Figurate Erythemas and Purpuras

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Disclosures

- None

Figurate Erythemas

Objectives

- Discuss the following figurate erythemas and treatments
  - Erythema Annulare Centrifugum
  - Erythema Marginatum
  - Erythema Migrans
  - Erythema Gyratum Repens
- Discuss the different types of purpuras and their etiologies
- Review basic methods of coagulation
- Review specific purpuric syndromes
- Discuss treatment modalities

Erythema Annulare Centrifugum

- Introduction
  - Superficial and deep forms.
  - More common in adults.
  - Peak incidence in 5th decade of life.
  - Duration: days to months, often self-limiting
  - Most commonly idiopathic, but can be related to infection or other exposures.
  - Reaction pattern or “hypersensitivity” reaction to one of many antigens

Pathogenesis

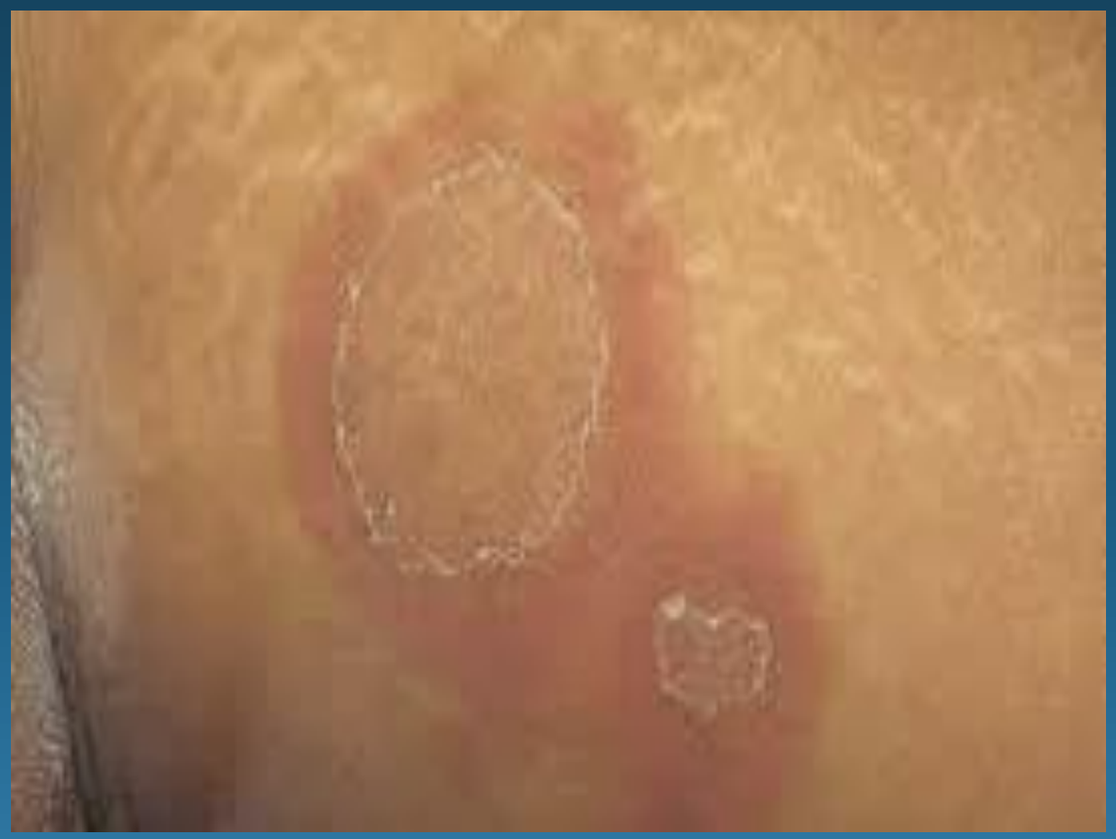
- Infectious causes:
  - Dermatophytes (Tinea Pedis)
  - Fungal: Candida, Penicillium in blue cheese.
  - Viruses (e.g. poxvirus, EBV, varicella-zoster virus, HIV)
  - Parasites and Ectoparasites (e.g. *Phthirus pubis).*

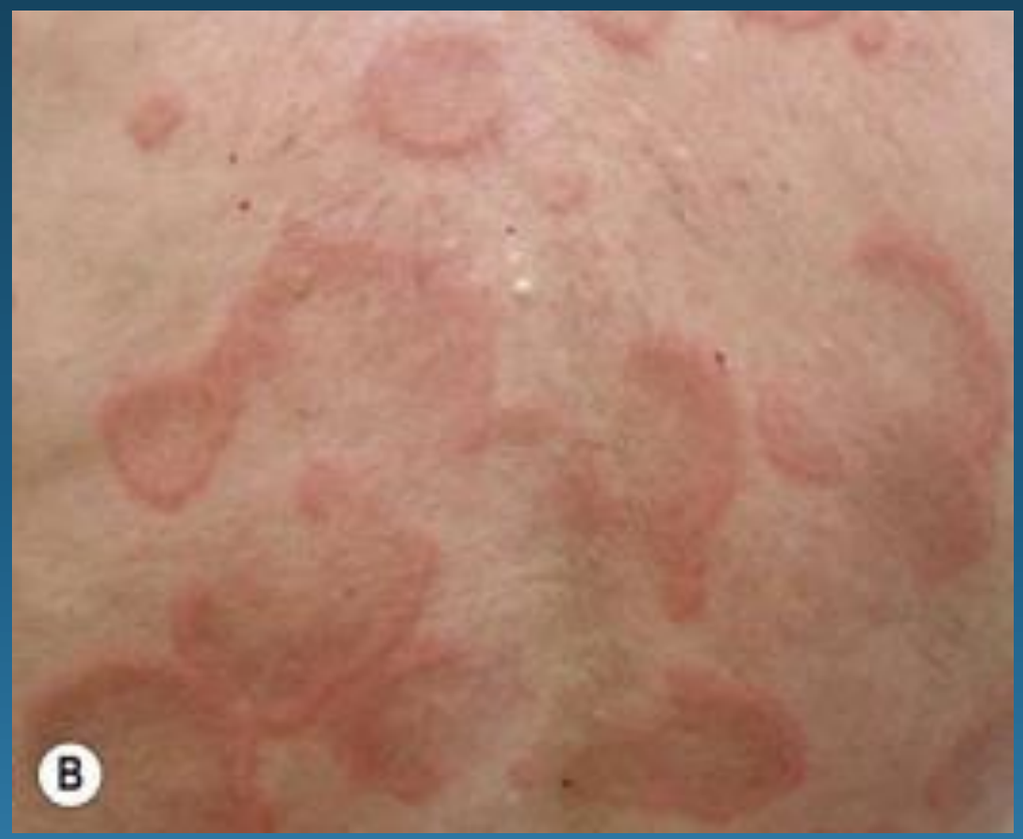
- Drug induced: diuretics, NSAIDs, antimalarials, gold, finasteride, amitriptyline, etizolam

- Other: Pregnancy, certain foods, autoimmune endocrinopathies, hyper-eosinophilic syndrome and occasionally, lymphomas and leukemia.

Clinical Features

- Initial lesions begin as firm pink papules that expand centrifugally and then develop central clearing.
- Can enlarge to greater than 6 cm.
- Favors upper legs, hips and trunk.
- In the superficial form, lesions are minimally elevated, and there is desquamation at the inner margin, i.e. **“trailing scale.”** +/- pruritus.
- In deep gyrate erythema, the advancing edges are indurated and raised, and there is usually no scale. Non-pruritic.
- As lesions resolve, PIH is common.



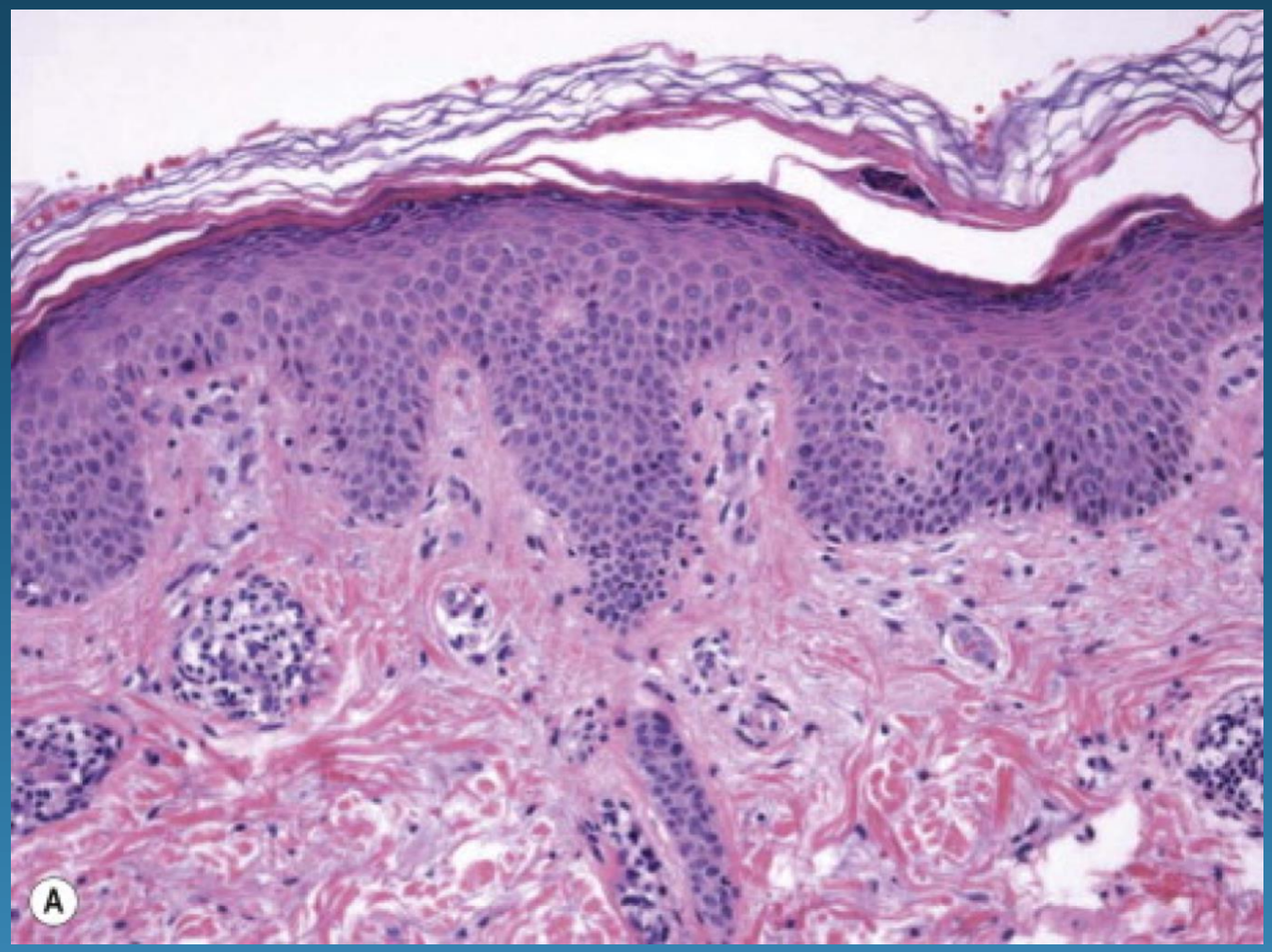


A) Superficial EAC
B) Deep Gyrate Erythema

Pathology

- Superficial lesions: mild spongiosis, focal parakeratosis, superficial perivascular lymphohistiocytic infiltrate
- Fairly tight aggregates around vessels, the so-called **“coat sleeve”** anomaly.
- Rarely eosinophils. Edema in the papillary dermis.

