Update on Infectious Exanthems... and Drug Eruptions
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Exanthems

- Abrupt onset
- Several areas of skin
- 65/100 children with fever and exanthem with infection* -72%; viral... most enteroviruses
- Can be direct or due to immune response... to virus or medication

*Br J Dermatol 1992;126:302
# Duke’s Classification of Exanthems

<table>
<thead>
<tr>
<th>First Disease</th>
<th>Measles</th>
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<tbody>
<tr>
<td>Second Disease</td>
<td>Scarlet Fever</td>
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<tr>
<td>Third Disease</td>
<td>Rubella</td>
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<tr>
<td>Fourth Disease</td>
<td>Duke’s disease</td>
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<tr>
<td>Fifth Disease</td>
<td>Erythema infectiosum</td>
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<tr>
<td>Sixth Disease</td>
<td>Roseola Infantum</td>
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Exanthems – Differential Diagnosis

- Viral infections
- Bacterial infections
- Drug eruptions
- Kawasaki
Healthy male with low grade fever
Facial erythema
Subsequent reticulated erythema on extremities
Mother is pregnant
Fifth's Disease

- Face
- Extremities, Torso
  - Palms/Soles usu spared
- Fades 2-3 wks
  - Waxes/Wanes with activity, heat, etc
- +/- Arthralgias: 8-10% pedi; 60% adults
Erythema Infectiosum

- Parvovirus B 19
- Respiratory; IP 1 – 2 wks
- Exanthem coincides with Ab
  - Serology or PCR
- Usually not ill-appearing
  - Myalgia
  - Low grade fever
  - Arthritis
- Pregnancy; Spont Ab, Hydrops, Stillbirth (✓ mat Ab)
- Seroprevalence: 20-30 y/o-60-70%; 60-70 y/o-80% (Clin Microbiol Rev 2002;15:485)
Papular Purpuric Glove Socks Syndrome

- Parvovirus B 19; others*
  *Human parechovirus 3

- Unique distribution
  - Acute edema/erythema
  - Often with enanthem; palate, pharynx, lips
Human Parechovirus 3

- Sepsis-like picture
  - Fever 80%

- Meningoencephalitis

- Neonates/Infants

- Exanthem (15 pts)
  - 1-5 days after fever onset
  - Disappeared 2-7 days

Pediatr Infect Dis J 2013;32:233
Hand Foot Mouth

- Droplet or contact
- IP 3-6 days
- Prodrome: decr appetite, sore throat, abd. Pain
- PCR or Serology
Hand-Foot-and-Mouth Disease
Hand Foot and Mouth

- Sausage shaped vesicles palms/soles
- Oral erosions
  - Can see feeding problems
- Erythematous papules on buttocks
- “Eczema coxsackium”
- Mild gastroenteritis
- Etiologies
  - Coxsackie A16, A2, A5, A6, A9, A10, B2...
  - Enterovirus 71
  - Others...
  - Pediatrics 2013;132:e149
Severe HFM and Coxsackie A6

MMWR 2012;61:213
JAAD 2013;69:736
Pediatrics 2013;132:e149

Exanthem and fever more severe
Hospitalization more common...
- dehydration, pain
Hand, Foot, and Mouth Disease

- Pts < 18 yrs
- NP and Vesicular fluid for PCR
- 104 pts; 66% with HFM involvement
- 41% with ≥ 5 sites
- 92% genotyped: CxA6 (51%), CxA16 (34%) - CxA10 (4), EV-71 (2), CxA9 (2), A8, B2, B3, E9 (all 1)
- Could not distinguish A6 v A16 with atypical or severe phenotype - except with Perioral lesions (CxA6)

Pediatr Inf Dis J 2014;33:e92
Neonate with congenital skin lesions
Severe brain malformation
Intrauterine HSV

- Early infection; 4-5% of neo. HSV
- Transplacental or ascending
- Skin lesions often present at birth
- Tzanck, Culture, PCR, Biopsy
- Microcephaly, brain malformation, eye
Intrauterine HSV

- 64 cases
- 5% of all neonatal HSV
  - > 2/3 w/o skin/CNS/eye
- Variation of cutaneous findings
  - Absence of vesicles/ bullae
  - Erosions
- Culture from skin results often delayed
  - 15 with lesions at birth; > 72hrs (median 10 d)

Pediatr Inf Dis J 2011;30 (2010 Aug 31 Epub)
Case History

- Previously healthy child with acute onset of fever, erythema, conjunctivitis
Case History

- On prednisolone (6 mg/kg/day) for pemphigus vulgaris

- Presented with fever, erythema, conjunctivitis after sibling began with similar illness
Measles

- **Definition**: Febrile rash and lab confirmation (Ab, PCR, virus isolation; NP/OP, Nasal, Throat, Urine)

- Declared eliminated in US in 2000
  - Outbreaks 1996 (58), 2008 (140), 2011 (220), Now

- 159 cases from Jan 1-Aug 24, 2013
  - NY (65), TX (25), NC (22), CA (15), OR, WA, AZ, CO, MN, MO, IL, IN, MI, FL, NJ, MD

