# Post-covid era: The new and unknown field

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From September 2020 to April 2021 Department of Biomedical Sciences in Rijeka of the Croatian Academy of Sciences and Arts organized seven international scientific conferences in collaboration with University of Rijeka, Medical Faculty and Clinical Hospital Center in Rijeka. The first cycle of five one day conferences were organized under the title COVID-19 MESSAGES I-V (see: 1) which were dedicated to all aspects of pandemics and their reflection on the society and University of Rijeka. Contributions of speakers and conclusions and recommendations were published in the book (see: 2).

The sixth COVID-19 conference was a traditional 4th Rijeka Forum on Neurodegenerative Diseases which was focussed on pandemics (see: 3). According to World Health Organization, as well as recently accumulated data long term consequences like chronic fatigue syndrome, respiratory, cardiovascular and neurological problems are more and more apparent and comprise more than 10 per cent of SARS CoV-2 infected individuals. So huge number of affected individuals worldwide will require interdisciplinary pre-

*Figure 1. Program Committee of Rijeka COVID-19 symposia:*

*Snježana Prijić Samaržija, rector of the University of Rijeka; Daniel Rukavina, Head of Academy Department of biomedical sciences in Rijeka; Alen Ružić, Head of the Clinical Hospital Center in Rijeka; Senka Mačešić and Marta Žuvić, Vice-rectors of the University of Rijeka; Tea Dimnjašević, Former president of the Student council of the University of Rijeka; Vladimira Vuletić, Head of the Department of Neurology, Clinical Hospital Center in Rijeka*

clinical and clinical approaches to determine causes and provide management options. This fact inspired us to organize symposium focussed on analyses and discussion of long-term consequences.

The symposium **"Post-COVID Era: The new and unknown field"** was held online on the 7th and 8th of April 2021. under the patronage of the Department of Biomedical Sciences in Rijeka of the Croatian Academy of Sciences and Arts, University of Rijeka, the Clinical Hospital Center (CHC) Rijeka, the Medical Faculty and Faculty of Health Sciences of the University of Rijeka and the Rijeka branch of the Croatian Medical Association. The symposium was opened with introductory talks of the president of the scientific committee, Daniel Rukavina, full member of Croatian Academy of Sciences and Arts and the Head of the Department of Biomedical Sciences in Rijeka of the Croatian Academy of Sciences and Arts, and president of the organizing committee Professor Alen Ružić, Head of the Clinical Hospital Center Rijeka. Furthermore, welcome addresses were given by Srđan Novak, Head of the Croatian Medical Association – Branch office Rijeka, Daniela Malnar, Dean of the Faculty of Health Studies and Goran Hauser, Dean of the Medical Faculty, University of Rijeka. Professor Snježana Prijić Samaržija, rector, expressed full support of the Rijeka University to the organization of this series of thematic symposia dedicated to COVID-19 pandemics in which she also participated actively both in development of the concept and organization.

In the brilliant introductory presentation **Pero Lučin** (Medical Faculty, Rijeka) made a brief overview of the cellular biology of viral infections on the example of two viruses: cytomegalovirus (CMV), as one of the largest DNA viruses, and SARS-CoV2 virus, as one of the largest RNA viruses. The initial part of the presentation indicated the interactions of CMV with infected cells. It demonstrated the complexity of membranous organelle rearrangements that occur during infection and lead to the formation of a compartment for assembly on new virions. Just if the membranous organelles are considered, CMV with its eighty gene products changes the organizational network of over three thousand cellular proteins to provoke the rearrangement of the membrane system. Based on this simple example, the presentation included the contemporary challenges of the cell biology research of viral infection focused on dealing with such a massive number of possible interactions and resolving these interactions. In the case of the SARS-CoV-2 virus, which also adapts the cell for its replication, the number of these interactions and the extent of cell rearrangement is far lower. Nevertheless, even on this far smaller scale, interactions are incredibly complex. To address these issues, the presentation included a simplified overview of the SARS-CoV2 life cycle at the level of infected cells, possible receptors for the virus entry, cellular sites of viral RNA replication, and biochemical mechanisms by which SARS-CoV2 inhibits the antiviral response of the cell and thereby weakens the host's non-specific immune response. The SARS-CoV2 replication scheme was used to explain the possible goals of antiviral action and display all antiviral drugs used so far to combat Covid-19 infection. By now, efforts in applying antiviral medications against SARS-CoV2 have been mainly focused on targeting the individual viral proteins and proteins of host cells needed for virus entry into the cells. In the final part of the lecture, the author presented results of its own studies on CMV in which antiviral effects are achieved by inhibition of the cellular phosphoinositide production, which blocked replication of CMV DNA. Phosphoinositide depletion had a similar impact in cells infected with the SARS-CoV2 virus. Such research shows that it is essential to conduct in-depth studies of cellular processes that contribute to the progression of viral infections and that disruption of cellular processes can also achieve antiviral effects. Since many drugs in use hamper cellular processes, it is also possible to found options for antiviral action and treatment among existing drugs.

