Complementary Medicine

Medicinal Leech Therapy

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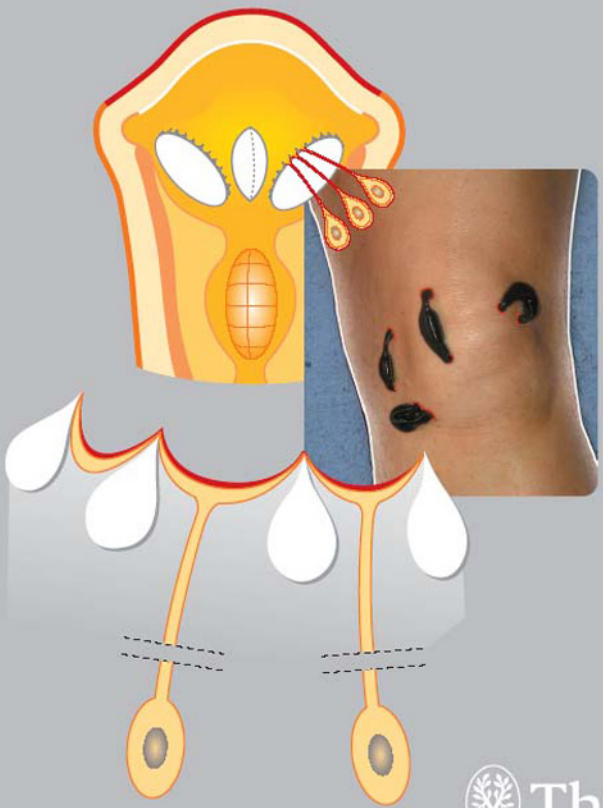

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Medicinal Leech Therapy

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Preface

The medicinal leech is a beautiful symbol of give-and-take and of sustainable resource management. *Hirudo medicinalis* is one of the oldest surviving animals on Earth. The first documented accounts of the use of leeches for medicinal purposes date back to the time of Hippocrates. There are two decisive factors in the survival of the "leech" species: a) the blood that it extracts from the host does not coagulate, and b) the leech bite is not painful. Hirudin, the anticoagulant compound in leech saliva, was isolated several years ago. In this modern age, hirudin is manufactured as a genetically engineered product, the efficacy of which has been tried and tested in large-scale, randomized controlled trials in a number of indications.

The retrospective on the therapeutic use of analgesic substances in leech saliva is a completely different story; these developments are still in their infancy, and the first systematic trials using live leeches were only conducted a few years ago. One phenomenon that was repeatedly observed during treatment and research with live leeches is that the relationship between leeches and humans is special. While the media would hone in on the "yuck factor," we constantly observed a great public interest in natural healing methods, especially leech therapy. Hundreds of people responded to our calls for volunteers for leech studies in Essen, Germany. In most cases, we had more than ten times more willing candidates than we actually needed for the study. Therefore, we often asked ourselves: Could the human mind possess something like a phylogenic memory for the positive effects of leeching? One could almost think that humans subconsciously know that leeching is good for them. The systematic studies of leeching performed in the last five years support this theory, and the interest of patients in leech therapy has grown accordingly. This trend started in Germany and spread to other parts of the world following the publication of our leeching study in the *Annals of Internal Medicine*" and, later, in *The New Yorker*. Thanks to these important articles on the medicinal leech and its therapeutic potentials, substantial interest in this ancient form of treatment has even spread to the USA.

After receiving numerous queries from Anglo-American countries, we ultimately decided to publish the present English edition of this book. By doing so, we would first like to offer scientific evidence to counteract the common misconceptions about leeches. Secondly, we would like to share our enthusiasm for the medicinal leech with others. Leeches are not disgusting creatures! They are classified as a medicinal product in Europe and as a medical device by the US Food and Drug Administration. Based on the scientific evidence, it no longer seems appropriate to classify the leech as a parasite—especially when one considers that humans have often pushed the leech to the verge of extinction because of its healing properties. As far as we are concerned, the leech is a "healing animal."

Our special thanks go to the Karl and Veronica Carstens Foundation for their many years of support for medicinal leech research. We also would not want to miss this opportunity to thank their Director, Dr Henning Albrecht, who shared our visions of scientifically tested integrative medicine, as well as Rainer Lüdtke, biometrician, for his very competent advice regarding statistical questions.

On behalf of all the authors, we wish you interesting insights into leech therapy and many successful treatments.

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Contents

1 Introduction

A. Michalsen, M. Roth

The return of the traditional treatment practice of leeching, or leech therapy, to modern medicine gave occasion to this book. Today, as was the case in the past, the use of leeches in medicine is drawing tremendous public attention. Positive and negative prejudices about leeches prevail, however these small protagonists can face them with great confidence. The fact that leeches have been used for more than 2000 years in the world's most important traditional medicine systems (including traditional European, Ayurvedic, and Chinese medicine) is in itself undeniable proof of the repeated success of leech therapy.

Nevertheless, it is essential to update and scientifically evaluate leech therapy in accordance with the current state of knowledge. According to I. W. Müller:

> *"Leeching is one of the oldest treatment methods around. It has survived for more than 2000 years since the beginnings of scientific medicine. Leeches were used by the billions, but this extraordinary mass experiment was poorly documented." [1]*

By combining traditional wisdom with modern biological and clinical study data, we can now give precise instructions for optimal leech therapy in hospitals and private practices.

As the title Medicinal Leech Therapy implies, the main objective of this book is to convey the most important elements of the successful practice of medicinal leeching. Apart from mastering the actual technique of leech application, these include a thorough and critical assessment of the indications for leech therapy, as well as a precise knowledge of contraindications and standard procedures for minimizing the risk of treatment complications. An in-depth knowledge of the biology of medicinal leeches (*Hirudo medicinalis* and *Hirudo verbana*), as well as skill and sensitivity in the handling of leeches are other important cornerstones of quality assurance.

Seen in a historical context it becomes apparent that there has been a shift in terms of the indications for medicinal leech therapy. In the past, leeches were mainly used to treat heart and circulatory problems, whereas now chronic inflammation and pain management are the primary indications. Over the last few decades, the medicinal leech has regained much of the former significance it had lost over the past 200 years. A century of "vampirism" and abuse, with all the negative consequences and adverse effects associated with it, led to a century of discrimination and general prejudice against leeches.

Today, the therapeutic properties of leeching can be demonstrated from an objective, scientific perspective based solely on the known activity of the specific chemicals in leech saliva. Leech therapy has gained acceptance in modern clinical medicine, initially because of the spectacular results it achieved in plastic and reconstructive surgery and, more recently, because of its proven effectiveness in treating chronic pain syndromes associated with degenerative joint disease.

However, opinions on leech therapy are still divided. On the one hand, stories about the clinical success of hirudotherapy usually generate a (welcome) positive response. On the other hand, problems (side effects, placebo effect, etc.) generally considered to be completely normal and permissible when associated with "clean" pills are frequently blown out of proportion and meet with undue suspicion when they happen to occur with leeches. This ambivalence is understandable considering that the "anonymity" and "sterility" (also in the figurative sense) of most modern remedies, tablets, scalpels, and injection needles contrasts starkly with medicinal leeches, which may seem as exotic or out of place as birds among airplanes.

Consequently, patients apply especially high standards when judging medicinal leeches. Because they literally have close encounters with the leeches, patients are often very concerned and sometimes downright suspicious about the efficacy and safety of leeching. For therapeutic reasons, the leech therapist needs to be able to provide the information needed to allay the patient's treatment concerns. Individuals administering treatments with live animals must have special qualifications. This book aims to provide the theoretical and practical knowledge required to meet these demands. It was written by physicians, alternative practitioners, and biologists mainly for physicians, alternative practitioners, and healthcare workers, but also for biologists and laypersons interested in this subject.

In order to be able to successfully practice leech therapy, we additionally recommend participating in practical training seminars. Compared to other techniques of natural and complementary medicine, leeching can be learned relatively quickly. Certain potential pitfalls can only be identified in the further course of practice. Seminars are designed to point out these hazards and, thus, contribute to optimizing the success of medicinal leech therapy in clinical and private practice. To ensure that leech therapy has a future and continues to be used, full compliance with the essential quality standards must be a top priority for all those administering this form of treatment. When these conditions are met, leeching will continue to be a useful and extremely effective treatment modality used at hospitals and private practices in a presumably ever-growing number of clinical indications.

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2 The History of Leech Therapy

E. Wittke-Michalsen

Leeching is one of the most ancient healing methods documented in the history of medicine. The first clearly identifiable account of leeching appears in ancient Sanskrit writings from India. According to Hindu mythology, Dhavantari, the physician who revealed the secrets of traditional Indian medicine to the world, held nectar in one hand and a leech in the other. The most extensive descriptions of leeching in the Indian literature appear in the writings of the physician Sushruta (100–600 B.C.E.). Leeching was also an ever-present force in traditional Chinese medicine (TCM), but was of lesser significance than in Indian medicine.

In Europe, medicinal leeching was viewed as a science-based therapeutic method right from the beginning. Leeching was an integral part of conventional and folk medicine from antiquity to the 19th century. Medicinal leeching initially remained primarily the domain of empirically minded physicians. Then, most proponents of medicinal leeching deduced its therapeutic efficacy within the framework of the prevailing scientific paradigms of their respective school of medicine. Leeching remained part of various systems of medicine through the centuries. The underlying basis for its use was the widespread belief in the concept of body humors (humoral pathology). This broad concept of disease was based on the notion that all illnesses are caused by an imbalance of one of the four body fluids, or humors (blood, phlegm, yellow bile, and black bile).

Leeching had a fixed and relatively modest range of indications in humoral pathology, the dominant paradigm in ancient European and Arabic medicine until the 17th century. Like bloodletting, leeching was mainly conceived as a means of eliminating the superabundance of blood, or plethora. The other main indications for leeching in early medicine were acute infection, local inflammation, heart problems, and circulatory disorders. Following the decline of humoral pathology, an age of misuse of leeching ("the age of vampirism") began in the 18th and 19th centuries. Mainly influenced by

the teachings of the French physician F.J.V. Broussais (1772–1838), the indications for leech application were extended for no rationally justifiable reason, and leeching was performed at an intensity of hitherto unknown proportions.

In most cases, it is not possible to reliably and accurately translate the historical classification of diseases, their underlying causes within the body, and the corresponding indications for treatment as defined by humoral pathology into the language of modern medicine. Basically, the historical definitions of disease types, constitutional causes, and treatments established based on the humoral concept of disease should be taken metaphorically, similar to the concepts of TCM and Indian medicine that are still present today.

Leeching in Ancient European Medicine

The first detailed description of the therapeutic use of leeches in ancient Greek medicine, which was influenced by Indian medicine, can be found in the poem *Alexipharmacia* by Nicandros of Colophon (200–130 B.C.E.). However, medicinal leeching first gained true significance in the Methodist School, which differentiated two main causes of disease, e.g. "constriction" and "dilation." Chronic headache, general febrile conditions, psychoses, epilepsy, ear ailments, liver disease, splenic and intestinal disorders, ischialgia, arthritis, and gout were the main indications for medicinal leeching; general diseases causing symptoms of hardening, heaviness, rigidity, tension, swelling, pain, and cramps (referred to as "*status strictus*" in the ancient nomenclature) were additional indications. Leeches were regarded primarily as tools for alleviating the tension associated with *status strictus*.

Advocates of the pneumatic theory of medicine valued leeches as a useful cure for "putrefaction" and "plethora" of blood. The object was to replace "bad blood" with "good blood." The therapeutic use of leeches became fashionable and had its first heyday around the middle of the 1st century C.E. An ancient writing credited to the school of the Roman physician Galen (129–199 C.E.) classified leeching as part of the system of elements (fire, earth, air, and water) and temperaments (sanguine, phlegmatic, choleric, and melancholic), the healthy balance of which required the drainage of excess corporal substances. Distinctions were made between plethora (superabundance)

and putrefaction of body fluids, as well as between qualitative and quantitative fluid excesses. Plethoric changes were treated by draining blood from the body, which was chiefly achieved by leeching and bloodletting. Disease management strategies were governed by popular beliefs regarding the movement of body fluids. According to the humoral concept of disease, organs or organ systems are not at risk of damage as long as the body fluids remain in motion and are excreted by the natural routes. However, if one part of the body is directly afflicted and the process becomes chronic, it should be treated locally in order to restore the healthy flow of humors. Ancient physicians therefore applied leeches for symptomatic local treatment of febrile and inflammatory diseases. Roman military physicians also used leeches to treat battle wounds.

Leeching in the Middle and Modern Ages

Leeching played a less important role than venesection and cupping in medieval Arabic medicine, where leeches were typically used to treat a variety of skin diseases and illnesses associated with the melancholic temperament (black bile). In Italy, on the other hand, physicians from the school of Salerno used leeches to remove excess body fluids in numerous indications. The teachings of Salernitan physicians gradually spread from Italy across all of Europe.

In the late age of Galenism, medieval physicians also used leeches primarily for "derivation" and removal of harmful fluids directly from an afflicted body part. They believed that the elimination of fluids by leeches promoted "internal combustion" (complete combustion of a body substance by natural organ heat) of residual disease material, thereby promoting natural healing. Leeching, as a simple systemic method for eliminating fluids, was indicated for treating conditions characterized by a general overabundance of fluids (e.g., fever) and could be used instead of venesection. The most important late-Galenic proponent of leeching was Abraham Zacuto (1575–1642), who expanded the range of indications for leeching and established the empirical basis for many physicians of the following years.

In the 17th century, the concept of humoral medicine put forward by Galen had to compete with new medical movements that arose from different streams of reasoning and that had different views on the practice of

bloodletting. Proponents of the school of iatrochemistry tended to reject all forms of bloodletting. They believed that any type of blood withdrawal could shorten one's lifetime and that, according to the Holy Scriptures, blood was the locus of the soul and the source of life energy. Since they believed that illnesses developed because the Archeus (the active principle of the body and mediator between body and soul) was infected with an *ideo morbus*, they reasoned that blood withdrawal would not cure the morbid thought underlying the disease. Still, the majority of iatrochemists continued the different practices of bloodletting with moderate restrictions.

The proponents of iatrophysics had a completely different opinion of medicinal leeching. Influenced by the discovery of the blood circulation, they believed that leeching was practically indispensable. Based on the laws of mechanics, iatrophysicists explained the effects of blood withdrawal in terms of changes in blood pressure, resistance, and velocity in response to bloodletting, resulting in a temporary redistribution of blood within the body with associated effects on the blood vessels, heart, and blood composition. A combination of iatromechanic theories and Galen's humoral concept of disease predominated in 18th century medicine. According to these paradigms, blood is a labile mixture of different substances and is therefore subject to putrefaction. Their proponents believed it was imperative to keep the blood in motion to prevent it from "thickening." Plethora, which they identified as the major cause of disease, was attributed to an imbalance of food input to blood consumption. Restoration of this balance, they believed, required fasting and physical exercise which, for practical reasons, frequently could not be performed rigorously and intensively enough to achieve adequate results. Therefore, they had to resort to an imitation of spontaneous bleeding, nature's remedy. The advantage of leeching was that it did not cause asthenia, a frequent complication of venesection and wet cupping. Furthermore, they reasoned that venesection did not eliminate blood effectively from individuals with a sanguine temperament (plethora) or a spongy, fleshy constitution because their blood accumulated mainly in the capillaries. If the superabundance of blood was predominantly located in the major blood vessels, as in patients with a choleric temperament, they believed that cupping was inadequate and that leeching was more effective. A special advantage of leeches was that they could be applied to parts of the body that were not amenable to cupping, for example the frontal vein, jugular vein, vessels behind the ears, temporal arteries, and hemorrhoidal veins. Furthermore, leeching was

considered to be a specific and dependable remedy for swelling, abdominal cramps, and pain in general, and for rheumatism, arthritis, ischialgia, nephritis, gout, and varicose veins in particular.

F. Hoffmann (1660–1742), a well-known proponent of iatromechanics, used leeches to treat a wide variety of acute disease conditions, as well as for disease prevention. The concept of plethora as a major cause of illnesses associated with thickening of the blood, the related putrefaction of body fluids, and the accumulation of fluids in various organs led physicians to conclude that leeching was an effective remedy for mental illnesses, melancholy, convulsions, pleurisy, asthma, and skin diseases and to implement this form of treatment accordingly.

By the beginning of the 19th century, leeching had become the predominant force in medicine. Because of the extremely high demand, English physicians had to resort to importing leeches from around 1810. This naturally put financial constraints on the spread of medicinal leeching. A leeching boom began in France, which had a rather large natural supply of leeches, and soon spread throughout all of Europe. Leeching was preferentially used instead of phlebotomy in almost all indications. The art of leech application became a profession in itself.

> *"The leader of this movement was F.J.V. Broussais (1772–1832), who proposed a new system of 'physiological medicine'. Broussais attributed nearly all illnesses to inflammation, and he believed that pathological changes in the capillary system of tissues were a key factor in these processes." [4]*

Since inflammations were thought to arise mainly in the capillary vessel territories and, since leeches primarily withdraw blood from the capillaries, leeching was administered as a universal cure, especially for abdominal diseases. Broussais combined older theories of medicine with the newer concepts of excitation and depression proposed by Brown (1735–1788), who believed that all diseases result from an excess (sthenia) or lack (asthenia) of stimulation and excitation. Broussais believed it was necessary to withdraw blood when there was excessive vital energy or an excess of blood-forming substances in the diet. According to Broussais, blood surplus causes excessive strength or excitation, which manifests itself as fever, inflammation, congestion, spasms, and pain. Furthermore, it can also cause asthenia indirectly by

preventing blood flow, leading to diseases such as apoplexy, asthma, and mental illnesses. Basically, virtually any disease could be classified as an indication for leeching depending on which medical paradigms were applied.

In the Broussaian age, the practice of leeching soon became so excessive that some of his contemporaries referred to it as "vampirism" (see Fig. 2.**1**). Up to 100 leeches were used in a single session, and several million leeches were used annually in countries like France, England, and Germany. "Broussaisism," as medicinal leeching was called for a while, inspired the "robes à la Broussais" design, a paisley-like depiction of the leech used to decorate garments worn by the women of society [1]. The French soon ex-

Fig. 2.**1** "Another 90 leeches, please!" Early 19th century caricature [7]

hausted their supply of leeches, especially since the natural habitats of the leech had been continuously diminished due to agricultural and industrial use. Increasing numbers of leeches had to be imported. By 1828, leeches had become the most important article in the *Materia Medica*, and roughly 100 million leeches were used each year in France alone. The price of leeches rose dramatically. Many physicians were therefore in favor of reusing old leeches and attempted to grow them in breeding facilities annexed to hospitals. Leech breeding was financed by the government, and military physicians were particularly worried that a shortage of leeches might affect their ability to treat battle injuries.

Leech Therapy in Recent Times

Around 1850, the practice of leeching gradually began to decline. This was partly due to the fact that leeches had by then been virtually exterminated in Central Europe and had to be imported from Central Asia, making them quite expensive. The main reason, however, was that the concept of cellular pathology introduced by Virchow (1821–1902) in the mid-1850s cast serious doubts on the older concepts of disease previously used as the justification for bloodletting. The subsequent discovery that diseases were caused by bacteria led to a virtual explosion of bacteriophobia. The use of leeches then dropped off rapidly, especially at hospitals. It was not possible to disinfect or sterilize leeches without killing them. Since medical education now took place in hospitals, physicians in training were rarely ever introduced to leech therapy, and this form of treatment fell into oblivion.

A major event in the history of medicinal leech therapy was the discovery by J. B. Haycraft (1857–1922) that the mouth and throat of the leech contained a substance that prevented the blood from coagulating; the compound was isolated and named hirudin in 1903/04. The specific effects of leeching could now be defined as a chemical process, that is, as a rational principle more closely in conformity with the conventional concepts of modern medicine and science. However, news of the recent discovery spread slowly—initially only among the scientific research community—and only the chemical compound itself attracted attention. The primary expectation of researchers was that this anticoagulant might have potential benefits in blood transfusion or that hirudin extracts might be useful in the treatment

of thrombosis, embolism, and infarction. However, the exorbitantly high costs of extracting the compound were too prohibitive for widespread use. The anticoagulant effect of hirudin was first noted in clinical/practical work nearly 25 years after the discovery of the compound. However, World War I and the resulting collapse of the leech trade pushed medicinal leech therapy once again into oblivion.

Leech therapy experienced a stronger revival in the 1920s. B. Aschner (1883–1960), a member of the group of naturopathic physicians, was then the main proponent of leech therapy. While developing his concept of constitutional therapy, he remembered the old bloodletting techniques and expounded them from new perspectives which, however, were strongly influenced by the humoral concept of pathology. The list of medical indications for leeching grew long again, and this uncritical use of the technique pushed leeching into the ranks of the so-called panaceas.

A specific domain of leech therapy was soon to be developed by the surgeon Termier. As the potentials of surgery increased, thrombus and embolism started to become more and more frequent postoperative complications. Termier remembered reading about the anticoagulatory effect of hirudin. Since it was too expensive to extract the drug, he recommended the direct application of leeches in 1922 so that hirudin could then be injected by the natural route. Termier called this technique "hirudinization of the blood." Within a few years, all renowned hospitals in Europe had started using leeches again for this medical indication.

> *"After its publication in 1935, H. Bottenberg's book—the first comprehensive description of this treatment modality in modern times, the greater part of which conforms to the needs and mindsets of practical physicians and which provides 52 vivid case reports demonstrating its success—fell on fertile ground. It remained a standard work for several years and is (and was) internationally acclaimed." [4]*

The plethora of indications for leeching was still too extensive. Bottenberg established the following general indications for leech therapy:

- All inflammatory processes and rheumatic diseases
- Passive congestions and spastic conditions

- Antidyscratic therapy (blood purification and regeneration) of toxicoses and mental illnesses
- Thrombosis and embolism
- Transudates and exudates
- When venesection is not possible for technical reasons (e.g., childhood, obesity, or joint contracture) or when treatment of a specific vessel territory is desired

Based on the scientific literature, Bottenberg also compiled a list of mechanisms of action, which was uncritically accepted by his imitators.

Once heparin and phenprocoumon (Marcumar) established themselves as the agents of choice for treatment and prophylaxis of thrombosis and embolism after World War II, the leech again disappeared from most hospitals in Central Europe and was also increasingly forgotten by practitioners.

In the 1970s, medicinal leech therapy achieved a remarkable international comeback thanks to the increasing use of leeches in the fields of general, plastic, and reconstructive surgery for treatment of postoperative venous congestion and graft rejection. Leech therapy simultaneously became increasingly popular in modern naturopathic circles in German-speaking regions. The reported successes of hirudotherapy in the context of naturopathic pain management and the results of several scientific studies by researchers from various university naturopathic departments on the effectiveness of leech therapy in the treatment of symptomatic joint diseases have since been widely received.

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3 The Biology of Leeches

M. Roth

Introduction

Roughly 600 leech species have been identified to date, but only about 15 are used in medicine. Leeches classified as "medicinal leeches" in the narrower sense have been used to treat patients around the world, especially in Europe and the United States, for centuries. Because of its excellent therapeutic properties, the medicinal leech described here is considered to be the favorite species. In the past, the medicinal leech was generally assumed to be a single species with regional color differences. Based on this logic, the two phenotypes with the most distinctive coloring were originally named *Hirudo medicinalis medicinalis* and *Hirudo medicinalis officinalis* (Fig. 3.**1a, b**). The latter, which is also known as the "Hungarian leech," was later renamed *Hirudo officinalis* after it was given species status. According to current scientific understanding, the different patterns on their body surfaces indicate that the two presumed phenotypes are indeed two different species: *Hirudo medicinalis* Linnaeus, 1758 and *Hirudo verbana* Carena, 1820. The species concept was recently proved by DNA analysis [26].

In leech therapy, the existence of two species seems to be irrelevant because both have been used as equivalents throughout history. As far as can be determined, no differences in their spectrum of activity are known or have ever been investigated. The composition of their saliva is also identical [24]. Since the natural supply of *Hirudo medicinalis* became scarce due to the intensive exploitation of leeches in the 19th century, *Hirudo verbana* has been virtually the only leech species used around the world for decades. Because the two species were originally assumed to be color variants of a single species, most authors (e.g., [39]) referred to both as *"Hirudo medicinalis,"* without differentiating between the two types. In this book, how-

Fig. 3.**1a** **There are no known differences in the activity spectrums of the close relatives *Hirudo medicinalis* and *Hirudo verbana* (Carena 1820).** The two medicinal leech species are used as equivalents. Because of overharvesting of *Hirudo medicinalis* in the 19th century, *Hirudo verbana* is now predominately used in medicine around the world. *Hirudo medicinalis* typically has a drop-shaped pattern on the lateral aspect of its body (from [26])

Fig. 3.**1b** ***Hirudo verbana*** (left) **can best be distinguished from *Hirudo medicinalis*** (right) **based on differences in color patterns on their ventral body surfaces.** (Photo by M. Roth)

ever, the terms "leech," "medicinal leech," and "Hirudo" will therefore be used synonymously to refer to both *Hirudo medicinalis* and *Hirudo verbana*.

While on the subject of terminology, it should also be noted that the leech is not a worm. The term "worm" (*vermis*) is no longer used in the zoological nomenclature because the animals formerly grouped under the heading of "*vermis*" are wormlike members of completely different groups, as is now known today. Nonetheless, the leech is currently classified in the nomenclature as an annelid or "ringed" worm, making the earthworm its close relative. The term "worm" has therefore prevailed, although there is now a distinction. The term is a graphic description as well because, according to a leading German dictionary, the Duden [10], "worm" also has the meaning "wriggler."

The fact that many people suffer from misconceptions about leeches needs no further explanation. In German, leeches are called "*Blutegel*," which is reminiscent of the word "*Ekel*" (disgust), but has completely different etymological roots. "*Egel*" derives from the Greek "echis" which, by the way, is related to "*Igel*" (hedgehog) and is the source of the Old High German word "*Blutigel*." "*Igel*" means "not a snake"—which is a good thing or we would otherwise be dealing with "blood snakes"! Though zoologically untenable, this might perhaps improve the image of the leech because, phonetically, it is not as closely related to "*Ekel*" (= "disgust," see above). The Swedish name is similar, namely "*igle*." The leech's role as a bloodsucker is emphasized in various other languages. For example, it is called "*sangsue*" in French, "*sanguijuela*" in Spanish, "*sanguisuga*" in Italian, "*bloedzuiger*" in Dutch, and "*sanguisugolam*" in Latvian (a very melodic name, indeed). In English, leech is derived from the Old English word "*læce*," which also meant "physician" in the Middle Ages.

The aim of this chapter is to convey knowledge of the biological characteristics of leeches from which information relevant to clinical practice can be derived and, secondly, to abolish misconceptions about leeches. Both patients and physicians suffer from misconceptions that can sometimes hamper treatment. The opposite is also the case, in that some experienced leech therapists make use of the unusual and archaic nature of this form of treatment to back up the merits of its unspecific active component. This mindset turns the leech into a kind of "performance artist" in the physician–patient relationship. This chapter will therefore elucidate leech biology from a treatment perspective.

The Evolutionary History of Leeches

Leeches were presumably "applied" very much earlier than the documented records of medicine show—although not by humans. In the Cambrian explosion of life form development roughly 400–500 million years ago, prehistoric annelids evolved as segmented invertebrates from the first multicellular organisms. These "arch-annelids" ultimately evolved into leeches. Since they were among the first hunters in the earth's history, they were one of the factors that guided selection and drove the pace of evolution. The prehistoric annelid was also an ancestor of humans. Segmentation is a consequential biological trait shared by the two species. Surprisingly enough, the blood of leeches and humans also has similarities, suggesting a common ancestry: Hemoglobin serves as the carrier of oxygen in medical leeches as well as in humans, but is dissolved in the respiratory fluid of the one (leech) and is stored in blood platelets/erythrocytes in the other (human).

Since the leech is a skeletonless invertebrate, confirmed fossil finds of Hirudinea are rare. The only two confirmed finds date back to the Jurassic period. Based on fossil evidence, we know that the general structure of the Jurassic leech was very similar to that of the modern leech [22]. Therefore, the basic model for Hirudo was already "set" at a very early stage of history, and the remaining time was available for "fine-tuning."

If one assumes that evolution follows a goal-oriented course, it might seem that Nature is intentionally making refinements that facilitate the development of cooperation between the "perpetrator" (leech) and the "victim" (mammals, patients, etc.).[1] The medical significance of the biochemistry of the leech clarifies this relation.

The saliva of leeches is a highly efficient and highly complex trait acquired over the course of the evolution of the species. The composition of the saliva was apparently a "main area of evolutionary development": When the leech bites its victim, the effect is a combination of at least 30 individu-

1 In the course of researching his comprehensive standard work *"Leech Biology and Behaviour,"* [39] R.T. Sawyer, an outstanding leech biologist, realized that the use of leeches throughout history was no coincidence but, rather, was to a large degree driven by evolutionary adaptation [7]. In the preface to his book, Sawyer describes the leech as a living pharmacopeia that is a reflection of human physiology.

al chemicals. However, only eight constituents of leech saliva have so far been characterized in terms of chemical structure and mechanism [2] (see p. 131 and Fig. 11.**1**). In some cases, the functional value of the compound (e.g., hirudin) to the leech is immediately apparent. Hirudin enables the blood to flow for some time without it clotting. This is the fundamental fact that makes the process possible at all. This anticoagulant protein serves to make the victim's blood flow more readily while the leech is sucking it and was therefore favored by evolution.

Calin (see p. 134 and Fig. 11.**1**) is another constituent of leech saliva. The main function of this protein is to induce secondary bleeding, which can last up to 12 hours. At first glance, you might wonder why the leech would need to produce a substance that makes the wound bleed for a relatively long time. After all, the leech detaches itself an hour or less after biting its victim and is no longer connected to the victim's blood supply. Consequently, the leech has no direct benefits to gain from the prolonged blood flow. Nature normally does not allow itself the luxury of producing a protein for no apparent reason. The answer to this puzzle may be that the secondary bleeding is designed to attract other leeches, which would function as a means of preserving the population. However, water movement alone is a well-known signal that serves this purpose, so it still would not be necessary to produce a protein with the same function. The most likely answer is that the induction of prolonged bleeding is designed to help the host cleanse the wound and thus serves as a simple yet effective means of disinfection. It reduces the risk of infectious diseases and sepsis, which the prey could contract through infection, for example with the leech-borne bacterium *Aeromonas* (see p. 143 ff), or through secondary contamination. The production of calin can therefore be interpreted as a form of "resource management." In other words, if the leech's prey dies of sepsis, it cannot return to the place where it was bitten, and if it develops a painful infection, it may not be able to come back, but a "satisfied" host is more likely to return. The inclusion of calin in leech saliva therefore functions to preserve the population of the leech's ecological niche (for the biochemistry of leech secretions, see Chapter 11, p. 131 ff). Leech saliva has other generally beneficial effects. Therefore, encounters between the leech and its victims within the ecological niche are not entirely coincidental because the victim is not unhappy about returning. This behavior establishes the basis for joint evolution characterized by species cooperation.

The prey or host animals, including humans, had millions of years' time to become accustomed to the leech. Though not systematically investigated, it is probable that animals ranging from lower species to mammals learned to "appreciate" the leech as a "therapist." This hypothesis is based on various evidence, for example, the fact that cattle with joint diseases apparently like going to leech-infested waters. According to reports that I have received from people in Greece and India, among other places, cattle seem to deliberately—as far as one can judge a cow's intentions–expose themselves to leech bites (i.e., "get treatment") for extended periods in order to leave the site more "light-footed" than before. Leech therapy has also been successfully introduced in modern veterinary medicine. Most dogs are said to be unusually quiet while the leech is "docking" onto them, as if they instinctively knew it was going to help them [32]. One can therefore assume that even *Pithecanthropus*, his ancestors and indeed *Homo sapiens*, also recognized and exploited the healing effects of the leech. In the Stone Age, people employed different techniques of venesection with and without leeches. They interpreted leeching as a simple method for "removal of evil spirits" [17]. Likewise, some paramedical therapists today refer to this as the "removal of the evil."

After prehistoric times, Hirudinea entered the written history of medicine and has since passed through it in waves of popularity. The information in ancient writings does not always allow one to clearly identify which of roughly 600 existing leech species was used. According to Arndt [1], 15 species are used for medicinal leech therapy. The natural leech supply was never seriously endangered before the 19th century, during which, however, entire leech populations were then devastated. Mainly supported by the teachings of the French physician Broussais, the practice of leeching grew explosively in the 19th century, which ultimately led to the outbreak of true "leech mania" or "vampirism" in Europe (see Chapter 2, p. 9). In those days, leeches were returned to nearby ponds after use. There was no fear of transferring diseases through microorganisms since people did not know that microbes existed. However, other practices led to a drastic reduction in the domestic leech supply. One such practice was the unrestrained removal of leeches from their natural habitats in order to ship them by the ton, for example from Hamburg to France, America, Australia, and England.[2] It is also safe to

2 Leech farms such as the "Stölter'sche Anstalt" in Germany could not produce enough leeches to meet the huge demand.

assume that many of the leeches died after the treatments and, thus, were never returned to the cycle of nature.[3]

German businessmen proposed the foundation of a prestigious leech trading company, the "*Actiengesellschaft Hirudinea*" in 1863 [31]. This seemed like a very promising business opportunity, but their idea came too late. In the age of Koch, Pasteur, and Virchow, leeching disappeared from the medical repertoire toward the end of the 19th century. The once endangered leech populations had a relatively long time to recover during the 20th century, but regained the justifiable attention of physicians in the second third of the century. Now that the mechanism of action of leeching was relatively well known, leeches were applied very selectively and usually in small numbers. This hiatus in the 20th century did not suffice for regeneration of European leech populations, because the required wetlands had meanwhile been lost through drainage or had otherwise become unfit for leech survival. A large portion of natural leech biotopes (e.g., shallow ponds in meadowlands) had been destroyed, and the remaining leeches no longer had access to the prey they needed for reproduction—namely mammals. Furthermore, environmental toxins have made it even more difficult for these sensitive organisms to survive in Europe. The number of natural leech habitats existing in Europe today is very small indeed.

