

Letter to the Editor

Ibn Sina (Avicenna) on Pathogenesis of Migraine Compared With the Recent Theories

From its dramatic rise in the seventh century, Islamic civilization has covered a large part of the globe, incorporating many subcultures and languages into its orbit (http://www.nlm.nih.gov/hmd/arabic/med_islam.html). Islamic medicine typifies that experience, being built on the theoretical and practical knowledge first developed in Greece and Rome. For Islamic scholars, *Galen* (d. ca. 210 AD) and *Hippocrates* (fifth century BC) were pre-eminent authorities, followed by Hellenic scholars in Alexandria. Islamic scholars translated their voluminous writings from Greek into Arabic and then produced new medical knowledge based on those texts. In order to make the Greek tradition more accessible, understandable, and teachable, Islamic scholars ordered and made more systematic the vast Greco-Roman medical knowledge by writing encyclopedias and summaries (http://www.nlm.nih.gov/hmd/arabic/med_islam.html).

Drawing upon Hellenic medical tradition, Islamic medicine developed its own traditions. In turn, medieval and early modern scholars in Europe drew upon Islamic traditions and translations as the foundation for their medical enterprise. It was through Arabic translations that the West learned of Hellenic medicine, including the works of Galen and Hippocrates (http://www.nlm.nih.gov/hmd/arabic/med_islam.html).

Of equal, if not of greater influence, in Western Europe were systematic and comprehensive works such as Avicenna's *Canon of Medicine*, which were translated into Latin and then disseminated in manuscript and printed form throughout Europe. During the 15th and 16th centuries alone, the *Canon of Medicine* was published more than 35 times (http://www.nlm.nih.gov/hmd/arabic/med_islam.html).

Avicenna's work represented one of the first scientific encyclopedia covering logic, natural sciences, psychology, geometry, astronomy, arithmetic, and music. In the *Canon of*

Medicine, Avicenna (980-1037 AD) surveyed the entire medical knowledge available from ancient and Muslim sources, supplementing this information with his own original contributions. The *Canon* became a standard of medical science, on a par with the works of Hippocrates (460-377 BC) and Galen (129-199 AD). The work could be found in all the important European university libraries. The *Canon of Medicine* consists of 5 books containing approximately 1 million Arabic words on 1000 pages, written in a completely systematic manner.¹

Avicenna begins his *Canon* with the following words: "It is my heart's desire, to start off with speaking about the general and common principles of both parts of medicine, that is, theory and practice."²

The *Canon* gained widespread popularity in the West only after the introduction of typography in the 15th and 16th centuries, but its impact throughout Europe remained steady until the end of the 18th century. Only a few modern European libraries now retain a complete *Canon of Medicine* (a 1482 edition in Paris, France; 1658 editions in Padua and Milan, Italy and a copy in Berlin). There is only 1 edition in a modern language (Russian), limiting an actual interpretation of this work.³

Recent articles considering history of theories of pathogenesis of migraine have ignored Avicenna.

Villalón et al⁴ summarized in their history of theories of pathogenesis of migraine, declaring that around 400 BC Hippocrates released migraine from the realms of the supernatural by attributing it to *vapours rising from the stomach* to the head.^{5,6} They pointed out that the Hippocratic/Galenic concept of migraine survived into the 17th century, when Thomas Willis published, in 1664, his hypothesis that "megrin" was due to dilatation of blood vessels within the head (the first enunciation of a vascular theory).^{5,6}

In 1873, Edward Liveing proposed that migraine was due to "nerve storms evolved out of the optic thalamus."⁵ Toward the end of the 19th century, attempts were made to reconcile both theories. Thus, Moebius stated in 1898 that "parenchyma is the master, circulation the servant," and that both brain and blood vessels dysfunctions were



Fig 1.—Photograph showing page 301 of Canon of Medicine in Arabic language, which is available in the Saab Medical Library in American University of Beirut, Lebanon.

necessary to produce an attack of migraine.⁵ Harold Wolff was then the first researcher to offer migraine a scientific basis.⁷⁻⁹

Nevertheless, in 1983, the vascular theory was apparently weakened when Lance et al¹⁰ demonstrated that blood flow changes similar to those known to occur in migraine could be produced by electrical stimulation of brainstem structures. This finding revived the neurogenic theory, stimu-

lating studies that investigated the relationship between the trigeminal nerve and the cranial vasculature.

