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Milestones in the History of Croatian Dermatology and Venereology: an Outsider's Insight

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SUMMARY While the first traces of interest in skin diseases date back to the 14th century recipes from Glagolitic manuscripts, the scientific beginnings of dermatovenereology might be associated with the beginning of the 19th century, when in the Rijeka region a 'new disease', called after the village of Škrlevo, was studied by Giovanni Battista Cambieri. This, however, has not been the only disease named after a Croatian toponym; in 1826, Luca Stulli of Dubrovnik was the first to describe the 'mal de Meleda', nowadays recognized as a form of hereditary palmo-plantar keratoderma. In 1876, Carl Heizmann, a Croatian from Vinkovci by birth, was one of the founders of the American Dermatological Association. In 1894, the first department for dermatologic and venereologic patients was opened at Sestre milosrdnice (Sisters of Charity) Hospital in Zagreb. The beginning of the 20th century brought an accelerated development to Croatian dermatovenereology; in 1910, while still in its experimental phase, the drug Salvarsan was used in Zagreb for the treatment of syphilis. In 1921, the chair of dermatovenereology was established at Zagreb School of Medicine, and in 1927, Franjo Kogoj was the first to describe the spongiform pustule. In 1950, Ante Vukas from Rijeka developed a special method of epidermotectoscopy. If one remembers that the first history of AIDS was written by the Croatian Mirko Dražen Grmek, it would be allowed to concur that the history of dermatology and venereology on the Croatian soil has been characterized by a fascinating profusion and dynamism.

KEY WORDS: Croatia, dermatology, history of medicine, venereology

'DERMATOLOGY' BEFORE DERMATOLOGY AND 'VENERELOGY' BEFORE VENEREOLOGY

If one ventures into writing about national milestones, one risks either to underestimate the notion of milestone or to overestimate it. To avoid these risks, I will try to be as concise as possible

and to leave to the public the judgment of the reach of importance of single contributions by Croatian dermatology and venereology to the general history of medicine.

Skin diseases had certainly been known long before physicians started to understand the importance of and to practice specialization. The first interesting trace of 'dermatological' topic found on the Croatian soil probably can be related to a 14th-century Glagolitic manuscript from the Vinodol area (western Croatia), representing a recipe dealing with skin disease (1). Of course in popular tradition not only a text but also an image used to witness the awareness of dermatologic phenomena, a wall painting from the 18th century in St. Elizabeth Chapel of Three-Holy-Kings Church in Komin (NW Croatia) shows the Hungarian saintly queen Elizabeth curing a superficial wound on a man's leg (2).

The first cases of syphilis emerged on the Croatian soil very short after it had been imported from the New World. In 1500, the disease was described in a soldier in Zadar, a year later in Trogir, and in 1502 in Dubrovnik. Marianus Sanctus, working there from 1527 to 1532, was curing syphilis with mercury ointments, while another famous physician of the time, Amatus Lusitanus, active in Dubrovnik from 1556 until 1558, described patients with 'French disease' in his work *Curatium medicinalium centuriam*, book VI, from 1566 (3).

The most curious, however, of all syphilis-related casuistry, was the still unresolved story of the 'Škrljevo disease'. The first written report on 2,600 cases of a 'new disease' was addressed to the municipal authorities of Rijeka in 1800 by the then prime physician of the city, Josip Mašić. The name to the disease (*morbus de Scharlievo*), however, was coined by another physician, Giovanni Battista Cambieri (1754-1838), who practiced in the village of Škrljevo near Rijeka (4). The 'new disease' was brought as a topic to the Medical Academy in Paris by the then leading doctor of the French Army in the Illyric Provinces. In 1816, Cambieri started to experiment with the cure for the disease, together with Ignác (Ignatius) Stáhly (1787-1849) from Budapest. In the period between 1818 and 1825, 2,259 cases of the disease were hospitalized in the city of Rijeka alone, and many more in the vicinities. New quarantines (lazarettos) were opened and the old ones re-opened in Rijeka, Bakar, and Kraljevica (visited by F. Hebra). L.V. Lagneau, in his famous 1828 *Traité pratique des maladies syphilitiques* (6th edition, 2 volumes, Paris, Gabon), called the disease '*mal de Fiume*.' Doctoral dissertations were written about the phenomenon in Padua (Lorenzutti, Santes, de Moulon, Rizzi) and Vienna (Melzer, Backes). Some

authors considered the Škrljevo disease a form of leprosy or scurvy, but the opinion prevailed that the epidemic was actually an exacerbation of endemic syphilis. By the mid-19th century, about 13,000 people had been declared infected by the disease. Since that was approximately 1/3 of the then total population of the region, no wonder that it raised serious doubt that the disease was not endemic syphilis (only) but a diagnostic fashion that masked various pathologies and maybe even reflected some contemporary sociopolitical moments, like avoiding French army recruitment (5).

