Summary

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Summary : Benediktos Adamantiades was born in Prousa, Asia Minor in 1875, studied at the Medical School of the University of Athens and specialised in ophthalmology in Paris. After being director of the Ophthalmology Department of Hippocration Hospital in Athens he developed significant scientific activities. During the annual meeting of the Medical Society of Athens on November 15, 1930, Adamantiades presented "A case of relapsing iritis with hypopyon" identifying the three major signs of the so called Adamantiades-Behçet's disease and insisting on a single clinical entity. In the same year, his lecture was published in the Proceedings of the Medical Society of Athens, and in 1931 in the French journal Annales d'Oculistique. In the year 1946, Adamantiades defined thrombophlebitis as the 4th major sign of the disease. Later, he presented the first classification of the disease by describing the ocular, mucocutaneous and systemic forms in a review work. He pointed out that the disease can occur for years as a monosymptomatic or oligosymptomatic disorder and that eye involvement and severe prognosis are more common in men than in women. In this work he also proposed the first diagnostic criteria. In addition to Adamantiades-Behçet's disease, Adamantiades described the interstitial keratitis in trachomatic patients to be a bacterial infection and classified the epidemic idiopathic hemeralopia. Further pioneer works were those on the marginal corneal degeneration, the posterior vitreous detachment, the measurement of the optic fundi and of the ocular pressure as well as investigations on trachoma and the pathogenesis of glaucoma. Adamantiades compiled over 150 scientific papers many of which marked a new stage in his field. He died in 1962 in Athens.

Keywords : Adamantiades, Adamantiades-Behçet's disease, history.

ARTICLE

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Benediktos Adamantiades (Fig. 1) was an important personality of the Greek medical community in the first half of the last century, but his scientific work has almost been forgotten outside his country. In addition to his major contribution to the description of Adamantiades-Beḥçet's disease as a single nosologic entity [1, 2], Adamantiades was the first physician who described the interstitial keratitis in trachomatic patients to be a bacterial infection [3, 4] and classified epidemic idiopathic hemeralopia [5]. He published the - for that time - large number of over 150 scientific works, many of which marked a new stage in his field and was a leader of the fight against epidemic eye diseases which constituted a serious medical problem in Athens of the 1920's, especially among the 1.5 million refugees who came to the city leaving Asia Minor after the war lost against Turkey in 1922 [6-9].

His life

Benediktos Adamantiades was born in Prousa, Asia Minor (nowadays Bursa, Turkey) in 1875 to a father who was a teacher [6-9]. His mother died when he was a child and later on, after having lost his father, he was fostered by his uncle, Metropolitan Bishop of districts in Thrace and Asia Minor, where he completed his elementary studies. Thanks to the financial support of his uncle Adamantiades was able to attend the "Megali tou Genous Scholi (Illustrious School of the Nation)" in Constantinople, which was well-known at that time for its high standards and excellent Greek teachers, and completed his secondary school studies there with distinction in 1892. Studying in that school and the influence of his uncle contributed to the formation of a personality with a classical education enriched by Christian and humanistic ideals. His plans to study at the Polytechnic School of Athens were annulled by his late arrival in the city, where he was confronted with the fact that the registration period had expired. In order not to lose an academic year, Adamantiades decided to register at the Medical School of the University of Athens in which he completed his studies in 1896 graduating with distinction. During his studies in Athens, the lectures of the renowned Professor of ophthalmology, A. Anagnostakis, aroused his special interest in the
With the end of his studies and because of the death of his uncle, financial reasons and the obligation to foster his younger sister Penelope, who lived on her own in Prousa, obliged Adamantiades to return to his city where he worked as a general practitioner for 10 years. During that time he gained the respect of the inhabitants of the district, of both Greek and Turkish origin, who simply called him "Doctor Benediktos". His interest in ophthalmology became more prominent and through the study of several thematic books, he was able to perform modern ophthalmologic examinations, such as refraction and fundoscopy, on a regular basis. From 1911 to 1914 he went to Paris to specialise in ophthalmology serving at Hôtel-Dieu, under Pr. Delapersonne, and at Quinze Vingts, under Professor Trousseau. The outbreak of the 1st world war obliged him to return to Prousa, where he was mobilised to serve as an officer-physician in the Turkish army in Dardanellia (nowadays Canakkale Bogazi). Because of a severe gastrointestinal disease he was dismissed one year later and returned to Prousa shortly to leave again for East Anatolia, followed by his sister, because of a banishment by the Turkish authorities. After the end of the 1st world war Adamantiades returned to Prousa and was elected president of the Greek community of the city. During the period 1920 to 1922 he closely cooperated with the Greek authorities of Asia Minor in the re-establishment of charities, health administration and Greek language schools for minors and adults. In 1922, after the defeat of the Greek army in Asia Minor, he accompanied millions of Asia Minor inhabitants of Greek origin as a refugee to Greece. He started immediately to serve as an ophthalmologist in Athens, where he led the fight against epidemic eye diseases, to be named in 1924 Director of the Ophthalmology Department of the Refugee Hospital of Athens (nowadays Hippocration Hospital). In his new duty he proved to be a persevering investigator with rare perspicacity and self discipline. Adamantiades was a founding member of the Greek Ophthalmologic Society in 1931. He developed into one of the most brilliant ophthalmologists in Athens in the first half of the last century. He married at a late age and died in 1962. His adoptive daughter, Evgenia Rangavi, was the first female ophthalmologist in Greece.

