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Review

Evolution of Management and Investigations of Cerebrovascular Diseases in Croatia

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A B S T R A C T

The author presents the history of management of cerebrovascular diseases (CVD) in Croatia since the beginning of medical health service in the country in the 19th and its evolution to the end of the 20th century. The foundation of the Zagreb School of Medicine in 1917 had paramount importance for the development of neurology, during the first period within the common specialty of neuropsychiatry. The interest for the CVD in Croatia became evident in the sixties of the past century, particularly when neurology has become a separate specialty in 1974. Fast progress in the field of CVD resulted from clinical applications of basic research and after discovery of risk factors in their occurrence. These advances and the appearance of a new medical specialty: intensive medicine, stimulated in Croatia the organization of the first Neurological Intensive Care Unit (ICU) in 1971. Clinical experience and investigations of the first neurological ICU stimulated this approach to CVD in other big hospitals in Croatia and in the surrounding countries. The results of new management were presented on national and international meetings, especially on 5 Zagreb Symposia on CVD. The concept of comprehensive care for CVD patients was promoted, as a continuum of prevention, early treatment – if necessary in the ICU, followed by modern rehabilitation. The described efforts were stopped due to the wars in the former Yugoslavia in the last decade of the 20th century. The process has been reinstated with new enthusiasm and new teams at the beginning of the 21st century after the postwar consolidation in Croatia and in the region.

Key words: *cerebrovascular disorders, stroke, Neurological Intensive Care Unit, intensive medicine, health services, electroencephalography, neurological diagnostic techniques, medical education, Croatia*

Introduction

The evolution of the concepts and practices in the management of cerebrovascular diseases (CVD) in Croatia demonstrates how modern advances in basic medical research and new concepts of the diseases have been introduced in a small country with a long European cultural tradition. The paper reviews these changes appearing at the end of the 19th and in the first half of the 20th century. For a long time stroke was regarded as a fatal condition, until new research in neurology started in the second half of the century. Stroke has not been any more regarded as an individual fate, but as a final result of slowly progressing development of the CVD, due to a number of factors, intrinsic and extrinsic. The CVD has been understood to be of various types and of different evolution, sometimes ending with an abrupt catastrophic accident: »stroke«. The new concept of CVD, initiated by neurologists, started in Croatia in the sixties, demanding a long path until it was accepted by medical community and introduced into practice through the appropriate organization of health services. The first neurological Intensive Care Unit (ICU) was founded in 1971, parallel with organized education of neurologists and practicing physicians, starting the same year with the Zagreb »Symposia on Cerebrovascular Diseases«. In a country with modest economic potentials the described advances were possible due to the endeavors of strong personalities introducing innovations in the management of this mass catastrophic disease. The program had to be continued with the education of the whole medical profession and of the general population, promoting the new concept of CVD, starting with prevention, early diagnostics, specific management and rehabilitation. Like many other economic and social activities, the evolution in managing the CVD was stopped due to the turmoil at the end in the former Yugoslavia, ending by the Croatian Defense War (1991–1995). The politics cruelly influenced this medical process, like

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many other human, economic and social spheres in the region. The described process has been however resumed with new energy after the postwar consolidation in Croatia and in the region at the beginning of the 21st century.

The early period of management of cerebrovascular diseases

Medical profession originated in Croatia in the 19th century. The majority of medical doctors, mostly from Croatia, many also from other countries of the Austro-Hungarian Empire, by origin Austrians, Germans, Checks, Slovaks etc, educated mostly in Austria or Germany, living in Croatia, were fully dedicating to local population. The major interest at that time was directed towards general hygiene, infections, trauma, general surgery, practicing medicine according to the then prevailing standards. Stroke (»apoplexy«) as a diagnostic entity, including other misdiagnosed brain diseases, being without an effective treatment, was out of interest of the then medical doctors, considered as a fatal condition, treated at home.

Croatian Medical Society (Hrvatski liječnički zbor) was established in the second half of the 19th century (1874) by medical doctors working in Croatia, in order to enable solving their professional and social status and to improve medical health service in the therapeutic and prophylactic activities. They founded in 1877 their professional journal: »Liječnički vjesnik« (»Medical Messenger«), published in Croatian. For several years it was the only medical journal in Croatia, reflecting the doctors' interests, trying to improve their everyday practices, writing reports on news in medicine from their own praxis and from foreign literature. Leading internists and general practitioners of that time, authors of the contributions, rarely sent contributions on neurological themes. So, a crossed hemiplegia was described by Gutschy in 1897[1], symptoms of hemorrhage in the internal capsule by Taussig in 1904[2], Belošević wrote on apoplectic bulbar palsy in 1932[3]. Physicians from the eastern Croatia (Slavonia) founded the Society of Slavonic Physicians (»Društvo Slavonskih liječnika«), with their monthly »Herald« (»Glasnik«) in 1877, published (in Croatian and German), mostly dedicated to relations to local population and their administration, giving hints on health education, public hygiene and information about their professional activities. There were no relevant reports on stroke.

