

INTERNATIONAL SEMINARS ON PLANETARY EMERGENCIES

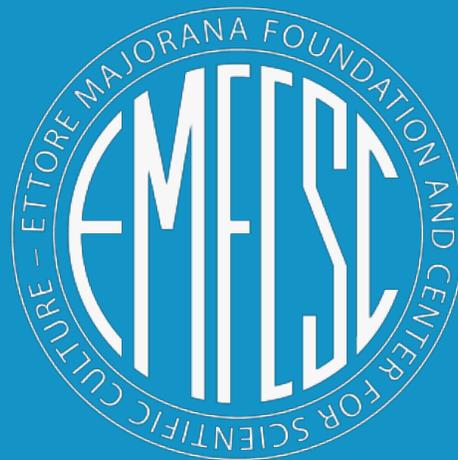
Executive Summary Plenary Report

56th Session

Chairman: A. Zichichi

Co-Chairman: C. Galbiati

8th – 14th August 2024



56th Session of the International Seminars on Planetary Emergencies Executive Summary

Overview

The 56th session of the International Seminars on Planetary Emergencies at the Foundation Ettore Majorana and Centre for Scientific Culture¹ (FEM) took place between 10-13 August 2024 in Erice, Sicily. The Seminars began in 1981, in midst of the Cold War. Each year, nuclear physicists, and advisors to leaders of the most powerful nations had the opportunity to freely exchange ideas and have discussions, at times very heated, thinking about the possible benefits in finding room for positive collaboration among nations that were on the brink of war. One significant result of those discussions was the historic Seminar in August 1987, where Professor Zhou Guang Zhao (Scientific Advisor to Premier Deng Xiaoping), Professor Edward Teller (Scientific Advisor to President Reagan), Professor Eugenij Velikhov (Scientific Advisor to President Gorbachev) and Professor Antonino Zichichi (Chairman of the International Committee 'Science for Peace', President and Founder of FEM), reached an Agreement for International Scientific Collaboration East-West-North-South without Secrecy and without Frontiers.

The Seminar this year had eight sessions in which 98 scientists, from 22 nations, participated and spoke. The following topics were discussed among a multi-disciplinary assembly of scientists, policy analysts and other experts:

- managing international conflicts and arms control,
- re-emerging infections and neurological diseases,
- the biological and social factors underlying metabolic and neurological diseases,
- children's health,
- pollution and the water crisis,
- combating wild-fires,
- climate geoengineering,
- defense against cosmic objects,
- disruptive impacts of solar storms,
- risks and challenges of artificial intelligence,
- the power sector and the energy transition.

The key messages of each of these eight sessions are summarized below.



Professor Zhou Guang Zhao (Scientific Advisor to Premier Deng Xiao Ping), Professor Edward Teller (Scientific Advisor to President Reagan), Professor Antonino Zichichi (Chairman of the International Committee 'Science for Peace') and Professor Eugenij Velikhov (Scientific Advisor to President Gorbachev), shaking hands after reaching the Agreement for International Scientific Collaboration East-West-North-South without Secrecy and without Frontiers.

¹ <https://ettoremajoranafoundation.it/>

Session 2 – Emerging/Re-emerging Infections and Neuronal Diseases

Session Chairman: Franco Maria Buonaguro (Chairman *Medicine and Biotechnology PMP*)

Speakers: Franco M. Buonaguro⁸, Ishwar Gilada⁹, Sofie Nyström¹⁰, Felice Iasevoli¹¹, Emanuele Buratti¹², and Rino Rappuoli¹³

Introduction

In the wake of the unexpected COVID pandemic, the scientific and healthcare community is looking for new preparedness strategies in terms of diagnostic, preventive and therapeutic tools. The pandemic event has shown the inability of the healthcare system to deal with a rapidly evolving airborne infectious disease that can overcome the quarantine approach with isolation of symptomatic infected patients, as transmission also occurs from subjects without respiratory symptoms (including the absence of cough) and without fever. The pandemic situation has also been aggravated by the difficulty of inducing effective and persistent herd immunity, capable of slowing down the rate of transmission, which can only be achieved for coronavirus infections with multiple vaccination cycles, in addition to masks and social distancing. Furthermore, the need for hospitals that can rapidly adapt to clinical needs has become evident, in particular the difficulty of hospitals to rapidly increase the number of intensive care units with oxygen masks to overcome the two-three weeks of respiratory failure. Finally, the speed of development of adequate diagnostic and therapeutic tools to identify people with viral infections to be quarantined and treated with antivirals and/or monoclonal antibodies.

