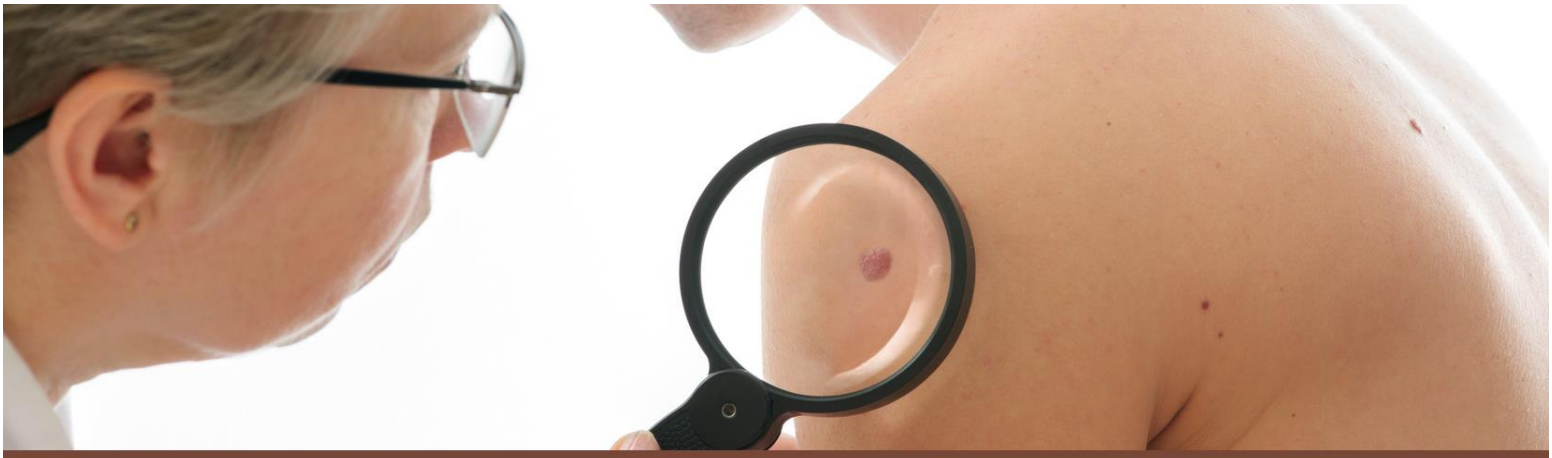

433 Teams

DERMATOLOGY

L 11- Dermatological Emergencies (BlisteringDisorders , Pempigus Valgaris, Drug Eruption)

This work, based on 432 teamwork plus our notes

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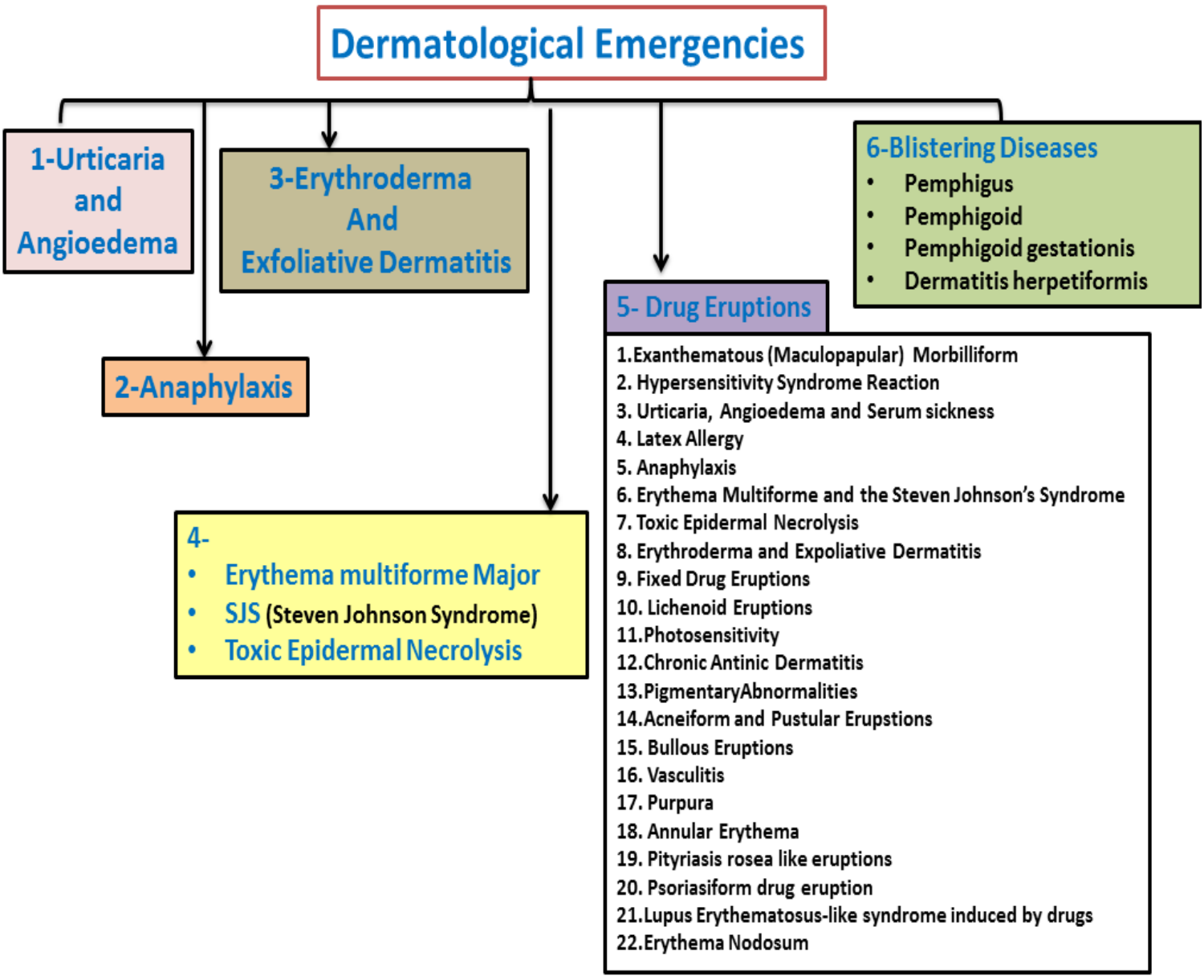
Mind Map


Dermatological Emergencies
1-Urticaria and Angioedema
2-Anaphylaxis
3-Erythroderma And Exfoliative Dermatitis
4-
Erythema multiforme Major
SJS (Steven Johnson Syndrome)
Toxic Epidermal Necrolysis
5- Drug Eruptions
1.Exanthematous (Maculopapular) Morbilliform
2. Hypersensitivity Syndrome Reaction
3. Urticaria, Angioedema and Serum sickness
4. Latex Allergy
5. Anaphylaxis
6. Erythema Multiforme and the Steven Johnson's Syndrome
7. Toxic Epidermal Necrolysis
8. Erythroderma and Expoliative Dermatitis
9. Fixed Drug Eruptions
10. Lichenoid Eruptions
11.Photosensitivity
12.Chronic Antinic Dermatitis
13.PigmentaryAbnormalities
14.Acneiform and Pustular Erupstions
15. Bullous Eruptions
16. Vasculitis
17. Purpura
18. Annular Erythema
19. Pityriasis rosea like eruptions
20. Psoriasiform drug eruption
21.Lupus Erythematosus-like syndrome induced by drugs
22.Erythema Nodosum
6-Blistering Diseases
Pemphigus
Pemphigoid
Pemphigoid gestationis
Dermatitis herpetiformis

An introduction mentioned by the doctor but not on the ppt

- **Important emergencies in Dermatology:**

1. Anaphylaxis is one of the most important emergencies in medicine (from voltarine for example) it's a type1 allergic reaction that happens within seconds → angioedema can kill the patient
2. TEN is the most killing dermatological emergency because risk of sepsis and an infection. (killing emergency that needs to be managed urgently)Its mortality is 30% in comparison to SJS which is 1-5% and is not as serious as TEN.
3. Pemphigus vulgaris is an important emergency (killing) and before the era of steroids the patients used to die due to sloughing of the skin which leads to septicemia. TEN is an important DDX

4. Necrotizing fasciitis (most commonly by Group A beta-hemolytic streptococcus, **Group B** strept): you acquire it post trauma or surgery and also seen in diabetics . violaceous and dusky red skin is an early presentation which can later extend to the fascia and deeper . It's treated by surgical debridement and antibiotics

5. Cellulitis: is a superficial infection with a well defined tender erythema. Predisposing factors: Portal for entry (wounds (especially between the toes), tinea pedis), diabetes, immunocompromised, etc. → you must treat the underlying cause to avoid consequences such as sepsis and death

6. **Pustules** in neonates needs to be investigated, you cannot depend on your clinical judgment as it could be a presentation of (**Candida, herpes**, etc.). the presentation is not typical in neonates for the present with pustules with no oral thrush in candida and in herpes they present with pustules

7. **Mucormycosis** is one of the fatal infections in **diabetic patients** when they have diabetic ketoacidosis around the sinuses and has a picture somewhat similar to Necrotizing fasciitis

8. Staphylococcal Scalded Skin Syndrome is common in children **(<6 yrs)**. SSSS is caused by the release of two exotoxins (epidermolysin toxins A and B) from toxigenic coagulase positive strains (**71** , 3A, 3B, 3C , 55)of the bacteria Staphylococcus aureus. They cause very superficial sloughing of the subcorneal sloughing . (all the nurses and doctors should be screened for staph carriers if a hospitalized patient was diagnosed with it). It may resemble TEN theoretically but clinically its more superficial that TEN . the initiating infection is usually in the form of crusting impetigo in the umbilical stump or nasopharynx.

9. Others include erythroderma , pustular psoriasis (pt mistaken to have sepsis) , inflammatory disoders , in children (histocytosis , ,astocytosis , hemangioma around orifices i.e oropharynx , eye) , ulcerating diseases like pyderma gangrenosum

Urticaria and Angioedema

- **Essentials of Diagnosis:-**

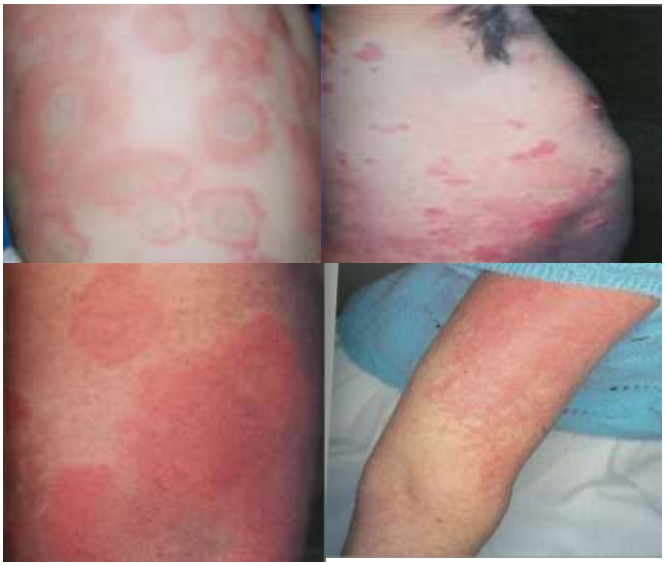
- Wheals or hives
- Evanescent: (disappears from a place and reappears on another) individual wheals disappear **within 24 hours** and often within minutes.
- Changing of configuration.

What's the difference between an urticarial wheal and urticated lesion?
Urticated: looks like urticarial wheals but it leaves marks (pigmentation for an example) unlike urticarial wheal. They may be painful , lasting for > 24 hours
Urticarial wheal: you know it by **history** + leaves no marks

- **What is the major mediator of Urticaria?**

Pathogenic mechanism:

- Immunologic Type I (IgE mediated) or Type III. Its immediate or quick
- Major mediator IgE and major effector cell is the Mast Cell
- Non immunologic (activation of the alternative complement pathway and direct release of histamine) from basophils or tissue mast cells by drugs or chemicals.
  - Transient swellings and erythema due to vasodilatation and fluid exudation.
  - Can be life threatening especially when associated with angioedema of the larynx. May take years to resolve.



Urticarial wheel , edematous and erythematous , you don't need a biopsy unless you are worried about urticarial vasculitis

Classification of Hypersensitivity Reactions:

Hypersensitivity is a state in which the immune responses frequently take place in such a way that cell damage occurs and harmful pathological lesions may occur.

5 types of hypersensitivity are recognized:

-Immediate (Antibody mediated):

Type I: Anaphylaxis

It is IgE-mediated. An antigen (allergen) reacting with specifically sensitized IgE that is fixed to mast cells through its FC portion. Degranulation of mast cells release of their mediators e.g. histamine, leukotrienes, ECF and NCF. The offending antigen is identified by intradermal prick tests giving immediate wheal and erythema reations or by provocation testing. There is a strong familial predisposition and a tendency to produce high levels of IgE. e.g. **anaphylaxis, utricaria, atopy**

Type III: Immune-Complex Reactions (arthus phenomenon)

The antigen reacts with specific circulating antibodies antigen-antibody complexes that act through: (a) complement activation and PMNL attraction inflammatory response. (b) platelet aggregation microthrombi and vasoactive amine release. E.g. **serum sickness (classical example , its was seen at the days of diphtheria Toxins)**, nephritis in SLE, Allergic **vasculitis, urticarial vasculitis** (can present like urtications , but may last for > 24 , leaves pigments , presents with fever + very important to rule out internal organ deposition so start with **UA** (for cast , RBC, Proteins)to detect kidney involvement + rule out other diseases), ? Bullous pemphigoid. (Immunocomplexes "antigen-antibody in excess" which then will deposit on other major organs like CNS , GIT, Liver, and most commonly Kidney and Joints .

N.B. remember that vasculitis can present with any of the following purpura , petechiae , ecchymosis

Acute Urticaria: less than 6 wks

Chronic Urticaria: more than 6 wks. Recurrent: 2 times a year.

Urticaria may accompany systemic Anaphylaxis or serum sickness reaction.

