

Giuseppe and Aloysius Frari's Works on Rabies and History of Frari Medical Family of Šibenik, Dalmatia

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This article is an attempt to reconstruct the family history of the Fraris, the famous Šibenik medical family. Three generations of physicians from the Frari family played an important role not only at medical and social scene of Šibenik in the 18th and 19th century, but also in Croatian and Italian medical history. I will try to provide important details on the lives, medical and social work, and publications of 5 members of the family, Giuseppe (Josip), Angelo Antonio (Anđeo Antun), Sebastiano (Sebastijan), Michele Carlo (Mihovil), and Aloysius (Luigi) Frari. I would also like to pay a special attention to the works on rabies, written by Giuseppe and Luigi Frari, which are among the earliest and most accurate Croatian works on the subject. To reconstruct the history of the family, I studied the relevant editions about the medical and social history of Šibenik, Dalmatia, Venice, and Croatia, together with the Fraris' publications and reflections. This was the first time Italian and Latin language works by Giuseppe and Luigi Frari on rabies were analyzed. The story on Fraris also documents that medical publishing was a common practice in Dalmatia in the 18th and the 19th century.

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In the thousand years of its history, the town of Šibenik on the Dalmatian coast of Croatia (Figure 1), has experienced a number of turbulent events (1,2). Like the entire region, it had had its share of wars and diseases, as well as seen the change of many political regimes and been a part of a number of states (1-4). However, turbulent history has also left its mark in the form of a large number of historical monuments, especially from the renaissance period.

Medicine in Šibenik has a rich and well described history (3,4). One of the town's most prominent medical families of in the 18th and the 19th century was the Frari family (3-23). Al-



Figure 1. Cityscape of Šibenik, as seen from the fortress. Picture postcard of Šibenik from the late 19th century, at the time of the last years of life of Luigi and Michele Frari. Available from: <http://www.istrianaet.org/istria/archives/photos/photochrom/dalmatia.htm>.

though the work of some members of the family has already been described in literature, mostly in Croatian and a little in Italian, French, and English (3-23), there is no overall assessment of the work, most important publications, and reflections of all the medical doctors in the Frari family. Some publications by Giuseppe, Angelo Antonio, and Michele Frari have already been evaluated by other authors, so for this occasion I decided to analyze medical works by Giuseppe and Luigi Frari, which, according to my knowledge, have not yet been translated or analyzed.

Giuseppe (Josip) Frari

Giuseppe Frari (Treviso 1738-Šibenik 1801) was the first of the Fraris who lived in Šibenik. He was a medical doctor who assumed the duty of the chief municipal physician (Croatian: “općinski fizik,” Italian: “medico primario”) in Šibenik in 1771, 16 years before the first Šibenik hospital was built (3-7,9). He was mentioned in literature as the municipal physician of Zadar as well (9). Before moving to Šibenik, he had a ten-year medical practice in Italy (4-6). He was well recognized for his medical work in Dalmatia, as well as for his publications (3-7).

Giuseppe Frari wrote a discussion about two citizens of Šibenik infected with rabies “*Rifles-*

sioni teorico mediche sopra una grave malattia dal dottor G. Frari medico primario di Sebenico in Dalmazia l'anno 1783,” which was published in Ancona in 1783 (5,6,9) (Figure 2). Although he died before Louis Pasteur was born (1822), his approach to rabies had characteristics of modern medical scientific observation. He reported a case of the patient Juraj Krnetić (“Sig. Zorzi Carnetich”), who was the first patient infected with rabies in his twenty years of practice (6).



Figure 2. The title page of Dr Giuseppe (Josip) Frari's “Theoretical medical reflections about a pernicious illness”, published in Ancona in 1783. The manuscript described rabies in two citizens of Šibenik in 1782 and 1783, with the data about incubation, symptoms, autopsy findings, and treatment options.

Impressed by the cruelty of its symptoms, Frari felt the urge to put down his observations on the case, together with a review of the literature (6). Juraj Krnetić, a 65 years old citizen of Šibenik was bitten on the hand by a domestic

cat. Four months later, the first symptoms appeared. The patient lost appetite and showed inability to swallow food, as well as insomnia. Pain appeared in the bitten arm and in that whole side of the body. After a few days, the patient's symptoms deteriorated, and convulsions, spasms, and depression appeared. At that time, Frari suspected that the man was bitten by an animal and concluded that these unusual symptoms had to be attributed to hydrophobia of the second grade (6).

