# Vasculitis

TUCOM
Dep. of Medicine
5th year
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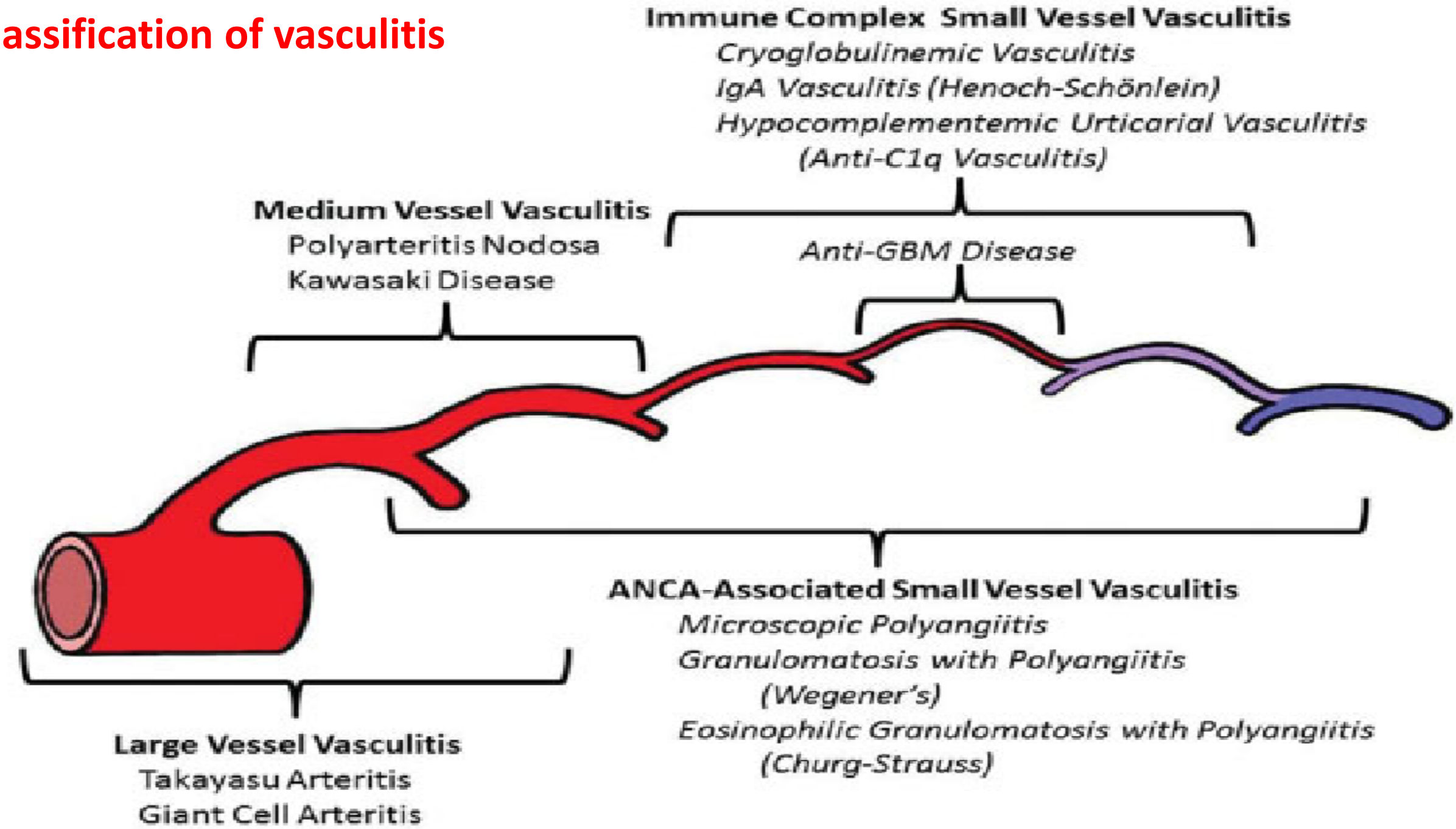
## Learning objectives:

1. Define vasculitis
2. Classify vasculitis
3. Clarify the clinical features common for vasculitis
4. Review the investigations of vasculitis
5. Outline the treatment of vasculitis
6. Explain the following conditions: ANCA - associated vasculitis, Takayasu arteritis, Kawasaki disease, Polyarteritis nodosa, Giant cell arteritis and polymyalgia rheumatic, Churg–Strauss syndrome, Henoch- Schonlein purpura and Behçet's disease.

**Vasculitis:** is characterized by inflammation and necrosis of blood-vessel walls, with associated damage to skin, kidney, lung, heart, brain and gastrointestinal tract. There is a wide spectrum of involvement and severity, ranging from mild and transient disease affecting only the skin, to life-threatening fulminant disease with multiple organ failure.

Vasculitis can be classified according to the size of the vessel involved, presence of ANCA and clinical presentation.

# Classification of vasculitis




on of vessel involvement by large vessel vasculitis, medium vessel vasculitis, and small vessel vasculiti

| Vessel size | Vasculitis | Clinical features | Investigations |
|---|---|---|---|
| Small | Wegener's granulomatosis | Upper respiratory tract (sinusitis, nasal crusting), Lower respiratory tract (nodules, fibrosis, haemorrhage), renal failure | Elevated ESR, CRP, cANCA<br>Biopsy shows small vessel vasculitis with granulomata |
| | Microscopic polyangiitis | Vasculitis skin rashes, joint pains, renal failure | Elevated ESR, CRP, classically pANCA (20% cANCA)<br>Histology: arteriolitis |
| | Churg–Strauss syndrome | Asthma, polyneuropathy, GI involvement, e.g. eosinophilic gastritis | Elevated ESR, CRP, eosinophilia, p or cANCA<br>Histology: eosinophilic vasculitis |
| Medium | Polyarteritis nodosa | Non-specific symptoms such as malaise, fevers, sweats, weight loss, abdominal pain | Mesenteric angiography demonstrating splenic/renal microaneurysms |
| Large | Takayasu's arteritis | Often asymptomatic<br>Affects large arteries from heart (e.g. subclavian)<br>Typically affects young women. More common in Far East | MRA or angiography demonstrating large vessel stenosis |
| | Giant cell arteritis (temporal arteritis) | Headaches, tender scalp, visual disturbance+/– stiffness in shoulders or neck. Age >60 years | Elevated ESR<br>Temporal artery biopsy |

## 24.65 Clinical features of systemic vasculitis

### Systemic

- Malaise
- Fever
- Night sweats
- Weight loss with arthralgia and myalgia

### Rashes

- Palpable purpura
- Pulp infarcts
- Ulceration
- Livedo reticularis

### Ear, nose and throat

- Epistaxis
- Recurrent sinusitis
- Deafness

### Respiratory

- Haemoptysis
- Cough
- Poorly controlled asthma

### Gastrointestinal

- Abdominal pain (due to mucosal inflammation or enteric ischaemia)
- Mouth ulcers
- Diarrhoea

