The Neurology of Aretaeus: Radix Pedis Neurologia

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Key Words

Aretaeus · Galen · Paralysis · Epilepsy · Migraine

Abstract

Aretaeus (Aretaios) was a physician born in Cappadocia in about the 2nd century AD, a student of medicine and physician in Alexandria. His works are found in eight books which espoused the physiological and pathological views of the Hippocratic principles derived from the pneumatists and the eclectic schools. Though he has been called the forgotten physician, it has been said that: ‘after Hippocrates no single Greek author has equalled Aretaios’. In order to give an indication of his neurological legacy, this paper offers a summary of and quotations from his principal neurological contributions: migraine, vertigo, tetanus, epilepsy, melancholia, strokes and paralysis. One of his most important discoveries was the notion that the pyramidal tract decussates.

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When he can render no further aid, the physician
alone can mourn as a man with his incurable
patient. This is the physician's sad lot.
Attributed to *Aretaeus*

Introduction

The value of the writings of Aretaeus re-emerged only in the 19th century, and undoubtedly established a basis, albeit a primitive one, for several many concepts of contemporary neurology [1]. He was neglected: ‘the forgotten physician’ [2]. Aretaeus (Aretaios) was a physician (fig. 1) born in Cappadocia in about the 2nd century AD. He studied medicine in Alexandria, and probably practised in Rome [3]. After Hippocrates, the school at Alexandria [4] cultivated the studies of Herophilus and Erasistratus to establish the rudiments of Greek medicine and anatomy by human dissections. The works of only a few have survived from this early period: Celsus, Dioscorides, Galen, Aretaeus and two Ephesians – Rufus and Soranus. Cappadocia occupied a portion of Asia Minor; originally independent, the Persians divided it into Pontus and an inland province called Cappadocia.

Francis Adams [5, pp. 472–473] considered Aretaeus a contemporary of Galen (131–201 AD) in the 2nd century AD: according to philologists, Aretaeus's Ionic dialect indicates the second century, which agrees with this estimate. Some scholars argue that Aretaeus lived in the 1st century AD and that Archigenes echoed the writings

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Fig. 1. Aretaeus (The National Library of Medicine; copyright statement: the National Library of Medicine believes this item to be in the public domain).

Fig. 2. *The Extant Works of Aretaeus, the Cappadocian* [5].

of Aretaeus [6, 7]. Others agree that he echoed the physiological and pathological views of the Hippocratic corpus derived from that eclectic school, but also the pneumatists stemming chiefly from Archigenes the Syrian physician and Athenaeus of Cilicia in the 1st century AD. They tried to link the four humours (blood, phlegm, black bile and yellow bile) to the fundamental role of ‘pneuma’, the air or spirit, in accord with Alexandrian teaching.

The eight books (four volumes) [5] of Aretaeus are: (1) *De causis et signis acutorum morborum libri duo*, (2) *De causis et notis diuturnorum affectuum libri duo*, (3) *De morborum acutorum curatione libri duo* and (4) *De morborum diuturnorum curatione libri duo*. In these books he discusses the causes, symptoms and treatment of many diseases. These include his much praised descriptions of tetanus, epilepsy, asthma, migraine, jaundice, diarrhoea, dropsy, elephantiasis, dysentery, diabetes, pneumonia and an early account of diphtheria. Also included are treatises of Rufus of Ephesus (c. 80–150 AD). Aretaeus’s contributions, unlike the dogma of Galen based largely on animal studies, rejected speculations, but drew on his own observations and experience [8], and is clearly identifiable as a distant link with modern medical scientific methods. He described unmistakably the clinical details of tuberculous consumption. He recognised diabetes mellitus: ‘The patient’s fiery thirst, his imperative desire to pass water, his dry mouth and parched skin; it is a wonderful malady, he says, a melting down of the flesh into urine’ [5, pp. 338–340, 485–486].

