.

The small number or lack of immune deposits in vessel walls that is characteristic of AAV differs from the moderate to marked vessel wall immune deposition that is characteristic of immune complex SVV. Although there are conceptual and practical difficulties in precisely establishing the break point, the presence of fewer versus more immune deposits distinguishes between AAV (with fewer immune deposits in vessel walls) and immune complex SVV (with more immune deposits in vessel walls). Antibodies binding to antigens appear to be a major initiator of pathogenic effector mechanisms

in both categories of vasculitis, but the exact mechanisms have not been fully elucidated.

The major clinicopathologic variants of AAV are microscopic polyangiitis, granulomatosis with polyangiitis (Wegener's), eosinophilic granulomatosis with polyangiitis (Churg-Strauss), and single-organ AAV (for example, renal-limited AAV).

Microscopic polyangiitis (MPA). MPA is necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Inflammation that is not centered on vessels, including granulomatous inflammation, is absent.

Granulomatosis with polyangiitis (Wegener's) (GPA). GPA is necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries, and veins). Necrotizing glomerulonephritis is common. Ocular vasculitis and pulmonary capillaritis with hemorrhage are frequent. Granulomatous and nongranulomatous extravascular inflammation are common. CHCC2012 adopted the recommendation of the American College of Rheumatology, the American Society of Nephrology, and the European League Against Rheumatism to replace "Wegener's granulomatosis" with "granulomatosis with polyangiitis (Wegener's)" (8–10).

Limited expressions of GPA occur, especially disease confined to the upper or lower respiratory tract (11), or the eye. These patients may have no identifiable evidence of systemic vasculitis, but when they exhibit clinical and pathologic changes identical to those seen in GPA respiratory tract involvement, and especially if they are ANCA positive, they should be included in the GPA category.

Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA). EGPA is eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels and associated with asthma and eosinophilia. Nasal polyps are common. ANCA is more frequent when glomerulonephritis is present.

The prominence of eosinophils in the blood and tissue is an essential feature of EGPA and thus is highlighted in the name. The eponym "Churg-Strauss syndrome" was replaced by "EGPA" in part to achieve nomenclature symmetry with MPA and GPA.

Limited expressions of EGPA confined to the upper or lower respiratory tract may occur. Many patients with otherwise typical EGPA do not have glomerulonephritis. Interestingly, only ~25% of patients with EGPA who have no renal disease are ANCA positive, whereas 75% with any renal disease and 100% with documented necrotizing glomerulonephritis have ANCA (12). Granulomatous and nongranulomatous extravascular inflammation, such as nongranulomatous eosinophil-rich inflammation of lungs, myocardium, and gastrointestinal tract, is common.

Immune complex small vessel vasculitis. Immune complex SVV is vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement, predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries). Glomerulonephritis is frequent. Arterial involvement is much less common in immune complex SVV compared to ANCA SVV.

When appropriate, immune complex vasculitis can be categorized as a vasculitis associated with probable etiologies (e.g., hepatitis C virus–associated cryoglobulinemic vasculitis) or as a vasculitis associated with systemic disease (e.g., lupus vasculitis or rheumatoid vasculitis).

Anti–glomerular basement membrane (anti-GBM) disease. Anti-GBM disease is vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with basement membrane deposition of anti–basement membrane autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents (13). "Anti-GBM disease" is a misnomer because anti-GBM antibodies are reactive not only with GBM but also with pulmonary alveolar capillary basement membranes; however, the use of "anti-GBM disease" is so conventional that the consensus was that this term should be retained. The eponym "Goodpasture's syndrome" has been used in the past for combined pulmonary and renal expression of anti-GBM disease.