A similar form of disease appeared also in the region of Dubrovnik (*Morbus brenensis*), later more thoroughly described by Niko Selak (6).

The beginnings of science-based practice

Another nosologic entity, the name of which has been related to a Croatian toponym, is *Mal de Melada* (the Mljet disease). It seems that Luca Stulli (1772-1828), a physician from Dubrovnik, was the first to describe 11 individuals from 3 families from the Mljet island, suffering from plantar and palmar keratosis (7). Thirteen years after Stulli's description, *Mal de Melada* (sic!) appeared in the 1839 Behrend's classification of cutaneous diseases, and later in the 1850 Domenico Marcocchia's inaugural thesis in Split. In 1896, Dr. Oskar Hovorka (1866-1930) reported on 14 cases of leprosy (!) on Mljet: the 'finding' was dismissed after the visit of Edvard Ehlers (1863-1937) from Copenhagen and Isidor Neumann from Vienna. The mystery was ultimately resolved by the work of a Croatian dermatologist Franjo Kogoj (1894-1983) and his assistant Srećko Bošnjaković (1900-1947) in the 1930s. According to their arguments and present-day knowledge, the Mljet disease may be considered specific autosomal recessive palmoplantar keratoderm(ia) or palmoplantar ectodermal dysplasia type VIII (caused by a deletion or mutation of the SLURP1 gene on the chromosome 8q) (8,9).

As early as the 19th century, several physicians chose topics for their doctoral dissertations in the field of dermatovenereology. Đuro Matija Šporer (1795-1884; Karlovac, Rijeka), better known for his pioneering work in balneology (one of the founders of Opatija health resort), wrote a dissertation on gonorrhea in 1819, and Franjo Zohar from Sinj and Zadar in 1827. In 1831, Ferko Gorjup from Osijek and Virovitica wrote a dissertation on syphilis, while in 1835, Nikola Ostoić from Hvar

wrote a dissertation relating skin color to the action of light (3). One of the most famous Croats working outside Croatia (at least when speaking of dermatovenereology) was Carl Heitzmann (1836-1896), born in Vinkovci (Slavonia, NE Croatia). In 1856, he excelled as the illustrator of the famous Hebra's dermatological atlas, while in 1872, he discovered the hematoblast (a pluripotent hematopoietic stem cell; the discovery was erroneously ascribed to Georges Hayem in 1877) (10). After he had exiled to the USA, Heitzmann was listed among the 16 founders of the American Dermatological Association (ADA) in 1876.

Among those who came to work in Croatia, without any doubt the most prominent was Fritz Schaudinn (1871-1906). Schaudinn, a German zoologist (protozoologist), worked in Rovinj (Istria) from 1901 until 1904. A year after he had returned to Germany, in 1905, Schaudinn together with Erich Hoffmann discovered the *Spirocheta pallida* (now *Treponema pallidum*). For his work, Schaudinn was three times nominated for the Nobel Prize for Physiology or Medicine: twice in 1906 (by Blanchard and Calmette) and a year later by Ipsen. In 1906, the Nobel Prize was given to Santiago Ramón y Cajal and Camillo Golgi (for their discoveries in neurohistology), while in 1907, the nomination came too late: Schaudinn had already succumbed to amebiasis.

Modern times, whenever they come

For Europe, modern times in dermatovenereology arrived as early as the end of the 18th century. In 1790, a new classification and description of cutaneous diseases was presented by Robert Willan (1757-1812) at the Medical Society of London. In 1801, Hôpital Saint-Louis, headed by Jean-Louis-Marc Alibert (1768-1837) was opened in Paris. A year later, Vincenzo Chiarugi (1759-1820) was appointed the first '*Lettore onorario di malattie cutanee e mentali*' at University of Pisa. In 1806, Alibert published *Description des maladies de la peau*, while in 1808, Willan's textbook *On cutaneous disease* appeared. In 1845, a classification of skin diseases in accordance with pathological anatomy was promoted by Ferdinand Hebra (1816-1880), head of Department of Dermatology at University of Vienna.