- Deep lesions: lymphoctic infiltrate with a sharply demarcated perivascular arrangement is present primarily within the mid and lower dermis.



Differential Diagnosis

- Tinea Corporis
- Annular Psoriasis
- Annular Urticaria
- Erythema Marginatum
- Allergic Urticarial Eruption
- Autoimmune disorders, including linear IgA bullous dermatosis, Sjögren’s syndrome and lupus erythematosus, can also have erythematous annular, arciform and polycyclic lesions.

Treatment

- If EAC is due to an underlying disorder, the skin lesions will usually resolve once the disease has been successfully treated
- Usually self-limited.
- Topical corticosteroids.
- Topical anti-pruritics and sedating antihistamines for pruritus.
- Systemic corticosteroids, however recurrence is common after discontinuation.
- Case Reports: Empiric use of antibiotics, anti-fungal agents, topical tacrolimus, topical calcipotriene, oral metronidazole, subcutaneous etanercept and subcutaneous interferon-alpha

Erythema Marginatum

- Cutaneous manifestation of Rheumatic Fever
- ~ 3% of patients with untreated group A β-hemolytic Streptococcal infections can develop acute rheumatic fever
- Latency period of 2-5 weeks before development of rheumatic fever
- Rash occurs in less than 10% of patients with acute rheumatic fever.
- Higher incidence in children, peak age 5-15 years.
- Associated findings: Jones Criteria: Carditis, Migratory Polyarthritis, Sydenham's chorea, fever and subcutaneous nodules.

Clinical Features

- Lesions begin as erythematous macules that spread peripherally and become patches or plaques, can be polycyclic, with NO scale.

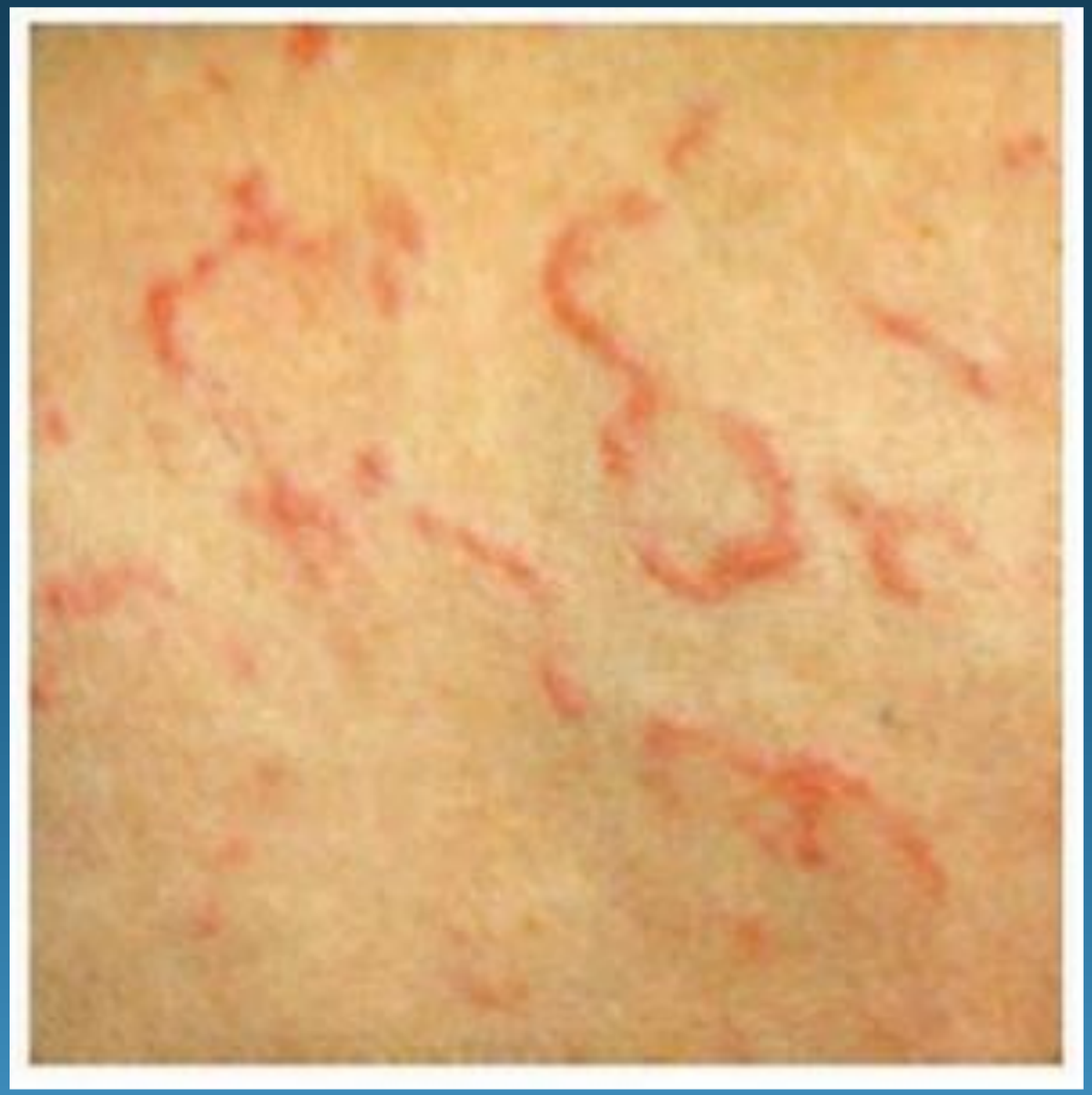
- Usually asymptomatic.

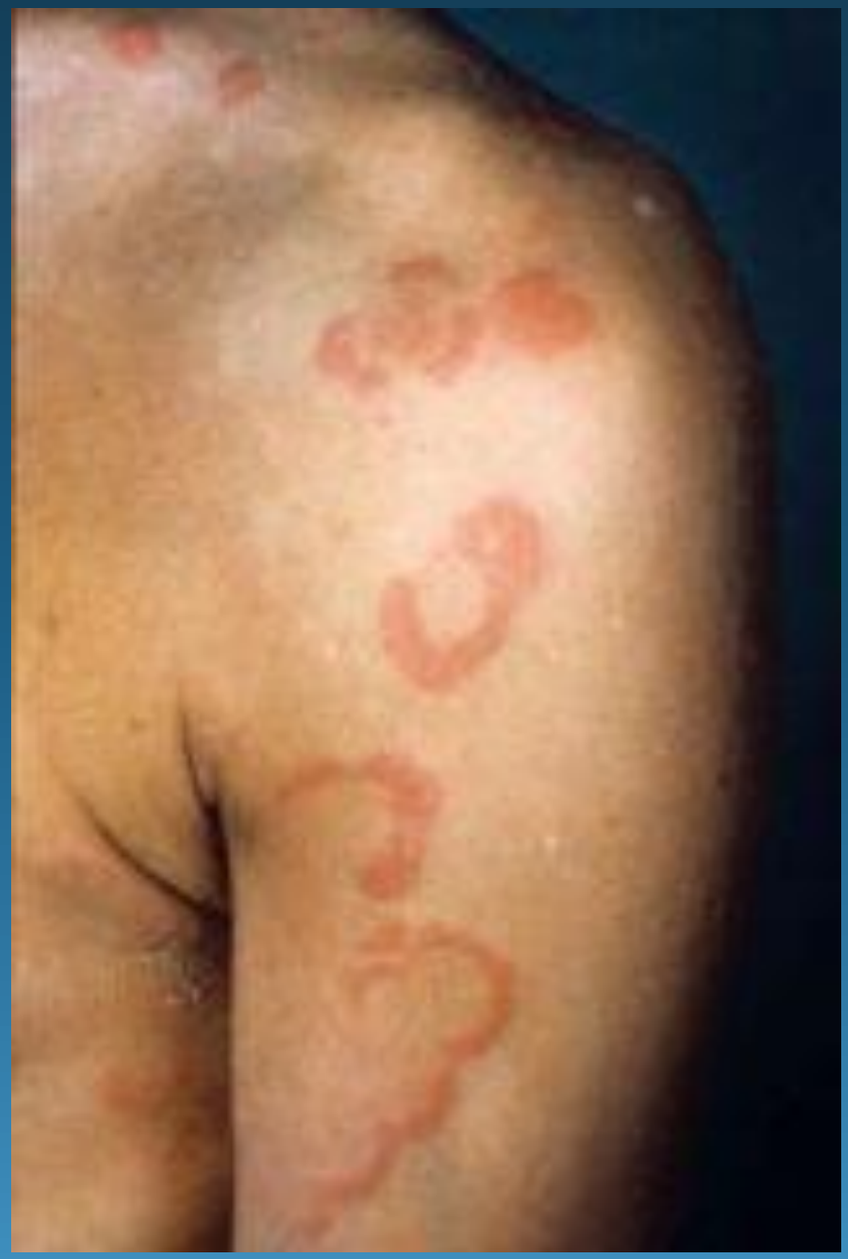
- Migrates over a period of 12 hours (by 2–12 mm).

- Lasts from a few hours to a few days – usually transient. Can recur over a few weeks.

- Most commonly on the trunk, axillae and proximal extremities, spares face.

Erythema Marginatum





Differential Diagnosis

- Annular urticaria
- Annular erythema of infancy
- Neutrophilic figurate erythema of infancy
- EAC
- Erythema Gyratum Repens
- Hereditary periodic fever syndromes (particularly *TNF receptor-associated periodic syndrome* [TRAPS])
- Kawasaki disease

Treatment

- Treat underlying rheumatic fever disease.
- No specific treatment for the rash.
- Lesions usually resolve spontaneously.
- Treatment of rheumatic fever does not usually affect the rash.

Erythema Migrans

- Initial cutaneous presentation of Lyme disease in 60-90% of cases

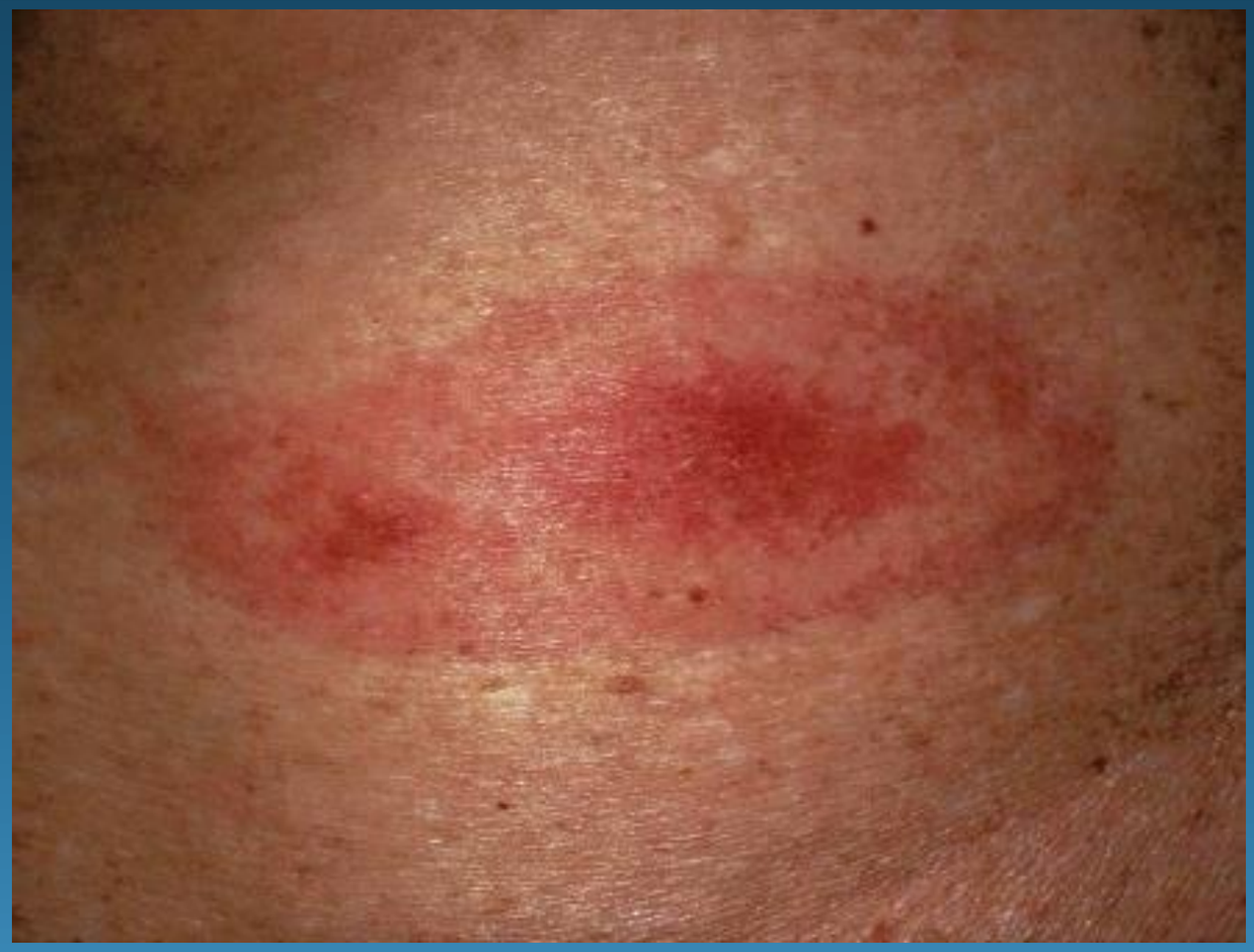
- Lyme disease infection is caused by the spirochete *Borrelia burgdorferi* and transmitted by species of the *Ixodes* tick

