THE EFFICACY OF MEDICINAL LEECHES IN PLASTIC AND RECONSTRUCTIVE SURGERY: A SYSTEMATIC REVIEW OF 277 REPORTED CLINICAL CASES

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Background: Although there are numerous case reports and small case series describing the experiences of leech therapy in various circumstances, there are relatively few large studies evaluating the effectiveness of leeching to relieve venous congestion. The therapeutic value of leeching is illustrated by these reports but the current literature lacks a cohesive summary of previous experiences. *Methods*: An electronic search of PubMed, the Cochrane library and the Centre for Reviews and Dissemination between 1966 and 2009 was used to retrieve human studies published in the English language evaluating outcomes following leech therapy. The 'success' and 'failure' of leech therapy were the primary outcome measures and secondary outcomes included complications, number of leeches used, pharmacological adjuncts and blood transfusion requirements. *Results*: In total, out of 461 articles, 394 articles met the exclusion criteria. The 67 included papers reported on 277 cases of leech use with an age range of 2–81 years and a male to female ratio of almost 2:1. The overall reported 'success' rate following leech therapy was 77.98% (216/277). In terms of secondary outcome measures, 49.75% of cases (N = 101) required blood transfusions, 79.05% received antibiotics (N = 166) and 54.29% received concomitant anticoagulant therapy. The overall complication rate was 21.8%. *Conclusion*: In the absence of robust randomized controlled trials on which the evidence may be based, this synthesis of current best evidence guides clinicians during the process of consenting patients and using leeches in their practice. © 2012 Wiley Periodicals, Inc. Microsurgery 32:240–250, 2012.

Bloodletting and the therapeutic use of medicinal leeches dates back to ancient Egypt.[1] Decades of reports of leech therapy in plastic and reconstructive surgery[2] and more recently the application of leeching for medical problems[3–6] has given *Hirudo* therapy a niche in contemporary medical practice. Plastic,[7–10] maxillofacial,[11] and other reconstructive surgeons[12,13] use leeches to aid salvage of compromised pedicled flaps,[2,14] microvascular free-tissue transfers[15–17] and venously congested extremities including digits,[9,18–25] nipples,[26,27] ears,[28–32] lips,[33,34] nasal tips,[12,35] and the penis.[36] After many years of use, *Hirudo medicinalis* received official FDA approval as a medical device in 2004.[37]

Leeches are useful to the reconstructive surgeon, as venous anastomoses can either become compromised or are not even attempted. When anastomoses are performed, venous thrombosis is a more common complication than arterial thrombosis[38] and it has been demonstrated in experimental flaps that acute venous obstruction is more damaging than acute and complete pedicle obstruction, where both arterial and venous supplies are involved.[39–41] There are a small number of experimental studies quantifying leech efficacy. A randomized control trial of leech treated venous compromised rodent epigastric skin flaps demonstrated a significant increase in flap survival rate,[42] and in a leech treated porcine model of venous compromised flaps, improved blood flow was objectively demonstrated using laser Doppler perfusion monitoring. In a case of human ear replantation, quantitative measurements of blood flow using injected fluorescein demonstrated an improvement of venous congestion after leech application.[43] The increased blood flow found throughout the leech treated flap is thought to be due to a combination of bleeding relieving obstruction and thus capillary pressure, and also by effects on the microcirculation caused by injection of the leech's vasoactive secretions.[44]

Although there are numerous case reports and small case series describing the experiences of leech therapy in various circumstances, there are relatively few large studies evaluating the effectiveness of leeching to relieve venous congestion.[2,23,45,46] Although the therapeutic value of leeching is illustrated by these reports, the current literature lacks a cohesive summary of previous experiences. The aim of this paper is to present current best evidence regarding the use of leeches by reviewing 277 cases retrieved from the literature. In the absence of robust randomized controlled trials on which the evidence may be based, such a synthesis of current best evidence may serve to elucidate the efficacy of leech therapy, and

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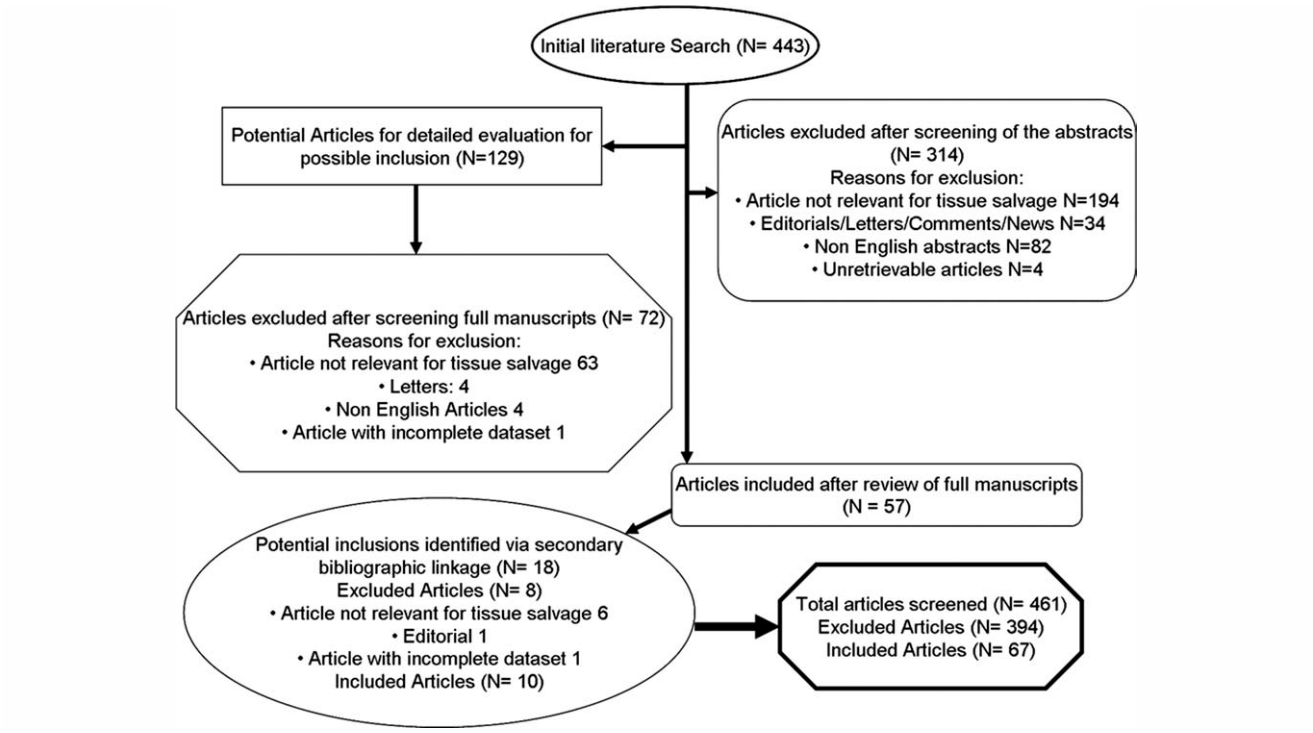

Figure 1. Citation attrition diagram documenting search process for the systematic review evaluating leech therapy for venous congestion post reconstructive or replantation surgery.

guide clinicians during the process of consenting patients and using leeches on their own patients.

