Cardiovascular system block

Pathology team 431

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Vasculitis

Vascular inflammatory injury, often with necrosis

- A clinico-pathologic process characterized by:

Inflammatory destruction of blood vessels →occlusion or destruction of the vessel → ischemia of the tissues supplied by that vessel.

Causes

- **Immune-mediated**
  - Immune complex deposition
  - Anti-neutrophil cytoplasmic antibodies (ANCAs)
  - Anti-endothelial cell antibodies
- invasion of vascular walls by **infectious pathogens**
- Physical and chemical injury

* Mainly the cause of vasculitis is **AUTOIMMUNE DISEASE** that begins in the vessel and destructs it.

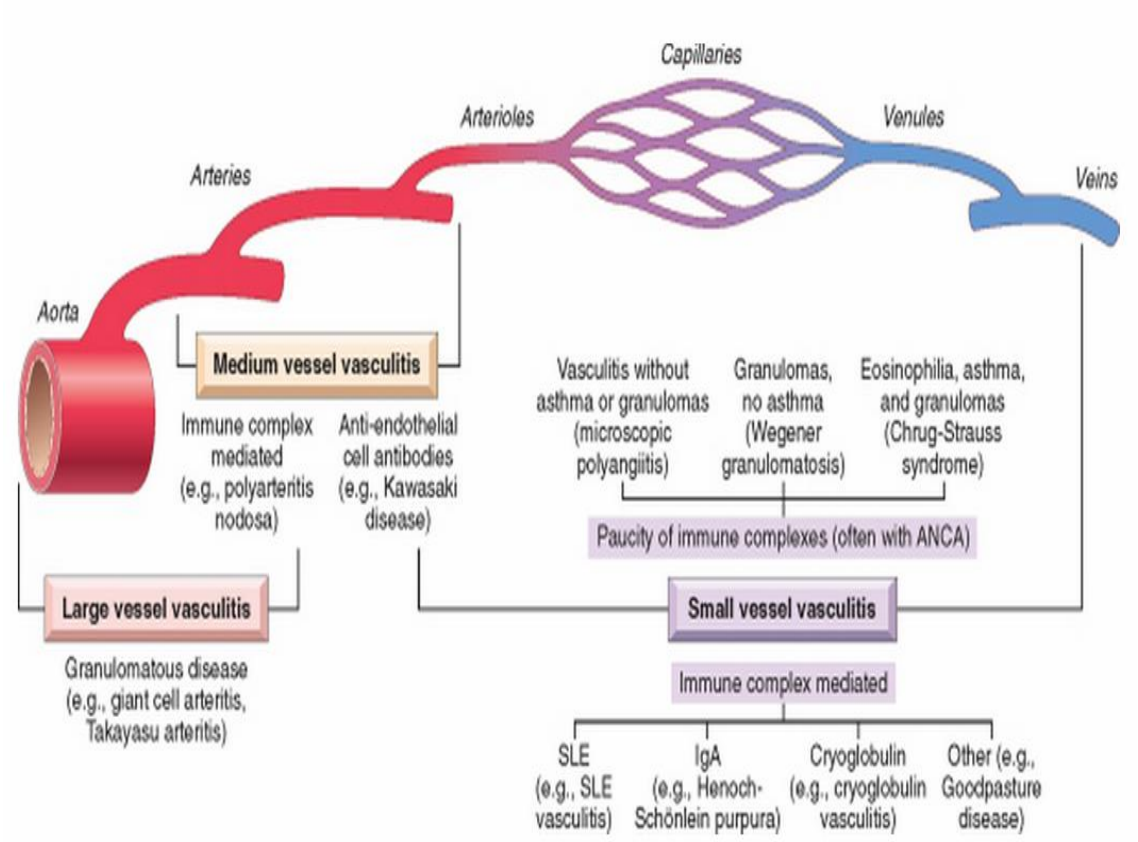
Classification

- Large-vessel vasculitis
  - Giant cell arteritis, Takayasu's arteritis
  - Behcet's disease, Cogan's syndrome
- Medium-vessel vasculitis
  - Polyarteritis nodosa
  - Buerger's disease, Central nervous system vasculitis, Kawasaki's disease, Rheumatoid vasculitis
- Small-vessel vasculitis
  - Wegener's, microscopic polyangiitis, Churg-Strauss syndrome
  - Cryoglobulinemic vasculitis, Henoch-Schönlein purpura,

Summary of Vasculitides

Vasculitides : is the plural of the word vasculitis

Vessel	Disease	Notes
Large	Giant-cell arteritis	>50. Arteries of head.
Medium	Polyarteritis nodosa	Young adults. Widespread.
Small	Wegener granulomatosis	Lung, kidney. c-ANCA.
	Microscopic polyangiitis	Lung, kidney. p-ANCA.



notice that in the figure there are Interfering between vessels range e.g: Large with medium (nothing in medicine 100%).

