Chronic wounds present a significant challenge, because there are few available treatment options for timely healing. Topical negative pressure devices have been used in a number of different types of wounds, including chronic wounds. They are believed to hasten wound healing by (1) maintaining a moist environment, (2) removing wound exudates, (3) increasing local blood flow, (4) increasing granulation tissue formation, (5) applying mechanical pressure to promote wound closure, and (6) reducing bacterial loads in the wound. Multiple nonrandomized, noncontrolled studies have reported that the use of these devices results in faster healing times and more successful closures. Five small randomized, controlled trials have also shown favorable outcomes with the use of topical negative pressure devices compared with conventional treatment. Adverse effects include discomfort, pain, and excessive tissue growth into the dressing. Complications are limited if the device is used properly. In light of the current treatment options, topical negative pressure devices may be considered useful as adjuvant therapy for chronic wounds; however, there is inadequate definitive evidence that wound healing is substantially better with these devices than with traditional therapy.

The management of chronic, nonhealing wounds has been a challenge to medical professionals in all fields. There are more than 2.8 million patients with chronic wounds, with billions of dollars spent on treatment each year in the United States. A chronic wound can be defined as a break in the skin that never heals, recurs, or takes a prolonged time to heal. The most common chronic wounds include arterial and venous leg ulcers, pressure sores, and diabetic ulcers. Depending on the type and cause of the wound, management can involve various combinations of the following treatment options: multiple dressings changes per day, compression, topical antimicrobial agents, debridement, partial skin grafts, bioengineered skin products, and growth factors. The standard of care for chronic pressure wounds includes frequent debriding, off-loading, maintaining a moist environment, using normal saline for cleansing, controlling infection, and providing adequate nutritional support. Despite current treatments, many chronic wounds fail to heal or persist for months to years. The use of topical negative pressure devices (also described as topical negative pressure or vacuum-assisted closure [VAC]) has gained popularity in surgical and wound-healing fields. The devices also represent a possible new treatment option for clinicians. The goal of the present review was to evaluate the strength of the trials that have been performed to determine the effectiveness of topical negative pressure devices in healing chronic skin wounds.

**DESCRIPTION OF THE DEVICE**

The topical negative pressure device consists of a foam dressing connected to an evacuation tube. A unit to provide negative pressure is applied to the other end of the evacuation tube. The dressing is composed of open-pore foam made of medical-
grade polyurethane ether or polyvinyl alcohol. The foam is cut specifically to fit within the wound. There are pores in the foam, ranging from 400 to 600 µm in diameter, to allow an open-cell system to create equal distribution of topical negative pressure to the entire wound. The evacuation tube is embedded in the foam and placed parallel to the wound. An adhesive drape is placed over the foam dressing and overlaps 3 to 5 cm onto normal skin to create a closed environment. Negative pressure can be delivered with a commercially available VAC device (VAC System; Kinetic Concepts Inc, San Antonio, Tex), wall suction, or surgical drainage bottles. All of the studies included in this review used the VAC device with either polyurethane ether foam or polyvinyl covering, with the exception of a few studies that used an alternate source of vacuum at the same settings as those of the VAC device.

PROPOSED MECHANISM OF ACTION

Topical negative pressure devices are believed to hasten wound healing by (1) maintaining a moist environment, (2) removing wound exudates, (3) increasing local blood flow, (4) increasing granulation tissue formation, (5) applying mechanical pressure to promote wound closure, and (6) reducing bacterial loads in the wound. Occlusive dressings maintain a moist environment, which is beneficial for wound healing. Topical negative pressure therapy uses a foam dressing with an adhesive drape covering the entire wound to create an occlusive dressing. Occlusive dressings prevent wound desiccation, increasing the rate of epithelialization, thereby leading to faster healing times. They also improve granulation tissue formation, particularly in chronic wounds. Moist wound environments create a hypoxic environment to stimulate angiogenesis, to encourage the proliferation of normal growth factors, and to increase fibrinolysis. Studies have shown that although bacterial colonization still occurs with occlusive dressings, the rate of clinical infection does not increase.

Although maintaining a moist environment results in faster wound healing, chronic wound fluid is believed to inhibit wound healing. Chronic wound fluid inhibits keratinocyte, endothelial cell, and fibroblast proliferation and contains low levels of glucose, albumin, and total protein. Studies have also shown elevated levels of proteolytic enzymes, particularly matrix metalloproteinases in chronic wound fluid, which may cause repeated tissue turnover and failed wound closure. Argenta and Morykwas reported removal of edema surrounding the wound, with volumes ranging up to 1000 mL of fluid per day.