METHODS

The search string ("Leeches"[Mesh] OR "Leeching"[Mesh]) AND ("Therapeutics"[Mesh] OR "therapy "[Subheading] OR "Treatment Outcome"[Mesh]) in Boolean format was used across the PubMed Database of the US National Library of Medicine, the Cochrane library and the Centre for Reviews and Dissemination. Bibliographic secondary linkage was used to retrieve additional papers. The time frame covered was 1966 to May 2009.

Inclusion Criteria

1. Human studies published in the English language and evaluating the outcomes following leech therapy for venous congestion of flaps and replanted appendages.

Exclusion Criteria

1. Articles including only descriptive data, historical articles, correspondence, editorials, and reviews
2. Studies with inadequate information or information that is not clearly portrayed or tallied, or studies that data cannot be used or extracted, specifically for the primary outcome.

Outcome Measures

The "success" and "failure" of leech therapy were the primary outcome measures. "Success" was defined as survival of the tissue/flap (even if a small amount of the flap needed debridement); whereas "failure" was considered to occur when excision of the whole flap or appendage was required or further procedure(s) were needed after leeching with or without secondary reconstruction.

Secondary outcomes included complications directly caused by the leech therapy, total number of leeches used, the use of pharmacological adjunctives and the requirements for blood transfusion. The type of study design was also evaluated.

Data Extraction and Analysis

A data extraction proforma was used for each article included in the review. All included studies and extracted data were further appraised by another author to ensure the accuracy of the collected data. Outcomes were only included in the analysis if they were specifically stated, and no assumptions were made on unreported (missing) data; specifically, when a particular rate was not disclosed it was not assumed to be zero.

Table 1. Detailed Analysis of the 67 Papers That Met Inclusion Criteria For Describing the Use of Leeches in Reconstructive Surgery

First author	Year published	Type of tissue	Sex (M, male; F, female; Age (years)	Total	Survived	Failed	Number of leeches used	Therapy time (mean; range) (days)
Derganc[2]	1960	Flaps	NM	20	20	0	3-6 BD – TDS	NM
Baudet[54]	1976	Free flap	M; 38	1	1	0	NM	2
Henderson[55]	1983	Scalp replantation	M; 28	1	1	0	4–8 every 12 hours	5
Holtje[33]	1984	Lip replantation	M; 44	1	1	0	100	10
Batchelor[6]	1984	Various	M:F = 6:1; 17–81	7	7	0	1 BD – 2 QDS	2.8; 2–4
Dickson[56]	1984	Pedicled Flap	F; 27	1	1	0	NM	4
Rao[57]	1985	Various	6M, 1F; 8–79	7	6	1	1 leech every 2 days – 1 QDS	5.3; 4–7
Lim[58]	1986	Free flap	M; 7	1	1	0	1 QDS	7
Mutimer[59]	1987	Ear replantation	M; 3	1	1	0	Continuous	7
Makin[60]	1987	Penile reconstruction	M; 44	1	1	0	2 OD	2
Mercer[50]	1987	Various	NM	6	6	0	NM	NM
Lucht[61]	1988	Free Flap	M; 47	1	0	1	NM	5
Baker[62]	1989	Digital replantations	M; 65	1	0	1	2–5 at all times	14
Brody[17]	1989	Digital replantations	M:F = 5:2; 4–57	7	6	1	1 BD	4.86; 3–6
Anthony[43]	1989	Ear replantation	M; 25	1	0	1	25	7
Bates[63]	1989	Various	M:F = 1:1; 25 & 44	2	1	1	20, 3	2
Snower[64]	1989	Free Flap	F; 62	1	0	1	NM	NM
Sadove [65]	1990	Ear replantation	M; 21	1	1	0	1 QDS	5
Wade [66]	1990	Various	M:F = 1:1; 24–46	4	4	0	NM	1–3
Evans[67]	1990	Hand Congestion	M; 40	1	0	1	4 applied, then continuously	4
Regan[68]	1991	Degloving Injury	M; 16 & 27	2	2	0	20 in 1st 7 days, 3–5 leeches/day for 2 weeks	1–2 weeks
Casady[69]	1991	Digital replantations	M; 46	1	1	0	6	3
Crawford[70]	1991	Lip replantation	F; 22	1	1	0	4	4
Lineaweaver[7]	1991	Various	M:F = 3:1; 11–63	4	4	0	4,18, 2 TDS, NM	3, 5, 6, NM
Rouholamin[71]	1991	Various	M:F = 7:1; 17–68	8	4	4	3 TDS	4–5
Foucher[46]	1992	Digital replantations	NM	33	20	13	NM	5
Husami[72]	1992	Lip replantation	M; 23	1	1	0	NM	9
Gross[25]	1992	Nipple Congestion	F; 20 2–60	4	2	2	10, 3, 2, 40	10, 3, 1, 7
Lineaweaver[8]	1992	Various	NM	7	1	6	NM	NM
Wells[73]	1993	Digital replantations	M; 19	1	1	0	1 every 4 hours	7
Rapaport[74]	1993	Ear replantation	M; 38	1	1	0	1 QDS	7
Gilhooly[75]	1993	Free flap	M; 67	1	1	0	3 OD	4
Hirase[76]	1993	Lip replantation	M; 34	1	1	0	19	7
Soucacos[77]	1994	Free flap	M:F = 4:1; 12–73	20	17	3	2–50	5; 1–10
Soucacos[22]	1994	Various	M:F = 22:7, 12–73	29	24	5	2–50; 2.7 leeches per day	Mean 5
Haycox[78]	1995	Free flap	M; 58	1	1	0	NM	22
Troum[79]	1995	Various	NM	13	9	4	NM	NM
Funk[29]	1996	Ear replantation	M; 28	1	1	0	1 TDS	5
Pantuck[12]	1996	Penile replantation	M; 37	1	1	0	1 OD–BD	5
de Chalain[44]	1996	Various	M:F = 1:2; 10–80	18	13	5	NM	3.3; 1hour–9 days
Varghese[80]	1996	Pedicled Flap	M; 67	1	0	1	2 BD	4
Walton[34]	1998	Lip replantation	M:F = 4:7; 2–49	11	11	0	NM	1 – 8
Mortenson[35]	1998	Pedicled flaps	M; 18	1	1	0	2 QDS	2
Utley[16]	1998	Pedicled flaps	M; 50–76	4	4	0	2, 6, 12 and 1 every 2–4 hours	2 hours, 1–4 days
Pereira[81]	1998	Digital replantation	F; 21	1	0	1	1 QDS	3
Cho[27]	1999	Ear replantation	M; 37	1	1	0	13 hrly and gradually decreased	7
Guneren[26]	2000	Nipple congestion	F; 24	1	1	0	1 TDS	3
Irish[82]	2000	Pedicled flaps	M; 55, 54	2	2	0	2, 4 QDS	4, 6

Table 1. (Continued)