For Croatia, 'modern times' arrived a few decades later. In 1894, Department of Dermatovenereology was opened at Sestre milosrdnice (Sisters of Charity) Hospital (Vinogradska) in Zagreb.

It was called Third Department (curing skin, genitalia, eyes, and otorhinolaryngological casuistry). The department was initially headed by Dragutin Mašek (1866-1956), an otorhinolaryngologist, and later (since 1919) by Aleksandar Blašković (working from 1911 until 1914 in Osijek). Soon, Department of Dermatovenereology (treating skin, genitalia, surgical, gynecological, and otorhinolaryngological patients) was opened at the Foundation Hospital in Zagreb as well, headed by Dragutin Schwarz. Schwarz was succeeded by one of the most successful dermatovenereologists in Croatia, Janko Thierry (1874-1939). Thierry, a University of Graz alumnus, started his career in Zagreb after 1901 and was probably the first specialist in dermatovenereology at all. In agreement with Paul Ehrlich, he tested the drug Salvarsan in 50 syphilis patients and published the first paper in the world on this topic (11).

Section of Dermatovenereology of the Croatian Medical Association was founded in 1920, and a year later, the Chair of Dermatovenereology at the newly founded University of Zagreb School of Medicine was assigned to Vladimir Ypolitovich Terebinsky (then in Kiev and Belgrade). Terebinsky was invited already in 1919, appointed in 1921, but he resigned in 1923, without ever actually taking the chair over (12). The chair was eventually, in 1923, assigned to Pavel Šavnik (born in Kranj, 1882, died in 1924), who arrived to his new position from Prague.

Probably the most prolific writer and the most influential dermatovenereologist in Croatia of all times was Franjo Kogoj (1894-1983), who took over the Zagreb Chair of Dermatovenereology in 1926. The impact of Kogoj's work and personality may be best illustrated by the numerous honors he was awarded: besides heading Department of Dermatovenereology (opened in 1928, under construction from 1924), he was dean of the University of Zagreb School of Medicine, *Doctor honoris causa* of universities in Ljubljana, Graz, Zagreb and Belgrade, and Vice-President of the Southern Slav Academy of Sciences and Arts (JAZU). In dermatological *milieu*, however, he is best known for his description of the spongiform pustule (an epidermal pustule seen in pustular psoriasis; optical microscopy had suggested the pustule be formed by infiltration of neutrophils into necrotic epidermis in which the cell walls persisted as a spongy-like network, but eventually electron microscopy demonstrated the neutrophils being located intercellularly) (13).

It would be wrong to think that Zagreb was the only center in Croatia to develop innovative techniques in dermatovenereology. In Rijeka (the locality of Sušak), in 1950, Ante Vukas (1910-1991) developed epidermotectoscopy as a special technique of examination of superficial architectonics of normal and pathologically altered skin. It was also the group of Sušak that, in 1975, as the first in the world introduced the use of human palatal tonsil epithelium as a test antigen in the indirect immunofluorescent assay (before, only monkey epithelium had been used), while in 1982, here, also for the first time in the world, large-area dermabrasion was performed (14,15).

Nowadays, dermatology and venereology in Croatia have been passing through a new epoch of dynamic development. After Croatia had gained independence, in 1993, Croatian Dermatovenereological Society and its journal *Acta Dermatovenereologica Croatica* (Editor-in-Chief: Jasna Lipozenčić) were founded (16). A series of reference centers have been appointed by the Ministry of Health and Social Welfare of the Republic of Croatia (Department of Dermatology and Venereology at University Hospital Center Zagreb, for the diagnosis of syphilis and Lyme diseases and six more centers, Department of Dermatology at Rijeka University Hospital Center for psoriasis) (17). The work by a Croatian medical historian Mirko Dražen Grmek (1924-2000), devoted to the history of AIDS, has been internationally recognized. The last but not the least, in May 2010, the 7th European Academy of Dermatology and Venereology Spring Symposium was held in Cavtat, Croatia. It was the best opportunity for hundreds of dermatovenereology professionals to witness not only the profusion of Croatian natural and cultural resources, but also the long-time variety of Croatian contribution to dermatovenereological science and practice.

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Elida Ideal soap; year 1934.
(From the collection of Mr. Zlatko Puntijar)