### Neurological

- Sensory or motor neuropathy

## Antineutrophil cytoplasmic antibody-associated Vasculitis (ANCA - associated vasculitis):

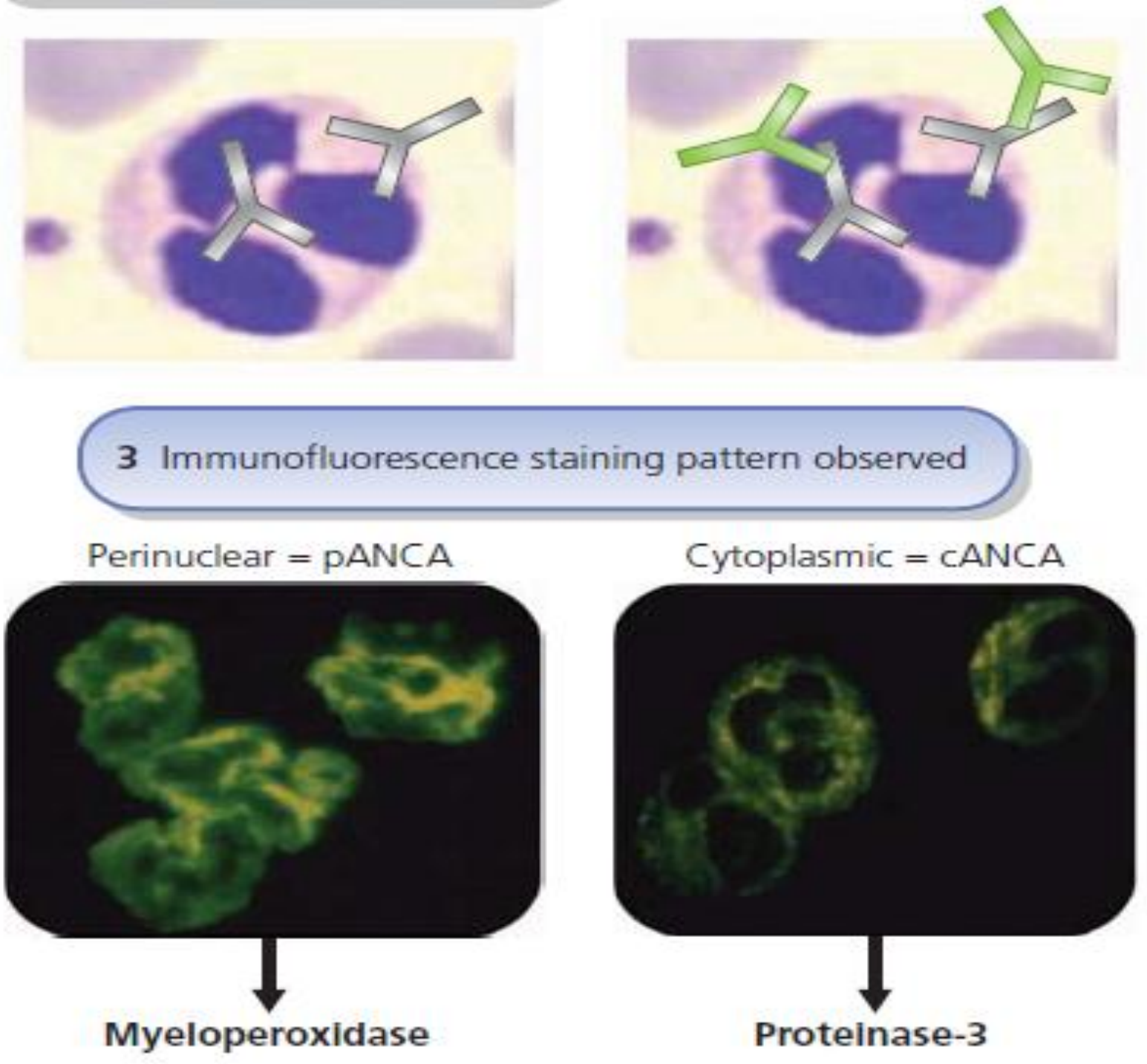
Antineutrophil cytoplasmic antibody-associated vasculitis (AAV) is a life-threatening disorder characterized by inflammatory infiltration of small blood vessels, fibrinoid necrosis and the presence of circulating antibodies to antineutrophil cytoplasmic antibody (ANCA).

