

George Higoumenakis (1895-1983), Greek dermatologist

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NOTE:

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Summary

This paper describes the Higoumenakis sign, enlargement of the sternal end of the clavicle in patients with late congenital syphilis, and the dermatologist after whom it is named. Several professors and doctors from the Medical School of the University of Athens opposed his actions especially at the University in Greece. His persistence led him to productive scientific activity in syphilis, leishmaniasis, and psoriasis. He became a member of the Greek parliament from 1964 to 1967 and eventually Minister of Hygiene - even though this may have been an imprudent political choice, due to the unstable socio-political status of that period. He died on 27 December 1983 at the age of 88.

Biographical details of the authors

Constantinos Frangos, MD is a research student at the Medical School of the National and Kapodistrian University of Athens, Greece. He has published several papers in English and Greek concerning inflammatory bowel diseases. His historical interests concern biographies of Greek physicians that managed to have an international impact in medicine.

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Childhood and University

Biography promotes discussion of ideas and has two main ingredients, the life of the man described along with his work and the results he has achieved.^{1, 2} The most compelling biographies, however, are those that portray the ambitions, the passions, the disappointment, the ‘peaks and valleys of one’s life’³ and the moral choices that characterize a scientist’s life.⁴

George Higoumenakis (Figure 1) was born on 26 August 1895 in the village Apóstoloi in the prefecture of Iráklion in Crete, the largest island in Greece.⁵

(Figure 1 here)

His father was Constantine Higoumenakis and his mother Maria who had two other sons and one daughter. Higoumenakis considered his mother to be the person who helped develop his character in the progressive manner that he followed for the rest of his life. He mentions, “if I became someone, I owe that to her.”⁶ George received his primary and secondary education in Iráklion and in 1912 was accepted at the Medical School of Athens. Only he and one other student, Aristeidis Michelidakis,⁷ entered the University of Athens after high school.

After graduating from high school, George decided to seek adventure before finishing his medical studies. He decided to volunteer to enlist in the army so that he could participate in the First Balkan War that had broken out on 17 September 1912. However, after the cessation of the Balkan wars of 1912-13 he returned to the Medical School of Athens and continued his studies; aiming to catch up with the courses he had missed. He became an assistant in the second department of Internal Medicine and in 1917 graduated with the mark of distinction, excelling particularly in Internal Medicine and Dermatology.

During his final examinations in Dermatology, Professor George Photinos (1876-1961) called upon all the consultants and registrars to listen to his ‘admirable student’. After the exams, Photinos said: “Do you want to become a dermatologist? I will teach you how to make a living out of it ...”⁸ Higoumenakis denied this gentle offer, because he was thinking of becoming an obstetrician-gynaecologist.

After University and Specialty: Paris, Berlin, Breslau, and Vienna

Higoumenakis’ first destination was Paris, as an intern at the Hospital Saint-Louis from 1919 until 1921. His main tutor was Professor Gaston Milian (1871-1945), a famous French dermatologist and an expert on syphilis,⁹ to whom he refers in his book *Hē klēronomikē syphilis deuterās geneas kai hē therapeia autēs*¹⁰ as his brilliant teacher. Milian also assigned Higoumenakis to prove whether or not there was hereditary syphilis of the second generation. The outcome of this research was two books^{11, 12} and several papers written in French,^{13, 14} which concerned hereditary syphilis. His extensive research gave him his first hint of the ‘sign of the clavicle’.¹⁵ In 1928 Milian presented a moulage (mold) before the French Society of Dermatology and Syphiligraphy depicting an enlargement of the sternal end of the clavicle in a patient with congenital syphilis. He cited Higoumenakis’ study of this subject¹⁶ and later on, wrote the prologue for Higoumenakis’ book on cutaneous Leishmaniasis.¹⁷

He was also interested in gonorrhoea and decided to go to Germany to see whether a new treatment had been developed for this disease. He stayed in Berlin for eleven months and Breslau for five. His teacher in Breslau was Joseph Jadassohn (1863-1936).¹⁸ His last stop was Vienna where he stayed from the summer of 1922 until the second half of 1923, studying under Professors Ernst Finger (1856-1939), J Kyrle (1880-1926),^{19, 20} and Salomon Ehrmann (1854-1926)²¹ and here he wrote on ‘lichen syphiliticus’.²²

