# EULAR points to consider in the development of classification and diagnostic criteria in systemic vasculitis

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**Abbreviations**

AAV Anti neutrophil cytoplasm antibody associated vasculitis

ACR American College of Rheumatology

ANCA Anti neutrophil cytoplasm antibody

CHCC Chapel Hill Consensus Conference

CRYO Cryoglobulinemic vasculitis

CSS Churg-Strauss syndrome

CT Computed Tomography

EULAR European League Against Rheumatism

ELISA Enzyme-linked immunosorbant assay

GBM Glomerular basement membrane

GCA– Giant cell arteritis

HIV – Human immunodeficiency virus

HSP Henoch Schönlein purpura

HV Hypersensitivity vasculitis

IIF – Indirect immunofluorescence

KD Kawasaki disease

LV Leucocytoclastic vasculitis

MRA Magnetic Resonance Angiography

MRI Magnetic Resonance Imaging

MPA Microscopic polyangiitis

PAN– Polyarteritis nodosa

PET - Positron Emission Tomography scanning

TAK Takayasu disease

WG Wegener's granulomatosis

**Abstract**

Objectives: The systemic vasculitides are multi-organ diseases where early diagnosis and therapy can significantly improve outcomes. Robust nomenclature reduces diagnostic delay. However, key aspects of current nomenclature are widely perceived to be out of date, these include disease definitions, classification and diagnostic criteria. Therefore, the aim of the present work was to identify deficiencies and provide contemporary points to consider for the development of future definitions and criteria in systemic vasculitis.

Methods: The expert panel identified areas of concern within existing definitions/criteria. Consequently, a systematic literature review was undertaken looking to address these deficiencies and produce 'points to consider' in accordance with standardised European League Against Rheumatism (EULAR) operating procedures. In the absence of evidence, expert consensus was used.

Results: There was unanimous consensus for re-evaluating existing definitions and developing new criteria. 17 points to consider were proposed, covering 6 main areas: biopsy, laboratory testing, diagnostic radiology, nosology, definitions and research agenda. Suggestions to improve and expand current definitions were described including the incorporation of ANCA and aetiological factors, where known. The importance of biopsy in diagnosis and exclusion of mimics was highlighted, while equally emphasizing its problems. Thus, the role of alternative diagnostic tools such as MRI, ultrasound and surrogate markers were also discussed. Finally, structures to develop future criteria were considered.

Conclusions: Limitations in current classification criteria and definitions for vasculitis have been indentified and suggestions provided for improvement. Additionally it is proposed that,, in combination with the updated evidence, these should form the basis of future attempts to develop and validate revised criteria and definitions of vasculitis.

## Introduction

The primary systemic vasculitides are a group of uncommon diseases (combined annual incidence >100 new cases per million),[1] some of which are associated with an untreated 1-year mortality of >80%.[2] Early diagnosis and treatment significantly improves outcome. Unfortunately, however, their relative rarity and heterogeneity frequently leads to diagnostic delay,[3] which could be improved by better nomenclature.

The terms 'disease definition', 'classification' and 'diagnostic criteria' are essential components of the nomenclature of any disease. However, they are frequently and incorrectly used interchangeably. For example the American College of Rheumatology (ACR) classification criteria for rheumatoid arthritis (RA) are unhelpful in diagnosing early RA.[4] In the vasculitides, each condition should be described (ie, disease definition), criteria listed to allow distinction from the general population and from similar, non-vasculitic 'mimic' conditions (ie, diagnostic criteria) and further criteria are required to distinguish one form of vasculitis from another (ie, classification criteria). The primary purpose of diagnostic criteria is to diagnose the conditions of individual patients, but they can also be used to distinguish one type of vasculitis from another. Classification criteria are primarily intended to generate homogeneous (usually 'classic') sets of patients for research.[5]

In the absence of validated diagnostic criteria for systemic vasculitis, the ACR classification criteria[5] and the Chapel Hill Consensus Conference (CHCC)[6] definitions are often used as substitutes.

