



## Spectrum of gustatory sweating, with especial reference to its presence in diabetics with autonomic neuropathy<sup>1-3</sup>

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Gustatory sweating is the induction in susceptible individuals of sweating, usually on the face, in response to eating. Only rarely will the phenomenon be triggered by smelling foods (1), and it is not triggered by thinking of foods, or chewing inert substance such as parafilm (2). It usually occurs within several seconds of the introduction of food into the mouth, but not into the stomach (by nasogastric tube) (3), and tends to persist throughout eating, suggesting that the initial peripheral stimulus is carried centrally by the taste buds. In mild forms it is a normal phenomenon, usually elicited by highly spiced or tasty foods, chocolates, and cheeses. Certain otherwise normal individuals may have an idiosyncratic response to one or several foods, and the mechanism of this sensitivity is not known. It may also be seen after parotid surgery (auriculotemporal syndrome) (4), cervical sympathectomy (usually bilateral) (1) and in diabetic neuropathy (2). The common denominator in these conditions seems to be damage to the autonomic nervous system.

In the auriculotemporal syndrome (Frey's syndrome) that follows parotid surgery (or similar lesions of the parotid gland), gustatory sweating occurs in the distribution of the auriculotemporal branch of the mandibular nerve. Since the auriculotemporal nerve receives autonomic fibers from the otic ganglion (mainly sympathetic fibers from the internal carotid artery and tympanic plexus via the lesser superficial petrosal nerve), it is presumed that parasympathetic secretomotor fibers initially destined for the parotid gland are interrupted

and reanastomosed with sympathetic fibers destined for the skin of the ear and temple. Since secretomotor parasympathetic fibers and sudomotor sympathetic fibers are cholinergic, no change in neurotransmitter occurs. The suggestions that sympathetic vasomotor fibers destined for the parotid gland resprout and innervate the auriculotemporal fibers is not tenable because the phenomenon is interrupted by atropine (4) and not by sympatholytic agents (1). The phenomenon is blocked by ganglion blocking agents (1), and apparently responds well to surgical destruction of the tympanic plexus (4). Destruction of the tympanic plexus in animals causes atrophy of the ipsilateral parotid (5), and it is reasonable to assume that successfully treated surgical patients will also have ipsilateral parotid gland hypofunction. Studies of parotid function in patients with the unilateral Frey's syndrome of auriculotemporal gustatory sweating may shed further light on the mechanism of this syndrome.

Less easy to understand is the syndrome after cervical sympathectomy (usually bilat-

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eral) (1). As with the auriculotemporal syndrome, the onset occurs weeks to months after the surgery and apparently does not correlate with relapse of the surgical condition. Although anesthetic block or excision of the stellate ganglion abolishes the gustatory sweating response in "normal" patients, it does not have a similar effect in postsympathectomy gustatory sweating. Sweating is more profuse if there is no ipsilateral Horner's syndrome. The distribution of sweating is the face and almost always the arm, corresponding to the distribution of innervation from the cervical sympathetic ganglia. Although sensitivity to circulating acetylcholine has been postulated as the mechanism of production of sweating, injection of cholinergic substances or acetylcholine does not reproduce the syndrome, and ganglionic blocking agents can interrupt the syndrome, suggesting that the response is neural rather than humoral. It is now felt that sprouting of cholinergic fibers into the area of the surgical lesion is the cause. Whether the sprouting axons arise from the thoracic sympathetic ganglia and meander past the surgical site, or whether they arise from the vagus nerve cephalad to the lesion is not established. Medical treatment with anticholinergic or ganglionic blockers offers some benefit but dosage schedules necessary to interrupt the syndrome produce unacceptable toxicity in most cases. No acceptable surgical procedure has yet been devised for treatment of this striking complication of sympathectomy.