Serum sickness:

5d 3weeks after initial exposure (type III) immune complex mediated reaction. From the excess antigen antibody deposit in the vessels and organs

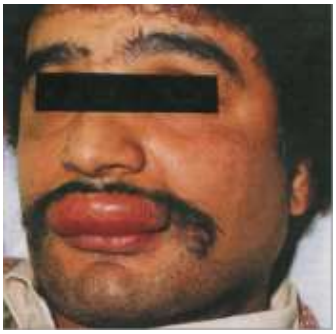
Exposure toxins i.e. anti-snake , anti-scorpion , drugs (classically)

Fever, Urticaria, Angioedema, Joint pain and swelling, lymphadenopathy, occasionally : nephritis or endocarditis with eosinophilia.

Minor form of Serum sickness: fever, Urticaria, **transitory** joint tenderness (without inflammation or other organ involvement).

N.B in serum sickness like reaction you won't see major organ involvement only fever , skin and maybe arthralgia

Angioedema

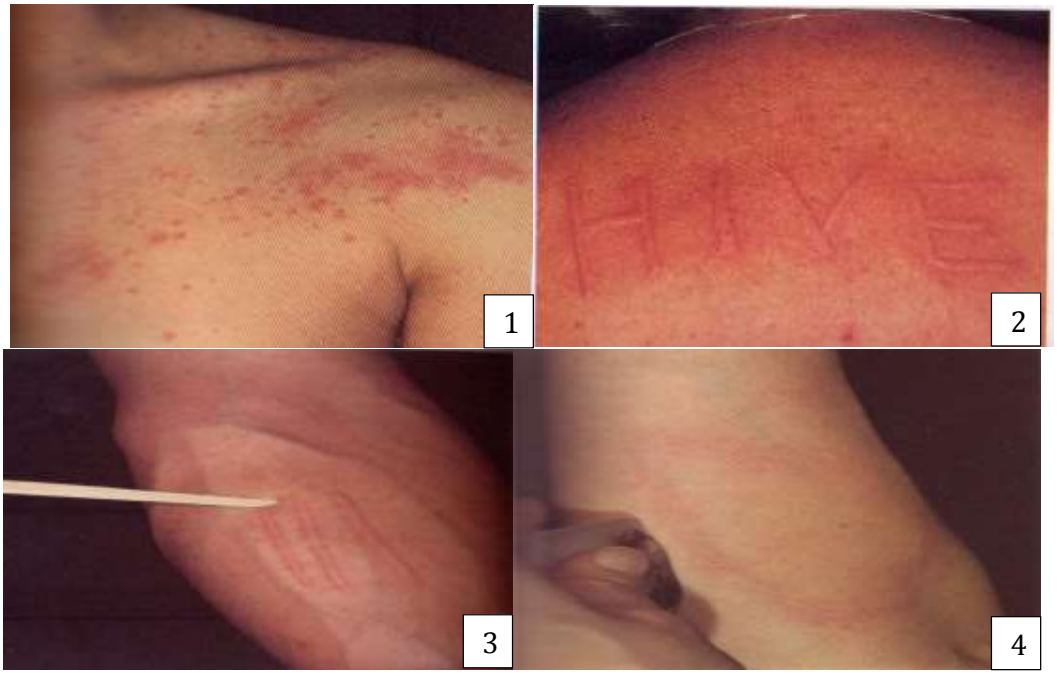


Angioedema: oedema Involving the deep dermis or subcutaneous and submucosal areas.
Why is it important? It may involve the airway like in oropharyngeal edema which is an emergency.

Causes of Urticaria and angioedema:

Drugs- Animal sera, vaccines containing egg protein, desensitizing agents, Antibiotics, ACEI, radiocontrast media, cylogenase inhibitors.
Foods, Inhalants, Infections, Autoimmune disease(SLE, autoimmune thyroiditis →its just an association , correcting the cause doesn't mean the urticaria will go), Insect bites, Physical causes (like in red dermatographism (axon or flare reflex)that happens in 5% of people upon scratching the skin they develop a wheal and flare)and it doesn't have to be investigated)
Hereditary causes, hereditary Angioedema. there are three types quantitative its due to C1 esterase deficiency , functional , and gene mutation (rare) .. C1 usually presents in the form of angioedema and gastric involvement without urticaria , however if such a presentation occurs in elderly adding the symptom of pitting and pain then its acquired C1 deficiency and thus you must R/O things such as lymphoma , solid malignancy , sometimes autoimmune (SLE)→ hereditary is an emergency which doesn't respond to steroids usually and they need anti-androgens such as danazol to stimulate the C1 esterase secretion
Vasculitis (most important things to rule out in purpura: Drug, infection, and autoimmune disease. Malignancy (ovarian and silent ones is a very rare cause that you have to rule out if the pt was clinically free before the purpura onset), Contactants, Idiopathic, SLE (can cause chronic urticaria), thyroid disease, Neoplasm (lymphoma, ca of lung and colon)

- Acute most commonly is due to infection and drugs
- In chronic urticarial we usually fail to find the cause (Idiopathic is the most common cause , 50% disappear after 6 months In acute (food, drugs and pollens are important causes)
- Physical causes (more information mentioned by the doctor):
  - Red dermatographism(commonest) : wheal after scratching the skin, it's associated with urticaria.
  - Cholinergic dermatographism: highly specific any **high temperature** getting sweaty , climbing the stairs he develops a pinpoint like (pen eraser size) urtication on the skin that disappears after few minutes. This is due to the release of Ach from the body heat → no need to investigate , its picked up purely by the pts description
  - White dermatographism is associated with atopy.
  - Cold urticaria: can cause drowning. May be associated with cryoglobulinemia
  - Vibratory urticaria: with vibration. Like people who work on mechanics
  - Solar: many types related to waves of light in the sun.



1-Eraser size (cholinergic urticaria)
2-3Dermatographism
4-Cold urticaria: (after applying an ice cube for 5-20 minutes) happens after rewarming not at the time of cold exposure.

Approach to the patient with chronic Urticaria.

- Start with history (drugs, food, other symptoms i.e. headache , abdominal pain , nasal , chest).
- Simple investigations like CBC (looking for eosinophilia, could be by drug, parasite, lymphoma(hodgekins), very high ESR (rule out malignancy by imaging according to the patients' gender and age "its optional"), rule out infections (ex: stool for parasites) , UA (vasclitis) skin prick test (food and inhalants (IgE)) , CXR, TFT, HCV, metabolic panel

Treatment:

- Elimination or avoidance of the causative agent. i.e. Drug
- **Nonsedating H_1 antagonists**. (the mainstay of treatment for urticaria and histamine mediated disorders) e.g. loratidine , claritine and cetirizine(can partially cross the BBB)
- Sedating H_1 antagonists (we give sedatives in dermatology in case of **itching** and non histamine mediated disorders to sedate the brain) i.e. diaphenhydramine
- Addition of H_2 antagonists ranitidine , cimetidine (lots of drug interactions)
- Corticosteroids (only with angioedema and acute not in chronic urticaria)
- Epinephrine (lifesaving in angioedema and anaphylaxis , give the patient a shot and send him to hospital for further management) → in the form of epipen then shift pt to hospital
- Montelukast (it's an anti leukotriene)
- Thyroxine

- Colchicine
- Sulfasalazine
- Immunosuppressive therapy
- Antimalarial can be given to treat the urticarial vasculitis
- Omalizumab (humanized anti igE monoclonal antibody)
- C1-esterase inhibitor deficiency: (we can't use systemic steroids and or antihistamines epinephrine here**) oral danazole,oral tranexamic acid** (given in excessive menorrhagia too), for emergency : C1 inhibitor concentrate, fresh frozen plasma. Estrogen & OCP should be avoided.

- **In acute emergency episodes:**

-Secure the airway
-I.V. line
-Adrenaline subcutaneous or I.M., repeated every 10 min.
-Diphenhydramine I.M. or I.V.
-Hydrcortisone I.V.
Patients with severe angioedema should be admitted for at least 24 hours observation particularly where laryngeal edema has occurred.

Anaphylaxis

- Essentials of Diagnosis:-
  - Laryngeal edema or bronchospasm or both.
  - Erythema, puritus, urtiaria or angioedma (any or all)
  - Vomitting, cramps, diarrhea.
  - Hypotension, cardiac arrythmia or shocks.

- General considerations:
  - Within minutes to hours, severe may be fatal.
  - **IgE mediated**
  - Chemical mediators are released
  - **Anaphylactoid reactions:** clinically similar reactions that involve the non-immunologic direct release of mast cells (non antigen-antibody) release of similar mediators e.g. (reactions to radiographic contrast media, aspirin, local anesthetics)
  - How is aspirin related to urticaria ? its unlikely to be a direct cause of urticaria , but can increase it , that's why pts with chronic attacks stop aspirin during the attack an resume in between
- Causative agents:
  - Drugs
  - Foods
  - Vaccines and Antisera (anti snake, anti scorpion)
  - Insects – bees, wasps

- Immunotherapy of allergic rhinitis, asthma or stinging insect sensitivity. (when they induce small quantities of allergen, it should be in a place that is prepared for resuscitation)
- Other cases:
  - Iodinated contrast media, aspirin, local anesthetics – anaphylactoid reactions.
  - Treatment of anaphylaxis

Erythroderma and Exfoliative Dermatitis

-Clinical features

Is defined as Erythema with or without scales affecting >90% of the body.

It's common in extreme of ages (neonates (immunity related, BSA in relation to weight) and old age (drug pharmacodynamics , immunity) and they are vulnerable for complications

-Complications:

Hypothermia , fluid and electrolyte loss, infection, HF(increase hemodynamic state), stress induced GIT ulcer, malabsorption, venous thrombosis, hypoalbuminemia due to loss from the skin.

- They behave a poikilothermic animals they adjust their body temperature to the outer one which can put them into the serious complication of hypothermia which is more serious than hyper
- The best outer temperature that suits our body is 23 degrees

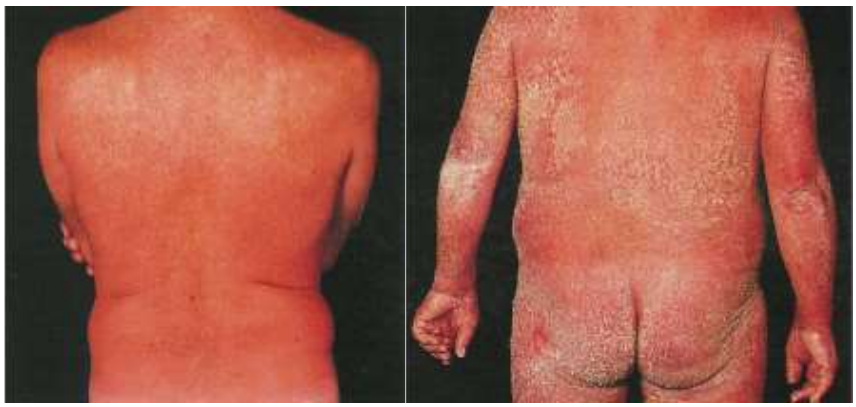
-Drug Etiology:

Sulphonamides, antimalarias, penicillin, phenytoin (carbamazepine (tegretol) , phenobarbitone)allopurinol for gout . steroid and NSAIDS

-Other causes

- psoriasis "it can present for the first time as severe erythroderma"
- drugs
- cutaneous T-cell lymphoma
- Solid malignancies
- severe atopic dermatitis, seborriac dermatitis
- PRP
- Sarcoidosis

- First 3 are the most common
- You have to ask about previous skin diseases and to take a >3 biopsies from different places (unless you're sure of the cause) and if you didn't know the cause repeat the biopsy every 4 months.



Generalized Erythema

Generalized Erythema with scales , erythrodermic psoriasis

Erythema multiforme Major, SJS, Toxic Epidermal Necrolysis

- Steven Johnson Syndrome SJS, TEN May represent variants of the same disease process.
- Clinically: Mucous membrane erosions (you can't diagnose SJS without it . usually the oral and eye mucosa are involved), target lesions
- Epidermal necrosis with skin detachment.
- SJS **< 10%** BSA of epidermal detachment, SJS –TEN Overlap **10-30%,** TEN **> 30%**
- EM minor little or no mucosal involvment, Preceding **herpes labialis** in 50% of EM
    - Systemic symptoms (fever , arthralgia ,sore throat)present in EM major and you will 2or 3 mucusal membrane involvmant & absent or limited in EM minor
    - In the erythema multiform , look for the target lesion . if you can't find them it doesn't exclude the dx . usually we don't see it SJS its atypical and crusted

Suspected etiologic factors: (the more severe the reaction it's a drug, and the less severe is with infections)

- Infections: Suspect an infection with SJS, erythema multiform minor and major (in SJS the most common causative infection is Mycoplasma pneumonia especially in children and in EM minor it's recurrent herpes), also always look for an infection in children. Other infections include histoplasmosis , parvovisrus (ORF virus of sheep nodules)
- **Drugs > 95% in TEN:** (but in SJS is it's around 50%) anticonvulsants, sulphonamides, allopurinol, NSAI.
- Neoplasia
- Collagen disease (less likely with TEN)
- Immunizations (some types of vaccines but not very common)

Risk factors for TEN:

- Slow acetylators (problem in getting rid of the metabolites, they usually have a family history of drug reactions (genetic background))
- Immunosuppression (HIV, Lymphoms) they have a high risk for drug reactions casing TEN because they have acquired **glutathione deficiency**, therefore, they can't scavenger the metabolites.

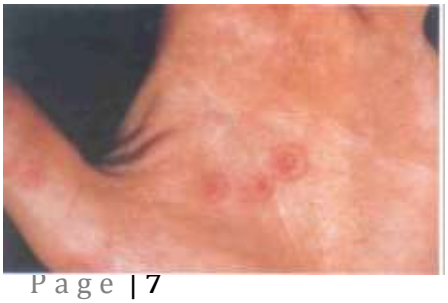
- Radiotherapy & anticonvulsants
- Specific HLA
- FDA recently recommended genotyping of all asians for the allele **HLAB 1502** prior **starting** Carbamazepine

Prognostic factors in TEN: (Mortality rate: 30% with TEN, 1-5% with SJS)
>BSA, extreme of age, low immunity, diabetes, high urea, low sodium bicarbonates (all are bad prognostic indicators), ?Metabolic base may trigger an immune response

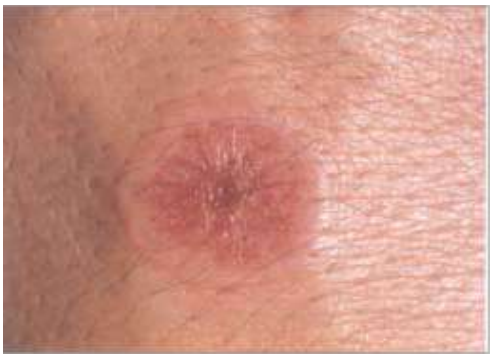
Major cause of death: Septicemia, electrolyte imbalance
Differential diagnosis:
- Pemphigus vulgaris(especially if there was bad oral mucosa involvement),
- SSSS (but it's more superficial and it doesn't have the raw red appearance of TEN),
- Kawasaki in children (they have erythema around the fingers, coronary involvement, conjunctival injection, strawberry tongue but not the chelitis of SJS. They have to be treated with aspirin and immunoglobulins immediately)

Pathogenesis
- Metabolic base may trigger an immune response
- Prognosis: related to extent of skin involvement.
- Mortality for TEN: 30% related to sepsis, fluid and electrolyte imbalance.

