THE USE OF AMNIOTIC MEMBRANE FOR WOUND HEALING IN BURN INJURIES
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**ABSTRACT**

**Background:** Burn injuries are associated with significant mortality and morbidity around the world. The care of burn wounds requires a great amount of medical resources, therefore it is important to find a wound dressing that accelerates wound healing and is readily available.

**Objectives:** This review article will provide an overview of the literature and background of the usage of amniotic membranes in burn patients. We will also discuss its properties of preventing infections, relieving pain, how it promotes and accelerates wound healing.

**Discussion:** Human amniotic membrane is now used around the world as a relatively cheap temporary dressing for burn wounds. It has been shown to promote wound healing, create a moist environment, reduce pain intensity, reduce scar formation, prevent water and electrolyte disturbances and also reduce the risk of infections. Research has also shown that it contains antimicrobial properties that could be of great benefit in burn patients and is compatible to use in developing countries because it is readily available, easy to obtain and sterilize, able to cover wounds of large size, protects the wound from excessive water and electrolyte loss, reduces pain intensity, requires fewer dressing changes and is also more cost effective than conventional dressings.

**Conclusion:** Amniotic membrane is a biological dressing that can be useful in the treatment of burn wounds. Further research should be conducted to investigate and understand the mechanisms of amniotic membrane for burn and wound care.

**INTRODUCTION**

Burns are the fourth most common type of injury, following motor vehicle accidents, falls, and interpersonal violence. The incidence of burn injuries is higher in developing countries. In Indonesia, it is estimated that around 195,000 deaths occur annually from burn injuries. According to the World Health Organization (WHO), there are high rates of mortality, with approximately 1.3 burn patients per 100,000 people in Southeast Asia. The patient's survival is highly dependent on the speed and effectiveness of wound healing. After the second week following a burn, it is believed that bacterial sepsis of the wounds is the leading cause of mortality in burn patients.

It is crucial to choose a simple, inexpensive, and widely available dressing because wound care involves a substantial amount of medical resources. Using amniotic membrane as a biological dressing to temporarily close a wound has been documented in the last century. The amnion is a thin tissue that forms the fetal membrane's innermost layer. In addition, current research indicates it is one of the most effective biological dressings for burn wounds. This review article will provide an overview of the literature and background of the usage of amniotic membrane in burn patients. We will also discuss its properties of preventing...
infections, relieving pain, and how it accelerates wound healing.

### HISTORY OF AMNION MEMBRANE USE IN WOUND

The amniotic membrane is the deepest layer of the placenta and can be detached with ease by blunt dissection. Histologically, the amniotic membrane consists of three primary layers: epithelium, basement membrane, and an avascular stroma. The membrane is avascular, tough, and transparent. In 1910, Davis was the first to utilize amniotic membrane for skin transplantation, which dates back over a century. The benefits stated at the time were pain reduction, reduced risk of infection, and healing support. Douglas did not discover the potential of amniotic membrane as a temporary burn wound dressing until 1952.

Burn wounds, chronic ulcers, intra-oral and genital reconstruction, hip arthroplasty, and corneal abnormalities are now treated globally with human amniotic membrane, a comparatively cost-effective and efficacious dressing. It can be acquired through cesarean sections under sterile conditions. It can be stored momentarily or preserved using glycerol, silver nitrate, antibiotic solution, or liquid nitrogen. The development of amniotic membrane applications expanded knowledge of its features and traits that could be utilized. In recent years, preservation techniques have also improved and become more widely available.

### HOW THE AMNION MEMBRANE WORKS

Multiple components in human amniotic membrane contribute to its anti-scarring, anti-inflammatory, anti-bacterial, and analgesic activities. Multiple cytokines, growth factors, metalloproteinases, and anti-inflammatory proteins are known to be exclusive to the amniotic membrane. Wound healing is greatly influenced by the inflammatory process, and the amniotic membrane can play a vital role in this regard.