The ACR classification criteria for vasculitis have sensitivities of 71.0% to 95.3% and specificities between 78.7 and 99.7%.[5] The most sensitive and specific criteria were for Churg–Strauss syndrome (CSS), giant cell arteritis (GCA) and Takayasu disease (TAK); hypersensitivity vasculitis (HV) was the least well defined condition (sensitivity 71.0%,

specificity 83.9%).[7] The ACR criteria have facilitated epidemiological and clinical studies. However, they have three main disadvantages:

1. The failure to include microscopic polyangiitis (MPA), which was not commonly used during the 1980s, despite its description in 1948.[8]

2. The lack of application of anti-neutrophil cytoplasm antibody (ANCA) as a criterion in the diagnosis of Wegener's granulomatosis (WG),[9],[11] MPA,[10] and CSS[12] (and also in polyarteritis nodosa (PAN), because of its absence).[13]

3. Use of the initial diagnosis made by the participating doctor as the gold standard.

The ACR criteria were derived by determining which features distinguished one form of vasculitis from another. Unsurprisingly, the ACR criteria demonstrate poor reliability when applied as diagnostic criteria,[14] as they were not designed for this purpose.

The CHCC definitions for primary vasculitis,[6] including MPA, describe features that should be present in a patient to warrant using a given term for either classification or diagnosis, but they do not specify what observations or criteria should be used to definitively determine that a given patients has a specific form of vasculitis. Attempts to validate CHCC definitions as diagnostic criteria (by including surrogate markers such as ANCA) have been unsuccessful.[15] [16]

There is widespread controversy in relation to the use of ACR criteria and CHCC definitions. A recent survey of an international panel of experts reflects this (Table 1). The majority felt the ACR criteria for PAN, CSS, Henoch–Schönlein purpura (HSP) and HV and CHCC definitions for WG, MPA and PAN were no longer fit for purpose. Paediatricians have already developed a set of classification criteria addressing new developments based on their experience in childhood.[17]

The European League Against Rheumatism (EULAR) convened an expert consensus group to consider re-evaluating definitions, classification and diagnostic criteria in

systemic vasculitis, in order to highlight areas which require updating or are of concern and indicate what should be considered next.

## Methods

### Working group

A consensus group was formed comprising 39 experts in vasculitis. In order to encourage universal acceptance of the conclusions, we incorporated multiple disciplines and nationalities: rheumatology (15), nephrology (7), immunology (5), internal medicine (3), pathology (2), paediatrics (2), otolaryngology (1), pulmonology (1), dermatology (1), radiology (1) and clinical epidemiology (1) were represented from 10 European countries, USA, Mexico and Japan.

The project conformed to the EULAR standing committees published standard procedures for the elaboration of recommendations.[18] Since the groups' findings were based on a systematic literature review rather than a data-driven approach, it is appropriate to use the term ‘points to consider’ rather than ‘guidelines’ or ‘recommendations’.

### Expert opinion

We used an iterative process to establish the major areas of concern/difficulties with the existing definitions/criteria. This involved a questionnaire to committee members who were asked to identify the key questions and issues relating to the current definitions, classification and diagnostic criteria, followed by a modified Delphi process. As a result, a set of questions was produced that provided the basis for a systematic literature search exploring studies on the diagnosis and classification of systemic vasculitis. These were used to fuel discussion and delineate points to consider as we develop and test new/updated definitions and criteria in the future.

### Literature review

We used the PubMed Medical Subject Headings (MeSH) database and Cochrane library. Where MeSH terms were unavailable (eg, MPA), free text was used. Searches were not limited by time or language; reference lists were manually searched. We excluded studies without abstracts; those with cohorts of less than 10 patients; case reports; reviews and letters. We examined relevant studies of all forms of systemic vasculitis including paediatric and secondary forms. Antiglomerular basement membrane (anti-GBM) disease was also explored since it is closely related to the vasculitides. Search strings were derived by consensus, for example to examine the role of ANCA in diagnosis, the following string was employed: ('vasculitis' (MeSH) or 'anti-GBM disease' (MeSH) or 'erythema induratum' (MeSH) or 'MPA' or 'cryo' or 'rheumatoid vasculitis' or 'nodular vasculitis' or 'infection associated vasculitis' or 'ANCA associated vasculitis' or 'immune complex vasculitis' or 'renal vasculitis' or 'drug induced vasculitis') and 'antibodies, antineutrophil cytoplasmic' (MeSH) and 'diagnosis' (MeSH).

We included all papers with an outcome identified in the Delphi exercise. Evidence was categorised according to the EULAR evidence hierarchy for diagnostic studies (Table 2).[19 20]

## Results and discussion

### Questions raised by Delphi exercise

A total of 10 questions were generated through the modified Delphi exercise (see Table 3). Some questions could only be addressed by supplementing published evidence with consensus.