His descriptions of migraine, diphtheria (‘ulcera Syriaca’), leprosy (‘elephantiasis Aretaei’), dysentery, pleurisy, pneumonia and asthma have only been revived in the last century [9–11]. He notably provided an account of adult coeliac disease [12]. However, although Hippocrates, Herophilus, Erasistratus, Galen and other ancient physicians were quoted and revered in the Middle Ages, Aretaeus’s works appear largely forgotten.

This paper offers a summary of and quotations from his principal neurological contributions in order to give an abbreviated indication of his neurological understanding, which re-emerged in the 19th and 20th centuries [11]. Quotations are based mainly on English translations from Adams [5] (fig. 2) and Hude (fig. 3) [9].

The Neurology of Aretaeus

Neurological disorders attracted his attention. Like many physicians such as Galen, he sought the soul or ‘pneuma psychikon’ (Latin: spiritus animalis) within the brain (encephalocentricity) – as opposed to Aristotle’s idea of cardiocentricity; in later medieval times, the soul was located in the cerebral ventricles. Three mental functions – the gathering of sensory perceptions for imagination, reasoning and memory – comprised the ‘sensus communis’ [1]. His texts include topics such as headaches, scotoma, epilepsy, tetanus, vertigo, melancholy,

Fig. 3. *Corpus Medicorum Graecorum* [9].

madness and paralysis [13, 14]. One of his most important discoveries was the notion that the pyramidal tract decussates, which accounted for crossed paralysis in apoplexy.

Paralysis of Motion and of Sensation

After the Hippocratic school, four scholars – Herophilus, Erasistratus, Aretaeus and Galen – appreciated the separate neural pathways responsible for motor and sensory functions, as well as the concept of ‘sympathy’ – the functional relationship of different parts not visibly connected [15]. In *Morborum acutorum, de curatione apoplexiae*, Aretaeus distinguished between the paralyses of motion and of sensation, and explained how apoplexy and injuries to the brain produce paralysis on the opposite side, but cord lesions caused homonymous (ipsilateral) paralysis [5, p. 306]:

Apoplexy is a paralysis, but a paralysis of the whole body, of sensation, of understanding, and of movement. But if the head be primarily affected on the right side, the left side of the body will be paralysed. If on the left side, the right. The cause of this is the interchange in the origins of the nerves... each of them passes over to the other side from that of its origin, decussating each other in the form of a letter X.

Here he plainly anticipated one important facet of 19th century cerebral localisation. He did not clearly separate spastic from flaccid paralysis, but Book 1, Chapter 7: ‘On Paralysis’ suggests upper motor neurone spasticity [5, 16]:

Sometimes the limbs lose their faculties while in a state of extension, nor can they be brought back into the state of flexion, when they appear very much lengthened; and sometimes they are flexed and cannot be extended; or if forcibly extended, like a piece of wood on a rule.

He also relates ‘phthisis of the pupil’ (presumably miosis) versus ‘platycoria’ or mydriasis. In addition, he speaks of the paralysed bladder: ‘it may lose its retentive powers or, on the contrary, be unable to express urine’. Causes of hemiplegia were a wound or blow to the head, exposure to cold, indigestion, venery or intoxication. An identical list was given by Soranus, another contemporary of Galen, and by Caelius Aurelianus in the 5th century AD [17]; but without systematic pathology, none of these scholars were able to analyse the pathogenesis of strokes [16].

Facial Palsy and Neuralgia

Aretaeus probably described facial paralysis: ‘Wherefore, the parts are sometimes paralyzed singly, as one eye-brow, or a finger...’ [5]. He described facial distortion [11, 18] in ‘cynic spasm’, a condition of unilateral facial muscle spasms reminiscent of hemifacial spasm:

But the distortion of the eye-brows, and of the cheeks, and of the muscles about the jaws and chin to the other side, if attended with spasm, has got the appellation of cynic spasm... But there is apt to be deception in cynic spasm; for to the spectator it appears as if the parts unaffected were those possessed by the disease.

Aurelius (Aulus) Cornelius Celsus (25 BC to 50 AD), physician to emperors Tiberius and Caligula, also described cynic spasm [19], a term later to be applied descriptively in tetanus as ‘risus sardonicus’ and ‘risus caninus’.

