

# Drug Rashes

- True drug allergy
- Amoxicillin non-allergic rash
- Serum sickness / SSLR
- Erythema multiforme
- Fixed drug eruption
- Stevens-Johnson Syndrome
- DRESS
- Erythema nodosum
- Other drug rashes



Common causes: antibiotics, anti-convulsants, NSAIDs

# Drug Allergy

- IgE-mediated true drug allergy rashes appear within 1 hour of drug ingestion
  - Occasionally slightly more than 1 hour if ingested with food that slows absorption
- Urticarial pruritic rash
  - May have flushing, angioedema
- May have [anaphylaxis](#): angioedema affecting airway, wheezing, hypotension, GI symptoms
- Common: beta-lactam antibiotics, NSAIDs, neuromuscular blockers
- Urticaria alone: treat with H1-blocking antihistamines and anti-itch therapy
  - [Anaphylaxis](#) – initiate emergency treatment with epinephrine IM and transport to ED
- Enter drug allergy on chart and inform patient to avoid the drug in the future
  - Consider allergist referral for confirmatory testing if unclear



[https://commons.wikimedia.org/wiki/File:Urticaria\\_child.jpg](https://commons.wikimedia.org/wiki/File:Urticaria_child.jpg)

# Amoxicillin non-allergic rash

- Delayed hypersensitivity reaction, *not* IgE-mediated, not a drug allergy
  - Occurs with other antibiotics and other drugs also
- Occurs in 10% of children given amoxicillin
- Starts on day 5-7 (range 2-16) after 1<sup>st</sup> dose
  - May start more quickly on re-exposure to same drug
- Pink or red, flat-topped, small macules & papules, torso, may spread to face & extremities
- Lasts ~3 days (range 1-6 days) whether amoxicillin stopped or not
- Reassurance
- Sometimes a rash while taking amoxicillin is a viral exanthem, commonly roseola, (amoxicillin was prescribed when the child was seen with fever as the only symptoms of the viral illness)



[https://commons.wikimedia.org/wiki/File:Amoxicillin\\_rash\\_11\\_hours\\_after\\_17th\\_dose.JPG](https://commons.wikimedia.org/wiki/File:Amoxicillin_rash_11_hours_after_17th_dose.JPG)

# Serum sickness / Serum sickness like reaction

- Serum sickness is a type III immune complex-mediated hypersensitivity reaction
  - More in adults: non-human-derived antitoxins, anti-thymocyte globulin, and monoclonal antibodies
  - Symptoms start 1-2 weeks after drug exposure
- SSLR appear similar but thought to have different pathogenesis
  - Common in children: cefaclor, penicillins
  - Symptoms start 5-10 days after drug exposure
- Fever, urticarial-like rash that may progress to purpura, arthralgias / arthritis, lymphadenopathy
  - No mucous membrane involvement
  - Individual lesions present > 24 hours (unlike urticaria)
  - SSLR symptoms milder than serum sickness
- Treatment: withdraw agent, supportive, prednisone course if fever > 38.5, extensive rash, significant arthralgia/arthritis





# Erythema multiforme

- Immune-mediated skin reaction to (90%) infections, drugs (esp penicillins in children)
  - NSAIDs, antibiotics, sulfonamides, anti-convulsants
- Target lesions (not always present) with dusky center
  - Extensor extremities first, spread to rest of body
  - Usually asymptomatic, but itch / burn
  - Lesions appear over 3-5 days, resolve over 2-3 weeks
  - EM minor: no mucosal involvement
  - EM major: mucosal involvement → ddx Stevens Johnson, admit if extensive mucosal lesions
  - Oral variant of drug-induced EM: oral bullae & ulcers
- Diagnosis: clinical
- Treatment: remove offending agent, supportive, (admit if mucosal involvement)



[https://commons.wikimedia.org/wiki/File:Erythema\\_multiforme\\_EM\\_02.jpg](https://commons.wikimedia.org/wiki/File:Erythema_multiforme_EM_02.jpg)

