Viral Dermatoses

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Senior Residents:
Disclosures

• No relevant financial relationships or conflicts of interest to disclose
Objectives

• Discuss human papillomavirus, including its oncogenic potential

• Discuss herpes viruses with an emphasis on the Epstein-Barr virus

• Discuss other viral exanthems, including associations of hand-foot-and-mouth disease
Human Papillomavirus (HPV)

- A dsDNA, non-enveloped virus that infects epithelia of skin or mucosa
- Causes an exciting array of warts in different size, shapes, colors...
- ...and anatomic locations
Awesome clinical spectrum of warts...

• Because > 130 subtypes of HPV

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Pathogenesis

Abrasions in skin allow HPV to reach basal keratinocytes, where it replicates.

Viral binding to skin cells requires L1, the major capsid protein.

HPV genes are transcribed:

- E1 + E2 are first, allowing transcription of the rest.
- E6 + E7 promote proliferation and amplify viral DNA.

→ hyperproliferation of keratinocytes.
E6 + E7 have a darker side

- E6 is an oncogene → degrades p53
- E7 is an oncogene → binds RB

When p53 is degraded and RB is bound, uncontrolled cell cycling may ensue

This may cause carcinogenesis in certain subtypes of HPV
Verruca vulgaris

- HPV 1, 2, + 4
Myrmecia

- HPV 1

From the Greek word for *ant hill*, referring to the clinical appearance of these plantar or palmar warts.
Verruca plana

- HPV 3 + 10
Epidermodysplasia verruciformis

- AR condition 2/2 mutation in EVER1/TMC6 or EVER2/TMC8 ➔ susceptibility to certain HPV subtypes

Clinically, 2 types of skin lesions:

- Tinea versicolor-like macules
- Verruca plana-like papules ➔ later develop SCC

• HPV 5 + 8
Condyloma acuminatum

- HPV 6 + 11

Condyloma in children always brings up the issue of sexual abuse. That risk is highest in kids > 3 years old. Infants < 1 year old probably acquired HPV through vertical transmission. Children 1 – 3 years old may be referred to child protective services on a case-by-case basis.
Verrucous carcinomas

- Verrucous carcinomas are low-grade squamous cell carcinomas, occurring in different locations:
  - Genitals – Buschke-Lowenstein tumor
  - Soles – Epithelioma cuniculatum
  - Oral mucosa – Oral florid papillomatosis
  - Shins – Papillomatosis cutis carcinoides

- Avoid radiation, may cause frank malignant degeneration
Laundry list of wart treatments

- Watchful waiting
- Cryotherapy every 1 – 3 weeks
- Manual debridement with No.15 scalpel blade
- IL Candida
- Topical 5-Fluorouracil nightly
- Salicylic Acid 17% home treatment
- Topical immunotherapies
  - Squaric Acid dibutylester (SADBE)
  - Diphenylcyclopropenone (DPCP)
- Measure serum zinc level and treat if low
- PO cimetidine
- Laser (PDL, utilizing hemoglobin as the chromophore)
- Bleomycin
- Duct tape
- Cidofovir
- Imiquimod
- Adapalene
- Podophyllin or trichloroacetic acid for genital warts
• RCT with n = 60 (common + plantar warts)
• Two interventions:
  – IL candida Q 3 weeks until clear, max of 3 sessions
  – Cryo Q 1 wk until clear, max of 10 sessions

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<tr>
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<th>IL Candida</th>
<th>Cryo</th>
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<tr>
<td>% pts clear</td>
<td>76.7%</td>
<td>56.7%</td>
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• IL candida statistically significant better response than cryo
“Donut” use cantharidin...