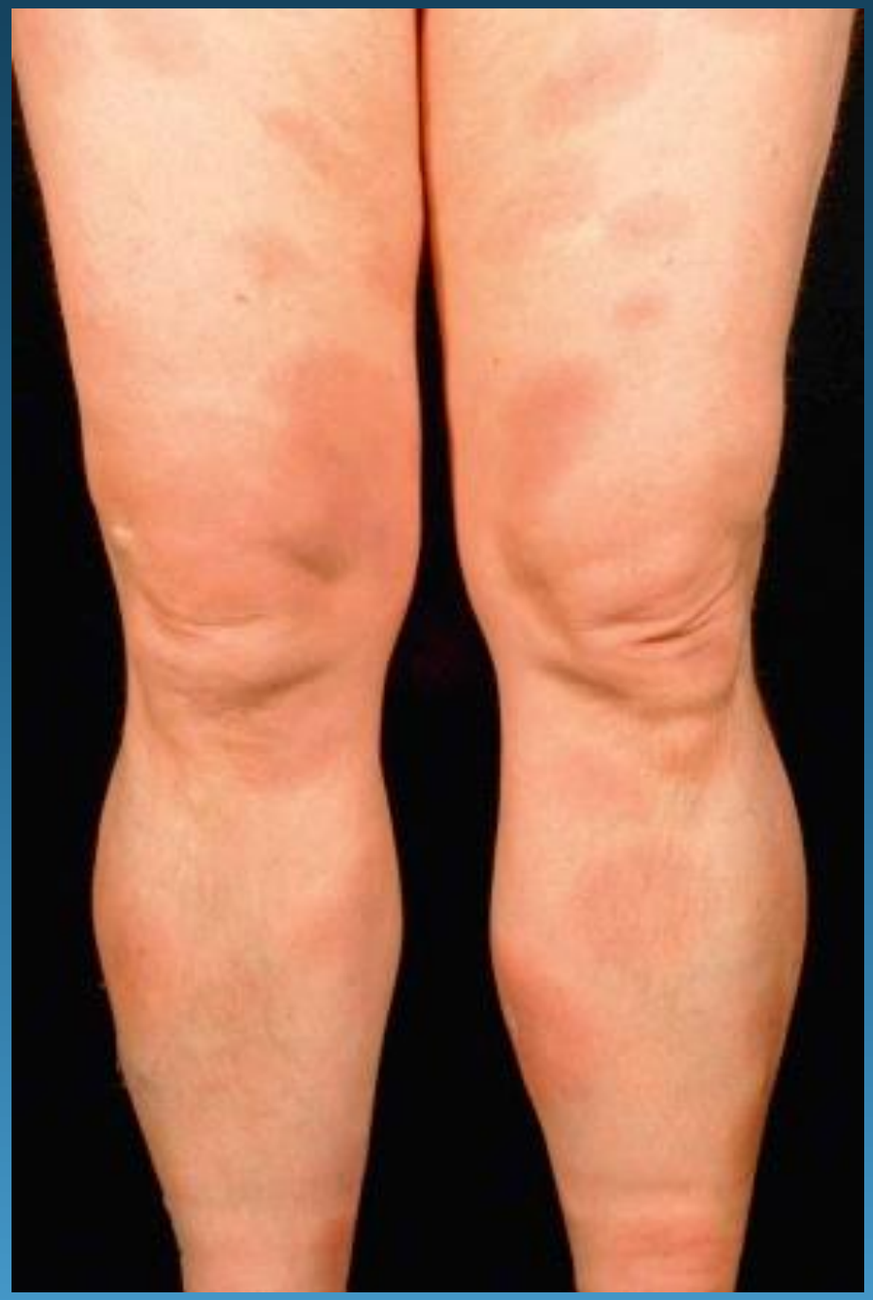
- Lyme disease is most prevalent in US and in Europe (Scandinavia and central Europe)

Clinical Features

- Typically 1-2 weeks after tick detachment
- Erythematous annular plaque with light-colored central area of a bull's eye appearance
- Favors trunk, axilla, groin and popliteal fossa
- Untreated, usually last four weeks
- Disseminated EM – EM and satellite oval-shaped widespread patches due to spirochetemia

Erythema Migrans





Stages and Major Organ Manifestations of Lyme Disease

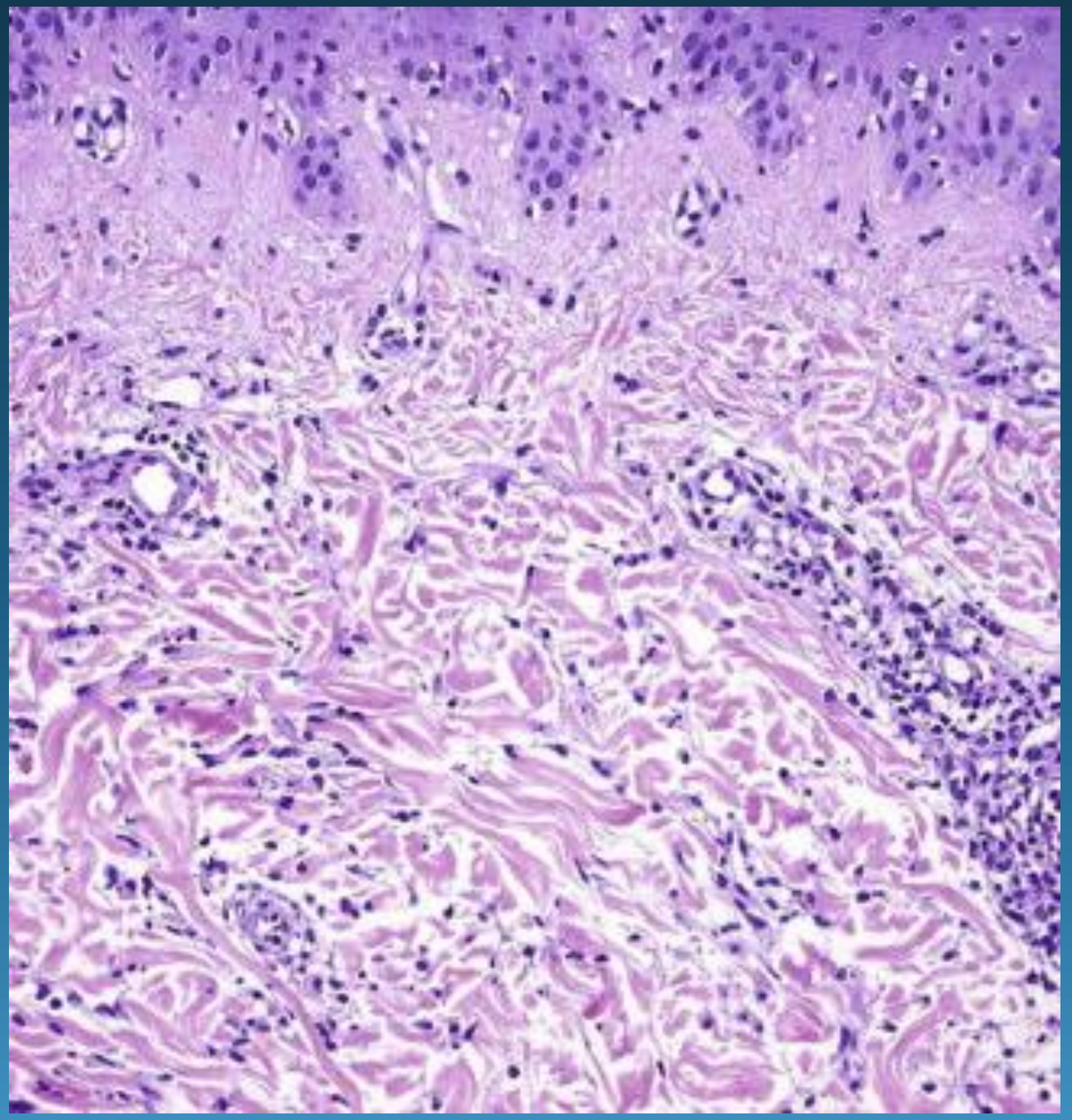
- Early Localized disease – EM, flu like symptoms, regional lymphadenopathy
- Early Disseminated disease – neural involvement (facial nerve common), migratory joint pain, carditis, conjunctivitis
- Chronic Disease – acrodermatitis chronica atrophicans, persistent neurologic and rheumatologic symptoms

Diagnosis

- Clinical presentation AND either history of exposure or laboratory evidence of infection
- PCR, culture, serological evidence
- Borrelia antibodies detection in serum might not be specific as peak specific IgM response is 3-6 weeks into infection
- Serologic tests will stay positive for months to years

Pathology

- Superficial and deep perivascular and interstitial infiltrate of lymphocytes, sometimes with abundant plasma cells and eosinophils
- Warthin-Starry stain is positive in 50% showing spirochetes



Differential Diagnosis

- Arthropod assault
- Erysipelas
- Cellulitis
- Non-pigmented fixed drug eruption
- Allergic contact dermatitis

