Updates in ANCA associated Vasculitis
Microscopic polyangiitis

M.Hakemi, M.D.
Shariati Hospital
TUMS
August 2024

Outline

1-Classification
2- Epidemiology
3-ANCA
4- Pathogenesis
5-Systemic features
6-Kidney involvement
7- Treatment?

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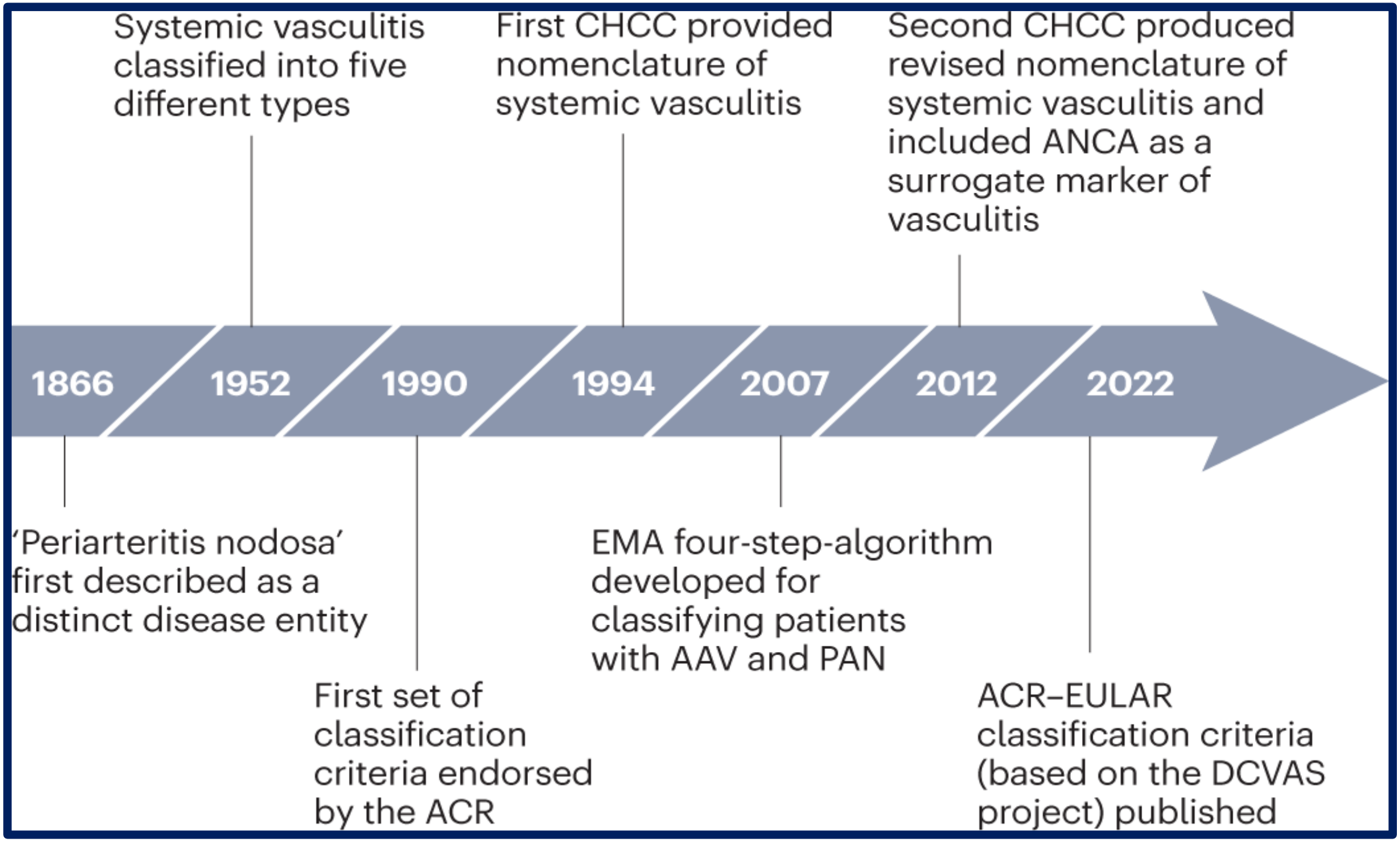

1866
‘Periarteritis nodosa’ first described as a distinct disease entity
1952
Systemic vasculitis classified into five different types
1990
First set of classification criteria endorsed by the ACR
1994
First CHCC provided nomenclature of systemic vasculitis
2007
EMA four-step-algorithm developed for classifying patients with AAV and PAN
2012
Second CHCC produced revised nomenclature of systemic vasculitis and included ANCA as a surrogate marker of vasculitis
2022
ACR–EULAR classification criteria (based on the DCVAS project) published

2012 International Chapel Hill Consensus Conference (CHCC)

Classification of vasculitides based on which type of vessels they target.

The important ones are:

- **Large vessels**
  - **Giant cell arteritis**
  - **Takayasu arteritis**
- **Medium vessels**
  - Polyarteritis nodosa
  - Kawasaki disease
- **Small vessels**
  - **Microscopic polyangiitis**
  - **Granulomatosis with polyangiitis**
  - **Eosinophilic Granulomatosis with polyangiitis**
- **Any vessel**
  - Infectious vasculitis
  - Vasculitis associated with other diseases

Small-vessel vasculitis (SVV)

- Antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV)
  - ◇ Microscopic polyangiitis (MPA)
  - ◇ Granulomatosis with polyangiitis (Wegener) (GPA)
  - ◇ Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA)
- Immune complex SVV
  - ◇ Anti–glomerular basement membrane (anti-GBM) disease
  - ◇ Cryoglobulinemic vasculitis (CV)
  - ◇ Immunoglobulin A (IgA) vasculitis (Henoch-Schönlein) (IgAV)
  - ◇ Hypocomplementemic urticarial vasculitis (HUV) (anti-C1q vasculitis)

Medium-vessel vasculitis (MVV)

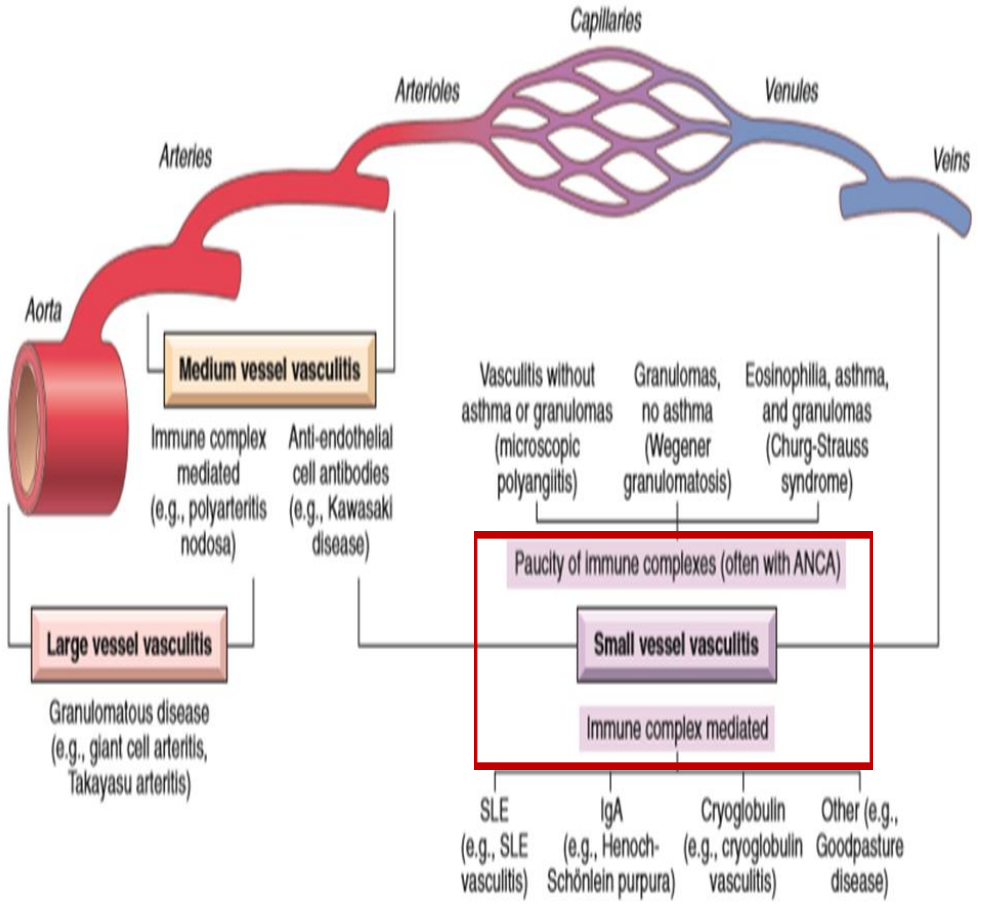
- Polyarteritis nodosa (PAN)
- Kawasaki disease (KD)

Large-vessel vasculitis

- Takayasu arteritis (TA)
- Giant cell arteritis (GCA)

Variable vessel vasculitis (VVV)

- Behçet disease (BD)
- Cogan syndrome (CS)



Curr Rheumatol Rep
https://doi.org/10.1007/s11926-024-01154-9

REVIEW

Classification Criteria for ANCA Associated Vasculitis – Ready for Prime Time?

Jens Rathmann[1] · Aladdin J. Mohammad[1,2]

Accepted: 5 June 2024

2022 ACR/EULAR classification criteria

	GPA		MPA		EGPA	
Clinical	**Nasal** *Crusts, discharge, ulcers, congestion, perforation*	+3	**Nasal** *Crusts, discharge, ulcers, congestion, perforation*	-3	**Asthma**	+3
	Cartilage *Ear, nose, stridor, endobronchial, saddle nose*	+2			**Nasal Polyps**	+3
	Hearing loss	+1			**Mononeuritis multiplex**	+1
Lab, imaging, serology	**Positive cANCA or PR3**	+5	**Positive pANCA or MPO**	+6	**Blood eosinophils** $\geq 1 \times 10^9$/L	+5
	Chest imaging *Nodules, mass, cavitation*	+2	**Chest imaging** *Fibrosis/ILD present*	+3	**Extravascular eosinophil rich inflamation on biopsy**	+2
	Granuloma on biopsy	+2	**Pauci-immune GN on biopsy**	+3	**Positive cANCA or PR3**	-3
	Sinus imaging *Effusion, consolidation*	+1	**Positive cANCA or PR3**	-1	**Hematuria**	-1
	Pauci-immune GN on biopsy	+1	**Blood eosinophils** $\geq 1 \times 10^9$/L	-4		
	Positive pANCA or MPO	-1				
	Blood eosinophils $\geq 1 \times 10^9$/L	-4				
Scoring	Sum scores 10 items ≥5 = GPA		Sum scores 6 items ≥5 = MPA		Sum scores 7 items ≥6 = EGPA	

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NATURE REVIEWS | DISEASE PRIMERS | Article citation ID: (2020) 6:71

PRIMER

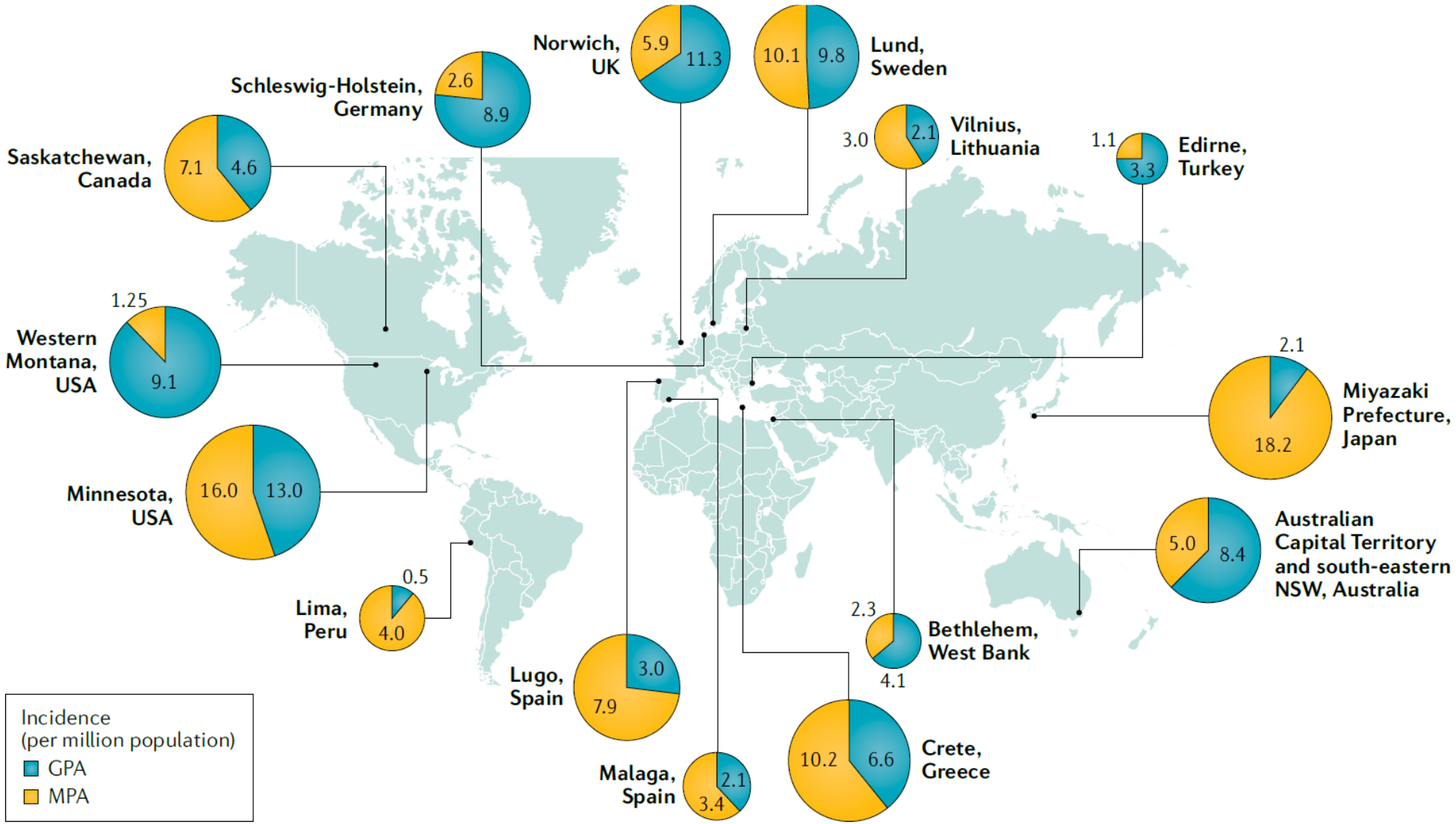
ANCA-associated vasculitis

A. Richard Kitching[1,2]✉, Hans-Joachim Anders[3], Neil Basu[4], Elisabeth Brouwer[5], Jennifer Gordon[6], David R. Jayne[7], Joyce Kullman[8], Paul A. Lyons[7,9], Peter A. Merkel[10], Caroline O. S. Savage[11], Ulrich Specks[12] and Renate Kain[13]

