

the C(1) hydroxyl group axial and the other substituent groups equatorial) is not altered by the refinement; nor was it expected to be altered. There are, however, significant changes in details of the skeletal structure. Furthermore, the structure determination is completed by the precise location of the hydrogen atoms. Because of the extraordinary biochemical importance of  $\alpha$ -D-glucose, we wish to present the atomic coordinates and the most important derived structural parameters without detailed comment at this time.

Our determination is based on intensity data of 1619 Bragg reflections from a crystal specimen (2) weighing 31.7 mg. The raw data from our automatic neutron diffractometer (3) were reduced by standard procedures (4) to a set of values  $|F_o(hkl)|^2$  and  $w(hkl)$ , where  $|F_o(hkl)|^2$  is the observed value of the square of the magnitude of the structure factor for reflection  $hkl$ , and  $w(hkl)$  is the weight of the observation. Absorption corrections were applied. In the least-squares refinement (5), the sum

$$S = \sum_{h,k,l} w(hkl) [|F_o(hkl)|^2 - |F_c(hkl)|^2]^2$$

was minimized by adjustment of an overall scale factor on the calculated structure-factor magnitudes  $|F_c(hkl)|$  and of three coordinates and six anisotropic thermal parameters for each atom. The discrepancy index

$$R = \frac{\sum_{h,k,l} ||F_o(hkl)|^x - |F_c(hkl)|^x|}{\sum |F_o(hkl)|^x}$$

is 0.060 when the exponent  $x$  is 1 and 0.059 when  $x$  is 2. A better indicator of the quality of the fit of the model to the data is the value 1.10 for the standard deviation of fit (6), which is close to the unit value expected at convergence for the correct model when the observational errors are normally distributed and correctly estimated.

The spatial configuration in molecule and crystal is specified completely by the atomic coordinates (Table 1) of the asymmetric unit molecule (7), in conjunction with the space-group symmetry and cell parameters determined by McDonald and Beevers (orthorhombic,  $P2_12_12_1$ ,  $a = 10.36 \pm 0.02$  Å,  $b = 14.84 \pm 0.02$  Å,  $c = 4.97 \pm 0.02$  Å, 4 molecules per cell).

All bond lengths and a selection of bond angles are shown in Fig. 1 (8). The six conformation angles (9) about

the pyranose ring bonds are: C(1)  $\rightarrow$  C(2),  $54.1^\circ$ ; C(2)  $\rightarrow$  C(3),  $-51.3^\circ$ ; C(3)  $\rightarrow$  C(4),  $53.3^\circ$ ; C(4)  $\rightarrow$  C(5),  $-57.5^\circ$ ; C(5)  $\rightarrow$  O(5),  $62.2^\circ$ ; O(5)  $\rightarrow$  C(1),  $-60.9^\circ$ . The computed standard errors of these molecular parameters, including contributions from errors in the unit-cell parameters (10), are as follows: C—C and C—O bonds, about 0.003 Å (except 0.006 Å for C(1)—O(1)); C—H and O—H bonds, 0.004 Å to 0.006 Å; bond angles involving only carbon and oxygen atoms,  $0.1^\circ$  to  $0.2^\circ$ ; C—O—H angles,  $0.2^\circ$  to  $0.4^\circ$ ; conformation angles,  $0.2^\circ$  to  $0.3^\circ$ . The thermal parameters have not yet been interpreted, and no corrections for thermal motion have been applied to any bond lengths or angles.

The hydrogen-bonding pattern established by McDonald and Beevers (1) is specified further by the precise location of the hydrogen atoms. The distances between the oxygen atoms and the angles at the hydrogen atoms in the five different hydrogen bonds are as follows: hydrogen bond O(1)—H(8) . . . O(5), 2.847 Å,  $161.0^\circ$ ; O(2)—H(9) . . . O(6), 2.776 Å,  $170.1^\circ$ ; O(3)—H(10) . . . O(2), 2.707 Å,

$164.8^\circ$ ; O(4)—H(11) . . . O(4), 2.773 Å,  $167.7^\circ$ ; O(6)—H(12) . . . O(3), 2.711 Å,  $169.7^\circ$ . The standard errors are 0.004 Å to 0.009 Å for the distances and  $0.3^\circ$  to  $0.4^\circ$  for the angles.