An important role on progress of medicine played the traditional ties between Croatia and the surrounding countries, especially those within the former Austro-Hungarian Empire, to which Croatia belonged for centuries until 1918, but also with nations, with whom the Croats lived for several decades in the two states of Yugoslavia (1918–1941 and 1945–1991), except a relatively short period during the Second World War, during the true occupation from German Nazis and Italian fascists, marked by terrible battles, great misery and big human, economic and cultural losses. The period after the Second World War was at the beginning characterized by rigid political and economic restrictions and by isolation from the advanced Western countries. After 1949, the year of ideological and political break between Tito and Stalin, a slow, but increasing growth of connections started between the then Yugoslavia and the Western countries. The connections of Croatian medical doctors with institutions in the Western Europe and USA were progressively promoted in education and science.

A large psychiatric hospital »Stenjevec« in Vrapče, on the periphery of Zagreb, was founded already in 1879, based on the old concept of psychiatric asylum. The first practical neurologist in Croatia, Primarius Ivan Herzog, with no academic ambitions, established the first neurological division within an internal medicine department in 1919 in the Zagreb general hospital (»Zakladna bolnica«)[4]. The foundation of the Zagreb School of Medicine was planned and officially initiated in the second half of the 19th century, when in 1874 the Law on the Organization and the Foundation of Zagreb University was enacted in the Croatian Parliament (»Hrvatski Sabor«), as result of efforts of Croatian intellectuals, who understood that cultural and economic development of the country was not possible without establishment of educated medical profession and a well-organized, sufficiently equipped health service. However, due to political tensions between Zagreb, the capital of Croatia, and Vienna, the capital of the Austro-Hungarian Empire, and the complex relations within the Empire, this was delayed to the very end of its existence in the academic year 1917/18, when a number of established specialists with some academic experience, of Croatian or foreign origin, was called to establish the chairs for the first Medical School in Zagreb. This was important landmark for Croatian culture and medicine, initiating also developments in neurology, including later interest in stroke.

The Chair and Department for Neuropsychiatry were established after the foundation of the School of Medicine, when Prof. Mihailo Lapinskij, the former professor and founder of neurology at the University in Kiev, eminent emigrant from the Soviet Union, living in Vienna, was invited to be the founder of the Zagreb Neuropsychiatry chair. Elected in 1921 the Head of the University Department of Neuropsychiatry[5], he was interested in research of vasomotor phenomena and vegetative nervous system, but he assembled a small team of doctors interested in neurology and psychiatry for purposes of teaching and practicing neurology and psychiatry. This period was mainly characterized by the clinical descriptions of stroke, according to the practice of that time, denoted by nihilistic attitude towards its management. Thus neurological disorders, including stroke, were still mostly treated at home, rarely in general hospitals. The only kind of prevention of stroke in patients with arterial hypertension was for many years the application of leeches (bloodsuckers), then attainable in every pharmacy.

Radoslav Lopašić, elected in 1932 for a new head of the University Department for Neurological and Psychiatric Diseases, reported in 1933 on cerebral arteriography[6], introduced into the praxis only after the Second

World War. The neuropathologist Pejčić-Marković reported in 1939 on cerebral aneurysms[7], while Danko Riesner, the founder of neurosurgery in Croatia, wrote in 1940 on intracranial hemorrhages[8,9]. It should be stressed that Primarius Ivo Glavan, one of the biggest enthusiasts in the history of Croatian neurology, working some time with Herzog, already in 1937 published the first modern book of neurology in Croatian: the cerebrovascular diseases were elaborated in 5 from 500 pages[10,5]. It was reedited and enlarged three times more, including more information on stroke, being for several decades the most popular neurological textbook in Croatia and in South Slavic countries.