Disease	Incidence * [7]	ANCA-Positivity	PR3-ANCA	MPO-ANCA	Predominant Organ Involvement	Rate of Renal Involvement [77]	RPGN [77]
GPA	1.9–13	~90%	~75%	~20%	Nose and sinuses, lungs, kidneys, joints, eyes	~70%	~50%
EGPA	0.8–4	~40%	<10%	30–40%	Lungs, upper airways, peripheral nerves, heart, skin	~25%	<15%
MPA	1.5–16	~90%	~25%	~60%	Kidneys	>90%	~65%

* per million person-years. Abbreviations: AAV: ANCA-associated vasculitis. ANCA: Antineutrophil cytoplasmic antibody. PR3: leukocyte proteinase 3. MPO: myeloperoxidase. RPGN: rapidly progressive glomerulonephritis. GPA: granulomatosis with polyangiitis. EGPA: eosinophilic granulomatosis with polyangiitis. MPA: microscopic polyangiitis.

AAV is an uncommon disease with an incidence of about 20 per million population per year in Europe and North America. There is a **slight male preponderance**. Incidence increases with age, with a peak in the **60- to 70-year** age range.


Norwich, UK
5.9
11.3
Lund, Sweden
10.1
9.8
Schleswig-Holstein, Germany
2.6
8.9
Saskatchewan, Canada
7.1
4.6
Vilnius, Lithuania
3.0
2.1
Edirne, Turkey
1.1
3.3
1.25
Western Montana, USA
9.1
2.1
Miyazaki Prefecture, Japan
18.2
Minnesota, USA
16.0
13.0
Australian Capital Territory and south-eastern NSW, Australia
5.0
8.4
0.5
Lima, Peru
4.0
2.3
Bethlehem, West Bank
4.1
Lugo, Spain
3.0
7.9
Crete, Greece
10.2
6.6
Malaga, Spain
2.1
3.4
Incidence (per million population)
GPA
MPA

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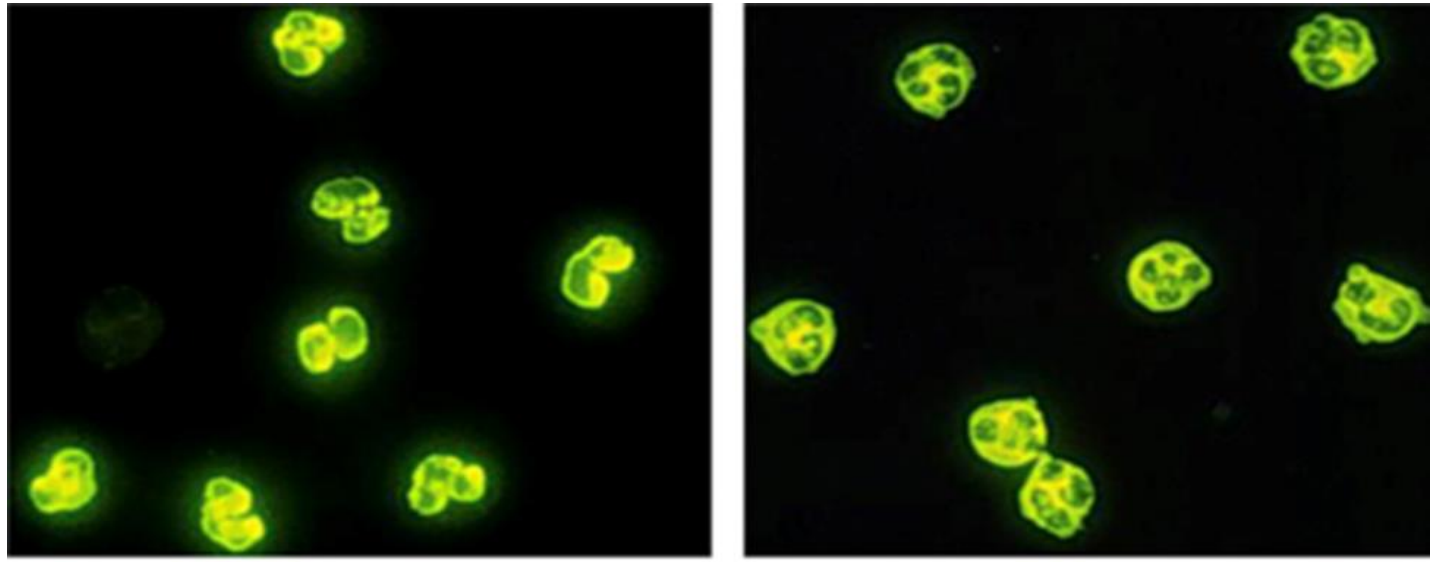
Anti Neutrophil Cytoplasmic Autoantibodies

ANCAs are autoantibodies directed against cytoplasmic antigens expressed in the primary granules of neutrophils and the lysosomes of monocytes.



P-ANCA Pattern

C-ANCA Pattern

ANCA-use in diagnosis

✓ **cANCA/PR-3**

- **Very specific for GPA**
- **Sensitive for diffuse disease**
- **Increasing recognition of false positives**
- **Less specific at very low titer**

✓ **pANCA/MPO**

- **Usually associated with MPA in > 50-75%, also 15% GPA**
- **Other associations: Infections,IBD, EGPA, drug induced**
- **False positives (by IIF) if ANA present**

ANCA-Negative Pauci-Immune Vasculitis

- ✓ A subgroup (10%) of patients with clinical features and pathology consistent with AAV remain ANCA negative.
- ✓ Failure of assay??? Ab against LAMP2???
- ✓ ANCA-negative patients are more likely to have renal-limited disease or less severe systemic disease.

ANCA- use in management

- **Often (not always) correlates with disease activity**
- **Increasing titer predictive of flare in SOME (not all) cohorts reported**
- **Negative ANCA in patient with high titer during prior flares has good negative predictive value**

DO NOT TREAT ISOLATED RISES IN ANCA TITER

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Int. J. Mol. Sci. 2020, 21, 7319