Return to Greece and Political Activity

In the early twentieth century there was a tendency for Greek medical university society to reject those doctors who had studied abroad. George N Papanicolaou (1883-1962) described Greece’s scientific environment in 1915 as desperately modest and closed to new ideas. He called Greece ‘a cemetery for research’.²³ George Cotzias (1918-1977), who first demonstrated L-Dopa as an effective treatment for Parkinsonism,²⁴ and Dennis Ikkos (1921-1993) are additional examples of other eminent Greek doctors

who studied abroad and were recognized by foreign institutions of higher education but who were rejected by Greek universities as faculty members.²⁵

In this climate, in 1923 Higoumenakis returned to Greece, believing it was time to begin his medical career. He first visited his old professor, G Photinos, who was now director of Andreas Syggros, a hospital that specialised in skin diseases. To Higoumenakis' surprise he was not offered a job as a doctor, despite his impressive studies abroad; he was quite offended by this treatment and considered it a sign of hostility from Photinos, possibly due to his rejection of his professor's offer before going to France in 1919. In the meantime he practised medicine privately at an office near the Centre of Athens and became a member of the Medical Society of Athens.

Later, Higoumenakis applied again for a position at Andreas Syggros. This time he went through a formal application procedure where Photinos was only one opinion on a three-member committee, and he was accepted. He worked there for four years, from 1925 until 1929. He mentions many disagreements with his old professor. This deterioration in his relationship with Photinos may have influenced the constant rejection of his doctoral theses submitted to the University of Athens from 1926 to 1942 (see below). In 1929 he resigned, having already accepted a much better position: that of director of the Department of Dermatology and Venereology in the Hospital 'Evangelismos' (15 September 1928) (Figure 2).

(Figure 2 here)

During his time as the director of Dermatology at the Hospital Evangelismos, in 1930 Higoumenakis married Alkmini Meïmaridou. They had three children: Nikos, Constantine and Helen. From 1938 until his retirement, Higoumenakis worked as a dermatologist at the General Hospital in Nikaia, Pireaus; while also practicing dermatology privately.

From 1924 Higoumenakis had shown a keen interest in participating in the sessions of the Medical Society of Athens.²⁶ Upon his return to Greece, Higoumenakis became a member of the Medical Society of Athens in 1924. Maybe his participation in the meetings of this society and others helped develop Higoumenakis interest in something very different from medicine yet similar in its immediate impact on people's lives: politics. In this regard he resembled the English dermatologist Sir Ernest Graham-Little (1867-1950).²⁶ In 1926 he became one of the founders of the Hellenic Dermatology and Venereology Union, a society interested in the discussion of modern issues of dermatology.²⁸ Moreover, we can find announcements of his in many other medical societies including: the Medical Society of Athens,²⁹ the Medico-Chirurgical Society,³⁰ the Hellenic Union of Dermatology and Venereology,^{31, 32} the Hellenic Urologic Society³³ and the French Society of Dermatology and Syphiligraphy.^{34, 35} The participation of Higoumenakis in the sessions of these societies draws a picture of a person who was very communicative and social and who had the courage to speak about his convictions.

From 1945 onwards he began to pursue significant political positions that required several thousand votes to be elected. His first achievement was to be elected as a member of the City Council of Athens in 1945 (Figure 3A) and subsequently he became a member and vice-president of the Greek Medical Council, the biggest syndicate fighting for doctor's rights. As a vice president of the Greek Medical Council, Higoumenakis fought for doctor's professional rights. He claimed that health provision for the poor classes of society should be provided free and he participated in more than one strike for doctor's professional rights.^{36, 37} His most important political achievement was to be elected a member of the Greek parliament with the progressive Centre Union party on 16 February 1964.