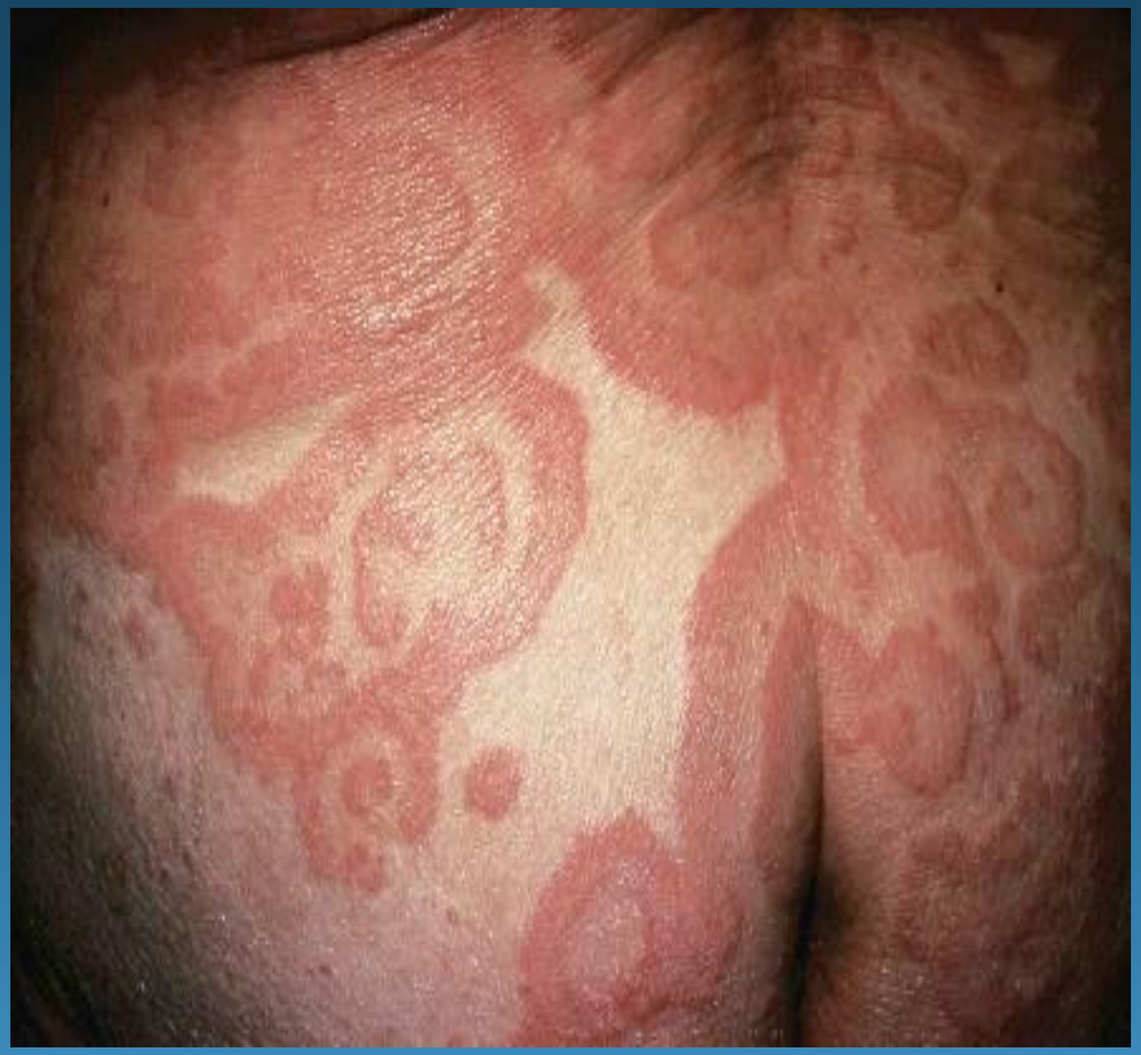
Treatment

Clinical features	Antibiotic		
	First choice for adults and children ≥8 years[*,†]	First choice for children <8 years and pregnant women; second choice otherwise[*]	Alternative choice[*]
Early localized disease	Doxycycline 100 mg (2 mg/kg) po q12h, 14–21 days[‡]	Amoxicillin 500 mg po q8h (50 mg/kg po per day divided q8h), 14–21 days[§]	Cefuroxime axetil 500 mg (15 mg/kg) po q12h, 14–21 days
Early disseminated disease or chronic disease, mild Cranial nerve palsy, 1st or 2nd degree heart block	Doxycycline 100 mg (2 mg/kg) po q12h, 14–28 days[‡]	Amoxicillin 500 mg po q8h (50 mg/kg po per day divided q8h), 14–28 days	Cefuroxime axetil 500 mg (15 mg/kg) po q12h, 14–28 days
	First choice	**Second choice**	**Third choice**
Early disseminated disease or chronic disease, severe Meningitis, radiculopathy, 3rd degree heart block	Ceftriaxone 2 g (75–100 mg/kg) iv once daily, 14–28 days	Cefotaxime 2 g (50–70 mg/kg) iv q8h, 14–28 days	Penicillin G 18–24 million units (200 000–400 000 units/kg) iv per day divided q4h, 14–28 days

Erythema Gyratum Repens

- Rare, males=females, Caucasians
- Gyrate polycyclic rapidly growing erythematous plaques with a trailing scale
- Migrates up to 1cm/day
- Wood grain resemblance due to “rings within rings” pattern
- Can be pruritic
- Additional findings: acquired ichthyosis, palmoplantar keratoderma and hypereosinophilia

Erythema Gyratum Repens



Erythema Gyratum Repens

- Unknown etiology, malignancy association >80% cases, i.e. the most specific paraneoplastic syndrome
- 1/3 patients= lung cancer, 8% esophageal cancer, 6% breast cancer
- The figurative eruption can precede, occur concurrently or appear after the diagnosis of the neoplasm
- Non-paraneoplastic cases: TB, CREST syndrome, pregnancy, bullous dermatosis

Differential Diagnosis

- Erythema annulare centrifugum
- Erythema migrans
- Resolving pityriasis rubra pilaris
- Erythrokeratoderma variablis

Erythema Gyratum Repens

- Treatment: identify and treat underlying malignancy

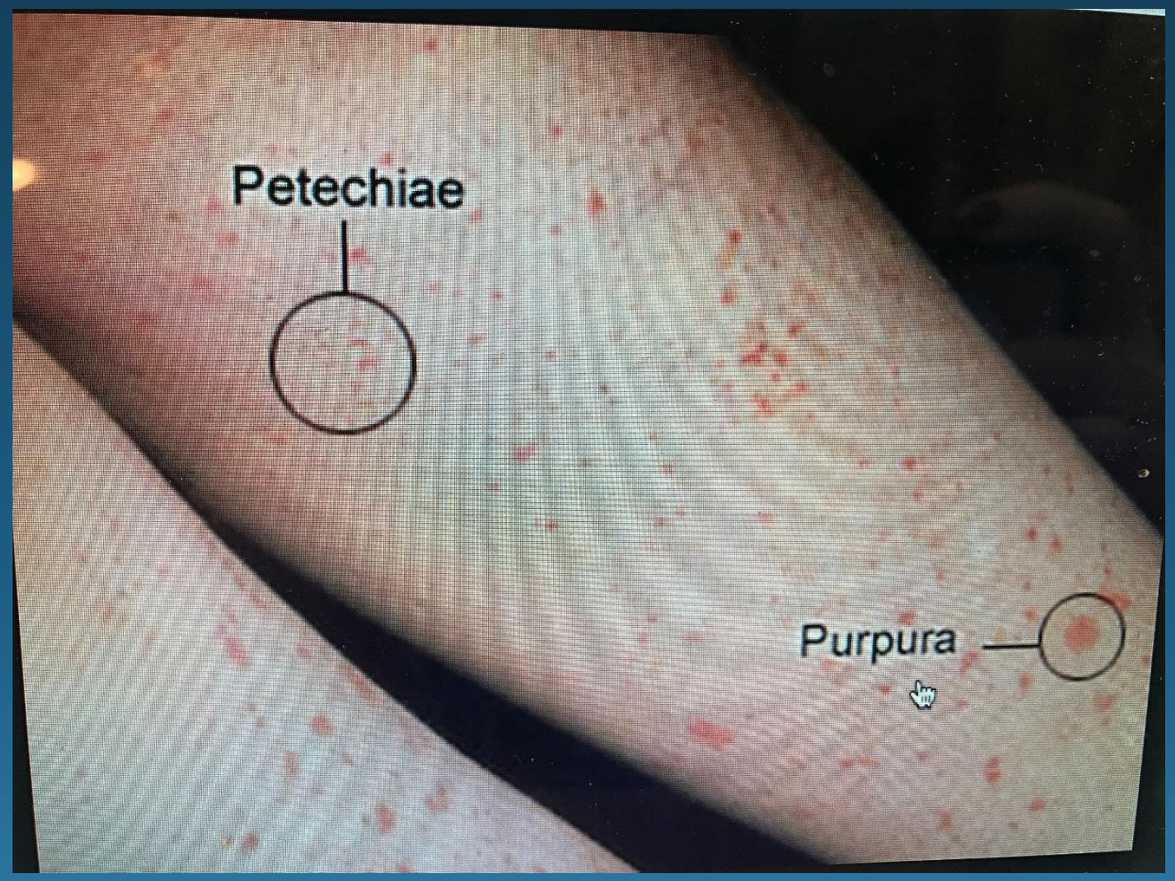
Purpuras

Definition

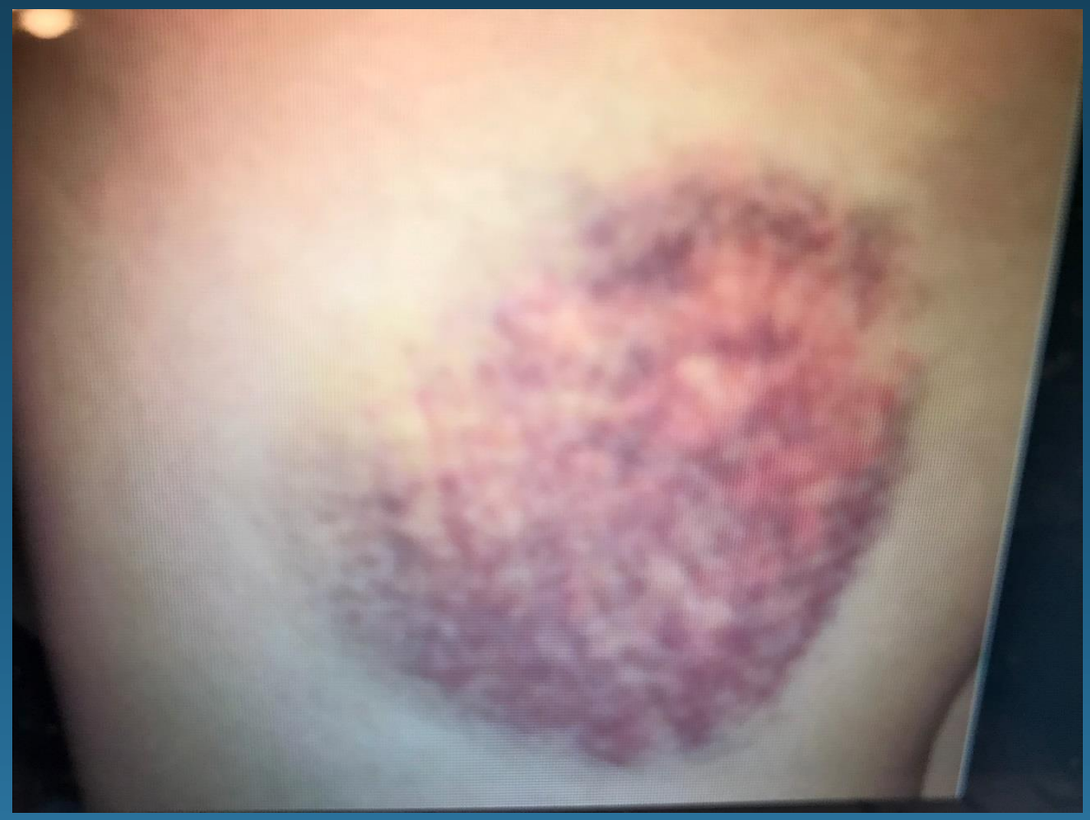
- Visible hemorrhage into the skin or mucous membranes.
- Divided into 6 subsets;
  - Petechiae
  - Macular Purpura
  - Macular ecchymoses
  - Palpable purpura
  - Non-inflammatory retiform purpura
  - Inflammatory retiform purpura

- **Petechiae** (<4 mm red-purple hemorrhagic macules):
  - Seen in: ITP, TTP, DIC, Platelet function defects, Aspirin/NSAID use, trauma, valsalva-manueaver, etc.
- **Macular Purpura** (5-9 mm red-purple hemorrhagic macules that don't blanch):
  - Seen in: Hypergammaglobulenima of Waldenstrom, thrombocytopenia
- **Macular Ecchymoses** (>1 cm red-purple-green patch due to bleeding in skin):
  - Seen in: Anticoagulant use, hepatic insufficiency, Vitamin K deficiency, DIC, Actinic purpura, steroid use, Vitamin C deficiency, Ehlers-Danlos disease, platelet function diseases, etc.