International Journal of
Molecular Sciences

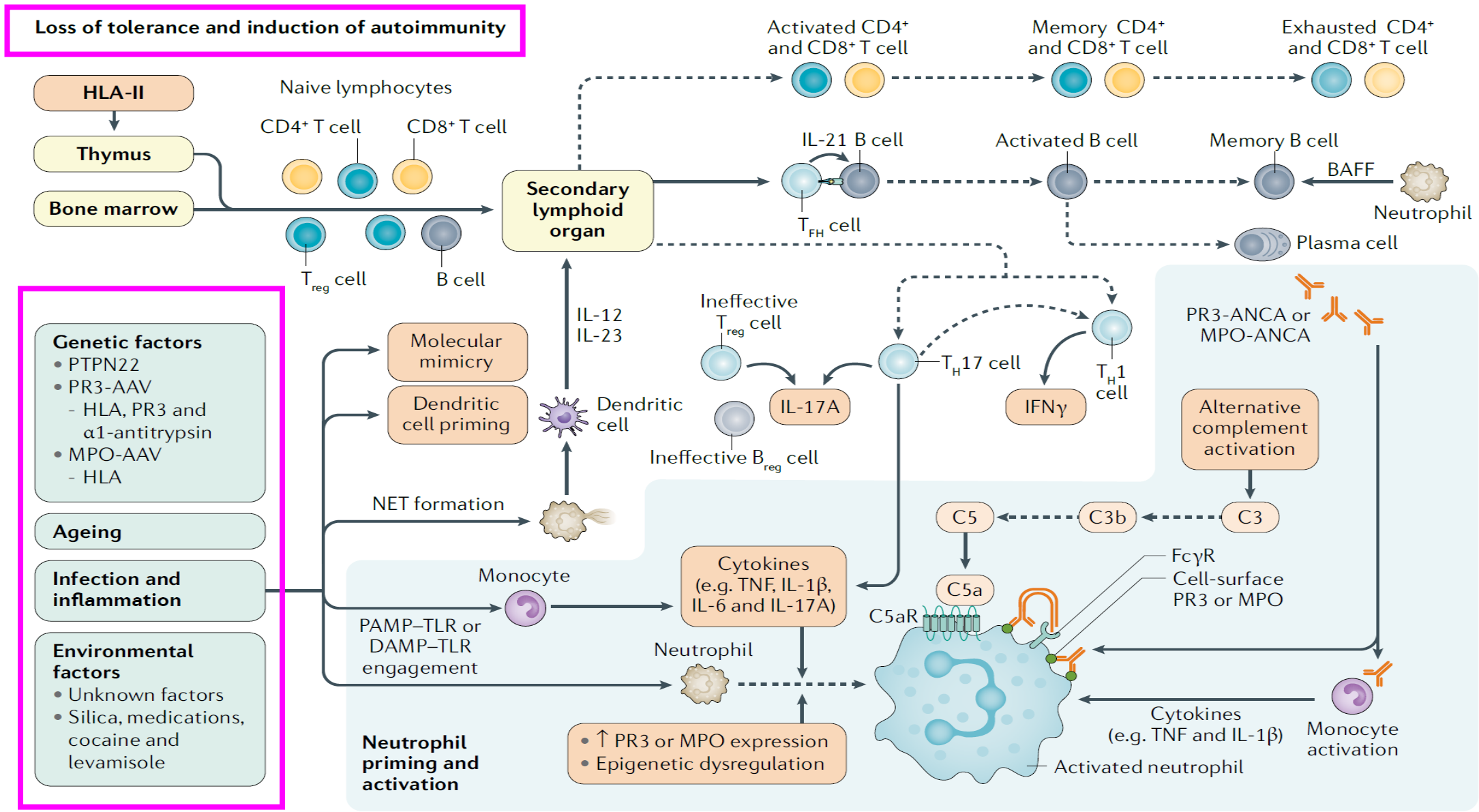
MDPI

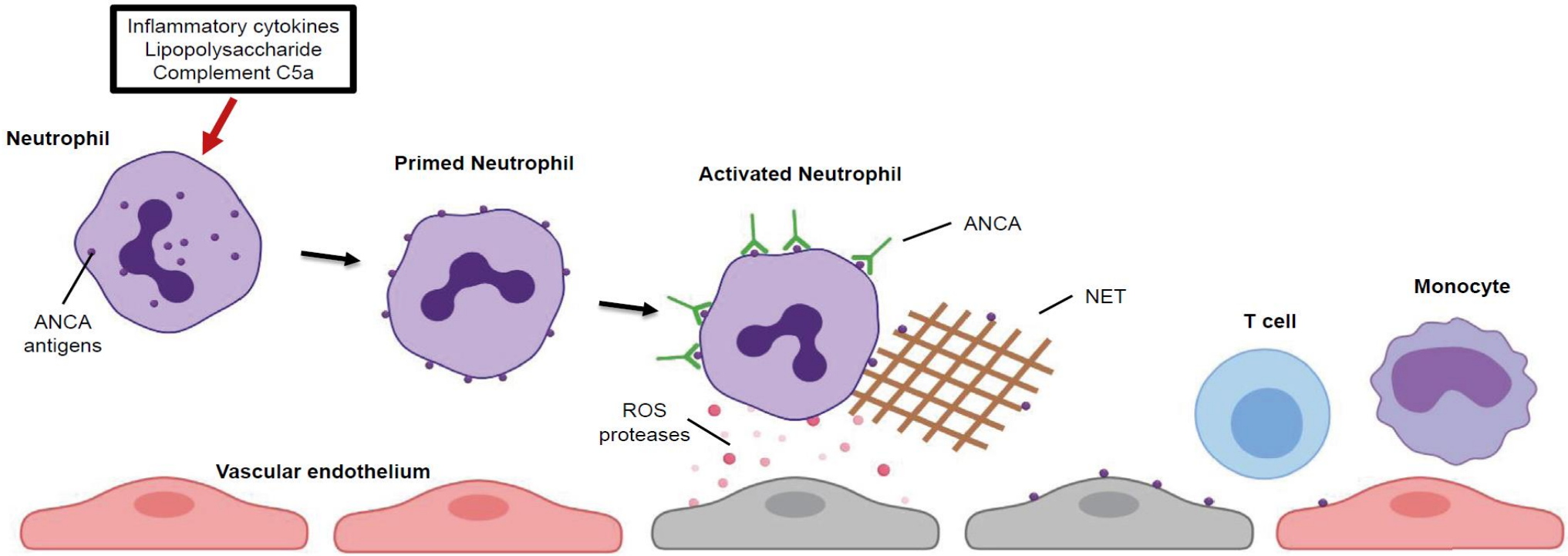
Review

Immunopathogenesis of ANCA-Associated Vasculitis

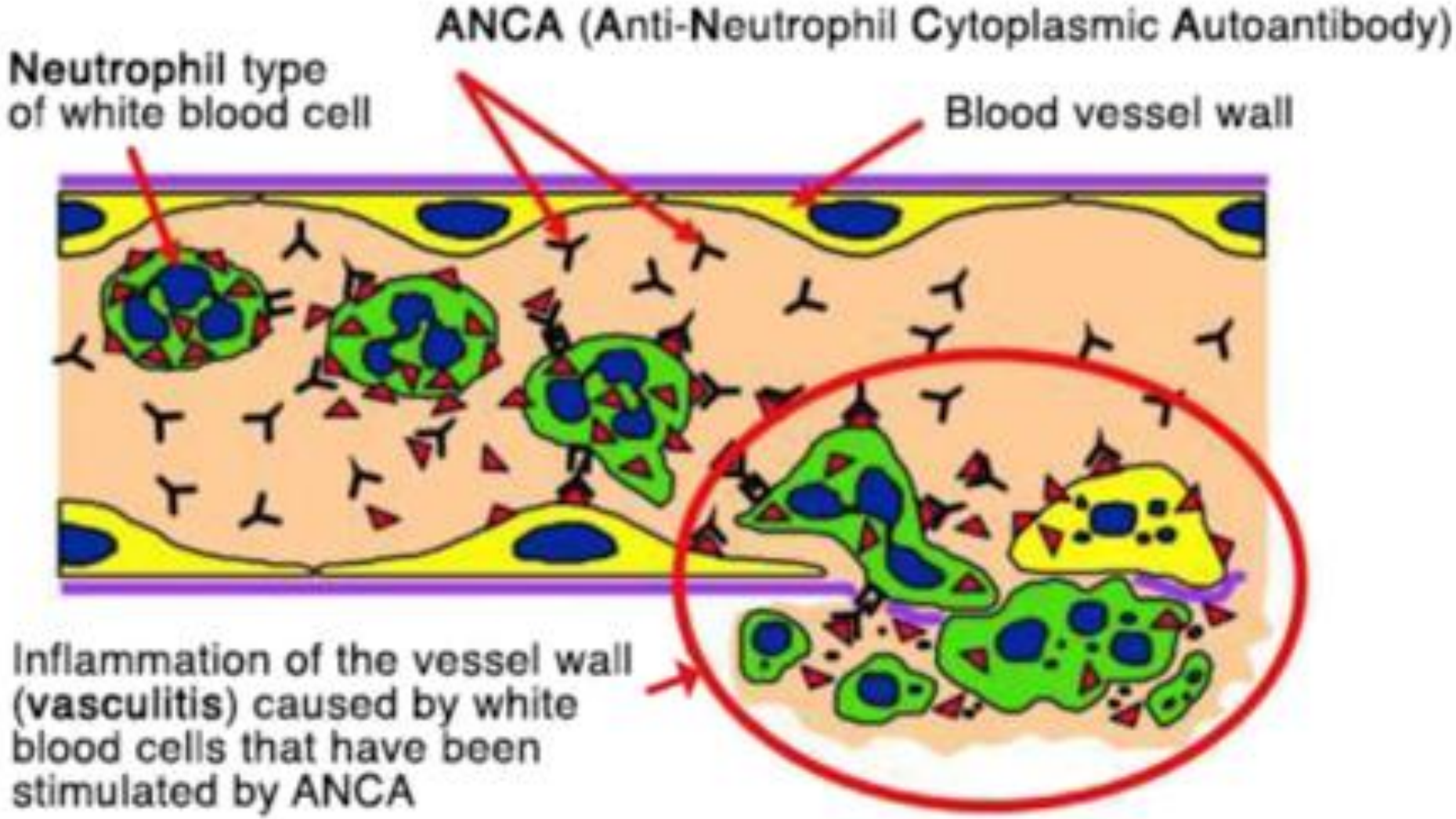
Andreas Kronbichler [1], Keum Hwa Lee [2], Sara Denicolò [1], Daeun Choi [3], Hyojeong Lee [3], Donghyun Ahn [3], Kang Hyun Kim [3], Ji Han Lee [3], HyungTae Kim [3], Minha Hwang [3], Sun Wook Jung [3], Changjun Lee [3], Hojune Lee [3], Haejune Sung [3], Dongkyu Lee [3], Jaehyuk Hwang [3], Sohee Kim [3], Injae Hwang [3], Do Young Kim [3], Hyung Jun Kim [3], Geonjae Cho [3], Yunryoung Cho [3], Dongil Kim [3], Minje Choi [3], Junhye Park [3], Junseong Park [3], Kalthoum Tizaoui [4], Han Li [5], Lee Smith [6], Ai Koyanagi [7,8], Louis Jacob [7,9], Philipp Gauckler [1] and Jae Il Shin [2,*]

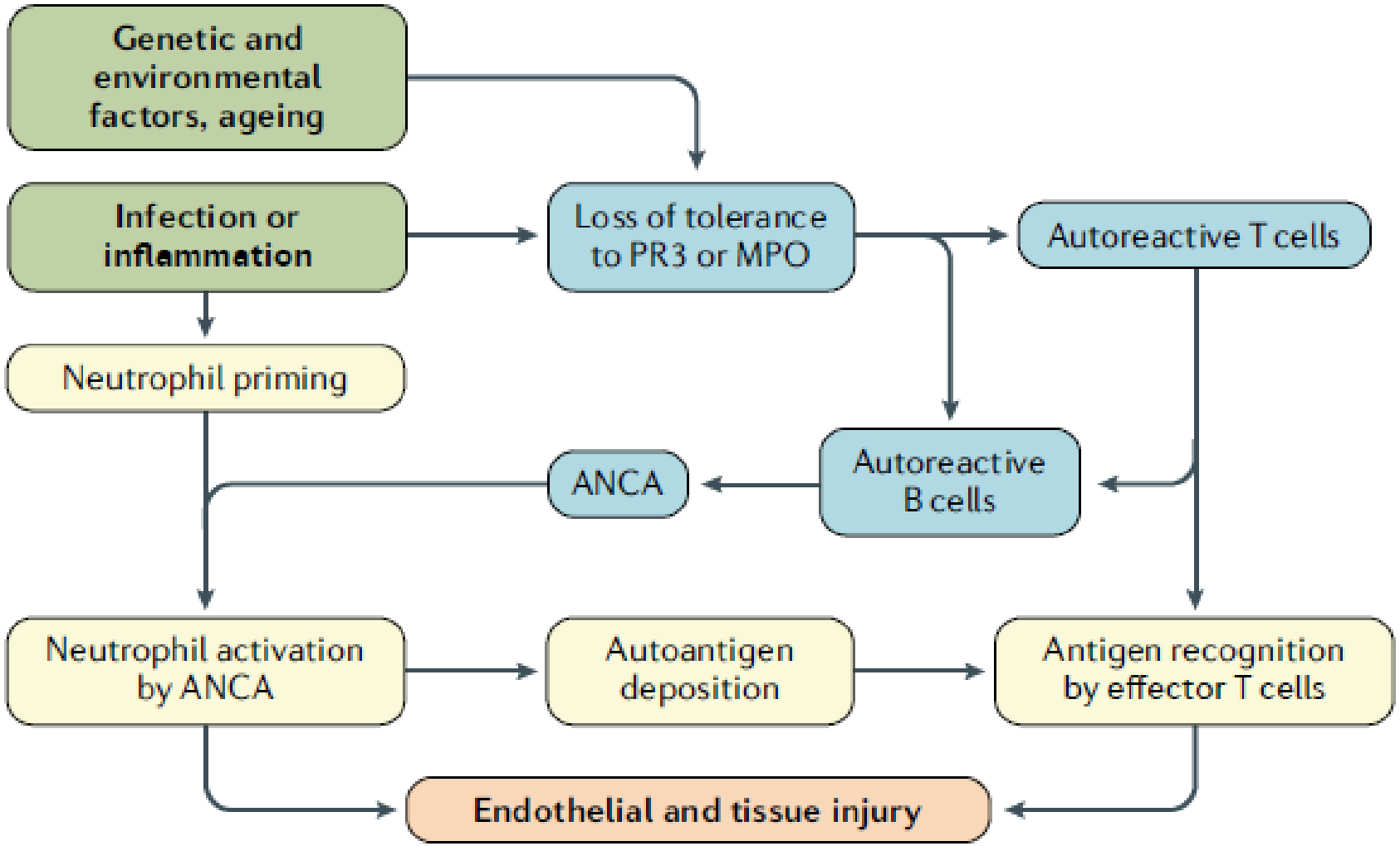
Loss of tolerance and the generation of effector responses in GPA and MPA.





ANCA autoantigens are normally sequestered in the primary granules of neutrophils. **Infection or other environmental stimuli** result in neutrophil priming, with movement of PR3 and MPO to the cell surface. **Binding of ANCA to these autoantigens** results in **activation of neutrophils**, which adhere to vascular endothelium. **Neutrophil degranulation** leads to the release of (ROS), proteases, and neutrophil extracellular traps (NETs), damaging the endothelium. Chemokines and tissue deposition of PR3 and MPO result in the **recruitment of autoreactive T cells and monocytes** augmenting tissue injury.


ANCA (Anti-Neutrophil Cytoplasmic Autoantibody)
Neutrophil type of white blood cell
Blood vessel wall
Inflammation of the vessel wall (vasculitis) caused by white blood cells that have been stimulated by ANCA


Genetic and environmental factors, ageing
Infection or inflammation
Loss of tolerance to PR3 or MPO
Autoreactive T cells
Neutrophil priming
ANCA
Autoreactive B cells
Neutrophil activation by ANCA
Autoantigen deposition
Antigen recognition by effector T cells
Endothelial and tissue injury

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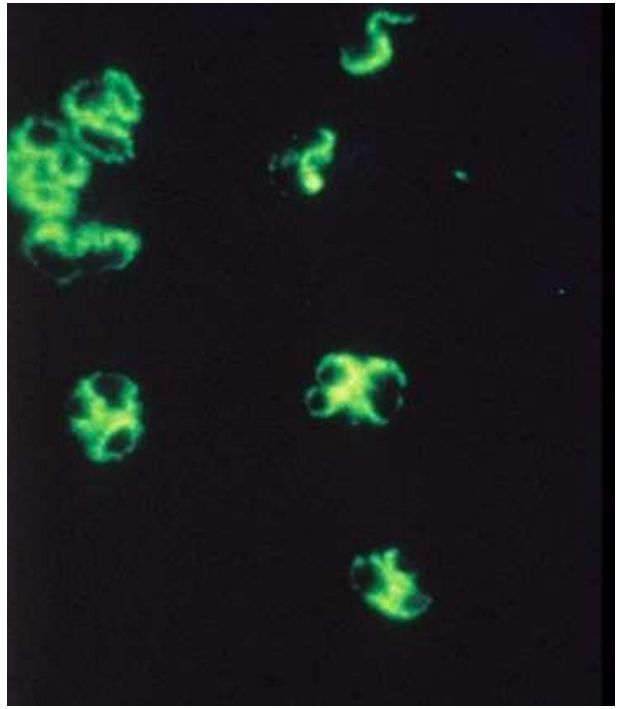
Microscopic Polyangiitis (MPA)

- Necrotizing small-medium vessel vasculitis
- Pulmonary and renal involvement most common
- Association with ANCA
  - perinuclear pattern (pANCA)
  - Anti-myeloperoxidase (MPO) specificity by ELISA (80-85% MPO positive)



Journal of Autoimmunity
Volume 112, August 2020, 102467

Microscopic polyangiitis: Clinical characteristics and long-term outcomes of 378 patients from the French Vasculitis Study Group Registry

Yann Nguyen [a], Christian Pagnoux [b], Alexandre Karras [c], Thomas Quéméneur [d], François Maurier [e], Mohamed Hamidou [f], Alain Le Quellec [g], Noémie Jourde Chiche [h], Pascal Cohen [a], Alexis Régent [a], François Lifermann [i], Arsène Mékinian [j], Chahéra Khouatra [k], Eric Hachulla [l], Jacques Pourrat [m], Marc Ruivard [n], Pascal Godmer [o], Jean-François Viallard [p], Benjamin Terrier [a], Luc Mouthon [a]...Xavier Puéchal [a]

Microscopic polyangiitis (MPA)

Constitutional manifestations:

- Fever (55%)
- Malaise, fatigue, flulike syndrome
- Myalgia (48%)
- Weight loss (72%)

Renal manifestations:

more than 80% of patients and on a spectrum from asymptomatic hematuria to necrotizing crescentic GN causing end-stage kidney disease. **(Risk of RRT 10%)**

Other manifestations :