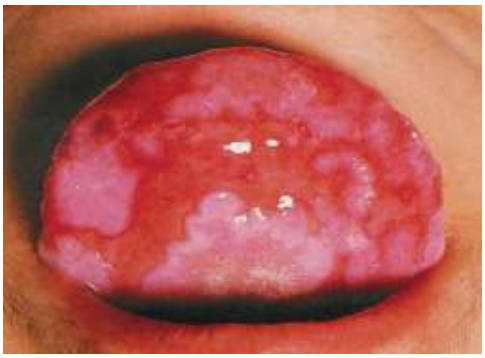
Management
- Early diagnosis, withdrawal of suspected drug
- Patient best cared in a burn (ideal place) or I.C.U.
- Replacement of I.V. fluids and electrolytes
- Don't add unnecessary treatment the pt is already getting a reaction from a drug , adding more will only make things worse
- Systemic corticosteroids-controversial → in TEN we don't start with it , yet in SJS if you start it early in the disease for a short period of 3-5 days may help , but not late as the mortality may increase
- Care for mucous membrane, eye involvement
- diagnose and treat complicating infections (take cultures if you suspect infection)
- pt will need high caloric and protein diet just like burns
- Prevention → never give the causing drug again it create a re-challenge reaction and a worse reaction
- Others which aren't used commonly include immunosuppressant therapy like acetylecysteine IV (used in panadol toxicity, cystic fibrosis (oral)), cyclosporine , these should be given early not late , ifliximab , etanercept



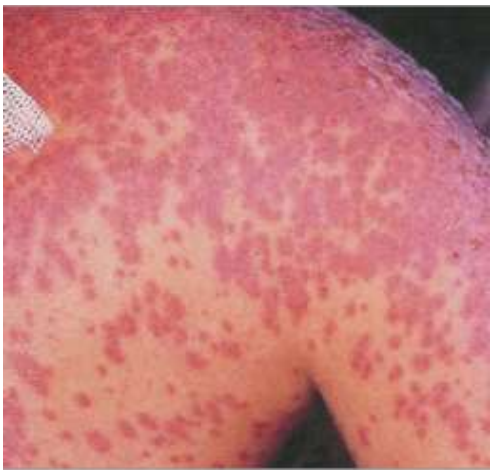
Target lesion classically its three concentric dark rim then light then inner most dark target (could be also in form of papule , vesicle , crust)
But Targetoid → not typical like the ones seen in SJS ,BP,Pemphegoid gestationis in pregnant woman



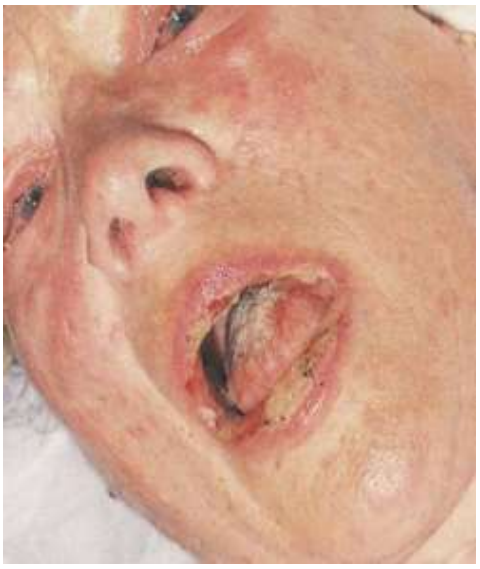
Erythema multiforme minor, crusting from a ruptured vesicle



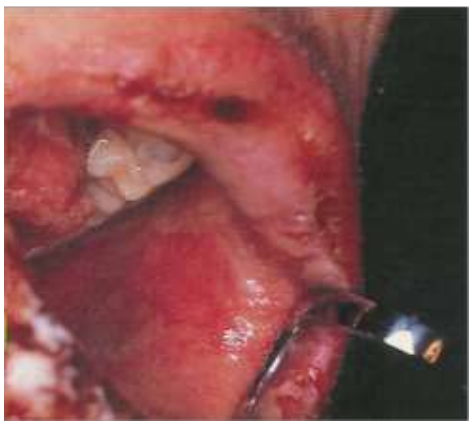
Mucosal involvement (EM major) Not SJS because it has les crustations here



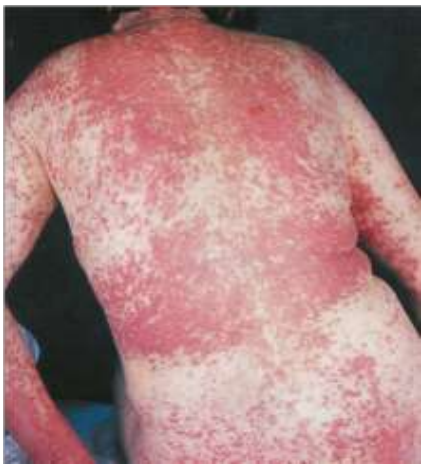
SJS : diffuse macular papular eruption with vesiculation on the shoulder (no target lesions here)



Severe crustation of the lips (severe cheilitis), the oral mucosa and eyes (irreversible damage to the eye) that's why here we need optha consultation or sometimes uro if you are worried about stricture

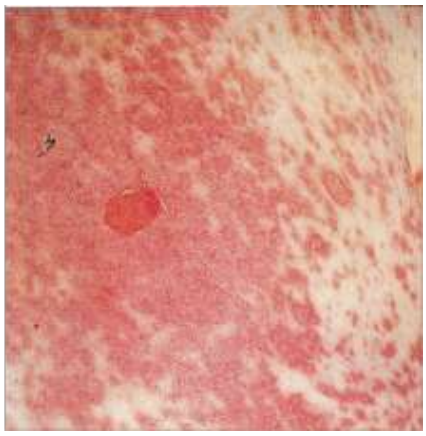


Ulceration of oral mucosa and crusts on the lips along with hard palate involvement

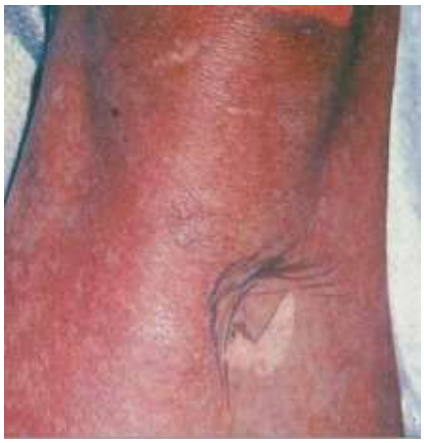


TEN because it's more than 30% of BSA it's early with an associated tenderness

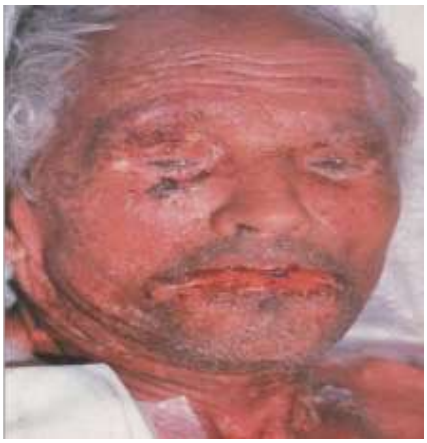
papular eruption



Raw appearance (closer view of the previous picture)



TEN resembles second degree burn if left untreated it will progress to sloughing



Eye involvement . TEN

TABLE 14-3 Kawasaki Syndrome CDC Diagnostic Criteria DDX

Symptom	Percentage of occurrence
Fever lasting longer than 5 days plus at least four of the following:	100%
1. Bilateral conjunctival injection	92%
2. Mucous membrane changes (1 or more)	100%
Red or fissured lips	84%
Red pharynx	72%
"Strawberry" tongue	32%
3. Lower extremity changes (1 or more)	
Erythema of palms or soles	72%
Edema of hands or feet	48%
Desquamation (generalized or periungual)	56%
4. Rash—erythematous exanthem	100%
5. Cervical lymphadenopathy (At least 1 node larger than 1.5 cm)	72%

Data from Velez-Torres R, Callen JP: *Intern J Dermatol* 26:96-102, 1987.

They don't have the cheilitis of SJS
And the peeling happens around the fingers in Kawasaki not all the fingers

TABLE 14-4 Kawasaki Syndrome Other Clinical Findings

Symptom	Percentage of occurrence
Arthralgias	24%
Cough	25%
Urethritis—sterile pyuria	75%
Aseptic meningitis and irritability	25%
Hepatitis—jaundice	20%
Diarrhea	28%
Hydrops of the gallbladder	5%
Vomiting	60%
Cardiac involvement	33%
Myocarditis	6%-24%
Pericarditis	4%
Coronary artery aneurysms	17%-31%

so if you get a 15 yr old with a MI . you must start aspirin and immunoglobulin early

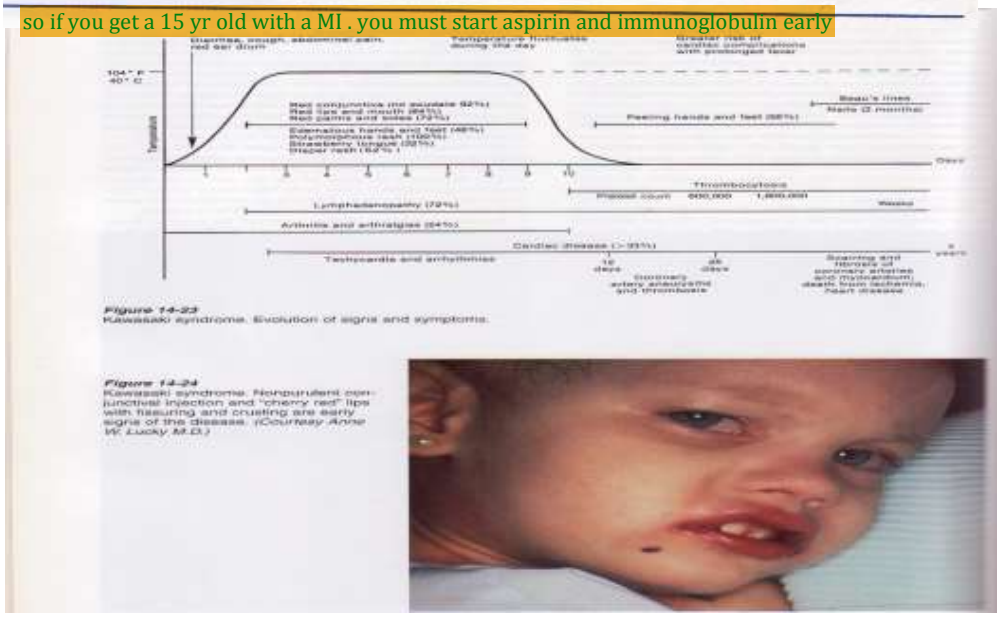


Figure 14-23
Kawasaki syndrome. Evolution of signs and symptoms.

Figure 14-24
Kawasaki syndrome. Nonpurulent conjunctival injection and "cherry red" lips with fissuring and crusting are early signs of the disease. (Courtesy Anne W. Lucky, M.D.)

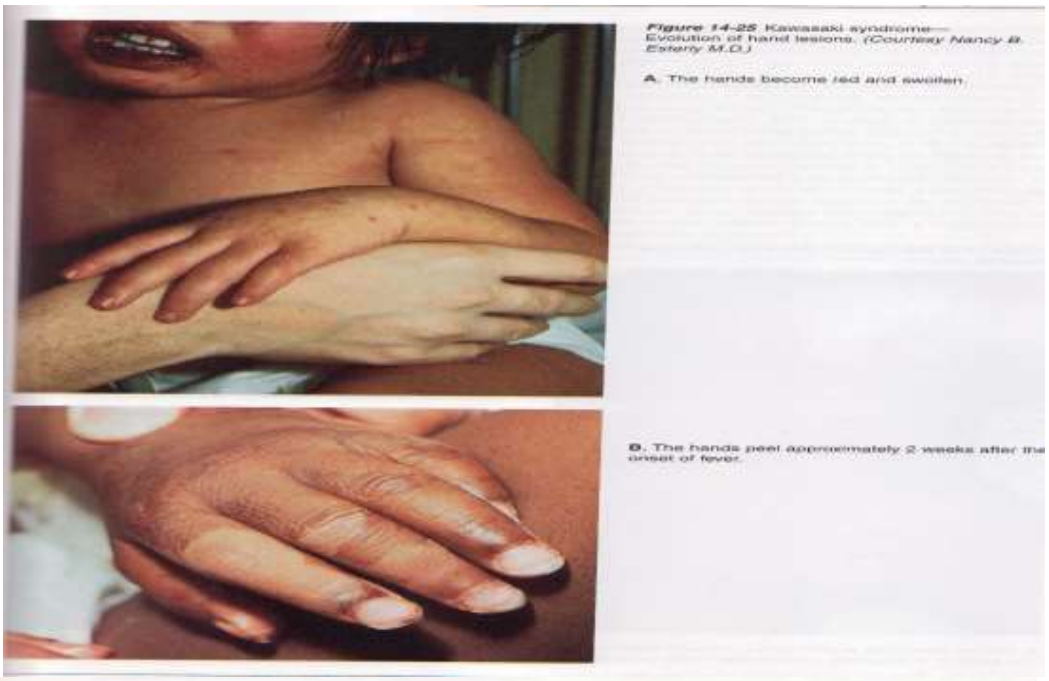


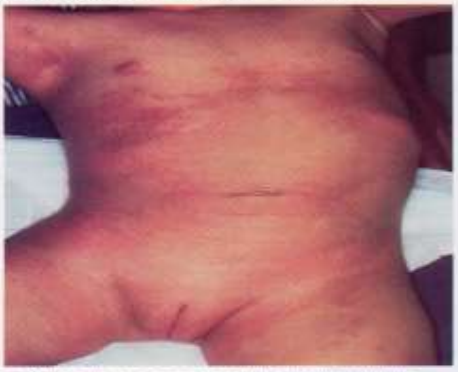
Figure 14-25 Kawasaki syndrome—Evolution of hand lesions. *(Courtesy Nancy B. Esterly M.D.)*

A. The hands become red and swollen.

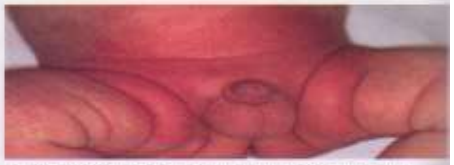
B. The hands peel approximately 2 weeks after the onset of fever.