The years following the Second World War were years of poverty, shortage and limited political and economic contacts with Western countries, so also with international medicine. After that period the increased chances appeared for special studies in countries of Western Europe and USA. Through the efforts of the then Dean of the Zagreb School of Medicine, Professor Andrija Štampar, a world known pioneer in public health medicine, one of the founders of the World Health Organization, a number of ambitious young assistants were sent to study modern medicine in the world leading centers. One of these was Sergije Dogan, then the young assistant of Professor Lopašić, granted for education at the National Institute for nervous diseases, Queen's Square (London), in Sweden and in the USA[5,11,12]. In the sixties, with the advent of new manpower, Dogan initiated a development of subspecialties in neurology, in line with such concepts in the advanced countries. The electroencephalography, pneumoencephalography, ventriculography and angiography were introduced gradually into clinical practice in Zagreb. A leading personality in Croatian neurology of that time, Dogan supported practices to admit stroke patients in neuropsychiatric wards at the University Hospital. So these patients were better observed and the doctors were able to get more experience in stroke and brain diseases. This example was followed in other parts of Croatia, while in some neighboring countries, according to the older tradition, stroke patients were still treated in internal medicine wards, mostly due to frequent cardiac or other internal complications, the most frequent causes of death after stroke.

The eminent Croatian leaders of the then common discipline of »neuropsychiatry« (Radoslav Lopašić, Josip Glaser and Desider Julius) founded in 1952 a specialized journal »Neuropsihijatrija« – Zagreb (renamed in 1977 »Neurologija«, in 1991 »Neurologia Croatica«), published in Croatian, from 1980 also in English; the journal was for a long time known for relatively good professional and research papers, reviews, case reports, with contributions from Croatia and other parts of the then Yugoslavia, also from collaborators from European countries and the USA. In the 50-ies an increased interest in Croatia for stroke among neurologically oriented neuropsycyhiatrists was noticed, reflected also in an increased number of publications on stroke. They reflected new approaches to stroke: Sušić and Hamel-Puškarić wrote on

Fig. 1. Sergije Dogan (1916–1979), neuropsychiatrist, Professor of Neurology, Head of the University Department of Neurology (1967–1979), and Chairman of the Chair of Neurology and Neuropathology, University of Zagreb.

cerebral hemorrhage (1947)[13], pathologist Knežević on extracerebral influences of stroke (1955)[14], Ivačić-Bohaček on the early treatment in stroke (1959)[15], Radošević on cerebral apoplexy (1959)[16], Barac et al. on the diagnostics of internal carotid thrombosis (1963)[17], Hamel-Puškarić et al. on the pathogenesis of hypertensive cerebral hematoma (1970)[18] etc. Certain progress may be seen even from the topics of their papers, showing the changing attitudes to the concept of stroke. Soon this interest was increased, when in 1971 neurology got autonomous chair at the Medical faculty in Zagreb, and in 1974 two independent specialties have been organized in Croatia: neurology and psychiatry. The concept of modern management of CVB patients started in Croatia relatively early, in the seventies of the 20th century, if compared with the progress in this field in surrounding European countries. However, it was hindered in the period of the last decade of the 20th century, first by political problems started then in Yugoslavia and followed by Milošević's army aggression on Croatia. It ended with a collapse of the old state, with big human tragedies, mass exiles and cruel mass killings. It finally ended with forming new, mostly national states in the region, including the Republic of Croatia in 1992, still at the beginning of the Croatian Defense War.

Towards the concept of comprehensive care of cerebrovascular patients

In the first half of the 20th century the approach of medical profession to stroke was conservative, like generally to neurological diseases, in Croatia like in the world, mainly epistemologically oriented, with limited diagnostic capabilities and with expectative attitude in their management. Medical nihilism and fatalistic approach prevailed to stroke, accepted as individual fate

connected mostly with heredity. At the end of sixties a new trend of experimental research started first in the USA big clinical hospitals, with experimental research directed to specific clinical problems. This decisively influenced the practical aspects of modern neurology, which was slowly changing to an active medical discipline, searching for new diagnostic technologies and for new, more radical methods of treatment and new approaches to prevention and restoration of neurological functions. In the last decades of the 20th century neurology has become also a science of relations between the human brain and the human mind, reaching the borders of understanding relations between the brain functions and the individual and collective human mental life. Under Dogan's influence a small team of neurologically interested neuropsychiatrists started fostering new specific fields – subspecialties in neurology: epileptology (Hajnšek), clinical neurophysiology (Dogan), cerebrovascular diseases (Barac), neuromuscular diseases (Jušić), multiple sclerosis (Hamel-Puškarić, Dupelj)[4,19].

