Viral Exanthems

Basic Dermatology Curriculum

Last updated November 21, 2013
The purpose of this module is to help medical students develop a clinical approach to the evaluation and initial management of patients presenting with typical viral exanthems.

By completing this module, the learner will be able to:

• Recognize morbilliform eruption as a prototype for viral exanthems
• Describe common presentations of pediatric viral exanthems
• Provide counseling for parents of children with typical viral exanthems
Definitions

Exanthem (exanthema)
– A rash that appears abruptly and affects several areas of the skin simultaneously
– Greek origin “exanthema” which means “a breaking out”

Enanthem (enanthema)
– An eruption upon a mucous membrane
Viral Exanthems

- Commonly described as “morbilliform” which means “composed of erythematous macules and papules that resemble a measles rash.”
- Difficult to distinguish from drug eruptions. A thorough history will aid in the diagnosis.
  - Viral exanthems are more common in children.
  - Drug eruptions are more common in adults.
Morbilliform Rash

Viral Exanthem

Drug Rash
Case One

Caleb
Case One: History

- **ID**: Caleb, 9-month-old male
- **HPI**: Caleb presents for evaluation of fever and rash. His mother noted a fever of 40°C two days ago. He appeared well and was eating and playing normally, so his mother was not alarmed. After the fever resolved, Caleb developed a red rash on his trunk that progressed rapidly over the past 24 hours.
- **PMH**: Caleb is up-to-date with vaccinations.
Based on Caleb’s history and exam, what is the most likely diagnosis?

a. Drug Eruption
b. Erythema Infectiosum
c. Measles
d. Roseola
e. Rubella
Case One, Question 1

Answer: d

Based on Caleb’s history and exam, what is the most likely diagnosis?

a. Drug Eruption (No medications)
b. Erythema Infectiosum (Low grade fever preceding characteristic lesions)
c. Measles (rare due to routine vaccinations)
d. Roseola
e. Rubella (rare due to routine vaccinations, see slide 61)
Roseola Infantum: Clinical Presentation

- Acute febrile illness, lasting approximately 3 to 7 days, often followed by the characteristic rash of roseola (in ~20% of infected children)

- **Prodrome**: High fever (39-40°C), palpebral edema, cervical lymphadenopathy, mild upper respiratory symptoms. Child appears well. As fever subsides, exanthem appears ("exanthema subitum" means "sudden rash").

- **Exanthem**: pink macules and papules surrounded by white halos. Begins on trunk, spreads to neck and proximal extremities. Lasts 1-3 days.
Roseola Infantum

- Synonyms: Exanthema subitum, Sixth disease
- Caused by *Human Herpesvirus* 6 (HHV-6) and less commonly *Human Herpesvirus* 7 (HHV-7)
- Mode of transmission unknown (possibly from nasopharyngeal secretions)
- Children 6 months – 4 years
- Most common exanthem before age 2
- No vaccine; infection results in immunity
HHV-6

- HHV-6 infection in children results in:
  - Subclinical infection
  - Acute febrile illness without rash
  - Exanthema subitum
- Seroprevalence of HHV-6 in the adult population is greater than 95%
- Reactivation in immunocompromised hosts may cause significant morbidity
- Reactivation of HHV-6 with drug exposure can lead to drug-induced hypersensitivity syndrome (DIHS)
Prognosis and Treatment

- Usually benign and self-limited
- HHV-6 is known to cause febrile seizure in children with infection, often without a rash
- Treatment may be necessary for atypical cases with complications and in immunosuppressed patients
Case Two

Keith
Case Two: History

- **ID**: Keith, 8-year-old male
- **HPI**: Keith was brought to the pediatrician by his mother because he developed low grade fevers several days ago, and now has red cheeks and a new rash on his body.
- **Meds**: No medications
- **PMH**: Keith is a healthy child, up to date with his vaccinations
How would you describe Keith’s rash?
Case Two, Question 1

Confluent, erythematous, edematous plaques on the cheeks - “slapped cheeks.” Erythematous reticular eruption on the trunk and extremities.
Case Two, Question 2

Based on the history and skin exam, what is the most likely diagnosis?

a. Drug Eruption
b. Erythema Infectiosum
c. Measles
d. Roseola
e. Rubella
Case Two, Question 2

Answer: b

Based on the history and skin exam, what is the most likely diagnosis?

