Clin Auton Res (2002) 12 : 179–184
DOI 10.1007/s10286-002-0045-7

HISTORICAL NOTE

Erin M. Dunbar
Todd W. Singer
Kelley Singer
Henry Knight
Douglas Lanska
Michael S. Okun

Understanding gustatory sweating
What have we learned from Lucja Frey and her predecessors?

Received: 25 May 2002
Accepted: 6 June 2002

E. M. Dunbar, MD (✉)
University of Florida
Department of Medicine
1600 SW Archer Rd
P.O. Box 100277
Gainesville, FL 32610, USA
Tel.: +1-352/265-0239
Fax: +1-352/338-9884

T. W. Singer, Esq.
Attorney at Law, Tulsa
Oklahoma

K. Singer, MD
Internal Medicine, Private Practice
Tulsa, Oklahoma, USA

H. Knight, D.Min.
University of Oklahoma
Department of Religion

D. Lanska, MD, MS, MSPH
Veterans Affairs Medical Center
Great Lakes VA Healthcare System
Tomah, Wisconsin, USA

M. S. Okun, MD
University of Florida
Mc Knight Brain Institute
and Department of Neurology

Abstract Gustatory sweating results from a disruption of the auriculotemporal nerve pathways. Damage to the nerve may cause a misdirected re-growth that results in parasympathetic innervation of sympathetic receptors and, therefore, facial sweating and flushing with gustatory stimulation. Over the past 300 years, the history of gustatory sweating has included observations of typhus-induced parotiditis, war injuries, and occupational accidents. Despite religious and personal persecution, Lucja Frey (1889–1943) systematically investigated gustatory sweating. Following the discovery of a German World War II document regarding Lucja Frey, an international committee was organized to research the history of gustatory sweating and of Dr. Frey's contributions to the understanding of the syndrome. Twenty original scientific publications from 1700 to 1950 on gustatory sweating were reviewed. Frey was the first to describe gustatory sweating as a disorder of both sympathetic and parasympathetic innervation. She proposed novel pathologic and pharmacologic mechanisms to explain the syndrome. Subsequent discoveries, including the work of André-Thomas in 1927, have provided a more complete understanding of gustatory sweating and the pathologic mechanism of aberrant neuronal regeneration.

Key words gustatory sweating · auriculotemporal syndrome · women in medicine · females in medicine · autonomic nerve disorder · autonomic nerve dysfunction

Introduction

Gustatory sweating results from a disruption of the auriculotemporal nerve pathways. Damage to the nerve or its branches may cause a misdirected re-growth that results in parasympathetic innervation of sympathetic receptors. Following the re-growth period, patients may report that gustatory stimulation leads to episodes of facial sweating and flushing. Most of the early literature on gustatory sweating failed to adequately address the causes and treatments of this phenomenon. Lucja Frey (1889–1943) (Fig. 1) systematically investigated gustatory sweating, which is now referred to as Frey's syndrome.

Frey's life and career were tragically altered by the events of World War II, which included religious and scientific persecution and ultimately her untimely death. In this paper we review the history of gustatory sweating, highlighting the contributions of many investigators, particularly those of Lucja Frey.

Fig. 1 Portrait of Lucja Frey.

Methods

Following the discovery of Lucja Frey's registration as a health professional, which was issued by the German government during World War II (Fig. 2), an international committee was organized to research the history of gustatory sweating and Dr. Frey's contributions. Twenty original scientific publications from 1700 to 1950 on gustatory sweating were obtained, translated from their original languages into English and reviewed. Interviews with living friends and colleagues provided personal and historical information.

Fig. 2 Lucja Frey's registration as a health professional, issued by the German government during World War II.

History of Gustatory Sweating

Over the past 300 years, the recorded history of gustatory sweating has included observations of typhus induced parotiditis, war injuries, and occupational accidents (Table 1). Perhaps the first case report was recounted by Paul Raymond in his 1888 paper, *Dés Éphidroses de la Face* [33], which noted that as early as 1740 [33] Kastremsky had described a patient with a peculiar perspiration when eating salty food. This report was followed in 1757 by that of M. Duphenix in *Observations sur les fistules du canal salivaire de Stenon* within his *Memoires de L' Academic Royale de Chirurgie* [15]. This report is frequently credited as the first case of gustatory sweating, but a review of the paper reveals an inconsistent account [18]. The paper describes a tragic hunting accident in which a boy suffered a deep pene-