New advances in stroke, one of the world's most frequent causes of morbidity and mortality in the developed countries, were rapidly increasing. Papers were published on cerebral circulation, on metabolic or pathophysiological mechanisms of stroke development. Epidemiological investigations on stroke were organized, searching for factors active in the origint of stroke, looking for efficient therapies[20–22]. Great influence on further development of the new concept of stroke and cerebrovascular diseases in the world were the two series of pioneer conferences: the »Princeton Conference on Cerebrovascular Disease« (from 1961 up to now) and the »International Salzburg Conferences on Research in Cerebral Circulation« (1965 to 1990). In these two series of conferences important role had colleagues, with some of whom also Croatian neurologists (Dogan, Barac) were collaborating with the then leading neurologists in the field, like John S Meyer (Houston), Carlo Loeb (Milano), Klaus J Zülch (Köln), Clark H Millikan and C Miller Fisher (Boston), John Marshall (London), Helmut Lechner (Graz), James Toole (Winston-Salem). Such meetings brought new dynamic concepts into research of stroke, exploring causes of its occurrence, searching for various individual »risk factors«, and for efficient therapeutic and prevention modalities.

Stroke stopped to be regarded the individual's fate, but a late consequence of identifiable risk factors or triggered by unfavorable pathophysiological mechanisms. In practice, we learned the importance to search for reliable indicators of individual risk factors and for the type of CVD. New trends developed in the prevention: the primary prevention in individuals or in the population at risk, while the secondary prevention should start after successfully treated stroke, in order to prevent its recurrence or progression of CVD. The management must start early after identification of modifiable risk factors (hypertension, diabetes, dyslipidemias, cigarette smoking, chronic stress) or possible etiologies: the therapy should be oriented rationally to risk factors or etiology.

This was one of the most important revolutions in the modern history of medicine, at the same time with a trend to treat hypertension and diabetes. The new discoveries needed a time, individual and common efforts to be generally accepted and to have visible results in broad population. The advances in understanding the true character of stroke were present also in Croatia, leading to changes in the concept and in the management of the CVD and stroke. It should be stressed that some of the international »pioneers« in the CVD lectured at the Zagreb meetings or in Pula (Croatia) at the International Neuropsychiatric Congresses: Lechner, Loeb, Marshall, Meyer, Toole.

The policy of treating stroke patients in neurological wards resulted in the fact, that at the end of the 60-ies two thirds of beds of the neurological divisions in Zagreb were acute patients with stroke. The patients were clinically observed: supportive and general therapy was used: antibiotics, cardiotonic therapy, infusions. The mortality of stroke patients was enormous, either by the accident itself or due to complications (infections, bedsores, pulmonary emboli etc). This was, however, an encouragement for engaged neurologists to try to follow the new trends introduced in countries with the advanced neurological practice.

The first Neurological Intensive Care Unit in Croatia

The author of this paper experienced personally the tragic gravity of stroke, when he felt, as a young neurologist, helplessness and frustrations in treating stroke patients, witnessing their dying in the neurology wards, sometimes young or in their best ages – up to five deaths in one day duty! During his residency in neuropsychiatry (1959–1962), in Surgery department (Vinogradska Hospital Zagreb), preparing to introduce a mitigated electroshock in psychiatric patients, he got acquainted with basic principles of anesthesiology and reanimatology[23]. Following reports on efficiency of »intensive medicine« in various medical branches (surgical, coronary units), he initiated in 1968 a program to apply the same principles in stroke patients[24,25]. The new discipline has developed during the seventh decade of the last century from anesthesiology and reanimatology. At this time the new concept of the CVD as a gradually developing process, was continuously promoted[26]. Barac's official proposal, supported by Dogan, the Head, and the Collegium of the Neurological Department of the University Hospital Center Zagreb, to organize a division for cerebrovascular diseases with Neurological Intensive Care Unit (ICU), was accepted at the Zagreb Community level. The program accentuated that the Neurological ICU must be under continued guidance of neurologists, experienced in stroke and familiar with principles of intensive medicine. The importance to identify the site and size, the cause and stage of the cerebral vascular lesion, was the primary goal of such ICU, enabling rational therapeutic measures, with uninterrupted follow-up of the patients[27]. The Unit started working under provisional conditions

in 1971. After the adaptation of one ward of the Department of Neurology it started functioning in 1974. Using the experience from the visits to the general ICU in Leeds (UK) and to the VA Hospital in New Haven (Connecticut, USA), the system of managing stroke patients in the Zagreb neurological ICU was constantly ameliorated. The organization of the Neurological ICU on these principles of management and our experience were reported on the First World Congress of Intensive Care (London1974) as the only report of intensive medicine applied in neurology[28].

