Henry Ford Hospital Medical Journal

Volume 9 | Number 4

Article 3

12-1961

Allergy to Leeches

Thos. J. Heldt

Follow this and additional works at: https://scholarlycommons.henryford.com/hfhmedjournal

Part of the Life Sciences Commons, Medical Specialties Commons, and the Public Health Commons

Recommended Citation

Heldt, Thos. J. (1961) "Allergy to Leeches," *Henry Ford Hospital Medical Bulletin*: Vol. 9: No. 4, 498-519. Available at: https://scholarlycommons.henryford.com/hfhmedjournal/vol9/iss4/3

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.

ALLERGY TO LEECHES*

THOS. J. HELDT, M.D.

The purpose of this contribution is to ring the bell of caution in the field of medicine to the end that the bite of the leech must be included in the disconcerting and even dangerous reactions to other insects,1 such as mosquitoes, spiders, bees,2,4 wasps,3 hornets,2,5 ants,6 and the lowly snail.7 In the mind of most lay people and in the mind of most doctors in fact, the medicinal leech is without blame and can be incriminated with difficulty, but it has been vulnerable throughout the centuries and its bite is not to be taken too lightly at the present time. However, the medicinal leech is one thing; the wild leech is quite another. It is very particularly the latter upon which the writer will center his attention with pertinent references to the former.

The leech is a parasite of the animal kingdom. A glance at the following Classification Table gives its usual taxonomy.

In general, it may be well to think of the leeches as falling into three groups: marine leeches, fresh water leeches, and terrestrial leeches. It is of course with the fresh water leeches that we are here concerned but a few words regarding the other two kinds will not be amiss. The marine leeches are quite secure in their salt-water habitat and feed largely on fishes. The terrestrial leeches have made history and gained recognition in divers ways. Sir J. E. Tennent¹⁹ gives account of how the land leeches routed an entire battalion of English soldiers from their wooded encampment in Ceylon. Hammerton²⁰ also refers to this incident in his discussion of the "Pigmy Trappers," and further mentions these leeches have surprised and slain sleeping human beings. Harmer and Shipley¹² record how a genus of the fresh-water leeches, the Limnatis, proved disconcerting to Napoleon's soldiers at the Nile in 1798.

CLASSIFICATION TABLE*

Phylum Annelida

Class Hirudinea

Order 1. Rhynchobdellida (No jaws, but proboscis; colorless blood). Family 1. Ichthyobdellidae (Fish leeches, mostly marine). Family 2. Glossiphonidae (Fresh water leeches). Genus Glossiphonia: Glossiphonia stagnalis Glossiphonia fusca Glossiphonia complanata Genus Placobdella: Placobdella montifera Placobdella parasitica Placobdella rugosa Order 2. Gnathobdellidae (With jaws, no proboscis, red blood, fresh water and terrestrial species. Family 1. Hirudinidae (Three toothed jaws, 5 pairs of eyes).

Includes Hirudo medicinalis and the horse leech (Haemopis mormatis (Aulastomum gulo).

Family 2. Herpobdellidae (With three muscular ridges in place of jaws; three pairs of eyes).

Genus Haemadipsa includes a number of pugnacious land leeches with notorious histories.

fi

ir

e)

01

sp

Ve

Genus Limnatis proved a nuisance to Napoleon's soldiers at the Nile.

Genus Trocheta is an English land leech that lives on earthworms. *For confirmations, variations, and amplifications see Selected References, 8 to 18.

*From Division of Neurology and Psychiatry. This investigative study was decided upon in July 1944. Request was made to the Research Committee of the Hospital and it was authorized as research project number 66. World War II responsibilities with personal health problems brought some protracted interruptions.

Fresh water leeches are common to the lakes, ponds, and creeks of the United States. Land leeches are less common but are well known to zoological gardens and most students of biology. When opportunity presents leeches feed avidly on the blood of vertebrates. Most leeches and especially the medicinal leech can ingest three times their own weight of blood. Since it requires from 9 to 12 months to digest such a repast meals may be few and far between. Leeches usually reproduce two times, during spring and summer. They are hermaphroditic, but the eggs of one parasite are fertilized by the spermatozoa of another leech. Leeches are of course of various sizes, from the barely visible horse hair size to several inches in length. The writer personally collected from the domesticated water buffalo of the marshes of the Marejo Island in the delta of the Amazon River a leech 6 inches in length and distended to 3 inches in width by the ingested blood.

A considerable literature has built up on the subject of leeches, both ancient and modern and in most languages. Hence, the bibliography for this article will be divided into Selected References and Supplementary References, to give better opportunity for checking and for verification. Extent of review will be judged on pertinence to the subject under discussion.

1

3

r

e

f

b

n

d

e

t

nes

the

ms.

in

zed

Drescher and Engel²¹ in 1947 present a noteworthy article on the medicinal leech in the Netherlands. After historical references and comments they outline the use of the medicinal leech in their homeland. They list 44 references in their bibliography, but inasmuch as they concern mostly the pharmaceutical aspects of the subject they will not here be inspected further.

It is judged that Albach²² in presenting his doctoral dissertation entitled: "Observations on the Therapeutic Use of Leeches with Particular Reflections as to Anaphylactic Appearances" made his primary consideration the determination as to leeches having a favorable effect on thromboses or thrombophlebitis. A secondary purpose is to note if anaphylactic reactions occur in the use of the medical leech.

In making his historical review Albach calls attention to some interesting data, including the following: Although blood-letting and cupping in all manner of ways were in common use by the Egyptians 3,000 years, B.C., and although used freely by Hippocrates (460-377 B.C.) and Erasistratus (300-250 B.C.) it was Nicander of Colophon (200-130 B.C.) who first used the leech medicinally. After him they were used freely by many: Themison of Laodicea (123-43 B.C., pupil of the great Asclepiades); Aretaeus of Cappadocia (30-90 A.D.); Galen (130-200 A.D.), and others. Antyllos,²³ notable Greek physician and surgeon (100-150 A.D.) was the first to use the leech-cut ("Blutegelschnitt"). If it be necessary to use leeches, and in case few are available, or a sparing number have been applied, it may prove expedient, at the time the leech has drunk his fill, to cut off his tail with a scissors ("... den Schwanz mit der Schere Abschneiden"). After the blood has run out of the leech it will reattach itself and will not let go until it is removed by ^{sp}rinkling some salt, soda, or ashes upon it. This observed fact is in use to this ^{very} day.

During the 19th century leeching in France reached an immeasurable degree, even to the extent that 100,000 leeches were used in one year in a single hospital. ("... an einer einzigen Krankenhaus Abteilung wurden bespielsweise jährlich 100,000 Stuck gebraucht;"). This popularity was in large part due to lectures by Francois Joseph Victor Broussais (1772-1830), so much so that his promoted methods were referred to as Broussaisism. Heinz Bottenberg at the time declared: Upon such enthusiastic excesses a repercussion must of necessity follow ("Auf so wilde Uebertreibungen musste notwendigerweise ein Rückschlag erfolgen".) Such spirited use of leeching received its setback over the ensuing years. Rokitansky in Vienna and Virchow in Berlin were developing more and more disbelief in the humoral theory, and this discredit had a dampening effect on blood-letting, cupping, and the use of leeches.

Albach (p. 7) says the best known and most widely distributed leech species are: Hirudo medicinalis, the German leech; Hirudo officinalis, the Hungarian leech; and Hirudo Sanguisuga, the horse leech. The habitat of H. medicinalis he gives as all of Europe, southwestern Asia, and north Africa; that of H. officinalis as southern Europe, Yugoslavia, Hungary, and Bulgaria. He further says that since the mad days of Broussaisism H. officinalis has been used almost exclusively in medical practice; the horse leech, since it elaborates no hirudin, is not used medically. Albach gives credit to "John H. Haycraft" (John Berry Haycraft 1857-1922),24 physiologist of Birmingham, England, for first isolating hirudin from the throat glands of the leech in 1884. After further declaring: "Der heute allein therapeutisch gebrauchte Blutegel ist der Hirudo officinalis" Albach describes the external colorings and markings of that parasite but he does not give those details necessary correctly to place that insect taxonomically. With references to different authors Albach records some general observations and anatomical details. Among them the following are of interest here: The life span of the leech is 10 to 20 years; it is not sexually mature until its 9th year; and, it must be 3 or 4 years old before it can be used therapeutically. The hirudin producing glands were discovered by Brandt in 1833.

