



## Purpura and Vasculitis

### Objectives :

- To differentiate between different types of purpura.
- To know the difference between inflammatory and non inflammatory purpura.
- To have an approach to diagnose purpuric lesions.
- To be familiar with serious and non serious conditions and when to refer to a specialist.

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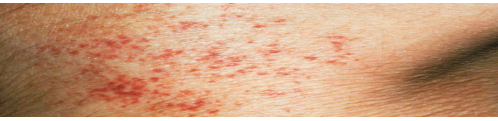
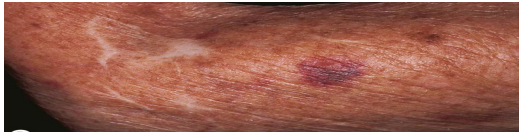

# Purpura

## ◀ Definition:

- Visible hemorrhage into the skin or mucous membrane. Purpura is extravasation of blood (venules most involved part) into the skin (commonest in lower limbs appear in direction of blood, for example, appear in the posterior surface of the bedridden patient ) or mucous membranes mainly it caused by Platelet disease, Coagulation defect and Blood vessel wall pathology.
- Mainly divided into 3 categories:
  - 1) **Palpable Purpura (Inflammatory)**
  - 2) **Non-palpable Purpura (non-inflammatory):**
    - Macular Petechiae (<4 mm)
    - Macular Purpura (5-9 mm)
    - Macular Ecchymoses (> 1 cm)
  - 3) **Retiform Purpura**

## ◆ Causes of non-palpable purpura:

- Trauma, pigmented purpura, actinic (solar) purpura.
- Poor dermal support of blood vessels e.g. “ topical or systemic steroid use”
- Vascular dysfunction: aging, scurvy, Ehlers-Danlos syndrome.
- Platelet dysfunction or Decreased Count: ITP, TTP, drug-induced thrombocytopenia, congenital/acquired platelet function defects
- Coagulopathies: hemophilia, cryoglobulinemia, anticoagulants, DIC, vitamin K deficiency, hepatic disease.

		
<p>This is an image showing petechiae. There are multiple small haemorrhage dots on the right cheek.</p>	<p>This is a macular purpura. This is a condition called solar purpura, usually appears in sun exposed areas in older people.</p>	<p>Macular Ecchymoses</p>

## ◆ Causes of non-palpable purpura:

### 1) Leukocytoclastic Vasculitis: - Small Vessels

- Medium Vessels
- ANCA-associated
- Others

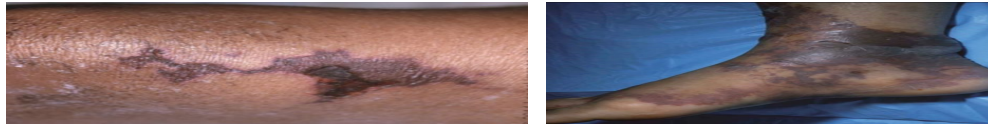
### 2) Not Leukocytoclastic Vasculitis:

- Erythema Multiforme
- Pityriasis Lichenoides Et varioliformis acuta (PLEVA)
- Pigmented purpura



## ◆ Causes of Retiform Purpura:

Heparin/Warfarin Necrosis	Cryoglobulinemia	Invasive Fungi	Ecthyma Gangrenosum	Protein C- and S- related	Polyarteritis Nodosa	Microscopic Polyangiitis
Livedoid Vasculopathy	Malignant atrophic papulosis (Degos' disease)	Sneddon Syndrome	Cholesterol Emboli	Calciphylaxis	Wegener's granulomatosis	Churg-Strauss Syndrome



### ◀ Clinical exam:

- **Purpura does NOT blanch with pressure**
- **Diascopy:** use of a glass slide to apply pressure to the lesion to differentiate erythema secondary to vasodilation (blanchable with pressure), from extravasation of blood (**non-blanchable**). All forms of purpura do NOT blanch with pressure.



