Module Instructions

- The following module contains a number of blue, underlined terms which are hyperlinked to the *dermatology glossary*, an illustrated interactive guide to clinical dermatology and dermatopathology.
- We encourage the learner to read all the hyperlinked information.
Goals and Objectives

- The purpose of this module is to help medical students develop a clinical approach to the evaluation and initial management of patients presenting with warts.

- By completing this module, the learner will be able to:
  - Identify and describe the morphology of various types of warts
  - Discuss the pathogenesis of warts
  - Develop an initial treatment plan for a patient with warts
  - Determine when vaccines can be helpful for wart management
Case One

Megan Driskell
Case One: History

- **HPI:** Megan is an 8-year-old girl who presents to her pediatrician’s office with bumps on her fingers and hands. They have been present for 3 months without change and are asymptomatic.
- **PMH:** no chronic illnesses or prior hospitalizations
- **Allergies:** no known allergies
- **Medications:** none
- **Family history:** no affected family members
- **Social history:** lives at home with parents and attends school
- **ROS:** negative
Case One: Skin Exam
Case One: Question 1

How would you describe these lesions?

a. Hyperkeratotic and umbilicated papules
b. Hyperkeratotic, endophytic papules
c. Hyperkeratotic, exophytic papules
d. Smooth and umbilicated papules
e. Smooth, exophytic papules
Case One: Question 1

Answer: c

How would you describe these lesions?

a. Hyperkeratotic and umbilicated papules (these papules are not umbilicated)

b. Hyperkeratotic, endophytic papules (these papules are growing outward, not inward)

c. Hyperkeratotic, exophytic papules

d. Smooth and umbilicated (marked by a depressed spot) papules (more characteristic of molluscum contagiosum)

e. Smooth, exophytic papules (these papules are not smooth)
Clinical Features of Verruca Vulgaris

- **Hyperkeratotic**, exophytic (growing outward), dome-shaped papules or nodules
- Most common on fingers, dorsal hands, knees or elbows but may occur anywhere
- Punctate black dots representing thrombosed capillaries
- May **koebnerize** – spread with skin trauma
Case One: Question 2

Verruca vulgaris is caused by:

a. Human immunodeficiency virus
b. Human papillomavirus
c. Pox virus
d. Herpes virus
e. Varicella-zoster virus
Answer: b

Verruca vulgaris is caused by:

a. Human immunodeficiency virus
b. Human papillomavirus
c. Pox virus
d. Herpes virus
e. Varicella-zoster virus
Human Papillomavirus (HPV): Overview

- Warts are caused by HPV
- HPV infects skin and mucosal epithelia
  - Infection causes hyperplasia of the epithelium = a wart
- HPV infects the basal keratinocytes of cutaneous and mucosal epithelium
Role of HPV in Cutaneous Disease

- HPV can be transmitted by skin-to-skin contact or through contaminated surfaces or objects
  - Patients can also spread virus from a wart to unaffected skin
- The type of HPV influences the wart morphology

<table>
<thead>
<tr>
<th>Type of Wart</th>
<th>HPV Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verruca vulgaris: common warts</td>
<td>HPV 2, 4</td>
</tr>
<tr>
<td>Verrucae plana: flat warts</td>
<td>HPV 3, 10</td>
</tr>
<tr>
<td>Palmoplantar warts</td>
<td>HPV 1</td>
</tr>
<tr>
<td>Condylomata acuminata: external genital warts</td>
<td>HPV 6, 11, 16, 18, 31, and more</td>
</tr>
</tbody>
</table>
Epidemiology

- One of the top three skin problems in children
- Peak prevalence is during adolescence (13-16 years old)
  - About 5-20% of teens are affected
- Also common younger and older people
  - About 1-5% of School-age children (5-12 years) are affected
- Males and females are equally affected
Clinical Features of Verrucae Planae: Flat Warts

- Skin-colored or pink
- Smooth-surfaced, slightly elevated, flat-topped papules
- Dorsal hands, arms, face (exposed surfaces)
Clinical Features of Palmoplantar Verruca

- Thick, endophytic (depressed into skin of sole) papules
- Mosaic warts: plantar warts coalescing into large plaques
Clinical Features of Palmoplantar Verruca

- Can accumulate a thick callus over and around the wart
- Plantar warts may be painful when walking
General Treatment Principles

- **Observation**: Chance of spontaneous resolution at 2 years is over 75%
  - Supported by cure rates of 20-70% in placebo groups of trials
- **Multiple treatments** are almost always needed for any treatment modality (laser, acids, cryotherapy, etc.)
- Start with therapies that minimize side effects and risk of scarring
Common Wart Treatment Options

- Treatments are often destructive and/or stimulate the immune system
  - There is no specific anti-HPV therapy (unlike HIV and viral hepatitis)
  - Only imiquimod is FDA-approved, specifically for treatment of genital warts, none are approved for warts in other locations