Table 1

Literature review of dustatory sweating	Gustatory stimulation	Pathological process	Nerve injury	Facial sweating	Autonomic nerves	Experiments (testing medium)
Kastremsky, 1740						
Duphenix, 1757		X				
Dupuy, 1816		?	X	X		nerve cuts (horse)
Brown-Se'quard, 1849	X			X		chocolate (self)
Baillerger, 1853	X	X				
Henle, 1855	X	X				
Be'rard, 1855		X				
Bergounhioux, 1859		X				
Rouyer, 1859		X				pH of fluid (saliva)
Botkin, 1875		X	?	X		Jaborans (animals)
Luchsinger & Nawrocki, 1880		X	X	X	S	electricity (horse)
Weir-Mitchell, 188?			X	X		electricity (animal)
Raymond, 1888	X	X	CN 5	X	S	nerves cut (animal)
Parkes-Weber, et al., 1897	X	X			S	
New & Bozer, 1922	X	X	X	X	S, ?P	
Frey, 1923	X	X	CN 5, AT	X	S, P	drugs (human)

Jaborans now known to be pilocarpine; *AT* Auriculotemporal N; *S* sympathetic N; *?* unsure; *P* parasympathetic N

trating wound to the left cheek. He reported peculiar symptoms: "Every time he chews his food, a transudation of clear droplets started to emerge on the skin that covers the face… it is evident that the liquid was the saliva that came through the skin since its natural pathway (Stenson's duct) has been damaged by the injury" [15]. The episode was terminated by surgical closure and a creation of a new conduit. It is clear that Duphenix's case was of a traumatic parotid fistula. The short delay between the accident and the liquid complication, the resolution after surgery, and the abundant quantity of dripping liquid are inconsistent with gustatory sweating [18].

Barthez, in his 1806 article *Nouveaux Éléments de la Science de L' hommo* [4], describes a "man with abundant one-side sweating when salt was placed on one side of tongue" [4, 12]. Barthez, unlike his predecessors, was able to reproduce observed symptoms of gustatory sweating with a simple experiment.

In 1816, Dupuy described inducible and reproducible sweating. He noted "gustatory sweating over the cheek area " while experimenting on horses [16]. Although the symptoms proved not to be gustatory sweating, his results and subsequent experiments helped define another cause for sweating as a result of sectioning cervical sympathetics [18].

Three early reports were stimulated by personal or family observations. In 1849, Brown-Séquard reported his own symptoms of gustatory sweating as "exaggerated physiological sweating" that occurred when he ate chocolate or spicy foods [12]. "A very abundant secretion of sweat on the face is experienced… every time that (my taste nerves are excited) by eating things too salty, too spicy, too sweet, in a word, anything with a strong taste. Movement of the jaw does not have anything to do with it" [12]. Brown-Séquard's accurate identification of the fluid as sweat and not saliva [13] was not immediately accepted.

Shortly after Brown-Séquard's description, Baillarger published two complete cases of gustatory sweating [3]. The descriptions include facial sweating and flushing after surgical drainage of a parotid abscess. As Baillarger noted, the parotid was often involved. He also discerned the relationship with gustatory stimuli, especially in the absence of chewing. He concluded that "it is reasonable to relate the exudation of the cheeks… [to] the obliteration of the two Stenson's ducts found at autopsy" [3]. He tested for the presence of saliva with starch and litmus paper and erroneously concluded that the "frankly alkaline" liquid "resembled saliva" [3].

Many other accurate accounts of gustatory sweating followed. In 1855, P. Bérard reported a parotid abscess associated with gustatory sweating. The patient, incidentally his father, reported unusual symptoms. "In the case where there is damage to some parts of the excretory apparatus of the saliva, it has been noticed a kind of clear dew on the surface of the cheek… At the moment of eating, his cheek became red and the saliva, that emerged as droplets, covered his cheek so quickly that there was no time to look for the orifices" [8].

In 1855, Henle reported that at the age of five he had an episode of parotitis followed by flushing and sweating [24]. He discussed a "triggering" of gustatory sweating, noting that any of the following could set off an episode: "slight stimulation of mucus membranes of the cheeks, a feather tip, increased nervousness, smoke, drinking or eating" [24].

