



# Wound Healing and Wound Care in Neonates: Current Therapies and Novel Options

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**GENERAL PURPOSE:** To provide wound care information that considers the specific physiology of neonates.

**TARGET AUDIENCE:** This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

**LEARNING OBJECTIVES/OUTCOMES:** After participating in this educational activity, the participant will:

1. Differentiate the use of hydrocolloids, hydrogels, foam dressings, and barrier creams in the neonatal population.
2. Identify issues related to the use of solvents, alginates, collagen dressings, and negative-pressure wound therapy in neonates.

## ABSTRACT

**OBJECTIVE:** To discuss what is known about the wound milieu in premature and full-term neonates, including the unique challenges pediatric clinicians face, the therapies that have proven effective, and the therapies contraindicated for use in neonatal wound healing to guide treatment that accounts for the specific physiological characteristics of this often overlooked population.

**DATA SOURCES:** Data were collected on neonatal wound healing from a wide variety of sources, including PubMed, Google Scholar, journals, and textbooks.

**STUDY SELECTION:** Selection criteria included publications focused on the differences and nuances of wound healing in neonates in comparison with all other age groups.

**DATA EXTRACTION:** Data were extracted based on articles covering wound healing therapies with proven effectiveness in neonates. Terms for neonatal wound care were compiled,

and then a comprehensive literature search was performed by the authors.

**DATA SYNTHESIS:** Although many therapies are safe for treatment of older children and adolescents, most have not been explicitly tested for neonatal use. This article reviews therapies with proven effectiveness and/or specific concerns in the neonatal population.

**CONCLUSION:** This review sheds light on the advantages and disadvantages of current standards of care regarding wound healing for neonates to direct researchers and clinicians toward developing treatments specifically for this delicate population.

**KEYWORDS:** alginate, adhesive, collagen dressing, foam, hydrocolloid, hydrogel, moisture-associated skin damage, negative-pressure wound therapy, neonate, wound healing

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## INTRODUCTION

Neonates, or those persons younger than 4 weeks, are an intrinsically transitional population. They have a wound-healing phenotype quite distinct from both fetuses and older infants. Although this population appears homogeneous, clinicians confront numerous wound care challenges unique to this group. Many of these challenges relate to the clinical environment and iatrogenic exposures critically ill neonates may experience,<sup>1</sup> such as IV line infiltration and extravasation, issues with nutrition and immune compromise, epidermal stripping from adhesives, and medical device-related pressure injury. Even typical infant experiences (fecal and urinary incontinence, prolonged dependent positioning, and immobility) can result in significant skin injury.<sup>2</sup> All of these risks are elevated in premature, critically ill, and chronically ill neonates.

The age of the neonate plays a critical role in wound healing physiology. Clinicians must simultaneously consider the limited capabilities of neonatal immunity, renal metabolism, hepatic metabolism, thermoregulation, and water/electrolyte balancing while caring for this group.<sup>3</sup> Prematurity, congenital conditions, malformations, and corrective surgeries can further complicate matters.<sup>4</sup>

Moreover, the unique properties of neonatal skin make wound care for this group even more complex. Neonatal skin is highly permeable to topical agents because the stratum corneum is incomplete, and preterm neonates will absorb topical agents directly because they lack a developed detoxification skin system.<sup>5</sup> Because of the accelerated formation of both granulation tissue and extracellular matrix in neonates, their wounds close rapidly. Critically, neonatal skin has decreased dermal-epidermal layer cohesion and an immature stratum corneum. The delicacy of neonatal skin and underlying structures helps explain why moisture-associated skin damage (MASD) is perhaps the most common type of neonatal skin injury. In particular, MASD injuries from IV extravasation occur at higher frequencies and cause more damage in neonates than in other age groups.<sup>6</sup> Other MASD risk factors include enterostomy and gastrostomy tube-based dermatitides, as well as the use of conventional wet-to-dry gauze dressings for wound care. Caustic effluent or leaks from ostomies and drains result in skin irritation and inflammation, which lead to hypertrophic granulation tissue formation or peristomal erosion and breakdown, all of which exacerbate leakage, tube fit, and ostomy bag placement issues. Further, given the high occurrence rate of diaper dermatitis (one of the most common etiologies of skin breakdown), it follows that neonatal wound care requires thorough research and careful consideration to treat.<sup>7</sup>

These factors, along with a reticence for conducting research on wound care in neonates, make neonates a highly vulnerable population whose standards of care are “institutional preference” at best and anecdotal at

worst.<sup>1</sup> A study of pediatric home health agencies in 2000 noted that most wound care involved applying hydrogen peroxide, iodine-based cleaners, or commercially available household soap to the wound area and then packing or covering the site in wet-to-dry gauze.<sup>8</sup> Although standards for wound care have markedly improved since the study, these results underscore how most neonatal wound care fails to account for the specific limitations of neonate physiology. As such, the aim of this review is to directly inform current treatment practices and provide footholds for researchers and clinicians alike to begin developing more age group-specific therapies for this overlooked population.

