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Message from the ESS President

Dear Colleagues, members, students and friends of the ESS,

It is told that our world is experiencing the biggest challenge since the Second World War; the only difference is that the enemy is nowadays invisible and that we are not separated into attackers and defenders but all are defenders. The COVID-19 pandemic has imposed social separation but has given us one major opportunity: to understand that in combat against this invisible viral enemy only pure science dissected from any personal motives can lead humanity to victory.

I am proud to chair the European Shock Society (ESS) whose members have been in the research and clinical battle forefronts against COVID-19 during the last year. Under the leadership of Marc Magele and Marcin Osuchowski, the ESS executive board published one of the first global reviews on SARS-CoV-2 and COVID-19 in the Shock journal (October 2020); the review offers an updated knowledge, inspires future research but, most importantly, raises awareness that the fight against SARS-CoV-2 needs to be led by all clinical and research experts on a daily basis. In this fight, everyone plays a major role and no single person can win without the help of the others.

Taking it from there, ESS progressed and, in collaboration with the European Group of Immunology in Sepsis, has produced two most recent reviews to provide guidance on pathophysiology and required modalities of basic research for COVID-19.

The activities of ESS during the difficult era of the pandemic could have never been so successful without the contribution of all members of the society and the members of the board. This devotion has recently led to the development of our new website – mainly thanks to the dedication of our secretary general, Andrea Szabó.

ESS is a wonderful world of people who are well aware how to stay scientifically and sentimentally united despite the restrictions in the physical person-to-person communication of our times. I wish that this unity paves the way to resolution of the new everyday difficulties that we have been facing since 2020.

Evangelos J. Giamarellos-Bourboulis
President of the European Shock Society

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Message from the ESS General Secretary

Dear ESS members,

First of all, I do hope that this newsletter reaches you, your family and your friends in good health and that you tolerate the pandemic-induced stress and new research and educational challenges well. It is always inspiring to experience how active the members of our society are when fighting on the battlefields of either an ICU or research bench by performing greatly modified daily duties during the present global health crisis. These hard times require great flexibility from all of us and I greatly acknowledge the continuous commitment of our members to fulfill the main aims of our Society. As a result of a common action of the ESS executive committee, a review paper entitled *"SARS-COV-2/COVID-19: evolving reality, global response, knowledge gaps, and opportunities"* was published in the October 2020 issue of the Shock journal. Despite the quick-evolving pandemic reality, the key messages of that review have remained valid.

During the last year, the **changes in the bylaws of ESS** (based on the decision of the General Assembly of October 11, 2019, Chania, Greece) were reported to the relevant Austrian authorities and the changes become effective (please see at our website; modifications include &18.5-9) in August 2020.

Pandemic-induced flexibility also manifested in an **online Executive Council Meeting** on October 13, 2020 with participation of Irshad H. Chaudry and Mark G. Clemens (retiring and interim Editors in Chief of Shock). The optimal date of the next ESS meeting was debated and a conclusion was reached whereby the congress president should make the final decision regarding the form and date of the next congress; this should be known in the first quarter of 2021. Issues regarding the website have also been discussed.

It is my pleasure to announce that **our website** underwent some facelift and a new mobile-friendly version was created (see also later). Special thanks to EC members **Stefanie Flohe, Borna Relja, Evangelos Giamarellos-Bourboulis, Marcin Osuchowski** and **Andreas-Barrat-Due** for their contribution by providing their own images. We are also grateful to Jon Fuller and his firm Rayzume for providing the digital services to ESS in that regard.

Global Sepsis Alliance

On the event of the General Assembly (held on October 15, 2020) of our sister society, the Global Sepsis Alliance (**GSA**), Konrad Reinhart - founder and president of GSA - stepped down and Niranjan "Tex" Kissoon was elected as the **new president**. In a letter of appreciation to Professor Reinhart, we expressed our gratitude for his lifetime achievement including establishment of GSA, World Sepsis Day/World Sepsis Declaration 2012, WHO Sepsis Resolution 2017, and WHO Global Sepsis Report 2020 as well as the organization of prestigious sepsis congresses (e.g. World Sepsis Congress, WSC Spotlight events). We also expressed our

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thanks for continuous support of our Society. We also assured the new president (Tex Kissoon) that ESS will continue the privilege of supporting the Global Sepsis Alliance and endorsing its important activities.

The European Medical Education Initiative for Advanced Bleeding Care in Trauma (**ABC-Trauma**; http://advancedbleedingcare.org/) requested renewal of **Marc Maegele, Cologne, Germany** as an ESS representative. In this alliance, an evidence-based European guideline on the early intra-hospital management of polytrauma patients is being updated. We wish Marc great success in his ongoing duty.