- a. Drug Eruption (No exposure to medications)
- b. Erythema Infectiosum
- c. Measles (Rare due to routine vaccinations, lacks this characteristic “slapped cheeks” exanthem)
- d. Roseola (Tends to occur in younger children with high fevers preceding a sudden rash that begins on the trunk)
- e. Rubella (Rare due to routine vaccinations, see slide 61)
Erythema Infectiosum: Clinical Presentation

- **Prodrome**: low-grade fever, malaise, headache, pruritus, coryza, myalgias, joint pain (more common in adult women)

- **Exantheme**: Begins with bright red cheeks (“slapped cheeks”) and as the facial rash fades over 1-4 days, a symmetric, erythematous, reticular (lacelike) eruption appears on trunk and extremities

- Eruption usually lasts 5-9 days
Diagnosis: Erythema Infectiosum

- Synonyms: Fifth disease
- Caused by Parvovirus B19
- Modes of transmission
  - respiratory tract secretions, percutaneous exposure to blood or blood products, and vertical transmission from mother to fetus
- Estimated incubation period from exposure to onset of rash usually between 1-2 weeks
- Individuals with erythema infectiosum are most infectious before onset of the rash
Epidemiology

- Most common in children 4-10 yrs old, but can affect all ages
- Tends to occur in epidemics, especially associated with school outbreaks in the late winter and early spring
- Secondary spread among susceptible household members is common, with infection occurring in ~ 50% of susceptible contacts
- Serologic studies show increasing prevalence of antibodies with age
  - In most communities, ~ 50% of young adults and often more than 90% of elderly people are seropositive
Diagnosis

- Detection of serum parvovirus B19-specific IgM antibody is the preferred diagnostic test
- Positive IgM test result indicates that infection probably occurred within the previous 2 to 4 months
Papular Purpuric Gloves and Socks Syndrome

- Rare presentation of Parvo B19 with painful and pruritic papules, petechiae, and purpura of hands and feet, often with fever and enanthem (oral erosions).

- Unlike the typical rash of Erythema Infectiosum, patients with this presentation are viremic and contagious --they should not be around those at risk:
  --pregnant women, immunocompromised pts

- May be IgM/IgG negative until 2-3 weeks later
Parvovirus B19

- Most infections are asymptomatic and unrecognized
- There is no specific treatment for uncomplicated parvovirus B19 infection
- Supportive therapy for relief of fatigue, malaise, pruritus, and arthralgia may be needed
- Generally resolves after 5-10 days, but can reoccur for months upon exposure to sunlight, hot temperature, exercise, bathing, and stress
Parvovirus B19: Complications

Some infections can be life-threatening

- Immunodeficiency
  - Can cause chronic erythroid hypoplasia with severe anemia

- Chronic hemolytic anemias
  - B19 is the most common cause of transient aplastic crisis in patients with chronic hemolytic anemias (i.e. sickle cell disease)
Parvovirus B19: Special Considerations

- **Pregnancy**
  - Infection occurring during pregnancy can cause hydrops fetalis*, intrauterine growth retardation, pleural and pericardial effusions, and death. The risk of fetal death is between 2% and 6.5% when infection occurs during pregnancy.
    - If a pregnant women has been in contact with children who were in the incubation period of infection or in anaplastic crisis, inform her of the small risk of infection and offer the option of serologic testing. Fetal ultrasonography can be useful.

- **Control measures**
  - Reduce transmission through hand hygiene, proper disposal of facial tissues, and avoidance of sharing eating utensils.

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*Hydrops fetalis: a condition in the fetus characterized by an accumulation of fluid, or edema, in at least two fetal compartments*
Case Three

Justin
Case Three: History

- **ID:** Justin, 6-year-old male
- **HPI:** Mother is concerned because he developed low grade fevers, painful ulcers in the mouth, and rashes on his hands and feet.
- **Meds:** No medications, Flintstone’s multi-vitamin daily, NKDA
- **PMH:** Justin is up-to-date with his vaccinations.
- **SH:** Justin attends elementary school in San Francisco.
- **FHx:** No family members with rash
Case Three, Question 1

How would you describe Justin’s lesions?
How would you describe Justin’s lesions?

