* **Vasculitis**
* **Means inflammation of the blood vessel wall.**
* **May affect arteries, veins and capillaries.**
* **What causes the inflammation?**
* **Immunologic hypersensitivity reactions:**
* **Type II : complement dependent**
* **Type III: immune complex mediated\*\***
* **Type IV : cell mediated**
* **Direct invasion by micro-organisms**
* **Etiopathogenesis
 Immunologic mechanisms**
* **Immune complexe deposition**
* **Responsible for most cases\*\*\***
* **Deposition of immune complex 🡪**
* **Activation of complement 🡪**
* **Release of C5a**
* **C5a 🡪 chemotactic for neutrophil**
* **Neutrophils 🡪 damage endothelium and vessel wall 🡪 fibrinoid necrosis.**
* **Endothelial damage 🡪 thrombosis 🡪**
* **Ischemic damage to tissue involved.**
* **Example of IC mediated Vasculitis = Henoch-Schonlein purpura**
* **Etiopathogenesis
 Immunologic mechanisms**
* **Type IV hypersensitivity: delayed type of hypersensitivity reaction**
* **implicated in some types of vasculitis due to presence of granulomas.**
* **Example: Temporal arteritis**
* **Direct Invasion:**
* **by all classes of microbial pathogens**
* **Rickettsiae**
* **Meningococcus**
* **Fungus**
* **Laboratory testing in vasculitis**
* **Antineutrophil cytoplasmic antibodies (ANCA)**
* **Erythrocyte sedimentation rate (ESR)**
* **Antineutrophil cytoplasmic antibodies (ANCAs)**
* **Are seen in some types of vasculitis esp small vessel vasculitis**
* **Are circulating ab reactive with neutrophil cytoplasmic ag = ANCA.**
* **The ANCAs activate neutrophils**
* **Cause release of enzymes and free radicals resulting in vessel damage.**
* **ANCA titers correlate with disease activity.**
* **Detected by immunofluorescence**
* **Two types of ANCAs**
* **Cytoplasmic (c-ANCAs):**
* **Ab directed against proteinase 3 in cytoplasmic granules.**
* **Cytoplasmic staining pattern**
* **Example: Wegener’s granulomatosis.**
* **Perinuclear (p-ANCAs):**
* **Ab directed against myeloperoxidase.**
* **Perinuclear pattern of staining**
* **Example: Churg-Strauss syndrome, PAN.**
* **Classification of Vasculitis : based on vessel size**
* **Large vessel Vasculitis:**
* **Giant cell arteritis \***
* **Takayasu’s arteritis \***
* **Medium vessel Vasculitis**
* **Polyarteritis nodosa (PAN)\***
* **Kawasaki’s disease\***
* **Thromboangitis obliterans (TAO)\***
* **Small vessel Vasculitis**
* **Hypersensitivity vasculitis**
* **Henoch Schonlein purpura\***
* **Churg Strauss syndrome**
* **Wegener granulomatosis \***
* **Clinical manifestations of vasculitis**
* **Clinical picture depends on the size and extent of the vessel involvement.**
* **Large vessel Vasculitis:**
* **Presents with loss of pulse or**
* **Stroke**
* **Medium vessel Vasculitis**
* **Presents with infarction or aneurysm**
* **Small vessel Vasculitis**
* **Presents with Palpable purpura\***
* **General features:**
* **Fever, weight loss, malaise, myalgias**
* **What do you see??**
* **Patient Profile # 1**
* **Old female patient presents with**
* **Headache in the temporal region**
* **Pain in the jaw while chewing**
* **Muscle aches and pains**
* **Develops problems with vision.**
* **On examination:**
* **Has nodular and palpable temporal artery.**
* **Labs:**
* **elevated ESR**
* **Biopsy: ( temporal artery)**
* **granulomatous inflammation with giant cells**
* **Diagnosis:**
* **Giant cell (temporal) arteritis**
* **Large vessel vasculitis
 Giant cell (temporal) arteritis**
* **Is the most common vasculitis\*\*.**
* **Occurs in women > 50 years (Female > male)**
* **Vessel involvement::**
* **Typically involves temporal artery and extra-cranial branches of external carotid.**
* **Involvement of ophthalmic branch of external carotid 🡪 blindness.**
* **Etiopathogenesis:**
* **Type IV hypersensitivity mediated reaction causing granulomatous inflammation.**
* **Giant cell arteritis: Pathology**
* **Affected vessel are cordlike and show nodular thickening.**
* **Microscopy:**
* **Focal Granulomatous inflammation of temporal artery**
* **Fragmented internal elastic lamina**
* **Giant cells.**
* Temporal (giant cell) arteritis
* **Giant cell (temporal) arteritis**
* **Clinical features:**
* **Fever, fatigue, weight loss**