<table>
<thead>
<tr>
<th>Primarily Irritating or Destructive</th>
<th>Primarily Immune-stimulating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryotherapy*</td>
<td>Imiquimod</td>
</tr>
<tr>
<td>Salicylic acid*</td>
<td>Candida antigen (IL)</td>
</tr>
<tr>
<td>Tretinoin cream</td>
<td>Immunotherapy: Squaric acid or DCNB</td>
</tr>
<tr>
<td>Shave removal</td>
<td></td>
</tr>
<tr>
<td>Adhesive tape</td>
<td></td>
</tr>
<tr>
<td>Laser</td>
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</tbody>
</table>

* = very common therapy, DCNB = dinitrochlorobenzene, IL=intralesional
## Approaches to Wart Treatment

<table>
<thead>
<tr>
<th>Number of Warts</th>
<th>Hand &amp; Foot</th>
<th>Face</th>
<th>Other Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Few</td>
<td>Salicylic acid</td>
<td>Cryotherapy Shave (surgical) removal</td>
<td>Cryotherapy Salicylic acid</td>
</tr>
<tr>
<td></td>
<td>Adhesive tape</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cryotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Laser</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Many</td>
<td>Salicylic acid</td>
<td>Cryotherapy Tretinoin cream</td>
<td>Imiquimod Tretinoin cream</td>
</tr>
<tr>
<td></td>
<td>Cryotherapy</td>
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For children, also consider observation, no active treatment.

*Treatments are listed from most favored (top) to less favored (bottom) in each box of the table.*
Cryotherapy

- Click here for an instructional video on cryotherapy
- Side effects of cryotherapy include:
  - PIPA (post-inflammatory pigment alteration)
    - hyperpigmentation or hypopigmentation
  - Scar
  - Pain
  - Blister
  - Nail dystrophy
Side Effects of Cryotherapy

- Post inflammatory hyperpigmentation after cryotherapy
- Ring Wart post-cryotherapy
Salicylic acid 17- 40%

- Mechanism: Keratolytic, loosens connections between keratinocytes, infected with HPV
- Applied and changed every 1-2 days, under occlusion (under tape or a bandage)
- Efficacy: Cure rate varies in individual studies (0-84%), similar to cryotherapy alone
- Cure rate improved by combining salicylic acid and cryotherapy
- Adverse effects: erythema, peeling, irritation, maceration (due to occlusion)
Case One: Question 3

Megan and her mom ask about treatment. You mention observation as an option. Approximately, what proportion of patients are wart-free at 2 years without treatment?

a. 10%
b. 30%
c. 45%
d. 60%
Case One: Question 3

Answer: d. 60%

Approximately, what proportion of patients are wart-free at 2 years without treatment?

a. 10%
b. 30%
c. 45%
d. 60%

Observation as a management option is also supported by the response rate in placebo groups, which typically ranges from 20-70%
Case One: Question 4

Megan and her mom prefer active treatment. Which of the following treatments would you try first?

a. Cryotherapy
b. Imiquimod
c. Laser therapy
d. Salicylic acid
Case One: Question 3

Answer: a. cryotherapy or d. Salicylic acid

Which of the following treatments would you try first?

a. Cryotherapy  
b. Imiquimod  
c. Laser therapy  
d. Salicylic acid

Cure rates for cryotherapy and salicylic acid are similar. Cryotherapy is more painful, while salicylic acid requires more effort on the part of the patient and caregivers. Lasers are not a first-line therapy. Cure rates for imiquimod are lower than salicylic acid and imiquimod is more expensive.
Case Two, Question 1

This 13-year-old girl has a single wart on her foot. What is your preferred approach with cryotherapy?

a. Freeze for 10 seconds, one time
b. Freeze for 30 seconds, one time
c. Freeze for 10 seconds, two times
d. Freeze for 30 seconds, two times
Case Two, Question 1

Answer d. Freeze for 30 seconds, two times
a. Freeze for 10 seconds, one time
b. Freeze for 30 seconds, one time
c. Freeze for 10 seconds, two times
d. Freeze for 30 seconds, two times

Options a and c would have too short an application time (freeze time) to cause sufficient damage.

Two freeze cycles performed and with adequate time to thaw is more effective, so options a. and b. are not preferred.

Treatment is also more effective if the thick overlying callus is removed – either sharply at the office or intermittently by the patient with a pumice stone at home.
Case Three

Jonathan Cohen
Case Three: History

- **HPI:** Mr. Cohen is a 17-year-old man comes into the clinic because of an increasing number of bumps on his penis over the last year.
- **PMH:** no chronic illnesses or prior hospitalizations
- **Allergies:** no known allergies
- **Medications:** none
- **Family history:** noncontributory
- **Social history:** studying economics at a nearby university
- **ROS:** negative
Case Three: Skin Exam
Case Three: Question 1

How would you describe these lesions?

a. Pearly, vesicular papules
b. Smooth, indurated plaques
c. Papillomatous, sessile papules
d. Waxy, stuck-on plaques
Case Three: Question 1