Most leeches now used in Central Europe for medicinal purposes are imported (mainly from Turkey) and are seldom grown domestically. Because the active constituents in leech saliva are effective ingredients in ointments and other topical products, the Turkish leech populations are very tightly monitored because leeches are very much in demand, alive or dead. Several tons of leeches, both fresh and frozen, are imported to Europe each year. Conservationists had hoped that recombinant hirudin manufactured from genetically modified bacteria and yeasts would soon be able to reduce the pressure on leech populations, but this hope has yet to be fulfilled. Because of the variety of constituents and complex mechanisms of action of leech

3 For the leech, treatment is an extreme feeding situation. Unlike the conditions in its natural habitat, where the leech must feed and detach quickly, the goal of leech therapy is often to have the leech extract as much blood as possible, i.e., to secrete as much saliva as possible. Treatment conditions are designed to achieve this purpose. This generally overtaxes the physiology of the leeches and a large percentage of them die after treatment if they are not returned to a suitable environment.

saliva, live leeches are more effective than pure hirudin in a number of cases. The number of live leeches used in Germany alone is probably around 300 000–400 000 each year. Assuming each leech weighs around 3 g, this equates to roughly 1.2 tons of leeches per year. On July 24, 2004, the American Food and Drug Administration (FDA) officially approved the leech as a "medical device" [37]) based on scientific evidence of the efficacy of leeching in diseases such as osteoarthritis of the knee [30]. This may spark a new round of pressure on the species. Although the approval of leech therapy may be good news for humans, it is not so great for the leech—at least not yet.

Ironically, the evolutionary feat of adapting to its prey ultimately resulted in more harm than good for the leech. Considering the beneficial effects of the leech, a discussion has arisen as to whether it is more biologically appropriate to classify the leech as "symbiotic" (a much more congenial and just description) rather than "parasitic" or "ectoparasitic." The roles of the protagonists have changed: Leeches are now being parasitized by humans. As mentioned above, the usefulness of the leech for humans is based on a survival strategy developed by the leech over the course of evolution. Considering that leeches have repeatedly been on the brink of extinction, it would be smart to develop new and efficient strategies to ensure their continued well-being for a change. For these reasons, *Hirudo medicinalis* was included in Appendix II of the Washington Endangered Species Act, which was designed to impose harvesting quotas and control leech trade. Under this agreement, it is mandatory for anyone buying or selling leeches to submit a CITES report form.[4] In other words, written permission to conduct the transaction must be documented by means of a CITES form whenever leeches are imported or exported. In Germany, the corresponding legislation is supervised and executed by the Federal Agency for Nature Conservation (BfN):

> *"A person who goes to the zoo, eats herring filets, keeps a caged parrot, or purchases a leech extract ointment to improve the blood flow rarely ever sees how these events are related. In*

4 CITES = Convention on International Trade in Endangered Species of Wild Fauna and Flora. CITES forms are used to prove the legality of trade in endangered species, that is, to determine whether and in what quantities it is permissible to remove representatives of this species from their natural environments.

countries around the world, including Germany, wild animals and wild plants are being removed from their natural environments for trade and manufacturing purposes. Many animals around the world are currently endangered because they are being used as foodstuffs, traditional remedies, or live commodities. On the initiative of the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety and the Federal Agency for Nature Conservation (BfN), criteria specifying ways in which the use of wild fauna and flora can be conducted in harmony with Nature have now been proposed." [6]

Ways to protect endangered species while protecting our own vital interests include the establishment and support of breeding farms for *Hirudo medicinalis* and *Hirudo verbana*, the development of further strategies to ensure their continued existence, and prudent planning of leech usage. We owe it to each individual creature to treat it humanely.

Anatomy and Function

In order to understand the structural concept of leech anatomy from a biological perspective, we will take a look at how the animal behaves in freshwater ponds. Its natural behavior is characterized by the following cycle of recurring events:

a) Quietly searching for food and observing potential prey while swimming slowly and floating near the water surface for extended periods; this can last months to years;
b) Quickly attaching to prey and feeding in a rapid series of movements; feeding is usually finished within a few minutes;
c) Submersion to a hiding place in the depths of the water body to rest and digest the meal; this resting period may last several months to years.

There is frequently a smooth transition from (c) to (a).

The leech can ingest relatively large amounts of blood (up to 10 times its body weight) each time it feeds. This allows the leech to survive for up to two years between feeding. This thrifty feeding behavior is partially due to

the limited supply of mammal hosts and is reflected in the simple but very advantageous body structure of the leech (Fig. 3.**2**). With respect to organ size, Hirudo consists almost entirely of a double-walled "digestive tube." The foregut, midgut (stomach), and hindgut occupy the largest volume of organs and tissues in both the filled and empty states. The foregut, comprising the mouth, pharynx, and esophagus, makes up roughly two tenths of the entire length of the animal. The midgut (stomach), which consists of 10 pairs of blind pouches, makes up five tenths of the total length. The three-part hindgut makes up roughly three tenths of the total length. Only one bacterium species is equipped for long-term survival in the leech stomach (cf. p. 142 ff). This species happens to be the symbiont the leech needs to digest its food: *Aeromonas biovar sobria veronii* (formerly called *Pseudomonas hirudinis* and many other names [14, 15]). This amazing coincidence is very helpful for medicinal leeching.

The leech stomach (crop) is an enormous "storage chamber" that enables the leech to survive for years without food. It is connected to the hindgut, the site where low-energy digestion takes place (anaerobic digestion can also be performed as needed). Even after the stomach contents have been fully depleted, the leech can subsist for months on its own body substance.

The leech has a small anterior sucker which surrounds its pointed apical mouth. The anus opens on the dorsal surface above the large rear sucker. The

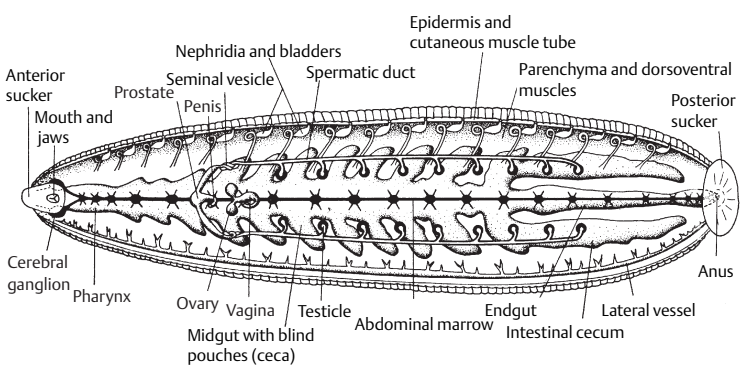

Fig. 3.**2** **Anatomical structure of the medicinal leech (ventral surface).** Secondary annulation is seen as folding of the body wall (adapted from Storer & Usinger, in [41])

leech also has two other types of excretory organs: the segmental nephridia and hermaphrodite (male and female) reproductive organs. Respiration takes place through the body wall. Hemoglobin dissolved in the blood transports oxygen to all parts of the body via a contractile capillary network. As an invertebrate animal, the leech has a soft body that lacks a skeleton. The body structure of Hirudinea resembles that of their phylogenetically close relatives, the earthworms (Annelida, Oligochaeta), in that it also displays segmentation. The body of the medicinal leech is composed of 34 segments. Segments 9–11 form the clitellum, the organ responsible for cocoon secretion, which is only visible in the summer months. The last seven segments form the large rear sucker.

Secondary annulations, consisting of 105 external rings (annuli), obscure the internal segments. Each segment is covered by up to five annuli. The annuli can stretch like an accordion. They provide skin reserves that expand to accommodate the large volumes of blood ingested during feeding. The annuli also assist in locomotion. Externally, the only sign of internal segmentation is the recurrent reddish orange/olive/black striped pattern on the back of *Hirudo verbana* and *Hirudo medicinalis* (Fig. 3.**1a**). No two patterns are exactly identical. Internally, segmentation is reflected by the metameric arrangement of the 32 ganglia, excretory bladders, nephridia, and seminal vesicles (Fig. 3.**2**).

As simple as the gross anatomy of the leech may initially appear, the individual structures are surprisingly complex. Its central nervous system, which is crucial for successful hunting, localization of enemies, and general coordination, is very highly developed and specialized (see p. 28 ff and 33 ff). The cephalic region of the leech fulfills attachment, biting, secretory, sucking, and locomotor functions, contains gustatory receptors, temperature receptors, and eyes, and is connected to the lower pharyngeal ganglion. The leech head was an early climax in increasingly specialized head development over the course of evolution. The body wall of the leech must also fulfill numerous tasks. The strong muscles of the body wall permit prolonged swimming, crawling, and respiratory movements and they help the leech to remain attached to its prey and other structures (see p. 31 ff).

Oral Anatomy and Function

The oral anatomy and function of medicinal leeches plays a central role in leech therapy. To find the right spot to bite, the leech must probe the host's skin. It uses highly sensitive chemical, heat, and touch receptors distributed most densely in the upper lip region to test the skin for the desired characteristics. If the leech tastes blood, glucose, or sweat, senses that the temperature is between 35°C and 40°C, and feels pulsating movements indicating the proximity of an artery, then it knows it has found a good feeding site.

The primary oral cavity (oral sucker) of the medicinal leech is separated by a velum from the secondary oral cavity (mouth) containing the jaws (Fig. 3.**3a**). Both can be retracted and extended. Before feeding, the leech starts to pump air into and out of the cavities and positions its jaws on its victim. While feeding, the leech slides its many-toothed jaws back and forth to slice into the victim's skin in a sawing motion, while the cavities (including the pharynx) contract and dilate rhythmically. The pumping motion creates a

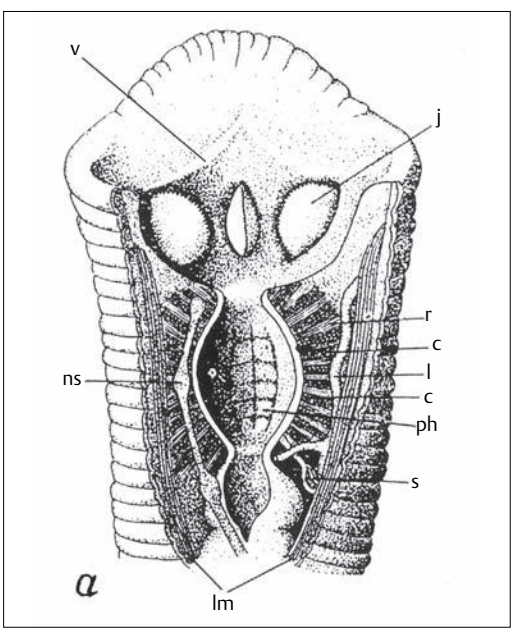

Fig. 3.**3 a** **Cross section of the oral sucker of the leech**
(from [19]).
Key to symbols:
j jaw
r radial muscles
c annular muscles
l lacunae
ph pharynx
s salivary ducts
lm longitudinal muscles
ns nervous systems
v velum

vacuum, which results in the suction of blood. This can readily be seen by the outside observer, especially in the final stages of feeding. The oral sucker spreads dorsally to form an upper lip (prostomium), which contains taste receptors. An adhesive substance (mucus) secreted by the oral sucker and the pharyngeal pump mechanism help the front and rear suckers achieve powerful suction pressure (roughly 0.2 atm). As a result, the leech can attach itself to almost any surface: Sandpaper or glasspaper of any grain size, Velcro, coarse or fine wire, or plastic wickerwork, and fabrics or even vertically positioned surfaces coated with Vaseline are no major problem for a leech to climb.

The feeding leech can lock its jaw so tightly that it is hard to pull it off–which one should not do anyway because of the risk of infection (see below). Due to its efficient attachment system, it is not so easy for hosts to brush the leech off their various body surface coverings. Tensile forces resulting from attempts to forcefully pull or knock off a feeding leech could cause the animal's body to rupture. This could result in regurgitation of gut contents, including the "leech bacterium" *Aeromonas*, into the wound, resulting in wound infection. Avulsion of an entire row of teeth seems a very unlikely cause of these infectious complications. Breakage of individual teeth that remain inside the wound to cause infection seems more conceivable.

The mouth of the medicinal leech is located in the anterior sucker. Just within the oral cavity are three jaws, the three sides of which form 120° angles, resembling the Mercedes-Benz symbol (Fig. 3.**3 a**). Figure 3.**3 b** provides a view of—or better, into—an oral sucker of a leech attached to a glass plate. The yellowish orange lenticular regions are the lips, which contain the hardened masses of muscle comprising the jaws. The bladelike jaws have 60–100 small teeth along their edges, as is seen from a dorsolateral view in Figure 3.**3 c**. Under a scanning electron microscope, interdental pores through which leech saliva is secreted can be identified (Fig. 3.**3 d**) [31].

Leech saliva is produced in discrete, scattered salivary glandular cells that do not connect to form a proper gland. The external openings distributed across the dental ridge between each pair of teeth are the endpores of a central canal, that is, the endings of the secretory ducts of the glandular cells. Antagonistic muscles at the base of the jaw work in concert to move the jaw back and forth in a semicircular motion similar to that of a circular saw. Through this muscle activity, the relatively small contact area of the curved, semicircular jaw penetrates deeper and deeper into the skin. Successive

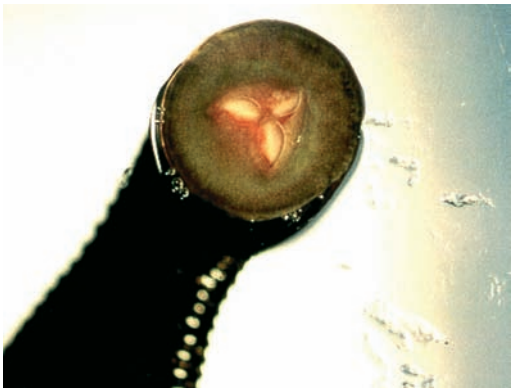

Fig. 3.**3 b** Oral sucker attached to a prewarmed glass plate. The pharynx (striped) is contracted. The leech has expelled all the air between the sucker and the glass. The pharyngeal muscles begin to contract rhythmically, creating the suction pressure required to withdraw blood. At the same time, the sawlike blades of the jaws of the leech (yellow) penetrate deeper and deeper into the host's skin while emitting pharmaceutically active substances. In the middle of the throat, at the imaginary point of intersection of the jaws, the pharynx now opens. (Photo by C. Morkel)

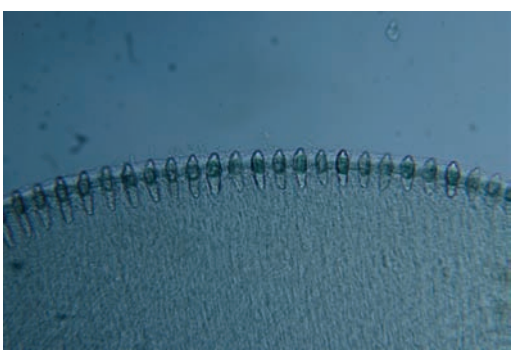

Fig. 3.**3 c** **Segment** (approximately one-third to one-quarter of the total jaw length) **of the leech jaw,** which can have up to 80 small, calcified teeth. The lower edge of the picture is equivalent to roughly 1.5 mm. The external openings (nephridiopores) of the salivary gland cells located roughly 5–10 mm away can be seen as discrete stripes in the hardened muscle tissue at the lower edge of the photograph. This anatomical configuration can be likened to a microsurgical/biochemical precision tool. (Photo by E. Schulte)

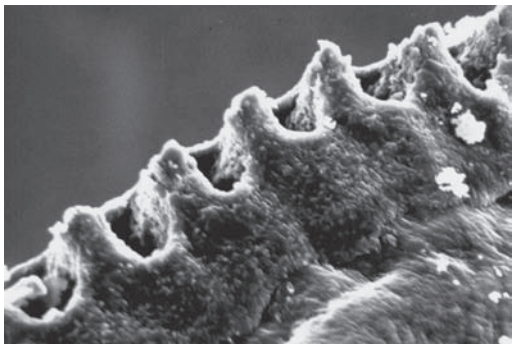

Fig. 3.**3 d** **Segment of the leech jaw showing the interdental pores** through which leech saliva and the substances contained in it are secreted. (Photo by C. Morkel)

penetration has two distinct advantages: First of all, it requires less force than, for example, a jaw with a linear tooth configuration. Secondly, the victim perceives less discomfort and is less likely to notice the bite. Thus, the chances are greater that the uninvited guest will go unnoticed. Leech saliva may also contain a substance with anesthetic properties that enhance this effect (for other chemicals in leech saliva, see Chapter 11, p. 131 ff). The leech secretes saliva into the wound through the interdental pores while sawing its teeth deeper and deeper into the host's skin. Mechanically speaking, the anatomical structures work like extremely efficient micropipettes that inject pharmaceutically active substances into the wound. No microsurgical tool can perform such complex functions with such high precision, not to mention the perfect coordination of the "interlocking" spectrum of action of the active constituents in leech saliva.

The pharynx (throat) connects the oral cavity with the esophagus (gullet). The esophagus is a muscular coat consisting of annular, longitudinal, and radial muscles (Fig. 3.**3 a**). It has the highest concentration of different muscle types in the leech body. These muscle groups interact to produce the rhythmic pharyngeal muscle activity that occurs while the leech is feeding. In the first phase of feeding (suction), radial muscles lead to active dilatation of the pharynx. In the second phase (transport), annular muscles are used for active pharyngeal contraction. These peristaltic movements of the pharynx start at a frequency of roughly 2.4 Hz and slow to approximately 1.2 Hz or less toward the end of feeding [18].

Leeches sometimes appear to "fall asleep" while feeding. Gently stroking the leech in the head/throat region can help them "wake up." Since the leech generally releases its "victim" voluntarily after about 20–60 minutes, it is better to wait for this natural end of feeding. When the leech is full, it usually opens its jaws and simply drops off the host. When this happens, towels, cellulose wadding, and the like should be at hand. A waterproof container filled approximately two thirds full with water (distilled water plus 1 g sea salt per liter is recommended) with a tight-fitting cover is also needed in which to deposit the leech, which has now expanded up to 10 times its original size. A leech occasionally feeds for up to two hours and may appear to have fallen asleep. If this happens, it is best to first detach the rear sucker to trick the leech into thinking that it is about to fall. In most cases, the leech will then release the oral sucker. If it does not, the sucker can be cautiously detached using a flat spatula (or a fingernail protected by a latex glove).

Skin, Muscles, Nerves, and Senses

The body wall of the leech has some remarkable features. As the interface between the leech and outside world, it must cope with the special demands of leech life. Therefore:

- It is extremely elastic;
- It performs respiratory functions;
- It serves as a barrier against harmful substances and infections;
- It permits osmoregulation and regulates the exchange of chemicals and gases;
- It functions like a single complex sensory organ;
- It can resist mechanical attacks;
- It can shed its outer layer (cuticula);
- It is pigmented for camouflage purposes;
- It serves as a means of species recognition;
- It works to prevent dehydration and protects the leech during winter hibernation and summer resting periods.

The entire body surface as well as the pharynx, oral cavity, and jaws of the leech are at least partially covered by cuticularized epithelium. Since

the epithelial cells are tightly linked, the cell connections can withstand the enormous tensile forces that occur during and after feeding. The skin is folded like an accordion when the stomach is empty, but stretches tremendously to accommodate the large volumes of blood ingested during feeding.

The leech epidermis is a porous collagen matrix covered by a cornified secreted layer (cuticula) that is shed approximately every 3–10 days by means of peristaltic motion (wavelike muscle contractions). The frequency of molting is determined by temperature, water quality, and the nutritional state of the leech. Molted leech skins look like floating white veils attached to plants or can be seen as white rings on the ground. A mucus layer consisting mainly of mucopolysaccharides overlies the fibrillar cuticula. The mucus layer is also sloughed off during molting. This double-layered mucus barrier prevents aquatic plant bacteria from coming in direct contact with the leech epidermis. Bacteria are also eliminated with each molt. Molting therefore serves as a natural means of hygiene.

Leech-keepers should take appropriate measures to facilitate the molting process. When changing the water in leech containers, all shed skins should be removed. Incomplete molting can result in serious injury or death. Remnants of old skin frequently cause tight and deep constrictions that can injure the leech epidermis, opening the way for bacteria to penetrate beneath the tough ring of the cuticula. Leeches that recover from these injuries often have ringlike scars at the injury sites. Rough objects such as sharp-edged stones and hard-leaved plants should therefore be placed in the leech container to facilitate molting. The leech can sometimes be helped out of its old skin by gently pulling on it. In the past, bundles of horse hair were placed in leech containers to facilitate molting.

Respiration and gas exchange are accomplished almost entirely via the dermis and the capillary network of the cuticula. The skin also regulates water inflow and outflow and ion and salt exchange, thus functioning as an excretory organ [40]. Transport can be accomplished both passively (with a concentration gradient) and actively (against a concentration gradient). The osmoregulatory function of the skin, which works in conjunction with nephridial excretion, is extremely important considering the extreme concentration gradients between the internal and external environments that must be regulated during feeding. The feeding leech must extract and eliminate water from the harvested blood while counteracting the influx of water. Therefore, it is vitally important to keep leeches in a properly adjusted saline solution.

When filled with harvested blood, the internal cavity must be protected from antagonists of all kinds. Unicellular mucopolysaccharide-producing mucus cells that are irregularly distributed throughout the skin are an important element of personal protection. According to Sawyer [39], the mucus produced by these cells performs a number of important functions: It prevents dehydration, protects the leech from physical and microbial attacks, and it assists in respiration, osmoregulation, winter hibernation, summer resting, and in excretion. Special chemicals in the mucus help leeches of the same species to recognize each other. Increased mucus production may be a sign that the leech is trying to protect itself from something, such as external chemical imbalances in sensitive parameters (pH, ammonia, water hardness, etc.), severe changes in temperature, disturbances, transportation stress, extended exposure to harsh sunlight, or microbial overload, etc. Excess mucus production sometimes occurs at the end of winter hibernation. The act of mucus hypersecretion in itself is not a disease, but may be a sign that something in the environment is disturbing the leech and should be removed. In most cases, there are simple solutions, such as washing the leech in a stream of lukewarm water or changing the leech's water (1 g of sea salt per liter of distilled water).

The leech skin contains a large number of sensory cells with various receptive qualities. Although distributed throughout the entire body, most are centralized in the head region (see below). Consequently, the leech encounters its occasional mammalian hosts with very keen senses. When using leeches for therapeutic purposes, it is important to remember and utilize this knowledge to influence the animal's behavior for its own good. Since the stimuli perceived via the ganglion nodes are integrated and coordinated, the skin of the leech can be viewed as a single sense organ [39].

The epidermis is characterized by metamerically arranged ornamental patterns that display individual differences, which are easily recognizable when observed under magnification. Most of these pigments are byproducts of excretion. Because of its external coloring, the leech fits in well with the surroundings on the pond floor or between leaves on the surface of the water (Fig. 3.**4**). This camouflage helps the leech to hide from its natural enemies and potential prey. When a leech has consumed up to 10 times its body weight in blood, it makes a tasty and nutritious snack for predators like birds and rodents. Therefore, the camouflage (and the ability to keep still) is of vital importance. However, the leech can turn the tables on a predator, even

Fig. 3.**4** **Camouflage pattern of *Hirudo verbana*.** The individually variable orange and green striped color pattern on the leech's body surface provides camouflage that effectively conceals the leech from natural enemies and potential hosts. (Photo by M. Roth)

if it is much larger than the leech. Even if the predator has only been injured by the leech, it will leave a trail of blood in the water that will attract lots of other hungry leeches, which can ultimately finish it off.

Alternating olive, russet, orange, and black stripes form a regular pattern on he dorsal region of the leech. *Hirudo medicinalis* tends to be predominantly reddish yellow, whereas *Hirudo verbana* is more dark green. The coloring of the two species is clearly different in the ventral region: *Hirudo medicinalis* has irregular blackish green spots, whereas *Hirudo verbana's* stomach region is a homogeneous olive green with two stripes along the edges (see Fig. 3.**1 b**).

The pharynx must perform considerable suction and pumping work (see above), so the tube of muscles in the body wall surrounding the pharynx has to be extremely well developed (see Fig. 3.**3a**). The leech jaw, which is formed by calcium encrustation and hardening of muscles, represents yet another form of muscle specialization. The muscle tube of the body wall generally consists of four layers (Fig. 3.**5**):

- A parallel layer of longitudinal muscles,
- A double layer of diagonal muscles,
- A transverse muscle layer,
- A dorsoventral muscle layer (used to flatten the body).

This muscle configuration permits four basic types of movement:

- On hard surfaces, the leech moves by alternately stretching and contracting its entire body. The large rear sucker remains attached to the surface while the small front sucker stretches forward and advances, making

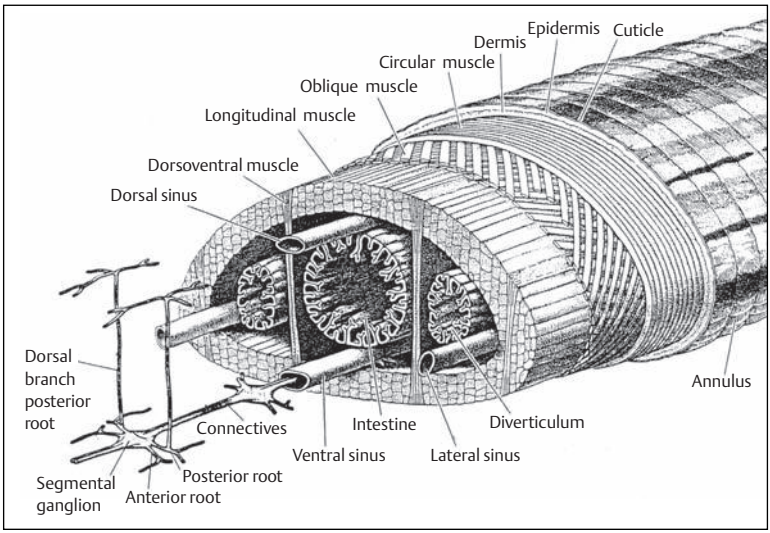

Fig. 3.5 **Block diagram of the midsection of the leech.** The thick body wall is a tubular structure consisting of annular, longitudinal, diagonal, and transverse muscles. Dorsoventral muscles allow the leech to securely attach itself and to drastically change its body shape. This extreme deformability allows the leech to slip through narrow cracks to hide from its enemies, including other leeches, even when its stomach is full. (Reprinted from [33], p. 15)

searching movements in the substrate or in the air. The leech can stretch up to several times its resting body length when extending. After advancing, the front sucker reattaches and the rear sucker glides across the surface in the direction of the head, where it also reattaches.

- The second type of movement is also accomplished by first attaching the front sucker and then drawing the rear sucker forward, but a loop is formed during the shortening phase. This resembles the way an inchworm crawls. Since leeches always move forward, the "head" is easy to spot. Furthermore, the oral sucker is much smaller than the rear sucker, but much better developed.
- When swimming, the medicinal leech moves its body up and down in dolphinlike waves of motion resembling a sinus curve. Similar to the way a dolphin uses its horizontal tailfin, the leech flattens and stretches it body while swimming in order to displace as much water as possible during the downstroke with minimal water resistance. The control and coordination

mechanisms responsible for these smooth movements have been the subject of several investigations [23, 39].

- In oxygen-deficient water, the leech fans water toward and past its body, which is usually spread flat and held in place by the rear sucker. The leech then makes whiplike movements with its body, the frequency of which can be modulated as needed. The objective is to draw fresher, more oxygen-rich water toward the body. This has also been referred to as "undulating ventilation."

The leech can dramatically change its body shape thanks to its pleated skin and extremely elastic neck muscle configuration. The dorsoventral muscles allow the leech to greatly flatten its body whenever this might be necessary, to hide in a narrow crevice for example. The leech body also has an amazing capacity to stretch both in and out of the water. A leech can lift its entire body except the rear sucker from the surface, for instance when "sniffing the air" to check out its surroundings. Once the leech has bitten its victim, it can be stretched to double or triple its normal length by pulling on the tail end of the leech. This demonstrates the extraordinary holding power and deformability of the sucker.

Because the leech can alter its shape so dramatically, leech containers should always be kept securely closed and air holes in the container should be small. Leeches can escape though the tiniest of cracks.

The nervous system of the Class Hirudinea is descended from the ladder-like nervous system of the earthworms. It consists of a cerebral ganglion, a ventral ganglion chain made of 21 ganglion pairs with approximately 200 neuron pairs each, and a posterior ganglion for the rear sucker. The stimuli received by the various sensory receptors are integrated and centralized in the 21 segmental ganglia, the large lower pharyngeal ganglion, and the caudal ganglion. The lower pharyngeal ganglion consists of four fused ganglia; the caudal ganglion consists of seven fused ganglia.

Like the overall central nervous system, the large leech neurons have been exceptionally well studied. They are also used as models for neural performance in higher animals. It is relatively easy to correlate the biochemical activity in and between leech cells to the leech's outward behavior. To a certain extent, biochemical processes, structures, cell types, and neurotransmitters, etc. in the leech are identical to those of some mammals, including humans. Serotonin, which can be found in Retzius cells, the largest leech neurons, mediates leech hunting behavior. High levels of serotonin

induce the leech to consume larger amounts of food (up to one third more), make the leech more eager to bite, soften the body wall, stimulate saliva production, and reduce the latency time for a leech to end its resting period and swim toward a stimulus center (prey) [29].

The finding that leech neurons are able to "solve math problems" aroused quite a bit of excitement. In the study in question, a computer was connected to two live leech neurons so that they could communicate with each other via the computer. When the one neuron was given an addition problem as input, it sent the second neuron the solution as output. This capability is based primarily on the modulation and transmission of electric impulses in the form of action potentials. This occurs, for example, when the leech regulates its blood pressure via the heartbeat [8, 13].[5]

The leech has five pairs of pigment cup eyes (ocelli), which it uses to detect shadows and, most importantly, shadow movement. The ocelli are embedded in the skin in the dorsal head region. Ocelli cells have a brush border (microvilli) and a transparent central vacuole. Each of these light-permeable cells is completely surrounded by a ring of black pigment. The configuration of these cells allows the leech to identify the angle of incidence of light and shadow movement in its surroundings. To test this theory, raise one hand to create a shadow above the head of a leech resting in water. In response to the stimulus, the leech will usually move toward the shadow within a few seconds.

In the oral region, especially in the skin of the upper lip (prostomium), the leech has thermoreceptors and two other types of sensory papillae that function as chemical receptors for different classes of substances [11]. We have found that certain substances also cause spontaneous defense reactions when they come in contact with the dorsal skin of the leech. Cigarette smoke, for example, is known to cause phobic reactions in leeches when placed in the vicinity of their anterior sucker. When the dorsal skin is exposed to cigarette smoke, the leech will also retreat into the water immediately, even if its head was submerged in water. A possible explanation for this response is that the broad distribution of chemoreceptors makes the leech a "floating tongue" and therefore provides a further rough orientation tool for locating prey.

5 Researchers hope to utilize the technically unparalleled complexity and performance of neural networks to develop chimeric technical, digital, and biological data media (neurochips).

Sensory papillae (sensory buds) that respond to light as well as touch, water movement, and pain (nociceptive tangoreceptors) are embedded in the annuli. These sensory cells are distributed throughout the entire body surface and are connected to the nodes of the ganglia, which integrate all sensory signals. Since the sensory papillae are located along the ridges of the annuli, they receive signals even when the leech is in an extremely contracted position. However, contraction creates skin folds that can exert shearing forces on touch receptors within the folds, thus sending false information signals.

The receptors that detect motion (vibration) can be exploited by leech hunters. Hitting the water with one's hand or a stick produces concentric ripples. The leeches will sense the vibrations–sometimes even from relatively great distances (several meters away)—and will flock directly toward the site of water motion. They quickly converge on the thing causing the commotion (which may or may not be a welcome meal). The leeches do not bite their find immediately since they first have to evaluate it for edibility. Only those moving objects that meet the leech's edibility criteria (which differ depending on the age of the leech) will be selected as prey. Young leeches are generally satisfied with cold-blooded animals as long as their body temperature has adjusted to ambient temperature, whereas older animals prefer warmer-blooded prey, i.e., mammals.

The leech is unique in the animal kingdom in that it is the only species with a head designed for feeding *and* locomotion. The leech head contains tactile, chemical, and thermal receptors, provides footing, and is an extremely efficient attachment organ. This is a very useful anatomical configuration for an animal that must do its feeding quickly. If the leech takes too long to bite and feed, the host may leave the water before the leech can finish. Its specialized head structure allows the leech to bite the host and attach itself the instant its sensors have located a suitable site to bite. This increasing specialization of the cephalic region with connections to the central nervous system was a result of the evolutionary process of cephalization.

Because they have such a well-developed nervous system, leeches are extremely sensitive animals. Improper handling and environmental disturbances, such as sudden changes in weather, extreme temperature and light variations, and exposure to various chemicals can have extremely detrimental effects. Leech therapy should be carried out in a quiet and relaxed setting. The leech may not bite if the therapist or the patient is very

nervous. Inexperienced handlers often use rough tactics when using their hands (or forceps!) to prevent the leech from escaping or when trying to get it to feed at a certain spot. Rough handling should always be avoided: It will only trigger pain receptors and evoke a fight-or-flight response, making the leech flee in the opposite direction. In particular, the handler should avoid touching the cephalic region, especially the eyespots and upper lip region. It is better to grasp the animal at least 2 cm below the head and coax it to feed at the right spot using a suitable form of enticement. A few drops of glucose will often do the trick. Alternatively, one can prick the patient's skin to draw a few drops of blood, increase the temperature at the target site by rubbing it with a warm wet towel, and so forth. Lard is also said to be helpful.