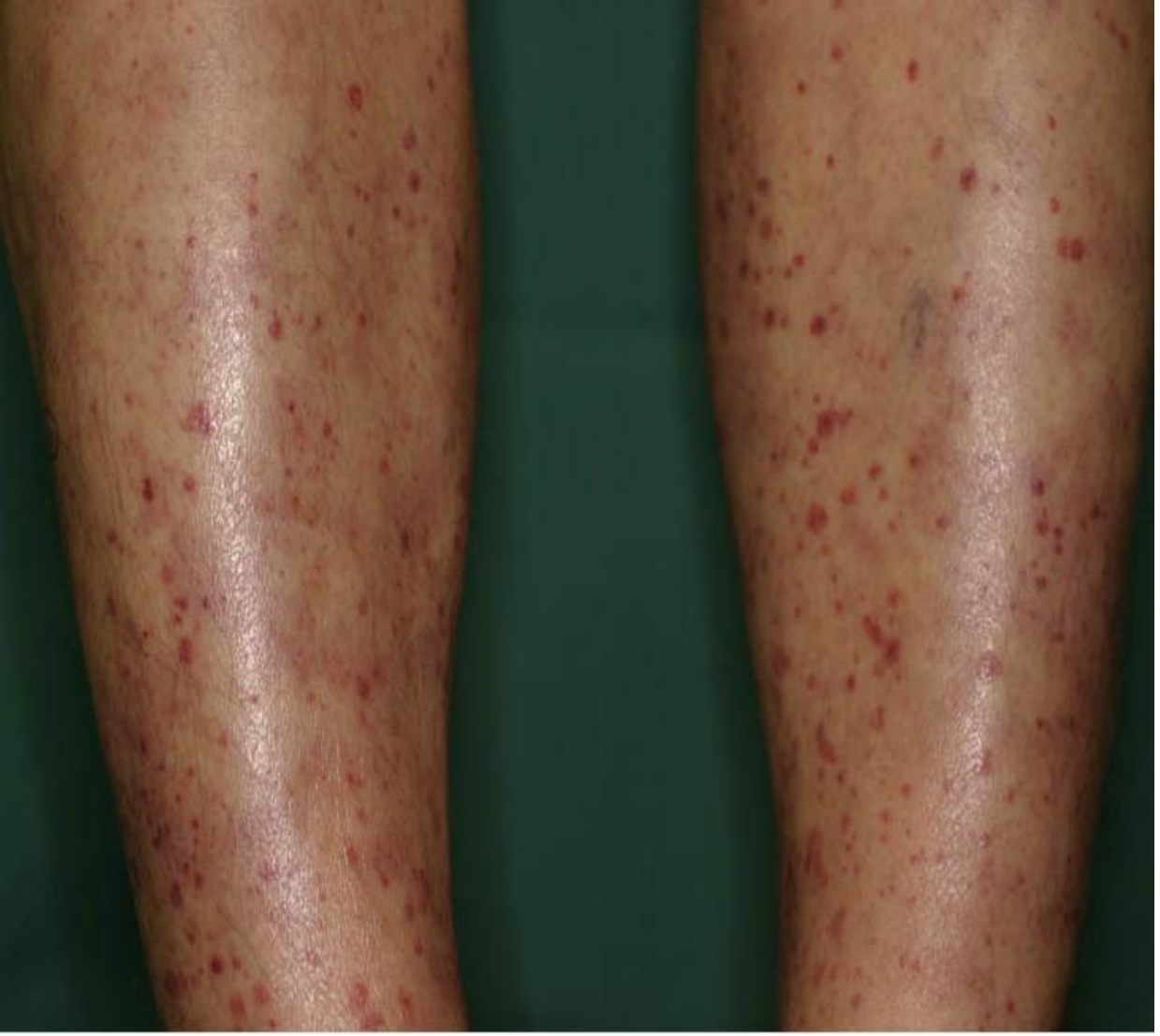
**Two main subtypes:**

**1- Microscopic polyangiitis:** is a necrotizing small-vessel vasculitis found with rapidly progressive glomerulonephritis, often in association with alveolar haemorrhage. Cutaneous and gastrointestinal involvement is common and other features include neuropathy (15%) and pleural effusions (15%). Patients are usually myeloperoxidase (MPO) antibody-positive or P- ANCA +ve.

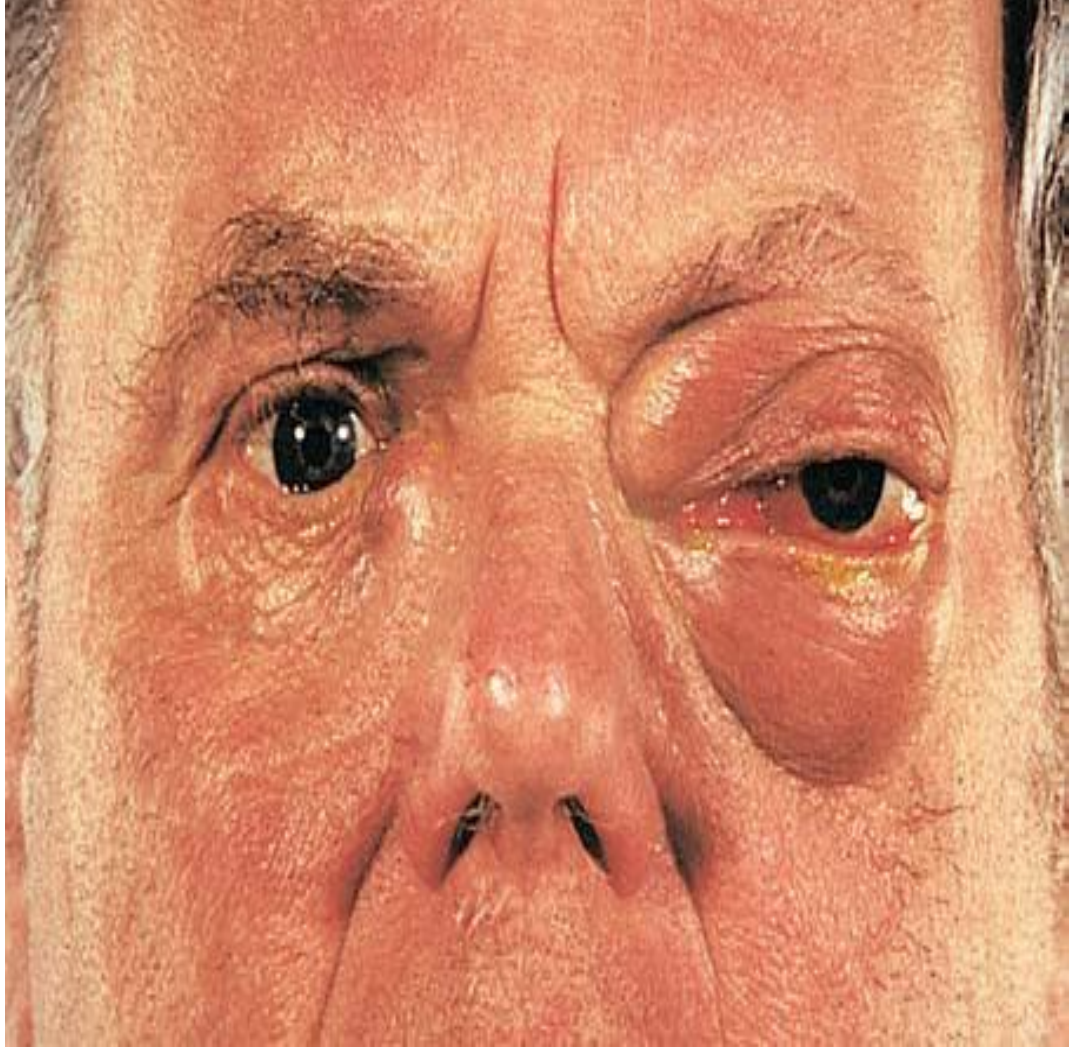
**2- Wegener's granulomatosis:** is characterized by granuloma formation, mainly affecting the nasal passages, airways and kidney. A minority of patients present with glomerulonephritis. C- ANCA +ve.

**Methods used to identify the subtype of ANCA.**





A 78-year-old woman with microscopic polyangiitis revealed palpable purpuric lesions and erythematous macules, scattered over her edematous legs.



Eye involvement in antineutrophil cytoplasmic antibody associated Vasculitis (Wegener's granulomatosis).

The most common presentations of Wegener's granulomatosis are epistaxis, nasal crusting and sinusitis (upper airway involvement), haemoptysis (lower airway involvement), deafness (inner ear involvement), and proptosis (inflammation of the retro-orbital tissue).

Patients with active disease usually have a leucocytosis with elevated CRP, ESR and C- ANCA. The diagnosis should be confirmed by biopsy of the kidney or lesions in the sinuses and upper airways.

Management for organ-threatening or acute–severe disease is with high-dose glucocorticoids (e.g. daily pulse intravenous methylprednisolone 0.5–1 g for 3 days, then oral prednisolone 0.5 mg/kg) and intravenous cyclophosphamide (e.g. 0.5–1 g every 2 weeks for 3 months), followed by maintenance therapy with lower-dose glucocorticoids and azathioprine, methotrexate or MMF. Plasmapheresis should be considered for fulminant lung disease. Rituximab in combination with high-dose glucocorticoids is equally effective as oral cyclophosphamide at inducing remission in AAV.

# Takayasu arteritis:

- Takayasu arteritis affects the aorta, its major branches and occasionally the pulmonary arteries.
- The typical age at onset is 25–30 years, with an 8 : 1 female-to-male ratio. It is most common in Asia.
- It is characterized by granulomatous inflammation of the vessel wall, leading to occlusion or weakening of the vessel wall.
- It presents with claudication, fever, arthralgia and weight loss. Clinical examination may reveal loss of pulses, bruits, hypertension and aortic incompetence.
- Investigation will identify an acute phase response and normocytic, normochromic anemia but the diagnosis is based on angiography, which reveals coarctation, occlusion and aneurysmal dilatation.
- Treatment is with high-dose glucocorticoids and immunosuppressant, as described for ANCA-associated vasculitis. With successful treatment, the 5-year survival is 83%.

