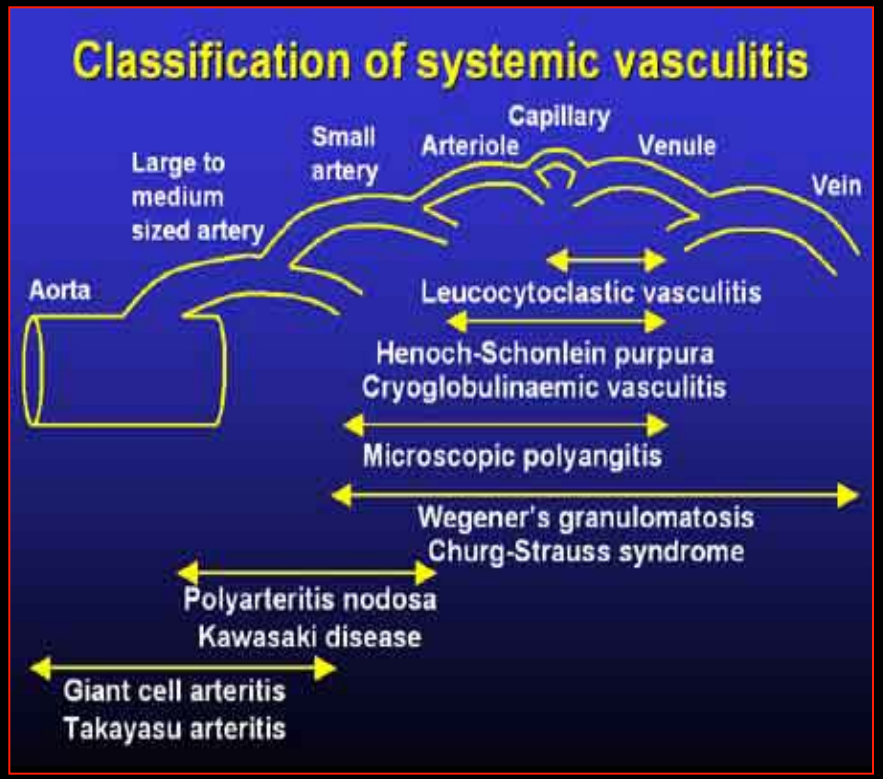
Wegener's Granulomatosis

By: Dr Maryam Sahebari

Wegener G.

Definition:

- Systemic necrotizing vasculitis
- Small & medium V.
- Granulomatous inflm.
  - Upper RespiratoryTract(ENT)
  - LowerRespiratoryTract (Lung)
  - Kidney



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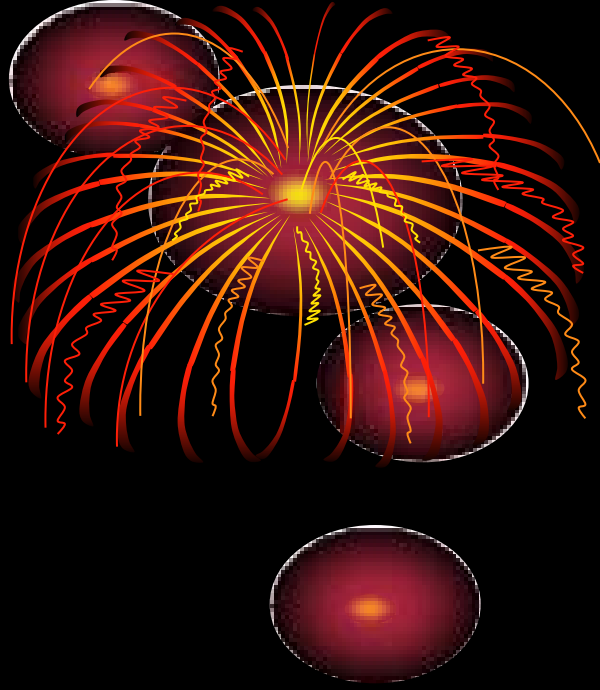
Wegener G.

Epidemiology:



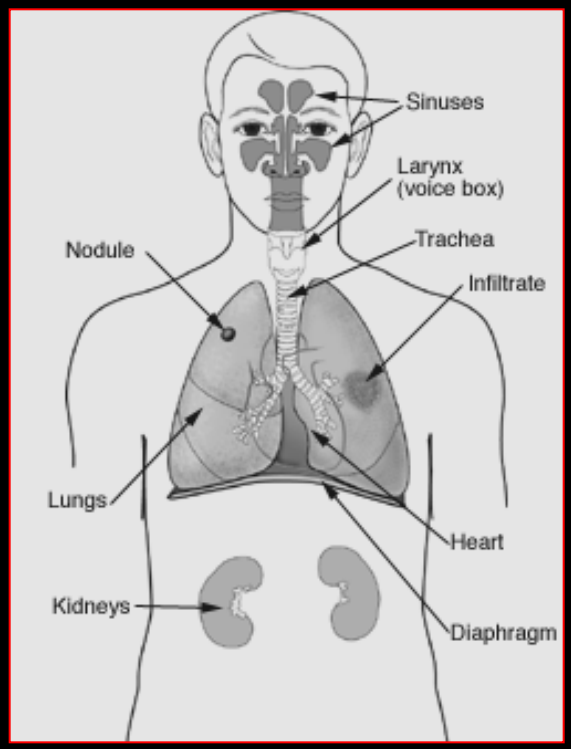
- Prevalence: 1/20,000-30,000
- M/F # 1
- Fourth & fifth decade: Mean = 40
- Age onset < 19: 15%
- White: 98%

By: Dr Maryam Sahebari

Wegener G.

Clinical findings:

- Constitutional
- Clinical triad:
  - URT(ENT)
  - LRT(Lung)
  - Kidney
- Initial presentation: ENT



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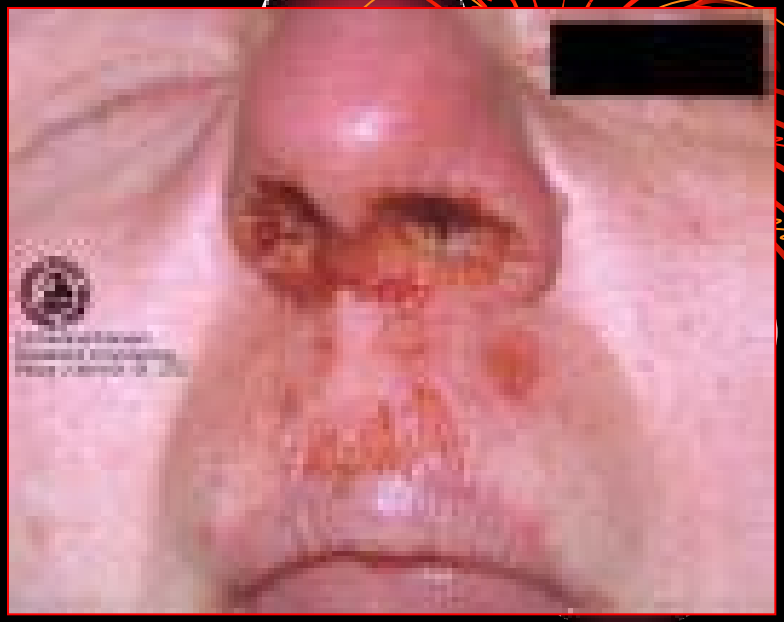
Wegener G.

URT: Nose

- Rhinitis
- Purulent/Bloody nasal discharge
- Epistaxis
- Nasal ulcer
- Runny nose
- Saddle-nose deformity



Wegener G.

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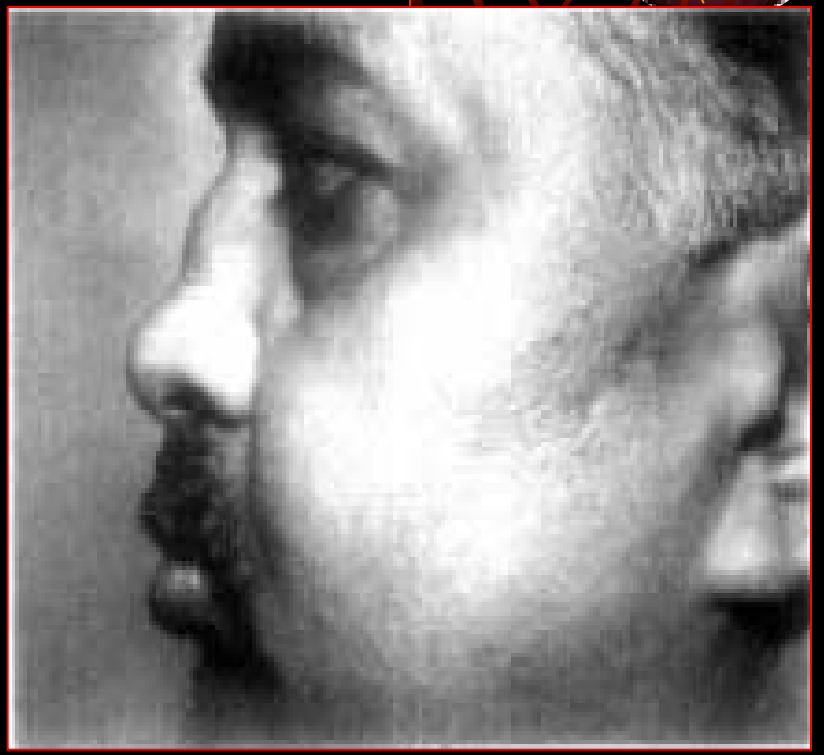
Saddle-nose deformity:



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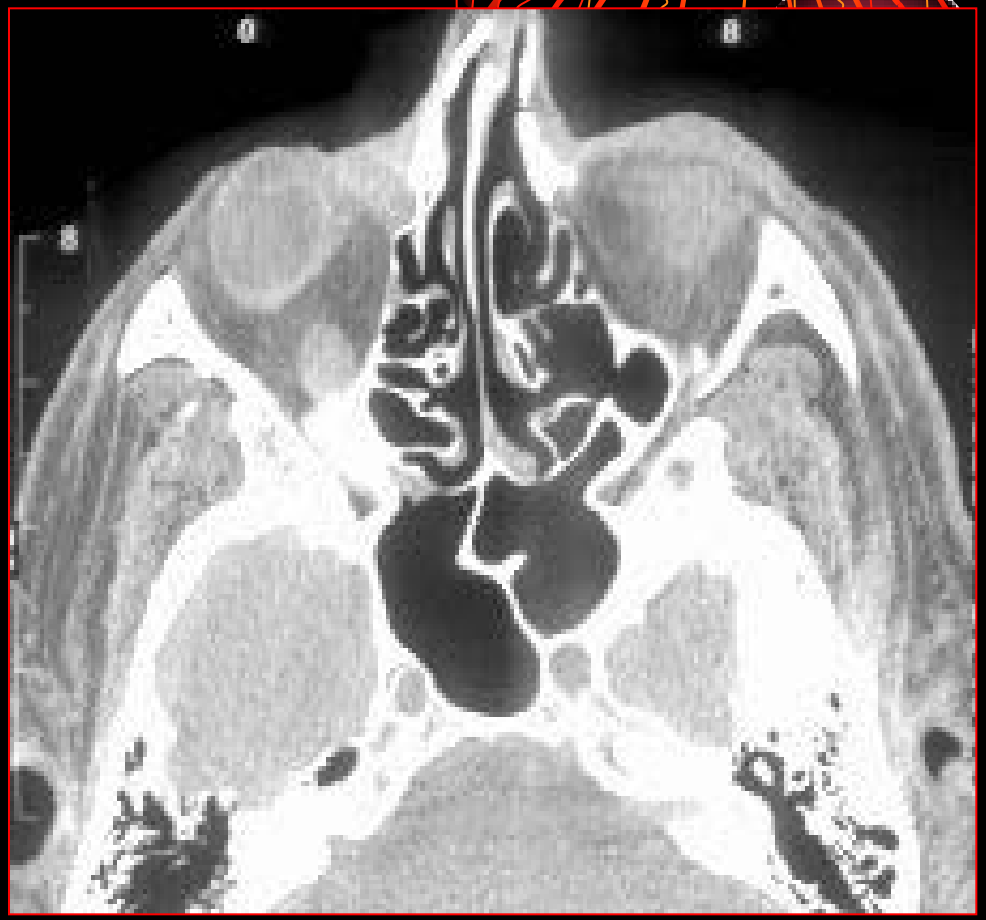
Wegener G.

URT: Sinus

- Pansinusitis



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Wegener G.

URT: Ear

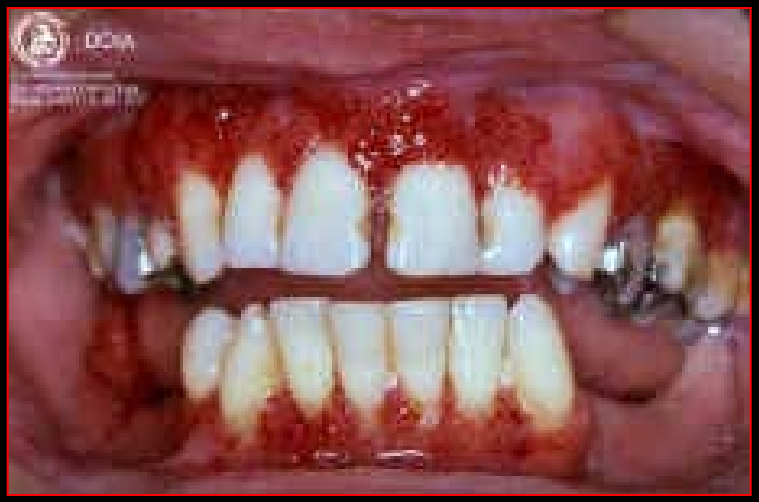
- Otitis media
- Hearing loss

By: Dr Maryam Sahebari

Wegener G.

Mouth:

- Oral ulcer
  - Perforation
- Strawberry gum hyperplasia



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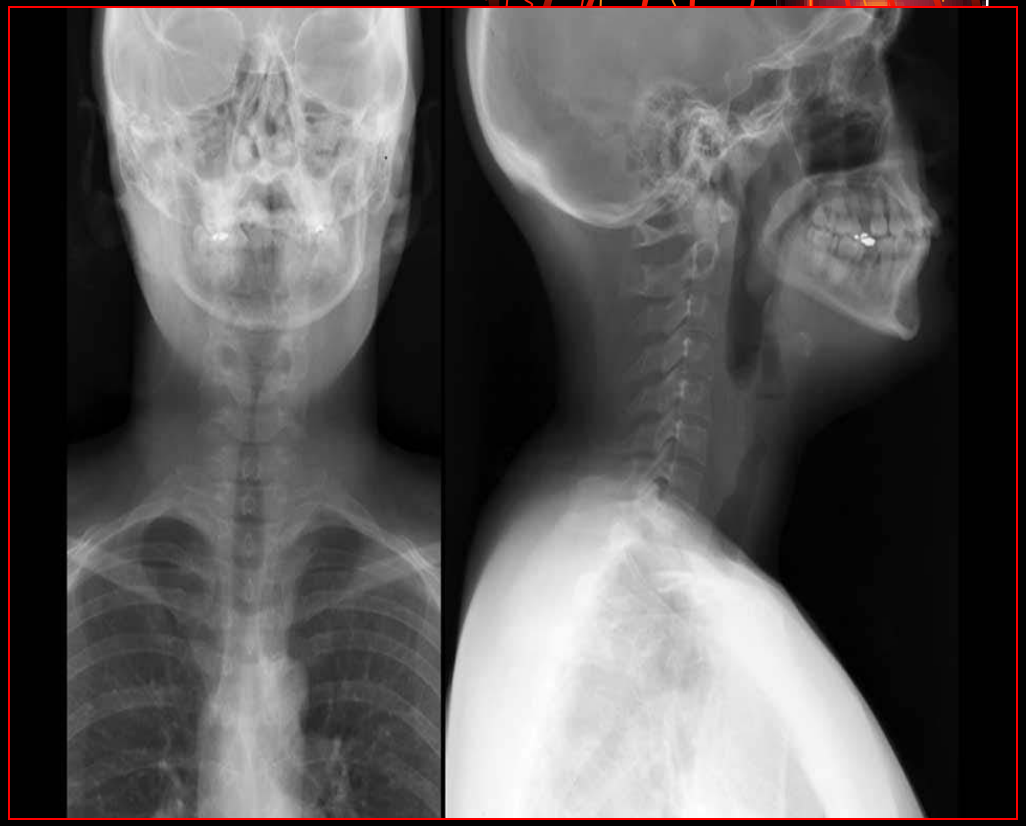
Wegener G.

Laryngotracheal:

- Hoarseness
- Stridor
- Subglottic stenosis
- Upper airway obstruction



Wegener G.

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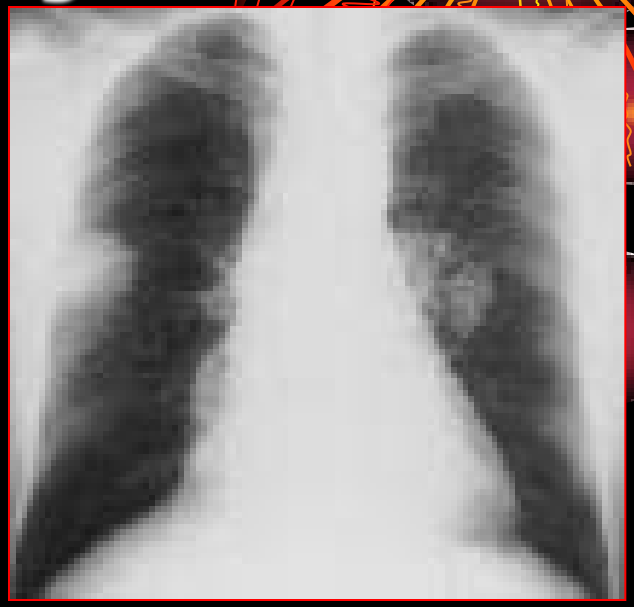
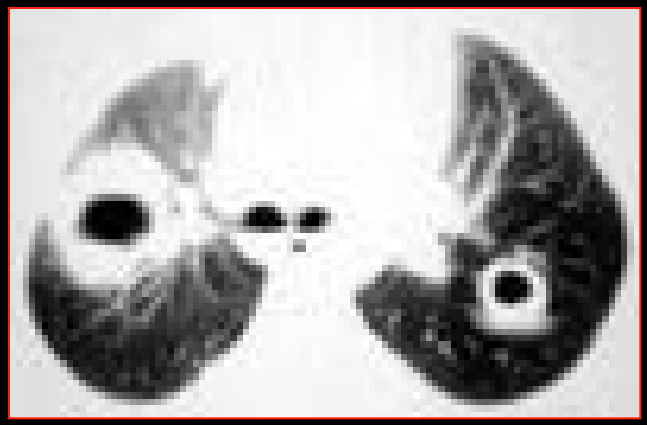
Lower respiratory tract:

- Pneumonia
  - Cough & Dyspnea
  - Hemoptysis
- Pleuritis
- Asymptomatic: 1/3
  - CXR
    - Nodule
    - Infiltration
    - Cavity





Wegener G.

