Viral Skin Infections

Dr. Ashraf Khasawneh
Skin lesions

- **Macule**: change in surface color without elevation or depression, less than either 5 or 10 mm in diameter
- **Papule**: circumscribed, solid elevation of skin with no visible fluid. pinhead to less than either 5 or 10 mm in diameter
- **Nodule**: similar to a papule. greater than either 5 or 10 mm in both width and depth. The depth differentiates a nodule from a papule
- **Pustule**: small elevation of the skin containing cloudy or purulent material
- **Vesicle**: circumscribed, fluid-containing, epidermal elevation generally considered less than either 5 or 10 mm in diameter
- **Bulla**: large vesicle described as a rounded or irregularly shaped blister containing serous or seropurulent fluid, equal to or greater than either 5 or 10 mm
- **Ulcer**: discontinuity of the skin exhibiting complete loss of the epidermis, portions of the dermis and subcutaneous fat
- **Crust**: dried serum, pus, or blood usually mixed with epithelial and sometimes bacterial debris
- **Lichenification**: epidermal thickening characterized by visible and palpable thickening of the skin with accentuated skin markings
Viruses causing skin lesions

• World wide
• Nonimmune individuals
• Humans sole reservoirs
• respiratory tract primary route
  – Mumps, Measles, Rubella
  – Erythema infectiosum and Parvovirus B19.
  – Roseola Infantum (Exantheme Subitum) and HHV6 and HHV7.
• Poxviruses.
• Herpes viruses
• Human papilloma virus
Measles (Rubeola)

- Paramyxovirus family, Morbillivirus genus.
- -ve sense, single-stranded RNA, enveloped
- Single serotype, prone to antigenic variation
- Sever illness in children associated with fever, rash and immunosuppression.

Epidemiology
- More than 6 months of age.
- Late winter and early spring.
- 95% infectivity. Communicability: 3-5 days before to 4 days after the appearance of the rash.
Exanthemes and enanthemes
Pathogenesis

- URT, intense infection as a result of viral replication and syncytia formation. Disruption of cellular cytoskeleton leads to the formation of inclusion bodies in the nucleus and the cytoplasm.
- Viremia and lymphatic dissemination (lymphoid tissue, BM, abdomen, skin, conjunctiva, UT, CNS)
- Viremic phase: infect B and T cells, PMN’s, CMI and humoral immunity depression, superinfection.
- Lymphoid tissue: Warthin-Finkeldey cells.
- Skin lesion: Vasculitis and skin rash, exantheme and enantheme (Koplik’s spots: red spots with bluish-white centre on the buccal mucosa).
- CNS involvement (encephalitis) due to cytotoxic (CD8) T-cells which react with virus infected cells.
Immunity

- CMI suppression for several months
- CMI at early stage mediate rash formation and is necessary for recovery
- Humoral peaks in 2-3 weeks, persist at low level.
- Life long immunity with neutralizing Abs
Clinical manifestations

• 5 day measles
• IP=7-18 days
• URT symptoms, conjunctivitis, fever. 1-3 days later Koplik’s spots (1-2 days), skin rash (maculopapular) 3-5 days, Lymphadenopathy (cervical lymph nodes).
• Infectivity: 3-5 days before and 4 days after rash appearance
• Mortality could reach 15-25% esp. in immunocompromised and malnourished.

COMPLICATIONS
• Bacterial superinfection in 5-15% (OM, sinusitis, pneumonia, encephalitis and mastoiditis)
• SSPE (1 in 100,000) chronic measles virus infection to CNS. Occur 2-10 yrs after infection. No treatment
• SSPE: personality change, intellectual deterioration, myoclonus, spasticity, tremor and ocular abnormalities.
Diagnosis

• Clinical Diagnosis.
• Viral isolation from oropharynx or urine.
• Multinucleated giant cells.
• Serology: ELISA, IF, PCR

