**WARTS FROM HELL**  
Ted Rosen, MD  
Baylor College of Medicine  
Houston, Texas

---

**Warts: Fast Facts**

- **Warts recognized Greco-Roman times**  
  Am J Clin Dermatol 2000;1:143-149
- **Common: Prevalence 3-20% of population**  
  Br J Dermatol 2001;144:4-11
- **Very common in children < 16 years of age**  
  Pediatr Dermatol. 2003;20:268-71 (USA)  
  J Babol Univ Med Sci 2003;5:1-6 (Iran)  
  Actas Dermosiifillogr 2008:99:111-118 (Spain)  
  J Formos Med Assoc 2008:107:21-29 (Taiwan)  
  J Dermatol 2008:35:413-418 (Turkey)
- **Spontaneous resolution rate high (2/3-3/4 2 yrs)**  

---

**INDICATIONS FOR THERAPY**

- Patient’s desire for therapy
- Pain, bleeding, itching, burning
- Disabling or disfiguring lesions
- Numerous or very large lesions
- Patient’s wish to prevent spread to self or to others
- Immunocompromise

Guidelines for care for warts. JAAD 1995;32:98-103  
Guidelines for the management of cutaneous warts Br J Derm 2001; 144:4-11

---

**THE IDEAL TREATMENT**

- Eliminate warts in nearly all patients treated
- Painless and non-scarring
- Require Rx of one wart (if multiple present)
- Require few treatment sessions
- Provide lifelong immunity
- Easily obtainable and low cost

**THE IDEAL TREATMENT DOESN’T EXIST**

---

**Wart Therapy Fast Facts**

- No single therapy is 100% effective
- No single therapy is uniformly superior to all reasonable alternatives
- Therapy involves trial and error
- Spontaneous resolution makes the evaluation of various therapies difficult
- Despite >6500 publications, reliable information is scant due to flawed methodology, poor quality reports and lack of randomized and/or placebo-controlled studies for virtually all Rx

---

**THEME**

- Salicylic acid, Lactic acid, Retinoids
- Trichloroacetic acid, Bichloroacetic acid
- Formaldehyde, Glutaraldehyde
- Podophyllin, Podophyllotoxin
- Interferon-alpha, Imiquimod
- Sensitizers (DNCB, SADBE)
- Cimetidine, IL Mumps or Candida antigen
- Bleomycin, 5-Fluorouracil
- Cryotherapy, Cantharidin
- Electrodesication, Laser ablation, PDT
- Thermotherapy, Ultrasound, Occlusion
- Acupuncture, Hypnosis, Botanicals
**Salicylic acid, Lactic acid, Retinoids**
Trichloroacetic acid, Dichloroacetic acid
Formaldehyde, Glutaraldehyde
Podophyllin, Podophyllotoxin
Interferon-alfa, Imiquimod
Sensitizers (DNCB, SADBE)
Cimetidine, II. Mumps or Candida antigen
Bleomycin, 5-Fluorouracil
Cryotherapy, Cantharidin
Electrodesiccation, Laser ablation, PDT
Thermotherapy, Ultrasound, Occlusion
Acupuncture, Hypnosis, Botanicals

---

**Duct Tape?**
- Applied for six days and removed
- Wart soaked with warm water
- Wart lightly debrided (emory board)
- Tape reapplied
- Continue process for 2 months
- Study: 51 patients, aged 3-22; Compared to Q2-3 week cryosurgery
  - 85% tape vrs 60% cryo Rx clear totally
  - Arch Pediatr Adolesc Med 2002;156:971-4

**DOES DUCT TAPE WORK? PART II**
Duct tape compared to corn pad (6wk)
16% duct tape, 6% placebo lesions clear
Study of 103 patients, aged 4-12
*Only applied ONE NIGHT per week*
*Done in Netherlands...Same “duct” tape?*
Arch Pediatr Adolesc Med 2006;160:1121

**Oral Acitretin**
- Limited experience: abn + normal hosts
- 0.5mg/kg daily x 2-3 months
- ? Benefit may be short-lived; ? F/U Rx
- Antiproliferative effects may inhibit viral replication and assembly within cell
- Off label: FDA-approved psoriasis
- AE: dyslipidemia; arthralgia, xerosis, cheilitis, alopecia
- COST (if no insurance coverage available)

**HIV+**
Monotherapy

HIV+ Acitretin 25mg/day x 2 months
Eur J Dermatol Venereol 2008; 18:346
**Oral Acitretin**

- Indian J Derm Venereol Leprol 2008;74:393-395
- Int J Dermatol 2006;45:480-482
- Pediatr Derm 1987;4:254-58 (Etretinate)

---

**Oral Zinc**

- Experience w/ case series: normal hosts
- Zn: Acetate, Gluconate, Sulfate
- QD 10mg/kg (3 doses, pc); 2-3 mo Rx
- 100mg ZnSO₄ = 22.5mg Zinc (max 150mg)
- ? MOA; Maybe increases APC activity
- Off label: FDA-approved: Zinc deficiency
- AE: GI distress; up to gastric perforation (microcytic anemia, copper deficiency)
- Binds: PCN, TCN, Quinolone, phytates
**Oral Zinc**