### ◀ How do we evaluate a patient with purpura?

- **History:** Family hx, Drug Hx, Medical hx
- **Physical examination:** Size, Type, Distribution, Mucous membranes.
- **Labs:** CBC & Differential, Bleeding time, PT & PTT

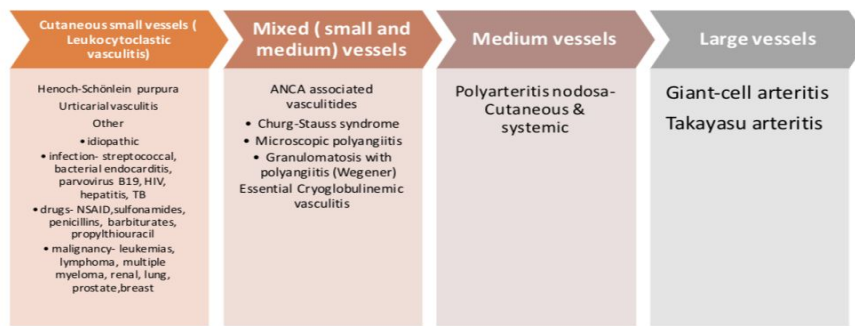
## Vasculitis

### ◀ Definition:

- Vasculitis represents a specific pattern of inflammation of the blood vessel wall.
- It can occur in any organ system of the body. **Vasculitis is an inflammatory destruction of blood vessels that results in occlusion or destruction of the vessel and ischemia of the tissues supplied by that vessel.**
- Cutaneous vasculitis could be limited to the skin, have secondary systemic involvement or a manifestation of systemic vasculitis.
- Can affect small, medium or large vessels (arterial and venous)
- Cutaneous involvement occurs almost exclusively with vasculitis of small and medium-sized vessels.

### ◀ Classification:

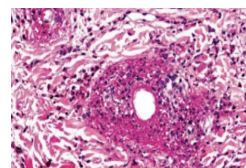
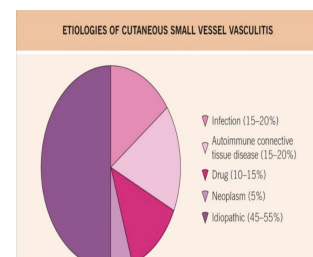
- Vasculitis is classified by the vessel size affected (small, medium, mixed or large)
- Clinical morphology correlates with the size of the affected blood vessels:
  - 1) **Cutaneous small vessels-** palpable purpura, urticarial lesions "urticarial vasculitis"
  - 2) **Small-medium vessels-** subcutaneous nodules, purpura, livedo reticularis, ulceration and necrosis of mainly medium vessel. **Medium (such as Arteries with muscular wall)** (also called **Mixed if small also involved**) → subcutaneous nodules, purpura, livedo reticularis, **Mononeuritis multiplex (wrist/foot drop), mesenteric ischemia, cutaneous ulcers, necrosis.**
  - 3) **Large vessels-** claudication, ulceration and necrosis. (ex: **Aorta, subclavian and carotid**) → **claudication, blindness, stroke, ulceration and necrosis**



**Note:** When we see subcutaneous vasculitis it can be limited to the skin and be dealt with easily, or it could be related to the skin and have a secondary cause, or the skin can be a manifestation of systemic involvement and that's a more serious condition. When we see skin involvement we typically think of small or medium vessels, with large vessels we rarely see skin involvement. vasculitis is a clinical and histopathological diagnosis.

## 1. Cutaneous small vessels vasculitis CSVV ( Leukocytoclastic vasculitis):

- Primarily involves the dermal postcapillary venules.
- Could occur as a primary process or could be secondary to an underlying cause.
- The majority of cases follow an acute infection or exposure to a new medication
- **Palpable purpura is the hallmark of this disease.**
- Pinpoint to- several mm in diameter. Manifestations on skin Purpura, urticaria, erythema-multiforme-like erythema, papules, nodules, pustules, blistering, erosion and ulceration occur, mainly in the lower extremities.
- They predominate on the ankles and lower legs, affecting mainly dependent areas.
- Usually asymptomatic and lesions resolve with residual post-inflammatory hyperpigmentation.
- Characterized by neutrophilic infiltration into the peripheral small dermal blood vessels.
- Pathogenesis An immune complex of an antigen (trigger) activate the immune system and cause vasculitis it lodge in vessel walls and activate compliments (type III allergic reaction).
- Constitutional symptoms (Fever, weight loss and myalgias) may accompany flares of CSVV including systemic symptoms. (rule out systemic vasculitis)
- 90% of patients will have spontaneous resolution of lesions within weeks, months.
- **Triggers :** **Infection-** streptococcal (hemolytic), bacterial endocarditis, parvovirus B19, HIV, hepatitis, TB. **Drugs-** NSAID, sulfa containing, penicillins, barbiturates, propylthiouracil, Thiazide and other drugs. **Chemical substance malignancy-** leukemias, lymphoma, multiple myeloma, renal, lung, prostate, breast, Collagen diseases. **Idiopathic or Others foreign antigens.**
- **Histopathology:**
  - Inflammation in the form of neutrophils (nuclear dust)
  - Vessel wall thickening
  - Erythrocyte extravasation
  - Fibrin deposit within the vessel wall.
- **Work-up:** CBC, renal profile, ANA, complement, ANCA, Skin biopsy (+/- DIF), History and PE.
- **Treatment:** Mainly supportive treatment because the disease will resolve on its own, we look for the cause and treat it, if it's cause by medications we stop them, if it's caused by an infection we treat the infection, sometimes these diseases can be severe and widespread, in these cases we give systemic steroids for a couple of weeks.