First author	Year published	Type of tissue	Sex (M, male; F, female; Age (years)	Total	Survived	Failed	Number of leeches used	Therapy time (mean; range) (days)
Akyurek[83]	2001	Ear replantation	M; 35	1	0	1	1 every hour for 3 days, then 1 every 2 hours thereafter	14
Chepeha[47]	2002	Free flap	M:F = 3:1; 49–73	8	8	0	3 per hour	6.6; 3–10
Guven[84]	2002	Ring avulsion injury	M; 35	1	1	0	1 leech 6 times a day	5
Sartor[51]	2002	Various	NM	7	2	5	5–17; mean 10.1	4.7; 3–7
Gideroglu[13]	2003	Pedicled flaps	M:F = 4:1; 39–58	5	4	1	2–3 QDS	4.4; 3–6
Ribuffo[85]	2004	Free flap	F; 42	1	1	0	2 daily	5
Duroure[86]	2004	Lip replantation	F; 29–61	3	2	1	NM	6
Mineo[87]	2004	Penile replantation	M; 32	1	1	0	1 every 3–4 hours (total of 6)	20 hours
Tuncali[23]	2004	Ring avulsion injuries	F; 48,60	2	2	0	1 every 4–6 hours	7–10
Frodel[11]	2004	Various	M	4	4	0	1 TDS–QDS	3–4
Ouderkirk[88]	2004	Flap	M; 40	1	0	1	NM	NM
Lazarou[89]	2006	Penile replantation	M; 25	1	1	0	12 hourly for 6 days then decreased	25
Ardehali [90]	2006	Pedicled Flap	F; 47	1	1	0	NM	5
Hullett[30]	2007	Replantation	M; 33	1	1	0	1 BD	3
O'Toole[91]	2008	Ear replantation	M; 60	1	1	0	Continuous	12
Ward[92]	2008	Pedicled flaps	M; 60	1	1	0	1 leech 5 times a day	4

NM, not mentioned; OD, once daily; BD, twice daily; TDS, three times per day; QDS, four times per day.

RESULTS

The article selection process for evaluating leech therapy for venous congestion post reconstructive or replantation surgery is displayed in Figure 1. In total, out of 461 articles, 394 articles met the exclusion criteria. Of the 67 included papers (see Table 1), one by de Chalain et al. and the other by Foucher et al., were not included as the authors had included the same data in subsequent papers where they reviewed their practices and presented it within a case series.[28,45–47] The case series by Foucher et al. had a total of 42 patients in which leech therapy was used, but only information on 33 patients was presented in the paper. The case report presented by Lineaweaver et al. reporting a latissimus dorsi lower limb reconstruction was excluded as the leeches failed to attach to the flap, and surgery ultimately was successful.[9] The indications for leech application are presented in Figure 2, and a topographical representation of the uses of leech therapy in clinical practice is illustrated in Figure 3.

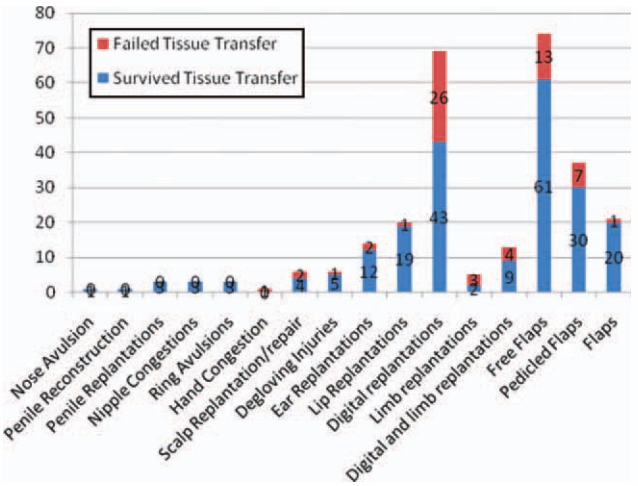

Figure 2. Distribution of the relative salvage rates with the use of leech therapy by literature review. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Primary Outcomes

Of the 65 included papers published between 1960 and 2008, there were 27 case series, 38 case reports and no randomized controlled trials. The relative number of publications per year can be seen in Figure 4. One paper presented a review of the literature prior to 1994 and a risk benefit discussion, which also included the author's observational study of their practice.[45] There were six articles/case reports focusing on digital replantations,[19,47–51] 1 hand,[52] 2 ring avulsions,[24,53] 8 on ear replantations,[29,43,54–59] 6 lip replantations,[33,34,60–63] 1 degloving injury,[64] 1 scalp replantation,[65] 3 penile replantations,[36,66,67] and 1 reconstruction,[68] 2 nipple congestions post breast surgery,[26,27] and 9 free flap series[69–77] and 25

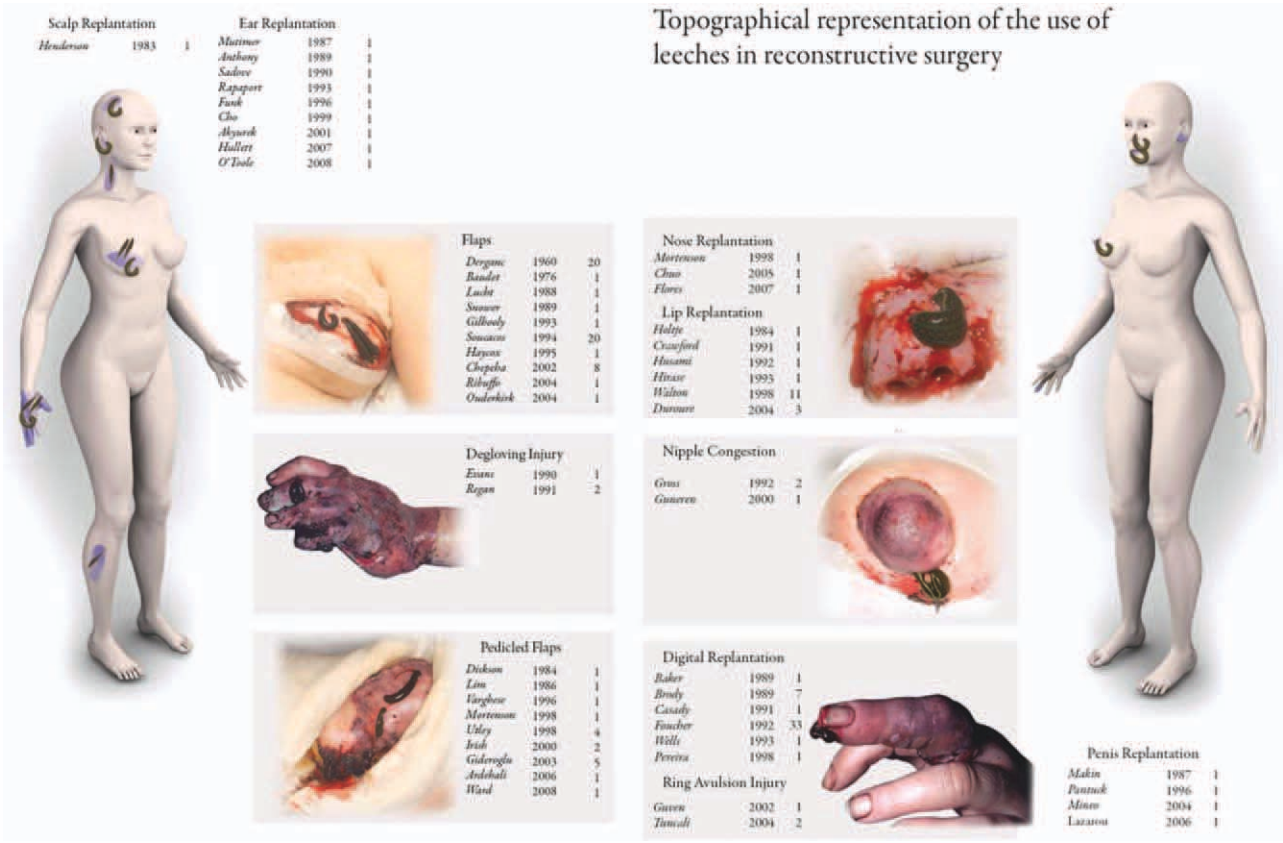

Figure 3. Topographical representation of the reported use of leeches in reconstructive surgery. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