TREATMENT AND PREVENTION

• Supportive treatment, observe complications (bacterial super infection)
• Live attenuated vaccine
• MMR: first (12 to 15 months) second (4-6 years), contraindicated: immunocompromised and pregnant women except AIDS pts.
• Immunocompromised pts (including infants) may be given IM immunoglobulin. Best results if given within 6 days of exposure.
• Mild Problems
  • Fever (up to 1 person out of 6)
  • Mild rash (about 1 person out of 20)
  • Swelling of glands in the cheeks or neck (about 1 person out of 75)
  • If these problems occur, it is usually within 7-12 days after the shot. They occur less often after the second dose.
• Moderate Problems
  • Seizure (jerking or staring) caused by fever (about 1 out of 3,000 doses)
  • Temporary pain and stiffness in the joints, mostly in teenage or adult women (up to 1 out of 4)
  • Temporary low platelet count, which can cause a bleeding disorder (about 1 out of 30,000 doses)
• Severe Problems (Very Rare)
  • Serious allergic reaction (less than 1 out of a million doses)
### National Vaccination Program

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG</td>
<td>Closest time after birth, meaning BCG vaccination.</td>
</tr>
<tr>
<td>DTP</td>
<td>At 2 months (121 days), meaning DTP vaccine.</td>
</tr>
<tr>
<td>IPV</td>
<td>At 2 months (121 days), meaning IPV vaccine.</td>
</tr>
<tr>
<td>OPV</td>
<td>At 2 months (121 days), meaning OPV vaccine.</td>
</tr>
<tr>
<td>Measles</td>
<td>At 2 months (121 days), meaning Measles vaccine.</td>
</tr>
<tr>
<td>MMR</td>
<td>At 18 months, meaning MMR vaccine.</td>
</tr>
</tbody>
</table>

### Jordan National Vaccination Program

- At birth: BCG (BCG)
- At 2 months: DTP + IPV + OPV + Measles
- At 18 months: MMR

The vaccination program includes a combination of vaccines to protect against various diseases, ensuring comprehensive protection for children.
Mumps

Swollen parotid gland
Mumps

- Paramyxovirus one antigenic type.
- -ve, ss-RNA, enveloped
- NH for attachment and F for fusion on envelope.
- Parotitis, aseptic meningitis in children.
- Acute orchitis and encephalitis in adults.

Epidemiology

- Frequent in 5-15 years old
- 30-40% of contacts do not develop clinical illness
- Communicable 7 days before to 9 days after.
- Late winter to spring.
Pathogenesis and immunity

• Local replication in RT and local lymph nodes, $1^{\text{ry}}$ viremia, reach salivary glands and CNS, $2^{\text{ry}}$ viremia then spread to organs (kidney).
• Viruria is common
• Tissue response characterized by cell necrosis and inflammation.
• IgM, then IgG (for life)
• CMI might contribute to pathogenesis and recovery from infection.
• Permanent immunity through neutralizing Abs
Clinical manifestations

- IP=12 to 29 days avg. 16-18 days.
- Fever and parotid swelling, Unilateral or Bilateral (7-10 days)

COMPLICATIONS

- 1-3 weeks after disease onset
- Meningitis 10%, encephalitis, transverse myelitis, Pancreatitis, orchitis 10-20%, Oophoritis.
- Rare: Myocarditis, nephritis, arthritis, thyroiditis, sensorineural deafness.
- Most complications resolve without sequale in 2-3 weeks.
Diagnosis and prevention

- Isolated in Saliva, CSF, Pharynx and urine
- Grown in primary monolayer of monkey kidney cell culture.
- Syncytial giant cells, viral hemagglutination.
- PCR
- Serology: ELISA, IF and neutralization test

- No specific therapy, only MMR two doses.
- Single dose 80% seroconversion; 90% after two doses.
Rubella (German measles)

- Mild benign childhood exantheme; Malaise, faint rash and arthralgia
- Profound effects on developing fetuses.
- Togavirus family, rubivirus genus.
- Enveloped, icosahedral, +ve ss-RNA genome
- Two glycoproteins E1 and E2
- One serotype, only in humans.
- Agglutinates chicks RBC’s, Trypsin treated human type O RBC’s.
- Virus enter the cell by viropexis. Genomic RNA encodes for nonstructural proteins and subgenomic RNA for structural proteins. Assembly occurs at the golgi or cytoplasmic membrane.
Epidemiology and pathogenesis

- Winter and spring, only 30-60% develop clinical apparent disease.
- Women of childbearing age, carry a risk of exposure during pregnancy
- Contagious 7 days before to 7 days after onset of rash
- Infected babies spread the virus 6 M after birth.