The opposite is also the case, in that the smell of virtually any essential oil will make the leech release its hold and react defensively. If, for example, you put a drop of tea tree oil on a glass rod and place it near the upper lip region, which is equipped with sensitive smell and taste receptors, the leech will normally release the host immediately. However, extremely intense stimuli may cause the leech to regurgitate, thus contaminating the wound with *Aeromonas* bacteria.

Before treatment, the intended bite site should be cleaned with plain water. An unperfumed soap (e.g., potash soap) can also be used if necessary. Nicotine transpiring through the skin can prevent biting, as can the smell of alcohol and garlic (leeches are "vampires" after all). To find out just how sensitive the gustatory receptors of the leech are, apply a single drop of perfume to the host, near the leech's head: The leech will not only open its jaws immediately, but will also writhe in pain, often bending the twitching cephalic region so far backward that the posterior sucker also detaches.

Failure of a leech to feed does not necessarily mean that it is not hungry (breeding centers generally deliver hungry leeches). This reluctance could be due to repulsive odors (perfume, nicotine, etc.) or simple inappetence (in the summer, for example, leeches are primarily geared toward reproduction). If all efforts fail, one cannot and should not force the leech to feed but should try one's luck with another leech.

When attempting to get the leech to stop feeding, it can be helpful to place a few salt crystals in the excreted fluids near the leech's head, but avoid overdosage as this may cause the leech to regurgitate its gut contents. To preserve or enhance their eagerness to feed, leeches should be kept

in a cool, dark place and left as undisturbed as possible. This calms their senses so that they can react all the more intensively to the stimuli (chemicals, temperature, light) that trigger their hunting instinct once they have located suitable prey.

Leech Behavior, Habitat, and Care

Developing a feel for the animals is important for proper care and successful therapeutic application of the medicinal leech. It is senseless to handle the leeches with forceps or to demote them to mere "medical devices." It will not suffice to keep the animals at the minimum subsistence level if one wants to achieve optimal treatment results with minimal side effects. To maintain leech vitality and a good quantity and composition of leech saliva with a low bacterial load, proper leech maintenance and adequate treatment preparations are essential. However, the treatment requirements must be compatible with the needs of the animals. In our leech breeding experience, we have found that keeping them in the proper conditions is the key to successful treatment. A specific understanding of the conditions appropriate to the species is essential for proper leech treatment and maintenance.

Because of environmental pollution and overharvesting, especially in the 19th century, the leech's natural habitats have become pretty rare. In Central Europe, there are only a few places left where medicinal leeches can be found in the wild. Quiet, shallow eutrophic ponds roughly 1–1.5 m deep with a loamy/peaty bottom (e.g., those in river plains) that are located off the beaten track are "ideal" biotopes for leeches. Since leeches deposit their cocoons containing 10–30 eggs each in the soil of the pond banks, the profile, mineral composition, flora, and fauna of the pond banks play a critical role in leech reproduction. The laying of cocoons in bank regions where the young are protected from dehydration and drowning (Fig. 3.**6**) can be interpreted as an early form of brood protection [25]. After hatching, young leeches first live off the yolk mass in the cocoon, returning through the spaces from which they hatched in order to feed. Young leeches then start to feed on benthic and planktonic organisms, then proceed to amphibians, and finally progress to mammalian prey.

It is important for the leech to have plenty of shaded resting and hunting places. The hungry leech prefers to observe the hunting ground from the water surface, so it likes to attach to floating leaves and the useful stable stems and leaves of submerged plants. The hunting leech locates water motion and/or shadow movements using its vibration receptors and five pairs of eyes.

Since leeches molt several times a month (every 3–10 days), they need hard-leaved plants such as Canadian waterweed (Elodea canadiensis) or other rough objects (branches, rocks, etc.) on the bottom of the pond to help them shed their skin. If molting is unsuccessful, sharp rings of the old cuticula can constrict around the body like a belt, resulting in life-threatening lacerations or strangulation. If this process has not gone too far, one can carefully finish pulling off the old skin using one's hands and a fingernail.

Such constriction may become chronic due to deep scar formation (or other causes) but does not necessarily mean the leech will die. Even leeches with "hourglass figures" can survive for quite a while, but their ability to

Fig. 3.**6** **Freshly laid cocoon on the banks of a leech breeding pond.** (The cocoon can be seen in the bottom left corner next to the 1-euro coin, which indicates the scale of the cocoon.) The protein shell, which the leech shed via peristaltic muscle movement, was initially white but has now transformed into a yellowish brown, spongy, hardened hollow cocoon. The cocoon contains 10–30 eggs, which will mature into fully developed leech young within a few weeks. (Photo by M. Roth)

swim is usually impaired and they appear to "stagger" through the water. Depending on the extent of nervous system injury, there may also be signs of paralysis, but the parts above the constriction are usually relatively intact. The part below the constriction site, generally down to the posterior end, may be completely paralyzed. These more severe injuries soon lead to death, especially since the anatomical constriction can severely impair digestion. Moderately severe injuries are best "treated" by simply leaving the injured animal undisturbed in a suitable environment. Since leeches have a high regeneration capacity, many will make an almost complete recovery from these lesser injuries. Incidentally, rest seems to play a central role in the treatment of almost all leech diseases.

In terms of feeding and reproduction, the "ideal" leech pond should contain various types of amphibians and fish, and it should serve as a watering place for warm-blooded land vertebrates. High organic loads are not as problematic for leeches as products of excretion (including those from leeches), such as ammonium and nitrite, or heavy metals and other environmental poisons. Because they are extremely sensitive to heavy metals and avoid water contaminated with them, medicinal leeches can be used as indicators of water toxicity [36]. Leeches are extremely sensitive to disinfectants. Even very low concentrations of chlorine can be fatal. The pond water should be < pH 7 and as soft as possible. If the oxygen content of the water is too low, the leeches can obtain sufficient oxygen through cutaneous respiration (oxygen enters through the body wall in the open air).

In captivity, leeches generally remain near the water surface, with the front sucker sticking out of the water and the rear sucker below the surface (when resting or hungry). They may also crawl around foraging or adhere to the walls of the container. Leeches frequently attach themselves to horizontal surfaces (like the lid of the container) for several hours at a time. Then, they position the two suckers at a variable distance from each other, so that they resemble either a hanging loop or a hammock (see Fig. 3.**8c**). It is not known whether this hanging activity is accomplished by energy expenditure (suckers and pharyngeal vacuum pump) or a specific adhesion effect (adhesive mucus secretion). However, it would almost seem as though the leeches relax while "hanging around."

Leeches not only increase their swimming activity when hunting, but also when the oxygen content or temperature of the water changes. In the past, it was generally assumed that leeches' swimming activity increases

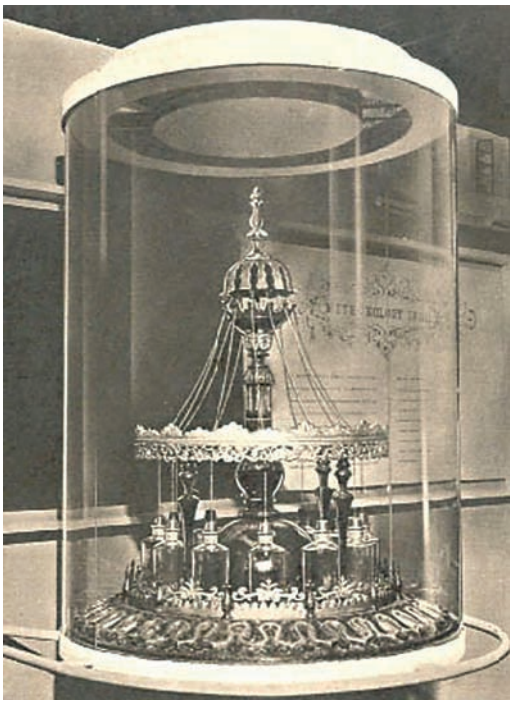

Fig. 3.7 **Merryweather's Tempest Prognosticator.** Leeches can sense when a storm is brewing. Based on this (still not definitively proved) ability, Dr. George Merryweather presented a "leech barometer" at the Great Exhibition of the Works of Industry of All Nations in London in 1851. Merryweather's Tempest Prognosticator consisted of a system of 12 jars containing leeches. When the atmospheric pressure changed suddenly, the leeches were supposed to crawl up to the top of the jar and touch a whale bone lever connected via a mousetrap mechanism and chain to a bell. Unfortunately, the idea of this "storm warning system" never caught on. (Photo by M. Packer)

in response to drops in barometric pressure before a sudden change in the weather, and they were extolled as living barometers. Leeches were sold as "Merryweather's tempest prognosticators" at the Great Exhibition of the Works of Industry of All Nations in London in 1851 (Fig. 3.**7**). Unfortunately, no one has been able to prove this claim so far [12]. Still, leech users generally report that the animals sometimes become more active before thunderstorms and are clearly more agitated during thunderstorms. Our observations in our own leech ponds confirm this. It would seem that the last word has not yet been spoken as regards this characteristic of the leech.

The physical and digestive activity of these poikilothermic animals is basically a function of temperature.[6] Shadow movement also makes leeches

6 The metabolic rate and chemical reaction rate double when the temperature rises by 10°C (see the so-called RGT rule).

become more active, presumably because it triggers their hunting instincts. Prolonged exposure to harsh sunlight can be lethal for leeches. Ironically, they sometimes remain in the blazing sunlight on half-dry banks until they dry up and die. It would seem that after they pass a certain irradiation and temperature threshold, their self-preservation instinct fails them. Like all poikilothermic animals, leeches like solar radiation exposure. Still, they should only be given moderate doses of sunlight to prevent their untimely death.

Leeches sometimes surface for no apparent reason and "swim laps" in the warm and sunny upper water zone (if the pond water and vegetation allow them). When swimming, leeches do not create horizontal waves like most fish, but generate dolphinlike, vertical sinus waves with their body stretched long and flat. This swimming activity is a sign that the leech is hungry.

A satiated leech behaves very differently from a hungry leech [29]. After a meal, the leech will retreat immediately to the bottom of the pond and crawl under a leaf or a rock or will slip into a dark crevice to digest its food in peace. Blood-filled leeches need to find safe, dark hiding places to protect themselves from hungry predators of their own or a different species. If anyone (e.g., the patient) wishes to keep a leech that has finished feeding, the leech must be placed in a separate container to protect it from its hungry relatives. Apart from water, the container should also provide comfortable hiding places (rocks, etc.) for the leeches.

In addition to the detection of movement, temperature, and shadows, the emission of specific substances from the blood also appears to play a role in the localization of prey by leeches. This is supported by the observation that approximately two to three weeks after feeding, satiated leeches are no longer attacked by other leeches, presumably because they no longer excrete telltale substances. This cannibalistic behavior may serve to help the leeches raise their young when the available food supply is scarce [27]. If attacked by only one leech, the attacked leech has a good chance of surviving thanks to its excellent regeneration capacity. After or during such attacks, the assaulted leech usually regurgitates blood. It may do this to create a diversion in order to flee. The same strategy can often be observed in older leeches attempting to protect themselves against too rude attacks by young leeches. This is one of the reasons why the linen bags or water in which leeches are transported may be stained with blood.

If there is more than one attacker, which can happen in a very dense population, the leech usually dies of its injuries or of subsequent complications.

The first digestion phase can take up to three months, at the end of which the first signs of an appetite reappear and saliva production peaks. Once fully satiated, the leech can survive up to two years or more without another meal. Depending on the age of the leech, it may take 3–18 months for completion of digestion and 4–21 months for full depletion of the stomach [19]. A calm "lifestyle" makes these long periods of starvation possible. Optimal utilization of food is achieved through diverticulation of the leech stomach, which creates an extremely large area in which to store food, and by lowering the metabolism through periods of rest.

Peace and quiet are essential for leech survival and reproduction. When kept in a spherical aquarium[7], leeches usually seek out a quiet, dark, protected hiding place between rocks on the floor of the aquarium. They also prefer shady positions when staking out prey. At first glance, a leech breeding pond may appear completely empty until one makes waves in the water. Then, often within a few seconds, hundreds of leeches will start swimming toward the source of the disturbance.

The leech must feed and drop off quickly before its host leaves the pond. Otherwise, it runs the risk of being stranded on dry land, where it will die of dehydration within a relatively short space of time (a few hours). Consequently, the leech must rapidly compare taste, temperature, and movement characteristics of its potential host (e.g., the pulse or fight-or-flight reactions) with a "target host profile" to determine the potential host's suitability for feeding. A leech must sense heat in order to bite. The ideal temperature range is 35–40°C, corresponding to the body temperature of mammals [29]. If the measured parameters fit the desired host profile, the leech quickly bites the target. It attaches its oral sucker perpendicular to the skin with the rest of its body dangling down, forming the characteristic hook shape (Fig. 3.**8a–c**). This hook shape is a sure sign that the leech has bitten. It then saws its three oval jaws back and forth in a rhythmic motion to slice through the skin. The jaws saw back and forth at a rate of roughly twice per second, assisted by the synchronous peristaltic movements of pharynx. The leech keeps feeding until the stretch receptors in its body wall signal that it is time to stop.

7 Because spherical aquariums allow the leeches to swim around without the stress of constantly turning corners, they are better suited for leech-keeping than rectangular aquariums.

Fig. 3.**8a** **View of a leech that has just bitten its host.** Total length of the animal is approximately 4 cm. The oral sucker (right) fans out during the biting and feeding process. The rear sucker (left) is used for attachment purposes only. The body surface is now relatively dry and the skin is folded like an accordion, especially in the anterior region. (Photo by M. Roth)

Fig. 3.**8b** **View of the leech during feeding.** Total length of the animal is approximately 10 cm. The front sucker (right) is attached perpendicular to the skin surface. The leech sucker and pharynx form the characteristic "hook sign," which shows that the leech has "docked on" successfully. The rear sucker (left) is somewhat larger than the front sucker and is exclusively used for adhesion purposes. During the feeding process, the blood is transported into the stomach in rhythmic contraction waves. At this early stage of feeding, the skin is still folded like an accordion. The surface is shiny due to the excretion of fluid components of the blood. (Photo by E. Schulte)

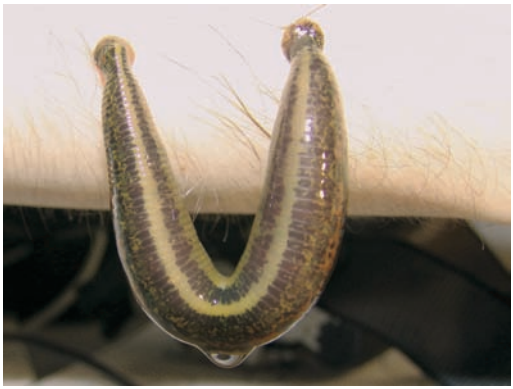

Fig. 3.**8c** **View of the leech just before completion of feeding.** Total length of the animal is approximately 10 cm. The front sucker (left) is approximately 0.6 cm in diameter. The skin, which was initially folded like an accordion, is now distended and smooth due to the ingested meal. The surface of the skin is now wet and droplets of moisture have formed. The moderate to large amounts of excreted fluid consist of fluid (serum) from the host's blood. When its stomach is full, the leech can weigh up to 10 times its original body weight. (Photo by E. Schulte)

Leech feeding is compulsive behavior [29]. It is hard to stop a leech from feeding, even by pulling on it or by applying other strong stimuli. If one cuts a feeding leech so that the ingested blood seeps out of its body, the leech will go on feeding for hours. This trait is exploited in the therapeutic technique called *bdellotomy*. First of all, this practice is cruel. Secondly, its therapeutic value is questionable because it does not increase the quantity of secreted saliva, and leech saliva keeps the wound open for several hours, anyway.

After a treatment, which is, after all, feeding time for the leech, the animal may regurgitate blood or even die. No diagnostic correlation between these events and the composition of the ingested blood has been identified based on the available literature or on the reports we have received. One reason may be that the clinical setting allows the leech to feed much more peacefully and extensively than it normally would in its natural habitat. Therefore, the leech tends to feed for longer and overeat. Overfeeding is associated with the risk of having a large clot of host blood form in the leech's stomach. Since there is not enough anticoagulant saliva left to dissolve the clot, the leech must resort to regurgitation. If this does not work, the clot often forms a

visible nodule of hardening and constriction that almost always ends fatally. When inspecting leech containers, reddish discoloration of the water due to regurgitation must be distinguished from greenish brown discoloration due to defecation. To osmotically assist leech digestion, the leech-keeper can dissolve roughly 1–2 g of sea salt in leech water and add it to the container.

Refusal to feed does not necessarily mean that a leech is not hungry (see p. 36).[8] Once satiated, the leech changes its behavior completely. It then avoids warm places, no longer reacts to water movements and chemical stimuli such as blood or sweat, and seeks out dark places at the bottom of the body of water.

Leeches require a minimum temperature of roughly 28°C for reproduction. Other than that they do not make any specific demands as regards temperature prior to their therapeutic use, although large fluctuations in temperature should be avoided. In nature, leeches survive scorching hot summers and extremely cold winters in mountain ponds. Cyclic temperature variations appear to be beneficial to the leech. Revitalization of leech populations can frequently be observed after a cold winter. The fact that leech activity increases and decreases depending on the temperature should be considered in treatment planning. It may be advisable to refrigerate the leeches and to perform the treatment in a cool place on hot summer days and to do the opposite in the winter months. Heat can make the leeches overactive, while cold can make them sluggish. The optimal temperature range for long-term maintenance of leeches used for medicinal purposes is 4–8°C, but room temperature is also acceptable. The fact that the bacterial growth rate also increases and decreases with temperature is another factor to consider.

Leeches are capable of learning. If you keep pushing them back into the water when they try to get out of the container, they will eventually stop attempting to escape [3]. This learning process occurs in three stages. When first placed in a container, they are restless and keep trying to get out. Leeches are true “escape artists.” They can change their body shape to fit through tiny holes and cracks. It is especially important to keep the lid on tight at this stage. In the second stage, the leeches become less restless. Their

8 Leeches are normally satiated and disinterested in eating for at least 3 months after a big meal. Leeches should be allowed to rest for at least this long before being sold to pharmacists and leech therapist.

initial escape attempts have failed and they have learned that it is impossible to escape. However, they will still try to escape whenever the opportunity presents itself. The absence of the lid usually does not go unnoticed for long! If they manage to escape, the leeches head straight for a dark hiding place, where they will die of dehydration if not found soon. Because they shrink when they lose water, they are easy to overlook. In the third stage, the leeches have almost completely abandoned the idea of escape. Now you can leave the container open, even for days at a time, and the animals will not try to get out. The fact that there was a way out seems to be almost completely erased from their memory. When left completely undisturbed in a suitable environment in a fishbowl for one or two months, even hungry and very active leeches will forget there was such an opportunity, even if you make big waves in the water. Dictated by their current experience, they will simply swim around the fishbowl unless one of the leeches comes up with the idea of trying to swim to the top. Then the others usually follow. Of course, this characteristic of leech behavior should never be used as an excuse to leave the leech container open!

Reproduction

Hirudo medicinalis and *Hirudo verbana* are not simultaneously hermaphroditic, but protandrous. In other words, they are first male and later female (see Fig. 3.**2** for a description of sex organs). Medicinal leeches reach sexual maturity at the age of two to four years, depending on the feeding frequency and quality of the food they consume. Mammalian blood seems to be essential for their sexual maturation. Leeches do not reproduce by self-fertilization but copulate with other leeches. Copulation normally takes place in the summer months, either in or out of the water, and can last up to 18 hours [19]. Since leeches can store sperm in their ovaries, the time between copulation and egg-laying can range from one to nine months (Fig. 3.**6**). The eggs are laid in cocoons, which are usually deposited in tunnels burrowed in the soil on the pond banks. The cocoons are produced by the clitellum, a gland-rich area located in the anterior third of the leech body. The clitellum secretes a viscous fluid, which is whipped to a creamy consistency by rapid muscle contractions. The leech then injects 10–30 eggs and a nutritive albumin substance called *hirudoin* into the cocoon. After the leech withdraws, hi-

rudoin gradually hardens and changes color from white to yellowish brown. The deposited cocoon has a fine inner lining and is filled with a yellowish brown, spongy protein substance. The cocoon stores water and protects the embryos from dehydration.

Whilst emerging from the spongy mass of the cocoon, the mother makes two small holes at each end of the now oval cocoon. The holes are roughly 0.5–1 mm in diameter and help the young leeches break free of the cocoon. Upon completion of development, the newly hatched leeches are roughly 1–2 cm in length and 1–1.5 mm in diameter. They do not undergo metamorphosis after hatching. When they hatch, their body is basically the same as that of the adult leech, except that they lack sex organs (Fig. 3.**9**). The duration of embryogenesis is extremely temperature-dependent, and may last anywhere from a few days to an entire winter. At the age of around three weeks, young leeches are able to pierce the skin of their prey. We have seen young leeches survive without food for up to six months after hatching. Young leeches have also been observed to return to a nearby cocoon, perhaps in order to feed on yolk. The fact that groups of young leeches sometimes form clusters in the soil on pond banks may be an extension of this behavior (Fig. 3.**9**) [28].

All mature leeches can lay eight or more cocoons within a period of 5–12 days in one summer. Like all parasites, they produce a relatively large number of progeny because they are exposed to several life-threatening attacks.

Fig. 3.**9** **Cluster of young leeches in peat substrate.** The animals are approximately four weeks old. Young leeches are fully developed (but not sexually mature) when they hatch, and they do not undergo metamorphosis. Young leeches and adult leeches form clusters under different conditions. Side length: 2 cm. (Photo by M. Roth)

Assuming a leech lays four cocoons containing 15 eggs each year, this would amount to 60 offspring per year. A large proportion of the offspring die before completion of development due to starvation, predation, and disease.

Medicinal Leech-Keeping and Breeding at Our Breeding Center

Comprehensive and precise knowledge of the behavior, biology, and ecology of leeches provides the basis for proper leech rearing, breeding, and maintenance. For both animal and patient welfare, this knowledge should be applied as fully as possible and not stripped to the bare necessities. This strategy is based on the simple experience and repeated observations that animal protection, endangered species protection, and quality management are by no means contrary to good biotherapeutics. Anything that promotes the growth and well-being of the leech promotes leech health, vitality, saliva composition, and appetite and, thus, is also beneficial to leech therapy. The one exception is microbial organisms, however. While relatively large quantities of specific bacteria are beneficial to the leech, the bacteria count in leeches to be used for therapeutic purposes should be kept to a minimum.

Consistent maintenance of domestically bred and imported leeches in a microbiologically and otherwise controlled and beneficial environment (e.g., in greenhouse ponds; see Fig. 3.**10**) keeps healthy bacteria in an ecological balance, stimulates leech saliva production, and ensures optimal suction strength. Measures should be taken to reduce the number of internal and external bacteria in leeches before their therapeutic use. After their last meal (e.g., blood from pigs raised under biologically controlled conditions), the leeches should be deprived of food for an extended period at a suitable temperature. This serves to eliminate foreign bacteria. Afterward, physiological bacteria, for example *Aeromonas* (see p. 143 ff), also decrease in number and are completely eliminated in most cases within six months to a year. However, the complete loss of *Aeromonas* generally leads to a massive loss of vitality for reasons that are still unclear.[9] Fasting also increases the animals'

9 *Aeromonas* may be coresponsible for the practical antibiotic situation in the leech intestine and stomach. Therefore, if complete elimination is to occur, we keep this period as short as possible.

Fig. 3.**10** **Leech breeding ponds at the ZAUG facility.** The ecology of the ponds fulfills the natural requirements of *Hirudo medicinalis*. Cocoons are laid in an area along the bank on the right. Camouflage nets protect the leeches from excessive sun exposure. The pretreated water is continuously cleaned by different types of filters. This helps to keep the natural bacterial flora in balance. (Photo by M. Roth)

readiness to feed, and the number of antithrombin units in leech saliva peaks after around three months of fasting [39].

A reduction in skin bacteria is achieved by gradually exchanging the leech water to continuously decrease the number of bacteria until the water is ultimately bacteria-free. Leech water can be kept germ-free by creating an environment which pathogens cannot enter and in which they cannot multiply.[10] Shortly before shipping, the leeches are washed to remove the remaining bacteria-infested skins. New methods for gentle preshipping leech skin disinfection are currently being tried and tested. Another agent is also being developed that supposedly allows the leech therapist to disinfect the leeches directly before use without causing any loss of vitality or therapeutic quality.

At our breeding center, the leeches deposit their cocoons in special land zones in the breeding ponds when all the conditions are right. Leeches are

10 Special surface materials and water filters serve to keep organisms such as *Pseudomonas aeruginosa* out of the system.

very particular about water quality, noise levels, substrate composition, feeding status, daylight hours, flora, fauna, and several other things. If they feel disturbed, they will not reproduce. We have learned this the hard way. Once, when the noise and distraction of work on a new sewage line exceeded the leeches' tolerance limit, they "punished" us by reducing cocoon production by one third.

Alternatively, leeches can be bred in aquariums. Only a few leeches are placed in each aquarium and encouraged to breed. The cocoons are deposited in areas reserved especially for this purpose.

The cocoons from these different sources are collected and allowed to hatch. We prefer to let Nature run its course and do not cut open the cocoons prematurely.

To keep the water clean and to prevent cannibalism, among other reasons, leeches are fed out of the water at our facility. The blood is given in pig bladders or intestines, linen cloths, or other suitable materials, depending on the age of the animal and the feeding method used. After a few days, the fed leeches are returned to their biotope or are transferred to a special feeding pond. After roughly 15 further feeding steps and a fasting period of no less than three months, the animals must complete a "purification stage" before being sold. Leeches to be used for breeding and imported leeches undergo an essentially identical but substantially shorter procedure, which varies depending on the feeding status and size of the leech. Relevant leech and water parameters are monitored during all of these steps. In particular, frequent microbiological analyses are performed to closely monitor the animals and the water during sensitive stages.

Careful handling of the animals is the basis of the success and high quality of our certified leech breeding center. We feel that creating a win-win situation for leeches and humans is the best way to ensure successful long-term use of this valuable resource in a manner that is in keeping with the times. This is rounded off by taking back used leeches and "putting them out to pasture." By applying this strategy, we hope to return the offspring to a suitable biotope to promote the development of the species.

Summary of Leech-Keeping Practice

- Leeches should be ordered early so they can have adequate time to rest before use. The leeches should ideally arrive two to three days ahead of the scheduled day of treatment. Ordering a surplus supply of leeches is not recommended unless adequate personnel and equipment are available to take care of them properly.
- Dead or sick leeches must be sorted out on arrival. Disease symptoms include: foul smell, limp and flabby skin consistency, pale skin, hard spots, nodules or strictures, head swelling, ulcers, pustules, red lips, white mucus covering, injuries, and traces of blood in some cases [33].
- When removed from the shipping container, the leeches should be washed under a gentle spray of lukewarm water.
- The size of the leech is primarily dependent on its age and feeding status. Medium-sized leeches are generally selected for leech therapy in humans. These individuals are roughly 5–7 cm long in the relaxed state. To reduce potential scarring and other problems, smaller leeches are used for treatments in the facial region or for other special applications. Larger leeches are also used in veterinary medicine, e.g., for horses.
- Recommended supplies for leech-keeping:
  1. Leech container and accessories

     The container can be purchased or made by the leech-keeper. Glass containers make it easier to visually inspect the leeches, but stoneware containers have the advantage of being heat-sterilizable. After each washing, all traces of disinfectant or detergent must be completely removed. Two- to three-liter canning jars filled roughly three quarters full of water can be used for temporary leech storage. One liter of water is sufficient for short-term leech storage (two to three weeks maximum with frequent water changes) of approximately 15–20 leeches. Special leech containers with a perforated insert are well-suited to leech storage. For longer-term storage, the number of leeches should be reduced accordingly. Calcium-free stones should be placed on the floor of the container. The stones should have sharp edges to assist the leeches with molting. Since leeches are able to escape through the tiniest of cracks, the container cover must be 100% "leech-proof." Gauze, cheesecloth, and fine-meshed synthetic netting, etc. are good cover materials. The edges of the covering should be tightly secured with an elastic band.

ZAUG GmbH, a leech breeding company in Biebertal, Germany, supplies two types of leech container (Fig. 3.**11 a, b**): One is made of glass ("Leech Eye") and the other of special clay ("Leech Pot"). The lid of the Leech Eye functions like an optical lens. The system comes complete with semiprecious stones and Canadian waterweed, a hard-leaved plant, to facilitate molting. The plants also absorb the products of leech metabolism and produce oxygen. This complete system allows 30 leeches to be kept for very long periods with little or no maintenance work required. The advantage of the Leech Eye system is that it gives you a continuous view of the splendidly colored leeches through a lens. This can be helpful in "desensitizing" skeptical or anxious patients. The Leech Eye is also a pretty desktop eyecatcher.

The Leech Pot can be recommended for practices with a high throughput of leeches. This system offers the advantages of easier cleaning and leech removal. The perforations of the pot insert are punched so as to create sharp edges that help the leeches to scrape and strip off their old skin.

Because of their cannibalistic tendencies [27], the feeding status of all leeches kept in a single pot should be the same.

Fig. 3.**11a** **The "Leech Pot" manufactured by ZAUG** is made of special clay and holds up to 30 leeches. Its perforated insert has a roughened surface that helps the leeches shed their old skins. The lid of the insert is locked by means of a bayonet catch. The outer pot is filled with water, and the insert is simply lifted into or out of the pot as needed. This makes it easy to change the water. (Photo by M. Roth)

Fig. 3.**11 b** **The "Leech Eye" manufactured by ZAUG** holds up to 20 leeches. The glass bowl of the aquarium is covered by a heavy lens that allows the leeches to be observed under magnification. Semiprecious stones and plants can be set up on the bottom of the container. The Leech Eye is an aquarium mainly used for attractively displaying leeches. This is useful for familiarizing patients with the animals. However, the system is also suitable for long-term leech-keeping. (Photo by M. Roth)

2. Leech water

   Water quality requirements:
   - Chlorine-free
   - Carbonate hardness < 9 dGH (German system)
   - pH < 7
   - Ammonium < 0.5 mg/L
   - Nitrate < 25 mg/L, nitrite < 0.4 mg/L
   - No heavy metals

   Rainwater is an excellent source of water because it usually has a low pH and lacks calcium. Spring water and well water may have high calcium concentrations and must therefore be tested for chemical and microbiological content before use. If your local tap water is unsuitable for leeches (ask your water supply company about the water composition), you can manufacture leech water as follows:

   Deionized or distilled water can be used, but must be supplemented with minerals. Distilled water is cheap and can be purchased at any gas station. Add around 0.3–0.5 g of sea salt (aquarium shop) to each liter

of distilled water. This solution is very similar to artificial pond water (APW) for leeches, but is much easier to make.

If the oxygen saturation level of the water is too low, the leeches will surface. The lower half of their body usually remains in the water while the upper half is exposed to the open air for cutaneous respiration. Because leeches can switch to cutaneous respiration in times of oxygen deficiency, it is normally not necessary to install an oxygen pump.

Bottled water (noncarbonated) is also suitable for leech-keeping, but gets rather expensive over time. Do not add salt to bottled water.

3. Cleaning and changing the water

In addition to good general health, the microbiological status of the leech is also important for medical leech applications. The lower the bacterial count, the better for the patient. However, a higher bacterial count seems to be healthier for the leech. The greater the degree of sterility, the higher the biological stress on the animal. *Aeromonas bi-ovar sobria*, the main leech bacterium, is essential for leech digestion. Leeches excrete the bacterium, which settles on the walls of the leech container. If the leeches are to be used one to three days after arrival, they should be washed under a gentle shower of lukewarm water when removed from the shipping container and again two to three hours before treatment. It is convenient to use a shower head. Alternatively, a sieve, the perforated insert of the leech container, or a latex-gloved hand can be used.

When leeches are to be kept for longer periods of time, the water should be changed every other day. Clean the leech container thoroughly before refilling it in order to reduce bacterial density. Using a second container (e.g., the one used to isolate individual leeches before treatment) facilitates the procedure. Carefully changing the water at least every other day serves to minimize the bacterial count (especially the number of *Aeromonas*). For long-term leech-keeping, it is sufficient to initially change the water once a week, then change the water daily and disinfect the container three days before leech use. The container should be disinfected regularly (once a week). When disinfecting the container, remember that even very small quantities of disinfectant can be lethal for leeches. If possible, use boiling water to sterilize the container. The molted skins of the leeches form gray to white veils (depending on their mucus content) on the water, which can often be

seen when changing the water. These can easily be filtered off by pouring the water through a small strainer. Avoid exposing the leeches to big temperature differences after changing the water.

Reddish discoloration of the water may be due to regurgitation of blood or to cannibalism (leeches should only be kept with leeches of the same feeding status to prevent cannibalism). At any rate, the water should be changed if this problem is detected. If cannibalism has occurred, the culprit must be identified and removed. Greenish brown discoloration occurs due to leech defecation. In this case, the water should also be changed.

4. Leech feeding

   Since leeches can survive for up to two years without food, it is generally not necessary to feed them.

5. Temperature and light

   Extreme temperature and light changes can be detrimental to the general state of the leeches. They remain calmest and healthiest in slightly darkened, cool places (ideally around 8°C for long-term storage).

6. Quiet is important for leeches

   When left undisturbed, leeches regenerate more quickly, have a lower oxygen demand, reproduce more frequently in breeding centers, and are more willing to feed. In addition, they produce fewer impurities in the water due to reduced metabolism.

