Neurologic Contributions of Bayard T. Horton

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Bayard Taylor Horton (1895-1980) (Fig. 1) received his M.D. degree in 1922 from the University of Virginia and then completed an internship at the University of Virginia Hospital. He was professor of biology at Emory and Henry College in Emory, Virginia, from 1923 to 1925. In 1925, Horton began his fellowship in medicine at the Mayo Graduate School of Medicine. He became a member of the Mayo staff in 1929. In 1940, he was appointed head of the Section of Clinical Investigation. He retired from the Mayo Clinic staff in 1958 and moved to Sun City, Arizona, where he was instrumental in the development of the Medical Research Section at the Boswell Memorial Hospital.

Horton was a tireless worker; he published numerous articles on topics including cold allergy, hypertension, and duodenal diverticula. Early during his career, he became known for his work on hypersensitivity to cold. His international reputation, however, was established with his lucid description of two headache disorders: histaminic cephalgia, now termed “cluster headache,” and temporal arteritis, now termed “giant cell arteritis.” Horton’s contributions also included investigating new medications such as dihydroergotamine (DHE-45) and E. C. 110 (a combination of ergotamine tartrate and caffeine) (Cafergot). The early recognition of medication-induced or rebound headache can be traced to Horton.

Horton was actively involved in numerous societies. From 1943 to 1944, he served as president of the Minnesota Society for Internal Medicine. He was the second president of the American Association for the Study of Headache from 1961 to 1963 and was the recipient of the Distinguished Clinician Award of the American Association for the Study of Headache in 1974. Horton was a member of the International Cluster Headache Research Group from its inception in 1979 until his death.

In this article, we focus attention on Horton’s seminal work on disorders of interest to neurologists: cluster headache, giant cell arteritis, and agents used in headache therapy.

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Cluster Headache

The debate concerning who rightly deserves credit for first describing cluster headache continues. In 1981, Sjaastad offered the following comments about this issue:

There may have been earlier indistinct and incomplete descriptions of Horton’s headache in the literature; they to some extent dealt with disorders probably not identical with our present concept of cluster headache. Horton’s description was a much more accurate one than that current at the time, and it focused interest on the syndrome to such an extent that it became an item in the diagnostic arsenal of every neurologist with any kind of self esteem. He laid the basis for the scientific study of cluster headache, and it is with this disorder that this name will deservedly be connected.

The clinical features of histaminic cephalgia (cluster headache), as characterized by Horton, are summarized in Table 1.

Horton’s description of a patient with histaminic cephalgia warrants review in that it superbly captures the salient features of cluster headache.

A woman aged 37 registered at the clinic Sept. 7, 1937, complaining of attacks of severe pain on the right side of the head and face. These episodes came on with clocklike regularity at night and night after night had awakened her at the same time, usually between 3 and 4 a.m. The pain often persisted until 10 or 11 a.m., after which time she generally was free from distress. During attacks her right eye watered and was congested, and there was stoppage of the right nostril. The taking of alcohol precipitated earlier attacks. The pain was made worse by stooping over. There was a sensation of throbbing in the involved region, but trigger zones were never present. The first episode of this character had occurred in 1920 and lasted for two weeks. Later episodes appeared in 1929 and in 1934. Nausea, vomiting and scotomas were never present. She had taken as many as 24 tablets of 5 grains (0.3 Gm.) each of acetylsalicylic acid in one night without relief. The application of ice packs to the right side of the head during attacks had given partial relief, and the intravenous administration of 0.2 to 0.3 mg. of ergotamine tartrate (gynergen) had relieved her. Physical and neurologic examinations revealed nothing significant except considerable tenderness over the right carotid and temporal vessels as well as tenderness over the upper part of the neck.

Horton not only characterized the clinical features of cluster headache but also devised a treatment plan. As sug-
gested by Goldblatt, Horton's tragic flaw may have been his "conviction that the use of histamine in the treatment of this syndrome [histaminic cephalgia] is as specific as insulin is in the treatment of diabetes mellitus." Unfortunately, this overshadows Horton's additional treatment recommendations that, to this day, are considered standard of care. In 1952, Horton wrote about the treatment of attacks.