- URT, LNs, viremia, skin and organs.
- CMI and Immune complexes, rash, arthritis.
- Maternal viremia, placental infection, spread to fetus and congenital infection.
- Pathogenesis of congenital defects: 1) vasculitis with impaired fetal oxygenation. 2) chronic viral infection leads to impaired mitosis, cellular necrosis and chromosomal breakage.
- Shedding of the virus in infected infants is prolonged (up to 30 months)
- Produce IgM and IgG antibodies to the virus, decrease to undetectable levels in 3-4 yrs.
- Viremia up to 8 days before rash to 2 days after.
- Virus shedding from oropharynx can be detected up to 8 days after onset of rash.
Pathology and immunity

- Mononuclear cell infiltration in tissues, Ca++ deposition is delayed in the metaphyses of long bones (Celery stalk).
- Ab titer peak after 2-3 weeks of onset
- Secretory IgA in respiratory tract
- Life long immunity.
- Reexposure: Transient Respiratory tract infection.
Clinical manifestations

- Three day measles.
- IP=14 – 21 days (16 average)
- Fever, URT symptoms, LNs (post cervical and postauricular).
- Macular rash 1-3 days (head, neck and trunk), faint rash
- Complications: arthralgia, arthritis, encephalitis and TCP.
- Risk for fetal damage is up to 80% in 2w, 6 – 10% by 14\textsuperscript{th}, 20-30% over all.
- Cardiac: PDA, Pulmonary valvular stenosis.
- Eye: Cataract, chorioretinitis, Glucoma, Coloboma, cloudy cornea, microophthalmia.
- Sensorineural deafness, enlarged Liver and Spleen.
- Thrombocytopenia, intrauterine growth retardation.
- CNS defects: microcephaly, encephalitis and mental retardation
- Late including DM, chronic thyroiditis, Subacute panencephalitis (SPE).
Diagnosis and treatment

- Diagnosis: Clinically is not enough.
- Isolated in Respiratory secretions, Urine and feces with
  - Cell culture.
  - RT-PCR.
  - Serology, IgM significance: (5%) not produced at all or persist for 200 days

- Supportive treatment
- Live attenuated vaccine
- MMRV: RA 27/3 human diploid fibroblast cell culture, female adults, hospital staff at risk, seroconversion in 95%
- Contraindications: IC and pregnant women
- Avoid conception for 3 months
Erythema infectiosum

- Parvovirus B19.
- Naked, icosahedral, SSDNA
- Three capsid proteins VP1-3
- cultured in BM cells, fetal liver cells.
- Globoside (P antigen) receptor found on erythroid progenitors, erythroblasts, megakaryocytes and endothelial cells.
- Primary site of replication is the nucleus of immature cell in the erythrocyte lineage.
- Clinical consequence is minimal unless pt compromised by chronic hemolytic process: sickle cell and thalassemia
- These pts might present with fever only. Then found to have anemia, and aplastic crises.
- Immunosuppressed pts (AIDS) with bone marrow failure, think of Parvovirus infection
Manifestations and diagnosis

- IP 4-21 days
- Fever, malaise, headache and myalgia and itching
- Indurated rash on the face (slapped-cheek) which spreads in 1-2 days to arms and legs
- LNs, enlarged spleen and liver.
- Illness lasts 1-2 wks, but rash may recur for 2-4 wks upon: exposure to heat or sunlight, on exercise or emotional stress.
- Sometimes associated with arthritis and vasculitis.
- Rare complications: hepatitis, Thrombocytopenia, nephritis and encephalitis.