Before 1964 however, and predominantly after 1940, the military and the monarchy were powerful proponents of the political right that ruled Greece until 1963. Significant socioeconomic changes took place between 1940 and 1963, resulting in a victory by the left-wing progressive Centre Union in the general elections of 1964 (Prime Minister George Papandreou). The period from 1964 to 1967, during which Higoumenakis was a member of the Greek Parliament, was a time of severe political and social turbulence; leading to a military coup d' état on 21 April 1967. During this time the central parliamentary government was very unstable and six separate governments came to power in quick succession. This political instability undermined the legitimacy of these governments but their ineffectiveness was further compounded by the unwillingness of the members of the Greek Parliament to work within the framework of the institutional rules and procedures. At the same time, the uncertainty in people's minds created by this state of affairs led to numerous strikes and demonstrations in the streets against the government.³⁸

After the victory of George Papandreou in 1964, the powerful right-wing forces were particularly hostile to the new government. A political scandal occurred, complicating matters and worsening the existing hostility, when Andreas Papandreou (the son of the prime minister) was accused of being involved in a left-wing secret organization within the army called 'ASPIDA'. King Constantine II took advantage of this situation and unconstitutionally appointed a government of his own (government Athanasiadis-Novas), without democratic election. This act, 'The Apostasy of July 1965', was considered the beginning of the end for parliamentary democracy, which was ultimately overthrown in the military coup in 1967.³⁹

Higoumenakis participated in these events and was not left untouched. He was appointed Minister of Hygiene in 1965 with the government of George Athanasiadis-Novas and was a cabinet minister from 11 May 1966 until 22 December 1966 with the government of Stephanos Stephanopoulos. This resulted in his being called an apostate and a traitor. He answered these allegations with a speech titled 'I believe in Democracy',⁴⁰ defending the ideals of democracy. A possible reason for Higoumenakis deciding to become a minister during this politically hot period was the promise by other politicians (more professional or leading, such as K Mitsotakis) of becoming a minister, something very much desired by every person; especially politicians.⁴¹ Unfortunately, history showed this government was unconstitutional, thus highlighting the mistakes of those who took part in it.

Despite the general interpretation of historians, we would like to note that Higoumenakis was a scientist among politicians. It is our opinion that it was erroneous of him to collaborate with the government of July 1965 because of the serious political problems of that period and the impact they had on the weakening of parliamentary democracy. However, at that time, this might not have been obvious to anyone, including Higoumenakis. Politics depends very much on impressions and less on logical deductions like those in science. Hence Higoumenakis possibly followed his logical instinct which, in combination with his desire to excel politically, led him to make an error in judgement, from an historical point of view.

(Figure 3 here)

Doctoral Thesis submitted: Accepted or Not?

A significant chapter of every scientist's life is his doctorate trial. It is the period when the young scientist acquires the mature thought required for future research and thereafter can be considered by the rest of the society as a capable and responsible scientist. For Higoumenakis, a doctorate came quite late (in 1946) considering his significant training abroad and his publications in international journals (which began as early as the 1920s).

Higoumenakis made four attempts to secure a doctorate from the University of Athens and each was denied. The title of his first thesis, submitted on 4 December 1925, was 'Hereditary syphilis of the second generation and its treatment'.⁴² Six months later, on 19 May 1926 his supervisor, Professor A Aravantinos, commented, referring to the French version of his 1925 book on hereditary syphilis

We must admit that the dissertation in its whole is characterised by a great deal of erudition [...] and great accuracy.

But we consider that the discussion on this doctoral thesis by the School is of no use, because according to the French original, it appears that the applicant is a doctorate of the Medical School of Paris. So we ask of the rector to inform him that the procedure of his thesis is from now on considered useless.⁴³

A few days later, on 28 May 1926, the rector I Alivizatos, after speaking with Higoumenakis himself and checking his titles, notes

Complying with the decision of the School, I checked the titles of the candidate, and found that they were all true and real ... Therefore, the candidate is suitable and the School should choose him.⁴⁴

Unfortunately, Higoumenakis sent a letter after that session⁴⁵ and resigned from his application; giving as the reason that he was offended that his word had been doubted and that he had been accused of presenting fake credentials. The denial of the Medical School of Athens to grant Higoumenakis a doctorate on the basis that he had presented fake credentials appears to be an excuse that hides a deeper reason. Higoumenakis claims to have presented true credentials and the rector appears to agree with him.