* **Temporal headache\* (MC symptom), facial pain.**
* **Painful, palpably enlarged and tender temporal artery\***
* **Generalized muscular aching and stiffness (shoulders and hip)**
* **Temporary / permanent blindness\***
* **Giant cell (temporal) arteritis**
* **Investigations:**
* **ESR: screening test of choice ; markedly elevated.**
* **Temporal artery biopsy : definitive diagnosis (positive in only 60% cases)**
* **Treatment:**
* **Corticosteroids (to prevent blindness)**
* **What do you see?**
* **Patient profile # 2**
* **Middle aged Asian woman presents with:**
* **Visual disturbances**
* **Marked decrease in blood pressure in upper extremity and**
* **Absent radial, ulnar and carotid pulses.**
* **Angiography shows:**
* **Marked narrowing of aortic arch vessels**
* **Biopsy:**
* **Granulamatous inflammation with giant cells**
* **Diagnosis:**
* **Takayasu’s arteritis (pulseless disease)**
* **Takayasu’s arteritis (pulseless disease)**
* **Is an inflammatory disease of vessels affecting**
* **the aorta and its major branches**
* **Seen in Asian women <50 years old.**
* **Vessel involvement:**
* **Typically involves the aorta\* and the aortic arch vessles\* (carotids, subclavian).**
* **Can also involve: pulmonary, renal, coronary**
* **Etiopathogenesis:**
* **Type IV hypersensitivity reaction causing granulomatous inflammation (granulomatous vasculitis)**
* **Takayasu’s arteritis**
* **Takayasu’s arteritis (pulseless disease)**
* **Pathology:**
* **Thickening of vessels ( aorta & branches) with narrow ( stenosis) lumen 🡪**
* **decreased blood flow**
* **Microscopic**
* **Similar to/indistinguishable from Giant Cell Arteritis**
* **Takayasu’s arteritis (pulseless disease)**
* **Clinical:**
* **Dizziness,syncope.**
* **Absent upper extremity pulse (pulseless disease)\*\***
* **Blood pressure discrepancy\* between extremitis : low in upper and higher in lower**
* **Visual disturbances**
* **Diagnosis:**
* **angiography**
* **Patient profile # 3**
* **Young male IV drug abuser with history of Hepatitis (HBV) presents with**
* **Hypertension, abdominal pain, melena, muscle aches and pains and skin nodulations.**
* **Biopsy of skin nodules:**
* **Segmental transmural inflammation of blood vessels with fibrinoid necrosis.**
* **Labs:**
* **HBsAg +ve**
* **pANCA +ve**
* **Diagnosis:**
* **Polyarteritis nodosa (PAN)**
* **Polyarteritis nodosa (PAN)**
* **A systemic disease.**
* **Vessel involvement:**
* **Affects medium sized & small muscular arteries\*.**
* **Typically involves vessels of**
* **Kidney, heart, liver, GIT and skin**
* **Spares the lung\*\***
* **Etiology:**
* **Mediated by type III hypersensitivity ( ag-ab complex deposition).**
* **Associations:**
* **strong association with HBV antigenemia**
* **hypersensitivity to drugs (IV amphetamines).**
* **Pathogenesis:**
* **immunecomplex deposition (e.g. HBsAg / anti- HBsAg)**
* **PAN**
* **Pathology:**
* **Transmural inflammation (involving all layers).**
* **Lesion in the vessel wall may**
* **involve entire circumference or part of it**
* **Fibrinoid necrosis**
* **Consequences:**
* **development of**
* **Thrombosis 🡪 infarction**
* **Weakening of vessel wall 🡪Aneurysms (kidney, heart and GI tract)**
* **PAN: Clinical features**
* **More common in young to middle aged men**
* **Signs and symptoms: due to ischemic damage.**
* **Target organs:**
* **Kidneys : Vasculitis/infarction 🡪 hypertension , hematuria, albuminuria.**
* **GI tract: Bowel infarction 🡪 abdominal pain, melena.**
* **Skin: Ischemic ulcers and nodules.**
* **Coronary arteries: aneurysms, MI**
* **Systemic manifestation: fever, malaise and weight loss.**
* **Cause of death: Renal failure MC COD**
* **PAN**
* **Laboratory findings:**
* **HbsAg positive in 30% of cases**
* **Hematuria with RBC cast**
* **Diagnosis:**
* **arteriography or biopsy of palpable nodulations in the skin or organ involved .**
* **Treatment:**
* **Untreated cases: almost fatal**
* **Good response to immunosuppressive therapy.**
* **Churg-Strauss Syndrome
(Allergic granulomatous angitis)**
* **Is a systemic vasculitis that occurs in persons with asthma\*.**
* **A variant of PAN.**
* **Involves small\* & medium vessels of**
* **upper/lower respiratory tract\***
