ACADEMICIAN FRANJO KOGOJ
AND ALLERGOLOGY IN CROATIA

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Summary
Franjo Kogoj was regular member of the Yugoslav Academy of Sciences and Arts (1947), first secretary and Vice-President elect for several terms of office of the Medical Science Section of the Yugoslav Academy of Sciences and Arts (1958-1973), long-standing head of University Department of Dermatology and Venereology, Zagreb University Hospital Center, and head of Department of Dermatology and Venereology, Zagreb University School of Medicine. Numerous papers by academician Kogoj address allergic events in the body and their role in the disease course and morphology, prognosis, prophylaxis and management. He wrote about experimental studies of allergic reactions in eczema and pruridermatitis, a term he introduced in dermatologic terminology to replace the terms neurodermatitis, endogenous eczema, prurigo-asthma and Besnier’s prurigo. He tackled the issues of allergy in many papers, always bringing something new in the field. The concepts elaborated in his paper entitled “Ein Vierteljahrhundert Vasculitis”, presented at the Deutsch-japanischer Angiologien Kongress held in Essen in 1973, were received with high interest. In 1965, the Center of Allergology of the Yugoslav Academy of Sciences and Arts on the island of Hvar was established on his initiative, first at premises adapted for this purpose, then moved to a modern building consisting of inpatient and outpatient departments, diagnostic laboratories of biochemistry, pulmonary function testing, electrocardiography, radiology, physiotherapy, and library in 1973. F. Kogoj and A. Brnobić were founders of the Section of Allergology of the Croatian Medical Association (1952), as an attempt at unifying the work of medical professions dealing with allergic diseases. Kogoj published about 230 scientific and professional papers, 70 of them addressing allergology and immunobiology issues; 5 books; several monographs; and valuable contributions in a number of handbooks and textbooks.

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A brilliant era in the history of the Zagreb University School of Medicine and Croatian Academy of Sciences and Arts ended with F. Kogoj.

**Key words:** Academician Franjo Kogoj and allergology; Pruridermatitis allergica chronic constitutionalis; Secretary of Medical Science Section of Yugoslav Academy of Sciences and Arts

**FRANJO KOGOJ IN CROATIAN MEDICINE**

Department of Medical Sciences of Yugoslav Academy of Science and Arts (YASA) has published Testimonial to the Late Academicians – Volume 28, 1985, dedicated to Franjo Kogoj, regular member of Zagreb YASA, presented at Commemorative Ceremony held on October 1, 1984 at YASA Home. Professor Sead Midžić, YASA associate member, wrote: “Academician Franjo Kogoj departed this life peacefully, quietly and gently, in acquiescence of harmoniously completed life, in his native place of Kranjska Gora, to which he had always been coming back. He was long-standing head of University Department of Dermatology and Venereology, and of School of Medicine Department of Dermatology and Venereology, dean and vice-dean of the Zagreb University School of Medicine for several terms of office, first secretary of YASA Department of Medical Sciences, and its elected vice-chairman for several terms of office (1958-1973). A brilliant era in the history of our School of Medicine and our medical sciences has terminated with his departure. We have lost him; however, he has bequeathed to us his great opus and
example that will always stimulate us to follow him as an ideal and an inexhaustible source of inspiration” [1]. He was elected regular YASA member in Zagreb in 1947. Kogoj devoted his life to the research, education and clinical work in the field of allergology and clinical immunology in dermatology and venereology [2].

Franjo Kogoj was born on October 13, 1894 in Kranjska Gora, Slovenia, where he died on September 30, 1983. He studied at Charles University School of Medicine and graduated from it in 1920. Then he served residency at University Department of Dermatology and Venereology in Prague, headed by Prof. Šamberg who offered him the position of assistant. In 1923, Kogoj stayed at University Department of Dermatology and Venereology in Brno, headed by Prof. Tryba, then at University Department of Dermatology and Venereology in Zagreb as assistant to Prof. P. Šavnik. As early as 1924, when Prof. Šavnik died, heading of the Department was taken over by Kogoj [1,2]. During the 1924-1926 period, he received training at large departments with Prof. A. Tryba (Brno), Prof. J. Jadassohn (Wroclaw), Prof. Pautrier (Strasbourg) and Prof. A. Sézary (Paris). In 1925, he habilitated as private Assistant Professor of Dermatology and Venereology at Masaryk University in Brno, with a thesis entitled “On sclerodermas and scrofuloderma” [1-4]. He found his scientific interest at Prof. Šamberg’s Department in Prague, where he mastered precision, systematic approach and morphology of skin lesions. Prof. Jadassohn aroused his interest in experimental studies he had dealt with throughout his professional life (e.g., dermatomycoses, pyoderma, syphilis, tuberculosis, etc.). Specific inflammation and morphogenesis of the pathologic substrate consequential to tissue sensitization led him to allergic phenomena. These considerations and presentation of allergy topics pointed to Kogoj’s work as a scientist and established his place in science [2].