Leeches are very sensitive to atmospheric conditions especially hot days and thunder showers. Albach (pp. 10-11) presents various methods used in applying leeches and encouraging prompt biting; the duration of attachment varies from 10 minutes to two hours depending on the sucking intensity and the temperament of the insect; it will fall off when it has obtained its fill; and, for some 24 hours there may be some bleeding where it was attached. He mentions that Dinand and Bottenberg had advanced studies to show that the leech could harbor a "leech-bacillus." However, investigations in the laboratories of the Hygienic Institute of the City University (Frankfort am Main), under the direction of Dr. Küster, did not confirm such findings, but instead showed that the ingested staphylococcus and the colon bacillus could live in the gut of the leech for months without noticeably disturbing its welfare. Albach (pp. 12-15) outlines with noteworthy comments the research studies of several investigators as to the pre-and post-operative use of leeches, and of parenteral injections of hirudin, in the hope of preventing or altering the formation of thrombi and emboli. Bleeding time and coagulability of blood is given due

consideration as are urinary excretion and changes. It is noted incidentally that the secretions of one leech can prevent in vitro the coagulation of 50-100 cc. of blood; on that basis the application of 60 leeches to a person at the same time could prevent the coagulation of his entire blood mass if that be estimated at 6,000 cc.

Albach cites (p. 17) Bosc and Delecenne²⁵ and Haupstein²⁶ as claiming that immunizing bodies are produced by the leucocytes of the patient in leech-therapy; and, Heisler that the application of 6 leeches in the course of 7 or 8 or more days can induce anaphylactic reactions. He firmly declares he disagrees in both instances.

Albach (pp. 18-19) briefly reviews two cases which to me have ear-marks of allergy to leeches. The symptomatology after the second application of the leeches is highly suggestive, but Albach made no immediate control studies, nor investigative comparisons, nor follow-up observations. Comparative injections of hirudin are carefully described, but concluding observation is voiced in this statement: "Eine Anaphylaxie oder etwas Aehnliches konnte von mir nicht festgestellt werden" (p. 21). (I could not confirm an anaphylaxis or a similar condition.) In support of this conclusion Albach records 16 case reports in the use of leeches for various conditions, varying from priapism to "cold abscess." (pp. 21-25).

He maintains that allergic and anaphylactic reactions to leech bite are merely local tissue responses. This for the reason that antigen-antibody elaboration to leech bite has not been proved. These deductions are clearly set forth in the 4th, 5th, 6th, and 7th statements of his summary:

"4. Infektionen durch Blutegel-Bisse sind möglich, aber offenbar selten. Meist handelt es sich um Erysipeloide. Diese dürfen nicht mit urticariösen Eczem oder anaphlaktischer Erscheinung verwechselt werden." (Infections due to leech bite are possible but obviously rare. They are involved mostly in the erysipeloids. These conditions are not to be confused wth urticarial eczema or with anaphylactic appearances.)

"5. Anaphylaktische Erscheinungen können auf Grund von Versuchen an 50 Fällen nicht bestätigt werden, weder beim Blutegel-Bis noch bei wiederholter intracutaner Impfung mit Hirudin." (Anaphylactic reactions, on the basis of investigative studies on 50 cases, have not been confirmed, neither by leech-bite nor by repeated intracutaneous injections of hirudin.)

"6. Rötungen, die bei beiden Applikationsarten gesehen wurden, sind nur lokale Reizungen der Vasomatoren-Endigungen mechanischer oder chemischer Art." (Erythemias, which may be seen with both methods of application, are only local irritations of vasomotor terminations of mechanical or chemical nature.)

"7. Die Antigen-Natur des Hirudin oder des Mundsekretes ist noch nicht erwiesen, deshalb mus vorläufig die Annahme einer Bildung von Immunkörpern und die Fähigkeit zur Auslösung anaphylaktischer Reaktionen abgelehnt werden." (The antigen nature of hirudin or of the oral secretions of the leech have not yet been

proved, therefore the assumption of the formation of immune bodies and the capacity to release anaphylactic reactions must be regarded as premature.)*

Sabrazès²⁷ opens his article with the statement: "I — Il est rare quon signale l'intolerance aux application de sangsues" (p. 642). Then he makes brief reference to the ancient use of the leech in India, Greece, and Rome with mention that its use was especially recommended by the School of Salerno. He says leeching was particularly promulgated by Nigrisoli's publication in 1665; more recently the studies of Derheims, Moquin-Tandon, Ebrard, and Busquet. Sabrazès then informatively reviews the work of Louis Vayson, with whom he seems very much in accord, except that he declares Vayson is in error when he states that the developing leeches of the Gironde aspirate blood from the engorged bodies of adult leeches, whereas the young leeches actually obtain their sustenance from frogs, tadpoles, and fishes.

Sabrazès remarks that at the time of his writing, 1933, that the average number of leeches sold per month by an important pharmacy in Bordeaux was from 30 to 100 at one franc 25 to one franc 50 per leech.

In "II" Sabrazès tries to answer these questions: "Y-a-t-i-l des cas de sensibilisation, des cas d'intolerance a l'egard des piqures de sangsues? Leur emploi risque t-il d'etre limite per cette evenualite?" (p. 644). He gives two case reports at some length. One of them, to my mind, is indicative of allergy to the leech bite (p. 644); and of it he remarks: "Ce cas releve probablement d'un etat de sensibilisation, sinon d'anaphylaxis." (p. 645).

In his "III," Sabrazès outlines the obtaining of hirudin from the heads of leeches; its use in thromboses and various diseases, and with appropriate comments and interpretations.

His discussion of "IV" opens with: "Les accidents du fait de l'application de sangsues sont rares. Il y a plus d'un siecle, Paul Jolly (Sur quelques accidents qui peuvent resulten de l'application des sangsues, Nouvelle bibliotheque medicale tomes III et IV Paris, 1827) leur consacrait un travail." Then with brief references to authors Pelletier and Hazard, Derheims, and Mayer as to the probability of septic material carried to the patient in the bite of the leech, he remarks: "Il est donc indispensable d'examiner les sangsues et d'ecarter les douteuses." He adds that except for the reaction of hypersensitivity he knows of no other risks in leeching beyond the foregoing then the tendency to lipothymie of some nervous patients and an occasional excessively prolonged bleeding after the leech has fallen off. Sabrazès concludes his article with this statement: "L'etude des sangsues est a nouveau d'actualite et souleve toujours des questions de biologie dont nous venons de laisser entrevoir l'interest." (p. 647). (The study of leeches is a new question of the hour which ever raises inquiries of biology which bring a welcome challenge to our interest.)

*In the closing statement of his article (p. 26) Albach remarks: "Meine hierüber (regarding details of hirudin effects after detachment of leech) zum Beweise angestellten Arbeiten and Versuche werde ich in einigen Wochen veröffentlichen." However, although eight subsequently published articles by Albach have been found, the title of not a one reflects any further study on leeching.

Jimenez, Miguel F.,²⁸ was much concerned in the first half of the 19th century about "accidents" his patients experienced in the application of leeches. He reported these "accidents" at some length. Outstanding is an urticarial reaction of considerable severity. He mentions two deaths resulting from this type of accident. Jimenez states these urticarial attacks, often with syncope, always came immediately on termination of the leech having obtained his fill of the patient's blood.