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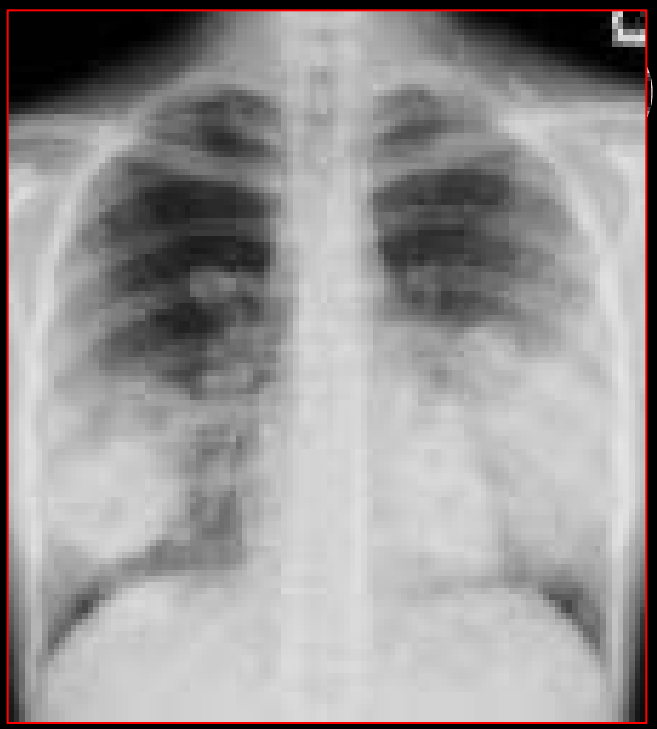
Pneumonia:

- Intractable pneumonia



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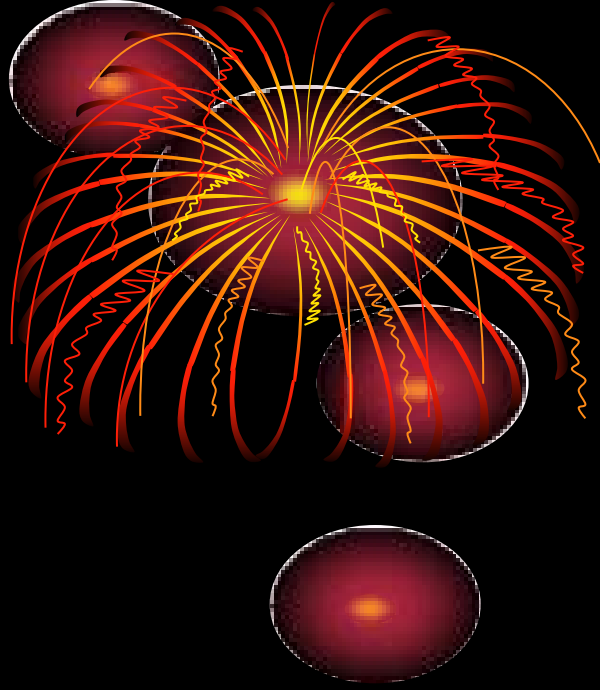
Wegener G.

Kidney:



- Asymptomatic
- Microscopic hematuria
- RBC cast
- Proteinuria & pyuria
- Azotemia
- Pathology:
  - Pauci-immune focal segmental necrotizing GN

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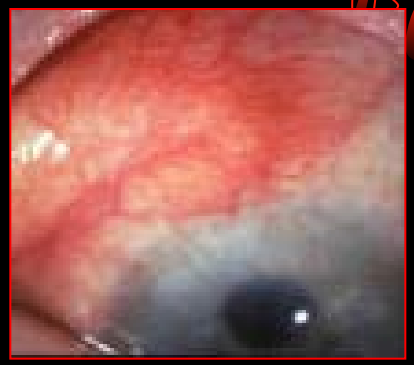
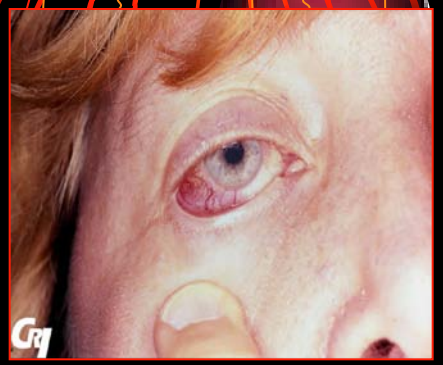
Wegener G.

Ophthalmic:

- Conjunctivitis, Scleritis
- Keratitis, Corneal ulcer
- Uveitis
- Dacriocystitis
- Proptosis
- Retinal vasculitis
- Optic neuritis
- Ophthalmoplegia
- Red eye syndrome





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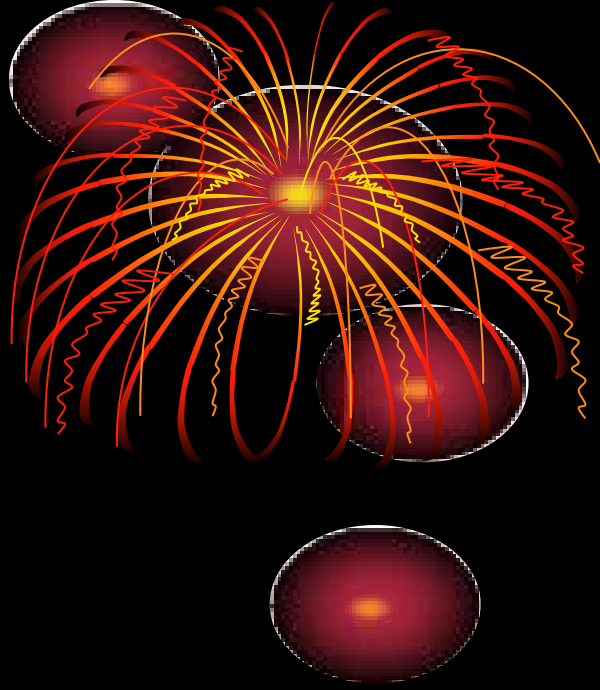
Wegener G.

Musculoskeletal:

- Arthralgias
- Myalgias
- Arthritis (<1/3)
  - Mono, Oligo, Poly
  - Migratory, Fixed
  - Symmetric, Asymmetric
  - Small, Large
  - Knee, Ankle
  - Positive RF: 50-60%



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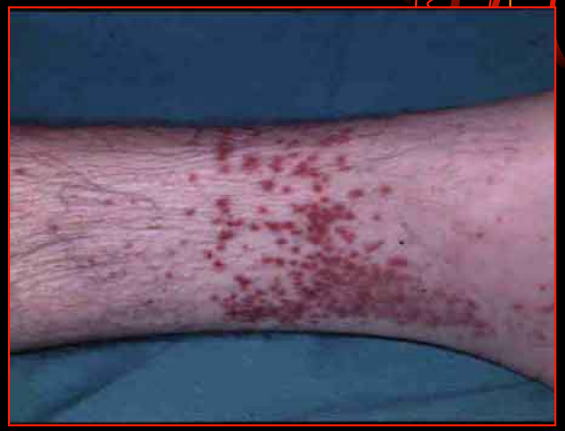
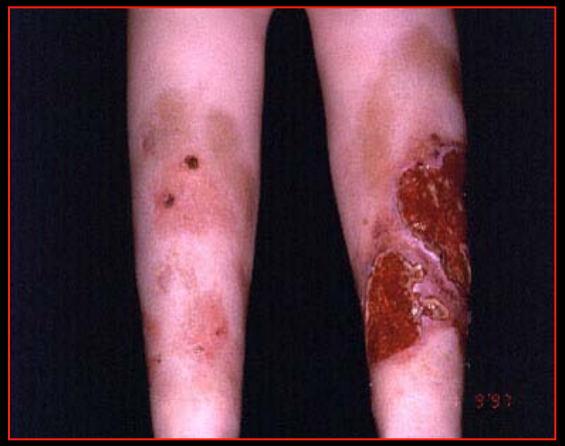
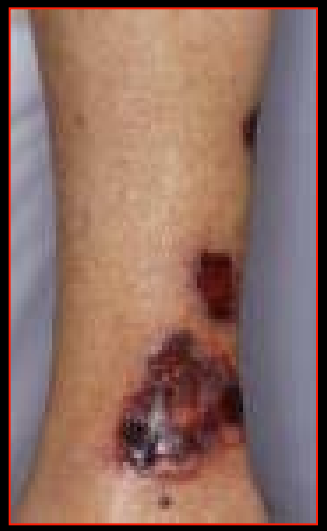
Wegener G.

Skin:

- Palpable purpura
- Ulcer
- Nodule
- Papule
- Vesicle
- Hemorrhagic lesion







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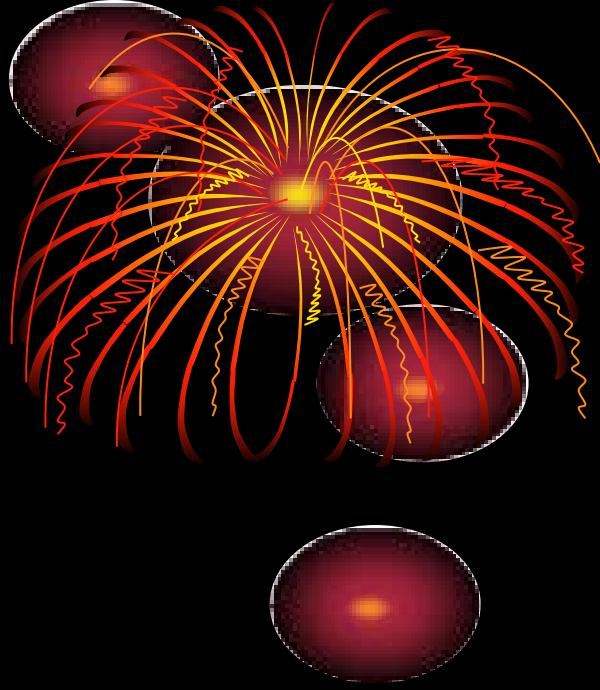
Wegener G.

Neurologic:

- Peripheral neuropathy
  - Mononeuritis multiplex
  - Polyneuropathy
- Cranial neuritis: 2, 6, 7
- CVA



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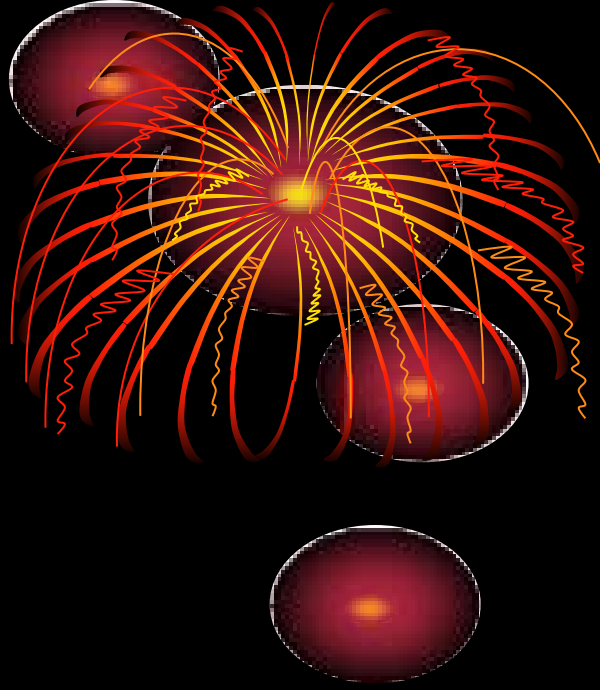
Wegener G.

GI tract:

- Asymptomatic
- Enterocolitis:
  - Abdominal pain
  - Diarrhea
  - GI bleeding
  - Ulcer



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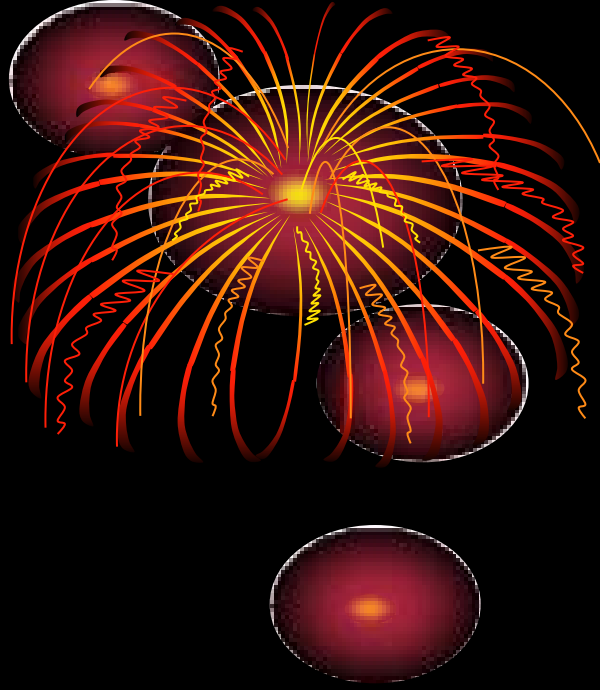
Wegener G.

Heart:



- Pericarditis
- Myocarditis
- Coronary vasculitis
  - MI, Angina
- Endocarditis

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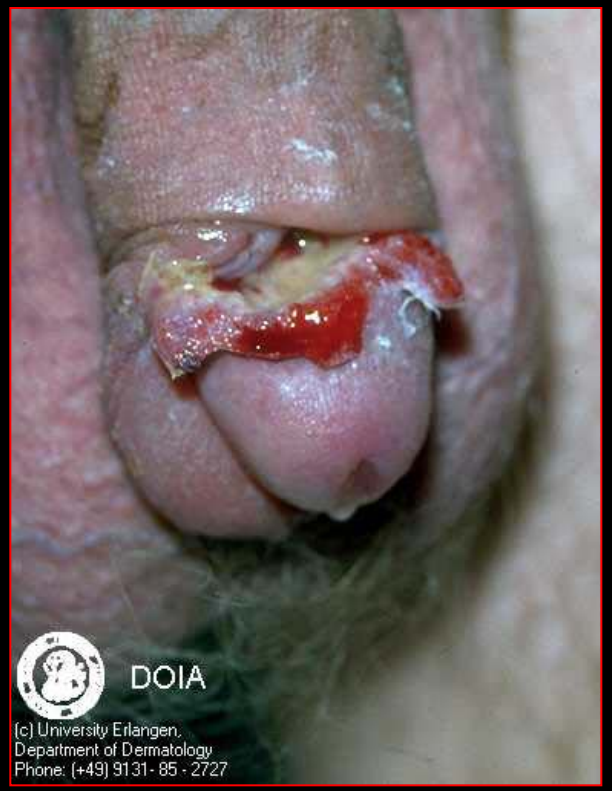
Wegener G.

Genitourinary:

- Ureteral obstruction
- Hemorrhagic cystitis



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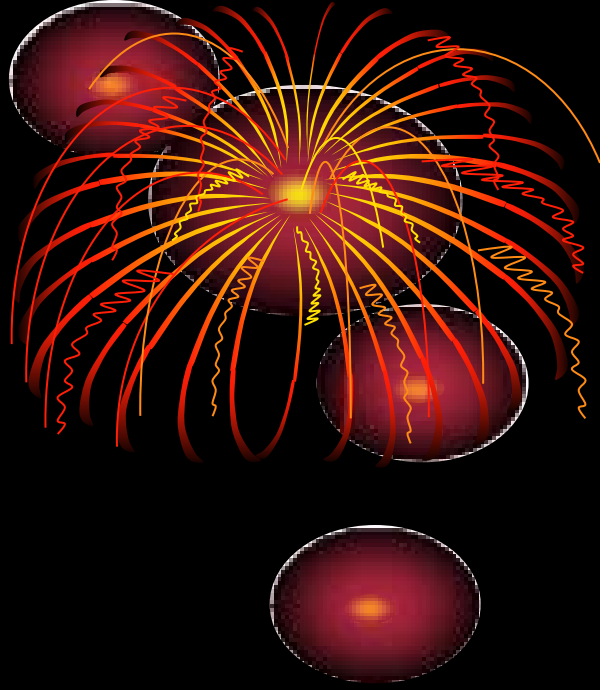
Wegener G.

Paraclinic:



- CBC, ESR, CRP
- BUN/Cr, U/A, LFT
- c-ANCA
- CXR, SinusXR
- Lung HRCTscan, Sinus CTscan
- Pathology
- Others

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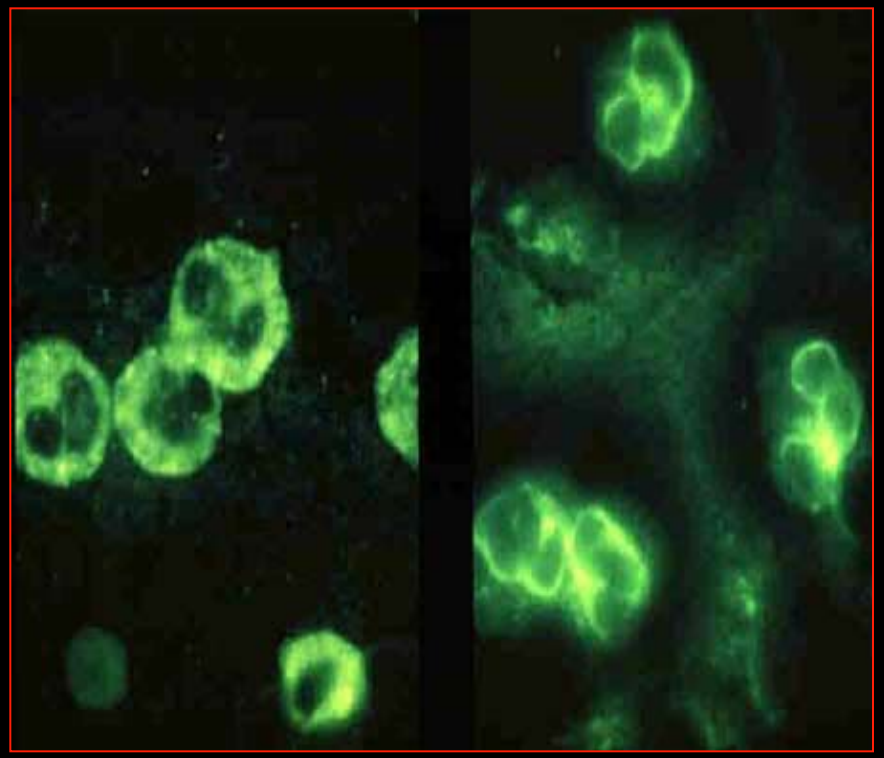
Wegener G.

Anti-Neutrophil Cytoplasmic Ab.

- c-ANCA: PR3

- c-ANCA specificity: 90%
- c-ANCA sensitivity:
  - Active: 90%
  - Remission: 40%
- Show activity: 64%



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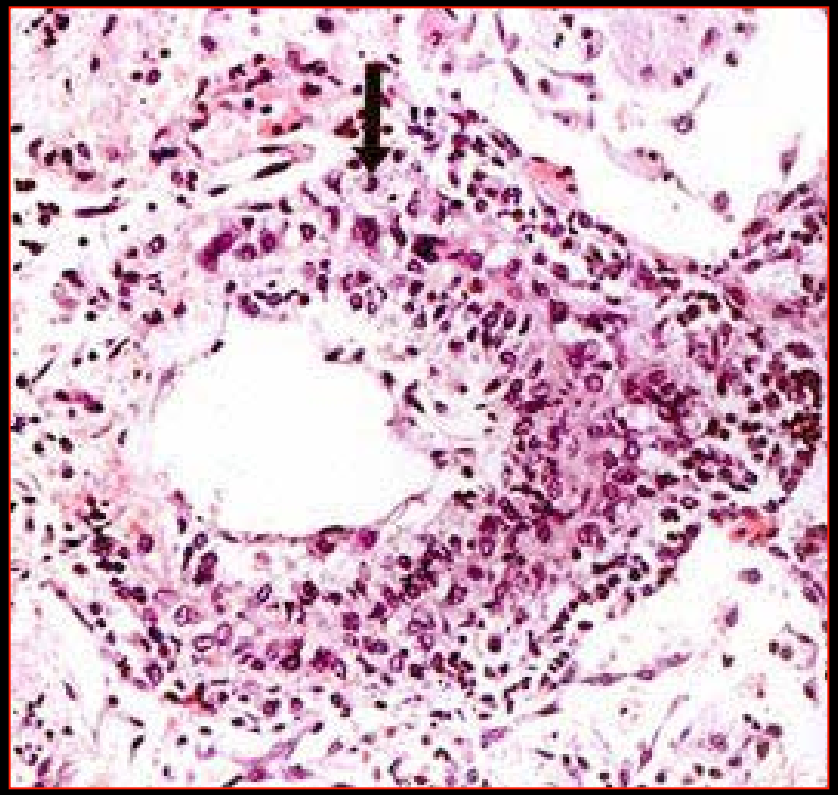
Wegener G.

Pathology:

- URT Bx: Sinus, Nose
- Renal Bx.
- Open Lung Bx.
- Pathologic triad:
  - Necrosis
  - Granuloma
  - Vasculitis



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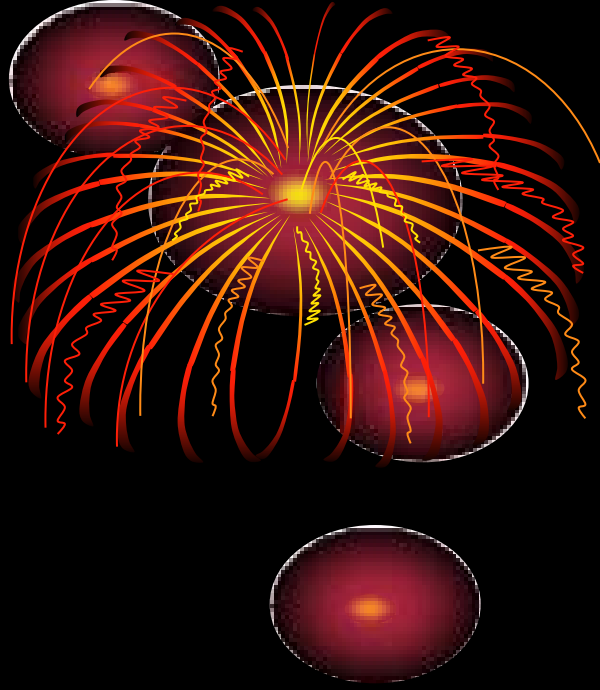
Wegener G.

