Adverse Cutaneous Drug Manifestations

Objectives :

Not given

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[Color index : Important | Notes | 433 notes | Extra]

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
- Most commonly in ICU and oncology patients. Scenario of elderly patient with multiple comorbidities or oncology patients on multiple medications.

Differential risk of adverse drug reactions amongst patient groups:

- Sex → females more than males (more medications than males)
- Age → extremes of ages. In elderly because of low immunity, pharmacokinetic (drug metabolism, distribution, eliminations, etc.) and dynamic (action of the drug) changes due to liver and renal impairment. Children 5% < Adults 30%
- AIDS → glutathione deficiency → 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.
- Sjogren's Syndrome → due to impaired lymphocyte response (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 intolerance, idiosyncratic reaction, small dose of drug then suddenly goes into hemolytic anemia
- **Immunological** could be type 1 , 3, 4 (cell mediated)
  - Unpredictable

Steps in the Approach to a Suspected Adverse Drug reaction:

1. Clinical Diagnosis cause and morphology
2. Analysis of Drug exposure. Viral vs Drug induced. Some viral illnesses like infectious mononucleosis can cause reactions to ampicillin.
3. Differential diagnosis

a. Viral, SSS, PV, AGEP (Acute generalised exanthematous pustulosis)
b. Erythroderma → Drug vs Psoriasis vs Cutaneous T cell lymphoma
c. Morbilliform rash in children → drug vs viral

4. Literature Search
5. Confirmation

a. Stop the drug to confirm. Not always feasible because some drugs have a long half life. Then re-challenge by giving the drug but it's unethical especially in severe reactions like TEN.
b. Hx., biopsy (not 100%, and won't show the drug) you confirm by stopping the drug you will see the reaction subside

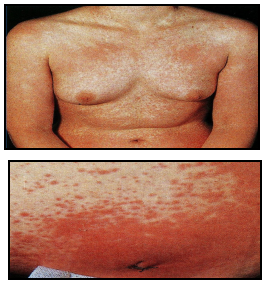
6. Advice to the patient to stop the drug and cross reactions especially when dealing with antiepileptics. They react with sulfa but not sodium valproate.
7. Reporting to licensing authorities and/or manufacturer

a. 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 antiepileptics which characteristically start after 2 months

Types of Clinical Reaction:

1. Exanthematous (Maculopapular) Morbilliform (2nd picture) – the most frequent

- Least serious and resolves spontaneously
- Erythema and macules, no pustule, vesicle, or blisters
- Usually seen in children on antibiotics (cefaclor).
  - If it was mild usually we don't have to stop the offending agent (ampicillin and amoxicillin) seen with EBV resembles scarlet fever
- Usually misdiagnosed as a viral infection
- Causes: penicillins, carbamazepine,allopurinol, gold salts

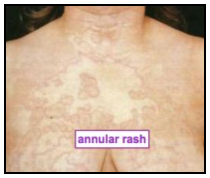


2. Hypersensitivity syndrome reaction

- An idiosyncratic serious (could lead to death) adverse drug reaction that involves skin and other organs.
- **Triad of fever, skin eruption and internal organ involvement.** (**hepatic** increased enzymes, 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** (no longer used in acne. Causes drug induced lupus, +ANA)
- SJS, TEN

3. Urticaria, angioedema, and serum sickness

- Transient wheals and/or large and deep skin colored swellings
- flushing, yawning, airway edema, sneezing, bronchospasm, laryngeal edema, hypotension, vomiting, diarrhea, arthralgia

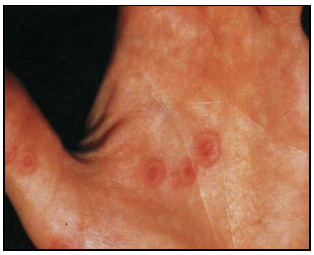


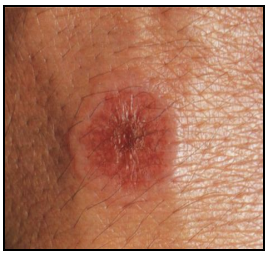
4. Latex Allergy

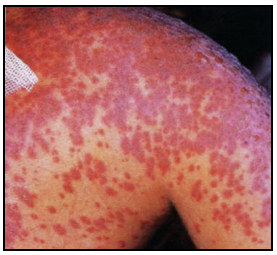
- Type 1 (IgE mediated) reaction to natural rubber latex proteins sometimes even the smell not only contact triggers a reaction
- Usually seen in children who are frequently examined (e.g. spina bifida) or nurses after taking off gloves could inhale latex particles and cause anaphylactic shock.
- Clinical 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, radiocontrast media, morphine, strawberry in large quantities