Kogoj was a versatile scientist. He entered the European and world’s scientific legacy by his clinical and scientific studies, in particular his histological discovery of the “spongiform pustule of Kogoj” in the diagnosis of pustular psoriasis. He contributed to the internationalization of Meleda disease (mal de Meleda), based on his epidemiological studies and histological verification of this genodermatosis. He was author of the film “Mal de Meleda” that was first released at XII International Congress of Dermatology in Washington, 1962 (4). Dorland’s Illustrated Medical Dictionary, published by W.B. Saunders, Philadelphia, 1974, brings the entry “Kogoj’s pustule: spongiform pustule of Kogoj” [1].

Kogoj advocated completion of the Department premises at Šalata, Zagreb, and University Department of Dermatology and Venereology was opened on December 9, 1928. In 1927, Kogoj was appointed professor and head of Department, which position he held until retirement in 1965, with interruption during World War II. From 1965 until 1980, Kogoj visited the Department daily, always ready to offer his valuable professional
assistance from his rich and inexhaustible treasury of knowledge [4]. At Department opening ceremony, he held a lecture entitled “On the causal problem in dermatology and in medicine in general”. Academician Kogoj said he was happy to speak in Zagreb as an outstanding cultural center, and he would invest all his efforts for the Department activities to contribute to the honor and reputation of the Croatian people both at home and abroad. Academician Kogoj performed this solemn promise honorably and completely through his numerous papers [4-11].

The Ljubljana University School of Medicine appointed him scientific and educational head of the University Department of Dermatology and Venereology during the 1955-1965 period. He served the position of dean in the academic years 1933-1934, 1946-1947, 1948-1949 and 1951-1952, and of vice-dean in the academic years 1952-1953 and 1953-1957. With his work, Academician Kogoj upgraded both Zagreb and Ljubljana University Departments of Dermatology and Venereology, the former being among the leading ones in Europe.

Kogoj continued his activities as director of the Institute of Clinical Medical Research, School of Medicine and Zagreb University Hospital Center from 1967 until 1974. He published about 230 papers in scientific and professional journals, periodicals, handbooks and textbooks, along with eight books and monographs (1-4). Especially prominent are his papers on the research into hereditary dermatoses, pyoderma, dermatomycoses, allergic diseases, keratodermas and management of skin diseases, syphilis in particular [2].

Kogoj was the first to use tests for assessment of allergic phenomena, was engaged in the study of endemic syphilis, Meleda disease, and introduced a new therapeutic procedure in the treatment of sporadic and endemic syphilis, thereby emphasizing the so-called critical moment, which he considered as an objective criterion on evaluating definitive cure in syphilis. Kogoj said: “We feel the unavoidable necessity of confirming the critical moment by a negative liquor finding because in early cases only such a procedure permits an immediate therapeutic intervention corresponding to the found condition and giving much more hope of success as that only later time” [12]. Of great importance are his papers on the genesis of pustular efflorescence, psoriasis, atrophoderma, dyskeratosis, scleroderma, pyoderma, eczema and eczematiform dermatoses, exanthema localization, and bullous dermatoses. He distinguished anergic, allergic-hyperergic and positive anergic forms on the basis of tuberculin reaction.

