**Invertebrate biology**

# New medical and scientific uses of the leech

*from Charles Lent*

USING leeches for bloodletting reached a medical apogee in the eighteenth and early nineteenth centuries. As everybody knows, the demise of this disgusting practice this century was a long-overdue triumph of science over superstition. Just when we thought that this slimy worm had disappeared from the physician's *vade mecum*, new therapies using leeches are emerging. Plastic surgeons use medicinal leeches to remove blood from post-operative occlusions, a procedure that increases the success of tissue transplants, reduction mammoplasty and the surgical re-attachment of amputated extremities and digits by reducing the frequency of necrosis. The chemicals secreted in leech saliva, important to these surgical procedures, are also being explored as therapeutic agents against several diseases, including atherosclerosis, thrombosis and cancer.

Leech biologists congregated recently* to discuss the medical and scientific uses of the leech, primarily the European species *Hirudo medicinalis* L, and its habit of feeding on mammalian, particularly human, blood[1]. Hungry leeches (Fig. 1) bite through the skin of mammals with their three jaws and make tri-radiate incisions (Fig. 2). Although both mammalian temperatures (my own work) and chemicals will evoke biting, the $Na^+$ and arginine found in blood are required for leech ingestive behaviour (E. Elliott, University of North Carolina). Leeches ingest massive blood meals of 900 per cent of their body weight, and their satiation often lasts for a year. Serotonin-containing neurones, including the well-characterized Retzius cells, are obligatory for the expression of leech feeding behaviour[2]. Skin temperatures excite synaptically these neurones to release serotonin into the periphery, where in turn it stimulates the pharynx to pump blood, the jaws to bite and gland cells to secrete saliva (Fig. 3). The salivary glands consist of large secretory cells (W. Wuttke & M.S. Berry, University College, Swansea) which are electrically independent of one another, fire $Ca^{2+}$-dependent action potentials[3] and are stimulated by serotonin to secrete their complex biochemicals. Leech feeding in the laboratory is similar to that in nature, where gut distension rather than optimal foraging is used (J. Wrona, University of Calgary).

*British Association of Leech Scientists Swansea, Wales, 10-12 July 1986.

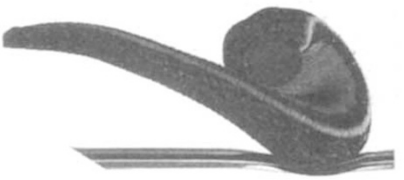

**Fig. 1** A hungry leech (*Hirudo medicinalis*) attached to the side of an aquarium. The two suckers of this annelid are easily distinguished. The large posterior sucker, adhering to the glass, is used in crawling. The smaller sucker at the head encloses the mouth, which has three jaws. This anterior sucker has an array of sensory structures used in feeding behaviour (courtesy of J.S. Flannery).

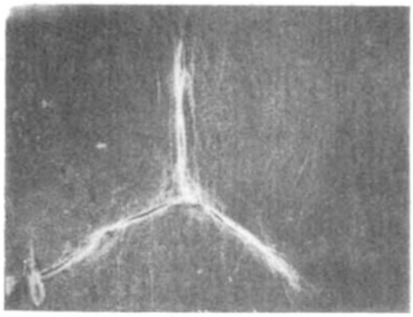

**Fig. 2** A single leech bite, consisting of a set of three incisions, one from each jaw (approximately 1 mm). This bite was made in parafilm on a 37°C surface, a method for assessing leech hunger. However, leeches make similar wounds in the skin of their prey, and both kinds of bites resemble the Mercedes-Benz logo.

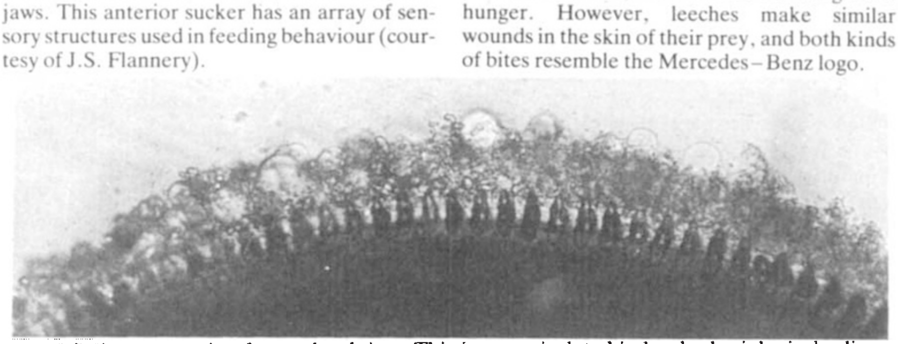

**Fig. 3** Salivary secretion from a leech jaw. This jaw was isolated in leech physiological saline with many of its gland cell bodies attached. The secretory response, which is seen as a halo of saliva along the cutting edge of the jaw, was evoked by a 20-min exposure to 1μM serotonin. A similar response is seen when the serotonin-containing Retzius cells fire high-frequency impulses. The saliva is secreted into ducts between the paired horny cutting teeth (about 60–70 pairs in each *Hirudo* jaw) and contains mucins and the anticoagulant hirudin.

*Hirudo* are most fascinating when feeding on humans. The colourful history of leeching, which pre-dated Christ by at least two centuries (A. Young, Lydiard Millicent, Swindon), was followed by modern case histories of its use in reconstructive surgery in Europe (P. Mahaffey, Withington Hospital, Manchester) and the United States (J. Upton, Harvard Medical School). After transplanting or reattaching tissues, venous return sometimes fails and reduces arterial supply, nearly always resulting in tissue necrosis. Mechanical and chemical attempts to prevent necrosis after venous failure have been unsuccessful. The leech removes the excess blood from occluded tissues and circumvents necrosis, which provides the necessary time (about 1 week) for capillaries to grow across the sutures. Leeching has a surprisingly low risk of infection (J. Cooper, Royal College of Surgeons, London) and leeches inoculate anticoagulants that are therapeutically beneficial, causing the bites to bleed for many hours after detaching.

Chemicals in leech saliva (Fig. 3) constitute an evolutionarily derived armamentarium against mammalian haemostatic clotting mechanisms. An anti-coagulant, hirudin, was described in leech saliva a century ago[4] and the DNA encoding this protein was cloned recently by biotechnologists at Transgéne[5]. Hirudin, a 65-amino-acid peptide that functions as anti-thrombokinase, is the most powerful natural anti-coagulant known (R. Sawyer, Biopharm, Swansea). The array of active agents in the saliva of several leech species includes a hyaluronidase (J. Edwards, Biopharm), a collagenase and two fibrinases. One fibrinase disrupts clots (R. Monroe, Morrison Hospital, Swansea) and the other, perhaps, atherosclerotic plaques (R. Baskova, Moscow State University). Salivary extracts from the giant leech *Haementeria* interfere dramatically with the metastatic growth of lung tumours and inhibit tumour cell collagenase (G. Gasic, University of Pennsylvania). Two salivary aparases prevent platelet aggregation by inhibiting their secretion of ATP (M. Rigbi, Hebrew University), but leech saliva does not contain anaesthetic. □


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