   If the leech therapist wishes to send the leeches into "retirement" after they have done their duty, they can be returned to a breeding center that maintains "retirement ponds." If the used leeches are to be killed, we recommend the gentle method of deep freezing the cold-blooded animals. After freezing, they can be placed in 90% alcohol solution if desired.

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4 The Technique of Leech Therapy

E. Wittke-Michalsen

In principle, leech therapy does not have to be performed at any specific time of day. However, for organizational reasons, it may be better to apply the leeches in the early morning or during the first half of the day because it sometimes takes up to two hours for the leeches to finish feeding. Morning appointments also ensure that the patient can be monitored for several hours and that the practice will be open for questions and additional care when needed. Patients who are reliable and experienced in monitoring the leeches themselves can be scheduled for afternoon appointments when only a few leeches are to be applied.

Certain weather conditions can affect leech behavior. For instance, it may be difficult to get the leeches to feed when it is very humid or when a storm is brewing. Great patience may be required. Humidity and barometric pressure changes can also affect patients with low blood pressure, who may develop autonomic dysregulation and circulatory problems.

The actual leech application procedure and related measures should be organized in such a way that the work can be done quietly and efficiently without pressure of time. The leech therapist should not be pressed for time. Otherwise, nervous agitation could spread from the therapist to all other parties involved.

In treatment preparation, it is very important to explain the treatment procedure in detail so that the patient will know exactly what to expect and what to do during and after leech application. Measures to reassure and relax the patient are also well taken. Overanxiety frequently causes sympathicotonia, resulting in a drop in blood flow and temperature in the extremities. This makes it harder to get the leeches to feed in peripheral sites (e.g., hand and foot joints), as we know from experience. Heat treatments to warm the target area prior to leech application can then be helpful (see below).

The following supplies are needed and should be gathered before starting a leeching session (Fig. 4.**1**):

- Fresh, unused, well-cleaned leeches (delivered at least 24 hours ahead)
- Small, sealable container for used leeches; should be partly filled with water
- Waterproof padding and towels
- Compresses, roller bandages, highly absorbent fleece material
- Adhesive tape
- Hot and cold water
- Scissors, disposable razor
- Surgical gloves
- Glass tube, small cupping device or cut-off disposable syringe if needed
- Blood pressure gauge
- Allergy medication, injection supplies, lancet or needle

Fig. 4.**1** **Materials required for leech therapy.** These materials should be gathered before starting treatment

Skin Preparation Measures

Perfumes, chemicals, and local drugs should not be applied to the skin at the intended application site for at least two days before treatment. Disinfecting the application site is not helpful because leeches are sensitive to strong odors and may not bite. It is not possible to achieve aseptic conditions without killing the leeches, anyway. It may be necessary to shave the application site if it is located in a part of the body that is densely covered with hair; it should then be shaved cleanly because sharp stubble can hinder the leech. Afterward, rub dry until the skin is rosy–hyperemization helps to get the animals to bite more quickly. Other measures to stimulate the blood flow and soften the skin (hot sponge or compress, red light, bathing the arms or feet in warm or hot water) can entice the leech to feed more quickly but are seldom necessary except when treating peripheral sites such as the joints of the foot or hand (e.g., for rhizarthrosis). Cupping is another suitable means of stimulating blood flow before treatment. Wetting the skin with water makes it easier for the leech to attach its suckers and can therefore facilitate feeding. Mostly, it is not necessary to "lure" the leech with sugar water.

Leech Application Procedure

Leech Selection

The leech therapist should only use healthy and active leeches—not those that are in the process of molting or resting lethargically at the bottom of the container. The ideal leech:

- Swims about quickly and lively in the water,
- Attaches to the handler's hand immediately when it is put in the container,
- Immediately draws up into an "O" shape when touched, and then extends the head region forward in searching movements.

Small to medium-sized leeches should preferably be used because the bites of smaller leeches are less painful and tend to heal faster.

Leech Application

The leeches should be taken out of the container by hand. Surgical gloves protect the handler from being bitten. A compress may make it easier to grasp the leech. If a leech attaches to the glove, then carefully remove the sucker. Never use tweezers or sharp instruments that could injure the leech. When treating a relatively large target area, for example a broad region of pain on the back (dermatome), several leeches can be applied at a time. Hold a large compress in one hand and place one to three leeches on the compress, then apply the leeches gently to the target area and hold down the edges of the compress. Release the compress after the patient has sensed multiple bites or local pain and rhythmic, pulsating movements can be seen in the curved neck of the leeches. Keep the target area warm and dark by loosely covering it with a towel or other material.

When treating a small target area, the leeches have to be applied one at a time. Grasp the tail region of the leech between the thumb and index finger (gently!) using a compress if necessary, and lower the head (more narrow, tapered, seeking end) to the target site. Keep guiding the leech back to the target site until it bites and starts to feed. Wetting the application site with water sometimes helps to make the leech bite faster.

If the leech attaches its sucker in the wrong place but has not bitten yet, the handler can carefully insert a fingernail under the edges of the sucker to detach it. Another good trick is to cut a hole in adhesive film and tape the film so that the hole is located over the intended application site (e.g., the thumb joint in patients with rhizarthrosis). A small glass tube, a disposable syringe with the bottom cut off or a small cupping glass can also be used to selectively apply one or more leeches to one or more target sites. Before removing the cupping glass, the handler should check to make sure that the leech has not started feeding yet.

To use an open syringe tube (2 mL or 5 mL, depending on the size of the leech), cut off the bottom of the syringe bluntly or obliquely, then smooth the edges under a flame. Now pull out the plunger and let the leech crawl in back first. Use the plunger or a piece of gauze to push the leech in just far enough that its head is still touching the application site. Once the leech starts to feed, take it out of the syringe so that it has adequate room to expand during feeding.

If the leech fails to bite for no apparent reason, it generally helps to prick the patient's skin with a sterile needle or lancet to draw a few drops of blood, which leeches find irresistible.

Note:
If a leech comes into contact with a patient's blood but fails to bite, it cannot, under any circumstances, be used on another patient and also must not be returned to the jar of fresh leeches!

Feeding Process

The leech should be left undisturbed while feeding. If possible, it should be covered with a compress and cotton padding to protect it from cold and light and to prevent the patient's skin from cooling. The covering material also absorbs the aqueous fluids the leech secretes while feeding (water and excess blood serum). The patient should be placed in a comfortable position, and the leech should have enough space to feed without the risk of being detached or crushed.

Note:
The blood serum secreted by the leech is just as potentially infectious as the blood itself. The leech therapist must therefore take the necessary precautions.

The leech will let go of its host as soon as it has finished feeding, which normally takes around 20–60 minutes. In rare cases, the leech may finish in as little as 10 minutes in parts of the body that are engorged with blood, but under unfavorable conditions, the leech may feed for up to two hours. Sometimes the satiated leech will remain attached and motionless. Gently tapping the leech or stroking it with a compress can help prompt the leech to wake up and continue feeding or detach itself. Never use force to make the leech loosen its bite! This could lead to infectious complications. Undue force could also make the leech regurgitate its stomach contents into the

wound, a major cause of infection. The right way to get the leech to let go is to gently shake its entire body several times or to gently loosen the supporting rear sucker with a fingernail so that the leech is pulled down by its own body weight. The leech will then drop off the patient of its own accord.

We strongly advise against using salt or other substances to make the leech let go by hurting or startling it. This can likewise make the leech regurgitate its stomach contents into the wound, resulting in wound infection.

Aftercare

The tripartite jaw of the leech makes a three-pronged bite wound. After the leech has dropped off, it usually takes 3–12 hours for the wound to stop bleeding. However, afterbleeding can last more than 24 hours when larger leeches are used. The slow drainage of blood is an important part of the treatment; in most cases, the amount of blood lost is of no systemic relevance. In our experience, premature stoppage of bleeding normally results in poorer treatment results and a higher rate of infection. The drainage of blood reduces venous congestion and prevents complications by washing out any bacteria that may have entered the wound.

When there is a good outflow of blood after leech feeding, the therapist should first cover the wound loosely and check the extent of bleeding 15–30 minutes later. If satisfactory, a loose dressing is applied and secured. The alleviation and improvement of symptoms in response to treatment may induce the patients to overexert themselves, which could increase the bleeding. As a precaution, patients should be advised to avoid strenuous physical activity until the bleeding stops naturally. Patients should also be advised not to increase their intake of fluids, as this could stimulate lymph flow, thus leading to increased water excretion. The patients should also be warned that their blood pressure will be slightly lower after treatment due to posttreatment resting and wound bleeding.

The primary dressing should consist of a sterile pad or compress covered by several centimeters of cellulose or gauze padding, which should be wide and thick enough to absorb all the blood oozing from the wound. The layers of padding should be loosely secured with a gauze bandage that is not so tight that it obstructs the blood flow. When treating large areas, especially in the trunk region, it is easier to secure the bandage using a towel held in place with safety pins or adhesive tape. The patient should be advised to

wear easy-care clothing that fits loosely enough to accommodate the thick dressing applied on the day of treatment. The bleeding usually stops on the following day, and a smaller dressing can then be used. When changing the dressings, a small amount of bleeding can occur if the scab is accidentally loosened.

The scabs come off by themselves after a week or so. In the meantime, the wound should be covered with an adhesive bandage to prevent infection due to scratching if the wound starts to itch (see Chapter 9, p. 108) and to protect the wound from traction and shearing forces from clothing. The patient should also avoid extended exposure to water in the next few days to keep the scabs from loosening prematurely. Waterproof bandages have proved to be effective in patients who plan to do hydrotherapy or go swimming a few days after leech application; the waterproof bandage should subsequently be replaced with a normal Band-Aid.

We recommend giving the patient an instruction leaflet (see Appendix) explaining the do's and dont's; the therapist should also note issuance of the instruction leaflet in the patient records. In addition, the patient should also be given an (emergency) phone number to call in case adverse effects should occur.

Bite wounds are, of course, an inevitable consequence of leeching, and bite marks may leave scars in patients who tend to develop keloids. Depending on the skin type, depigmentation generally occurs in the bite region and lasts a variable period of time. The edges of the three-pronged wound swell over a period of 12–48 hours, during which the patient may feel slight tension, heat, and reddening due to dilation of the blood vessels. A slight tearing and pulsating sensation may also be perceived. The wound area becomes discolored like a normal bruise. It initially turns pale red to violet and then turns yellow after around two weeks. Discoloration is normal—it is not a sign of infection and does not need treatment! The bite site will be recognizable for a while longer. It quickly shrinks in size and turns pale and should no longer be visible after a few weeks. The healing leech bite is frequently associated with a variable degree of itching similar to that of a bigger mosquito bite. Wet compresses soaked in vinegar–water solution or curds can alleviate severe itching.

Excessive bleeding is a rare complication of leeching. The historically known cases can be attributed to the use of excessive quantities of leeches and/or disregarding contraindications. A large leech may be able to cause

severe blood loss if applied to a major blood vessel situated near the body surface. The simplest and most reliable way to stop the bleeding is to compress the wound by means of a pressure bandage. If needed, wound suture or cauterization is even more efficient.

The most frequent complication of leeching is secondary wound infection, the main causes of which are premature stoppage of bleeding and scab loosening due to premature dressing changes or scratching, in which case skin bacteria can infiltrate the wound. Therefore, it is especially important to mentally prepare the patient for itching and to prevent scratching by applying suitable dressings. Particular caution is required when the wound is located in a part of the body where mechanical stimuli aggravate the itching, i.e., in places where clothing constantly rubs against the skin.

5 Indications for Leech Therapy

P. Flecken, A. Michalsen

Venous Disease; Varicose Veins

Venous disease is one of the best-established traditional indications for leech therapy. There is a plethora of case reports and empirical studies on the subject, including clinical investigations of the efficacy of leeching for postoperative prevention of thrombosis before the advent of heparin, which is now the standard prophylactic agent. The postoperative use of leeches for prevention of thrombosis was proposed by the French surgeon Termier as far back as the 1920s. His recommendation was first adopted in France and was later implemented successfully in numerous hospitals around the world. In addition to its fibrinolytic and viscosity-enhancing effects in the blood, leeching also has bactericidal and some spasmolytic activity that may have a very positive effect on the patient's general condition. Leeching was therefore a permanent institution at many hospitals for many years and was readily performed even though it was relatively time-consuming in terms of changing the dressing and caring for the animals.

In the end, comparative studies from this period were unable to demonstrate that leech therapy could reliably prevent thromboembolism. This was presumably due to the unreliable pharmacokinetics and poorly controllable anticoagulatory effects of leeching. After the advent of heparin, leeching rapidly lost its foothold in thrombosis prophylaxis and is no longer used for this indication today. In deep vein thrombosis, the systemic effects of leeches are insufficient; hence, it must be assumed that they do not have any relevant systemic fibrinolytic activity. In modern medicine, the use of leeches for adjuvant treatment of acute deep leg vein thrombosis cannot be justified because the established drugs used for initial anticoagulation constitute a contraindication for leeching.

In venous disease, medicinal leech therapy can be recommended for treatment of acute superficial phlebitis and chronic venous insufficiency (CVI) associated with varicose veins and postthrombotic symptom complex. Leech therapy is particularly useful for symptomatic treatment of varicose veins. Although it cannot eliminate the venous dilatation and valvular insufficiency of varicosis, leeching is valued as a tool for quickly alleviating the symptoms associated with the disease. In most cases, the symptoms of swelling, pain, and perceived heaviness in the region of varicose veins or perivenous tissues improve significantly after leech application. We must stress that, when used to treat symptomatic varicosis, leech therapy should be administered in combination with other effective treatment modalities, especially those for relief of venous congestion. Important pillars of chronic venous insufficiency management include weight normalization for obese patients, physical therapy, and Kneipp's system of hydrotherapy. For optimal treatment results, supportive measures (e.g., support or compression stockings and medicinal wraps) should be continued and/or incorporated into combined treatment strategies. In any case, the patient should always be advised that leech therapy improves the symptoms but not the appearance of varicose veins.

Spider-burst must be differentiated from symptomatic varicose veins. Most patients seeking treatment for this mainly asymptomatic form of venous dilatation are women expecting cosmetic improvement. Leech therapy can, in fact, improve the cosmetic appearance of spider-burst veins, but there are no reliable data for objective quantification of the treatment results. As with CVI, it is important to inform patients with spider-burst veins that leeching often does not change the appearance of their condition and that the leech bites can even result in small scars or depigmentation.

In most cases, leech application has a significantly positive effect on the course of superficial phlebitis. Patients often perceive a noticeable improvement of symptoms right after treatment. Due to the potent anti-inflammatory, blood-thinning, and lymph flow–accelerating effect of leech secretions, the symptoms of swelling and pain rapidly subside, and the local letting of blood has a decongesting effect in the affected region.

In acute phlebitis, our experience has shown that the application of a larger number of leeches in a single session achieves the best results. In chronic venous disease, on the other hand, it is better to apply a smaller number of leeches in a series of treatments.

Practical Procedure

Target sites for leech application must be identified while the patient is standing to ensure that the blood vessels are in their maximum filling state. Leeches should never be applied to a visible or palpable vein, but always perivenously, that is, slightly proximal or lateral to the vein. Once the target sites have been identified, the leeches can be applied while the patient is lying down. As soon as the bleeding has stopped and dark crusts have formed, cooling compresses should be applied to the leech bites. We have found curd or lemon wraps to be effective for this purpose; these supportive measures enhance the results of treatment and reduce and/or eliminate the itching and swelling that often occur following treatment. The patient should keep the leg elevated during the first two days after treatment. The leech therapist should specifically advise the patient never to scratch on or around the leech bites since this could cause inflammation and permanent depigmentation of the bite marks.

The "dosage" guidelines provided below should be interpreted as reference values that must be adjusted to the individual needs of each patient. Based on our experience in practice, we also recommend that leeching should not be performed on patients with venous diseases on hot days unless absolutely necessary.

Acute Phlebitis, Acute Superficial Thrombosis

Six to ten closely spaced leeches are applied perivenously. Leeching should be performed two to three times within a period of approximately one week until the symptoms have subsided completely. Blood counts should be obtained before any repeat treatments are administered.

Postthrombotic Syndrome Secondary to Deep Leg Vein Thrombosis

Leeches can be applied to the affected region for superficial adjuvant therapy (only after completion of pharmacological anticoagulant therapy!). Repeat treatments can be considered if the initial treatment resulted in good improvement of symptoms and prolonged therapeutic effects. To avoid problems with wound healing, leeches should never be applied directly to regions with marked signs of dermatitis or ulceration.

Chronic Venous Insufficiency

The symptoms of CVI (e.g., feeling of heaviness, pain, swelling, and itching in the legs) typically occur after orthostatic stress. The severity of symptoms, not the cosmetic appearance, determines the need for treatment.

Four to six leeches are evenly distributed lateral to the affected veins. The treatment should be repeated at four- to six-week intervals, i.e., after the therapeutic effect subsides. In the case of severe varicosis in the thigh and calf regions, it may be necessary to apply more leeches (10–12) around the vein in order to cover the symptomatic region adequately. Blood counts should be obtained prior to bilateral or repeat leech applications.

Special recommendations apply when treating venous ulcers in the calf and forefoot region associated with severe CVI. We advise against applying leeches directly to the ulcers, even though good results have reportedly been achieved with this practice in isolated cases. Instead, we recommend that a few leeches be applied to the healthy skin roughly 2–10 cm proximal and lateral to the edges of the ulcer wounds.

Spider-Burst Veins

The number of leeches used depends on the extent of venous dilatation. As a rule, no more than four to five leeches are required for a focal area of spider-burst veins. The leeches can be applied directly in and around the spider-burst region.

Arthrosis

Since one would not expect the primary activity of leeching to develop in the joints and joint cartilage, the effectiveness of leeching in the treatment of symptomatic joint diseases raises important questions about the mechanism of action of leech saliva. Clearly, the therapeutic action of leeching must be due to other mechanisms. As is well known, chronic pain syndromes associated with degenerative joint diseases are characterized not only by cartilage destruction accompanied by inflammatory reactions within the joint, but also involve a number of surrounding structures supporting the joint, the tendon/muscle/ligament system, and secondary changes in the periarticular connective tissues (see also Chapter 6, p. 88). Two suf-

ficiently verified physical therapy techniques for treatment of degenerative joint disease—thermotherapy and massage—target these underlying factors externally.

The "injection" of the chemicals in leech saliva into the affected tissues surrounding the joint has various beneficial effects on periarticular structures. The local anti-inflammatory and circulation-enhancing effects of leech saliva have a positive effect on the affected tissues and metabolic processes. In addition, blood and lymph drainage lead to local decongestion with further beneficial effects. The basic regulation model proposed by Pischinger may also provide a better understanding of the effects of leech therapy. While attempting to elucidate the pathogenesis of various diseases, Pischinger did not focus on cellular processes, but on the connective tissue or in protein regulation and storage [1]. Proteins are stored in the ground substance as collagens, proteoglycans, and glycosaminoglycans. If the amount of protein deposits exceeds the individually variable protein degradation capacity, alternative pathways of extracellular transport must be used, and microangiopathies, macroangiopathies, and inflammations may therefore develop. The deposits involved are protein metabolites (e.g., glycated protein end products) that cannot be broken down any further. These factors may play a role in chronic degenerative diseases associated with impaired capillary perfusion and reduced vascular–endothelial function. The impact of leeching on the postulated changes remains speculative. However, one can certainly assume that the combined effects of the different compounds in leech saliva and the local decongestive effects of leeching have a positive effect on the cell environment, and that leeches are thus able to exert a positive influence on metabolic activity in the periarticular region.

Frequency of Leech Application for Arthrosis Pain Management

The frequency of leech application is determined primarily by the patient's response to the initial treatment. In the majority of patients, the symptoms improve significantly after the first treatment. Treatment is repeated after the primary effect wears off. A large observation study conducted at the hospital in Essen, Germany, showed that, out of a total of 400 patients with arthrosis of the knee, primary leech application had no significant effect in 15 % of the patients, a positive effect that lasted three to four months in 35 % of the patients, and a positive effect that lasted from six months to more

than 12 months in the remaining 50%. In a small portion of patients (< 10%), a significant treatment effect was first observed after the second treatment. If the initial response to leech therapy is unsatisfactory, treatment should be repeated once or twice, no more than eight weeks after the initial treatment. If the patient fails to respond to three treatment attempts, further treatment attempts will probably also fail, so no more attempts should be undertaken. Since leeches can be applied repeatedly in patients who respond to the treatment, leech therapy can be used for long-term symptomatic treatment of arthrosis. However, there are no clinical studies which compare the efficacy of leech therapy to conventional therapy of arthrosis.

In practice, it is frequently the patient who informs the leech therapist that the effects of the initial leech treatment are wearing off and makes an appointment for the next treatment. The intervals between treatments generally remain the same for the individual patient. We have found a biannual rhythm of treatment to be effective for most patients with joint disease. Allergization is a rare but possible side effect of leeching. It is therefore important to watch for signs of allergization, that is, the occurrence of adverse effects following subsequent treatments. If increasing skin reactions develop over the course of treatment (see Chapter 9, p. 110), the intervals between treatments should be extended and the patient should initially be given antihistamines. If the skin reactions get worse, leech therapy should be discontinued.

Leech Application Sites and Techniques in Different Indications

Knee Arthrosis (Gonarthrosis)

A total of four to six leeches are usually applied around the affected joint (Fig. 5.**1 a, b**). One or two of the leeches should be placed on the points of maximum spontaneous or palpatory pain. Many leech therapists like to use four equally spaced periarticular points called the “eyes of the knee” as the application sites. However, the selected application sites must coincide with the points of spontaneous and palpatory pain, as well as with connective tissue sites that elicit pain when pinched. For practical reasons, the so–called Kibler's skin fold rolling test should be done beforehand to facilitate application site selection (see Fig. 6.**2**, p. 89). Joint position also determines the sites of greatest pain. Gonarthrosis patients with genu valgum (knock knees) tend to have more pain in lateral periarticular joint structures and muscle

Fig. 5.**1a, b** **Leech application sites on the knee** (**a:** From [5]; **b:** Photo by Kliniken Essen-Mitte)

insertions, and more leeches should be applied to these points accordingly. Patients with genu varum (bowlegs), on the other hand, have greater pain in medial joint structures, especially the insertion of the pes anserinus, and these sites should be targeted accordingly. If there is pain in the knee cap region (e.g., retropatellar pain syndrome), leeches can be applied directly along the edges of the patella. However, as a general rule, an adequate amount of subcutaneous tissue must be present for a successful and reliable outcome of leech therapy.

Patients with arthrosis of the knee should be advised of the importance of physical therapy. Exercises (knee training) designed to strengthen the quadriceps muscles, which is generally atrophied due to restricted use, is an important part of the overall treatment concept. The successful alleviation of pain after leech therapy is generally accompanied by a direct improvement of joint function, thus improving the general conditions for exercise. The patient should be reminded of the importance of continued exercise therapy for long-term treatment success. At the same time, the patient should also be warned to refrain from overexercising the joint on the first few days of improvement since this would undermine the effects of treatment.

Although pain localization is important when selecting the leech application sites, hirudotherapy can be successfully performed in patients without localized pain and tenderness. In this case, the four periarticular points around the knee should be used as standard application sites. Up

to now, study data do not suggest a correlation between the stage of arthrosis and the efficacy of leech therapy. In radiologically confirmed cases, success rates achieved in patients with advanced knee arthrosis and those with mild or beginning knee arthrosis and pain were equally good. Before starting treatment, imaging studies should be performed to confirm the diagnosis of arthrosis. Experience has shown that knee pain due to other causes, especially traumatic meniscopathy, responds poorly to leech therapy.

Baker cyst is a frequent secondary finding in patients with arthrosis of the knee. Clinical practice has shown that leeching frequently brings about a significant reduction in cyst size and improvement of symptoms when application sites proximal to or directly on the cyst are used.

Shoulder Arthrosis

Due to the complex structure of the shoulder joint, arthrosis of the shoulder has manifold causes that are inadequately described by the commonly used term "humeroscapular periarthritis." In leech therapy, a pragmatic regional pain management approach can be recommended. A total of four to eight leeches are generally applied to sites around the shoulder joints while targeting the points of maximum pain and trigger points. Pain points frequently reflect pain from the anterior and posterior joint capsules and the proximal course of the anterior biceps muscle. The leeches should be distributed in the front and back shoulder regions (Fig. 5.**2**). When administering the treatment on an out-patient basis, a proper dressing technique is

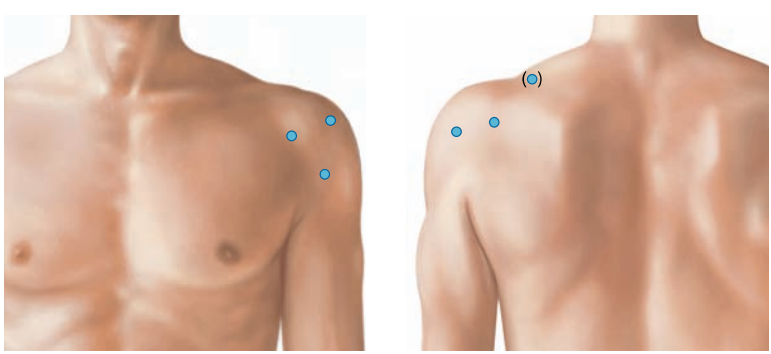

Fig. 5.**2** **Leech application sites on the shoulder** (From [5])

indispensable yet also difficult due to the complexities of the shoulder joint.

Hip Arthrosis

Unlike the knee and shoulder joints, the hip joint is poorly accessible to leech secretions because it is deeply embedded in muscle tissues. Therefore, leech therapy of the hip is generally successful only in slim patients or when there is major involvement of superficial muscles and tendons in the overall pain syndrome. Especially in obese patients, leech secretions generally cannot penetrate the thick layer of subcutaneous tissue to get near enough to the joint. Considering the size of the hip joint (and initial blood test results), eight to ten leeches are applied to the skin directly over the hip joint and greater trochanter (Fig. 5.**3**). Due to the intensity of treatment, only two initial treatment attempts should be made when testing for a treatment response.

Ankle Arthrosis

Leech therapy has also proven successful in practice in the treatment of arthroses of the ankle. Three to 6 leeches can be applied medially and laterally (Fig. 5.**4 a,b**)

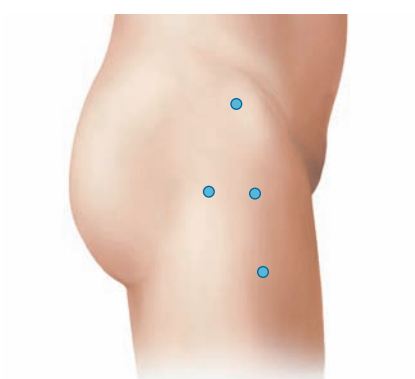

Fig. 5.**3** **Leech application sites on the hip** (From [5])

Fig. 5.**4 a, b** **Leech application sites on the ankle** (Photos by: **a**, Ullrich + Company, Renningen; **b**, Kliniken Essen-Mitte)

Small Joint Arthrosis

In principle, leeches can be successfully applied to peripheral joints of the hand and foot for treatment of arthrosis, but certain tissue conditions must be met. Leeches must not be applied to finger and toe joint regions that are not covered by a sufficient amount of subcutaneous tissue. If applied to regions with thin cutaneous and subcutaneous covers, the leeches generally will not have an adequate effect, and delayed wound healing and complications may occur. When treating the lesser metacarpophalangeal joints of the second to fifth digits, one or two leeches are normally used. Leech therapy works well in arthrosis of the saddle joint of the thumb (rhizarthrosis). One to three leeches are generally applied over the ball of the thumb, and

Fig. 5.**5** **Leech application sites on the saddle joint of the thumb** (for rhizarthrosis treatment; (from [5])

another one or two leeches are applied directly proximal to the saddle joint or at the intersection between the first and second median (acupuncture point: LI-4; Fig. 5.**5**).

The sites of pain indicated by the patient should always guide application site selection. Leeching is also an efficient modality for treating arthrosis of the first metatarsophalangeal joint and podagra. It is important to warm and stimulate blood flow in peripheral sites before applying the leeches. We recommend giving these patients a warm hand or foot bath before treatment. Leeching is not very effective in improving the symptoms of polyarthrosis of the fingers (Herberden arthrosis) and is generally not recommended for the finger region anyway because the skin is too thin.

Rheumatic Diseases

Rheumatoid Arthritis

Rheumatoid arthritis (chronic polyarthritis) is not a clear indication for leech therapy. Older studies generally do not differentiate sufficiently between inflammatory and activated degenerative joint diseases, and more recent study findings suggest that leeches should not be used to treat acute joint inflammation in patients with rheumatoid arthritis (see Chapter 6). Primary symptoms of swelling in larger proximal joints without marked reddening

or clear evidence of inflammation in laboratory tests (C-reactive protein and blood sedimentation rate), are potential indications for leeching.

Fibromyalgia Syndrome

Local techniques for symptomatic treatment of fibromyalgia should be used with restraint since they could obstruct self-help and lifestyle measures and keep the patient from coming to terms with the disease. Leech therapy has been reported to achieve good results in patients with rheumatic soft-tissue complaints and fibromyalgia syndrome many times over. However, in light of the multilocational nature of pain and unclear causes of the disease, local leech therapy would appear to be a lesser priority. The primary treatment options are classical naturopathic methods such as moderate exercise, hydrotherapy, and "mind–body medicine" (relaxation techniques, stress reduction, coming to terms with the disease), as well as psychosomatic therapy. Leech therapy may be worth a try in patients with severe yet primarily localized tenderness (e.g., in the pes anserinus of the knee joint or iliosacral joint). However, the 18 tender points used for diagnosis do not necessarily correspond to the optimal leech application sites. Leech therapy should always be incorporated in the overall treatment concept as a supplement to the primary therapy.

Tendovaginitis (Lateral Epicondylitis) and Tendinitis

Epicondylitis

Lateral epicondylitis (tennis elbow) is a common problem that frequently responds poorly to the usual conservative treatment attempts. The typical course of the disease is characterized by relapses upon resumption of the trigger activity and increasing functional restriction of the arm. Leech therapy often takes effect within a few days, and it achieves a significant and longer-lasting improvement of symptoms than conventional therapies. For acute epicondylitis, three to six leeches are placed directly over the inflamed lateral condyle and surrounding tissues while taking care to avoid veins in the vicinity (Fig. 5.**6a, b**). The treatment can be repeated after one week if necessary. After treatment, the patient should refrain from using the arm for

Fig. 5.**6 a, b** **Leech application sites on the elbow** (for treatment of lateral epicondylitis) (Photos by: **a**, Ullrich + Company; **b**, Kliniken Essen-Mitte)

a few days and keep it elevated as often as possible in order to prevent local side effects.

When lateral epicondylitis becomes chronic, compensatory strain leads to spreading of the regional pain syndrome and, ultimately, to involvement of the medial epicondyle and humeral and ulnar muscles. Therefore, these sites should also be treated in patients with chronic tennis elbow.

The efficacy of leech therapy in purely medial epicondylitis (golfer's elbow) is unclear.

Leech therapy is a simple yet effective local treatment for painful insertion tendopathies, and patients with these complaints are commonly seen in leeching practice. Inflammatory involvement of the insertion of the greater trochanter is particularly common. Tensor faciae latae syndrome can also be easily treated by applying several leeches to the region of the severely painful fascia.

There are no data and/or clear expert opinions on the efficacy of leech therapy in the treatment of tendovaginitis at other sites.

Vertebrogenic Pain Syndromes

Leech therapy is an excellent alternative for treatment of vertebrogenic pain syndromes, especially when the physical examination reveals painful hardening of muscles and connective tissue in the paravertebral region. Patients with rapid flushing (red dermographism) are also good candidates for leech therapy. Leech therapy should then be integrated into a comprehensive

treatment concept. Leech therapy often alleviates vertebrogenic pain immediately, thereby improving the baseline conditions for physical therapy and kinesitherapy, which are also required. In hospitalized patients, staff should be reminded not to perform wet physical therapy or local thermotherapy measures for a few days after leeching. When leeches are to be applied in vertebral positions, the leech therapist should carefully explain the technique of leeching because not being able to see the leeches may give the patient an added sense of insecurity.

Most therapists consider local leech therapy to be particularly useful for treatment for the following types of vertebrogenic pain:

Lower Back Pain (Lumbago)

(Lumbar disc herniation or other primary causes must be excluded before starting treatment.) With the patient lying prone or bending comfortably forward, the therapist should apply six to eight leeches on either side of the spinal column, thereby targeting the areas of most severe muscle hardening (Fig. 5.**7**). Leech therapy can be a useful adjunct to physical therapy and pain management concepts for lumboischialgia and chronic pain due to lumbar disc herniation. In these cases, the potent antiphlogistic effect of leech saliva can be very beneficial.

Fig. 5.**7** **Leech application sites on the back** (for treatment of low back pain; From [5])

Iliosacral Joint Point

Two to four leeches are applied bilaterally to the painful iliosacral joints (usually with the patient lying down).

Cervical Spine Syndrome and Cervicobrachialgia

Leech therapy is an excellent treatment alternative in patients with muscular hypertonia and pain radiating from the brachial region. It can also be considered in patients suffering from cervical cephalalgia. With the patient sitting comfortably, leeches are applied bilaterally to the painful shoulder girdle muscles and paravertebrally up to the level of C3–C5. Before applying leeches to the nuchal region, the leech therapist should first check to ensure there is an adequate thickness of subcutaneous tissue. When treating brachialgia and carpal tunnel syndrome accompanied by severe muscular pain in the shoulder girdle region, it is generally useful to apply leeches on and around acupuncture point GB-21.