Kogoj’s educational and scientific work was abundant in original ideas and procedures, for which he was recognized as one of the leading dermatologists worldwide. He was member of the Standing Expert Council for Therapy Issues of the Federal Healthcare Institute and of the Federal Council for Coordination of Scientific Activities; chairman of the Committee for Medical Sciences and of the Expert Group for Dermatology, Venereology and Allergology; member of the Science Council of the Socialist Republic
of Croatia (SRC); chairman of the Association of Institutions and Organizations for Medical and Pharmaceutical Research in SRC; delegate of the Yugoslav Council of Academies to the Committee for Science and Technology Coordination; member of the Executive Committee for the Foundation of the School of Medicine in Rijeka; member of Deutsche Akademie der Naturforscher Leopoldina and New York Academy of Science; and corresponding member of the Slovenian Academy of Science and Arts, Serbian Academy of Science and Arts, Bosnia and Herzegovina Academy of Science and Arts, Schweizerische Akademie für medizinische Wissenschaften and Österreichische Akademie der Wissenschaften. He was chairman, honorary member, corresponding member or regular member of forty international and Yugoslav dermatological and medical societies and professional-organizational bodies [2-4].

Kogoj was invested with a number of high federal orders. He received the Federal Governmental Award for his textbook *Dermatološka propedeutika* (Dermatologic prope-deutics, 1949); SRC Life Achievement Award (1962); AVNOJ Award (1966); and a number of other certificates of merit. He received the title of *Doctor honoris causa* on four occasions in 1962 at Graz University; honorary doctoral degree in medical sciences in 1961 at Ljubljana University, in 1968 at Zagreb University, and in 1970 at Academy of Military Medicine in Belgrade [1-4].

The great contribution of Academician Kogoj to Croatian dermatology and venereology, allergology in particular, is inarguable.

THE HISTORY OF ALLERGOLOGY IN CROATIA WITH ACADEMICIAN KOGOJ’S INITIATIVE

A detailed account is given of the history of allergology in Croatia as directly related to Academician Kogoj. In 1909, Prof. Ernst Mayerhofer drew attention to and with his coworkers wrote in 1928 in Liječnički vjesnik (Lijec Vjesn) about the role of cow’s milk allergy in infants and children. Ivan Hugo Botteri was among the first in the world to introduce cutaneous testing in the diagnosis of echinococcosis. These developments and those contributed by Prof. Kogoj made the basis of allergology in Croatia.

Besides numerous papers in dermatology and venereology, Prof. Franjo Kogoj also earned his place in allergology and clinical immunology. His papers *O alergologiji* (On allergology); *L'allergie, c'est la vie* (Allergy, that’s life) from 1926; *Dijagnostika alergijskih bolesti* (The diagnosis of allergic diseases); and those on drug allergy, urticaria, strophulus, prurigo and allergoderma were major scientific contributions in the field of allergology [13]. Prof. Vuletić contributed greatly to Croatian allergology with his papers on the diagnosis and therapy of bronchial asthma and pollenosis (Lijec Vjesn 1931-1934). In 1948, Prof. Kogoj together with Prof. Brnobić opened Allergology Unit and Outpatient
Clinic for Occupational Diseases at University Department of Dermatology and Venereology in Zagreb. In 1956, on the initiative of Academician Kogoj, Prof. Jakac established Laboratory of Allergology at Braća Sabol University Department of Dermatology and Venereology in Rijeka, and in 1957 Prof. Vukas opened Division of Allergology at Dr. Z. Kućić University Department of Dermatology and Venereology in Rijeka.

On the initiative of Academician Kogoj, YASA organized Symposium on Allergy and published the papers presented in 1952. Along with the editor F. Kogoj (dermatology and venereology), the experimental aspects of allergy were addressed by Petar Sokolić, endocrine system by Vuk Vrhovac, bronchial asthma by Vinko Vuletić, allergy and digestive tract by Arpad Hahn, tuberculosis by Stanko Ibler, allergy in neurology by Radovan Lopašić, ENT by Srečko Podvinec, dental medicine by Ivo Ćupar, and occupational allergic diseases by Branko Kesić.

In 1952, also on the initiative of F. Kogoj, Section of Allergology with dozens of members was established at Croatian Medical Association (CMA). F. Kogoj was the first Section chairman and was later elected life honorary chairman [13].

