VESICULAR ERUPTION OF VIRAL INFECTION IN TROPICAL COUNTRIES

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- Individual predisposition
  - Skin barrier
  - Personal hygiene
  - Nutritional status

- Environmental
  - Temperature
  - Humidity
  - Geographical position

Important role in some infectious diseases (Fungi, Bacterial, VIRUS)
- **Viral skin disease** → **skin rashes**

- **Vesicula / vesicle**:
  - Elevated lesions
  - Circumscribed
  - Filled with clear fluid
  - Ø < 0.5 cm

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**Exanthema**

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**Vesicular lesions**

- Immune disorder
- Other non-infectious condition
- A number of viral infection
  - Varicella
  - Herpes zoster
  - Hand foot mouth disease
  - Herpes simplex
VARICELLA
(Chicken pox)

- Acut primary Varicella Zoster Virus (VZV) infection
- Highly contagious
- Acquired by:
  - Inhalation infected respiratory droplet
  - Direct skin contact with infected lesion

Etiology

- VZV: Varicella zoster virus
- Member of the Herpes virus family
Epidemiology

- Worldwide
- $\varphi = \sigma$
- Children $>>$
- Temperate climates:
  - 90% : children $< 10$ years of age
  - $< 5% : > 15$ years of age
- Tropical countries:
  - Mean age $\uparrow$
  - Susceptibility among adults is greater

VZV

Pathogenesis

mucosa of respiratory tract and oropharynx

Multiplication

Primary viremia

RES

(2 weeks)

Secondary viremia

Incubation period

Symptom & lesion
Clinical finding

- Incubation period: 10 days – 3 weeks
- Prodromal symptom:
  - Children: low grade fever proceed / simultaneously with onset of the rash
  - Older children / adult: 2-3 days of fever, malaise, backache.
  - Some patient: sore throat, dry cough

- Faint macular \([24 \text{ hours}]\) “tear drop” vesicle on erythematous base \(\rightarrow\) pustula \(\rightarrow\) crusted.

- Vesicle:
  - \(\varnothing 2-3 \text{ mm},\) elliptical, long axis parallel to the skin fold
  - Superficial, thin walled surrounded by irregular area of erythema \(\rightarrow\) “dewdrop on rose petal”
  - The fluid become cloudy-pustula-drier, beginning in the center \(\rightarrow\) umbilicated \(\rightarrow\) crust \(\rightarrow\) (1-3 weeks) fall of spontaneously \(\rightarrow\) shallow pink depression \(\rightarrow\) gradually disappear.
Rash:
- Centrally distribution
- Begin on the face, scalp → trunk, upper limb
- Evolve in crops next 12-24 hours
- New crops continue appear for about 7 days
- Seldom on the palm & sole
- In area of inflammation (diaper rash sunburn) vesicle ≥
- Could be in the mucous membranes
- Pruritus (+)

Distinctive feature:
- Simultaneous presence in any area of the skin of lesion in all stages

Fever:
- Persist as long as new lesions continue to appear
- The height proportional to the severity of the rash
Diagnosis

- Clinically, based on:
  - The appearance and evaluation of the characteristic rash.
  - History of exposure within the proceeding 2-3 weeks

Supporting laboratory

- Tzanck smear: multinucleated giant cell
- Histopathologic, serologic, immunofluorescen, isolated virus from cell culture
Complication

- Normal children:
  - <<<
  - >> secondary bacterial infection
  - Secondary bacterial pneumonia, otitis media, supportive meningitis <<<

- Adult
  - ↑
  - >> primary varicella pneumonia

Treatment

<table>
<thead>
<tr>
<th></th>
<th>Children</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>20 mg/Kg, 4x/day 5 days</td>
<td>5 x 800mg/day 7 days</td>
</tr>
<tr>
<td>Valaciclovir</td>
<td>3 x 1000mg/day 7 days</td>
<td></td>
</tr>
<tr>
<td>Famcyclovir</td>
<td>3 x 500mg/day 7 days</td>
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</tbody>
</table>
Symptomatic:
- Antipiretic
- Antihistamin
- Secunder infection (+)
  → antibiotic effective against S. aureus & streptococcus β hemolyticus