The intravenous administration of 1 cc of dihydroergotamine (DHE-45) frequently will abort an attack in 1-5 minutes, if it is administered at the onset of the attack. The breathing of 100% oxygen will alleviate an attack to a marked extent, especially if the attack is mild and if the patient resorts to the use of oxygen promptly. If the attack has fully developed and has persisted for several minutes, it is likely to run its course irrespective of the drug employed. A rectal suppository which contains 2 mg of ergotamine tartrate and 100 mg of caffeine, if used at bedtime, frequently will prevent nocturnal attacks.

Horton also found that corticotropin was useful in the management of this syndrome. "In a control study of nine additional cases of severe histaminic cephalgia, attacks of pain were blocked for various periods of time in eight of nine cases by the intravenous administration of corticotropin."

GIANT CELL ARTERITIS

Although Hutchinson likely reported the first case of temporal arteritis, Horton and colleagues in 1932 described two additional cases, one of which involved a 55-year-old woman and the other of which was a 68-year-old man. They stated that,

The clinical pictures which these two cases present are similar in many ways, and seem to represent a definite clinical syndrome. Both patients were admitted to the Clinic in the spring of 1931 because of fever, weakness, anorexia, loss of weight, anemia, mild leukocytosis, and painful, tender areas over the scalp and along the temporal vessels. These manifestations had been present for from four to six weeks.

In subsequent articles, Horton further emphasized the systemic features. Horton recognized headache as a cardinal symptom of temporal arteritis. "The physician should be aware of headache in the senior citizen. It may forbode, among many things, the insidious onset of temporal arteritis, a disease that can be easily overlooked in its early stages." He also noted that the headache of temporal arteritis can vary—"But all patients agree that it differs from any other headache they may have previously experienced."

Horton was likely one of the first to describe so-called jaw claudication in association with temporal arteritis. "Its significance was not appreciated until I finally realized, during the years 1942-1944, that the pain of chewing, referred to by patients as difficulty in chewing or 'lockjaw,' is an exercise phenomena and represents intermittent claudication of the jaw."

Ophthalmologic complications associated with temporal arteritis, ranging from visual loss to double vision, were also characterized by Horton. Although not the first to describe blindness in patients with temporal arteritis, he recognized early on the importance of visual loss. "Sudden loss of vision in one eye in an elderly person with headache and symptoms of sepsis and high sedimentation rate should indicate to the physician that the patient most likely has temporal arteritis."

Horton described the pathologic changes associated with temporal arteritis.

Microscopic examination gave evidence of chronic periarteritis and arteritis. Complete necrosis of the media was often observed, and the media had been replaced by a granulomatous type of lesion in which numerous giant cells were invariably present. The large number of giant cells constitutes the most characteristic feature.

Horton emphasized that temporal arteritis is not a localized disease confined to the temporal arteries. In 1935, this...
### Table 1.—Clinical Characteristics of Histaminic Cephalgia

<table>
<thead>
<tr>
<th>Character</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Males &gt;&gt; females</td>
</tr>
<tr>
<td>Family history</td>
<td>None</td>
</tr>
<tr>
<td>Age at onset (yr)</td>
<td>30-40</td>
</tr>
<tr>
<td>Prodrome</td>
<td>None</td>
</tr>
<tr>
<td>Aura (visual)</td>
<td>None</td>
</tr>
<tr>
<td>Site of pain</td>
<td>Unilateral, maximal pain in ocular area, may extend into temple, neck, and face</td>
</tr>
<tr>
<td>Character of pain</td>
<td>Boring, burning</td>
</tr>
<tr>
<td>Severity of pain</td>
<td>Excruciating</td>
</tr>
<tr>
<td>Onset to peak pain</td>
<td>Minutes (rapid)</td>
</tr>
<tr>
<td>Duration of pain</td>
<td>15 minutes to several hours</td>
</tr>
<tr>
<td>Frequency of attacks</td>
<td>2-20 per wk</td>
</tr>
<tr>
<td>Periodicity of attacks</td>
<td>Clocklike regularity</td>
</tr>
<tr>
<td>Cluster phenomena</td>
<td>Exacerbations and remissions are common</td>
</tr>
<tr>
<td>Autonomic accompaniments</td>
<td>Ipsilateral nasal congestion, rhinorrhea, conjunctival injection, ptosis (Homer’s syndrome), lacrimation, Bradycardia often present during attack</td>
</tr>
<tr>
<td>Behavior during headache</td>
<td>Pacing</td>
</tr>
<tr>
<td>Nocturnal attacks of pain</td>
<td>Frequent</td>
</tr>
<tr>
<td>Triggering factors</td>
<td>Alcohol, sleep</td>
</tr>
</tbody>
</table>

