Drug Eruptions

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Outline

- Pathophysiology of drug eruptions
- Morbiliform (maculo-papular)
- Urticaria
- Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Adverse Drug Reactions (ADRs)

‘A response to a medicine which is noxious and unintended, and which occurs at doses normally used in man’

- 3-6 % of hospital admissions
- 10-15 % of hospitalised patients
- Type A ADRs- 80%
- Type B ADRs- 15-20%

Pathophysiology

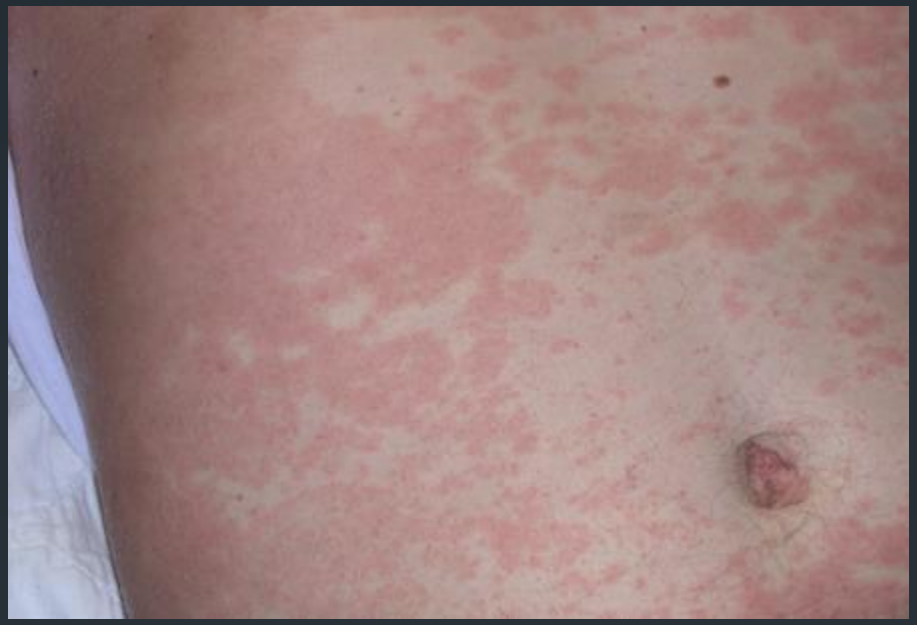
Hypersensitivity reactions

- Type I- urticaria, angioedema and anaphylaxis. *eg. insulin*
- Type II- hemolysis and purpura. *eg. Penicillin, cephalosporins, sulfonamides, rifampicin*
- Type III- serum sickness, urticaria. *eg. Quinine, salicylates, chlorpromazine, sulfonamides*
- Type IV- contact dermatitis, morbiliforme reactions and photoallergic reactions. *Contact hypersensitivty to topical medications eg. neomycin*

Non Immunological

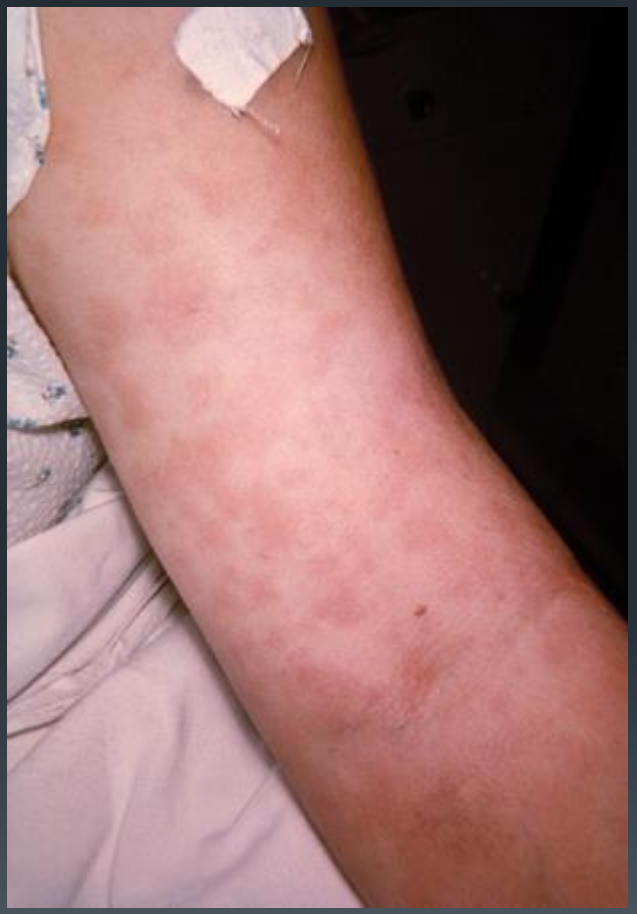
Accumulations, adverse effects, direct release of mast cell mediators, idiosyncratic reactions, intolerance, overdosage or phototoxic dermatitis.