In addition to providing an optimal wound bed environment, topical negative pressure has been shown to increase local blood flow to the wound site in initial animal studies. Adequate perfusion is essential to proper wound healing in order to provide nutrients and inflammatory mediators to the wound and to remove local edema. Chronic wounds that are edematous, with poor circulation, may benefit because of the decrease in hydrostatic pressure in the capillaries, which would allow increased return of fluid proximally. Increased blood flow may also help to remove bacteria from the wound and thereby decrease bacterial wound colonization.

An important factor in wound healing is the growth of granulation tissue. Initial animal studies by Morykwas et al showed a significant increase in the rate of granulation tissue formation in wounds treated with the VAC device compared with control wounds treated with saline-moistened gauze. It is postulated that this phenomenon occurs because of the applied force across the wound. In vitro studies have shown that mechanical forces can promote keratinocyte growth and protein synthesis, possibly through alterations of integrins. Disruption of these transmembrane proteins may transmit extracellular signals to the cytoplasm, resulting in matrix molecule synthesis and cellular proliferation. Also, intermittent application of pressure has the potential for repetitive release of second messengers. The actual mechanical strain applied to the wound by topical negative pressure may provide the stretch that is believed to be necessary to stimulate cell proliferation.

Applying negative pressure to wound beds may draw wound edges together as a form of reverse tissue expansion. As noted earlier, the application of mechanical stresses to the edges may promote cell growth to reapproximate wound edges at a more rapid rate. One animal study of an ischemic wound exhibited faster granulation tissue growth from the edges as well as faster epithelialization in topical negative pressure–treated wounds.

Infected wounds disturb the normal equilibrium of the wound healing process. Infection is believed to prolong the inflammation phase, to deplete complement components, to disrupt normal clotting, to inhibit angiogenesis, to create friable granulation tissue, and to disturb leukocyte function. Wound infection is suggested when quantitative cultures show bacterial levels that are higher than 10⁵ organisms per gram of tissue. In animal studies, Morykwas and colleagues showed that there was a significant decrease in the number of organisms in topical negative pressure–treated wounds compared with control wounds. The level of organisms remained lower than 10³ organisms per gram of tissue after postinoculation day 5. Bacterial counts of less than 10⁵ organisms per gram of tissue are also associated with successful, spontaneous wound healing.

Based on results from initial animal studies, it has been suggested that intermittent applications of pressure in cycles of 5 minutes on, 2 minutes off is optimal for increased granulation tissue formation and optimal local blood flow. It has also been suggested that the optimal negative pressure is 125 mm Hg, because studies of acute porcine wounds treated with 125 mm Hg showed a significant increase in the rate of granulation tissue formation compared with wounds treated with either 25 or 500 mm Hg.

CLINICAL TRIALS AND REVIEWS

The effectiveness of topical negative pressure devices is best determined by looking at primary outcomes of improved wound healing. The Food and Drug Administration’s Guidance for Industry draft document suggests that improved wound healing can be evaluated by incidence of complete wound closure, accelerated wound closure, facilitation of surgical closure, or improved quality of heal-
A literature search was performed with MEDLINE via PubMed. All clinical trials of chronic wounds using the topical negative pressure devices were reviewed. The number of randomized, controlled trials was limited to 6 studies. Many of the studies on the VAC apparatus use non-validated surrogates, such as change in wound area or volume or formation of granulation tissue, thus limiting their interpretability. The Food and Drug Administration stresses that quality studies should use control wounds, randomization, and blinding if possible. With this device, neither a vehicle control nor blinding is feasible, so all studies are constrained by this limitation. Another feature of a powerful study is the use of appropriate statistical analysis to determine significance, and this is missing from some of the studies on the VAC.4

There have been some case series of topical negative pressure devices in chronic wounds. These initial studies did not use controls or randomization. The case series that were reviewed concluded that topical negative pressure devices are beneficial to the healing of chronic wounds.9,18-22 Wound type varied from pressure ulcers to diabetic wounds. A few studies looked at outcomes related to wound closure by surgical means.19-21 They concluded that topical negative pressure devices were effective, because a majority of the wounds healed either without the need for surgery or with surgical intervention (secondary suture, graft, or flap). The other case series evaluated change in wound size19 and mean time to complete granulation tissue growth.22 A retrospective chart review looked at quantitative bacterial cultures and found that topical negative pressure therapy increases bacterial bioburden in the acute and chronic wounds reviewed.23 However, the authors did not see a correlation between the bacterial bioburden and the overall beneficial effect on healing with the VAC device.23