As he realized that it was too late to wash out the wound, Frari decided to apply the methods which would slow down the effect of the poison. He started the treatment by bloodletting and rubbing in a remedy made of mercury in the area around the scar, which became led-colored. He also put compresses on the patient's chest and prescribed enema. Finally, he applied a powder made of cinnabar, "as proposed by Cob and used by some Chinese and English," mixed with some violet syrup. Nevertheless, the symptoms deteriorated and seizures became more and more frequent. For seizures to appear, the patient needed only to see water, nevertheless drink it. The mere sight of water made him cover his face with a blanket or jump out of the bed furiously and beg others not to bring any liquid to him (6).

Afterwards, the bitten arm became paralyzed, and pain appeared, together with the respiratory problems and constipations. On one of Frari's visits, on the fifth day from the onset of symptoms, the patient tried to bite his son and, as he was prevented, he escaped outside and was found after two hours on the rooftop of a nearby house freezing and shivering. Later that day, his appetite recovered, and he even had a meal. In the evening, he looked terrible, with his eyes sparkling, all confused and talking nonsense (6).

The next morning he peacefully laid or sat in his bed, with raucous voice, breathing hardly. Some hours later the patient, although overwhelmed with sadness, drank half a glass of wine, but in the evening he became all cold, motionless, barely pronouncing words. That night, yellow

foam came out of his mouth, his tongue was sticking out, and, about 3 o'clock after midnight, the patient passed "from this into another life" (6).

Frari continued with his observations on this disease, and tried to explain the phenomena which accompanied it (6).

According to Frari, the incubation of this disease could last from several days up to several months, or even several years. The longer incubation period was attributed to the position of the bite far from the course of the major blood vessels. Frari thought that the poison, which consisted of evaporative particles, inside the organism changed into a form in which it could be mixed with the body liquids, ie, blood and lymph. This caused increased viscosity of blood and lymph, but also of the secretions of glands, which resulted in symptoms such as hard respiration, constipation, altered pulsations, rheumatic pains, and dry mouth. Frari attributed the symptoms of aversion toward water, convulsions, and seizures of rage to the transmission of the poison from blood into the nervous liquids, which altered their contents and resulted in the impairment of the nervous function. As Frari said, cervical plexus, which innervated the pharyngeal muscles, was specially attacked (6).

In Frari's opinion, the disease appeared spontaneously in animals, which was specially enhanced in hot summers and during long term heat. He demonstrated this with the fact that a greater number of affected dogs was observed in Šibenik during the previous summer, which had been long and with long lasting excessive heats. Frari also provided a description of the infected dog. It was an animal with bowed head, the tongue sticking out, foam on its mouth, and the tail between the legs, wandering around and biting other dogs and sometimes humans (6).

Frari considered that the treatment of the disease from the second stage on was mainly unsuccessful, but that it was important to treat the wound at the site of the bite. He mentioned

the possibility of amputation in case of deep wound or multiple bite wounds. In case of smaller wounds, Frari mentioned the need to treat the wound by cutting of the parts of the tissue; washing out with sea or mineral water or vinegar; burning the wound; or extracting the poison out of the wound by special suction devices. These methods, as he said, were the preventive methods, but could suppress the development of the disease (6).

He found the treatment with the mercury a successful method and described the preparation of mercury unguent in detail. Frari said that mercury, applied into the organism by rubbing in, interfered with the poisonous substance, and that it could suppress the progression of the disease. He claimed that this method was proved by the experience of numerous educated physicians. He also claimed that some liquid remedies, such as chicory soups or nitrated water, when prepared on favorable temperature and diluted, might help in soothing long lasting insomnias. Frari also said that cinnabar powder should also be used because it could slow down the progression of hydrophobic poison. Among other methods, Frari recommended bloodletting and purgatives, such as English salt and rhubarb. He finally recommended seeking the physician as early as possible after the bite, so that the patient could be helped on time (6).

The second case of rabies in Šibenik that Frari described was the case of a young peasant girl Antica Vušić (Antonia Vusich), who was bitten on the arm and ear by a dog. The municipal surgeon Pietro Rosa treated the girl for a while with the intention to stimulate scarification as early as possible. After two months, the patient lost appetite and refused to drink liquid. She finally died in a couple of days. Frari found her two hours before death lying motionlessly in her bed, with foam on her mouth. It is interesting that this girl did not show any signs of violent behavior, or any wish to bite – she was, on the contrary, exceedingly quiet (6).