Jimenez judged that the causes of these occasional reactions of his patients to leeches could be included under two general headings: First, the type and activities of the leeches themselves; secondly, the health conditions found in the persons to whom the leeches were applied. Under the first heading he included the species of leech, time of year in which the leech was used, whether the leech had been used on a patient before and whether these leeches inoculated the patient with some poisonous principle at the time of the bite. Under the second heading the class of disease or condition being combatted, regions of the body to which the leech was applied, and lastly the constitution, predisposition, or particular idiosyncrasies of the patient. Jimenez discusses each factor in turn. As to the species of leech he says only the gray or medicinal leech (Sanguisuga medicinalis) was used. He recounts how this type of leech was applied to three patients simultaneously from the same container. One patient developed urticaria, the other two showed no unusual reactions. He remarks that he is certain from his observations in every month of the year that time of year is not a factor in causation. He further comments that the re-use of the leeches does not seem to be a factor for such re-use is common in some of the hospitals, yet there is no increase in the number of untoward reactions reported. As to the inoculation of a poisonous substance at the time of the bite, he declares that he can only associate it with the particular status of the patient and not with the annelid.

Jimenez cites 15 different disease conditions for the 18 cases he reports and firmly concludes that it is not the disease which is the determining factor in the urticaria and the cerebral congestion encountered. He says further that he has never seen urticaria due to the application of leeches in patients with high fever such as in scarlatina and like conditions, although leeches were often used in such cases. He further concludes that the particular area of the body to which the leech is applied is also not a causal factor.

In referring to the cause of this recurrent accident, after leeches have been applied a second time to the susceptible patient, "to constitution, predisposition, or idiosyncrasies of the individual," Jimenez says: "It is with a feeling of advancing a subterfuge," but he adds: "It is very probable that this conception embodies the cause or one of the true causes of the repetitive morbidity." He likens the condition experienced by the patient to the occasional effect seen in the eating of "clams, crabs, etc." He makes a further point in saying that he has never seen this "accident" affect children under the age of eight, although leeches were applied frequently in order to avoid phlebotomy.

Jimenez, Lauro Maria,²⁹ a niece of Miguel F. Jimenez, apparently stimulated by the earlier observations of her uncle, made painstaking studies of the leeches

of the lower half of the Valley of Mexico. She investigated specifically those leeches which were at the time being used medically. She studied three species in particular. These species were collected from the streams and canals within a 100 mile radius of Mexico City. She describes fully and gives drawings of four species, but only three of these were consistently used in medical applications. Except for one species, to avoid confusion, she named the species according to the province in which the leech was collected. Glossiphonia granulosa was the leech most commonly used and apparently most collected. It was also found to be the chief offender. Hirudo Tehuacanea and Hirudo Queretaro she says were both thoroughly innocuous so far as precipitating morbid accidents. She briefly identifies Bdella Ixmiquiltanea as she does the genus Aulastoma but these are passing references only. In her article Lauro Jimenez gives credit to "a clever pharmacist of this city" (Herrara) for suggesting that the Glossiphonia granulosa secretes a poisonous substance which is injected at the time of its bite. Jimenez judges that the poison secreted by gland cells associated with the proboscis is minimal in effect when the leech has been cleanly kept. She adds that she has not been able to demonstrate any actual gland in dissection of the mouth of the leech.

Jimenez (L. M.) sums up her annotations in the following:

"1. Three species of medicinal leeches have been studied best in Mexico: the Glossiphonia granulosa, the Hirudo Tehuacanea and the Queretanea.

"2. The accidents which have been observed as a consequence of the application of leeches have been brought about by the Glossiphonia granulosa which appears to carry a buccal gland which secretes a poisonous liquid.

"3. The leeches of this species generally do not produce such accidents when they have lived for some time in clean water which is frequently changed.

"4. Furthermore, a special constitution in the patient is necessary for the reaction, a matter not known until now.

"5. The accidents consist of an urticaria more or less general, congestive attacks in the head, and swooning attacks which are sometimes fatal.

"6. The bites of the Queretaro and the Tehuacan are completely innocuous.

"7. These species extract a quantity proportional to their number: a little more than half a dram for each of them.

"8. In view of the terrible accidents produced by the Glossiphonia and the

inoffensive bites of the Tehuacan and the Queretaro, it is not only useful but essential that there be acclimatization of the latter in this capital (Mexico City).

"9. And considering one of the causes which opposes this intention, the manner in which they reproduce, it is convenient to remove this, by providing the animals with the proper places where they can deposit their progeny, i.e., in adequate tanks."

In September 1866 Jimenez (L. M.)³⁰ reported: "Another Poisoning by Glossiphonia." She outlines the reactions of her patient, a woman 33 years of age, in

adequate manner. She concludes: "One recognizes that she was under the influence of poisoning caused by the Glossiphonia. But in this case, what could be the determining factor in the dangerous accident? It was not a bad quality which the leeches had acquired, from a poor condition of the waters in which they lived, because they had been placed and guarded with great care; neither could this be a predisposition or an individual condition of the patient, because in other cases, she had had no trouble from the use of the same kind of leeches."

"It is necessary to search in another part for the explanation of the phenomenon. It will be remembered that it is not strange that other animals used as food, acquire poisonous properties during the days in which they are occupied with reproduction. It seems to me that it is not an unreasonable idea to admit that this was the cause in this case. In fact, I remember on the same day the solicitude with which these leeches cared for their numerous progeny, sheltered under the abdomen."

"Maybe in the moment of fecundation, there is produced in this animal a toxin which is absorbed by the same wound which is made by the stylet which it has in its mouth; the pathological accidents produced by some of the mollusks, without heads, do not admit of another origin. They are produced when the embryo leaves the egg, they fix themselves under the branchial region and appear to be there naturally. The shell-fish eaten in that state causes eruptions of urticaria with swelling of the face, and sometimes suffocation and other nervous symptoms."

Jimenez, L. M., in the details of her article refers to the studies of Mendoza, Gumesindo and Herrara, Alfonso.³¹ These professors of pharmacy open their article with the following statement: "Clinical experience has demonstrated a fact which science has not yet resolved, namely, the urticaria produced by the bite of the leech which is used here." They then refer to article by M. F. Jimenez in 1844. They recount in clearcut manner the symptoms recorded by Jimenez. These authors declare: ". . . the annelid used in this capital, at least in our time, is not of the genus Hirudo de L. Sanguissuga de Savigny or Jatrobdella de Blainville, which is the only kind used in Europe, but it is of the genus Blossibdella de Blainville, or Glossiphonia of Moquin Tandon. They promptly call attention to, ". . . a difference in the structure of the mouths of these two genuses, which distinguishes the tribes; the Hirudo has three mandibles armed with small teeth, similar to those of a saw and the Glossiphonia lacking these mandibles, and instead has a small tube with a long, fine bristle, like a sound or fine trocar. Thus, the first provides for suction by scarification by the mandibles, while the second makes a perforation by introducing the natural trocar deeply into the dermis, in a manner similar to that of the mosquito (culex pipiens) whose tube is similar but not the same as that of the Glossiphonia ... " Then follows a comparison of the inflammatory wheals produced in keeping with the size of the two insects. The "clear liquid" secreted in the mouths of both facilitates the punctures made and is a further factor in the untoward reactions of some persons. The authors quote Blainville, ". . . speaking of the accidents which take place in Europe from the bite of the medical leech, 'It is necessary to believe that the inflammation occasionally produced by the bite of the leech depends on

505

r

S

,,

n

the difficulty which the animal has in biting — and perhaps also in the mucous material more or less altered, held in the buccal disc and introduced into the wound.'" "Mendoza and Herrara then emphasize the following:

"There is something which has been well proven, according to the reports which we have seen from the practitioners, namely, that the use of the Glossiphonia some time after its removal from the original water source only rarchy produces the phenomenon in question. This leads us to believe that the liquid introduced into the wound is more irritating because of the kind of food which the leech has in its natural state; it is well known that this has a great influence on the secretions of an animal; furthermore, it is a fact that our leeches live in swampy places; it has also been proved that the more swampy the natural habitat, the more poisonous the buccal secretion; when the annelids are kept in a barbershop, the nature of the waters is changed, i.e., previously they were in contact with animal materials and vegetables in decomposition, but now they are in contact with clean and edible things. One must take into consideration the frequency of the change of water and its effect on the diminution of the burning quality of the buccal secretion. The clam (Mytilus Edulis), although in a distinct manner, produces phenomena very similar to those which originate from the Glossiphonia when one does not take the precaution of washing it repeatedly before eating it. To all this, the following objection could be raised: What is the reason that all persons to whom the annelid is applied do not experience the symptoms which are the object of this investigation? We believe it could be answered that here we have the idiosyncrasies, temperament and nature of the disease, the age of the person, and the place of application which we would call predisposing causes; then it is a fact well explored that even the bite of the mosquito, which we have taken as the point of comparison, does not have the same effect in various persons, although the poisonous liquid has been introduced by the bite into each individual. The same observation has been made with respect to the accidents originating from the ingestion of clams. Gervais says 'We believe that the intoxication with these animals is in some cases the result of an individual predisposition.' "

Some of the deductions of Mendoza and Herrara are given in the followings language:

"1. The Glossiphonia has a liquid or buccal secretion of more irritating quality when less time has elapsed since it was captured, and when the place of its habitation

has been more swampy.

"2. The secretion is less poisonous when the time of captivity has been greater and when the number of washings has been greater.

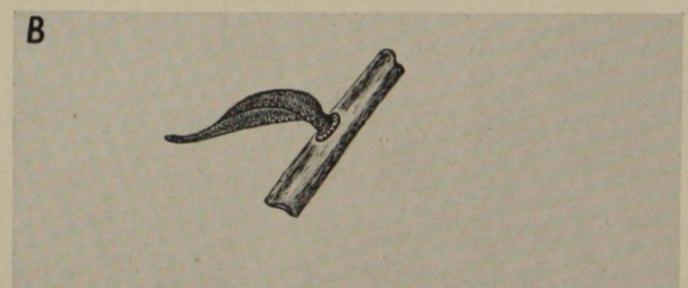
"3. The accidents produced are in relation to what we have called predisposing causes."

Then with the caution: To avoid the use of "recently caught" leeches; and, the suggestion: that the "genus Hirudo" be used ". . . in place of the Glossiphonia,

which for some cause produces such alarming symptoms and even death at times," — the authors close their contribution with this further deduction:

'In conclusion, we shall state that the indicated phenomena would by chance call the attention of the European naturalists, so much so that some of them believe



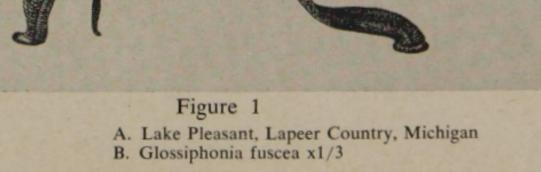


r

g

d,

a,



it is impossible that the genus Glossiphonia could serve as a leech for the extraction of blood; and in proof of this assertion, we see such as was expressed by Fremond in his excellent monograph on medicinal leeches: 'Some authors have written that the black leech, the common leech, and the humble leech are used indiscriminately. It is an error to be refuted: the black leech, not being other than the Aulostama vorax, the common, the nephelis octoculata, the deprunida, a glossiphonia, it is entirely impossible that they could be used, since they are not able to pierce the skin of a man.' Against this observation, we present the simple authentic fact (as amply presented in the foregoing), and with proof so disagreeable that it even involves death itself.''*

Paulet³² in 1808 reports a case, that of an adult woman to whom 6 leeches were applied, 3 to each arm. Apparently one of the leeches very directly punctured a communicating artery between the "cubital and radial arteries," and forthwith a considerable hemorrhage of arterial blood was at hand. The arresting measures common at the time were to no avail. The bleeding was so free and excessive that real disquietude was aroused in both patient and the doctor. Paulet finally stopped the flow of blood effectively by placing his thumbs on each side of the puncture wound. He sums up his observations as follows: "1. That leeches may sometimes puncture an artery or a vein." "2. That in the use of this type of insect it is important to assure one's self that there is not some artery projecting into the area where it is planned to make the application, which is really easily determined by the presence or absence of arterial pulsation." "3. That the compression of an arterial vessel with the fingers, when it is practical, is the means, not only very gently but also most prompt and the most certain in a case such as here reported; and, that an hour of such compression accompanied by calm and confidence is thoroughly sufficient to produce the desired effect."

Stuart³³ in 1805 introduces his, "Observations on the Occasional Injurious Effects of Leeches," with this statement: "Physicians observing the bites of leeches to be occasionally followed by troublesome inflammation, ulceration, and gangrene, have attributed these to some venomous quality of the insect. But, as the precautions founded on this opinion, have proved ineffectual in obviating the evils noted, the opinion may be justly suspected to be fallacious."

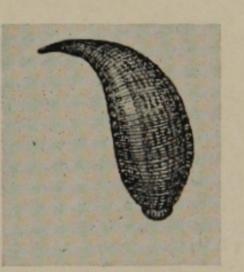
He then describes three species of leeches common in his area (Pa., N. Y., N. J.) at that time without designating them by name, but he adds: ". . . the large brown leech is the species most generally employed in medicine." After a general review of the functioning of this leech he further states: "I attribute them (injurious effects upon the patient) to the state of the system, or to that of the particular patient to which the leeches are attached. . . . because the effects mentioned never occur, except in such cases as evidence the presence of a morbid diathesis, general or local, in the patient to which they are applied; and, because they frequently

*I am very much indebted to Conrad R. Lam, Chief Surgeon in Division of Thoracic Surgery in the Henry Ford Hospital for the translation into English of the 4 Spanish articles listed under numbers: 28, 29, 30, and 31, in the Selected References.

do occur where such diathesis exists." Stating "I have seen many," he reports a case in point, — that of an adult male to whom leeches had been applied to an inflamed perineum. After explanatory details Stuart concludes: ". . . that bad consequences are to be apprehended from leeches when applied in an inflammatory diathesis before general bleedings have been performed; in a general gangrenous diathesis; in an extremely irritable habit; and last, when applied to a patient actually affected with inflammation, ulceration and gangrene."

Telo and Panciroli³⁴ report two cases of local hypersensitivity to Hirudo officinalis. Appended to their article is the following summary in English.

"Two rare cases of abnormal cutaneous reactions to medical blood leech are presented in this article.



S

r

T

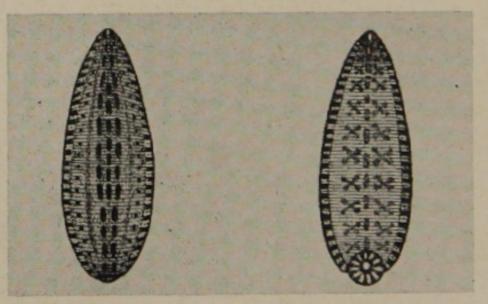
al

y

ry ed



Anterior sucker, enlarged, showing pit from which proboscis is projected.



Ventral View Dorsal View Glossiphonia fusca

Figure 2

"The first regards a subject with obvious signs of an allergic diathesis, who was afflicted with an asthma of mixed etiology, in the multiple sensitized phase, and in whom the first bite of the medical leech, gave rise to no abnormal reactions, but in whom the second bite (10 days later) caused local reactions in the form

of a swollen erythema, a severe pruritus of the histamine type, and an eosinophilia in the blood.

"In the light of these facts, the successful therapy with synthetic antihistamines, and the rapid cutaneous reactions which follow the injection of a protein extract of the leech, appear to substantiate the etiopathogenetic hypothesis of the AA, concerning an acquired hyperergy to Hirudo officinalis.