### Points for consideration

The results of the literature search were grouped into three main diagnostic topics (Table 4). The following discussion combines the results of the literature search and expert opinion and attempts to cover the questions raised through the modified Delphi exercise. From the results, 17 'points to consider' were extrapolated (Table 5).

**Diagnostic tools**

*Biopsy*

Histology is fundamental to the diagnosis of most forms of vasculitis and more importantly, perhaps, the exclusion of mimics. This is best highlighted by brain biopsy in central nervous system (CNS) vasculitis, where despite the potential for significant iatrogenic morbidity and variable yield (36% to 83%),[21 22] it remains the gold standard investigation due to its role in identifying alternative diagnoses such as infection. Significant variation exists in the utility of biopsy depending on the target organ. For example, the yield of kidney and temporal artery biopsies is high (80%[23 24] and 87%[25] respectively). In contrast, *ear, nose and throat (*ENT) and transbronchial biopsies have a low reported sensitivity (0% to 42%).[23 26,,30]

Clinically directed biopsies can improve yield as exemplified in the nerve,[31 32] lung[23] and temporal artery.[25] Further studies examining temporal artery sampling support the need for a prompt biopsy to reduce unnecessary corticosteroid exposure[33,,36];adequate sampling by length (0.5–2 cm)[33 37 38] with multiple sectioning[39] and bilateral biopsies,[25] in view of the problem of skip lesions. It would be difficult to justify the latter routinely. A more effective approach may be sequential sampling of cases where the first biopsy is negative, in patients with a high pretest probability of GCA.[40]

Although previous proposed criteria and definitions have incorporated histology, there are no universally recognised histological criteria and little evidence to justify the inclusion of specific pathological features. Perhaps the exception is IgA as an essential criterion in the diagnosis of HSP. In a study of 182 cases of skin vasculitis, the presence of IgA was 98% sensitive for the clinical diagnosis of HSP; however, the specificity was very low (24%)[41]

*Laboratory testing*

The discovery of specific autoantibodies characterised by immunofluorescence patterns, cytoplasmic ANCA (cANCA) and perinuclear ANCA (pANCA) and subsequently by the relevant target antigens, proteinase 3 (PR3-ANCA) and myeloperoxidase (MPO-ANCA),

has been a major advance in the diagnosis of small vessel vasculitis,[42] particularly WG and MPA. Sensitivity of ANCA varies significantly (34% to 92%)[10 11 43 – 47] due to non-standardised assays,[11 48] different study designs,[14 44] differences in treatment, disease activity and disease type in the populations studied. MPO-pANCA predominates in MPA and PR3-cANCA in WG, however, this is not absolute. Geographical variation has been observed with the presence of MPO-pANCA in 60% of a cohort of Chinese patients with WG.[49] In contrast, specificity is consistent between studies.[10 43 45] Most studies include disease controls, predominantly containing patients with inflammatory bowel disease, systemic lupus erythematosus (SLE) and RA, rather than healthy controls. However, the ideal control group should include vasculitis mimics.[10 42]

The combined use of indirect immunofluorescence and ELISA provides optimal performance.[11 10 50 51] A meta-analysis of seven studies provided a weighted pooled sensitivity of 85.5% and specificity of 98.6% for MPO-pANCA and PR3-cANCA in the diagnosis of WG, MPA or renal limited vasculitis.[43] PR3-ANCA and MPO-ANCA are the only ANCA specificities with proven diagnostic value for small vessel vasculitis. However, additional ANCA specificities may emerge as useful diagnostic markers in future.[52]

The prevalence of ANCA in CSS is lower than in WG or MPA (38% to 73%). ANCA-positive CSS is associated with a higher frequency of glomerulonephritis.[12]

In some vasculitides, the absence of ANCA can be of value. For example, in PAN, which, historically, has been difficult to differentiate from MPA.[13 53 – 55]

ANCA are only present in low titre or completely absent in all other vasculitides such as GCA[56] and Kawasaki disease (KD).[57] ANCA are not 100% specific for vasculitis; they are found in other autoimmune diseases and vasculitis mimics such as SLE,[58] RA,[59] HIV,[60] tuberculosis,[61 62] inflammatory bowel disease,[63] primary sclerosing cholangitis,[64] drug reactions (eg, cocaine[65] and propylthyourracil[66]), infective endocarditis and septic shock.[67]