Anti-GBM disease is categorized as an immune complex disease based on the in situ formation of immune complexes composed of autoantibodies bound to basement membrane in glomerular and pulmonary alveolar capillaries. Although the hemorrhagic pulmonary lesions often lack overt leukocyte infiltration, anti-GBM disease is a vasculitis because cellular and humoral inflammatory mechanisms are responsible for the injury (13). In addition, necrotizing anti-GBM glomerulonephritis is an overtly inflammatory process affecting glomerular capillaries and, although anti-GBM pulmonary disease often has little or no identifiable leukocyte

infiltration, conspicuous neutrophilic inflammation may occur in some cases of acute anti-GBM pulmonary hemorrhage (14).

Cryoglobulinemic vasculitis (CV). CV is vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with cryoglobulins in serum. Skin, glomeruli, and peripheral nerves are often involved. The term "idiopathic" or "essential" may be used as a prefix to indicate that the etiology of CV is unknown. As with other vasculitides, when the etiology is known, this can be designated in the diagnosis, e.g., hepatitis C–associated cryoglobulinemic vasculitis.

IgA vasculitis (Henoch-Schönlein) (IgAV). IgAV is vasculitis with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). IgAV often involves the skin and gastrointestinal tract and frequently causes arthritis. Glomerulonephritis indistinguishable from IgA nephropathy may occur. Any segment of the gastrointestinal tract can be affected, but small bowel involvement is most common.

The consensus to replace the eponym "Henoch-Schönlein purpura" with IgAV is based on the compelling body of literature indicating that abnormal IgA deposits in vessel walls are the defining pathophysiologic feature. In patients with either systemic IgAV or renal-limited IgA nephropathy (IgAN), IgA1 in serum and in tissue deposits has reduced terminal glycosylation in the hinge region (15). There also are emerging data suggesting that patients with IgAV and IgAN have circulating abnormally glycosylated IgA1, and possibly glycan-specific IgG antibodies that form IgA1–IgG anti-IgA1 immune complexes (16). IgG antibodies directed against the abnormal glycosylation putatively bind to IgA1 molecules and localize in vessel walls, causing inflammation.

As with other vasculitides, IgAV can occur as a single-organ vasculitis. Isolated cutaneous IgAV is analogous to IgAN without systemic disease. Patients with renal-limited IgAN or single-organ cutaneous IgAV may subsequently develop systemic IgAV. IgAV can be associated with and possibly caused by other diseases, such as liver disease, inflammatory bowel disease, and ankylosing spondylitis. The onset of symptomatic IgAV is often associated with an upper respiratory tract or gastrointestinal infection.

Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis). HUV (anti-C1q vasculitis) is vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (i.e., capillaries, venules, or arterioles), and associated with anti-C1q antibodies. Glomerulonephritis, arthritis, obstructive pulmonary disease, and ocular inflammation are common features. Anti-C1q antibodies are one of the most distinctive findings in HUV (17,18). Hypocomplementemia, and to a lesser extent urticaria, occur in other immune complex SVV, such as lupus vasculitis. Consideration was given to recommending the term "anti-C1q vasculitis" in preference to "HUV." Consensus was not reached to recommend this as the primary term, but there was agreement that the pathophysiologic link between anti-C1q and HUV was strong enough to at least introduce this term in parentheses with the more conventional "HUV."

Variable vessel vasculitis (VVV). VVV is vasculitis with no predominant type of vessel involved that can affect vessels of any size (small, medium, and large) and type (arteries, veins, and capillaries). Behçet's disease and Cogan's syndrome are the 2 examples included in CHCC2012. They are included as primary categories of vasculitis rather than vasculitis associated with a systemic disease, because of the frequency of vasculitis.

Behçet's disease (BD) vasculitis. BD vasculitis is vasculitis occurring in patients with BD that can affect arteries or veins. BD is characterized by recurrent oral and/or genital aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal, and/or central nervous system (CNS) inflammatory lesions. Small vessel vasculitis, arteritis, arterial aneurysms, and venous and arterial thromboangiitis and thrombosis may occur.