COVID and Long-COVID issues, Franco Maria Buonaguro and Ishwar Gilada focused on the initial global difficulty in managing the pandemic, particularly in low- and middle-income countries, where in addition to limitations in diagnostic reagents, the limited availability of oxygen-supported intensive care units was a critical limitation. Furthermore, the country's economy did not allow for an appropriate population-based vaccination program, in the context of a high burden of infectious diseases, including HIV and multidrug-resistant TB.

During the current low-rate endemic COVID infection, the long-COVID disease is becoming a critical problem. Long COVID or long-haul COVID is a group of health problems that persist or develop after an initial period of COVID-19 infection. Symptoms can last for weeks, months or years and are often debilitating¹. The World Health Organization defines long COVID as an infection that begins three months after the initial COVID-19 infection, but other agencies define it as an infection that begins four weeks after the initial infection. Long COVID is characterized by a large number of symptoms that sometimes disappear and then reappear. Commonly reported symptoms of long COVID are fatigue, memory problems, shortness of breath, and sleep disorders.

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¹¹ Associate Professor, Department of Neurosciences & Reproductive Sciences, "Federico II" University, Naples, Italy.

¹² Scientific Coordinator & Group Leader of Molecular Pathology, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy.

¹³ Scientific Director of Fondazione Biotechnopolo di Siena and National Pandemic Center, CNAP, Siena, Italy.

Several other symptoms may also occur, including headaches, mental health issues, loss of smell or taste, muscle weakness, fever, and cognitive dysfunction. Symptoms often get worse after mental or physical efforts, a process called post-exertional malaise. There is a large overlap in symptoms with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)².

The causes of long COVID are not yet fully understood. Hypotheses include lasting damage to organs and blood vessels, problems with blood clotting, neurological dysfunction, persistent virus or a reactivation of latent viruses and autoimmunity. Diagnosis of long COVID is based on (suspected or confirmed) COVID-19 infection or symptoms—and by excluding alternative diagnoses. Estimates of the prevalence of long COVID vary based on definition, population studied, time period studied, and methodology, generally ranging between 5% and 50%³. Prevalence is less after vaccination. Risk factors are higher age, female sex, having asthma, and a more severe initial COVID-19 infection. As of August 2024, there are no validated effective treatments¹. Management of long COVID depends on symptoms. Rest is recommended for fatigue and pacing for post-exertional malaise. People with severe symptoms or those who were in intensive care may require care from a team of specialists. Most people with symptoms at 4 weeks recover by 12 weeks. Recovery is slower (or plateaus) for those still ill at 12 weeks. For a subset of people, for instance those meeting the criteria for ME/CFS, symptoms are expected to be lifelong. Globally, over 400 million people have experienced long COVID. Long COVID may be responsible for a loss of 1% of the world's gross domestic product³.

Several Funds have been made available for research programs by major health institutions to identify the pathogenic cause of this syndrome and develop the appropriate therapy in particular the NIH Recover project, the European Commission, and the World Health Organization. The data available so far support the importance of inflammation and immune and autoimmune response in the development of Long-COVID and PASC (post-acute consequences of SARS-CoV-2 infection). Neuro-PASC, including chemo-fog state (present in cancer patients treated with chemotherapy and even CAR-T therapy) and cognitive impairment have been associated with auto-immune status⁴ and cytokines/chemokines CSF (Cerebrospinal Fluid) imbalance including CCL11⁵.