Superficial, round erosions on the tongue and soft palate.

3-7 mm oval-shaped vesicles with erythematous halos on palms.
Case Three, Question 2

Based on the history and skin exam, what is the most likely diagnosis?

a. Aphthae
b. Hand-Foot-and-Mouth Disease
c. Herpes simplex virus
d. Porphyria cutanea tarda
e. Varicella-zoster virus
Case Three, Question 2

Answer: b

Based on the history and skin exam, what is the most likely diagnosis?

a. Aphthae (known as canker sores, limited to mouth)
b. Hand-Foot-and-Mouth Disease
c. Herpes simplex virus (usually affects gums and lips as well)
d. Porphyria cutanea tarda (usually presents later in life with blistering and scarring on the dorsal hands)
e. Varicella-zoster virus (expect trunk involvement)
Case Three, Question 3

Which of the following is responsible for causing Hand-Foot-and-Mouth Disease?

a. Adenovirus
b. Coxsackie virus A16
c. Cytomegalovirus
d. Echovirus 22
e. Epstein-Barr Virus
Case Three, Question 3

Answer: b

Which of the following is responsible for causing Hand-Foot-and-Mouth Disease?

a. Adenovirus (family of viruses, most often with upper respiratory tract syndromes)
b. Coxsackievirus A16
c. Cytomegalovirus (a common herpes virus)
d. Echovirus 22 (viral exanthem with less specific presentation than HFMD)
e. Epstein-Barr Virus (causes Infectious Mononucleosis)
Hand-Foot-and-Mouth Disease: Clinical Presentation

Prodrome
- Fever, sore throat, malaise for 1-2 days

Exanthem (skin lesions)
- Progression of lesions: Bright pink macules and papules → painful vesicles with erythematous halos → erosions with surrounding erythema

Enanthem (oral lesions)
- Erythematous erosions resembling aphthae (“canker sores”)

Distribution (highly distinctive)
- Starts in the mouth: tongue, buccal mucosa, hard palate
- Presents later on hands and feet, with occasional involvement of buttocks, diaper area, or elbows.
Hand-Foot-and-Mouth Disease

Common culprits
- Coxsackievirus A16 (CVA16), A6 (CVA6) and enterovirus 71 (EV71)
  - HFMD can also be caused by other types of Coxsackieviruses, echoviruses, enteroviruses
- Infection with EV71 can be serious and sometimes fatal. EV71 is more common in Asia. Individuals with EV71 will appear ill with additional symptoms, such as aseptic meningitis or encephalitis.
  - Other types of nonpolio enteroviral infections can also manifest with serious, systemic disease.
- Individuals with CVA16 may appear uncomfortable, but are non-toxic.
- Individuals with CVA6 may have a more severe rash.

Timing
- Common in late summer and early fall
- Incubation period of 4-6 days
Prognosis and Treatment

Prognosis
- HFMD is typically a benign, self-limited illness that resolves within 10 days.
- It is highly infectious.

Treatment is supportive.
- Provide relief for fevers, and pain.
Case Four

Jasmine
Case Four: History

- **ID**: Jasmine, 4 year-old female
- **HPI**: She was brought to the pediatric clinic by her mother. She has been sick for three days with fever, cough, runny nose, headache, muscle pain, fatigue, and rashes all over her body.
- **Meds**: No medications, NKDA
- **PMH**: Jasmine is up-to-date with her vaccinations.
- **SH**: Jasmine is in pre-school, grandmother babysits
- **FHx**: No family members with rash
How would you describe Jasmine’s rash?
How would you describe Jasmine’s rash?

Generalized, nondescript, pink erythematous macules and papules
Case Four, Question 2

Based on the history and skin exam, what is the most likely diagnosis?

a. Drug eruption
b. Herpes simplex virus
c. Miliaria crystalline
d. Nonspecific viral exanthem
e. Varicella-zoster virus
Case Four, Question 2

Answer: d

Based on the history and skin exam, what is the most likely diagnosis?

a. Drug eruption (Jasmine takes no medications)
b. Herpes simplex virus 1 (Expect orolabial involvement)
c. Miliaria crystalline (Presents with small clear vesicles with no inflammation)
d. Nonspecific viral exanthem
e. Varicella-zoster virus (Presents with vesicles and pustules)
Nonspecific Viral Exanthems

The majority of exanthems that you will encounter will be nonspecific and difficult to categorize.