The Unit was organized in two functional sub-units: a) intensive therapy unit (ICU in the strict sense) and b) intensive observation unit. The principles of management enabled establishing new approaches to management in various types of stroke (intracerebral hemorrhage, cerebral infarction – embolism or thrombosis, precerebral stenosis, subarachnoidal hemorrhage), or, less often, in acute neurological dysfunctions due to internistic disorders or closed cerebral trauma. The intensive medicine concept, including careful observation and follow up, maintaining vital functions and immediate applying of necessary medical therapy, was primarily developed to assure a prompt and efficient resuscitation of critically ill, using modern facilities and pharmacological preparations to restore impaired vital functions – the cardio-circulatory and respiratory failures in the first place, regulating them in a critical period[29]. A dilemma arose whether to organize a neurological emergency service within the General ICU of the University hospital, or to organize it within Neurological Department itself. The latter view prevailed, not only due to the large size of the University Hospital (1200 beds), with many specialized disciplines, on the principle that specially experienced neurologists must be responsible for the continuous care for these patients. Other specialized ICUs were organized afterwards in the University hospital (surgical, coronary, internal medical, neurosurgical, pediatric), with the ideology: cooperation, not competition[30]. The results of stroke patients' management realized by the neurological ICU team was reported on scientific national or international meetings, especially in the Zagreb »Symposia on Cerebrovascular Diseases«. The education of younger neurologists and of the ward nurses was constantly improving. Neurologists interested in this field of activity from Croatia (Ledić, Baturić, Reić) and the leading neurologists from other Yugoslav republics: Bokonjić (Sarajevo, Bosnia and Herzegovina), Kartin (Ljubljana, Slovenia), Popovski (Skopje, Macedonia) were collaborating with the Zagreb ICU, the younger colleagues being educated in this type of management. Consecutively such management was organized in other big hospitals of Croatia: Osijek, Rijeka, Split, and of Yugoslavia: Ljubljana, Belgrade (1987), Sarajevo (1989), Skopje etc.

The functions of the Neurological Intensive Care Unit

From the very beginning it was established as the most important task of the ICU manpower to proceed the necessary diagnostic and therapeutic steps immediately after admission. The Unit had about 300 admissions of acute cerebrovascular patients per year, with a continuous tendency of increase, for several reasons: the growth of the population in the region, the aging of the population and the changes in the practices in referring patients early to the hospital. Because of specific treatment noticed in medical community, some patients were sent to the Department from the remote parts of the country, even by air. The Unit had air conditioning facilities, in-built facilities for oxygen, compressed-air and negative pressure, electronic equipments for diagnostic and therapeutic purposes. A team of up to 7 neurologists, trained in emergency medical services, some of them also in clinical neurophysiology and ultrasonography, in close collaboration with anesthesiologists, cardiologists and other specialists in the hospital, formed a team for continuous medical work.

The main principles and the first experiences of managing stroke and other emergent neurological patients were described in the summarizing paper on the ICU[29], followed by other reports, postulated the »early treatment of cerebrovascular dysfunctions« and the »education of all participants in health service and of the population«[31–34]. Every acute stroke patient had to be admitted to the ICU: patients with cardiocirculatory instability, with a recent neurological deficit or with tendency towards progression were admitted to »intensive therapy unit« and treated until the process was sufficiently stabilized. After that period the treatment was continued in the »intensive observation unit«. The stroke patients with relatively stable general condition were admitted straight to the »intensive observation unit«. The history of the disease, neurological and somatic findings, laboratory investigations have aimed to ascertain the clinical diagnosis as early as possible. In case of stroke, the detailed diagnosis (type, location and size, the stage and time of the accident) was necessary for appropriate therapy. The management was instituted immediately and the diagnostic procedures performed in parallel. The neurophysiological diagnostic methods (EEG) were regarded as useful, in spite of their nonspecificity, for their inoffensiveness and the possibility of repeating them, having in mind the simple diagnostic repertoire of that period[35–37]. Doppler ultrasonography or echo-encephalography were performed as a bed-side diagnostics for the same reason, and rheoencephalography for some questions in the diagnosis and prognosis of stroke[38]. Neuroradiological investigations (then available brain CT and angiography) were applied when serious differential diagnostic problems existed, or when neuro- or vascular surgery were considered, or to follow-up the evolution of the process[39,40]. Biochemical analyses served sometimes for specific purposes in the diagnosis of possible concomitant internal or infectious disease; cerebrospinal fluid investigations were performed in the then standard indications, but also in the diagnostic efforts (localization, duration and stage of the vascular process)[41], relating them to clinical, neurophysiologic or ra-

diological data. To-day, with the existing diagnostic possibilities (MRI, SPECT etc), they will be used rarely, e.g. in diagnosing meningeal infection.