In 1956, the manufacture of testing and desensitization allergens was initiated at the then Serovaccine Institute (later Institute of Immunology). The International Symposium of Allergology was held in 1964 in Zagreb, Split and Hvar, organized by YASA in collaboration with the CMA Section of Allergology. The European Climatic Center for Treatment of Allergic Diseases was founded on the island of Hvar, on the initiative of F. Kogoj and Grga Novak as YASA chairman. In 1961, members of the CMA Section of Allergology organized the First Congress of Yugoslav Allergologists, with F. Kogoj as president of the Organizing Committee.

The First Convention of Yugoslav Allergologists was held in 1962 in Dubrovnik [13]. Section of Allergology continued its activities in the time to come, including its engagement in the Association of Yugoslav Allergologists. Jubilee celebration of the 40th anniversary of the foundation of the Section of Allergology entitled Allergologia Croatica 1952-1992 was held in October 1992 at Croatian Academy of Science and Arts (CASA) under the auspices of the CASA Department of Medical Sciences. Plenary lectures on Academician Kogoj and Prof. Mayerhofer paid due reverence to these greats of allergology. Some of the papers presented at the meeting have been published in Rad Hrvatske akademije znanosti i umjetnosti, Medicinska znanost, Vol. XXVII, Zagreb, 1994:466 [13].

FRANJO KOGOJ IN ALLERGOLOGY AND CLINICAL IMMUNOLOGY AS APPLIED IN DERMATOLOGY AND VENEREOLOGY

Many Kogoj’s papers deal with allergic events in the body and their impact on the morphology and course of disease, its prognosis, prophylaxis and treatment [14-52].
These include papers on anticutins and procutins, superimposed tuberculin reactions, superimposed epicutaneous reactions, superimposed tuberculin-trichophytin reactions, and experimental studies of allergic reactions in eczema and pruridermatitis; he introduced the latter term in dermatologic terminology instead of neurodermitis and endogenous eczema, prurigo-asthma and prurigo Besnier [4]. In many of his papers, Kogoj tackled the issues of allergy, always bringing some new concepts, as allergy was his favorite field of interest [11]. He described numerous intriguing observations in the field of dermatology and elaborated in detail the issue of symptom complex in dermatology; he thoroughly investigated particular syndromes and semi-syndromes, and the issue of pruritus as a symptom. In 1962, he wrote the chapter on urticaria, strophulus, prurigo and pruritus in the complementary part of Jadassohn’s *Handbuch der Haut.*

Throughout his professional life, Kogoj was intensively engaged in scientific research up to 1980, as evidenced by the great number of his papers (about 50) published upon retirement. In these papers, he continued dealing with his favorite topics of medicamentous exanthema, medicamentous dermatopathies, eczema, pruridermatitis (atopic dermatitis), pruritus, superimposed trichophytin reactions, effect of serotonin on allergic skin tests, allergic events on the skin, so-called corticotropin therapy in dermatology, and role of histamine in eczematous reaction. His latest concepts elaborated in the paper entitled *Ein Vierteljahrhundert Vasculitis,* presented at the Deutsch-japanischer Angiologen Kongress held in 1973 in Essen, aroused high interest indeed [3,4,52]. Kogoj published his papers in Croatian, Slovenian, Czech, Polish, Bulgarian, German, French, Italian and English languages, thus being recognized and known all over the world. He mostly wrote his papers alone and some in collaboration with his coworkers Šavnik, Tryba, Jadassohn, Bošnjaković, Farkaš, Franković, Žuka, Ante Vuletić, Gušić, Štefanija Puretić, Milavec, Brnobić, Gizela Luković, Fettich, Zambala, Schwarzwald, Žmegač, Davor Perović and Verena Kogoj-Bakić. He tackled allergy topics in *Problematica ekzema* (The problems of eczema) and *Bolesti kože 1. i 2. dio* (Skin diseases, Parts 1 and 2; 1970 and 1971), a textbook for physicians and students; these books he wrote in collaboration with his coworkers. With these books, Kogoj completed his trilogy on *Dermatološka propedeutika, Spolne bolesti* and *Bolesti kože,* where he elaborated allergology, overall dermatology and venereology, along with dermatology and venereology propedeutics [2,4].