Higoumenakis' second attempt for a doctoral diploma concerned a thesis he submitted concerning 'Oriental Sore and its Treatment'. The supervisor was G Photinos who, at the session of the medical school on 31 May 1935,⁴⁶ denied him the diploma. The reasons given were scientific inaccuracy, great exaggerations, and unbelievable imagination.⁴⁷

An article from a Greek medical newspaper of that time, *Iatrikai Athinai*, comments on this decision; supporting Higoumenakis. The article seems to imply that the denial was based more on the personal hostility between Photinos and Higoumenakis and it mentioned

We must confess with honest our defeat by Mr Professor of Venereology [Photinos], concerning the condition of the propter legem claim on behalf of Iatrikai Athinai for the right of Mr Higoumenakis to receive a doctorate.

Mr Photinos, after having delayed to submit his reviewing report and now urged by our complaint, has submitted it, thus complying with the law, and has found a new way not to grant his opponent [Higoumenakis] a doctorate diploma.

Taking advantage of his personal relationships with some of the Professors, his enticing "give-and-take" transactions with others and the absence of some [professors], has succeeded in producing a decision of the School [Medical School, University of Athens], of which the judges and the reviewer, we must say, can brag of, while we, who have intervened with a propter legem manner, and the immediately interested person, are not able to oppose the decision with any judicial action.

Hence, we have but to congratulate the winners. And we do this, even though, we are obliged to feel sad, together with all the other doctors, for the condition of the School this victory reveals.⁴⁸

The third attempt was made in 1936 when Higoumenakis submitted a thesis titled 'Psoriasis'.⁴⁹ This was also denied, because Photinos, who was appointed again as a supervisor, claimed that the definition of psoriasis which Higoumenakis had proposed was unthinkable.⁵⁰ Higoumenakis suggested that psoriasis was a viral illness, possibly attributable to the smallpox virus. Despite this denial by the Medical School of Athens, Higoumenakis published his observations in two scientific journals.⁵¹

The final attempt came in 1942 when Higoumenakis submitted to the Medical School of Athens a thesis entitled 'On a study of the immunising effect of the skin against syphilis'. This was also denied, and this time Higoumenakis was forbidden to apply again for a doctorate.^{52,53}

Eventually, in 1946 Higoumenakis received a doctorate diploma from the Medical School of the Aristotelian University of Thessalonica, under the title 'The sign of the clavicle and its significance in the diagnosis of hereditary syphilis'.

The proceedings of the Medical School of Athens describes a series of letters between Higoumenakis, Photinos, and other doctors that, while on some occasions praise Higoumenakis for his persistence in scientific research; mostly accuse him of being a mendacious person who practises medicine without moral boundaries and blames the school for his own inadequacy.^{54, 55} It is worth mentioning that, in his fourth attempt, the school board decided that it was better not to accept his dissertation because this would lead society to regard Higoumenakis as a hero who managed to overcome the school's continuous rejections.⁵⁶

But then why did Higoumenakis continue applying? We might find the answer in Higoumenakis' character. Surely we can understand that he was persistent, neither did he listen to the advice of Photinos to keep a 'low profile'.⁵⁷ In the *Proceedings of the Medical School of Athens*, we find a letter in which Higoumenakis accused Photinos of being a person who ruled without leaving openings for others to excel.⁵⁸ Apart from strong will, we can see that he possessed great confidence; possibly emanating from his professional, scientific and personal achievements in life. In a discussion with Higoumenakis' son,

Nikos described his father as an unconventional person, who could not stand any profound injustice or unjustified suppression.⁵⁹