Bergounhioux was convinced that mastication stimulated gustatory sweating [9]. In a patient with facial swelling, pain, and flushing following a parotid injury, Bergounhioux successfully demonstrated based on the "acid reaction" of the secreted fluid that this "phenomenon involved sweat" [9].

Etiology of Gustatory Sweating

In 1888, Paul Raymond published two comprehensive studies, *Ephidroses de la Face I and II*, of lesions of the cervical sympathetic chain, a syndrome similar to gustatory sweating [33]. To determine how the sudoriparous phenomenon related to the sympathetic nervous system, Raymond reviewed the animal dissections and previous secretion experiments Dupuy [16, 17], Berard [8], and Nawrocki [30]. Raymond proposed several etiologic causes for the abnormal production of sweat. These included injury to the central nervous system (where sweating appeared in all body parts), injury to the cervical sympathetics (where hyperhidrosis, paralysis and flushing were confined to the ipsilateral head), injury to peripheral and cranial nerves (5^{th} and 7^{th}), and "irritation" of reflex origins of the nerves that carry touch, taste, and smell. He noted that the latter explanations were more likely responsible for gustatory sweating [33].

Raymond was likely acquainted with Langley's 1898 paper, which coined the term "autonomic nervous system." Raymond states that the "autonomic sympathetic system" is responsible for "the development of cutaneous flushing and sweating" [33]. The term parasympathetic was also used in 1905 by Langley, who attempted to understand phenomenon like those seen in gustatory sweating [26]. Raymond was aware that the studies performed previously yielded contradictory results regarding the pathogenesis of hyperhidrosis or gustatory sweating [33]. He published a comprehensive review and editorial that provided much insight for later scientists.

One of these scientists was F. Parkes Weber, who in 1897 accurately described a case of a nineteen-year-old boy who developed sweating and flushing on his left ear and face following an episode of parotiditis. That required incision and drainage [35]. Weber accurately re-

ported the presence of a six-month time delay in the onset of symptoms (enough time for re-growth to occur), and concluded that the symptoms were possibly due to "temporary compression of vaso-motor fibres" [35]. Weber wrote, "[t]he scar is partly adherent to the parotid salivary gland, and I suppose that when physiological swelling of the gland takes place during eating, the scar is dragged on in some way, and the nerve fibers which are involved in it become compressed that their function is temporarily completely abolished" . He further noted that "some nerve fibers have been cut through or destroyed by previous suppuration" [35].

Weber and a local house physician, Steiner, postulated that the time delay was due to scar contraction and that it may "merely be an abnormal reflex from the mucous membrane of the mouth (and possibly from the stomach) in a neurotic patient" [35]. Frey's 1922 publication contains many of the same features as Weber and Steiner's report, yet Frey provides no reference to this report, suggesting that she may have been unaware of its existence.

B. Gorman New and Hermann E. Bozer reported that "hypersecretion (was) due to irritation of the secretory fibers of the facial nerve" [31]. New and Bozer cited the work of Adamkiewicz, who demonstrated that "in healthy persons, faradic stimulation of the facial nerve produced sweat secretion" [1]. The two investigators also noted the latency to symptoms and the role of the spinal cord as a potential regulator of secretory nerves.

Unsure "whether the lesion was irritative or paralytic," they postulated that the "explanation appears to be possible only on assuming the existence of both secretory and inhibitory fibers of sweat glands" [31]. New and Bozer added a potential new mechanism, "faulty regeneration of the facial nerve," but did not elaborate on the specifics. Like Raymond, they believed the research to date yielded much contradictory evidence, and therefore they did "not feel warranted in drawing any conclusions as to the pathologic physiology" [31].

In 1923, Lucja Frey, a neurologist in Warsaw, published *Le Syndrome du Nerf Auriculo-Temporal* [19], the first complete description of the anatomy, pathology, potential mechanisms, and potential treatments of gustatory sweating [14, 19].

Frey's attention to detail is noteworthy. A twenty-five year old patient had been injured "by a rifle bullet behind the angle of the (left) lower jaw." Five months later, he was "ashamed by the excessive 'voracity' of perspiration" (and flushing) during meals" [19]. Frey obtained a history, performed a meticulous examination and then subjected the patient to tests including the Bordet-Wasserman test, electric stimulation, photography, and the administration of foods and medicines [19]. She drew important conclusions, at least partially due to the novel use of medications (Table 2).