**Vanda Juranić - Lisnić** (Medical Faculty, Rijeka) gave an insight to the pathophysiological aspects of SARS-CoV-2 infection. Epidemiological data on the global level are underlining the enormous number of deaths, but also the high prevalence of post-COVID changes in health, functional and work capacity, as well as on the quality of life. These topics are linked to the development of vaccines and the importance of broad vaccination. Within the overall program of the Symposium, this presentation of methodology and principles in the development of antiviral vaccines brought an important dimension and significantly contributed to the understanding of the area. As the head of the Crisis Staff of CHC Rijeka **Martina Pavletić** presented the post-COVID period from her personal and professional experience. She was a key person who in cooperation with the team of the Centre for Proteomics of the Medical Faculty in Rijeka (Vanda Lisnić Juranić and Stipan Jonjić) established in CHC Rijeka first laboratory for molecular diagnostics within the emergency medical service. In his lecture, **Alen Protić** (Medical Faculty, Rijeka) presented in detail the clinical features of the most complex forms of SARS-CoV-2 pneumonia with severe respiratory insufficiency, clinical conditions that are frequent associated, as well as the holistic approach to the treatment of most demanding patients. Special attention was given to the methods and protocols of respiratory support in these patients, and to other complementary therapeutic measures. The exceptional heterogeneity of post-COVID symptomatic patients certainly represents one of the key challenges in current routine work in pulmonology.

**Ljiljana Bulat Kardum** (Medical Faculty, Rijeka) summarized the existing knowledge, personal, institutional and international experiences and highlights the need for high individualization of diagnosis and treatment. Long-term changes in the lungs and respiratory failure with a significant impact on the quality of life after the acute phase of SARS-CoV-2 infection are presented in detail by **Igor Barković** (Medical Faculty, Rijeka). According to the

presented data, patients after Severe Acute Respiratory Syndrome (SARS) have some similarities with Middle East Respiratory Syndrome (MERS). They have a long-term respiratory complications prevalence of 30%, although after one year only 10% of them have changes in the lung parenchyma that can be objectify with modern imaging methods, at first by computed tomography (CT).

Modern imaging techniques, primarily CT, are a key diagnostic tool in the acute phase of COVID infection, but also in the further monitoring and guidance of treatment in these patients. **Melita Kukuljan** (Medical Faculty, Rijeka) emphasized the angiocentricity of pathophysiological changes in COVID and post-COVID patients, the frequency of thromboembolic events and local thrombotic complications in the lungs, as well as the microangiopathic specifics of this new disease. Through citations from recent literature, but also illustrating by examples from her personal and institutional practice, she argued number of possible variants of changes in the lung parenchyma. It is ranging from CT findings known as "ground glass", regional consolidations, peribronchial and perivascular tissue thickening, reticulation, bronchiectasis, occurrence of nodular formations, pulmonary septal thickening, to a number of rare changes of open specificity and sensitivity within COVID and post-COVID clinical cases.