Higoumenakis sign (the Clavicle Sign) and his other works

In 1927 Higoumenakis described in Greek the enlargement of the sternal end of the clavicle as a sign of late congenital syphilis, and subsequently he published in French in 1928 and in German in 1930.⁶⁰⁻⁶² He described it as mostly appearing between the ages of 15 years and 56 years. However, clavicular thickening has been noticed in other diseases as well; including sternoclavicular hyperostosis, sternoclavicular osteoarthritis, low-grade chronic osteomyelitis, condensing osteitis of the clavicle and Tietze syndrome.^{63, 64} Nevertheless, Higoumenakis gave radiological evidence of the sign and an explanation for its production, associating the side of the thickening with the handedness of the patient. The anatomical reason is that the sternal (medial) end of the clavicle is preformed of connective tissue and is ossified between 11 and 22 years of age by a secondary ossification centre. The body of the clavicle is ossified from two primary centres, one medial and one lateral, which appear during the fifth and sixth weeks of intrauterine life. The biological reason is that *Treponema pallidum*, carried in the blood stream of the foetus, becomes as readily localized in the connective tissues as in the lymphatic spaces and other organs of the foetus and may remain in the connective tissues and bones without manifestation in childhood.⁶⁵ The mechanical reason is that later in life the frequent movements of the arms during heavy work and the constant friction of the clavicle against the sternum set up irritation; the treponemata are reactivated and through their toxins produce chronic periostitis which results in hyperostosis. The enlargement of the sternal end of the clavicle reaches a permanent stage about the age of puberty, and hence becomes a valuable permanent stigma of prenatal syphilis (Figure 4).

(Figure 4 here)

Future authors confirmed the presence of the sign, with some being more agreeable as to its significance,⁶⁶ others less;⁶⁷ and still others disagreeing with the mode of production, while others agreed.⁶⁸ Histologically, it is a case of sclerotic bone involvement, representing the permanent residual of prior bony inflammation.^{69, 70} Over thirty authors (along with Higoumenakis) commented on this sign during the period from 1930 to 1980, leading to its general acceptance (Table 1, online Supplement Document).

Nevertheless, if we search texts older than those of Higoumenakis (1927)⁷¹ we can find occasional descriptions of acquired or congenitally syphilitic affection of the sternal end of the clavicle (Table 2, online Supplement Document). Descriptions begin in 1851 with Philippe Ricord, who describes enlargement of the sternal end of the clavicle in a patient with acquired syphilis;⁷² and continue to 1926 when John Stokes claimed that this sign was very rare (four cases out of 202).⁷³ In Russia this sign is called Avsitidiysky-Higoumenakis sign, after G Higoumenakis and I Avsitidiysky (И. Авситидийского). According to Kozhevnikov,⁷⁴ Avsitidiysky described similar results in his thesis of 1891⁷⁵ and proposed this name. However, in western journals the sign is generally ascribed to Higoumenakis.

Cutaneous Leishmaniasis

In 1930 Higoumenakis wrote 'Le bouton d'Orient'.⁷⁶ This failed to be accepted as an essay for a Greek competition because he was accused of claiming a method of curing oriental sores as his, while actually it belonged to Hulusi Behçet (1889-1948). This book, combined with an essay of his on a new atypical form of oriental sore,⁷⁷ made his position more eminent among foreign dermatologists. Hulusi Behçet⁷⁸ and Alfred Marchionini (1899-1965)⁷⁹ mention him as a specialist for the disease in Greece.

Up to that point he considered that the causative agent of Oriental sore and Kala-Azar were different⁸⁰ but in 1938 he published a paper supporting the view that the agent responsible for the two forms of the disease is the single parasite of Wright (*leishmania tropica*), which had to be identical to the parasite of Donovan (*leishmania donovani*).⁸¹ He thoroughly explained why his patients with definite cutaneous leishmaniasis had systemic symptoms including nausea, vomiting and fever; and patients that had passed Kala-Azar presented cutaneous lesions, without finding Wright's parasite. Moreover, he claims that the two parasites are identical under the microscope and he gives an extensive review of the contemporary literature on this subject. The difference in the clinical syndrome is due to the place of inoculation of the

parasite: when inoculated in the skin we have oriental sore; when inoculated in the viscera, we have Kala-Azar. Nevertheless, we can easily recognise in his descriptions cases of post kala-azar dermal leishmaniasis (PKDL), leishmaniasis recidivans, and possibly viscerotropic leishmaniasis (because in one case of cutaneous leishmaniasis, the parasite of Wright was found in the bone marrow and in the liver).