## METHODS

To address the lack of wound care resources focusing on the limitations of neonate physiology, studies on both established and novel wound care options with efficacies explicitly confirmed in neonates were reviewed for this discussion. Data were synthesized from a multitude of sources such as PubMed and Google Scholar using neonatal wound care terms compiled by the authors. A thorough database search was then conducted to identify articles focusing on therapies specifically indicated for premature and full-term neonates. Studies on those products that are not recommended for use on neonates were also reviewed.

## DISCUSSION

### Current Therapies for Neonatal Wound Healing

There are a few goals fundamental to all wound treatment regardless of patient age. These include (1) infection identification, control, and treatment; (2) the establishment and maintenance of a clean and hydrated wound bed; (3) debridement or removal of necrotic or devitalized tissue if present; and (4) wound protection or barrier formation to prevent secondary infection, skin breakdown, or dehydration.<sup>9</sup> Informed product choices require caregivers and clinicians to consider these goals, as well as the phase of wound healing and the specifics of the patient's condition—all of which are dynamic and require vigilance.

Currently, enough data are available to recommend using hydrocolloids, hydrogels, foams, barrier films, and barrier creams as first-line treatments for neonatal wounds (Table). Each of these products will be discussed in this review. In addition, the characteristics of each product will be described at the beginning of each section, followed by discussions on when each would or would not be appropriate. By the end of each section, a clinician should have the relevant information needed to make informed decisions about when and why to use a particular product for neonatal wounds.

### Hydrocolloids

Hydrocolloids represent a class of moldable dressings composed of a gently adhesive carbohydrate base (commonly

**Table 1. SUMMARY OF VARIOUS WOUND CARE PRODUCTS INDICATED FOR USE ON NEONATES**

Product Class	Positive Characteristics	Negative Characteristics	Advised Use Cases	Unadvised Use Cases
Hydrocolloids	Moldable Gently adhesive Interacts with wound fluid to form hydrating gel Moisturizes skin Barrier against wound contamination Protects skin from adhesive damage	May detach and migrate if it absorbs too much liquid	Barrier to prevent adhesive, pressure, and extravasation injuries Irregular wound shape, size, or location	Heavy exudate Exposure to nearby body fluids
Hydrogels	Donates water to the wound Prevents ambient water loss Alleviates pain Aids selective autolytic debridement of nonviable tissue Available in multiple occlusive and semioclusive varieties Use without other products often leads to sufficient healing and satisfactory cosmetic results	Can require days or weeks to go into effect Requires frequent assessment to prevent or manage maceration May need overlying secondary dressing to prevent migration or dehydration May be difficult to maintain on certain irregular wounds	Superficial wounds with adequate perfusion and nonexcessive exudate Wounds in the proliferative and remodeling stages	Patients without skilled caregivers at home Irregular wound shape, size, or location
Foams	Absorb excessive exudate Can be cut to form Create a physical barrier and cushion ideal for use as a primary barrier Can employ silicone-based adhesives that are ideal for premature skin Only needs to be changed when strikethrough is present Can tailor dressing changes to needs of the neonate	Require frequent changing when used on exudative wounds to prevent maceration May require secondary dressings to stabilize	Wounds with excessive exudate Irregular wound shape, size, or location Mitigation or prevention of pressure ulcers	Heavy exudate Wounds that would require adhesive dressings to stabilize the foam
Barrier films	Semipermeable Protects skin Gentle adhesive properties	Nonabsorptive	Securing lightweight catheters to prevent friction and caustic substance injuries Preventing iatrogenic MASD	Heavy exudate
Barrier creams	Protects skin	Nonabsorptive	Preventing iatrogenic MASD Both petroleum and zinc oxide-based barrier creams can be applied to wound sites in between diaper changes to mitigate diaper dermatitis	Heavy exudate

Abbreviation: MASD, moisture-associated skin damage.