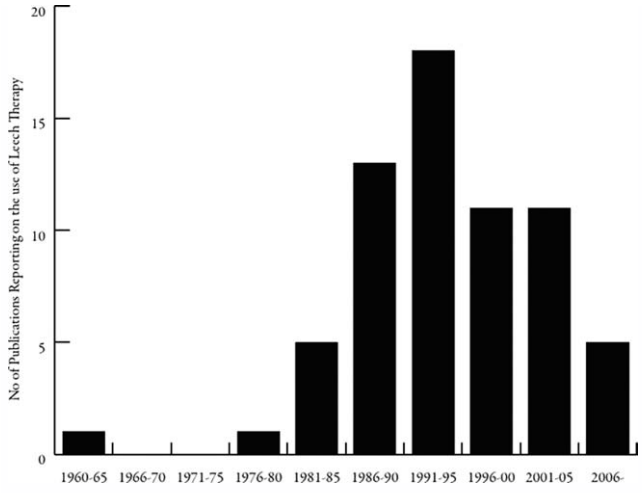

Figure 4. The relative number of publications reporting the use of leeches in reconstructive surgery over time.

articles including a variety of flaps or mixed case series[2,7,12,14,16–18,23,35,45,78–91] (See Table 1). The included articles yielded a total of 277 patients receiving leech therapy, with an age range of 2–81 years and a male to female ratio of almost 2:1. The overall reported "success" rate following leech therapy was 77.98% (216/277). The tissues were deemed unsalvageable and excised in 22.02% (61 out of 277) of the cases.

The distribution of the relative salvage rates are illustrated in Figure 2. Free flaps (26.71%), were the most common indication for leech therapy in this series, followed by digital replantations (24.91%), pedicled flaps (13.36%), various flaps (where the author did not differentiate between free or pedicled) (7.58%), lip replantations (7.22%), ear replantations (5.05%), distal upper limb replantations (the authors did not differentiate between digits and the limbs) (4.69%), scalp replantations and degloving injuries (2.17%), proximal upper limb replantations (1.81%), ring avulsions, penile replantations, and nipple congestions (1.08%). One penile reconstruction, a single congested hand and one nose avulsion (0.36%) completed the series. The 100% success rate of the small number of ring avulsions, nose avulsion, penile replantations and reconstruction, and nipple congestion were encouraging, although the small numbers involved preclude any meaningful inferences. The lip replantation group fared well, with an overall success rate of 95%. The digital replantation group reported a salvage rate of 62.3% which is only slightly lower than the reported suc-

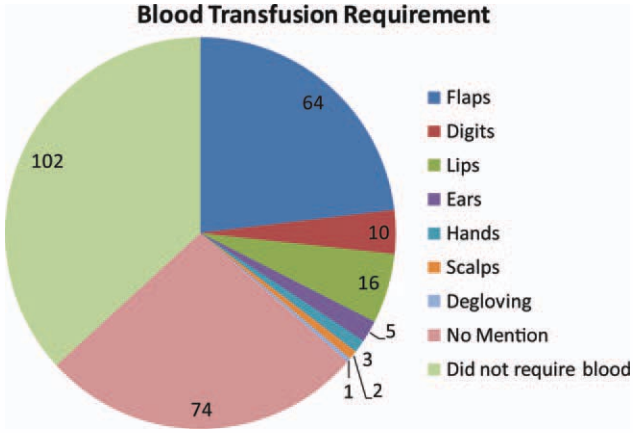

Figure 5. The reported need for blood transfusion, by units of blood, associated with the use of leeches. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

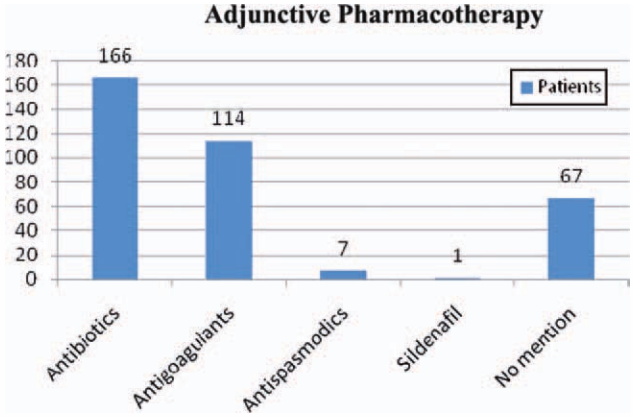

Figure 6. The reported use of adjunctive medications to aid the use of leech therapy. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

cesses of Foucher in his seminal series.[47] Mixed flaps' failure rate was 4.76%.

Number of Leeches Used

The number of leeches was highly variable, ranging from one leech per day to as many as one every hour. The time interval between applications was similarly varied, ranging from hourly to once a day for 22 days.

Blood Transfusion

Blood transfusion is often required for patients due to the continuous blood loss during and for several hours following leech therapy (see Fig. 5). Thirteen (13) articles did not mention whether or not blood transfusion was required. Out of the 52 articles reporting the use of blood transfusions, 49.75% of cases ($N = 101$) required blood transfusions.

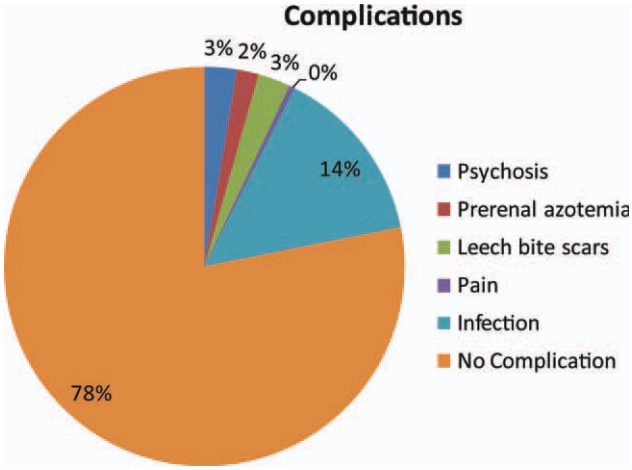

Figure 7. Reported complications associated with the use of leeches. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Adjunctive Pharmacotherapy

Eleven (11) articles did not mention whether or not any type of adjunctive medication was used (See Fig. 6). Of the remaining 54 articles, 79.05% of their patients received antibiotics ($N = 166$), 54.29% received concomitant anticoagulant therapy ($N = 114$), and 3.33% ($N = 7$) received antispasmodics. One patient (0.48%) received sildenafil.

Complications

Of the 61 articles reporting on complications, 18 articles reported complications of leech therapy (See Fig. 7). Of the 229 patients described in the 61 articles, there was a 21.8% complication rate ($n = 50$). The infective complication rate was 14.4% ($N = 33$). Rare complications (<3% each) included leech bite scars, psychosis, prerenal azotemia and very rarely, pain ($N = 1$, 0.4%). The complications that were not related to leech therapy were not reviewed.