"The second case on the other hand reacted to the first bite of the leech with a large hemorrhagic pruriginous halo in the hepatic area at the point of the bite. This manifestation was insensible to the action of antihistamines, of slow resolution, and not accompanied by ematological changes.

"The etiopathogenesis of the manifestations seen in the second case, is pictured in the light of their hypothesis, as one in the vast field of idiosyncrasy, with a particularly strong capillary toxicity due to acquired miopragic factors."

Heisler³⁵ in his chapter entitled: "Blutegel" (pp. 1236-1238) reports two seriously septic cases. He confidently describes the effective use of leeches in the recovery of these patients obviously experiencing generalized septicemia, when other measures of therapy had failed. He also briefly outlines three additional cases of patients experiencing anaphylactic reactions.

Orszagh and Alfoldy³⁶ report the preparation of "a coagulative serum prepared by injecting hirudin into animals." This article is cited to show that leeches are currently inviting considerable attention.

Shope³⁷ of the Rockefeller Institute of Medical Research published January 17, 1957 in the Journal of Experimental Medicine a very thought provoking article entitled: "The Leech as a Potential Virus Reservoir." In telling manner it outlines the technique used in injecting leeches with two different viruses, and records (p. 381): "The preservation of hog cholera virus in the bloody gut contents of leeches for as long as 3 months and the similar preservation of myxoma virus for as long as 5 months suggests that the viruses are well protected from physical and chemical factors that might be operative in the open. This relatively long period of survival conceivably could be of importance as a mechanism for the preservation of viral agents in matter, despite the fact that virus seems not to multiply in the leech, and that the leech serves only as a mechanical reservoir."

Additional sidelights on leeches are not difficult to unearth. However, it is judged that the foregoing are sufficient to underscore the warning found in the introductory paragraph.

A Case Report: A highly dynamic, sociable married man of 34 was admitted to the Dermatological Service of the Hospital at 10 p.m. on July 9, 1944. He was disturbed and somewhat fussy about some skin lesions just above his left ankle. He declared that they were painful and disconcerting because "They seem to make me



Figure 3

Left ankle showing old scar of former leech bite, and two lesions of recent leech bites.

feel miserable all over." Staff members of the Division of Dermatology apparently told him that the lesions were due to poison ivy and a solution of gentian violet was applied during the morning of July 10th.

Since the author had known the man and his family personally for some five or six years he paid the patient a friendly visit. At the time of that visit the patient was somewhat upset and declared: "The doctors tell me this is poison ivy, but you know there isn't any poison ivy within a mile of where I got this." (What did you get?) "Leech bites — two of them. I pulled both of them off and killed them with a stone and this is the second time leeches have done this to me." (Tell me.) "Back in July 1936 I was organizing a market for the Kroger people at Owosso, Michigan. I was there a couple of weeks, so on Sunday afternoon I went to the Genesee or Shiawassee River for bass. I didn't have any waders so I just hopped into the water in my shorts. Somewhat later I spied a leech on my left ankle that's the scar there now. I pulled it off. The next morning about 10 or 12 hours after I had pulled the leech off there was a great deal of swelling and I went to a doctor in Flint. That doctor and my superintendent at the time thought that probably in my work I had bruised my ankle with a splinter of pork bone. It took eight days for me to get over it and here I am with a leech bite a second time. If you look at those places carefully on my left ankle, although it's hard to see with all that violet paint on, you can see where the two leeches had their suckers attached." Inspection really did reveal telltale markings which were evident even a few days later and more so after much of the gentian violet was removed.

The writer solicitously presented the complaints of the patient to Dr. Frank R. Menagh, physician in charge of Division of Dermatology. The doctor listened at-

tentively and thoughtfully, — then remarked: I've never heard of it, much less seen it. Looks like poison ivy to me."*

The skin lesions came under control and permitted the patient to be discharged on July 14th. During the time of his stay in the Hospital the writer further revewed his findings with the chief of the Division of Dermatology. The dermatologist was reluctant to consider leeches the cause of the lesions in question. However, the patient remained vehemently positive in his declarations to the writer. Accordingly, the latter undertook a bit of research in behalf of the problem. The lesions such as remained were photographed. (Fig. 3).

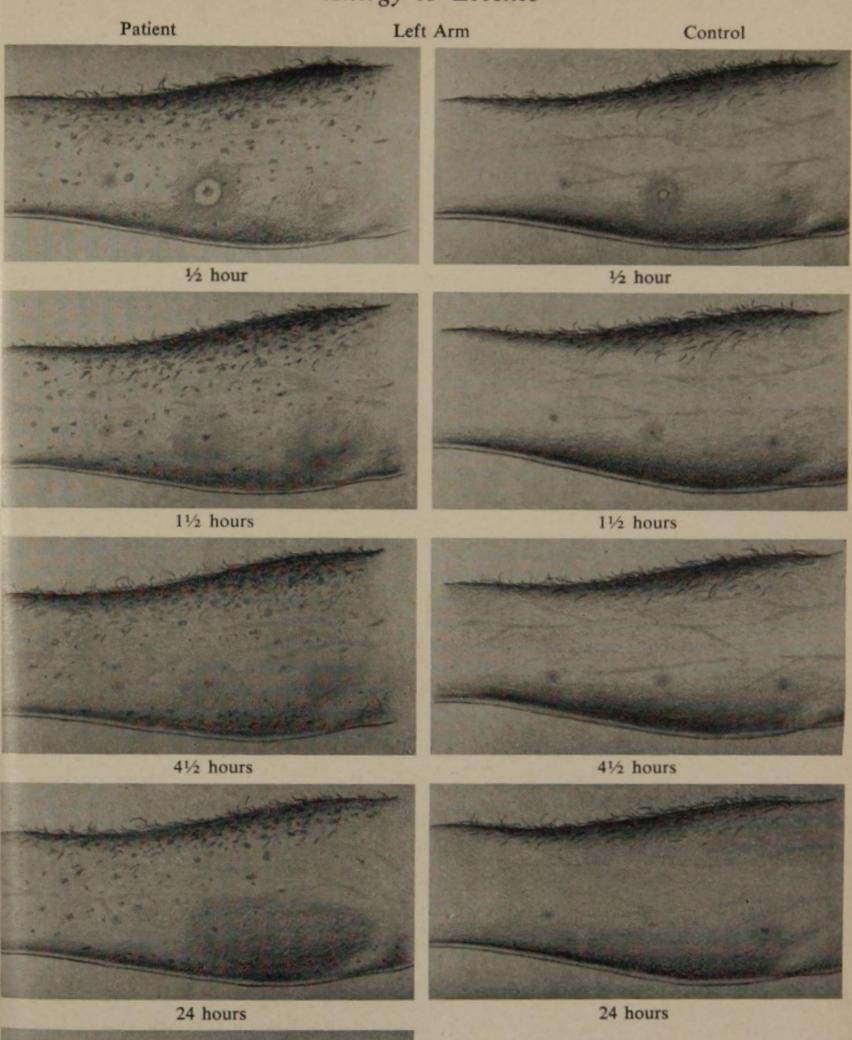
Next, it was undertaken to identify the leeches in question. Hence, the writer accompanied the patient to the area where the leeches lived** and he was successful in catching three of them. (Figs. 1 and 2) He used these as specimens and had them identified and classified and then sent them to the laboratory for the making of extracts which might be used as injection material. After some time the injection material was ready and the patient submitted to an intracutaneous injection of the material in his forearm, together with an injection of normal saline as a control. The writer, as a control, had similar injections. To these injections the patient had a positive reaction to the leech extract whereas the writer had no reaction. This test was in no way convincing to the dermatologist. Hence, the writer after some weeks obtained some hirudin from a commercial firm in New York City. Tests were again carried out. The patient showed a positive reaction to the hirudin but the writer, as a control, showed no reaction.

protruded, - no teeth seen.