Further General Indications

Sudden Hearing Loss

Leech therapy can be considered for treatment of sudden hearing loss although no scientific study data on this subject have been published up till now. In most cases, two leeches are applied: one in the region of the mastoid process, the other over the angle of the jaw in front of the ear. A total of two to three treatments can be administered at three- to four-day intervals.

Tinnitus

The available data as regards leech therapy and other complementary medicine techniques is not sufficient for an objective assessment of the treatment response in patients with this syndrome, which is difficult to treat and of unclear etiology. Numerous reports of the success of leeching have been heard in practice. However, the mechanism of action of leech therapy is still unclear, and unspecific effects (placebo effect) must also be considered. Considering the fact that the treatment possibilities for tinnitus are limited, a treatment attempt with leeches can be justified in severe cases. The sites of

leech application are the same as in sudden hearing loss, but a total of six treatments should be administered at one- to two-week intervals.

Otitis Media

The practice of leeching to treat otitis and otitis media is especially widespread in Eastern Europe and is partially backed up by study data [2]. The leech application sites correspond to those used for sudden hearing loss and tinnitus. Two treatments are administered three to four days apart.

Ocular Circulation Disorders

If leech therapy is not contraindicated because of concomitant anticoagulatory medication, one to two leeches each can be applied in the temple regions. When used to treat microangiopathy, a series of three treatments should be administered at three- to four-day intervals. For long-term improvement of ocular perfusion, leeches can initially be applied at two-week intervals and later at four-week intervals.

Peripheral Circulation Disorders / Peripheral Occlusive Arterial Disease

Peripheral occlusive arterial disease is one of the central manifestations of arteriosclerosis. Leech therapy is unlikely to produce significant improvement of the vascular lesions underlying this common disorder. The transient effects of leeching on the viscosity and rheology of the blood would also appear minor compared with those of established drug treatment options. Still, patients report time and again that leech therapy led to improvement of intermittent claudication, thereby lengthening the distances they could walk and/or reducing the intensity of their symptoms when the leeches were applied to peripheral locations, for example for treatment of gonarthrosis or varicose veins. As for the mechanism of action, leeching may work by improving connective tissue hyperalgesia or pseudoradicular factors. These observations can justify attempts with leeches in cases where other treatments have failed. Four to six leeches should be applied proximal to the affected sites. Leech therapy should only be performed in patients with Fontane stage I–II disease and should never be used to treat gangrene. When used to treat secondary ischemia-related dermatosis, leeches should

be applied significantly proximal to the affected areas of the skin. The leech therapist must beware of concomitant medications, such as clopidogrel or phenprocoumon (Marcumar), which are frequently prescribed to patients with peripheral occlusive arterial disease.

Abscesses

A number of positive case reports in the literature support the use of leeches for treatment of abscesses associated with inflammation [3]. In most cases, three to four leeches are applied to the reddened and inflamed area immediately proximal to the abscess at intervals of several days.

Hematoma

If a large bruise does not go away within a few weeks and causes discomfort, treatment with leeches can be considered. Case reports exist on the use of leeches to treat hematomas in various locations [4]. In most cases, a single treatment in which four to six leeches are placed directly on the bruise is sufficient.

Herpes Zoster

Leech therapy has established itself as a viable alternative for treatment of herpes zoster (shingles), although scientific study data are not available. Timely initiation of treatment no more than seven days after the initial appearance of symptoms is essential. Otherwise, the chances of success are poor. As a rule, the leeches are applied paravertebrally in the affected dermatome and only on the back, even if there are lesions on the front of the body. In a series of four to five treatments, four leeches each are applied from dorsal to ventral at three- to four-day intervals.

Adjuvant Therapy for Inflammatory Diseases of Internal Organs

Leech therapy can be a useful adjuvant when administered supplementary to a primary internal medical treatment. Four to six leeches are applied to the cutivisceral segment over the affected organs. Depending on the severity of the disease and the patient's response to treatment, leeching can be repeated every three to seven days.

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6 Leech Therapy in Rheumatic Disease

U. Storck

To fully understand why leech therapy works in such a wide range of applications, one must realize that the therapeutic activity of leech therapy (which is still not fully understood) is not based on a single mechanism of action, but on a combination of multiple effects. If conceived as a form of local drug therapy, a complex model would have to be used to explain the pharmacological action of leeching. The leech could then be compared to a drug that acts locally in a palm-sized region. It reduces the viscosity of the blood in that region while simultaneously dilating the blood vessels, accelerating the lymph flow, inhibiting platelet aggregation, blocking numerous mediators of tissue infection, and exerting local analgesic and anesthetic effects, thus minimizing the pain of treatment. The active role and sensitivity of the leech is a special feature of leech therapy. The leech is equipped with an extremely sensitive nervous system, which it uses to inspect the host and the host's blood. The dosage of secreted saliva is presumably adjusted in accordance with the leech's "preliminary examination findings."

Specific indications for leech therapy were described in the previous chapters (gonarthrosis, varicose veins, etc.). Based on an understanding of its multifactorial mechanisms and aspects for its symptom-specific application, leech therapy can also be recommended to treat rheumatic diseases and chronic pain syndromes of the musculoskeletal system, as we know from 35 years of experience with this treatment modality.

Muscle Tension

Muscles make up over 42% of body mass. Assessment of muscle tension is a basic part of any medical assessment of diseases of the locomotor system. The 424 striated muscles constitute the largest parenchymatous organ of the human body. In musculoskeletal mechanics, the muscles form the link between static and motor activity. Nearly all diseases of the musculoskeletal system are characterized by impairment of muscle function. Muscle tension can be defined as abnormal variation between muscle tension and muscle tone. A quantitative classification of muscle tension can be useful when assessing the appropriateness of leech therapy for treatment of patients with painful chronic and vertebrogenic muscle tension (Table 6.**1**).

Focal bands or zones of hardening within a muscle are classified according to the main muscles associated with them. In medical terminology, localized areas of hardening within a muscle are referred to as *myogelosis*. Myogelosis must be differentiated from actual muscle tension, in which a muscle group or cord exhibits a variable degree of muscle tension. Muscle tension is classified according to which the main muscle or muscle nearest the body surface is affected. The severity of muscle tension generally correlates with the response to local leech therapy.

Painful trigger points are important for treatment planning. Myofascial trigger points are important target sites for leech application. There are two types of trigger points: active and latent. Active trigger points exhibit pain spontaneously without application of external stimulus, whereas latent trigger points give rise to pain only on pressure. Moreover, trigger points must be differentiated from tender points. The 18 tender points used for diagnosis

Table 6.**1** Classification of muscle tension

Grade	Classification	Physical examination findings
0	Normal	Soft, no muscle tension
I	Mild muscle tension	Countertension slightly increased
II	Moderate muscle tension	Marked countertension
III	Severe muscle tension	Hard, maximum countertension

of fibromyalgia are not specific target sites for leech application per se (see Chapter 5, p. 77).

Specific areas of myogelosis are useful for pain localization and should be evaluated carefully before leech therapy. Myogelosis is characterized by reversible colloidal changes within a muscle. If myogelosis persists for long periods of time, destruction of muscle fibers occurs in a process characterized by increased nuclei, loss of transverse striation, and degeneration of myofibrils.

When evaluating a patient, it is important to note that tonic and phasic muscles differ with respect to the types of contractility and metabolism associated with them. Pain, inactivity, overactivity, improper use, poor posture and trauma can lead to shortening of tonic muscles and to weakening of phasic muscles. The maximum isometric muscle tension in tonic muscle fiber groups is greater than that in phasic muscle fiber groups. However, tension build-up is much faster in phasic muscles. Loss of elasticity occurs in predominantly tonic muscle groups, and predominantly phasic muscles fatigue more rapidly.

Most skeletal muscles have approximately equal fractions of tonic and phasic muscles. The iliopsoas muscle is a good example of the shortening tendency of tonic muscles. Because of its proximity to various organs in the abdomen and pelvis, it very often shortens in response to functional isorders of these organs (e.g., diseases of the colon and urogenital tract). The iliopsoas muscle can easily be tested but is difficult to palpate, and physicians frequently forget to check for iliopsoas shortening. Shortening of the iliopsoas muscle plays a major role in many pain processes. In the lumbar spinal region, psoas shortening leads to chronic hyperlordosis, which is accompanied by the well-known symptoms of facet syndrome and Baastrup disease. Local pain in the hip region is not uncommon. On closer inspection, some of these cases turn out to be iliopectineal bursitis.

The muscles in the neck and lumbar region are most frequently utilized to maintain body posture. This constant use leads to typical pathological changes in the neck region, including palpable areas of hardening within the muscles and surrounding tissues, as well as reduced range of motion of neck and shoulder muscles. This frequently leads to the development of cervicobrachialgia.

The postural mechanisms for vertebral joints in the lumbar region have greater distances to overcome. A well-developed muscular apparatus is able

to actively contract and support the body in order to counteract the normal lever effects on the lumbar spine that occur during daily activities.

If the musculature is impaired, passive postural and support mechanisms must bear the full brunt of this lever action. In all pain syndromes characterized by the described signs and symptoms, the main goal of treatment is to break the vicious circle of symptom worsening (Fig. 6.**1**).

These reflex mechanisms often have such an enduring effect that limited range of motion and pain often persist long after the cause (e.g., disc herniation) has been eliminated. When included as part of a balanced physical therapy and therapeutic exercise program, local and symptom-specific leech therapy often achieves very long-lasting effects, which can be very useful in the initial stages of multidisciplinary therapy. Chronic vertebrogenic and joint pain syndromes due to degenerative rheumatic disorders and sports injuries are some of the many practical areas of application for leeches.

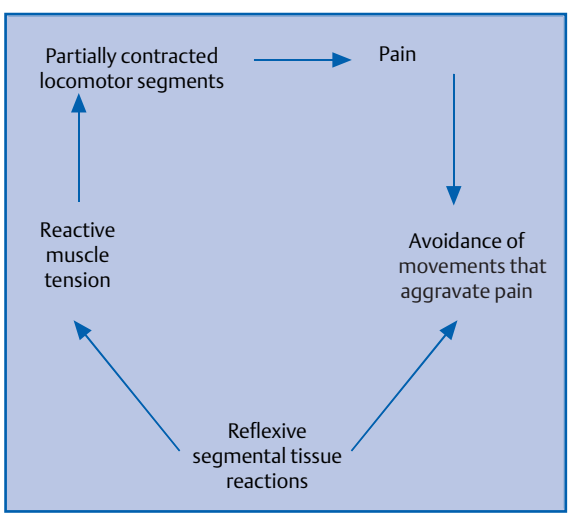

Fig. 6.**1** Vicious circle of symptom worsening

Inflammatory Reactions in Connective Tissue and Connective Tissue Zones

The connective tissue plays an important role in pain chronification processes and, thus, in treatment planning. Disorders of local metabolism are frequently implicated as the cause of myogelosis, a typical accompanying symptom. The chronic pain process affects not only the muscles, but also the subcutaneous connective tissues and fatty tissues. Strain and visceral afferent pain signals (due, e.g., to abdominal organ diseases) can also lead to painful changes (indurations) in connective tissues, as in muscles. Painful areas of connective tissue hardening are referred to as *connective tissue zones*. While the causes of connective tissue zone development and the role of sympathicotonically controlled vasomotion are not yet fully understood, trophic changes in the tissues result in clinical signs of reduced capillary perfusion.

Gonarthrosis-related painful hardening of the pes anserinus is a common example of a chronic connective tissue zone or connective tissue induration. The constant interplay between overloaded active and passive muscle tissues in the knee, one of the largest joints of the body, leads to constant irritation. This is especially common in the tibial knee region, where typical zones of connective tissue hardening nodules ("medial knee zones") can be palpated. The zones exhibit reduced mobility, hardening, and considerable pain even on gentle pressure. The pain becomes more intense in response to lifting or rolling of skin folds in the region. This is classified as a positive response to the Kibler's skin fold test (see Fig. 6.**2**). Upon visual inspection, the skin in the affected area often appears livid and/or pale and clearly distinct from its surroundings. Similar processes can be observed at the insertions of the muscles that support and move another large joint, namely the hip. Connective tissue zones can frequently be palpated around the greater trochanter.

To our surprise, many patients with unilateral coxarthrosis do not experience the most severe pain in the affected hip, but on the opposite ("wrong") side. This confirms the assumption that the associated pain may be caused not so much by the morphological changes in the joint as by the active and passive elements of movement on the side bearing the additional strain. Specific pathological changes in connective tissues, especially in the paravertebral region, may provide the decisive evidence needed to establish the indication for leech therapy.

Fig. 6.**2** Palpation and "rolling" of skin folds (Kibler's skin fold test) (Photo: Kliniken Essen-Mitte)

Empirically, most leech therapists will confirm that the presence of painful connective tissue zones correlates with a high probability of a successful outcome of leech therapy. The clinical procedure for the diagnosis of connective tissue zones is summarized in Table 6.**2**. In practice, palpation of the vertebrogenic/periarticular region generally provides excellent clues as to where the leeches should best be applied. Kibler's skin fold test is especially useful in these cases.

At our center, patients with acute arthritis, especially rheumatoid arthritis, have not been treated with leeches up to now based on the rationale that no additional blood-thinning or vasodilatory measures should be carried out at

Table 6.**2** Diagnosis of connective tissue zones

1. Visual inspection
   - — Skin color and vasomotion: Livid, pale, or congested appearance, swelling (connective tissue edema) or tissue atrophy
2. Palpation (e.g., Kibler's skin fold test)
   - — Check for adhesion to fasciae
   - — Compare volume of skin folds on both sides
   - — Assess consistency of skin fold
3. Pain assessment
   - — Pinching pain (sharp, epicritical), sometimes "pleasant pain"

a site of increased vessel filling, i.e., at the site of the pathological process. Bottenberg [1] described a method of leech therapy for erysipelas that would appear feasible for treatment of patients with acute arthritis. According to the Bottenberg method, leeches are applied 5 cm cranial to the edge of the process in order to improve venous and lymph return. After the symptoms of redness and heat have subsided in response to physical therapy and pharmacotherapy, leeching can be very useful for reducing or eliminating pain in patients with inflammatory rheumatoid arthritis. However, the primary antirheumatic therapy must not be interrupted during leech therapy.

Indurations from earlier episodes of inflammation also respond well to treatment with four to six leeches.

The shoulder is the joint with the largest range of motion, and the muscle and tendon tensile tracts there run in several different directions. (The long head of the biceps tendon must extend through the intra-articular cavity in order to reach its attachment on the supraglenoid tubercle.)

Local inflammatory processes frequently occur at the junctions to the active musculoskeletal system, often resulting in a limited range of shoulder motion. The inflammation is accompanied by the development of adhesions in active and passive caudal capsule segments, which normally fold and unfold like an accordion. In the universal nomenclature, this condition is referred to as *periarthropathia humeroscapularis*. A universal name was necessary because of the diversity of causes and terminology problems encountered when attempting to establish a detailed specific diagnosis. Areas of hardening can be palpated along the edges of the muscle groups, especially in the sites described above. Periarthropathia humeroscapularis is treated with a combination of massage, physical therapy, and other circulation-enhancing physical treatment measures. Leech treatment can also be incorporated into the treatment concept and is at least equally as effective.

Tender points within a painful insertion of the deltoid muscle are often attributed to fibromyalgia syndrome. The pectoral muscles extend from the scapula across the shoulder joint, and the rotator cuff forms the soft roof of the shoulder joint. Biomechanical disorders of the shoulder joint render both pectoral and rotator cuff muscles susceptible to inflammation. Leech therapy can be recommended for treatment of such inflammations if the affected muscles are accessible to the leeches.

Insufficiency of the muscle pump promotes the development of indurations. Indurations may occur in the musculoskeletal system, as well as in superficial veins and surrounding tissues. Leech therapy is an efficient method for treating phlebitis and residual indurations in the immediate vicinity of an inflammatory process. It is important to relieve the veins from orthostatic pressure during and up to 24 hours after leech therapy. This can be achieved by applying elastic bandages or by elevating the feet. The patient should be instructed to activate the muscle pump by contracting and relaxing the calf and thigh muscles for 10 minutes every hour while the feet are elevated. The area of induration should be significantly softer and the dark livid discoloration much paler after three to four sessions with up to six leeches. The analgesic effect should be noticeable after the first session.

In summary, musculoskeletal pain syndromes associated with secondary muscular tension, connective tissue zones, and myogelosis are suitable indications for leech therapy. In a comprehensive treatment approach, leech therapy should ideally be combined with physical therapy and physical exercise training. The rapid analgesic effects of leech therapy will establish better functional prerequisites for physical treatment measures. Leech application sites should be selected in accordance with the local findings, especially trigger points and painful areas of muscle hardening and myogelosis.

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7 Leech Therapy in Plastic Surgery

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Theory

In modern medicine, corrective plastic surgery is mainly indicated for reconstruction of cutaneous defects caused by accidents, burns, tumor resection, and postoperative wound-healing disorders. Reconstructive plastic surgery is also frequently required for elimination of functional deficits associated with scar contracture. The range of corrective surgery includes repairs using local skin flaps (proximal flaps), such as advancement and rotation flaps. Reconstructive surgery, on the other hand, encompasses the use of local skin flaps with a vascularized pedicle (e.g., pectoralis major flaps and latissimus dorsi flaps), as well as microsurgical tissue transfers using graft material from adjacent and distant sites.

Unlike the other techniques, microsurgical tissue transfer and replantation surgery require a complete interruption of blood flow to the vascularized tissue pedicle. In some cases, the blood supply must be interrupted for several hours. The blood vessels (arteries and veins) that supply the grafted tissues must therefore be reconnected by microscopic anastomosis. Latissimus dorsi flaps are frequently employed as microsurgical transplants, especially in plastic reconstruction of large defects.

In all of these techniques, the blood supply to the grafted tissues must be partly or completely (microsurgical transplants) interrupted and redirected. Traction or pressure-related changes in tissue tension or changes in blood flow patterns can therefore lead to impaired perfusion in the grafted tissues. Failure of the vascular anastomosis is one of the most feared complications of microvascular surgery. Thrombosis or insufficiency of anastomosed arteries can have various causes, such as collapse or spasm of the affected vessels. Thrombosis or insufficiency of anastomosed veins occurs less frequently. Ischemia is a typical sign of arterial thrombosis. When this complication

occurs, the transplant turns visibly pale during surgery or within a few hours after surgery. If one briefly applies gentle pressure to the ischemic transplant with one's finger (or a cotton swab), the return of capillary blood flow to the affected region will be significantly delayed or absent after one releases the pressure. If the arterial blood supply remains interrupted or inadequate, the graft will die within a few hours to days, depending on the temperature of the transplant. An ischemic transplant will sometimes have a marbleized or grayish blue appearance and a pale center. Failure of blood to emerge from an exploratory incision or puncture confirms the suspicion of ischemia.

If arterial complications occur, revision of the vascular anastomosis must be performed as quickly as possible. Ischemia is frequently caused by insufficiency of the reconnected vessels, but may also be due to vessel wall injury or trauma-related vasospasm. Since hypoxia and electrolyte imbalances may also induce vasospasms, electrolyte testing should be performed regularly during the postoperative period. However, in many cases the exact cause cannot be determined. Patients at risk for these complications should be monitored in the intensive care unit (ICU). Hemoglobin levels should also be measured to ensure adequate oxygen transport and to determine whether a blood transfusion is required. Oxygen tissue pressure in the transplant should be monitored by intravital microscopy.

In pedicle flaps, perfusion problems may develop, but imbalances between arterial supply and venous drainage are more common. Deficient venous return leads to venous congestion or—in the worse case–thrombosis. Blue discoloration of a transplant is the classic sign of venous congestion. The skin becomes increasingly mottled, especially in areas with the worst blood drainage, which is usually along the edges of the transplant. If the drainage problem persists, discoloration increases, and the transplant changes from violet to blue to black. Significant volume enlargement of the transplant further aggravates the venous insufficiency problem.

Transplant patients should therefore be monitored at frequent intervals (in the ICU), particularly in the first few hours and days after surgery. Potential complications can then receive immediate and continuous attention.

Leeching has been used for decades to alleviate perfusion problems in skin grafts, and the efficacy of leeching in this indication has been repeatedly demonstrated. Since the 1980s, leech therapy has regained recognition in the medical literature after initial publications by Upton's group in the United States and Mahaffey's team in Europe gave this treatment modality

new impetus. A publication that significantly contributed to this development and awakened the general interest in leeching in plastic surgery was a case report about the successful use of medicinal leeches to salvage the reattached ear of a boy in the United States [4].

In 1985, the right ear of a five-year-old boy from Medford, Massachusetts was bitten off by a dog. After several hours of surgery, his doctors succeeded in reattaching the ear. The blood vessels of the ear were reconnected by microscopic anastomosis. Microsurgical anastomosis of arteries requires a great deal of skill on the part of the surgeon, and reattachment of hair-thin veins, which are usually collapsed in these cases, is extremely challenging. The chances of the ear surving were slim, although one artery and multiple veins had been anastomosed. The reattached ear soon developed symptoms of venous insufficiency and started to turn blue and swell. Dr. Upton, the attending Army surgeon, applied several leeches to the affected ear region to relieve the venous congestion. His only experience with leeches until then had been in the treatment of poorly perfused skin grafts. The circulatory situation in the reattached ear then improved rapidly, and the boy was discharged from the hospital with an intact ear.

Historically, the successful use of leeches, especially Hirudo medicinalis, for treatment of insufficient flap perfusion following plastic surgery, particularly facial surgery, has been known for over a century. The first reports in the literature describe the successful application of medicinal leeches to restore circulation in nasal skin grafts [1] and skin flaps threatened by venous congestion [2]. Dieffenbach (1792–1847), a Berlin surgeon accredited as one of the fathers of modern facial surgery, also described the successful use of leeches after plastic surgery in 17 cases [7].

Today, medicinal leeches are frequently used to remedy postoperative complications in local flaps, pedicle flaps, and microsurgical transplants, especially in the facial region. Leeches are used when transplant healing is at risk because of hemodynamic complications or venous insufficiency. Venous congestion is a critical complication that requires immediate attention. Venous drainage problems frequently occur in the immediate postoperative period. Leeching can be particularly useful for restoring blood flow in crushed tissues (e.g., after horse bite injuries). After local perfusion has been restored, wound healing and integration of the transplant can proceed.

Leeches can also be applied to intraoral transplants, but intensive monitoring is required and the hospital personnel must be specifically trained.

Since the leeches cannot be "kept on a leash," potential escape routes such as the base of the tongue, larynx, and pharynx must be blocked off by tamponade. It may be necessary to continuously monitor the patient for the entire duration of treatment. When treating intubated or tracheotomied patients, proper blockage of the cuff is required.

Venous congestion of a skin flap associated with the consecutive development of thrombosis or hypoperfusion in the flap is a grave complication. Flap necrosis will occur if the circulatory situation does not improve. This can lead to infection or sepsis, ultimately resulting in total or partial loss of the transplant. The release of necrotoxins is another problem.

Medicinal leeches are used to salvage flaps with immediate postoperative symptoms of venous congestion that have not responded to initial treatment attempts. It is crucial to intervene early, i.e., in the stages where the perfusion problems are still reversible and little or no hypoxic damage has occurred. Initial or immediate measures include the removal of sutures to lower excessive wound tension, relief of pressure on the flap (decompression), and the elimination of hematoma under the flap. Further local measures include scarification (creating multiple punctures with a sterile needle) to establish blood drainage via the skin and the application of heparin-soaked sponges to prolong the drainage. Blood clots cannot develop if the congested blood is not allowed to coagulate and occlude the vessels and if drainage bleeding is established. Depending on the extent of surgery, a single intravenous dose of cortisone (intraoperatively or postoperatively) can be considered for postoperative edema prophylaxis. Cortisone should not be administered as a standard prophylactic treatment because it can increase blood coagulation, which would impede blood drainage. Continuous heparin administration can also be considered in the postoperative phase after microsurgical tissue transfer. Low doses of heparin should be administered intravenously via a perfuser. The question of whether hydroxyethyl starch (HAES) has a positive effect on transplant perfusion is still debatable, especially since a prolonged increase in arterial bleeding can be expected to occur in patients with venous insufficiency. HAES is supplied in products like HAES-steril and Plasmasteril.

Although altered, the sensibility of cutaneous pedicle flaps and sliding flaps remains largely intact. Local treatment measures therefore produce a variable degree of pain. Most patients describe the leech bite as relatively painless. This is due to the anesthetic compound secreted by the leech while

feeding. Because of the vasoactive substances in leech saliva, blood usually oozes from the bite wound for hours without the need for heparin compresses. If multiple leeching sessions are to be performed, blood counts should be monitored at close intervals. When treating neonates and infants, the volumes of blood removed by the leeches may soon become hemodynamically relevant. Caution is therefore advised when performing leeching in these patients.

We have found that the Y-shaped leech bite wound generally heals without any major problems. Most importantly, it does not cause any esthetically relevant scarring. The scope, nature, and potential risks and benefits of the leeching procedure must be fully explained to the patient in advance of treatment. This takes away the patient's apprehensions about the animals and/or this unusual form of treatment. The treatment is generally well-tolerated and accepted by well-informed patients. Continuous monitoring of the patient may be advisable when leeches are applied in the facial region (see above).

Once the leech has started to feed, it generally does not change positions until it has finished. Peristaltic body movements signal that the leech is feeding. The leech will also change positions if the primary feeding site does not have enough blood to satisfy its appetite. The patient and the leech should therefore be closely monitored to make sure that the leech does not wander off to some other part of the body. When the leech is full, it generally drops off the bite site and is not interested in finding more food.

When used for treatment of venous insufficiency, leech therapy quickly leads to a visible improvement of transplant circulation in most cases. The number of leeches applied and the number of treatment sessions required depends on the size of the transplant or target area and on the response of the transplant to the leeches. Bite wound infections have been rare occurrences in our patient populations. However, almost all of our patients undergoing minor skin graft surgeries receive perioperative "single shot" antibiotic therapy, and those undergoing major surgery receive extended antibiotic therapy. A bite wound infection may still develop if there is a persistent oxygen deficit within the transplant. When leeches are used properly, infection of the bite wound with germs from the patient's skin is more likely than infection with leech bacteria. If one forcefully detaches a feeding leech, it may regurgitate and contaminate the wound with gut bacteria. Recent studies have shown that *Aeromonas hydrophila*, a microorganism that

colonizes the leech gut, has developed increasing resistance to a number of standard antibiotics, including cephalosporins such as ticarcillin and clavulanic acid [8]. Consequently, the use of gyrase inhibitors is now recommended.

Case Studies

Case 1 (Figs. 7.1–7.3)
Female patient with a basal cell carcinoma near the tip of the nose. Treatment consisted of resection and island flap repair. The transplant exhibited signs of venous congestion after surgery. A leech was applied to drain off the excess blood. The circulatory situation improved significantly, and the transplant healed completely without any further complications.

Fig. 7.**1–3** **Two leeches were applied to this frontal lobe transplant in the nasal apex region** (left)
Healing stages. The leech application sites are still visible, the circulatory situation has normalized, and the transplant is fully integrated (middle)
View of the fully integrated transplant nine months after treatment (right)
(Photos: University Hospital Eppendorf, Hamburg)

Case 2 (Figs. 7.4–7.7)

This young female was treated for a horse bite injury in the right buccal region. The horse's broad front teeth had torn off a narrow pedicled flap of skin from the right cheek and crushed the tissues in the medial flap region. The wound was treated and sutured. Venous congestion developed in the distal part of the flap (area of livid discoloration) due to insufficiency of venous return through the crushed tissues. Leech therapy was therefore performed. The circulatory situation normalized after a single leech bite.

Fig. 7.**4** **Horse bite injury.** A horse had bitten off a narrow pedicled flap of skin from the cheek, causing this right buccal defect

Fig. 7.**5** **Livid discoloration along the edges of the wound,** reflecting serious hypoperfusion and imminent necrosis of the affected tissues

Fig. 7.**6** **Leeches were applied to the problem area of the skin flap**

Fig. 7.**7** **The same cheek a few years after treatment.** The entire flap of skin was saved and facial nerve function seems to be intact. There is no scar contracture when the patient smiles (Photos 7.**4**–7.**7**: University Hospital Eppendorf, Hamburg)

Case 3 (Fig. 7.8)

A tubed pedicle transposition flap was used for defect repair. Venous congestion developed even before transposition of the harvested flap. After multiple leech applications, the circulatory situation improved and the transplant was saved. The tubed pedicle flap technique described by the Berlin dentist Hugo Ganzer in 1917 [3] is seldom used today, but is still important in a small number of indications.

Fig. 7.**8** **After livid discoloration developed, two leeches were applied to the distal region of the tubed pedicle flap**

Case 4 (Figs. 7.9, 7.10)

A local rotation flap was used to treat this right foot defect resulting from sarcoma resection. Hypoperfusion occurred postoperatively in the critical field[1] of the transplant. Immediate leech therapy led to normalization of the circulatory situation. The entire transplant was saved.

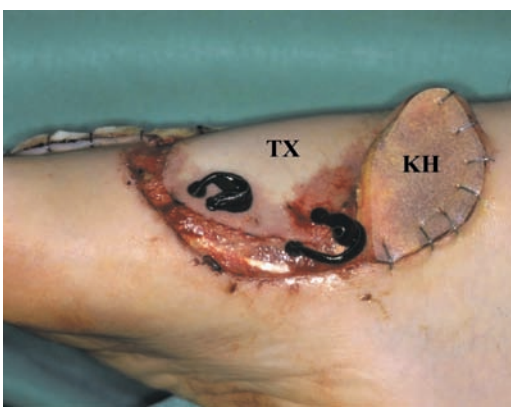

Fig. 7.**9** **Poorly perfused areas of skin along the margins of the transplant** (TX). Artificial skin transplant (KH) for temporary residual defect coverage in the immediate vicinity

1 The area where critical oxygen supply deficits are most likely to occur.

Fig. 7.**10** **Leech application has stopped the progressive demarcation of the transplant margins and prevented the tissue loss associated with flap necrosis.** The transplant appears to be well incorporated three weeks after primary surgery. The edges of the wound seem to be well supplied with blood. The split skin graft in the region of the former artificial skin also appears to be healing well

Case 5 (Figs. 7.11–7.13)

This patient had a basal cell carcinoma in the right facial region. Treatment consisted of excision and reconstruction. A multilayered advancement flap was used for buccal reconstruction and a nasolabial island flap for nasal alar reconstruction. Blood flow to the island flap was impaired after surgery. A leech was applied to the poorly perfused region of the flap. Wound healing then proceeded uneventfully without skin loss.

Fig. 7.**11–13** **A leech was applied to the poorly perfused region of the island flap** (Photos 7.**8**–7.**13**: University Hospital Eppendorf, Hamburg)

Fig. 7.**14** **Hypoperfusion with livid discoloration of the tongue.** A leech was applied near the tip of the tongue (Photo: University Hospital Eppendorf, Hamburg)

Case 6 (Fig. 7.14)

Intubated patient (tracheostoma). Treatment consisted of extensive tumor resection in the head and neck region. Lingual hypoperfusion developed after surgery, which was successfully treated by applying a single leech to the tongue. The oral cavity was blocked off by tamponade to prevent the leech from migrating into the gastrointestinal tract. The patient was continuously watched by a staff member while the leech was in place.

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8 Contraindications

P. Flecken, A. Michalsen

Knowledge of the following contraindications is imperative to prevent serious malpractice errors with negative consequences.

Hemophilia, Anticoagulant Medications

Any type of congenital or acquired hemophilia or concurrent medication with the anticoagulants Marcumar, warfarin, heparin, or heparinoids is an absolute contraindication to leech therapy. Patients should be specifically asked to subjectively assess whether they have any abnormal bleeding tendencies. In the observation study performed by researchers at Essen-Mitte Hospital, extremely prolonged bleeding from the leech bite was observed in isolated cases. Retrospective case analysis revealed that these patients had undiagnosed tendencies to increased bleeding. Aspirin and clopidogrel are not contraindications per se, but the number of leeches applied should be reduced in the first treatment session, and the patient should be asked about bleeding tendencies. If clopidogrel and aspirin are being used in combination, then clopidogrel should be discontinued five days before leech therapy if medically feasible. Bleeding time after leeching may be significantly prolonged in patients taking high-dose fish oil or gingko biloba products. These patients should also temporarily discontinue these medications before leech therapy.

Anemia

Any type of treatment involving blood removal is generally contraindicated in patients with anemia or bone-marrow suppression.

Erosive Gastritis and Potential Gastrointestinal Bleeding

Upper gastrointestinal bleeding occurred on the day after leeching in one of our patients with gastroscopically confirmed erosive gastritis. This adverse event was also reported in another patient with coronary artery disease who was taking aspirin to inhibit platelet aggregation. Therefore, leech therapy should not be performed in patients with known peptic ulcers or erosive gastritis because the potentially systemic effects of hirudin may increase the risk of gastrointestinal bleeding.

Acute Stages of Infectious Disease

Experience has shown that the administration of leech therapy during the acute stages of infectious diseases may lead to subjective weakness and impaired wound healing. According to the broader concepts of naturopathic medicine and humoral pathology, any treatment that extracts blood from patients with infectious diseases is generally considered to be counterproductive and is not recommended. In plastic and reconstructive surgery, where leeching must often be performed in patients with severe infections, antibiotics are administered concomitantly with leech therapy.

Serious Organic Disease and Immunosuppression

Leech therapy should never be performed in patients with severe, unstable organic disease or marked immunosuppression (chemotherapy). Severe, chronic yet stable organ diseases such as cirrhosis of the liver (warning: coagulation disorders!), connective tissue diseases, dialysis, immune diseases, and diseases of the blood-forming organs are relative contraindications. Leech therapy can be performed with concomitant antibiotic therapy if the patient has normal blood coagulation in the absence of anemia or immunosuppression if there is a justifiable indication (pain management). Leech therapy is contraindicated in individuals with HIV infection. No treatments involving the removal of blood should be performed in patients with cachexia of any cause. Leech therapy can be administered to patients on cor-

ticosteroids if the drug is given in low to medium doses and if the patient does not have a history of wound-healing disorders or cortisone-related skin changes ("cortisone skin").