Infection vs. Noninfected

Of the 33 patients that developed an infection, the replant/flap savage rate was 37.4% ($N = 12$) (See Fig. 8). In the 196 patients where an infection was not encountered, the tissue survival rate was 88.3% ($N = 173$).

The reported pathogens responsible for the infections are reported in Figure 9.

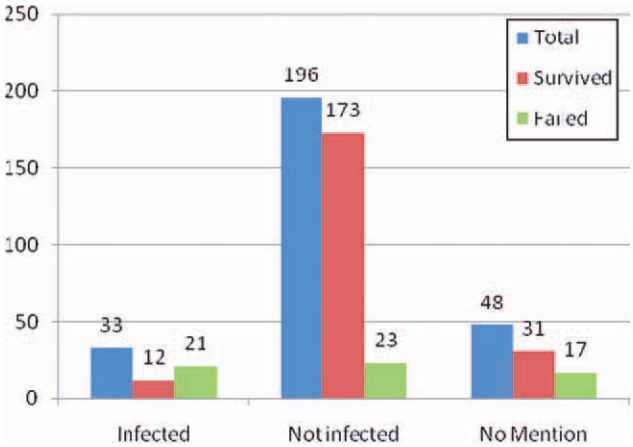

Figure 8. Outcomes of leech therapy in the presence or absence of infection. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

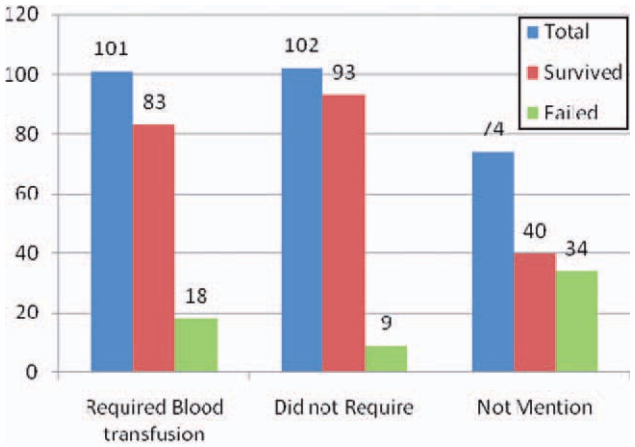

Figure 10. Salvage-related outcomes of leech therapy for patients who did or did not require blood transfusion. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

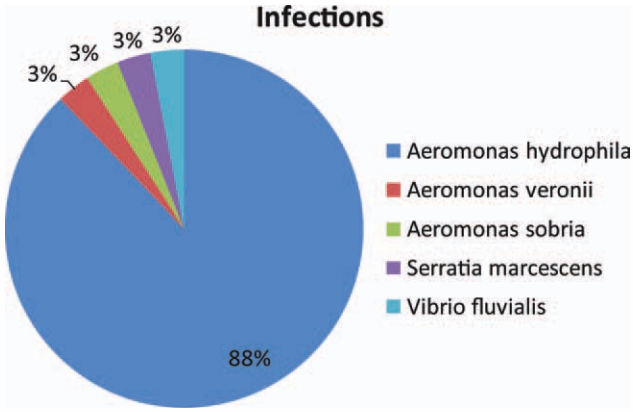

Figure 9. Pathogens cultured from soft-tissue infections that occurred in the presence of leech therapy. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Blood Transfusion vs. No Transfusion

The salvage rate of the tissues in which patients required blood transfusion was 82.2% (83/101) and in those who did not require blood transfusion, the tissue survival rate was 91.2% (93/102) (See Fig. 10).

DISCUSSION

The reporting of individual case reports and small series of patients having leech therapy, after peaking in the early 1990s, has become less frequent as the publication of novel information becomes less likely. This trend may reverse as the importance of the different species of medicinal leech in use, and the potential differences are further investigated. The European medicinal leech is one of vanishingly few animal species with direct application in modern medicine and *Hirudo medicinalis* has been approved by the United States Food and Drug Administration as a prescription medical device. However a recent article has highlighted that there are at least three species of European medicinal leech, and that leeches marketed as *Hirudo medicinalis* are actually *Hirudo verbena*.[92]

This study of 277 cases from the literature exhibited a wide reported range of indications along with a good overall efficacy of leech therapy. Our data, in line with previous studies, support the use of leeches to aid salvage of replanted extremities and free tissue transfers. It is important to note that tissues should be assessed clinically before application of leeches, and there is experimental evidence that they should not be used to attempt salvage when there is mixed arterio-venous insufficiency. A well designed rat study showed that the use of multiple leeches was detrimental to flap survival.[93]

Almost 50% of our dataset (52 articles/101 cases reporting on the use of blood transfusions) required blood transfusions. The need for blood transfusion during and after leech therapy is a well-known phenomenon[45,76,94] due to the continuous blood loss after leech removal. It is advised to check the full blood counts of patients before and after leech therapy, especially children. Our findings show that the need for blood transfusion was not associated with a decreased salvage rate, nor were the other rare complications including leech bite scars, psychosis, and prerenal azotemia.

Of the 54 articles reporting on the use of pharmacotherapy alongside leech therapy, almost 80% of patients received antibiotics ($N = 166$), over 50% received concomitant anticoagulant therapy ($N = 114$), and a small number received antispasmodics.

The overall complication rate associated with leech therapy of 21.8% was relatively high. The infective complication rate of 14.4% ($N = 33$) gives more credence to the policy of antibiotic prophylaxis such as quinolones, which have good resistance profiles to *Aeromonas* species. Previous reviews have reported infection rates of between 4.1 and 20%.[18,45,80,87,95,96] The review by de Chalain et al. (1960–1994) reported an infection rate of 17.59%, though there was no clear methodology on how the literature review was conducted and which reports were included or excluded.[45] *Aeromonas hydrophila* was reported as the commonest cause of infection (87.9% of total infections), but we now know that these were likely to have been misidentified,[97,98] and *Aeromonas veronii*[99–101] was the likely pathogen. Isolated reports of infections due to *Serratia marsescens*,[51] and *Vibrio fluvialis*[86] were also reported. The knowledge regarding leech microbiota is advancing due to new molecular methods to identify the culturable and non-culturable symbionts of the leech. In the noninfected group the salvage rate was 88.3% which dropped to 37.4%, when the tissue became infected. These results are broadly in line with the second largest series from the literature reporting on the effect of infection, de Chalain's meta-analysis, which reported on a total of 19 cases of *Aeromonas* infection (nine replants, three free flaps, and seven pedicled flaps) with an overall salvage rate of 31.8%, compared with a salvage rate of 60–80% in noninfected tissues.[45] In our experience, and that of others, surgical site infections (SSIs) due to leech application result in additional antibiotic therapy, extended hospital stays, rehospitalization or removal of nonviable tissues.[87] A recent clinical study has shown the proportion of patients becoming infected after leech therapy was significantly greater in the group of patients that did not receive a prophylactic antibiotic treatment.[95] There is emerging evidence from recent studies that high levels of resistance to first generation cephalosporins, penicillins (via b-lactamases), tetracyclines, and augmentin are present. Fluoroquinoles seem to be consistently active, and our experience suggests that prophylactic fluoroquinolones seem to be mandatory given the preponderance of infection.[102] The recently reported case of a MDR (multi drug resistant) *Aeromonas* strain is concerning[103] when you combine this finding with recent environmental isolates from European natural water sources demonstrating a plasmid mediated fluoroquinolone resistance in *Aeromonas* strains. Isolates obtained from a Swiss lake and the Seine River containing *Aeromonas* with the qnrS2 plasmid that encodes fluoroquinolone resistance.[104]N

It is important to note the limitations of this study. The flap size is not mentioned in the papers, and the whole idea of "success and failure" is easier to address with relatively small replantations, whereas it is much more difficult in large flaps. Several articles did not include information regarding complications, the need for blood transfusion, or whether and adjunctive medication was used. A significant number of papers do not comment on antibiotic prophylaxis or treatment, or what type of antimicrobials was used. The number of leeches was highly variable, ranging from one leech per day to as many as one every hour, indicating there is no scientific basis as yet to guide us. The time interval between applications was similarly varied, ranging from hourly to once a day for 22 days.