In 1786, Frari was accused of being responsible for the death of a great number of citizens during the epidemics of unknown contagious fever, probably typhus or plague, which appeared in Šibenik in 1783 (Figure 3) (3,5-7,9). In response to these accusations, he wrote “*Storia ragionata delle malattie acute insorte nella città di Sebenico in Dalmazia l'anno 1783*,” an elaboration on the epidemic, addressed directly to the Venetian senator Giovanni Minotto. In 120 pages of the elaboration published in Ancona, he described the conditions in the town, the course of the illness, autopsy findings, theoretical discussion, and the methods of treatment (7). He put the blame for the epidemic on hot and humid air in the summer before the outbreak, which was accompanied by intensive humidity and unusual heat in autumn and winter, lack of favorable winds which would ventilate the town, starva-



Figure 3. The title page of Dr Giuseppe (Josip) Frari's "Evidence based history of illnesses that emerged in Šibenik in Dalmatia in 1783 and 1786", published in Ancona, in 1786. The manuscript described the epidemics of unknown contagious disease (probably typhus) in Šibenik in 1783 and 1786, and gave a detailed description of unfavorable hygienic conditions in Šibenik at that time.

tion which struck many of the Venetian provinces at the time, poor nutritional and clothing habits, and bad water (5,7). He also gave a detailed description of poor hygienic conditions in Šibenik at the time (5,7,9): Šibenik was a town with high buildings and narrow streets which often could not be insolated or ventilated adequately (7). The streets were often dirty, filled with stinking, stagnating water and a nauseating smell coming from entrances (7). Giuseppe Frari concluded that there was a lack of educated people in the town who would warn against the perilous effects of the poor hygienic conditions (7). On the last three pages, Frari provided demographic data, duration of illness, and the date of death of 37 patients who were treated by him and died in the outbreak of 1783, out of a total of 800 persons who got ill (7). The methods of treatment Frari recommended were the following: 1) to evacuate the stagnating contagious fluids out of the region in order to prevent their entrance into the blood, 2) to countereffect their consequences in the most efficient way, 3) to prevent and attenuate blood viscosity. The latter consisted principally of bloodletting and prescribing various drinks, such as the juice of barley, mallow, weed, depurated niter, and a bit of vinegar and honey (7). Giuseppe Frari also emphasized that people unfairly tended to blame and punish the physician when things go wrong, for which he cited several historical examples (7). The publication is also interesting for numerous proverbs, mostly in Latin and Italian, such as the following, probably Dante's: *Ma finalmente non ebb'io in pensiero, Che un' Istoria narrar, che dica il vero* (Finally, I should not worry if I tell a story which says the truth).

Giuseppe Frari's two sons Angelo Antonio and Sebastiano also became physicians (4-6,9).

Angelo Antonio (Andeo Antun) Frari

Angelo Antonio Frari (Šibenik 1780-Venice 1865) (Figure 4) graduated in medicine from



Figure 4. Dr Angelo Antonio (Andeo Antun) Frari (Šibenik 1780 – Venice 1865). The municipal physician and the head of the lazaretto of Split (1806-1821), the protomedicus, and the president of the Maritime Health Magistrate of Venice (1835-1843), famous epidemiologist, and the first Croatian historian of medicine (6,10).

Padua University in 1801 (4-6,10,12) and acquired further medical education in Vienna as a student of the famous public health ideologist and the founder of hygiene as a science, Dr Johan Peter Frank (4,10,12).

As a prominent epidemiologist, he became the municipal physician in Split and headed the lazaretto of Split in the period of Napoleon's government (1806-1813), and later, until 1821. He was famous for his efforts and success in the improvement of the Dalmatian quarantine system and municipal hygiene (4-6,9-14). Frari, astonished with the poor sanitary conditions and poverty in Dalmatia, undertook numerous actions in order to improve the sanitary conditions. He warned the Napoleon's governor Vincenzo Dandolo about the tragic health and social situation in Split and its surroundings. He also incited the launching the new Law on Health Issues, which was officially accepted in 1812, together with the "Instructiones sur les Lazarets", which were

mostly composed by Frari (5,10,12). During this period of his life, Frari was also very effective in the suppression of plague epidemics in Split, Makarska, and in some regions of Montenegro and Albania (4,5,9-12). In 1815, he himself got ill, but cured himself by cutting the bubonic masses and treating them with oil and sweat (12).