Complications:



- Renal:
  - CRF: 42%
  - ESRD: 11%
- Non-renal:
  - Saddle-nose deformity
  - Tracheal & subglottic stenosis
  - Blindness & ophthalmoplegia

By: Dr Maryam Sahebari

Wegener G.

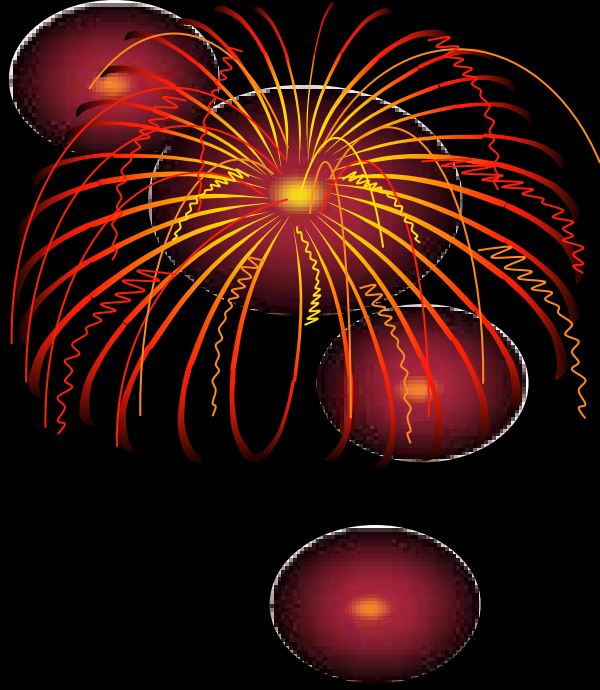
Churg-strauss syndrome (CSS)

Chapel Hill : 1994

An eosinophil-rich and granulomatous inflammation and necrotizing vasculitis of the medium-sized vessels involving the respiratory tract in association with asthma and eosinophilia

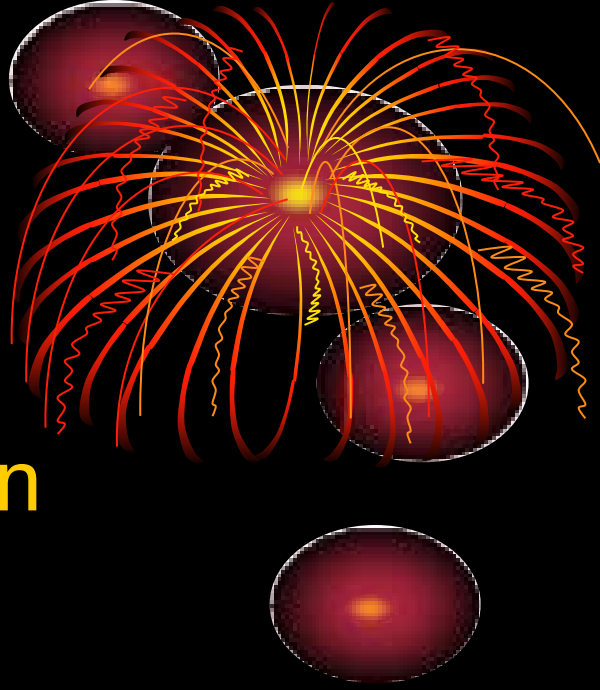
By: Dr Maryam Sahebari

Clinical features



- Three distinct phases :
- 1.prodrome phase
- 2.Allergic phase
- 3.vasculitic phase

Epidemiology



Annual Incidence : 3 per million

Mean age : 40 years

F/M : 1/1-3

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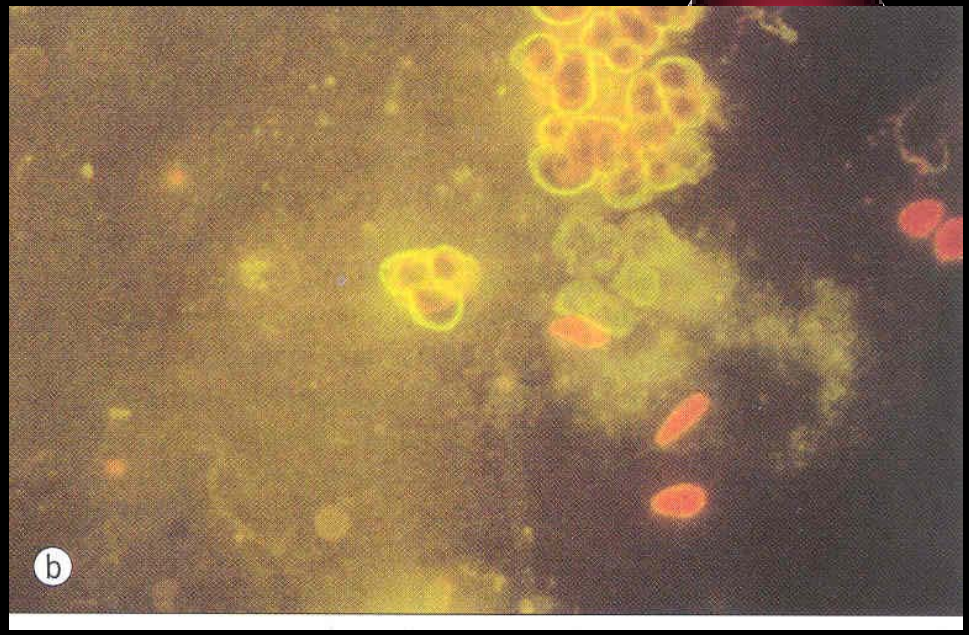
Laboratory test

Eosinophilia >1500

MPO-ANCA +



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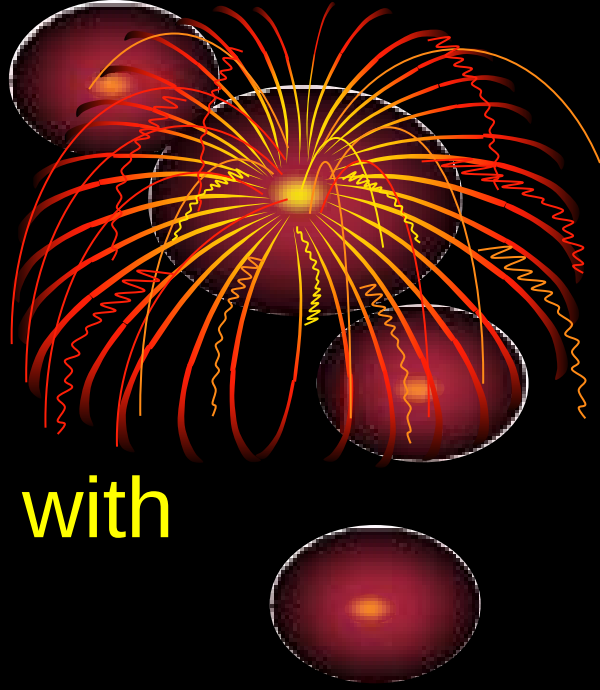


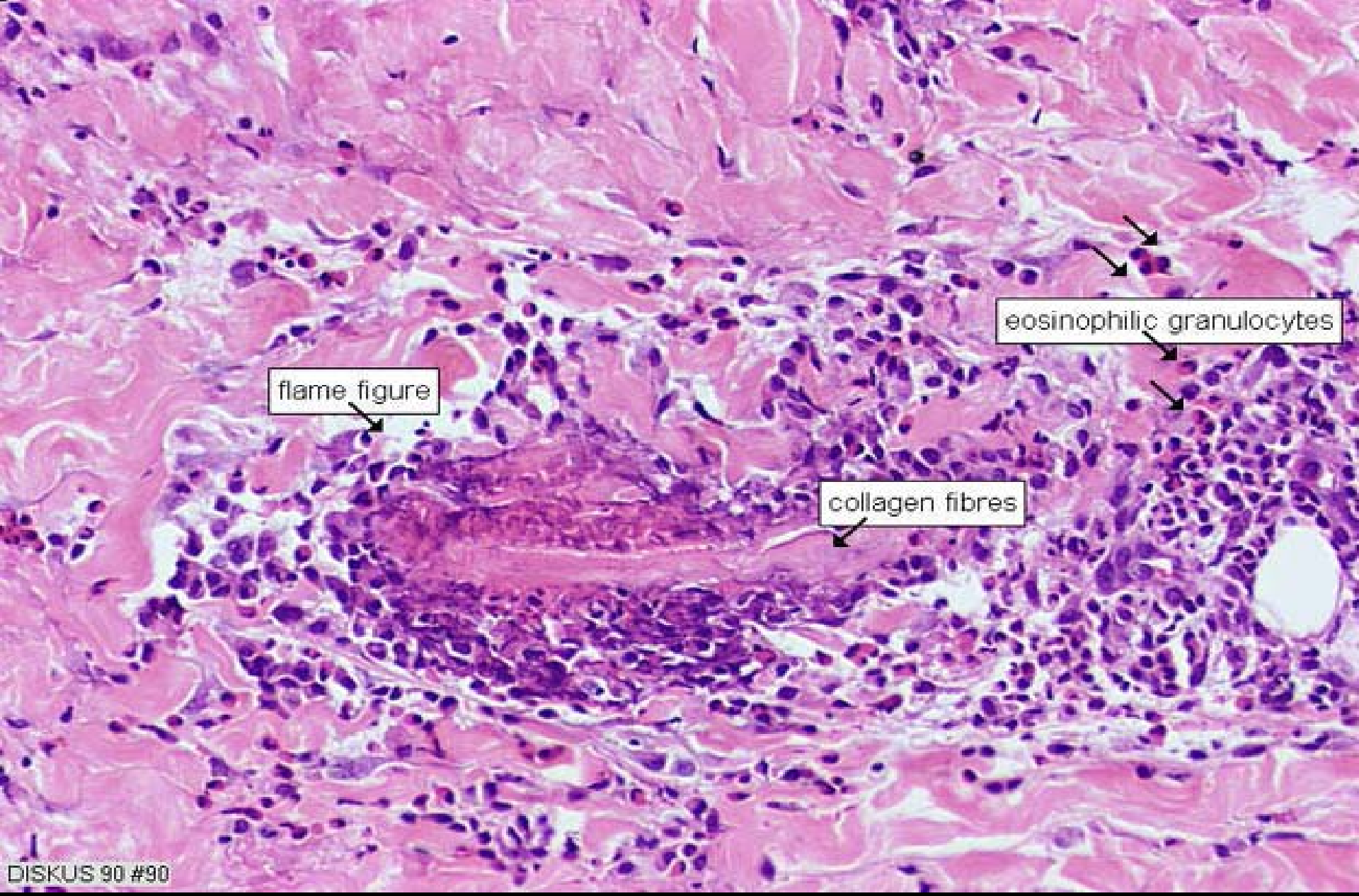
- Based on the documentation of necrotising vasculitis with eosinophils occuring in a patient with adult onset asthma and allergic rhinitis

Biopsy :

Necrotizing vasculitis

extravascular granuloma

eosinophilic tissue infiltration



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ACR

1.Asthma

2. Eosinophilia

3 . Mononeuritis multiplex or mononeuropathy or polyneuropathy

4. Pulmonary infiltrates ,non fixed

5. Paranasal sinus abnormality

6. Extra vascular eosinophils

4 of 6 criteria,sensitivity : 85% ,specificity : 99.7%

By: Dr Maryam Sahebari

Microscopic Polyangiitis

- Small vessel vasculitis
- Clinically distinguished from PAN by:
  - Rapidly progressive glomerulonephritis
  - Pulmonary involvement
  - P-ANCA positivity
  - Normal visceral angiography
  - No association with Hep B antigenemia

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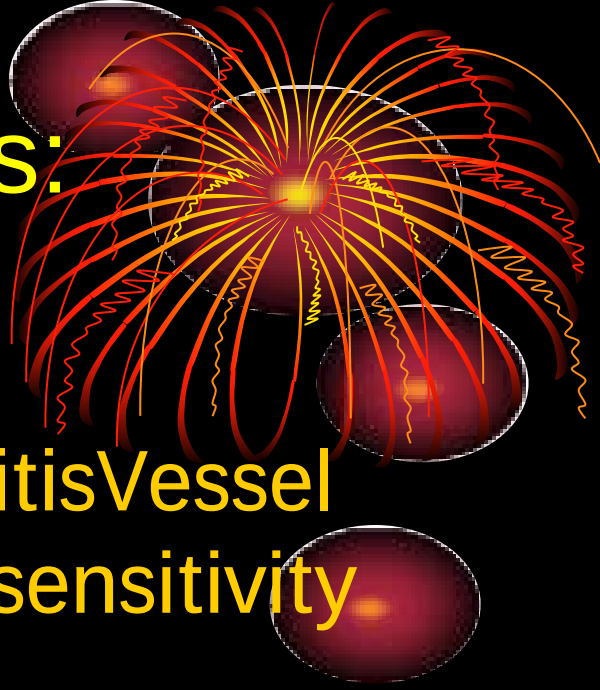
HypersensitivityVasculitis: DEFINITION



- Heterogeneous group of vasculitisVessel wall inflammation due to hypersensitivity reaction to one Ag
- Leukocytoclastic vasculitis
- Small vessel vasculitis
- Predominantly cutaneous vasculitis

- The patient is a 40-50 years old man or woman
- Skin lesion

  In dependent regions

  Macular petechia → Palpable purpura

  They become larger and confluent → Plaque

  In crop

  Asymptomatic

  Usually heal in 1 week, rarely last more than 1 months
- Edema in ankle and foot
- Fever, anorexia, myalgia, arthralgia

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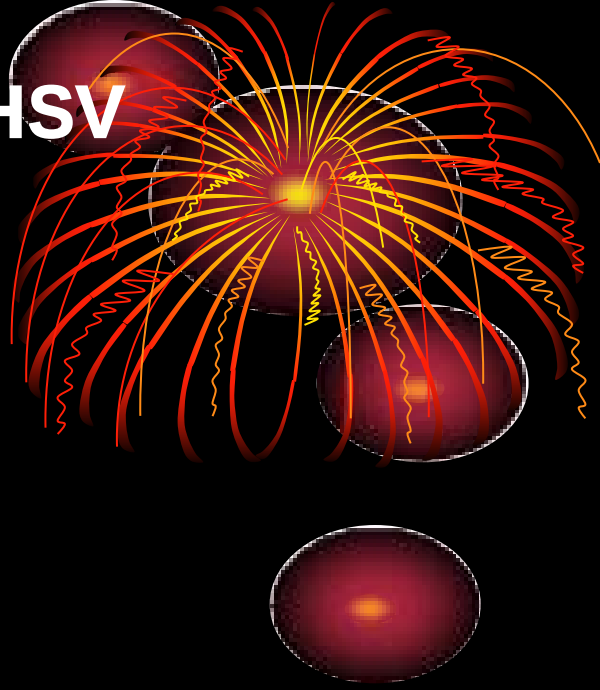
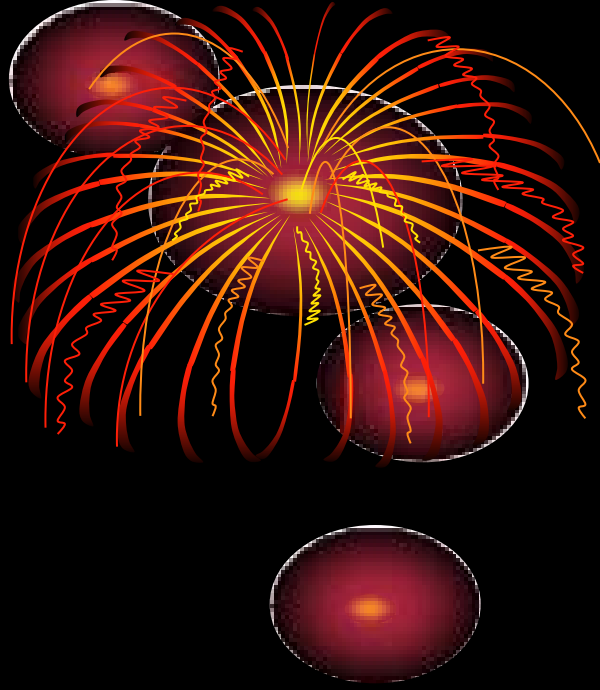
ACR Criteria for Classification of HSV (1990)



- Age at disease onset > 16 yr
- Medication at disease onset
- Palpable purpura
- Maculopapular rash
- Biopsy including arteriole and venule: granulocyte (neutrophils, eosinophils, or both) in a perivascular or extravascular location

ETIOLOGY OF CLA



- Exogenous Ag

1. Drugs
2. Infections

- Endogenous Ag

1. Malignancies
2. Collagen vascular diseases
3. Systemic diseases

By: Dr Maryam Sahebari

PATHOLOGY

- Inflammatory infiltration within and around the small vessel walls
- **Leukocytoclasis**
- **Extravasation of RBC’s**
- **Disruption of blood vessels architecture**
- **Endothelial swelling and proliferation**

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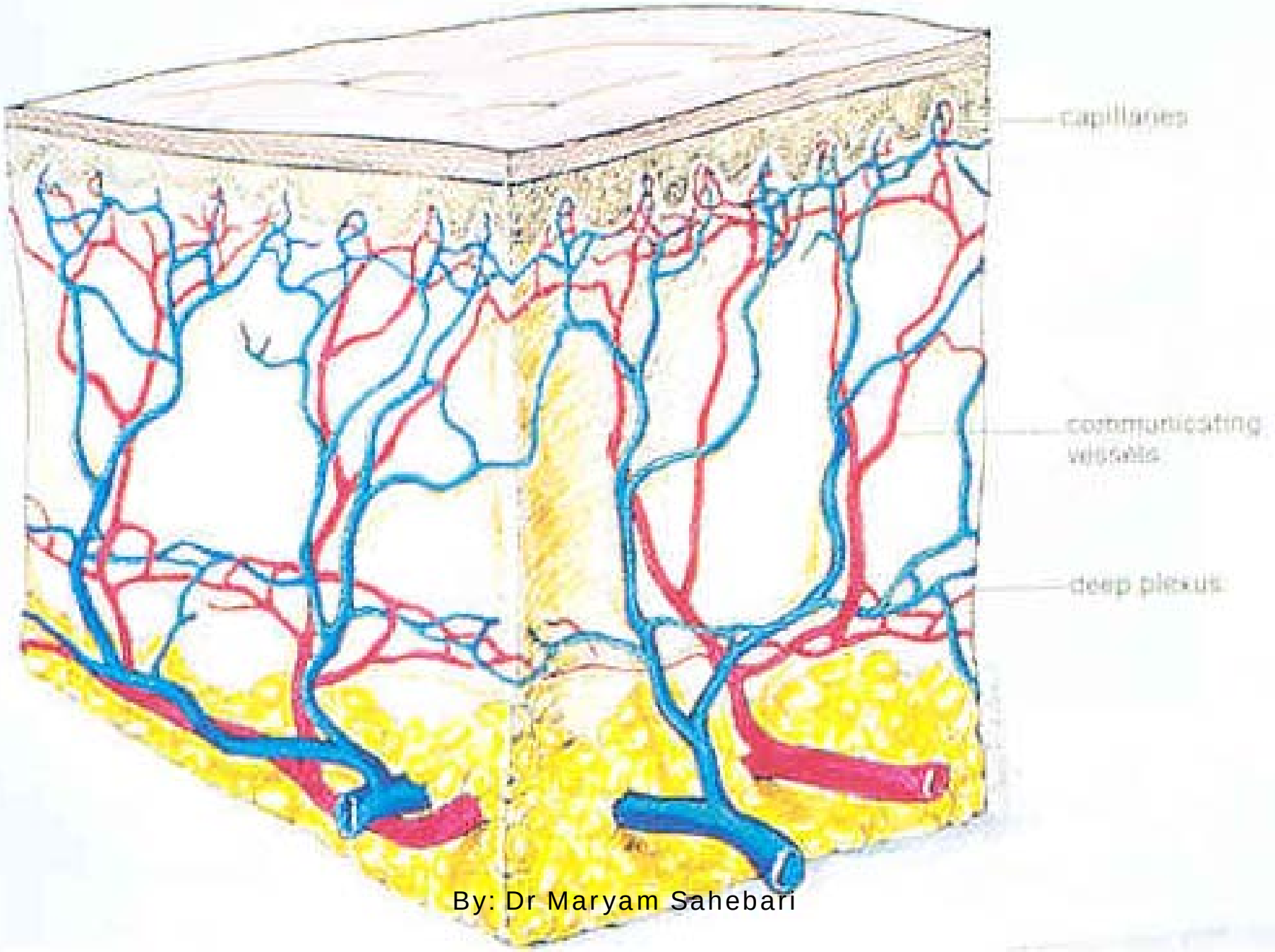