Connecting the dots between virus amyloids and neurodegenerative diseases. Sofie Nyström reported a further COVID-related neurological issue: specific fragmentation of the spike (S) protein can produce peptides, characterized by the property of precipitating and generating amyloids (amyloidogenic peptides)^{6,7}. The full-length folded Spike-protein did not form amyloid fibrils, but amyloid-like fibrils with evident branching were formed during 24-hour co-incubation of the S protein with the protease neutrophil elastase (NE) in vitro. NE efficiently cleaved the S-protein, making the exposure of amyloidogenic segments and accumulation of the amyloidogenic peptide 194–203, part of the most amyloidogenic synthetic spike peptide. NE is overexpressed at inflamed sites of viral infection. These data propose a molecular mechanism for potential amyloidogenesis of SARS-CoV-2 S-protein in humans facilitated by endoproteolysis. The prospective of S-protein amyloidogenesis in COVID-19 disease associated pathogenesis is important to understand the disease and long COVID-19. In particular, such results showed that the spike fragments can contribute to anomalous coagulation, not sensible to heparin treatment, and accelerate the neurological process characterized by fibril formation as in Alzheimer and Parkinson disease^{8,9}.

Circulating biomarkers, genetic signatures and neuroimaging correlates of neuronal damages in acquired and congenital neurological and behavioral disorders. Felice Iasevoli reported the link of neurodegeneration and psychiatric disease (i.e. schizophrenia) to SARS-CoV-2 infections^{10,11} and current innovative approaches through the analysis of circulating brain vesicles. Genetic and epigenetic alterations involved in DISC-1 based amyloid-like fibrils' generation¹², misassembling of DISC-1 in specific areas of brain^{13,14} and the interference with dopamine metabolism¹⁵ have been previously reported. The intersection of COVID-19 and schizophrenia has attracted significant attention due to the pandemic's impact on mental health, particularly in individuals with pre-existing psychiatric conditions. In a group of studies from Felice Iasevoli's staff, the impact of COVID-19 pandemics on mental health of multiple patients' samples has been delineated^{16,17}, including the first study with original data on the level of COVID-19-associated distress in severe mental disease patients¹⁸. More recent studies have highlighted the impact on brain functions of putative long COVID, including the occurrence of psychiatric disturbances. Research has identified several circulating biomarkers that are altered in COVID-19 patients, which may contribute to neurological complications, including cognitive dysfunction and potential exacerbation of psychiatric disorders such as schizophrenia¹⁹. Proteins like Glial Fibrillary Acidic Protein (GFAP), Neurofilament Light Chain (NfL), and inflammatory cytokines (e.g., IL-6, TNF- α) have been significantly altered in COVID-19 patients. These biomarkers are associated with central nervous system (CNS) function and may indicate neuronal damage or inflammation linked to cognitive impairment. Furthermore, specific microRNAs (miRNAs), including miR-146a and miR-155, have shown dysregulation in COVID-19 patients²⁰. These miRNAs are implicated in neuroinflammatory responses and may serve as prognostic indicators for cognitive dysfunction following infection²¹.

Among patients with severe mental disorders, schizophrenia patients were at the higher risk of detrimental consequences of COVID-19 pandemics and long COVID effects, due to both biological and social factors²². Indeed, it has been reported that schizophrenia pathophysiology may involve neuroinflammatory lesions, at least in the early stages of neurodevelopment, including disruption of DISC-1-mediated functions. These putative neuroinflammatory damages may overlap with the inflammatory responses seen in COVID-19. Cytokines such as IL-1 β and IL-6 are elevated during psychotic episodes and may also be increased in COVID-19 cases, suggesting a shared inflammatory pathway that could exacerbate symptoms in vulnerable populations²³. Moreover, it has been hypothesized that the neuroinvasive potential of SARS-CoV-2 might increase the risk of psychosis in individuals with schizophrenia.