Owing to his numerous scientific and professional papers, Kogoj was member of editorial boards of a number of renowned scientific and professional journals, i.e. 5 domestic and 12 international journals. At professional conventions, he presented more than 100 case reports, and took active part in vivid discussions at congresses and conventions in Croatia and abroad. He was cited in a number of papers published in Liječnički vjesnik, Zentralblatt für Haut- und Geschlechtskrankheiten, Excerpta Medica, etc., reviewed many books in domestic and international periodicals, wrote congress re-
ports, worked on Medical Encyclopedia and other encyclopedic editions. He was Editor-in-Chief of the following publications: Izvješća Dermatovenerološke klinike u Zagrebu (1952); Simposion o alergiji (1952); Symposium allergologicum internationale Zagrabiae-Spalati-Phari (1964); Peti kongres dermatovenerologa Jugoslavije, Zagreb (1965); Radovi Medicinskog fakulteta u Zagrebu (1953-1958); and Simpozij o alergozama respiratornog trakta, Hvar (1957). He organized three national congresses of dermatology and venereology (Split, 1930; Zagreb, 1933; and Ljubljana, 1957); I. naučni sastanak dermatovenerologa FNRJ (Zagreb, 1950); I. kongres alergologa Jugoslavije (1963); and Dies italicus-jugoslavici medicinae destinati (Hvar, 1968 and 1971). He initiated Interclinical Meetings of Departments of Dermatology and Venereology Zagreb-Graz, which were alternatively held at the respective departments every 1-2 years. The main leit-motif of Kogoj’s work was and remained throughout his career: Salus aegroti suprema lex [4,11].

He was especially engaged in the topics of allergology. He published books on prurigo, urticaria, staphylococci, and medicamentous exanthema [4]. He was not only interested in the clinical manifestations of allergic hypersensitivity in dermatoses but also in the biological process of sensitization [1]. Kogoj showed restraint in adopting the terms of atopy and atopic diseases, defined by Coca as hereditary susceptibility to allergic sensitization induced by atopens and provoked by atopic reagins, if the author also considered urticarial reaction as atopic allergy. Kogoj considered eczema as allergic dermatosis and a professional disease. The rate of these disorders is relatively high in individuals at occupational exposure to antigens that can induce allergic hypersensitivity of the skin. The number of these patients is constantly increasing. The cutaneous allergic reaction is expected to disappear upon cessation of allergen exposure, which is achieved in most but not all cases. Eczema does not clear when the process has turned chronic, even if the patient’s skin is not exposed to the sensitizing antigen anymore. The reason for eczema relapses has not yet been fully elucidated. Perhaps a prolonged reaction of the hypersensitive tissue is involved, and the process of hypersensitivity might in part be explained by immune induction of cellular disintegration of the unrecognized and damaged cell [1,4].

It was on Kogoj’s initiative that the YASA Allergology Center was opened in 1965 in Hvar, first in the premises adapted for this specific purpose, and in 1973 moved to the newly constructed premises with the ward, clinics, diagnostic laboratories for biochemistry tests, pulmonary function testing, electrocardiography, radiology, physiotherapy, and library [1].