Prodrome

▪ No indicative symptom complex
▪ Nonspecific associated symptoms
  ▪ Fever, headache, myalgia, fatigue, respiratory or gastrointestinal complaints

Exanthem:

▪ No unique lesion morphology or distribution
Nonspecific Viral Exanthems

Prognosis
- Most nonspecific exanthems resolve over 1 week without treatment.

Common Causes
- Nonpolio enteroviruses
  - More common in summer months
- Respiratory viruses
  - Adenovirus, rhinovirus, parainfluenza virus, etc.
  - More common in winter months
Classic viral exanthems

- **Measles** (Rubeola) and **Rubella** (German measles) are classic viral exanthems that are uncommon in the United States due to routine vaccinations.
- Diagnoses are confirmed with serology and cases must be reported to local or state health departments.
Case Five

Ana
ID: Ana is a 4-year-old female
HPI: Previously healthy girl presents with a 1 week history of cough, runny nose, fever, sore throat and red eyes.

- She went to her pediatrician 2 days ago and was prescribed Augmentin (amoxicillin and clavulanate) for presumed pharyngitis.
- Yesterday, Ana developed a red rash which started on her face and has spread to her trunk. Her mother would like to know if the rash is from her new medication.
**PMH:** Ana has never received vaccinations due to her mother’s fear regarding autism.

**Meds:** The augmentin was started 24 hours before the onset of her rash.

**FHx:** You also discover that a close family member recently visited from the Netherlands, who also developed a similar rash.
Case One: Skin Exam

**Physical Exam:** Ana is an ill-appearing child who presents with a morbilliform rash with erythematous macules and papules.

- Lesions have coalesced on the face and neck.
- Rash has spread to her trunk and extremities (not shown)
Exam Continued

- Inspection of Ana’s mouth reveals, bluish-white dots on the mucosal surface. These are called Koplik spots.
Case Five, Question 1

Based on the history and exam, what is the most likely diagnosis?

a. Drug Eruption
b. Erythema Infectiosum
c. Measles
d. Roseola
e. Rubella
Case Five, Question 1

Answer: c

Based on the history and exam, what is the most likely diagnosis?

a. Drug Eruption (Too soon for an exanthematous drug eruption. Refer to the module on drug reactions for more information)

b. Erythema Infectiosum (Eruption begins with bright red cheeks followed by a reticular eruption on the trunk and extremities)

c. Measles

d. Roseola (Tends to occur in younger children with high fevers preceding a sudden rash that begins on the trunk)

e. Rubella (Rash tends to spread more quickly, covering the body in 24hrs. See Slide 61)
Measles: Clinical Presentation

- **Prodrome**: Fever, Malaise, Conjunctivitis, Cough, Coryza*

- **Exanthem**: Erythematous macules and papules begin on the face and spread cephalocaudally and centrifugally (by the 3rd day, the whole body is involved).

- **Enanthem**: Koplik spots (occur in prodromal period)

- **Recovery**: Clinical improvement begins within 2 days of appearance of the rash. The rash tends to fade after 3-4 days and will last around 6-7 days.

*Coryza: “head cold” with nasal congestion, rhinorrhea, sore throat
Measles (Rubeola)

- Measles is a viral disease spread by respiratory droplets
- Incubation period tends to be 8-12 days from exposure to onset of symptoms
- Patients are contagious from 1-2 days before onset of symptoms (3-5 days before the rash) to 4 days after appearance of the rash
- Immunocompromised patients can be contagious for the duration of the illness
Measles (Rubeola)

- Incidence of measles has decreased substantially where measles vaccination has been instituted.
- Most cases of measles in the United States are imported with spread to unvaccinated individuals.
- Measles is still common in many developing countries (parts of Africa and Asia) and outbreaks repeatedly occur in communities who do not accept vaccinations (e.g. religious community in Netherlands).
Diagnosis

- Measles is diagnosed clinically, however, all cases of suspected measles should be serologically confirmed and reported immediately to the local or state health department without waiting for results of diagnostic tests.