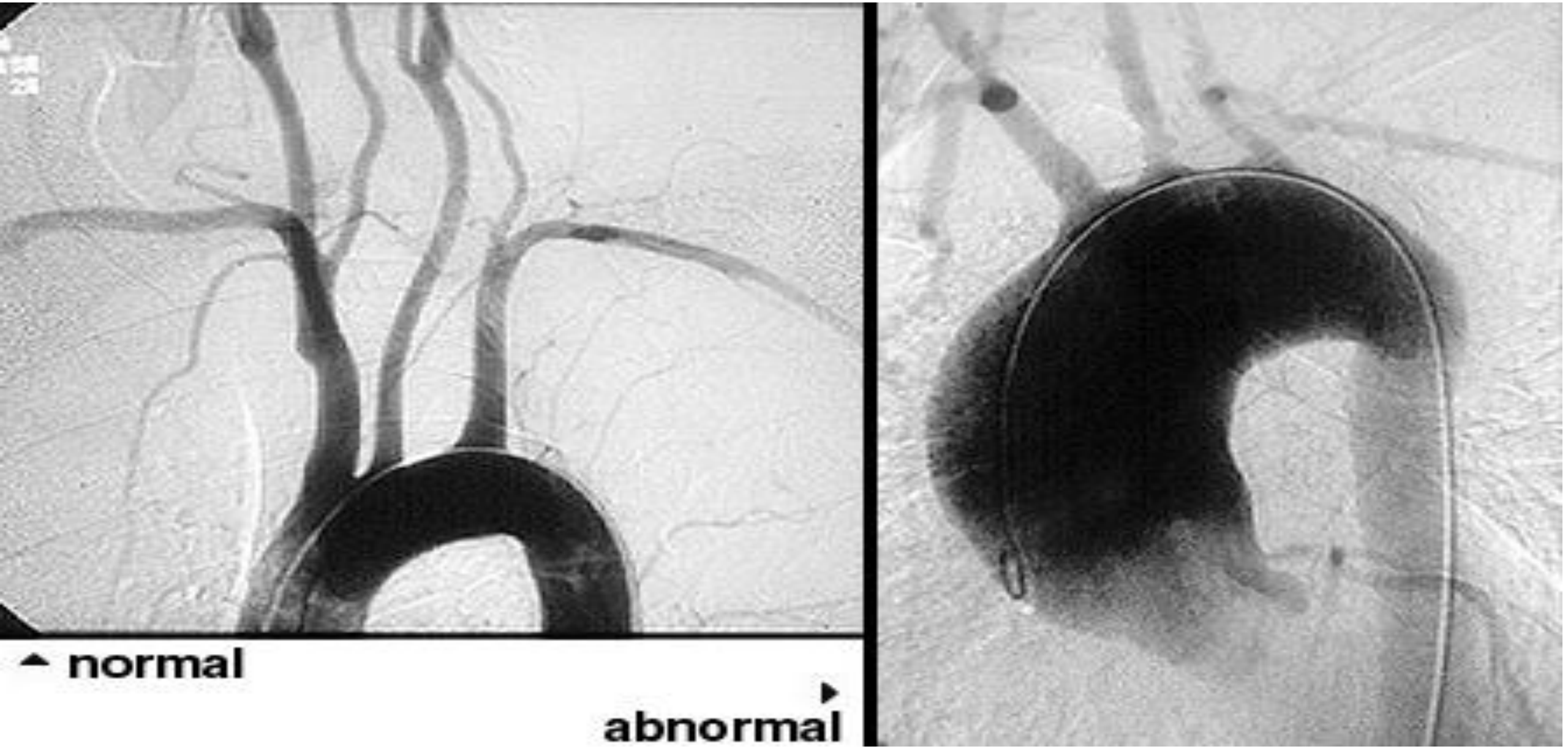


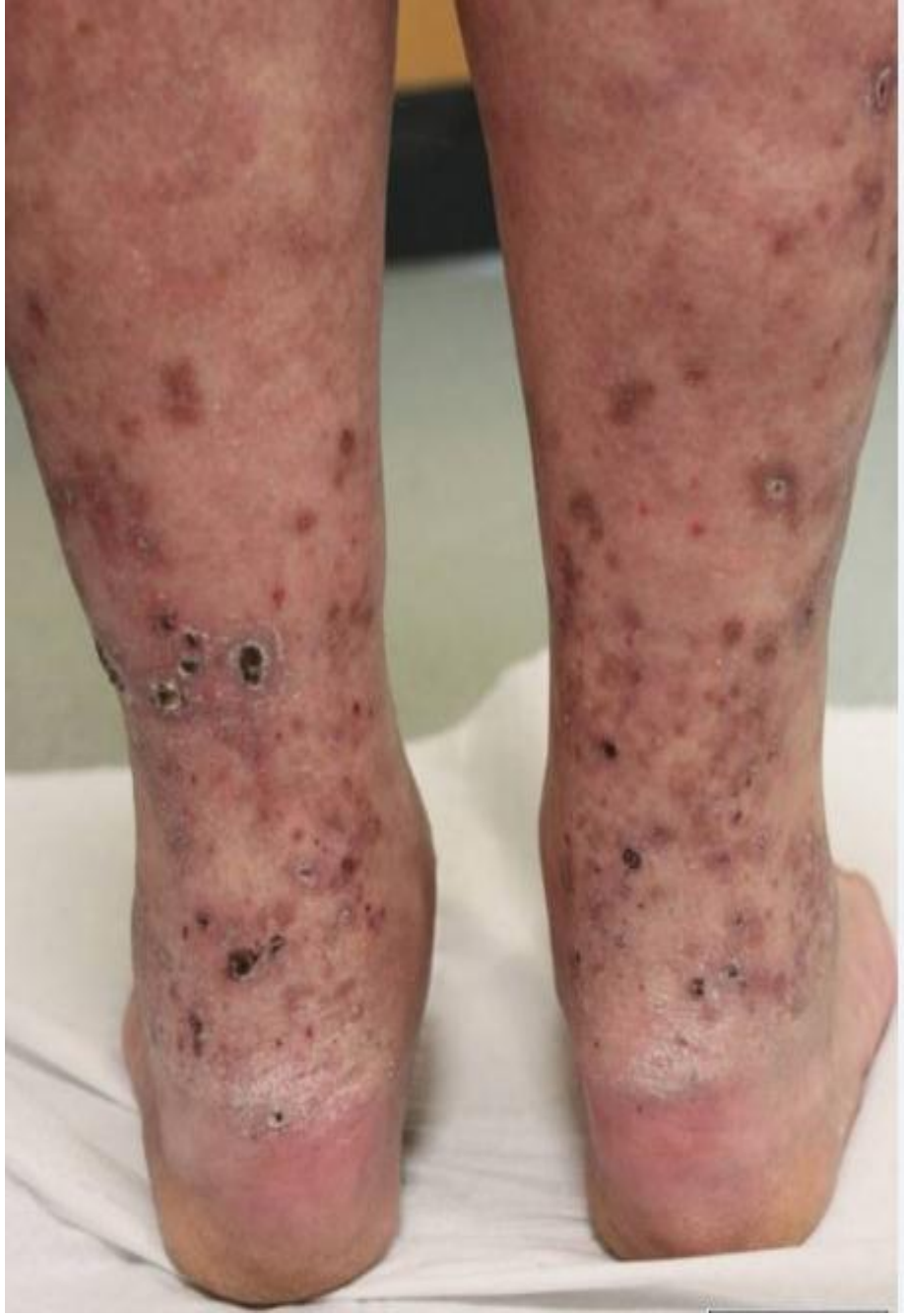

**Figure shows a normal aortic arch *on the left*, with narrow, smooth blood vessels. *On the right* is an example of an abnormal aortic arch in a patient with Takayasu's, with obvious dilation of the ascending aorta on the left side of the picture.**

## Kawasaki disease:

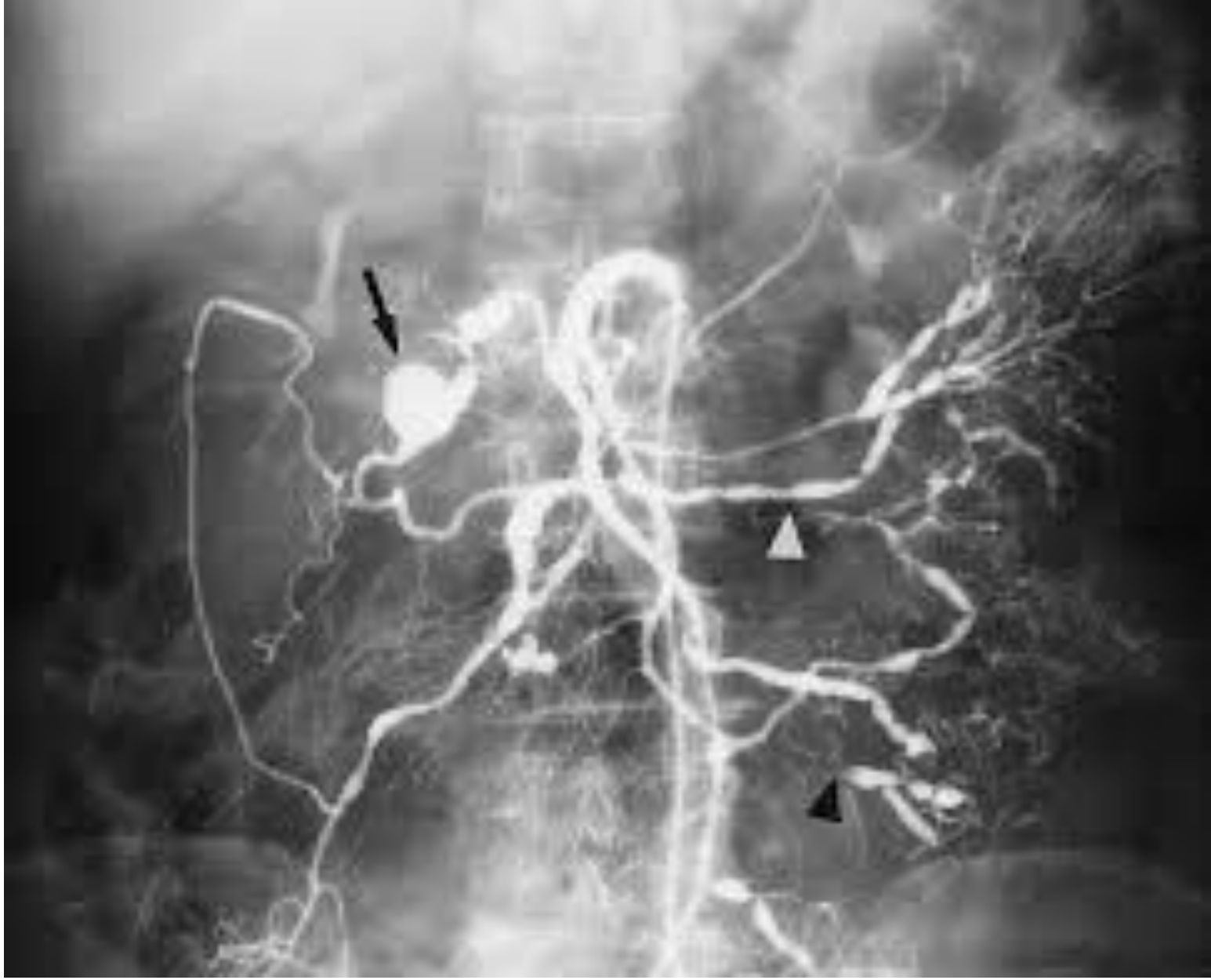
- Kawasaki disease is a vasculitis that mostly involves the coronary vessels. It presents as an acute systemic disorder, usually affecting children under 5 years.
- It occurs mainly in Japan and other Asian countries, such as China and Korea, but other ethnic groups may also be affected.
- Presentation is with fever, generalised rash, including palms and soles, inflamed oral mucosa and conjunctival injection resembling a viral exanthem.
- The cause is unknown but is thought to be an abnormal immune response to an infectious trigger.
- Cardiovascular complications include coronary arteritis, leading to myocardial infarction, transient coronary dilatation, myocarditis, pericarditis, peripheral vascular insufficiency and gangrene.
- Treatment is with aspirin (5 mg/kg daily for 14 days) and IVIg (400 mg/kg daily for 4 days).

## Polyarteritis nodosa:

- Polyarteritis nodosa has a peak incidence between the ages of 40 and 50, with a male-to-female ratio of 2 : 1. The annual incidence is about 2/1 000 000. Hepatitis B is an important risk factor.
- Presentation is with fever, myalgia, arthralgia and weight loss. Skin lesions are palpable purpura, ulceration, infarction and livedo reticularis.
- Pathological changes comprise necrotising inflammation and vessel occlusion, and in 70% of patients arteritis of the vasa nervorum leads to neuropathy, which is typically symmetrical and affects both sensory and motor function.
- Severe hypertension and/or renal impairment may occur due to multiple renal infarctions but glomerulonephritis is rare (in contrast to microscopic polyangiitis).
- The diagnosis is confirmed by conventional or magnetic resonance angiography, which shows multiple aneurysms and smooth narrowing of mesenteric, hepatic or renal systems, or by muscle or sural nerve biopsy, which reveals the histological changes described above.
- Treatment is with high-dose glucocorticoids and immunosuppressants, as described for ANCA-associated vasculitis.