• ...or you could end up with this ringlike arrangement of warts

Especially if the warts are larger (> 5 mm) to begin with
Human Herpesviruses

Natalie Edgar, DO
Human Herpesviruses (HHV)

- Double-stranded DNA viruses
- Pathogenesis sequence
  - $1^\circ$ infection $\Rightarrow$ latency $\Rightarrow$ reactivation

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Human Herpesviruses (HHV)

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Epstein-Barr Virus (HHV-4)

• One of the most ubiquitous viruses, infecting 90-95% of adults worldwide
• Utilizes the CD21 cell surface receptor to infect B lymphocytes
• Virus remains latent in B-cells and periodic reactivation may occur
• Variety of clinical diseases
Epstein-Barr Virus (HHV-4)

Mononucleosis ampicillin eruption

- Generalized, pruritic, erythematous to copper-colored macules
- 7-10 days after starting aminopenicillin abx for presumed strep pharyngitis
- 80-100% of pts
- Not a true hypersensitivity
- Also in CMV infection
Epstein-Barr Virus (HHV-4)

Hydroa vacciniforme

- Childhood-onset photodermatosis that resolves by adulthood
- Photodistributed, hemorrhagic crusted papulovesicles that heal w/ scarring
- Study found 94% of children with typical disease, had lesional T-cells positive for EBV
Epstein-Barr Virus (HHV-4)

Gianotti-Crosti Syndrome

- Acute, symmetric papular eruption on the face, extremities, & buttocks
  - Spares the trunk
- EBV > Hepatitis B
- Likely represents a virus-induced delayed hypersensitivity
Epstein-Barr Virus (HHV-4)

Drug Reaction with Eosinophilia and Systemic Symptoms

- CMV, HHV-6, HHV-7 have also been implicated in conjunction with medication and genetics
- Morbilliform eruption with follicular accentuation and facial edema 2-6 weeks after initiating drug
- Peripheral eosinophilia and systemic symptoms
Epstein-Barr Virus (HHV-4)

• Other clinical presentations include
  – Genital ulcers (aka Lipschutz ulcers)
  – Hypersensitivity to mosquito bites
  – Oral hairy leukoplakia
  – Lymphoproliferative disease
  – Nasopharyngeal carcinoma
  – Smooth muscle tumors
Enteroviruses

• ssRNA

• Most common exanthem:
  - Hand-foot-and-mouth disease (HFMD)
HFMD

Vesicles on palms and soles

Erosive stomatitis

Onychomadesis
HFMD Enteroviruses

• Most common: **Coxsackie A16**

• Cardiopulmonary and neurological complications: **Enterovirus 71**

• Superinfection in those with atopic dermatitis: **Coxsackie A6**
  – “Eczema coxsackium” is a Kaposi’s varicelliform-like eruption
Measles (Rubeola)

- RNA virus in the *Paramyxovirus family*
- Incidence greatly decreased with vaccination
- Prodrome: *fever with 3 C’s*
  - Cough, conjunctivitis, coryza (nasal congestion)
Measles

Koplik spots

Cephalocaudal spread
Measles

- Late complication: **Subacute sclerosing panencephalitis**

- Treatment: **Vitamin A**
  - Low Vit A is associated with increased measles related morbidity and mortality
Erythema Infectiosum (EI)

- Fifth Disease
- Parvovirus B19 infection
  - ssDNA
- Most common in school aged children
Slapped cheeks

Lacy extremity-predominant exanthem
Erythema Infectiosum (EI)

- **Arthritis** occurs in 10%
  - Most commonly small joints (hands, wrists)
  - 30-60% of adult women

- Greatest susceptibility of fetal infection: **<20 weeks gestation**
  - Risk of fetal anemia resulting in *hydrops fetalis* and possible miscarriage
Another manifestation of Parvovirus B19...

Papular-purpuric glove and sock syndrome
Which HPV derived protein degrades p53 and is implicated in carcinogenesis?

A) E1
B) E3
C) E6
D) E7
A child with atopic dermatitis suffers from HFMD and suddenly develops a Kaposi's varicelliform-like eruption. What virus is associated with this occurrence?

A) Coxsackie virus A16  
B) Coxsackie virus A6  
C) Enterovirus 71  
D) Chikungunya
Summary

- Certain subtypes of human papillomavirus may cause squamous cell carcinoma when E6 degrades p53 and E7 inactivates RB

- Epstein-Barr virus is a herpes virus that is associated with a wide range of dermatologic conditions, including hydroa vacciniforme, Gianotti-Crosti syndrome, and DRESS syndrome

- Coxsackie A6 is an enterovirus that may cause a widespread eruption termed “eczema coxsackium” in atopic patients
References

1. Bolognia Ch 78, 79, 80, 81, 87


3. [http://www.regionalderm.com](http://www.regionalderm.com)


5. Hurwitz Ch 15, 16


Thank you!