* **heart, spleen, peripheral nerves, skin , kidney.**
* **Pathology:**
* **Inflammation of vessel wall (eosinophils)**
* **Fibrinoid necrosis**
* **Thrombosis and infarction**
* **Churg-Strauss Syndrome
(Allergic granulomatous angitis)**
* **Features very similar to PAN but patients with CSS have:**
* **History of atopy**
* **Bronchial asthma, allergic rhinitis and**
* **peripheral blood eosinophilia.**
* **Microscopy:**
* **Similar to PAN**
* **Labs:**
* **peripheral eosinophilia , high serum IgE,**
* **p-ANCA\***
* **Patient profile # 4**
* **A 4 year old Japanese child presents with**
* **Fever, redness of eyes and oral cavity**
* **Swollen hands and feet**
* **Rash over the trunk and extremities**
* **Peeling of skin and**
* **Cervical lymphadenopathy.**
* **Labs:**
* **ECG changes consistent with myocardial ischemia**
* **Diagnosis:**
* **Kawasaki Disease (mucocutaneous lymphnode syndrome)**
* **Kawasaki’s disease**
* **Is also known as mucocutaneous lymphnode syndrome.**
* **Is an acute self limited febrile illness of infants and children (< 5 yrs).**
* **Is endemic in Japan , Hawaii**
* **One of the manifestations is vasculitis (coronary artery).**
* **In other words:**
* **KD is a childhood vasculitis that mainly targets coronary arteries.**
* **Coronary artery involvement:**
* **can lead to coronary thrombosis or aneurysm formation and its rupture.**
* **Clinical features : Kawasaki’s disease**
* **Clinical findings:**
* **High fever**
* **Erythematous rash of trunk and extremities with desquamation of skin.**
* **Mucosal inflammation : cracked lips, oral erythema**
* **Erythema, swelling of hands and feet.**
* **Localized lymphadenopathy (cervical adenopathy)**
* **MCC of an acute MI in children\*\*\*\*\*\***
* **Lab:**
* **Neutrophilic leukocytosis**
* **Thrombocytosis : characteristic finding**
* **High ESR**
* **abnormal ECG (e.g. acute MI)\*\*\*\*\***
* **Patient profile # 5**
* **A young smoker male patient from Israel presents with C/O**
* **Pain in the foot**
* **Which is severe and present even at rest**
* **On examination:**
* **Presence of ulcers and blackish areas over the fingers and toes.**
* **Some missing digits.**
* **Biopsy from lower limb vessel:**
* **Acute inflammation of vessel wall with Obliteration of vessel lumen by a thrombus.**
* **Diagnosis: Thromboangitis Obliterans (Buerger’s Disease)**
* **Buerger’s Disease**
* **Also known as Thromboangitis Obliterans.**
* **Is a peripheral vascular disease of smokers.**
* **Pathology:**
* **Earliest change: Acute inflammation involving the small to medium sized arteries in the extremities (tibial, popliteal & radial arteries).**
* **Inflammation of vessel 🡪 thrombus formation 🡪 obliterates lumen 🡪 ischemia  gangrene of extremity.**
* **Inflammation also extends to adjacent veins and nerves.**
* **Involvement of entire neurovascular compartment.**
* **Buerger’s Disease**
* **Buerger’s Disease**
* **Clinical findings:**
* **Young-middle age, male, heavy smoker\***
* **Israel\*, Japan, India.**
* **Symptoms start between 25 to 40 years**
* **Early manifestation:**
* **Intermittent Claudication in feet or hands**
* **Cramping pain in muscles after exercise, relieved by rest**
* **Late manifestation:**
* **Painful ulcerations of digits**
* **Gangrene of the digits often requiring amputation.**
* **Buerger’s Disease**
* **Diagnosis:**
* **biopsy**
* **Rx:**
* **early stages of vasculitis frequently cease on discontinuation of smoking.**
* **Small vessel vasculitis**
* **Small vessel vasculitis
Hypersensitivity (leukocytoclastic) vasculitis**
* **Refers to a group of immune complex mediated vasculitides.**
* **Characterized by:**
* **Acute inflammation of small blood vessels**
* **Manifesting as palpable purpura\*\*\*.**
* **Organs involved:**
* **Usually skin ( other organs less commonly affected).**
* **Hypersensitivity (leukocytoclastic) vasculitis**
* **May be precipitated by**
* **Exogenous antigens**
* **Drugs**
* **E.g. aspirin/penicillin/thiazide diuretics**
* **Infectious organisms**
* **E.g. strep/staph infections,TB,viral diseases**
* **Foods**
* **Chronic diseases**
* **E.g. SLE, RA etc.**
* **Hypersensitivity (leukocytoclastic) vasculitis**
* **Pathology:**
