Vacuum assisted closure is being increasingly used for wound management. This review examines the history of its development and appraises the current evidence on its use so far.

Keywords: Vacuum assisted closure; Topical negative pressure; Vacuum sealing technique; Sub-atmospheric pressure; Dressings; Wound management; Acute wounds; Chronic wounds.

Introduction

Vacuum assisted closure (VAC) is a relatively new technology with applications in a variety of difficult to manage acute and chronic wounds. It is known by many pseudonyms—TNP (topical negative pressure), SPD (sub-atmospheric pressure), VST (vacuum sealing technique) and SSS (sealed surface wound suction).1

It involves the application of open cell foam to a suitable wound, adding a seal of adhesive drape and then the application of sub-atmospheric pressure to the wound in a controlled way.2 Encouraging results in terms of rates of healing have been reported in the literature but there is a relative paucity of randomised controlled trials with significant numbers to substantiate the findings. This article reviews some of the work published so far and explains the postulated mechanisms of action of the VAC as well as some of its reported clinical applications to date.

The VAC Technique

VAC uses medical grade open cell polyurethane ether foam (which is FDA approved for open wounds) as a dressing.2 The pore size is generally 400–600 μm (thought optimal for tissue growth).2 This foam is cut to fit and closely applied to the selected wounds. An evacuation tube with side ports, which communicate with the reticulated foam, is embedded in it. The aim of the reticulation being that the negative pressure will be applied equally to the entire wound bed. An adhesive drape is then applied over the area with an additional 3–5 cm border of intact skin to provide an intact seal.

The evacuation tube is connected to an adjustable vacuum pump and a canister for collection of effluent. The pump can be adjusted in terms of both the timing (intermittent vs. continuous) and magnitude of the vacuum effect. In general an intermittent cycle (5 min on, 2 min off) is employed as this has been shown to be most beneficial.2

Guidelines have been produced to aid in administration of this technique (Table 1). Effectively the technique converts an open wound into a controlled and temporarily closed environment.
Research and Experimental Work

The VAC was first investigated by Morykwas and Argenta et al. in 1997.² Their work followed on from studies of negative pressure years previously that had suggested it might improve wound healing. Early work suggested that negative pressure increased blood flows as evidenced by hyperaemia.³ Morykwas and Argenta² used a swine model to investigate the effect of negative pressure applied via the VAC on wound healing. They postulated that it might have application in chronic wounds but had no animal model available on which to mimic this state (Table 2). They, therefore, produced acute wounds on pigs and attempted to extrapolate their findings to what might reasonably be expected in chronic wounds. They compared the VAC with the standard treatment for wound dressings—saline soaked wet to moist dressings. Each subject had two wounds, one treated with the VAC and one a control treated with standard dressings. Four parameters were measured. The effect of the VAC on Doppler measured flows in the wound and adjacent tissues (five subjects), the amount of granulation tissue formation (10 subjects, five continuous VAC vs. control, five intermittent VAC vs. control), bacterial clearance (five subjects) and nutrient flow/random pattern flap survival (five subjects).

They found that the peak blood flows as measured by Doppler ultrasonography were recorded with a 125 mmHg vacuum setting. Flows gradually decreased after this, falling below the baseline observed at room pressure at 400 mmHg. Interestingly the flows also declined after 5–7 min of pressure returning also eventually to baseline (Fig. 1). The flows were seen to increase again with re-establishment of flow with an optimum off time of 2 min and an optimum cycle of 5 min on, 2 min off—the current regimen favoured by clinicians. However, from the authors’ later reported clinical experience of 300 chronic wounds⁴ they now recommend an initial 48 h continuous administration followed by the standard intermittent regime. This is from anecdotal rather than rigorous clinical evidence. Certainly from the early animal study² intermittent pressures did produce significantly improved healing rates (63.3 vs. 103.4%).