In 1984, Moskowitz¹¹ showed that trigeminovascular axons from blood vessels of the pia mater and dura mater released vasoactive peptides producing a sterile inflammatory reaction with pain. During this neurogenic inflammation, the trigeminal ganglion is stimulated and this induces neurogenic protein extravasation; then some vasodilator



Fig 2.—Photograph showing page 302 of Canon of Medicine in Arabic language, which is available in the Saab Medical Library in American University of Beirut, Lebanon.

peptides are released, including calcitonin gene-related peptide, substance P and neurokinin A.

At no point, for historical context, was the work of Avicenna referenced in regard to migraine. Interestingly, Avicenna’s speculations regarding the pathogenesis of migraine almost resembled the recent neuro-vascular theory, centuries before, as summarized in the Table.

It could be concluded that Ibn sina (Avicenna) was the first medical scholar to address neurovascular

theory of migraine. An increase in the availability of a translation of his work, the *Canon of Medicine*, should spread recognition of his research and expertise, especially in the study and treatment of the nervous system.

Noha Abokrysha, MD

Department of Neurology, Cairo University, Kaser Al-Aini Hospital, Al-Manyal, Cairo, Egypt

Table.—Comparison of Ibn Sina's Theories and Recent Theories of Migraine Pathogenesis

Ibn Sina theory	Recent theory
May be from the bone of skull.	The trigeminal nerve, which innervates the meninges, is intricately involved in migraine. There is increasing evidence that events intrinsic to the cerebral cortex are capable of affecting the pain sensitive vascular structures (eg, in the dura mater, base of the skull, and scalp). ¹²
Or from the membrane underneath the bone of skull (dura mater).	
Or due to substances reaching the side of migraine either from outer veins and arteries (extra cranial).	Most of the arterial concepts of migraine have been focused on the enlargement of intracranial surface-of-the-brain arteries resulting from their exposure to nitric oxide (NO). Moreover, the effects of the release of peptides such as calcitonin gene-related peptide (CGRP) on the extracranial vessels by their corresponding trigeminal nerve branches are adversely affected. ¹³ The elevation of CGRP in the external jugular venous blood of patients with acute migraine with aura was documented. ¹⁴
Or from brain itself and its meninges (pia mater).	Migraine is a primary brain disorder most likely involving an ion channel in the brain stem nuclei, a form of neurovascular headache in which neural events result in dilation of blood vessels aggravating the pain and resulting in further nerve activation. The key pathway for the pain is the trigeminovascular input from the meningeal vessels. These nerves pass through the trigeminal ganglion and synapses on second-order neurons in the trigeminocervical complex. ¹³ Current hypotheses, besides noradrenaline and acetylcholine, immunohistochemical studies have demonstrated the presence of several vasodilator transmitters in perivascular nerves supplying intracranial blood vessels, including 5-HT, vasoactive intestinal peptide, NO, substance P, neurokinin A, and CGRP. In any case, cranial vasodilatation leads to the resultant increase in perivascular (trigeminal) sensory nerve activity, which provokes headache and other symptoms. ¹⁵⁻¹⁷

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APPENDIX I

Translations

His words in latin letters	Translation into English
fasl fi al-shakika Asbab al-shakika Min Dakhel al-Raas	Chapter of migraine Causes of migraine pain May be from the bone of skull. Or from the membrane underneath the bone of skull. (Dura mater)
Fi Al – gheshaa Al-mobatten le-azem al-gahf Wa takoon al mawad wasela ela mawdehe Ema min al-wareed Aw Al-sharaieen al-kharega Aw min al-demagh nafseh wa hogabeh	And it will be due to the substances reaching the side of migraine either from outer veins and arteries (extra cranial) Or from brain itself and its meninges (pia mater)

*Figures 1, 2 represent pages from chapter of migraine.