Prevention
- Live attenuated viral vaccine (Oka strain)
  - Children age 1-12 years: single dose
  - ≥ 13 years of age: twicw dose (4-8 weeks)

- Passive immunization:
  VZV specific immunoglobulin 125μ/10 Kg (VZIG)
Herpes zoster (shingles)

- Acute inflammatory, unilateral dermatom
- Having dermatologic and neurologic manifestation
- Caused by VZV

Epidemiology

- 15-20% of population
- 1.5 - 3.0 per 1000 person per year in all ages
- 7 - 11 per 1000 person per year in person > 60 year of age
- The population ages
- $\sigma = \varphi$
- Sporadically throughout the year, no seasonal prevalence

Risk factor

- Old age
- Cellular immune dysfunction

Pathogenesis

Reactivation of VZV latent in sensory ganglion
Clinical finding

- Prodromal symptom:
  - Pain and paresthesi
  - Several days (1-3 weeks)
  - Immunocompetent
    - < 30 year of age <<
    - > 60 years of age >>

- Erythematous maculae & papulae $\overset{(12-24 \text{ h})}{\rightarrow}$ vesicles $\overset{(7-10 \text{ days})}{\rightarrow}$ dry and crust $\rightarrow$ crust persist 2-3 weeks.
- Closely grouped of vesicle on erythematous base, evolve more slowly then variola.
- New lesions: 1-4 days (7 days).
- The area applied by the trigeminal nerve, particularly ophthalmic division.
- The thoracic from T3-L2
- Older people: - more severe
  - last longer
Diagnosis

- Based on clinical sign & symptom
  - Tzanck smear, histopathology
  - Definite diagnosis: culture
Complication

- Cutaneous, Ocular, Neurologic, Visceral

<table>
<thead>
<tr>
<th>Complications</th>
<th>Visceral</th>
<th>Neurological</th>
<th>Visceral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous VZV dissemination</td>
<td>Neuritis</td>
<td>Meningo-encephalitis</td>
<td>Abnormal sensations</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>Herpetic meningitis</td>
<td>Herpes zoster</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Scarring</td>
<td>Ophthalmic herpes zoster</td>
<td>Herpetic meningitis</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Cerebral</td>
<td>Ophthalmic herpes zoster</td>
<td>Herpetic meningitis</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Zoster gangrenosis</td>
<td>Ophthalmic herpes zoster</td>
<td>Herpetic meningitis</td>
<td>Herpes zoster</td>
</tr>
<tr>
<td>Seizures</td>
<td>Ophthalmic herpes zoster</td>
<td>Herpetic meningitis</td>
<td>Herpes zoster</td>
</tr>
</tbody>
</table>


Treatment

**Immunocompetent adult:**
- Acyclovir 5 x 800mg 7 days, or
- Valacyclovir 3 x 1000mg 7 days, or
- Famcyclovir 3 x 500mg 7 days
- Symptomatic treatment
- Treatment of complication
Zoster vaccine
FDA: prevention of Herpes zoster in adult >> year of age

Herpes Zoster Vaccine in Older Adults and the Risk of Subsequent Herpes Zoster Disease

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Stephanie R. Blauke, MD, MPH
Lisa S. Ny, MPH
Steven J. Jacobson, MD, PhD

Context: Approximately 1 million episodes of herpes zoster occur annually in the United States. Although pharmacoeconomic data provided evidence that herpes zoster vaccine works in a select study population under idealized circumstances, the vaccine needs to be evaluated in field conditions.

Objective: To evaluate risk of herpes zoster after receipt of herpes zoster vaccine among individuals in general practice settings.

Design, Setting, and Participants: A retrospective cohort study from January 1, 2007, through December 31, 2009, of individuals enrolled in the Kaiser Permanente Southern California health plan. Participants were immunocompetent community-dwelling adults aged 60 years or older. The 79,761 members in the vaccinated cohort were age matched (1:3) to 237,188 unvaccinated members.

Main Outcome Measures: Incidence of herpes zoster.