Other authors recommend various regimes for certain clinical situations, again mostly from their anecdotal experience. In general reduced pressures (50–75 mmHg) are employed for chronic ulcers and other cases where pain may be of concern or for example to encourage skin grafts to take.⁴ Higher pressures may be used for larger cavities or some acute traumatic injuries,⁴ however, these recommendations, as we have said, all stem from anecdotal evidence.

Banwell et al.,¹ have found immediate application of the VAC following injury/debridement to produce good results (from their experience with acute and traumatic wounds). They recommend changes of dressing every 4–5 days (but every 48 h if any evidence of infection) from anecdotal evidence.

Many groups have attempted to corroborate Argenta and Morykwas’ findings of increased local blood flows with a vacuum in a human model. Skagen and Henrikson⁵ looked at negatively applied pressure in a specially designed circumferential chamber applied to human forearms. They surprisingly showed decreased flows at only 40 mmHg (as evidenced by Xenon wash out studies) increased vascular resistance and vasoconstriction (later shown to be abolished by nervous blockade). This was corroborated in further work by the same author.

His work contrasted with a study by Fentem and Matthews⁶ which looked at negative pressure applied to the fore arms of healthy volunteers and this time showed the expected increased flows with application of negative pressure. However, neither of these groups were directly comparable to the original animal model.

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Table 1. Clinical management: negative pressure therapy

| Susan Mendez Eastman Advances in skin and wound care vol. 14 no 6 Nov/Dec 2001 |
|---|---|
| Guidelines for use of the VAC |
| 1. Gently remove previous dressing and discard as per local institutional protocol |
| 2. Aggressively cleanse wound and peri-wound area |
| 3. Debride necrotic tissue if applicable |
| 4. Achieve haemostasis |
| 5. Shave bordering hair if necessary |
| 6. Dry and prepare the peri-wound skin |
| 7. Select appropriate foam dressing |
| 8. Select appropriate sponge kit to fill the cavity |
| 9. Size and trim the drape to cover an area around the wound large enough to secure the foam and to maintain an air tight seal |
| 10. Gently place the foam into the cavity covering the entire wound base including sides, tunneling and undermining |
| 11. Apply tubing to the foam |
| 12. Cover the foam and an area of healthy surrounding tissue with the drape in order to accomplish an airtight seal |
| 13. Attach tubing from the wound to tubing in the canister placed in the VAC unit. Ensure clamps are unclamped |
| 14. Program the appropriate pressure and cycle in the computerized unit and begin treatment |

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as they applied circumferential pressure to normal skin with out a foam inter face rather than using foam diffused negative pressure over a discrete cutaneous wound. The numbers of volunteers were also comparatively small.

The original study used alginate casts of the wounds to determine healing/amount of granulation tissue formation. The findings were of 103% increase relative to the controls in the intermittent pressure group (G 35.3% CI) and 63.3% (G 26.1% CI) in the continuous group. Bacterial clearance was also measured in the original study/the wounds were inoculated with S. aureus and S. epidermidis and counts were found to be significantly reduced after 4 days of the VAC dressing. The non-VAC treated group’s levels of bacteria peaked at day 5 anecdotally this has been confirmed in humans with fewer courses of antibiotics.7, 8

Furthermore Gustaffson et al. showed VAC assisted closure to be effective in patients with deep sternotomy wound infections a series of 16 patients with infections monitored by CRP level were closed successfully in an average of 9 days with demonstrable falling CRP levels. They were all alive and infection free 3 months later. Scholl et al. reported success in their recent series of 13 patients with sternal osteomyelitis. A closure rate of 100% was noted at 14 months. Buttenschoen et al. looked at a small series of ankle fracture patients with endotoxaemia and rise in acute phase proteins treated with the VAC. The toxemia and acute proteins settled with time.

However, one case report highlights the fact that the VAC may not always positively affect bacterial clearance. The authors report a case where a patient with a difficult groin wound treated with the VAC developed a severe anaerobic infection (it improved with VAC cessation and antibiotics).

