Areteus of Cappodocia.
Views on diphtheria

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BIOGRAPHY

Areteus (Figure 1), native of Cappadocia, lived in Alexandria, between the 1st and 2nd century AD. He was a representative of the Eclectic School (Greek: Εκλεκτική Σχολή), and wrote his manuscripts in Ionian dialect, in such a way that no medical author of antiquity surpasses him in his vivid portrayal of various diseases. Little is known concerning his life. Among his extant works are “De causis et signis acutorum morborum”, the “De causis et signis diuturnorum morborum”, the “De curatione acutorum morborum”, and the “De curatione diuturnorum morborum”. His eight books granted him an honourable place among the greatest of medicine [1].

ON DIPHTHERITIS

Although the disease’s cause was actually unknown, Areteus, committed to the principal of the total observation of things, described diphtheria (diphtheritis), its symptoms, complications and treatment. He noticed that the disease’s prevalence among children and youngsters was higher, as the appearance of the false membranes was more frequent. He stated, though, that surgical interference (probably tracheotomy or laryngectomy) was completely secure [2]. In his work “On Uvula’s Diseases”, mentioning several types of angina (Greek: κυνάγχη), Areteus had separated the membranes (hymens) into unilateral, and bilateral like wide cloths or bat wings. In the case of bilateral stigma, he named the membranes “strap” (Greek: ιμάντιο) [2].

On the next chapter, “On the Palatine Tonsil’s Ulcers”, he categorized all types of tonsil ulcers, mentioning the usual benign and harmless ulcers, and the uncommon, infectious and at times deadly forms. According to Areteus, the benign ulcers, small and surfaced, were free of pain and inflammation. On the contrary, the infectious ones were fouling, wide and deep, covered with white or black phlegm. His admirable description of diphtheria continued in the same chapter with the following words “if this cover is deep, it is called “eschara” (Greek: εσχαρα). Around it, the area is inflammatory, red and painful. The presence of smaller scattered reddish rashes at the beginning causes wide ulcers after their merging. In case of the disease spreading towards the opening of the mouth cavity, it reaches the uvula and cuts it out. The disease continues its spread to the tongue, gums, and towards mouth corners, and even the teeth get blackish, sensitive and tremble. The inflammation reaches the neck and then the sufferer has only a few days before he dies by inflammation, fever, bad breath, and

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A vivid presentation of croup (sharp obstruction such as a case was “sudden, as both lungs and heart could not sustain ulcers, bad odour and bile humours (phlegm)”. He had also completely understood the diphtheritic laryngitis, when writing “the sufferers breathe heavily and deeply as they need cool air to sustain fever, while expiration is light, and hoarseness or voice absence is present. The symptoms worsen, and the patients suffer until they fall down and die” [2].

Aretaeus, like a philosopher of ancient times, prior to discussing treatment, mentioned some demographic information, “the disease appears mostly among children and youngsters, but also in older patients. This disease is widespread in Egypt and Syria” [2, 3].

Writing on treatment, he considered diphtheritis an acute disease, an emergency situation which needed a rapid medical response before it proved fatal. Stating that an offensive strategy was needed to cure the affected, he proposed enemas, phlebotomy, compresses, poultices, re-heating, suction cups and surgery. Having faith in the theory of the humours he believed that bleeding (Greek: αφαίρεση, especially in the elbow area with a wide phlebotomy, or repeated enemas, could reduce the volume of liquids, and save the patient from “gallows-like” drowning. Bandages were to be applied on the feet, ankles, knees, wrists, elbows and arms. According to his theory if imminent drowning was expected, new incisions should be made and some suction cups used [2].

Aretaeus recorded a plethora of per os formulations and poultices. As cementing medications the following were proposed: sumac (Rhus coriaria), Acacia arabica dissolved in honey or water, parasites from the roots of rockrose (Cistus), earth from Samos, Limnos or Sinopi, and unripe grapes. In more serious cases myrrh, costus (an aromatic root), and the herb Conium maculatum should be applied. In the case of “escharas” gum (gummi) and niseste, both waterlogged with pomegranate or dates decoction, alongside a mush of pitisani or wild fig (Greek: τρίχας, fig tree species in Messina), were recommended [2].

Finishing his pharmaceutical suggestions on diphtheria, he noted some very strong medicines. Realizing that the wounds which he called diphtheres, had a progressive dispersion, he proposed that cauterezation was the approved solution, but was an inapplicable method due to local sensitivity. Thus, medications with similar properties should be used. The remedy contained alum with honey, part of the oak’s bark (Greek: κικίς), dried pomegranate juice, and a mix of copper stones (Greek: χαλκίτι), kadmeia (zinc oxide) and vinegar or rhubarb (rheum) [4].

In terms of applications, Aretaeus, suggested inhalations, powder forms, and liquid pouring directly on uvula, while reeds, feathers, and small but wide tubes could be used for the purpose [4].

In his final reference on diphtheria, he split patients into those who were on the route to recovery, and those who would eventually die. Among the former, when the “escharas” were dropped, apoptosis of the “diphtheres”, the remaining ulcers, could cause nerve spasms due to muscle distortion. Thus the physicians were to apply milk, niseste, pitisani, fig, flaxseed, and Trigonella foenum graecum, in order to soften the area as well as the whole body. The unfortunate patients suffered until corrosion of the uvula to the bone, combined with inflammation of the epiglottis, had reached a critical point where swallowing was impossible, and hunger would eventually finish them off [4].

DISCUSSION

The eminent classical author from Cappadocia, Aretaeus, was the only one who used the term eschara to define the lesions of diphtheria, and diphtheres for the false membranes. These terms are still used to characterize diphtheria [5]. He not only gave a remarkable description of diphtheria, which has stood the test of time, but also established the use of alum for the centuries to come.

This remedy had been forgotten and had fallen into oblivion, until Bretonneau unearthed it from Aretaeus’ writings, realising that alum gargles and insufflations of alum were sufficient to stop the development of the false membranes. Bretonneau started using alum in 1825, with surprisingly good results [6, 7]. The beneficial role of the presence of alum is still studied: it improves antibody titres against the diphtheria toxoid protein, proving Aretaeus’s
intellect and prescience [8]. Gifted with a unique faculty for observing pathological phenomena, he was able to elaborate upon earlier texts, enriching them with his own original findings and numerous thoughtful reflections, forming a sophisticated synopsis of knowledge on diphtheria, which remains a point of reference to the present day [9].

**Keywords:** Aretaeus, diphtheria, membranes, escara, alum.

**Conflict of interest**
All authors state that there is no conflict of interest related to this paper.

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**REFERENCES**