Frari, as a supporter of the Franch revolutionary ideas, had to leave Split in 1821 and stayed in Zadar for a short period. In 1822, he left Dalmatia for good and moved to Verona and three years later to Venice, where he was active as an epidemiologist and writer. He served as the *protomedicus* of Venice and the president of the Maritime Health Magistrate of Venice from 1830 until 1843 (10,12,13). In 1835 he went to Egypt, as a consultant in the suppression of plague (4-6,8-13).

Angelo Antonio Frari published a number of medical papers (4-6,8-14). In Padua, in 1817 (2nd edition in Split 1820), he published a description of typhus fever in Split and the surrounding area (the towns of Trogir and Kaštela, and the island of Brač), called "*Storia dell febbre epidemica che regno a Spalato e luoghi vicini nell'anno 1817*" (5,6,9-12). Frari named the illness typhus because it, apparently, resembled the yellow fever (typhus icteroides) in its symptoms and changes found on the autopsies (12).

His later work "*Cenni storici sull'isola di Poveglia e sulla sua importanza sotto l'aspetto sanitario*" (Venice 1837) provided arguments in favor of the quarantine protection system, in particular of the one on the island of Poveglia at the entrance to Venice (12). Antonio Frari obviously found the quarantine protection system extremely important, which even brought him to the conflict with the *protomedicus* of the Austrian Littoral, Dr Franz Weber, who proposed certain restrictions of the quarantine system, in order to stimulate the Mediterranean steamship traffic (13). The issue of the quarantine system finally led Frari to his involuntary retirement in 1843, since he was accused of cor-

ruption related to public health and quarantine system (13).

Angelo Antonio Frari's capital work was "*Della peste e della pubblica amministrazione sanitaria*" (Venice 1840), which is considered the world's best general history of the plague epidemics up to that time. In almost 1000 pages, he described plague epidemics in the world and, in particular, Dalmatia in great detail (4-6,8-14,17). In this overall review, he discussed various diagnostic possibilities, methods of treatment, and reported on autopsy results, and methods of disinfection, describing the methods such as fumigation (15). Frari was convinced that the cause of the disease was a specific contagious germ ("*germe del contagio*"), even though the bacillus of plague (*Yersinia pestis*) was discovered as late as in 1894 (10).

Antonio Frari's scientific work and medical practice was especially praised by Frari's close friend Nikola (Niccolo) Tommaseo, the famous Šibenik-born Italian and Croatian writer, novelist, and revolutionary politician in his "Intimate Diary" and poems dedicated to doctor Frari (1,5,6,8,10,12). Tommaseo, on Frari's proposal, even wrote a letter of protest to the Austrian Emperor regarding poverty and poor sanitary conditions in Dalmatia (8).

Angelo Antonio Frari was awarded by the Austrian Emperor Franz Joseph I for his epidemiologic work in Dalmatia ("*medaglia d'oro di onore del merito civile per servizi prestati in circostanze di peste*", ref. 5,12,14). Angelo Antonio Frari was described as the first Croatian historian of medicine (10,16).

Sebastiano (Sebastijan) Frari

Sebastiano Frari (Šibenik 1773-1827) was the older son of Giuseppe Frari, who was also a physician (5,10,12). He graduated from Padua in 1793 and became the illustrious Šibenik chief municipal physician and a communal politician (4-6,9,10,12,16). He died relatively early (12)

and, unfortunately, little is known on his life and publications.

The third brother of Sebastiano and Angelo Antonio, Giuseppe (Joisp) Frari junior, joined the fraternity of St. Dominic and became a monk (12).

Michele Carlo (Mihovil) Frari

Michele Frari (Split 1813-Padua? 1896), Angelo Antonio's son, was a renowned professor of obstetrics in Padua from 1843 until 1889 (5,12,17,18). He was the author of many obstetrical articles and the inventor of various obstetrical instruments, including the so-called Frari Forceps (Figure 5) (18).



Figure 5. An obstetrical instrument from the time of Michele Carlo (Mihovil) Frari. Michele Frari was the professor of obstetrics in Padua from 1843 until 1889 and the inventor of a type of obstetrical forceps (18).