Finally, the original animal study looked at nutrient flow as evidenced by random pattern flap survival. In the five subjects that the VAC treated, flap wounds showed 21% increased graft take relative to controls (p value <0.05). The wounds were further split into pre treated post-treated and pre and post-treated groups and showed increasing levels of graft survival but inter-group differences were not significant due to small numbers.2

Many groups have subsequently looked at use of the VAC to increase graft take rates/survival. It theoretically provides the perfect conditions for graft take: a suitable wound bed, firm fixation and prevention of shearing forces, adaptation to various concave/convex surfaces, evacuation of sub-graft haematomas and seromas and reduction in infection.1 Take rates for the VAC have been reported at above 90%.1

Mullner et al. prospectively studied 45 patients with various wounds to which the VAC was applied. There was no control group and again the recommendations on settings for the VAC were based on anecdotal evidence but an 80% reduction in size during the period of study in 12 of the 17 pressure sores studied was found. Furthermore, all of the 12 soft tissue injuries responded well enough to allow early grafting. This was with 48 h conventional wet to moist dressings prior to commencing treatment with the VAC.

Chronic leg ulcers have been specifically studied by a group in France. In their group of 15 ulcers that had

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Table 2. Indications, contra-indications and guidelines for use of the VAC. (Compiled from the KCI website)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Guidelines</th>
<th>Cycle setting (following initial 48 h continuous period)</th>
<th>Dressing change interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcers</td>
<td>Continuous, 50–75 mmHg</td>
<td>48 h (12 h with active infection)</td>
<td></td>
</tr>
<tr>
<td>Acute wounds</td>
<td>Intermittent, 125–175 mmHg</td>
<td>As above</td>
<td>48 h (12 h with active infection)</td>
</tr>
<tr>
<td>Flaps, grafts and burns</td>
<td>Continuous, 75–125 mmHg</td>
<td>None. Remove dressing after 3–5 days</td>
<td>72 h (12 h with active infection)</td>
</tr>
</tbody>
</table>

**Contra-indications**
- Malignancy with the wound
- Untreated osteomyelitis within the wound
- Non-enteric and unexplored fistula
- Necrotic tissue with eschar present (debride first)

**Precautions**
- Active bleeding, difficult wound haemostasis, antico-agulant therapy
- Close proximity to blood vessels/organs (ensure cover with tissue or protective barrier)
- Care with irradiated or sutured blood vessels or organs
not responded to several other treatment modalities, the VAC produced a greater than 50% reduction in size in four patients, and greater than 25% reduction in size in six patients over only 6 days. Reduction in oedema, as we have mentioned, is thought to be one of the mechanisms of action of the VAC.

It is difficult to quantify. Various groups are attempting to, however, by high frequency ultrasound scanning and electrical impedance measurements. Dry tissue weights and displacement techniques have also been used.1

One of the early criticisms of the VAC system was that it might be needlessly expensive for example could the same results be obtained simply with wall suction or surgical suction drains. The counter-argument to this being that the VAC provides a safe system with controlled programmable application with a measured magnitude of vacuum with a failsafe alarm. No one knew for example what the effect of an inadvertent air leak in a system without an alarm might be. Wall/bed head suction would be uncontrolled with no alarm. Surgical drainage bottles would allow mobility but also deliver high pressures over short periods—not necessarily practical or effective.

Morykwas et al.13 attempted to clarify the matter again with their experimental swine model they simulated the various methods of vacuum applications. High pressure for short periods produced only 5.9% increase in granulation tissue by day 8. The standard 125-mmHg regimen had granulated to skin level by this time!

An air leak was simulated in a third group (by producing a hole in the drape) these wounds actually increased in size by 197% on average. Presumably due to desiccation and necrosis. The authors concluded that wall suction/surgical drainage bottles were neither safe nor effective when compared to the VAC.