- 62.5-87.7% success rate reported
- Failures ascribed to too low a dose, noncompliance due to GI symptoms, or too short treatment regimen
- Patients do better when serum Zn levels rise (quadruples, on average)

- Br J Dermatol 2002;146:423-31
- JAAD 2009;60:706-708

**Problem Patient**

3 year history

Failed:
- 5% 5-FU, Imiquimod 5%, Tazarotene 0.1% (+ combinations of above three topicals)
- LN₂, Electrodesiccation

Let's try Zinc (10mg/kg ZnSO₄) PLUS Acitretin 25mg/day

**PDT**

- Experience: Normal hosts; Case series & RCT
- Pre-treatment preparation:
  - Flat warts: No prep
  - Common/Plantar: Pared or Salicylic acid & curettage
- 20% 5-Δ-ALA; Occlusion 3-6 hours
- Red, White or Blue lights; Dose = 50-125J/cm² (Majority w/ red light and 50-75J/cm²)
- Re-treatment every 3-14 days (Majority every 2 weeks)
- Requires 2-4 treatment sessions; 70-90% cure
- PAIN in 1/5 warts so treated severe; require Rx

Photodermatol Photoimmunol Photomed 2006;22:304


**FOOT PDT**

5-Δ-ALA + White Light up to 3x

Int J Dermatol 2007;46:1180-84

**FINGER PDT**

5-Δ-ALA + Red light (635nm) 3-4x

PDT
5-ALA + Red Light up to 2x
Br J Dermatol 2003;149:1087-88

PDT
• J Dermatol 2008;35:658-661
• JEADV 2007;21:1170-1174
• Int J Dermatol 2007;46:1180-1184
• Br J Dermatol 2003;149:1087-1088
• J Photochem Photobiol 2001;61:30-34
• Lancet 2000;355:963-966
• Clin Exp Dermatol 1999;24:154-159
• Dermatology 1995;191:346-347

INTRALESIONAL BLEOMYCIN

Bleomycin

• Experience case series: abn+norm hosts
• Commercial bleo: Mixture of bleomycins
• 15 unit vial; Reconstituted to 1U/ml with bacteriostatic water or 0.9% saline
• Stability: 10-28 days refrigerated; 1-14 days room temp. post-reconstitution
• MOA: Breaks DNA; Aberrant synthesis and replication of DNA (RNA and Protein, also)
• Off label: FDA-approved cancer therapy

Intralesional Bleomycin

• Soak with tap water to soften wart
• Inject intralesionally to induce “blanch”
• Also introduced by “scarification”
• Process repeated Q2-4 weeks
• Immediate or delayed pain; vasospasm post-Rx dyschromia and scar formation
• Contraindicated: Raynaud’s, PVD, pregnancy (Category D)
• COST: 15 unit vial = $200-350

Intralesional Bleomycin

• Soak with tap water to soften wart
• Inject intralesionally to induce “blanch”
• Also introduced by “scarification”
• Process repeated Q2-4 weeks
• Immediate or delayed pain; vasospasm post-Rx dyschromia and scar formation
• Contraindicated: Raynaud’s, PVD, pregnancy (Category D)
• COST: 15 unit vial = $200-350
IL Bleomycin
Dilution: 1 unit/ml
Q3weeks, 1-4x

Indian J Dermatol Venereol Leprol 2009; 75:262-67

Note Dyschromia and scars!

IL Bleomycin
Dilution: 1 unit/ml
Q5weeks, 1-5x

J Dermatolog Treat 2006;17:112-116

Renal transplant
Failed salicylic acid
Failed cryotherapy
Failed cantharidin
Failed laser ablation

Intralesional Bleomycin

- Summary of all studies to 2006: 23-99% cure rate, with plantar warts being more resistant
- More recent studies compared IL Bleomycin head-to-head, same patient, with cryosurgery

<table>
<thead>
<tr>
<th>Pts Rx # (Max)</th>
<th>Interval</th>
<th>Bleo Cure Rate</th>
<th>Cryo Cure Rate</th>
<th>Sites Treated</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 44</td>
<td>2 weeks</td>
<td>86.4%</td>
<td>86.2%</td>
<td>Hands Feet</td>
<td>Dermatol Online J 13(3):4, 2007 (1/2 unit/ml)</td>
</tr>
<tr>
<td>N = 73</td>
<td>3 weeks</td>
<td>97%</td>
<td>82%</td>
<td>Hands Feet +</td>
<td>Ind J Derm Venereol Leprol 75:262-267, 2009 (1 unit/ml)</td>
</tr>
</tbody>
</table>