Purpura and Petechiae



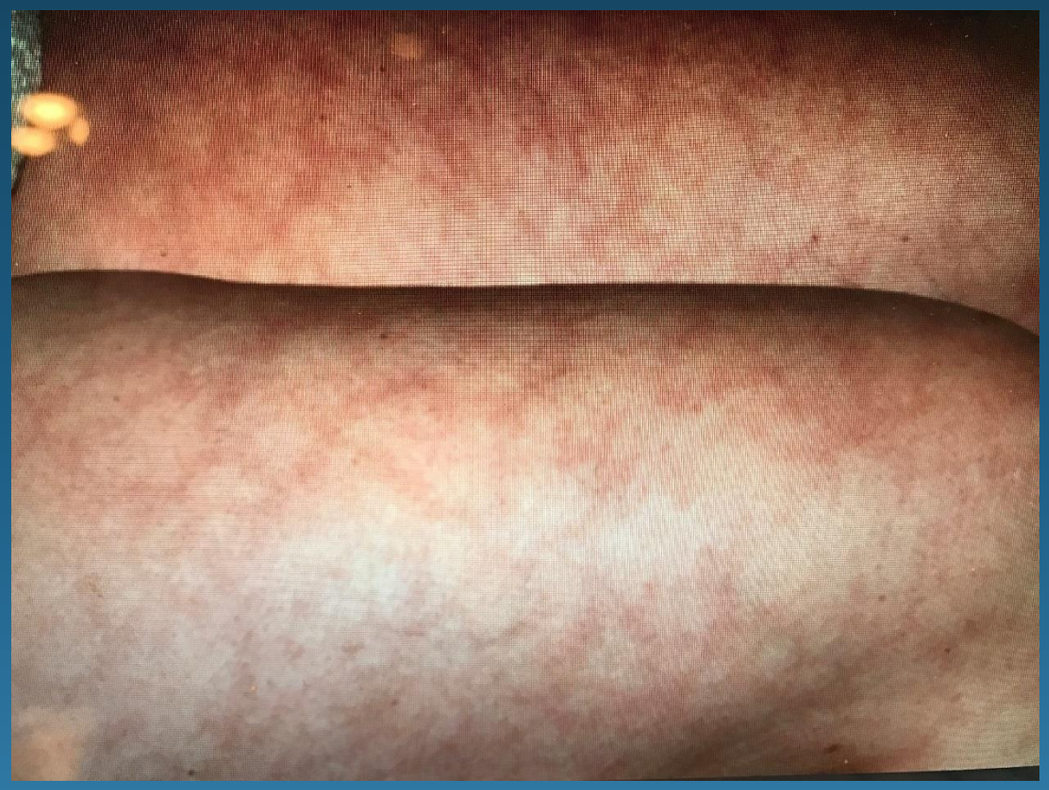
Macular Ecchymosis



- Macular purpuras are all due to hemorrhage, with mild inflammation and extravasated red blue cells causing what is seen in the patient.

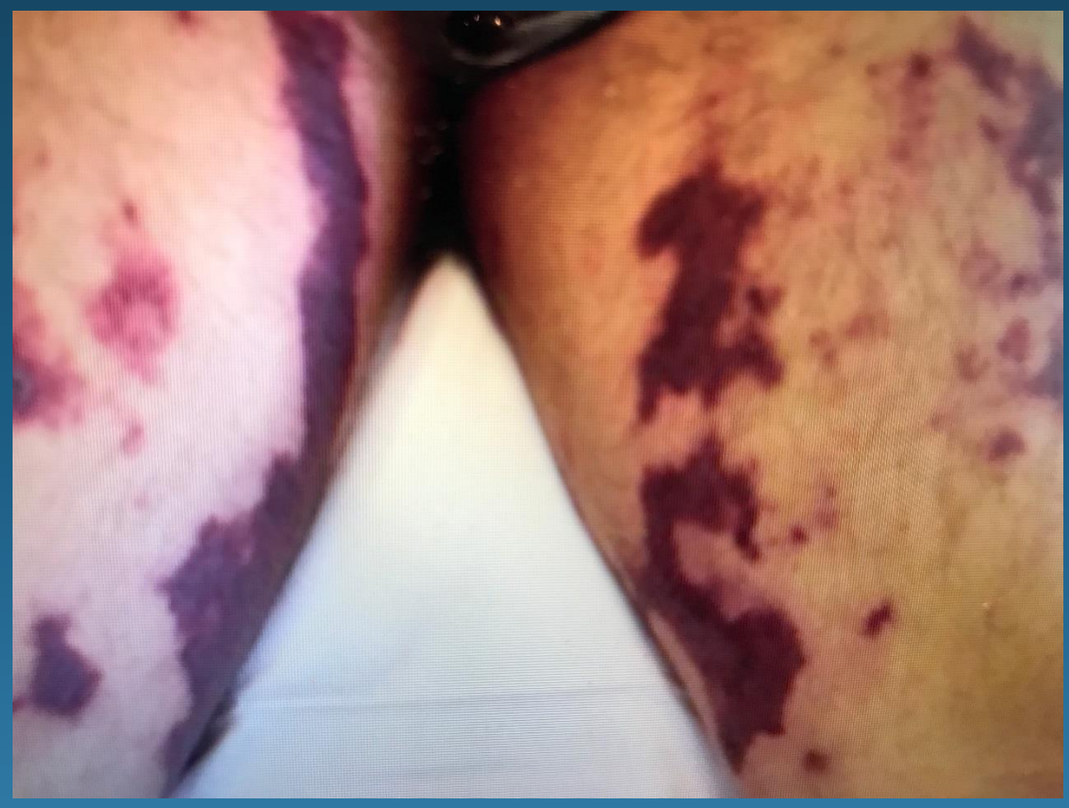
- **Palpable Purpura**: (raised, non-blanching inflammatory purpura with erythema)
  - Seen in: Idiopathic, infection IgG/IgA/IgM complexes, Hypergammaglobulinemic purpura of Waldenstrom, Urticarial vasculitis, Mixed cryoglobulinimia, Rheumatic vasculitis, ANCA associated diseases, etc.
- **Non-inflammatory retiform purpura** (mottled lace-like livedo reticularis pattern causing a purple-ish discoloration):
  - Seen in: Heparin necrosis, thrombocytosis, TTP, cryoglobulinimia, ecthyma gangrenosum, Protein C/S deficiency, warfarin necrosis, livedoid vasculopathy, cholesterol emboli, etc.
- **Inflammatory retiform purpura** (visible hemorrhage into skin or mucous membranes in the livedo reticularis pattern):
  - Seen in: IgA vasculitis, mixed cryoglobulinimia, polyarteritis nodosa, chillblains, wegener's granulomatosis, livedoid vasculopathy, etc

Livedo Reticularis



- Seen due to blood flow regulation in dermal and subcutaneous vessels- and shows a net like pattern

Retiform Purpura



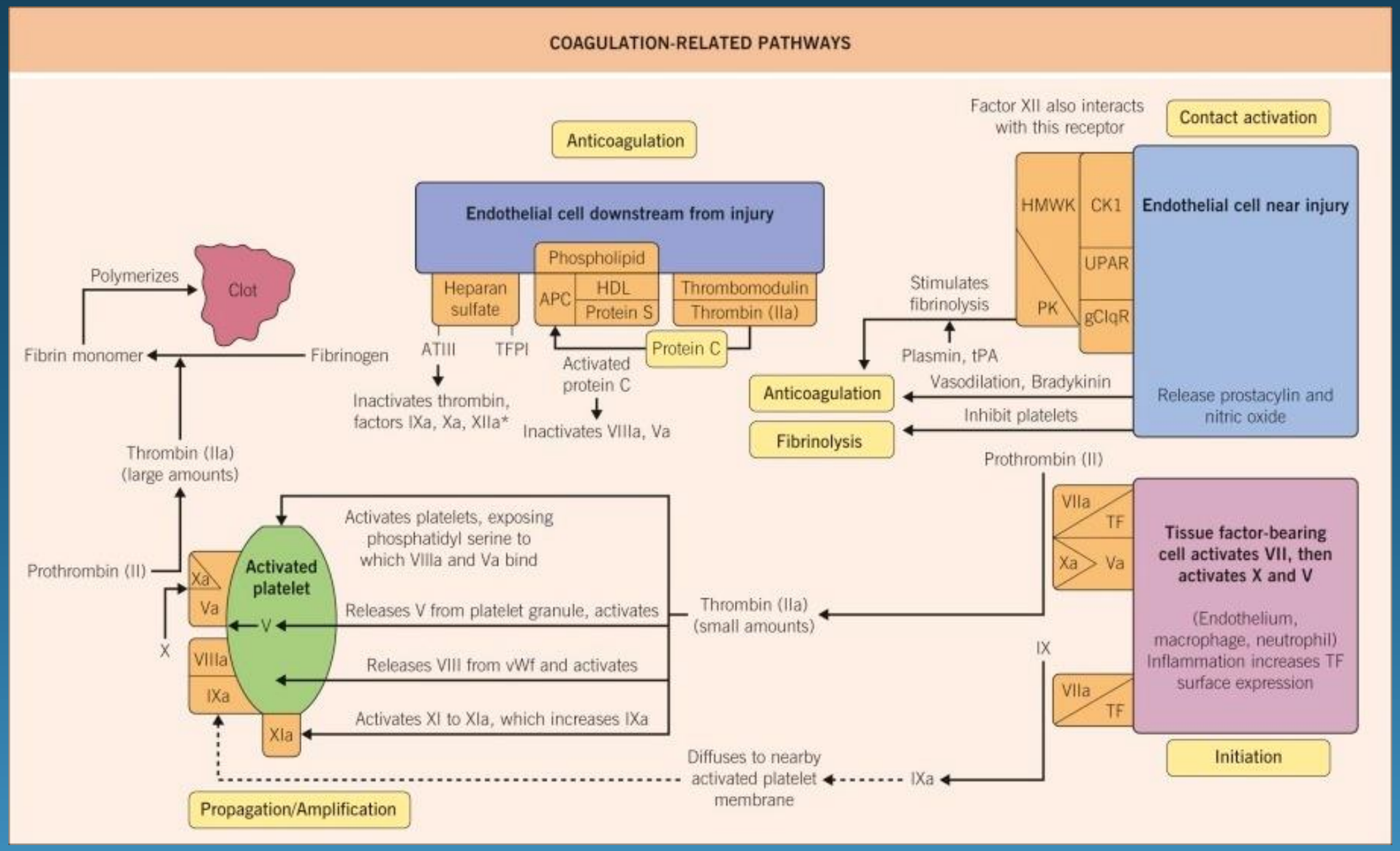
- Retiform purpura is due to occlusion of vessels that cause the livedo reticularis; distinguish the 2 by presence or absence of purpura.