The size of the device and necessity of mains electricity was a potential pitfall in terms of patient acceptability. Encouragingly success with smaller portable mini-vac devices was soon reported.14 In one series of skin grafted patients seven out of nine were successfully treated with the portable device. The mini-vac is now widely available.

As applications for the VAC increase, new questions are posed and answered as to how best to use it. The VAC has been employed to aid closure where wounds have become infected and/or closure is difficult.7 However, negative haemodynamic effects have been observed in some of these cases.15 They hypothesized that the interposition of a muscle flap attenuates these negative haemodynamic effects.

A further example of current controversy surrounding use of the VAC would be enterocutaneous fistulae. This has been cited in the past as a contraindication to using the VAC but some groups have reported success. Two published case reports highlight successful use of the VAC both in expeditious healing of two...
enterocutaneous fistulae and in palliation of skin excoriation resulting from the fistulous exudates. Both patients had been managed nil by mouth, with total parenteral nutrition and VAC therapy to the site. Current recommendations from the manufacturer state that it may not be used on unexplored fistulae.

Other novel uses presented in case reports include successful application of the VAC in resection and reconstruction for advanced scalp malignancy, placed: orbital skin grafting, as an aid in construction of a neo-vagina without resulting contraction or need for stenting, and the salvage of a ventral hernia repair with mesh that was infected with M.R.S.A.

As we have mentioned although there are many case reports and reports of centres’/and authors’ experiences of the VAC in the literature there are few randomised controlled trials. Evans and Land undertook a review of the literature into the application of the VAC for chronic wounds in 2001. They found only two trials that were randomized and prospective with some attempt at blinding. In both the evidence was weak due to small sample size and methodological limitations. Important parameters such as cost, quality of life, pain and comfort were not assessed. Joseph et al. took 24 patients with 36 wounds (chronic of various aetiologies) and randomized to wet to moist dressings or the VAC. The end point was reduction in wound volume. Results were a 66% reduction in volume with the VAC and only 20% with the wet to moist dressings.

McCallon et al. studied 10 patients who were randomized in the same way all of whom were diabetics with post-operative foot wounds the end points were days to healing and change to surface area. The VAC was superior (statistically significant) in both parameters. Clare et al. retrospectively reviewed the notes of 17 patients who had had diabetic or dysvascular non-healing wounds treated by the VAC. Fourteen of the 17 were successfully healed with the VAC. In a large series of 300 wounds 175 chronic, 97 sub acute and 31 acute, 296 showed significant increases in granulation, there were no controls.

Mechanisms of action

Wounds generally heal by primary, where edges are brought into close apposition for example by suturing, or secondary intention, where the wound edges are not opposed and a matrix of small blood vessels and connective tissue must be formed in between in order for keratinocytes to migrate across the surface and re-epithelialise the defect. It is a complex, intricate process. The aims of the process can be considered as minimization of blood loss, replacing any deficits with new tissue (granulation) and restoring an intact epithelial barrier as quickly as possible. In order to achieve healing debris must also be removed; any infection controlled and inflammation eventually cleared. The wound then heals with granulation, remodeling of the connective tissue matrix and finally maturation.

The rate of healing may be limited by vascular supply and the capacity of the wound to form new capillaries/matrix. Any disruption in the various processes involved—proliferation, angiogenesis, chemotaxis, migration, gene expression, protein production can lead to a chronic wound. When we consider the postulated mechanisms of action of the VAC and how they tie in with our generally accepted ideas surrounding the way wounds heal it is easy to suppose a likely benefit in quicker resolution of wounds.