Table 2

Frey's pharmacologic tests and treatments		
Medication	Effect	Mechanism
pilocarpine	+ GS	(P agonist)
atropine	– GS	(P antagonist)
adrenalin	paleness, coolness	(S agonist)
physostygmine	paleness, coolness	(P agonist, indirect)
amyl nitrate	flushing	(vasodilation)
other drug studies: stenson's duct size, pilomotor reflex, scope of symptoms		
Novel human treatment		
Scar ablation		
Alcoholic neurolysis		
Partial extirpation of AT		

* Many treatments still used today
GS gustatory sweating; *P* parasympathetuc; *S* sympathetic

Lucja Frey: Life and Works

Little is known about Lucja Frey. She was born November 3, 1889 in Lwow, Poland where she finished high school and studied mathematics under professor S. Smoluchowski [14]. Frey moved to Warsaw to study medicine, receiving her degree in 1913 and passing her medical boards on June 3, 1923 [7]. Two months later, and prior to the issuance of her official medical license, she published her paper on gustatory sweating [19], which was widely accepted as the most complete on this topic [2, 5, 36]. She then returned home to Lwow, where she became a Senior Associate Clinician in Neurology at the University, under professor Kazimierz Orzechowski [6, 32]. Frey was one of the first female academic neurologists in Europe. She was known among her colleagues as an exceptional scientist and was described as "modest, quiet, [and exhibiting] an ant-like work ethic" [6,25]. Frey was uniquely meticulous in her work [6, 25].

Frey's contribution to gustatory sweating can best be understood in the context of her life. There was much political unrest in Poland before and after WWII. In 1938, Frey's husband, Marek, was arrested and presumably killed by Soviet police. She raised a daughter alone and continued her scientific pursuits. Early in her career, Frey published important works on the mapping of the human brain and the histology of the nervous system [14, 19]. Her 1925 book, *First Steps in Learning the Topography of the Brain* [22], discussed anatomical changes in brain tissue, Charcot's joints, a case of a brain aneurysm of the plexus of the medulla, and multiple sclerosis [19, 20, 21, 22, 23]. Her pathological studies noted that multiple sclerosis was more than just a disease of the myelin and that it also involved axonal degeneration [19].

The *Medical Yearbook of the Polish Republic* lists Frey

as working at the prestigious Jewish Hospital on Rappaporta Street in Lwow in 1936 [6]. During the Soviet and German occupations, she was forced to work in other Jewish Clinics in the ghetto. On June 22, 1941, Germany invaded the Soviet Union and occupied Lwow. Acts of plunder and brutality against the Jewish population in this area escalated [7]. The German "Einsatzgruppe," or mobile killing squads, harassed and killed Jews and political dissidents. The Jewish Committee of Lwow had only 3,000 survivors of approximately 100,000. Dr. Lucja Frey was not among them and it is unknown what other of her papers and observations were lost.

Lucja Frey: Important Contributions to Gustatory Sweating

Frey was not aware of all previous observations on gustatory sweating when she wrote her 1923 paper. She cited Baillarger [3], Bergounhioux [9], Botkin [10], Bouveret [11], Rouyer [34] and Lipsztat, in her discussion, but left out many other investigators. Frey accurately described the constellation of symptoms in gustatory sweating, including warmth, flushing, sweating, and altered tactile sensation. She was the first to define gustatory sweating as a disorder of both sympathetic and parasympathetic innervation. She knew that the physiologic secretion of the parotid gland was determined by both the glossopharyngeal nerve (parasympathetic) and other fibers of the sympathetic system. Based on her drug experiments (Table 2), she observed that the unaffected side of the face produced a "more fluid saliva," and concluded that this was due to parasympathetic innervation. She further observed that the injured side produced "more thick, and scarcer saliva" and determined that this was due to a pathologic "preponderant influence of [the] sympathetic system" [19]. "Based on the presence of the thicker saliva [in this patient]," she concluded that the "reflex action [of the auriculotemporal nerve], when affected by the phenomenon of gustatory sweating, produced a "irritation syndrome," resulting in "parasympathetic fibers [which have] partially lost conductivity" [19]. Frey identified the auriculo-temporal nerve as responsible for the syndrome and argued that it was the missing link between eating, gustatory stimulation, and facial sweating [19].