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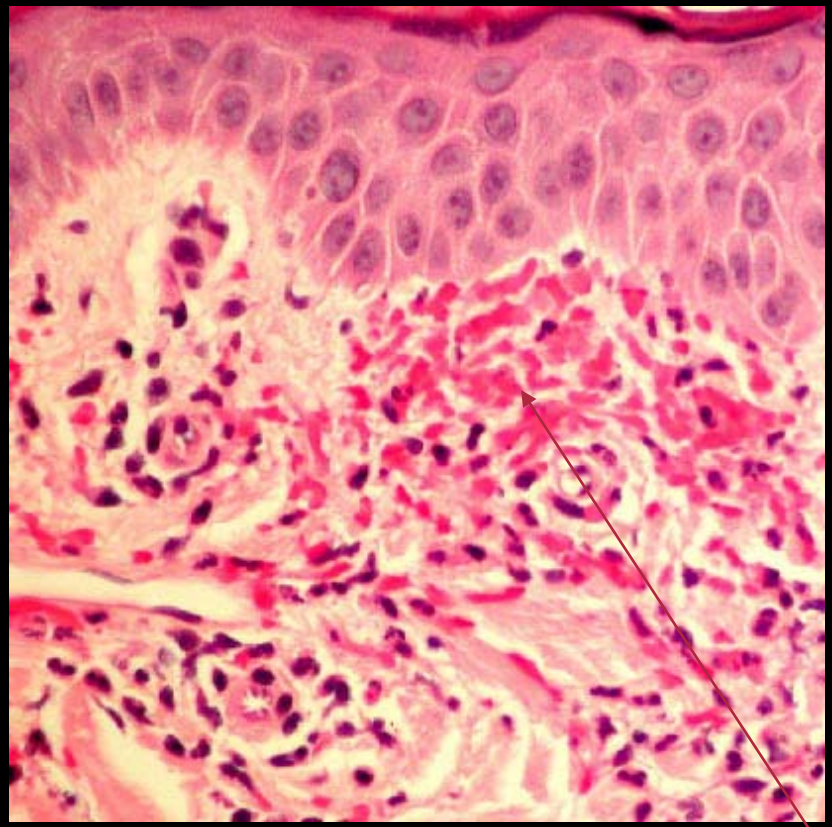
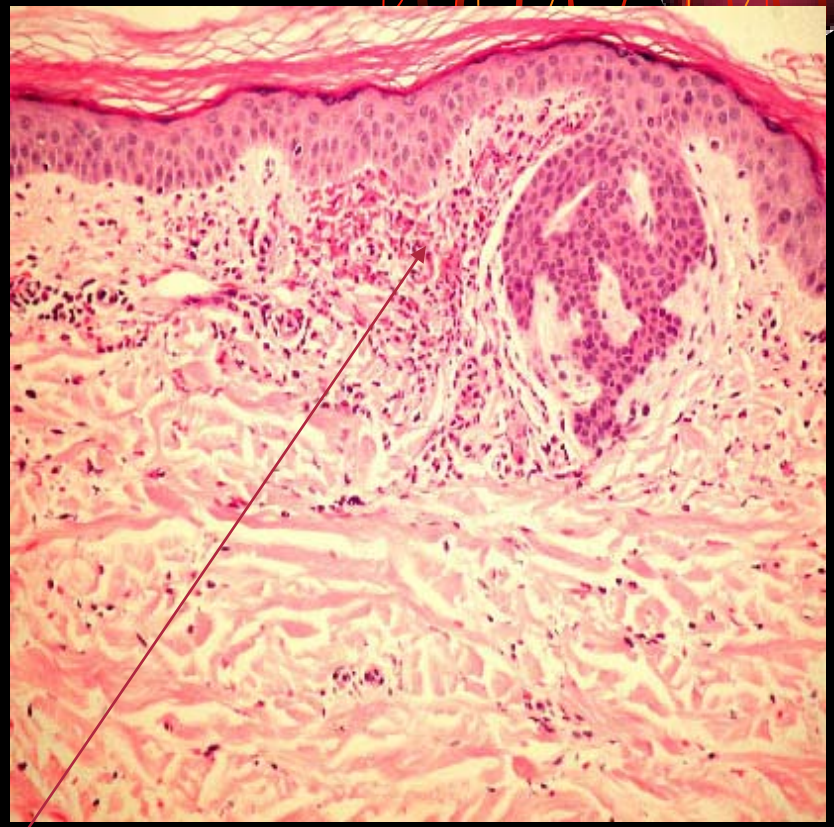
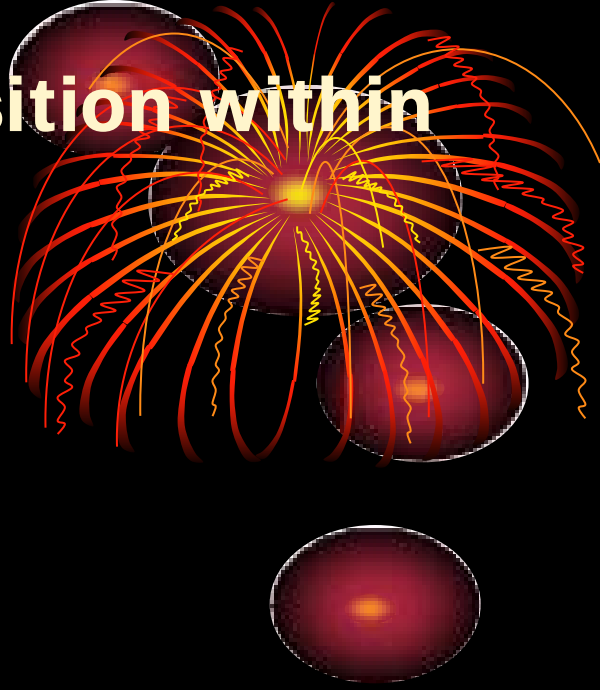


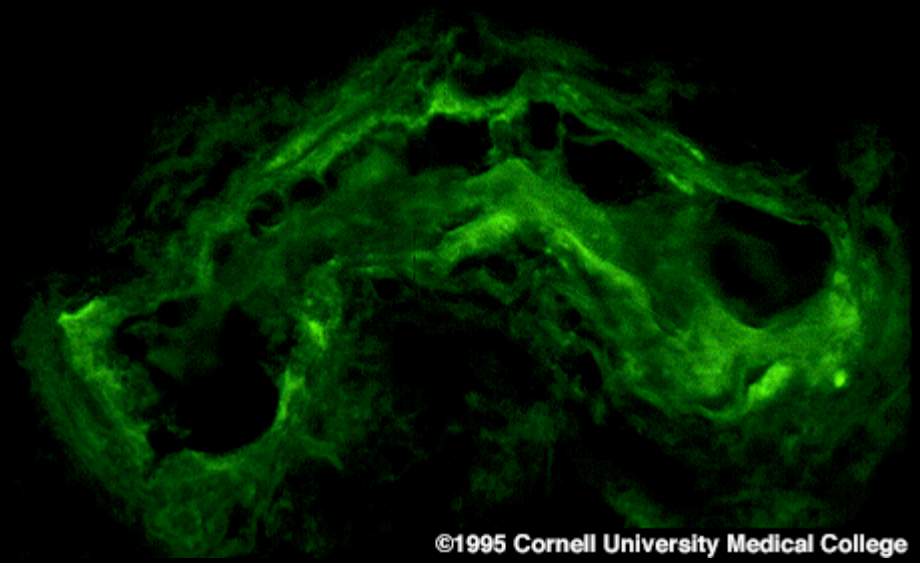


Extravasation of RBC's

By: Dr Maryam Sahebari

DIF: Ig and complement deposition within and around the vessel





IgM deposition around vessel wall

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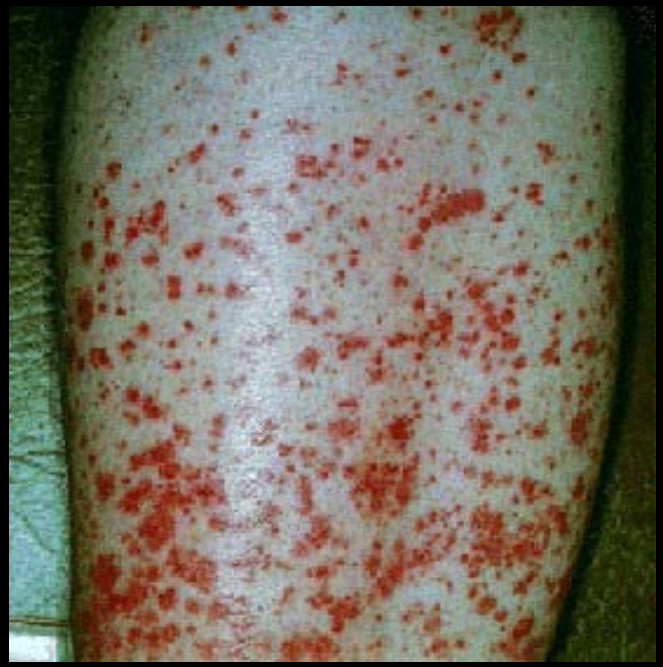

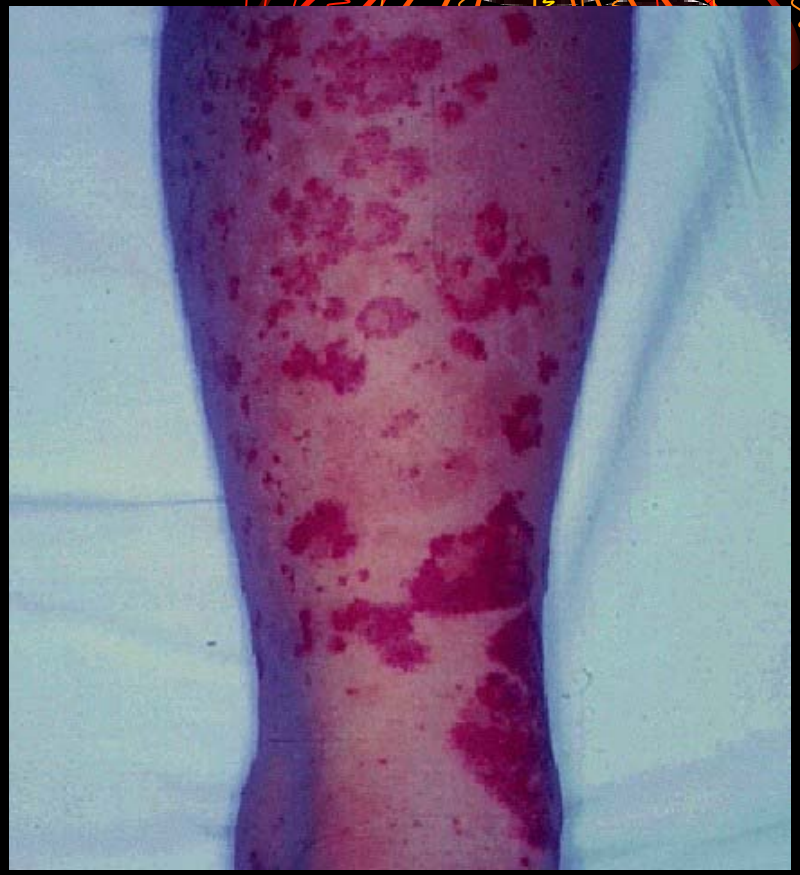

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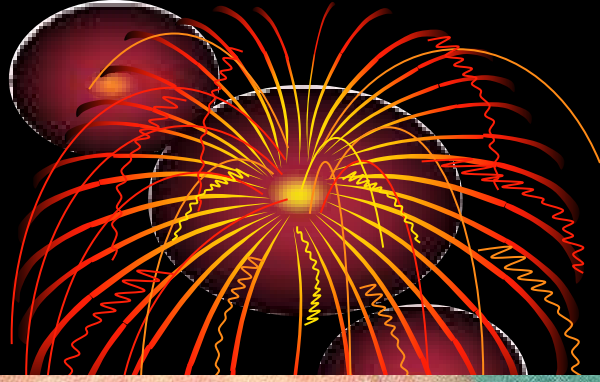
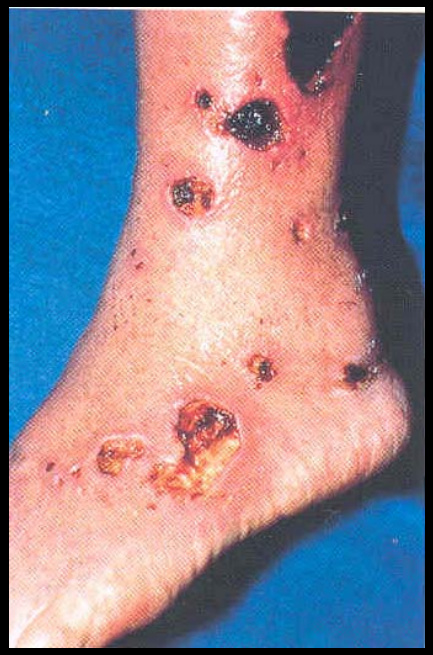
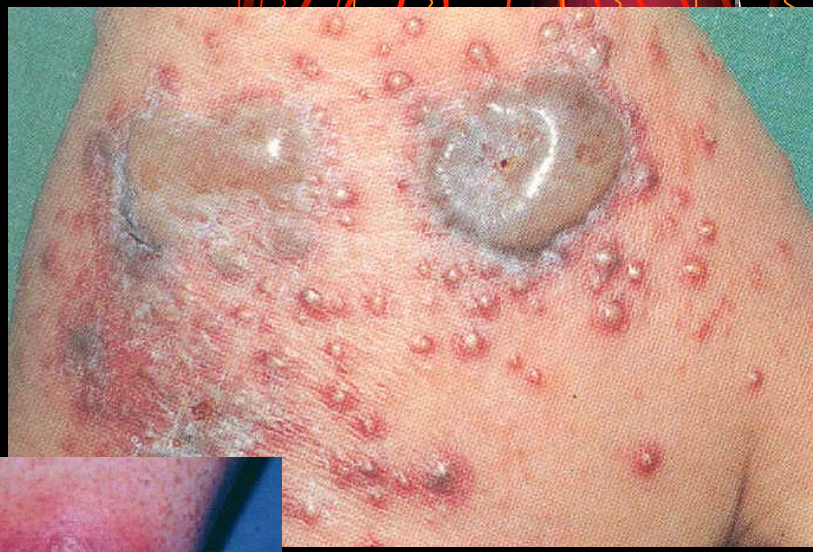
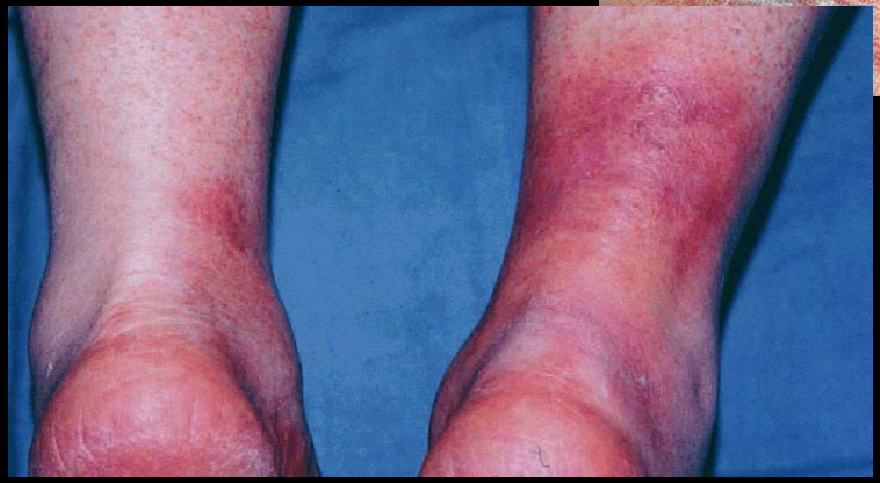








By: Dr Maryam Sahebari

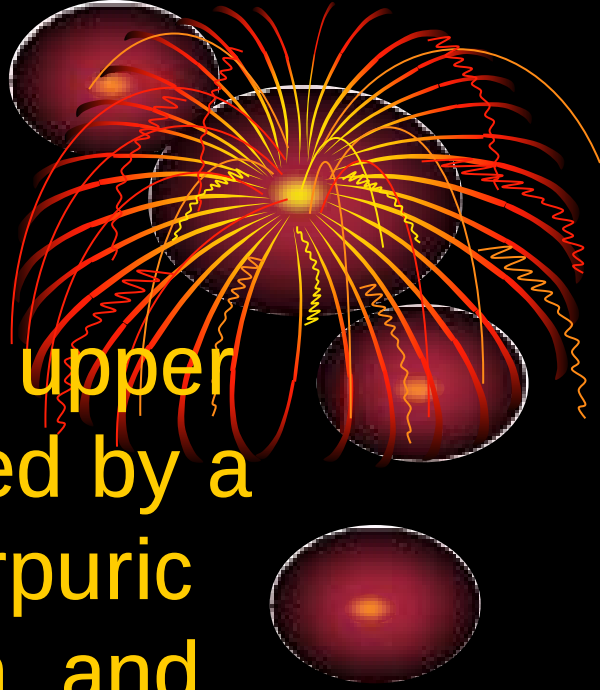
Laboratory findings

- Mild leukocytosis, eosinophilia
- Complement is normal
- ESR
- Cryoglobulinemia
- Microscopic hematuria
- RF+
- May be with internal organ involvement

Henoch-Schonlein Purpura

- complex-mediated form of small vessel vasculitis that is associated strongly with IgA deposition within blood vessel walls.
- ACR criteria
- Palpable purpura
- Age ,20 years at disease onset
- Bowel angina
- Granulocytes in arteriole or venule walls on biopsy

By: Dr Maryam Sahebari



- The hallmarks of HSP include an upper respiratory tract infection followed by a syndrome characterized by a purpuric rash, arthralgias, abdominal pain, and renal disease.

- Adults can be affected by HSP, and have a greater tendency toward prolonged disease courses (with recurrent bouts of purpura) than do children. Colicky abdominal pain, presumably secondary to gastrointestinal vasculitis, is a common characteristic of HSP, and frequently occurs within a week after the onset of rash.

- the abdominal pain in HSP occurs before the onset of purpura, and may be difficult to distinguish from an acute abdomen.

Mild glomerulonephritis is common and generally self-limited, although some patients will develop end-stage renal disease.

Diagnosis

- In children with mild manifestations, the clinical history alone may be sufficient to confirm the diagnosis. In more serious cases or when there is sufficient doubt about the diagnosis, biopsy of an involved organ is essential. Unlike other forms of immune complex-mediated disease, however, direct immunofluorescence will reveal florid IgA deposition.

Cryoglobulinemic Vasculitis

- Cryoglobulins are immune complexes that are characterized by their tendency to precipitate from serum under conditions of cold. Cryoglobulins, detectable to a varying degree in a wide array of inflammatory conditions, are not invariably pathogenic. **In some patients, however, cryoglobulins** deposit in the small- and medium-sized blood vessels and activate complement, leading to cryoglobulinemic vasculitis.