Removal of oedema/exudate management

Localised oedema can compress the vascular and lymphatic systems in a wound. The VAC removes excess fluid and, therefore, is thought to restore the vascular and lymphatic flow. Practically, the next best wound dressing (wet to moist saline dressings) involves labour intensive and potentially hazardous dressing changes. The VAC ensures a closed environment for wounds and, therefore, adheres to universal precautions. They also need to be accessed far less frequently. The VAC system allows collection of the removed fluid for analysis. Some centres have shown high levels of proteolytic enzymes in chronic wounds and burns. These enzymes if left in situ could result in matrix degradation and a non-healing wound environment. They have also been demonstrated in the effluent from VAC treated wounds along with cytokines and various acute phase proteins.

Reduction in levels of bacteria

Infection is known to impede wound healing. Reduced levels of bacteria have been demonstrated in VAC treated wounds. It has also been demonstrated that VAC treated wounds require fewer courses of antibiotics relative to conventionally treated

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wounds\textsuperscript{7,8} This is thought to be due to multiple factors: the positive effect of removing excess wound fluid on local blood and lymphatic flows, greater amounts of oxygen made available for the bacteria killing oxidative bursts and the closed nature of the system. Gouttefangeas \textit{et al.}\textsuperscript{31} measured the cellular content of the foam from the VAC and found high levels of granulocytes, cd4, cd5 and T cells. They supposed the foam to be an attractive habitat for immune cells, partially recruited by a foreign body reaction.

However, one recent study of 25 patients undergoing VAC treatment suggests there may be a negative effect on bacterial clearance.\textsuperscript{32} In this study, serial cultures showed that bacterial colonization increased significantly during treatment. Though of note, the treatment was beneficial in most cases with rapid wound healing and there were no controls to provide meaningful comparison.

### Mechanical stress causing granulation tissue formation and angiogenesis

Ilizarov \textit{et al.} showed that applied mechanical stress to tissues stimulated mitosis and found that new vessels were formed as a result.\textsuperscript{33,34} This and the reduction in oedema could explain changes in blood flow and new vessel formation. However, further theories suggest that the vacuum may directly affect vasomotor tone and vaso-active mediators or simply have a mechanical effect forcing the blood through the area more quickly.\textsuperscript{1}

It is thought that \textit{in vivo} the external forces applied to cells through the extra cellular matrix are balanced by intracellular cytoskeletal forces with integrins acting as trans-membrane bridges. This balance is thought to be disturbed by application of the VAC leading to release of various intra cellular second messengers which together cause changes in expression of immediate early genes which results in matrix molecule synthesis and, therefore, proliferation.\textsuperscript{33} The presumption is that this also occurs when the vacuum on the foam is released, causing progressive up-regulation when the vacuum is applied intermittently. This is born out by the finding of more granulation tissue in wounds where the vacuum is applied intermittently.\textsuperscript{2}

Recent work in China\textsuperscript{35} also found that levels of the matrix metalloproteinases 1, 2 and 13 were reduced over time in five chronic wounds treated by the VAC technique. Lower levels of these MMP’s would presumably lead to reduced collagen and gelatin breakdown and aid wound healing.\textsuperscript{35} A further Chinese group recently examined the protein Bcl-2.\textsuperscript{36} They found that expression of this protein was increased in an animal model on treatment with VAC therapy. This protein helps modulate apoptosis, and the results of the study suggest that the VAC may promote the healing process partly through modulation of apoptosis.

### Reverse tissue expansion/skin stretching

The vacuum is thought to encourage migration of keratinocytes across wound defects. A pure in-drawing produced by the vacuum, the so-called ‘mechanical creep’ effect. This is well seen in abdominal wounds treated by the VAC where a centripetal effect is observed.\textsuperscript{37} It can also be compared to the stretching of tissue produced by tissue expanders used prior to skin grafting procedures.

### Complications

When used within recommendations, complications resulting from the use of the VAC are infrequent—but do occur.

#### Pain

Most wounds treated by the VAC are painful by their very nature—for example; burns, pressure sores and infected wounds. However, as with all ‘dressings’ this pain can be exacerbated by dressings changes. Although VAC treatment carries the advantage of fewer dressings changes, strategies to minimize pain should be employed.\textsuperscript{38} A small percentage of patients in the larger series\textsuperscript{4} reported VAC treatment itself to be painful, but none withdrew from VAC treatment as a result.