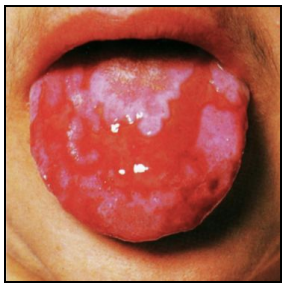
6. Erythema Multiforme (target lesions) and Steven Johnson's Syndrome

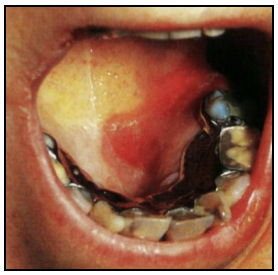


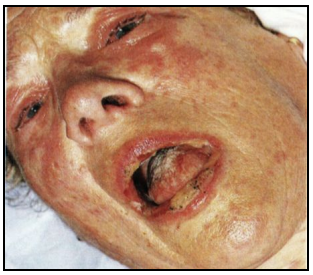




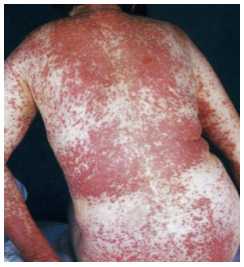
Erythema multiforme can be caused by drugs or more commonly herpetic.

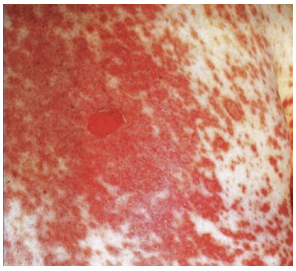


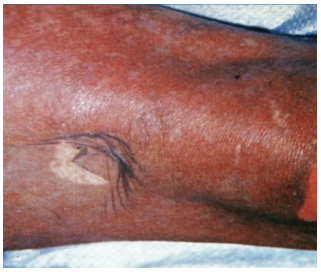




7. Toxic Epidermal Necrolysis



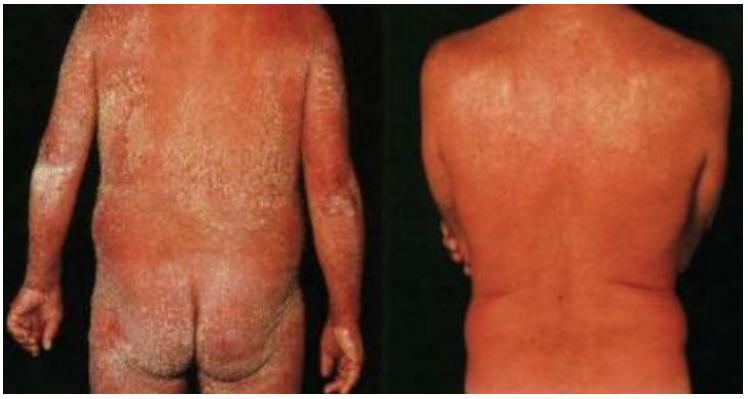




Complete sloughing of skin below granular layer (SSSS).

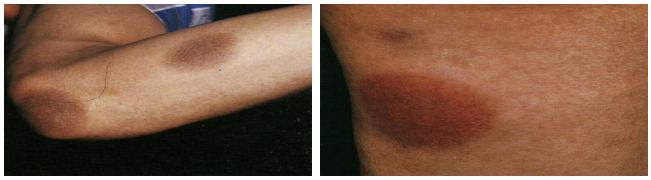
8. Erythroderma and Exfoliative Dermatitis

Could be caused by drugs, inflammatory skin disease, cutaneous lymphoma, psoriasis.



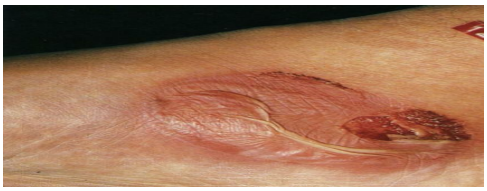
9. Fixed Drug Eruptions

- A drug reaction that happens the same time and **place** each time the pt takes the drug. It reoccurs in the same place this is why it's called fixed.
- Classically its dark brown, grayish, very well demarcated and round
- Sharply demarcated, could be brownish/dusky red, inflammatory/pigmented/vesicular/blister.
- Could be type 1 hypersensitivity. Happens every time the patient takes the medications (can occur with paracetamol use)