Giant-Cell (Temporal) Arteritis

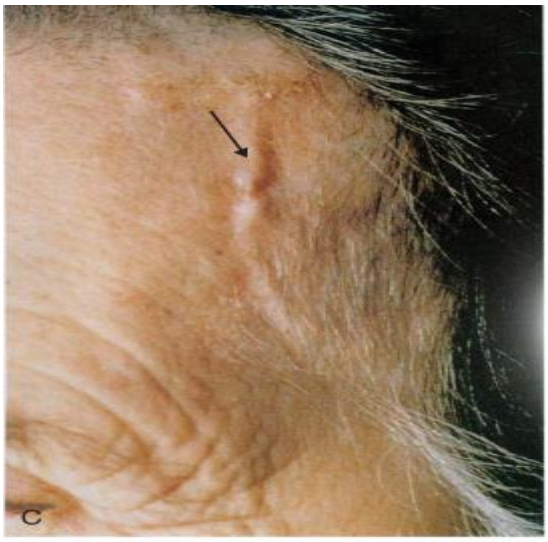
- The most common
- Chronic, typically **granulomatous inflammation** of large to small-sized arteries **(N.B.! Small sized artery NOT arterioles)**
- Principally affects the arteries in the head-especially the temporal arteries
- Rarely the aorta (*giant-cell aortitis*)
- Unknown cause
- Likely **immune origin**, T cell-mediated.
- An immune origin is supported by the characteristic granulomatous response with associated helper T cells, a correlation with certain major histocompatibility complex (MHC) class II haplotypes, and a therapeutic response to steroids.
- The extraordinary predilection for a single vascular site (temporal artery) remains unexplained

- Granulomatous inflammation
- Temporal arteries
- Immune origin: (MHC) class II haplotypes
- Above 50
- Segmental
- Granuloma + giant cell + inflammatory cells infiltration may end with FIBROSIS

Giant-Cell (Temporal) Arteritis (cont.)

Clinical features

- > 50 years of age
- Vague symptoms:
  - Fever, fatigue and weight loss
- May involve facial pain or headache
- Pain most intense **along the course of the superficial temporal artery**, which is painful to palpation



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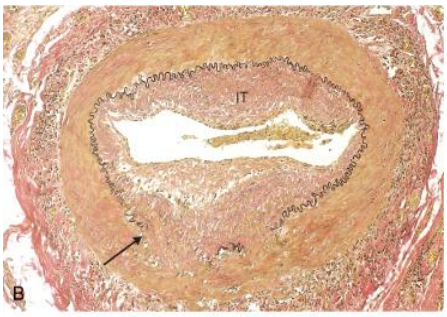
Nodularity, thickness and firm vessel
Can be segmental process



