# Clinical uses of the medicinal leech: A practical review

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# Clinical uses of the medicinal leech: A practical review

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## ABSTRACT

The medicinal leech, *Hirudo medicinalis*, is an excellent example of the use of invertebrates in the treatment of human disease. Utilized for various medical indications since the ancient times, the medicinal leech is currently being used in a narrow range of well-defined and scientifically-grounded clinical applications. Hirudotherapy is most commonly used in the setting of venous congestion associated with soft tissue replantations and free flap-based reconstructive surgery. This is a comprehensive review of current clinical applications of hirudotherapy, featuring a comprehensive search of all major medical search engines (i.e. PubMed, Google Scholar, ScientificCommons) and other cross-referenced sources. The authors focus on indications, contraindications, practical application/handling of the leech, and therapy-related complications.

KEY WORDS: Complications, contraindications, hirudotherapy, indications, medicinal leech

## Introduction and Historical Perspective

The medicinal leech, *Hirudo medicinalis*, is one of the few examples of the use of invertebrates in the treatment of human disease. The word *leech* is likely derived from the old English word for physician, *laece*.[1] Leech therapy has been administered since ancient times. A painting in an Egyptian tomb from around 1500 BCE depicts the use of medicinal leeches.[2,3] Hirudotherapy has also been reported by Themison of Laodicea in the year 50 BCE.[4] Leech therapy played an important role during the seventeenth and eighteenth centuries, at which time it was used for medicinal "blood-letting" and "purification" – a practice believed to cure a variety of ailments from gout to headaches.[3,5,6] The use of leeches likely gained popularity among practitioners of phlebotomy due to its ability to achieve more gradual rate of blood loss. According to some, the therapy may have been so popular that leech shortages were reported in Europe during that time.[3] Enthusiasm for leech therapy waned in the late nineteenth and early twentieth century, but scientific interest in *Hirudo medicinalis* continued.[5,6] In the early 1880s Haycraft first noted the antithrombotic properties of leech saliva and Jacoby discovered the anticoagulant factor in leech saliva and named it *hirudin* in 1904.[7] Hirudotherapy re-emerged as an adjunct to plastic, reconstructive, and trauma surgery in the 1970s and 1980s.[3,5,6] In the 1980s, French microsurgeons began using leeches to assist with distal digital replantation involving arterial repairs only.[8] Today, the medicinal leech is often used to treat venous congestion in the settings of microvascular replantations, reconstructive surgery, and traumatology.[2,9,10] This review focuses on the biology and current therapeutic applications of the medicinal leech.

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## Methods

A comprehensive search of major medical search engines (i.e. PubMed, Google Scholar, ScientificCommons) was conducted. The following list of search terms was utilized, in various permutations: (a) leech therapy; (b) medicinal leech; (c) hirudotherapy; (d) indications; (e) contraindications; (f)

complications; (g) infections. Literature reports most relevant to the focus of the current review were then incorporated into the manuscript as part of the general discussion, topic-specific discussions, or both. Topic-specific references were subsequently tabulated according to the corresponding subject area.

## Basic Biology of Leeches

First named by Linnaeus in 1758, *Hirudo medicinalis* is abundant in freshwater systems of North America and Europe.[11,12] Leeches are usually hermaphroditic, but require a second leech to reproduce.[12] They belong to the phylum *Annelida*, class *Hirudinea*. *Hirudo medicinalis* is the species that inflicts the deepest bite and the most prolonged post-bite extravasation in its class.[1] Being essentially a segmented worm without an exoskeleton, the medicinal leech is a very specialized annelid both anatomically and behaviorally.[2,13] It consists of 102 annuli (each of which usually consists of five segments).[14] *Hirudo medicinalis* can grow to approximately 12 cm in length, with its resting length being about one-third of its maximal length.[14] The leech crawls using a large posterior sucker.[12] Posteriorly, the leech has three jaws arranged in a triradiate configuration that attach to and bite through human skin and a smaller anterior sucker that is utilized for feeding.[14]