Coagulation

Coagulation

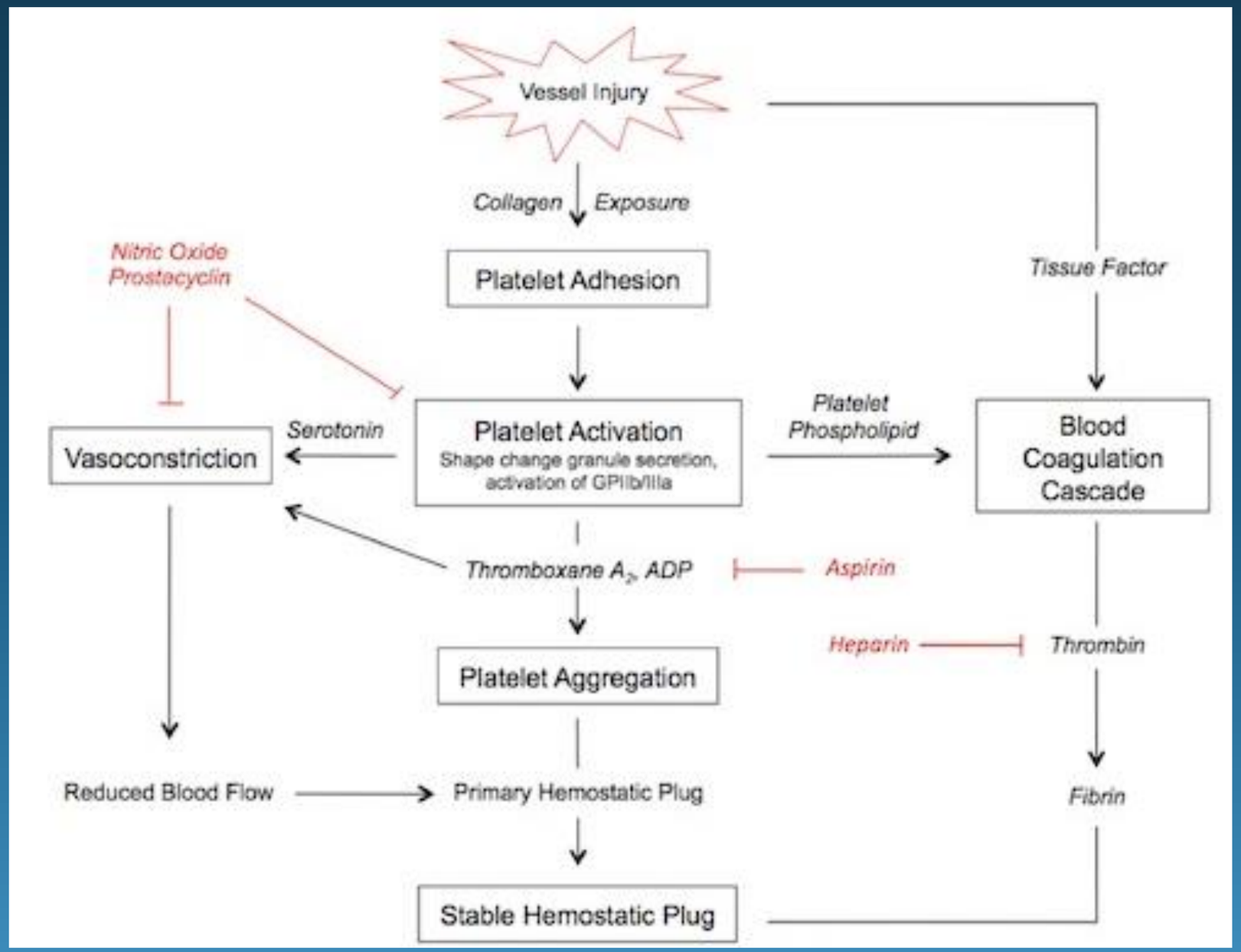
- Primary hemostasis consists of the formation of a platelet plug that is sufficient for minor injuries to the microvascular system
- If the size of the vessel or injury is too large, secondary hemostasis with clot formation is necessary
- Too little clotting → death by hemorrhage
- Too much clotting → thrombosis, embolus, necrosis
- Requires extensive regulation and balance between procoagulant, anticoagulant, and fibrinolytic pathways

Coagulation Related Pathways

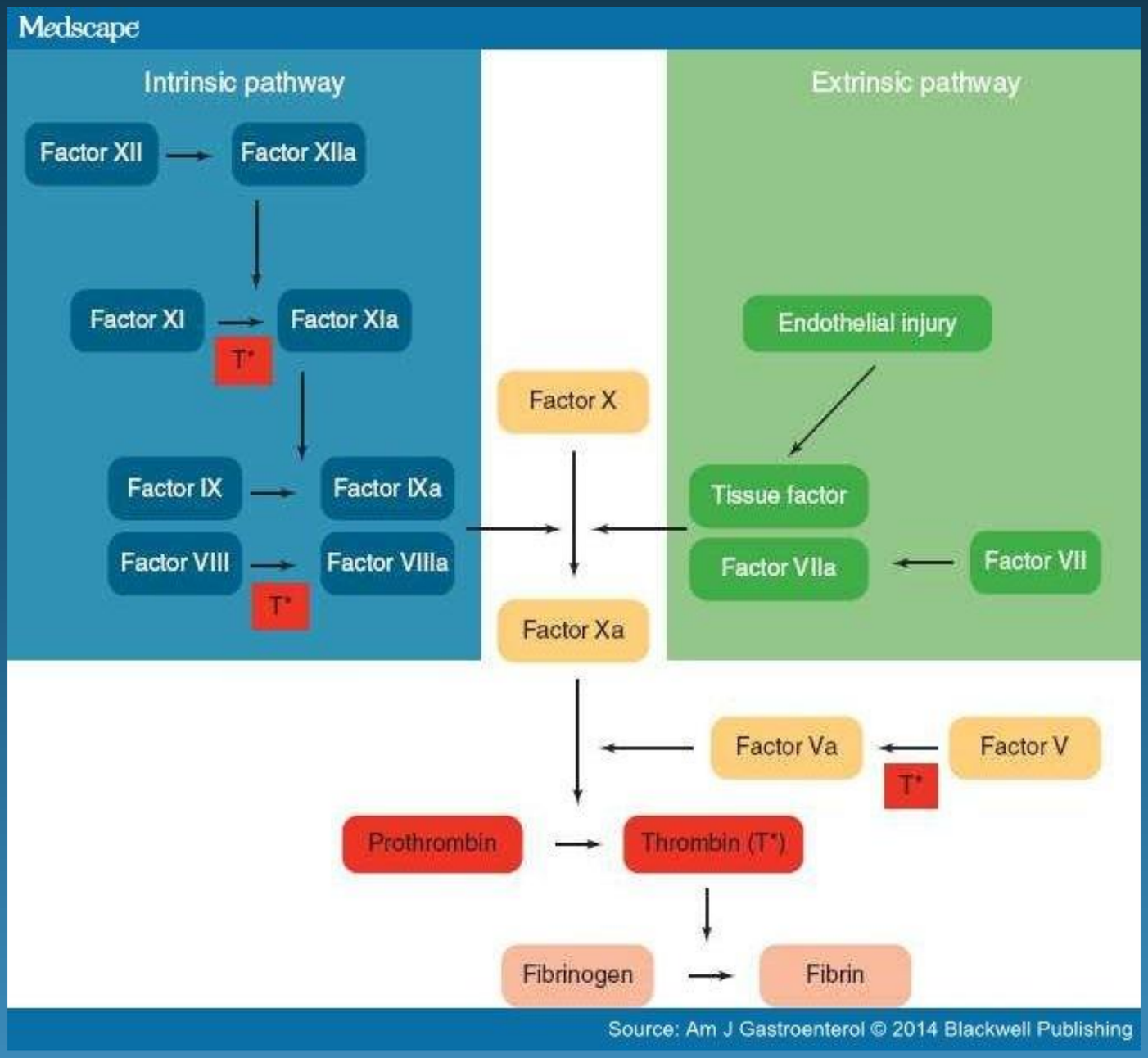


Dermatology. 3rd Edition, Bolognia.

Platelet Plug (Primary Hemostasis)



http://www.sharinginhealth.ca/multimedia/images/hemostasis_Kathryn_Dorman.jpg


Medscape
Intrinsic pathway
Extrinsic pathway
Factor XII
Factor XIIa
Factor XI
Factor XIa
T*
Factor IX
Factor IXa
Factor VIII
Factor VIIIa
T*
Factor X
Factor Xa
Endothelial injury
Tissue factor
Factor VIIa
Factor VII
Factor Va
Factor V
T*
Prothrombin
Thrombin (T*)
Fibrinogen
Fibrin
Source: Am J Gastroenterol © 2014 Blackwell Publishing

Thrombin (factor II)

- Generated in small amounts from primary clot
- Activates platelets, leads to binding of procoagulant factors
- Also stimulates release of factor V from platelet granules
- Activates tissue factor VIIa
- Activates Factor IX to IXa and Factor X to Xa

Anticoagulant pathway

- Initiation phase of clotting is down-regulated by tissue factor pathway inhibitor (TFPI) and antithrombin III (ATIII)
- Both bound to heparin sulfate molecules on endothelial cells
- Capture activated clotting factors and prevent them from leaving the vicinity
- TFPI can inactivate factor Xa; ATIII can neutralize thrombin, factor IXa, Xa, XIIa
- Thrombomodulin/protein C/protein S
- Important in large vessels
- Thrombin from clot bind to thrombomodulin, and thus loses it ability to cause procoagulatory effects
- Activates protein C → inactivates Factor Va, VIIIa

Tests for Coagulation

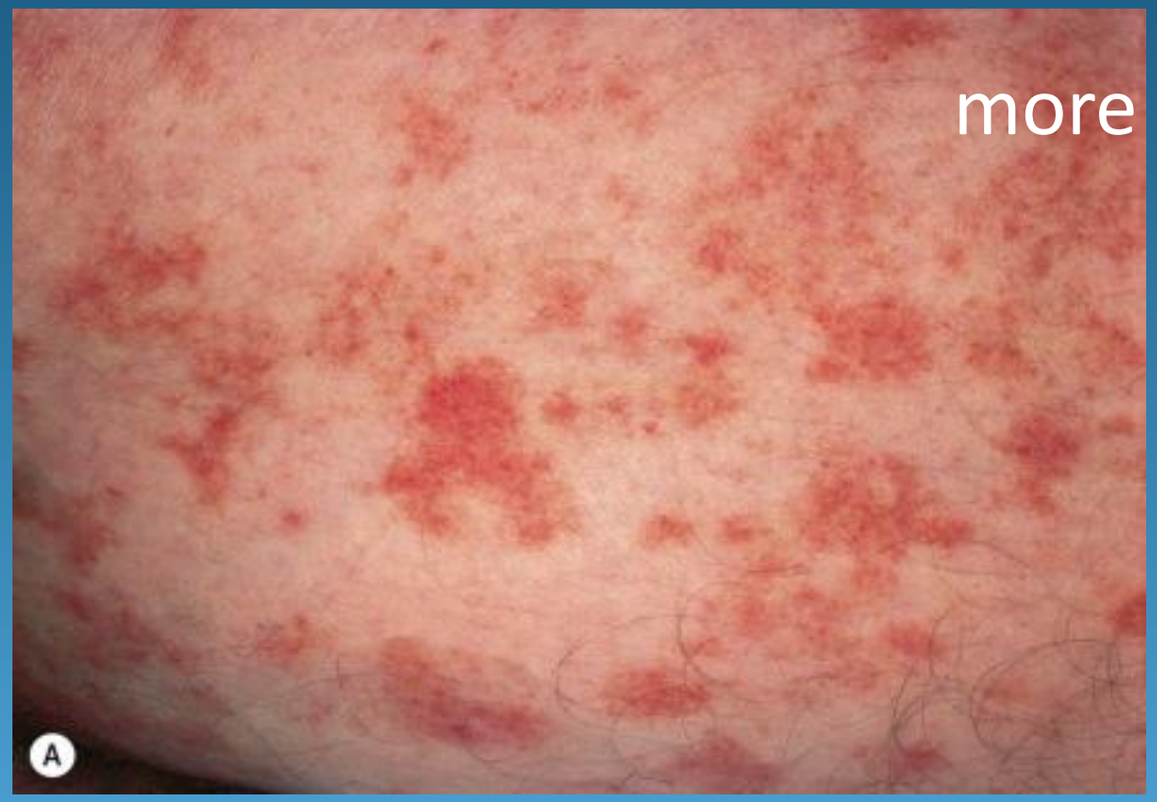
- Thorough history and physical exam
- Labs: Platelet count, PT, and APTT
- If PT or APTT prolonged, can repeat testing using 1:1 mixture of pt plasma and normal plasma ->if time normalizes then there is a factor deficiency
- Prolonged PT + normal APTT: factor VII deficiency or use of PO anticoagulant
- Prolonged APTT + normal PT: use of Heparin, lupus anticoagulant, acquired factor VIII deficiency, or von Willebrand Disease
- Prolonged PT + APTT: fibrinogen deficiency, prothrombin, factor V or Factor X deficiency