Six prospective, randomized, controlled studies evaluating the effectiveness of topical negative pressure devices have been completed to date (Table). Five of the 6 studies have also concluded that topical negative pressure is effective, since the VAC groups had greater decreases in wound volume or area.1,24-27 However, these findings were only significant in 3 of the studies.1,26,27 Two of the studies looked at time to healing and found that it was insignificantly decreased in the VAC groups.24,27 One study concluded that in pressure sores there was no significant difference (P = .09) in the time to decrease wound volume by 50%.28 Most studies used moist gauze dressings on control wounds except for 1 study that used hydrocolloid gel26 and 1 study that used an “HP [Healthpoint System] dressing” (Accuzyme [a papain-urea debridement ointment], Iodosorb [hydrophilic beads with 0.9% cadexomer iodine in gel or foam], and Panafil [a papain-urea-chlorophyll-copper ointment]; Healthpoint Ltd, Houston, Tex).25 The number of patients who completed the trial was small in 1 study; the number of wounds was small in 4 studies; and, randomization was inadequate in only 1 study.27

A review by Evans and Land29 concluded that since there have been only 2 small clinical trials, there is weak evidence of the superiority of topical negative pressure devices over saline gauze dressings in managing chronic wounds. The authors caution against using these trials to make any definitive conclusions, as the trials were small and had methodological flaws. Also, an evidence report by the Agency for Healthcare Research and Quality also concluded that there is insufficient evidence to support the effectiveness of the VAC device in the treatment of chronic wounds.30 The agency included 6 trials in their review.

**CLINICAL USE**

Topical negative pressure devices have been used in many different types of wounds. Current indications include traumatic wounds, infected wounds (with caution), sternal and abdominal dehiscences, skin graft fixation, wound bed preparation, pressure ulcers, venous ulcers, and diabetic ulcers.31 Chronic wounds are still the most difficult wounds to treat regardless of the use of the topical negative pressure devices. Traumatic wounds are believed to be the best responders to topical negative pressure, but there are also high, rapid success rates in skin graft fixation.

Specific regimens for treatment vary depending on the type of wound and the practitioner. For chronic ulcers,23 continuous pressures of 50 to 125 mm Hg are suggested, depending on patient tolerance, because there may be more pain associated with higher pressures. With some pressure ulcers, use of topical negative pressure can be switched to intermittent (5 minutes on, 2 minutes off) after the first 48 hours. Dressing changes should be every 48 hours and possibly every 12 hours if the wound is infected. Contraindications, including necrotic tissue, neoplasms, blood dyscrasias, fistulae, infections, and open body cavities,31 are limited. They are not absolute, and physicians are advised to use clinical judgment.

The safety of the device should be evaluated by looking for deterioration of the wounds after commencement of treatment.4 Deterioration can be seen as erythema, pain, discharge or infection, tissue necrosis, requirement of repeated debridement, surgical interventions, or increased ulcer size.4 Complications with proper use of the devices have been limited and minimal. Some of the more common complications have included discomfort and pain at higher pressures and excessive growth of tissue into the foam dressing, causing bleeding. Therapy should be stopped if any of the complications occur or if there is purulence or hematoma formation.13,31 The presence of an air leak is detrimental and should be avoided. One study has shown that an unregulated air leak in the adhesive drape leads to significant progression of the wound as a result of dehydration and necrosis.17

Philbeck et al32 extrapolated data from Medicare records to evaluate the cost-effectiveness of topical negative pressure devices in the treatment of chronic wounds. The average cost for saline gauze–treated wounds was $23 465 compared with $14 546 for wounds treated with topical negative pressure. This outcome was based on shorter treatment times for wounds treated with topical negative pressure vs saline gauze–treated wounds (97 days vs 247 days). The article suggests that treatment of chronic wounds was adequate in only 1 study.27

**Table**

- **Wound type**
  - Pressure ulcers, diabetic ulcers, venous ulcers, and traumatic wounds

- **Indications**
  - Chronic wounds
  - Open body cavities

- **Contraindications**
  - Necrotic tissue, neoplasms, blood dyscrasias, fistulae, infections, and open body cavities

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wounds with topical negative pressure may be more cost-effective than traditional therapy with saline gauze. Currently, the VAC device is covered by Medicare, some Medicaid plans, the Veterans Affairs Healthcare System, and some private insurers for the treatment of chronic wounds. This coverage means that there is little out-of-pocket expense for most patients.

**CONCLUSIONS**

Topical negative pressure devices have been used to aid in the healing process for many types of wounds. There are many potential benefits of topical negative pressure, including earlier closure of some wounds, decreased dressing changes, and minimal adverse effects. Most clinical trials to date have reported favorable results with topical negative pressure therapy. However, to our knowledge, there have not been any unflawed, randomized, controlled clinical trials studying the use of such devices for chronic wounds. Use of these devices is still best implemented as adjunctive therapy to standard treatment. Larger multicentered, randomized, controlled clinical trials are needed to provide better evidence of improved wound healing in chronic wounds.