The feeding behavior of *Hirudo medicinalis* is controlled predominantly by the neurotransmitter serotonin which is abundant in the largest neuronal cell of the leech, the Retzius cell.[15,16] The actual act of feeding is stimulated by the proximity of mammalian-range temperature and by the sodium and arginine in blood.[16] Leeches can be very discriminating in their feeding patterns, preferring blood from certain species.[12] Hungry leeches tend to rest at the water's edge and can swim with great accuracy toward objects that produce waves.[15,17,18] While some leeches feed on other small invertebrates, others feed exclusively by temporarily attaching to various animals using a very powerful clinging sucker.[2,12] Certain species use blade-like jaws to incise the skin of the host; other species secrete enzymes that help digest an opening through the skin.[2,12] The host is frequently unaware of this attack due to the natural anesthetic substance secreted in the leech saliva. The leech also produces one of the most potent anticoagulants known, hirudin, a 65-amino acid peptide that inhibits thrombin-catalyzed conversion of fibrinogen to fibrin and prevents the host blood from clotting.[12,19] Other important substances secreted by salivary glands of the leech include vasodilators (antihistamines) and hyaluronidases.[20] Of interest, some leeches are capable of ingesting up to nine times their body weight, which may represent an entire year's nourishment.[12] It is important to note that leeches are colonized by endosymbiotic bacteria, mostly *Aeromonas spp*, that aid in the digestion of blood within their digestive system.[2] The presence of these bacteria, while usually of no consequence to the host, can occasionally contribute to localized (cellulitis/abscess) and/or systemic (gastroenteritis/sepsis) infections.[10,21] At times, these infections can be very serious, even life-threatening (i.e. myonecrosis, sepsis).[22,23]

## Mechanism and Rationale for Hirudotherapy

Contemporary leech therapy is most often used in the setting of localized venous congestion or hematoma. Venous congestion occurs with native venous thrombosis or with venous outflow thrombosis in a vascular graft or replanted tissue.[6,10] Reports of hirudotherapy in the setting of soft tissue hematomas include leech applications for large scrotal and lingual hematomas.[24,25] In this particular setting, the goal of leech application is to avoid the need for surgical intervention.[24,25]

The actual volume of blood drawn by a single leech is minimal, approximately 2 mL to 20 mL per feeding.[5,26,27] Following extraction of this small volume of blood, the leech usually becomes satiated within 10 to 30 min, detaches from the host, and will not re-feed unless purged by incision of the posterior crop.[12,26-28] However, due to the presence of hirudin in the leech saliva, continued oozing from the leeching site well after the leech has detached allows therapy sessions to be temporally spaced by up to 6-8 h.[5] Of interest, the secretions from a single leech have been found to prevent *in vitro* coagulation of 50-100 mL of human blood.[19] Because the leech bite site on the host may continue to ooze blood for as long as 24 to 48 h, the benefit from leech phlebotomy is thought to far exceed the individual meal volume. In cases of hirudotherapy for retained hematomas, continued drainage of dark non-clotted blood from leech attachment sites suggests that resolution of the hematoma may be ongoing for some time after leech detachment.[25] Leeches will detach spontaneously after they are maximally engorged. At this point, they should be removed and disposed of as biohazardous after sacrifice in 70% alcohol.[10] If a leech does not detach, this may indicate arterial insufficiency, and the leech should be removed with 5% topical cocaine, which will paralyze the leech. The leech must not be forcibly detached, and alcohol must not be applied while the leech is still attached.[1] Basic handling of the medicinal leech is described in Figure 1.

While modern use of leech therapy revolves around providing a temporary substitute/bridge for venous outflow in the setting of critical venous congestion of tissue reconstruction/flaps, one must always differentiate between venous congestion and arterial ischemia within the tissue being considered for hirudotherapy.[10] This is because the use of leeches in tissue with compromised arterial inflow will not only fail to promote tissue healing but may also contribute to introducing bacterial contamination of the ischemic tissue.[10,21]

The subsequent sections describe details of the most widely reported applications of hirudotherapy, focusing on clinical indications, risks, and benefits of leech therapy. Finally, a section on infectious complications of hirudotherapy follows.