Severe Allergic Diathesis

In patients with known protein allergies, the possibility of an allergic reaction to the foreign proteins in leech saliva must be considered. Leech therapy should not be performed in patients with a history of severe allergic diathesis and severe systemic reactions. Leech therapy can be performed with concomitant antihistamine therapy if the patient has only mild or uncertain intolerance reactions.

Pregnancy

Treatments involving the withdrawal of blood are generally contraindicated during pregnancy. Furthermore, leech therapy might result in side effects that would require treatment with chemical drugs.

General and Local Wound-Healing Disorders

The normally harmless leech bite can lead to local complications in patients with diseases associated with impaired wound healing (e.g., diabetes mellitus). The case history must be thoroughly evaluated to determine whether any relative contraindications to leech therapy exist. In patients with localized areas of impaired wound healing (e.g., leg ulcers), leeches should not be applied directly to the affected region as this may create potential foci for new ulcers.

Keloids

Leech bites can result in keloid formation in patients who tend to develop keloids. Patients should therefore be questioned about their history of scarring and keloids.

Lack of Patient Consent

Leech therapy should never be performed without the patient's consent. We recommend the use of a written informed consent form similar to the ones used for other invasive treatments. At the first consultation, the leech therapist should have the patient sign the consent form and give the patient written information describing the procedure (see Appendix).

9 Safety and Adverse Effects of Leech Therapy

A. Michalsen

Leech therapy rarely ever leads to serious complications. Observance of the contraindications mentioned in Chapter 10 and proper performance of the treatment procedure serve to minimize adverse effects. The local pain of treatment and short-term itching are regular side effects. Prior to treatment, the patient should be advised accordingly and asked to sign a consent form describing the relevant side effects (see Appendix). Prevalence data from systematic and prospective studies are only available for some of the different side effects of leech therapy. The following analysis was compiled using the data from published efficacy studies and case reports, as well as from personal observations. Quality control data on adverse events documented in more than 1000 cases treated at Essen-Mitte Hospital, mostly for treatment of degenerative joint disease, were also included in the analysis.

Local Pain During Treatment

Perceptions of the local pain of leeching vary. Most patients describe a local dragging pain that occurs immediately after the leech bites and persists for around one to five minutes. As more and more saliva is introduced into the tissues, the anesthetic effect of leech saliva begins to take effect. The intensity of the pain of the leech bite and the first phase of feeding is generally described as mild or negligible (depending on the individual's pain threshold), but some patients find the pain more intense, similar to that of a wasp sting. The perceived intensity of the leech bite varies from one individual to another. Subjective pain ratings range from "hardly noticeable" to "mild" (similar to the pain of stinging nettle) to "similar to a wasp sting" (very rare). A slight (or sometimes somewhat stronger) rhythmic pulling sensation is usually noticed for the first one to three minutes after the start of feeding.

Whether stimuli of exactly the same intensity are perceived as painful or are not perceived at all is certainly dependent on the individual's personality, but also depends on that person's concentration on the leech or attitude toward leech therapy. The size of the individual leech's jaw, the strength of the bite, the intensity of suction, and the volume and composition of the leech saliva also play a role. Many people never even notice the leech bite, for example when they are bitten under water while their attention is focused on something else. Frequently, the more anxiously the patient focuses on the leech preparing to bite, the higher the pain perception. The leech therapist should keep this in mind during the preparation phase and during treatment. A diversion can sometimes be helpful. It is also helpful to allow the patient to "get to know" "his" or "her" leech and to reassure the patient by handling the leech in a confident manner. If latex gloves must be worn for hygienic reasons, the leech therapist should never use forceps on the leech. Many patients lose their aversion to leeches when they are shown how elegantly they swim and the beautiful colored pattern on their back is pointed out. Many people report that the patient's attitude toward the leeches changes from negative to positive after a positive treatment experience. Most of the apprehensions projected onto the leech are based on archaic fears rather than on objective facts. We also advise against killing leeches in front of the patients. If the leech is to be killed after treatment, the animal should be frozen and placed in a 90% alcohol solution a few days later.

Local Itching

Transient itching at the site of the leech bite in the first few days after treatment is very common and should not be mistaken for an allergic reaction. In the study of the efficacy of leech therapy in patients with osteoarthritis of the knee described in Chapter 10 (p. 121), roughly 70% of patients treated with leeches developed local itching that lasted a mean of two days. Transient itching occurs at a comparable frequency, but stronger intensity levels in many cases where leeches were applied to more peripheral joints, for example the thumb, but at lower levels after treatment of large joints and vertebrogenic zones, according to empirical assessments. The patient hould be advised of these side effects prior to treatment. The patient should never scratch the leech bite, especially after initial wound closure,

because this frequently delays wound healing. We recommend local cooling remedies (curd wraps, cold moist wraps, vinegar wraps). For more severe itching, commercial antipruritic products (e.g., Fenistil ointment) or oral antihistamines may be used. Some leech therapists prescribe concurrent oral antihistamines for patients with a known history of severe reactions (itching and skin reddening) to leech therapy. Isolated reports describe brief recurrences of moderate itching in certain situations (e.g., high temperatures) over the course of several months after an otherwise uneventful course of leech therapy.

Hypotension and Vasovagal Attacks

Patients with a history of developing vasovagal attacks or syncope (fainting) before other invasive treatment methods may also develop such a reaction at the start of or during leech therapy. One survey showed that vasovagal attack occurred in one out of 1000 leech treatments performed at our hospital. Therefore, the leech therapist should always ask about the patient's prior history of vasovagal attack or fainting before procedures such as blood sample collection or acupuncture. To guard against vasovagal attack, the patient should drink plenty of fluids before and during treatment, and treatment should always be performed in a calming environment while the patient is lying down. Two outpatient cases of hypotension and vasodepressor syncope following leech therapy were also observed. Both patients had known arterial hypertension and were on triple antihypertensive medication, which they continued taking as usual. A few hours after leech therapy, both patients developed a brief attack of benign syncope. It is important to remember that leeching has a known antihypertensive effect when treating patients on antihypertensive medications. Patients should drink plenty of fluids. If there is a strong flow of blood from the leech bite, the patient's blood pressure should be monitored and antihypertensive medications should be adjusted as needed.

Blood Loss

Leech therapy is always associated with a certain degree of blood loss, which is clinically irrelevant in most cases. In the clinical trial by Michalsen et al. [3], the mean hemoglobin loss was 0.7 mg/dL, and clinically relevant blood loss did not occur in any of the patients studied. However, there have been isolated observations of stronger afterbleeding with a corresponding decrease in hemoglobin, particularly in cases where a leech was inadvertently applied directly to a superficial vein. According to the records of Essen-Mitte Hospital, a clinically relevant decrease in hemoglobin (> 3 mg/dL) occurred after leech therapy in two patients, one of whom required a blood transfusion (after being treated with six leeches for osteoarthritis of the knee). Asked retrospectively, one of the patients stated that she had, in her opinion, experienced prolonged wound bleeding in the past. In another case, afterbleeding from the leech bite lasted over 36 hours and had to be stopped with a cutaneous suture. Extensive coagulation tests were then performed but did not reveal any specific coagulation disorder. Prior occurrences of abnormal bleeding seem to be anamnestically important, and patients should be specifically asked about such events. Anticoagulants are important concurrent medications to watch for. If low-dose aspirin is prescribed in combination with other platelet aggregation inhibitors (clopidogrel, Iscover, Plavix) or high-dose fish oil (Omacor), a smaller number of leeches (three to four) should initially be used. Blood counts should always be obtained before starting leech therapy. To reliably prevent the loss of relevant quantities of blood, the leech therapist should never use more than 12 leeches in a single treatment session.

Impaired Wound Healing, Superinfection, and Allergies

After the leech drops off, the edges of the three-pronged wound generally swell for 12–48 hours accompanied by a feeling of local tension, heat, and reddening. Small blood spots (ecchymoses) develop below the skin around the leech bite. Larger collections of blood rarely develop. As with superficial bruising, the blood spots are initially reddish violet, then turn yellowish, and finally disappear within around two weeks. Localized inflammation,

sometimes with papulous elevation of the bite sites, is a relatively common problem that is often accompanied by itching (see above). These inflammations usually subside quickly when iced and left undisturbed. The cause of this wound-healing disorder is unknown. Improper handling, especially early stoppage of afterbleeding from the wound, squeezing the head of the leech with forceps, forceful removal of the leech before it has finished feeding, and failure to keep the animals in fresh water, have frequently been implicated as potential causes. However, this has also been observed to occur after proper leech handling in isolated cases. Theoretically, local infection with *Aeromonas hydrophila* is a potential cause, but there has been no microbiological evidence so far of the presence of *Aeromonas hydrophila* in the wound secretions from the affected patients. More severe local inflammations are most commonly caused by secondary wound contamination or irritation due to mechanical irritation, such as scratching and rubbing. The patient should be thoroughly advised of the importance of protecting the wound from mechanical irritation. According to the hospital survey, more severe localized inflammations occurred in three isolated cases: One patient developed erysipelas and two developed moderate lymphangitis. All cases resolved quickly in response to antibiotic treatment with cephalosporins and/or gyrase inhibitors. Strict adherence to contraindications and localization recommendations minimizes the risk of localized inflammation. In unclear cases where progressive and painful skin reddening develops, especially if associated with increased temperature, the leech therapist should know to administer antibiotics immediately. Pseudolymphomas may occur in rare cases; these papulous efflorescences are caused by an arthropod reaction to the leech bite [5, 4]. Currently, there is no data by which to assess the precise frequency of this adverse effect. To our knowledge, a total of three documented and confirmed cases have been reported.

It is difficult to distinguish secondary wound-healing disorders from potential allergic reactions. Precise data on the frequency of allergic reactions to leech bites are not available. Local itching, a common side effect of leeching, should not be interpreted as an allergic reaction. Unequivocal allergic reactions such as transient urticaria and locodistant swelling have been reported in a few isolated cases. However, localized symptoms, reflex erythema, and urticarial dermographism in psychovegetatively labile individuals have been observed more often. An older case report describes the occurrence of a short-term anaphylactic shock after application of six

leeches to the temple region [4]. Some leech therapists administer systemic antihistamines for treatment of local allergic reactions with (empirically) good success. However, the good response rate to antihistamines is not proof per se of an allergic cause: A certain rate of placebo response to antihistamines must also be taken into account. The possible boosting of an existing antibiotic allergy by leech therapy was also proposed in a case report [1].

When interpreting local reactions that occur following leech therapy, it is important to remember that the proteases in leech saliva release various types of nonimmunological mediators. Furthermore, such reactions can be aggravated by psychovegetative factors. All in all, there are only a few cases in which an association between leech therapy and the occurrence of allergic reactions has been proved with sufficient certainty. However, allergic reactions may potentially occur after exposure to any foreign proteins. Contact dermatitis has also been observed after use of leech ointment [2].

Short-term reactive swelling and/or tenderness of proximal lymph nodes has occasionally been reported, but most commonly in patients with delayed wound healing. These symptoms have most frequently developed in the groin region after application of leeches for treatment of the knee joint, hip joint, or varicose veins. Rapid and uneventful disappearance of lymph node swelling is described in all of the case reports.

Sepsis

Sepsis due to systemic infection with *Aeromonas hydrophila* has been repeatedly observed after leech application in reconstructive surgery indications, but not in any of the other relevant fields of use. This supports the conclusion that the risk of *Aeromonas hydrophila* sepsis is increased only in patients with severe underlying diseases or immunosuppression, which is often the case in surgical candidates for leech therapy. We therefore recommend concurrent antibiotic treatment for all surgical patients receiving leech therapy (see Chapter 7). In the remaining fields of use, primary antibiotic therapy does not appear to be necessary according to the current state of knowledge, but relevant contraindications must be observed.

Antibiotics in leech therapy
Concurrent antibiotic therapy (starting at least six hours before leech therapy) is recommended for all surgical patients. In all other indications, previous experience indicates that concurrent antibiotic therapy is not necessary. Patients with multiple comorbidities can receive antibiotics for three days (first choice: gyrase inhibitors such as ciprofloxacin or Ciprobay). Gyrase inhibitors are also indicated for treatment of significant cases of inflammation (tissue reactions that are clearly more severe than normal) or delayed occurrences of phlegmonous inflammations or lymphangitis.

Transmission of Infectious Diseases

Today, medicinal leeches are generally only used once. Therefore, there is no risk of the indirect transfer of infectious diseases from one patient to another. Primary infection with *Aeromonas hydrophila* is clinically relevant only when leeches are applied to surgical transplants. Concurrent antibiotic treatment is therefore recommended for infection prophylaxis in these cases (see above). The transmission of other bacterial or viral pathogens to humans within the context of leech therapy has not been observed so far. The leech therapist should naturally make sure to purchase leeches from suppliers who breed the leeches under controlled conditions (e.g., ZAUG in Germany).

Scarring

When left undisturbed, leech scars usually quickly shrink to hardly visible or invisible tiny three-pronged marks that disappear completely within one to three weeks. However, if wound healing is impaired due to scratching or secondary wound infection, the scars may remain visible for significantly longer periods of time. Papulous skin changes persisting for several months have also been reported in isolated cases. In one case, a permanent "arthropod reaction" was also reported to occur after leech treatment (see above).

Significant scarring may occur particularly when leeches are applied to areas with thin skin and thin layers of subcutaneous tissue or joint regions where the skin is in constant motion. The wearing of restrictive clothing after treatment, for example around the knees, can also result in scar formation.

For esthetic reasons, restraint is advised when using leeches in the facial region or in other clearly visible and cosmetically relevant parts of the body. Here, we again stress that it is necessary to thoroughly inform the patient about the potential risks of treatment, including scarring, and to obtain written informed consent from the patient before going ahead with the treatment.

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10 The Scientific Basis of Leech Therapy

A. Michalsen

Compared to conventional pharmacological and interventional treatment modalities, leech therapy has a very broad range of uses in various fields of medicine. To understand why this is so, one must analyze the potential and known mechanisms of leech therapy. The efficacy of leeching is based on a combination of multiple effects resulting in hemodilution (venesection), modification of local tissue rheology, segmental (reflex) counterirritation, and antinociception. In other words, leech saliva contains a range of bioactive substances that exert manifold pharmacological effects.

The relevance of the different underlying mechanisms varies for each clinical indication. In this chapter, the clinical indications for leech therapy will be grouped according to the primary mechanism involved. This type of classification is purely theoretical. Furthermore, the current data suggests that the simultaneous action of multiple mechanisms may be responsible for the clinical effectiveness of leeching in nonsurgical indications.

Mechanisms of Leeching and Their Clinical Correlatives

Anticoagulation and Hemodilution

When a leech bites, the bite wound immediately begins to bleed and continues to bleed for several hours. This prolonged bleeding is due to the presence of hirudin and other anticoagulant substances in leech saliva and it is the most relevant mechanism of leeching in plastic and reconstructive surgery. Leeching achieves extensive local venous drainage and improves the hemorheological characteristics of the blood to effectively counteract postoperative venous congestion and imminent tissue necrosis. Although

the secretion of hirudin by the leech only represents a local tissue injection, systemic effects of hirudin are also presumed to occur. In a cohort of 23 patients, a reduction of viscoelasticity and aggregation tendency of the blood was observed four weeks after a single leech treatment in the lumbar region, while the hematocrit and plasma viscosity values remained unchanged [5]. Considering the short plasma half-life of hirudin, the authors proposed that differential stimulation of erythropoiesis might be responsible for the long-term modulation of hemorheological parameters. However, such systemic effects of leeching are of little importance in surgical indications for leech therapy.

Leeching is no longer recommended for prevention and treatment of thrombosis. Modern drugs such as heparin and coumarin have reliably effective and controllable pharmacological effects and are now preferred for these indications.

Analgesic and Anti-inflammatory Effects

A number of the known biochemicals in leech saliva exhibited analgesic and anti-inflammatory properties in experimental studies [2, 16, 17] (see Chapter 11 for more information on the biochemistry of leech saliva). Recent studies on hirudin and thrombin inhibitors have highlighted the direct anti-inflammatory effects of these substances in addition to their known anticoagulant effects. Experimental studies by researchers at the University of Lausanne have received much attention [10]. The investigators first produced antigen-induced joint inflammation in experimental animals and then treated the animals with subcutaneous doses of recombinant PEG hirudin for 13 days. Significant scintigraphic reduction of inflammation and histological reduction of synovial thickening occurred within seven days. These findings suggest that the inhibitory effect of hirudin acts not only on the thrombin system, but also on inflammatory processes at the cellular level. In another study, they showed that hirudin inhibits a number of proinflammatory cytokines in synovial fluid [22]. In leech therapy, it is important to bear in mind that a leech bite represents only a single hirudin “injection” and that the half-life of natural hirudin is shorter than that of recombinant PEG hirudin. As already mentioned, hirudin normally works in combination with many other anti-inflammatory substances in leech saliva. This additive effect is presumably very significant.

The jaws of the leech pierce the skin so that these potent biologically active substances can penetrate into the deeper tissues. Hyaluronidase (spreading factor), an enzyme in leech saliva, further facilitates the penetration and diffusion of these pharmacologically active substances into the tissues (see Chapter 11). Experimental research data on commonly used topical antiphlogistic drugs can be used to draw certain general conclusions about the accumulation of locally administered substances in body tissues. After topical application of diclofenac gel to the knees of patients with knee joint effusions, the drug could be detected in the deep periarticular tissues and body compartments [15]. With the additive effect of hyaluronidase, it is highly probable that the antiphlogistic substances in leech saliva can penetrate deep enough to exert significant effects on periarticular myofascial structures and perhaps even on intra-articular structures. A recent study showed that periarticular myofascial structures play an important role in the development of chronic joint pain and regional pain syndromes in patients with osteoarthritis [4]. A systemic anti-inflammatory effect of leech therapy is less plausible, especially in light of the prolonged effect of a single leech bite.

Segmental and Antinociceptive Effects

As a rule, any treatment that causes irritation of the cutis and subcutis will trigger local antinociceptive and segmental effects. This is the rationale behind the use of specific antinociceptive substances such as capsaicin (Spanish pepper) in pain treatment. These mechanisms are also involved in acupuncture and in the skin stimulation techniques employed in traditional European medicine (Braunscheidt's technique, cupping, etc.). The extent to which a single leech bite activates such mechanisms is not known and is difficult to determine in experimental models. However, it would seem plausible that the antinociceptive effects of the leech bite might enhance the other primary mechanisms of leeching. The significance of segmental organization is often stressed in the historical literature. For example, one author states that leeches should be applied to the margins of the liver for treatment of hydropic liver congestion and to a defined connective tissue "headache zone" for treatment of migraines [3]. For the unbiased researcher, these theories can be interesting and merit further investigation. At present, the available study findings are insufficient to reliably determine whether there are clinical indications for leeching based on these mechanisms.

Effects on Lymph Flow and Connective Tissues

In addition to the aforementioned pharmacological effects, some investigators postulate that leeching improves lymph flow. The available data on this subject is sparse and stems from older studies [14]. Clinical experience with leech therapy in joint disease and pain management does not give any strong evidence in support of such an effect. There are no empirical reports of a specific effect of leech therapy on concomitant lymphedema. However, previous clinical studies have demonstrated the efficacy of leech therapy, even in patients without palpable tissue abnormalities or lymphedema. Likewise, some practitioners postulate that local leech therapy is especially effective in patients with so-called connective tissue zones. However, subanalyses of two large studies on leech therapy in the treatment of osteoarthritis of the knee did not show any correlation between the extent of local connective tissue zones and the clinical efficacy of treatment [13]. Based on the current state of knowledge, the effects of leech therapy on lymph flow and connective tissues seem to be of little relevance to pain management, but the stimulation of lymph flow might be more important in the treatment of symptomatic varicosis. Further clinical studies are needed for a reliable assessment of such effects.

Traditional and Constitutional Concepts of Efficacy

In European, humoral, and Arabian medicine, as well as in Ayurveda and Traditional Chinese Medicine (TCM), leeching is closely associated with the constitutional theories and concepts of disease. In these systems of medicine, local and systemic states of surplus and deficit, heat and cold are considered when assessing the patient. All of these systems describe treatments involving local skin irritation and venesection as "drainage of surplus fluids." It is theoretically possible yet methodologically difficult to analyze treatment responders according to these criteria. First of all, adequate standardization of the relevant terminology and clinical classifications is lacking. Secondly, responder analyses require a very large number of cases and a study design amenable to such an analysis. In our studies we were unable to demonstrate a correlation between the efficacy of leech therapy and initial hematocrit levels, the extent of blood extracted by the leech, or the body mass index (BMI), which were used as approximate parameters of constitution. However, no specific techniques of constitutional medicine (e.g., tongue

diagnosis) were used to evaluate the patients. Therefore, it is not possible to rate the response to leech therapy based on traditional concepts of constitutional medicine at present. Even though the models underlying these traditional concepts now have a more metaphorical sense that does not comply with modern pathophysiological concepts and action principles, the fact that they served as the basis for proper and presumably successful leech treatment for centuries must be emphasized. Comprehensive scientific analyses of leech therapy should therefore take such aspects into consideration if possible.

Proof of Efficacy in Specific Clinical Indications

Plastic and Reconstructive Surgery: Acute Postoperative Venous Congestion

Leech therapy has been used to treat acute postoperative venous congestion since the 1960s. In this indication, leeching is now an internationally established modality that can be classified as a standard treatment method (see Chapter 7). A number of published case studies, case series, and uncontrolled studies demonstrate the efficacy of leech therapy in these patients [9, 19, 23]. Venous congestion and subsequent thrombosis are serious and feared complications of skin flap transplantation and limb reconstruction surgery. The successful use of leeches to treat postoperative venous congestion after plastic and reconstructive surgery was mentioned by Dieffenbach as early as 1827 [25]. The first comprehensive international publication on the subject was by Derganc and Zuravic, who described their results in a series of 20 patients in 1960 [6]. Objective proof of the improvement of blood flow was later provided by Doppler laser studies performed by Hayden [8].

Various animal experiments, some of which had a randomized study design, have convincingly demonstrated that leech therapy improves perfusion in transplanted skin regions and is superior to other treatment modalities used to restore normal blood supply and drainage. However, controlled clinical studies are still lacking. The feasibility of performing randomized controlled trials is limited because it is hard to standardize the field of indication and the treatment procedure for postoperative venous congestion. Furthermore, the overall number of cases is very small. Because leeching is now

an established form of treatment in this indication, it would seem ethically untenable to withhold the treatment from patients in the control group of a study. Consequently, it is very unlikely that such a study will ever be performed. The situation is similar to that of numerous surgical indications where a treatment form is viewed to be the standard treatment method even though the treatment lacks the high-level proof of efficacy defined by the criteria of evidence-based medicine. Numerous observation studies and case series on the use of leech therapy to treat acute venous congestion have been published in the international literature since 1960. In spite of the lack of controlled studies, one can therefore conclude that there is sufficient clinical proof of the efficacy of leech therapy for this indication.

Thrombophlebitis and Varicose Veins

Before the advent of heparin, leech therapy was an established method for acute treatment of deep leg vein thrombosis and superficial thrombophlebitis [14]. Many older nurses and doctors from different departments remember using leeches to treat such cases. With the arrival of heparin, which was before the age of randomized controlled studies, leech therapy quickly lost much of its former significance, but it has still retained significance as a niche application for treatment of symptomatic varicosis and superficial thrombophlebitis in medical practice. A multitude of case studies and case series on this subject can be found in the older internal medicine literature. Bottenberg's book on leech therapy was an authoritative work of the times [3]. Indian researchers used technology-based methods for objective classification of the effects of leech therapy in a more recent uncontrolled clinical trial in 20 patients with venous ulcers in patients with complicated varicose veins. A single leech application reportedly led to a significant anti-edematous effect in 19 out of 20 patients and produced healing of the previously refractory venous ulcers in all patients studied [1]. Because of the lack of a control group, it is not possible to determine whether the effect of leech therapy was a specific effect. There are no other uncontrolled or controlled studies on this subject. As in many other diseases, years of successful traditional practice provide a broad base of empirical evidence of efficacy, but only little evidence that fulfils the criteria of evidence-based medicine. Controlled studies must therefore be performed in order to obtain a more specific efficacy assessment. Since leech therapy does not have cosmetic ef-

fects on varicose veins and because effective physical methods for edema treatment are available, these studies should concentrate on the efficacy of leeching in alleviating the symptoms of varicose veins and in healing venous ulcers. However, these studies cannot be conducted without financial support. Sufficient research funding is crucial for achieving scientific proof of the efficacy of leech therapy.

Arthrosis, Arthritis, and Chronic Pain Syndromes

These are clearly the predominant indications for leech therapy in modern medical practice. Historically, leeches were mainly used for treatment of arthritis urica and abscessing infectious joint diseases. For epidemiological reasons, degenerative joint diseases are more prevalent in the European population today. As their frequency has steadily increased, so these diseases have become more and more prominent in clinical leech therapy in the last decades.

Osteoarthritis of the Knee (Gonarthrosis)

Symptomatic gonarthrosis is one of the best studied indications for leech therapy. In outpatient clinics and on hospital wards such as the former Department of Naturopathic Medicine at Moabit Hospital in Berlin, leech therapy has long achieved very high subjective success ratings after single periarticular leech applications in patients with painful osteoarthritis of the knee. Our research team published a pilot study on the efficacy of leeches in the treatment of painful osteoarthritis of the knee in 2001 [12]. Sixteen consecutive patients with confirmed, long-standing cases of painful gonarthrosis that was worse on one side were included in the study. A single treatment with four to six leeches was performed in 10 patients, and standard treatment was continued in the other six. In this controlled but nonrandomized study, leech therapy achieved a rapid and significant (approximately 60%) reduction of pain compared to the control group. The difference in pain reduction became statistically significant three days after treatment and was even more pronounced four weeks after treatment. At the end of the study, pain intensity in the leech therapy group was rated "1" on a scale of 0–10. The observed course of joint pain over time is shown in Figure 10.**1**.

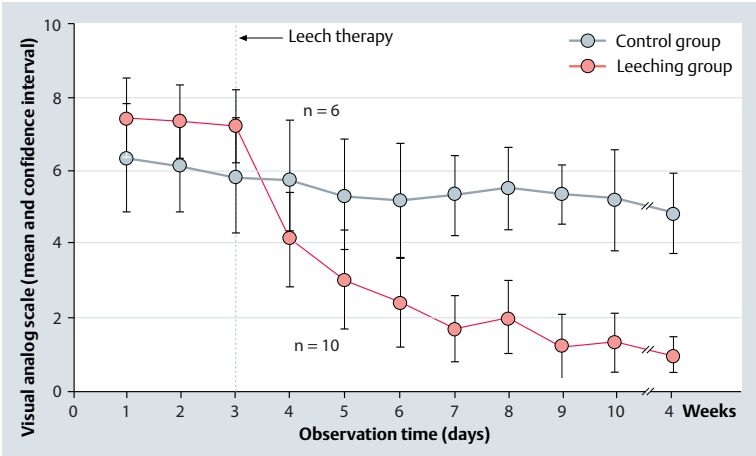

Fig. 10.**1** **Results of a controlled pilot study in patients with osteoarthritis of the knee.** Course of pain scores in patients treated with leeches versus standard treatment

Encouraged by these promising results, we initiated a larger randomized study at the Essen-Mitte Hospital with funding from the Karl and Veronica Carstens Foundation [11]. All 51 patients included in the study had long-standing radiologically and clinically confirmed osteoarthritis of the knee. The patients were randomly assigned to groups receiving a single leech treatment (n = 24) or topical diclofenac gel (n = 27). Diclofenac, the conventional standard treatment, was applied several times a day for a total of four weeks. Patients were followed for a total of three months. Symptoms were documented in detail using a validated and established questionnaire, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC visual analog scale). The WOMAC questionnaire was completed on days three, seven, 28, and 90. WOMAC total scores were also analyzed. The WOMAC questionnaire was used to obtain a pain score, joint function score, morning stiffness score, and total score. Again, the results clearly weighed in favor of leech therapy. A significant reduction of pain occurred three days after the leech treatment, and maximum pain relief was measured on day seven. At the three-month end point, the pain scores were still lower than the baseline scores. Leech therapy was clearly superior to the reference treatment

at the first two sampling dates, although the statistical significance of the difference decreased after that. During the entire study period, the WOMAC joint function, morning stiffness, and total scores of patients who received leech therapy were consistently better than those of patients in the control group. Quality of life, which was assessed at one month, was also significantly better in the leech therapy group. No serious adverse events were observed. Moderate local itching that lasted for two to three days was frequently reported. The courses of the WOMAC pain scores and joint function scores over time are shown in Figures 10.**2** and 10.**3**.

This randomized study demonstrates that leech therapy is a highly effective and reliable method for treatment of painful osteoarthritis of the knee. The fact that absolute pain reduction was slightly lower than in the pilot study can be attributed to the randomized study design. In the pilot study, the patients specified which method of treatment they wished to receive, whereas in the second study, the patients were randomly assigned to the different treatment arms. Because of the lack of blinding, placebo and suggestive effects may have been a significant influence. To test this hypothesis, all the patients in the latter study were questioned about their expectations in regard to treatment outcome directly after randomization. Not surprisingly, patients in the leech therapy group had much higher expectations than those in the diclofenac group. The outcome expectations were included in an adjusted statistical analysis, which showed that they did not affect

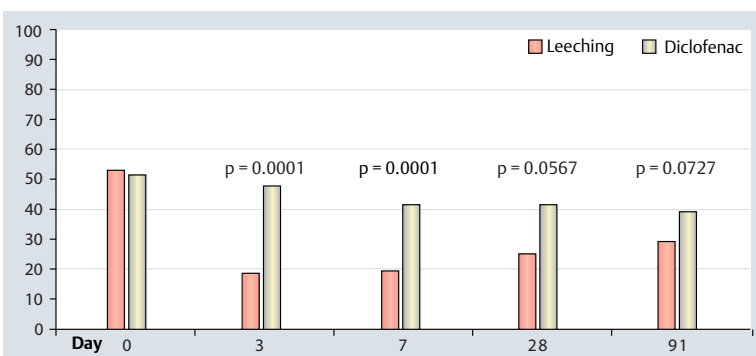

Fig. 10.**2** **Randomized study of the efficacy of leech therapy in 51 patients with osteoarthritis of the knee.** WOMAC pain score

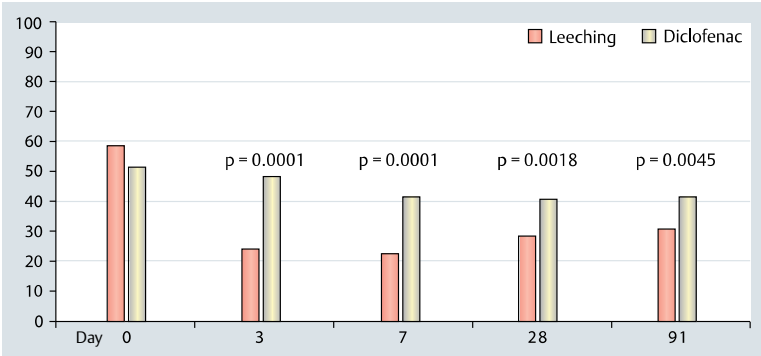

Fig. 10.**3** **Randomized study of the efficacy of leech therapy in 51 patients with osteoarthritis of the knee.** WOMAC joint function score

the treatment outcomes or the observed group differences. This allowed us to conclude that placebo or suggestive effects did not have a significant influence on treatment outcome.

A third intervention study with a comparable randomized controlled study design was performed by researchers at the Free University of Berlin. A total of 52 patients (mean age: 68 years) were included in the study. Patients in the leech therapy group (n = 26) received a single leech treatment, and those in the control group (n = 26) received a single transcutaneous electrical neuromuscular stimulation (TENS) treatment. The investigators used a crossover study design in which the two three-week treatment periods were separated by a three-week wash-out period. Symptoms were evaluated using the validated Lequesne index, which is comparable to the WOMAC index. The Free University study also demonstrated that a single local leech treatment induced significant pain reduction and improvement of joint function, and that the effects of leeching were still measurable nine weeks after treatment [21].

To summarize, three studies demonstrating the good clinical efficacy of leech therapy for treatment of osteoarthritis of the knee have been performed so far. Two of these were randomized, controlled trials. According to the criteria of evidence-based medicine, this can be classified as very reliable evidence.

Nevertheless, additional studies are urgently needed. The duration of the effect of leeching needs to be determined in longer-term studies, and the potential benefit of early repetition of leech treatment should also be assessed. In addition, adverse effects of leech therapy should be documented in large patient populations to improve the risk-to-benefit assessment. A retrospective study by Essen-Mitte Hospital in which approximately 400 patients with osteoarthritis of the knee received a single leech treatment provides preliminary data on the long-term effects of leech therapy. Ninety percent of these patients experienced a significant reduction of pain, which lasted one to three months in 27% of cases, four to nine months in 33%, and 10 months and longer in 26%. The need for analgesic medications decreased in 72% of patients overall, and decreased for a duration of more than one year in 32%. Except for frequent local itching and occasional skin reddening, adverse events were rarely observed [20]. At present, we can conclude that leech therapy is a useful and safe method for treatment of symptomatic gonarthrosis. The clinical relevance of leeching becomes all the more important in light of the well-known adverse effects associated with prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors. Moreover, the efficacy of arthroscopic interventions has been challenged by preliminary blinded intervention studies in which no significant efficacy differences between sham operations and arthroscopic interventions could be determined.