Pigmented Purpuric Eruptions

- Diseases characterized by petechial hemorrhage likely due to capillaritis
- Minimal inflammation and hemorrhage of superficial papillary dermal vessels
- Source of inflammation unknown and no coagulation abnormalities
- Several variants

Schamberg's Disease

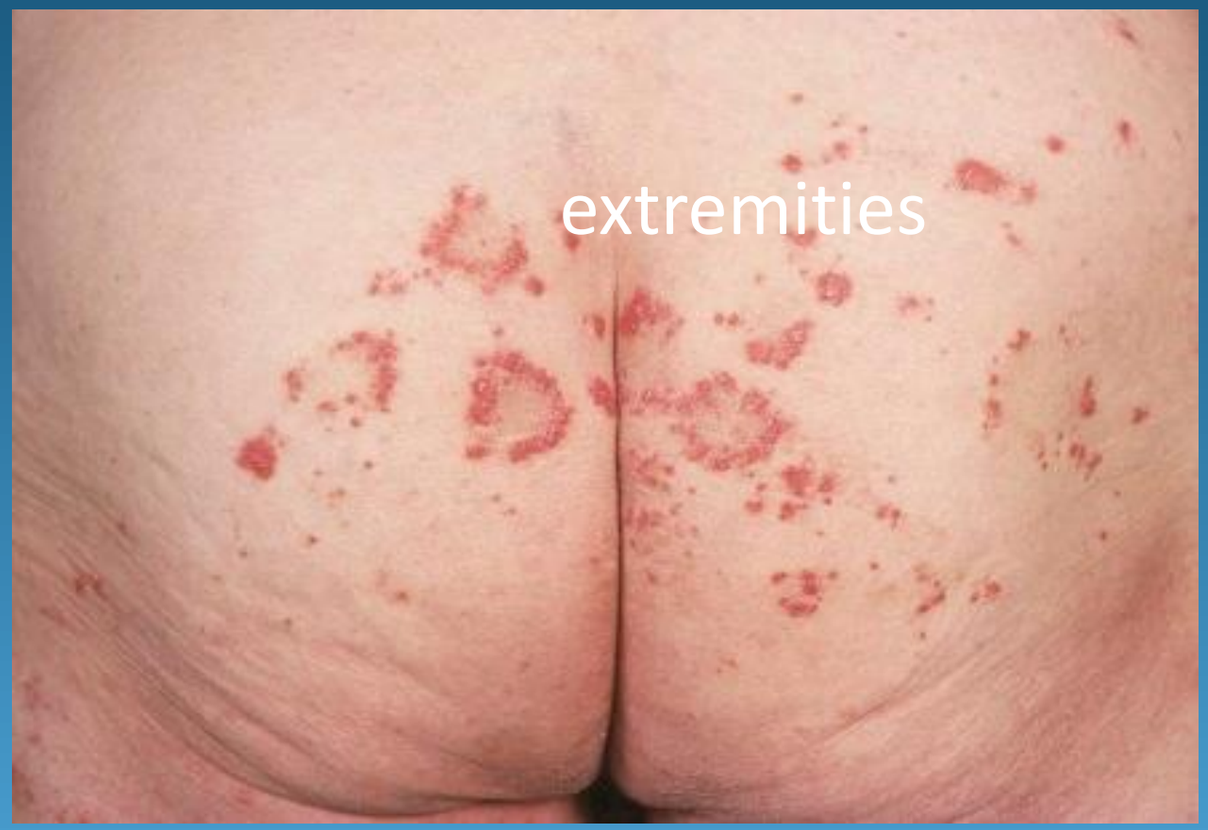
- Yellow-brown patches with an oval to irregular outline, pinpoint petech
- Most common form, peak frequency in middle aged to older men
- Usually involves lower extremities
- Stasis purpura clinically has more hem



Bolognia, “Dermatology”, figure 22.5a

Purpura annularis telangiectodes of Majocchi

- Uncommon, adolescents, young adults, especially women
- 1-3 cm annular plaques that slowly expand, punctate telangiectasias and petechiae within border, possible yellow center
- Trunk, proximal lower extremities

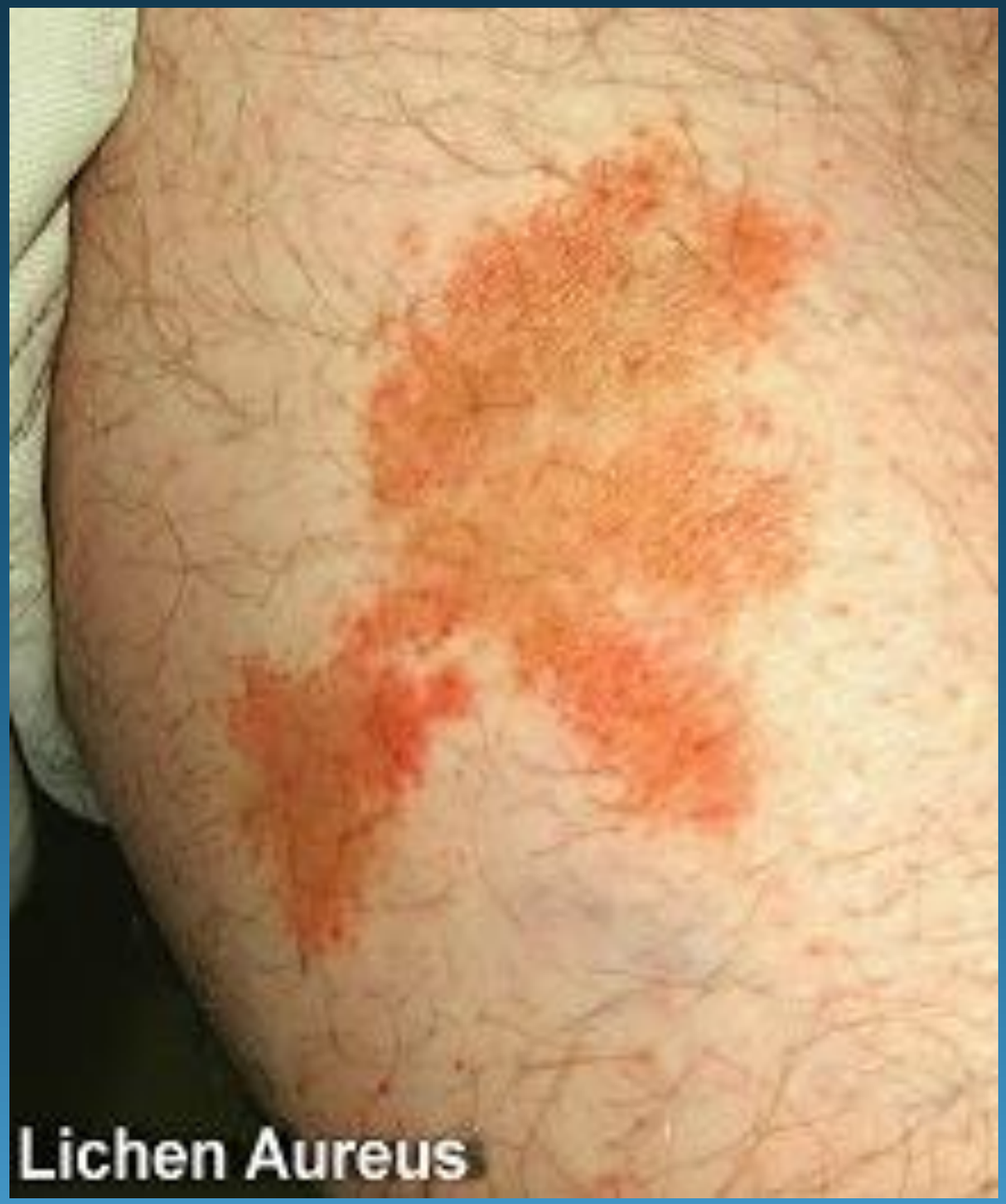


Bolognia, “Dermatology”, figure 22.6

Rare Variants

- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum: Schamberg like- purpuric red-brown lichenoid papules
- Eczematid-like purpura of Doucas and Kapetanakis: Scaly petechial or purpuric macs, paps and patches, usually pruritic
- Lichen aureus: solitary patch, color varies from golden to rust to purple brown

Lichen Aureus



http://www.cortesedermatology.com/dermatitis-images.html

Histology

- Red cell extravasation, endothelial swelling, perivascular lymphs, and hemosiderin containing macrophages

- Lichen aureus and Gougerot-Blum variants are characterized by lichenoid infiltrate

- Eczematid like purpura of Doucas and Kapetanakis often has spongiosis, patchy parakeratosis

Treatment

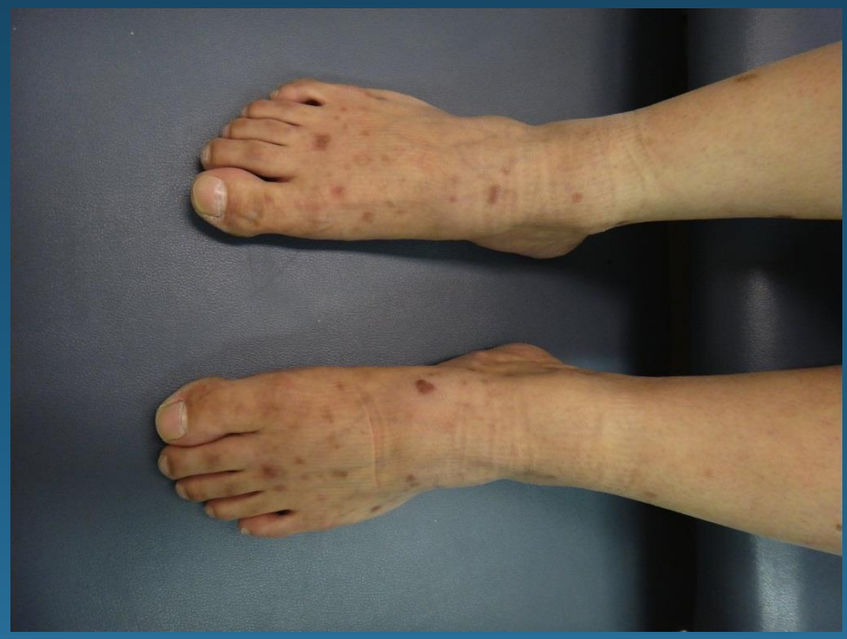
- Topical steroids especially if pruritic
- PUVA, NBUVB
- Ascorbic acid 500 mg BID with Rutoside 50 mg BID
- Cyclosporine