Maculopapular/ morbiliforme eruption



Drug eruption due to phenytoin

When the clinical presentation is a maculopapular rash, the cause is drug induced in 50% to 70% of adults and 10% to 20% of children.



Hypersensitivity rash due to penicillin

Maculopapular/morbiliforme eruption

Primary differential diagnosis:

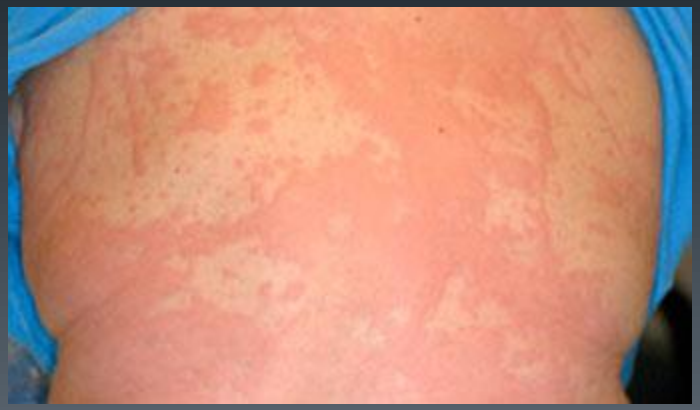
- drug eruptions (particularly in adults)
- Anaphylaxis
- viral exanthems (particularly in children)
- rickettsial infections
- bacterial infections
- rheumatological diseases,
- systemic diseases

Initial clues to the correct category are derived from the history and clinical setting.

- Review complete medication list! *Antibiotics (especially sulphonamides, penicillins, cephalosporins), anticonvulsants, and allopurinol may have a rate of up to 5%. Chemotherapy?*
- Interval between introduction of a drug and onset of the eruption.
- Risk factors? *Female gender, older age, and immunosuppression*
- Urgent considerations- Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis.

Urticaria

- Hives/ whealing of the skin
- Raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis that are very pruritic.
- Some cases are complicated by a swelling of the deeper dermis and tissues (angio-oedema), with laryngeal oedema the most dreaded variant, potentially causing respiratory distress and death.



Urticaria

- Acute (<6 weeks)
- sudden-onset
- Isolated lesions lasting a few hours at a time
- Possible precipitants- recent illness, medication use (eg. Penicillins, cephalosporins, NSAIDs, diuretics, diuretics), travel, foods, new perfumes/dyes/lotions/creams, new pets, contact with nickel/industrial chemicals, sun/cold exposure, exercise

- Chronic (>6 weeks)
- Recurrent whealing of skin at least twice weekly
- Cause rarely identified

- Physical

- mechanical pressure, vibration, thermal (hot or cold) contact, UV light, water exposure, exercise, or stress.

Stevens Johnson Syndrome and Toxic Epidermal Necrolysis

- Severe cutaneous adverse reactions

- SJS has <10% total body surface area (TBSA) involvement
- SJS/TEN overlap has 10% to 30% TBSA involvement
- TEN has >30% TBSA involvement.

Epidemiology

Incidence
SJS: 1 to 6 cases/million person-years
TEN: 0.4 to 1.2 cases/million person-years