By: Dr Maryam Sahebari

Behcet's disease

- **Huluci Behcet 1937**
  - ★ **First description as a triad**
- **Autoimmune disease**
- **Systemic Vasculitis**

By: Dr Maryam Sahebari


RRC
Origin BD?
Caucasian
East Asian
UNITED KINGDOM
OSLO
SWEDEN
FINLAND
LONDON
COPENHAGEN
PARIS
LISBON
Lake Ladoga
BARENTS SEA
Mys Lopatka
SEA OF OKHOTSK
Aldan
Lena
Yenisey
Angara
Ob'
Amur
Argun
Lake Baikal
Harbin
Milan
SARAJEVO
TUNIS
BUCHAREST
CHISINAU
Donets
TUNISIA
VALLETTA
GREECE
İstanbul
TRIPOLI
TURKEY
KAZAKSTAN
Lake Balqash
Aral Sea
Caspian Sea
SAHARA
NICOSIA
BEIRUT
SYRIA
BAKU
UZBEKISTAN
BISHKEK
ALMATY
TASHKENT
DUSHANBE
TURKMENISTAN
TEHRAN
AMMAN
LIBYA
EGYPT
NIGER
Nile
CHINA
Chengdu
Shanghai
T'AI-PEI
TAIWAN
Indus
Salween
Brahmaputra
AFGHANISTAN
ISLAMABAD
KUWAIT
IRAN
HIMALAYAS
Luzon Strait
Jiang
CHAD
N'DJAMENA
SAUDI ARABIA
DOHA
ABU DHABI
MASQAT
PAKISTAN
Delhi
NEPAL
BHUTAN
Ganges
Mekong
HANOI
MANILA
Karachi
DHAKA
Calcutta
SUDAN
OMAN
INDIA
BURMA
LAOS
PARACEL
VIETNAM
PHILIPPINES
VIENTIANE
BANGUI
ERITREA
CENTRAL AFRICAN REPUBLIC
YEMEN
Bombay
Pune
Hyderābād
RANGOON
SPRATLY ISLANDS
DJIBOUTI
THAILAND
CAMBODIA
ETHIOPIA
BAY OF BENGAL
BANDAR SERI BEGAWAN
ARABIAN SEA
Bangalore
MALAYSIA
UGANDA
KIGALI
KENYA
SOMALIA
Palk Strait
BORNEO
KUALA LUMPUR
SINGAPORE
NAIROBI
MOGADISHU
SRI LANKA
INDIAN OCEAN
MALE
Kilimanjaro
TANZANIA
DAR ES SALAAM
Surabaya
JAKARTA
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BD Diagnosis

(ISG Criteria)

Recurrent Oral Aphthosis

Plus two of :

- **Recurrent genital ulceration**
- **Eye lesions**
  (Uveitis and/or Retinal vasculitis)
- **Skin lesions**
  (Pseudofolliculitis or Erythema nodosum)
- **Positive Pathergy test**

By: Dr Maryam Sahebari

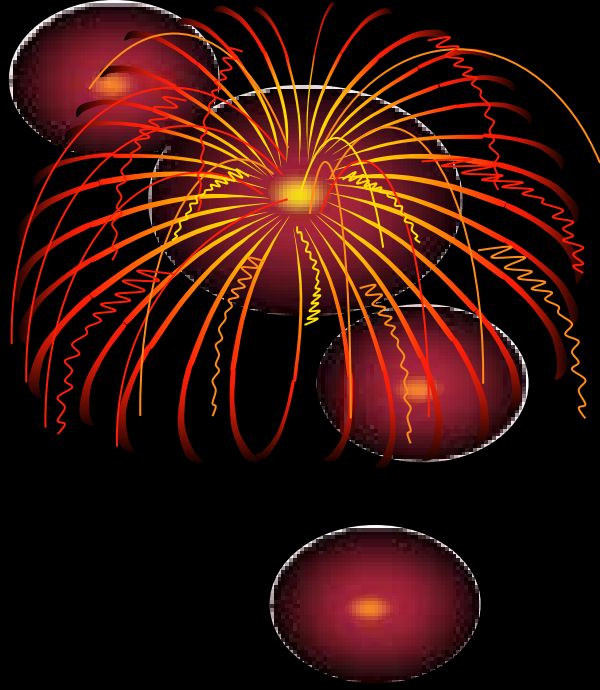
Behcet's disease

(Clinical manifestations)

- Articular
- CNS
- Gastro-intestinal
- Vascular
- Cardiopulmonary
- Renal
- Epididymitis
- Others

By: Dr Maryam Sahebari

SCENARIO



HSP

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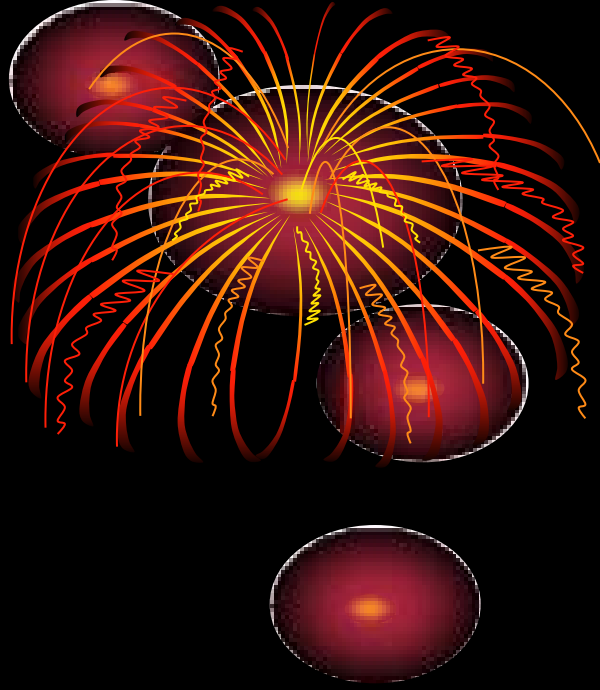

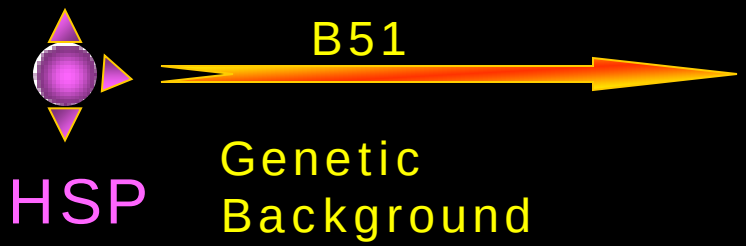

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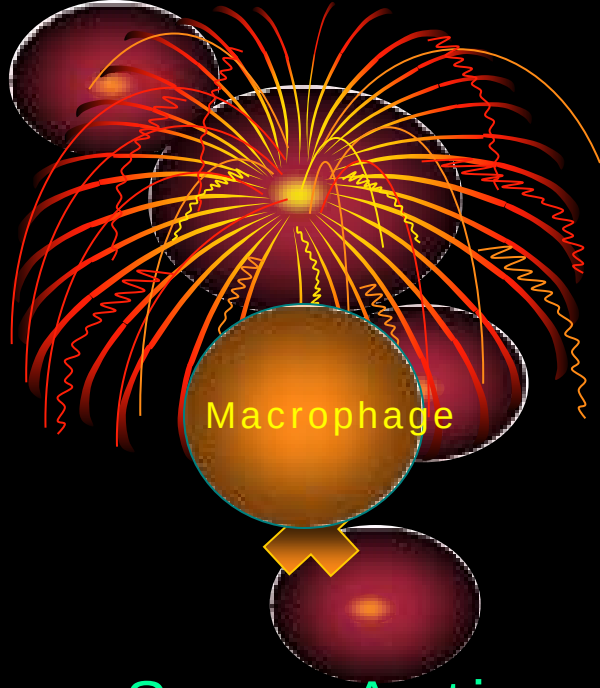
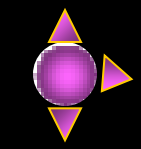


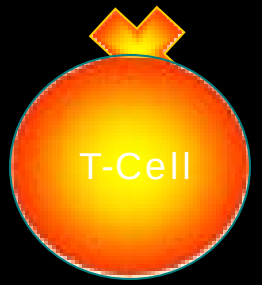


B51

Genetic Background

Super Antiger

HSP



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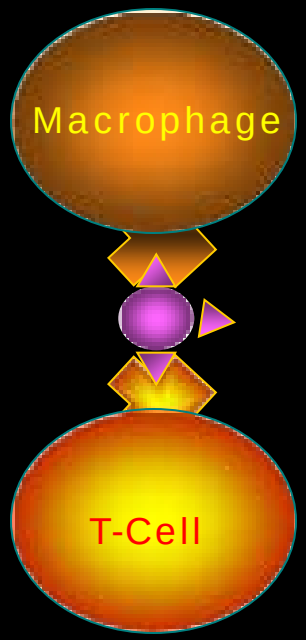

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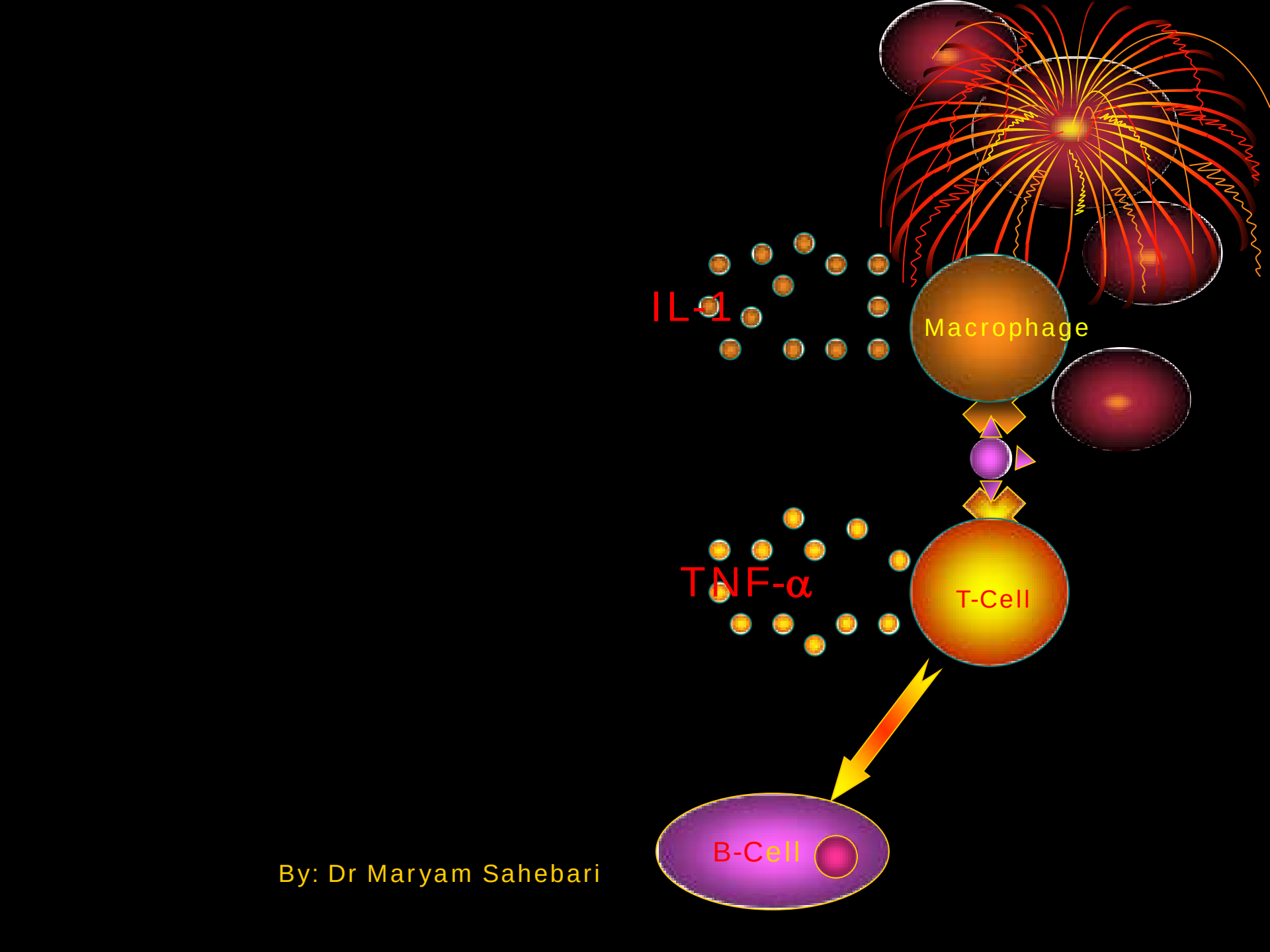

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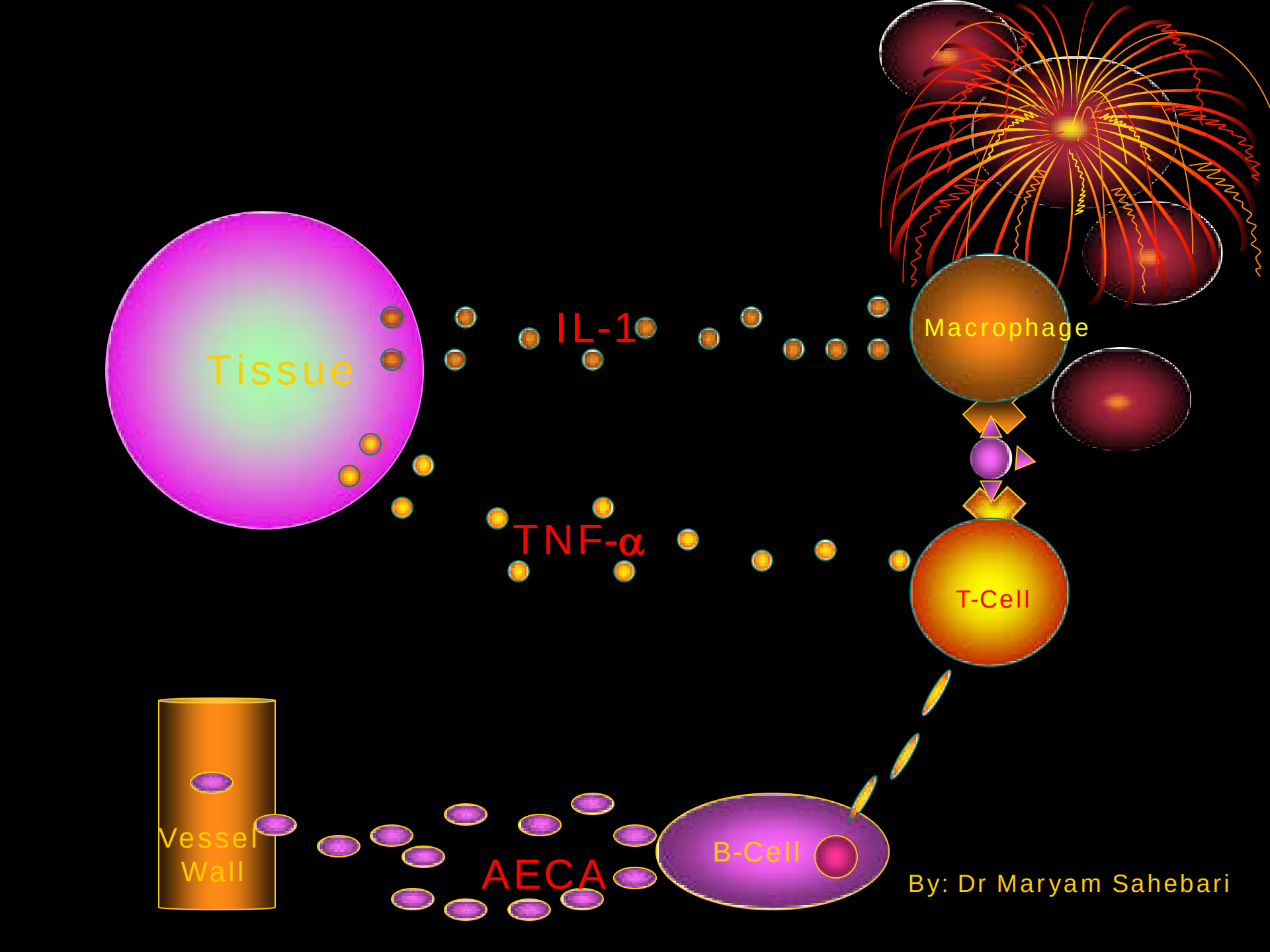
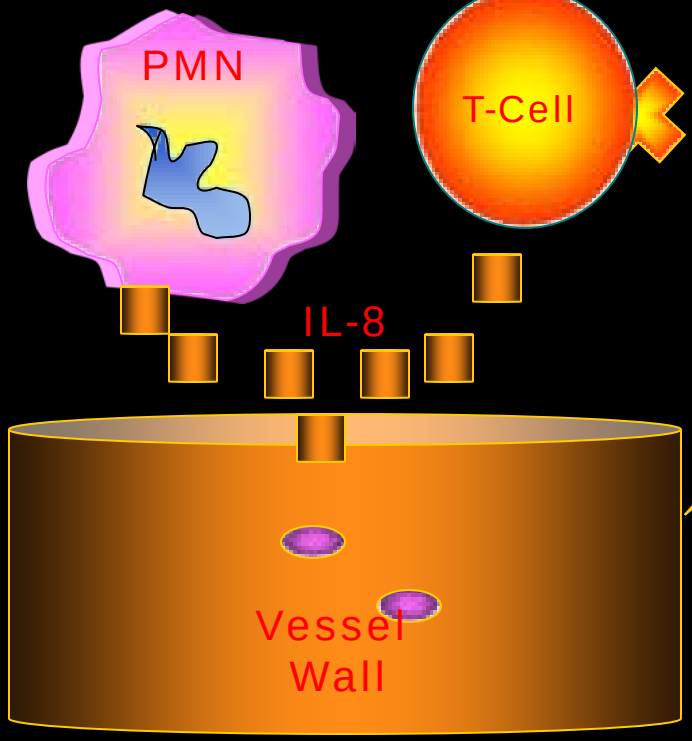

Tissue
IL-1
Macrophage
TNF-α
T-Cell
Vessel Wall
AECA
B-Cell
By: Dr Maryam Sahebari

THROMBOSIS



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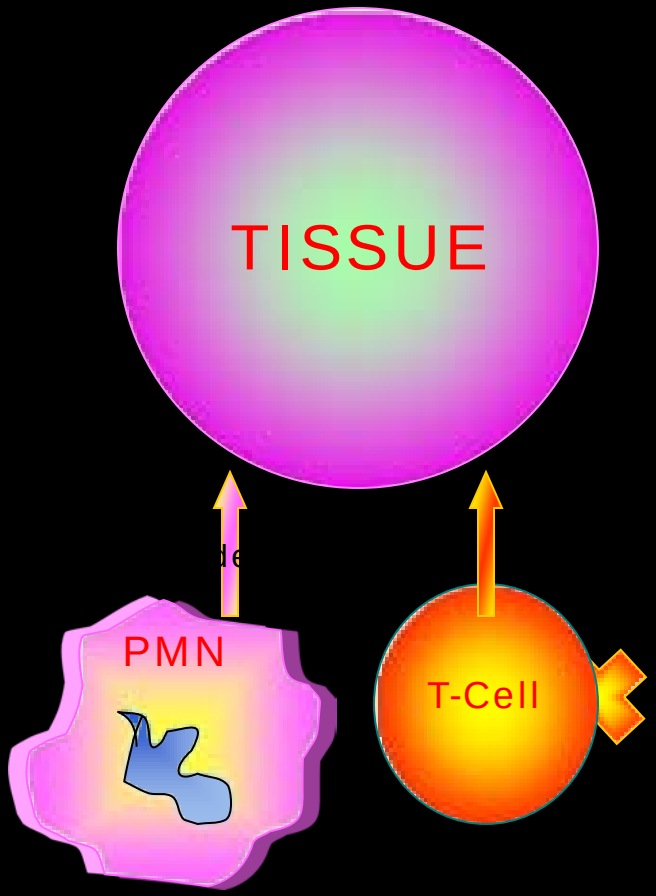