Before Nicholas André (1756) and Fothergill (1773) described ‘tic douloureux’, Aretaeus described a pain in which ‘spasms and distortions of the countenance took place’, possibly a hint of trigeminal neuralgia.

Tetanus

In Chapter 6 of *De curatione tetani id est rigoris*, Hippocrates describes tetanus in a ship’s master after a crush injury of his finger by an anchor; Aretaeus also fully described tetanus [20, 5, p. 253]:

Tetanus in all its varieties is a spasm of an exceedingly painful nature, very swift to prove fatal, but neither easy to be removed. They are affections of the muscles and tendons about the jaws; but the illness is communicated to the whole frame...

Opisthotonos bends the patient backward, like a bow, so that the reflected head is lodged between the shoulder-blades; the throat protrudes; the jaw sometimes gapes, but in some rare cases it is fixed in the upper one; respirations stertorous; the belly and chest prominent... the abdomen stretched, and resonant if tapped; the arms strongly bent back in a state of extension; the legs and thighs are bent together...

The causes of these complaints are many; for some are apt to supervene on the wound of a membrane, or of muscles, or of punctured nerves, when for the most part, the patients die; for, spasm from a wound is fatal... An inhuman calamity! An unseemly sight! A spectacle painful even to the beholder! An incurable malady!

Mental Illnesses

In *On The Causes and Symptoms of Chronic Disease*, Chapter 5, Aretaeus left us a lucid picture of mania and melancholia (black bile), linking them: 'I think that melancholia is the beginning and a part of mania...'. In Chapter 6, melancholia [21] was a state of despondency; man's delirium could be brought on by melancholy, and when signs of joy briefly appeared it was evidence of mania: a clear reference to 'bipolar disorder'. Those disposed to mania were:

...irritable, violent and given to joy and childish things... And they with whose madness joy is associated, laugh, play, dance night and day, and sometimes go openly to the market crowned, as if victors in some contest of skill; this form is inoffensive to those around. Others have madness attended with anger; and these sometimes rend their clothes and kill their keepers... Depressives, termed melancholics, were 'dull or stern, dejected or torpid without manifest cause'. And they become 'dispirited, sleepless'; if the illness was more severe they showed 'hatred, avoidance of the haunts of men, lamentations and the desire to die'.

The cause of the disease 'is seated in the head and hypochondriac region..., seated in the bowels, sometimes commencing in both together, and the one imparting it to the other' [5, p. 303].

Epilepsy

In Chapter 5 of *De causis et signis acutorum morborum*, 'de epilepsia sive morbo comitiali' is described. Epilepsy was a disease of a cold and humid nature, originat-

ing in the brain or nerves. Purging, dietary regulation, cautery, heating and phlebotomy were some of the remedies favoured by Aretaeus and Galen. Epileptic seizures were clearly identified [5, pp. 243, 296, 399–400, 468]. He recorded (Book 1, Chapter 5, 'On the Paroxysm of Epileptics'): 'the person lies insensible; the hands are clasped together by the spasm; the legs not only plaited together, but dashed about hither and thither by the tendons.'

He mentioned an olfactory aura and sluggishness, vertigo, heaviness of the tendons, plethora and distension of the veins in the neck, and much nausea (Book 1, Chapter 5) and:

But, if it be near the accession of the paroxysm, there are before the sight circular flashes of purple or black colours, or of all mixed together, so as to exhibit the appearance of the rainbow expanded in the heavens; noises in the ears; a heavy smell; they are passionate, and unreasonably peevish. They fall down then, some from any such cause as lowness of spirits, but others from gazing intently on a running stream, a rolling wheel, or a turning top. But sometimes the smell of heavy odours, such as of the gagate stone (jet), makes them fall down...

He also described focal fits with retention of consciousness, which were treated by stretching or binding of the affected parts:

But those to whom the affection has become habitual, whenever the disease recurs, and has already seized the finger, or is commencing in any part, having from experience a foreknowledge of what is about to happen, call, from among those who are present, upon their customary assistants, and entreat them to bind, pull aside, and stretch the affected members; and they themselves tear at their own members, as if pulling out the disease; and such assistance has sometimes put off the attack for a day.