- Transmitted through respiratory route
- Spring months
- Viremia last 7-12 days

- Diagnosis: PCR, and serology: IgM-specific Ab

- Treatment: no definitive treatment, immunoglobulin
Parvovirus B19

“Slapped cheek” rash

ADAM
Roseola Infantum (Exanthem Subitum)

- HHV6, HHV7.
- HHV6 has two variants A and B.
- Replicates in CD4+ T-lymphocytes
- All population has Abs against it by age 5yrs
- HHV6-B associated with Exanthem Subitum. A and B associated with febrile illness with or without seizure and rash.
- Common in 6 months- 2 years
- Exanthem Subitum: Fever (39°C), 3-5 days later Faint macular rash appears that spread from trunk to extremities.
- EBV, Adenovirus, coxsakieviruses and echoviruses cause similar manifestations.
- Can cause latent infection in T-cells and become reactivated with immunosuppressive status.

- Diagnosis: seroconversion, culture and PCR

- Treatment: ganciclovir and foscarnet.
Roseola infantum
<table>
<thead>
<tr>
<th></th>
<th>RUBEOLA</th>
<th>RUBELLA</th>
<th>ROSEOLA</th>
<th>ERYTHEMA INFECTIOSUM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>Paramyxoviridae</td>
<td>Togaviridae</td>
<td>HHV6,7</td>
<td>Parvovirus b19</td>
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<tr>
<td><strong>Incubation Period</strong></td>
<td>7 – 18</td>
<td>14 - 21</td>
<td>unknown</td>
<td>7– 10</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Respiratory</td>
<td>Respiratory</td>
<td>Oral secretions</td>
<td>Respiratory</td>
</tr>
<tr>
<td><strong>Epid</strong></td>
<td>All ages &gt;6 months</td>
<td>6 -18 months</td>
<td>6months-2yrs</td>
<td>All ages 5-15 yrs</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td>Maculopapular</td>
<td>Maculopapular</td>
<td>Maculopapular</td>
<td>Maculopapular</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td>Begins on the head, then trunk and extremities</td>
<td>Begins trunk → arms &amp; neck face- legs – 3d</td>
<td>Begins trunk → extremities</td>
<td>Face → arms &amp; legs</td>
</tr>
<tr>
<td><strong>Prodrome</strong></td>
<td>3 – 5 d low-mod fever, hacking cough, coryza, conjunctivitis, kopliks after 2-3 days</td>
<td>Mild catarrhal , retroauricular, post cervical, post occipital lymphadenopathy</td>
<td>Mild URT illness</td>
<td>Headache, fever, sore throat, coryza and abd pain for 2-3 days</td>
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<tr>
<td>Symptoms</td>
<td>Fever, cough, conjunctivitis, koplík’s spots</td>
<td>Low grade fever, upper respiratory symptoms</td>
<td>High fever, occasional late sudden rash</td>
<td>Mild fever, malaise, headache, myalgia and itching</td>
</tr>
<tr>
<td>Infectivity</td>
<td>3-5 days before and 5 days after rash appearance</td>
<td>7 days before – 7 days after onset of rash</td>
<td>From time of exposure till symptom development</td>
<td>3rd day of fever and 1st day of rash</td>
</tr>
<tr>
<td>Rash</td>
<td>Lateral neck, ears, hairline → back, abdomen, thigh → feet on 2nd</td>
<td>Faint rash over head, neck and trunk last 1-3 days</td>
<td>rash appears on the trunk and spreads over the body. The rash's spots blanch (turn white) when touched</td>
<td>Rash 3 stages 1. Slapped cheek 2. Maculopapular on 3rd as face fades 3. Lacy or reticulated appearance rash – fades central clearing pruritic lasts 2-39 days</td>
</tr>
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<td></td>
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<tr>
<td><strong>Illness duration</strong></td>
<td>3-5 days</td>
<td>1-3 days</td>
<td>3-5 days</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td>Bacterial superinfection, encephalitis, keratitis, SSPE</td>
<td>Arthritis, congenital infection</td>
<td></td>
<td>Aplastic crisis, arthritis, arthralgia</td>
</tr>
<tr>
<td><strong>Fetal infection</strong></td>
<td>No</td>
<td>Yes- Multiple defects</td>
<td>No</td>
<td>Yes- still birth</td>
</tr>
<tr>
<td><strong>Vaccine</strong></td>
<td>Live attenuated</td>
<td>Live attenuated</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>