Degenerative Diseases of Other Joints and Myofascial Pain Syndrome

In clinical practice, leeches are used to treat degenerative joint disease in many other locations besides the knee. According to a survey of leech therapists, the main joints treated for this condition are the shoulder, the thumb, and the ankle. The application of leeches to the hip joint for treatment of coxarthrosis is also possible but less promising because the hip is poorly accessible to leeches. Furthermore, painful insertion tendinopathies and myopathies play a less important role in the pathogenesis of pain in coxarthrosis than in gonarthrosis. The application of leeches to finger and toe joints is generally not recommended because of the increased risk of delayed wound healing. However, when the subcutaneous tissue layer is thick enough and the potential risks and benefits of leeching have been thoroughly considered, treatment with leeches is possible. An unpublished observation study conducted by researchers at the University of Moscow, which was presented at

the European Congress of Rheumatologists in 2002, prospectively analyzed the effect of leech therapy on periarticular pain/trigger points, arthralgia, joint mobility, and morning stiffness in 51 patients with degenerative joint disease in various locations and in 51 patients with rheumatoid arthritis. Leech therapy achieved a significant improvement of function, arthralgia, and morning stiffness in nearly all patients in both diagnosis groups [18]. Further specific studies on the efficacy of leeching in other forms of degenerative joint disease are currently lacking. In light of the promising results achieved in gonarthrosis studies, clinical investigators should concentrate on testing the efficacy of leeching in degenerative diseases in other commonly treated joints.

The situation is much the same for myofascial pain syndrome. Lower back pain and iliosacral joint pain syndrome are two conditions that are commonly and successfully (subjectively) treated with leeches, but the corresponding data from clinical trials are lacking. Humerolateral epicondylitis is another frequent indication for leeching. No clinical/scientific assessment of the efficacy of leeching in these diseases is possible at present.

In the classical literature, leeching is often recommended for contusions and sprains. Reduction of swelling and pain in response to leech therapy has been observed in case studies and in practical experience [14]. The use of leeches in sports medicine (e.g., in professional soccer) is now on the increase. Based on these observations, it would probably be safe to conclude that leeching must be effective, but controlled clinical trials should be carried out to obtain scientific proof of efficacy.

Inflammatory Arthritis

Arthritis urica is one of the main indications for leech therapy specified in the older literature. In his book, Bottenberg [3] describes a number of successfully treated cases that support the use of leeches in this indication. In those days, drugs like ibuprofen and allopurinol, which are now the standard treatment options, were not available. On the other hand, modern clinical studies on the efficacy of leech therapy for treatment of arthritis patients are lacking. Consequently, the use of leeches should be reserved for chronic and refractory cases.

Articles in the older and more recent literature contradict each other with respect to the use of leeches for treatment of chronic polyarthritis (cP) and rheumatoid arthritis (rA). One center for rheumatic diseases that specializes

in leech therapy takes a very reserved approach to using leeches for treatment of cP (see Chapter 6). In the previously mentioned observation study [18], leech therapy led to significant improvement of rheumatic joint diseases and an accompanying decrease in laboratory parameters of inflammation. At present, the data in the literature does not provide sufficient proof of efficacy. We advise against applying leeches directly to joints affected by acute inflammation, but leeching can be attempted in the intermittent stage after the acute inflammation has subsided.

Otitis media, Tinnitus, and Other Ear Diseases

Diseases of the ear, especially otitis media, are major indications for local leech therapy in the older literature and in Bottenberg's book. The leeches were applied in the mastoid or tragus region. Baskova's renowned team at the University of Moscow conducted a clinical study on the use of leeches to treat ear diseases [19]. In this interesting study, 273 patients with either otitis media, otitis externa, or tinnitus were divided into three treatment groups. Group 1 was treated by leech therapy alone, Group 2 received a local injection of fresh leech saliva extract, and Group 3 received the normal standard treatment (antibiotics for ear infections, hemodilution for tinnitus). Leech therapy exhibited significant superiority in alleviating the symptoms of otitis externa and tinnitus but did not exert any demonstrable effect in otitis media. The effect of injected leech extract was roughly one third lower than that of natural leech therapy. Despite the positive results achieved in otitis externa and tinnitus, these study findings should be interpreted with caution, especially in the case of tinnitus. Very frequently, the good efficacy demonstrated in preliminary drug and acupuncture studies could not be confirmed later in large-scale randomized clinical trails. However, reports of the good effects of leech therapy in tinnitus are frequently heard in practice. Clinical studies on this subject would be most welcome.

Hypertension and Cardiovascular Diseases

Cardiovascular disease was a main indication for leech therapy for centuries. In the first half of the 20th century, it was normal to apply leeches for treatment of stroke and heart attack [7]. The underlying mechanisms involved are the systemic anticoagulative effects of hirudin and the stimulation of

segmental reflex mechanisms by the leech bite. After the advent of aspirin for thrombolysis and inhibition of platelet aggregation, the significance of leech therapy rapidly declined. Recombinant hirudin was later utilized and investigated in modern myocardial infarction treatment regimens. Unlike the heparins, direct thrombin inhibitors like hirudin do not need antithrombin III as a cofactor. Moreover, hirudins are able to inactivate fibrin-bound thrombin. Because of the strong anticoagulant potency of these biochemicals, a high incidence of hemorrhagic adverse effects occurred in preliminary studies using the first recombinant hirudin analogs (desidurin, lepidurin). The hirudins were therefore initially unable to become established drugs for primary treatment of myocardial infarction. A novel hirudin (bivalirudin) has meanwhile achieved very promising results in clinical trials. Heparin-induced thrombocytopenia type II (HIT-2) is an established indication for hirudin today. Promising new low molecular weight direct thrombin inhibitors for treatment and prevention of arterial and venous thrombosis (ximelagatran, melagatran) are also hirudin derivatives. Regarding the use of natural leech therapy for treatment of coronary syndromes and thrombosis, insufficient proof of efficacy, insufficient pharmacological standardization, and insufficient controllability preclude the use of leeches in these patients.

In the past, leech therapy was commonly used to treat arterial hypertension. The acute and medium-term antihypertensive effects of repeated moderate venesection are known and have been documented in various studies [24]. Likewise, the hypovolemic hemodilution that occurs due to the extraction of blood by the leech can also be classified as an antihypertensive effect. However, modern antihypertensive treatment regimens include a great number of reliable and effective antihypertensive drugs, as well as effective lifestyle changes. Consequently, leech therapy is now largely seen as a welcome adjuvant therapy rather than as a first-line treatment.

The older literature refers to the special benefits of leech therapy in the treatment of hypertension in individuals with a “plethoric constitution.” The application of leeches to specific areas of the body (segmental hypertension zones, neck region, etc.) is also described. However, study data on this subject is not available. In principle, the consideration of such nosological aspects in studies of the potential efficacy of leech therapy in patients with refractory arterial hypertension would also be desirable.

Special Features of Clinical Research with Leeches

The fact that it is currently not possible to conduct blinded clinical trials on leech therapy poses a principal problem in assessing efficacy. The characteristic nature and protracted course of leech feeding does not lend itself to treatment blinding. In modern clinical research, blinding is no longer an absolute prerequisite as long as randomization is performed. "Effectiveness" is the sum of all specific and unspecific (placebolike) effects. Unlike "efficacy," "effectiveness" very validly describes the actual clinical degree of effect of a treatment method as it is also rated in practice. Nonblinded studies define the effectiveness of a treatment method. Unspecific effects always occur, regardless of the treatment method. To approximately define these placebo effects, patients should be asked about their expectations in regard to treatment outcome using a standardized questionnaire before the start of treatment (see gonarthrosis study on p. 121). "Outcome expectation" can then be included in the statistical analysis of treatment effects. It would also be useful to compare the intensity of leeching in the different studies. This would generate more precise dose–effect data that could be useful for weighting the specific and unspecific effects of leech therapy.

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11 The Biochemistry of Leech Saliva

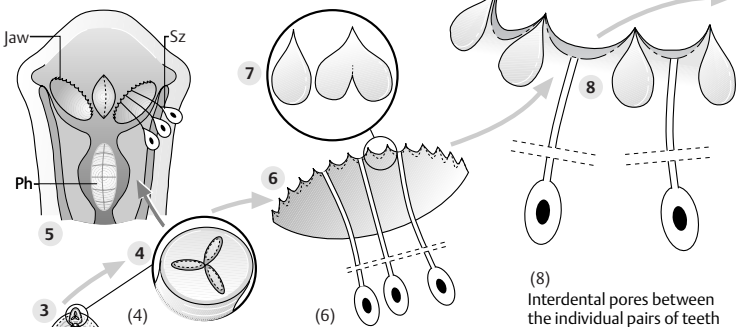
U. Gross, M. Roth

The comeback of leech therapy can be attributed to an increased understanding of the pharmacologically active substances in leech saliva, among other things. The most obvious effect of the leech bite is venesection. However, compared to the pharmacological effects, blood withdrawal is only of secondary importance. During the process of feeding, leeches secrete a complex mixture of different biologically and pharmacologically active substances into the wound. The individual saliva components are produced in scattered salivary gland cells that do not merge to form a proper gland. The cell bodies are located in the pharyngeal region. The excretory ducts of the gland cells are distributed across the dental ridges of the jaws and emerge between each of the calcified teethlets (cf. Fig. 3.**3 a–d**, p. 24 ff). No microorganisms have been identified in leech saliva to date. The various active substances in leech saliva produce different effects within the body of the host (Fig. 11.**1**, Table 11.**1**). In addition to humans, the leech preys on most mammals, birds, and poikilothermic animals. A characteristic effect of the leech bite in humans is the prolonged, wound-cleansing oozing of blood from the leech bite. Although bleeding from the leech bite stops after only 30 minutes in most other warm-blooded animals, it lasts an average 12 hours in humans[1].

1 For many years, it was assumed that this was a nonsensical biological "overreaction," indicating that humans were not the "intended" hosts. However, it is now known that prolonged bleeding from the leech bite is an "intentional" effect of nature that is achieved by a specific protein, calin. This refutes the theory that prolonged wound bleeding is a coincidental hyper-reaction. It would appear that the wound-cleansing effect associated with it makes biological sense for the leech (see p. 125).

(5)
The pharynx (Ph) contracts rhythmically (peristalsis) to pump blood ingested through three-pronged wound to the stomach. The chemicals in leech saliva are produced by scattered salivary cells (Sz) located in the connective tissues. Tubular salivary ducts connect them to the jaws.

(7)
The leech teeth are calcified structures embedded in the hardened muscle mass of the leech jaw. They appear heart-shaped in this view; in cross-section, they look like elongated teardrops.

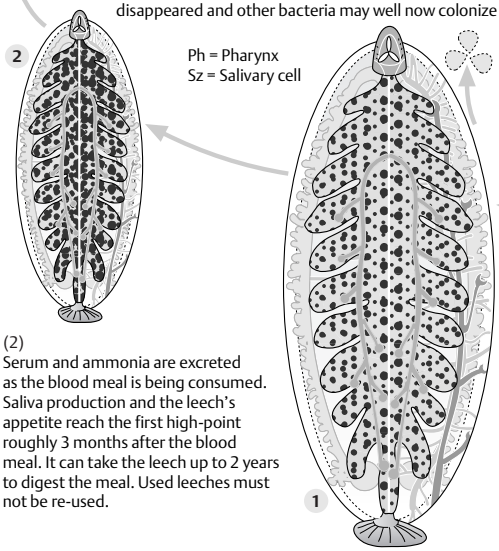


(4)
The tripartite jaw of the leech, as viewed from above, is the mechanism central to treatment (see Fig. 3.3a, p. 24).

(6)
The salivary cells do not merge to form a proper gland. They are basically germ-free.

(8)
Interdental pores between the individual pairs of teeth form the openings of the excretory ducts of the salivary cells (see Fig. 3.3d, p. 26 ff), through which the various chemicals in leech saliva are secreted into the bite wound.

(3)
Within around 2 years' time, the blood meal is completely digested and the leech begins to consume its own body substance. Aeromonas colonies have largely disappeared and other bacteria may well now colonize the leech stomach and intestine.



Mammal blood is probably essential for the production of leech offspring and cocoons. The leeches lay their cocoons in wet soil on the water banks. Each cocoon contains 10 to 30 young leeches, which do not undergo metamorphosis.

(2)
Serum and ammonia are excreted as the blood meal is being consumed. Saliva production and the leech's appetite reach the first high-point roughly 3 months after the blood meal. It can take the leech up to 2 years to digest the meal. Used leeches must not be re-used.

(1)
The venesection effect of leeching consists of the extraction/uptake of 10 to 50 milliliters of blood within a range of around 20 to 120 minutes. Roughly the same amount of blood oozes out of the wound during the ca 12-hour afterbleeding phase. The blood is stored in the 10 pairs of lateral ceca in the leech stomach. The leech can consume 5 to 10 times its weight in blood.

Components of the Saliva of the Medicinal Leech

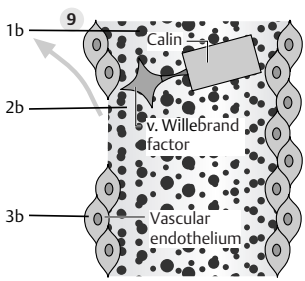
Hirudin

Hirudin is the best known component of leech saliva. It was named by Jakobj around 1903/4 [18]. Hirudin is sometimes used to describe all active substances in leech saliva. Therefore, there may sometimes be a confusion of terms. In reality, "hirudin" refers only to one specific active substance in leech saliva (see below), the structure of which is known and the function of which is now largely understood. The ability of leech saliva to inhibit blood coagulation was discovered over a century ago [12]. The first anticoagulant compound in leech saliva was isolated and identified by Markwardt [15] in the mid-1950s. This is the protein now known as hirudin. The hirudin molecule consists of a chain of 65 amino acids with a high proportion of aspartic acid and glutamic acid, both of which are aminodicarbonic acids. It inhibits blood coagulation by selectively binding to thrombin in the blood of the host animal. Hirudin binds with thrombin to form an inactive complex with a very low dissociation constant (10^{-10} mol · l^{-1}) [16].

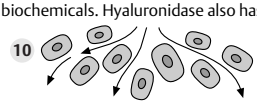
In this chapter, we will describe the final pathway of blood coagulation and how this is related to hirudin. Figure 11.**2** shows the most important events in blood coagulation and their relation to this thrombin inhibitor. Prothrombin is converted to thrombin through the action of the enzyme thrombokinase. The glycoprotein fibrinogen is then broken down into fibrin

Fig. 11.**1** **The biological interaction between leech and patient.**

(9) Leech saliva contains hirudin, a chemical that inhibits blood coagulation. It also contains calin, a substance that keeps the wound open for roughly 12 hours by binding with and thereby inactivating von Willebrand factor. The seepage of blood from the wound (the actual venesection effect) constitutes an additional wound cleansing effect.



(10) Hyaluronidase functions as a "spreading factor." It facilitates the removal of mucopolysaccharides from the interstices, thus opening the door for subsequent biochemicals. Hyaluronidase also has an antibiotic effect.



(11) A carboxypeptidase A inhibitor and histamine-like substances dilate the capillaries around the leech bite, thereby increasing the flow of blood into the bite region.

(12) Anti-inflammatory substances such as eglins and bdellins promote healing.

Table 11.1 **Components of medicinal leech saliva that exert effects in the host's body**

Substance	Effect on the host
Hirudin	Inhibits blood coagulation by binding to thrombin
Calin (saratin)	Inhibits blood coagulation by blocking the binding of von Willebrand factor to collagen Inhibits collagen-mediated platelet aggregation
Destabilase	Monomerizing activity Dissolves fibrin Thrombolytic effects
Hirustasin	(Serine proteinase) Inhibits kallikrein, trypsin, chymotrypsin, and neutrophilic cathepsin G
Bdellins	Anti-inflammatory Inhibits trypsin, plasmin, and acrosin
Hyaluronidase	("Spreading factor") Increases interstitial viscosity Antibiotic
Leech-derived tryptase inhibitor (LDTI)	(Tryptase inhibitor) Inhibits proteolytic enzymes of host mast cells
Eglins	Anti-inflammatory Inhibit the activity of α-chymotrypsin, chymase, subtilisin, elastase, and cathepsin G
Factor Xa inhibitor	Inhibits the activity of coagulation factor Xa by forming equimolar complexes
Complement inhibitors	May possibly replace natural complement inhibitors if they are deficient
Carboxypeptidase A inhibitors	Increases the inflow of blood at the bite site
Suspected saliva components:	Effect on the host
Histaminelike substances	Vasodilator. Increases the inflow of blood at the bite site
Acetylcholine	Vasodilator
Anesthetic substance	Anesthetic

Data based on [4, 18, 11, 23]

monomers through the action of thrombin. The fibrin monomers polymerize with thrombin to form fibrin polymers. Fibrin then forms a clot by forming new peptide bonds. When hirudin binds with thrombin, it blocks this process. It thereby inhibits fibrin production and prevents clot formation.

Hirudin acts similar to heparin but has various advantages over this commonly used drug [17]:

1. Unlike antithrombin III and heparin, hirudin does not need cofactors.
2. Hirudin is exclusively selective for thrombin.
3. Hirudin is not acted upon by peptides and enzymes in the blood.
4. Hirudin is excreted in unchanged form via the urine.

A disadvantage of hirudin is that there are no known antagonists for it. If hirudin is overdosed, this means that there is no antidote. However, overdosage is very unlikely when living leeches are used according to standard recommendations.

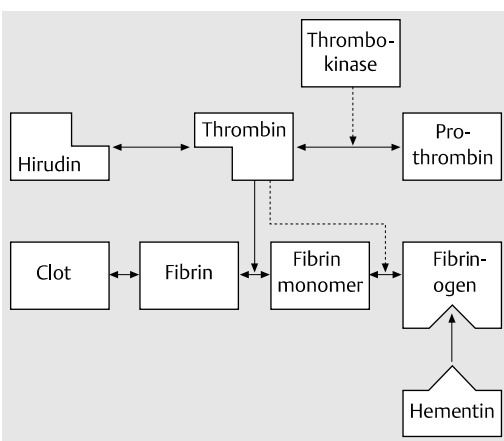


Fig. 11.2 **Final stage of blood coagulation, with the two different points of attack of hirudin and hementin.** Hirudin bonds with thrombin to form an inactive complex. Hementin breaks down fibrinogen. Both mechanisms lead to the same effect, namely inhibition of coagulation (see text for details)

Other Components of Leech Saliva

An **anesthetic substance** and a histaminelike **vasodilator** in leech saliva may start to work even before hirudin is secreted into the wound. Since no compound that fits this description has been identified, the presence of an anesthetic substance in leech saliva is still the subject of debate. The vasodilator serves to widen blood vessels in the region of the bite wound, thus increasing the volume of blood withdrawn from this area [13, 23]. Leech saliva also contains **calin**, a protein that has the following functions:

(a) Inhibition of collagen-mediated platelet aggregation and adhesion;
(b) Inhibition of von Willebrand factor-dependent platelet adhesion to collagen in the vessel walls, thereby preventing wound closure [2, 17] (Fig. 11.**3**).

This is the biochemical basis of prolonged bleeding from the leech bite, which normally persists for roughly 12 hours. Theoretically, this prolonged bleeding has a host-preserving function, in that the outflow of blood cleanses the wound, which prevents the host from developing a potentially lethal sepsis. It therefore makes good biological sense.

Destabilase, a monomerizing enzyme that dissolves fibrin, was also found in the saliva of medicinal leeches [5, 6]. **Proteinases** and **proteinase inhibitors** present in the saliva of the medicinal leech were described by Baskova und Zavalova [4]. Some of these substances are adsorbed on the surface of the host's damaged blood vessels, and some mix with the blood

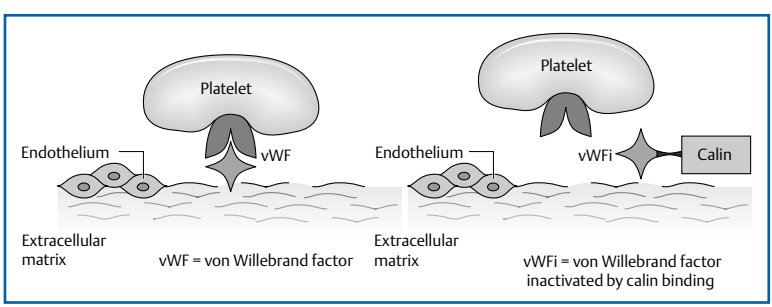


Fig. 11.**3** **The diagram shows the point of attack of calin.** Binding with calin inhibits von Willebrand factor, resulting in prolonged wound bleeding

oozing from the wound. Some proteinases are secreted by symbiotic bacteria *(Aeromonas sobria)* in the leech's digestive tract. The leech gut wall also produces and secretes proteolytic enzyme inhibitors. Proteinase inhibitors from the medicinal leech belong to a group of proteins that inhibit the catalytic activity of different proteolytic enzymes. Proteinases are also secreted outside the gut of the medicinal leech. Some proteinases (e.g., bdellins) are scattered throughout the entire body surface of the animals. **Bdellins**, for example, are found in the leech gut and saliva alike. These proteinases function as inhibitors of trypsin, plasmin, and acrosin. Depending on their elution behavior in ion exchange chromatography, bdellins are divided into two main types, bdellin A and B, both of which can form multiple subtypes. The bdellins, as well as **bdellostasin** and **eglin**, were shown to have a neurite-stimulating capacity [8]. **Hirustatin** is yet another proteinase inhibitor found in the saliva of the medicinal leech. This compound belongs to the group of serine proteinases and occurs in two isoforms, which differ only by a single amino acid. Hirustatin inhibits kallikrein, trypsin, chymotrypsin, and neutrophilic cathepsin G.

Tryptase inhibitors have also been isolated from medicinal leech extract. Tryptase itself plays a key role in the pathogenesis of allergic and inflammatory reactions associated with impaired mast cell function. Tryptase is also involved in diseases such as asthma, rheumatoid arthritis, and psoriasis. **Leech-derived tryptase inhibitor (LDTI)** is one of the better analyzed tryptase inhibitors. LDTI binds to active tryptase centers. In one study, 20 µM of recombinant LDTI blocked the replication of HIV-1 virus in host cells [1]. The biological function of LDTI is thought to be as follows: Leeches secrete LDTI in order to inhibit the proteolytic enzymes (tryptases) released by the host's mast cells when the leech punctures the skin. This is the leech's way of protecting itself from proteolytic enzymes in the oral region while it feeds.

Eglins are another group of anti-inflammatory, low molecular weight proteins isolated from leech extract. They inhibit the activity of α-chymotrypsin, chymase, subtilisin, and the neutrophilic proteinases elastase and cathepsin G.

Factor Xa inhibitor is a further leech saliva component that acts on the coagulation cascade. Factor Xa catalyzes the conversion of prothrombin to thrombin during the process of blood coagulation. Factor Xa inhibitor forms a stable equimolar complex with Factor Xa, thus inhibiting its activity.

A carboxypeptidase A inhibitor enhances kinin-induced blood flow during leech feeding. This substance may also help to dissolve any blood clots that may form when the leech is feeding.

Complement inhibitors have also been isolated from leech extracts. These substances may be useful in patients with deficiencies of the natural inhibitors. They may also be able to counteract unwanted complement activation, as occurs in anaphylactic shock, chronic inflammation, and sepsis.

Hyaluronidase (orgelase), another enzyme in leech saliva, is involved in the digestion of hyaluronic acid. As the "spreading factor," it opens the interstices, paving the way for other active substances in leech saliva to reach the deeper tissues. In mouse experiments, hyaluronidase was also found to have antibiotic properties. It probably exerts this effect by attacking the mucous capsule of streptococci [23].

Baskova et al. [3] used different methods to demonstrate that a number of as yet unidentified substances are present in leech saliva. By one-dimensional electrophoresis, they identified more than 60 bands with molecular weights ranging from 11 to 483 kD. Two-dimensional electrophoresis indicated that there are more than 100 substances. Comparisons of mass spectrometry data with protein databases indicate that eight of the detected saliva proteins are known. (Discrepancies between this figure and the substances listed above are due to the use of different extraction methods. Extracts were only obtained from the leech head region in some cases, and from the entire body in others.) The unidentified substances are presumed to be simple variants of the known proteins and/or other bioactive saliva components.

This leaves plenty of possibilities for future biochemical research. Several interesting riddles remain to be solved, for example the question of whether leech saliva contains potential anesthetic substances or other pharmaceutically useful compounds, especially anti-inflammatory and vasoactive substances.

Components of the Saliva of Other Leeches

The saliva of other leech species also contains several anticoagulant substances. The secretions of different leech species have variable effects on the coagulation cascade as they contain different anticoagulant substances. Thus, different species (e.g., *Hirudo* and *Haementaria*) inhibit coagulation in different ways.

Recombinant Anticoagulants

For many years, natural hirudin was extracted from *Hirudo medicinalis*, the supply of which is limited. Hirudin is a relatively small compound with a simple composition. Therefore, researchers quickly succeeded in cloning the molecule in baker's yeast and producing sufficient quantities of recombinant hirudin [14]. The recombinant form is identical to natural hirudin. It has the same biochemical and pharmacological characteristics as hirudin from the medicinal leech [19]. Modification of the amino acid composition of recombinant hirudin has improved its pharmacological characteristics [7]. A novel substance called leech carboxypeptidase inhibitor (LCI) was isolated from *Hirudo medicinalis.* The fully functional inhibitory protein is obtained by overexpression of LCI in *Escherichia coli* into yeast medium. LCI is a globular protein that remains stable over a wide pH range [22]. A *synthetic* gene for hirustatin was synthesized by polymerase chain reaction and expressed in baker's yeast. The biological activity of the synthesized protein was identical to that of the corresponding protein from *Hirudo medicinalis* [9].

Proteins from the saliva of other leeches have also been cloned. A synthetic gene encoding the amino terminal domain of ghilanten, an anticoagulant protein found in the leech *Haementeria ghilianii,* was constructed and expressed in yeast [21].

It remains to be seen whether compounds synthesized from the medicinal leech will function the same as the intact leech. This chapter has shown that the saliva of the medicinal leech contains numerous potent bioactive substances. Leech saliva can therefore be described as a natural combination drug product.

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12 Bacterial Flora of the Medicinal Leech *(Hirudo medicinalis)*

J. Graf

The efficacy and safety of leech therapy in the different fields of use are important issues. Clinical experience and scientific studies have shown that the treatment pain is generally mild and that adverse reactions to the components of leech saliva are rare and mild to moderate in severity. Likewise, the possibility of leech-borne transmission of bacterial or viral infections is a current and clinically relevant concern. The mandatory practice of disposing of medicinal leeches after they have been used once effectively eliminates the possibility of microbial diseases being transmitted from one patient to another due to leech therapy. However, normal bacteria present in the leech's digestive tract can also be transmitted to the patient and may pose a potential risk of bacterial infection. We will therefore elucidate the microbiology of the medicinal leech and discuss the diagnostic and therapeutic implications of these microorganisms.

Intestinal Symbiosis of the Medicinal Leech

The modern physician likes to practice medicine under strict conditions of precision and sterility. However, when administering treatments with live animals, it is impossible to achieve the customary level of sterility because all animals are colonized by natural bacteria. These symbionts help the animal by synthesizing essential nutrients, digesting food, and killing harmful organisms [22, 44]. The human intestine exhibits impressive bacterial diversity. Hundreds of different bacterial strains have been isolated from the gut of humans by culture techniques, and culture-independent methods suggest that the actual number of intestinal strains may be twice as high [17, 18,

22]. The intestine of the medicinal leech is likewise colonized by bacteria but exhibits very little bacterial diversity compared to many other animals [15]. In this chapter, we will describe the current state of knowledge on the bacterial flora and antimicrobial mechanisms of the intestine of *Hirudo medicinalis*.

The so-called stomach (crop) of the leech, which occupies the majority of the space in the digestive tract, serves as the storage site for ingested blood [39]. The leech's stomach is unlike that of vertebrate animals in that it extracts water and salt from the blood. In this capacity, it works similar to the human intestine, where the reabsorption of fluids and salts occurs. The leech stomach is also able to store ingested red blood cells. The actual process of digestion and nutrient absorption takes place in the intestine [37], which is much smaller than the stomach. Therefore, most investigators who studied the bacterial flora in the leech's digestive tract probably isolated the bacteria from the leech's stomach. However, this cannot always be determined with certainty because of the sometimes minimalist descriptions of study methods.

Surprisingly, only a single bacterial species was isolated from the leech stomach in the first microbiological studies reported. This bacterial symbiont was named *Bacterium hirudinicolum* by Lehmensick and Hornborstel in 1941 [29]. Ten years later, Büsing and co-workers renamed it *Pseudomonas hirudinis* [6, 7]. The presence of only a single bacterial species in the leech contrasts sharply with the great diversity of bacterial flora found in the digestive tract of most other animals. The bacteria isolated from leeches tested positive for beta-hemolysis and were found to produce extracellular proteases and lipases. Because of the pure culture of these enzymes, which could be important for blood digestion, these bacteria were classified as symbionts.

The exact role of the symbiotic bacteria in the symbiosis is still not fully understood, but three potential functions have been proposed [7, 15, 16]:

1. The bacteria may help to digest ingested blood.
2. The bacteria may produce essential nutrients for the leech.
3. The bacteria may prevent the growth of other bacteria.

The classic proof that a bacterium is involved in blood digestion or nutrient synthesis is antibiotic inactivation of the bacterium. Antibiotic susceptibility tests can be used to determine whether the bacterium is involved in the

synthesis of a nutrient such as vitamin B_{12}, which is present in low concentrations in the blood. Two groups of researchers have studied the effects of different antibiotics on the physiology of leech digestion. Büsing and coworkers [7], who treated medicinal leeches with chloramphenicol (1 mg per mL of blood), observed a reduction in water loss and nitrogen excretion after feeding. Two factors to consider are:

1. Chloramphenicol passes relatively quickly from the intestine into the blood (at least in humans).
2. The animals were given relatively high doses of the drug.

Consequently, it is impossible to ascertain with certainty whether the antibiotic actually had a direct effect on the leeches. Zebe et al. observed a reduction in oxygen uptake and NH_3 excretion in leeches treated with kanamycin [47]. Again, very high doses of the drug were used (1 mg per mL of kanamycin). However, unlike chloramphenicol, kanamycin is poorly absorbed by the intestine, so it probably had a smaller effect on the animals [16]. All in all, these findings at least suggest that the symbionts influence the metabolism and physiology of the medicinal leech.

Aeromonas, Intestinal Symbiont of the Medicinal Leech

In the 1960s, the symbiont discovered by Lehmensick was renamed *Aeromonas hydrophila* [27]. *Aeromonas* taxonomy has since undergone complex changes and many new species have been described [2, 8, 23, 25, 26]. Classical biochemical identification is not always straightforward, and very discrete differences in 16S rRNA gene sequences of the different strains must be detected [1, 13, 34]. Another well-known problem is incorrect identification of the different *Aeromonas* species by commercial test kits, especially the older systems. Most investigators who studied the bacterial flora of the medicinal leech in the past only used commercial test kits to identify the symbionts, most of which were identified as *Aeromonas hydrophila* [5, 11, 30, 31, 33, 35, 38, 41]. Some of the isolates that were identified as *Aeromonas sobria* [12, 33] probably should have been classified as *Aeromonas veronii biovar sobria* because the 16S rRNA gene sequence is different. Our group identified

the symbionts as *Aeromonas veronii biovar sobria* using commercial test kits supported by additional tests; identification was subsequently confirmed by 16S rRNA gene sequencing [14]. Our analysis revealed that many species isolated from the leech stomach had atypical biochemical test reactions consistent with the presence of *Aeromonas hydrophila*. For example, one group of symbionts tested positive for esculin hydrolysis, which is characteristic of *Aeromonas hydrophila*, but its 16S rRNA sequence was identical with that of *Aeromonas veronii biovar sobria*. Other investigators recently reported similar difficulties in biochemical identification of *Aeromonas* strains [1]. Furthermore, leeches from other breeders or from other regions may be—colonized by different bacterial species.

Exact taxonomic identification is probably of lesser importance in clinical medicine because *Aeromonas hydrophila* and *Aeromonas veronii biovar sobria* cause similar infections in humans and the same safety precautions apply for both leech species [25]. To my knowledge, no reports of notable infections occurring after application of leeches to well-perfused parts of the body of individuals with an intact immune system have been mentioned in the literature. If blood supply to the application site is impaired, there is an increased risk of wound infection which, however, can be prevented by prophylactic administration of antibiotics. Quinolone antibiotics such as ciprofloxacin and ofloxacin or third-generation cephalosporins such as ceftriaxone should preferably be used for this purpose [19, 21, 28, 38, 42, 45]. First-generation cephalosporins and penicillin are not recommended because resistance to these drugs is a widespread problem. Still, resistance to the recommended antibiotics can also develop [40, 45]. Accurate differentiation between the two *Aeromonas* species is important for microbiologists because investigators still have not succeeded in distinguishing virulent *Aeromonas* strains from benign types. Both *Aeromonas* strains are widespread. They both occur in the water and sediment of rivers and lakes. More importantly, both can cause bacterial infections in humans.

Of the 15 known *Aeromonas* strains, the three that most frequently cause diseases in humans are:

1. *Aeromonas hydrophila*
2. Aeromonas *media*
3. *Aeromonas veronii biovar sobria* (often erroneously called *Aeromonas sobria*)

Compared to many other bacterial pathogens, these *Aeromonas* strains are not of major clinical importance. The most common manifestations of *Aeromonas* infection are diarrhea and wound infection. The diarrhea usually clears up without antibiotics, and the wound infections usually occur in small wounds that were exposed to contaminated lake or river water. Although relatively uncommon, a severe course of infection can occur in patients whose immune systems are suppressed due to surgery, multiple trauma, liver cirrhosis, or other reasons. An extensive review of the available data on this subject has already been published [25].