GEORGE M. BROWN  
HENRI A. LEVY

Chemistry Division, Oak Ridge  
National Laboratory\*, Oak Ridge,  
Tennessee

#### References and Notes

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2. We thank Professor A. VanHook of the College of the Holy Cross for growing crystals for us.
3. W. R. Busing, H. G. Smith, S. W. Peterson, H. A. Levy, *J. Phys. (Paris)* **25**, 495 (1964).
4. See for example, G. M. Brown and H. A. Levy, *ibid.*, p. 497.
5. We used various modified versions of "OR FLS, A Fortran Crystallographic Least-Squares Program," W. R. Busing, K. Martin, H. A. Levy, Report No. TM-305, Oak Ridge National Laboratory, 1962.
6. This quantity is given by the expression  $[S/(n-p)]^{1/2}$ , where  $n$  is the number of observations and  $p$  is the number of parameters adjusted.
7. Our coordinates when referred to the right-handed axis system of the crystal describe the molecule in correct absolute configuration. The McDonald and Beevers coordinates describe the optical antipode. The absolute configuration is known from chemical work relating  $\alpha$ -D-glucose to D-tartaric acid, the absolute configuration of which was established by application of the x-ray anomalous scattering effect by A. F. Peerdemann, A. J. van Bommel, J. M. Bijvoet, *Koninkl. Ned. Akad. Wetensch. Proc. Ser. B* **54**, 16 (1951).
8. The drawings, except for the lettering, were executed automatically through use of an X-Y plotter program of our co-worker Dr. C. K. Johnson (see Abstracts of Annual Meeting of American Crystallographic Association, Bozeman, Montana, 1964, p. 22).
9. For definition see G. M. Brown and H. A. Levy, *Science* **141**, 921 (1963).
10. Standard errors computed without the contributions from the errors of the unit-cell parameters are generally smaller by 30 to 50 percent. These are the errors which are relevant in considering parameter shifts between our structure and that of McDonald and Beevers.

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## Histoplasma Capsulatum from the Liver of a Bat in Colombia

Abstract. Of 135 bats (eight species), one of the species *Glossophaga soricina soricina*, a nectar-feeding bat from Girardot, Colombia, harbored *Histoplasma capsulatum*. The microorganism was cultured from the liver. This is the second report of recovery of this fungus from bat tissue.

*Histoplasma capsulatum* has been isolated from the tissues of various mammals (1); Shacklette *et al.* (2) were the first to isolate it from the

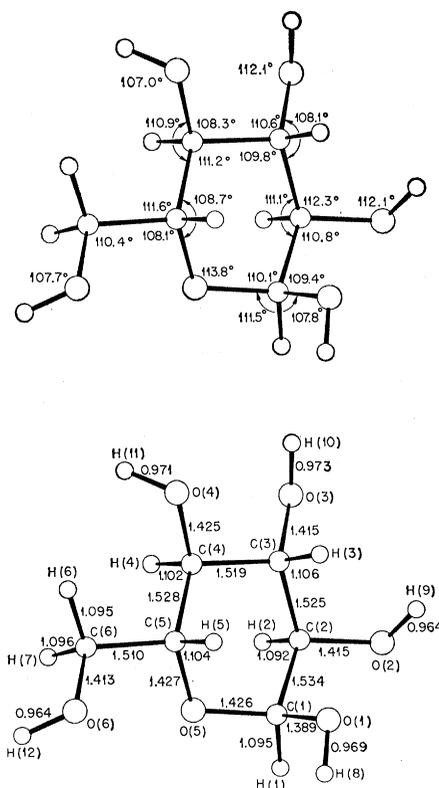


Fig. 1. Bond angles (top) and bond lengths (bottom) in the  $\alpha$ -D-glucose molecule. The molecule is represented to scale as it is found in the crystal.

liver and spleen of bats (*Chilonycteris 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, pH 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) iso-

lated *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.

C. J. MARINKELLE

E. GROSE

Department of Microbiology,  
Universidad de los Andes,  
Bogotá, Colombia

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6. We thank C. O. Handley, U.S. National Museum, Washington, D.C., for assistance in identifying the bats.

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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); mis-

takes 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).