This is supported by findings that show elevated levels of inflammatory markers in both conditions, indicating a possible link between viral infection and exacerbation of psychiatric symptoms²⁴. Understanding the relationship between circulating biomarkers, COVID-19, and schizophrenia may be crucial for developing targeted interventions. Circulating biomarkers could serve as valuable tools for predicting cognitive outcomes and managing mental health issues post-COVID-19 for multiple reasons: i) monitoring levels of inflammatory cytokines might help assess the risk of cognitive decline or psychotic episodes in affected individuals; ii) identifying specific biomarkers that correlate with disease severity can inform therapeutic strategies aimed at mitigating both neurological and psychiatric complications arising from COVID-19. As a general take-home message, clinicians should consider the combined effects of physical health (COVID-19) and mental health (mostly in schizophrenia cases) when treating patients during

and after the pandemic. This includes regular assessments of circulating biomarkers to tailor interventions effectively. The interplay between COVID-19 and schizophrenia through circulating biomarkers underscores the need for integrated healthcare approaches that address both physical and mental health challenges posed by these conditions. These considerations strengthen the idea that more research should be undertaken for expanding our knowledge on the topic.

Identifying fluid biomarkers for neurodegenerative diseases. Emanuele Buratti reported on the TAR-DNA binding protein (TDP-43) an amyloidogenic protein which plays a major pathogenic role in patients affected by amyotrophic lateral sclerosis (ALS), and for such reason with high potentiality for the early diagnosis of such disease still requiring standardized biomarkers²⁵. TDP-43 could play some role also in the neurodegenerative disorders associated with S-protein amyloidogenic peptides^{26,27}, which are mitigated by the TREM2 interaction²⁸. From a health and early diagnosis perspective, it therefore becomes imperative to find a way to observe fibril formations or other forms of alterations in patient's biofluids. In fact, although post-translationally modified forms of TDP-43 (pmTDP-43) can be detected in ALS brain and spinal cord postmortem, current bioassays have shown variable performance in quantifying these species in biofluid samples.

To address this gap, our lab together with a USA-base foundation called TargetALS, we have focused on developing novel ALS blood-based biomarker assays that are specific, sensitive, reproducible, affordable and minimally invasive, and are based on analyzing the blood platelet component. Platelets express a large number of neurotransmission-related proteins and contain mitochondria as well as pre-mRNAs, splicing factors and ribosomes to subserve signal-dependent RNA processing and de novo protein synthesis. We have therefore hypothesized that TDP-43 could be involved in these activities in platelets in a manner that parallels its known regulation of RNA processing and translation in situ in neuronal synapses. The detection of disease-related RNA-level changes in platelets and synapses is also likely to reflect nuclear hypofunction of TDP-43 in megakaryocyte and neuronal nuclei, respectively. We have then used transcriptomic analyses to expose possible disease-related differences in TDP-43-associated RNAs. This complementary approach provides the further advantage that RNAs can be differentially detected and quantified with high sensitivity. These results have been recently published²⁹ and have confirmed that indeed platelets could represent an excellent substrate for novel biomarker analysis which could not just be limited to ALS but also to all the other neurodegenerative diseases that could have connection with Alzheimer and Parkinson disease.

Emerging and re-emerging pandemics preparedness. Rino Rappuoli highlighted the necessity of global preparedness for future pandemics. The health and scientific gaps highlighted by the emergence of the pandemic due to the SARS-CoV-2 infection, has led to the establishment of CEPI, the Coalition for Epidemic Preparedness Innovations³⁰, a global partnership focused on the 100-day strategy for the characterization of new epidemic pathogens and the development of vaccines, and a greater involvement of policy makers at the national and international levels, including the G7 and G20. Within the context of preparedness for emerging and re-emerging diseases, Rino also highlighted the role of the scientific community in monitoring communicable diseases at high risk of epidemic outbreaks and in supporting new scientific developments to accelerate the production of appropriate preventive (e.g., vaccines) and therapeutic (immune and antiviral tools) strategies, as well as innovative regulatory

procedures to safely accelerate and standardize approval procedures. In this regard, he highlighted the role of CNAP, the Italian National Center for Pandemic Preparedness³¹, funded in 2022 by the Italian government and IUMS, the International Union of Microbiological Societies³². For this reason, the overall final message of the session was that scientific societies, with adequate government support, can significantly contribute to the development of effective preparedness strategies.

