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HISTORICAL VIGNETTE

Frey Syndrome Before Frey: The Correct History

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Objective: **To review the chronology of publications on gustatory sweating before Frey's landmark publication.** ***Methods:*** **Reports on Frey syndrome were reviewed, and all references given to publications before 1950 were obtained and examined. References to prior publications in the obtained articles were similarly reviewed. The cases described in these publications were analyzed for their compatibility with the accepted clinical symptoms of Frey syndrome.** ***Results:*** **Despite numerous references, the case described by Duphenix in 1757 is most probably a traumatic parotid fistula. The first reported case of Frey syndrome should be attributed to Baillarger in 1853.** ***Key Words:*** **Frey syndrome, history, autonomic nervous system, sweat, parotidectomy**

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In 1923, Lucie Frey, [1] a neurologist at the University of Warsaw, published her landmark study on the "syndrome du nerf auriculotemporal." She described a 25-year-old patient who, 5 months after a gunshot wound to the parotid region, developed facial sweating, as well as local facial skin flushing during meals. Thus the syndrome that has become to bear Frey's name is characterized by sweating and flushing resulting from gustatory stimulation, independent of mastication. These symptoms develop several months to years after an external trauma or surgical procedures to the parotid area or to the cervical sympathetic chain. Symptoms continue unabated without treatment.

While "Frey syndrome" is a well-accepted eponym, the first case of Frey syndrome is routinely attributed (in 22 references to date) to M. Duphenix[2]; a historical report to that account has even been published.[3] In 1757, Duphenix described a patient who was injured by a deer in a hunting accident. A deep penetrating wound to the left cheek was present, through which a malar bone fracture could be appreciated. The wound, in which a clear liquid drainage was observed whenever the patient was eating, remained open for more than 4 months. After a surgical closure and the creation of conduit toward the oral cavity, the laterofacial liquid drainage appeared to have stopped. This is obviously a traumatic parotid fistula; even the title that Duphenix chose for his report suggests so.[2]

It is surprising that anyone could interpret this description as Frey syndrome. The presence of an open cheek wound, the near-certainty that Stenson's duct was severed (the masseter was visible through the wound), the short delay between the accident and the complication, the resolution of the symptoms after surgical treatment, and the quantity of liquid pouring out during meals, all speak against Frey syndrome. Duphenix measured the amount of fluid secreted through the wound on several occasions: 2 ounces in 15 minutes, 3 ounces in 18 minutes, and 4 ounces in 28 minutes, corresponding roughly to 60 to 100 mL. A maximal sweat secretion rate has been measured at about 2 to 20 nL/min per gland.[4] The face has about 250 glands/cm^2 [5]; thus the maximal facial sweat rate should be 500 to 5,000 nL/min/cm^2 or 5 to 50 mL/min/m^2. Assuming that maximal sweat secretion rates are observed in Frey syndrome and that a large surface is involved (e.g., 7 × 7 cm or about 50 cm^2), the maximum amount of sweat liquid that can be collected is 250 μL/min. For 20 minutes, the maximal sweat output of such a surface is 5 mL. This is much less than the quantity Duphenix was able to gather from his patient, notwithstanding technical means available 250 years ago, as well as possible evaporation and collection losses.

Recently[6,7] credit was given to Dupuy,[8] who was supposed to have described. in 1816, "gustatory sweating over the cheek area in patients . . . ." As the title of Dupuy's report implies,[8] it is an early experimental work on horses. While Dupuy's descriptions bear little relation to Frey syndrome, the work is quite interesting and probably represents one of the first studies examining the effects of sectioning the cervical sympathetics. Clear description of the ocular signs was given, some 50 years before Horner described the symptom bearing his name.[9]

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In 1853, Baillarger[10] described five cases and reviewed the case of Duphenix. Two of the cases (cases 2 and 6) are typical salivary fistulas, one of long duration and one after drainage of an abscess. One of the cases (case 5) appears to be a parotid abscess (with symptoms lasting only a few days) that resolved after an incision and drainage; this complete resolution of symptoms is not seen in Frey syndrome. The two other cases (cases 1 and 4) represent typical Frey syndrome, following surgical drainage of parotid abscesses. However, probably because of Duphenix's interpretation, and because at the autopsy of one of these patients Baillarger believed that Stenson's ducts were blocked, he proposed that the fluid appearing during meals was an outpouring of saliva through the skin because of a blockage of Stenson's duct.[10] Despite this incorrect interpretation, we should probably regard Baillarger's publication as the first report of Frey syndrome.