Key Practice Guidelines

- A type and screen (crossmatch) should be sent before the onset of leeching and kept up to date.
- Leeches should not be administered to patients unwilling to have a blood transfusion if there is any other alternative available—and if it is necessary, there should be a well-documented discussion of the risks.
- Prophylactic antibiotics should be administered to all patients being treated with leeches.

The best current evidence suggests quinolone antibiotic therapy, although a recent case report has reported a MDR (multidrug resistant) aeromonas strain.[103]

CONCLUSION

Despite the limitations of retrieval of information available from published series, the current paper presents the current "best evidence" from a large clinical series, and is a valuable resource which can help guide surgeons in their use of leeches and consenting patients. Despite the widespread use of leeches worldwide, there are insufficient prospective studies with large enough numbers to inform the microsurgical specialist on the implications of leech speciation and *Aeromonas* subtypes. It is important to note that there are proponents of alternative methods to relieving venous congestion,[105–107] and a comprehensive systematic review of the chemical and mechanical alternatives to leech therapy has been recently published.[108] Our future research efforts will aim towards an interdisciplinary, prospective multicenter study combining genetic clarification of leech types, hematological parameters, outcome analysis, and isolates from surgical wounds.

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REFERENCES

1. Whitaker IS, Rao J, Izadi D, Butler PE. Historical Article: Hirudo medicinalis: Ancient origins of, and trends in the use of medicinal leeches throughout history. Br J Oral Maxillofac Surg 2004;42: 133–137.
2. Derganc M, Zdravic F. Venous congestion of flaps treated by application of leeches. Br J Plast Surg 1960;13:187–192.
3. Michalsen A, Deuse U, Esch T, Dobos G, Moebus S. Effect of leeches therapy (Hirudo medicinalis) in painful osteoarthritis of the knee: A pilot study. Ann Rheum Dis 2001;60:986.
4. Michalsen A, Lüdtke R, Cesur O, et al. Effectiveness of leech therapy in women with symptomatic arthrosis of the first carpometacarpal joint: A randomized controlled trial. Pain 2008;137:452–459.
5. Michalsen A, Moebus S, Spahn G, et al. Leech therapy for symptomatic treatment of knee osteoarthritis: Results and implications of a pilot study. Altern Ther Health Med 2002;8:84–88.
6. Bäcker M, Lüdtke R, Afra D, et al. Effectiveness of leech therapy in chronic lateral epicondylitis: a randomized controlled trial. Clin J Pain 2011;27:442–447.
7. Batchelor AG, Davison P, Sully L. The salvage of congested skin flaps by the application of leeches. Br J Plast Surg 1984;37:358–360.
8. Whitaker IS, Izadi D, Oliver DW, Monteath G, Butler PE. Hirudo Medicinalis and the plastic surgeon. Br J Plast Surg 2004;57:348–353.
9. Lineaweaver WC, O'Hara M, Stridde B, Valauri FA, Buncke HJ. Clinical leech use in a microsurgical unit: The San Francisco experience. Blood Coagul Fibrinolysis 1991;2:189–192.
10. Lineaweaver WC, Hill MK, Buncke GM, et al. Aeromonas hydrophila infections following use of medicinal leeches in replantation and flap surgery. Ann Plast Surg 1992;29:238.
11. Rao J, Whitaker IS. Use of Hirudo medicinalis by maxillofacial surgical units in the United Kingdom: Current views and practice. Br J Oral Maxillofac Surg 2003;41:54–55.
12. Frodel JL, Barth P, Wagner J. Salvage of partial facial soft tissue avulsions with medicinal leeches. Otolaryngol Head Neck Surg 2004;131:934–939.
13. Mineo M, Jolley T, Rodriguez G. Leech therapy in penile replantation: A case of recurrent penile self-amputation. Urology 2004;63:981–983.
14. Gideroglu K, Yildirim S, Akan M, Akoz T. Immediate use of medicinal leeches to salvage venous congested reverse pedicled neurocutaneous flaps. Scand J Plast Reconstr Surg Hand Surg 2003;37: 277–282.
15. Connor NP, Conforti ML, Heisey DM, et al. Augmented blood removal after medicinal leech feeding in congested tissue flaps. J Rehabil Res Dev 2002;39:505–512.
16. Dabb RW, Malone JM, Leverett LC. The use of medicinal leeches in the salvage of flaps with venous congestion. Ann Plast Surg 1992;29:250–256.
17. Utley DS, Koch RJ, Goode RL. The failing flap in facial plastic and reconstructive surgery: Role of the medicinal leech. Laryngoscope 1998;108:1129–1135.
18. Lineaweaver WC, Hill MK, Buncke GM, et al. Aeromonas hydrophila infections following use of medicinal leeches in replantation and flap surgery. Ann Plast Surg 1992;29:238–244.
19. Brody GA, Maloney WJ, Hentz VR. Digit replantation applying the leech Hirudo medicinalis. Clin Orthop Relat Res 1989;245:133–137.
20. Durrant C, Townley WA, Ramkumar S, Khoo CTK. Forgotten digital tourniquet: Salvage of an ischaemic finger by application of medicinal leeches. Ann R Coll Surg Engl 2006;88:462–464.
21. Gur E, Eldor A. Medicinal leeches for the salvage of a replanted digit. Isr Med Assoc J 1999;1:62.
22. Shenfeld OZ. Successful use of the medicinal leech (Hirudo medicinalis) for the treatment of venous insufficiency in a replanted digit. Isr Med Assoc J 1999;1:221.
23. Soucacos PN, Beris AE, Malizos KN, Kabani CT, Pakos S. The use of medicinal leeches, Hirudo medicinalis, to restore venous circulation in trauma and reconstructive microsurgery. Int Angiol 1994;13:251–258.
24. Tuncali D, Terzioglu A, Cigsar B, Aslan G. The value of medical leeches in the treatment of class IIC ring avulsion injuries: Report of 2 cases. J Hand Surg Am 2004;29:943–946.
25. Valauri FA. Aeromonas hydrophilia infection complicating digital replantation and revascularization. J Hand Surg Am 1991;16:181–182.
26. Gross MP, Apesos J. The use of leeches for treatment of venous congestion of the nipple following breast surgery. Aesth Plast Surg 1992;16:343–348.
27. Güneren E, Erolu L, Akba H, et al. The use of Hirudo medicinalis in nipple-areolar congestion. Ann Plast Surg 2000;45:679–681.
28. de Chalain T, Jones G. Replantation of the avulsed pinna: 100 percent survival with a single arterial anastomosis and substitution of leeches for a venous anastomosis. Plast Reconstr Surg 1995;95:1275–1279.
29. Cho BH, Ahn HB. Microsurgical replantation of a partial ear, with leech therapy. Ann Plast Surg 1999;43:427–429.
30. Kim KS, Kim ES, Hwang JH, Lee SY. Microsurgical replantation of a partial helix of the ear. Microsurgery 2009;29:548–551.
31. Talbi M, Stussi JD, Meley M. Microsurgical replantation of a totally amputated ear without venous repair. J Reconstr Microsurg 2001;17:417–420.
32. Otto A, Schoeller T, Wechselberger G, Ohler K. [Successful ear replantation without venous anastomosis by using leeches]. Handchir Mikrochir Plast Chir 1999;31:98–101.
33. Walton RL, Beahm EK, Brown RE, et al. Microsurgical replantation of the lip: A multi-institutional experience. Plast Reconstr Surg 1998;102:358–368.
34. Höltje WJ. Successful replantation of an amputated upper lip. Plast Reconstr Surg 1984;73:664–670.
35. Mortenson BW, Dawson KH, Murakami C. Medicinal leeches used to salvage a traumatic nasal flap. Br J Oral Maxillofac Surg 1998;36:462–464.
36. Pantuck AJ, Lobis MR, Ciocca R, Weiss RE. Penile replantation using the leech Hirudo medicinalis. Urology 1996;48:953–956.
37. Rados C. Beyond bloodletting: FDA gives leeches a medical makeover. FDA Consum 2004;38:9.
38. Kubo T, Yano K, Hosokawa K. Management of flaps with compromised venous outflow in head and neck microsurgical reconstruction. Microsurgery 2002;22:391–395.
39. Su CT, Im MJ, Hoopes JE. Tissue glucose and lactate following vascular occlusion in island skin flaps. Plast Reconstr Surg 1982;70:202–205.
40. Angel MF, Ress AM, Amiss LR, Morgan RF. Age and tolerance to secondary ischemia in rat epigastric flaps. Microsurgery 1994;15: 652–654.
41. Angel MF, Knight KR, Biavati MJ, et al. Timing relationships for secondary ischemia in rodents: The effect of arteriovenous obstruction. J Reconstr Microsurg 1991;7:335–337.
42. Lee C, Mehran RJ, Lessard ML, Kerrigan CL. Leeches: Controlled trial in venous compromised rat epigastric flaps. Br J Plast Surg 1992;45:235–238.
43. Anthony JP, Lineaweaver WC, Davis JW, Buncke HJ. Quantitative fluorimetric effects of leeching on a replanted ear. Microsurgery 1989;10:167–169.
44. Whitaker IS, Cheung CK, Chahal CAA, et al. By what mechanism do leeches help to salvage ischaemic tissues? A review. Br J Oral Maxillofac Surg 2005;43:155–160.
45. de Chalain TM. Exploring the use of the medicinal leech: A clinical risk-benefit analysis. J Reconstr Microsurg 1996;12:165–172.
46. Foucher G, Merle M, Braun JB. Distal digital replantation is one of the best indications for microsurgery. Int J Microsurg 1981;3:263–270.
47. Foucher G, Norris RW. Distal and very distal digital replantations. Br J Plast Surg 1992;45:199–203.
48. Baker CA, Nayduch DA. Medicinal leech therapy: A case study. Orthop Nurs 1989;8:21–24.
49. Casady L, Scaduto J. Thumb replantation: A case study. Orthop Nurs 1991;10:24–25.
50. Wells MD, Manktelow RT, Brian Boyd J, Bowen V. The medical leech: An old treatment revisited. Microsurgery 1993;14:183–186.