gelatin, pectin, or cellulose).<sup>6</sup> This carbohydrate base interacts with fluid in the wound to form a hydrating gel, which absorbs excess water and prevents desiccation of both the wound and surrounding skin. Hydrocolloids both moisturize the wound and provide a barrier that prevents wound contamination and protects the skin from injury by other adhesive products. Hydrocolloids represent a very useful tool in the neonatal population

for a variety of reasons. They can be shaped into patterns that are useful given the spectrum of size and body habits that one encounters in developing infants. They are excellent at protecting the neonatal skin and offer a number of protective features that can be employed. These properties make hydrocolloids the preferred option for areas at risk of adhesive, pressure, and extravasation injuries; however, the hydrophilic property of hydrocolloids

presents some pitfalls in certain wound types and locations. Heavy exudate or exposure to other nearby body fluids can disrupt the gel's composition and cause the dressing to detach or migrate. Further, the gel itself can migrate into nonoptimal locations such as tracheostomy sites or other appliances.<sup>6</sup>

### Hydrogels

Hydrogels are composed primarily of water, propylene glycol, and carboxymethylcellulose crosslinked into a three-dimensional hydrophilic polymer.<sup>10,11</sup> This combination hydrates the wound bed by donating water to the application site while preventing ambient water loss, which relieves pain and aids in selective autolytic debridement of nonviable tissue.<sup>6</sup> These actions are most critical during the proliferative stage of wound healing because both granulation tissue formation and re-epithelialization require wound debridement.

Hydrogels are available in multiple occlusive and semi-occlusive dressing varieties such as spreadable amorphous gels, sheets, or films and hydrogel-embedded gauzes that also provide a mechanical debridement effect.<sup>10</sup> Superficial wounds with adequate perfusion and nonexcessive exudate will benefit the most from hydrogels; already maximally hydrated, their ability to absorb further fluid from the wound bed is limited.<sup>10,12</sup>

There are, however, important issues to consider before using hydrogel dressings. Notably, hydrogels can require days or weeks to go into effect, often making them inappropriate for pediatric patients and their caregivers at home without skilled home care. Maceration is probably the most common adverse effect of hydrogel use.<sup>6</sup> As a result, hydrogel dressings require frequent caregiver assessment of the placement and integrity of the dressing and the surrounding skin. If left unattended, the dressing can migrate or dehydrate if not sufficiently protected by an overlying secondary dressing.<sup>6</sup> In addition, difficulties with dressing placement and maintenance can increase with particular wound locations, sizes, and complexities. Although this fact applies to both neonates and other patient populations, neonatal skin is more prone to transepidermal water loss and undue environmental heat transfer.<sup>6,13</sup> Although hydrogel-based dressings alone can often sufficiently heal neonatal skin while providing satisfactory cosmetic results, the aforementioned inefficiencies of hydrogels have the potential to inhibit proper wound healing in some cases.

### Foams

Foam dressings can be composed of natural (cellulose-based) or synthetic (polyurethane blends) materials, but all share an underlying spongy architecture that grants these dressings the ability to absorb excess exudate.<sup>14–16</sup> In addition, they can be cut to form, making them ideal for

irregularly shaped wounds. Foam dressings also create an elemental physical barrier and cushion that can be used as a primary dressing for protection, absorption, and protection against pressure injuries. Foam dressings are often used as secondary dressings to protect neonates with epidermolysis bullosa from movement damage and to prevent the fusion of adjacent rubbing tissues.<sup>17</sup>

However, as with any dressing used in exudative wounds, they must be changed when saturated to avoid damaging healthy skin surrounding the dressing. Another drawback of foams is that they are generally nonadhesive and may not stay in place without a secondary stabilizing dressing (and again, adhesives present a clinical challenge when dealing with fragile skin). However, foam-based products that employ a silicone adhesive are ideally suited for premature neonatal skin because they do not cause injury upon application. The foam itself is also specially designed so that it only needs to be changed once strikethrough is apparent. This allows dressing changes to be spaced out and tailored to the individual needs of the neonate, minimizing dressing changes and discomfort.

### Barrier Creams and Barrier Films

Barrier films are a distinct class of semipermeable synthetic dressings.<sup>14–16</sup> Barrier films provide protection and a measure of gentle adhesion, which can be vital for a patient population that does not tolerate other adhesive agents well. Some clinicians apply liquid barrier films prior to adhesives to prevent epidermal stripping at the time of dressing removal.<sup>17</sup>

The ideal use for barrier creams is to prevent or alleviate MASD and other issues related to neonatal skin sensitivity. For example, gentle and sterile application of bland emollients such as petrolatum is recommended for almost all variants and stages of ichthyosis.<sup>18</sup> The combination of a barrier product with stoma paste or wafer can be useful for managing MASD.<sup>9</sup> Further, both petroleum and zinc oxide-based barrier creams can be applied to wound sites in between diaper changes to mitigate diaper dermatitis development and severity.<sup>7</sup> Because neonates are more prone to MASD, barrier films and barrier creams should be used to lessen the likelihood of iatrogenic MASD.