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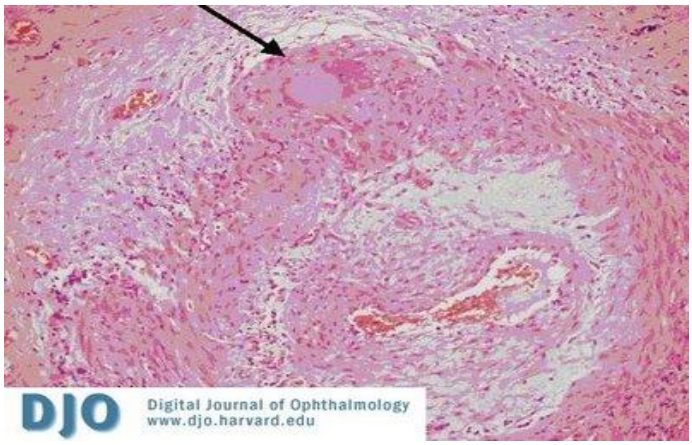
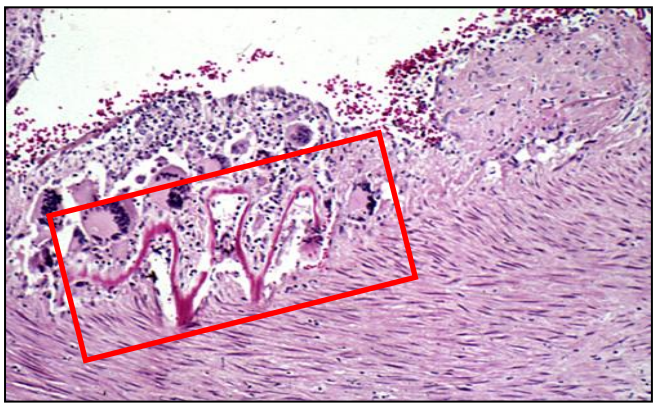
The granuloma is centered on

The internal elastic lamina

Giant cell arteritis



Superficial **temporal artery biopsy** - **intimal thickening and medial damage, giant cells with inflammatory cell infiltration** in the internal elastic lamina



Giant cell (temporal) arteritis.
Disruptions of the elastic lamina with inflammation and giant cells.

Segmental inflammatory lesions with intimal thickening , medial granulomatous inflammation with giant cells and chronic inflammatory cells and internal elastic lamina fragmentation .

Giant-Cell (Temporal) Arteritis (cont.)

- Definite diagnosis depends on:

Biopsy of an adequate segment and histological confirmation

- Treatment: **corticosteroids**

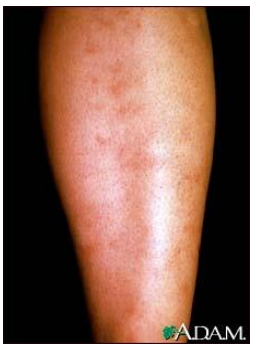
Polyarteritis Nodosa (PAN)

- **Systemic involvement (autoimmune disease)**
- **Small or medium-sized muscular arteries**
- But **not** arterioles, capillaries, or venules
- Typically involving **renal and visceral** vessels (It does NOT affect the lung)

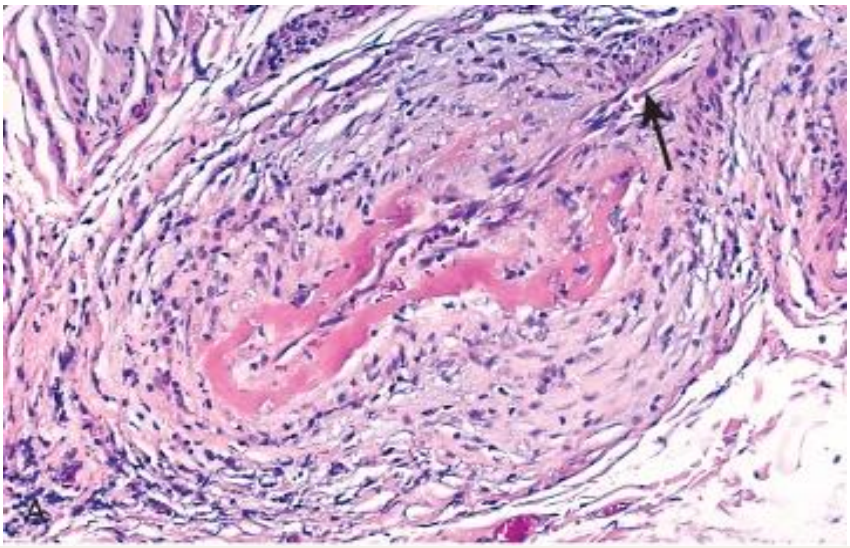
- It is the PROTYPE of vasculitis>
- Systemic
- Episodic (sometime present and sometime not)
- Young Adults
- involving **renal and visceral** vessels
- **No** association with ANCA
- With **FIBRINOID NECROSIS**
- No grnuloma or gaint cell, you just see (classic vasculitis) what is usually seen in inflammation

Polyarteritis Nodosa (PAN) (cont)