51. Pereira JA, Greig JR, Liddy H, Ion L, Moss ALH. Leech-borne Serratia marcescens infection following complex hand injury. Br J Plast Surg 1998;51:640–641.
52. Evans J, Lunnis PJ, Gaunt PN, Hanley DJ. A case of septicaemia due to Aeromonas hydrophila. Br J Plast Surg 1990;43:371–372.
53. Guven H. The use of leeches in the management of a ring avulsion injury. Eur J Plas Surg 2002;25:162–164.
54. Mutimer KL, Banis JC, Upton J. Microsurgical reattachment of totally amputated ears. Plast Reconstr Surg 1987;79:535–541.
55. Sadove RC. Successful replantation of a totally amputated ear. Ann Plast Surg 1990;24:366–370.
56. Rapaport DP, Breitbart AS, Karp NS, Siebert JW. Successful microvascular replantation of a completely amputated ear. Microsurgery 1993;14:312–314.
57. Funk GF, Bauman NM, Rinehart RJ, Mankarious LA. Microvascular replantation of a traumatically amputated ear. Arch Otolaryngol Head Neck Surg 1996;122:184–186.
58. Akyürek M, Safak T, Keçik A. Microsurgical ear replantation without venous repair: Failure of development of venous channels despite patency of arterial anastomosis for 14 days. Ann Plast Surg 2001;46:439–442; discussion 442–443.
59. O'Toole G, Bhatti K, Masood S. Replantation of an avulsed ear, using a single arterial anastamosis. J Plast Reconstr Aesthet Surg 2008;61:326–329.
60. Crawford CR, Hagerty RC. Survival of an upper lip aesthetic complex using arterial reanastomosis only. Ann Plast Surg 1991;27:77–79.
61. Husami TW, Cervino AL, Pennington GA, Douglas BK. Replantation of an amputated upper lip. Microsurgery 1992;13:155–156.
62. Hirasé Y, Kojima T, Hayashi J, Nakano M. Successful upper labial replantation after 17 hours of ischemia: Case report. J Reconstr Microsurg 1993;9:327–329.
63. Duroure F, Simon E, Fadhul S, et al. Microsurgical lip replantation: Evaluation of functional and aesthetic results of three cases. Microsurgery 2004;24:265–269.
64. Regan PJ, Roberts JO, Sabapathy SR, Roberts AH. Use of the medicinal leech to salvage specialized skin jeopardized by venous impairment. Injury 1991;22:161–163.
65. Henderson HP, Matti B, Laing AG, Morelli S, Sully L. Avulsion of the scalp treated by microvascular repair: The use of leeches for post-operative decongestion. Br J Plast Surg 1983;36:235–239.
66. Mineo M, Jolley T, Rodriguez G. Leech therapy in penile replantation: A case of recurrent penile self-amputation. Urology 2004;63:981–983.
67. Lazarou EE, Catalano G, Catalano MC, Leon YC, Gorman JM. The psychological effects of leech therapy after penile auto-amputation. J Psychiatr Pract 2006;12:119–123.
68. Makin CA, Edwards L. Application of leeches to reduce swelling after reconstructive surgery. Br J Urol 1987;59:189.
69. Baudet J, LeMaire JM, Guimberteau JC. Ten free groin flaps. Plast Reconstr Surg 1976;57:577–595.
70. Lim CL. Successful transfer of "free" microvascular superficial temporal artery flap with no obvious venous drainage and use of leeches for reducing venous congestion: Case report. Microsurgery 1986;7:87–88.
71. Lucht F, Aubert G, Seguin P, Tissot-Guerraz F, Relave M. Postoperative skin-flap decongestion, leeches and *Aeromonas hydrophila*. J Hosp Infect 1988;11:92–93.
72. Snower DP, Ruef C, Kuritza AP, Edberg SC. Aeromonas hydrophila infection associated with the use of medicinal leeches. J Clin Microbiol 1989;27:1421–1422.
73. Gilhooly MG, McLoughlin PM, Phillips JG. Salvage of a microvascular scalp reconstruction with Hirudo medicinalis. J Oral Maxillofac Surg 1993;51:1150–1152.
74. Soucacos PN, Beris AE, Malizos KN, Xenakis TA, Georgoulis A. Successful treatment of venous congestion in free skin flaps using medical leeches. Microsurgery 1994;15:496–501.
75. Haycox CL, Odland PB, Coltrera MD, Raugi GJ. Indications and complications of medicinal leech therapy. J Am Acad Dermatol 1995;33:1053–1055.
76. Chepeha DB, Nussenbaum B, Bradford CR, Teknos TN. Leech therapy for patients with surgically unsalvageable venous obstruction after revascularized free tissue transfer. Arch Otolaryngol Head Neck Surg 2002;128:960.
77. Ribuffo D, Chiummariello S, Cigna E, Scuderi N. Salvage of a free flap after late total thrombosis of the flap and revascularisation. Scand J Plast Reconstr Surg Hand Surg 2004;38:50–52.
78. Dickson WA, Boothman P, Hare K. An unusual source of hospital wound infection. Br Med J (Clin Res Ed) 1984;289:1727–1728.
79. Rao P, Bailie FB, Bailey BN. Leechmania in microsurgery. Practitioner 1985;229:901–905.
80. Mercer NS, Beere DM, Bornemisza AJ, Thomas P. Medical leeches as sources of wound infection. Br Med J (Clin Res Ed) 1987; 294:937.
81. Bates M, Kneer K, Logan C. Medicinal leech therapy: An overview (continuing education credit). Orthop Nurs 1989;8:12–17.
82. Wade JW, Brabham RF, Allen RJ. Medicinal leeches: Once again at the forefront of medicine. South Med J 1990;83:1168–1173.
83. Lineaweaver WC. Aeromonas hydrophila infections following clinical use of medicinal leeches: A review of published cases. Blood Coagul Fibrinolysis 1991;2:201–203.
84. Rouholamin E, Harris D. "Reach for a leech": Leeches and microsurgery. Injury 1991;22:159–160.
85. Troum S, Floyd WE. Upper extremity replantation at a regional medical center: A six-year review. Am Surg 1995;61:836–839.
86. Varghese MR, Farr RW, Wax MK, Chafin BJ, Owens RM. Vibrio fluvialis wound infection associated with medicinal leech therapy. Clin Infect Dis 1996;22:709–710.
87. Sartor C, Limouzin-Perotti F, Legré R, et al. Nosocomial infections with *Aeromonas hydrophila* from Leeches. Clin Infect Dis 2002;35:E1–E5.
88. Ouderkirk JP, Bekhor D, Turett GS, Murali R. Aeromonas Meningitis complicating medicinal leech therapy. Clin Infect Dis 2004; 38:e36–e37.
89. Ardehali B, Hand K, Nduka C, Holmes A, WOOD S. Delayed leech-borne infection with *Aeromonas hydrophilia* in escharotic flap wound. J Plast Reconstr Aesthet Surg 2006;59:94–95.
90. Hullett JS, Spinnato GG, Ziccardi V. Treatment of an ear laceration with adjunctive leech therapy: A case report. J Oral Maxillofac Surg 2007;65:2112–2114.
91. Ward C, Craw L, Cherian A, Delos-Reyes M, Joseph S. Medicinal leeches: Taking a bite out of venous congestion. Nursing 2008; 38:28–30.
92. Siddall ME, Trontelj P, Utevsky SY, Nkamany M, Macdonald KS. Diverse molecular data demonstrate that commercially available medicinal leeches are not Hirudo medicinalis. Proc Biol Sci 2007;274:1481–1487.
93. Schlaudraff KU, Bezzola T, Montandon D, Pepper MS, Pittet B. Mixed arterio-venous insufficiency in random skin flaps in the rat: Is the application of medicinal leeches beneficial? J Surg Res 2008;150:85–91.
94. Whitaker I, Izadi D, Oliver D, Monteath G. Hirudo medicinalis and the plastic surgeon. Br J Plas Surg 2004;57:348–353.
95. Whitaker IS, Josty IC, Hawkins S, et al. Medicinal leeches and the microsurgeon: A four-year study, clinical series and risk benefit review. Microsurgery 2011;31:281–287.
96. Bauters TGM, Buyle FMA, Verschraegen G, et al. Infection risk related to the use of medicinal leeches. Pharm World Sci 2007; 29:122–125.
97. Abbott SL, Seli LS, Catino M, Hartley MA, Janda JM. Misidentification of unusual Aeromonas species as members of the genus Vibrio: A continuing problem. J Clin Microbiol 1998;36:1103–1104.
98. Abbott SL, Cheung WKW, Janda JM. The genus Aeromonas: Biochemical characteristics, atypical reactions, and phenotypic identification schemes. J Clin Microbiol 2003;41:2348–2357.
99. Kikuchi Y, Graf J. Spatial and temporal population dynamics of a naturally occurring two-species microbial community inside the digestive tract of the medicinal leech. Appl Environ Microbiol 2007;73:1984–1991.
100. Maltz M, Graf J. The type II secretion system is essential for erythrocyte lysis and gut colonization by the leech digestive tract symbiont Aeromonas veronii. Appl Environ Microbiol 2011;77:597–603.