- Testing includes:
  - Serology: Anti-measles IgM and IgG, isolation of measles virus or identification of measles RNA
  - Histologic evaluation of skin lesions or respiratory secretions may show syncytial keratinocytic giant cells
Management

- Uncomplicated measles is self-limiting, lasting 10 to 12 days.
- Treatment in the majority of cases is supportive (antipyretics, fluids).
- Malnutrition, immunosuppression, poor health, and inadequate supportive care can worsen the prognosis in any patient. In developing nations, measles is a major cause of infant mortality.
- Vitamin A supplementation has shown to be of benefit in the treatment of measles.
Complications

- Groups at increased risk for complications of measles include immunocompromised hosts, pregnant women, malnourished individuals, and persons at extremes of age.
- Most common complications include otitis media, pneumonia, laryngotracheobronchitis (croup), and diarrhea. Hepatitis, thrombocytopenia, and encephalitis occur less commonly.
- Pneumonia is the most common fatal complication of measles in children and the most common complication overall in adults.
Another Classic Exanthem: Rubella (German measles)

Clinical presentation

• Low-grade fever, headache, sore throat, rhinorrhea, cough
• Conjunctivitis and lymphadenopathy
• Pruritic, pink to red macules and papules which begin on face and spread to neck, trunk, and extremities over 24 hours
• 20% with petechial lesions on soft palate and uvula (Forchheimer's sign)

Treatment is usually supportive

- All women of child-bearing age with suspected rubella should be screened for pregnancy
- Infection during pregnancy may can result in miscarriage, fetal death, or cause congenital rubella syndrome
## Viral Exanthem Summary Table

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<tr>
<th>Viral Syndrome</th>
<th>Causative Virus</th>
<th>Exanthem/Enanthem</th>
<th>Age/Epidemiology</th>
<th>Associated Symptoms</th>
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<tbody>
<tr>
<td>Roseola</td>
<td>HHV-6 (HHV-7)</td>
<td>Erythematous macules and papules surrounded by white halos.</td>
<td>Infant-Preschool</td>
<td>High fever x 3 days, then rash. Mild URI sx. Complications: febrile sz.</td>
</tr>
<tr>
<td>Erythema Infectiosum</td>
<td>Parvovirus B19</td>
<td>Erythematous &quot;slapped&quot; cheeks, followed by reticulate erythema on body</td>
<td>School-age</td>
<td>Low-grade fever</td>
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<tr>
<td>Hand-Foot-and-Mouth Disease</td>
<td>Coxsackie A16, A6; Enterovirus 71; others</td>
<td>Oval vesicles on palms, soles, buttocks; oral erosions.</td>
<td>Infant-Preschool</td>
<td>Fever, sorethroat, respiratory and GI sx.</td>
</tr>
<tr>
<td>Measles</td>
<td>Measles</td>
<td>Erythematous macules and papules; spread from head down. White erosions on buccal mucosa (Koplik spots)</td>
<td>Majority of cases in US are imported.</td>
<td>Prodrome: Fever, Malaise, Conjunctivitis, Cough, Coryza Infectious complications.</td>
</tr>
<tr>
<td>Rubella</td>
<td>Rubella</td>
<td>Pruritic pink macules and papules, spread from head down over 24 hrs. Petechial lesions on soft palate (Forsheimer’s sign)</td>
<td>Majority are vaccinated.</td>
<td>Fever, HA, URI sx, conjunctivitis, lymphadenopathy. Congenital rubella syndrome.</td>
</tr>
</tbody>
</table>
Take Home Points

- Exanthems are rashes that occur abruptly and affect multiple areas of the skin simultaneously.
- Morbilliform means “composed of erythematous macules and papules that resemble a measles rash.”
- Most cases of viral exanthems are nonspecific and resolve without treatment.
- Distinct viral exanthems are seen in erythema infectiosum, roseola infantum, Hand-Foot-and-Mouth Disease, measles and rubella.
- Careful history taking and physical exam help establish the diagnosis.
- In the case of measles and rubella, clinical diagnosis should be serologically confirmed and reported.
Acknowledgements

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References


References


- Jordan J. Clinical manifestations and pathogenesis of human parvovirus B19 infection. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2013.

To take the quiz, click on the following link:

https://www.aad.org/quiz/viral-exanthems-learners