About 10 years ago, a patient came from one of the suburbs of Detroit to the Eye Department of the Henry Ford Hospital to have a clinically applied medical leech removed from one of his orbital areas. Its harmless removal occasioned considerable concern at that time. Should it be desired to remove a leech before it has drunk its fill, it is easily done with a sprinkle of salt or soda upon it; blowing tobacco smoke upon it, or, touching it lightly with the burning end of a cigarette.

**Lake Pleasant, Lapeer County, Michigan. (See Fig. 1)

^{*}Such a sincere remark of 17 years ago is not uncommon even today. A letter to the American Medical Association contained this comment in the reply: "Although an allergic response from a leech is theoretically possible it is not likely to be common. Leeching is still being used in many areas and among many peoples, particularly among some foreign populations. It is certainly not a necessary nor recommended medical procedure." An inquiry to the U. S. Department of Health, Education, and Welfare brought in its reply this remark from the National Institute of Allergy and Infectious Diseases: "In regard to your question concerning the use of *Hirudo medicinalis*, I do not know of any place in the United States in which it is being used for medicinal purposes." In wonderment the author telephoned the Health Commissioner of Detroit and forthwith was given four verified addresses where living medical leeches can be obtained. The writer proceeded to one of the addresses and readily procured the dispensable leech. (V. C. Piaskowski Drugs, 7542 Michigan Avenue, at Florida, Detroit, Michigan). Mr. Slezak, the pharmacist, had a lively stock of leeches. "These are the Hirudo officinalis imported from Spain, 'They have no teeth.'" (Have call for them?) "Oh yes, the doctor upstairs prescribes them frequently and then there are other doctors." (names three additional doctors). Inspection of the anterior sucker of the procured leech clearly showed the distal end of its proboscis in the pit from which the proboscis is





One week

No noticeable residuals

Figure 4

Reactions to intracutaneous injections of normal saline (0.025 ml., 0.9%); leech extract (0.25 ml., 1:10,000); hirudin (0.25 ml., 1:1,000,000); from left to right.

It was then planned to try the extraction material again but the dermatologist judged that it would not be dependable because: "First of all - you are two different types of person. The patient is a high type freckled redhead and you are more of stoic German disposition. His skin is more sensitive, yours more resistant. The only thing to do is to find a control who is more like the patient." A young redheaded interne finally volunteered. Intracutaneous tests were made. (Fig. 4) "That's not proof enough" said the dermatologist. So next, leeches again had to be obtained and it was not until August of 1946 that the author succeeded in persauding the very reluctant patient to submit to the leeches again and to help him obtain the leeches. However, the leeches were obtained from the original locale, four of them, and two of them were finally applied to the left forearm of the patient on August 24, 1946, under the supervision of the dermatologist; a third to the left forearm of the interne volunteer; the fourth to the left forearm of the writer. Observations were carefully checked by both the dermatologist and the writer and accurately recorded.* The patient responded with active reactions and required seven days of thoughful therapeutic attention. (Fig. 5) Reactions of the controls were negative. Also, the author had no reaction to leech bites in the tropical waters of the Amazon in 1958. Both the dermatologist and the writer were convinced that the patient did possess an allergy to the leeches in question, namely, the Glossiphonia fusca (Figs. 1 and 2) The Placobdella rugosa was found in the same waters as the G. fusca and it is judged that it too must be held under suspicion.

The dermatologist recorded his observations and interpretations in the hospital record of the patient as follows:

"This note is placed in the history at the request of Dr. Heldt giving our opinion of the reactions which occurred when the leeches were recently placed on the left forearm of this patient. The two leeches engorged themselves and dropped off spontaneously. This patient was observed during the period when these leeches were in place. It was found then and immediately after their removal that he had a perfectly typical wheal, such as would occur in an individual who was allergic to the material to which he was contacted. The reaction showed a wheal about 2½ cm. in diameter and this, in turn, was surrounded by a large areola. Following this, during the next 24 hours and to a less extent in the succeeding 3 or 4 days this patient showed a very vigorous reaction in this forearm. The arm swelled greatly, was hard and brawny and the patient had a typical febrile reaction.

"Our opinion as to the type of reaction here is as follows: this patient was definitely allergic, and the initial reactions were those of an individual who was

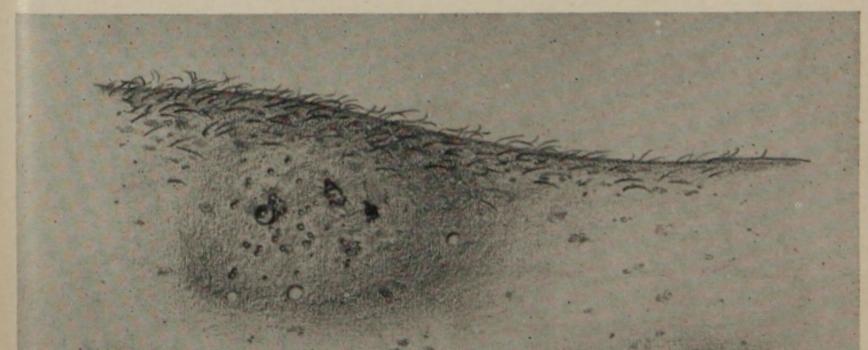
*Two leeches were applied and attached themselves to the left forearm of the patient at 3:45 in the afternoon of August 24, 1946. At 4:15 the leeches had taken their fill and fell off. Post-detachment bleeding after one leech stopped at 4:50; after the other at 7:10 p.m. A well marked wheal was present at the site of attachment by the time the leeches had obtained their capacity. Elevation of temperature was minimal throughout the seven days; pulse, however, was 110 for much of that time. WBC on August 26th, 27th, and 31st were between 10,050 and 10,750, PMN 76 to 57, PME 1-2, Lymphocytes 23-42; Hgb and RBC well within average. Fifty-one hours after detachment of the leeches swelling of the patient's left arm was very noticeable. It measured four inches more at left elbow than at the right.

allergic to the protein material which was absorbed through the epithelium and the traumatized areas as a result of the presence of the leeches on the skin. Whether this was only anti-coagulant or whether there was other protein material due to the presence of the leeches, it is of course, impossible to say. However, associated with this vigorous reaction, there was also an invasion of the lymph channels by bacteria, giving rise to an acute but short-lived lymphangitis which was responsible for the fever.

"This is not an unknown sequence of events. It occurs frequently around the face, particularly the cheeks, ears, eyes, and lips. The portal of entry here is usually an injury or fissure somewhere around the face, and there are other complicating features such as migraine, Bell's palsy, etc. in some of these patients. All of these, we feel, are part of the allergic response to the invasion of the lymph channels by infected organisms. In these cases when this recurs a number of times, the swelling frequently becomes permanent and in this instance, it has been diagnosed as an elephantiasis nostras dura which is due to the invasion of the causal organism."

The important and mutual deduction of the observing physicians then is, that the patient is allergic to leeches and the controls are not.

In conclusion, since many of the fresh-water lakes, streams, and ponds of the United States are populated with leeches, and since terrestrial leeches inhabit some of its wet lands, the medical profession and its unitary constituents must beware of the deleterious potentialities of the parasite leech now and in the future.



ľ

d

S

d

C

ıt

of is

d

15

as

45 ff. ell

er, 50

ge.

Figure 5

Reaction of patient; left arm, to two leech bites at 48 hours.

SELECTED REFERENCES

1. MacLaren, W. I., Eisenberg, B. C., Frank, D. E., and Kessler, J.: Reactions to insect allergins. The incidence of response to testing among allergic and non-allergic persons, California M. J. 93:224, 1960.