101. Graf J. Symbiosis of Aeromonas veronii biovar sobria and Hirudo medicinalis, the medicinal leech: A novel model for digestive tract associations. Infect Immun 1999;67:1–7.
102. Whitaker IS, Kamya C, Azzopardi EA, et al. Preventing infective complications following leech therapy: Is practice keeping pace with current research? Microsurgery 2009;29:619–625.
103. Wang EW, Warren DK, Ferris VM, Casabar E, Nussenbaum B. Leech-transmitted ciprofloxacin-resistant Aeromonas hydrophila. Arch Otolaryngol Head Neck Surg 2011;137:190–193.
104. Cattoir V, Poirel L, Aubert C, Soussy C-J, Nordmann P. Unexpected occurrence of plasmid-mediated quinolone resistance determinants in environmental Aeromonas spp. Emerging Infect Dis 2008;14:231–237.
105. Mozafari N, Ghazisaidi MR, Hosseini SN, Abdolzadeh M. Comparisons of medicinal leech therapy with venous catheterization in the treatment of venous congestion of the sural flap. Microsurgery 2011;31:36–40.
106. Conforti ML, Connor NP, Heisey DM, Hartig GK. Evaluation of Performance Characteristics of the Medicinal Leech (Hirudo medicinalis) for the treatment of venous congestion. Plast Reconstr Surg 2002;109:228.
107. Hartig G, Connor N, Heisey D. Comparing a mechanical device with medicinal leeches for treating venous congestion. Otolaryngol Head Neck Surg 2003;129:556–564.
108. Azzopardi EA, Whitaker IS, Rozen WM, Naderi N, Kon M. Chemical and mechanical alternatives to leech therapy: A systematic review and critical appraisal. J Reconstr Microsurg 2011;27:481–486.