## Hirudotherapy for Soft Tissue Hematomas

Extensive lingual swelling (macroglossia) represents an acute airway emergency.[25] Most frequently attributed to seizure-related activity, traumatic macroglossia may also arise from blunt or penetrating injuries to the lower face that lead to the development of a large lingual hematoma.[25,26] In the setting

of blunt trauma to the face, macroglossia can be secondary to bleeding from the fracture site at the mandibular symphysis via dissection into the sublingual space.[25] Non-traumatic lingual swelling has also been associated with prone positioning in spinal surgery and cleft palate repair.[27,29] Although lingual swelling has been traditionally treated expectantly, it is generally agreed that airway management should be performed early in anticipation of increasing swelling to prevent acute airway emergency.[25,30] Once the tongue becomes massively swollen, a cycle of venous and lymphatic congestion begins, contributing to persistent/worsening swelling.[31] Reported therapeutic alternatives in this setting include head elevation, manual reduction of the tongue, and corticosteroid administration.[25,27,29,31]

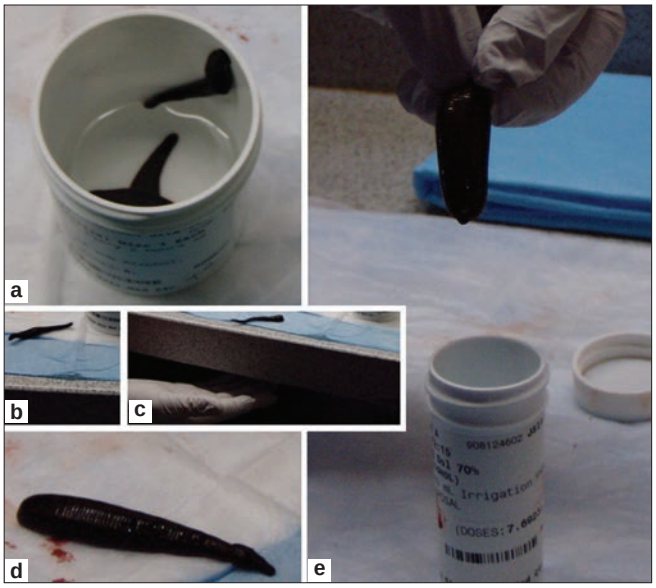


**Figure 1:** Pre- and post-application handling of the medicinal leech: (a) Leeches are delivered in a clean container provided by a certified hirudotherapy supplier; (b and c) Leeches are able to move quite quickly on flat surfaces – it is important not to drop or lose a leech when handling it; (d) Satiated leech is visibly distended and moves slower; (e) The leech is being placed into a 70% alcohol solution during the post-application disposal process

Medicinal leech application has been reported to be successful in the management of massive post-traumatic lingual swelling.[25,26] Clinical results have been satisfactory, with resolution of swelling and only minor post-leeching glossal puncture marks.[25] Table 1 contains a list of clinical reports describing hirudotherapy in the setting of lingual swelling.

## Hirudotherapy in Tissue Flap Reconstructions

Perhaps the best established modern application of leech therapy is in tissue flap reconstructions. Despite our improving understanding of tissue perfusion, flaps continue to fail for a variety of reasons. The most common reason for tissue flap failure is inadequate venous outflow. Most authors agree that the initial step in this setting should be surgical exploration and examination of the venous pedicle to alleviate venous insufficiency. Only when venous compromise is determined to be surgically irreparable of if surgery is contraindicated should hirudotherapy be considered.[1] Table 2 lists examples of hirudotherapy in this clinical setting. In one paper, hirudotherapy was associated with morbidity, including the need for blood transfusions.[33] In another report, the use of leech therapy was described in the setting of heparin-induced thrombocytopenia associated with lower extremity tissue flap failures.[34] In this case, the patient underwent an initial soleus flap placement, which failed despite an intact Doppler signal throughout the pedicle. Subsequently, a microvascular gracilis flap was constructed but began failing in the immediate postoperative period, despite re-exploration-proven patency of both artery and vein. After stopping all heparin administration, hirudotherapy was started, with flap viability maintained until shortly after discontinuation of leech therapy on Day 7. At that time, muscle necrosis ensued. During subsequent workup, it was shown that the patient had heparin-induced thrombocytopenia. In this case, the observation of flap salvage using hirudotherapy – and thus hirudin, the natural non-heparin anticoagulant present in leech saliva – may have constituted indirect evidence that the initial flap insufficiency was associated with heparin-induced thrombocytopenia, especially in the context of immediate gracilis flap failure following discontinuation of leech