Results: Herpes zoster vaccine recipients were more likely to be white, women, with more outpatient visits, and fewer chronic diseases. The number of herpes zoster cases among vaccinated individuals was 80/8 in 1,416 person-years (1.04/100 person-years; 95% confidence interval [CI], 0.92-1.21), and for unvaccinated individuals it was 690/550 person-years (1.26/100 person-years; 95% CI, 1.21-1.31). In adjusted analysis, vaccination was associated with a reduced risk of herpes zoster (hazard ratio [HR], 0.49; 95% CI, 0.42-0.58). Infection occurred in all age strata and among individuals with chronic diseases. Risk of herpes zoster differed by vaccination status to a greater magnitude than the risk of unrelated acute medical conditions, suggesting results for herpes zoster were not due to bias. Diphtheritic herpes zoster (HR, 0.37; 95% CI, 0.23-0.69) and hospitalizations coded as herpes zoster (HR, 0.35; 95% CI, 0.24-0.51) were less likely among vaccine recipients.

Conclusions: Among immunocompetent community-dwelling adults aged 60 years or older, receipt of the herpes zoster vaccine was associated with a lower incidence of herpes zoster. The risk was reduced among all age strata and among individuals with chronic diseases.

HAND, FOOT & MOUTH DISEASE (HFMD)

- Acute infection
- Caused by non-polio enterovirus
- Usually mild and self-limited
Etiology

- Major causative agent are:
  - Coxsackie virus A 16 (CVA 16)
  - Human enterovirus 71 (HEV 71)
  - Coxsackie virus A 10 (CVA 10)
- Genus enterovirus family Picornaviridae

Epidemiology

- Worldwide
- Temperate climate: fall and summer >>
- Topical countries: throughout the year
- Sporadic outbreak & epidemic
- Recent years: several EV 71 associated outbreak in Australia, Singapore, Taiwan, China, Vietnam.
- Children < 10 years of age: >>
Hand, foot, mouth disease kills 70 in Vietnam

VIETNAM: A surging outbreak of hand, foot and mouth disease has killed 70 people so far this year in Vietnam and infected more than 23,000, mostly children under 5, state-controlled media reported Thursday. Most of the cases have been reported in the country’s south, and enterovirus 71, or EV-71, is the dominant strain circulating in Vietnam, Nguyen Van Bi, head of the Ministry of Health’s Department of Preventive Medicine, was quoted by Thanh Nien newspaper as saying.

EV-71 can result in a more serious form of the common childhood disease leading to paralysis, brain swelling or death. This year’s outbreak is a sharp uptick from recent years. Since 2008, about 10,000 to 15,000 cases were reported per year with about 20 to 30 children dying annually. — AP

Pathogenesis

- Transmission via:
  - Fecal – oral route
  - Respiratory inhalation (<<)
- Ingested / inhaled virus → ensues in the oropharynx and / or GI tract → viremia
Clinical findings

- Incubation: 3 – 7 days
- Non specific prodrome:
  - Low grade fever
  - Malaise
  - Throat / sore mouth
  - Abdominal pain / upper respiratory tract symptoms
  - Cervical & submandibular lymphadenopathy
- Oral lesion and cutaneous lesions

Oral lesions

- Painful
- Few in number
- Tongue, buccal mucosa, hard palate
- Bright pink macules, papules → vesicles with surrounding erythema → erode → yellow to grey erosions surrounded by erythematous halo
Cutaneous lesions

- Palm, soles, slides of hands and feet, buttock >>
- Red macules → clear, oval, elliptical (football-shaped) /triangular vesicles with surrounding red halos → crusting → (7-10 days) heal.