The World Health Organization declared 2020. the World Year of Nurses / Technicians and Midwives before anyone could have guessed that this year would be the beginning of this epochal pandemic that would bring new, huge challenges to these professions. **Snježana Juričić** (Clinical Hospital Center, Rijeka) spoke on this topic, and through statements from the scientific literature, but also experiences at the level of CHC Rijeka presented the key role of nursing during the COVID pandemic. This is emphasized through the special organization of work, new protocols, methods and procedures, but also illustrated by the unexpectedly high level of physical and emotional involvement of nurses in the functioning of the health system during the COVID pandemic. Some available research emphasized important reflections of the pandemic on private lives and the emotional status of nurses and technicians. New knowledge and competencies, provided systematic education and gained experience for all positive aspects of the pandemic, which has made great strides in the professional and scientific field of nursing. In addition to SARS-CoV-2 infection, in pandemic circumstances the health system was faced with a number of tasks in the organization and implementation of health care for non-COVID patients also. Clinical research, guidelines and procedures from the organization of health care institutions with an emphasis on post-COVID protocols for the control of nosocomial infections and the functioning of health care systems in the "new normality" were presented by **Morana Magaš** (Faculty of Health Sciences, Rijeka).

Cardiovascular involvement represents a significant portion of clinical manifestations, and includes some important predictors of outcome in patients during and after SARS-CoV-2 infection. This includes the area of myocardial injury whose pathophysiology is extremely complex and in which there is not yet a precise quantification of the contribution of individual components of systemic and local pathological events. Distinguishing the inflammation and / or disproportion between the needs and availability of oxygen as mechanism responsible for myocardial injury from viral myocarditis, the presentation of fulminant forms and a review of available scientific evidence within this area were all presented by **Alen Ružić** (Medical Faculty, Rijeka**).** The lecture included new insights and attitudes of international expert teams related to the treatment of acute coronary syndrome in COVID patients and particularly raises the question of the role of fibrinolytic therapy and delayed endovascular procedures when possible. An extremely significant area of thromboembolic events in the circumstances of COVID infection with accompanying complex reactions of the immune and coagulation systems was clearly and broadly presented by **Luka Zaputović** (Medical Faculty, Rijeka**).** Patients with pre-existing cardiovascular diseases and / or high cardiovascular risk profile represent the most at-risk group for the development of severe clinical forms of COVID infection and were at highest risk for adverse outcomes. Recent observational studies have shown that SARS-CoV-2 virus infection is statistically significantly associated with the occurrence of atrial fibrillation. The complexity of the area is underscored by the fact that the risk factors for the development of severe forms of COVID-19 infection overlap with the risk factors for thromboembolic events. Also, epidemiological studies have indicated concomitantly above-average high risks of COVID-19 infection and thromboembolic events in elderly and less mobile patients with special emphasis on those staying in nursing homes or social care facilities. The established pathophysiological mechanisms in COVID-19 infection include a hypercoagulable state with the high incidence of deep vein thrombosis, pulmonary embolism and other thromboembolic events.

Lectures from the scientific area of neuroscience and neurology have followed the excellent lectures in cardiology. First was **Nenad Bogdanović** (Karolinska Institutet, Stockholm, Sweden), who held an insightful lecture about the cognitive problems that can follow an active COVID-19 infection. Most of the talk was focused on the current knowledge of COVID-19 neurotropism and the way systemic inflammation can contribute to neurodegenerative processes in the central nervous system. The conclusion was that there is a strong need to identify neurological damage as a long-term consequence of COVID-19 infection in patients, as is hypothesized for other neurotropic viruses.

In an excellent lecture **Paolo Manganotti** (University Medical Hospital, Trieste, Italy) on the topic of peripheral neurological symptoms in the post-COVID-19 era focused on the potential of COVID-19 virus to induce autoimmune reactions, and thus influence the onset of classical peripheral nervous system autoimmune diseases such as Guillain-Barre syndrome and Miller-Fisher

syndrome. One of the key points was that there is a challenge of diagnosis in these patients as most clinical neurophysiological diagnostic methods require close contact with the patients, which is not possible in acute COVID-19 infections.