* **acute inflammation of small blood vessels (arterioles, capillaries, venules)**
* **Neutrophilic infiltrate in vessel wall.**
* **Leukocytoclastic refers to nuclear debris from disintegrating neutrophils**
* **The neutrophils undergo karyorrhexis.**
* **Erythrocyte extravasation**
* **Hypersensitivity (leukocytoclastic) vasculitis**
* **C/F:**
* **The disease typically presents as palpable purpura\* involving the skin principally of lower extremities.**
* **May also involve other organs**
* **Lungs🡪 hemoptysis**
* **GIT🡪 abdominal pain**
* **Kidneys 🡪 hematuria and**
* **Musculoskeletal system 🡪 arthralgia**
* **brain, heart**
* **Hypersensitivity (leukocytoclastic) vasculitis**
* **Diagnosis:**
* **Skin biopsy is often diagnostic.**
* **Treatment:**
* **removal of offending agent**
* **Patient profile # 6**
* **A 14 year old child with history of URT infection develops:**
* **Polyarthritis**
* **Colicky abdominal pain**
* **Hematuria with RBC casts**
* **Palpable purpura localized to lower limbs and buttocks.**
* **Lab:**
* **Neutrophilic leukocytosis**
* **Deposition of IgA-C3 immune complex : in skin and renal lesions**
* **Henoch Schonlein purpura (HSP)**
* **A variant of hypersensitivity vasculitis.**
* **Seen in children\*\* (MC vasculitis in children) , rare in adults.**
* **Etiopathogenesis:**
* **Usually occurs following an upper respiratory infection\*.**
* **Caused by deposition of IgA-C3 immune complexes in vessel wall.**
* **Vessels involved:**
* **Arterioles, capillaries and venules of**
* **Skin, GIT,Kidney,musculoskeletal system.**
* **Henoch Schonlein purpura (HSP)**
* **Clinically characterized by:**
* **Palpable purpura over extensor aspects of arms and legs.**
* **commonly limited to lower extremities/ buttocks.**
* **Involvement of**
* **GIT 🡪 colicky abdominal pain, melena**
* **Musculoskeletal system  Arthralgia (non migratory), and myalgias**
* **Kidneys  hematuria due to focal proliferative GN.**
* **Lung 🡪 rare**
* **Henoch Schonlein purpura (HSP)**
* **Lab:**
* **Neutrophilic leukocytosis**
* **Deposition of IgA-C3 immune complexes : in skin and renal lesions**
* **Rx: steroids**
* **Wegener Granulomatosis (WG)**
* **Is characterized by:**
* **Necrotizing granulomatous inflammation of URT and LRT and**
* **Granulomatous vasculitis of the same areas plus kidneys.**
* **Therefore patients have:**
* **Lesions of the nose, sinuses and lungs\* (upper & lower respiratory tract) and**
* **Kidney\***
* **Highly associated with c-ANCA\*\***
*
* **Wegener Granulomatosis**
* **Pathology: two different types of lesions**
* **Granulomatous Vasculitis**
* **involving small vessels of URT and LRT and kidneys.**
* **Necrotizing granulomatous lesions**
* **in the above sites.**
* **Granuloma formation with giant cells**
*
* **Wegener Granulomatosis**
* **Clinical features**
* **Persons most commonly affected by WG are**
* **middle aged 40-50 yrs (Peak incidence)**
* **Male> females**
* **Respiratory tract signs and symptoms dominate the clinical picture:**
* **Upper respiratory tract (nasopharynx, sinuses, trachea)**
* **Chronic Sinusitis, ulcers of nasopharyngeal mucosa.**
* **Saddle nose deformity\* : Nasal cartilage destroyed**
* **Lower respiratory tract**
* **Recurrent pneumonia with**
* **Nodular lesions which undergo cavitation**
* **Kidney: Crescentric glomerulonephritis 🡪 can cause renal failure.**
* **Lab:**
* **c-ANCA\* present in 90% of patients with active disease (good marker of disease activity)**
* **Specific for WG**
* **Chest radiograph:**
* **bilateral nodular infiltrates or cavitary lesions.**
* **Diagnosis:**
* **biopsy**
* **Treatment:**
* **Cyclophosphamide**
* **Danger of hemorrhagic cystitis and Transitional cell carcinoma**
* **Steroids**
* **Without treatment 80% die within 1 year**
* **Infectious vasculitis**
* **Fungal vasculitis: vessel invading fungi**
* **Mucor, Aspergillus ,Candida.**
* **Rocky Mountain spotted fever**
* **Rickettsia rickettsiae**
* **Disseminated meningococcemia:**
* **Small vessel vasculitis 🡪 petechial hemorrhages**
* **Infective endocarditis\***
* **Roth’s spots in retina**
* **Janeway’s lesions on hands (painless)**
* **Osler’s nodes on hands (painful)**
* **Glumerulonephritis**