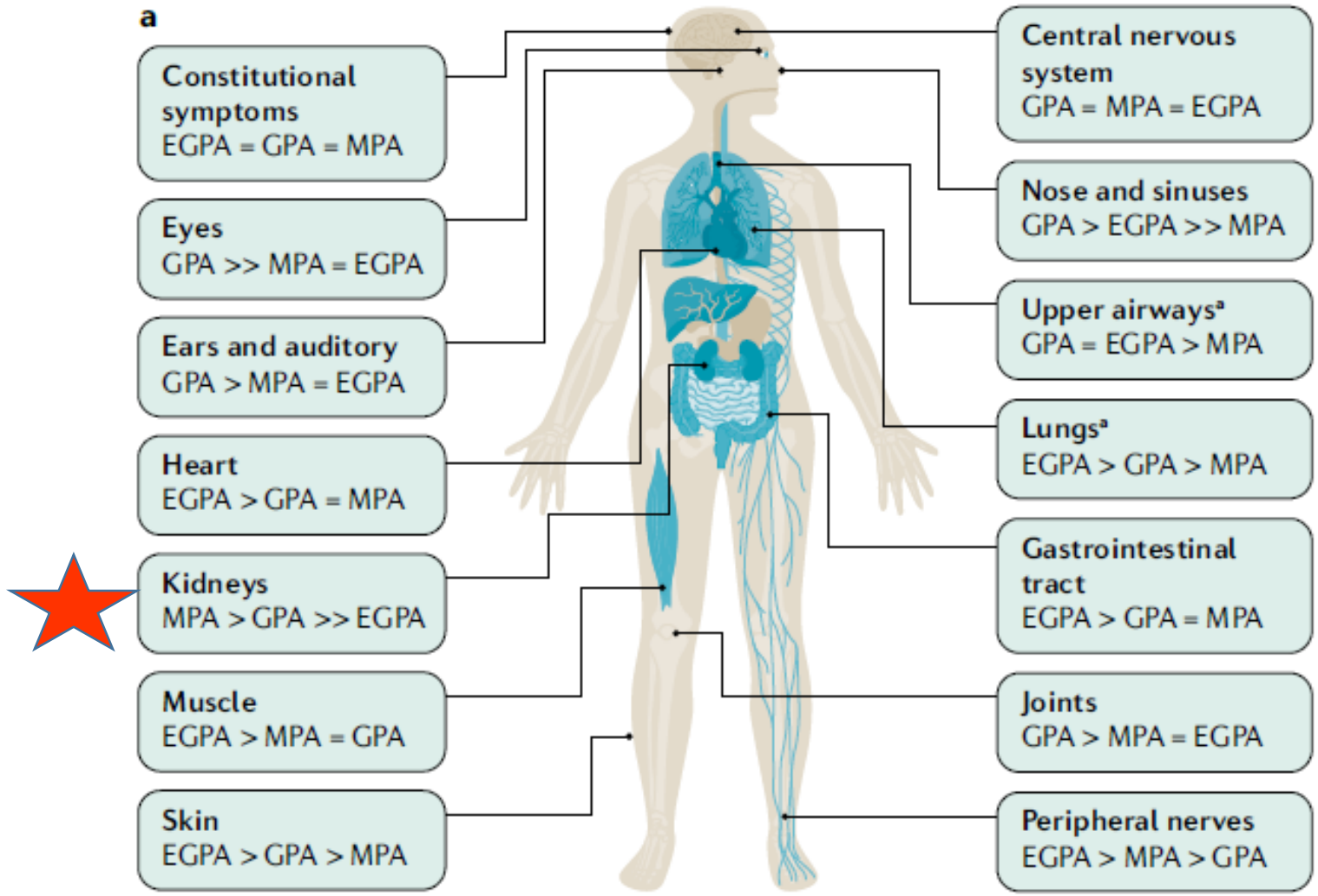
Skin - Rash (50%), Arthralgias (10-50%)

Pulmonary - Hemoptysis (11%), dyspnea, cough

Cardiovascular – Chest pain, symptoms of heart failure

Gastrointestinal (GI) - GI bleeding, abdominal pain

Neurologic - mononeuritis multiplex (57%); CNS- (seizures) (11%


a
Constitutional symptoms
EGPA = GPA = MPA
Eyes
GPA >> MPA = EGPA
Ears and auditory
GPA > MPA = EGPA
Heart
EGPA > GPA = MPA
Kidneys
MPA > GPA >> EGPA
Muscle
EGPA > MPA = GPA
Skin
EGPA > GPA > MPA
Central nervous system
GPA = MPA = EGPA
Nose and sinuses
GPA > EGPA >> MPA
Upper airways[a]
GPA = EGPA > MPA
Lungs[a]
EGPA > GPA > MPA
Gastrointestinal tract
EGPA > GPA = MPA
Joints
GPA > MPA = EGPA
Peripheral nerves
EGPA > MPA > GPA

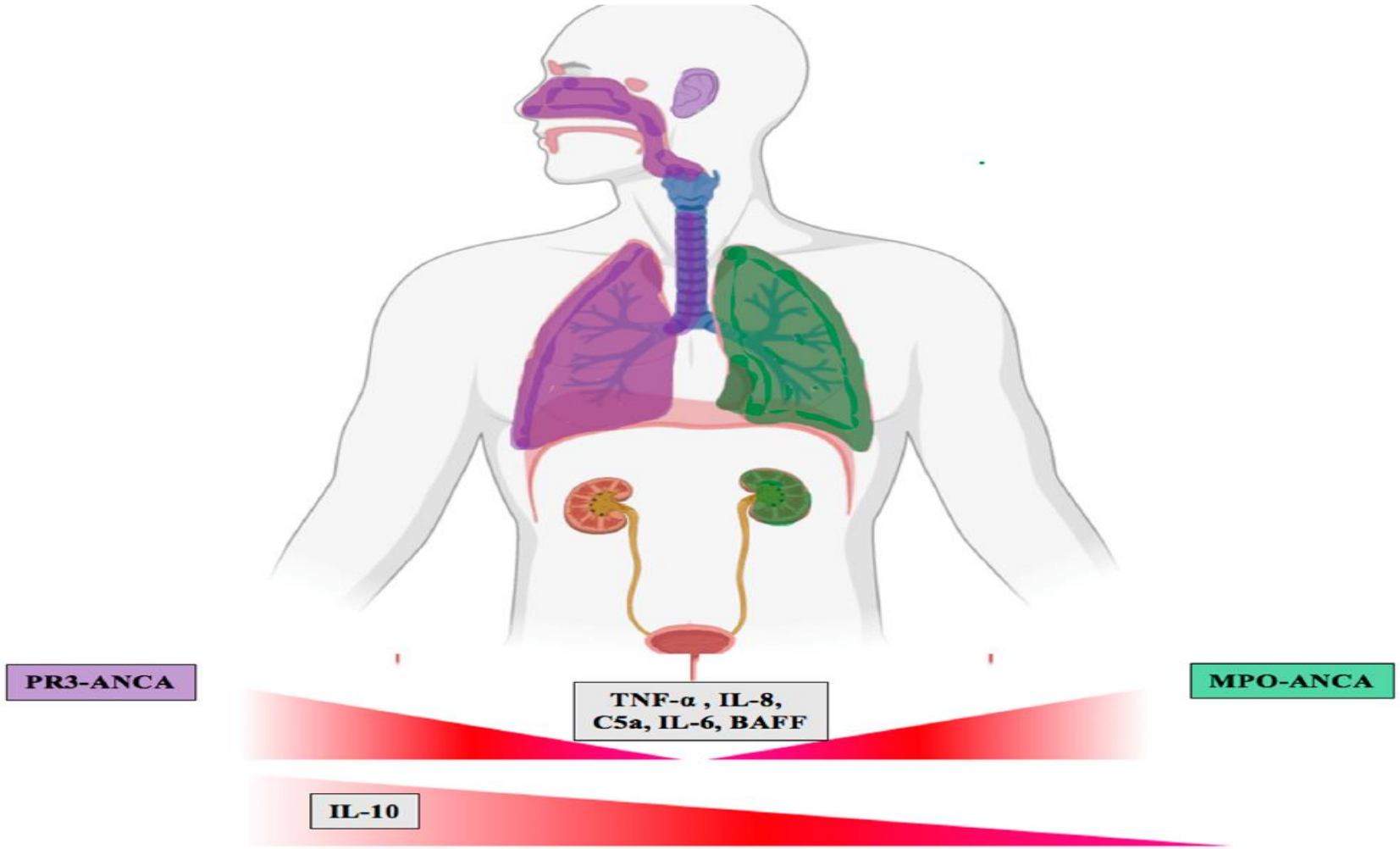


Figure 2. Phenotypes of ANCA serotypes. PR3-ANCA (purple) affects the ear nose and throat (ENT), the upper and lower respiratory tract and the kidneys in around 50–60% of cases, while MPO-ANCA (green) primarily affects the lungs and kidneys. Tumor necrosis factor (TNF)-α, C5a, interleukin (IL)-6, IL-8, and B cell activating factor (BAFF) are elevated in both PR3- and MPO-ANCA. IL-10 is elevated only in PR3-ANCA and is decreased in MPO-ANCA.

Serotype versus Clinical Syndrome

- ANCA antigen specificity is more closely associated with disease phenotype/prognosis than the clinical syndrome
- PR3-ANCA
  - Granulomatous inflammation
  - More extensive extrarenal involvement
  - Higher relapse rate
- MPO-ANCA
  - Renal-limited disease
  - More kidney scarring
  - Carries an overall worse renal prognosis

AT THE FOREFRONT
UChicago Medicine

Some patients with GPA or MPA present with vasculitis limited to a single organ, such as the kidneys, ENT tract or lungs, which may represent the early stages of AAV.

However, in MPO- ANCA+ patients with MPA, isolated renal disease or isolated pulmonary fibrosis is not infrequent.

- ✓ A minority of MPO- ANCA+ patients with MPA also have anti- glomerular basement membrane antibodies and exhibit a hybrid disease phenotype.
(Dual-Positive ANCA and Anti-GBM Disease)

- ✓ Moreover, individuals with systemic lupus erythematosus or systemic sclerosis can be MPO- ANCA+ and develop some features of AAV, especially the vasculitic pattern of glomerulonephritis.

Table 1 | **Comparison of the three syndromic presentations of AAV**

Feature	GPA	MPA	Eosinophilic GPA
Incidence	0.4–11.9 cases per 1 million person-years	0.5–24.0 cases per 1 million person-years	0.5–2.3 cases per 1 million person-years
Prevalence	2.3–146.0 cases per 1 million persons	9.0–94.0 cases per 1 million persons	2.0–22.3 cases per 1 million persons
Typical age of onset (years)	45–65	55–75	38–54
Male: female ratio	1:1	1:1	1:1
2012 revised CHCC definition[145]	Necrotizing granulomatous inflammation, usually involving the upper and lower respiratory tract; necrotizing vasculitis affecting predominantly small-to-medium vessels (such as capillaries, venules, arterioles, arteries and veins); necrotizing glomerulonephritis is common	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (such as 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	Eosinophil-rich and necrotizing granulomatous inflammation, often involving the respiratory tract; necrotizing vasculitis predominantly affecting small-to-medium vessels; associated with asthma and eosinophilia; ANCA$^+$ is more frequent when glomerulonephritis is present
Frequency of ANCA	PR3-ANCA$^+$: 65–75% MPO-ANCA$^+$: 20–30% ANCA$^-$: 5%	PR3-ANCA$^+$: 20–30% MPO-ANCA$^+$: 55–65% ANCA$^-$: 5–10%	PR3-ANCA$^+$: <5% MPO-ANCA$^+$: 30–40% ANCA$^-$: 55–65%
Key innate immune cell	Neutrophil	Neutrophil	Eosinophil
Relapse rate	Higher than MPA (or MPO-AAV)	Lower than GPA (or PR3-AAV)	Relapse is frequent

RPGN: 80-100%

AAV, ANCA-associated vasculitis; ANCA, anti-neutrophil cytoplasmic antibody; CHCC, Chapel Hill Consensus Conference; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, myeloperoxidase; PR3, leukocyte proteinase 3.

Table 2. Comparison of Clinical Features by ANCA Specificity

	PR3-ANCA	MPO-ANCA
Demographics	50-70 y	60-80 y (mean, 10 y older than PR3-ANCA)
Geography	Northern Europe, North America	Southern Europe, Asia
Genetic risk alleles	*HLA-DP, PRTN3, SERPINA1*	*HLA-DQ*
Pathology	Necrotizing vasculitis, granulomatous inflammation	Necrotizing vasculitis, no granulomatous inflammation
Renal	More acute presentation	More common, more chronic injury on biopsy, may have a slow indolent course, more likely renal limited, isolated interstitial kidney disease (rare), usually MPO-ANCA
Respiratory involvement	More common; nodules, cavitation, and central airway disease more specific to PR3	Less common; may be chronic lung fibrosis, peripheral reticulation, honeycombing and usual interstitial pneumonia more specific to MPO
Upper airway disease	More common, destructive lesions (nasal perforation, saddle nose)	Rare
Outcomes	More likely to have resistant disease	Worse long-term survival (more chronic injury)
Relapse rate	Higher	Lower
Treatment	May respond better to rituximab than cyclophosphamide	Similar response to rituximab and cyclophosphamide

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; MPO, myeloperoxidase; PR3, proteinase 3.

These classification criteria should be applied when a diagnosis of small or medium vessel vasculitis has been made, to classify a patient as having microscopic polyangiitis. Alternate diagnoses mimicking vasculitis should be excluded prior to applying the criteria.