SJS and TEN

Aetiology

Infections

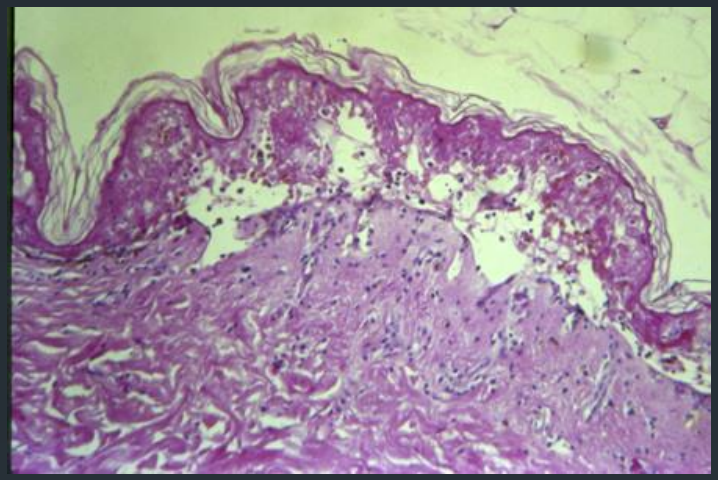
- Upper respiratory tract infections
- Pharyngitis
- Otitis media
- Mycoplasma pneumoniae
- Herpes
- EBV
- Cytomegaloviruses

Drugs

- Anticonvulsant agents
- Antibacterial sulphonamides
- Antibacterial and antifungal antibiotics
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Allopurinol
- Analgesics
- Antimalarials
- Corticosteroids
- Anti-HIV medicines, such as nevirapine
- Selective COX-2 inhibitors
- Lamotrigine
- Antihelminthics.

SJS and TEN

Pathogenesis



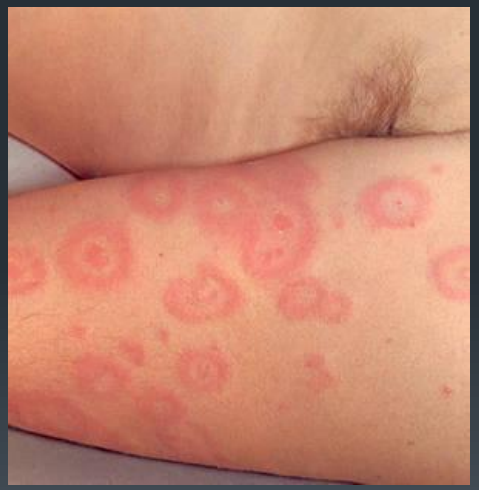
Histopathology of SJS/TEN

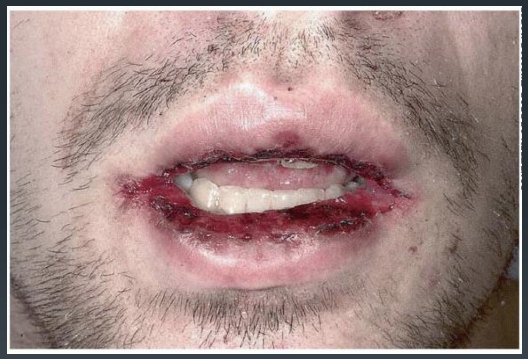
- Keratinocyte apoptosis mediated by cytotxic T-lymphocytes (CD8) in SJS and TENS is modulated by plasma TNF-alpha and interferon-gamma- both are increased in patients with SJS and TEN.
- 3 possible pathways: Fas-Fas ligand interaction; perforin/granzyme B; and granulysin-mediated.

SJS and TEN

SJS Signs and Symptoms :

- ✓ Prodromal phase: fever, malaise, arthralgia, myalgia +/- vomiting and diarrhoea.
- ✓ Ulceration of the skin and two or more mucosal surfaces (eg. Mouth, urethra, lungs, conjunctivae).
- ✓ Typical target lesions develop, often on the palms or soles with blistering in the centre.





TEN Signs:

- ✓ Wide-spread erythema followed by epidermal necrosis with loss of large sheets of epidermis. Mucosae severely affected.

SJS and TEN

Treatment

- Withdrawal of causative agent!
- Dressings and topical antibiotics
- IV fluids and nutritional support
- IVIG

Prognosis

Prognosis is best when:

- Patients are <50 years of age
- The total body surface area (TBSA) involved is low
- Patients are transferred to a burn centre
- Patients do not have sepsis
- Patients do not require antibiotics.

SJS- approximately 5% mortality rate
TEN- approximately 30% mortality rate

SJS and TEN

August 2013: the FDA issued a safety announcement advising that anyone who develops a rash, blister, or some other skin reaction while taking acetominophen should stop using the drug and seek medical care immediately. The drug poses a risk SJS and TEN.

Summary

- Adverse drug reactions are common
- Most drug eruptions are benign, but a small percentage, including angioedema, Stevens-Johnson syndrome and toxic epidermal necrolysis can be life threatening!
- Treatment of drug eruptions is generally supportive