Monitoring of vital functions (ECG, arterial and central venous pressure, respiration, temperature) was used according to the established intensive medicine criteria. The purpose of emergency therapy had to establish optimal cerebral circulation, having in mind hemodynamic and biochemical influences, perfusion pressure, oxidative, water and electrolyte metabolism upon cerebral metabolism, autoregulation and microcirculation[42]. The »algorhythms« of diagnostic techniques were changed, depending what diagnostic methods had been available at some time and place, how they were accessible and what specific purpose they served.

The following principles in emergency therapy of stroke patients were adopted:

A. General systemic therapy was aiming to ensure adequate cardiocirculatory and respiratory functions[29], improving local and general cerebral circulation and metabolism in the following steps: 1. Achieving optimal cardiac output to assure satisfactory brain perfusion pressure[43]. 2. Correcting circulatory deficiencies aiming at lowering the risk of secondary damage in the brain, normalizing excessively high or excessively low arterial pressure, achieving the optimal general circulation and perfusion pressure needed for actual type and stage of stroke (hemorrhage or ischemia), respecting the age of the patient etc[44]. 3. Good respiratory function assures the adequate brain oxygenation and the acid-base balance. 4. Water, electrolyte or glucose disturbances must be corrected as soon as possible, having possibly fatal influences on the microcirculation, acid-base balance, deteriorating all the mentioned functions: »an appropriate infusion therapy is of special importance«[45]. In patients with the altered consciousness or bulbar symptoms, total parenteral alimentation (TPA) assured the appropriate nutritive and therapeutic corrections, with a control of biochemical, clinical and neurophysiologic parameters. »The TPA may be considered as specific therapeutic approach in the treatment of neurological patients«[46].

B. Specific therapy was directed to specific problems in the actual cerebral process: different modes of therapy were applied in cerebral hemorrhage or in ischemia (stenosis or thrombosis with »penumbra« and perifocal edema). In such situations a choice was among then available therapies: anticoagulants (heparin), molecular weight Dextran and corticosteroids[47–49]. Analyzing our results with anticoagulant therapy[47] we warned, still in 1974, the temporal limits for indication of the application of anticoagulants: 6 hours from the start of thromboembolic stroke was in our opinion the longest possible period for starting heparin therapy, to reduce the risk of cerebral hemorrhage. Our warning was a forerunner of the present concept of the »therapeutic window«, the permitted time from stroke for application of anticoagulant therapy in the strict conditions in the present day »stroke units«, with still existing dilemmas between 3 and 6 hours for the »window«, depending on individual specific factors. Surgery was chosen as a therapy in some cases of cerebral hematoma or in cerebrovascular insufficiency due to Carotid artery disease[50–53]. It was difficult to draw a sharp distinction between conservative and surgical management: both were aimed to improve the local and collateral circulation, to regulate cerebral metabolism, and to prevent secondary complications in the brain or elsewhere in the body: the surgical management was indicated in situations when surgery had to achieve results not obtainable by conservative management. »Such an organization of the specific intensive care unit for cerebrovascular and other neurological emergency patients requires a prompt diagnosis and subsequent follow-up of the pathologic process, enabling the medical staff to apply the appropriate therapy in every stage of dynamic changes during the acute brain dysfunctions. This treatment in acute cerebrovascular and other neurological diseases aims to minimize the actual brain lesion, preventing secondary cerebral and other complications, treating the patients in the acute dynamic phase of stroke, even though the life itself may not be in danger at that moment. Appropriate emergency management improves final results, reducing invalidism and mortality«[29].

Education of neurologists and their collaborators

In 1971 Dogan initiated the first Zagreb »Symposium on Cerebrovascular Diseases«, organized with Poljaković and Barac at the end of the same year, as well as with leading neurologists in Zagreb (V Hudolin, M Ferković) and representatives of primary contact family doctors (V Boltar-Haramінčić). The leading idea was to educate appropriately the neurologists and the primary contact doctors on the advances in understanding stroke and CVD. The aim of such meeting was to assure the close collaboration between neurologists and general practitioners, as a precondition for successful prevention and early management of patients with stroke and the CVD. Special attention of the first Symposium was attributed to the task of primary health physicians in the early diagnosis of the CVD patients and early referring Stroke patients to the hospital, the continuous post-stroke management and rehabilitation of CVD patients. The Symposium ended with a full success; it was decided, that such meetings should be continued in the periods of two or three years to improve the collaboration of all participants and to take pace with fast advances in the field. The 2nd Symposium in 1974 was dedicated, among others, to the organization of intensive therapy of cerebrovascular diseases[54]. A number of the contributions reported on their experience, but also to the deficiency of properly educated neurologists. Awareness of possibilities in the new approach to the stroke patient was an important message. Slowly, but continuously, the amelioration was seen in all parts of Croatia, like the increased interest for such approach in all republics of Yugoslavia. The topics of the five Zagreb CVD symposia (Table 1) were dedicated to various aspects of CVD: epidemiology, risk factors, diagnostics of incipient and slowly progressive disturbances of cerebral circulation, methods of diagnosis, evaluation of