Thus ANCA analysis should not be abused for general screening purposes. Selectivity of test ordering improves positive predictive value[51] and the use of ANCA requesting guidelines to avoid indiscriminate use may be justified.[68]

*Diagnostic radiology*

Radiological diagnostics are of increasing use in the assessment of large vessel vasculitis. Traditionally, conventional contrast angiography has been an essential criterion in the diagnosis of TAK.[69] [70] More recently, the less invasive applications of CT angiography and magnetic resonance angiography (MRA) have produced similar diagnostic performance (sensitivities of 95%[71] and 100%[72] respectively and specificity of 100%[71] [72] for both, where contrast angiography is the reference standard). They provide the added advantage of visualising mural changes, although, overall the performance of angiographic techniques in early disease is poor. In contrast MRI and ultrasound (US) both detected mural inflammation,[73],[74],[75] which may be useful in early diagnosis, but are inferior to angiography in late disease.[73] [75] [76] In future, early diagnosis of large vessel vasculitis may be facilitated by positron emission tomography scanning (PET) scanning. Retrospective studies suggesting sensitivities of 60% to 92% and specificities of 99% to 100% in the diagnosis of large vessel vasculitis, with greater sensitivity in detecting wall inflammation compared to MRI.[77],[78],[79] There is, however, insufficient evidence at present to advocate PET as a standard in diagnostics, especially in view of its considerable radiation dose when combined with CT.

US and MRI,[80],[81],[82] but not PET[83], may be a useful alternative to temporal artery biopsy for the diagnosis of GCA. In a meta-analysis of 23 studies (2036 patients), the diagnostic value of US in GCA, using the 'halo' sign, a dark area around the temporal artery vessel, provided a weighted sensitivity and specificity of 69% and 82% respectively, compared to biopsy and 55% and 94% compared to ACR criteria. Abnormal findings appear to increase the likelihood of disease, thereby justifying a biopsy, while negative results decrease the post-test probability and reduce the need for a biopsy.[84] The presence of bilateral halos may obviate the need of biopsy.[80] Alternatively, 3T MRI of cranial arteries provides high diagnostic sensitivity (89% to 94%) and specificity (92% to 100%) in

detecting vessel wall inflammation, although studies are based on small numbers performed at a limited number of centres.[81] [82]

The available evidence to support other radiological strategies is not convincing.

Abdominal angiographic abnormalities, particularly microaneurysms, are regarded as synonymous with PAN. However, studies assessing angiography in PAN have included a significant number of patients with MPA.[85],-,[87] Reported sensitivities are variable (58% to 89%) and one study described a specificity of 89% in populations with suspected medium vessel vasculitis. In practice, despite the absence of evidence, the risks of formal angiography encourage increased use of digital subtraction angiography and MRA as alternatives.

In terms of granulomatous antibody-associated vasculitides, CT and MRI can be useful in diagnosing ENT disease.

Compared to CT, sinus visualisation with MRI is sensitive (92%) in detecting inflammatory changes in WG.[88] In contrast, MRI is poor in delineation of destruction (5% of cases) compared to CT (40% of cases).[89] Although not diagnostic, they are necessary for guided biopsies that may lead to a diagnosis.

The use of radiology in CNS vasculitis is controversial. The lack of a gold standard has caused difficulties in assessing its diagnostic performance in this rare and heterogeneous condition. Conventional angiography has low specificity (14% to 60%)[21] [90] and variable sensitivity (15% to 92%).[91] Angiography alone is not pathognomonic and must be interpreted in the clinical context. Distinguishing reversible vasospasm is a particular problem. MRI, CT and MRA have a role, but no investigation provides diagnostic certainty.

*Surrogate markers*

It is clear that currently available diagnostic tools are imperfect, thus future criteria, at least in the short term, will rely heavily on clinical surrogate markers.

The ACR classification criteria is dominated by clinical characteristics.[5] Supplementing CHCC definitions with clinical features and biomarkers to form diagnostic criteria has not been effective in WG and MPA, however, alteration of the criteria improves their performance[16] as classification criteria in WG (specifically by not excluding cases with hypereosinophilia) but not in MPA. The development of novel biomarkers may ultimately prove superior to biopsy, which provides suboptimal yield in practice.

**Classification tree**

We recommend the development of updated criteria and re-evaluation of current disease definitions.

A preliminary nomenclature scheme based upon a classification tree was agreed as work in progress and provides a basis for future validated classification and diagnostic criteria.