Rash. A rash appears soon after the onset of fever. Several symptoms have been described. The most common forms are urticarial and a diffuse, deep red, maculopapular eruption (Figure 14-26, *A*). Less often the rash resembles erythema multiforme, scarlet fever, or the erythema marginatum seen in rheumatic fever. Dermatitis in the diaper area is common. The perineal rash usually occurs in the first week of the onset of symptoms. Red macules and papules become confluent (Figure 14-26, *B*). Desquamation occurs within 5 to 7 days. Perineal desquamation occurs 2 to 6 days before desquamation of the fingertips and toes (Figure 14-26, *C*). Vesiculopustules may develop over the elbows and knees.

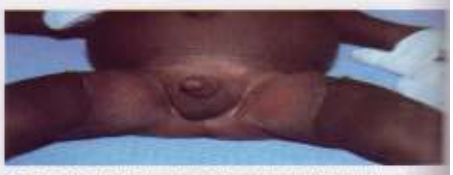
Figure 14-26 Kawasaki syndrome—erythematous exanthem rash.



A. Diffuse, blanching, erythematous, macular exanthem. The eruption is frequently concentrated in the perineal area.



B. Red macules and papules appear in the perineal area 2 to 4 days after the onset of the illness. The rash becomes confluent and desquamates within 5 to 7 days. Desquamation of the fingertips and toes occurs 2 to 6 days later.



C. The skin of children with diaper-area inflammation peels at the margin of the rash. *(Courtesy Anne W. Lucky M.D.)*

Drug Eruptions

Definition: it's the uptake of any substance for any given purpose whether treatment , non-therapeutic or for investigation that would lead to one of the skin manifestations below
Incidence: ranges depending where you take the sample from 1-30 % or even more such as in AIDS pts
Differential risk of adverse drug reactions amongst patient groups:

- Sex →females more than males because they tend to consume more
- Age → extremes of ages . in the elderly because of the low immunity , pharmacokinetic (drug metabolism , distribution , eliminations etc.) and dynamic (action of the drug) changes due to liver and renal impairment
- AIDS→ glutathione deficiency where they can't scavenge certain metabolites of drugs , they also react strongly to septrin (sulfa) in AIDs can reach up to 50 % in comparison to the healthy (population
- Sjogrenis Syndrome→ due to impaired leukocyte dispense . they react more than SLE and RA
- Route of administration→ I.V. Prone to anaphylaxis , but the **most sensitizing root is topical** (e.g. topical antihistamine → this will lead to a cross reaction where you can't use systemic anymore and bad reaction can happen
- Other cross reactions happen with hair dyes , some oral hypoglycemic , sulfa tends to cross react with aromatic compounds like procainamide

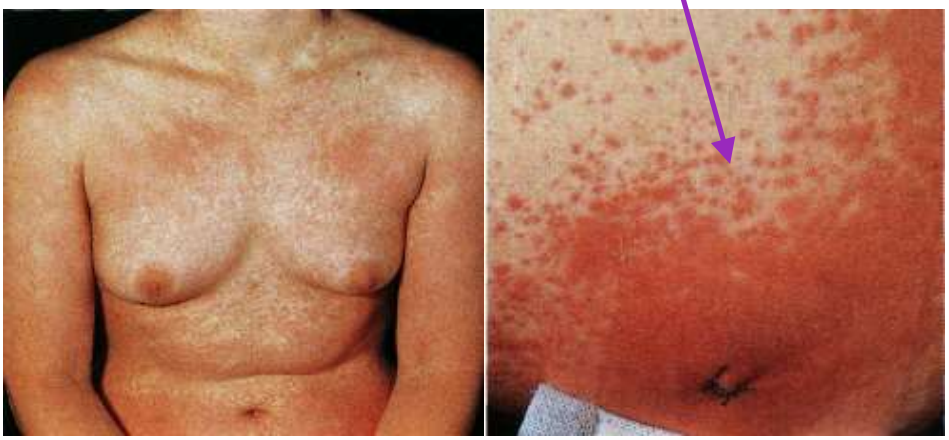
Classification and Mechanism of Drug Reactions

- Non immunological
- Predictable
- Unpredictable like intolerance , idioyncratic reaction ,small dose of drug then suddenly goes into hemolytic anemia
- Immunological → could be type 1 , 3, 4 (cell mediated)
- Unpedictable

Steps in the Approach to a Suspected Adverse Drug reaction

- Clinical Diagnosis
- Analysis of Drug exposure
- Differential diagnosis →viral , SSS ,PV , AGEP (Acute generalised exanthematous pustulosis) other putular drugs vs. drug
- Literature Search
- Confirmation → HX. , biopsy (not 100% , and won't show the drug in the biopsy) you confirm by stopping the drug you will see the reaction subside then you re-challenge by giving the drug but that's unethical especially in severe reactions like TEN
- Advice to the patient → to stop the drug and cross reactions especially when dealing with anti epileptics . they react with sulfa but not sodium valproate
- Reporting to licensing authorities and/ or manufacturer
- Evanescent you mainly face it in the ICU , oncology → they have a chart to track down the causing drug , usually such reactions need two weeks before arising , but other may start earlier or even later like **anti-epileptics** which characteristically start after 2 months
- **Types of Clinical Reaction:**

1. **Exanthematous (Maculopapular) Morbilliform – the most frequent**



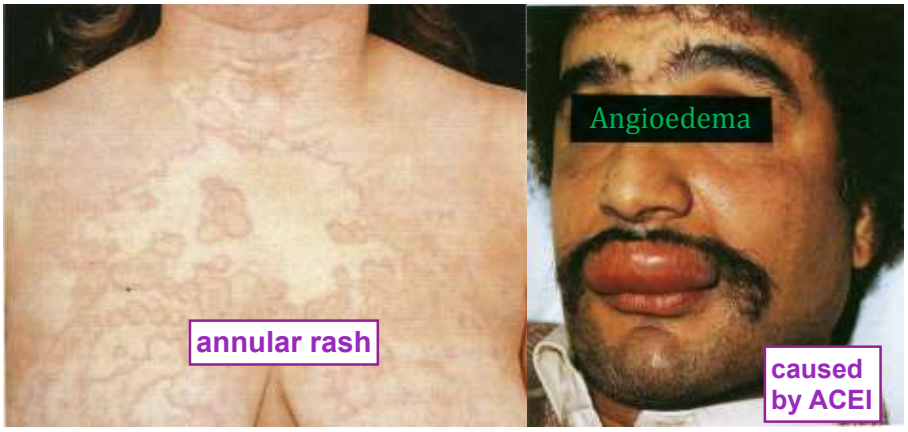
Erythema , macules,
And They have no pustule, vesicle , or blister
Usually seen in children on antibiotic(cefaclor) . and usually in children we confuse it with a viral infection
if it was mild usually we don't have to stop the offending agent
ampicillin and amoxacillin you see it with EBV
resembles scarlet fever

2. **Hypersensitivity Syndrome Reaction**

- **Triad of fever, skin eruption and internal organ involvement. (hepatic , lymph nodes , kidney , pneumonitis)**
- Potentially life threatening syndrome
- First exposure
- **Anticonvulsants (classically)** , sulfonamide, dapsone, allopurinol - most frequently associated with HSR →you address it as phenytoin HSR for example
- Other Drugs : Azathioprine, Minocycline (that's why no longer used in acne because it also causes drug induced lupus , +ve ANA)
- SJS , TEN

high liver enzymes

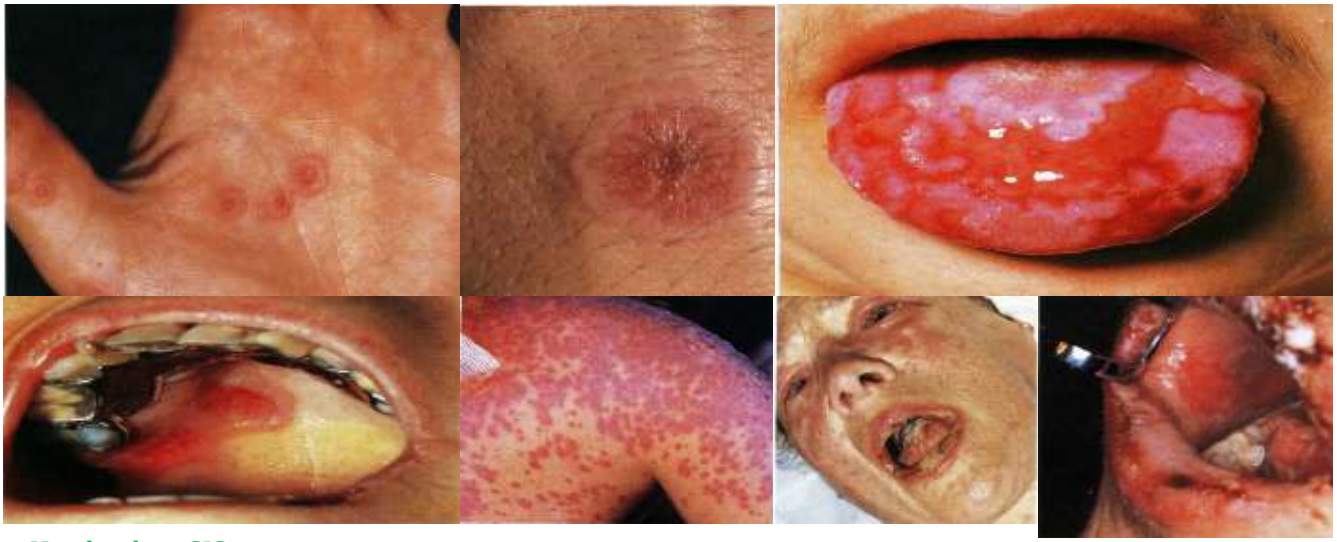
3. **Urticaria, Angioedema and Serum sickness**



4. **Latex Allergy**

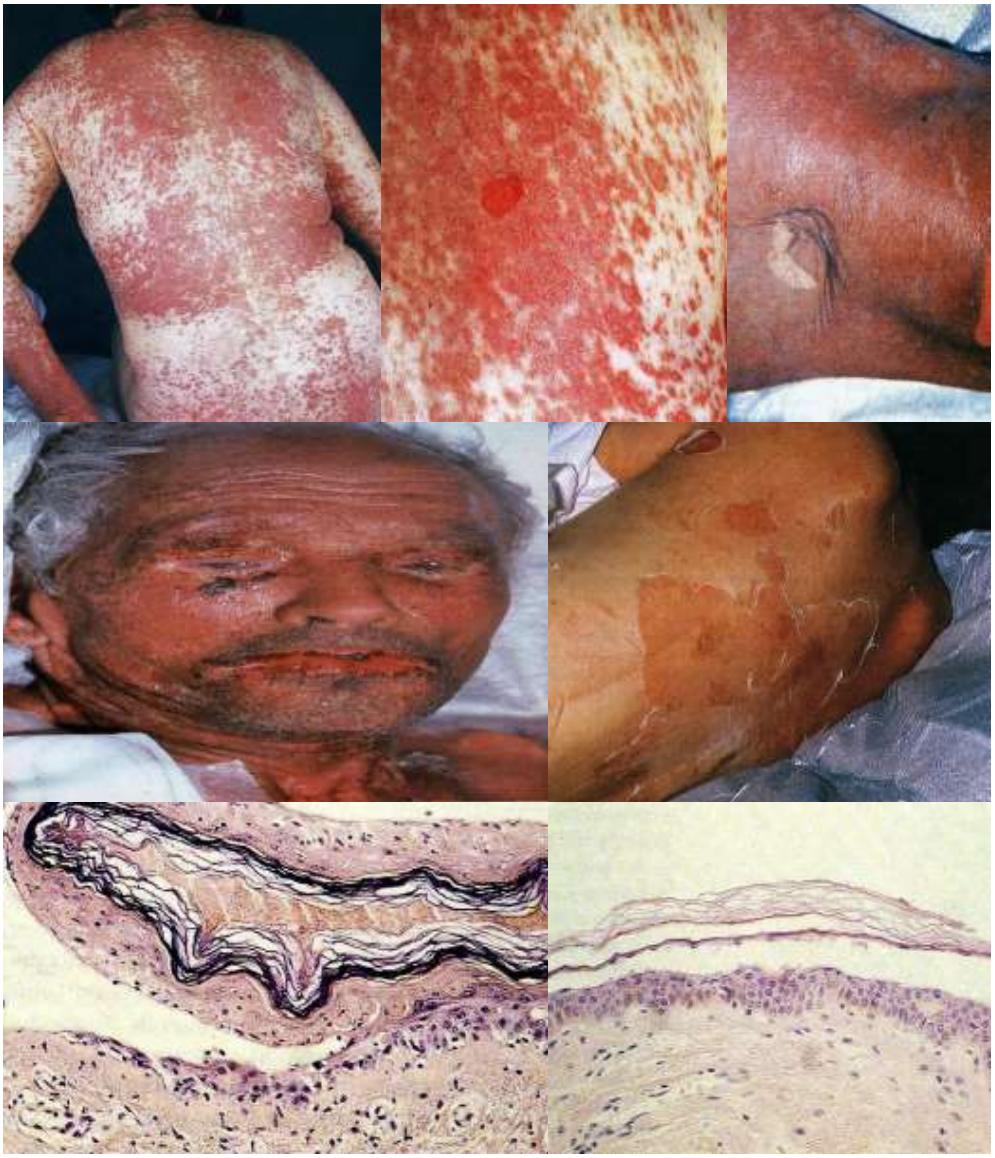
- **Type 1 reaction** to natural rubber latex proteins → sometimes even the smell not only contact triggers a reaction
- Clinical Manifestations – Contact Urticaria, Fatal Anaphylaxis
- Foods that cross react with latex proteins : Banana, Kiwi, Avocado, Chestnuts