Diabetic patients with autonomic neuropathy may present with a similar syndrome (2). The similarity of the syndrome in diabetes to that occurring in postsurgical patients makes it most reasonable to assume that a lesion has occurred in the autonomic nervous system with subsequent sprouting between healthy cholinergic axons and diseased ones. A careful study of diabetic patients manifesting this phenomenon revealed widespread deficits in the sympathetic and parasympathetic nervous systems (2). The missing bit of information in these cases is whether diabetic patients suffering from autonomic neuropathy are able to sprout and regenerate axons; certainly the

presence of gustatory sweating in these patients is at least circumstantial evidence that such a phenomenon occurs. Nerve biopsies in diabetic patients with painful neuropathy have demonstrated abnormal sprouting of small, unmyelinated fibers roughly of the size of postganglionic sympathetic nerves, and abnormal relationships of these sprouts to Schwann cells (6). This suggests that abnormal sprouting and unusual relationships of unmyelinated fibers to Schwann cells may be the anatomic bases for painful diabetic neuropathy. In view of this histological evidence, it seems reasonable to suggest that the mechanism for gustatory sweating in diabetic patients with autonomic neuropathy is also axonal degeneration with abnormal sprouting from contiguous axons. Since in gustatory sweating it is presumed that the stimulus to the sweat glands originates in the dorsal motor nucleus of the medulla, and is diverted to sympathetic cholinergic axons destined for the face and perhaps the arm, it is likewise plausible that adrenergic vasomotor impulses from the cervical sympathetic chain cause the other less constant parts of these syndromes such as goose flesh, vasoconstriction, paraesthesias and flushing.

Evaluation of diabetic patients with gustatory sweating should include tests of autonomic function and documentation of the gustatory phenomenon. Tests of autonomic function should measure blood pressure, peripheral temperature, etc. The following tests are recommended:

1) Measurement of recumbent and standing blood pressure and pulse, four times per day.

2) The response of body temperature (central and peripheral) to ambient temperatures of 19 to 21 C (7, 8). Maximal skin venous dilation will cause a toe temperature of 32 C; at a toe temperature of 25 C the blood flow is approximately 3 ml/100 ml per minute; at 22 C there is virtually no measurable blood flow. The measurements should be made for 1 hr, monitoring air temperature, body core temperature, and toe temperature. The normal response is a drop in toe temperature indicating vasoconstriction and heat preservation. Patients



with autonomic neuropathy will have a toe temperature above 25 C, indicating failure of peripheral vasoconstriction.

3) The response of central areas of body, face, and feet to sweating induced by either heat or injections. Sweating can be measured either visually or by application of Guttman's powder. The ambient temperature should be raised until the sublingual temperature rises one degree centigrade, or until brisk sweating has occurred over the forehead (9).


4) The response of pupils to dilute solutions of cocaine 4%, epinephrine 1/10,000 and methacholine 2.5%. The normal eye will pupillodilate to cocaine and will not respond to the dilute epinephrine or methacholine solutions. The denervated pupil will not respond to cocaine, will dilate in response to epinephrine, and will constrict after pilocarpine (10).

5) The response of skin to interdermally injected histamine (0.05 mg in 0.1 ml). The normal response is a triple flare. Absence of the "axonal response" indicates denervation (10).

6) The response of blood pressure and pulse to a Valsalva maneuver. This is accomplished in the recumbent position, with a blood pressure cuff placed on the arm, and an electrocardiograph recording the pulse. The patient is instructed to take a deep breath and hold it for 10 to 15 sec, and then to gradually exhale. Blood pressure is measured before breath-holding, just before the end of breath-holding and every 15 sec thereafter for 1 min. Pulse is recorded continually. The normal response is hypotension and tachycardia toward the end of breath-holding, and an over-shoot of the blood pressure with a pulse slowing after breath-holding is terminated. Absence of this pulse-ratio (9, 11) and absence of a blood pressure over-shoot (10) indicates failure of the autonomic nervous system to respond to the Valsalva maneuver.

7) Cold pressor test. Ice is applied to the forehead for 1 min and its effect upon blood pressure and pulse is measured every 15 sec for 5 min. The expected response is a

rise in blood pressure. Absence of a rise in blood pressure indicates deficient autonomic function (12).

8) Gustatory sweating. The patient is questioned specifically about those foods that induce gustatory sweating, and in what areas the sweating occurs. The patient is offered one or two of these test foods, and 1 teaspoon of Worcestershire sauce, a chocolate bar, and two squares of American cheese. The sweating response is documented either visually or by using a topically applied indicator agent. The distribution of sweating is compared with that induced by heating. 

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