Amnion can be used to facilitate the treatment of burn injuries by improving wound Table 1. Summary of literature review

<table>
<thead>
<tr>
<th>Author</th>
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</thead>
<tbody>
<tr>
<td>Mohammadi et al.</td>
<td>Human amniotic membrane dressing: An excellent method for outpatient management of burn wounds</td>
<td>2008</td>
<td>In a randomized controlled clinical experiment with a single-blind, amniotic membrane was associated with faster wound healing, fewer needs for skin grafts, and less discomfort compared to the control group.</td>
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<tr>
<td>Branski et al.</td>
<td>Amnion in the treatment of pediatric partial-thickness facial burns</td>
<td>2007</td>
<td>Significantly fewer patients treated with amnion required dressing changes.</td>
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<tr>
<td>Koob et al.</td>
<td>Biological properties of dehydrated human amnion/chorion composite graft: Implications for chronic wound healing</td>
<td>2013</td>
<td>Using enzyme-linked immunosorbent assays (ELISA), human amnion allografts were examined for the presence of growth factors, including TGF-, EGF, PLGF, bFGF, GCSF, and cytokines including IL-4, IL-6, IL-8, and IL-10.</td>
</tr>
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<td>Haugh et al.</td>
<td>Amnion membrane in diabetic foot wounds: A meta-analysis</td>
<td>2017</td>
<td>A meta-analysis of ulcers of the extremities treated with amnion membrane showed a significantly greater success rate than conventional dressing during a 6-week period.</td>
</tr>
<tr>
<td>Mao et al.</td>
<td>Anti-microbial peptides secreted from human cryopreserved viable amniotic membrane contribute to its anti-bacterial activity</td>
<td>2017</td>
<td>The anti-microbial activity of amniotic membrane against common pathogens in chronic wounds, mediated by anti-microbial peptides (AMPs) including human beta-defensins (HBDs), was demonstrated.</td>
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healing, creating a moist environment, reducing pain intensity, minimizing scar formation, preventing water and electrolyte disturbances, and minimizing the risk of infection. Human amnion is typically applied to burns of the second degree that have already been debrided. It is applied to the wound until it has fully healed, which depends on the severity of the wound and exudate. Full-thickness burns may also be covered temporarily with amniotic membrane in preparation for more permanent wound closure. It has also been demonstrated that the amniotic membrane promotes the migration and adherence of epithelial cells in burn wounds.5,11

**CURRENT EVIDENCE SUPPORTING THE USE**

The anti-inflammatory effects of amniotic membrane have been extensively discussed. The stromal matrix of the amniotic membrane has shown an ability to inhibit the expression of potent pro-inflammatory cytokines such as IL-1 and IL-1.14 The inflammatory cytokine IL-1 mediates the extravasation of phagocytes and lymphocytes to the site of inflammation and plays a crucial role in the inflammatory cascade. Amniotic membrane contains IL-1 receptor agonists (IL-1RA) that can inhibit immune cell migration. It also contains IL-10, which is able to inhibit important inflammatory factors such as TNF-α, IL-6, and IL-8, which promote neutrophil and granulocyte migration to the site of inflammation.15 Amniotic membrane has the ability to downregulate these pro-inflammatory cellular components. It also contains hyaluronic acids in large quantities, which act as a ligand for CD44 that helps the adhesion of lymphocytes.16

Human amniotic membranes have antimicrobial properties, making them an optimal temporary biological dressing for burn injuries. It is able to provide mechanical protection against infectious organisms and also contains transferrin, bactricidin, β-lysin, lysozymes, and immunoglobulins.17,18 These molecules were shown to possess anti-bacterial effects against

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The amniotic membrane has also been shown to promote migration and adhesion of epithelial cells in burn wounds. Some growth factors that contribute to this are epidermal growth factor (EGF), placental growth factor (PLGF), transforming growth factor α (TGF-α), basic fibroblast growth factor (bFGF), and granulocyte colony-stimulating factor (GCSF). These growth factors also promote angiogenesis, the development of new blood vessels from the capillaries that already exist.12 It also contains anti-inflammatory cytokines, including IL-4, IL-6, IL-8, IL-10, and tissue inhibitors of metalloproteinase (TIMP) 1, 2, and 5.13

Table 2. Summary of the benefits of amniotic membrane for burn wound healing

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bacteria that are often seen in burn patients, such as groups B and A Streptococcus, enterococcus faecalis, Escherichia coli, Staphylococcus saprophyticus, Lactobacillus, Pseudomonas aeruginosa, and Acinetobacter. Amniotic membrane tested in infected excised granulating burn wounds have also been reported to decrease the number of bacteria. To increase its anti-microbial properties, a technique using impregnation of silver nitrate can be used. Silver nitrate impregnation is performed by placing the amniotic membrane in light-proof bottles for two hours in a solution of 0.5% silver nitrate. Comparing silver-impregnated amniotic membrane to uncoated amniotic membrane, a randomized in vitro study revealed a significant reduction in bacteria when treated with silver-impregnated amniotic membrane.