**His scientific work**

During the annual meeting of the Medical Society of Athens on November 15, 1930, Adamantiades presented in a lecture with the title *A case of relapsing iritis with hypopyon*, a 20-year-old male patient with the three major signs of the disease. The disease had begun at the age of 18 with oedema and ulcerations on the left leg diagnosed as thrombophlebitis. During the following 2 years (1928-1930) the patient developed recurrent iritis with hypopyon in both eyes which led to blindness and atrophy of the optic nerve, scrotal ulcers healing with scars, oral aphthous ulcers and sterile arthritis in both knees. The latter three signs were recurrent. Bacterial cultures of the knee and anterior eye chamber punctures were found sterile and the inoculation experiments in animals were negative, while in cultures from scrotal ulcers and a tonsilar abscess staphylococi had grown. In the same year, the lecture was published in the Proceedings of the Medical Society of Athens [1] and in the following year in the French journal *Annales d'Oculistique* [2]. Adamantiades brought together the genital ulcers, the arthritis and the ocular
signs in connection as signs of a single disease. He referred to the important publications by Reis [10] and Gilbert [11], who described similar cases, backed the hypothesis of a bacterial focal illness, induced by staphylococci, which had been initiated by Gilbert [12], and responded to the comment of the physician V. Vasilopoulos, that the case can be classified to the already described so-called "metastatic ophthalmias" which indicate a generalised infection, with the phrase "I would like to comment to my colleague that the disease, which Gilbert reports as aetiological (notice: induced by staphylococcus), does not correlate to all types of iritis, but to this iritis with recurrent hypopyon, which now constitutes a clinical entity" (Fig. 2). In the year 1946, Adamantiades reported on two further patients and defined thrombophlebitis as the 4th major sign of the disease [13]. Later, he presented the first classification of the disease by describing the ocular, mucocutaneous and systemic forms in a review work [14]. He pointed out that the disease can occur for years as a monosymptomatic or oligosymptomatic disorder and that eye involvement and severe prognosis are more common in men than in women. In this work he also proposed the first diagnostic criteria. In 1958, Adamantiades published his last work on the neurological complications of the disease [15].

In addition to his work on Adamantiades-Behçet's disease, Adamantiades described in 1926 and 1928 the interstitial keratitis in trachomatic patients to be a bacterial infection through the Koch-Weeks bacillus [3, 4]. He observed an epidemic character of the disease associated with the malnutrition of the Asia Minor refugees. Twenty-five years later, similar observations were made in malnourished populations in Africa and Pagès from Morocco confirmed Adamantiades' reports [16].