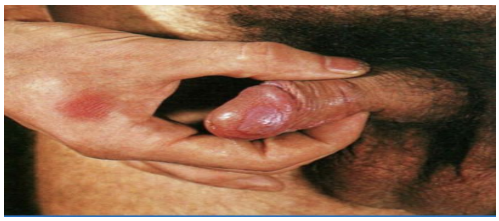


Most classical form of drug eruption with no other DDX

Sharply demarcated erythema with a blister

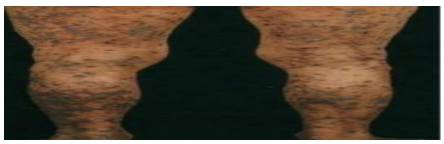


Sharply demarcated erythema with a ruptured blister and an associated crustation



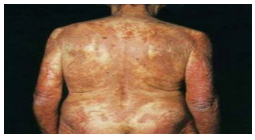
Classical in males in the form of a blister in the glans penis and erythema in the hand. Usually they are young males on **minocycline** Can be misdiagnosed as STD.

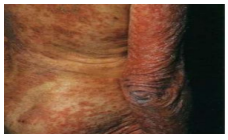
10. Lichenoid eruptions



- Lesion resembles lichen planus, violaceous, scaly, papules, diffuse (may be localized), mucosal involvement It's a more persistent reaction.
- Associated with: ACE inhibitors, Beta blockers

- Psoriasiform → commonly with lithium, BB, and antimalarials





<table>
<tr><th colspan="2">11. Photosensitivity</th></tr>
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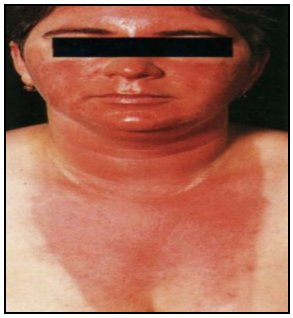
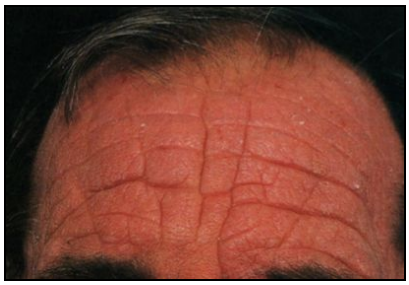
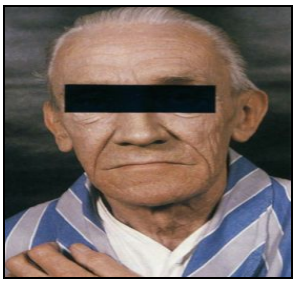
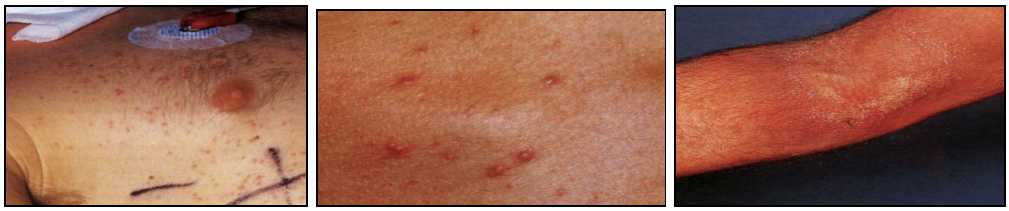
- Types:
  - Phototoxic (more common) → Irritation (non immune mediated) e.g. psoralen, doxycycline
  - Photoallergic → allergy to a particular component e.g. doxycycline

</td><td>  </td></tr>
<tr><th>12. Chronic actinic dermatitis</th><th>13. Pigmentary abnormalities</th></tr>
<tr><td>  </td><td> 
Causes: bleomycin, amiodarone, clofazimine, minocycline</td></tr>
<tr><th colspan="2">14. Acneiform and pustular eruptions</th></tr>
<tr><td colspan="2">  </td></tr>
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- Monomorphic papulopustular eruption non-comedonal think of systemic steroid use
- Seen in post pubertal, post RTA on steroids
- Don’t confuse this with drug induced acne (antipsychotics and phenytoin)