Table 1: Clinical reports describing the use of *Hirudo medicinalis* in the setting of soft tissue hematomas

| Study (Reference) | Type of report | Number of patients | Clinical details | Comments |
|---|---|---|---|---|
| Grossman *et al.*[25] | Case report | 1 | Lingual swelling secondary to blunt trauma. Early nasotracheal intubation was performed. Following initial leech therapy, a laceration was found in the dorsal aspect of the tongue. | Two cycles of 6 leeches applied 6 h apart. The patient was placed on broad-spectrum antibiotics during hirudotherapy. |
| Lee *et al.*[26] | Case report | 1 | Blunt trauma resulting in sublingual hematoma in a patient with chronic liver disease and associated coagulopathy. Swelling developed over several days. No intubation was required. | Patient received prophylactic antibiotics during leech therapy. Authors recommend second or third-generation cephalosporin. |
| Heckmann *et al.*[32] | Case report | 1 | Report of a large forearm hematoma following cardiac catheterization. Following development of neurologic/motor deficits in the median nerve distribution, compartment syndrome was suspected. Hirudotherapy resulted in significant improvement over the subsequent 24 h. No further treatment was required. | An estimated 145 mL of blood was evacuated by a total of 13 leeches. At the three-month follow-up, the patient's median nerve function was normal.<br>This report constitutes a very controversial use of leech therapy, with standard therapy of suspected compartment syndrome being surgical decompression. |

Table 2: Clinical reports describing the use of *Hirudo medicinalis* in the setting of tissue flap reconstructions

| Study (Reference) | Type of report | Number of patients | Clinical details | Comments |
|---|---|---|---|---|
| Kim *et al.*[35] | Case report | 1 | Plantar reconstruction using the medial sural artery perforator-free flap. Postoperative venous insufficiency was treated successfully with hirudotherapy. | |
| Top *et al.*[36] | Case report | 1 | Distally based sural flap in the treatment of chronic venous ulceration. Distal venous congestion in one patient was treated successfully with hirudotherapy. | All patients received perioperative antibiotics based on culture results from their ulcers. |
| Aydin *et al.*[37] | Case report | 1 | Posterior interosseous flap to the left distal forearm. Postoperative venous insufficiency was successfully treated with leech therapy. | |
| Chepeha *et al.*[33] | Case series | 8 | A series of patients with free tissue transfers to the head and neck region. All patients in this series developed venous obstruction deemed unsalvageable by surgery or thrombolytic therapy. Patients were treated with hirudotherapy. | Average duration of leech therapy was 6.6 days, with average transfusion requirement of 13 units per patient and mean ICU stay of 9.6 days. |
| Bank *et al.*[38] | Case report | 1 | Basal cell carcinoma of the nasal columella. After Mohs and several composite grafting procedures, the flap appeared acutely congested. The patient underwent successful hirudotherapy. | The authors described a technique wherein the leech was sutured to the underlying tissue to prevent its translocation into the nasal cavity. Of note, leech transmigrations into body cavities have been described. |
| Frodel *et al.*[39] | Case series | 4 | Successful salvage of soft tissue avulsions of the face (ear, nose, lip, and scalp). Each case was characterized by a small pedicle with adequate arterial inflow but compromised venous outflow. | Leeches were applied every 6-8 h for 3-4 days. Broad-spectrum antibiotics were utilized during hirudotherapy. All flaps were viable, but with significant scarring. |
| Irish *et al.*[1] | Case series | 2 | Successful salvage of thrombosed median forehead flap and a congested iliac crest osseocutaneous flap with hirudotherapy. | Leeches applied every 6 h for 4 (forehead) and 6 (iliac crest) days. Supplemental iron was administered to patients, but no transfusion was required. |
| Medina *et al.*[34] | Case report | 1 | Authors describe two lower extremity flap failures associated with heparin-induced thrombocytopenia. The initial soleus flap failed despite intact Doppler signal throughout the pedicle. Subsequently, a gracilis flap was placed but became congested. After exploration showed patent vein and artery, heparin was stopped and hirudotherapy was initiated. The free flap improved with initiation of leech therapy, but failed promptly after leech applications were discontinued 7 days later. | Hirudotherapy was applied for 7 days, with continued flap viability throughout that time period. The flap progressed to muscle necrosis shortly after leech therapy was discontinued. Subsequent workup demonstrated the presence of heparin-induced thrombocytopenia. The patient was treated with argatroban and underwent successful cross-leg flap and skin graft reconstruction. The patient was discharged to home on warfarin anticoagulation. |