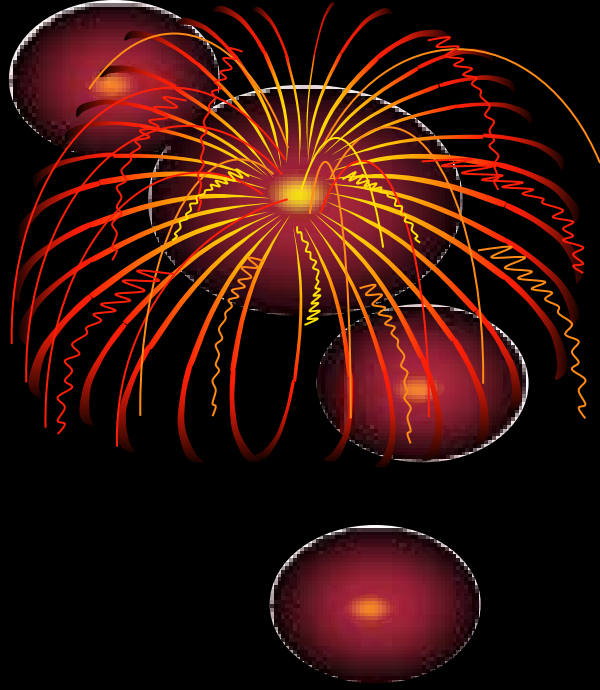

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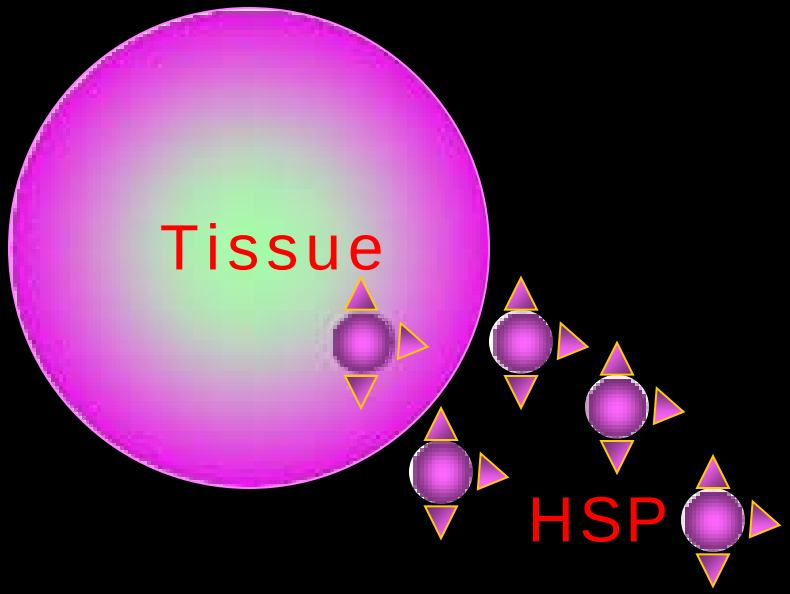

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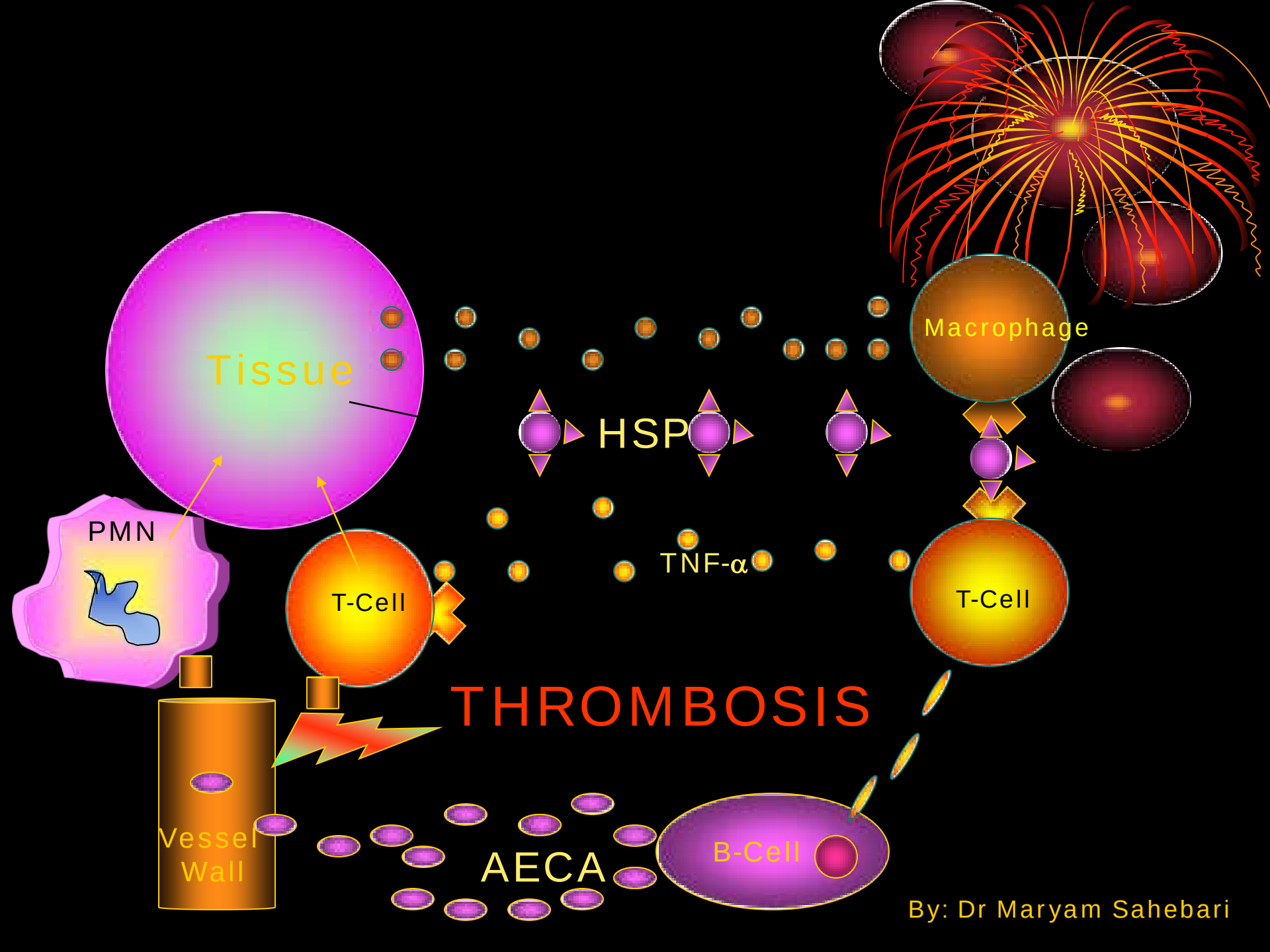
Tissue
Macrophage
HSP
PMN
TNF-α
T-Cell
T-Cell
THROMBOSIS
Vessel Wall
AECA
B-Cell
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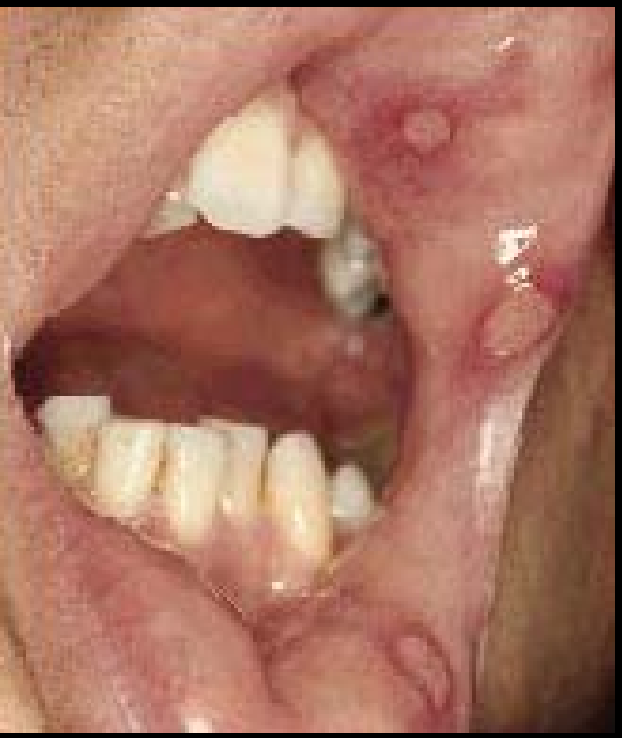
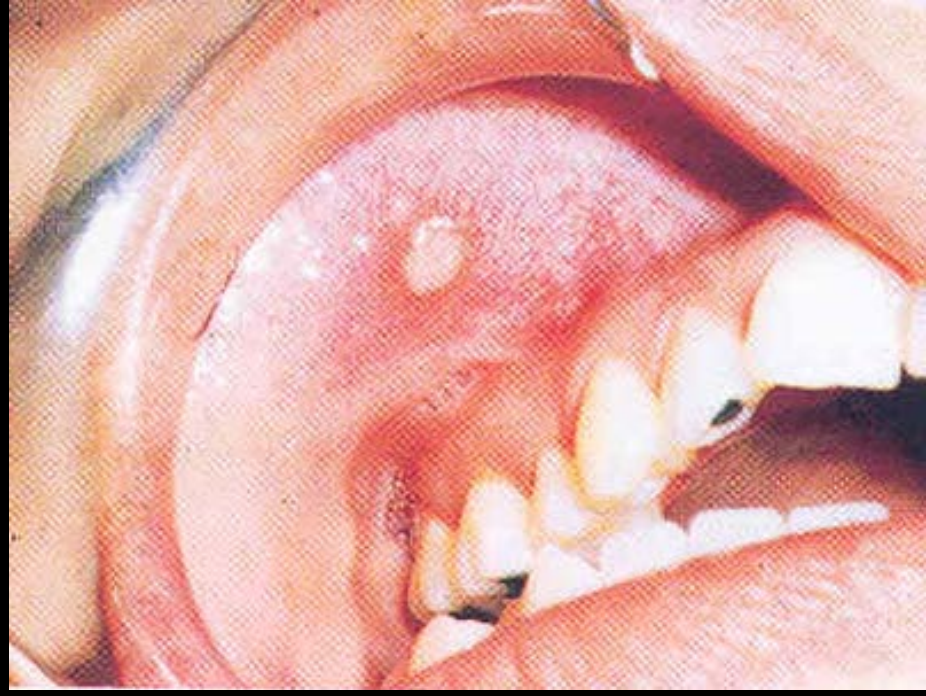
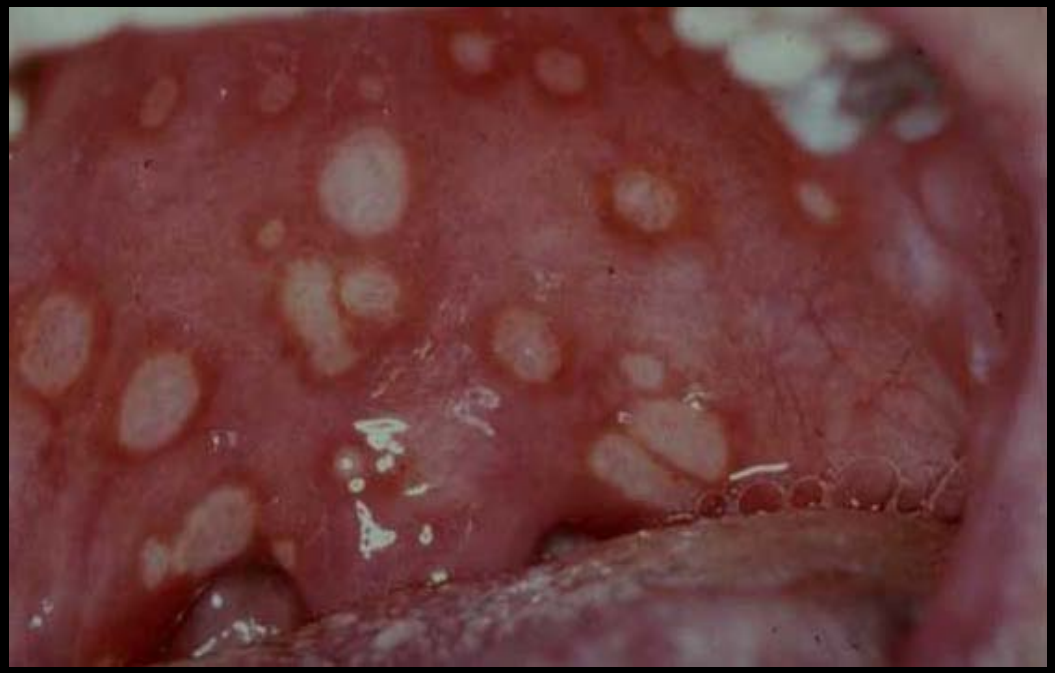
Oral ulcers







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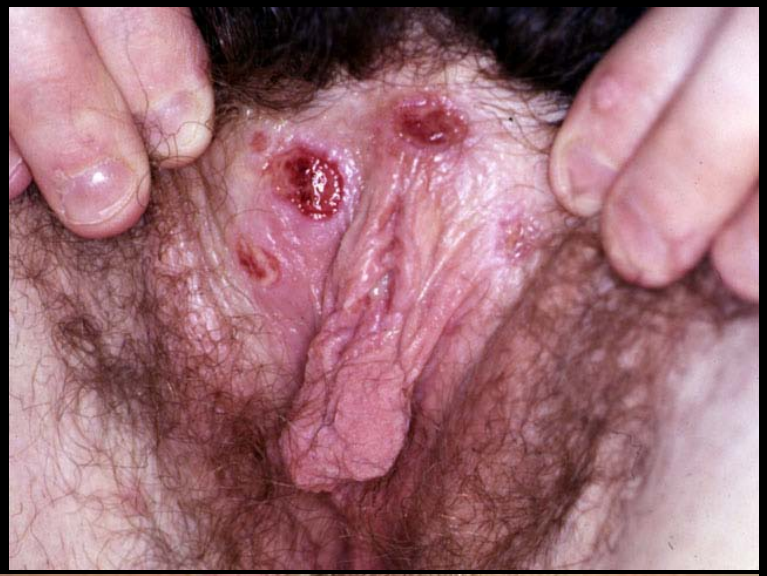
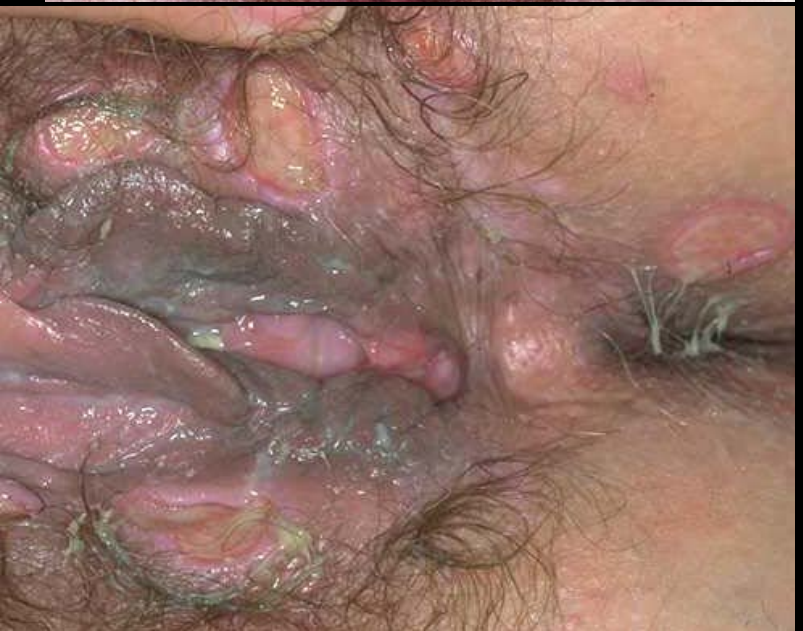
Genital ulcers





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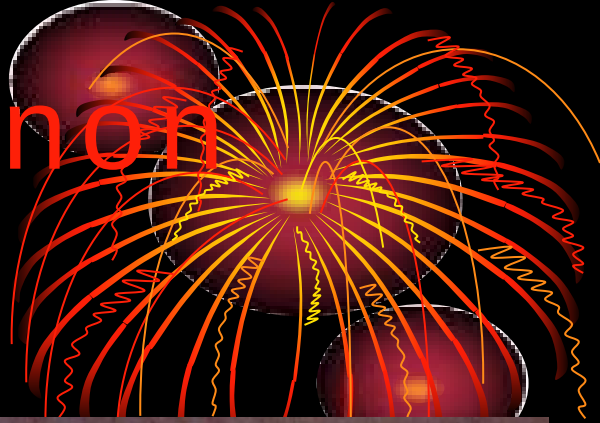
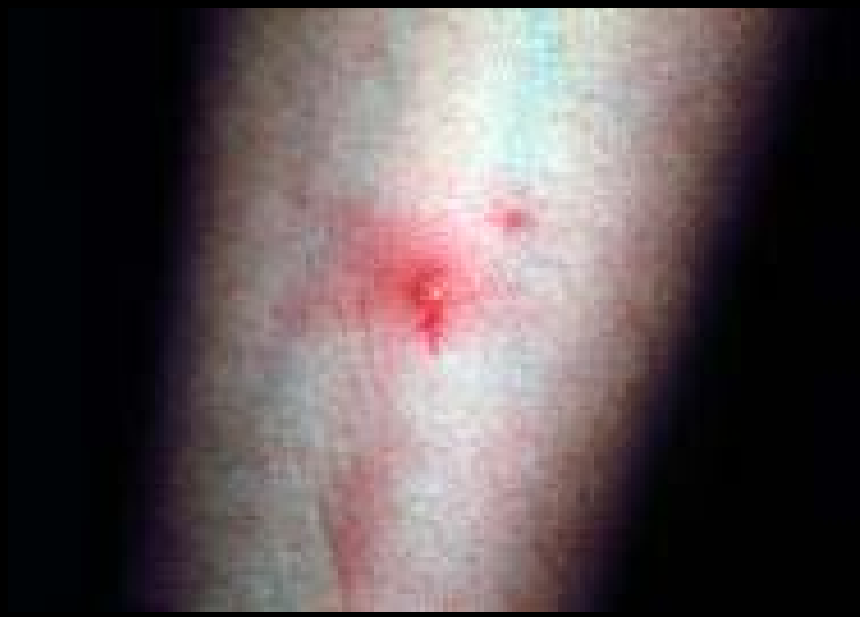
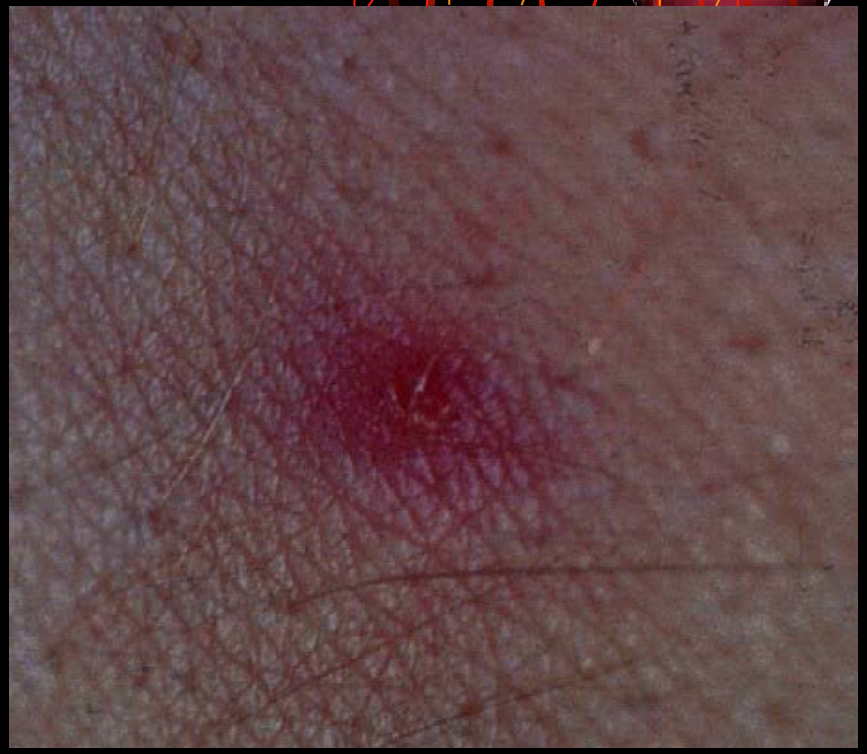
Pathergy phenomenon