## 1. Henoch-Schönlein Purpura

- HSP is a specific form of CSVV.
- Most commonly occurs in children <10 yrs, can be seen in adults.
- Associated with a **preceding respiratory tract infection**. A **viral infection or streptococcal pharyngitis** is the usual triggering event (specially upper respiratory infection with hemolytic streptococcus in children), other triggers: bacterial infections, foods, drugs ( aspirin, penicillin), lymphoma
- Duration is 6-16 weeks
- Intermittent palpable purpura on extensor extremities and buttocks.
- **Characterized by: purpura, arthralgias, abdominal pain and renal disease** (when you see systemic involvement in a child you suspect Henoch-Schönlein Purpura) appears on the extensor aspects of the extremities → ( mainly lower legs and to a lesser extent on the forearms) and buttocks bullae is a bad sign if you see it
- **IgA-dominant** immune deposits in walls of small blood vessels. **IgA-mediated vessel injury** (Histologically; LCV, IgA, C3 and fibrin deposits) IgA, C3 and fibrin depositions have been demonstrated in biopsies of both involved and uninvolved skin by immunofluorescence techniques.
- Arthralgias and arthritis (upto 75%)
- GI involvement (50-75%): Abdominal pain and/or melena. GI bleeding, acute surgical abdomen, enterorrhagia, and intussusception also paralytic ileus may occur.
- Renal involvement (40-50%): Renal vasculitis often mild but can be chronic. Progressive glomerular disease “ crescentic glomerulonephritis”, renal failure (adults has increased risk for renal complication and prolong kidney involvement). Renal complication Most dangerous )
- Pulmonary hemorrhage can be fatal.
- May be associated with an underlying malignancy in adults.
- **Treatment:** supportive. (bed rest, pain relieve, antibiotics in strep throat infection, Systemic steroids for severe cases with systemic involvement, Abdominal pain- H2 blockers, corticosteroids, NSAIDs are best avoided ( renal & GI complications). Usually resolves without sequelae, 5-10 % persistent or recurrent disease.



## 2. Urticarial Vasculitis

- Recurrent episodes of painful, persistent urticarial lesions that last > 24 hours and often resolve with residual hyperpigmentation.
- Fixed urticarial lesions that when biopsied will have vasculitis, if we suspect this disease we have to check complement level, if the patient has hypocomplementemia (low C4 or C3) means that the disease is serious and has more systemic involvement.
- 3 clinical features distinguish the skin lesion of urticarial vasculitis from urticaria:
  - 1) Urticarial lesions that last **longer than 24 h** and are fixed
  - 2) On resolving there is postinflammatory hyperpigmentation
  - 3) Lesions are rather painful with burning sensation, rather than pruritic
- + There will be elevated ESR, decreased Serum C3, C4 and a positive ANA.
- May occur with or without angioedema.
- May be associated with constitutional symptoms and arthritis.
- Patients with hypocomplementemia are more likely to have systemic involvement (MSK involvement is the most common extracutaneous manifestation).
- Associated disorders include: autoimmune CTD's (Lupus, Sjogren's), viral infections, Leukemia, Drugs (ACEI, penicillin, sulfonamides, fluoxetine and thiazides), gammopathies ( IgG & IgM).
- Labs: elevated ESR, decreased Serum C3, C4 and a positive ANA.



- **Management :** History & physical exam. Ix- CH50, C3, C4, C1q, ANA, dsDNA,(exclude SLE) Anti-SSA & Anti-SSB, HipB&C, lupus band test. Treatment is based on the systemic effects of the disease, extent of cutaneous involvement and previous response to treatment (remove the offending agents). Cutaneous involvement→ (symptomatic NSAIDs & antihistamines), if these fail → colchicine, hydroxychloroquine, dapsone if these fail or if the patient has systemic disease → corticosteroids + steroid sparing agent (azathioprine, mycophenolate mofetil, rituximab). Prognosis: Most cases are idiopathic and improve spontaneously after few months.