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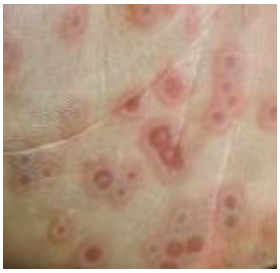
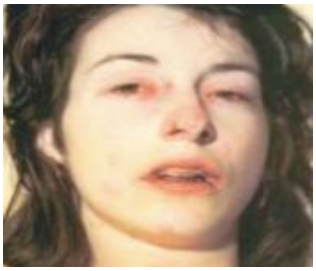
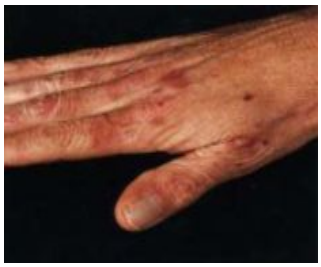
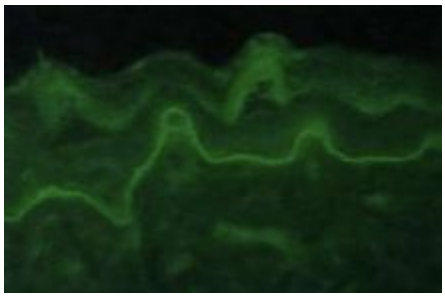
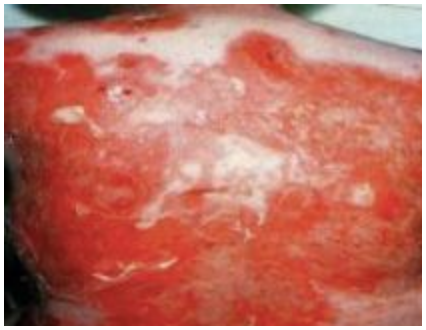
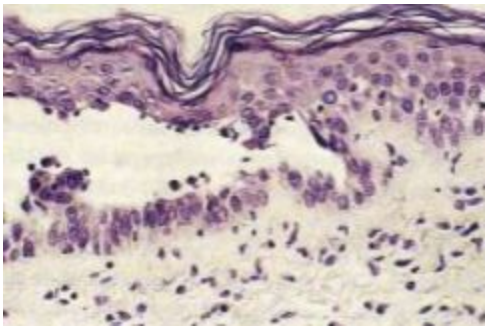
</table>

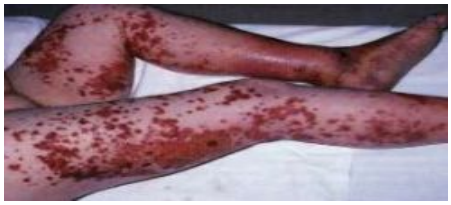
15. Bullous eruptions:

- **All may have a bullous component:**
- Fixed drug eruptions.
- Erythema Multiforme (Stevens-Johnson syndrome, erythema multiforme 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 **NSAIDs** or antibiotics "nalidixic acid". They have normal porphyrin level).
- Anything not clinically typical think of drug eruptions e.g. bullous pemphigoid in atypical area.

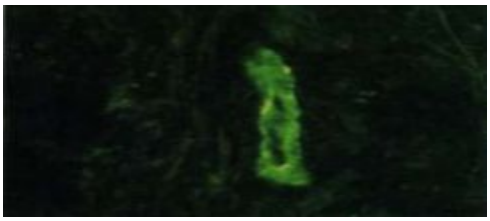
Erythema Multiforme		Pseudoporphyria
		
• Target like lesions that consist of 3 zones dark- light – dark		• Seen in sun exposed area (hand) showing blisters and crustation.

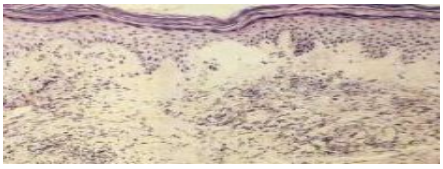
Drug induced Bullous pemphigoid	
	
• Tense blister because the split under the epidermis (subepidermal)	
Drug induced pemphigus	
	
Superficial pemphigus (foliaceus) unlike vulgaris of TEN. The more superficial the more crustations you will see and no raw appearance. Causes: penicillamine, captopril	Separation (intraepidermal) above the basement membrane. Acantholytic cell seen when there's detachment of the keratinocyte in Pemphigus Vulgaris 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 it's subepidermal but there is the sloughing component.

