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# Topical treatment of chronic wounds

Joseph A. Woelfel

University of the Pacific, [jwoelfel@pacific.edu](mailto:jwoelfel@pacific.edu)

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## Topical Treatment of Chronic Wounds

Chronic wounds most commonly include pressure ulcers (also called decubitus ulcers or bed sores), diabetic foot ulcers, burns, and varicose ulcers. They are generally difficult to heal and are often resistant to therapy.<sup>1</sup>

Most pressure ulcers occur in the lower part of the body. The elderly and bedridden spinal cord injury patients are prone to these ulcers. Common complications include osteomyelitis, sepsis, and death.<sup>1</sup>

Measures to prevent pressure ulcers include recognizing patients at-risk, reducing bed rest, reducing constant pressure, assessing and maintaining nutritional status, and preserving skin integrity. Treatment is often based on the extent of the wound. Staging of ulcers is a common practice and relates to ulcer depth. Stage 1 is identified by nonblanchable redness of intact skin. Stage 2 is characterized by ulcer extension through the epidermis or dermis. Stage 3 ulcers extend through the full thickness of the skin into the subcutaneous tissue and create a crater. Stage 4 effects include tissue necrosis with muscle, bone, or underlying structural damage.

Treatment of ulcers involves: 1.) daily assessment, 2.) cleaning with sterile saline at each dressing change, 3.) use of occlusive, vapor-permeable or hydrocolloid dressings, 4.) use of debriding techniques or medications to remove necrotic tissue, and 5.) use of topical antibiotics for local colonized infection.<sup>2</sup>

Agent	Indication <sup>3</sup>	Cost <sup>3,4**</sup>	Comments <sup>3,4</sup>
<b>Enzymatic Chemical Debridement</b>			
<ul style="list-style-type: none"> <li>Papain, Urea (<i>Accuzyme, EtheZyme</i>, etc.) available as an ointment</li> <li>Papain, Urea, Chlorophyllin Copper Complex (<i>Panafil, Ziox</i>, etc.) available in an ointment or spray</li> </ul>	<ul style="list-style-type: none"> <li>Pressure ulcer, stage 2 to 4</li> <li>Burn eschar</li> <li>Diabetic foot ulcer</li> <li>Varicose ulcer</li> </ul>	<ul style="list-style-type: none"> <li>\$54.55 30 gm tube (\$1.81/gm)</li> <li>\$88.00 30 gm tube (\$2.93/gm)</li> </ul>	<ul style="list-style-type: none"> <li>Papain is the proteolytic enzyme that debrides necrotic, nonviable tissue. Viable tissue is unharmed.</li> <li>Urea supplements papain action by exposing sulfhydryl groups in necrotic tissue to papain action.</li> <li>Chlorophyllin Copper Complex inhibits hemagglutination and inflammatory properties of protein degradation products. It promotes healthy granulation, decreases inflammation, and reduces wound odor.</li> <li>Papain/urea ointment has been shown to have greater efficacy than collagenase ointment.<sup>1,5</sup></li> <li>Products vary in papain content which may affect efficacy. <i>Accuzyme</i> contains 830,000 units per gm. <i>Panafil</i> contains 521,700 units per gm.</li> <li>Do not use peroxide or heavy metal containing agents due to papain inactivation (e.g. zinc containing products, silver sulfadiazine creams).</li> </ul>

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Agent	Indication <sup>3</sup>	Cost <sup>3,4**</sup>	Comments <sup>3,4</sup>
<ul style="list-style-type: none"> <li>Collagenase (<i>Santyl</i>) available as an ointment</li> </ul>	<ul style="list-style-type: none"> <li>Pressure ulcer, stage 2 to 4</li> <li>Burn eschar</li> <li>Diabetic foot ulcer</li> <li>Varicose ulcer</li> </ul>	\$60.35 30 gm tube (\$2.01/gm)	<ul style="list-style-type: none"> <li>Collagenase is specific for digestion of collagen in necrotic tissue. Collagen composes about 75% of dry tissue.</li> <li>Optimal pH for enzymatic action is 6 to 8; avoid acidic agents for cleansing.</li> <li>Peroxide does not affect its efficacy.</li> <li>Do not store above 77 degrees F.</li> </ul>
<ul style="list-style-type: none"> <li>Trypsin, Castor Oil, Peru Balsam (<i>Granulex, Xenaderm</i>) available as a spray</li> </ul>	<ul style="list-style-type: none"> <li>Pressure ulcer, stage 1 to 4</li> <li>Burn eschar</li> <li>Varicose ulcer</li> </ul>	\$19.41 113 gm spray (\$0.17/gm)	<ul style="list-style-type: none"> <li>Trypsin is a mild debriding agent for necrotic tissue.</li> <li>Castor oil and Peru Balsam are protectants providing a soothing, protective barrier. Peru Balsam also reduces wound odor.</li> <li>Trypsin/Peru balsam/castor oil was not better than mechanical gauze debridement as shown in one study.<sup>1,6</sup></li> </ul>
<b><i>Iodine Compounds</i></b>			
<ul style="list-style-type: none"> <li>Cadexomer Iodine available as a gel (<i>Iodosorb</i>) or as a sheet (<i>Iodoflex</i>)</li> </ul>	<ul style="list-style-type: none"> <li>Chronic non-healing, exuding wounds such as pressure or leg ulcers, exuding, infected wounds</li> </ul>	\$59.77 40 gm gel (\$1.49/gm) \$49.83 1x3 sheet (\$16.61/sheet)	<ul style="list-style-type: none"> <li>Contraindicated in patients with iodine sensitivity, Hashimoto's thyroiditis, non-toxic nodular goiter, and in children.</li> <li>Potential risk of interaction with lithium due to systemic absorption of cadexomer iodine.</li> <li>May accelerate rate of wound healing, reduce pain, help remove exudate, and stimulate granulation tissue formation.<sup>9</sup></li> </ul>
<b><i>Regrowth Stimulants</i></b>			
<ul style="list-style-type: none"> <li>Becaplermin, rh-PDGF (<i>Regranex</i>) available as a gel</li> </ul>	<ul style="list-style-type: none"> <li>Pressure ulcer, stage 2 to 4*</li> <li>Diabetic foot ulcer</li> </ul>	\$595.56 15 gm tube (\$39.70/gm)	<ul style="list-style-type: none"> <li>PDGF is a recombinant formulation of platelet-derived growth factor which promotes cell mitogenesis and protein synthesis for granulation tissue formulation.</li> <li>Adequate blood supply to the affected area is needed for efficacy.</li> <li>Efficacy is dependent on absence of necrotic tissue.</li> </ul>