Palpable purpura with ulceration

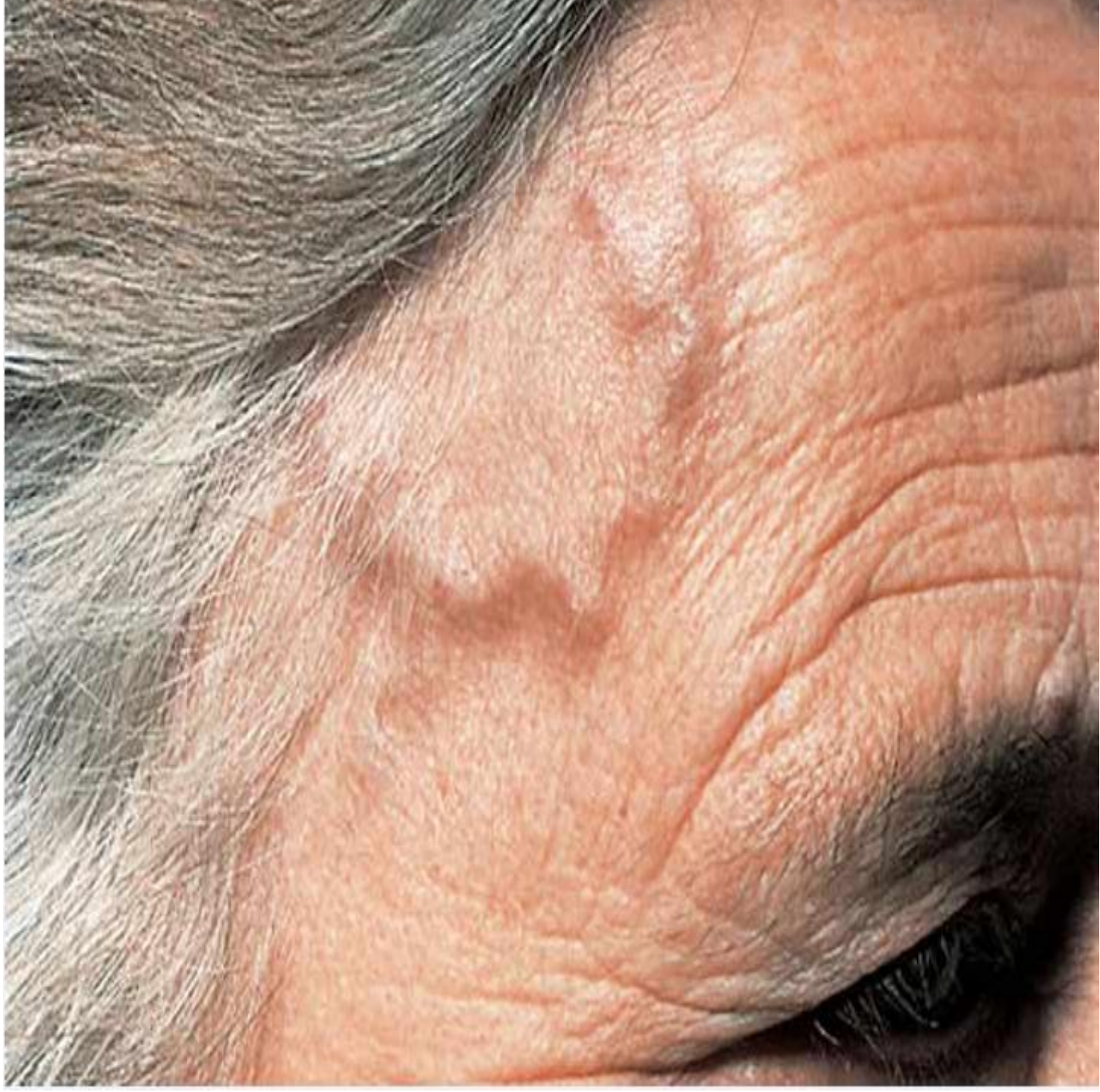


Magnetic resonance angiography, which shows multiple aneurysms and smooth narrowing of mesenteric, hepatic or renal systems

# Giant cell arteritis and polymyalgia rheumatica:

- Giant cell arteritis (GCA) is a granulomatous arteritis that affects any large (including aorta) and medium-sized arteries. It is commonly associated with polymyalgia rheumatica (PMR), which presents with symmetrical, immobility-associated neck and shoulder girdle pain and stiffness.
- Many patients with GCA have symptoms of PMR, and many patients with PMR go on to develop GCA if untreated, it is a different manifestations of the same underlying disorder.
- Both diseases are rare under the age of 60 years. The average age at onset is 70, with a female-to-male ratio of about 3 : 1. The overall prevalence is about 20 per 100 000 in those over the age of 50 years.
- Clinical features: The cardinal symptom of GCA is headache, which is often localized to the temporal or occipital region and may be accompanied by scalp tenderness. Jaw pain develops in some patients, brought on by chewing or talking. Visual disturbance can occur (most specifically amaurosis) and a catastrophic presentation is with blindness in one eye due to occlusion of the posterior ciliary artery. Rarely, neurological involvement may occur, with transient ischaemic attacks, brainstem infarcts and hemiparesis.

- In GCA, constitutional symptoms, such as weight loss, fatigue, malaise and night sweats, are common. With PMR, there may be stiffness and painful restriction of active shoulder movements on waking. Muscles are not otherwise tender, and weakness and muscle-wasting are absent.
- Investigations: reveals an elevated ESR, with a normochromic, normocytic anaemia. Elevated CRP and abnormal liver function. Characteristic biopsy findings are fragmentation of the internal elastic lamina with necrosis of the media in combination with a mixed inflammatory cell infiltrate. Diagnostic yield is highest with multiple biopsies and multiple section analysis (to detect 'skip' lesions). A negative biopsy does not exclude the diagnosis.
- Treatment: Prednisolone should be commenced urgently in suspected GCA because of the risk of visual loss. Response is dramatic, such that symptoms will completely resolve within 48–72 hours of starting therapy in virtually all patients. use higher doses in GCA (60–80 mg prednisolone) than in PMR (15–20 mg). In both conditions, the glucocorticoid dose should be progressively reduced, guided by symptoms and ESR, with the aim of reaching a dose of 10–15 mg by about 8 weeks.