Michele Frari also published a textbook on obstetrics "Obstetrics theoretical and practical" (18-20). As a response to criticism by Dr Ferdinando Moroni, Dr Ghirrotti from Padua vehemently defended Frari's work and accused Moroni of ignorance and avidity (as "being the aspirant on the position at the Cathedra in Padua") (20). Ghirrotti discussed the obstetrical issues which were mentioned in the Frari's textbook, such as symphysiotomy, pelvic/fetal head diameters, fetal/maternal auscultation, geminal and extra-uterine pregnancy, mola, menstrual cycles, anatomical variations of the uterus, maternal alimentation, infertility, and death *in utero*. He concluded that Professor Michele Carlo Frari was a highly qualified obstetrician and skilled surgeon, reliable and extremely appreciated for his

work, and that his textbook was "written according to true principals of the art, with the right criteria and argumentation, based on proper experience and on opinions of celebrated obstetricians of various nations" (20). A second edition of the book appeared in 1876 (19).

Michele Frari also participated in the social life of Šibenik. In 1889 he took part in the discussion about possible location of Nikola Tommaseo's monument in Šibenik (17).

Aloysius (Luigi) Frari

Luigi Frari (Šibenik 1813-1898) was Sebastiano's son, who also served in Šibenik as the chief municipal physician (Figure 6) (6,9). Since he was only sporadically mentioned in various publications, his life and work had to be reconstructed from a variety of surviving sources.

In 1840 in Vienna he published his inaugural dissertation (Figure 7) at the Padua University about rabies "*De rabie canina*" (6,9,21-23). Perhaps, more than for his medical work, he was famous for his political and social activity and writing (3,6,20-23). He was the mayor of Šibenik and is especially remembered for his work in improv-



Figure 6. Photograph of Dr Aloysius (Luigi) Frari made in "Giuseppe Popovich" atelier in Split. The original is the property of Roksanđa Smolčić, Zagreb.

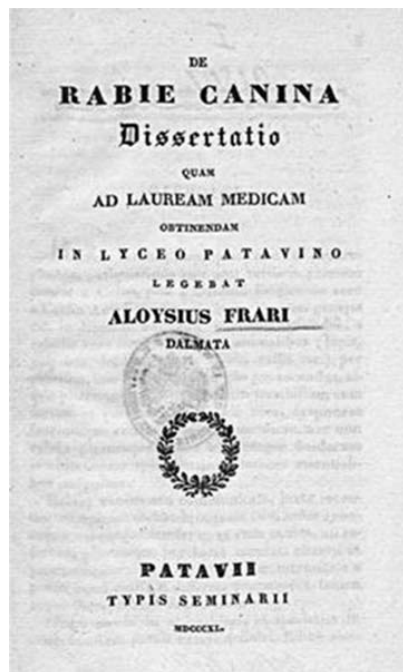


Figure 7. The title page of Aloysius (Luigi) Frari's Inaugural dissertation about rabies from 1840. It should be noted that the text was published with decorations and obvious attention paid to the esthetics, characteristic for the dissertations in Padua at that time (23).

ing the town's infrastructure (3,6,23-26). As a mayor ("il Podestà"), he also fought against a possible abolition of the Diocese of Šibenik in 1872. In an article published in "La Dalmazia Cattolica," addressed directly to the Austrian Emperor, Luigi Frari provided substantial religious and civil arguments for preserving the Diocese of Šibenik (22). Luigi Frari was also the president of the Šibenik Theatre Society, which financed and built Šibenik "Mazzoleni" Theater in 1870, one of the oldest in Croatia (2). He was a well known member of Šibenik's intellectual and social elite of that time (2), who collaborated with Nikola Tommaseo in gathering Slavic people proverbs in the Šibenik region (8,17). Although he was accused of being a Dalmatian autonomist, the radical autonomists at that time criticized him to be "a man of mild colors" (2,23-26).