In 1925, in a work on "epidemic idiopathic hemeralopia" Adamantiades classified the course of avitaminosis A in three stages, namely hemeralopia, xerophthalmia with Bitot's spot, and keratomalacia [5], a classification that is nowadays also in use.

Further pioneer works were those on the marginal corneal degeneration or marginal furrow keratitis first described by Terrien [17], on the posterior vitreous detachment (Weiss' ring), on the measurement of the optic fundi and of the eye pressure as well as investigations and development of new concepts for trachoma and the pathogenesis of glaucoma [7]. Adamantiades compiled over 150 scientific papers many of which marked a new stage in his field.

Adamantiades-Behçet's disease

Adamantiades-Behçet's disease is a chronic, multisystemic inflammatory disorder, which is clinically characterised by relapsing oral aphthous and genital ulcers, and ocular vascular lesions [18-21]. The disease may affect small and large vessels in almost all organs [22]. Adamantiades-Behçet's disease is a universal rare disorder with varying prevalence and a peak of onset in the 3rd decade of life [23]. It occurs endemically in the Eastern Mediterranean area and in Central and East Asia. Although several immunological abnormalities and a genetic predisposition have been demonstrated, the exact pathogenesis remains to be elucidated. The most probable hypothesis is that of an autoimmune late reaction induced by
infectious or other antigens in genetically predisposed individuals.

The first description of the disease goes back to the 5th century B.C. when Hippocrates of Kos (460-377 B.C.) described in his 3rd *Epidemion* book, case 7, an illness, whose manifestations fit very well with the cardinal signs of Adamantiades-Behçet's disease. It was the ophthalmologist A. Feigenbaum who paid attention to the context of the Hippocratic text in correspondence with Adamantiades-Behçet's disease [24]. In the medical literature there are reports of patients with a symptom complex that resembles Adamantiades-Behçet's disease since the 18th century [25].

Behçet was aware of the first publication of Adamantiades in the *Annales d'Oculistique* and included it in the references of his first report in 1937 [26]. In 1941, Jensen from Denmark, being aware of Behçet's work but not of that of Adamantiades, first used the term "Behçet's syndrome" to describe a patient with the triple symptom complex and ulcerous haemorrhagic colitis and established the pathergy test as a diagnostic criterium [27, 28]. In 1944, Berlin and Ephraim described simultaneously the disorder in necropsy material of a patient from Tel Aviv [29] and in another patient from Haifa [30]; both referred to the important work of Jensen and used the name of Behçet in the titles of their publications. In 1946, Feigenbaum and Kornblüh first used the term "Behçet's disease" and considered it as a manifestation of a chronic septic condition connected with a constitutional disorder in their description of 4 additional patients from Jerusalem [31]. However, it was Ollendorff-Curth, former vice chair of the Department of Dermatology, Virchow Hospital in Berlin (Pr. Buschke) and immigrant to the United States who, knowing the work of Behçet as she had met Behçet in Berlin, made the term "Behçet's syndrome" popular with two publications which reported on two American patients [32, 33]. By reading the second publication of Ollendorff-Curth [33] it becomes obvious that she had gone through the publications of Jensen, Berlin and Ephraim (which were written in English) but she did not have detailed knowledge of Adamantiades' work (written in French), although she included the latter in her references. Adamantiades himself, in one of his communications in 1956 six years before his death, reported that he had only become cognisant of Behçet's publications after the 2nd world war [34].

Later, several authors, who got access to the work of both authors, added the name of Adamantiades to the one of Behçet in their descriptions [25]. The term "Adamantiades-Behçet's disease" honours both of the first recognisers of the several manifestations of the disease to constitute a unique entity in modern times and is, therefore, advisable to be used for naming this disorder.

References


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32. Ollendorff Curth H. Behçet's syndrome, abortive form (?) (recurrent genital

Figure 2. *Original text of the response of B. Adamantiades to the comment of the physician V. Vasilopoulos during the annual meeting of the Medical Society of Athens on November 15, 1930, proving his belief that his reported case constitutes a new clinical entity.*