Cogan's syndrome (CS) vasculitis. CS vasculitis is vasculitis occurring in patients with CS, which is characterized by ocular inflammatory lesions, including interstitial keratitis, uveitis, and episcleritis, and inner ear disease, including sensorineural hearing loss and vestibular dysfunction. Vasculitic manifestations may include arteritis (affecting small, medium, or large arteries), aortitis, aortic aneurysms, and aortic and mitral valvulitis. The primary ocular vascular target for inflammation in CS is the small vessels in the vascularized layers of the anterior globe, i.e., from outer to inner: conjunctiva (conjunctivitis), episclera (episcleritis), sclera (scleritis), and uvea (uveitis). Inflamed small blood vessels invade the adjacent normally avascular corneal stroma and cause the very distinctive interstitial keratitis of CS.

Single-organ vasculitis (SOV). SOV is vasculitis in arteries or veins of any size in a single organ, with no features that indicate that it is a limited expression of a systemic vasculitis. The involved organ and vessel type should be included in the name (e.g., cutaneous small vessel vasculitis, testicular vasculitis, CNS vasculitis). Vasculitis distribution may be unifocal or multifocal (diffuse) within an organ or organ system. Some patients originally diagnosed as having SOV will develop additional disease manifestations that warrant reclassifying

the vasculitis as one of the systemic vasculitides (e.g., cutaneous arteritis later becoming systemic PAN).

If the features of a vasculitis that is confined to one organ indicate that it is a limited expression of one of the systemic vasculitides, this vasculitis should be considered a limited expression of that category of vasculitis rather than an independent SOV. Clinical, laboratory, and pathologic features are useful in distinguishing SOV from an isolated expression of systemic vasculitis (19). Concluding that an isolated vasculitis is a limited expression of a systemic vasculitis does not imply that the vasculitis will or will not subsequently evolve into systemic disease.

There is a distinctive form of CNS SOV (primary CNS vasculitis) that is not an isolated expression of a systemic vasculitis (20,21). As with other SOV, a diagnosis of primary CNS vasculitis requires determining that CNS vasculitis is not a component of a systemic vasculitis (e.g., GCA, BD, MPA, GPA, EGPA), caused by infection (e.g., syphilis), or associated with a systemic disease (e.g., lupus, sarcoidosis).

Primarily because there are no specific biomarkers for TAK and GCA, it is not possible to know if any or all examples of SOV aortitis are limited expressions of TAK or GCA. Isolated aortitis can also be associated with an infection (e.g., syphilis) or systemic disease. For example, some patients with IgG4-related systemic disease develop aortitis as the only vasculitic manifestation (22).

Vasculitis associated with systemic disease. Vasculitis can be associated with and may be caused by a systemic disease. The name (diagnosis) should have a prefix term specifying the systemic disease (e.g., rheumatoid vasculitis, lupus vasculitis, sarcoidosis vasculitis, relapsing polychondritis vasculitis, etc.).

This category of vasculitis associated with systemic diseases and the following category associated with probable etiologies often are considered to be *secondary vasculitides*, whereas the other categories have been considered *primary (or idiopathic) vasculitides*. Categorization into primary versus secondary vasculitis becomes problematic as more and more etiologies of the former are discovered.

Vasculitis associated with probable etiology. If a vasculitis is associated with a probable specific etiology, the name (diagnosis) should have a prefix specifying the association (e.g., hydralazine-associated microscopic polyangiitis, hepatitis B virus–associated polyarteritis nodosa, hepatitis C virus–associated cryoglobulinemic vasculitis, syphilis-associated aortitis, serum sickness–associated immune complex vasculitis, cancer-associated vasculitis, and many others). Hematologic and solid organ neoplasms, as well as clonal B cell lymphoproliferative disorders and myelodysplastic syndrome, can be associated with and may cause vasculitis.

Epilogue

Disease names and definitions evolve over time as medical knowledge and understanding advance, which is why CHCC2012 is being proposed to replace CHCC1994. The goals are to make this nomenclature system more relevant and more valuable by including additional categories of vasculitis, and by adjusting names and definitions based on current trends in usage and on advances in the understanding of disease manifestations and mechanisms.

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All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Jennette had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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