# Fixed drug eruption

- Antibiotics (esp TMP-SMX, penicillins, fluoroquinolones, tetracyclines), NSAIDs, acetaminophen, anti-convulsants (esp carbamazepine), anti-malarials
- Tends to recur in same location if re-exposed to same drug
- Usually single lesion, round-oval, dusky red-brown-black plaque
  - Lesion may itch or burn
  - Common locations: lips, hands, feet, genitalia
  - Usually 30 min – 8 hours after ingest drug, but can take up to 2 weeks to appear
- Stop offending drug and avoid in the future
- Symptomatic treatment (itch relief)
- Spontaneously resolves in 7-10 days
  - May have post-inflammatory hyperpigmentation



[https://commons.wikimedia.org/wiki/File:Drug\\_eruption2.jpg](https://commons.wikimedia.org/wiki/File:Drug_eruption2.jpg)

# Stevens-Johnson syndrome

- Severe, potentially fatal drug reaction
- Anti-convulsants (phenytoin, carbamazepine, phenobarbital), NSAIDs, sulfonamides
- Continuum with toxic epidermal necrolysis (TEN)
  - < 10% BSA epidermis detached = SJS
  - > 30% BSA epidermis detached = TEN
- Symptoms begin 1 week – 1 month after drug started
  - Prodrome fever; malaise, myalgias, arthralgias
  - Tender skin, atypical targets, vesicles and blisters, progress to sheet-like skin detachment, erosions
  - Nikolsky sign: sloughing with gentle lateral pressure / rubbing
  - Painful mucosal involvement in 90%: crusts and erosions
- Stop offending agent, initiate supportive resuscitation (vascular access, fluids, analgesia, wound care), transfer to higher level of care (may need burn center)



[https://commons.wikimedia.org/wiki/File:Steven\\_Johnsons\\_Syndrome.jpg](https://commons.wikimedia.org/wiki/File:Steven_Johnsons_Syndrome.jpg)



Source: [Wikimedia Commons](#)

# DRESS

- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Severe drug reaction with rash, lymphadenopathy, organ involvement, eosinophilia, atypical lymphocytes
- Anti-convulsants, sulfonamides, vancomycin, anti-TB drugs
- Latent phase 2-8 weeks after starting drug
- Red maculopapular rash → coalesces, may cause purpura, target lesions, exfoliation
  - Torso and extremities
  - 50% mucosal involvement, milder than SJS/TEN
- Facial edema common
- Systemic: fever, lymphadenopathy, visceral organ effects
- Stop offending drug, initiate supportive care, transfer patient to higher level of care



<https://www.dresssyndromefoundation.org/>

[Additional images](#)



# Erythema nodosum

- Delayed type hypersensitivity reaction
- Triggers: drugs (penicillins, sulfonamides, OCPs), infections, pregnancy, systemic illnesses e.g. sarcoid
- Erythematous to dusky tender nodules on shins, bilateral
  - Less commonly: legs, buttocks, arms, face
- May have prodrome 1-3 weeks prior: fever, malaise, arthralgias, URI symptoms
- Self-limited, resolves in 1-2 months
- Supportive care: analgesia, compression stockings, elevation, rest



# Other Drug Rashes

- Acute generalized exanthematous pustulosis (AGEP)
  - Numerous tiny sterile pustules on a background of erythema and edema
  - Beta-lactam antibiotics, sulfonamides, tetracyclines
  - Rash starts 1-2 days after begin new drug, resolves w/desquamation over 2 weeks
- Drug-induced pemphigus
  - Mucosal blisters/erosions, flaccid skin blisters, + Nikolsky sign
  - Penicillins, cephalosporins, vancomycin
- Hypersensitivity vasculitis
  - Palpable purpura, esp on legs, days to weeks after drug exposure
  - Beta-lactam antibiotics, sulfonamides
- Drug-induced photosensitivity
  - Tetracyclines, sulfonamides, fluoroquinolones
  - Sunburn-like rash (phototoxic) or eczematous (photoallergic) in sun-exposed areas
- Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)
  - Sharply demarcated erythema in intergluteal or inguinal folds and other flexural folds
  - Amoxicillin and other penicillins, ceftriaxone, clindamycin, erythromycin
- Red man syndrome
  - Flushing, erythema, pruritis with vancomycin infusion