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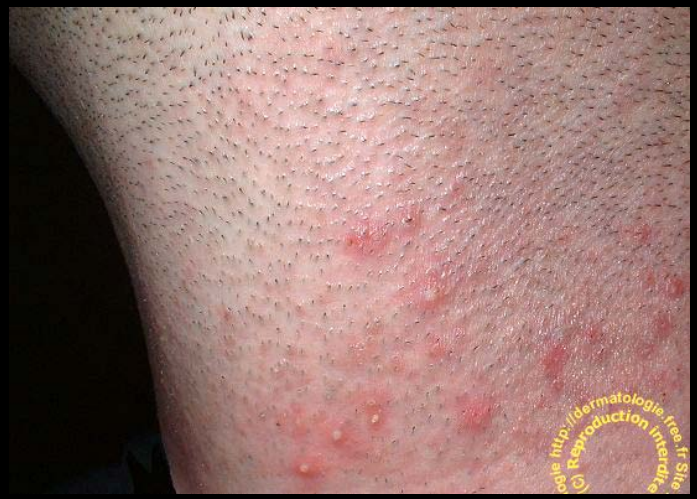
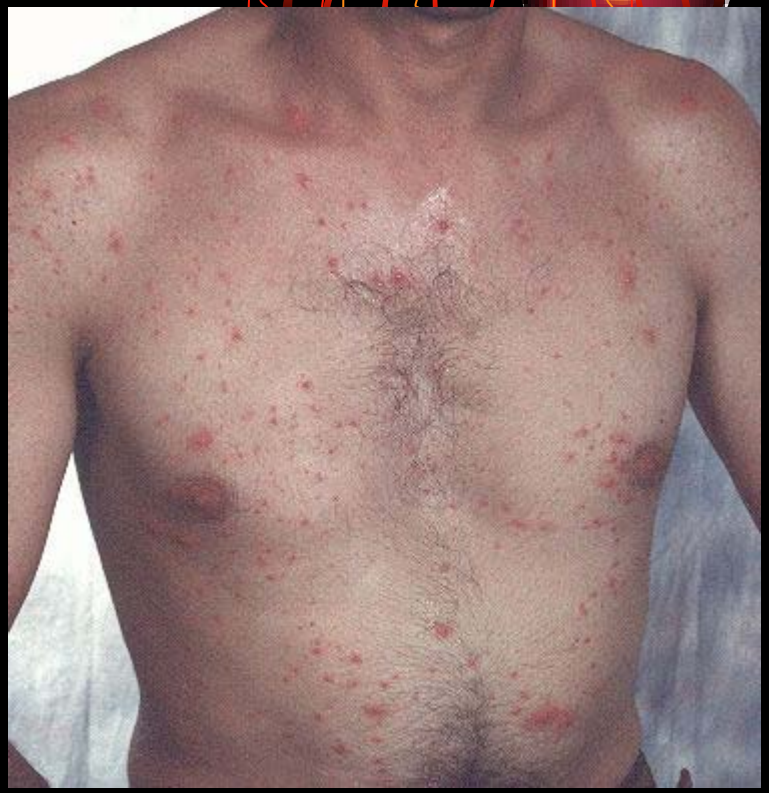
Skin lesions





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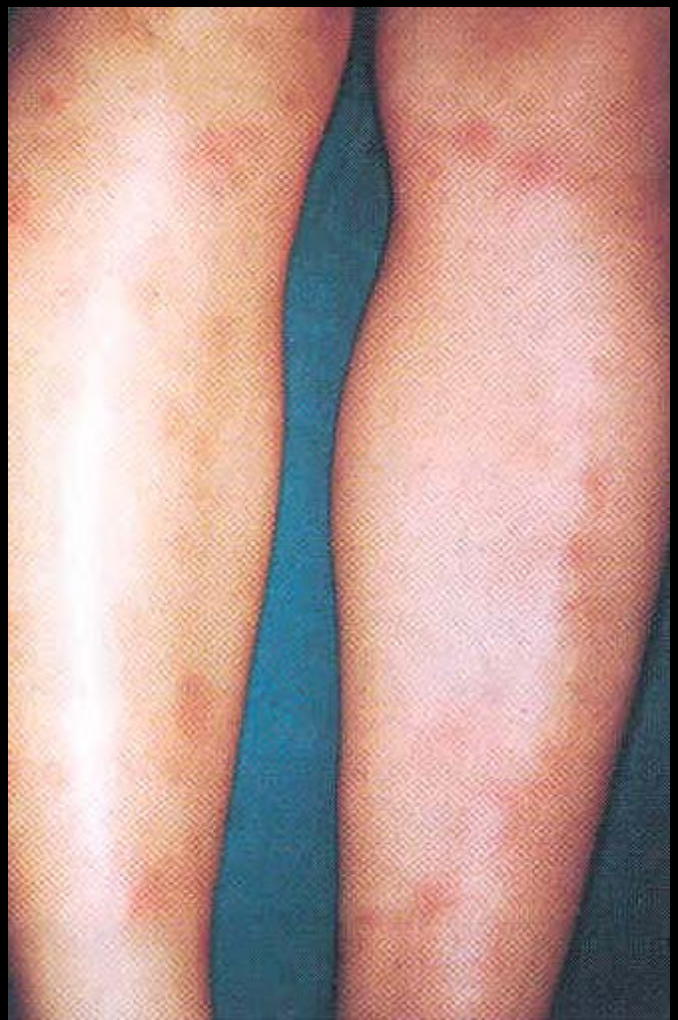
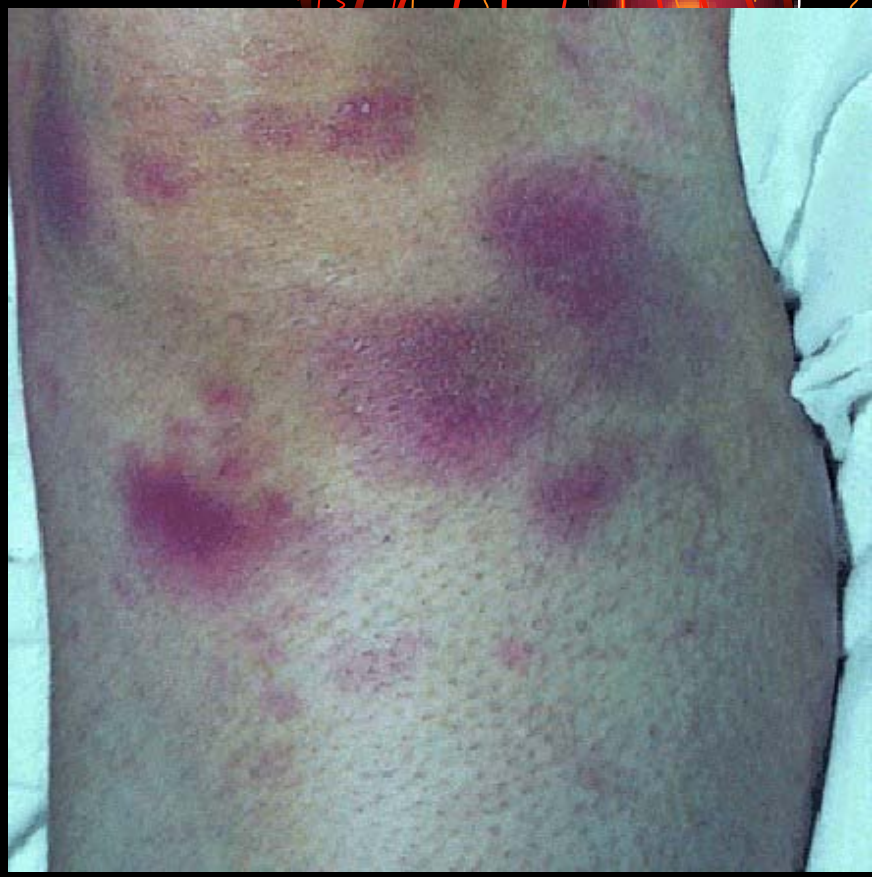
Skin lesions





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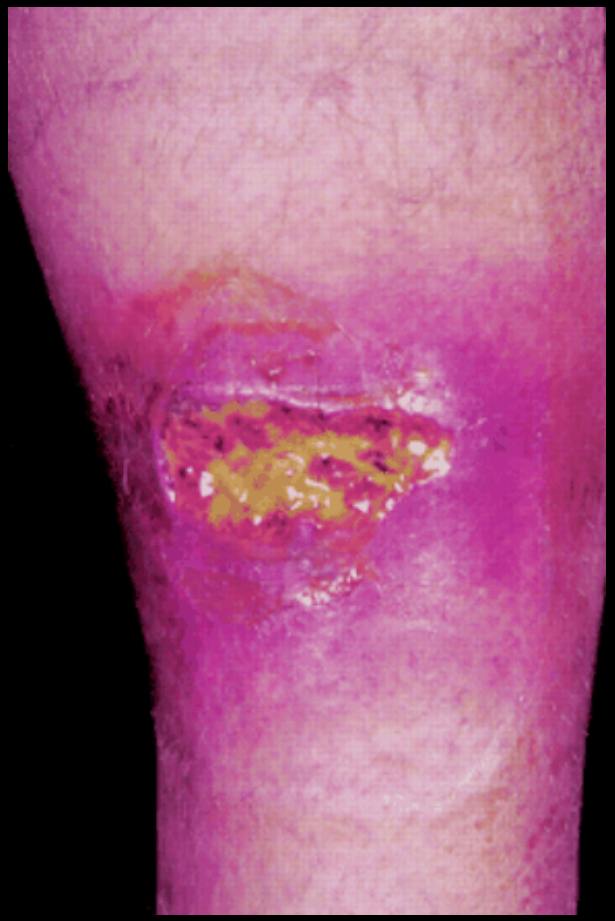
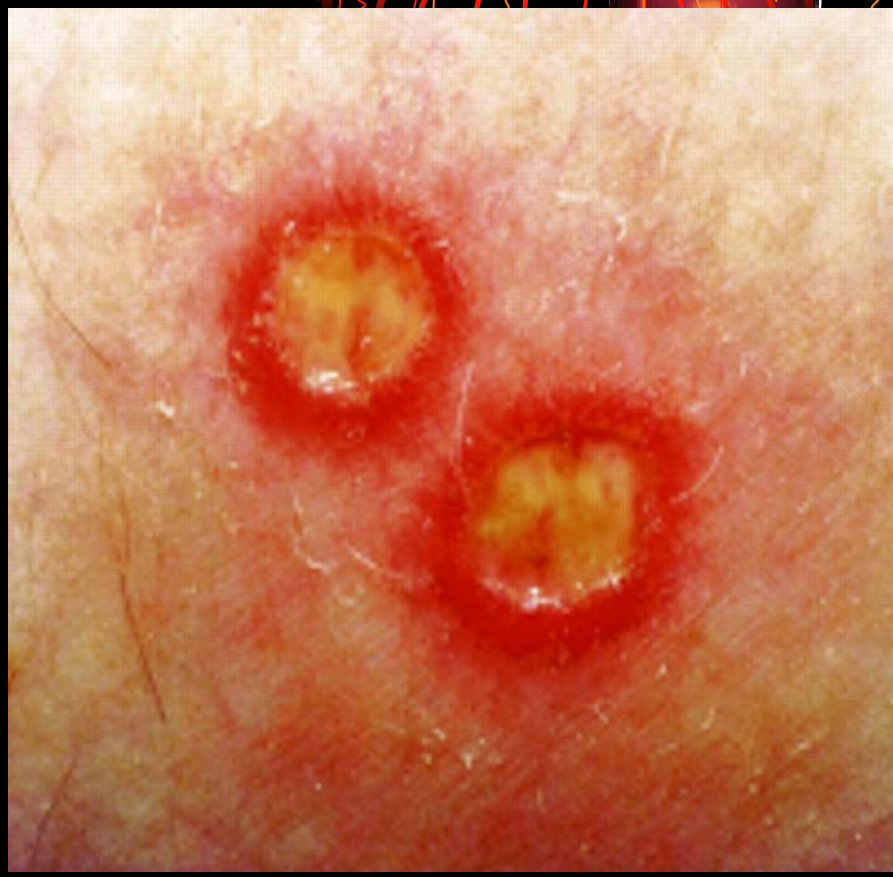
Skin lesions





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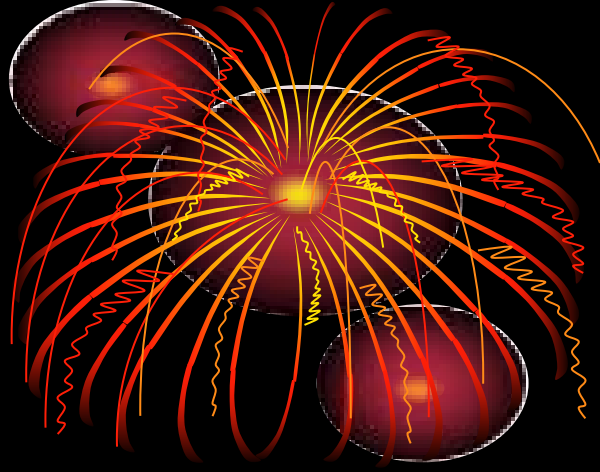
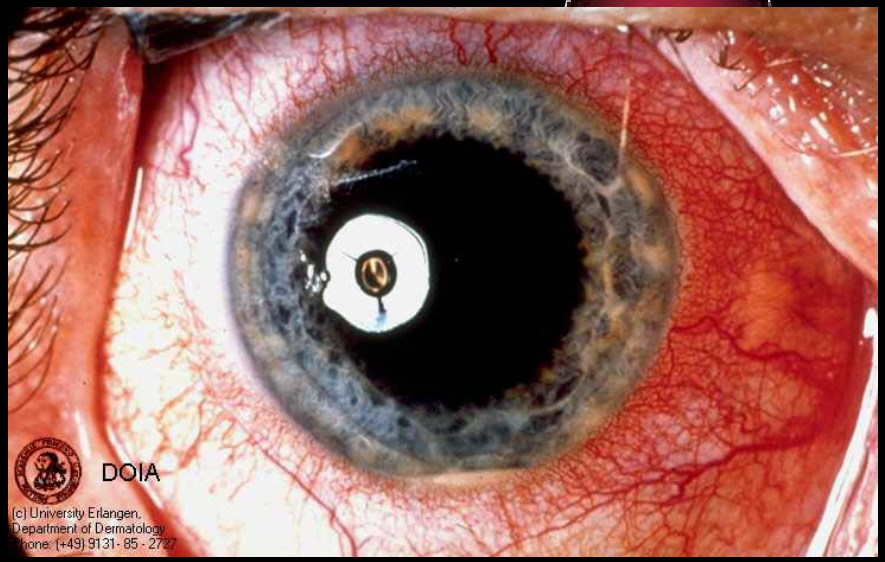
Eye lesions



- Anterior uveitis
  - Decrease in visual acuity
  - Red eye
  - Periorbital pain
  - Photophobia
  - Discoloration of iris



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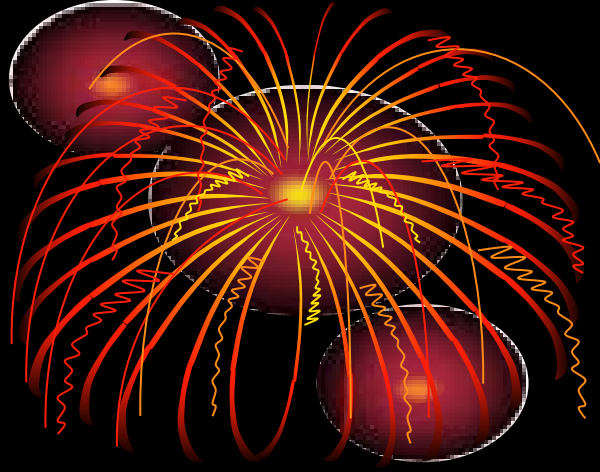
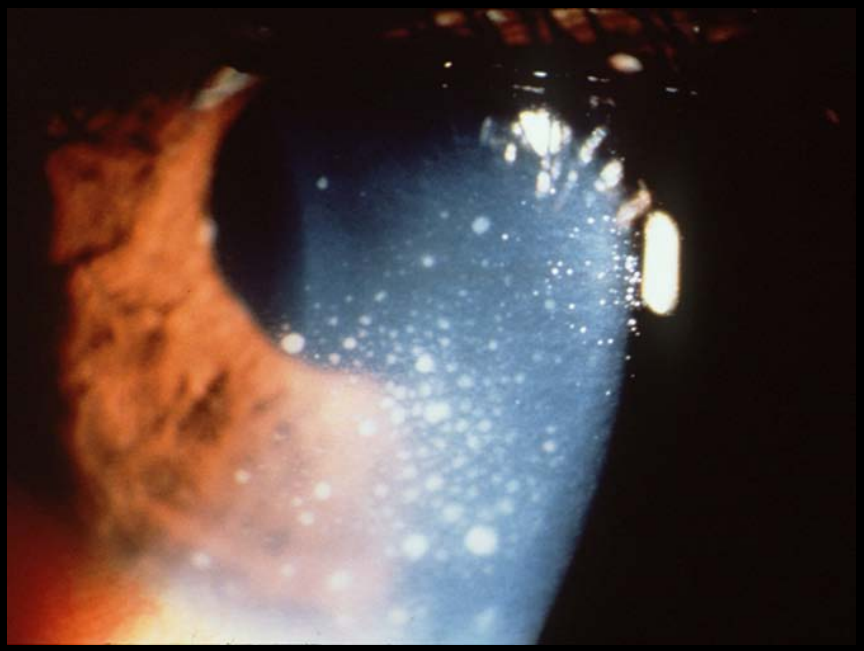
Eye lesions



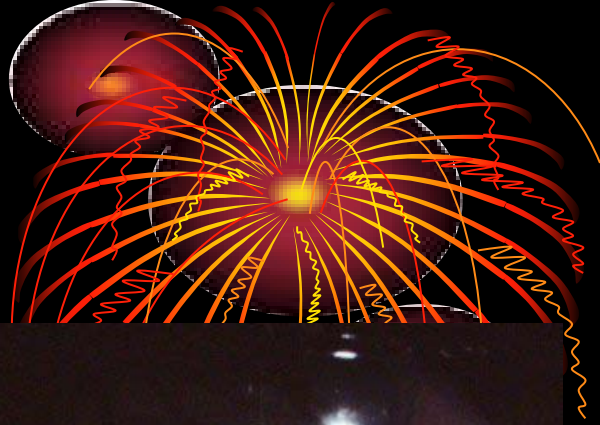
- Anterior uveitis
  - Decrease in visual acuity
  - Red eye
  - Periorbital pain
  - Photophobia
  - Discoloration of iris
  - Flare and KP in anterior chamber

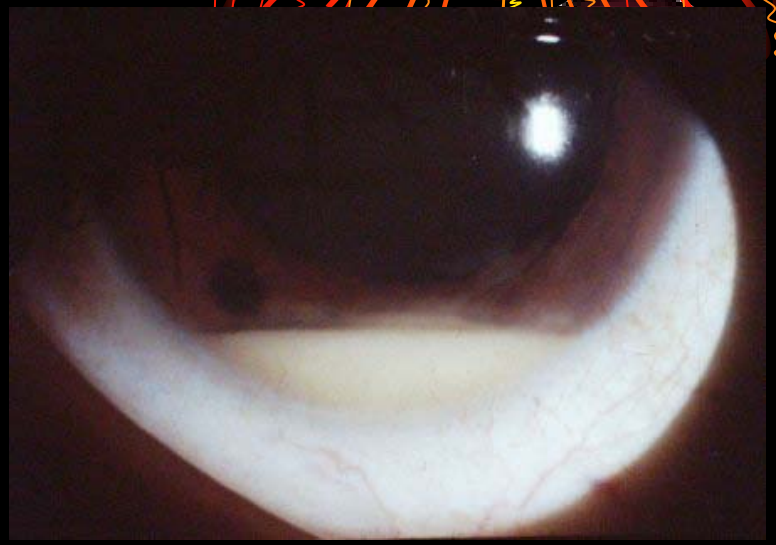


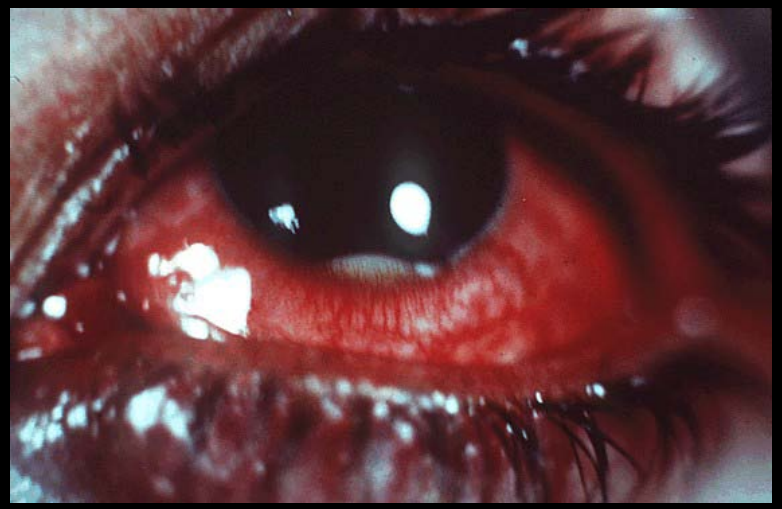
By: Dr Maryam Sahebari

Eye lesions

- Anterior uveitis
  - Decrease in visual acuity
  - Red eye
  - Periorbital pain
  - Photophobia
  - Discoloration of iris
  - Flare and KP in anterior chamber
  - Hypopion (%8.7)