After his death on 19 March 1898, his unknown friend, signed as "Un amico," published a sonnet about him (translation from Italian by the

author of the article). The document is the property of Roksanda Smolčić and it was presumably also published in "Il Dalmata" in 1898 (23):

*Sacred old man, tender like seraphim
Husband, father, citizen, brother
Upon your bier* a kiss of esteem
Upon your cold coffin tears and flower*

*You were gentle, good, you were faithful
Like Gabriel the angel resembling
I try to soothe, in this painful
Part of earth, my cry and suffering*

*The tired eyes are forever closed
But your spirit noble and devout
Flies bright and pure to bosom of the Lord*

*And in your silent grave, in autumn and spring
Sacred old man, of hair white,
Dream in peace your dream everlasting*

*bier n, "bara" in Italian, is the old English word for a movable plane on which a coffin or a corps is placed (according to Metcalf J, Thompson D, editors. Illustrated Oxford English dictionary. London, Oxford: Dorling Kindersley and Oxford University press; 1998).

Luigi Frari's inaugural dissertation on canine rabies included the history of the disease, its epidemiology, the paths of infection, methods of prevention, clinical symptoms, effects of the agent in the body, and the methods of prophylaxis and treatment (21). Two of nine additional theses which were defended by Frari, and mentioned in his dissertation, were also related to rabies – one on prophylaxis and the other one on the prolonged incubation period (21).

The dissertation itself, however, was not the result of Frari's experimental work but an outcome of studying literature and summarizing collected papers. Luigi Frari, as 27-year-old laureate of medicine at the time, as he himself admitted, did not have enough experience in the area. A greater part of dissertations defended at Padua, Vienna, and Budapest at that time were also of informative and compilation character (16,23).

The text, although written more than 160 years ago, resembles modern conceptions of that disease (21,27-29).

In the dissertation, Frari clearly described the possible ways of disease transmission (“bite, contact with saliva”), as well as the favorable conditions for the transmission such as excessive heat. The details about the progression of the illness in dogs and humans were also described. The representation and behavior of an infected dog was clearly depicted (the paralysis of the posterior limbs, the curved and flabby tail, the need to bite cats, dogs and, finally, humans), as well as the usual naive denying of the danger on the master’s part. Frari said that the development of the disease in animals was particularly stimulated in hot summers, cold winters, sexual deprivation, and when the animals were fed with bloody meat. In humans, the course of the disease was divided, similar to modern literature (27-29), in the prodromal, hydrophobic, spastic, and adynamic stage. The incubation period (“10 to 17 days, exceptionally up to several years”) and each stage were thoroughly described, as well as both the mental condition of the patient in various stages and reactions of other people. Seizures were described in a very good and even dramatic way; the patient would become physically very strong, aggressive, and dangerous, after which a period of self-pity, penitence, and depression followed. The factors which provoked the seizures were light or shining objects, such as reflection and murmur of water or the reflection in mirror, as well as fresh air (aerophobia). Frari also described various clinical expressions of the disease in humans and dogs, including the so called quiet, non-furious forms of the disease. He also clearly stated that the site of the disease was in the nervous system and that the infection spread through the nerves from the site of the bite toward the spine and brain. According to Frari, the salivating glands of the patient were those which excreted the agent of the infection (“the poison”). Frari correctly attributed the inability to swallow to the pharyngeal spasm of neurological nature. The differential diagnosis mentioned by Frari – the rage of psychological origin – is among the first mentioned

in modern medical literature (29). Also, medical history of rabies provided by Frari was similar to those given in modern literature (27-29). Epidemiologic measures for suppressing further infection proposed at the end of the text (to bury the nude cadaver into a deep grave, to burn his clothes and furniture, to wash the rafters and paint the room) are both interesting and practical.

The crucial difference between Frari’s approach to rabies and that of the modern literature is that Frari was not aware of the existence of microorganism – the RNA virus of rabies. He attributed the infection to a poison (“virus” in Latin). Besides, Frari knew nothing about the possibility of post-expositional prophylaxis by means of passive immunization with immunoglobulin and active immunization, which was the merit of Louis Pasteur’s epochal discovery in 1885 (28). Frari mentioned the prophylaxis which mainly consisted of wound treatment by washing out, excision, burning with caustic devices, such as mercury, arsenic, and application of various unguents and powders. Frari declared that a correct prophylaxis of that kind could, according to various observations, suppress the development of the disease. Therefore, it is not surprising that even the contemporary literature attributes an exceptional importance to wound treatment, such as washing out with soap, the method which was also highlighted by Frari (27-29)

The diagnostic possibilities were much more limited at that time and consisted of anamnesis, inspection, and recognition of symptoms, as opposed to today’s methods of isolation of the virus and measuring of the antibodies’ quantity in the serum or liquor (28,29).