Clinical	Nasal bloody discharge, ulcers, crusting, congestion or blockage, or nasal septal defect /perforation	-3
Diagnostic Tests	pANCA or anti-MPO ANCA positive	+6
	Fibrosis or interstitial lung disease on chest imaging	+3
	Pauci-immune glomerulonephritis on biopsy	+3
	cANCA or anti-PR3 ANCA positive	-1
	Serum eosinophil count ≥ 1 ($\times 10^9$/L)	-4

Sum scores for 6 items. A score of ≥ 5 is needed for classification of MPA

ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic anti-neutrophil cytoplasmic antibody; MPO: myeloperoxidase; pANCA: perinuclear anti-neutrophil cytoplasmic antibody; PR3: proteinase 3

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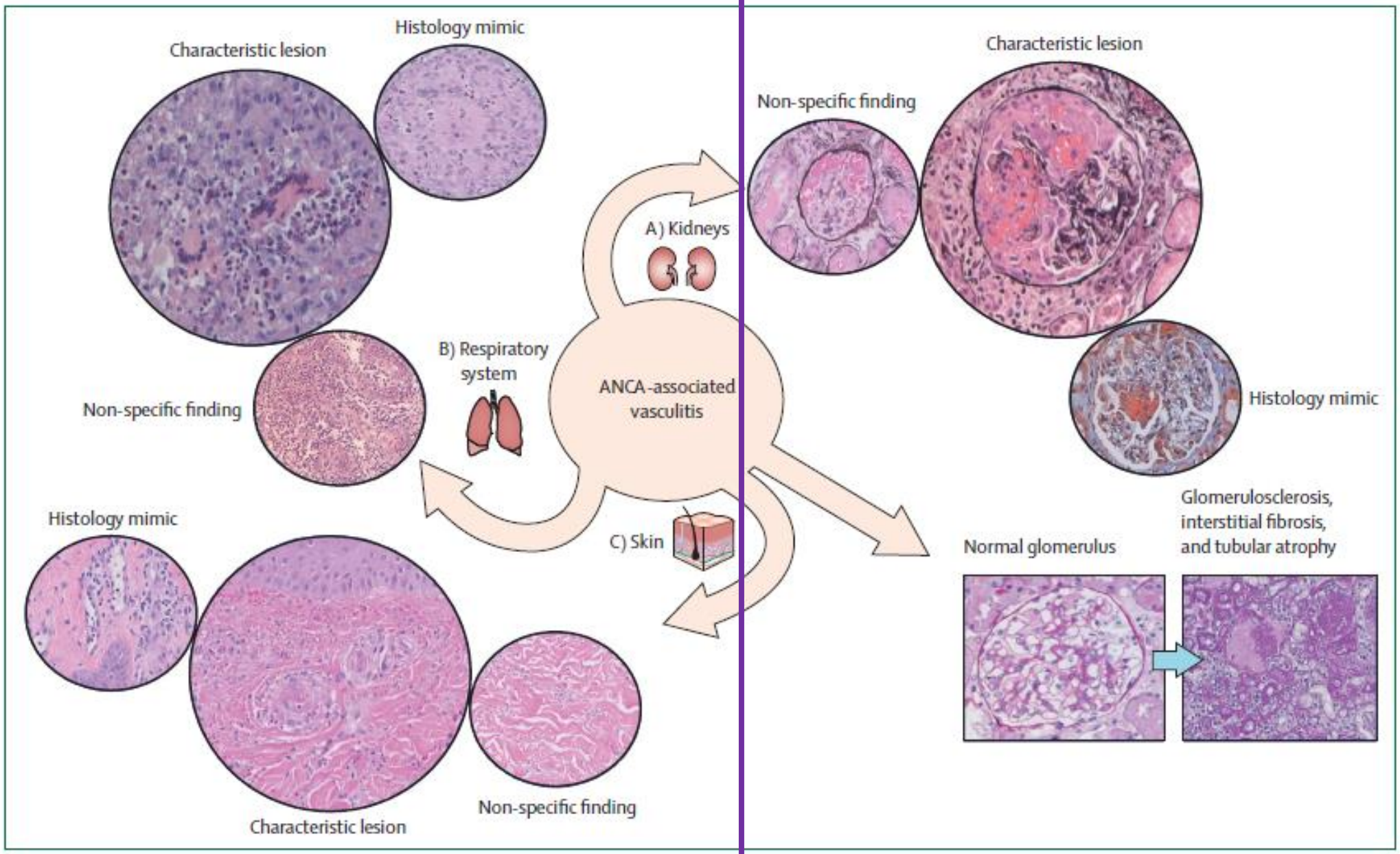
In the kidneys, the characteristic lesion in AAV is segmental necrosis of glomerular capillary loops, with little or no deposition of immunoglobulin
or complement, termed '**pauci- immune'**
focal necrotizing (and crescentic) glomerulonephritis.


Characteristic lesion
Histology mimic
Non-specific finding
A) Kidneys
B) Respiratory system
ANCA-associated vasculitis
C) Skin
Histology mimic
Characteristic lesion
Non-specific finding
Non-specific finding
Characteristic lesion
Histology mimic
Normal glomerulus
Glomerulosclerosis, interstitial fibrosis, and tubular atrophy

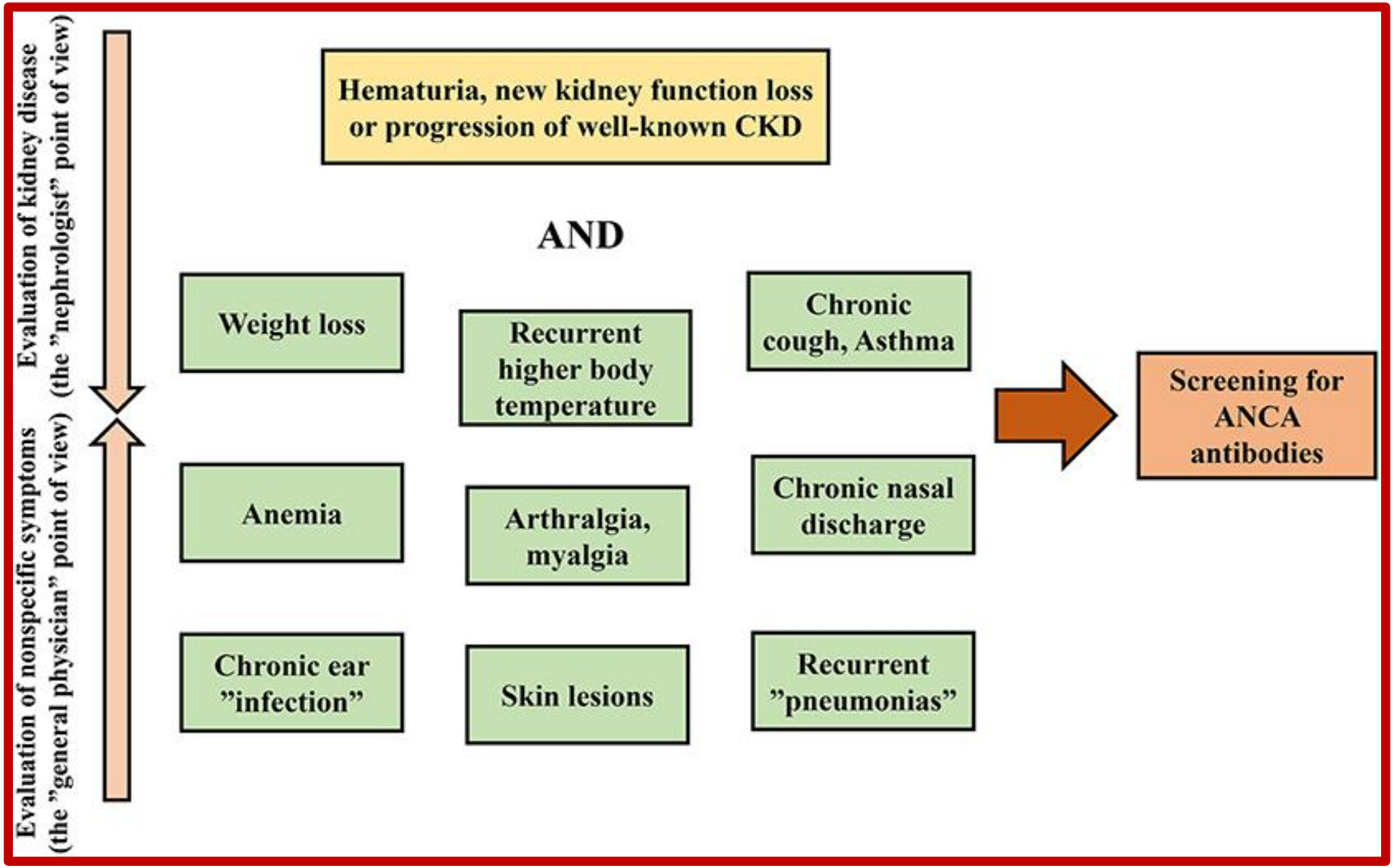
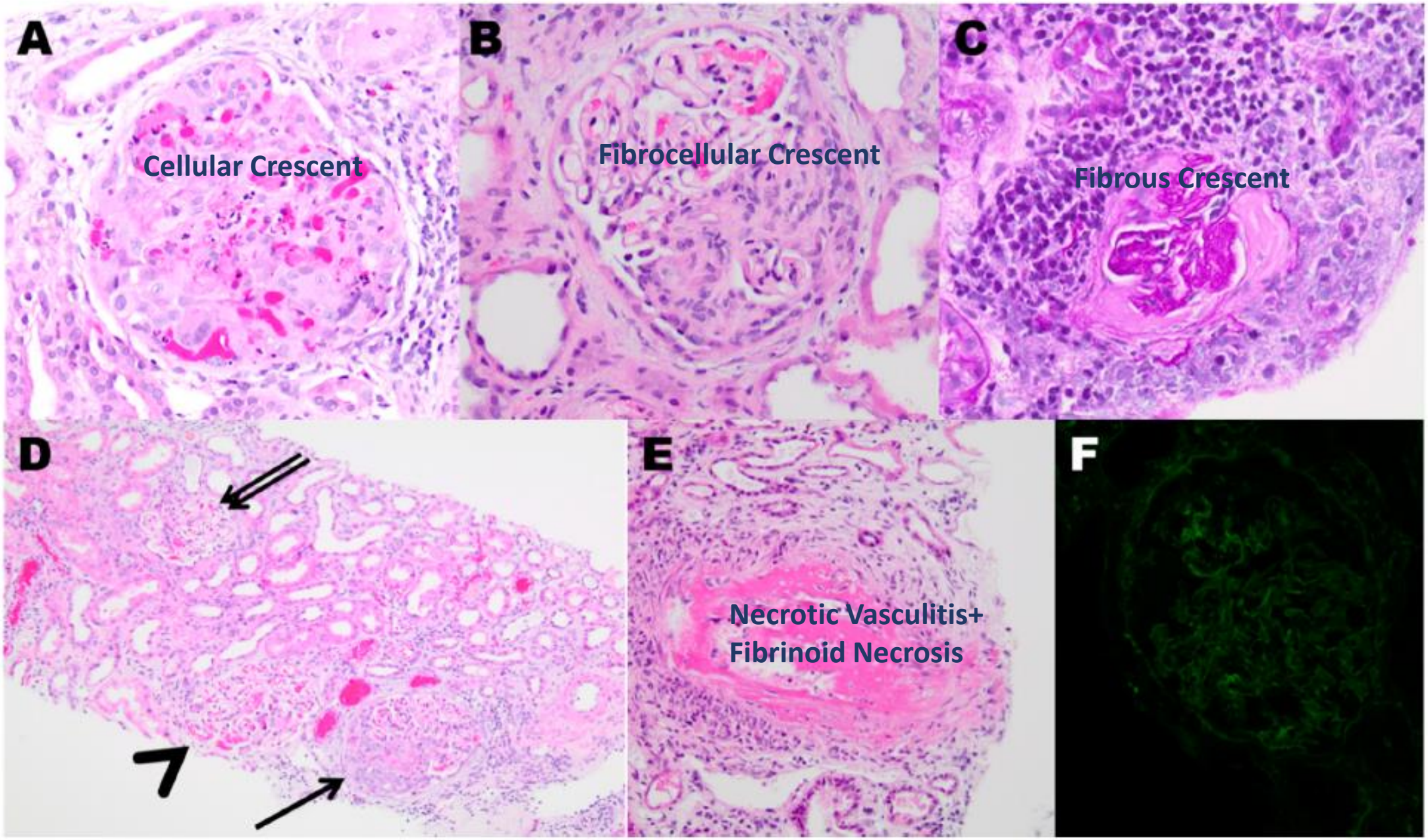
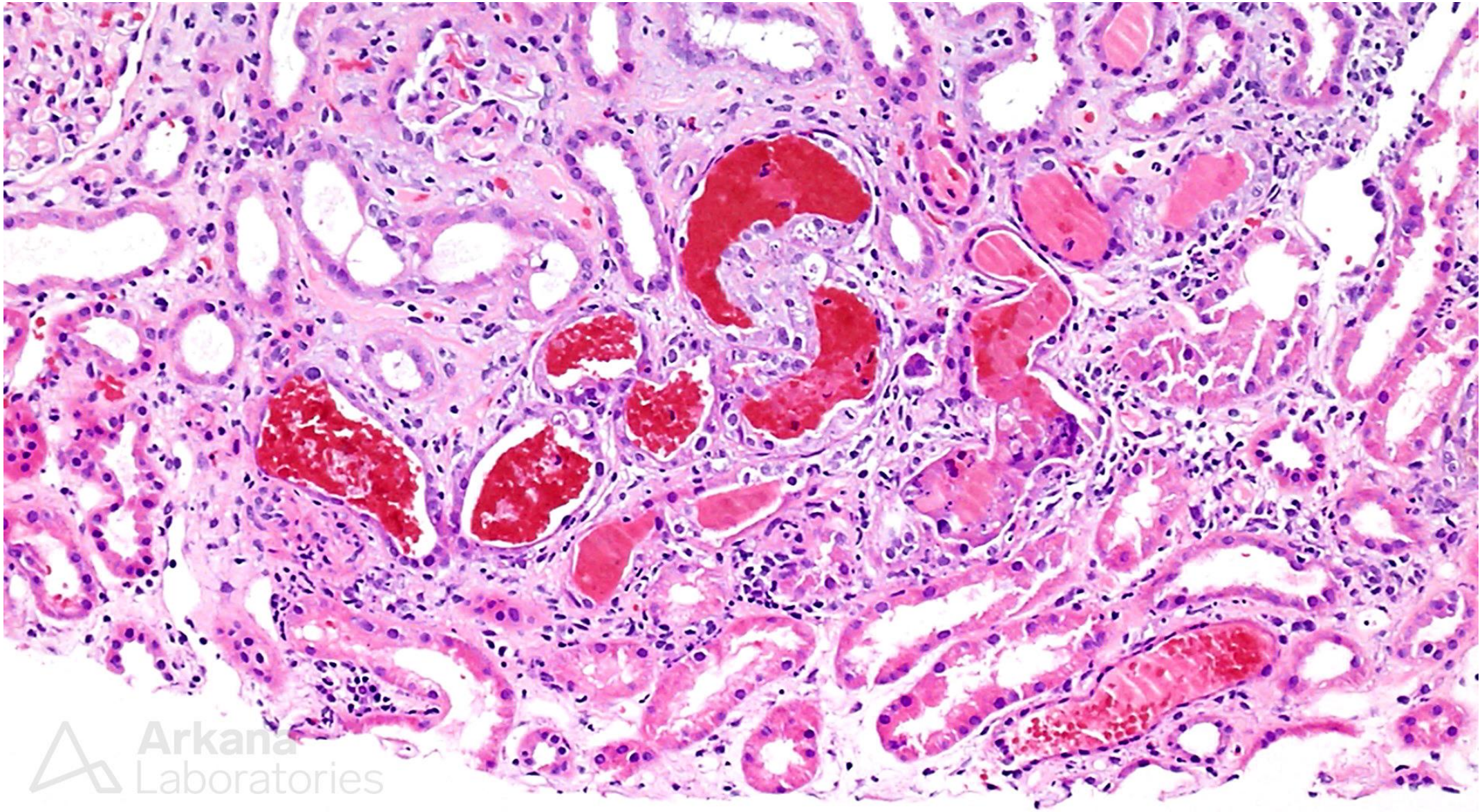