"The area of the face affected by this phenomenon . . .presents itself in the form of a triangle . . . the area corresponding almost exactly to the region of the auriculotemporal nerve" [19]. In addition, "hyperaesthesia of all modes of sensitivity: redness, increase temperature, and perspiration [occurred] each time the rear part of lingual mucosa (was) stimulated" [19].

Frey produced a diagram to explain the exact autonomic innervation (Fig. 3), which was reproduced with some modification [28]. In addition, she accurately incorporated the time delay of her patient's symptoms into a proposed pathological mechanism and concluded that "irritation of the nerve may . . . be due to its compression by scars, resulting from a prolonged suppuration" [19].

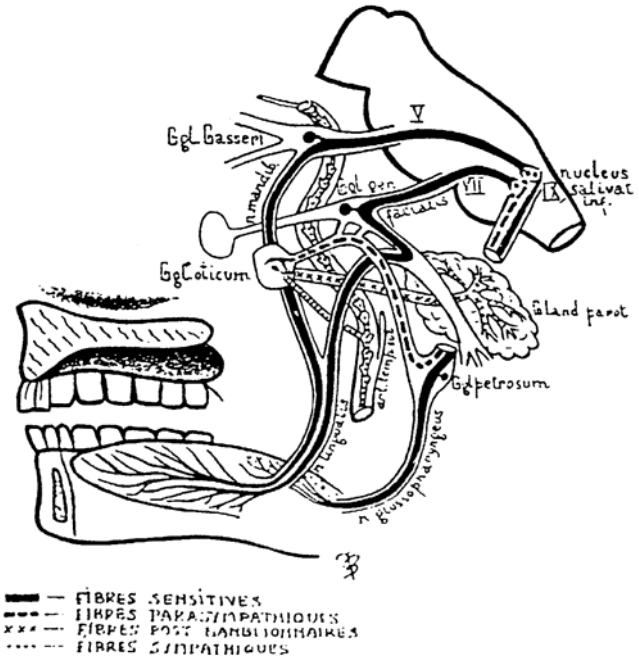

Fig. 3 Diagram used to illustrate Frey's paper in *Revue Neurologique* (Frey, 1923) (which itself was reproduced from Muller, *Das vegetative Nervensystem*, Berlin, 1920, p. 75).

Frey also proposed "ablation of the scars to release the nerve which was compressed, alcoholic neurolysis, and partial extirpation of the auriculotemporal nerve."

Conclusion

The causes and treatments of gustatory sweating have been elusive. Lucja Frey published the first complete report of the symptoms, pathology, etiology, and treatments and recognized that the syndrome had both parasympathetic and sympathetic components. Errors in her description included the idea of an irritation syndrome, a discussion of a partial paralysis of the parasympathetic fibers innervating the parotid gland, the attribution of the time delay to scar formation, and a lack of an explanation for vasodilation [19]. Despite these errors, the work stands as an important contribution to gustatory sweating. Herman commented that "even though the legacy of Frey's work is not extensive, each of her published works possesses great scientific depth, leaving a strong mark in the collective accomplishments of science." Recent discoveries have provided a more complete understanding of gustatory

sweating and the pathologic mechanism of aberrant neuronal regeneration [36], a concept first postulated by New and Bozer, and more clearly described by André-Thomas [2].