#### Infection

One case report has been published highlighting the occurrence of Toxic Shock Syndrome following VAC treatment,\textsuperscript{39} another mentioned in this article reported a wound infection by anaerobes which resolved on cessation of VAC treatment and the institution of a course of antibiotics.\textsuperscript{10} Frank pus within the wound to be treated is a contra-indication to treatment with the VAC. The manufacturers and body of opinion in the literature suggest that the wound bed should be debrided and prepared prior to treatment and any necessary antibiotic treatment commenced. However, the original studies reported enhanced clearance of
bacteria in VAC treated subjects, and the clinical experience reported by many groups suggests a positive effect on avoidance of infection. No direct comparison has been made in a clinical trial of infection rates specifically in VAC vs. non-VAC treated patients.

**Bleeding**

The authors found no mention in the literature of haemorrhage as a complication of VAC therapy. But, the manufacturers do recommend the device is not used in patients whose wounds are actively bleeding, or where haemostasis was difficult. Use of controlled suction over a period of time on a bleeding wound would have obvious adverse consequences.

**Fluid depletion**

One recently published case report mentioned two cases of patients at extremes of age (10 months and 82 years). Both patients suffered fluid depletion following VAC treatment for skin loss following meningococcal septicaemia and chronic leg ulcers, respectively. In both cases, large amounts of fluid had been lost from the wounds over the course of their treatment. This problem should be considered and managed appropriately where large amounts of effluent are collected by the VAC.

**Cost-effectiveness**

Considering the VAC and traditional dressings in terms of cost, one might suppose a greater cost for treatment would be attached to the VAC. A certain cost is attached to the purchase or hire of a VAC unit but a published analysis reported that overall, cost of VAC treatment is lower. Shorter treatment times and fewer additional interventions helping to reduce the cost. Philbeck Jr et al. reviewed the case notes of 1032 patients with chronic wounds treated in the community with the VAC after failing to respond to conventional dressings. They reviewed the time taken to heal as well as analysed costs. The results were compared with published reports of costs of treating same types of wounds with conventional dressings. The average wound in the VAC treated patients took 97 days and $14,546 to heal. The average wound of the same type treated conventionally took 247 days and $23,465 to heal.

**Summary**

From our own experience, the VAC is a promising new technology in the field of wound healing. With multiple applications in a variety of wounds including those that can prove difficult to heal: pressure sores, amputation sites, skin grafts, lower limb ulceration, sternotomy wounds, burns and abdominal wounds. Broadly speaking, the applications are for both acute and chronic wounds, salvage procedures or as an adjuvant therapy to improve results of various surgical procedures.

KCI Medical (the manufacturers of the VAC) summarise the indications for the VAC as chronic open wounds (diabetic ulcers and stage 3–4 pressure sores) acute and traumatic wounds, flaps and grafts, sub-acute and dehisced wounds as well as partial thickness wounds. They advise that non-enteric and unexplored fistulas and wounds containing necrotic tissue and eschar should not be treated with the VAC.

Its use is also contraindicated on wounds containing untreated osteomyelitis or malignancy (due to the effect on cellular proliferation). The scientific basis for the VAC has been tested rigorously and the theories surrounding its’ mechanisms of actions explored. Centres around the world continue to explore various applications of the VAC and to attempt to improve the way it is used. Our centre has extensive but unpublished experience using the VAC. It has been successfully used for diabetic amputation wounds, fasciotomy wounds, closure of laparostoma and non-healing venous ulcers. However, the VAC is costly and there is a need for larger randomised controlled trials to prove the effectiveness of the technique in the various patient groups suggested by the current anecdotal evidence. We have commenced a randomised controlled trial to address some of the issues raised in this review.

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technique. [see also 44–45].

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