Although his conclusions are now considered inaccurate in the modern view of these diseases, since the two parasites are different and not identical as Higoumenakis claimed;^{82, 83} they attracted the attention of esteemed dermatologists of his time (Behçet, Marchionini, Castellani). Aldo Castellani (1874-1971) invited him to become Member of the Editorial Advisory Board of *Dermatologia Tropica*, which Higoumenakis considered a great honour.⁸⁴

Psoriasis

Higoumenakis claimed that a virus caused psoriasis. Specifically he wrote: ‘Psoriasis is a chronic, infectious disease in all probability attributable to an unknown dermato-epitheliotropic poison, resembling smallpox virus. It is characterized by silver-white dry scales situated on a reddened, leaf-like base of various shape and size’.⁸⁵

Higoumenakis’ son, Nikos, mentions that Professor George Merikas considered this essay very important, although it was proven wrong by future experiments; because psoriasis is considered to have an immunological aetiology.⁸⁶ Nevertheless, viruses have been implicated in the pathogenesis of psoriasis, as reported by Lionel Fry and Barbara Baker: ‘Viruses such as HPV5, retroviruses, and human endogenous retroviruses (HERVs) have been detected in psoriatic skin, but their roles in disease pathogenesis, if any, are unknown’.⁸⁷

Gonorrhoea

Higoumenakis wrote a review on the treatment of gonorrhoea with diathermy.⁸⁸ He invented a special thermophore, which was produced by the French factory Minerva under the name Thermophore Higoumenakis. This helped to prevent urine being spilled over the patient during the therapy.⁸⁹

Conclusions

Higoumenakis published widely outside his own Greek language (see Higoumenakis’ bibliography, online supplement document). As doctor and politician, he has not been well known but his achievements have had a significant part to play within his own country.

Acknowledgements

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Figures

Figure 1

Picture and signature of George Higoumenakis (1895-1983)



Figure 2

G Higoumenakis (sitting in the middle) with the members of his staff at the Dermatology and Venereology Department of the Hospital Evaggelismos

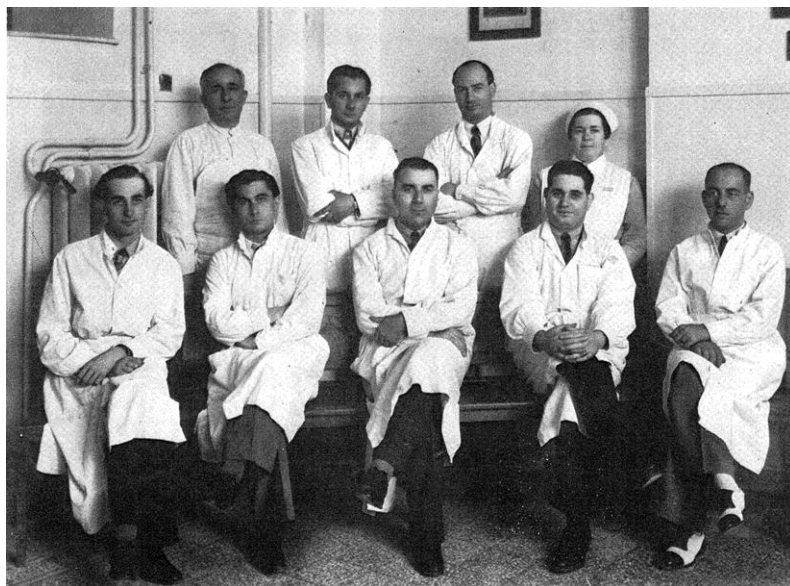


Figure 3

3A G Higoumenakis (left) besides the chancellor of Germany Konrad Adenauer (1876-1967) (middle), on his welcoming in Athens (1950s) and his announcement as Citizen of Athens honoris causa.