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**Table. Clinical Trials**

<table>
<thead>
<tr>
<th>Source, y</th>
<th>Study Type</th>
<th>Intervention</th>
<th>Chronic Wound Type</th>
<th>Outcomes</th>
<th>Study Flaws</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joseph et al,2000</td>
<td>Prospective, randomized, controlled</td>
<td>Continuous at 125 mm Hg with dressing changed every 48 h Control: wet to moist gauze dressing changed 3 times daily</td>
<td>Pressure ulcers, traumatic wounds, dehiscence wounds, venous insufficiency ulcers, and radiation-induced wounds (VAC, n = 18; control, n = 18)</td>
<td>Significant decrease in wound volume (decrease by 78% vs decrease by 30%) over 6 weeks (P &lt; .001), wound depth most significant (P &lt; .001) 64% of VAC-treated wounds showed granulation tissue on histologic examination</td>
<td>Small number of wounds Grouped all wound types together Blinded?</td>
</tr>
<tr>
<td>McCallon et al,2000</td>
<td>Prospective, randomized, controlled</td>
<td>Continuous at 125 mm Hg for first 48 h, then Intermittent at 125 mm Hg Control: saline gauze</td>
<td>Postoperative diabetic foot ulcers (VAC, n = 5; control, n = 5)</td>
<td>Decreased time to satisfactory healing (22.8 d vs 42.8 d) Decreased surface area (28.4% vs 9.5%)</td>
<td>No statistical analysis Small number of wounds Subject to bias</td>
</tr>
<tr>
<td>Ford et al,2002</td>
<td>Prospective, randomized, controlled, crossover</td>
<td>Continuous with dressing changed Mon, Wed, and Fri HP dressing (Accuzyme, Iodosorb, and Panafil) changed once or twice daily</td>
<td>Full-thickness pressure ulcers (n = 3)</td>
<td>Greater mean % reduction in ulcer volume with VAC (VAC, 51.8%; HP dressing, 42.1%) (P = .46) Decreased inflammation in VAC group (fewer PMNs/lymph nodes) Increased number of capillaries in VAC group, suggesting more granulation tissue Significant decrease in wound depth (P &lt; .05) and volume (P &lt; .005) Insignificant decrease in wound length and width</td>
<td>Small number of wounds One patient with maceration complication in VAC group Did not address pain, patient preference, or length of treatment needed Different wound types evaluated Known infected wounds</td>
</tr>
<tr>
<td>Eginton et al,2003</td>
<td>Prospective, randomized, crossover</td>
<td>Continuous at 125 mm Hg with dressing changed 3 times a week Control: hydrocolloid wound gel and gauze dressing changed daily</td>
<td>Large diabetic foot wounds (n = 7)</td>
<td>Insignificant decrease in median ± SEM time to readiness for surgical therapy (6 ± 0.52 d vs 7 ± 0.81 d; P = .19) Significant wound surface area reduction in VAC wounds (P &lt; .05) No significant change in quantitative bacterial load for both groups No difference in time to decrease wound volume by 50% Equal effectiveness in formation of granulation tissue</td>
<td>Small number of patients</td>
</tr>
<tr>
<td>Mouses et al,2004</td>
<td>Prospective, randomized, controlled</td>
<td>Continuous at 125 mm Hg with dressing changed every 48 h Control: moist gauze</td>
<td>Full-thickness wounds (traumatic wounds, infected wounds, dehiscence wounds, pressure ulcers, and miscellaneous) (VAC, n = 29; control, n = 25)</td>
<td>Insignificant decrease in wound surface area with VAC (VAC, 51.8%; HP dressing, 42.1%) (P = .46)</td>
<td></td>
</tr>
<tr>
<td>Wanner et al,2003</td>
<td>Prospective, randomized controlled</td>
<td>Continuous Control: wet to dry or wet to wet with Ringer solution, gauze changed 3 times daily</td>
<td>Pressure sores (VAC, n = 11; control, n = 11)</td>
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</tbody>
</table>

**Abbreviations:** HP, Healthpoint System; PMNs, polymorphonuclear leukocytes; VAC, vacuum-assisted closure.
Women's Health: A Call for Papers

We invite manuscripts reporting the results of original research, especially randomized clinical trials on topics of particular interest to women's dermatologic health. This includes diseases that are more common in women as well as sex differences in treatment effects. Cultural issues affecting women's health and dermatologic complications of menopause will be considered. Manuscripts received by December 1, 2005, will have the best chance for consideration for the March 2006 theme issue of the Archives of Dermatology which supports the theme issue of the JAMA & Archives family of journals. Our usual rigorous editorial review process with no advance promise of acceptance for publication will be used for manuscripts submitted for the theme issue. High-quality submissions not accepted for this theme issue may be considered for other issues of the Archives. Please follow the Archives' Instructions for Authors regarding authorship, submission, and formatting requirements. The instructions may be found at www.archdermatol.com.