Evaluation of kidney disease (the "nephrologist" point of view)
Evaluation of nonspecific symptoms (the "general physician" point of view)
Hematuria, new kidney function loss or progression of well-known CKD
AND
Weight loss
Recurrent higher body temperature
Chronic cough, Asthma
Anemia
Arthralgia, myalgia
Chronic nasal discharge
Chronic ear "infection"
Skin lesions
Recurrent "pneumonias"
Screening for ANCA antibodies

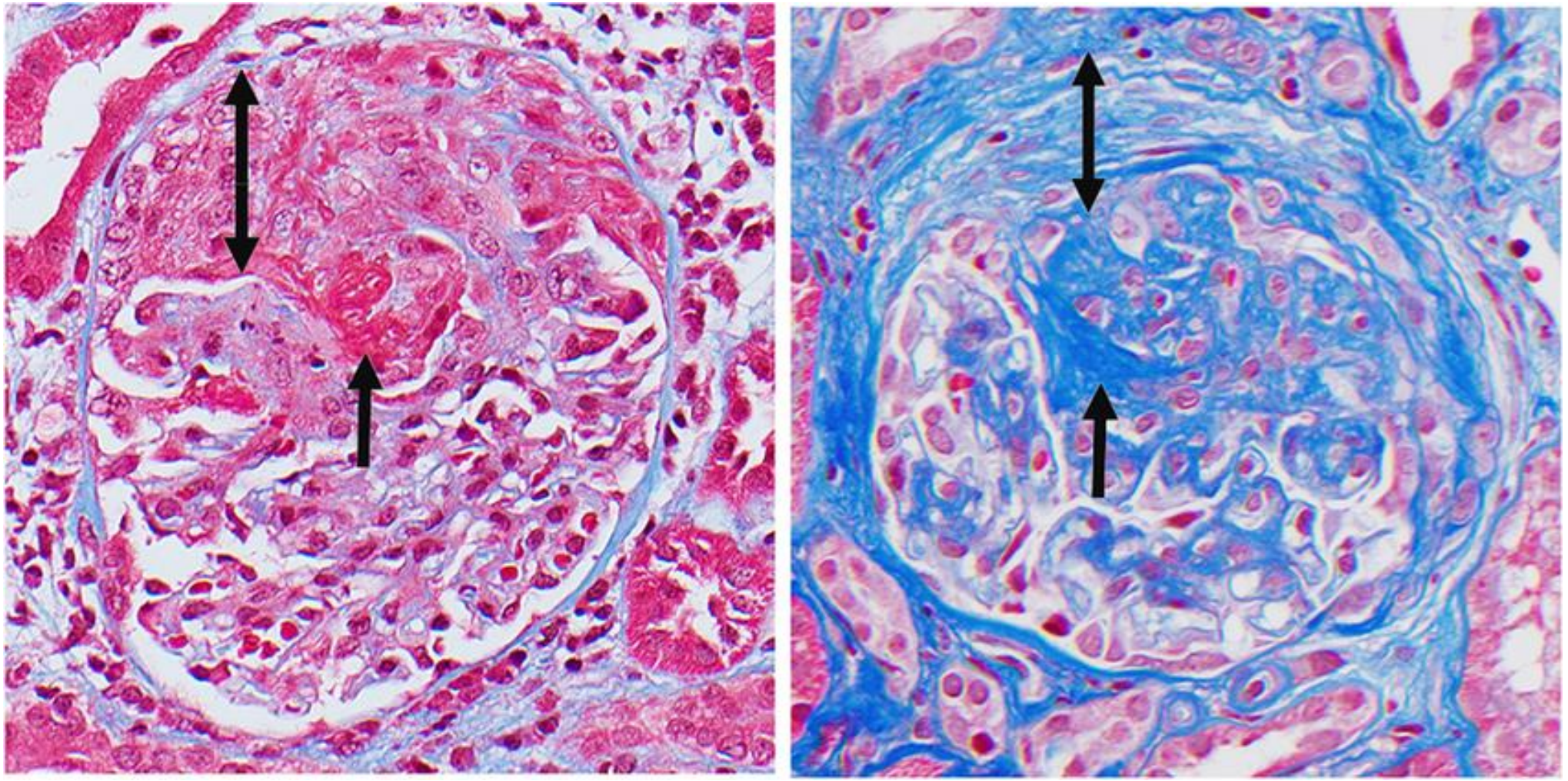
Table 2. Classification of ANCA-associated glomerulonephritis *.

Class	Criteria
Focal	≥50% of glomeruli are normal
Crescentic	≥50% of glomeruli have cellular crescents
Sclerotic	≥50% of glomeruli are globally sclerosed
Mixed	Not fulfilling any of the above criteria


A
Cellular Crescent
B
Fibrocellular Crescent
C
Fibrous Crescent
D
E
Necrotic Vasculitis+
Fibrinoid Necrosis
F