Answer: c

How would you describe these lesions?
A. Pearly, vesicular papules
B. Smooth, indurated plaques
C. Papillomatous, sessile papules
D. Waxy, stuck-on plaques
Clinical Features of external genital warts

- Compared to warts on the hands or feet, genital warts are *not* hard or hyperkeratotic
- Sessile (broad-based) papules
- May be papules or large confluent plaques
- External genitalia, perineum, perianal, inguinal fold
Comparison of molluscum and genital warts

Molluscum Contagiosum
(smooth, dome-shaped papules with central umbilication)

External Genital Warts
(papillomatous, exophytic papules and plaques)
What additional information is especially important to care for this patient?

a. Medications
b. Sexual history
c. Surgical history
d. Allergies
Answer: b. Sexual history

- What additional information is especially important to care for this patient?
- Why:
  - to determine if the patient is at risk for anal HPV infection
  - to discuss the contagious nature and risk of spreading to others and receipt from others
  - to consider symptoms of additional concomitant STI
External Genital Warts (EGW)

- HPV infection is one of the most common STIs
  - Highest incidence rates for men and women is during 20-34yo
  - Risk factors: sexual intercourse at an early age, numerous partners, unprotected exposure
- Effective prophylactic HPV vaccine is available for prevention of genital warts
HPV Infection

- Genital HPV infection is transmitted by sexual contact from partners with clinical or subclinical infection
- Some HPV types are associated with neoplasia (16, 18, 31, 33-35, 40, 45)
- Immunosuppression (organ transplant, HIV) can lead to infections that are more:
  - frequent, persistent, and difficult to treat
  - Patients with HIV and anal warts are also at higher risk of anal squamous cell carcinoma
Case Four: Question 3

Which of the following treatments could you use for external genital warts?

a. Cryotherapy
b. Imiquimod
c. Podophyllin
d. All of the above
Case Four: Question 3

Answer: d

Which of the following treatments could you use for external genital warts?

a. Cryotherapy (liquid nitrogen is used to freeze and destroy the infected tissue)

b. Imiquimod (interferon inducer is topically applied 3x per week for 16 weeks)

c. Podophyllin (this anti-mitotic agent is topically applied, twice daily for 3 days, wait 4 days, then repeat the cycle)

d. All of the above
Treatment (cont.)

- Surgical (destructive) methods can be used to treat genital warts
  - Laser
  - Electrocautery
  - Scissor or Shave debulking

In addition, it is important to counsel patients about the risk of transmission and malignancy.

- CDC patient handout

Always use protective mask due to aerosolized HPV virus in the smoke plume.
Prevention: HPV Vaccine

- Two HPV vaccines are licensed by the FDA and recommended by the CDC
  - Gardasil™ and Cervarix™
- Both vaccines are effective against HPV types 16 and 18, which cause most cervical cancers
Prevention: HPV Vaccine

- **Gardasil:**
  - quadrivalent vaccine against HPV 6, 11, 16, 18
  - Gardasil-9 against those 4 plus HPV 31, 33, 45, 52, 58
- **FDA-approved:**
  - for females and males, 9-26 years old
  - to prevent genital warts and HPV-related genital cancers
- **Ceravix:** bivalent vaccine against HPV 16, 18
- **FDA-approved:**
  - for females 10-25 years old (not approved for males)
  - to prevent HPV-related genital cancers
Case 5, Question 1

Parker is a 13-year old girl with warts on her fingers. She and her mother have heard that there is a vaccine that can treat warts and they want Parker to receive it. What is the best response to this request?

a. No, because she’s too young to get the vaccine.
b. No, because the types of warts (HPV) are different.
c. Yes, it will help treat and prevent warts.
d. Yes, it’s approved for this condition
Case 5, Question 1

a. No, because she’s too young to get the vaccine.
b. No, because the types of warts (HPV types) are different.
c. Yes, it will help treat and prevent warts.
d. Yes, it’s approved for this condition

Answer b.
The HPV vaccines are FDA-approved for males and females 9-26 years old (option a) for prevention, not treatment (option c) of external genital warts and HPV-associated genital cancers (option d), not common warts on the hands, face, feet, etc.
The FDA-approved vaccines are not composed of the HPV types that cause common warts (correct answer, option b)
Take Home Points

- Warts are caused by human papilloma viruses
- Numerous morphologies exist: common, flat, palmoplantar, external genital
- Treatment is difficult, so observation for spontaneous resolution is reasonable
- There are many treatment options available
- Vaccines have been developed to reduce HPV-associated neoplasia, and some have efficacy for external genital warts
Acknowledgements

- This module was developed by the American Academy of Dermatology Medical Student Core Curriculum Workgroup from 2008-2012.
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- Peer reviewers: Renee M. Howard, MD, FAAD; Erin F. D. Mathes, MD, FAAD, FAAP.
- Thanks to the Society for Pediatric Dermatology for help with revisions.
End of Module


To take the quiz, click on the following link:

https://www.aad.org/quiz/warts-learners