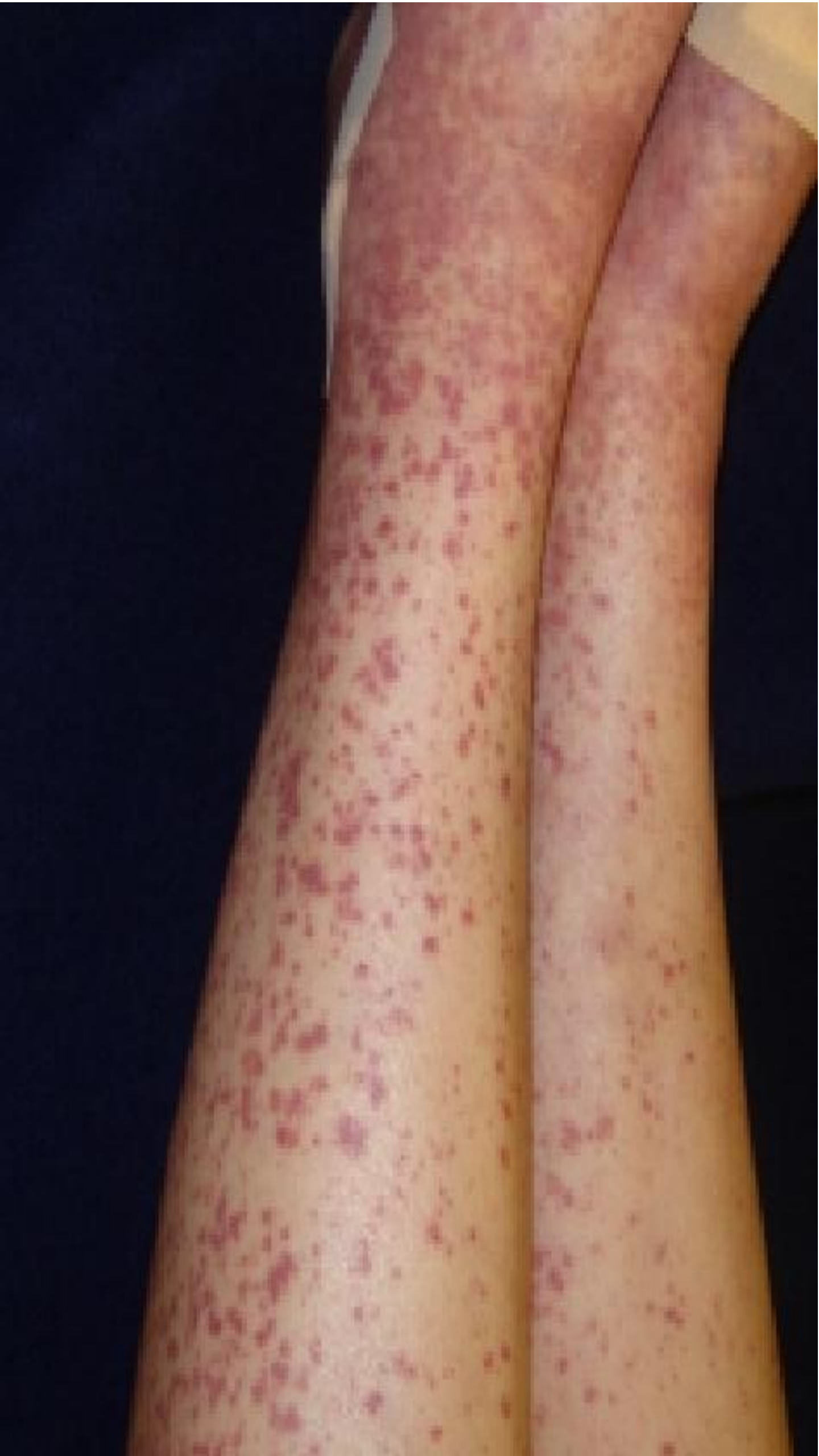


## Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome):

- Is a small-vessel vasculitis with an incidence of about 1–3 per 1 000 000. It is associated with eosinophilia.
- characterized by allergic rhinitis, nasal polyposis and late-onset asthma that is often difficult to control. The typical acute presentation is with a triad of skin lesions (purpura or nodules), asymmetric mononeuritis multiplex and eosinophilia. Pulmonary infiltrates and pleural or pericardial effusions due to serositis may be present. Up to 50% of patients have abdominal symptoms provoked by mesenteric vasculitis.
- Investigations: raised levels of ESR and CRP and an eosinophilia. antibodies to P- ANCA or C- ANCA can be detected in up to 60% of cases. Biopsy reveals a small-vessel vasculitis with eosinophilic infiltration of the vessel wall.
- Management is with high-dose glucocorticoids and cyclophosphamide, followed by maintenance therapy with low-dose glucocorticoids and azathioprine, methotrexate or MMF.

## Henoch- Schonlein purpura:

- It is a small-vessel vasculitis caused by immune complex deposition following an infectious trigger.
- It is predominantly a disease of children and young adults. The usual presentation is with purpura over the buttocks and lower legs, accompanied by abdominal pain, gastrointestinal bleeding and arthralgia. Nephritis can also occur and may present up to 4 weeks after the onset of other symptoms.
- Biopsy of affected tissue shows a vasculitis with IgA deposits in the vessel wall.
- Henoch- Schonlein purpura is usually a self-limiting disorder that settles spontaneously without specific treatment. Glucocorticoids and immunosuppressive therapy may be required in patients with more severe disease, particularly in the presence of nephritis.



## Behçet's disease:

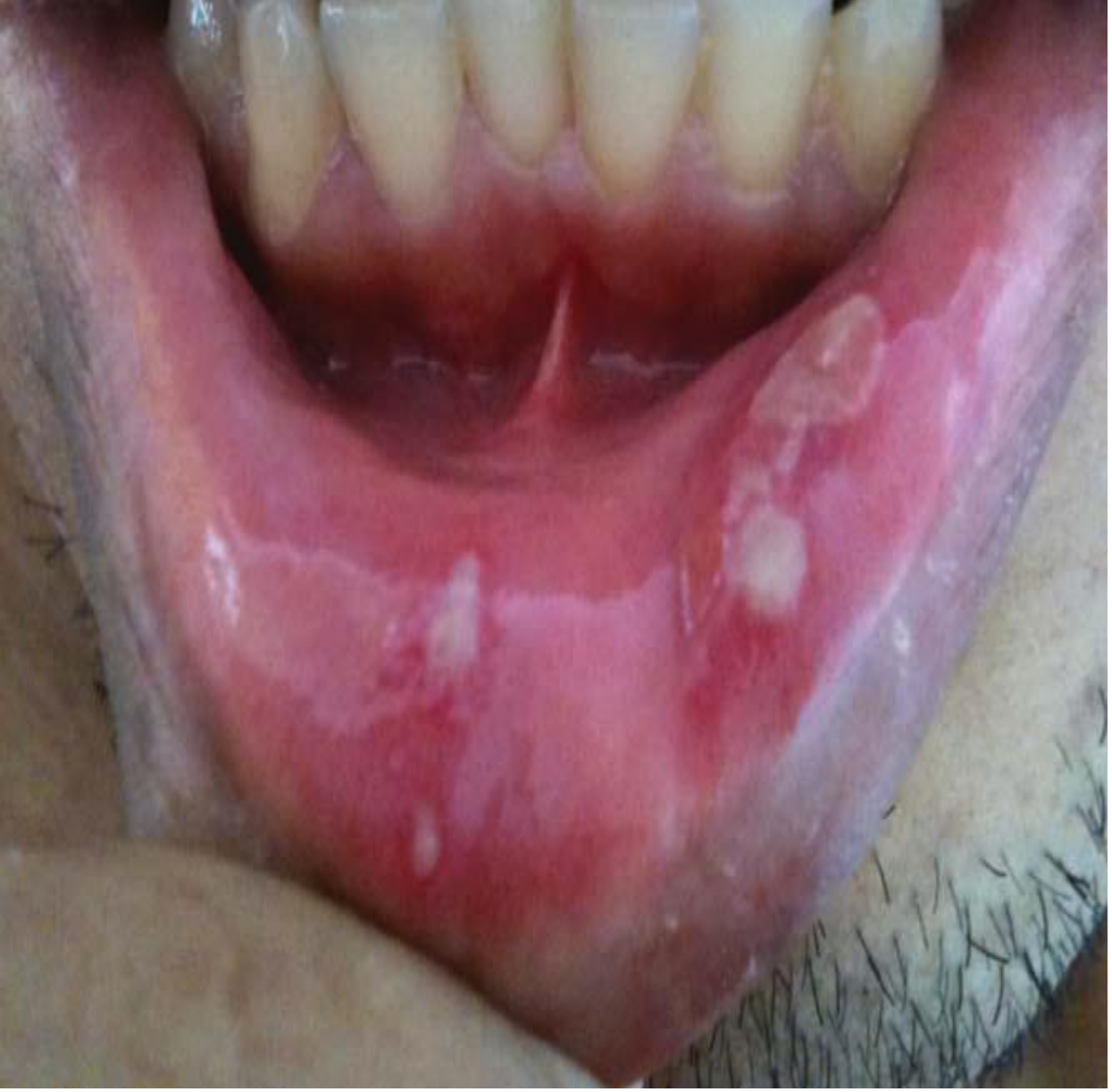
- This is a vasculitis of unknown aetiology that characteristically targets small arteries and venules.
- Common in 'Silk Route' countries, around the Mediterranean and in Japan, where there is a strong association with HLA-B51.
- Oral ulcers are universal. Unlike aphthous ulcers, they are usually deep and multiple, and last for 10–30 days. Genital ulcers are also a common problem, occurring in 60–80% of cases.
- The usual skin lesions are erythema nodosum or acneiform lesions but migratory thrombophlebitis and vasculitis also occur. Ocular involvement is common and may include anterior or posterior uveitis or retinal vasculitis. Neurological involvement occurs in 5% and mainly involves the brainstem although the meninges, hemispheres and cord can also be affected, causing pyramidal signs, cranial nerve lesions, brainstem symptoms or hemiparesis. Recurrent thrombosis also occur.