  - Most unvaccinated (82%), 42 imported (50% from WHO European region)

  MMWR 2013;62:741
Measles

- March 13, 2013; *Intentionally* unvaccinated adol to NYC from London
- Source of largest outbreak in US since 1996
- 3500 contacts
- 58 cases
  - No cases in persons with documented vaccination
  - Last case on 6.9.2013; limited by high vaccination coverage in area

MMWR 2013;62:752
Measles

- Outbreak in NYC in 2011
- Index case with 2 immunizations
- 88 contacts; 4 cases with either 2 prior doses or confirmed IgG response
- All cases confirmed and with typical clinical picture
- First report of transmission from twice vaccinated Clin Infect Dis 2014 Feb 27 Epub
Mycoplasma pneumoniae-Induced Rash and Mucositis (MIRM)

- Difference from drug or viral induced SJS/EM
- Generally w more limited skin involvement
  - vesiculobullous
- Oral>Ocular>GU mucosal involvement
  - mucositis alone seen in 34%
- Most with excellent recovery; ATB (!), IVIG, steroids
  - resistance (TCN or fluorquinolone)
- Recurrence rarely

*J Am Acad Dermatol* 2015;72:239
*Pediatrics* 2011;127:e1605
Genetic Determinants of Adverse Drug Reactions

- HLA-B*15:02 screening FDA recommended
  - Carbamazepine use; Asians

- Aromatic anticonvulsants with similar risk
  - Phenytoin

- CYP (Cytochrome P450) enzymes involved in metabolism of anticonvulsants
  - CYP2C9/CYP2C19 related to PBS/Phenytoin metabolism

- Useful screens for this group of medications

J Hum Genet 2015;60:413
Case

- A child is seen with rapidly developing morbilliform erythema, facial edema, and fever. These findings were noted approximately 21 days after starting carbamazepine. Laboratory studies show 13% eosinophilia and elevated liver functions.
Case

1. Stevens-Johnson syndrome
2. Serum sickness – like eruption
3. Urticaria multiforme/Giant urticaria
4. Drug reaction with eosinophilia and systemic symptoms (DRESS)
5. Presidential fever
Case

- 1. Stevens-Johnson syndrome
- 2. Serum sickness – like eruption
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### Case

Which of the following viral conditions is associated with DRESS?

A – Echovirus 8 infection  
B – Hepatitis A infection  
C – HHV-6 reactivation  
D – Influenza A  
E – Parvovirus infection
Case

- A – Echovirus 8 infection; has not been reported
- B – Hepatitis A infection; has not been reported
- C – HHV-6 reactivation; multiple reports of such; ? Due to cytotoxic T cell activation w cross reaction with drug and organ toxicity (also EBV, CMV)
- D – Influenza A; has not been reported
- E – Parvovirus infection; has not been reported
## DRESS – Associated Medications

<table>
<thead>
<tr>
<th>Anti-infectives</th>
<th>Anti-convulsants</th>
<th>Anti-hypertensives</th>
<th>Biologics</th>
<th>NSAIDs</th>
<th>Misc</th>
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</thead>
<tbody>
<tr>
<td>Dapsone</td>
<td>Carbemazepine</td>
<td>Amlodipine</td>
<td>Imatinib</td>
<td>Celecoxib</td>
<td>Allopurinol</td>
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<tr>
<td>Ampicillin</td>
<td>Lamotrigine</td>
<td>Captopril</td>
<td>Vismodegib</td>
<td>Ibuprofen</td>
<td>Ranitidine</td>
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<tr>
<td>Linezolid</td>
<td>PBS</td>
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<td>Vemurafenib</td>
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<td>Minocycline</td>
<td>Phenytoin</td>
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<td>TMP/SMX</td>
<td>Valproate</td>
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<td>Vancomycin</td>
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<td>INH</td>
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DRESS – Systemic Concerns

- Autoimmune disease –
  - Grave’s
  - Type 1 DM
  - AA
  - Autoimmune hemolytic anemia

- End organ disease… most commonly renal

Semin Cutan Med Surg 2014;33:2
DRESS - Management

- Stop the suspected medication
- Steroids... systemic v topical
- Retrospective study
  - 50 consecutive pts with d/c Dx: 38 prob or confirmed
- Potent topical steroids v Systemic steroids
  - Systemic tx not felt nec for mild disease
  - Systemic use felt to be assoc with viral reactivation (HHV6) and more severe/prolonged course (*)

JAAD 2015;72:246
DRESS and HHV 6
Corticosteroids

- Retrospective evaluation of 29 pediatric cases
- All HHV6 + and 80% of HHV6 – pts received CS
- Shorter time to cessation of progression of disease
- Fewer days with fever
- Suggestion of shorter hospitalization
- Conclusion of *more severe illness* with HHV6 + and *better outcome* in both with systemic steroid use

Br J Dermatol. 2015 Apr;172(4):1090-5
Summary

- Variety of new presentations of older disorders
- Severe drug eruptions associated with infections
- Severe drug eruptions determined by genetic considerations