Clinical picture



- Largely young adults
- Typically episodic, with long symptom-free intervals
- Because the vascular involvement is widely scattered, the clinical findings may be **varied and puzzling**
- Fever and weight loss
- Examples on systemic involvement:
  - Renal (arterial) involvement is common
  - Hypertension, usually developing rapidly
  - Abdominal pain and melena (bloody stool)
  - Diffuse muscular aches and pains
  - Peripheral neuritis
- **Biopsy** is often necessary to confirm the diagnosis



Mixed infiltrate of neutrophils, eosinophils, and mononuclear cells, frequently accompanied by **fibrinoid necrosis**

Polyarteritis Nodosa (PAN)

- All stages of activity (from early to late) may **coexist** in different vessels or even within the same vessel
- Later, the acute inflammatory infiltrate is replaced by **fibrous (occasionally nodular) thickening of the vessel wall** that can extend into the adventitia
- **No association with ANCA**
- Some 30% of patients with PAN have hepatitis B antigenemia
- If untreated, the disease is fatal in most cases
- Therapy with **corticosteroids** and other immunosuppressive therapy results in remissions or cures in 90%

Polyartirits Nodosa is characterized by: 1) does not affect the lung

2) Shows different stages of activity

3) Fibrinoid necrosis (histopathology)

4) 30% of patient with hepatitis B

Antigenemia: The presence of an antigen in circulating blood < active infection

Complications

- **Vessel rupture**
- **Impaired perfusion:**
  - Ulcerations
  - Infarcts
  - Ischemic atrophy (not infarction)
  - Haemorrhages in the distribution of affected vessels may be the first sign of disease

Antineutrophil Cytoplasmic Antibodies (ANCA)

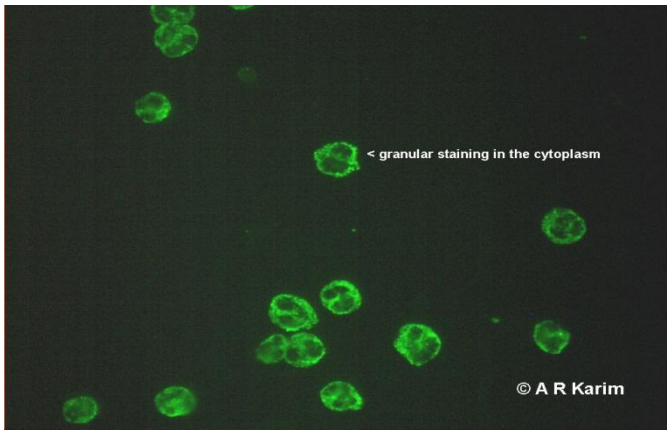
- **Cytoplasmic localization (c-ANCA)** -> the most common target antigen is proteinase-3 (PR3)
  - typical of **Wegener granulomatosis**
- **Perinuclear localization (p-ANCA)** -> most of the autoantibodies are specific for myeloperoxidase (MPO)
  microscopic polyangiitis and Churg-Strauss syndrome

- ANCAs serve as useful diagnostic markers for the ANCA-associated vasculitides
- Their levels can reflect the degree of inflammatory activity

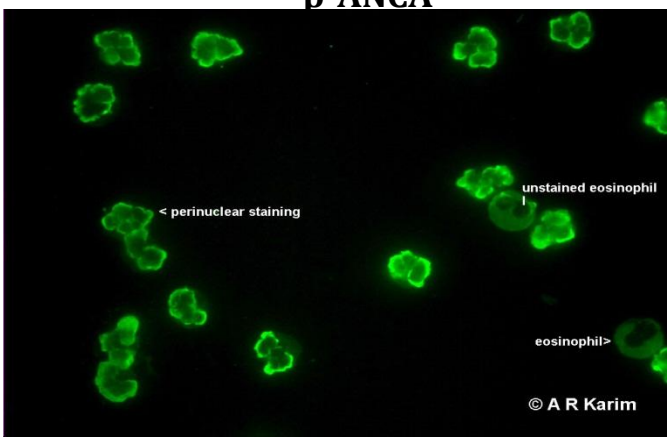
ANCA-associated vasculitides

- **Wegener's granulomatosis**: granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small to medium-sized vessels (C-ANCA)
- **Microscopic polyangiitis**: Necrotizing vasculitis affecting the small vessels. (P-ANCA)
- **Churg-Strauss Syndrome**: Eosinophil-rich and granulomatous inflammation involving the medium-sized vessels, and associated with asthma and eosinophilia (P-ANCA)

c-ANCA



p-ANCA



ANAC : two types of antibody (c_ANCA & p-ANCA) which are produced against some enzyme inside the neutrophils (PR3 & MPO),and it's measured in the blood and help to diagnose the activity of the disease. (if it's increased that mean sever if it's decreased that mean mild) and it affect small blood vessel.