**Criteria for the diagnosis of Behçet's disease:**

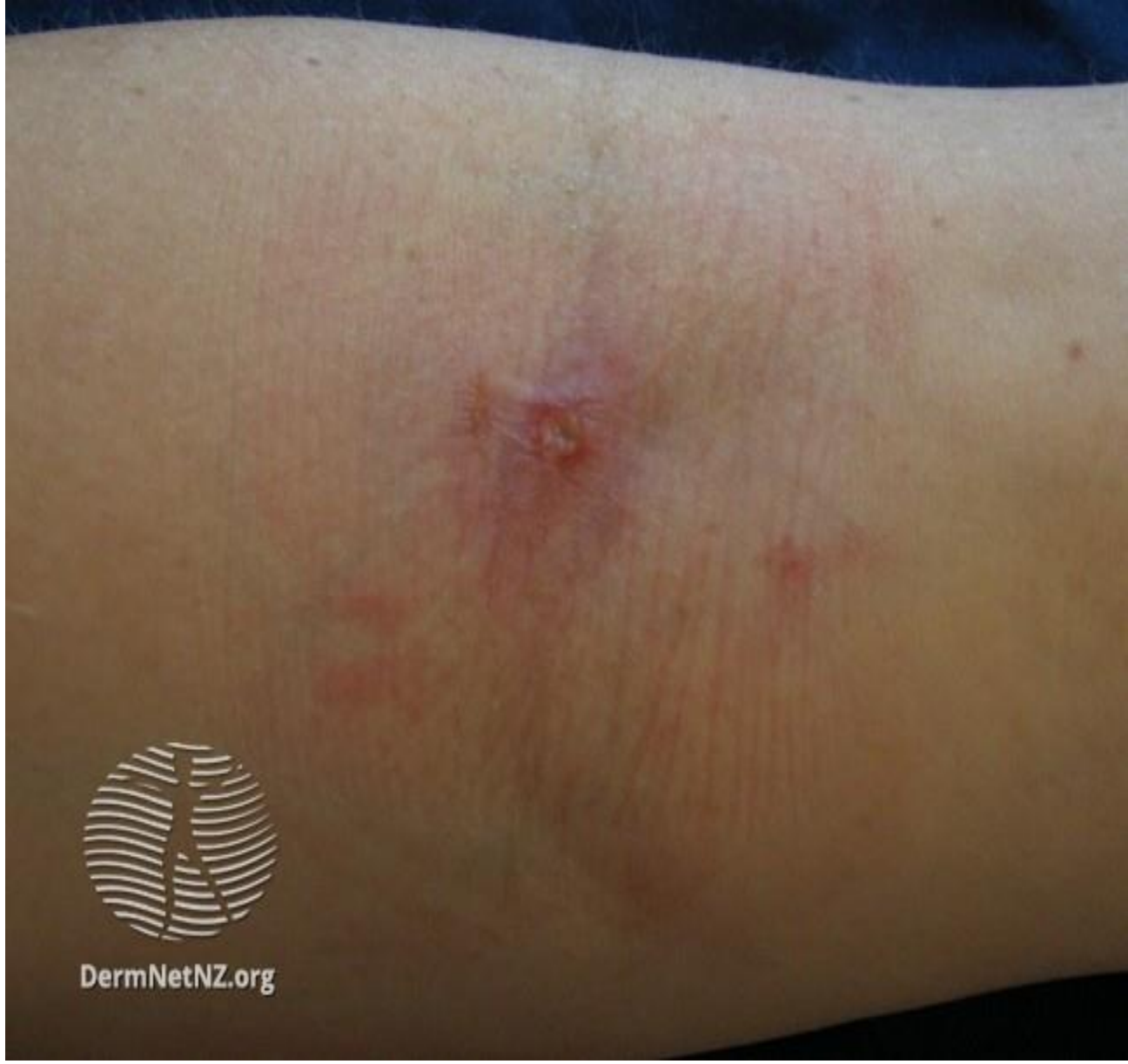
**Recurrent oral ulceration: minor aphthous, major aphthous or herpetiform ulceration at least three times in 12 months *plus* two of the following:**

- **Recurrent genital ulceration**
- **Eye lesions: anterior uveitis, posterior uveitis, cells in vitreous on slit-lamp examination, retinal vasculitis**
- **Skin lesions: erythema nodosum, pseudofolliculitis, papulopustular lesions, acneiform nodules**
- **Positive pathergy test (pricking the skin with a needle and looking for evidence of pustule development within 48 hours.)**

**Treatment: Oral ulceration can be managed with topical glucocorticoid preparations (soluble prednisolone mouthwashes, glucocorticoid pastes). Colchicine can be effective for erythema nodosum and arthralgia. Thalidomide (100–300 mg per day for 28 days initially) is very effective for resistant oral and genital ulceration but is teratogenic and neurotoxic. Glucocorticoids and immunosuppressants are indicated for uveitis and neurological disease.**



Oral aphthous lesions




Pathergy at the site of blood tests in patients with Behcet disease

# Thanks