TABLE 1
ZAGREB »SYMPOSIA ON CEREBROVASCULAR DISEASES«

1971: 1st Symposium	(Dec 10–11)
Aims: Close collaboration between neurologists and general practitioners. Appropriate education of neurologists and non-neurologists in clinical approach to CVD.	
Topics: Role of primary health physicians in diagnosis, management, rehabilitation and resocialization of Stroke patients, Possibilities of prevention of CVD.	
1974: 2nd Symposium	(May 9–11)
Topics: Epidemiology of CVD, Transitory ischemic attacks, Management of Stroke, Intensive therapy in CVD patients.	
1979: 3rd Symposium	(Dec 6–8)
Topics: Risk factors for CVD: Hypertension, Diabetes mellitus, Disturbances of metabolism, lipoproteins and coagulation, Other, Early disturbances of cerebral circulation, Working capacity of CVD patients.	
1985: 4th Symposium	(Dec 5–7)
Topics: Epidemiology of CVD, Early and slowly progressive forms, Evaluation of therapy, Indications for surgical treatment.	

management of CVD, vascular surgery and neurosurgery in their treatment, neuropsychological changes, rehabilitation of CNS patients etc.

The Zagreb CVD Symposia became popular among neurologists, collaborating specialists and general practitioners, not only in various parts of the former Yugoslavia, but attracted many eminent lecturers from European countries (Germany, Austria, Czechoslovakia, Italy etc). At the last one, in 1990, 256 papers were presented. It was repeatedly warned, that there were no unique schemes in the management and treating stroke because of the need to identify individual risk factors and actual pathologic mechanisms leading to stroke, in order to apply the individual rational therapy[55–57]. The founder of the first neurological ICU in the region and one of the initiators of the Zagreb CVD Symposia was invited on the 1st Yugoslav Symposium on emergency conditions in Neurology (Beograd, November 1990)[58], to report as a first speaker on organization of intensive care unit in neurology.

In the former state, when Croatia was a part of Yugoslavia, due to insufficient and old-fashioned methods of official data acquisition and their elaboration, we did not have reliable data on stroke morbidity and mortality[59]. The number of epidemiological studies was small, performed by various methodologies. The data on the incidence and mortality rates of CVD differed whether taken from the official vital statistics or obtained from specialists on the ground of specific analyses, depending on the availability of sophisticated diagnostic methodologies. In the official report from 1991 the mortality rate for CVD (In Croatia was estimated 182.8/100.000 for the year 1989[60]. In a systematic follow-up study of cerebrovascular diseases, performed by Poljaković at al. after 1971,

Fig. 2. 3rd Zagreb Symposium on Cerebrovascular Diseases (Deember 6 – 8, 1979). Presidency of the Opening Ceremony: V Filipan (Zagreb), P Kartin (Ljubljana), B Barac (Zagreb), P Ledić (Rijeka), V Hudolin (Zagreb), K Orovčanec (Novi Sad), Z Poljaković (Zagreb), P Baturić (Zadar).

in collaboration with specialists from the WHO (Geneva)[61], as a longitudinal study of epidemiological follow-up of CVD in Zagreb, a constant increase in the number of stroke accidents was found: the average annual stroke incidence rate in 1972 was 202/100.000, it reached 234 in 1982, and 250 in 1988, with a significantly higher number of the diseased in the middle ages population (40 – 60 years). In the same study they found a favorable influence of new admittance and management policy in the Zagreb neurological ICU wards on the outcome of new stroke patients: the mortality in the first 48 hours after the accident decreased from 39% in 1974 to 30% in 1983, while the recurrences of stroke in patients surviving the first 14 days of hospitalization decreased from 17.9% from the years 1974–1975 to 13% in 1982–1983, showing good results of the secondary prevention. These data implied both positive and negative influences of social, economic and health services factors on the appearance and outcome of stroke, showing that invalidism of CVD can

Fig. 3. 3rd Zagreb Symposium on Cerebrovascular Diseases – Session of the Symposium.

be diminished. The progress of such a large program was slow, the programs of prevention, appropriate therapy and necessary rehabilitation, without a strong support of the whole society not being possible.