therapy.[34] An example of leech therapy in the setting of free-flap reconstruction is shown in Figure 2.

## Hirudotherapy in the Setting of Severe Soft Tissue Injury and Surgical Replantation

Vascular congestion poses a significant challenge in reconstructive surgery. Traumatic injury with extensive soft tissue loss and/or the need for replantation constitutes an important indication for medicinal leeching.[40] Clinical signs that should prompt consideration of hirudotherapy in these settings include the development of tissue edema, purple discoloration, and warmth of the reconstructed/replanted tissue – all suggestive of ongoing venous congestion in the presence of preserved arterial inflow.[41,42] Application of hirudotherapy in the setting of surgical replantation of a digit can be seen in Figure 3 and Table 3.

## Hirudotherapy in Penile Replantation

A well-known entity in urologic trauma, penile amputation poses a difficult surgical problem.[10,45] The current approach to penile replantation involves reapproximation of the urethra and corporal bodies with microsurgical anastomosis of the dorsal vein. Adequacy of postoperative venous outflow is critical to the success of replantation.[45] Prior to the common use of microvascular techniques, non-microsurgical penile replantations were plagued by skin loss, urethral strictures and fistulae, loss of the glans penis, and sensory deficits.[46] Anecdotal evidence suggests that the success of non-microsurgical replantation may be augmented with the adjunctive use of hirudotherapy [Table 4].[45]

## Less Common and Controversial Applications of Hirudotherapy

Among the less common applications of hirudotherapy,

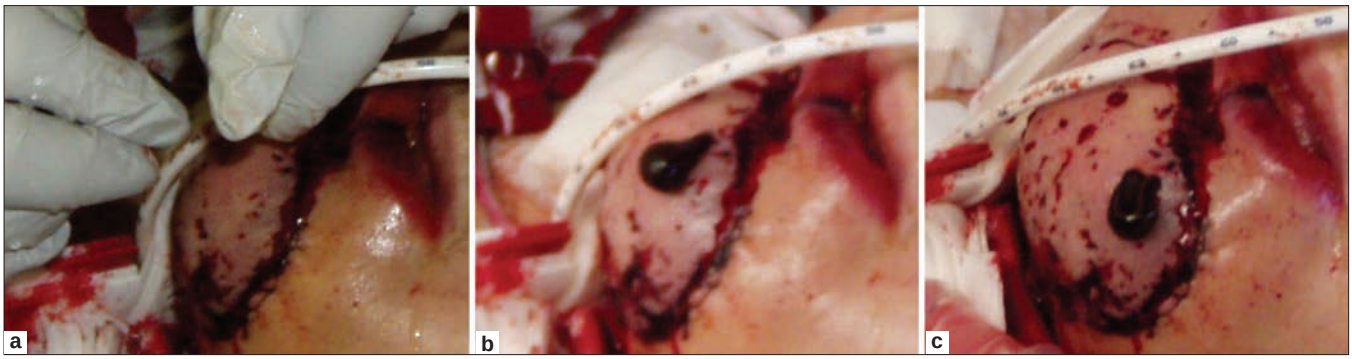


**Figure 2:** Application of hirudotherapy to a facial free flap-based reconstruction complicated by early postoperative venous congestion: (a) The leech is applied directly to the flap; (b) The leech attaches; (c) As feeding continues, the leech grows in size until it becomes satiated