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 31. CNAP, The National Pandemic Center <https://www.biocnopol.it/en/national-pandemic-center-cnap/>.
 32. IUMS, The International Union of Microbiological Societies <https://iums.org/>.

Appendix 1: Agenda

INTERNATIONAL SEMINAR ON PLANETARY EMERGENCIES 56th Session

Erice, 8_14 August 2024

Paul A.M. Dirac Lecture Hall – Patrick M.S. Blackett Institute

Thursday 8 August 2024

Arrivals

20:00 Dinner

Friday 9 August 2024

09:30 PMP Meetings

20:00 Dinner

Saturday 10 August 2024

09:30 Welcome and Introductory Remarks:

- Fabrizio Zichichi (introducing Antonino Zichichi)
- Antonino Zichichi (via video)
- Mrs. Daniela Toscano Pecorella, Mayor of the Municipality of Erice, Italy
- H.E. Rev. Msgr. Pietro Maria Fragnelli, Bishop of Trapani, Italy
- Hon. Roberto Di Mauro, Deputy for Energy and Public Utilities of the Sicilian Region, Palermo, Italy
- Dr. Fabio Ciciliano, Head of the National Department of Italian Civil Protection, Presidency of the Council of Ministers, Rome, Italy

10:30 Keynote Address: Cristiano Galbiati

11:00 Coffee Break

11:30 Session 1: Managing international conflicts and arms control

Session Chairman: William Barletta, *Chairman Mitigation of Catastrophic Risks PMP*

11:30 Tariq Rauf: *The growing threat of nuclear weapons*

11:45 William Barletta: *New Nuclear Delivery Systems*

12:00 Richard Lanza: *Risk Assessments and Nuclear Arms Control*

12:15 Karen Hallberg: *Conflict management and the Pugwash process*

12:30 Discussion

13:30 Lunch

15:30 Session 2: Emerging/Re-emerging infections and neuronal diseases

Session Chairman: Franco Maria Buonaguro, *Chairman Medicine and Biotechnology PMP*

15:30 Franco M. Buonaguro: *Long COVID disaster and update of current outbreaks/epidemics*

15:40 Ishwar Gilada: *Avian Influenza and COVID pandemic update in India*

16:00 Sofie Nyström: *Connecting the dots between virus amyloids and neurodegenerative diseases*

16:15 Felice Iasevoli: *Circulating biomarkers, genetic signatures and neuroimaging correlates of neuronal damages in acquired and congenital neurological and behavioral disorders*

16:30 Emanuele Buratti: *Identifying fluid biomarkers for neurodegenerative diseases*

16:45 Rino Rappuoli: *Emerging and re-emerging pandemics preparedness*

17:00 Discussion

18:00 Adjourn
20:00 Conference Dinner

Sunday 11 August 2024

09:30 Session 3: The power market and the energy transition

Session Chairman: Carmine Difiglio, *Chairman Energy PMP*

09:30 Carmine Difiglio: *Introduction, Energy security and the power sector*

09:40 Peter Hartley: *A costly transition*

10:00 Alessandro Clerici: *The electrical power system within the global energy trends*

10:20 Ashutosh Shastri: *Walking the tightrope of regulation and markets for a low carbon energy transition- emerging lessons learn from the UK/European Experience*

10:40 Teresa A. Gorman: *Can the US EPA mandate net zero?*

11:00 Discussion

11:45 Coffee Break

12:15 Session 4: Managing International Conflicts

Session Chairman: William Barletta, *Chairman Mitigation of Catastrophic Risks PMP*

12:15 Nichole Argo and Lydia Wilson: *Psychological pathways to international conflict*