c-ANCA → PR3(enzyme inside neutrophils) = **Wegener's granulomatosis**

p-ANCA MPO (enzyme inside neutrophils = **Microscopic polyangiitis** and **Churg-Strauss Syndrome**

Leukocytoclastic Vasculitis/ Microscopic Polyangiitis

also k/a Microscopic Polyarteritis, Hypersensitivity Vasculitis

- **Necrotizing vasculitis** that generally affects capillaries as well as arterioles and venules of a size smaller than those involved in PAN
- Rarely, larger arteries may be involved

If it affects the large arteries, how can we distinguish it from Polyarteritis Nodosa (PAN) which also affects the large vessel ?

1) **Microsopice polyangitis doesn't show different stages (PAN shows that)**
2) **Microsopice polyangitis affects the lug (PAN not affect the lung)**

- *All lesions of microscopic polyangiitis tend to be of the **same age in any given patient***
- *Necrotizing glomerulonephritis (90% of patients) and pulmonary capillaritis are particularly common*

Pathogenesis :

- Causes: an **antibody response** to **antigens** such as **drugs (e.g., penicillin), microorganisms (e.g., streptococci),** heterologous proteins, or tumor proteins
- This can result in immune complex deposition, or it may trigger secondary immune responses
- **p-ANCAs** are present in more than 70% of patients
- Depending on the organ involved, major clinical features include:
  - **Hemoptysis** (coughing up of blood)
  - **Hematuria** (is the presence of red blood cells in the urine and)
  - Proteinuria (is presence of an excess of serum proteins in the urine)
  - Bowel pain or bleeding
  - Muscle pain or weakness
  - **Palpable cutaneous purpura**

- Same age in any given patient = all blood vessels show the same features in any patient

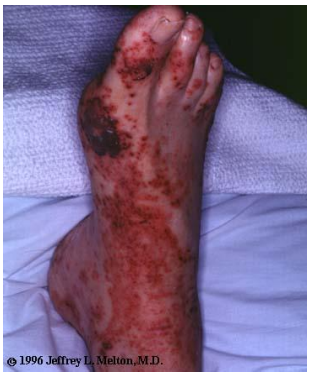
- Heterologous proteins = foreign protein (found in the organism)

- Necrotizing glomerulonephritis: may be secondary to haemolytic streptococcal infection

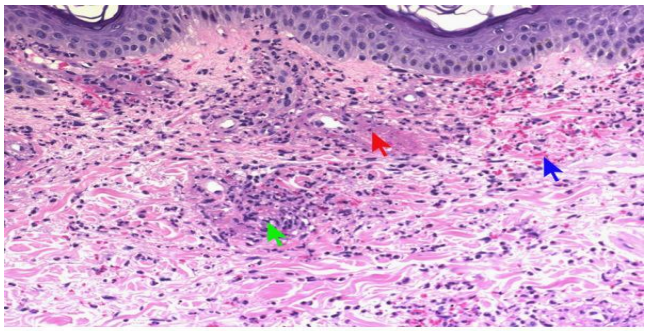
Also, it presents with hematuria (blood in urine)

- Pulmonary capillaritis: it presents with hemoptysis (blood stained sputum)

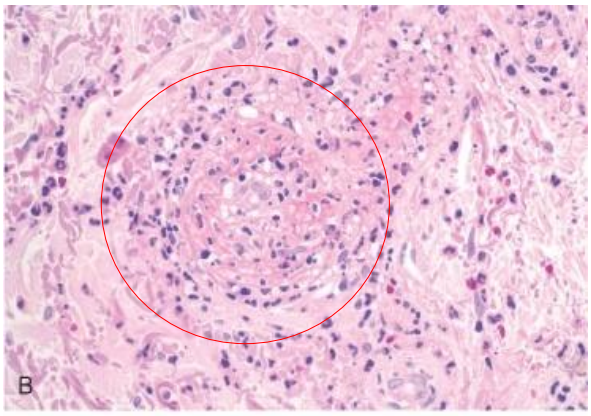
- Which ANCAs? **(Important to know)** P-ANCAs



Leukocytoclastic vasculitis, foot.
The purpuric eruption
(Subcutaneous bleeding patches)
tends to be most pronounced on
dependent areas.