Aretaeus distinguished acute epileptic paroxysms from the chronic diseases characterised by epilepsy. He reported depressed fracture as one acute cause. He differentiated epilepsy from 'hysterical suffocation' by lack of convulsions in the latter. Centuries before Hughlings Jackson, he observed the aura, tongue biting, incontinence and the post-epileptic state:

The person lies insensible... The tongue protrudes, so as to incur the risk of a great wound, or of a piece of it being cut off should the teeth come forcibly together with the spasm... The utterance of a moaning and lamentation... when they come to the termination of the illness. There are unconscious discharges of the urine, and watery discharges from the bowels... At the termination they are torpid in their members, at first experience

heaviness of the head... and are languid, pale, spiritless and dejected.

A comprehensive discussion is given by Eadie and Bladin [22].

Vertigo

On the Causes and Symptoms of Chronic Disease, Book 1, Chapter 3 describes vertigo and scotoma as equivalent. However, although he describes tinnitus, he does not clearly relate vertigo to a disorder of the inner ear. Aretaeus lucidly relates the symptoms and recognises a primary form, and attacks secondary to ‘cephalæa’, or as warning of mania, or epilepsy:

Vertigo arises as the successor of cephalæa; but also springs up as a primary affection... If darkness possess the eyes, and if the head be whirled round with dizziness, and the ears ring as from the sound of rivers rolling along with a great noise, or like the wind when it roars among the sails, or like the clang of pipes or reeds, or like the rattling of a carriage, we call the affection Scotoma (or Vertigo); a bad complaint indeed, if a symptom of the head, but bad likewise if the sequela of cephalæa, or whether it arises of itself as a chronic disease. For, if these symptoms do not pass off, but the vertigo persist, or if, in course of time, from the want of any one to remedy, it is completed in its own peculiar symptoms, the affection vertigo is formed, from a humid and cold cause. But if it turn to an incurable condition, it proves the commencement of other affections – of mania, melancholy, or epilepsy, the symptoms peculiar to each being super-added.

Headaches and Migraine

Both the Hippocratic school (c. 460–370 BC) and Celsus’s *de Medicina* (c. 30 AD) [23] yield recognisable portraits of migraine sufferers [24]. Several Latin translations and Adams’ English translation (1856) have noted Aretaeus’s classification of headache, well expounded by Koehler and van de Wiel [25], who translated sections from Hude’s Greek text published in 1958 [9]. Aretaeus (*On the Causes and Symptoms of Chronic Diseases*, Book 1, Chapter 2: ‘De cephalæa’; fig. 4), says that cephalalgia[s] are headaches lasting a few days, and ‘cephalæa’ are headaches lasting days or weeks without remission. Of cephalalgia:

If the head be suddenly seized with pain from a temporary cause... the disease is called Cephalalgia... In certain cases... the

Fig. 4. De cephalæa. *On the Causes and Symptoms of Chronic Diseases*, Book 1, Chapter 2.

pain ... remains in the half of the head. This is called Heterocrania, an illness by no means mild, even though it intermits, and although it appears to be slight it sets in acutely, it occasions unseemingly and dreadful symptoms; spasm and distortion of the countenance..., nausea; vomiting of bilious matters, collapse of the patient, but if the effect be protracted, the patient will die; or if more slight and not deadly it becomes chronic; there is much torpor, heaviness of the head, anxiety and weariness. For they flee the light; the darkness soothes their disease: nor can they bear readily to look upon or hear anything disagreeable; their sense of smell is vitiated.

Aretaeus used the word ‘heterocrania’ (Galen’s hemi-crania) to indicate its location in half of the head and described headache attacks recognisable as migraine [26]. Although symptomatic headache was also probably identified by Aretaeus, the terms ‘heterocrania’ and ‘cephalæa’ may be compared with what today we would call migraine and tension-type headaches, respectively [25].