The treatment of the disease once it has developed was, and still is, generally unsuccessful (27-29). Frari mentioned the antiphlogistic drugs, but said that they were of no real effectiveness. Today, however, due to improvement of the supportive therapy, a small number of patients can

survive the disease. However, according to Frari, even at that time, some patents could survive rabies, although extremely rarely.

The preventive immunization of health professionals and domestic animals against rabies was, of course, impossible at that time. Still, Frari declared that physicians had to approach patients with great caution, since even the clothes contaminated with the infected saliva presented a threat, even after a longer period of time (Frari used the term “fixed nature of the poison,” which was also used by Pasteur (28). Frari also warned that a dead animal could still be contagious.

Finally, Frari’s dissertation was also interesting from the ethical point of view, since Frari advised that the dying patient should be approached and cured in a proper way and should be spared irritations and unwanted spectators. According to Frari, the factors that could provoke seizures in the patient should be removed. In a particularly merciful way, Frari understood the condition of the patient and affirmed that all possible measures should be undertaken in order to nurse and respect the patient “until death comes upon the scene.”

Frari’s Latin is stylistically beautiful and very readable, and I truly enjoyed translating and analyzing the text. It is well known that Padua dissertations had to be written with special attention to the style and taste (16,23).

Discussion

The story of the Frari family is an example of a family tradition in the medical profession in Dalmatia (Figure 8).

Although different authors have already mentioned the importance of certain members of the Frari family (3-26), I hope that my overall analysis of the whole family and their work provided a better understanding of the Fraris, their medical practice, and the medical history of the town of Šibenik and Dalmatia in the 18th and the 19th century.

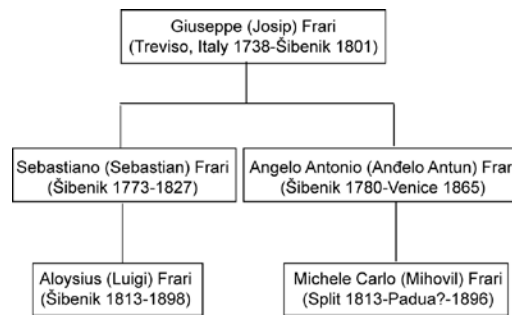


Figure 8. The Frari family tree. Three generations of the Fraris are mentioned, all of them were medical doctors. The tree is reconstructed out of references 3-6,9-12,15,16,23 and the data from the Croatian Official Register.

Clearly, the Frari family and particularly some of its members (Angelo Antonio, Giuseppe, Luigi, Michele) played a considerable role in Croatian and Italian medical history (9,10,12,15,18,23). The history of the Fraris also witnesses about the responsibilities and work of Dalmatia’s municipal physicians (4,9,23).

The observations of Giuseppe Frari on rabies obviously in a great deal inspired his grandson Luigi. Similarities to his grandfather’s work in description of symptoms, course of the illness, the effect of the poison in the body, and treatment options are apparent. Still, as opposed to Giuseppe, Luigi attributed less significance to treatment with mercury and emphasized wound treatment, in particular washing out of the wound. He also greatly emphasized the nervous damage, but gave less emphasis to the changes of the body liquids, except the saliva which he considered as the path of infection. However, it is interesting that Giuseppe Frari was completely familiar with the symptoms of hydrophobia, which he also divided into stages. He even talked about the poisonous particles, perhaps somehow predicting Louis Pasteur’s and other discoveries 100 years later!

Rabies, as a disease, was mentioned in various texts from the earliest history: in Egypt, Mesopotamia, and Greece (27,28). In ancient Rome, Celsus established a relationship between hydro-

phobia in humans and rabies in dogs, and recommended cauterization of the bite wound. Galen recommended excision of the wound (21,27,28). Later, in the Middle Ages, various authors all over Europe described the disease and epidemics, but until the beginning of the 19th century the texts about rabies were mostly sporadic (27,28). However, it should be emphasized that the prominent Italian physician Fracastoro, as early as 1546, described the incubation and clinical symptoms of rabies (27,28).

I assume that Luigi Frari, when choosing rabies as the subject for his dissertation, was in a great deal inspired by his grandfather's work. On the other hand, interest in rabies was almost a trend in the early 19th century (27,28). It was the time when the systematic and experimental approach to rabies began (27,28). Zinke in 1804 proved the infectivity of the saliva and Stimson and others in 1821 infected dogs with saliva of an infected human (28).