5. **Anaphylaxis → type 1 vs. Anaphylactoid reactions→** non-immunological e.g. aspirin , radio contrast media , morphine , strawberry in large quantities
6. **Erythema Multiforme and the Steven Johnson's Syndrome**



Hard palate SJS

7. **Toxic Epidermal Necrolysis**



Dusty erythema , cheilitis , severe mucosal involvement in conjunctiva and the eye

This is SSS an important DDX Here the sloughing is more superficial , its subcorneal

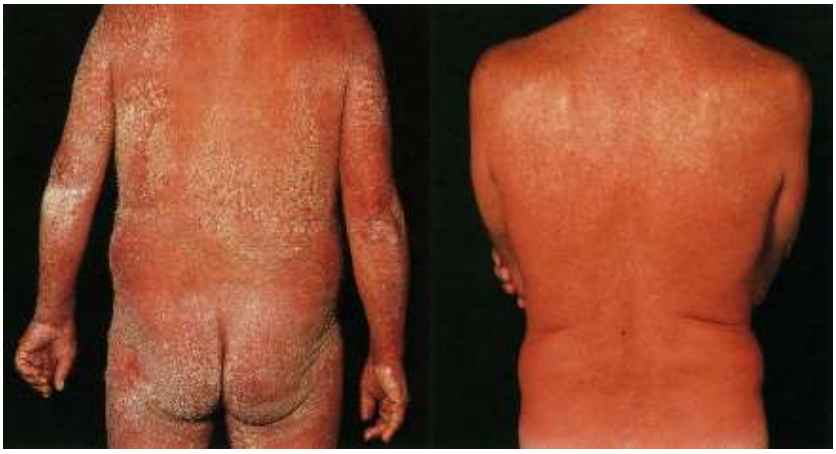
To differentiate the age here is less than 6 years

Histopath of SSS you can see the splitting at the level of the subcorneal epidermal layer

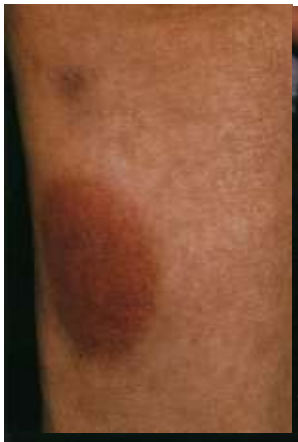
Unlike TEN where all the epidermis is removed

Superficial Epidermal sloughing in TEN like in pemphigus. Outer note: dermatophyte infections in the hand in gives a hard tense blister even though its epidermal why? Because a lot of keratin is there

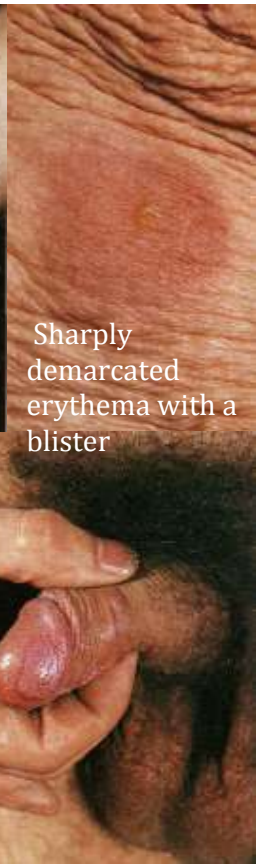
8. **Erythroderma and Expoliative Dermatitis**



9. **Fixed Drug Eruptions**



Most classical form of drug eruption with no other DDX



Sharply demarcated erythema with a blister

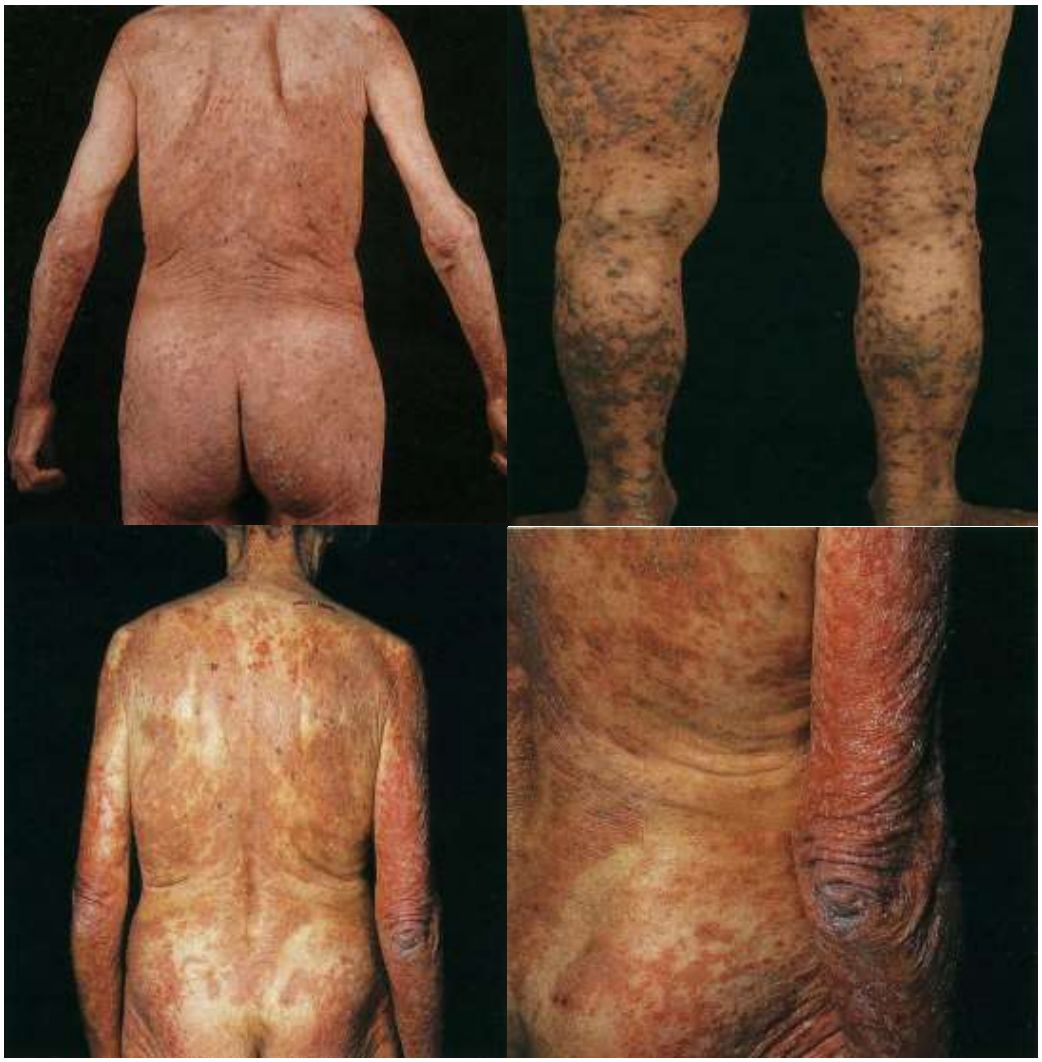
Sharply demarcated erythema with a ruptured blister and an associated crustation

9. A drug reaction that happens the same time and place each time the pt takes the drug

Classically its dark brown , grayish , very well demarcated and round
Can be a result of any drug even paracetamol . can be pigmented or even inflammatory in the form of blistering

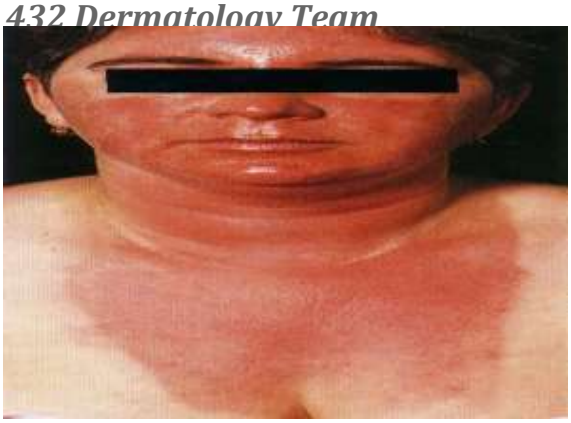
Classical in males in the form of a blister in the glans penis and erythema in the hand .
usually they are young males on minocyline for acne

10. **Lichenoid Eruptions**



Lesion resembles lichan planus , violaceous , scaly , paplules , diffuse (may be localized) , mucosal involvement
It's a more persistent reaction

Psoriasiform → commonly with lithium , BB, anti-malarial



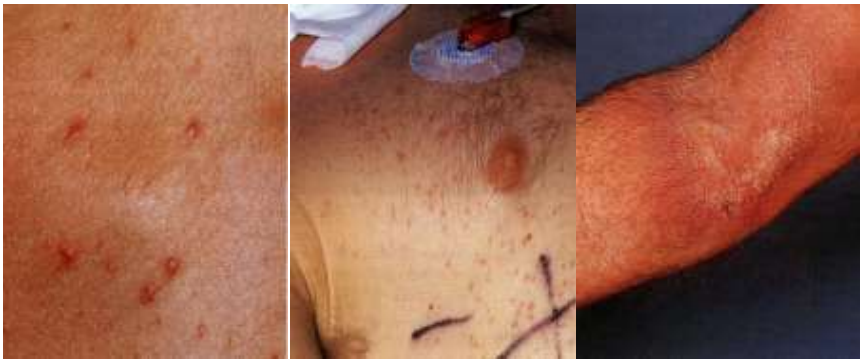
11.Photosensitivity

2 types

1- Photoxic → more common , its non-immune mediated more of an irritation e.g. psoralen , doxacyclin for acne
2- Photoallergic → pt is allergic to a particular component

12.Chronic Antinic Dermatitis

13.PigmentaryAbnormalities



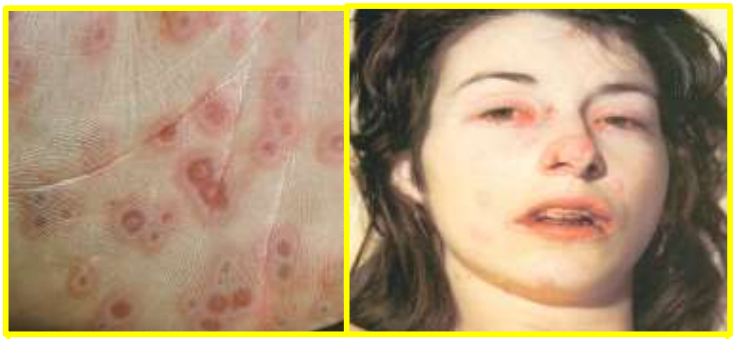
14.Acneiform and Pustular Erupstions

Q : you are called to the ward for a monomorphic papular eruption non-comedonal → steroid

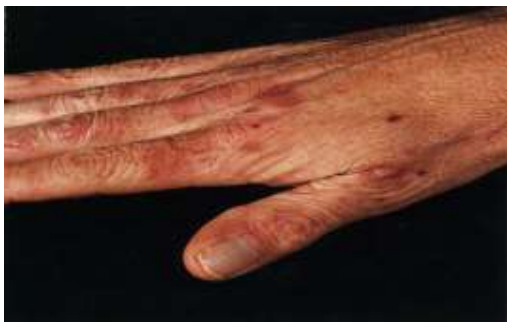
15. Bullous Eruptions

All may have a bullous component:

- Fixed drug eruptions.
- Erythema Multiforme (Stevens-Johnson syndrome, erythema multiform major /minor).
- Drug induced Vasculitis.most common is in the form or purpura , but it can be a papule , vesicle , pustule, blister
- Drug induced TEN (Widespread blistering).
- Drug induced **Porphyria** (abnormality in heme synthesis pathway .the pt will have a blister at the sites of sun exposure) and **Pseudoporphyria** (it happens in patients with renal diseases on dialysis and taking anti-inflammatory or antibiotics "nalidixic acid". They have normal porphyrin level).

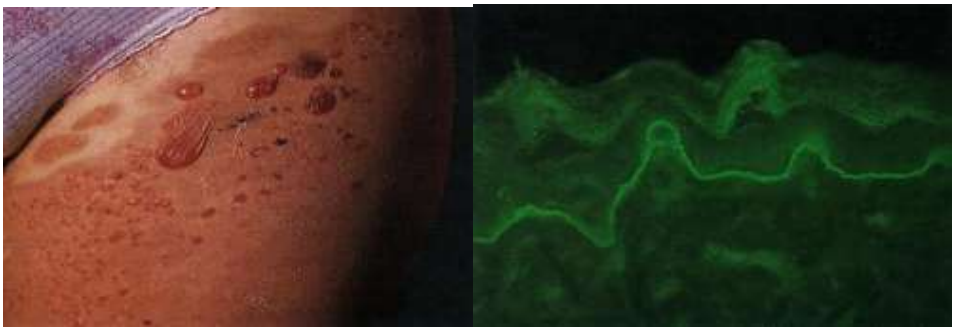


Erythema Multiforme
(Target like lesions that consist of 3 zones dark-light – dark)



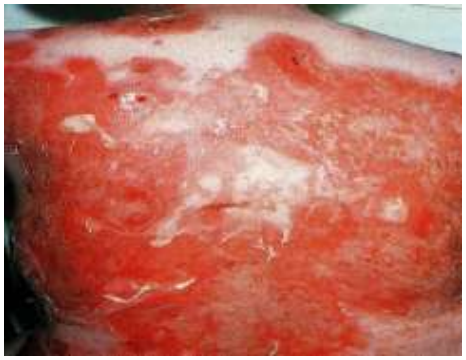
Pseudoporphyria seen in sun exposed area (hand) showing blisters and crustation.