His description of various headaches has been exhaustively quoted in most 20th century texts and papers [9, 24, 25, 27, 28], showing that after 1,800 years he has finally achieved recognition. Of the above passage, Macdonald Critchley [29] rightly commented that the reference to death is foreign to contemporary experience, but suggests that Aretaeus might have observed a patient with aneurysmal subarachnoid haemorrhage.

In keeping with practices of his time, Aretaeus advocated (*On the Cure of Chronic Disease*, Book 1, Chapter 2) bloodletting from a peripheral vein or from a scalp vein. If that failed to secure relief he advised:

...we must take the thick quill of a goose, and having scooped the nervous part of it into teeth like a saw, we are to push it down the nostrils as far as the ethmoid cells, then shake it with both hands so that the part may be scarified by its teeth. Thus we shall have a ready and copious flow of blood.

Later in the Byzantine period, following Aretaeus, Orisbasius (325–403 AD), advised purging and bloodletting in hemicranias [30]. Alexander of Tralles (525–605 AD) advised bloodletting from the side opposite to the headache, and Paul of Aegina (625–690 AD) recommended opening the veins of the nose [31].

Discussion

Aretaeus left many clinical accounts ‘of unsurpassed accuracy and elegance’ [5, p. xii]. His principal works in Greek were unknown until translated into Latin by Junius Paulus Crassus (Venice, 1552) with the original Greek edition reprinted in Paris in 1554. The English edition (Moffat, 1785) [32] was succeeded by the versions of Francis Adams (1856) [5] and C. Hude (Berlin, 1958) [9]. These are probably reliable translations of the remnants of the original manuscripts, despite the long interval.

Yet the originality of his work has been questioned by Wellman [33], and Allbutt [34] in a scholarly review remarked: ‘Aretaeus was a copyist, as was Aetius’, a view

disputed inter alia by Neuberger [35]. His use of the Ionic dialect has been criticised as ‘consciously archaic’, though plainly reflecting the Hippocratic corpus, particularly the aphorisms, and ‘he sometimes quotes, mostly silently, from the Homeric Iliad’ [12]. Douglas Guthrie’s *History of Medicine* [36] (1960), comments that ‘his valuable contributions to medicine passed unnoticed, and by the early historians he was regarded as a frank copyist who borrowed from the writings of Archigenes (c. AD 100) whose original works are lost’ (p. 71). However, Garrison’s praise [37] is unqualified. Similarly, Neuberger [35] reminds us:

... one thing stands out as certain, after Hippocrates no single Greek author of whom we have knowledge has equalled Aretaios, and no work in the entire literature so nearly approaches to the true spirit of Hippocratism, both in description of disease and in therapeutic principles, as the work of the Cappadocian... . He trod the strait path of true, thoughtful, critical observation of nature... .

Aretaios drew a series of pictures of disease difficult to rival, hardly to be excelled. He ever strove after more certain diagnosis, ever kept in view one chief aim – a simple method of treatment, as far as possible in conformity with nature.

It appears that both Hippocrates and Archigenes influenced his ideas, yet all scholars learn from acknowledged classic texts. No further original material is likely to emerge, and there appears to be no overt criticism of his writings from Galen or other contemporary sources. Aretaeus has been praised for his skilful observation and thoroughness of clinical description, which in many instances such as migraine, epilepsy, and the crossed motor pathways have led to his dissertations being considered seminal works.

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Erratum

In the article by Pearce J.M.S., entitled 'The Neurology of Aretaeus: Radix Pedix Neurologia' [Eur Neurol 2013;70:106–112, DOI: 10.1159/000352031], please amend the following: unfortunately, the captions for the illustrations have been wrongly placed. Referring in sequence to the actual figures published, the captions should read: Fig. 1. The Extant Works of Aretaeus, the Cappadocian [5]; Fig. 2. Corpus Medicorum Graecorum [9]; Fig. 3. De Cephalea. On the Causes and Symptoms of Chronic Diseases, Book 1, Chapter 2; Fig. 4. Aretaeus, The National Library of Medicine®.