The major role of allergology and clinical immunology in dermatology and venereology is well known. This makes the research in the field initiated and systematically performed by Academician Franjo Kogoj at University Department of Dermatology and Venereology in Zagreb highly valuable indeed. Allergology and clinical immunology
in dermatology and venereology were his favorite fields of work and research he pursued in his rich scientific opus. He always tended to elucidate allergic manifestations on the skin or some other organ, and to clarify immune events causally related to these manifestations [4,14-52]. Kogoj began his systematic work on the issues of allergology and immunology as early as 1928, with his paper O alergiji (On the allergy) [14]. Since then, in his papers he used to bring some new concepts along with those widely known. Dermatoses may occasionally show similar or nearly identical symptomatology; therefore they can be differentiated and classified as allergic or non-allergic lesions only on the basis of the pathogenetic mechanism of their onset [4]. Kogoj discussed the role of many other substances and factors involved in allergic and immune reactions, such as spreading factor, histamine, acetylcholine, serotonin and peripheral nervous system [23]. Vulgar eczema was his favorite topic, addressed in many of his papers. In his monograph Problematika egzema (The problems of eczema, 1947), Kogoj presents the complex nature of the issue concerning manifold terms, hypotheses and theories, statements and facts. Eczema only refers to a skin manifestation where lesions involve the epidermis and occur consequentially to allergic sensitization. It develops in individuals free from hereditary allergy burden but have general predisposition for sensitization and special predisposition for eczema. All other dermatoses, no matter how similar or even clinically identical to vulgar eczema, should not be considered as vulgar eczema. Various dermatitides (e.g., d. eczematosa, d. detritiva, d. simplex, d. varicosa, d. pediculosa, d. solaris, d. intertriginosa) and so-called seborrheic eczema (d. seborrhoeica), by Kogoj termed “dermatitis dyseborrhoeica”, are not vulgar eczema because they are underlain by sebaceous gland dysfunction rather than allergic sensitization [4,21,42,43,46]. Neither is dermatitis eczematosides allergica vulgar eczema, although its clinical picture may occasionally be quite identical to that of vulgar eczema, because the pathogenetic mechanism of its occurrence differs from vulgar eczema. It is in fact an eczematoid allergoid formed by hematogenous or lymphogenous dissemination of secondary eczematogen from the focus to the specifically sensitized skin [38,42]. Pruridermatitis (neurodermitis) is also an allergic dermatosis and may in some circumstances present the same clinical picture as vulgar eczema, on eczematization in particular, but it is not eczema [4,22,44]. Here, the process of sensitization takes place in connective tissue and blood vessels, and can only manifest on the genetic basis predisposing to hypersensitivity reaction [4,22,44,47]. The term “atopy” is only acceptable to denote atopic disease that manifests following previous sensitization underlain by genetic predisposition [4,44].

Kogoj bequeathed us with a rich opus of works thoroughly elaborating allergic and immune events, to mention only Urtikarija, strophulus i prurigo (Urticaria, strophulus and prurigo), published in the book Bolesti kože (Zagreb, 1971) and in the great Jadassohn’s Handbuch der Haut (1962) [4,34,35]. Based on his studies, he concludes that prurigo
remains one of the most complex and inadequately clarified issues in dermatology. It is characterized by the prurigo papule located in the epidermis. Prurigo of Hebra is always an allergic dermatosis caused by some exogenous allergen. The paper *Dijagnostika alergijskih oboljenja* (The diagnosis of allergic diseases, by F. Kogoj, A. Brnobić and J. Fettich, 1962) extensively presents general indicators of allergic state and specific allergic tests used in vivo and in vitro in the diagnosis of allergic diseases (36). Results of the authors’ own research into vulgar eczema, pruridermatitis, strophulus, prurigo, urticaria, and some other allergic and non-allergic dermatologic and non-dermatologic diseases are tabularly presented [4,36].

Kogoj’s paper *Ein Vierteljahrhundert Vasculitis*, presented at the Deutsch-japanischer Angiologen Kongress in Essen, 1973, aroused high interest [4,52]. Kogoj used to emphasize that every problem deserves to be paid due attention and efforts irrespective of the positive or negative outcome of the results expected because the outcome will show whether the problem has or has not been properly set [53].

F. Kogoj and A. Brnobić were founders of the CMA Section of Allergology in 1952, with the intention to integrate the work of medical professions related to the study of allergic events. In 1965, the YASA Allergology Center in Hvar was founded on Kogoj’s initiative. Almost all activities required in allergology and clinical immunology have been available at the Center since 1973. Kogoj published around 230 scientific and professional papers, some 70 of them dealing with the issues in allergology and immunobiology. He wrote 5 books, several monographs, and a number of precious contributions to handbooks and textbooks in the field. Upon retirement, Kogoj used to visit the Department until 1979, still working hard and having published more than 50 papers, the last one in 1977 [4,52].

Academician Kogoj received high orders, awards and decorations not only at the national level but also from other European and non-European countries for his extraordinary scientific, professional and educational work as well as for his numerous social activities [4,10,11].

Academician Kogoj departed this life but his work and achievements live. It will certainly take decades for such a bright figure, such a man, humanist, organizer, educator, health professional and researcher to appear in our environment.

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Sažetak

Akademik Franjo Kogoj i alergologija u Hrvatskoj


S njime je završila sjajna era povijesti Medicinskog fakulteta Sveučilišta u Zagrebu i HAZU.

Ključne riječi: Akademik Franjo Kogoj i alergologija; Pruridermatitis allergica chronica constitutionalis; Tajnik Razreda medicinskih znanosti JAZU