In 1859, Rouyer[11] briefly described three cases of gustatory sweating. One case followed a bullet wound to the parotid area and is probably a typical case of Frey syndrome. In the other two cases, gustatory sweating was attributed to parotitis, although both patients had parotid abscesses. Most probably, these patients had their parotid abscess drained and developed a typical case of Frey syndrome. Following Baillarger,[10] Rouyer also believed that the Stensen's duct was blocked and that the saliva somehow found its way to the skin.

In 1850, Brown-Séquard[12] discussed the possible production of facial sweating when eating spicy foods. He essentially described his own case of an exaggerated physiological sweating,[13] an interesting historical note that was largely echoed in the literature.[1,14–18] Nevertheless, the possibility of facial sweating was described and this undoubtedly helped later authors to correctly understand the nature of the fluid observed in the cases they reported.

In 1875, Botkin, from St. Petersburg, also described a case of gustatory sweating after drainage of a parotid abscess.[18] The case description is rather short, and the interpretation ambiguous: although the symptoms are maximal on the cheek and during meals, apparently the entire half of the body can be involved and eating, as well as walking, excitement, and so forth, could induce the symptoms. Botkin cited Brown-Séquard's report and probably because of that, and because the symptoms involved a large body area, he interpreted the skin fluid as sweat.

In 1888, Paul Raymond[16,17] wrote two seminal reports on the "Ephidroses de la Face" in which the role of the autonomic sympathetic system in the development of cutaneous flushing and sweating appears established. One of the patients described has a case of Horner's syndrome with gustatory facial sweating and flushing. This is one of the first reports of gustatory facial sweating and flushing following a lesion of the cervical sympathetic chain.

The first case of Frey syndrome in the English literature was described by Weber[19] in 1897. It is also the first case of bilateral Frey syndrome. The patient had bilateral scars in the parotid area, after incision and drainage of "previous suppurations." Like Baillarger's, the clinical description is exact, with flushing, sweating, a clear relationship to gustatory stimuli, and an absence of the effect of chewing.

In 1922, a year before Frey's description, New and Bozer[14] reported on three cases of "Hyperhydrosis of the cheek associated with injury of the parotid region." Two of the patients had drainage of a parotid abscess, and the third one had a traumatic injury to the preauricular area.

Peter Bassoe[15] reported, in 1932, the first case of Frey syndrome following parotidectomy, which is the most frequent etiologic factor in Frey syndrome today.

Although Lucie Frey[1] did not describe the first case of gustatory facial sweating and flushing, she certainly deserves to have the syndrome named after her. She not only correctly described the symptoms, but also accurately put in perspective the relevant autonomic innervation of the parotid gland and facial skin. By pinpointing the role of the auriculotemporal nerve in the syndrome, Frey provided the missing link between eating and gustatory stimulation on one side and facial skin sweat production on the other. It remained to André Thomas[20] to correctly explain the physiopathology by postulating the aberrant regeneration theory.

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EDITORIAL FOOTNOTE

This is a most interesting article from the historical viewpoint. It is my assumption that the authors submitted it in response to the article by Linder et al. in the *Laryngoscope* (1997;107:1496–1501), which credited the Frey syndrome to Duphenix, Dupuy, and Baillarger. Other authors on the same subject begin with a one- or two-paragraph history of the syndrome before proceeding to their recommendations on treatment. Of greatest interest is the article by New published in 1922 that describes several cases of the syndrome and relates them to episodes in which there was neither trauma nor surgery. Apparently in the 1800s, typhus, typhoid, and drainage of suppurative abscesses were associated with the later development of gustatory sweating.

It is apparent to me that Lucie Frey was the first to recognize the development of the syndrome as an abnormality of both the parasympathetic and sympathetic innervation, although she concluded that there was a partial paralysis of the parasympathetic fibers innervating the parotid gland. Gustatory excitation was attributed to a reflex arc involving the glossopharyngeal nerve and the posterior tongue to the salivary nucleus. The nucleus gave rise to fibers that traveled back through the tympanic nerve or Jacobson nerve to the petrous nerve through the otoganglion with postganglionic fibers following the trigeminal nerve providing the parasympathetic stimulation. Sympathetic fibers traveled from the superior cervical chain to the otic region.

Frey's important contributions were her recognition of the sympathetic and parasympathetic innervation of the parotid gland, a reflex arc explaining the gustatory sweating and the relationship with the auriculartemporal nerve, and the delayed onset of the syndrome from the time of injury to the development of the gustatory sweating. She does give recognition to authors Baillarger, Bergounhioux, Botkin, Bouveret and Rouyer, who had reported on this in the 1800s.

The accepted explanation of the aberrant innervation of the parasympathetics to the sympathetics is credited to Thomas. If we were to make a real issue of who actually explained the results of gustatory sweating after parotidectomy, perhaps we should call this Thomas syndrome.

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