Intravenous Cidofovir

- Limited experience: abnormal hosts
- 3.5 to 5.0mg/kg (Probenecid + hydration)
- Q2 weeks; Multiple courses over 5-6 mo
- Halts DNA synthesis, Fragments HPV DNA; Upregulates caspase-3
- Off label: FDA-approved CMV retinitis
- AE: nephrotoxic; iritis/uveitis; neutropenia (metabolic acidosis; teratogenic?)
- COST (1 vial ~$1500 + infusion costs)
Intravenous Cidofovir

- JEADV 2006;20:202-205
- JAAD 2006;55:533-536
- Arch Dermatol 2004;140:13-14

Topical Cidofovir

- Limited experience: normal + abn hosts
- 1-3% compounded in bland ointment
- QD-BID (mostly QHS) x 1-8 weeks
  Few cases cycle: 2wk on -- 2wk off
- Halts DNA synthesis, Fragments HPV DNA; Upregulates caspase-3
- Off label: Not FDA-approved
- AE: Local erythema, scaling, irritation, (nephrotoxicity; allergc contact)
- COST (30 gram = $750-1000)

<table>
<thead>
<tr>
<th>%</th>
<th>Regimen</th>
<th>Clear</th>
<th>Age</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>QD</td>
<td>4/7</td>
<td>Pediatric</td>
<td>BJD 2008;160:223</td>
</tr>
<tr>
<td>1%</td>
<td>QD</td>
<td>1 HIV+</td>
<td>Adult</td>
<td>Int J STD AIDS 2006;19:175</td>
</tr>
<tr>
<td>2.5-5.0%</td>
<td>QOD</td>
<td>2/2</td>
<td>Transplant</td>
<td>Transplant Int 2006;20:238</td>
</tr>
<tr>
<td>1%</td>
<td>BID</td>
<td>1 GVHD</td>
<td>Adult</td>
<td>Transpl Infect Dis 2005;7:158</td>
</tr>
<tr>
<td>1%</td>
<td>QD</td>
<td>1 ALL</td>
<td>Pediatric</td>
<td>BJ 2005;152:386</td>
</tr>
<tr>
<td>1%</td>
<td>QD</td>
<td>2/4 HIV+</td>
<td>Adult</td>
<td>Ann Dermatol Venereol 2004;131:445</td>
</tr>
<tr>
<td>3%</td>
<td>BID</td>
<td>1 HIV+</td>
<td>Adult</td>
<td>JAAD 2004;3:340</td>
</tr>
<tr>
<td>1%</td>
<td>QD</td>
<td>1 HIV+</td>
<td>Adult</td>
<td>Surg Med Oral Path Oral 2000;90:713</td>
</tr>
<tr>
<td>1%</td>
<td>BID</td>
<td>10/10 HIV+</td>
<td>Adult</td>
<td>JEADV 2000;14:484</td>
</tr>
<tr>
<td>3%</td>
<td>BID &amp; QD</td>
<td>2/2</td>
<td>Pediatric</td>
<td>JAMA 1997;278:1236</td>
</tr>
</tbody>
</table>
Others…. 

- **Imiquimod 5% (debridement/occlusion)**
  - BJD 2005;152:122
  - BJD 2005;143:1026
  - Ann Derm Venereol 2000;80:134
  - Ann Intern Med 2000;132:95

- **Intralesional Candida Antigen (multiple Rx’s)**
  - J Drugs Dermatol 2005;8:268
  - Arch Dermatol 2005;141:589
  - Pediatr Derm 2003;20:268
  - Cutis 2002;70:185
  - Arch Derm 2000;136:1274

- **Intralesional interferon alfa-2a**
  - Clin Exp Derm 2008;34:16
  - Arch Dermatol 1986;122:272

- **Botanicals**
  - Tea Tree Oil: Complement Ther Clin Pract 2008;14:225
  - *Thuja Occidentalis* Extract: Nurse Practitioner 2006;31:53

- **Hypnosis**
  - Am J Clin Hypnosis 2005;47:259
  - Altern Ther Health Med 2002;8:144
  - Am J Clin Hypnosis 1992;35:1
  - Psychosom Med 1990;52:109

Theory: Induce local T-cell response
Inject 0.1cc Candida Antigen to large wart(s)
Re-injection Q 2-4 weeks; total of 5-10x
58-74% Complete response; ~20% no benefit
Distant warts may also respond (~40%)
Adding concomitant INF alfa-2b no better
Arch Derm 136:1274, 2000
Arch Derm 137:451, 2001
Arch Derm 141:589, 2005
WARNING: PAINFUL, PURPLE DIGIT
Dermatitis 16:216, 2005

Why Might Botanical Work?

- Contents of stem-leaf extract
- Isopimaric acid
- Deoxypodorhizone
- Isopicrodeoxypodophyllotoxin
- Dexopodophyllotoxin

Hypnosis

- Allegedly works best with children
- My success rate is 0 for 6
- Your experience may differ!?!?
- Practitioner 220:305, 1978
  - Aust NZ J Psychiatry 16:30, 1982
  - Psychosom Med 52:109, 1990
  - Am J Clin Hypnosis 35:1, 1992
  - Altern Ther Health Med 8:144, 2002
  - Am J Clin Hypnosis 47:259, 2005