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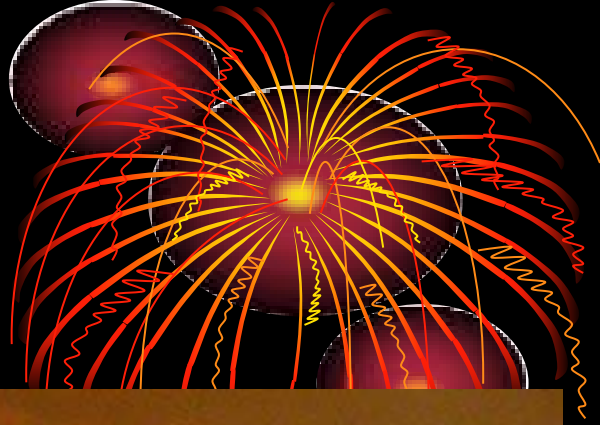
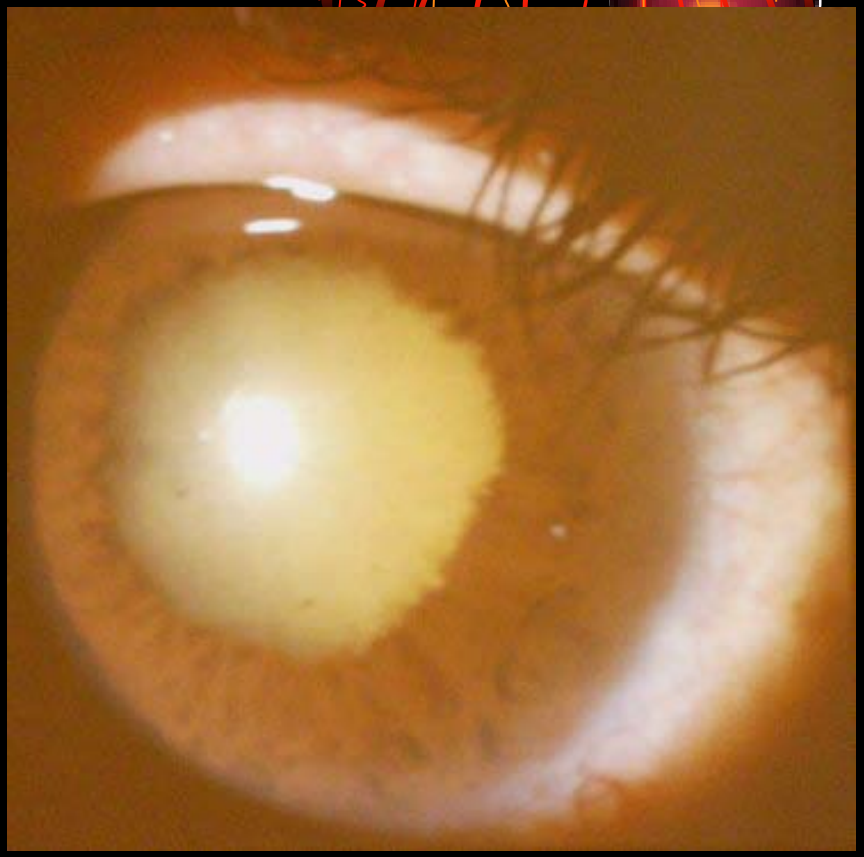
Eye lesions



- Posterior uveitis
  - Vitreitis
  - Macular edema
  - Papillaitis
  - Optic atrophy
  - Retinal detachment



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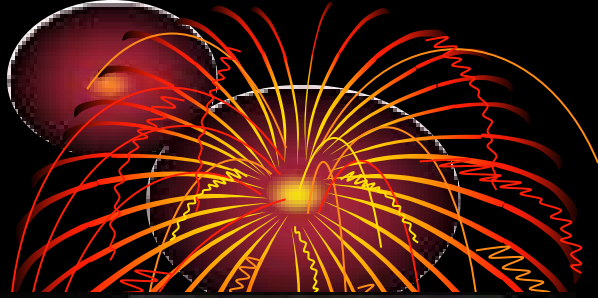
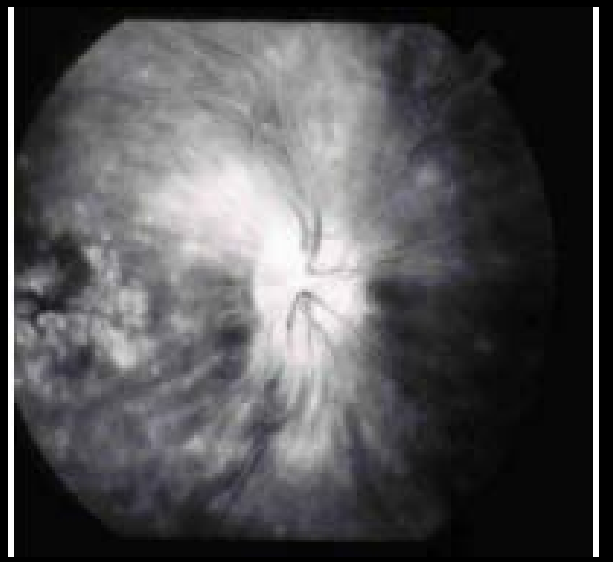
Eye lesions

- Anterior uveitis
- Posterior uveitis
- Retinal vasculitis
  - Perivascular sheeting
  - Retinal hemorrhage
  - Retinal infarction





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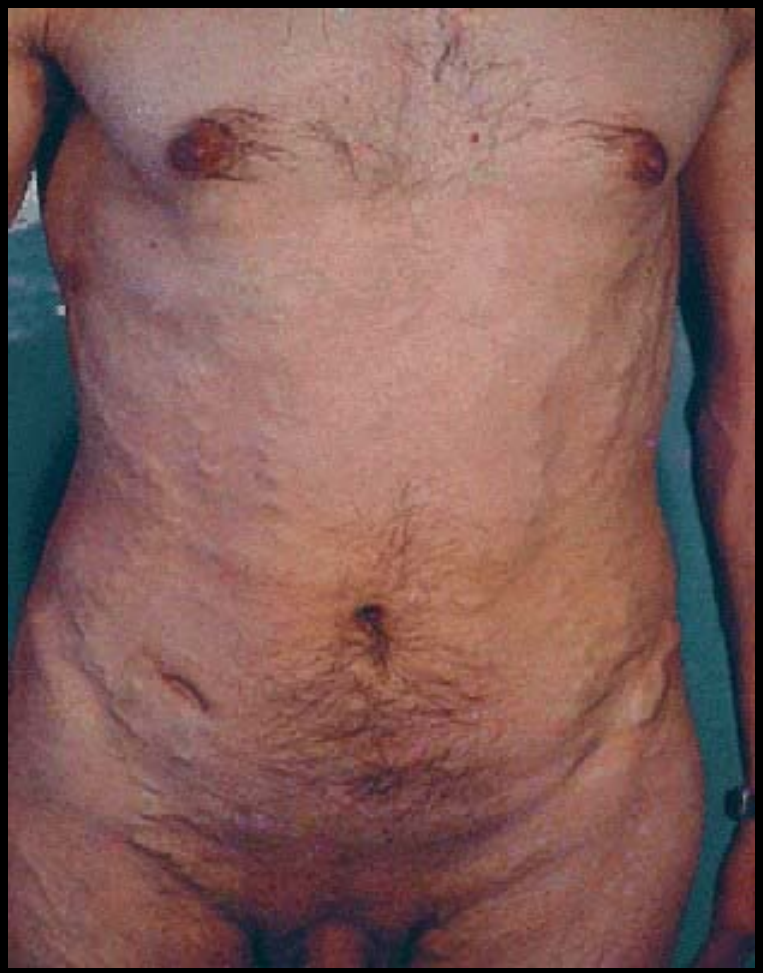
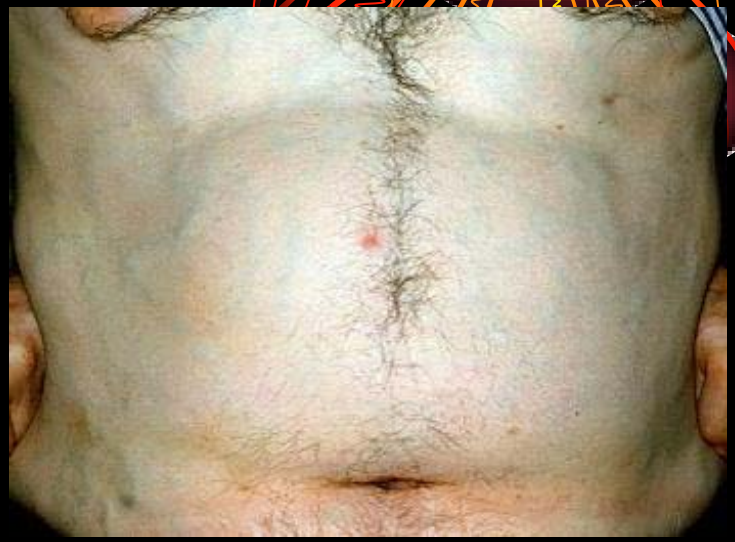
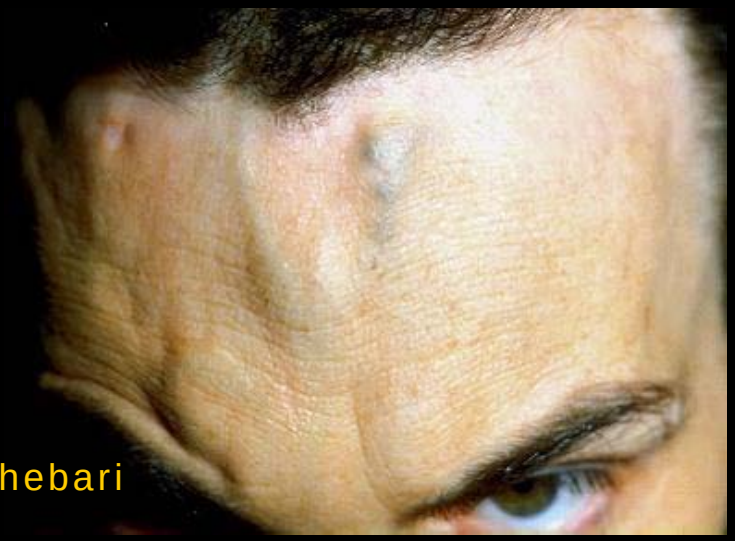
Vascular lesions







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Vascular lesions

- Venous thrombosis
  - Deep vein thrombosis in lower limb (%6)
  - Superficial phlebitis (%2.3)
  - Large vein thrombosis (%0.9)
- Vasculitis
  - Aneurysm (%0.4)
  - Arterial thrombosis (%0.1)

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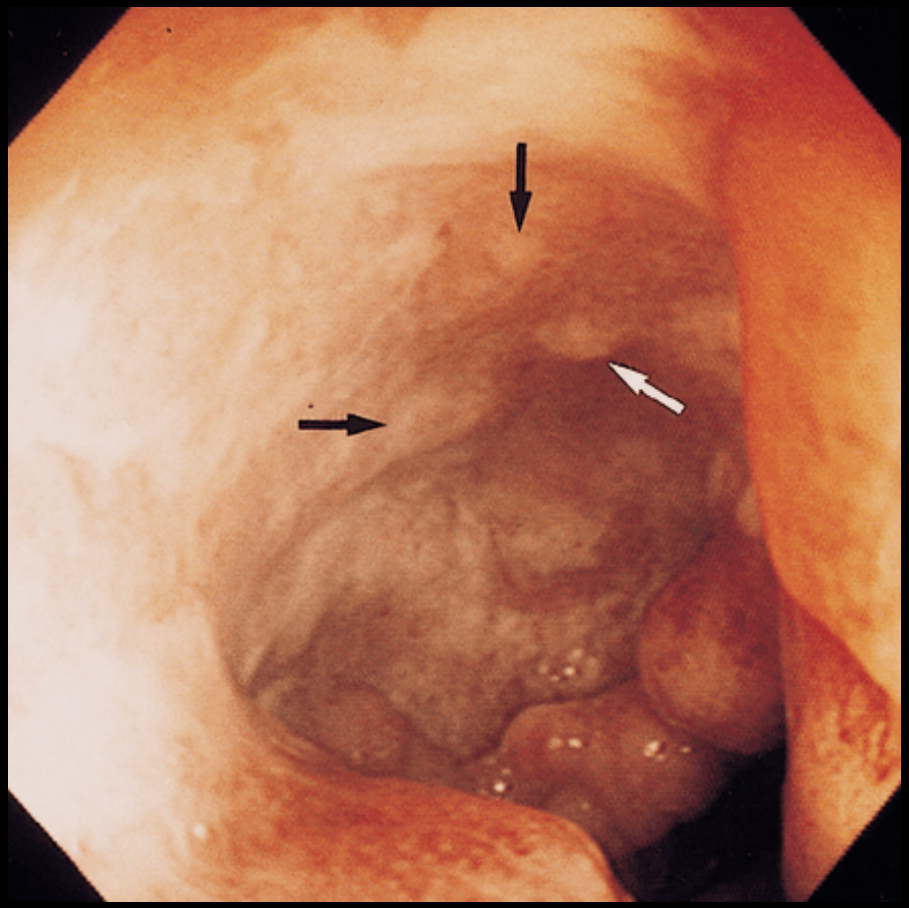
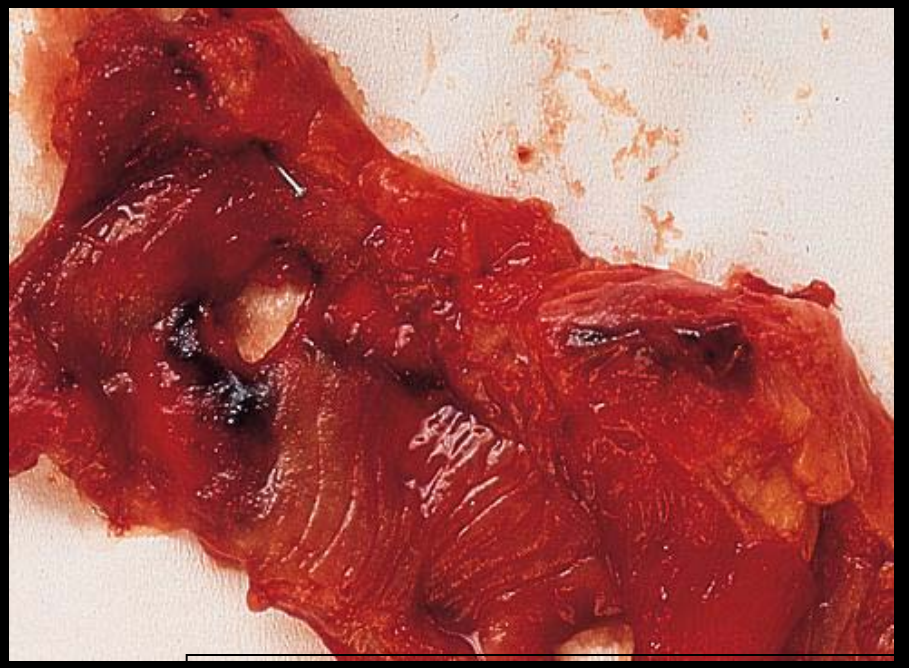
Gastrointestinal lesions

Ulcer



Diffusely scattered punched-out ulcers in the ascending colon



Bowel perforation due to intestinal ulceration

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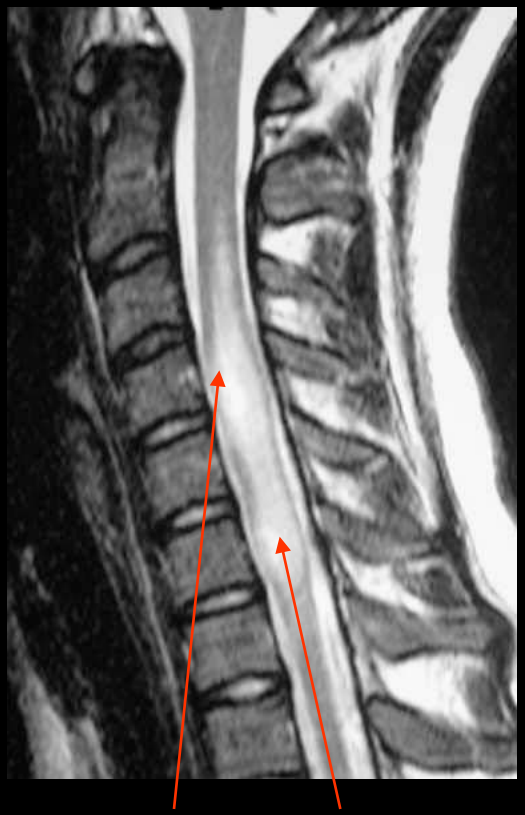
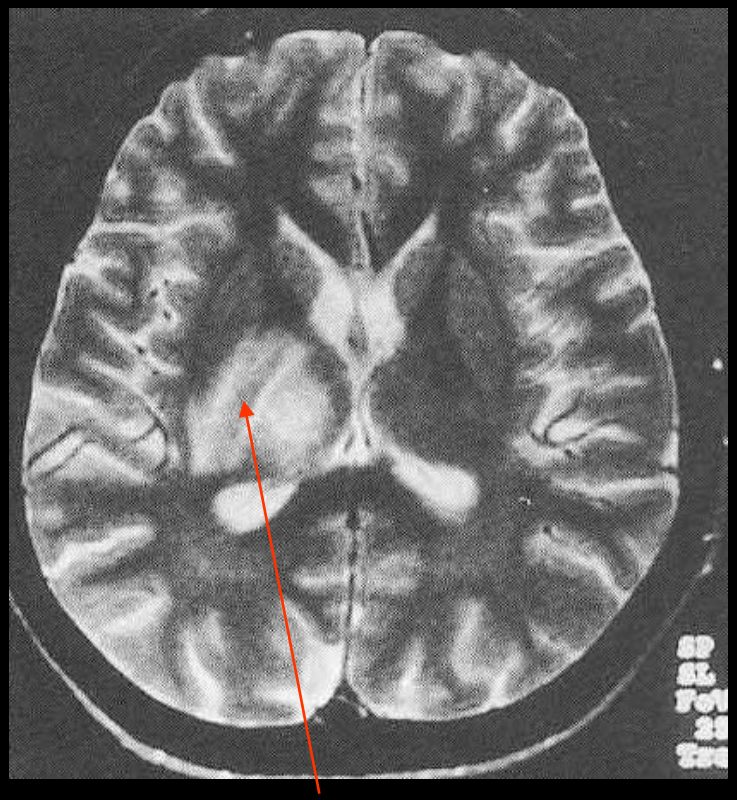
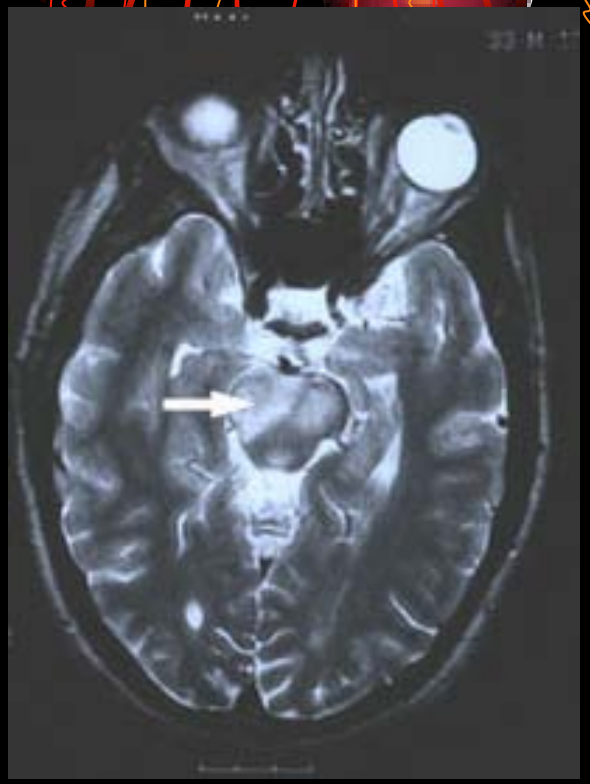
Nervous system involvement

Parenchymal lesions







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