In addition to its anti-inflammatory and anti-bacterial properties, amniotic membrane promotes wound healing by stimulating the migration of keratinocytes, which results in re-epithelialization of the wound. By activating c-Jun, a crucial transcription factor for the progression of re-epithelialization, the amniotic membrane initiates a complex signaling network of events. This has been demonstrated by in vitro wound healing studies. C-Jun is an indispensable component of activator protein-1 (AP-1), an early response transcription factor involved in cell proliferation, differentiation, migration, apoptosis, inflammatory responses, and tumorigenesis. c-Jun is essential for the formation and organization of epidermal cells during wound healing. Amniotic membrane also includes Type IV and Type VII collagen, fibronectin, and lamilins 1 and 5, which stimulate epithelial cell proliferation and adhesion.

**DRAWBACKS**

In developing countries with a large incidence of burns, treatment should remain efficient and cost-effective. The risk of infection in burn wounds is high as burn patients tend to have longer stays in the hospital. The nature of the burn wounds and the immune compromise effects of burns need intensive diagnostic and therapeutic procedures.

Amniotic membranes as dressings for burn wounds are compatible in developing countries because it is readily available, easy to obtain and sterilize, and more cost-effective than conventional dressings. The other benefits include the ability to cover large-size wounds, protect wounds from excessive water and electrolyte loss, reduce pain intensity, and require less dressing changes. In research comparing the cost analysis of amniotic membrane grafts to other biocompatible skin replacements, it was determined that amniotic membrane grafts are much less expensive than other biocompatible skin substitutes. One study revealed that although items containing amniotic membrane had a higher initial cost, the patients who were treated with these items had much reduced costs at the conclusion of their therapy for chronic diabetic foot ulcers. This study revealed that 92% of patients with diabetic foot ulcers saw healing at six weeks, whereas only 8% did so with regular care, thereby justifying the high initial cost of therapy.

Concerns with the usage of amnion membrane center around the difficulties of screening the material for viral infections and contamination. The danger of disease transmission must be weighed against the therapeutic advantages and the donor’s known traits. Amniotic membrane that has been preserved or used fresh have both been found to function well for wound care. Ideally, serologic testing should be done in the case of a maternal donor for the amniotic membrane. With fresh amniotic membrane, the time of procurement until the transplantation is short. With preserved amniotic membrane, there is more flexibility in the time of usage. Preserving amniotic membrane would
necessitate the use of a refrigerator, making it problematic in locations with limited resources. Additionally, amniotic membrane has quick decomposition, weak mechanical characteristics, and impractical shapes.

**FUTURE DIRECTION**

Over the last century, the medical application of amniotic membrane has progressed from a sheet for topical administration to the skin to more sophisticated forms such as micronized dehydrated membrane, amniotic cytokine extract, and solubilized powder injections for regeneration. Many of its positive applications as a natural biocompatible material are not yet well recognized. Future developments that could be of high benefit would be to investigate how amniotic membrane could be optimized in order to facilitate its applications. This could be by researching how amniotic membrane could be used in combination with other materials and properties and incorporating technologies such as 3D printing, nanotechnology, and tissue engineering. The advancement of technology in medicine has helped and will continue to improve wound care using amniotic membrane in various forms such as suspension, gel, and sponge.

**CONCLUSION**

Burns are complicated injuries that can result in substantial morbidity and death.
Infection, slow wound healing, scarring, and discomfort are the obstacles that burn care physicians must overcome. Burn wounds can be treated using amniotic membrane as a biological bandage. In developing countries, the benefits, procurement feasibilities, and use of amniotic membrane are advantageous. Even though amniotic membrane has been utilized for wound treatment since the previous century, new studies have demonstrated its benefits. To examine and comprehend the mechanism of amniotic membrane for burn and wound treatment, further research is required.

CONFLICT OF INTEREST
There was no conflict of interest in writing this research report.

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AUTHOR CONTRIBUTION
All authors contributed equally in writing the report on the results of this study, from the stage of proposal preparation, data collection, analysis, and presentation of the final report.

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9. Douglas B: Homografts of fetal membranes as a covering for large