Microbiology of the Leech

Bacterial flora in the intestine of *Hirudo medicinalis* can best be assessed by bacterial cultivation or DNA analysis of samples obtained from the leech intestine. In most studies described in the literature, commercial test kits were used for biochemical identification of cultured bacteria. *Aeromonas* was isolated from the medicinal leech in all of the relevant studies. The isolated strain was most commonly identified as *A. hydrophila*, followed by *A. veronii biovar sobria*. In our study, 99.5% of the cultured bacteria were identified as *A. veronii biovar sobria*. In several culture studies, *Aeromonas* was the only genus identified, but some investigators have found others. Without quantitative data on the number of isolates, it is difficult to assess the role of these bacteria in the leech. In order to determine whether bacterial infection is a potential hazard, it is imperative to know whether these bacteria colonize the leech intestine, body surface, or other organs and to obtain quantitative data on the bacteria. Although they are metabolically active, most of the bacterial species cannot be cultivated in the laboratory. For example, only about 0.1% of the bacterial species present in lake water can be isolated by cultivation. Although most disease pathogens in humans can be cultivated, "only" 30–50% of all intestinal bacteria can be cultivated in the laboratory [17]. Consequently, other bacteria that are difficult to impossible to cultivate under laboratory conditions may also be present in leeches. In an as yet unpublished study, we isolated DNA from the leech intestine and stomach and then amplified the 16S rRNA gene and cloned it in a plasmid (Worthen, Gode, and Graf, unpublished data). By sequencing individual plasmids, we gained an insight into the bacterial flora of the leech without bacterial cultivation.

Preliminary analyses suggest that, in addition to *A. veronii biovar sobria*, the leech stomach may also be colonized by another bacterial species that is distantly related to one of the symbionts in the human intestine, namely *Bacteroides*. These findings suggest that the leech stomach is probably colonized by more microorganisms than originally assumed. Still, the number of bacterial species is surprisingly small. Other bacterial species colonize the intestine of the leech; the predominant species are *A. veronii* and the relative of *Bacteroides* mentioned above.

Reports of the renewed use of medicinal leeches for treatment of local impairment of venous perfusion arising as a complication of plastic and microvascular surgery have been published since the early 1980s [20]. A major consequence of impaired blood flow is local weakening of the patient's immune system. Because of local immunosuppression, bacteria can easily colonize the surgical wound and cause infection. Bacterial infections following the application of leeches to poorly perfused tissues have therefore been reported in numerous cases [3, 9, 10, 30–32, 41, 43, 46] (cf. Chapter 9). These infections can be prevented by antibiotic prophylaxis. Two important things to remember are:

1. The impairment of blood flow makes these patients susceptible to wound infection.
2. Multiple leeches must be applied in multiple treatment sessions.

In this indication, no medication is as efficient as leeching. This makes impaired tissue perfusion distinctively different from most other indications for leech therapy. Microbiological tests identified *A. hydrophila* or *A. veronii biovar sobria* as the cause of the leech-associated wound infections in almost all of the reported cases. *Vibrio fluvialis* and *Serratia marcescens* were implicated as the causative pathogen in one case each [36, 43].

Antimicrobial Properties of the Leech Intestine

In contrast to the diversity of bacterial flora in the intestines of most animals, the current data suggests that only very few bacterial species colonize the intestine of the medicinal leech. This lack of diversity serves to enhance the safety of leech therapy in humans. Furthermore, current findings sug-

gest that certain substances in the leech stomach inhibit the growth of many bacteria or may even kill the bacteria, which is very interesting from a therapeutic perspective. These antibacterial substances may be produced by the leech itself or by its symbionts. Alternatively, they may already be present in the ingested blood.

Indergand and Graf studied the ability of clinical isolates of *Escherichia coli, Pseudomonas aeruginosa,* and *Staphylococcus aureus* to colonize the medicinal leech [24]. The leeches were fed pure cultures of the bacteria (dissolved in a blood meal)], and the concentrations of the bacteria in the leeches were measured at various sampling times. Interestingly, *E. coli* concentrations in the leech intestine decreased over time. In control experiments, the same blood meal was not fed to the animals but incubated in vitro and studied under otherwise identical test conditions. *E. coli* concentrations also decreased in the control samples. This suggests that an antimicrobial substance in the blood of the animals may remain active .

The complement system, an important defense against infections, can be activated by the classic or alternative complement pathway. Since complement is heat-labile, heat treatment of the blood meal inactivates complement and allows *E. coli* to grow inside the leech and in the ingested blood. The corresponding studies suggest that complement (in ingested blood) remains activated and kills sensitive bacteria inside the leech digestive tract for a certain period of time. This hypothesis is supported by evidence from experimental studies with *A. veronii* mutants that were made incapable of synthesizing lipopolysaccharides, thus making them susceptible to complement-mediated killing [4]. The mutants were unable to colonize the leech unless the blood meal had been heat-treated, and complementation of the mutants with the intact operon restored their ability to colonize the leech. These results indicate that complement in freshly ingested blood remains active in the digestive system of the leech and kills sensitive bacteria.

Pseudomonas aeruginosa and *Staphylococcus aureus*, the other two bacterial species investigated by Indergand and Graf, were able to survive in the leech intestine but their growth was significantly inhibited [24]. These findings suggest that the ingested blood must be modified by the leech, the intestinal symbionts of the leech, or both, and that this modification inhibits bacterial growth–at least that of the investigated bacterial strains [15]. Immediately after ingestion, extraction of water and salt from the blood meal occurs in the leech's digestive tract; the extracted portion is then excreted via

the nephridia. Theoretically, all of these processes could have influenced the growth of the investigated bacteria. Alternatively, or in addition, the leech or its symbionts may produce substances that inhibit bacterial growth.

One of our broader goals is to elucidate the effects of these processes on the bacterial flora of the leech and to identify any antimicrobial substances that may be involved. We therefore performed experiments based on the rapid growth of *A. veronii* in the leech stomach [14]. The number of *Aeromonas* symbionts in the leech stomach doubled approximately once every hour at 21°C, which was equal to the proliferation rate in a rich culture medium. Proliferation ceased at end concentrations of 5×10^7–1×10^8 colony-forming units (CFU) per mL. These findings suggest that the symbiont is resistant to antimicrobial substances. If mutants that are unable to colonize the leech intestine can be found, then important clues to the identity of the corresponding active substance in the leech intestine can be obtained by analyzing the mutants.

The available studies indicate that there are barriers to colonization at various levels that the naturally occurring leech symbionts can overcome but many other bacterial species cannot. Antimicrobial components in the ingested blood also play an important role. Other bacterial species may be able to colonize the leech intestine under certain conditions, for example if the ingested blood is not fresh or if the leech is weakened, for instance due to extended periods of starvation.

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13 Medicinal Leeches in Integrative Medicine

G. Dobos

Ten years ago, when I started to work at a hospital where leeches had been routinely used for years in the treatment of painful osteoarthritis of the knee I was skeptical. I had spent the past 12 years training in internal medicine at Freiburg University Hospital and had spent two years doing research in the United States. I could not seriously see myself approaching my former colleagues as a proponent of leech therapy for gonarthrosis, especially as there was not a single study on the efficacy of leeching in that indication.

At first I tried to close my eyes to leeching as a treatment option. However, the numbers of patients who spontaneously reported how leeching had dramatically reduced their pain could not be ignored. In most of our patients, osteoarthritis was a secondary diagnosis. It was evident that leech therapy had achieved a significant reduction of pain intensity or, in many cases, had completely eliminated the pain. After leeching, patients were able to climb stairs again without any problems and gross swelling in the knee region was no longer detectable.

I found a way out of the dilemma after I was appointed Chief of Staff of the Model Clinic for Complementary and Integrative Medicine at Kliniken Essen-Mitte, an academic teaching hospital at the University of Duisburg-Essen. I called for the systematic study and inclusion of leech therapy in our therapeutic program. Dr. Andreas Michalsen, Assistant Medical Director of our department, applied the medicinal "magical creatures" with great care, enthusiasm, and scientific curiosity. Through our efforts over many years, together with the biological expertise of Dr. Manfred Roth and the practical experience of Dr. Ulrich Storck and Petra Flecken, leeching developed into a dynamic field of medicine.

The tremendous response to reports about our work in scientific journals and the media signaled the need for the present book. The publication of our

leech studies had sparked a growing interest and requests for information from doctors, therapists, and patients in Germany.

Impressive treatment successes in the fields of plastic and reconstructive surgery had earlier marked the beginning of an international renaissance of leech therapy. In alternative medicine, leeches are mainly used for treatment of symptomatic joint diseases and local pain syndromes. Over 1500 leech treatments have been administered for these problems at Kliniken Essen-Mitte in recent years. However, not a single severe adverse event has been observed. The most frequent side effects are itching at the bite site, which generally disappears within a few days, and prolonged bleeding from the leech bite. As mentioned elsewhere in book, leeching is contraindicated in certain cases, for example, in patients with coagulation disorders, those taking anticoagulant drugs, and immunosuppressed patients.

All in all, it seems to me that leech therapy is a good candidate for the currently developing concept of **Integrative Medicine**, an approach that integrates established conventional medicine with natural healing techniques, Complementary Medicine, and Mind–Body medicine. The term "Integrative Medicine" should be taken metaphorically. We interpret it as the ability to "speak different languages." Proponents of Integrative Medicine use a practical combination of different proved techniques of conventional medicine (we avoid the term "allopathic medicine" because of the historically negative connotations attached to it), applied naturopathy, and Mind–Body medicine. In addition, they utilize active behavioral adaptation strategies to overcome disease. The integrative therapist approaches the individual case without prejudice. The decision regarding which treatment modality to implement is based on a thorough assessment of the available scientific evidence regarding the treatment method in question (external evidence) and the therapist's own experience (internal evidence).

Why Integrative Medicine?

In the past decades there has been a considerable shift in the types of disease affecting European society. Rapid advances in medicine have mitigated the fears associated with acute infection, and there has been a steady decline in the number of infection-related deaths.

Chronic diseases, on the other hand, have meanwhile become the scourge of (Western) civilization. The majority of people over 65 years suffer from chronic conditions that have led to a veritable explosion of healthcare costs. In Germany alone, approximately 80% of all expenditures in the healthcare system are associated with treatment of chronically ill patients. The most common chronic conditions include musculoskeletal pain syndromes and osteoarthritis, both of which frequently lead to a significant loss of quality of life. Medical treatment of these diseases is not only a financial problem, but also a therapeutic dilemma.

Many chronic conditions do not respond well to conventional treatments. According to the usual recommendations and graduated treatment strategies, these patients are gradually switched from less to more potent drugs, with a corresponding amplification of the profile of side effects. Still, drug treatment rarely succeeds in completely eliminating chronic disease. Besides increasing treatment costs and side effects, multidrug treatments also increase the risk of drug interactions, which are often unclear and pose a further set of problems for the chronically ill patient.

In many cases long-term drug treatment eventually results in serious adverse events that may require hospitalization or outpatient treatment, or may impede the continuation of pharmacological treatment. Some of these complications end fatally. According to official statistics, over 100000 individuals in the United States die each year as a result of adverse drug reactions [1]. Over 16000 of these deaths are associated with nonsteroidal anti-inflammatory drugs, the medications chiefly used for pain management in arthrosis patients [2]. Considering this dilemma, alternative treatment options are of particular interest.

Integrative Medicine in Germany

The first clinical department of naturopathy was founded at the Benjamin Franklin Hospital of the Free University of Berlin in 1989. The first doctoral thesis on leech therapy was also published at this institution. Over a decade later, in 2002, the University of Rostock opened a department of naturopathy, which mainly focuses on the potentials of complementary medicine in the field of rehabilitation.

In 1999, the first department of internal medicine specializing in integrative medicine was established at Kliniken Essen-Mitte as a model clinic sponsored by the State of North Rhine-Westphalia. The department has 54 beds for inpatients, a day clinic, and an outpatient clinic. Its goals encompass the research, evaluation, and application of complementary treatment strategies and their integration in mainstream clinical care. Since its founding, the department has treated over 10000 patients on an inpatient, semi-outpatient, and outpatient basis. More than 1500 of these patients have received leech therapy for various indications. In October 2004, the first and only Chair of Complementary and Integrative Medicine in Germany was established at the University of Duisburg-Essen. This was made possible through funding from the Alfried Krupp von Bohlen and Halbach Foundation. Its clinical and academic background provides the ideal model and means to integrate current alternative medicine research findings into the framework of mainstream hospital care.

Example: Leech Therapy for Osteoarthritis of the Knee

The use of leeches for pain management in osteoarthritis of the knee is a prime example of the paradigm of Integrative Medicine. Although leech therapy may sound exotic in our part of the world, it has been used since antiquity. Scientific studies confirm the positive effects of leeching on knee pain in osteoarthritis. The onset of analgesic effect occurs after a mean period of three days following a single application of four to six leeches to the knee region; pain is reduced by an average of 60% in roughly 80% of patients with gonarthrosis [3]. Leeching has long-lasting analgesic action: pain is reduced by 70% for at least three months, and the need for analgesic drugs is reduced by 45% for up to 10 months. Thus the efficacy of leeching is far superior to that of all other known methods of pain treatment in patients with osteoarthritis of the knee. In many cases therefore leeching makes it possible to decrease and/or eliminate other analgesic/antiphlogistic treatments and consequently, their potential side effects.

Respecting the Wishes of the Patient

The treatment method prescribed is based not only on the scientific evidence and a cost–benefit comparison, but also on the patient's attitude toward the treatment. As is well known, compliance is particularly low when drugs with a high potential for side effects are prescribed for treatment of chronic disease. Interestingly enough, the majority of patients treated with leeches become enthusiastic advocates of the method. Some even develop a special relationship with "their leeches." Once, after we applied for a research grant, the reviewers commented that they could not imagine that patients would voluntarily subject themselves to such a treatment. In response, we conducted a survey of nearly 400 former patients to quantify the "yuck factor." The survey revealed that less than 10% of all patients had initial qualms before treatment, and these generally disappeared after the first treatment. In fact, after recent newspaper reports, our department and the ZAUG leech breeding center in Biebertal, Germany have received hundreds of calls from people interested in leech therapy. Other national and international centers report a similar response.

How Does Leeching Fit into CAM?

In German medical CAM education and training, leech therapy is classified as a so-called drainage technique. The concept of "drainage" has its origin in humoral pathology. It is based on the notion that health complaints are caused by an imbalance of body fluids or "humors." Although this concept is founded on ancient systems of medicine, there is scientific evidence supporting the efficacy of leeching and a number of other methods of humoral drainage. Apart from leech therapy, these include venesection and fasting, as well as the therapeutic use of diuretics and laxatives.

Medical curriculae specify another treatment approach, or "whole system" treatment methods. This includes Ayurvedic medicine and traditional Chinese medicine (TCM). In Ayurveda, leeches are prescribed for a wide range of ailments. Also, the use of dried leeches has a long tradition in traditional Chinese herbal medicine. A large number of leech farms still exist in China today, but most of them specialize in the manufacture of dried Hirudo products. After an initial skepticism, our visiting Chinese physicians have

shown a tremendous interest in the secrets of "Western leech therapy" and plan to implement this knowledge in China when they return. Our Chinese colleagues are particularly interested in techniques combining classic alternative treatments with leech therapy. Three good examples are the use of fasting cures, local compress administration, or acupuncture as a basic pillar of pain management. The effects of these basic treatments intensify those of leech therapy.

Leech therapy has significantly contributed to the globalization of alternative medicine in the past few years. This English language edition of *Medicinal Leech Therapy* is a byproduct of this development.

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14 Legal Aspects of Leech Therapy in the EU and USA

M. Aurich, J. Graf

For the German first edition of the present book, which was published by HAUG Verlag, it was only necessary to present the legal aspects of leech therapy subject to German jurisdiction. The present English-language edition of the book, however, is an internationally oriented version. As such, it must provide an expanded view of the legal issues pertaining to leeching in order to guarantee a successful implementation of leech therapy in the USA and other countries. We feel that it is appropriate to compare and discuss the currently different legal classifications of the medicinal leech as a "medical device" in the USA and as a "drug / medicinal product" in the European Union (EU). The standards of both systems of drug law have undergone considerable change in the last decades. This requires a short introduction to the drug law systems of the USA and EU (see below). The medical systems of the USA and EU are structured differently, as are those of different countries within the EU. Therefore, specific rules may apply only to certain countries. Those pertaining only to Germany, for example, are marked "German law." In order not to expand the scope of the legal aspects of leech therapy disproportionately, the authors ask the readers to independently research the national regulations for the described legal areas to ensure the performance of leech therapy in conformity with the law. The information below provides important points of reference.

In addition to abiding by the general rules of good treatment practice, persons administering leech therapy must consider important legal aspects of treatment. Leech therapists can be confronted with liability, regulatory, and criminal law problems, which pose legal risks to the profession. Patients expect to receive the best possible treatment with safe and effective drugs. This chapter outlines the legal issues specifically related to leech therapy. General responsibilities of healthcare professionals are not included.

To protect the patient and the leech therapist from legal repercussions, the following questions should be answered before the start of leech therapy:

- What is the legal status of leech therapy under drug law regulations?
- What qualifications must a leech therapist have in order to administer the treatment?
- Is the leech therapist adequately informed about potential risks?
- Has the patient been properly informed about how to recognize potential side effects?
- Do animal and environmental protection rules apply?
- What legal requirements apply to the disposal of used leeches?

What is the Legal Status of Leech Therapy?

Summary Comparison of Drug Law and Medicinal Products Law of the USA and the EU and the Implications for Leech Therapy

USA

The Pure Food and Drug Act, also known as the Wiley Act, was passed in the USA in 1906, creating a uniform national legislation for the food and drug sector. In 1938, the Wiley Act was abrogated and substantially amended and replaced by the Federal Food and Cosmetic Act, or Copeland Act, which is still in force today [1]. The Federal Food, Drug and Cosmetic Act itself has meanwhile been amended [7]. The aforementioned legislation lays down the statutory requirements, not only for foods and cosmetics, but also for drugs and medicinal products. Today, proof of quality, efficacy, and safety of drugs and medicinal products prior to their being placed on the market is statutorily regulated by comparable high-quality approval procedures in both the USA and the EU.

EU

The harmonization of drug laws within the EU commenced with the passage of Council Directive 65/65/EEC in 1965 [2]. Considerable aspects of drug law in the EU were extensively harmonized by various later directives. EU directives are to be implemented in form and content via the national legislation of the Member States. Further requirements may apply in the Member States

as long as they do not obstruct the free movement of goods and are in conformity with the EU constitution. Unlike the USA, the different Member States of the EU have different national regulations for foodstuffs and medicinal products, the basic standards of which, however, are identical. The EU system of drug law has a three-part structure:

1. EU-wide regulations that apply throughout the EU and which are enforced and controlled by the EU.
2. National regulations that apply in a given country and which are nationally controlled but are mutually recognized by several other EU Member States.
3. National regulations that apply only in a given country and are nationally controlled by that country.

This three-part structure can also be seen in the framework of the alternative approval procedures in the EU. In addition to receiving approval for certain drugs by the EU administration (central authorization procedure), it is also possible to receive national approval (decentralized authorization) for various drugs from an EU Member State with a mutual recognition procedure that allows for the extension of medicinal product approvals to other EU Member States. Unlike the USA, regulations for drugs [2] and medicinal products [4] are regulated by different legal norms in the EU.

Current Legal Status of Medicinal Leeches as Drugs / Medical Devices in the USA and EU

USA

In 2004, the medicinal leech was approved by the US Food and Drug Administration (FDA) as "an adjunct to the healing of graft tissue when problems of venous congestion may delay healing, or to overcome problems of venous congestion by creating prolonged localized bleeding" (quoted from the 510(k) summary of statement for medicinal leeches as a medical device and the product information sheet from Leeches USA). The decision to classify medicinal leeches as a medical device was based on the use of medicinal leeches prior to 1976, clinical experience, the manufacturing process, and past clinical use. This allows Ricarimpex SAS to sell leeches through suppliers to licensed practitioners, such as physicians and veterinarians, in the USA according to section 801.109 of the Code of Federal Regulations.

The use of medicinal leeches for research, education, or extraction of active compounds is not regulated by the FDA. Leeches can be purchased from US-based scientific or medical suppliers such as Leeches USA. Because *Hirudo medicinalis* is an endangered species, their import falls under the jurisdiction of both US Customs and US Fish and Wildlife Services; both agencies should be contacted prior to importing the animals to ensure their safe arrival.

EU (Using Germany as an Example)

The medicinal leech was not comprehensively classified as a drug/medical device until the year 2004. In Germany, however, the sale of medicinal leeches was controlled, in part, by the drug authorities. The medicinal leech was unequivocally classified as a medicinal product by the German drug authorities in the framework of implementation of the Twelfth Amendment to German Drug Law (AMG) on July 30, 2004 [5]. The AMG passage that includes the medicinal leech under the definition of a medicinal product designed for medical use (section 2 [1]) reads: "Medicinal products are substances or combinations of substances used to cure, alleviate or prevent diseases, suffering, bodily injuries or pathological complaints." Section 3(3) of German Drug Law also includes the "bodies of living animals" as a substance group.

However, because of the legal consequences of the German Drug Law, *Hirudo medicinalis* is not directly and by nature a "medicinal product." The answer to the question of whether a substance or a preparation of substances is a medicinal product depends on the intended use (German Drug Law §2.1). The concept of "medicinal product" is directly associated with a desire to "market" the active agents or drugs. Medicinal products covered by the German Drug Law may only be marketed by a pharmaceutical company holding an appropriate manufacturing license (German Drug Law §13) and/or distributed by a pharmaceutical business licensed for wholesaling (German Drug Law §52a) and dispensed by a pharmacy. This gives rise to the first important question regarding the treating practitioner's liability towards the patient. It needs to be established whether leeches for use in medical treatment are products of a pharmaceuticals manufacturer with a valid "permit for the production of animal active agents and human drugs under the German Drug Law §11." Leeches originating from other sources, for example medicinal leeches caught in the wild (without official approval), and the use of such leeches for medicinal purposes on a patient are

breaches of the law both on conservation and on species protection (see p. 164). They also breach the German Drug Law (e.g., §9).

With the entry into force of the 14th amendment of the German Drug Law on September 6, 2005 [3], leeches for medicinal applications were included in the licensing obligation by means of a change of definition in the German Drug Law. To implement the content of the legal amendment, §141 set an interim period until September 1, 2008, for licensing applications. A legal medicinal product license for medicinal leeches under the standards of the above licensing procedure will only be possible based on their specific properties as "living drugs."

If side-effects emerge during treatment, a drug manufacturer is obliged to record and evaluate them and, where applicable, report them to the Federal Drugs Monitoring Office (this is mandatory for licensed medicinal products). The manufacturer is also obliged to inform treating practitioners and patients of new developments and potential side-effects, via the packing insert (German Drugs Law §63b). This currently applies to medicinal leeches in Germany. To implement this statutory requirement, the drugs manufacturer relies on information about side-effects supplied by treating practitioners. The practitioners are not bound to supply this by (German) law, but should actively support this procedure, designed to protect patients, as part of their responsibilities as treating practitioners.

Why Has Drug Legislation in the USA and EU Classified Medicinal Leeches Differently?

The respective definitions of "medical device" and "drug/medicinal product" in the USA and EU do not directly account for the different classifications of medicinal leeches in drugs legislation. One approach to an explanation might be that the drugs authorities in the USA and EU hold different views of the mechanisms of action of leeches. Seen in isolation, the suction or letting functions of the medicinal leech would tend towards classification as a medical device, as in the USA. On the other hand, the medicinal functions of the active agents support classification of the medicinal leech as a medicinal product, as in the EU. Given the growing interest in leech therapy and the leech's potential as an effective natural therapy, an international harmonization of views would be desirable in the next few years.

What Qualifications Must a Leech Therapist Have?

As trained healthcare professionals, physicians and nonmedical practitioners have the formal authorization (under German law) to perform leech therapy on a patient provided the patient agrees to the treatment. However, leech therapy is still not included in the (German) national curriculum for physicians, and there are no national training regulations for nonmedical practitioners. The training of nonmedical practitioners in the technique of leech therapy is therefore left to the discretion of the training institution. Considering liability and malpractice issues, physicians and nonmedical practitioners are advised to complete a certified training program in leech therapy before administering the first treatment if their school did not provide comprehensive and certified training in leech therapy. They will then be able to give proof of their qualification should a legal dispute arise.

Many physical therapists are also interested in administering leech therapy as an adjunctive treatment. However, as physical therapists are not allowed to perform any invasive treatments on their patients, they would be taking an incalculable legal risk if they did so. Section 5 of the German Non-medical Practitioner's Ordinance [6] states that anyone working as a nonmedical practitioner without a license as specified in section 1 of the ordinance will be fined or sentenced to up to one year's imprisonment.

Has the Patient Been Properly Informed of the Potential Risks of Treatment by the Leech Therapist?

Leech therapy is associated with certain risks, and the therapist is obliged to comprehensively inform the patient about these potential hazards. All patients must be informed of the general risks associated with leech therapy (allergic reactions, secondary and primary inflammation, scarring) before administering the treatment. Specific risks must be explained on a case-by-case basis when applicable, especially when leeches are applied to critical sites in the face or neck region. The leech therapist must obtain the patient's explicit consent to the proposed treatment with proof that the patient was informed of the potential risks of treatment (see "Information for Patients" in the Appendix).

Has the Patient Been Properly Informed about How to Recognize Potential Side Effects?

In addition to explaining the potential adverse effects of leeching, the leech therapist must also instruct the patient on how to react if such side effects do occur. The patient should always be able to contact the person who administered the treatment so that potential adverse reactions can be assessed and treated as quickly as possible. Severe adverse reactions requiring prescription medications are rare. The medications needed to treat these complications can only be prescribed by a physician. Therefore, if the attending leech therapist is a nonmedical practitioner, he or she must inform and enlist the assistance of a physician immediately.

Do Animal and Environmental Protection Rules Apply?

Medicinal leeches are medicinal devices (USA) and medicinal products (EU). Although animal protection rules may have to take the back seat, they should not be neglected or ignored—that is, insofar as they do not contravene environmental protection, hygiene, and disease control regulations. Releasing medicinal leeches into the wild is in violation of drug laws, environmental protection laws, and hazardous waste disposal regulations (under German law).

What Legal Requirements Apply to the Disposal of Medicinal Leeches after Use?

There are basically three ways to dispose of used leeches in compliance with the law (German law). Used leeches may be:

1. Returned to a "leech retirement" pool, (this has, however, been banned by the German drug authorities in July 2006).
2. Killed by freezing.
3. Killed by immersion in alcohol.

After they are killed, the leeches should be disposed of as hazardous waste materials as they are potentially infectious (in Germany they are classified

as Class 18 02 02 waste). Small practices that do not have an industrial waste disposal system can place the leeches in a tightly sealed container and dispose of it with their general waste.

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Appendix

Check List: Materials for Leech Therapy

- Fresh, unused, well-cleaned leeches (delivered at least 24 hours ahead)
- Small, sealable container for used leeches; should be partly filled with water
- Waterproof padding and towels
- Compresses, roller bandages, highly absorbent fleece material
- Adhesive tape
- Hot and cold water
- Scissors, disposable razor
- Surgical gloves
- Glass tube, small cupping device or cut-off disposable syringe if needed
- Blood pressure gauge
- Allergy medication, injection supplies, lancet or needle

Check List: Leech Therapy Procedure

- After informing the patient thoroughly about the treatment, check the patient for contraindications and have them sign the consent form.
- Send the patient to the bathroom before starting the procedure.
- Expose the target area and position the patient on a surface protected by waterproof material.
- Locate and inspect the leech application sites. Mark off borders of application site with tape for site restriction if needed.
- Use low lighting to create a quiet, darkened environment.
- Select leeches and apply them with the aid of a cupping glass or modified syringe.

- If the leech does not bite within five minutes, wet and warm the patient's skin (immerse in warm water or apply a warm towel, etc.).
- If the leech still fails to bite, use a lancet to prick the patient's skin.
- Monitor the patient continuously until the leeches drop off, or give the patient a bell to ring when the leeches have fallen off. Have gauze and a suitable container for the used leeches ready.
- Cover the wound loosely, check the extend of bleeding 15–30 minutes later, and if satisfactory, cover it with a thick absorbent dressing.
- Remind the patient about afterbleeding from the leech bite and make sure the patient has your telephone contact information.

Pain Journal Used to Document the Results of Leech Therapy

Address of medical practice: .....

Office phone: .....

Mobile phone: .....

Patient's last name: .....

First name: .....

Change in knee complaints after leech therapy

1 How many hours/days passed before you noticed the first signs of improvement of knee pain and other symptoms?

.....

.....

.....

.....

.....

2 Change in knee complaints over the course of time (days):

.....

.....

.....

.....

.....

The first entry in the journal should be made three days prior to leech therapy. Please rate the severity of symptoms on a daily basis (each evening) by marking the number on the pain scale that best reflects the symptom intensity on that day (0 = No symptoms, 10 = Maximum symptom intensity).

Pre-treatment Ratings										
No Symptoms										Maximum Symptom Intensity
Day –3 / Date										
0	1	2	3	4	5	6	7	8	9	10
Day –2 / Date										
0	1	2	3	4	5	6	7	8	9	10
Day –1 / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date of Leech Therapy:										
0	1	2	3	4	5	6	7	8	9	10

Post-treatment Ratings										
No Symptoms										Maximum Symptom Intensity
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10
Day / Date										
0	1	2	3	4	5	6	7	8	9	10

Information for the Patient and Consent Form

Dear Patient,

You are scheduled to receive leech therapy. The treatment may produce side effects, which are usually harmless and temporary.

The following side effects may occur:

Common side effects:
- Mild pain during treatment
- Prolonged afterbleeding (bleeding from the leech bite)
- Itching and reddening of skin around the leech bite (allergy-like reaction)

Rare side effects:
- Infection (skin infection)
- Temporary enlargement of lymph nodes
- Pigmentation disorders/scarring at site of leech bite
- Temporary swelling of treated part of the body, arm, or leg

Some side effects require treatment (compression bandages for bleeding, antibiotics for infection, antihistamines for allergies, etc.).
If side effects should develop, please contact us by phone or come in to the medical practice/clinic for assessment.

Contraindications: Leech therapy should not be performed in patients with:
- Anticoagulant co-medications (e.g., Marcumar)
- Hemophilia, hematological diseases
- Acute gastric ulcers or erosive gastritis
- Anemia
- Immune deficiency due to AIDS, chemotherapy, etc.
- Severe chronic diseases (advanced-stage cancer, dialysis, etc.)
- History of poor wound healing (associated, e.g., with poorly controlled diabetes mellitus, obesity, and long-term cortisone treatment)
- Known allergy to any of the active substances in leech saliva
- Tendency to develop keloids or scarring

Aftercare

We recommend that you come in for a dressing change on the day after treatment.

You should come in again for a check-up three to seven days after treatment or sooner if complications arise.

I consent to the proposed treatment (leech therapy) and aftercare measures.

Dr. / Mr. / Ms. ..... has explained the potential side effects to me. To my knowledge, none of the above-mentioned contraindications apply.

I have no further questions.

.....
Place and date signed

.....
Patient's signature

.....
Place and date signed

.....
Signature of doctor/leech therapist

Pretreatment Information for Leech Therapy Patients

Dear .....

You are scheduled for leech therapy at (time) ..... on

(date) ..... . This important information is for you to read in advance of your appointment.

Do not use any perfumed lotions, shower gels, and medical ointments or oils on the day before the treatment or on the day of the treatment.

You must inform the leech therapist if you are taking any blood-thinning medications (anticoagulants).

The entire leech therapy procedure will take two to three hours. Please schedule your time accordingly. On the day of the treatment, you should rest and elevate the affected limb as frequently as possible.

Continue to elevate the limb frequently for at least two days after treatment.

We recommend that you come in to have the dressing changed on the day after the treatment, and that you present for a check-up three to seven days after treatment.

Once the leeches have dropped off, the leech bite will be covered with a thick absorbent dressing which may restrict your movements. Loosely fitting clothing or wide (open-toe) shoes should be worn over the dressing.

It is not advisable to drive a car during this time.

State medical programs and basic medical insurance policies usually do not cover the costs of leech therapy.

If you have any further questions, please call us during office hours for assistance:

Tel. ..... .

Best regards,

Leech Therapy Procedure

Dear Patient,

You were referred to us for leech therapy, and the doctor who administered the treatment told you about its potential side effects and contraindications. This information sheet will give you and the subsequent care physician important details regarding further treatment.

Once the leeches have finished extracting blood, the target region is covered with a thick absorbent dressing, which should be left in place until the following day. We recommend that you refrain from all strenuous activities on the day of the treatment and elevate the treated limb as frequently as possible.

You will have been given additional dressing material. If the primary dressing becomes soaked with blood from the leech bite, then cover it with the additional dressing material. Contact our institute/practice if heavy bleeding continues or if you are worried about any other side effects. Call the regular number during office hours or the following number after hours:

Tel. ..... .
The dressing should be changed on the day after treatment. This should preferably be done at our institute/practice.

Itching and reddening of the skin around the leech bite may occur. These symptoms are usually harmless and are presumably part of the leeching effect. They usually respond well to simple remedies such as curd compresses, ice, and insect bite ointments (antihistamines). Contact us or another physician immediately if the symptoms become more severe (fever, chills, circulation problems, etc.).

Approximately one week after treatment, we will contact you to ensure that the treatment was completed properly. This quality control measure is for your safety and for our records.

If you or the subsequent care physician should have any further questions during the course of aftercare, please call us during office hours at the

following phone number for assistance: ..... .

Yours sincerely,
Your Treatment Team

Index

Page numbers in *italics* refer to figures.