References

1. Adamkiewicz A (1878) Zur Physiologie der Schweisssecretion. Arch f. Path. Anat.: l xxv, pp. 555–560
2. André-Thomas (1927) Le double réflexe vaso-dilatateur et sudoral de la face consécutif aux blessures de la loge parotidienne. Les pararéflexes. Revue Neurologique 4:447–460
3. Baillarger J (1853) Mémoire sur l'obliteration du canal du Sténon. Gazette médicale de Paris 23:194–197
4. Barthez (1806) Nouveaux Éléments de la Science de L' hommo, Paris, vol II
5. Bassoe PN (1932) Auriculotemporal syndrome and other vasomotor disturbances about the head: "auriculotemporal syndrome" complicating diseases of parotid gland, angioedema of the brain. Med Clin North Am 16: 405–412
6. Bennett JD, Pietruski J (1993) Lucja Frey (1889–1943) in the 50th anniversary of her tragic death and 70th anniversary of the auriculotemporal syndrome. Otolaryngologia Polska 47 (4): 378–382
7. Bennett JD (1994) The woman behind the syndrome: Frey's syndrome – the untold story. Journal of the History of the Neurosciences 3 (2):139–144
8. Bérard PH (1855) Cours de physiologie, fait à la Faculté de médecine de Paris, vol 4
9. Bergounhioux (1859) La Gazette de Hôspitaux, Paris
10. Botkin S (1857) Über die Reflexerscheinungen im Gebiete der Hautgefässe und über den reflectorischen Schweiss. Berliner Klinische Wochenschrift 7:81–83
11. Bouveret L (1880) Des sueurs morbides. Thesis. Paris, p. 148
12. Brown-Séquard CE (1850) Production de sueur sous l'influence d'une excitation vive des nerfs du goût. Compte Rendu Société de Biologie 1:104
13. Brown-Séquard CE (1850) Remarques sur la précédente note. Compte Rendu Société de Biologie 1:449–450
14. Burton MJ, Brochwicz-Lewinski M (1991) Lucja Frey and the auriculotemporal nerve syndrome. Journal of the Royal Society of Medicine 84 (10): 619–620
15. Duphenix M (1757) Obervations sur les fistules du canal salivaire de Stenson. I. Sur une playe compliq la joue ou le canal salivaire fut déchireé. Mémoires de l'Académie royale de chrirugie III:431–439
16. Dupuy LE (1816) Sur l'enévement des ganglions gutturaux des nerfs trisplanchniques sur des chevau. Journal de médecine, chirurgie, pharmacie, Paris 37:340–350
17. Dupuy LE (1873) Enchondrôme de la parotide. Bull Mem Soc Anat Paris, xlviii:261–262
18. Dulguerov P (1999) Frey Syndrome Before Frey: The Correct History. Laryngoscope 109:1471–1474
19. Frey L (1922) Le syndrome du nerf auriculo-temporal. Revue neurologique, Paris 30 (2):97–104
20. Frey L (1923) Zespól nerwu uszno-skroniowego. Neuro Pol
21. Frey L, Orzechowski K (1925) Zmiany anatomiczne w chorobie Charcota. Neurol Pol 8:196
22. Frey L (1925) Przyczynki do nauki o topografji w trzonie mozgowym. Ogniska w wyzszych pietrach mostu Varola. Neur Pol 8:124
23. Frey L (1926) Przypadek tetniaka splotwatego rdzenia. Neurol Pol 9:21
24. Henle (1855) Handbuch der rationnellen pathologie, 3rd ed, vol 1, p. 236
25. Herman E (1958) Neurolodzy Polscy (Warszawa: Panstwowy Zaklad Wydawnictw Lekarskich), pp. 225–227
26. Langley JN (1905) The Autonomic Nerves. Vereeniging Secties voor Wetenschappelijken Arbeid. Voordrachten gehouden voor de medische en natuurphilosophische studenten der Universiteit van Amsterdam. no. 4
27. Medical Yearbook of the Polish Republic (1936) Warsaw, pp. 525, 549
28. Mitchell SW (1872) Injuries of Nerves and their consequences. Lippincott, Philadelphia, p. 377
29. Müller (1920) Das Vegetative Nervensystem, Berlin, p. 75
30. Nawrocki F (1878) Weitere Untersuchungen über den Einfluss des Nervensystems auf die Schweissabsonderung. Centralbl. F. d. med. Wissensch xvi, pp. 721–724
31. New GB, Bozer HE (1922) Hyperhydrosis of the check associated with the parotid region. Minnisota Medicine, vol 5
32. Orzechowski C (1924) Action antinévralgique des médicaments agissant sur le systéme nerveux de la vie végétative. C R Seances Soc Biol Fil 91(Dec 27):1475–1476
33. Raymond P (1888) Des éphidroses de la Face I and II. Arch Neurol (Paris) 15: 212–217
34. Rouyer J (1859) Sur l'éphidrose parotidienne. Journal de la physiologie de l'homme et des animaux 2:447
35. Weber FP (1897) Clinical cases V: a case of localized sweating. Transactions: Clinical Society of London 31: 277–280
36. Williams JG, Prince ME (1999) Frey's Syndrome: A Case of Aberrant Nerve Regeneration. The Dalhouse Medical Journal, Halifax, Nova Scotia, Canada, May