- Drug induced bullous pemphigoid

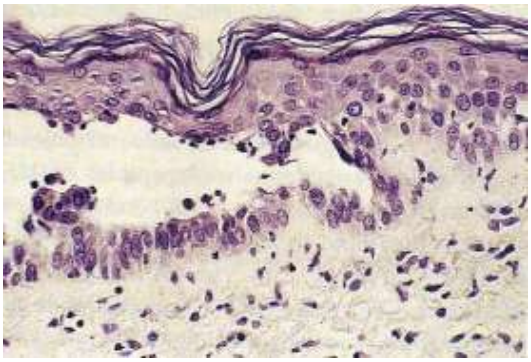


In bullous pemphigoid
→Tense blister because the split under the epidermis (subepidermal.)

- Drug induced Pemphigus



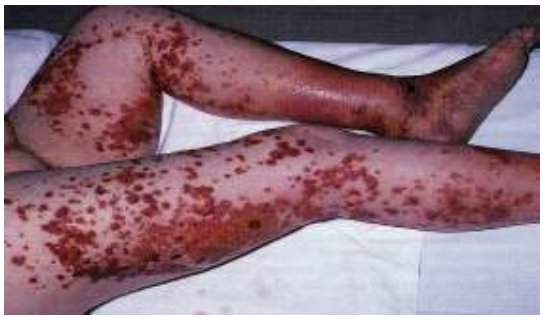
Superficial pemphigus (foliaceus) unlike valgaris of TEN . the more superficial the more crustations you will see and no raw appearance
Classical drug causing it is penicillamines and captopril

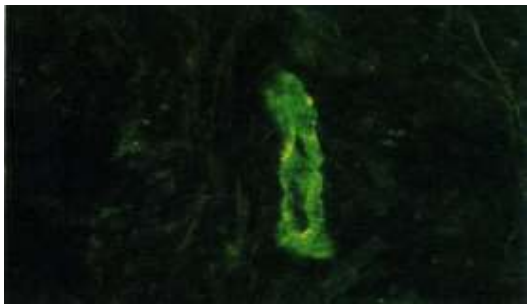


Separation (intraepidermal) above the basement membrane .
n.b. anything below the basement membrane will create a tense type of blister . anything above will create an easily ruptured blister except if caused by a dermatophyte in the hand and feet because of the thick stratum cornea , same with the TEN its subepidermal but there is the sloughing component

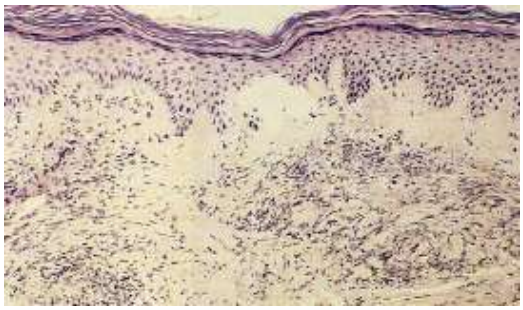
here in the histopath we see Acantholytic cell seen when we have detachment of the keratinocyte in Pemphigus Valgaris

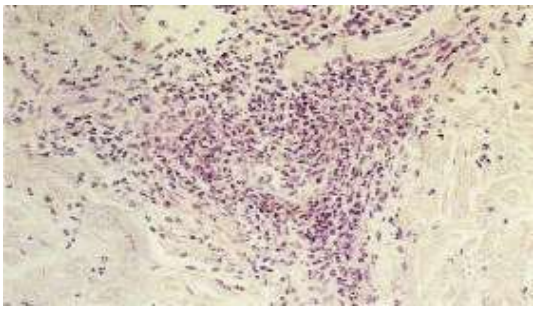
16. Vasculitis





purpura

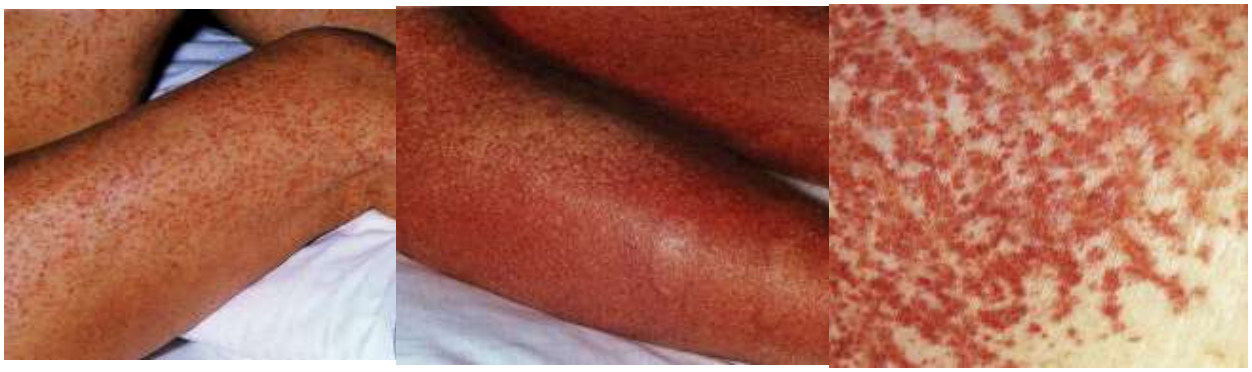




Inflammation around the blood vessel with neutrophil infiltrate

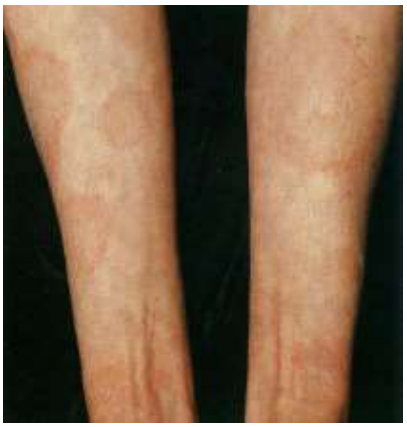
17. Purpura

- **Most common causes of purpura:**
- Autoimmune diseases
- Infections
- Drugs

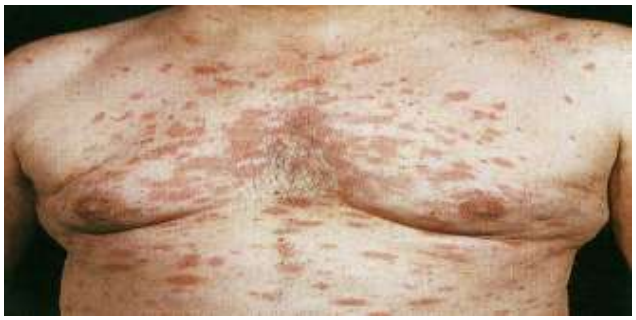


Classical purpuric eruption

18. Annular Erythema

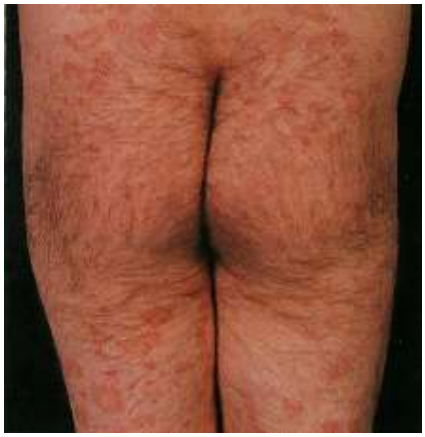


19. Pityriasis rosea like eruptions



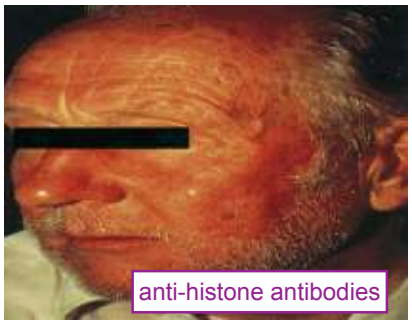
Erythematous , scaly rash running along the **cleavage line** of the skin

20. Psoriasiform drug eruption



Rarely seen de novo from the drug its exacerbated but lichenoid may be initiated denovo

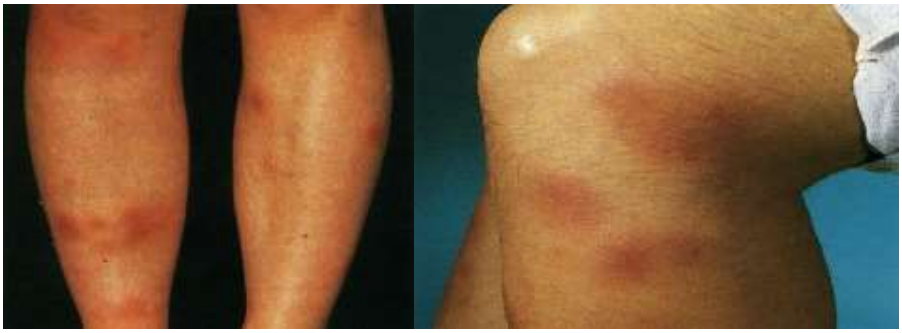
21. Lupus Erythematosus-like syndrome induced by drugs



The most common drugs: Hydralazine,procainamide, sulfonamide, Minocycline, INH

The presentation is milder than the actual disease and once you stop it should resolve

22. Erythema Nodosum



-It is due to inflammation of subcutaneous fat (panniculitis).

- Causes: TB (most common cause in our region), penicillin, tetracycline, OCP. minocinin western counties sarcoidosis and IBD→ to Dx you need a deep biopsy up to fat to determine which subtype septal , lobular , vascular ..

Blistering Diseases

A. Introduction:

Well-circumscribed skin lesions containing fluid, if it is ≤ 5 mm we call it **vesicle**, and if it is > 5 mm it is called **bulla.**

Helpful skin findings in evaluating a patient with blister:

- Distribution: generalized skin and oral cavity.
- Symmetry
- Associated lesions.
- Additional types of skin lesions-urticaria. BP may present with a highly pruritic urtecaria for a long time, up to 1 yr before the blistering . PG aslo
- Characteristic of blisters.

Useful tests in evaluating vesiculobullous diseases:

- Cultures (bacteria, viruses, fungi).
- Smears from blisters (bacteria, dermatophytes, multinucleate giant cells of H.S).
- Skin biopsy – non infectious causes.

Special tests necessary to diagnose blistering skin disorders:

- Routine histology
- Electron microscopy (EM) to diagnose epidermolysis bullosa (EB) "another name: mechanobullous disease".
- Immunofluorescence (IF) to diagnose immunobullous disorders.
- Urine porphyrin to diagnose Porphyria Cutanea Tarda (PCT).

Zinc levels to diagnose acrodermatitis.

- Characteristics of blisters: flaccid or tense.
- Superficial blister: also called **subcorneal** blister (seen in "SSSS", milia caused by miliaria crystallina → obstruction to apocrine glands with excessive sweating it creates an easily ruptured vesicle). The blister rupture easily so sometimes we won't see it.
- Intraepidermal blister: as seen in pemphigus vulgaris. Its flaccid with slouphing
- Pemphigus foliaceus is higher up than vulgaris below stratum corneum (has crustation without raw appearance, less severe than vulgaris).
- The BP and PG are tense and subepidermal below the basement membrane
- For impetigo: order gram stain and culture for bacteria. Herpes simplex and zoster you do Tzank and culture . biopsy here
- Fungal infections are superficial but tense.
- Skin dermatophytes: present as small vesicles between the toes. When we suspect tenia I'm not sure) do scraping for KOH and fungal culture, then we order biopsy for HIV, H&E stain and for IF when we suspect autoimmune disease.
- "Acrodermatits is due to zinc deficiency could be inherited in children or acquired in adults mostly among alcoholics and malnourished individuals. Blisters with crustation are periorofacial (mouth , anus , genetalia i.e. body openings).

- Blister: well-circumscribed skin lesion contains fluid, pus, blood, or can be clear. Sized between 0.5-1 mm. small→ vesicle , large→ blister
- Blisters are not always caused by autoimmune diseases reaction.
- Blisters could be caused by:

1. burns
2. infections (herpes simplex, herpes zoster (dermatomal): the patient suffers from severe neurotic pain days before the appearance of blisters, impetigo: honeycomb thrust blisters over the umbilicus stump or nasopharynx, coxsackie or any funny viral infection "hand, foot, mouth disease").
3. Friction (mechanical)
4. Allergic reaction
5. Contact dermatitis → vesicle and eczema complex "deep seated blisters" vesicle around the fingers
6. Drugs → bullous fixed drug eruption , erythema multiformi , porphyra and psuedoporphyra , BP
7. Insect pits → lower lip and exposed area
8. Diabetic bullae "diagnosis of exclusion → do IF, skin biopsy, and examine for autoimmune disease".
9. Lupus.

- The most important reliable and sensitive and specific method to diagnose autoimmune disease is direct immunofluorescence (IF).
- Helpful skin signs when evaluating a patient with blisters: distribution and the involvement of the oral cavity (as seen in pemphigus vulgaris→ the pt presents for years as such at the dentist before being discovered), generalized or localized, symmetry of the rash, associated skin lesions like urticaria.
- There is an entity in children called mechanobullous epidermolysis bullosa disease it's a genetic disease with different mode of inheritance characterized by blister formation at birth or early childhood they will have a blister with any minimal injury

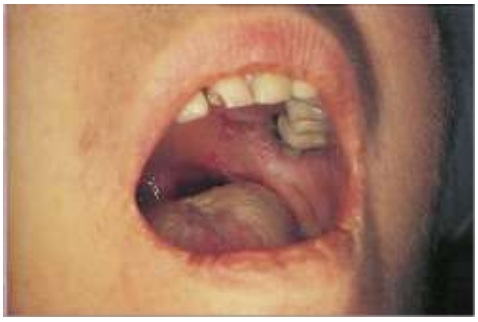
B. Pemphigus:

- ✓ Flaccid blisters intraepidermal, weeping painful erosions.
- ✓ Mucous membrane involvement. → may be the starting lesion
- ✓ Positive Nikolosky's sign. sloughing of the intact skin next to the blister.
- ✓ Positive asboe – Hansen sign or (bulla spread sign). spread of the bulla when we press over it.
- ✓ Acantholysis and intra-epidermal cleft. IgG auto antibodies attack desmosomplyin which adheres keratinocytes together, results in detachment of keratinocytes and floating of cells. This is mainly in Vulgaris
- ✓ **IgG and C3 in the intercellular space of epidermis. Very characteristic .**Another disease which produces such a picture is carotinemia
- ✓ IF: surface antibodies to epidermal cell surface antigens – titer reflects disease activity.
- ✓ Rare, lethal, autoimmune blistering disease.
- ✓ Age – sixth decade of life. M=F , strong genetic predisposition . more common in jews up to 17/1m in the kingdom its mainly In the south
- ✓ Classification of pemphigus:

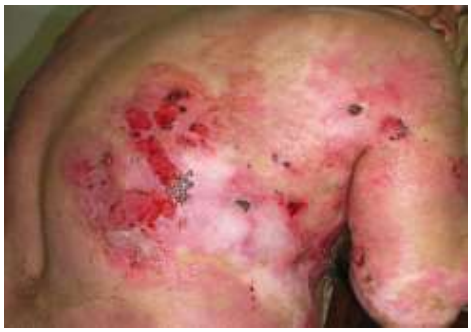
1. Pemphigus vulgaris→ blistering and fatal
2. Pemphigus vegetans→ nodules could be transmitted to p.vulgaris if not treated properly.
3. Pemphigus foliaceus→ in the epidermis and below the stratum corneum
4. Pemphigus erythematosus: localized resembles SLE (more benign and localized with crustations).
5. Pemphigus fogoselvagem: endemic is seen in Tunisia and Brazil due to **black fly** insect pits in people with genetic tendency to develop pemphigus.