A series of international conferences dedicated to rheoencephalography – a bioimpedance method applicable in investigations of cerebral circulation and in the CVD diagnostics, was organized in Zadar (Croatia) by Petar Baturić[62]. Zagreb was also an esteemed center (In Croatia) and ex-Yugoslavia for the ultrasonographic diagnostics of cerebral circulation, known through Vida Demarin's intensive teaching in a series of postgraduate courses on this inoffensive and relatively inexpensive diagnostic tool. Special tribute should be paid to the traditional International Neuropsychiatric Pula Symposia (INPS), especially in the period after 1985, when Helmut Lechner (Graz), the founder of the Salzburg Symposia, was elected as one of the two Secretaries General of the INPS, dealing also with CVD problems.

The Zagreb CVD Symposia were successful in their didactic programs, the scientific and practical initiatives in the field, starting collaboration of medical specialists and primary contact physicians, in some degree informing also the general population. They stimulated neurologists in Croatia and in other Republics of the former Federation, connecting also Croatian medicine with the European and world advances in the field.

The concept of comprehensive care for cerebrovascular patients

During the described period of hardly two decades neurologists in Croatia were alerted to accept the new concepts of the CVD. The concept of comprehensive care for patients with CVD included prevention, early diagnosis, intensive management, neurological rehabilitation and resocialization[63]. This was reported at the 13th World Congress of Neurology in 1985[64]. Zagreb and Croatia followed successfully new trends started in developed countries, in some aspects even pioneering in the process of new approaches in the intensive management of the CVD. This specific approach to public health problems in neurology resulted in formation of a WFN Research Group on Organization and Delivery of Neurological Services, which used the experience of Croatian concept of comprehensive care of CVD[65].

The process interrupted by the war has been reinstituted in Croatia at the beginning of the 21st century after relative political and economic consolidation in in the region. New leaders in this development, Professor Demarin and her team, have made successful efforts to innovate the described process across Croatia and in the surrounding countries, with new achievements in the diagnosis and management of patients with most efficient, scientifically based methods: the detailed recommendations on the management of the CVD and stroke have been proposed and published[66,67]. The »Stroke units«, as a specialized type of Neurological ICU have been recommended as the useful method in stroke management.

Our early experience may still be usefully applied in developing countries with insufficient sophisticated technologies, using the present knowledge in the modest medical conditions. On the basis of our activities in the WFN during more than two decades[65], we strongly believe that the principles of the described concept, supported and possibly modified by new knowledge, may be applicable for every culture and every region, with necessary modifications, taking into account the specific social, cultural, religious and economic factors, respecting local tradition.

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RAZVOJ LIJEČENJA I ISTRAŽIVANJA BOLESTI KRVNIH ŽILA MOZGA U HRVATSKOJ

S A Ž E T A K

Autor prikazuje povijesni razvoj liječenja i istraživanja cerebrovaskularnih bolesti (CVB) od početaka medicinske zdravstvene službe u Hrvatskoj potkraj 19. i njezina razvoja do kraja 20. stoljeća. Naglašava važnu ulogu osnivanja Medicinskog fakulteta Sveučilišta u Zagrebu za razvoj neurologije u okvirima tadašnje neuropsihijatrije. Interes za CVB javio se tek u šezdesetim godinama 20. stoljeća, kad se neurologija 1974. godine bila razvila u Hrvatskoj u samostalnu specijalnost. Brzi napretci na području krvožilnih bolesti mozga bili su rezultat novih spoznaja u temeljnim istraživanjima i otkrića faktora rizika u njihovu nastanku. Spomenute spoznaje i pojava nove medicinske struke – intenzivne medicine, potakli su u Hrvatskoj 1971. g. osnivanje prve neurološke jedinice intenzivnog liječenja (JIL). Nova klinička iskustva i istraživanja u prvoj neurološkoj JIL potakli su sličan pristup organizaciji liječenja CVB u drugim velikim bolnicama u Hrvatskoj i susjednim zemljama, te bila su predstavljena na domaćim i međunarodnim skupovima, a osobito na 5 zagrebačkih simpozija o CVB. Bio je predložen koncept cjelovite brige o bolesnicima s CVB kao neprekinuta djelatnost prevencije, rano započetog liječenja – prema potrebi u okvirima JIL, te suvremene rehabilitacije. Opisani napori bili su prekinuti ratnim zbivanjima u zemlji, ali su nastavljeni u 21. stoljeću s novim entuzijazmom i novim timovima nakon poslijeratne konsolidacije u zemlji i u regiji.