DERM ROUNDS: A day in the life of the inpatient consult service

(Handout: Price, HN;2019)

*Please note clinical photos in the slide presentation will not be shared

- **Drug eruptions (DE): drug eruption diagnoses are heavily based on clinical appearance and ***history*****. Ensure you consider a broad differential and rule out other causes. A drug timeline can be very helpful in patients on polypharmacy.**
    - *Morbilliform eruptions*
    - Drug hypersensitivity reaction (DHS)
    - SJS/TEN continuum
    - Reactions to chemotherapy/targeted-drugs

Type of DE	Onset	Incidence	Clinical	Common drugs
Morbilliform	4-21 days	35% of children	Pink to violaceous macules and papules on truck and extremities; rare MMs, can have low grade fever	Beta-lactam Abx, AED^, NSAIDS
DHS*	2-6 weeks	Unclear (1 in 1,000 to 1 in 10,000 in adults)	Febrile prodrome, morbilliform skin changes, facial edema, conjunctivitis, mucositis, lymphadenopathy	Aromatic AEDs, lamotrigine, sulfa antibiotics
SJS/TEN (continuum)	Prodrome 1-3 weeks after medication	10% of all cases occur in children; overall rare	Morbilliform to targetoid plaques to full epidermal necrosis, bullae and vesicles; prodrome of fever, fatigue, sore throat, LAD	Phenobarbital, sulfa antibiotics, lamotrigine, carbamazepine

- *See criteria table
- ^Anti-epileptic drugs

WARNING SIGNS for Drug eruptions
1. The presence of mucosal involvement
2. Systemic clinical manifestations
3. Facial swelling
4. Lymphadenopathy
5. Blister formation
6. Pustules and denuded skin
7. Fever N 38°C (100.4°F)

SJS/TEN criteria—almost always drug induced

Table 2 SJS/TEN classification scheme

1. Bullous erythema multiforme—epidermal detachment involving <10% of BSA with localized typical targets or raised atypical targets
2. Stevens-Johnson syndrome—epidermal detachment of <10% of BSA with widespread erythematous or purpuric macules or flat atypical targets
3. SJS/TEN overlap—epidermal detachment of 10-30% of BSA with widespread purpuric macules or flat atypical targets
4. Toxic epidermal necrolysis with spots—epidermal detachment of >30% BSA with widespread purpuric macules or flat atypical targets
5. Toxic epidermal necrolysis without spots—large sheets of epidermal detachment involving >10% of BSA without purpuric macules or target lesions

BSA, body surface area; *SJS/TEN,* Stevens-Johnson Syndrome/toxic epidermal necrolysis.
Modified from Bastuji-Garin et al.[43]

From: Waldman R, Whitaker-Worth D, Grant-Kels JM. Cutaneous adverse drug reactions: Kids are not just little people. Clin Dermatol. 2017 Nov - Dec;35(6):566-582. doi: 10.1016/j.clindermatol.2017.08.007. Epub 2017 Aug 4. Review. PubMed PMID: 29191348.

RegiSCAR[17]	J-SCAR Criteria[30]
Acute rash	Maculopapular rash >3 weeks after initiating offending drug
Reaction suspected to be drug related	Prolonged clinical symptoms after drug discontinuation
Hospitalized	Fever > 38°C
Fever >38°C	Liver abnormalities or other organ involvement
Lymphadenopathy at two or more sites	Leukocyte abnormalities (leukocytosis, atypical lymphocytosis, or eosinophilia)
Involvement of at least 1 internal organ	Lymphadenopathy
Blood count abnormalities (lymphopenia, eosinophilia, or thrombocytopenia)	HHV-6 reactivation

HHV, human herpesvirus; *J-SCAR,* Japanese Research Committee on Severe Cutaneous Adverse Reaction; *RegiSCAR,* European Registry of Severe Cutaneous Adverse Reactions.

*RegSCAR and J-SCAR are not validated in children or adults with drug hypersensitivity syndrome but can be useful to asses likelihood of DIHS/DRESS.

From: Waldman R, Whitaker-Worth D, Grant-Kels JM. Cutaneous adverse drug reactions: Kids are not just little people. Clin Dermatol. 2017 Nov - Dec;35(6):566-582. doi: 10.1016/j.clindermatol.2017.08.007. Epub 2017 Aug 4. Review. PubMed PMID: 29191348.