The proposed scheme will accommodate the following features:

1. The group raised concerns that ‘inflammation of blood vessels’, the true pathological definition, captured many diseases not considered to be clinical forms of vasculitis. Future criteria should focus only on clinically relevant vasculitis defined as a disease where pathological evidence of blood vessel inflammation is considered to be an important part of the disease. Thus, all forms of vascular disease will be defined as either ‘vasculitis’ or ‘predominantly non-inflammatory vasculopathy’. The latter would include atherosclerosis, haemolytic uraemic syndrome and fibromuscular dysplasia.

2. The use of eponyms should be reviewed. There is evidence linking Dr F Wegener with the Nazi regime, but how substantial this link is remains undetermined.[92] Similar concerns have led to the removal of the term ‘Reiter’s syndrome' in favour of reactive arthritis.[93] The committee has discussed this further with EULAR and ACR and have prepared a document raising the relevant issues which is currently being reviewed by

the German society of rheumatology. We recognise that an alternative to the term for WG could be ANCA-associated vasculitis with granulomatosis (Wegener's granulomatosis).

In general, it was agreed that wide-scale abandonment of historically established terms would cause confusion and therefore any change would need to be introduced gradually, with initial retention of the old names in addition to the new, more appropriate names.

3. The name for any disease should, where possible, reflect its pathophysiological basis. Our understanding of specific aetiologies in vasculitis is limited, but expanding. A significant proportion of patients with PAN and cryoglobulinaemic vasculitis (cryo) carry hepatitis B[94] and C[95] infections, respectively and there is evidence to suggest that these viruses induce direct vessel damage via immune complex formation. This should be reflected in their definitions and names.

4. Age is worthy of inclusion in the definitions of some forms of vasculitis, but not all.

   The spectrum of large vessel vasculitis has traditionally been set according to age[5] with a cut-off of 50 years between GCA and TAK. The concept of 'age at disease onset' should be considered (as per the ACR criteria)[5] since many patients with TAK present several years after their true disease onset with symptoms such as claudication. Age is currently used to define HSP, but at least 10% of cases occur in adulthood.[50] Adults with HSP often follow a distinct clinical course from children, in particular, with worse renal outcomes.[96] In contrast, KD is mainly a paediatric disease. Adult cases are rare and benign.[97]

5. Vasculitis is divided into primary and secondary forms. Primary entities may move into the secondary category if aetiologies are discovered.

Secondary vasculitis includes vasculitis due to infection, drugs, malignancy and connective tissue diseases.

6. The use of predominant vessel size and type will remain a major discriminator. In addition to ‘small’, ‘medium’ and ‘large’, a ‘no predominant vessel size’ category would be incorporated. This allows the inclusion of syndromes such as Behçets disease, CNS vasculitis, Cogan's syndrome and relapsing polychondritis.

## Conclusions

There is currently no gold standard test for the diagnosis of vasculitis. We have critically appraised the value of biopsy, serology and radiology for diagnosing vasculitis to define an evidence base from which to modernise current definitions and criteria. We have identified areas of potential improvement in current definitions and criteria. The available evidence is insufficient to make definitive recommendations for diagnostic criteria. However, the points represent position statements to allow the development of future definitions and validated diagnostic/classification criteria. There is clear consensus among the international community to embrace this challenge. This work provides the foundation for a proposed large multicentre study to develop new criteria from prospective cohorts that would take current diagnostic testing into consideration.

## Footnotes

- Funding EULAR Executive Secretariat, Ministerio de Cienciae Innovación, SAF 08/04328 (MCC), and the American College of Rheumatology.
- Provenance and peer review Not commissioned; externally peer reviewed.
- Competing interest None.

**Tables**

Table 1 Percentage of committee dissatisfied with disease criteria/definition*

| Disease | ACR (%) | CHCC (%) |
|---|---|---|
| GCA | 38 | 27 |
| TAK | 45 | 27 |
| PAN | 76 | 59 |
| KD | n/a | 14 |
| WG | 43 | 68 |
| MPA | n/a | 59 |
| CSS | 76 | 36 |
| HSP | 86 | 14 |
| HV | 75 | n/a |
| LV | n/a | 41 |
| Cryo | n/a | 36 |