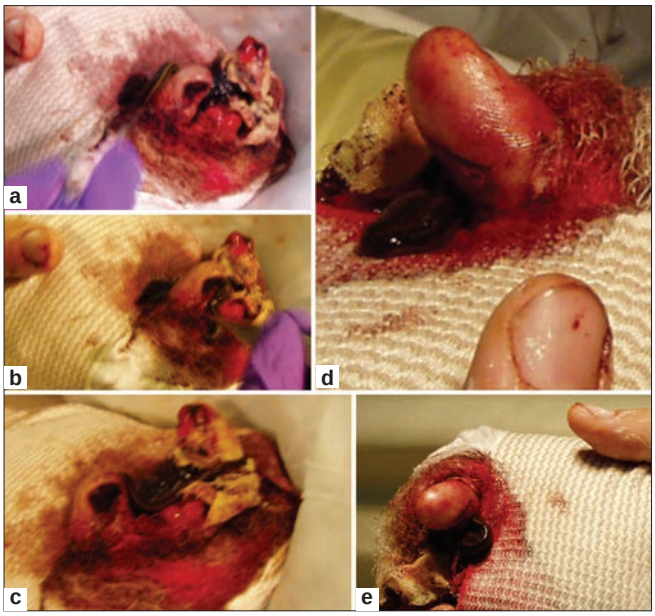


**Figure 3:** Leech therapy application in a case of digital replantation: (a and b) Application of the leech using non-traumatic forceps – the leech is held until it attaches; (c) Following successful attachment, the leech starts feeding; (d and e) The leech grows in size as it continues to feed

Heckmann *et al.*, described the successful use of the medicinal leech for the treatment of forearm compartment syndrome.[32] However, this therapeutic approach is very controversial, and it has to be emphasized that hirudotherapy does not constitute the standard of care for any type of compartment syndrome.[47] The authors of this review concur with the published criticism of the initial report – undertaking the risks associated with nonoperative approach to extremity compartment syndrome is currently not justified. Nevertheless, for the sake of factual completeness, this report was included in the review.

Due to the presence of anti-inflammatory substances in the saliva of medicinal leeches, leech therapy has also been used in recent times to treat localized inflammation and pain. Michalsen *et al.*, recently published a randomized controlled trial that demonstrated significantly better pain relief among patients with osteoarthritis of the knee treated with leech therapy compared with topical diclofenac therapy.[48] This use of hirudotherapy remains experimental [Table 5].

## Special Topics in Hirudotherapy: Infectious Complications

Leeches should be obtained from appropriately regulated commercial sources.[25] They represent a potential vector of blood-borne diseases, including the human immunodeficiency virus (HIV) and hepatitis viruses.[25,49,50] The leech bite leads to direct communication between the leech digestive tract and the host soft tissue, The most commonly encountered infectious agent during hirudotherapy is the Gram-negative rod, *Aeromonas hydrophila*, a prominent component of the leech intestinal flora.[22] However, infections with *Pseudomonas spp* and *Vibrio spp* have also been reported.[12,51] Because of the intimate contact between the leech and the patient, infections associated with hirudotherapy occur in 2.4–20% of patients who do not receive antibiotic prophylaxis.[2,22] A wide range of clinical infections have been reported including cellulitis, flap necrosis, extensive muscular necrosis, and even septic shock.[2] Ischemia produces local immunosuppression – another reason why hirudotherapy should be reserved for areas with adequate arterial supply.

*Aeromonas spp*. produce beta-lactamase, so penicillins and first-generation cephalosporins are ineffective. The organisms most often involved in hirudotherapy-associated bacterial infections are usually sensitive to second and third-generation cephalosporins, aminoglycosides, chloramphenicol, fluoroquinolones, and trimethoprim.[1]

## Conclusions

Modern leech therapy utilizing *Hirudo medicinalis* is based on sound scientific principles and has resulted in important patient care enhancements. Leech therapy is most often used in the settings of localized venous congestion associated with flap reconstructions and surgical replantations. Hirudotherapy has also been used to treat soft tissue swelling and hematomas in trauma. Infectious complications can be minimized by obtaining leeches from appropriate commercial sources and utilizing effective antibiotic prophylaxis against *Aeromonas*.

