liver and spleen of bats (*Chilonycterus rubiginosa fusca*). During a survey on trypanosomiasis of bats from central Colombia in 1964, 135 bats were collected from caves near the villages of Nilo, Villeta, Girardot, and Tocaima (Dept. Cundinamarca) and Borbur and Yopal (Dept. Boyacá). The bats examined were distributed as follows: 15 *Peropteryx macrotis macrotis* (Wagner), 23 *Phyllostomus discolor* Wagner, 6 *Phyllostomus hastatus hastatus* (Pallas), 5 *Glossophaga sorcina sorcina* (Pallas), 21 *Carollia perspicillata perspicillata* (Linnaeus), 4 *Artibeus lituratus* Olfers, 59 *Desmodus rotundus rotundus* (Geoffroy), and 2 *Myotis nigricans nigricans* (Schinz).

Plates containing Sabouraud medium, *p*H 7.0, were directly inoculated with liver tissue and feces of the bats and were then incubated at 26°C; no antibiotics or other substances were added either to medium or specimens. One of the inoculations produced a positive culture of *Histoplasma capsulatum*. This inoculation came from the liver tissue of a nectar-feeding bat, (*Glossophaga sorcina sorcina*, caught near Girardot. Emmons *et al.* (*3*) isolated *Histoplasma capsulatum* from droppings of a *Glossophaga sorcina*, but cultured feces collected directly from this bat did not show the fungus. According to a review of histoplasmosis by Orozco (*4*), the disease is not uncommon in man in Colombia. The importance to public health of histoplasmosis in animals may be related to the role played by infected animals as indices of the geographic distribution of *Histoplasma capsulatum* (*5*). Whether or not bats can disseminate the organism remains to be determined.

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Absence of Taste-Bud Papillae in Familial Dysautonomia

Abstract. *No fungiform papillae could be found on the tongues of 30 patients with familial dysautonomia. In ten of these patients a search for vallate papillae was made, but none were found. Inspection of the tongue may thus be useful for diagnosing this rare disease, even in infants. Absence of these sensory receptors suggests that the multiple sensory deficits found in persons with familial dysautonomia may be related to defects in the peripheral receptors.*

Familial dysautonomia is a rare, inherited disease which affects the sensory, motor, and autonomic nervous systems. The disease appears to be inherited as a single recessive trait and is largely limited to Jewish families. Prominent in the symptomatology are an absence of tears, postural hypotension, dysphagia, and "crises" of vomiting, hypertension, cutaneous blotching, and sweating, often induced by emotional stress (*1*).

Much of the autonomic dysfunction appears to be related to an insufficiency of the parasympathetic nervous system (*2*), but the sensory defect is not easily explained. The existence of a sensory disturbance was suspected initially because children with dysautonomia were able to sustain severe injuries, even fractures, without much discomfort. Objective evidence for one aspect of the apparently widespread sensory deficit in dysautonomia was noted in patients given intradermal injections of a strong solution of histamine (1 mg/ml). In normal persons this treatment produces a sensation of intense, burning pain in a wide area radiating from the site of injection. Within a few minutes, a flare develops over the area where the pain is felt. In the dysautonomic patient, both the pain and the flare are strikingly absent (*3*).

Another example of sensory deficiency in dysautonomic patients is inability to perceive or discriminate among the various modalities of taste. When presented with varying concentrations of acidic or sweet solutions, the dysautonomic patient is able to discriminate only the very concentrated solutions from distilled water (*4*); mistakes in the identity of the solution are frequent. We now describe, an anatomical defect which appears to be diagnostic for familial dysautonomia and which may account for the diminished, or absent, sense of taste.

The dorsal surfaces and tips of tongues of 30 patients with familial dysautonomia, ranging in age from 3 weeks to 26 years, were examined with a modified dissecting microscope at magnifications up to 40. In ten of these patients the posterior surface of the tongue was examined by grasping the tongue, pulling it forward, and using a laryngeal mirror when necessary.

The dorsal surface of the tongue in the healthy person is covered with numerous conical, filiform papillae interspersed with fungiform papillae. The distribution of the latter is greatest near the tip and lateral surfaces (Fig. 1). Posteriorly, there are 7 to 15 large, vallate papillae arranged in a V-shaped configuration, with the apex of the V in the midline, pointing posteriorly. The fungiform and vallate papillae contain most of the taste buds in the normal individual.

Careful examination of the tongues of dysautonomic patients revealed a complete absence of both fungiform and vallate papillae, even in patients with relatively mild clinical symptoms. The tip of a tongue from one of these patients is shown in Fig. 2. The large dark spots representing the fungiform papillae (Fig. 1) are absent. The histological examination revealed no structures resembling fungiform papillae, and no taste buds were found in any other areas of the epithelium.

Specimens of tongue from two patients with familial dysautonomia also were examined histologically. One was a biopsy specimen from a 20-year-old man, taken from an area near the tip of the tongue; the other was a section taken from the anterior third of a tongue obtained at autopsy from a 10-month-old infant.

Since the absence of fungiform papillae in patients with familial dysautonomia appears to be characteristic of the disease, diagnosis may be easily made in newborn, and perhaps in premature, infants, because fungiform papillae are normally present in large numbers even at these ages. Support for the diagnosis may be obtained from the histamine test (*3*) and the pupillary reaction to 2.5 percent methacholine (*5*).