6. Drug-induced pemphigus→ is seen with the use of penicillamines and Captopril (sulfahydryl) . it happens in genetically predisposed individuals
7. Paraneoplastic pemphigus→ with chronic lymphocytic leukaemia, nonHodgkin's lymphoma and other malignancies. In histo you see it as a mixture of LichenPlanus ,Erythema Multiformi, and pemphigus
8. IgA pemphigus →Rare

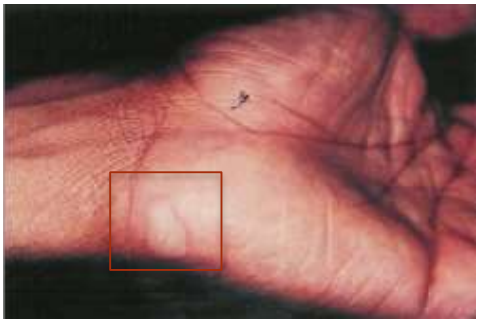
- Pemphigus: a group of autoimmune diseases, one of the most lethal dermatosis in dermatology and the patient might die if we didn't treat it properly.
- Systemic steroids are life-saving among pemphigus patients.
- Pemphigus vulgaris is an autoimmune disease characterized by skin and **mucous membrane** involvement (opposite to bullous Pemphigoid).



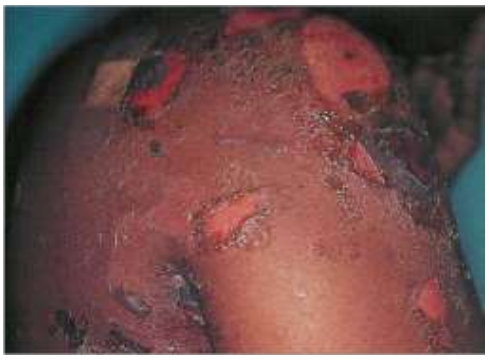
The starting lesion of pemphigus, painful ulcer in the palate that can stay for a few months up to one year without skin involvement. We diagnose by direct immunofluorescence



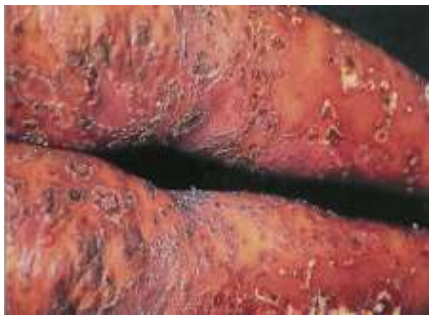
The superficial type of pemphigus "pemphigus foliaces". With a lot of superficial erosions and crustations.



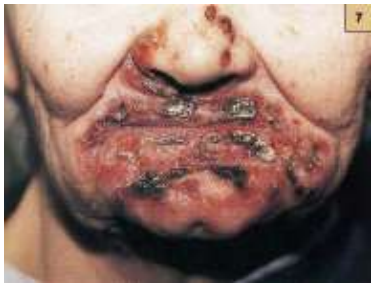
Blistering non blistering → early lesion of pemphigus



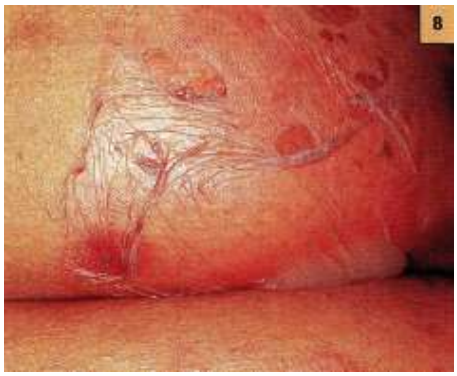
Many crustations of the superficial type of pemphigus + erosions



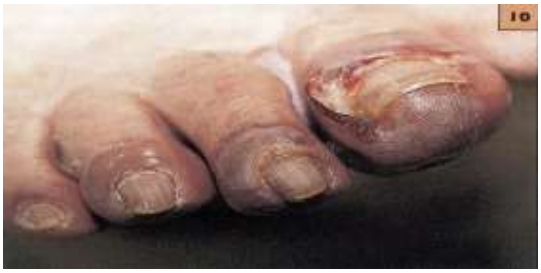
Multiple crustations "pemphigus foliaceus". Its mild



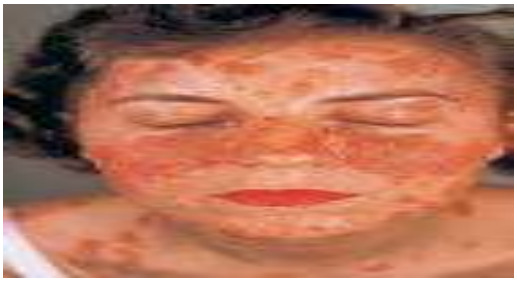
Multiple crustations "pemphigus foliaceus".



The classical pemphigus vulgaris, scalded like there is sloughing of the entire epidermis "severe"

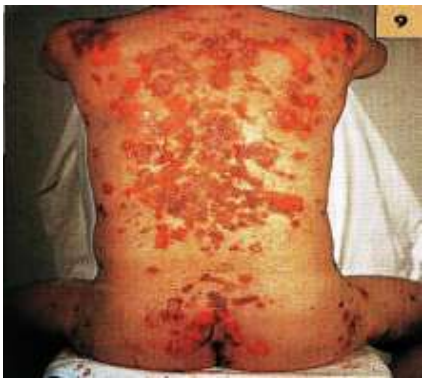


Localized type of pemphigus "pemphigus vegetans".

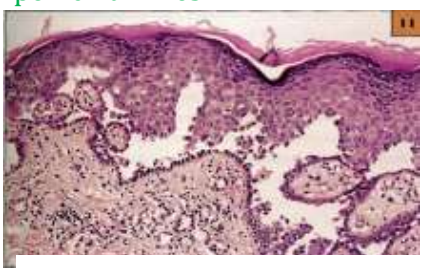


Pemphigus erythematosus. Subtype of vulgaris seborrheic dermatitis like picture , lupus like picture

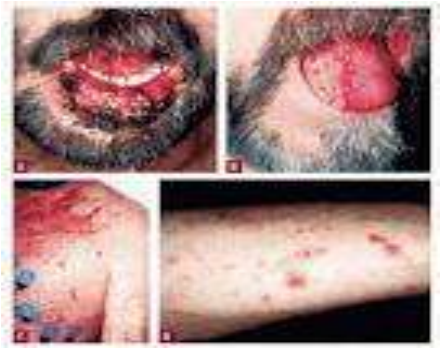
Axilla with papule and nodule like lesions → pemphigus vegetans (usually in flexures)Localized type if left untreated with turn to the severe vulgaris form



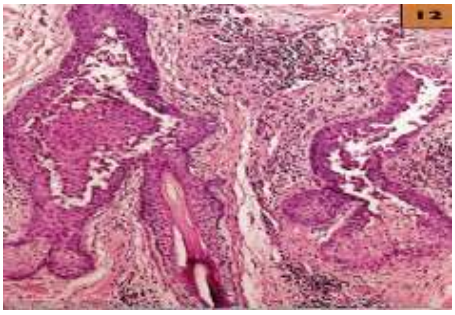
Drug induced pemphigus . you see a lot of erosions with penicillamines



White = blister
Inside = acantholytic cells floating in pemphius



Paraneoplastic with many findings , lichenoid , blistering , crustations
Do a biopsy



Direct IF shows intracellular deposition of IgG and C3 in pemphigus vulgaris.

Investigation:

1. Skin biopsy – light microscope.
2. Immunofluorescence: **IgG and C3 in intercellular substance of epidermis**. Levels reflect the activity of the disease.

Treatment:

1. Systemic corticosteroids.
2. Immunosuppressive therapy (e.g. Azathioprine, Mycophenolate, Mofetil, Cyclophosphamide). Steroid sparing
3. IVIG (Intravenous immunoglobulin) for resistant cases.
4. Anti CD-20 for resistant cases, Rituximab

- Pulse steroid can be used for resistant cases but there is a risk of arrhythmias, so we have to monitor the patient.
- The patient will develop steroid-side effects after using it for 6 weeks, and to avoid these side effects we should switch the patient gradually to immunosuppressive therapy.

C. Pemphigoid:

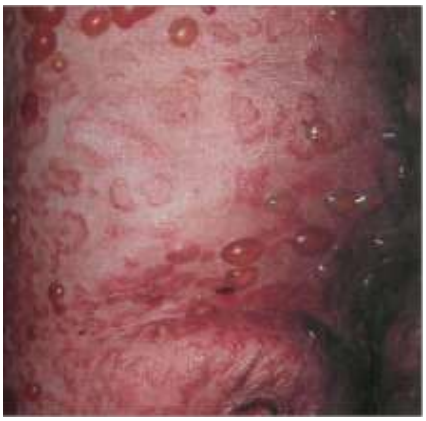
Bullous Pemphigoid, Herpes Gestationis, Cicatricial Pemphigoid: group of autoimmune sub-epidermal blistering disorders with circulating IgG and basement membrane zone (BMZ)-bound IgG antibodies (ABS) and C3.

1. Bullous Pemphigoid:

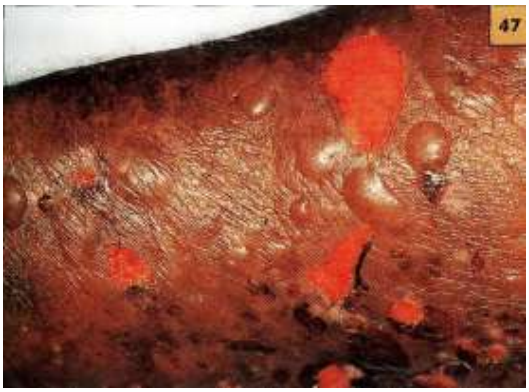
- ✓ Large bullae on erythematous plaques or normal appearing skin.
- ✓ No or only mild involvement of mucous membrane.
- ✓ **Sub-epidermal blister. So it's tense**
- ✓ **IgG, C3 at dermal-epidermal junction.**
- ✓ Antibodies against the basement membrane zone in the patients' serum.

- ✓ Age : Elderly
- ✓ Relatively benign
- ✓ Clinical manifestation:
- Local Erythema, Urticaria, Pruritus
- Tense blisters, lower part of abdomin, groin, flexors of Arms & legs.
- Negative Nikolsky's sign
- Course: Variable, untreated B.P. Localized, Spontaneous Remission, generalized.
- **Drug induced are not typical and you find them in acral , palms and soles**

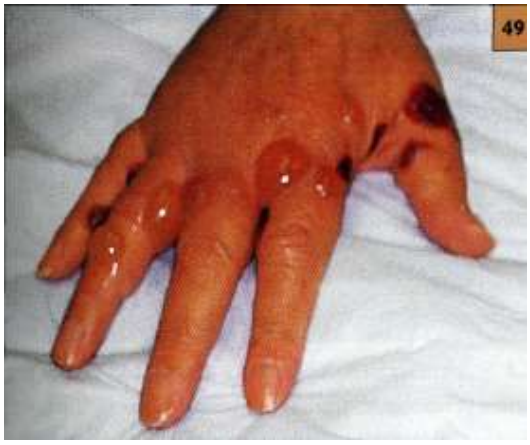
- **Diagnosis:**
  - ✓ CBC: Eosinophilia - 50%
  - ✓ IgE: - 70%
  - ✓ HIST → subepidermal blister
  - ✓ DIF most sensitive and specific
  - ✓ IIF
- **Rx**
  - ✓ Topical (if mild/localized bulla or urtication)
  - ✓ Systemic: Steroid
  - ✓ Antibiotics: Tetracycline, Minocin"Minocycline" as an anti inflammatory for mild and localized disease.
  - ✓ Dapsone
  - ✓ Immuno Suppressive
  - ✓ (Azathioprine, Mycophenolate, Mofetil)
  - ✓ In resistant cases : ivIg ,anti –CD20 immunotherapy (rituximab)



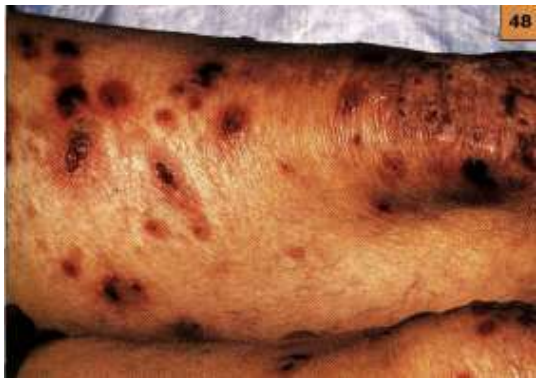
Multiple tense bulle some of them may be hemorrhagic, with crustation, little arythemia somewhat annular, the patient might present with urticated-like lesion about one year before the appearing of blister + it's very itchy.