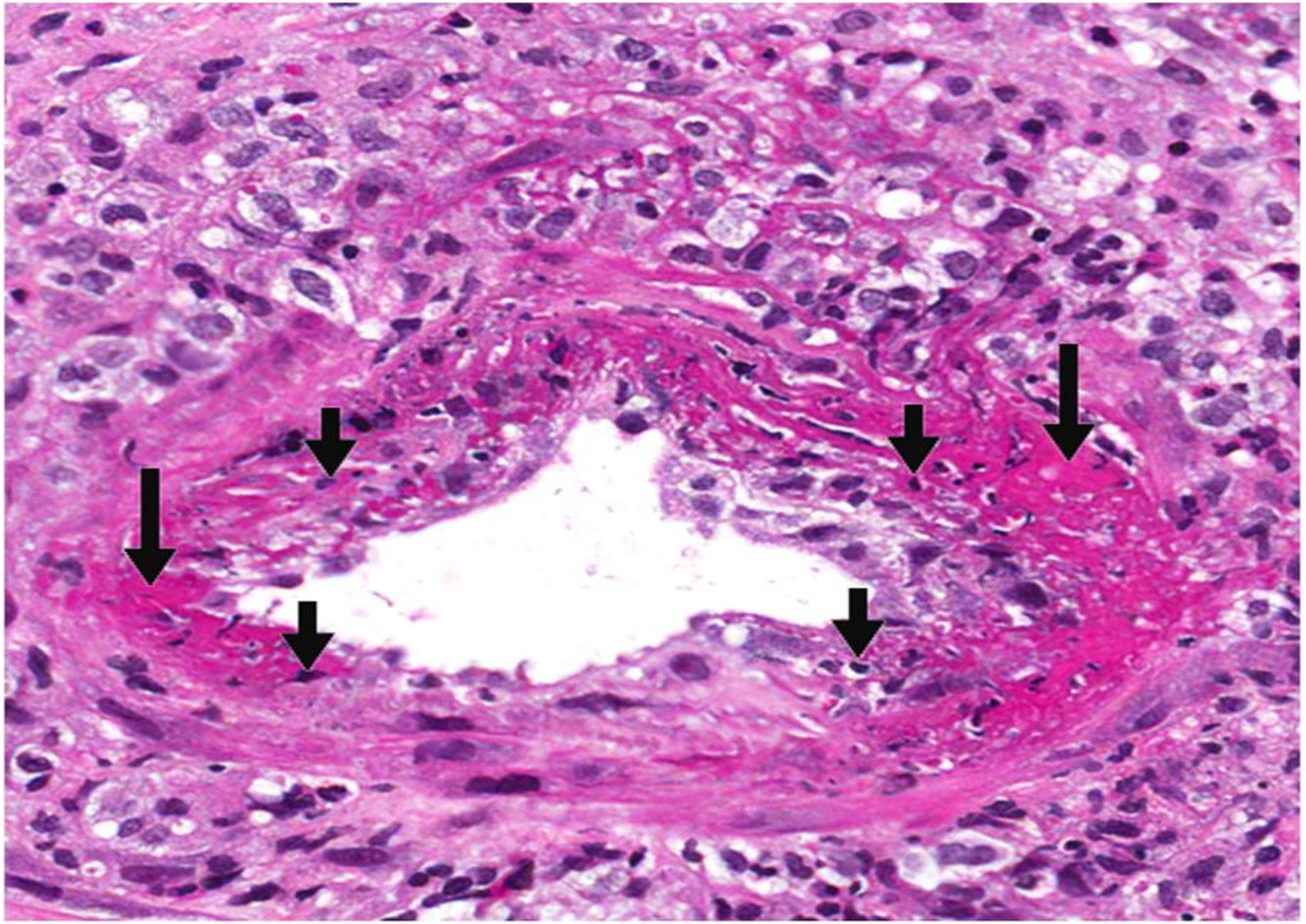
RBC casts

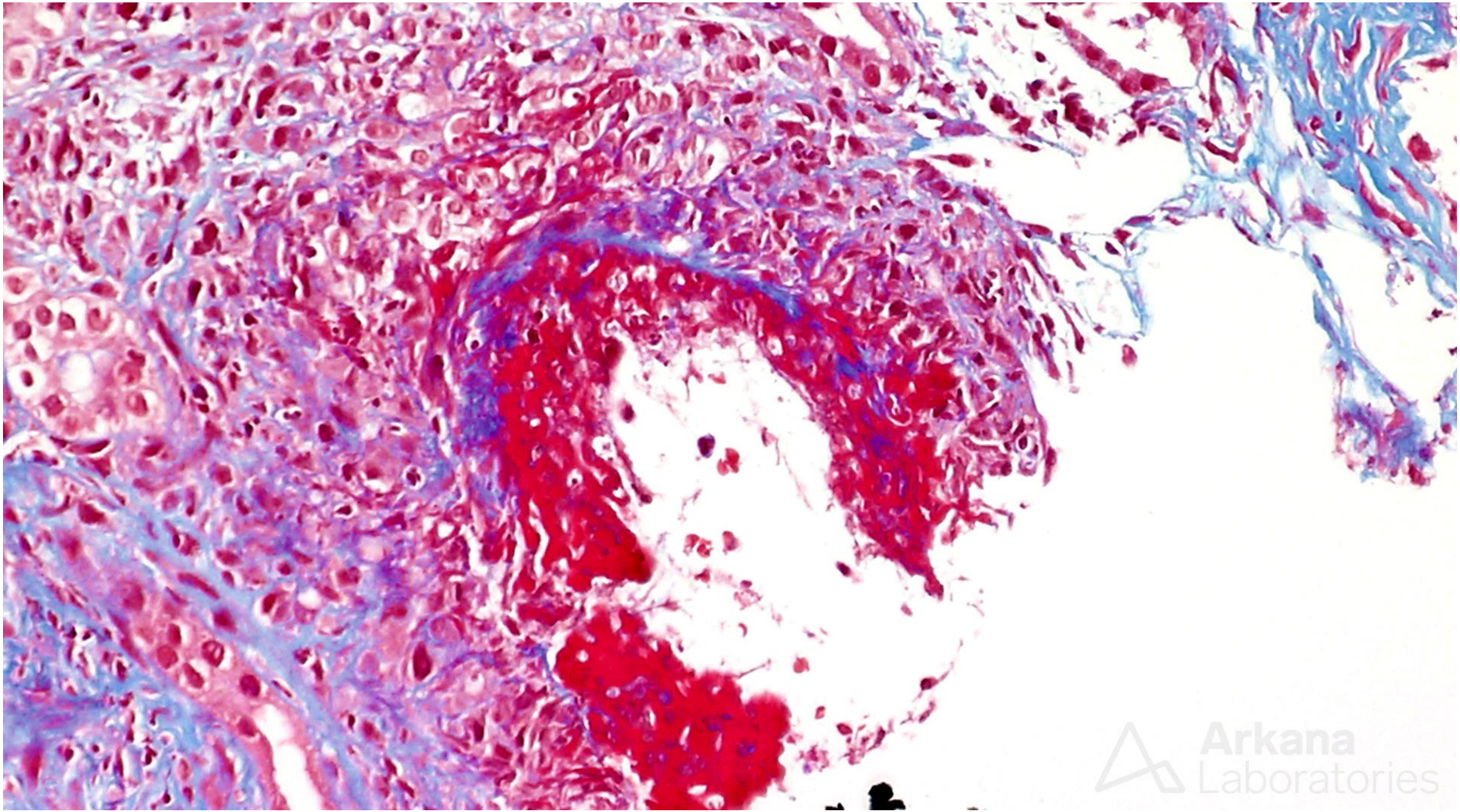


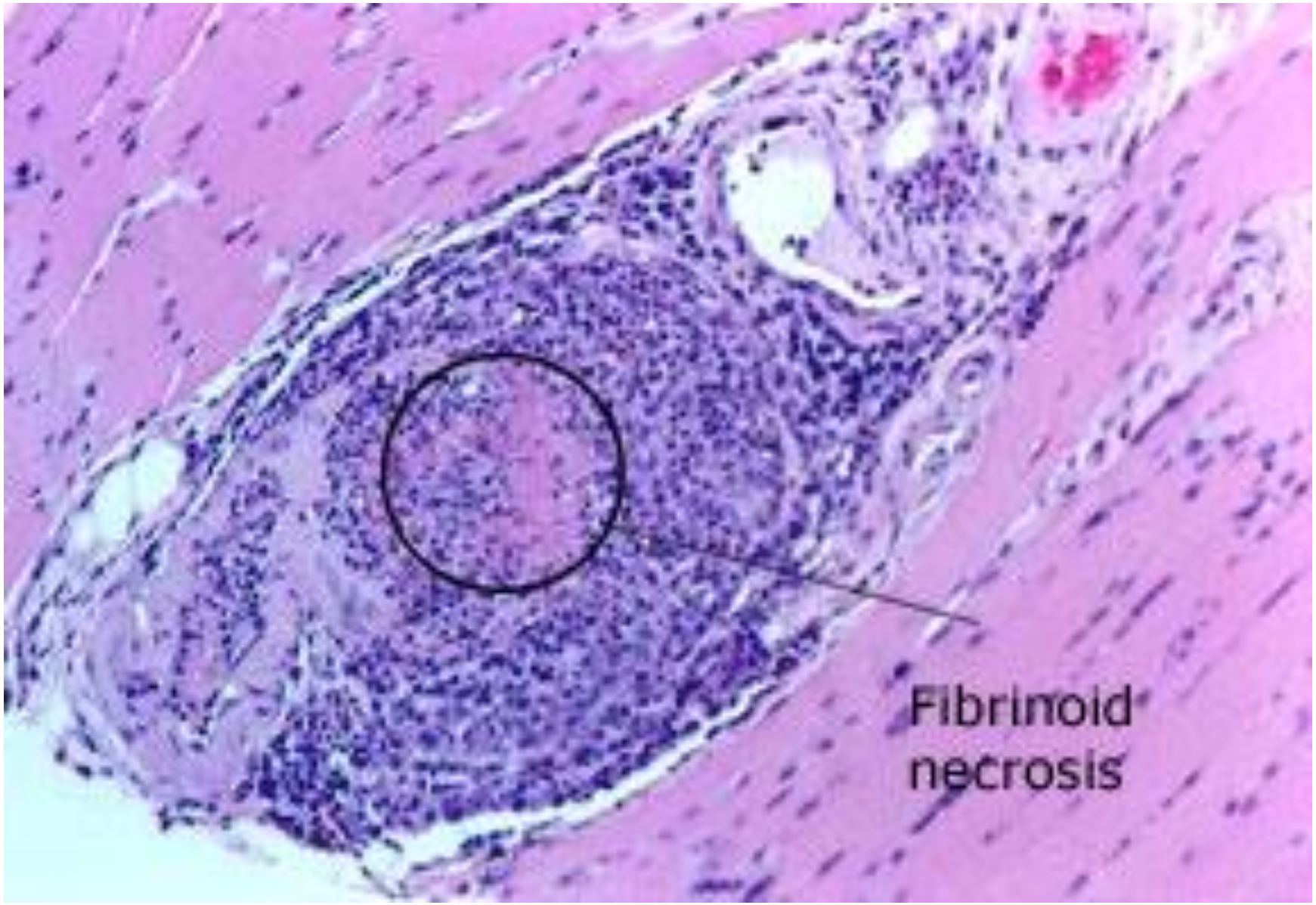


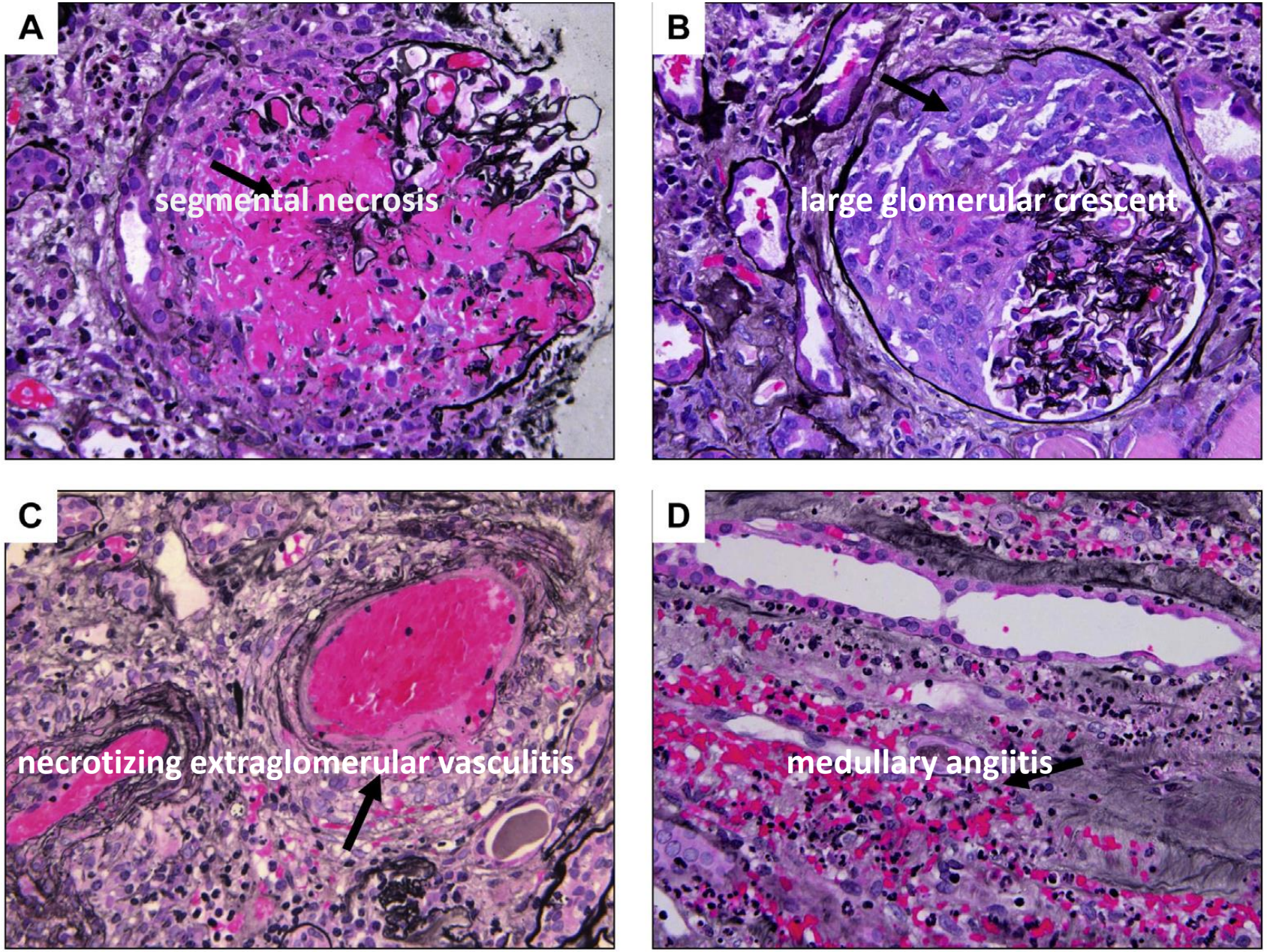
Left panel: active glomerulonephritis with segmental fibrinoid necrosis (short arrow) and cellular crescent (double arrow).
Right panel: sclerotic glomerulonephritis with segmental sclerosis (short error) and fibrotic crescent (double arrow)

Arteritis with fibrinoid necrosis

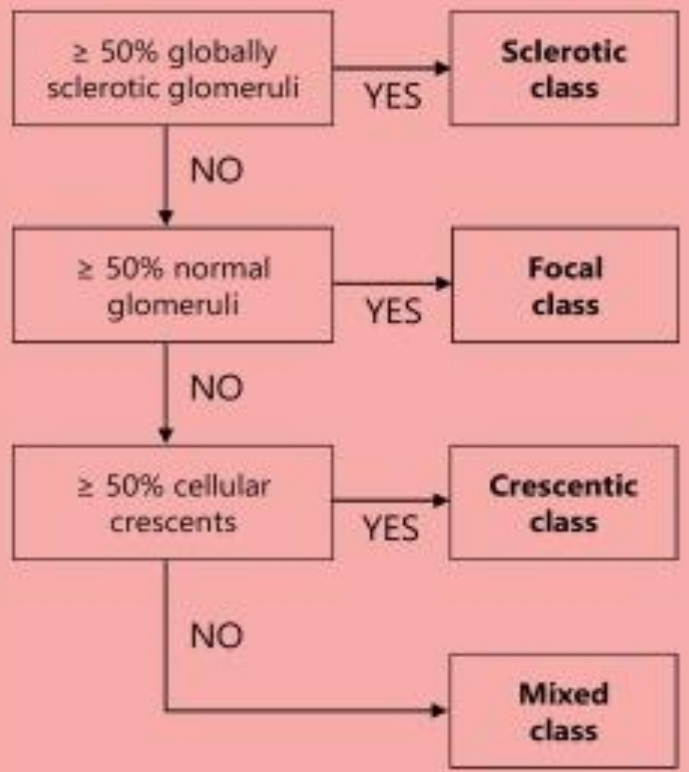



Arkana
Laboratories


Fibrinoid
necrosis


A
segmental necrosis
B
large glomerular crescent
C
necrotizing extraglomerular vasculitis
D
medullary angiitis

Histopathological classification



ANCA Renal Risk Score

Risk factor	Points
Normal glomeruli	
> 25%	0
10-25%	4
< 10%	6
IF/TA	
≤ 25%	0
> 25%	2
GFR at diagnosis	
> 15 mL/min	0
≤ 15 mL/min	3

Total	Risk group
0	**Low**
2-7	**Medium**
8-11	**High**

Mayo Clinic Chronicity Score

	Points			
	0	1	2	3
GS	< 10%	10-25%	26-50%	> 50%
IF	< 10%	10-25%	26-50%	> 50%
TA	< 10%	10-25%	26-50%	> 50%
	0			1
CV	Thickening			
	Intima < media			Intima ≥ media

Total	Grade
0-1	**Minimal**
2-4	**Mild**
5-7	**Moderate**
≥ 8	**Severe**

The prognostic value of two histopathologic classification models of ANCA-associated glomerulonephritis: A prospective study

Christodoulou M.[1], Moysidou E.[1], Lioulios G.[1], Stai S.[1], Bandis K.[1], Flaris N.[2], Nikolaidou C.[2], Fylaktou A.[3], Papagianni A.[1], Stangou M.[1]

[1] School of Medicine, Aristotle University of Thessaloniki, Department of Nephrology, Hippokration Hospital, 54642 Thessaloniki, Greece.
[2] Department of Pathology, Hippokration General Hospital, 54642 Thessaloniki, Greece.
[3] Department of Immunology, National Histocompatibility Center, Hippokration General Hospital, 54642 Thessaloniki, Greece.

Background: Berden Classification and ANCA renal risk score (RRS) are classification models, aiming to rate renal histology and outcome in patients with ANCA-associated vasculitis /Glomerulonephritis (AAV/GN). In the present study we compare their ability to predict renal function outcome in short and long term follow up.

Methods: N=94 AAV/GN patients

- Kidney biopsy
- Classification according to Berden and RRS
- Same treatment protocol
- 60 months of follow-up
- Renal function recorded at three (T3), six (T6) and sixty (T60) months of follow-up
- Results compared to both classification systems

Results:

- Patients were grouped as Focal (n=24), Crescentic (n=35), Mixed (n=21) and Sclerotic (n=14), and had significant differences in eGFR at T3 only, while the percentage of those requiring hemodialysis differed at T0, T3, T6 but not at T60.
- According to RRS, patients were classified as Low (n=8), Medium (n=47) and High (n=39) risk, and showed significant differences in both eGFR levels, proportion of hemodialysis, at T0, T3, T6 and end-stage kidney disease (ESKD) at T60.
- Even patients classified as Mixed (Berden) and as Medium or High risk (RRS) had significant improvement from T0 to T6, $p=0.001$, $p<0.0001$, $p=0.05$, respectively. Relapse could not be predicted by either system.

Journal of NEPHROLOGY
official journal of the Italian Society of Nephrology

Conclusions: Neither system could predict renal function outcome or need for hemodialysis in the short term, but RRS showed a clear superiority in predicting renal function outcome and ESKD after long term follow up.

ANCA positive Conditions
DD

	PR3-ANCA (mostly cANCA)	MPO-ANCA (mostly pANCA)	Other
ANCA-Associated Vasculitis			
GPA	75%	20%	5% ANCA negative
MPA	30%	60%	10% ANCA negative
EGPA	5%	45%	50% ANCA negative
Renal-limited vasculitis	10%	80%	10% ANCA negative
Drug-induced vasculitis Hydralazine	10%	90%	Often high titer, dual positivity for MPO and PR3
Nonvasculitis Conditions			
Systemic lupus	2%	10%	10% atypical ANCA
Endocarditis	15%	5%	
Inflammatory bowel disease	Negative	Negative	Atypical ANCA, various antigens: ulcerative colitis (50%-67%), Crohn disease (6%-15%)
Primary sclerosing cholangitis	Negative	Negative	Atypical ANCA, various antigens: 60%-80%
Cystic fibrosis	Negative	Negative	Atypical ANCA pattern, directed against BPI (90%)

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; BPI, bactericidal/permeability-induced protein; cANCA, cytoplasmic antineutrophil cytoplasmic antibody; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; MPO, myeloperoxidase; pANCA, perinuclear antineutrophil cytoplasmic antibody; PR3, proteinase 3.