12:35 Bilal Ayyub: *Modeling Complexity of Conflicts including Economic, Structural and Psychological Perspectives*

12:50 Francesca Giovannini: *Application to NATO, Russia and Ukraine*

13:05 Tariq Rauf: *Rapporteur's Report – Paths Forward in the Conflict in the Middle East*

13:15 Discussion

14:00 Lunch

16:00 Session 5: Perspectives, Risks and Challenges of Cyber Security and AI

Session Chairman: Axel Lehmann, *Chairman Future of Cyber Security and AI PMP*

16:00 Axel Lehmann: *Introduction*

16:05 Hamadoun Toure: *Current Status and Associated Challenges of AI*

16:17 Sun Kun Oh: *Challenges to AI and its Global Position from an Asian Perspective*

16:29 Arthur Miller: *The Brave New World of Machines that Make Art, Create Prose and also Think*

16:41 Pavan Duggal: *Emerging Legal and Policy Trends Impacting AI and Generative AI*

16:53 Anna Pouliou: *Immediate Privacy and Cyber Risks from AI and Countering Legislation*

17:05 Alex Ntoko: *Advanced Information Management System and Artificial Intelligence*

17:17 Pier Paolo Menchetti: *AI in Health*

17:30 Discussion

18:00 Adjourn

20:00 Conference Dinner

Monday 12 August 2024

09:30 Session 6: Global wildfire emergency and other threats to civil infrastructures

Session Chairman: William Barletta, *Chairman Mitigation of Catastrophic Risks PMP*

09:30 Jim Lambert & Bilal Ayyub: *Systems analysis of wildfire emergency*

09:45 Ranger Dorn: *Erice wildfire scenarios*

10:30 Wildfire discussion

10:45 Robert Rosner: *Solar Geoengineering*

11:05 Anatoly Zaitsev: *Update on defense against cosmic threats*

11:20 John Organek: *Solar Storm Disruptions of Power & Communications*

11:30 Coffee Break

12:00 Session 7: Pollution and Water Crisis

Session Chairman: Lorne Everett, *Chairman Pollution and Water Crisis PMP*

12:00 Dan Stephens: *Groundwater Contamination: A History of Unintended Consequences*

12:20 Shammy Puri: *Scarcity Plus Global Water Pollution-A Ticking Time Bomb?*

12:40 Vijay Singh: *Water Security in the World's Most Populated Country, India*

13:00 Hugo Loaiciga: *Water and Energy Provision in a Changing World: Prospects for the 21st Century*

13:20 Discussion

14:00 Lunch

16:00 Session 8: Biological and social developmental factors in the epidemic of metabolic and neuro-behavioural diseases

Session Chairmen: Stefano Parmigiani & Fred vom Saal, *Chairmen Environment and Health PMP*

16:00 Christopher Kassotis: *Environmental contaminants (and mixtures), developmental disruption and neurometabolic health effects*

16:20 Mary Gilbert: *Thyroid hormone insufficiency mediates important adverse effects of chemical pollution and nutritional deprivation on brain development*

16:40 Jose Hernandez: *Prematurity and low birth weight as risk factors for obesity in early childhood and adulthood*

16:55 Steven Andrew Haas: *The Wounds they Carry: The Long-Term Impacts of Childhood Exposure to War*

17:20 Discussion

18:00 Adjourn

20:00 Gala Dinner with Sicilian Folk Music

Tuesday 13 August 2024

10:00 Wrap-Up Session (press will be present)

10:00 Fabrizio Zichichi, Session Moderator

10:10 PMP Chairs' Reports

11:00 Fabrizio Zichichi, *Plenary Discussion of PMP Priorities with PMP Chairs' Panel*

12:00 Cristiano Galbiati, *Closing Remarks*

12:30 Fabrizio Zichichi, *Plenary Discussion – Synopsis: 2024 Seminars and Plans for 2025*

13:30 Adjourn Plenary Sessions/Lunch

19:00 Dinner

Wednesday 14 August 2024

Departures