### 3. Acute hemorrhagic edema of infancy

- A very rare form of CSVV.
- The child is well-appearing.
- Seen primarily in children between 4 and 24 months of age.
- Annular, circular or targetoid purpuric plaques on the face and extremities.
- Tender, non-pitting edema of acral sites.
- Extracutaneous involvement is rare.
- Benign clinical course with spontaneous resolution within 1-3 weeks



## 2-Small to medium vessel vasculitis (Mixed): ANCA-associated Vasculitides

- **Characterized by:**
  - Involvement of small to medium-sized vessels
  - The presence of antineutrophilic cytoplasmic antibodies (ANCA)
  - An overlapping spectrum of organ involvement
- **Each have distinguishing clinical and laboratory features:**
  1. Microscopic polyangiitis (MPA). 2. Wegener's granulomatosis. 3. Churg-Strauss syndrome.

### 1. Microscopic polyangiitis

- Vasculitis of capillaries, venules and medium-sized arteries.
- In terms of skin manifestations we'll see palpable purpura, erythematous macules and patches, splinter hemorrhages and ulcers( [as you can see these are non specific things that we will see in the other types as well](#)).
- **The systemic symptoms and blood work will differentiate this type from the others.**
- Constitutional symptoms, and mainly **renal and lung involvement**, crescentic necrotizing glomerulonephritis and alveolar hemorrhage.
- **Positive P-ANCA.**
- Absence of granuloma formation



- **Pics:** These are not classic, just to show you there might be some purpuric involvement and erythematous patches and plaques in the lower legs, but you won't be able to diagnose these clinically.

<p><b>2. Granulomatosis with polyangiitis (Wegener)</b></p>	<ul style="list-style-type: none"> <li>● Necrotizing granulomatous inflammation of the <b>upper and lower respiratory tracts.</b></li> <li>● Pauci-immune glomerulonephritis.</li> <li>● Systemic vasculitis that can involve the skin and oral mucosa.</li> <li>● <b>Positive C-ANCA and Anti-PR3.</b></li> <li>● The most common mucocutaneous manifestations: <ul style="list-style-type: none"> <li>● Palpable purpura.</li> <li>● Oral ulcers(image B).</li> <li>● Strawberry gums.</li> <li>● Papulonecrotic lesions on the extremities.</li> </ul> </li> </ul> 
<p><b>3. Churg-Strauss syndrome</b></p>	<ul style="list-style-type: none"> <li>● Systemic involvement includes asthma and allergic rhinitis typically precede vasculitic phase.</li> <li>● <b>Elevated blood eosinophil count.</b></li> <li>● Cutaneous vasculitis in approximately half of patients.</li> <li>● Histologic features consist of eosinophils, extravascular granulomas and Vasculitis.</li> <li>● Laboratory findings are similar to Wegener's with the additional findings of <b>peripheral eosinophilia</b> and <b>elevated serum IgE levels.</b></li> </ul>

**3-Medium vessel vasculitis (Polyarteritis nodosa):**

- Segmental multisystem vasculitis of predominantly **medium-sized arteries.**
- Systemic and cutaneous variants both can present with palpable purpura, livedo racemosa, retiform purpura, ulcers, subcutaneous nodules or peripheral gangrene.
- **Is a rare Necrotizing vasculitis affecting small and- medium-sized arteries of the dermis and subcutaneous tissue Localized to the skin with limited systemic involvement, usually neuropathy (progression to classical polyarteritis nodosa is an exception.)**
- **It is the only type that has skin involvement and purely medium-sized arteries.**
- The cutaneous variant has a chronic, more benign course; it may be accompanied by mild systemic symptoms (fever, myalgias, arthralgias and peripheral neuropathy). **Patients should be followed carefully and regularly evaluated to exclude the development of systemic involvement (Systemic involvement is uncommon except for Peripheral neuropathy).**
- Extracutaneous manifestations of the systemic variants include: Fever, arthralgias, myalgias, paresthesias, abdominal pain, orchitis and renovascular hypertension.
- Treatment and prognosis: Cutaneous PAN runs a chronic course lasting months to years and has a waxing and waning phenomenon. Patients are generally treated with NSAIDs and oral steroids. Immunosuppressive drugs can also be used in low doses in more severe kinds of cutaneous PAN and as steroid-sparing drugs(sulfapyridine, or methotrexate)