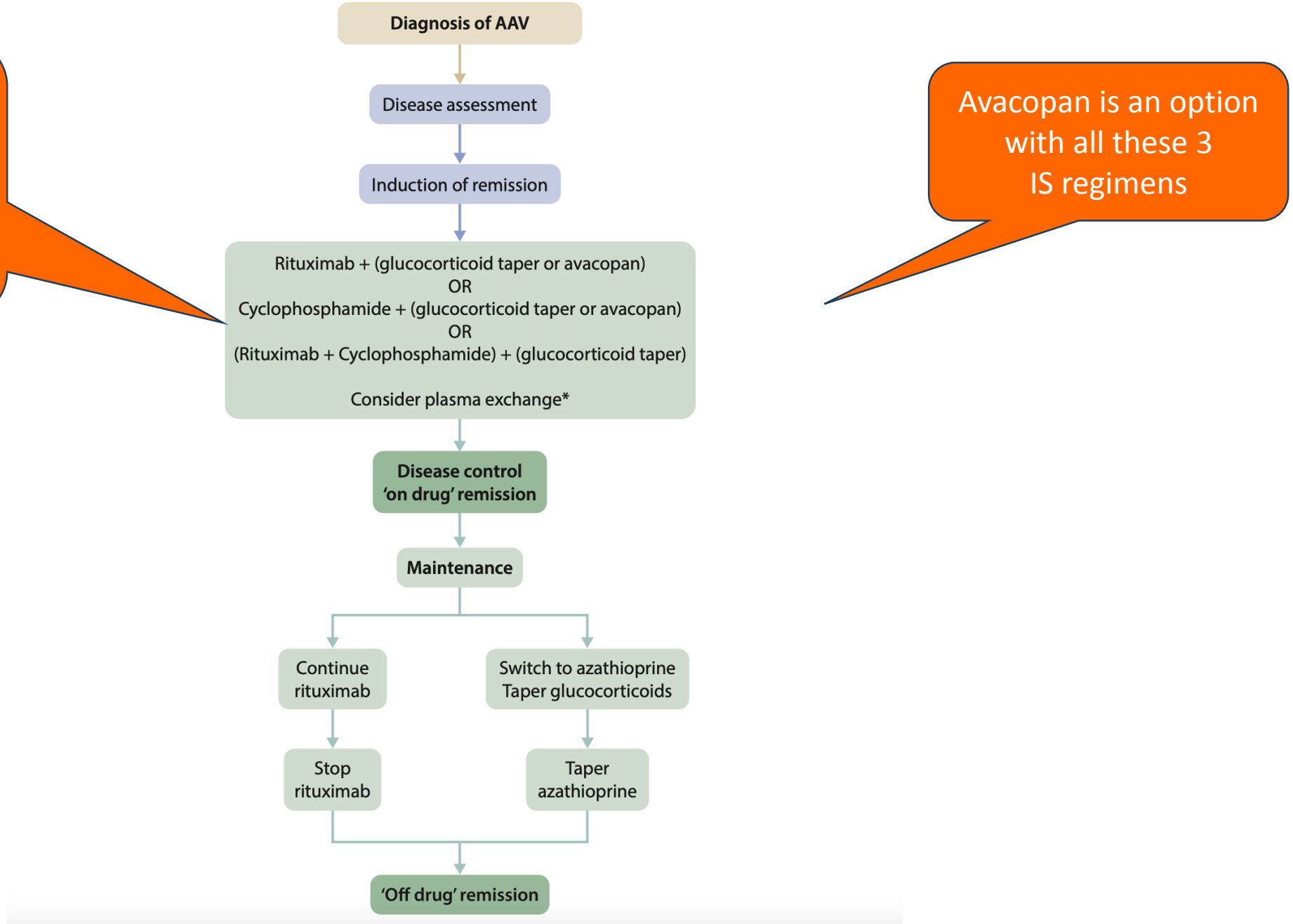

BVAS
Birmingham Vasculitis
Activity Score


VDI
Vasculitis Damage Index

Table 1 – VDI and AVID scores by category

	VDI		AVID	
Category	Baseline	End of follow-up	Baseline	End of follow-up
Musculoskeletal	11	20	16	27
Skin	3	5	16	33
Ocular	17	29	28	57
Ear/Nose/Throat	84	124	150	232
Pulmonary	20	44	9	27
Cardiovascular	21	45	39	80
Peripheral vascular disease	3	8	-	-
Gastrointestinal	1	1	1	1
Renal	30	84	42	108
Neuropsychiatric	16	37	-	-
Neurological	-	-	41	67
Psychiatric	-	-	6	9
Endocrine	-	-	23	32
Hematology/Oncology	-	-	1	3
Other	24	34	42	96
Total	230	431	414	772

The goal is to achieve disease control
What we call:
An on drug remission



Avacopan is an option with all these 3 IS regimens

How do we choose between these options ?

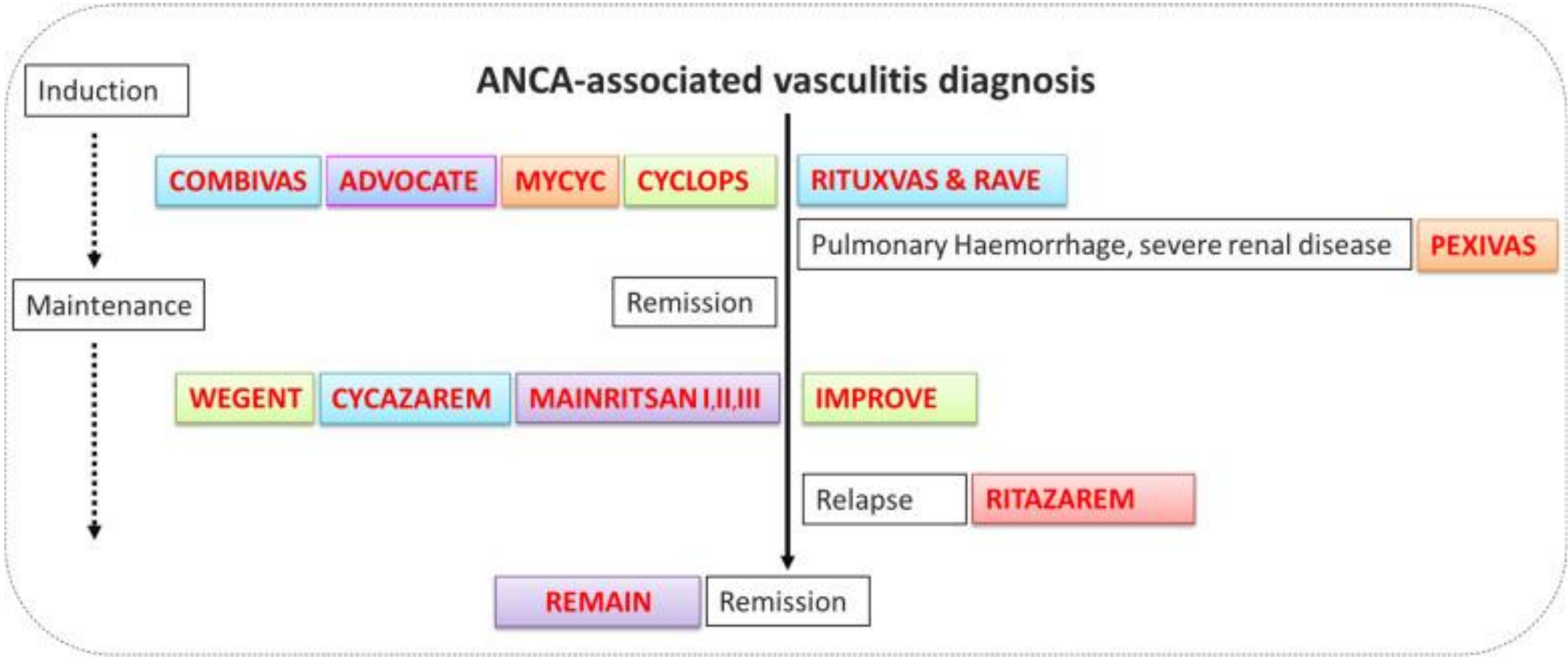
CPA is still an effective ttt
Many Nephrologists still prefer to include or use CPA in pts w/ more advanced kidney disease
We do not have robust clinical tirla data supporting Rtxmb without CPA

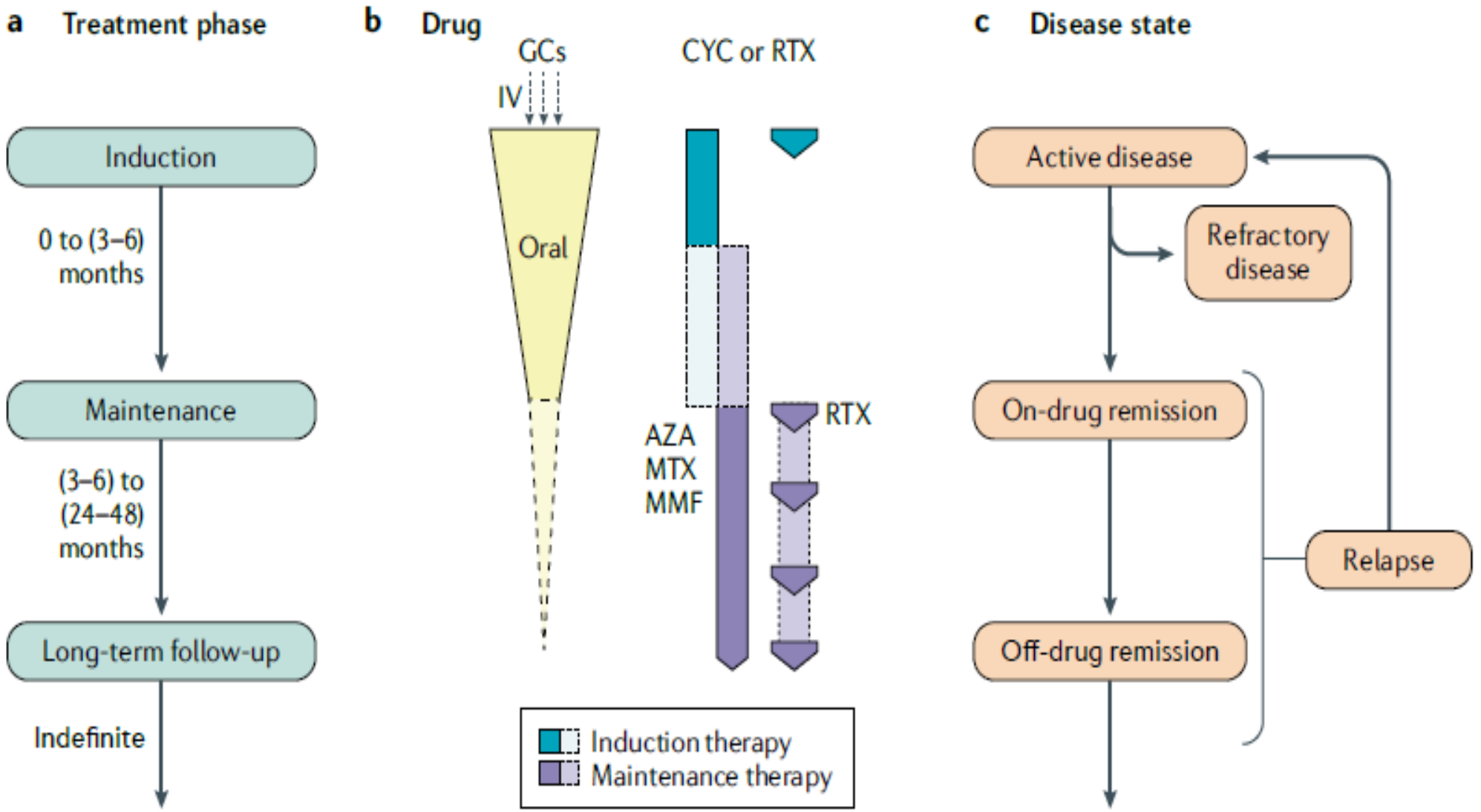
Rituximab preferred	Cyclophosphamide preferred
• Children and adolescents • Pre-menopausal women and men concerned about their fertility • Frail older adults • Glucocorticoid-sparing especially important • Relapsing disease • PR3–ANCA disease	• Rituximab difficult to access • Severe GN (SCr >4 mg/dl [354 µmol/l]), combination of two intravenous pulses of cyclophosphamide with rituximab can be considered

Figure 77 | Factors for consideration when choosing between rituximab and cyclophosphamide for induction therapy of AAV. AAV, ANCA-associated vasculitis; ANCA, antineutrophil cytoplasmic antibody; GN, glomerulonephritis; PR3, proteinase 3; SCr, serum creatinine.

Combination Tx

Ritxmb 1000 mg x 2 + CPA pulse x 2


ANCA-associated vasculitis diagnosis
Induction
COMBIVAS
ADVOCATE
MYCYC
CYCLOPS
RITUXVAS & RAVE
Pulmonary Haemorrhage, severe renal disease
PEXIVAS
Maintenance
Remission
WEGENT
CYCAZAREM
MAINRITSAN I,II,III
IMPROVE
Relapse
RITAZAREM
REMAIN
Remission


a
Treatment phase
Induction
0 to (3–6) months
Maintenance
(3–6) to (24–48) months
Long-term follow-up
Indefinite
b
Drug
GCs
IV
Oral
CYC or RTX
AZA
MTX
MMF
RTX
Induction therapy
Maintenance therapy
c
Disease state
Active disease
Refractory disease
On-drug remission
Relapse
Off-drug remission

Conclusion

1-AAV is multisystem disease with varied clinical manifestations which are sometimes non- specific

2- AAV can remain undiagnosed for months or years until think about it and request ANCA testing

3- Role of renal biopsy

4- Early treatment is advised and should be initiated as soon as a diagnosis is probable

5- Assessment of prognosis and residual organ damage

5-Monitoring disease activity and risk of relapse