Blood vessel with :
- infiltrating and fragmenting neutrophils



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Wegener Granulomatosis

Triad:

- *Acute necrotizing granulomas* of the upper and lower respiratory tract (lung), or both
- *Necrotizing or granulomatous vasculitis* affecting small to medium-sized vessels (most prominent in the lungs and upper airways)
- *Focal necrotizing, often* ***crescentic, glomerulitis***

- No causative agent, although immune complexes are occasionally seen

- Clinically, this resembles PAN except that there is also respiratory involvement.

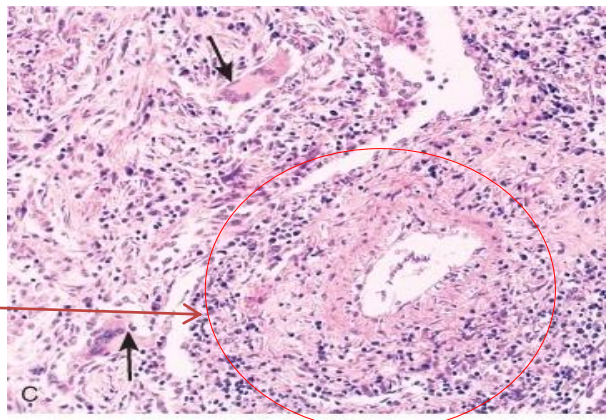
- Kidney severity is variable

(Focus on the 3 clinical features)

Wegener Granulomatosis (cont)

- 40-50 years
- Associated with **C-ANCA**
- Without Rx -> 80% die
- With Rx -> 90% live (not cured)
- The Rx -> immunosuppression

Vasculitis of a small artery with adjacent granulomatous inflammation including epithelioid cells and giant cells *(arrows)*.

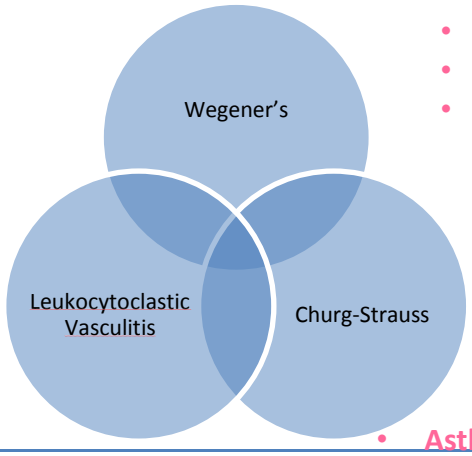


Churg-Strauss syndrome

Female's doctor said it is not important

- Eosinophil-rich and granulomatous inflammation involving the respiratory tract and necrotizing vasculitis affecting small vessels
- Associated with asthma (alleregy) and blood eosinophilia
- Associated with p-ANCAs.

Necrotizing Granuloma



- **Sinusitis**
- **Crescentic glomerulitis**
- **Pulmonary nodules**

Hypereosinophilia

- **Asthma**
- **Pulmonary infiltrates**
- **Myocarditis**

- **Pulmonary capillaritis**
- **Glomerulonephritis**
- **Sensory neuropathy**

1) Polyartiritis Nodosa does NOT affect which Vessel :

a) Renal vessel

b) Liver Vessel

c) Coronary Vessel

d) Pulmonary Vessel

2) 75 year old woman presents with Fever and **severe headaches. What is the most likely diagnosis?**

a) Takayasu arteritis

b) Giant cell arteritis

c) Aortic dissection

d) Polyarteritis nodosa

e) Wegener's granulomatosis

3) c-ANCAs are found in:

a) Polyarteritis nodosa
b) Microscopic Polyangiitis
c) Wegener's granulomatosis
d) Churg-Strauss syndrome

Answers:

d

b

c