2. Shaffer, J. H.: Some aspects of insect allergy, Henry Ford Hosp. M. Bull. 9:191, 1961.

3. Shaffer, J. H.: Wasp sting, J. A. M. A. 177:280, 1961.

4. Shaffer, J. H.: Stinging insects - A threat to life, J. A. M. A. 177:473, 1961.

5. Shaffer, J. H.: Insects and man (editorial), J. A. M. A. 177:505, 1961.

6. Allington, H. V.: Ant bite, J. A. M. A. 176:477, 1961.

7. Poling, J. W.: The host snail, Army 12:52, 1961.

8. Beddard, F. E.: Leech. Encyclopaedia Britannica, 11th ed. Cambridge, England, 1911, v.16.

9. Leeches. Encyclopedia Americana, New York, Americana Corp., 1941, v.17, pp. 191-2.

10. Hegner, R. W.: Invertebrate Zoology, New York, Macmillan, 1933, pp. 321-25.

11. Ward, H., and Whipple, G.: Fresh-Water Biology. First ed., New York, John Wiley, 1918. (Chapter by Moore, J. Percy).

12. Harmer, S. F., and Shipley, A. E.: Cambridge Natural History, London, Macmillan, 1896, v.2 pp. 406-08.

13. Royal Natural History, Invertebrates, vol. VI, Leeches, pp. 441-44, 1896.

14. Cambridge Natural History, Worms, Rotifers, Polyzoa. v2, pp. 392-407, 1910.

15. Ebrard, E.: Nouvelle monographic des sangsues medicinales: description, classification, nutrition, reproduction, croissance, qualities des diverses races, mulplication dans les bassins, les barrails, les marais, et les etangs; du commerce des sangsues et de ses fraudes, legislation, du degorgement, des maladies, et de la conservation, etc. Paris, J. B. Bailliere & fils, 1857, 494pp. (Surg. Gen. Cat., Ser. I, v.4, p. 43)

16. Bosc, Louis Augustin Guillaume (1759-1828): Histoire naturelle des vers, contenant leur description, et leurs moeurs. 2éme ed., Paris, Roret, 1830, 3v. Des Sangsues. v.1 pp. 271-90.

17. Nachtrieb, H. F.: The Leeches of Minnesota (Geological and Natural History Survey of Minnesota) Zoological Series No. V, Part III by Moore, J. Percy, 1912.

18. Miller, J. A.: A study of the leeches of Michigan, with key to orders, suborders, and species, Ohio J. Science 37:85, 1937.

19. Tennent, (Sir) Jas. E.: Ceylon, an account of the Island, physical, historical, and topographical, with notes on its natural history, antiquities, and productions, London, Longman, Green, Longman & Roberts, 1859, v.1 p. 305.

20. Hammerton, J. A.: Wonders of Animal Life. Pigmy Trappers, London, Waverly, 1930, v.4, p. 1721.

21. Drescher, G. N., and Engel, H.: De medicinale bloedzuger in Nederland. Pharmaceutische Weekblad (Amsterdam), 82:555, 1947. (44 Refs.).

22. Albach, Erwin (Frankfurt am Main): Beobachkungen bei der therapeutischen Blutegelverwendung mit besonderer Berücksichtigung anaphylaktischer Erscheinungen. (Inaugural Dissertation zur Erlangung de Doctorwarde in der gesamten Medizin) 30pp. Gelnhausen. Kalbfleisch. Feb., 1939.

23. Sarton, G.: Antyllos. In, Introduction to the History of Science, Baltimore, Williams & Wilkins, 1927, v. 1 p. 280.

24. Haycraft, J. B.: Ueber die Einwirkung eines Secretes des officinellen Blutegels auf die Gerinnbarkeit des Blut, Arch. f. exper. Path. u. Pharmakol. 18:209, 1884.

25. Bosc and Delecenne: Imputrescibilité de sang rendu incoagulable par l'extrait de sangsue, C. R. Acad. des Sc. 123:465, 1896.

26. Haupstein, P.: Die Blutegelbehandlung der Thrombophlebitis (Thrombose) nach Operationen und im Wochenbett, Med. Welt 8:1723, 1934.

27. Sabrazè, J.: I. Le renouveau des application de Sangsues. Le Livre de Louis Vayson of Bordeaux. (Revival in the medical use of leeches. Review of book by Louis Vayson of Bordeaux). II. Sensibilisation et intolerance aux piqures de Sangsues. (Sensitivity and intolerance to puncture by leeches). III. L'hirudine of l'hemophiline (Hirudin or hemophiline). IV. Incidents et accidents locaux (Situational incidents and accidents). Gaz. Sc. Méd. 54:642, 1933.

28. Jimenez, Miguel F.: Sobre los accidentes a que de lugar en Mexico, la applicacion de sanguijuelas, Sociedad Filoratrica de México, Periodico I:213-218, 1845.

29. Jimenez, Lauro Maria: Apuntes sobre Algunas de las Especies de las Sanguijuelas de Mexico (Annotations on several of the species of leeches in Mexico). Gaceta Médica I:483, 1865.

30. Jimenez, Lauro Maria: Another poisoning by the Glossiphonia, Gaceta Médica (México) II:267, 1866.

31. Mendoza, Gumesindo and Herrara, Alfonso: Observation on the leech which is used in this capital. Imprenta de Inclan (Inclan Press). Cerca de Sto. Domingo No. 12. México, Feb., 1865. (From: Pamphlets Vol. 4768, Army Medical Library, Washington, D. C.)

32. Paulet, Jean-Jacques (1740-1826): Observation sur le danger de l'application des sangsues à certaines parties. J. gén. de méd., de chir., et de pharm. 32:269, Soc. de méd., Paris, 1808.

33. Stuart, J.: Observations on the occasional injurious effects of leeches, Philadelphia Medical Museum (Philadelphia) 1:416, 1804-05.

34. Telo, W., and Panciroli, E.: Osservazioni cliniche su due rari casi di ipersensibilita locale al sanguisugio, Il policlinico 61:1674, 1954.

35. Heisler, A.: Aus Forschung und Erfahrung. Landarzt and Naturheilverfahren. Blutegel, Hippocrates 50:1236, 1937.

36. Orszagh, O., and Alfoldy, J.: A congestive serum prepared by injecting hirudin into animals, Lancet 1:28, 1940.

37. Shope, R. E.: The leech as a potential virus reservoir, J. Exper. Med. 105:373, 1957.

SUPPLEMENTARY REFERENCES

Bottenberg, Heinz.: Neue Gesichtspunkte fur die Blutegelbehandlung. Munch. Med. Wschr. 90:128, 1943.

Bottenberg, Heinz.: Nuevos puntos de vista en el tratamiento por sanguijuelas. Actual. med. Granada. 33:100, 1947.

Bottenberg, Heinz: Die Blutegelhandlung ein veelseitiges, Verfahren des biologischen Medizin, 128 pp. Stuttgart. Hippokrates. 1935. (Surg. Gen. Cat. 4th Ser. Vol. 2, 1937.)

Bottenberg, Heinz: Wissenschaftliche und praktische Fragen zur Blutegelbehandlung. Hippokrates 7:677, 1936.

Fermond, C.: Monographie des sangsues médicales, contenant la description, l'education, la conservation, la reproduction, les maladies, l'emploi, le dégorgement et le commerce de ces annélides, suivie de l'hygiène des marais à sangsues, Paris, 1854.

Fermond, C.: Mémoire sur la conservation et la reproduction des sangsues officinales et médicinales, J.d. conn. med. prat., Paris, 18:374, 1850-51.

Gervais, P., and van Beneden, P. J.: Zoologie médicale. Exposé méthodique du règne animal, basé sur l'anatomie, l'embryogenie et la paleontologie; comprenant la description des espèces employees en médicine, de celles qui sont venimeuses et de celles qui sont parasites de l'homme et des animaux. Paris, J. B. Baillière & fils, 1859, 2v.

Moquin-Tandon, Chrétien Horace Bénédicte Alfred (1804-1836): Monographie de la famille des hirudinees. Nouv. éd., revue et augmentee, Paris, 1846, 2v. (Surg. Gen. Ser. I, Vol. 9 p. 442).