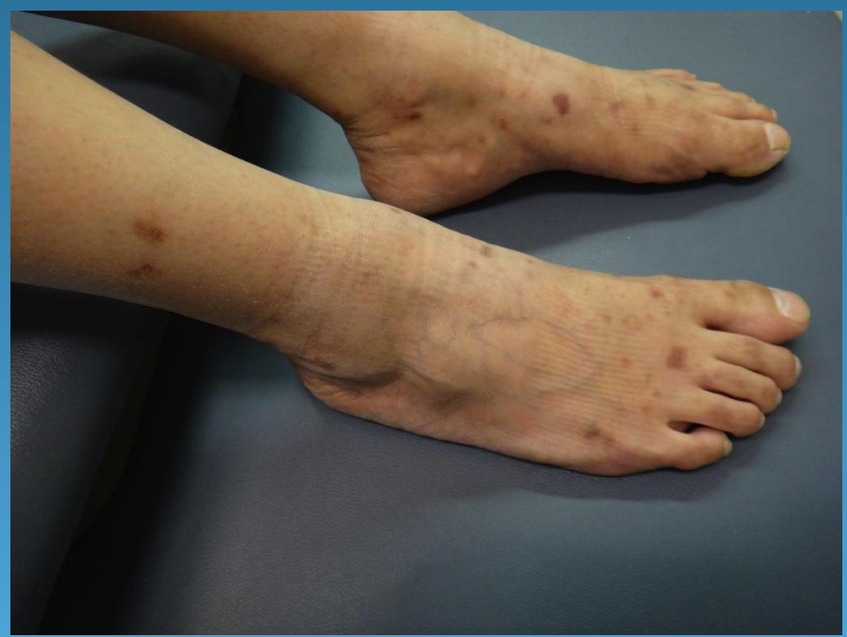
Hypergammaglobulinemic Purpura of Waldenstrom

- Associated with a hypergammaglobulinemia
- Presence of small circulating immune complexes containing IgG or IgA rheumatoid factor
- IgG and IgA rheumatoid factors are highly soluble, which may explain the speed with which lesions appear and resolve
- Can be primary or secondary
- In younger patients, it is usually primary, but eventually patients may develop an autoimmune connective tissue disease (usually Sjogren's)
- Complications include the development of a monoclonal gammopathy, lymphoma, or multiple myeloma
- Differential Dx: classic cutaneous small vessel vasculitis syndromes

Hypergammaglobulinemic Purpura of Waldenstrom

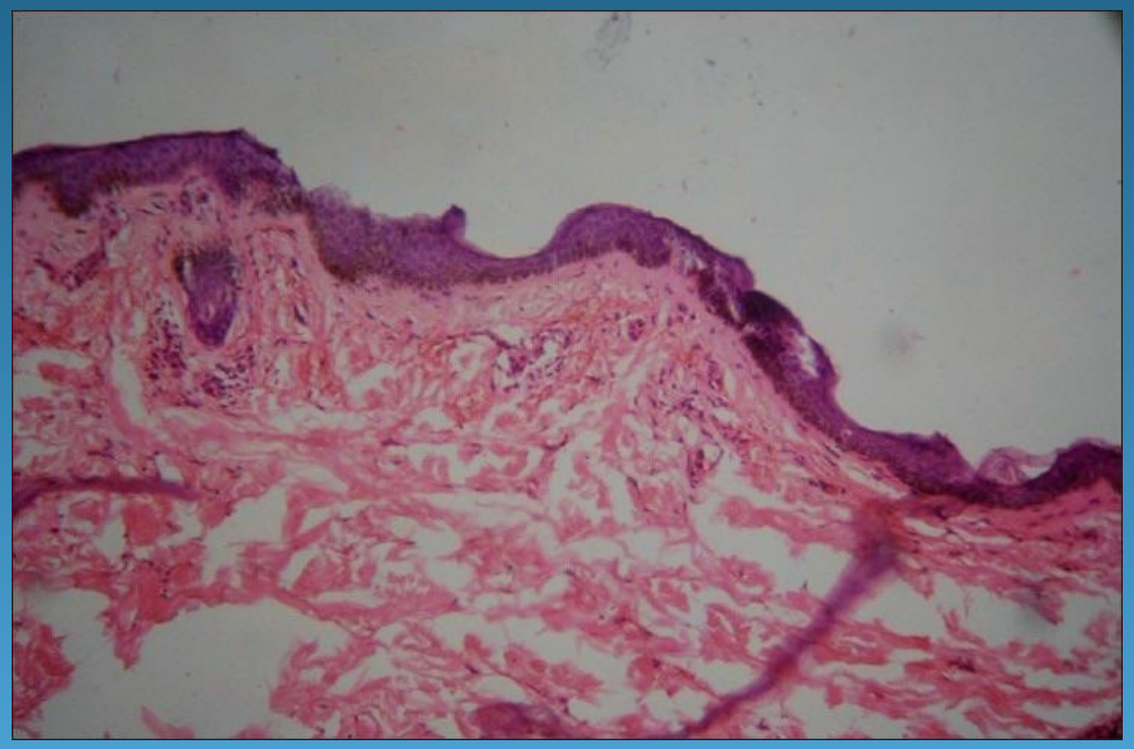
- Usually affects women
- Mild pruritus, tingling, or burning may precede the presence of purpura
- Symptoms are exacerbated by prolonged standing, tight fitting garments, and heat
- Petechiae or larger purpuric macules on lower extremities is the most common presentation
- Labs: Polyclonal hypergammaglobulinemia, elevated ESR, anti-Ro and anti-La Abs are usually present and may predict a higher likelihood of developing autoimmune connective tissue disease
  - Standard RF assays will only detect IgM, therefore they will not detect IgG or IgA





Pathology

- Histopathology may show hemorrhage, a mild perivascular infiltrate, or a leukocytoclastic vasculitis
- Image shows dilated superficial capillaries, extravasation of red blood cells, and sparse mononuclear infiltrate without evidence of vasculitis



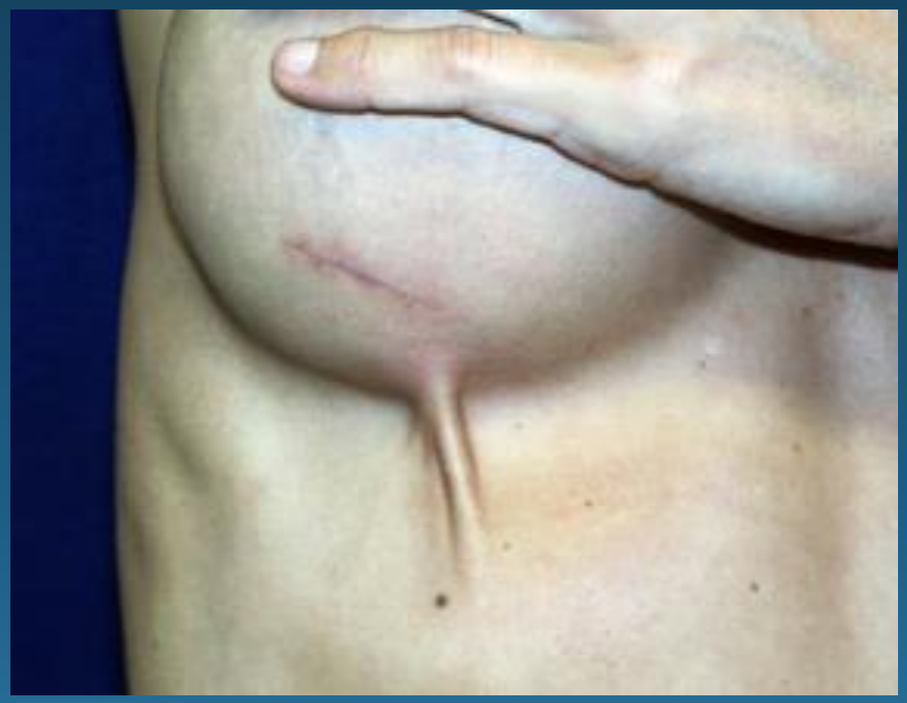
Treatment

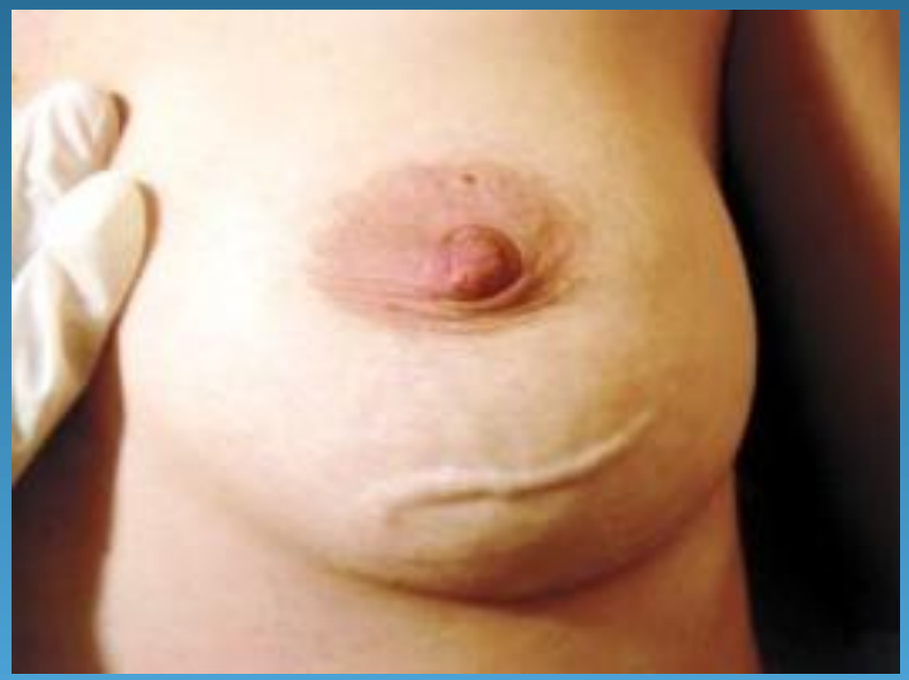
- Limited treatment options
- Aspirin
- Support stockings
- Avoidance of triggers such as alcohol, prolonged standing

Mondors Disease:

- First described in 1939 by Henri Mondor
- Superficial thrombosis (SVT)
- Self limited
- Most commonly seen in patients aged 30-60 year old
- Female > male; 3:1

Clinical Presentation





- Predisposing factors include:
  - Increased coagulation state
  - Thoracic surgical procedures
  - Breast surgery
  - Tight clothes
  - Mammary infections
  - Pendulous breast
  - Chronic inflammatory disease states
- Presents as a fibrous painful cord, with or without skin retraction, and with or without local inflammation.
- Can present on the chest well, involving other venous areas, and following breast disease

Work up

- Complete history and physical
- Ultrasonographic to confirm
- Mammography if suspicion of breast cancer

- Most cases are idiopathic
- In a pool analysis of the four largest and most recent series:
  - Idiopathic (32.5%)
  - Breast Cancer (6.3%)
  - Iatrogenic (11.9%)
  - Inflammation (4.8%)
  - Trauma (32.5%)
    - Including: injury, muscular, heavy load, tight support, thrombophilia, hormone therapy

Treatment

- Mondor’s on chest wall: Spontaneous resolution in 2-8 weeks
- Other locations: less known, can consider anticoagulation and etiologic management if known. Surgery in persistent cases
- Mondor’s after breast surgery: This is not a thrombotic process. Reports suggest that manual rupture of the fibrous bands ensures immediate functional recovery and pain relief.
- Penile Mondor’s: conservative treatment.
- There is approximately 13% recurrence

Conclusion

- Reviewed the four “classic” figurate erythemas: erythema annulare centrifugum, erythema marginatum, erythema migrans, and erythema gyratum repens
- Reviewed specific purpuric syndromes and treatment modalities
- Provided practical applications for these dermatological conditions

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Thank You