3B G Higoumenakis (right) with his political associate Konstantinos Mitsotakis (former Prime-minister of Greece) (middle)

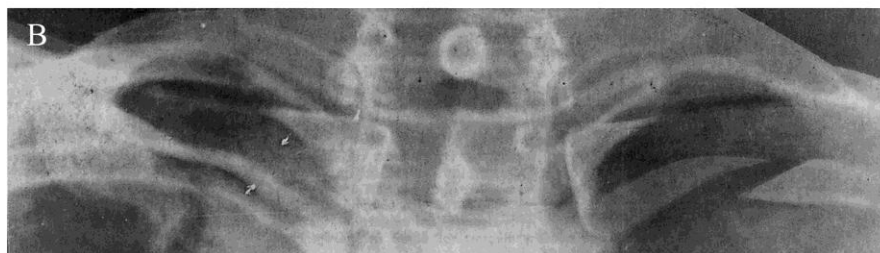
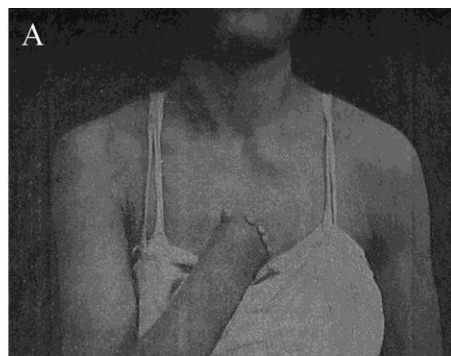


Figure 4

4A. Sign of the clavicle left, on a patient suffering from congenital syphilis and presenting partial agnesia of the right hand, because of which she is forced to use the left hand.

4B

Osteitis of the sternal end of the right clavicle, with vesicular formations, on a patient present the sign of the clavicle (Higoumenakis sign). Source: *Iatrikai Athinai* 1937;4:83-95, with the permission of the National Library of Greece.



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- 28 This Union was different from the Hellenic Association of Dermatology and Venereology, founded by G Photinos some years earlier. Higoumenakis and others wanted to create a new society, where Photinos would not have influence; it seems that Photinos was somewhat absolute in his opinions and this created frustration from other doctors. Moreover, Photinos and Higoumenakis were in conflict from 1924 already
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Supplementary Material

Table 1. Authors who describe Higoumenakis sign (clavicle sign) in patients with late congenital syphilis from 1930 until 1980, along with a brief description of patients and findings.

No.	Author (Year)	Brief description of patients and findings
1	Pratsicas (1927) ¹	2 patients, young age and 50 years old. Clavicle sign was present.
2	Phloros (1927) ²	1 Patient, 18 years old with clavicle sign of Higoumenakis
3	Bezecná (1931) ³	15 patients with congenital syphilis. 5 patients (30%) presented the clavicle sign.
4	G Higoumenakis (1931) ⁴⁻⁶	6 patients with clavicle sign at the right sternal end
5	Pliškin (1932) ⁷	3 patients with the clavicle sign.
6	Efstathianos (1934) ⁸	2 patients. 19 and 18 years old. Clavicle sign present
7	Dorne and Zakon (1935) ⁹	12 patients. 14-27 years old. Clavicle sign present always.
8	Miskjian (1936) ¹⁰	Case report. 16 years old girl with clavicle sign
9	G Higoumenakis (1936) ¹¹	1 patient with clavicle sign
10	G Higoumenakis (1937) ¹²	20 patients, 15-56 years old. Sign of the clavicle in all.
11	Smyrniotis (1937) ¹³	7 patients with congenital syphilis. Definite clavicle sign (with vesicular formation in x-ray) in 3 of them
12	Glickman and Minsky (1937) ¹⁴	1 patient with congenital syphilis, 56 years old. Clavicle sign left in a left-handed person.
13	British Medical Journal (1938) ¹⁵	Suggestion to pay attention to the clavicle sign
14	Grafe (1939) ¹⁶	100 patients with congenital syphilis. Clavicle sign in 25 patients (25%)
15	Spiethoff (1939) ¹⁷	Clavicle sign is frequent in congenital syphilis and can help in its primitive diagnosis and therapy.
16	Lutz (1940) ¹⁸	95 patients with congenital syphilis. After Hutchinson's tooth and periosteal skull lesions, clavicle sign was most frequent.
17	Yang (1940) ¹⁹	6 patients. 19-29 years. Clavicle sign present.
18	Dax and Stewart (1940) ²⁰	64 patients with congenital syphilis, 18-73 years. Clavicle sign in 19 patients (29.7%).
19	Gertler (1940) ²¹	1 male patient, 18 years old. Clavicle sign present.
20	Oldach (1941) ²²	92 Patients with congenital syphilis. Clavicle sign in 5 (5,5%) patients.
21	Umlandt (1941) ²³	103 with congenital syphilis, 1 to 40 years old. Findings: a. 0 patients in out of 35 (0%) in years 1-12 b. 8 patients out of 34 (23,8%) in years 13-20 c. 10 patients out of 35 (33,3%) in years 21-40. d. 18 patients out of total 103 (14,6%), ages 1-40. e. 18 patients in 68 (26,5%) in years 13-40.
22	Nair and Chetty (1942) ²⁴	130 patients. 0-40 years old. Clavicular thickening at the sternal end was found in 103 (79,2%). Until the age of 15 only 18 out of 103 had the clavicle sign and from 18 to 40 years old, 85 patients had the sign.
23	Wang (1943) ²⁵	21 with definite congenital syphilis, 16-36 years old. 18 out of 21 had the clavicle sign
24	Lahiri (1943) ²⁶	5 patients, 8-12 years old. Clavicle sign present.
25	Laird (1950) ²⁷	115 patients, 3-75 years old. "The clavicle is particularly accessible to clinical examination and often provides valuable evidence in the diagnosis of congenital syphilis. The inner third of the clavicle, usually the right, and more commonly in males, often presents definite thickening (17 out of 32 males/ 19 out of 63 females)".
26	Fiumara (1965) ²⁸	1 Patient male (in a whole family case report), 35 years old. Clavicle sign present