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Agent	Indication <sup>3</sup>	Cost <sup>3,4**</sup>	Comments <sup>3,4</sup>
<ul style="list-style-type: none"> <li>Phenytoin (<i>Dilantin</i>) prepared as a suspension of the contents of a 100 mg capsule mixed with 5 mL sterile saline or powder applied directly to wound</li> </ul>	<ul style="list-style-type: none"> <li>Pressure ulcer, stage 2*</li> <li>Burn eschar*</li> <li>Diabetic foot ulcer*</li> <li>Varicose ulcer*</li> </ul>	\$34.84 100 capsule bottle (\$0.35/capsule)	<ul style="list-style-type: none"> <li>Phenytoin may stimulate proliferation of fibroblasts, enhance granulation tissue, decrease wound exudate, promote collagen deposition, and decrease bacterial contamination.<sup>7</sup></li> <li>Topical phenytoin appears to be effective and safe for healing soft tissue wounds [Evidence level B, lower quality RCT].<sup>7,8</sup></li> </ul>
<b>Topical Antibiotics</b>			
<ul style="list-style-type: none"> <li>Bacitracin, Neomycin, Polymyxin B (<i>Neosporin</i>) as an ointment or cream</li> <li>Bacitracin, Polymyxin B (<i>Polysporin</i>) as an ointment</li> </ul>	<ul style="list-style-type: none"> <li>Prevention or treatment of superficial infection</li> </ul>	\$6.36 30 gm tube (\$0.21/gm) \$6.78 30 gm tube (\$0.23/gm)	<ul style="list-style-type: none"> <li>Ointment dosage forms are difficult to remove.</li> <li>May have cytotoxic effects which may delay wound healing.</li> <li>Allergic reactions may occur.</li> <li>Bacteria may become resistant with prolonged use.</li> </ul>
<ul style="list-style-type: none"> <li>Gentamicin (<i>Garamycin</i>) available as an ointment or cream</li> </ul>	<ul style="list-style-type: none"> <li>Prevention or treatment of superficial skin and soft tissue infections due to susceptible gram-negative and gram-positive organisms.</li> </ul>	\$3.60 15 gm tube (generic) (\$0.24/gm)	<ul style="list-style-type: none"> <li>Ointment dosage forms are difficult to remove.</li> <li>May have cytotoxic effects which may delay wound healing.</li> <li>Allergic reactions may occur.</li> <li>Bacteria may become resistant with prolonged use.</li> </ul>
<ul style="list-style-type: none"> <li>Silver Sulfadiazine [<i>Silvadene, SSD, Dermazin</i> (Canada)] available as a cream</li> </ul>	<ul style="list-style-type: none"> <li>Prevention of infection in second and third degree burns</li> <li>Prevention or treatment of infection in chronic wounds*</li> </ul>	\$14.68 1% 85 gm jar (generic) (\$0.17/gm)	<ul style="list-style-type: none"> <li>May have cytotoxic effects which may delay wound healing.</li> <li>Allergic reactions may occur.</li> <li>Bacteria may become resistant with prolonged use.</li> <li>Do not use with papain-containing enzymatic debriding agents.</li> </ul>

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<b>Wound Cleansers</b>			
<ul style="list-style-type: none"><li>• Sterile Saline (Normal Saline for Irrigation, 0.9%)</li></ul>	<ul style="list-style-type: none"><li>• General wound cleaning and rinsing</li></ul>	Not available	<ul style="list-style-type: none"><li>• Best for general wound cleaning and rinsing.</li><li>• Note: avoid other wound cleaners such as povidone iodine (<i>Betadine</i>), chlorhexidine gluconate (<i>Hibiclens</i>), hypochlorite solution (<i>Dakin's Solution</i>), benzalkonium chloride solution, acetic acid solution. They can disturb granulation tissue and be cytotoxic if not diluted or used too vigorously.<sup>1</sup></li><li>• Hydrogen peroxide 3% solution may delay healing but 20% solution acts as a healing enhancer.<sup>1</sup></li></ul>

\* non-FDA-approved indication

\*\* Cost information is approximate as of the time this chart was prepared. It is based on manufacturer stated internet website prices, observed retail pharmacy prices, and www.drugstore.com listings. Actual selling prices may differ.

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Level	Definition
A	High-quality randomized controlled trial (RCT) High-quality meta-analysis (quantitative systematic review)
B	Nonrandomized clinical trial Nonquantitative systematic review Lower quality RCT Clinical cohort study Case-control study Historical control Epidemiologic study
C	Consensus Expert opinion
D	Anecdotal evidence In vitro or animal study

Adapted from Siwek J, et al. How to write an evidence-based clinical review article. *Am Fam Physician* 2002;65:251-8.

**Project Leader in preparation of this Detail-Document:** Joseph A. Woelfel, Ph.D., FASCP, R.Ph., Assistant Editor

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