Although semipermeable, barrier films are generally nonabsorptive, so clinicians treating exudative wounds should consider alternatives to barrier films or use them alongside other products.

### Wound Care Products with Specific Concerns in Neonates

Many adhesives commonly used without issue in older children and adults such as paper tapes, plastic tapes, and surgical glue are ill-suited for neonates. Use of these adhesives in newborns can cause significant epidermal stripping and dermatitis. Any adhesive products must be used strategically with serious consideration given

to the properties of neonatal skin. For example, it has been shown that dressings with a soft silicone adhesive prevent epidermal stripping, as does applying a skin barrier product prior to the dressing.<sup>9</sup> In addition, specific oil-, alcohol-, organic-, and silicone-based adhesive removers exist, which can reduce or even prevent epidermal stripping. Although oil-based products are effective in removing medical adhesives, their long drying times mean they are problematic in instances where the site will soon undergo reapplication. Alcohol-based and organic solvents are generally not recommended for neonates because of potential toxicity, especially given their high surface area-to-body weight ratio and increased skin permeability. Silicone-based removers tend to work best for patients with highly fragile skin because they form a layer between the skin and the adhesive and dry quickly after application without residue.<sup>19</sup>

Alginates are highly viscous hydrophilic gels or gums created from purified extractions of chain-forming polysaccharides found in brown algae.<sup>6</sup> Alginates are useful in exudative wounds in older children and adults because they absorb water from their surroundings.<sup>14-16</sup> Although it is common practice to use alginate-derived products on neonates in the ICU, applying them to large mucosal wounds on neonates can significantly dehydrate the wound bed to the point of systemic electrolyte deficiency.<sup>6</sup> Subsequent hyponatremia and hypocalcemia can both lead to seizures. As a result, clinicians must exercise extra caution when selecting these dressings.

Collagen dressings are acellular tissue dressings derived from purified bovine connective tissue.<sup>6</sup> These dressings both supplement and stimulate collagen, which makes them ideal for slow-healing or large wounds. Although these dressings are purified and acellular, they are ultimately xenografts, which may stimulate adverse reactions such as systemic inflammation from the neonate's immature immune system.<sup>15</sup>

### Negative-Pressure Wound Therapy

In negative-pressure wound therapy (NPWT), a foam dressing is applied to the wound site to contain the vacuum suction created by a small electric pump.<sup>20</sup> At a macroscopic scale, NPWT removes excess wound drainage and edema from the wound without desiccating the tissue.<sup>21</sup> At a microscopic scale, the subatmospheric pressure generated by NPWT appears to stimulate the localized release of growth factors, enhance cellular recruitment and migration to the wound site, promote local angiogenesis, and improve blood flow to the wound.<sup>22</sup> In addition, the application of negative pressure to wounds via occlusive dressings appears to simultaneously diminish the activity of bacterial enzymes, reduce overall bacterial burden within the wound, and protect the wound from secondary contamination.<sup>22</sup>

Research into the application of NPWT for adults has shown it to be a safe, inexpensive, and easy-to-use option for treating wounds with low incidences of pain and complications.<sup>20</sup> In practice, NPWT has seen use with a wide variety of adult patients; clinicians use NPWT to treat acute and chronic pressure injuries, traumatic wounds (including open fractures or those containing surgical hardware), infected or contaminated wounds, and a multitude of diverse surgical wounds.<sup>20,23,24</sup> Unfortunately, most NPWT studies and reports limit their focus to adult patients, and thus too few data exist to sufficiently support using NPWT as a first-line treatment for neonatal wounds. Despite this, neonatal patients are the most likely pediatric patients to see postoperative wound management with NPWT given the high rates of severe pressure injuries, abdominal wall malformations, and necrotizing enterocolitis in this population. This application is substantiated by NPWT's ability to control fluid losses, mitigate wound dehiscence, and prevent compartment syndrome.<sup>24</sup>

Many NPWT treatment guidelines in adults have been translated to children, with most studies demonstrating that a 25- to 50-mm Hg setting for premature infants is sufficient to reduce the risk of fluid loss, dehydration, electrolyte abnormalities, and hemodynamic instability.<sup>25</sup> When choosing the appropriate negative-pressure setting, clinicians must consider that the mean arterial pressure of a neonate is approximately equal to the gestational age. Therefore, a 40-week-gestation neonate should have a mean arterial pressure of 40 mm Hg, and it stands to reason that setting the pressure of the wound vacuum to 50 mm Hg would have detrimental effects on the patient's skin. As a result, consider keeping the wound vacuum setting less than the mean arterial pressure.