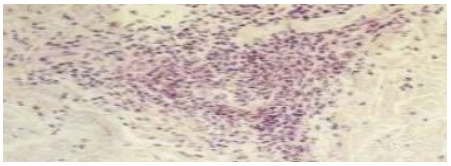
16. Vasculitis



Purpura





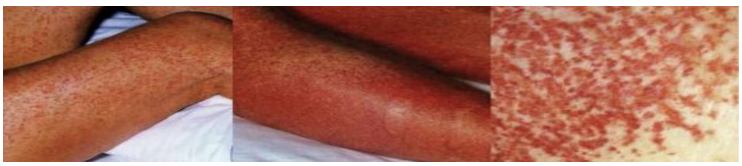


Inflammation around the blood vessel with neutrophil infiltrate

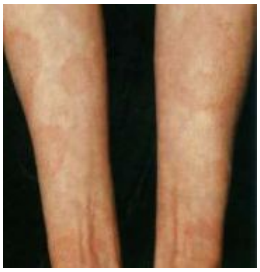
17. Purpura

Most common cause of purpura:

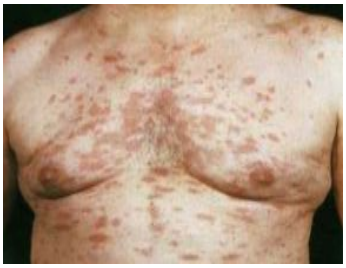
- Autoimmune diseases
- Infections
- Drugs



18. Annular erythema

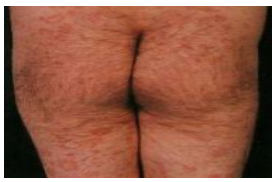


19. Pityriasis rosea like eruptions



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

20. Psoriasiform drug eruptions

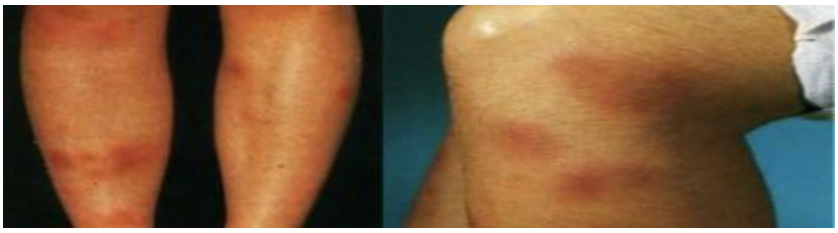


- Rarely seen de novo from the drug its exacerbated but lichenoid may be initiated denovo

21. Lupus Erythematosus-like syndrome induced by drugs

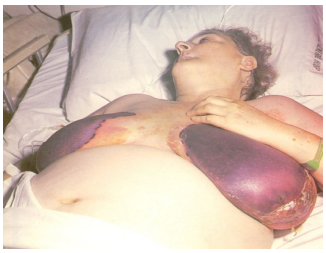
- The most common drugs:
  - Hydralazine,procainamide, sulfonamide, Minocycline, INH
- The presentation is milder than the actual disease and once you stop it should resolve

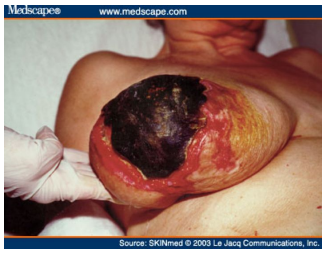
22. Erythema nodosum

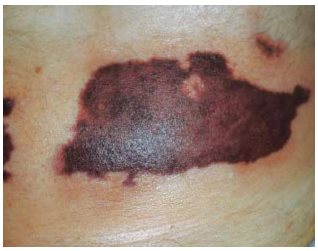


- It is due to inflammation of subcutaneous fat (panniculitis).
    - Causes: TB (most common cause in our region), penicillin, tetracycline, OCP. minocycline, western counties sarcoidosis and IBD
    - Dx you need a deep biopsy up to fat to determine which subtype septal, lobular, vascular.

23. ACDR related necrosis







- After **oral** drug or at **sites of injection**
- **Warfarin cutaneous necrosis:** Idiosyncratic
- **Onset:** 3-5 days of anticoagulation therapy.
- **Due to** a **transient hypercoagulable state and thrombus formation. In the beginning**
- **Risk factors:** high initial dose, obesity, female, hereditary deficiency of protein C, protein S or antithrombin III.
- Sharply demarcated, deep purple to black necrosis.
- Lesions vary with severity of reaction: petechiae to ecchymoses to tender hemorrhagic infarcts to extensive necrosis → deep tissue sloughing/ ulceration.
- Usually single. On areas of abundant fat. Acral areas spared.
- Coagulation studies: within normal limits
- **Course/ Prognosis**
    - May subside/heal by granulation or require surgical intervention.
    - **Life threatening if extensive** in an elderly debilitated patient.
    - Heparin causes less severe reactions than warfarin