

WHAM Evidence summary: Enzymatic debridement for pressure injuries

Emily Haesler, PhD, P Grad Dip Adv Nurs (Gerontics), BN, Fellow Wounds Australia^{1,2,3}



1. Adjunct Professor, Curtin Health Innovation Research Institute, Wound Healing and Management (WHAM) Collaborative, Curtin University, Perth, Australia
2. Adjunct Associate Professor, Australian Centre for Evidence Based Aged Care, La Trobe University, Melbourne, Australia
3. Honorary Senior Lecturer, Australian National University Medical School, Australian National University, Canberra, Australia

CLINICAL QUESTIONS

What is the best available evidence for enzymatic debridement to promote complete healing and/or improvement in wound bed condition in pressure injuries (PIs)?

SUMMARY

Evidence from three randomized controlled trials (RCTs),¹⁻⁴ two^{1,4} of which were included in a network meta-analysis,⁵ provided *Level 1* evidence supporting use of a collagenase to debride PIs to promote complete healing.¹⁻⁵ *Level 2*⁶ and *Level 3*^{7, 8} evidence suggested use of a collagenase to debride PIs was associated with superior improvements in the wound bed condition compared with sharp⁶ or autolytic debridement.^{7, 8} *Level 1* evidence^{9, 10} found no difference between a collagenase and other types of enzymatic debridement for achieving PI healing. Expert opinion (*Level 5*) suggested that the urgency of debridement,¹¹⁻¹⁵ vascularisation of the wound bed,¹⁶ type of tissue to be debrided,¹⁷ the patient's tolerance of the treatment,^{18, 19} and financial cost^{1, 3, 20, 21} are all considerations when selecting

a method for debriding PIs. This evidence supported a *Grade B* recommendation (a weak recommendation).²²

CLINICAL PRACTICE RECOMMENDATIONS

All recommendations should be applied with consideration to the wound, the person, the health professional and the clinical context:

Where available, enzymatic debridement can be used to remove devitalised tissue from pressure injuries in the presence of adequate vascularisation and in the absence of a need for rapid removal of non-viable tissue (Grade B).

SOURCES OF EVIDENCE

This summary was conducted using methods published by the Joanna Briggs Institute.²²⁻²⁴ The summary is based on a literature search combining search terms related to PIs and enzymatic debridement. Searches were conducted in CINAHL, Medline, the Cochrane Library and Google Scholar for evidence published up to November 2019 in English. Levels of evidence for intervention studies are reported in the table below.

BACKGROUND

Debridement is the process of removing devitalized tissue (e.g. necrotic tissue or bacteria/biofilm) from the wound bed. One method of debriding a wound is enzymatic debridement—the use of exogenous

Table 1: Sources of evidence and the level

Level 1 Evidence	Level 2 Evidence	Level 3 Evidence	Level 4 Evidence	Level 5 Evidence
Experimental Designs	Quasi-experimental Designs	Observational – Analytic Designs	Observational – Descriptive Studies	Expert Opinion/ Bench Research
1.a Systematic review of RCTs ⁵ 1.b Systematic review of RCTs and other designs ^{16, 18, 28} 1.c RCT ^{1-4, 9, 10, 29}	2.d Pre-test – post-test or historic control study ^{6, 30}	3.d Case – controlled study ^{7, 8}	Level 4.b Cross-sectional study ²⁹	5.b Expert consensus ¹¹⁻¹⁵ 5.c Bench research/ single expert opinion ^{17, 19, 31, 32}

enzymes that digest proteins (collagen and/or fibrin) in necrotic tissue.⁵ Enzymes used for debridement include general proteolytics (active against a broad range of protein matter), fibrinolytics (active against fibrin) and collagenases (selective action against collagen).^{19, 28} Collagenase ointment appears to act on lower levels of necrotic tissue, working from the bottom of the wound bed up.²⁵ Papain-based enzymatic debriding agents act from the top of the wound down, and act against all protein that contains cysteine,¹⁷ working best in the presence of urea.^{17, 25}

CLINICAL EVIDENCE

Evidence from primarily pre-1980s studies reporting positive impact of enzymatic debridement for chronic wounds (some studies including PIs) is summarized in narrative in two systematic reviews.^{18, 25} Both reviews^{18, 25} reported primarily low level evidence at high risk of bias outlining the clinical benefits of enzymatic debriding agents, with some small studies offering favourable comparisons to placebo treatment. These studies provided early support for using enzymes to debride chronic wounds more slowly and with generally low levels of pain²⁵ (both *Level 1*).

Enzymatic debridement to promote complete healing

A network meta-analysis of RCTs⁵ (two RCTs,^{1, 4} n = 61 participants in total) showed collagenase ointment was associated with an increase in complete healing within up to 16 weeks compared with advanced wound dressing (risk ratio [RR] = 2.12, 95% confidence interval [CI] 1.06 to 4.22), with 176 more PIs per 1,000 likely to heal. However, the studies were at high risk of bias and certainty in the result was low⁵ (*Level 1*).

In an RCT at high risk of bias (n = 27 PIs),^{2, 3} collagenase ointment was associated with an increase in complete healing within 84 days compared with autolytic debridement using a hydrogel (collagenase 69% versus autolysis 21%, p = 0.02),^{2, 3} as well as faster healing rates² (*Level 1*).