GCA – Giant cell arteritis; TAK – Takayasu disease; PAN – Polyarteritis nodosa; KD – Kawasaki disease; WG – Wegener's granulomatosis; MPA – Microscopic polyangiitis; CSS – Churg-Strauss syndrome; HSP – Henoch Sconlein purpura; HV – Hypersensitivity vasculitis; LV – Leucocytoclastic vasculitis; Cryo – Cryoglobulinemic vasculitis

* 22 participants

Table 2: The EULAR evidence hierarchy for diagnosis based on study design

| Grade | Evidence |
|---|---|
| Ia | Meta-analysis of cohort studies |
| Ib | Meta-analysis of case control studies |
| IIa | Cohort studies |
| IIb | Case control/cross sectional comparative studies |
| III | Non-comparative descriptive studies |
| IV | Expert opinion |

Table 3: Questions generated by the Delphi Exercise

| |
|---|
| 1. Which diseases should be included in future classification/diagnostic criteria? |
| 2. Should there be upper or lower age limits for certain vasculitides ? |
| 3. What methodologies should be used to create classification/diagnostic criteria? |
| 4. What is the role of biopsy findings in diagnosis? |
| 5. What is the role of ANCA in diagnosis? |
| 6. What is the importance of vessel size and vessel type when considering criteria? |
| 7. What is the role of radiographic imaging in diagnosis? |
| 8. What is the role of surrogate markers in diagnosis? |
| 9. Should we identify and exclude 'mimics' prior to making the diagnosis of vasculitis ? |
| 10.Shall we cease to use eponyms as primary names for the vasculitides ? |

Table 4: Number of citations identified versus number found suitable for evaluation

| Topic | Identified citations | Selected citations |
|---|---|---|
| Tissue pathology | 2724 | 64 |
| Laboratory testing | 1063 | 68 |
| Diagnostic radiology | 7138 | 46 |

Table 5: Points to consider in the development of classification criteria and definitions in the systemic vasculitides

| | Statement | Level of Evidence |
|---|---|---|
| | *Biopsy* | |
| 1. | Although histology is fundamental to the diagnosis of vasculitis and exclusion of its' mimics, biopsy of affected organs is not always possible and yields vary significantly according to conditions and target organs | III |
| 2. | Temporal artery biopsy (TAB) is an important tool in the diagnosis of GCA | Ia |
| 3. | Cases of Henoch Schönlein Purpura (HSP) usually have IgA deposits present on biopsy | IIb |
| | | |
| | *Laboratory Testing* | |
| 4. | ANCA testing plays an important diagnostic role in suspected small vessel vasculitis | Ia |
| 5. | In suspected Polyarteritis Nodosa (PAN), the absence of ANCA has diagnostic value | IIa |
| 6. | The role of clinical features and additional surrogate biomarkers for vasculitis is likely to have an important role in the development of future diagnostic criteria | IV |
| | | |
| | *Diagnostic Radiology* | |

| | | |
|---|---|---|
| 7. | Computer aided tomography (CT) and magnetic resonance angiography (MRA) techniques can replace standard angiography in the diagnosis of Takayasu's disease (TAK) | IIa |
| 8. | Ultrasound and high resolution MRI may have a role in the diagnosis of GCA | US Ia<br>MRI IIa |
| 9. | The role of abdominal angiography in the diagnosis of adult PAN is unclear | III |
| 10. | CT and MRI may be useful in diagnosing ENT involvement associated with WG/CSS | III |
| 11. | The role of radiology in the diagnosis of central nervous system (CNS) vasculitis is unclear | III |
| | *Nosology* | |
| 12. | The nomenclature in use for distinguishing between "disease definitions", "classification" and "diagnostic" criteria is confusing and should be clarified wherever possible. | IV |
| 13. | Nosology of different forms of vasculitis should be a reflection of their aetiopathogenesis wherever this has been determined. In the absence of this, definition must rely on a clear accurate description of the salient features of the condition. | IV |
| 14. | The use of eponyms should be reviewed if a more rational approach to nomenclature can be developed, based on aetiopathogenesis, but their retention is necessary at present to avoid confusion. | IV |
| | *Definitions* | |
| 15. | Age is worthy of inclusion in the definitions of some forms of | III |

| | | |
|---|---|---|
| | vasculitis, but its role should not be overstated | |
| | *Research agenda* | |
| 16. | Future criteria initiatives should include all forms of vasculitis, providing definitions of less common syndromes not covered by CHCC | IV |
| 17. | The development of a classification tree will provide the foundations to future criteria | IV |

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