Data from references 4 through 10.

In 1945, Horton and colleagues published the first report of dihydroergotamine in the treatment of migraine. Of the 120 patients studied, 56% experienced complete relief in 1 to 4 hours, and in 19%, the duration and severity of the attack were markedly reduced. Intravenous administration of dihydroergotamine was also found to provide almost immediate relief in a case report of a woman with migraine. They noted that, “She was observed during an acute attack and was completely relieved within two minutes after receiving 1 c.c. of D.H.E.-45 intravenously.”

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**Horton’s Role in Therapeutic Investigations**

Horton had an important role in the development of several symptomatic medications, specifically dihydroergotamine and ergotamine tartrate, for use in migraine and cluster headache. In 1945, Horton and colleagues published the first report of dihydroergotamine in the treatment of migraine. Of the 120 patients studied, 56% experienced complete relief in 1 to 4 hours, and in 19%, the duration and severity of the attack were markedly reduced. Intravenous administration of dihydroergotamine was also found to provide almost immediate relief in a case report of a woman with migraine. They noted that, “She was observed during an acute attack and was completely relieved within two minutes after receiving 1 c.c. of D.H.E.-45 intravenously.”

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**INITIAL DESCRIPTION OF MEDICATION-INDUCED HEADACHE**

Peters and Horton were the first to warn physicians of the potential adverse effects of excessive use of ergotamine-containing preparations. “A rebound phenomenon occurs—a withdrawal headache begins and more ergotamine tartrate is taken to combat the withdrawal headache. A vicious cycle develops, and it takes more and more ergotamine tartrate to produce the desired effect.” This likely represents the first account of ergotamine-withdrawal headache, which is also known as medication-induced headache or rebound headache. Horton and Peters did not...
observe this medication-induced headache phenomenon with the prolonged use of dihydroergotamine.

Horton was likely the first to institute a detoxification program for ergotamine-overuse headache. Horton and Peters\(^{22}\) noted that many patients with this condition required hospitalization for several days, during a "stormy time" when the offending medication was discontinued. They found that nasal oxygen, 100% oxygen, used for several minutes each hour for several days was "effective in treating ergotamine-withdrawal headache."\(^{22}\)

Horton,\(^{6}\) in further discussing treatment, admonished that, "Habit-forming drugs, such as morphine and codeine, have no place in the treatment of periodic or chronic headache. Their use eventually creates a new problem which becomes more difficult to handle than the original headache."

CONCLUSION
Horton's two outstanding contributions to neurology were his characterization of two headache disorders: histaminic cephalgia, now termed "cluster headache," and temporal arteritis, now termed "giant cell arteritis." He not only described these two headache disorders but also devised a treatment plan for both. In regard to giant cell arteritis, he and colleagues characterized the biopsy findings. Horton's contributions to headache research also include studies of ergotamine tartrate and dihydroergotamine. Moreover, he recognized the phenomenon of ergotamine-induced headache.

Horton,\(^{23}\) in speaking of the genius of Dr. William J. Mayo, cofounder of the Mayo Clinic, attributed this to the "genius of vision": "Great men have always been the ordained leaders of mankind. They have sought not greatness, but truth, and in so doing, have found both." Horton, also, found both.

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REFERENCES