Cerebrovascular incidents in the post-COVID-19 time was the focus of a lecture by **Zdravka Poljaković** (University Hospital Zagreb, Croatia). The audience listening this lecture could hear interesting findings, such as that the incidence of stroke in COVID-19 patients was quite low, albeit it is followed with higher mortality than in patients without COVID-19. Interestingly, small vessel disease strokes and microhemorrahages occured more frequently in COVID-19 patients, as well as cases of cerebral sinus thrombosis and PRESS. Finally, professor Poljaković pointed out that there can be non-specific MRI changes in COVID-19 patients, whose impact is yet to be elucidated for now.

The symposium was closed with a riveting lecture from **Vladimira Vuletić** (Medical Faculty, Rijeka) on the topic of movement disorders and the post-COVID-19 neurological syndrome. The lecture was focused on the similarities between the COVID-19 infection and certain neurodegenerative diseases like Parkinson's disease, with regards to early symptoms such as anosmia. The talk covered several interesting case reports of patients who developed complicated parkinsonian syndromes at the time of COVID-19 infections. The development of a Post COVID Neurological Syndrome (PCNS) was also a focus of the talk, with examples of patients developing a certain "COVID brain fog" and various neurological symptoms, such as headache, problems with smell and taste and dizziness, in the post-COVID-19 period. The lecturer concluded that we need additional studies to confirm or refute the trigger effect of SARS-CoV-2 on the neuroinflammatory and neurodegenerative processes leading to the development of parkinsonian symptoms.

The symposium was closed by an interesting round table discussion chaired by professor **Nenad Bogdanović**, where all lecturers had an opportunity to answer numerous questions by the audience and discuss the topics of their presentations with peers.

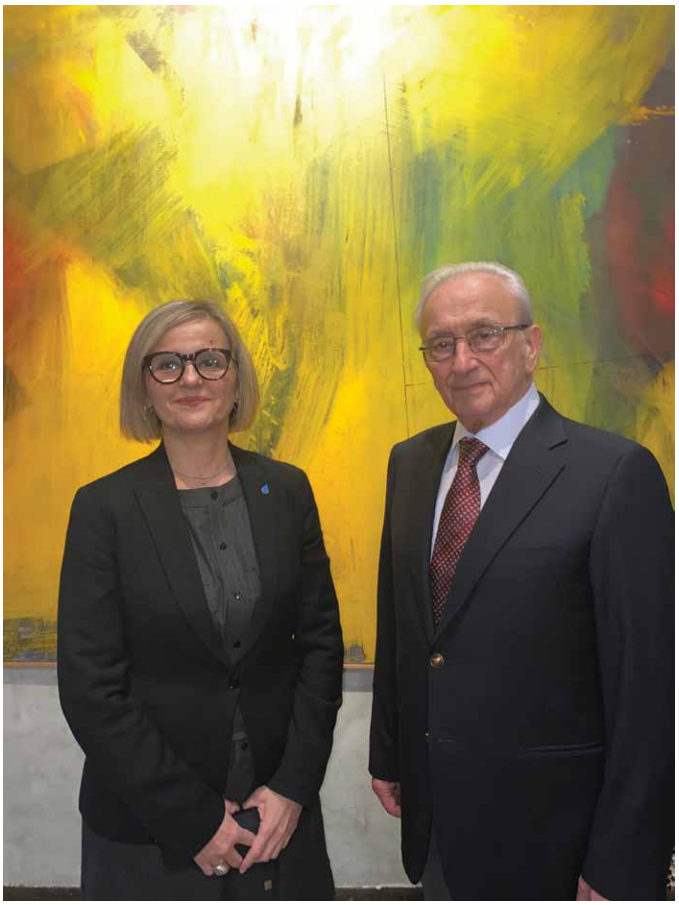

*Figure 2. Co-chairmen of the Program Committee of Rijeka COVID-19 symposia: Snježana Prijić Samaržija and Daniel Rukavina*

## References:


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