Because of the fragility of the neonatal tissue, a contact barrier such as a petroleum jelly-soaked matrix between the sponge and skin helps to prevent adverse events. If intact fascia or more sturdy endogenous tissues are present, a contact barrier may be avoided. Further, the wound vacuum itself can be set to an intermittent or continuous setting, although empiric evidence would suggest that continuous NPWT produces less pain in pediatric patients.<sup>26</sup> The constant change between the on and off cycle with the intermittent setting can be startling to neonates.

For the neonatal population, NPWT is advantageous because it is less prone to inadvertent removal and requires noticeably fewer dressing changes. Further, the NPWT system has been known to reduce pain and anxiety for both the patient and caregiver and minimize the burden of having two direct care nurses for frequent dressing changes. When compared with conventional neonatal wound treatments, NPWT's fewer dressing changes reduce treatment costs.<sup>27</sup>



However, keeping a close and accurate assessment of the fluid shifts within the neonate is important. Given that the total blood volume of a neonate is 100 mL/kg, if too much blood or fluid is inadvertently taken out, it could lead to hypotension and more disastrous outcomes. Another cause of concern is that the rapid rate of granulation for neonatal wounds can make NPWT more difficult for this group. In order to stop granulation tissue from incorporating into the foam dressing, caregivers should change NPWT dressings every 5 to 7 days.<sup>28,29</sup> Although complications such as skin maceration and dermatitis more commonly occur when using NPWT on neonates, single-barrier agents or contact layers on the at-risk skin will prevent these complications in most cases.<sup>30</sup>

### Limitations

The pace and scope of biomedical research mean that a single paper cannot exhaustively cover a topic on its own. Thus, it is very likely one or more additional products or product classes were overlooked or not selected for this article. Further, this literature review did not discuss specific examples of products from each class but instead chose to focus on the principles of the class as a whole. It is likely that specific products from a given class address the shortcomings of the class as a whole and therefore may not fit within the confines of these purposefully broad generalizations. Similarly, the design of an individual product may be modified in such a way that would make it inappropriate for use on neonatal wounds. As such, a clinician would most benefit from this review by using it as a guide to the landscape of neonatal wound care and looking into product specifics for each individual use case.

### CONCLUSIONS

Because neonatal bodies lack many of the developed features seen in older patient groups, it is inappropriate to use certain conventional wound care products on neonates simply because they work for older patients. Rare cases may necessitate the use of adhesives, alginates, or collagen dressings on neonatal wounds, but the vast majority of neonatal patients would benefit from substituting these products for those with explicitly verified efficacies. Currently, enough data are available to recommend using hydrocolloids, hydrogels, foams, barrier films, and barrier creams as first-line treatments for neonatal wounds.

This review aims to improve current neonatal wound care protocols and inspire others to include neonates in future wound care research. Experimentation with NPWT on neonates has already improved treatment for numerous conditions in this group, and it may only be a matter of time until NPWT becomes a first-line treatment for

neonatal wounds. The adoption of NPWT in neonatal care illustrates how investigators could modify current treatments for adults into neonate-appropriate variants. Through similar research, it may even be possible to engineer adhesives, alginates, and collagen dressings suitable for neonatal wounds. As both the quantity and quality of neonatal wound care research improve, medicine will gain more effective tools to treat this vulnerable population.

### PRACTICE PEARLS

- Neonates have a wound healing phenotype distinct from fetuses and older infants, so clinicians should be mindful of the therapies used when caring for this population.
- Hydrocolloids are useful for different scenarios because of their pliability, but their composition can be easily disrupted when exposed to body fluids. In contrast, hydrogels help to hydrate the wound bed but often require days or weeks to go into effect.
- Foam dressings have a spongy architecture that makes them ideal for absorbing excess exudate, but they cannot remain in place without a secondary stabilizing dressing. On the other hand, barrier creams can serve as a light adhesive but are generally nonabsorptive.
- Many adhesives commonly used in older children and adults are not suitable for neonatal patients because they can cause epidermal stripping and dermatitis.
- Although the majority of NPWT studies have focused on adult patients, NPWT may prove beneficial for neonates, but clinicians should take extra care and consideration when implementing this therapy. ●

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**Registration Deadline:** May 31, 2022 (physicians); June 3, 2022 (nurses).

### PAYMENT

- The registration fee for this CE activity is \$17.95 for nurses; \$22.00 for physicians.