An early RCT²⁶ (n = 17 PIs) at high risk of bias reported a non-specific fibrinolytic (streptokinase/streptodornase) was associated with slower healing than autolytic debridement using a hydrogel, but the difference was not significant. In most countries, this treatment has been superseded by contemporary enzymatic debriding agents²⁶ (*Level 1*).

In a cohort study at high risk of bias (n = 434 PIs),²⁷ collagenase ointment was associated with statistically significantly higher rates of healing by 12 months compared with sharp debridement (collagenase 22% versus sharp debridement 11%, hazard ratio [HR] = 1.85, 95% CI 1.28 to 2.68, p = 0.001)²⁷ (*Level 2*). However, healing rates in both groups were low and may not be clinically significant.

Enzymatic debridement to promote improvement in the wound bed condition

In a cohort study at low risk of bias (n = 114),⁶ collagenase ointment was associated with significantly greater improvements in overall score (p = 0.022) and in necrotic tissue score (p = 0.0001) on the Bates-Jensen Wound Assessment Tool (BWAT) compared to wounds receiving sharp debridement. There was no significant difference in change in wound surface area between the two debridement methods. Both groups received concurrent negative pressure wound therapy⁶ (*Level 2*).

In a case-controlled study at low risk of bias (n = 557 PIs), collagenase ointment was associated with improved granulation by 12 months compared to autolytic debridement using medicinal honey (collagenase 100% granulation versus honey 38%, odds ratio [OR] = 1.384, 95% CI 1.057 to 1.812, p = 0.018).⁷ This finding was supported by an observational study at low risk of bias that reported treatment of PIs (n = 46,054) with collagenase ointment was associated with requiring fewer follow-up visits compared to medicinal honey, including lower rates of hospital readmission (OR = 0.86, 95% CI 0.80 to 0.94, p = 0.0002)⁸ (both *Level 3*).

Comparisons between different types of enzymatic debridement

Two RCTs,^{9, 10} both at moderate risk of bias, showed no significant difference in healing outcome measures between collagenase ointment and debridement with papain-urea (n = 26 PIs)⁹ and debridement using a fibrinolytic (n = 78 PIs)¹⁰ (both *Level 1*).

CONSIDERATIONS FOR USE

The following points should be considered when performing enzymatic debridement:

- Adequate wound bed vascularity should be established before performing debridement¹⁶ (*Level 1*).

- In limbs/heels with poor vascularity or ischemia, dry stable eschar should usually be left undisturbed, except when infection is suspected. When infection is suspected, consult an appropriate medical practitioner¹¹⁻¹⁶ (*Levels 1 and 5*).
- Enzymatic debridement is appropriate when the need to remove devitalised tissue is not clinically urgent. In the presence of extensive necrotic tissue, crepitus, fluctuance or signs of advanced cellulitis or sepsis, more rapid methods of debridement (e.g. surgical/sharp debridement) should be performed¹¹⁻¹⁵ (*Level 5*).
- Papain-urea could be selected when excessive necrotic tissue is present and collagenase could be selected for wound beds containing excessive fibrous tissue or mixed non-viable tissue¹⁷ (*Level 5*).
- Individuals may experience pressure injury pain and/or burning sensations from enzymatic debridement. Diluting the enzymatic agent in hydrogel might help reduce pain¹⁹ (*Level 5*) and maintain a moist healing environment¹⁸ (*Level 1*).
- Economic analyses^{1, 3, 20, 21} suggest that enzymatic (collagenase) debridement is associated with lower financial costs than using sharp debridement,²¹ autolytic debridement with medicinal honey (although the difference was not statistically significant)²⁰ or using an advanced wound dressing only.^{1, 3}
- Manufacturer instructions,²⁹ local policies and national regulation should always be followed when selecting products, including when selecting a compatible wound dressing to apply²⁹ (*Level 5*).

CONFLICTS OF INTEREST

The author declares no conflicts of interest in accordance with International Committee of Medical Journal Editors (ICMJE) standards.

FUNDING

The development of this WHAM evidence summary was supported by a grant from The Western Australian Nurses Memorial Charitable Trust.

ABOUT WHAM EVIDENCE SUMMARIES

WHAM evidence summaries are consistent with methodology published in

Munn Z, Lockwood C, Moola S. The development and use of evidence summaries for point of care information systems: A streamlined rapid review approach, *Worldviews Evid Based Nurs*. 2015;12(3):131-8.

Methods are provided in detail in resources published by the Joanna Briggs Institute as cited in this evidence summary. WHAM evidence summaries undergo peer-review by an international review panel. More information is available on the WHAM website: <https://www.whamwounds.com/>.

WHAM evidence summaries provide a summary of the best available evidence on specific topics and make suggestions that can be used to inform clinical practice. Evidence contained within this summary should be evaluated by appropriately trained professionals with expertise in wound prevention and management, and the evidence should be considered in the context of the individual, the professional, the clinical setting and other relevant clinical information.

PUBLICATION

This evidence summary has been published in *Wound Practice and Research*:

Haesler E. Evidence summary: Enzymatic debridement for pressure injuries. *Wound Practice and Research*, 2020; 28(4) 192-4.

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