**Table 3: Selected clinical reports describing the use of *Hirudo medicinalis* in the setting of severe soft tissue injury and surgical replantation**

| Study (Reference) | Type of report | Number of patients | Clinical details | Comments |
|---|---|---|---|---|
| Kind *et al.*[41] | Case series | 3 | Three cases of adult ear reimplantation. All cases involved microvascular anastomoses. Patients underwent either immediate or delayed hirudotherapy, as based on the presence of venous congestion within reimplanted ears. | As a part of multi-modality approach, leech therapy was beneficial in maintaining viability of reimplanted tissue. Other therapies used herein included aspirin, dextran infusion, heparin infusion, thrombolytics, and warfarin. |
| Miller *et al.*[43] | Case series | 3 | In this report, two pediatric patients underwent nasal replantations following dog bites and one adult patient underwent nasal replantation following a sharp amputation due to farming injury. Leech therapy was used to treat postoperative venous congestion in the replanted tissue. | Complete replant survival was not accomplished in all cases and delayed definitive surgical revision was required. However, the resulting deformity was less than the original defect in all three cases. |
| Cho *et al.*[42] | Case report | 1 | Authors reported a case of partial ear replantation without venous repair. | Adjunctive use of hirudotherapy was employed in order to remedy the acute postoperative venous congestion. |
| Hullett *et al.*[40] | Case report | 1 | Leech therapy was used as adjunctive treatment following surgical replantation and repair of an ear avulsion. | Venous structures were not amenable to repair, with resultant venous congestion and threat to replanted tissue. |
| Trovato *et al.*[44] | Case report | 1 | Successful ear replantation with arteriovenous anastomosis (no suitable artery could be identified). | Dextran and hirudotherapy (every 4-6 h for 9 days) were employed to promote venous drainage. Packed red blood cells' transfusion was required. |

**Table 4: Clinical reports describing the use of *Hirudo medicinalis* in the setting of penile replantation**

| Study (Reference) | Type of report | Number of patients | Clinical details | Comments |
|---|---|---|---|---|
| Mineo *et al.*[45] | Case report | 1 | Authors described a case of self-inflicted amputation of the distal penis treated with primary surgical reimplantation. After the patient developed bullous edema of the glans penis, the application of leeches to the affected area resulted in salvage of the distal penis. Additional debridement of the glans was needed at 2 weeks, with traditional wet-to-dry saline dressing application until complete wound healing. | Each leech therapy session utilized three leeches, with a total of six treatments performed over 20 h. Leeches spontaneously detached and were replaced every 3 to 4 h. The patient reported sensation of the glans, normal erection and voiding at two months. |
| Pantuck *et al.*[10] | Case report | 1 | A case of a patient who underwent penile replantation following complete amputation with a kitchen knife. On the second postoperative day, the patient developed penile venous congestion and hirudotherapy was started. Despite the associated 4-g hemoglobin drop, the patient experienced significant relief of the edema within 24 h. After 5 days, venous congestion had resolved and hirudotherapy was discontinued. | The tissue where leeches were applied was cleaned with sterile water and draped to prevent leech migration. One to two leeches were applied daily to the distal penis. Leeches were allowed to feed until satiated, with spontaneous detachment noted after approximately 20-45 min. Leeches were discarded in 70% alcohol. |

**Table 5: Selected clinical reports describing the use of *Hirudo medicinalis* in less common and controversial clinical applications**

| Study (Reference) | Type of report | Number of patients | Clinical details | Comments |
|---|---|---|---|---|
| Heckmann *et al.*[32] | Case report | 1 | Authors reported a patient with forearm compartment syndrome. Hirudotherapy was used as the main therapeutic approach. | In a letter to the editor, Schenker *et al.*[47] asserted that forearm compartment syndrome is a surgical emergency and that delaying surgical treatment may be deleterious to the patient. The authors of this review agreed with this comment. |
| Michalsen *et al.*[48] | Randomized controlled trial | 51 (24 leech, 27 diclofenac) | Significantly greater pain relief at Day 7 with leech therapy as compared to topical diclofenac. | Other apparent benefits in this study of hirudotherapy included improved function, stiffness, and overall quality of life. The authors of this review emphasized the investigational nature of this therapeutic approach to osteoarthritis. |

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