- Infectious related eruptions
  - Eczema cocksackium
  - Staph scalded skin syndrome
  - Unusual presentations of common bugs: lice, scabies
  - Strep infections
  - Mycoplasma induced eruptions

Table II. Proposed diagnostic criteria for classic cases of *Mycoplasma*-induced rash and mucositis

Classification	MIRM
Detachment	<10% BSA
No. of mucosal sites involved*	≥2
Few vesiculobullous lesions, or scattered atypical targets	Yes
Targetoid lesions	±
Evidence of atypical pneumonia	
1) Clinical	Fever, cough, positive auscultatory findings
2) Laboratory	Increase in MP IgM antibodies, MP in oropharyngeal or bullae cultures or PCR, and/or serial cold agglutinins

BSA, Body surface area; *MIRM*, *Mycoplasma*-induced rash and mucositis; *MP*, *Mycoplasma pneumoniae*; *PCR*, polymerase chain reaction.
*Rare cases have <2 mucosal sites involved.

- Reaction patterns (if time):
  - Urticaria multiforme
  - Urticaria

TABLE 4 **Distinguishing Features of Urticaria Multiforme, Erythema Multiforme, and Serum-Sickness–Like Reactions**

Feature	Urticaria Multiforme	Erythema Multiforme	Serum-sickness–Like Reactions
Appearance of individual lesions	Annular and polycyclic wheals with central clearing or ecchymotic centers	Classis target lesion with annular lesions with purpuric or dusky, violaceous center (may blister), middle ring of pallor and edema, outer ring of erythema or blisters	Polycyclic urticarial wheals with central clearing; may appear purpuric
Location	Trunk, extremities, face	Involvement of palms, soles common	Trunk, extremities, face, lateral borders of hands and feet
Duration of individual lesions	<24 h	Days to weeks	Days to weeks
Fixed lesions	No	Yes	Yes
Total duration of rash	2–12 d	2–3 wk	1–6 wk
Mucous membrane involvement	Oral edema common, no erosions or blisters	May see oral erosions or blisters of lips, buccal mucosa, and tongue; rarely involves conjunctivae, nasal, or urogenital mucosa; usually involving only a single site	Oral edema common, no erosions or blisters
Facial or acral edema	Common	Rare	Common
Dermatographism	Yes	No	No
Fever	Occasionally, low-grade	Occasionally, low-grade	Prominent, high-grade
Associated symptoms	Pruritus	Mild pruritis or burning	Myalgias, arthralgias, lymphadenopathy
Common triggers	Antibiotics, immunizations, viral illness	Herpes simplex virus, other viral illness	Antibiotics
Treatment	Discontinue any new or unnecessary antibiotics or medications; combinations of H1 and H2 antihistamines may be helpful; systemic steroids can be helpful in more recalcitrant cases	Supportive care; early institution of systemic steroids can sometimes be helpful	Discontinue any new antibiotics or medications; H1 and H2 antihistamines; supportive care; consider systemic corticosteroids

From: Shah KN, Honig PJ, Yan AC. "Urticaria multiforme": a case series and review of acute annular urticarial hypersensitivity syndromes in children. Pediatrics. 2007 May;119(5):e1177-83. Review. PubMed PMID: 17470565.

TABLE 5 Principal Differential Diagnostic Considerations for Urticaria Multiforme

Urticaria variants
Erythema multiforme
Serum sickness and serum-sickness–like reactions
Viral exanthem
Erythema marginatum
Lupus erythematosus (neonatal, subacute cutaneous)
NOMID (neonatal multisystem inflammatory disorder)
Kawasaki disease
Urticarial vasculitis and other vasculitides
Juvenile rheumatoid arthritis
Figurate erythema (eg, erythema annulare centrifugum)
Lyme disease (secondary)

TABLE 1 Diagnostic Criteria for Urticaria Multiforme

Typical annular and polycyclic morphology and configuration to urticarial lesions
Transient, ecchymotic skin changes may be present
Absence of true target lesions and/or skin necrosis or blistering
Absence of mucous membrane involvement with blisters or erosions
Duration of individual lesions of <24 h
Dermatographism
Angioedema but not arthralgias or arthritis
Angioedema typically involves the hands and/or feet but may also involve the periocular or oral mucosa; children with significant edema of the feet may find walking difficult, which should not be confused with arthritis or arthralgias
Favorable response to antihistamines
May require combination therapy with a long-acting antihistamine such as cetirizine in conjunction with a short-acting agent such as diphenhydramine or cetirizine in conjunction with ranitidine
Modest but not-significant elevations in acute-phase reactants may be present
White blood cell count, erythrocyte sedimentation rate, or C-reactive protein level may be mildly elevated but does not demonstrate the elevations typically seen in patients with rheumatologic disorders, serious systemic infections, or Kawasaki disease

From: Shah KN, Honig PJ, Yan AC. "Urticaria multiforme": a case series and review of acute annular urticarial hypersensitivity syndromes in children. Pediatrics. 2007 May;119(5):e1177-83. Review. PubMed PMID: 17470565.

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