2

Moquin-Tendon, (A.) Mémoire sur la sangsue de cheval ou haemopis chevaline, haemopis sanguisuga moq. Jour. de med et chir. de Toulouse, IX:102;140, 1845-6.

Brandt, Johann Friedrich: Blutegel (Naturhistorisch). Encylopädisches Wörterbuch der Medicinschen Wissenschaften, 5:624, 1830.

Brandt, Johann F.: Versuch einer Anatomie und Physiologie des medizinischen Blutegels (Sangsuisuga medicinalis). Memoires de l'academia des Sciences de St. Petersbourg, 2:vi-viii, 1833.

Brandt, Johann F.: Sanguisuga. In: Johann Friedrich Brandt and Julius Theodor Ratzeburg. Medizinische Zoologie, Berlin, 1833, v. 2.

Brandt, Johann F.: Bemerkungen uber die im vollendeten letzen (zweiten) Bande der von Brandt und Ratzeburg herausgegebenen medinischen Zoologie entheltenen neuen anatom. physiologischen Beobachtungen am medicinischen Blutegel. Annalen der Pharmacie, (Liebig), 11:69, 1834.

Nigrisoli, Hieronymi: Progymnasma de hirudinum applicatione interne parieti uteri in puerperis et mensium suppressione; de succi citrei et limonii viribus et usu in febricitantibus et puerpens; de vena in febribus malignis fecanda an superior an inferior; de Romana muliere per biennium utero gerente. Guastalla 1665. 4. Falc. Bur.

Nigrisoli, Hieronymus (1621-89): Progymnasmata in guibus novum praesidium medicum apposito, videlicit hirudinum internae parti uteri in puerperii, et mensium suppressione expositur, rationibus, auctoritatibus, et experimentis confirmatur, de vena in febribus malignis secanda disseritus, et alia medicis non solum, sed omnibus bonarum litterarum coltoribus utilia simul atque jucunda expenduntur. 197 pp. Salisburgi, J. B. Mayer, 1689. (S. G. Ser. I. v. 9, p. 943).

Derheims, Jean Lambert (1798-*). Histoire naturelle et medicale des sangsues, contenant la description anatomique des organes de la sangsue officinale, avec des considerations physiologiques sur ces organes; des notions tres-etendues sur la conservation domestique de ce ver, sa reproduction, ses maladies, son application, etc. 165 pp. Paris, J. B. Bailliere, 1825. (S. G. Ser. V. 4, p. 158).

Vayson, Louis: Guide pratique des eleveurs de sangsues. 2ème èd. 230 pp. Paris, J. B. Bailliere, 1855.

Ledoux, Auguste: Recherches comparatives sur les substances principales qui suspendent la coagulation du sang. Archives de Biologie. XIV:63, 1895-6.

Reutter, Louis: Traite de matiere mèdicale, dorgues vegetables, drogues animales et de chimie vegetale. Paris J. B. Bailliere & fils, 1923.

Dickinson, W. L.: Note on leech-extract and its action on blood, J. Physiol. 11:566, 1890.

Mayer, L.: Pathogenesis of postoperative embolism. Treatment with leeches, Beruxelles med. 10:312, 1930.

Dimitru, V. and Somnes, G. O.: Action Therapeutique de l'hirudine dans les phlebites, la septicemia, et dans quelques affections le nature microbienne. Presse méd. 39:1359, 1931.

Stoia, I.: Results obtained in therapy of septicemic conditions by injection of plasma obtained by application of leeches, Spitalul. 52:490, 1932.

Weil (P. E.) and Boye: Note sur les extraite disseches de tetes de sangsues. Compt. rend. Soc. de biol., Par., 66:345, 1909.

Weil (P. E.): Action physiologique et hemorrhagipare chez le lapin des extraits desseches de tetes de sangsues. Ibid., 516.

Weil, E., and Boye, G.: Recherches physiologiques sur les applications le sangsues en clinique humaine, Semaine Med., Paris 29:421, 1909.

Weil, (E.): The leech in medical treatment. Med. Press & Circ., Lond., 89:166, 1910.

Weil (E.) and Mouriquand, G.: L'hemorrhagic secondaire tardine et grave consecutive a l'application de sangsues. Bull. Soc. med. d hop. de Lyon, 10:499, 1911.

Weil, E., Mouriquand, G., and Chalier, J.: Pouroir hemolytique de l'hirudine de Sachse. Bull.

Soc. med. d. hop. de Lyon, 10:30, 1912.

Kretter, K.: Therapeutic effect of leeches in thrombosis. Polska Gaz. lek. 14:796, 1935.

Cowie, D. M.: On hirudin and hirudin immunity, J. Med. Research, 24:497, 1911.

Marshall, E. K.: The toxicity of certain hirudin preparations, J. Pharmacol and Exper. Therp. 7:517, 1915-16.

Vera, M. and Loeb, L.: Immunization against the anticoagulating effect of hirudin, J. Biol. Chem. 19:305, 1914.

518

*National Library of Medicine, Washington, D. C., was unable to supply year of death.

van Geertruyden — Bernard, M: Contribution a l etude de l'action de'hirudine sur les accidents anaphylactiques, Paris 1921.

Denis, M. A.: Les sangues en medicine. 72 p. Lille. Societe d'Edition du Nord. 1933. These – Lille – No. 34).

Bruck, F.: Leeches as substitutes for venesection. Wien. med. Wchnschr. 93:422, 1943. (German)

Walker, J. W.: Leech infection, case (with hypochromic anemia). East African M. J. 20:114, April 1943.

Lilienthal, H.: Coronary thrombosis, proposed treatment by hirudin. J. Mt. Sinai Hosp. 10:135, 1943.

Chin, T. H.: Leech infection in man. Chinese M. J. 60:241-43, Sept. 1941.

Reeves, B.: Leech infection in Middle East. J. Roy. Army M. Corps 77:205, 1941.

Hirst, G. K.: Effect of polysaccharide — splitting enzyme (from leech extract) on streptococcal infection. J. Exper. Med. 73:493, 1941.

Claude, A.: "Spreading" properties and mucolytic activity of leech extracts. Proc. Soc. Exper. Biol. and Med. 43:684, 1940.

Meyer, O.: New principle in treatment of poliomyelitis (application of leeches over inflamed jugular vein). Internat. Bull. M. Research & Pub. Hyg. (A44-P): 5-9, 1944.

Claude, A.: Spreading properties of leech extracts and the formulation of lymph. J. Exp. Med. 66:353, 1937.

Dastugue, G.: Sensitizing or antagonistic action of some synthetic antihistamine on the denervated leech preparation, comparison with atropine. C. R. Soc. Biol., Paris 146:647, 1952 (French).

Faust, E. C.: Leech infestation. In: Modern Med. Therapy in Gen. Practice. Balt., Wm. Wood 1940. v. 2, p. 1970.

Morhardt, P. E.: Le renouveau des sangsues. Presse méd., 57:882, 1949.

Press, A.: (A case of hemorrhage due to application of leeches.) Harefuah, Tel Aviv, 34:50, 1948 (In Hebrew).

Glick, S., and Ritz, N. D.: Hypochromic Anemia secondary to leeching. New England J. Med. 256:409, 1957.

Gilkes, M.: Leech bite of the cornea. Brit. J. Ophthal. 41:124, 1957.

Mitchell, J. F. O.: Leeches as endoparasite (in upper respiratory tract). J. Laryng. & Otol. 65:370, 1951.

Lal, M. G.: Anticoagulant activity of Indian cattle leech. Nature. 166:480, 1950.

Ehrenberg, F.: Modern therapy with leeches. Berl. med. Ztschr. 1:183, 1950 (German).

Weiler, P.: Antibiotic activity of leeches, leech bacteria (Bacteria hirudinis) and their bacteriafree filtrate. Experientia 5:446, 1949.

Reeves, B.: Leeches as temporary endoparasites in upper respiratory tract. J. Laryng. & Otol. 60:369, 1945.