Laboratory test

- No tests are indicated
- Epidemic (+) → stool and throat cultures → determining the strain → determining possible complication
- (Viral culture, PCR)
Diagnosis

History and physical examination

Complications

- Rare
- Painful oral lesions → dehydration
- Secondary infection
- Aseptic meningitis most common serious complication
- E 71: severe disease with encephalitis, encephalomyelitis, myocarditis pulmonary oedema, pulmonary hemorrhage, death.
### Table 2: Clinical staging and management of enterovirus 71 infection [41]

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Manifestations</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hand, foot, and mouth disease</td>
<td>Symptomatic treatment only</td>
</tr>
<tr>
<td>2</td>
<td>CNS involvement</td>
<td>Fluid restriction, osmotic diuretics for increased intracranial pressure, and</td>
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<tr>
<td></td>
<td></td>
<td>furosemide for fluid overload (CVP &lt; 8 cm H2O), intravenous immunoglobulins</td>
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<tr>
<td></td>
<td></td>
<td>for encephalitis and/or polio-like syndrome and close monitoring of heart rate,</td>
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<tr>
<td></td>
<td></td>
<td>blood pressure, oxygenation, coma scale and blood glucose</td>
</tr>
<tr>
<td>3</td>
<td>Cardiopulmonary failure</td>
<td>Phosphodiesterase inhibition, milrinone, to increase cardiac output, early</td>
</tr>
<tr>
<td></td>
<td></td>
<td>intubation with positive pressure mechanical ventilation with increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>positive end expiratory pressure for pulmonary edema, and high frequency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>intubation if pulmonary edema/hyperglycemia persists or severe hypoxemia</td>
</tr>
<tr>
<td>3A</td>
<td>Hypertension</td>
<td>Add isotropic agents such as dopamine and epinephrine</td>
</tr>
<tr>
<td></td>
<td>Pulmonary oedema</td>
<td>Rehydration for lung edema, dyspnea, apnea or central hyperventilation, and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sufficient chest effort to avoid intubation</td>
</tr>
<tr>
<td>4</td>
<td>Convalescence</td>
<td>Rehabilitation for limb weakness, dysphagia, apnea or central hyperventilation,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and sufficient chest effort to avoid intubation</td>
</tr>
</tbody>
</table>

HFMD: hand, foot, and mouth disease; CNS: central nervous system; CVP: central venous pressure.

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**Treatment**

- ↓ morbidity
- Prevent complication
- Supportive Tx, symptomatic Tx
- No effective antiviral agent
- Adequat fluid intake
  - Intravenous hydration if necessary
- Antipiretic
- Secondary infection (+) → oral and/or topical antibiotic
Herpes simplex

- Caused by Herpes Simplex Virus (HSV) (the herpes virus family)
- 2 mayor antigenic:
  - Type 1: facial, oral, labial inf.
  - Type 2: genital inf.
  (the predilection of a specific viral serotype to a particular anatomic site appears to be changing)
- Acquired by direct contact with infected secretions / actual mucocutaneous lesions
- Primary or recurrent

- Primary HSV 1 Inf. : Childhood disease
- HSV 2 inf. :
  - Mainly after puberty
  - Often Transmitted sexually

- Tzanck smear
- Viral culture
Herpetic gingivostomatitis

- Children: 1-5 years of age
- Incubation: 5 days
- Fever, malaise, excessive dribbling
  Eating and drinking difficulties
  Foul breath odor
- Vesicles on erythematous base
  Painful, swollen, gray erosions and ulcerations
  (palate, tongue, gingival)

- The gums swollen, inflamed, bleed easily
- Regional lymph nodes enlarged and tender
- Perioral lesions: lips, cheeks, chin
- Tends to be self limited
- 10 days → 2 weeks
- Complications:
  - Dehydration
  - Encephalitis

- Supportive therapy: fluids, analgesic
- Specific antiviral therapy:
  - Acyclovir 5 x 200mg/day ≥ 5 days / Valacyclovir/Famcyclovir children 15mg/day 7 days
  - Must effective start within 3 days of disease onset
Herpes labialis

- Must common type of recurrent herpes inf.
- Reactivation latent in the cells of the trigeminal ganglion
- On the lips: vermilion border >>
- Prodromal symptom:
  - Tingling, burning, itching → (1-2 days) localized clusters of small vesicles / erosion on an erythematous base
- Topical and oral antiviral agent
Differential Diagnosis

- Impetigo
- Insect bite
- Contact dermatitis
- Erythema multiforme
- Drug eruption
- Scabies
- Apthous stomatitis
- Herpangina