

# The Role of Zinc in Wound Healing

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**T**he importance of nutrition in the management of a patient with a wound should never be underestimated. Zinc, a trace mineral, plays a fundamental role in the overall success of many body functions. Because zinc deficiency can negatively affect wound healing, it is an issue clinicians need to consider in the overall care of patients with wounds.

Testing for zinc deficiency is a challenge, as the serum zinc levels may not be indicative of the microcellular state.<sup>1</sup> As well, zinc levels fluctuate with serum albumin, further muddying the significance of the blood levels. Significant zinc deficiency is most likely to be of concern in patients with excessive GI losses, heavily draining wounds, malnutrition,<sup>2</sup> burns, psoriasis, chronic alcoholism and severe surgical trauma.<sup>3</sup>

This article reviews zinc deficiency, exploring the cellular effects of zinc on wound healing during each phase and highlighting the clinical observations

to be made at the macroscopic level when zinc levels are diminished. The wound healing phases are hemostasis, inflammation, proliferation and maturation.<sup>4</sup> Current clinical practice recommendations for zinc supplementation are discussed.

## Hemostasis

Immediately after skin injury, the hemostasis phase begins, with platelet adhesion to form the fibrin clot that will stop blood loss.<sup>5</sup> Activation of the platelets by the intrinsic pathway causes the platelets to change shape, allowing them to aggregate together.<sup>6</sup> In a patient with a low zinc level, the platelets have a decreased ability to aggregate as described, resulting in increased bleeding time. It is believed that this is related to the role of zinc in thrombotic factors in the platelet and endothelium. It has been shown that this bleeding problem can be reversed with appropriate zinc levels.<sup>6</sup> Delayed platelet aggregation and prolonged bleeding times will delay the onset and strength of inflammation.

## Inflammation

During the inflammation phase, a number of important factors align for wound healing and appropriate immune response.<sup>7</sup> Zinc is a required component of proliferating cells, including the cells of inflammation, neutrophils and macrophages.<sup>8</sup> Zinc is partially responsible for synthesis of protein, DNA, RNA and cell proliferation.<sup>2</sup> Neutrophils, simply speaking, clear the wound of debris and signal the inflammatory cytokines, growth factors and enzymes.<sup>9</sup> Macrophages clean the wound through phagocytosis, secrete growth hormones, recruit fibroblasts, create an initial framework for granulation and secrete nitric oxide, which has many functions, including vasodilation, thrombolysis, angiogenesis and cell regulation.<sup>4,8</sup> Both neutrophils and macrophages are affected by low zinc levels that can cause disturbance in their functions. The result could be increased bacterial burden, wound debris, weakened immune response by



the pro-inflammatory cytokines, reduced cell signalling, poor framework creation and slowed angiogenesis.

Also occurring during the inflammation phase is free-radical action. Free radicals are effective in killing pathogens but also need to be kept in balance by antioxidants. Zinc is an essential part of antioxidant function as part of the zinc-copper superoxide dismutase<sup>10</sup>; and a reduction of their action can prolong the inflammatory process in chronic wounds.<sup>2</sup> A prolonged inflammation phase will predispose the patient to infection and delayed healing.<sup>9</sup>

The need for zinc is greatest during the inflammation phase. A person with a zinc level on the low end of the normal range could dip into a sub-therapeutic range during this time, resulting in a negative effect on wound healing.<sup>7</sup>

### **Proliferation**

During proliferation, fibroblasts play a major role in creating new tissue. This cannot happen unless angiogenesis has laid down a healthy network to support fibroblast proliferation. Fibroblasts are also responsible for collagen synthesis, which forms the scaffolding within the extracellular matrix among the capillary buds to build granulation tissue.<sup>11</sup> Over time, the disorganized collagen will break down with the help of metalloproteinases and rebuild in a more orderly fashion.<sup>4</sup> Zinc is required to maintain cell wall stability, DNA, RNA and protein synthesis and to encourage proliferation of fibroblasts.<sup>1,2,7</sup> An absence of adequate zinc at the cellular level would result in poor, delayed granulation and wound closure. The fibroblasts would likely be less numerous or effective. The

number of capillary buds would be reduced or not present, depending on the extent of deficit. Collagen deposition would be scarce. It has been shown that higher levels of zinc available to wound cells will stimulate and hasten the function of the enzymes repairing the wound.<sup>7</sup>