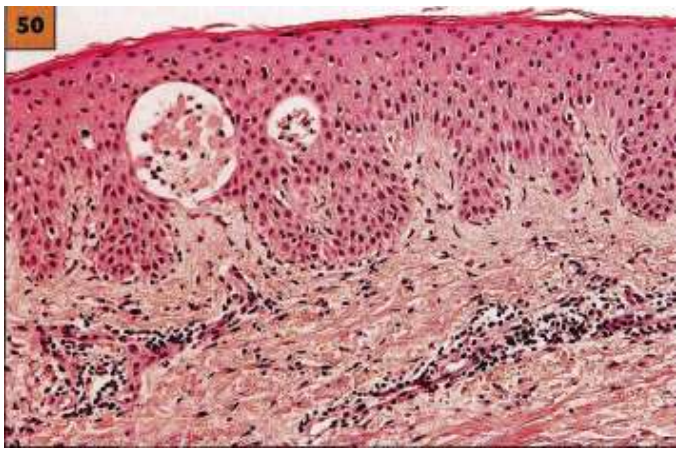
Erosion of ruptured tense blister in BP.

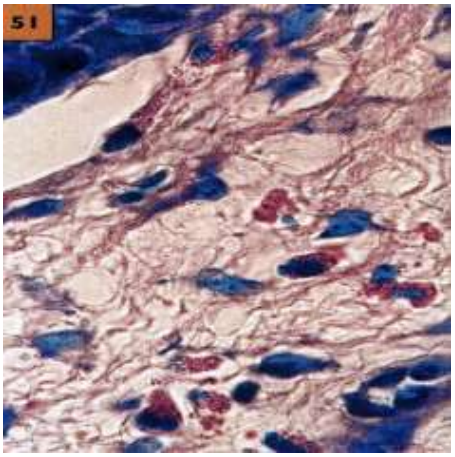


Tense blister and crustations in BP.



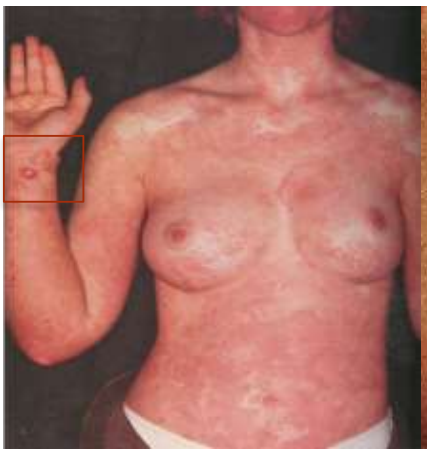
Multiple crustations after rupture of blister in BP.



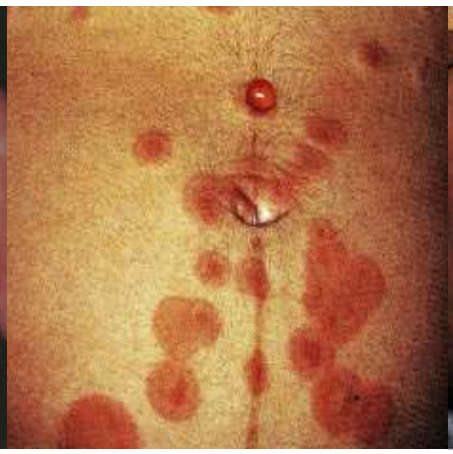


D. Pemphigoid gestationis:

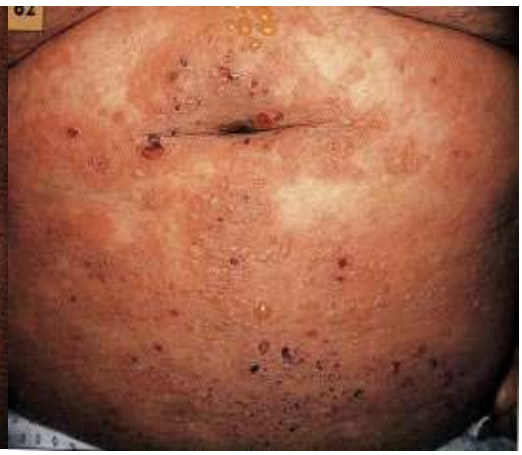
- ✓ Commonly seen among pregnant ladies. Called herpes Gestationis = resemble herpes because its vesicular but it's not actual herpes
- ✓ Erythematous urticarial Plaques, alone or with papules, vesicles, blisters, erosions, most on abdomen, proximal extremities.
- ✓ Intense pruritus
- ✓ **Sub epidermal** blister (Basement membrane zone)
- ✓ C_3 (more than IgG), IgG at BMZ, H.G. Factor in Patient's Sera
- ✓ Usually starts at the 2nd, 3rd Trimester.
- ✓ Flares at post partum, OCP (never give OCP in a patient with PG in the first weeks postpartum)
- ✓ Purely anti-HLA antibodies from the paternal placenta and so The more the peak of pregnancy = the patient will get it earlier with each pregnancy. Occasionally up to 5% it may skip a pregnancy
- ✓ Treatment is potent steroids, avoid the systemic in the 1st trimester.
- ✓ Topical drugs, drying agents and antiseptic to prevent infections "caring for the blister"
- ✓ For blisters = systemic therapy.
- ✓ For pruritis = anti histamine.
- ✓ S/E of medications = small for gestational age sometimes prematurity due to the disease



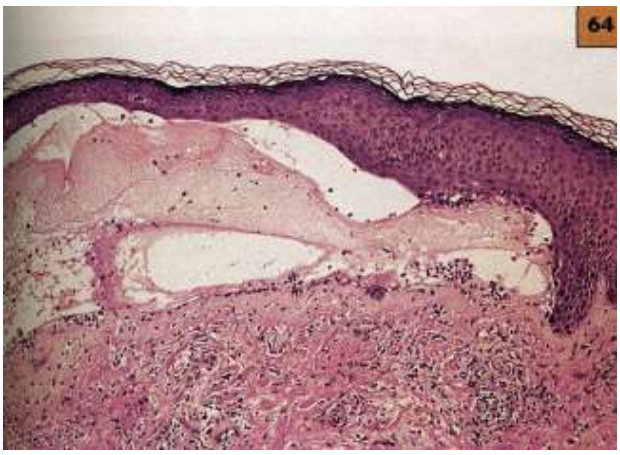
Wide spread Erythema and urtication. With tense blisters on the right wrist



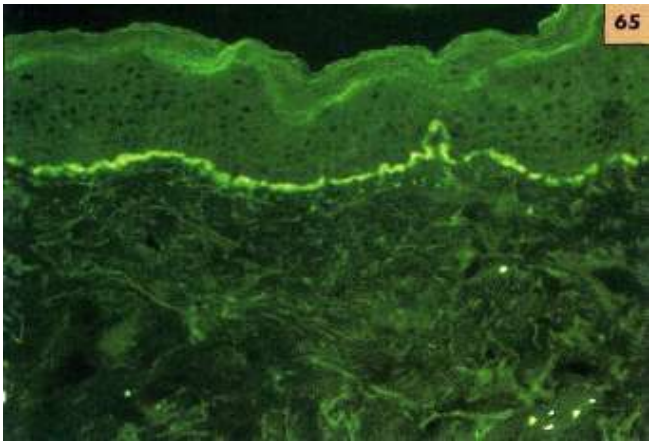
-Tense blister and multiple periumbelical **targetoid** lesions in the abdomen in PG.
-BP and PG can have targetoid lesions as well.



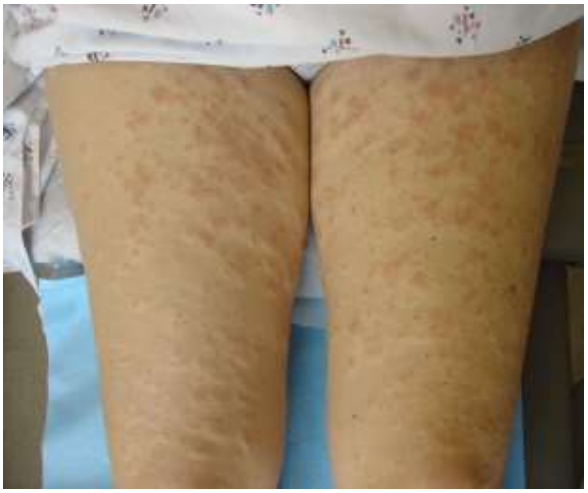
Blisters and vesicles in PG.



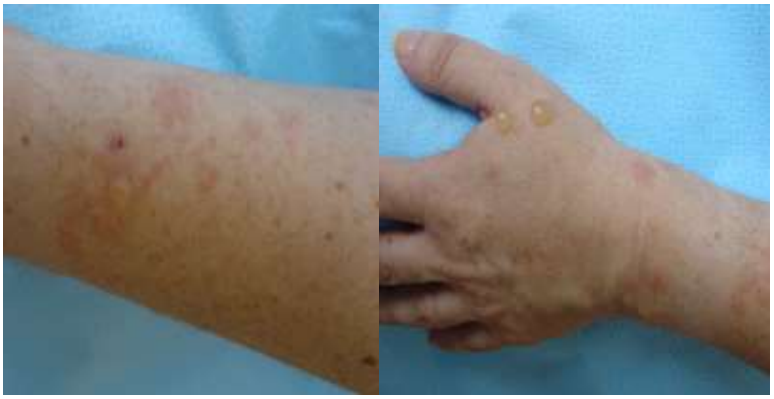
Subepidermal blister in PG.



IF shows C3 and IgG deposition in the BM



PUPPP disease of pregnancy: pruritic urtication papules and plaques of pregnancies could be confused with BP, that's why we need to do biopsy.



Tense blister

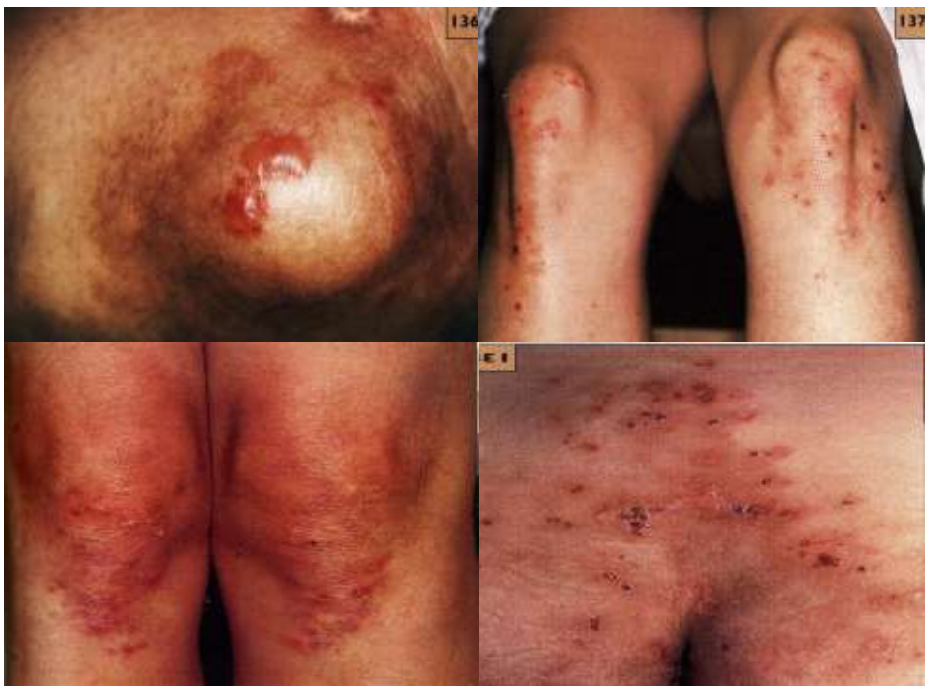
E. Dermatitis herpetiformis

- ✓ **Severe Pruritis**
- ✓ Associated with gluten sensitive enteropathy. Related to celiac disease "same AB"
- ✓ Pruritic tense blisters on extensors
- ✓ **Pathology**
  - Sub epidermal blister, prominent neutrophil infiltration
  - Dif: granular IgA in dermal papillae

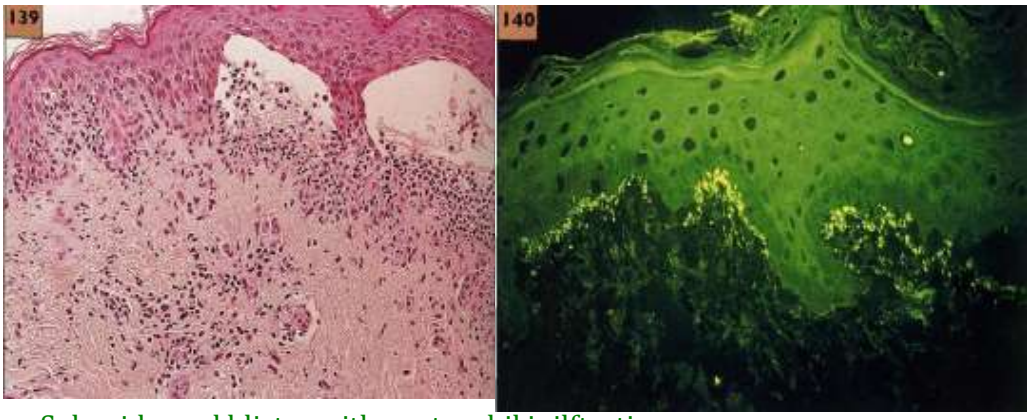
- ✓ **Treatment:**

  - Gluten free diet
  - Dapsone – 1st line of treatment
  - Sulfa pyridine- 2nd
  - Tetracycline and Nicotinamide in localized

Dermatitis Herpetiformis:
Autoimmune disease characterized with severe pruritis in the form of a vesicular eruption , most of the time we won't see any blisters because it's very pruritic and the patient will excoriate the rash before the appearance of blister.
It comes in groups over the elbows, lower and upper back.
To role out DH = do IF
Could be one of the invisible dermatosis, only capiliary pruritis. If we take a biopsy from the normal skin "covered area" you will find IgA granular deposition "characterstic for DH".
Same as celiac disease antibodies but in the skin . There is risk of developing intestinal lymphoma if not treated . first drug of choice is dapsone not systemic steroids



Multiple scratches with no blisters or vesicles in the extensors



Subepidermal blister with neutrophil inilftration
And IF shows dermal IgA in the dermal papillae