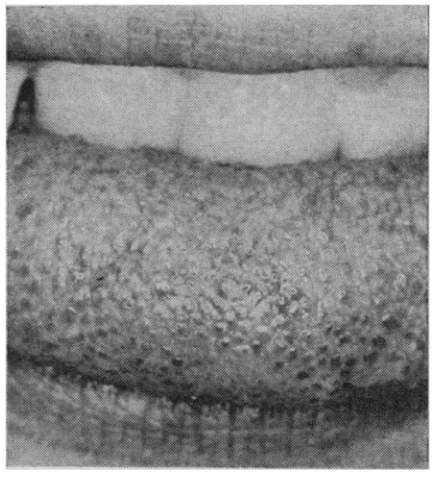

Fig. 1. Tip of the tongue of a healthy child. The dark spots represent blood vessels seen through the clear epithelium of the fungiform papillae.

This observation may also advance our understanding of the disease. The absence of taste buds provides an anatomical basis for deficiency in taste discrimination. It also raises the question of how much of the symptomatology might be attributed to some general defect in peripheral receptors. The mechanism for the absent axon flare is primarily peripheral (*6*). Many other features of the disease—the subnormal response to oxygen and carbon dioxide (*7*), postural hypotension, and areflexia—may also have their origin in defects of peripheral receptors.

In test animals, severing the chorda tympani is followed by disappearance of the taste buds (*8*). Examination of the tongue in four human subjects with a history of destruction of the chorda tympani incidental to middle ear surgery revealed, in two of them, a very striking reduction in fungiform papillae. Although we cannot say now whether the papillae are present but inapparent because of some transformation, or whether they have disappeared, the finding does demonstrate a strong interdependence of the papillae and their neural connections and suggests that a neural deficiency during the development of the fetus might result in lack of formation of papillae and the associated taste buds. A recent finding favors this possibility. In the embryonic chick that is functionally denervated with botulinum toxin, the effector organ, in this instance skeletal muscle, fails to develop normally (*9*).

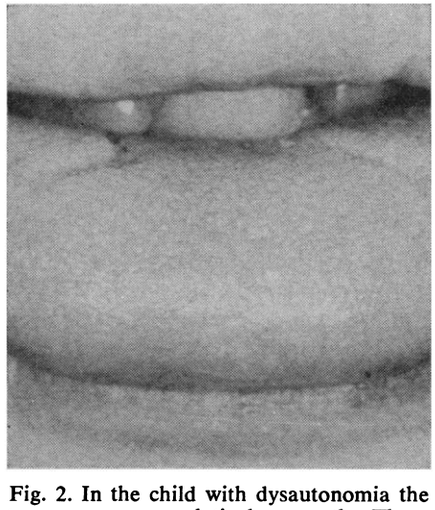

Fig. 2. In the child with dysautonomia the tongue appears relatively smooth. There are no fungiform papillae.

A study with the electron microscope (*10*) of the sequence of development of the fungiform papillae and taste buds in rats revealed that the papillae develop in the absence of any demonstrable neural elements in the immediate vicinity. Nerves then grow inward, and taste buds appear. Thus the papillae appear to arise in response to some non-nerve stimulus. Hence the basic mechanism for dysautonomia may not be neurogenic. A deficiency in some non-neural, controlling factor may be primary, such as the salivary gland factor described recently by Levi-Montalcini (*11*).

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X Chromosome DNA Replication: Developmental Shift from Synchrony to Asynchrony

Abstract. *The X chromosome in* Melanoplus differentialis *is negatively heteropycnotic in the early spermatogonial cell generations but positively heteropycnotic in the final premeiotic interphase. Autoradiography after administration of tritiated thymidine reveals that this condensation change is paralleled by a change in the time of DNA replication in the X chromosome relative to that in the autosomes.*

Sex chromosomes which show precocious condensation during interphase (positive heteropycnosis) are asynchronous in DNA replication; DNA synthesis continues in such chromosomes after it ceases in most other chromosomes (*1*). Developmental changes in the pattern of chromosome condensation are well known and provide an opportunity for testing the possible correlation of replication sequence and heteropycnosis. We have studied DNA replication in testicular cells of the grasshopper *Melanoplus differentialis* in which a striking change in the pattern of X chromosome condensation occur. Thus the X is positively heteropycnotic and forms a typical sex chromatin body in the final premeiotic interphase and meiotic prophase (Fig. 1*b*), but the X is negatively heteropycnotic in the earlier spermatogonial cell generations where no sex chromatin body is visible at interphase (Fig. 2*b*) and where the X is slightly undercondensed at metaphase (Fig. 3, *b* and *d*) (*2*, *3*). We have observed a developmental change in the relative time of X-chromosome replication which parallels this change in chromosome condensation.

Melanoplus differentialis males (*4*) under light CO_2 narcosis were injected with tritiated thymidine (*5*) and either killed after 25 minutes or given at that time a second injection of nonradioactive thymidine (*6*) and then killed at 2- to 4-hour intervals from 4 to 46 hours after injection. The testes were fixed, stained in bulk by the Feulgen reaction, and squashed, and autoradiographs were prepared (*7*).

We have confirmed earlier reports (*2*, *3*) that the X chromosome in younger spermatogonia can be identified during interphase by its characteristic position (Fig. 2*b*); the X can be positively identified at this site in late