The revolution in the approach to rabies was made by Louis Pasteur in 1885, when he successfully immunized an infected boy (27,28). In 1889, Babes and Leps produced the anti-rabies serum (28). In 1903, Remlinger confirmed the ultramicroscopic nature of the causative agent and Negri discovered the inclusions in neurons (28).

The texts on rabies written by other Croatian authors were also not uncommon, even before Louis Pasteur.

In 1831 in Zagreb, publisher Franjo Župan published a text in Croatian on the possibilities of treatment after the bite of an infected animal (9). However, this text was a translation of a German text by the priest Tomislav Mikloušić (9). In 1837 a text in Croatian concerning royal orders on curing and preventing the spreading of rabies was published by the Typography of the Budapest University (9). However, this text was not originally Croatian but a translation from a Latin original (9). In 1832, Zagreb municipal physician, Croatian *protomedicus*, and the well-known patriot, Aleksa Vancaš defended

his inaugural dissertation on the topic of rabies at the Budapest University (8,9,23,30). This paper was important because it described the prevalence of rabies in certain countries for the period 1809-1818, and the author clearly declared that the illness was of infective nature. The term "*contagium*" was used for the non-evaporative matter which caused the disease (8,9,23). Vancaš stressed the need of public health measures in order to prevent the spreading of rabies, but unlike Giuseppe and Luigi Frari, he did not describe the illness in detail or from various aspects (21,23). After Aleksa Vancaš and Luigi Frari, inaugural dissertation on rabies was also defended by Hinko Kuničić (Vienna 1847), the Austrian military doctor, and Ivan Janson from Pečuh (Pecsz, Hungary), Osijek municipality physician (graduated in Budapest 1848) (9,23). Kuničić described the symptoms of rabies in humans and animals and stressed that dogs were the reservoir of the disease, but as well as Giuseppe Frari, wrongly concluded that the dogs got ill spontaneously due to deprivation in sexual activity, anger or frustrations (23). In 1844 Josip Lalić, a teacher from Vrbovec, published in Vienna his work in Croatian entitled "The ways of treatment of rabies or the bite of furious dogs in humans and domestic animals" (9,27,31). The methods of post-exposition prophylaxis described by Lalić were of a popular, non-medical, character, but still they partly resembled the methods described by Giuseppe and Luigi Frari: washing out of the wound with vinegar or urine of another person, burning of the wound, treatment with the extracts of insects of the genus of *Cantharidae* (Spanish Fly), the extracts of plants for external and internal application, such as the extracts of the *Gentianum* and *Compositae* genera (21,27,31). On the other hand, previously mentioned Hinko Kuničić accused Lalić of being a quack (23).

Liječnički Vjesnik, one of the oldest Croatian medical journals, published a series of texts, annual health reports (32), as well as various observational papers on rabies in the period from

1877 to 1886. These resembled Fraris' and other mentioned works, but appeared much later (33,34). The first Louis Pasteur Institute in Croatia was established relatively late, in 1918 in Zagreb (28).

It can be concluded that the publication by Giuseppe Frari from 1783 and the dissertation of Luigi Frari from 1840, were among the earliest texts on rabies written by Dalmatian or Croatian authors. These texts included everything that was known in Europe at the time about the history, epidemiology, infectiveness, clinical course, effect of the agent, and the modalities of prophylaxis and treatment of rabies. Obviously, the texts were the reflections of the comprehensive contemporary conceptions about rabies. The value and the credibility of these texts in the global context should not be questioned. Luigi Frari's dissertation was defended at the Padua University, which was at that time one of the most excellent universities within the Austrian Monarchy and Europe in general. Dalmatian physicians from the 18th and 19th century in general studied medicine in Padua, which was even their official duty for a period of time (4,16,23,35). In the 19th century, some 200 candidates from Dalmatia, Istra, and Rijeka graduated in medicine from Padua (4,9,16,23,35).

As I already said, in this period there was also a significant publishing activity on the subject of rabies in other regions of Croatia (9,23). This could be the subject of a future historical research. Besides that, inaugural dissertations published by a number of Croatian authors in that period in Vienna, Budapest, Padua, and Pavia (8,9,16,23,35) contain valuable information (9,23), and should be further assessed.

Further research on the topic of the Frari family is still needed. Future studies should be conducted to assess their position and importance in the general social and intellectual history of central and southeastern Europe.

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