ANCA-Associated Vasculitis

GPA · MPA · EGPA · Small-vessel disease that destroys kidneys and lungs in days

PULMONARY-RENAL
= treat now

RECOGNIZE IT *a multisystem illness masquerading as something benign*

ENT & UPPER AIRWAY

Classic for GPA. Chronic sinusitis unresponsive to antibiotics, **epistaxis**, nasal crusting, **saddle-nose deformity**, otitis media, hoarseness and **subglottic stenosis**. Often present for months before diagnosis.

LUNG & KIDNEY

Diffuse alveolar hemorrhage — breathlessness, hypoxia, falling hemoglobin, with or without hemoptysis. **Rapidly progressive glomerulonephritis** — rising creatinine with an **active urinary sediment**. This combination is the emergency.

SYSTEMIC & OTHER

Fever, weight loss, arthralgia. **Palpable purpura**, **mononeuritis multiplex**, scleritis or episcleritis. **EGPA** adds **asthma, eosinophilia and nasal polyps**, and carries a specific risk of **cardiomyopathy**.

CONFIRM IT *serology plus tissue, but do not let the biopsy delay treatment*

Test	Interpretation
ANCA serology	**PR3-ANCA (c-ANCA)** associates with **GPA**; **MPO-ANCA (p-ANCA)** with **MPA** and renal-limited disease. **ANCA-negative disease exists** — roughly 10% — so a negative result does not exclude it when the clinical picture is convincing.
Urine microscopy	**Dysmorphic red cells and red cell casts.** The single most useful bedside test — look at it yourself, and repeat it, because renal involvement can be silent until the creatinine climbs.
Kidney biopsy	**Pauci-immune necrotizing crescentic glomerulonephritis.** Confirms the diagnosis and, importantly, **quantifies chronicity**, which predicts renal recovery and informs how aggressively to treat.
Imaging & other	CT chest for nodules, cavitation and hemorrhage; CT sinuses. Send **anti-GBM antibodies** in parallel — double-positive disease occurs and changes management. Check **complement**, which is typically **normal** in ANCA vasculitis.

INDUCE REMISSION *severe disease means organ- or life-threatening*

1. **Severe disease** — life- or organ-threatening, including glomerulonephritis and alveolar hemorrhage — is treated with **glucocorticoids combined with either rituximab or cyclophosphamide**. Rituximab is recommended for induction in severe GPA and MPA, and is generally preferred for relapsing disease and in those wishing to preserve fertility.
2. **Combining rituximab with cyclophosphamide** reduces cumulative cyclophosphamide exposure, and may allow glucocorticoid minimization with improved responses.
3. **Avacopan**, an oral C5a receptor antagonist, is used alongside rituximab or cyclophosphamide specifically to **reduce glucocorticoid exposure** — a major driver of long-term harm in this disease.
4. **Plasma exchange is not recommended routinely.** Consider it for **creatinine above 3.4 mg/dL**, patients **requiring dialysis or with rapidly rising creatinine**, and **diffuse alveolar hemorrhage**. This is a substantial narrowing from older practice.
5. **Non-severe disease** — sinusitis, arthralgia, limited skin involvement without organ threat — can be induced with glucocorticoids plus methotrexate, and does not need cyclophosphamide.

MAINTENANCE & SUPPORTIVE CARE *the part that determines long-term outcome*

MAINTAIN REMISSION

Rituximab is recommended for maintenance in severe GPA and MPA, with azathioprine or methotrexate as alternatives. Continue for **at least 18 months to several years** — relapse is common, and PR3-ANCA disease relapses more than MPO. Monitor for **relapse clinically and by urinalysis**, not by ANCA titre alone.

DO NOT FORGET

Pneumocystis prophylaxis with TMP-SMX for anyone on cyclophosphamide or substantial steroid — and in GPA it may also reduce upper-airway relapse. **Check immunoglobulins before and during rituximab**. **Bone protection**, vaccination before immunosuppression, cardiovascular risk reduction, and **fertility counseling with cyclophosphamide**.

TELL THE THREE APART *they share a treatment backbone but differ in organs and prognosis*

Disease	Typical serology	Distinguishing features
GPA granulomatosis with polyangiitis	**PR3-ANCA** in most	**Upper airway destruction** — saddle nose, subglottic stenosis, destructive sinusitis. **Lung nodules that cavitate.** Granulomatous inflammation on biopsy. **Relapses more often** than MPA.
MPA microscopic polyangiitis	**MPO-ANCA** in most	**No granulomas and no upper-airway destruction.** Dominated by **glomerulonephritis** and **alveolar hemorrhage**, often with pulmonary fibrosis. More insidious onset.
EGPA eosinophilic GPA	**ANCA-negative in about 60%**	**Asthma, nasal polyps and eosinophilia** precede the vasculitis by years. **Cardiac involvement** is the leading cause of death and is commoner in ANCA-negative disease. **Mepolizumab** is used for relapsing or refractory non-severe disease.

FOLLOW THEM UP *relapse is common and mostly detected on routine review*

WHAT TO MONITOR

Urinalysis and creatinine at every visit — renal relapse is silent. Plus symptoms, ESR/CRP, complete blood count, and **immunoglobulin levels on rituximab**. Watch for **subglottic stenosis** in GPA, which can progress without systemic activity and needs ENT assessment rather than more immunosuppression.

DAMAGE vs ACTIVITY

Distinguish **ongoing inflammation** from **accrued damage** — a fixed creatinine, established stenosis, or chronic sinus disease will not respond to escalating immunosuppression, and treating damage as activity exposes patients to avoidable infection. **Infection is a leading cause of death** in treated vasculitis.

PEARLS & PITFALLS

- **Look at the urine yourself.** Red cell casts turn a vague systemic illness into a same-day rheumatology and nephrology emergency.
- **A negative ANCA does not exclude the diagnosis.** Around 10% are seronegative — treat the clinical picture.
- **Falling hemoglobin with hypoxia is alveolar hemorrhage** until proven otherwise, even without hemoptysis.
- **Plasma exchange is now reserved** for severe renal failure, dialysis dependence, rapidly rising creatinine, or alveolar hemorrhage — not for everyone.
- **Do not treat relapse on an ANCA rise alone.** Titres correlate imperfectly; treat the patient and the urine.
- **Prescribe PCP prophylaxis** with the immunosuppression, not after the first opportunistic infection.

References: 2021 ACR/Vasculitis Foundation Guideline for the Management of ANCA-Associated Vasculitis · EULAR 2022 and KDIGO 2024 ANCA vasculitis recommendations · PEXIVAS and ADVOCATE trials.

Educational aid; verify doses against local protocol, renal function, and patient factors.

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