### **Maturation**

The maturation phase of wound healing focuses on collagen and wound strength. There is a fine balance among the building, organizing and breakdown of collagen to reach the final tensile strength over approximately two years. This work is done by fibroblasts, metalloproteinases, epidermal cells and endothelial cells.<sup>11</sup> The maturation of collagen is dependent on adequate zinc levels.<sup>7</sup> The metalloproteinases that help to digest collagen and stimulate the orderly growth of new collagen contain a zinc ion.<sup>4</sup> A deficiency in zinc could cause reduced wound strength and increased risk of skin breakdown in the future.<sup>7</sup>

### **Macroscopic Perspective**

The clinician should be alert to the clinical signs of ineffective hemostasis and control of bleeding at the wound site as well as the serum bleeding times. Another trigger for a

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clinician to consider a low zinc level may be a delayed, chronic inflammatory response in a wound prone to infection and lacking the usual presentation of inflammation expressions such as pain, heat, edema, loss of function and erythema. The wound may become stalled in the inflammatory phase, or the clinician may see slow granulation and cellular proliferation. The result could be a wound with poor tensile strength and easily damaged scar tissue when compared with other wounds. The signs of zinc deficiency overlap with signs of other wound healing problems such as use of anticoagulants or poorly controlled blood glucose and prolonged inflammation. It is the responsibility of the clinician to be aware of all potential causes of delayed wound healing and create a comprehensive plan of care to address the causes.

### Zinc Supplementation

Current recommendations for the management of pressure injuries does not suggest zinc supplementation as a stand-alone treatment for poorly healing wounds.<sup>2,12</sup> At the time of this publication, current best practices suggest that most balanced diets will include the recommended amount of zinc without supplementation<sup>13</sup> and that evidence is lacking to support oral zinc supplementation in those with adequate dietary intake.<sup>12</sup> In order to determine the quality of the patient's diet,

it is recommended to consult with a registered dietitian who can provide a comprehensive review of the patient's nutritional status.

The patient should undergo a nutrition screening with a reliable and validated tool.<sup>12</sup> This will objectively determine if a balanced diet is being consumed to meet the body's macro- and micro-nutrient needs. If a balanced diet is not being consumed, it is recommended that a vitamin and mineral supplement be used to augment.<sup>2,12</sup>

If a zinc deficiency is accurately diagnosed and needs to be treated, current recommendations state no more than 40 mg elemental zinc daily can be supplemented for a limited period, as deemed appropriate by a prescriber.<sup>2</sup> High zinc levels will adversely affect wound healing as well. Zinc at high levels is known to interfere with copper metabolism and may render additional problems with wound healing. Up-to-date, evidence-based information regarding nutrition and zinc supplementation can be found online through "PEN: Practice-based Evidence in Nutrition."<sup>13</sup> Collaboration with a dietitian and the rest of the integrated team is essential to determine any special dietary needs of patients with wounds.

### Conclusion

It has been determined that zinc plays a vital role throughout all wound healing phases. When

### About Zinc

- Zinc is an essential trace mineral for wound healing.
- Zinc deficiency can negatively manifest in all four stages of wound healing.
- There is insufficient evidence to demonstrate that people without zinc deficiency benefit from zinc supplementation.
- All patients with wounds should have a nutritional screening completed, in consultation with a dietitian, to determine dietary needs.
- Vitamin and mineral supplements may be required for those with dietary deficiencies.
- An excellent resource for up-to-date, evidence-based nutrition information, "PEN: Practice-based Evidence in Nutrition," can be found at [www.pennutrition.com/home.aspx](http://www.pennutrition.com/home.aspx).

zinc levels are low in the cellular environment, all four phases of healing are affected. In order to provide the highest quality patient care, the clinician should be alert to the possibility of zinc deficiency and collaborate with the team to investigate dietary adequacy and address deficiencies. 🍷

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