No.	Author (Year)	Brief description of patients and findings
27	K Higoumenakis (1968) ²⁹	3 patients with late congenital syphilis, 25, 42 and 48 years old. Clavicle sign present in all.
28	Robinson (1969) ³⁰	85 patients with congenital syphilis (ages not mentioned). Clavicular thickening in 4 out of 85. Possibly didn't have bigger ages
29	Fiumara and Lessell (1970) ³¹	271 North American patients altogether, mean age 29,2 years old. Clavicle sign present in 107 (39.4%) patients with 37 (44%) men and 70 (37A%) women.
30	Fiumara (1974) ³²	3 patients with late congenital syphilis, treated and then affected with acquired syphilis. Clavicle sign in all.
31	Fiumara and Lessell (1983) ³³	100 Carribean patients with late congenital syphilis, mean age 30,7 years old. Clavicle sign in 81% of the patients

Table 2. Authors describing similar lesions with Higoumenakis sign (clavicle sign), before Higoumenakis (1927). Brief description of patients and findings.

No.	Author (Year)	Brief Description of patients and findings
1	Gilbert ³⁴ , cited in Diday ³⁵	Young lady observed two swellings develop: one on the left clavicle and the second at the inner edge of the right sterno-cleido-mastoideus muscle. Possibly, signs of congenital syphilis
2	Ricord (1851) ³⁶	40 year old male patient. Enlargement of the sternal end of the right clavicle in acquired syphilis, obtained at age 25.
3	Bärensprung (1864) ³⁷	3 week year old baby. Enlargement of left sternoclavicular end.
4	Parrot (1872) ³⁸	1-month girl. Clavicles were affected at their sternal ends
5	Taylor (1875) ³⁹	12 patients with congenital syphilis, until 2 years old. One patient 10 weeks old has acute enlargement of the sternal end of the right clavicle
6	Laschkewitz (1878) ⁴⁰	12 year old girl with late congenital syphilis and an enlargement of the clavicle
7	Fournier (1886) ⁴¹	hyperostosis of long bones as rather frequent, particularly among the tibia, the cubitus and the clavicle
8	Avsitidiysky (1891) ⁴²	He reports on periostitis of the sternal end of the right clavicle many times in patients with congenital syphilis, possibly due to mechanical reasons
9	Gaucher and Rostaine (1903) ⁴³	27-year old woman. Augmentation in volume of the medial end of the left clavicle, acquired syphilis.
10	Schneider (1921) ⁴⁴	Lesions of osteochondritis in the sternal end of the clavicle
11	Stokes (1926) ⁴⁵	202 cases of congenital syphilis. Clavicular thickening in 4 of the patients (possibly small ages).

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