Finally, I thank all of you for your ongoing support and I wish to encourage you to support us by convincing your colleagues to join ESS – for their own benefit and as well as of our Society.

Yours,
Andrea Szabó

The Treasurer's Corner

Hello dear ESS team,
In the wake of the COVID-19 pandemic, we have fiscally lived a benign life since we have not incurred any substantial losses except for the expenses regarding the changes in the bylaws of ESS and a remarkable facelift of our website (kudos to the ESS secretary!). Yet, for the more bearish among us who have witnessed how quickly a liquidity can evaporate, my above statement may feel like a false comfort given that the number of our active (read: paying) members has been slightly decreasing. Well, the dwindling numbers of paying ESS members may have been caused by the most serious changes in the day-to-day life across the entire planet. These globally-resonating events definitely provoke a pause and reflection. It is definitely a moment for our former and new community members (as well as the executive ESS board) to ponder the value and benefits (professional and human alike) that can be derived from working and growing together.

Speaking of more earthy benefits: if you have failed to pay your ESS membership for 2020/21 on time, we sincerely ask you to please consider doing it now. Currently, a fixed 2-year membership fee of EUR 100 for regular members and EUR 50 for student members applies. I will send you reminders - please be kind not to ignore them as ESS existence relies on your membership.

Thank you very much, ESS folks – much appreciated!

Your treasurer,
Borna Relja

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The clinical features and experiences of COVID-19

2020 has just passed but will remain as an extraordinary historic year that hit the globe with a pandemic outbreak caused by SARS-CoV-2. By today, more than 100 mill SARS-CoV-2 cases are documented and more than 2 million have died according to worldmeters.info. COVID-19 has hit some countries harder than others, but everyone has had their everyday life changed due to different kind of restrictions and lockdowns trying to limit the spread of the coronavirus and to reduce strain on the healthcare system. Vaccination has just started and hopefully 2021 will be the year that the pandemic slowly ceases. However, SARS-CoV-2 will probably be with us for years potentially as a recurrent seasonal infection in large parts of the world like influenza.

Signs and symptoms: The ISARIC partners (International Severe Acute Respiratory and Emerging Infections Consortium) is a global federation of clinical research networks, that regularly has issued a report on aggregated data on hospitalized COVID-19 patients. By November 2020, 95966 cases had entered the database with a laboratory confirmed SARS-CoV-2 infection[1]. The most common symptoms seen at hospital admission were fever (60.2 %), shortness of breath (59.1 %), cough without sputum (38.4 %), fatigue (35.6 %) and altered consciousness (21.9 %). The three most frequent comorbidities were hypertension (46%), chronic cardiac disease (29.2 %) and diabetes (16.4 %). However, age is the most important risk factor for severe disease and death. Twenty percent required treatment at an ICU or high dependency unit (HDU) which is comparable with other reports. Although respiratory symptoms predominate, surprisingly many patients have been admitted to hospitals without requiring supplemental oxygen (>25%)[2,3], and the distribution of combination of different symptoms have been diverse (e.g., abdominal discomfort and pharyngitis in several patients). Moreover, many physicians have been baffled by the clinical picture of silent hypoxemia, which was extensively covered in the media during the initial phase of the pandemic. The disease course has not been easy to predict where some patients have recovered fast whereas others have experienced severe disease progression companioned by long lasting ICU stays, and too many patients have died.

The mortality has varied considerably in different reports[4]. It is tempting to believe that this is closely connected to the immense pressure on hospitals and healthcare systems some countries and districts have experienced during the pandemic. The ISARIC database document a mortality of 34.5% among those patients admitted to ICU/HDU. Two large pragmatic trials that have enrolled thousands of patients, The RECOVERY- and the WHO Solidarity study, refer to overall 28-day mortality of 23% and around 11%, respectively, whereas the mortality among mechanical ventilated patients were 41.1% and in between 29-37% (dependent on which study control arm), respectively[2,3]. In Norway, effective lockdown-policies were effectively introduced during the initial phase of the pandemic, which partly may explain a favorably lower ICU-mortality (18.4%) compared to other regions[5].

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COVID-19 and research: We have never witnessed such a massive research activity including several RCT as well as basic and translational studies on a specific subject as we did during 2020. A search on pubmed on *COVID-19*, limited to the year 2020, give 89350 hits. In addition, news and media have been filled with information on COVID-19, also including press release on scientific reports which sometimes never have reached publication in a medical journal. The information load has been overwhelming and difficult to sort.

Rapid clear answers to treatment questions have the potential to save thousands of lives. However, the conclusions must not be based on rumors but on large clinical trials. This requires a well-organized network, a simple setup, multi-center structure able to include enough patients quickly and to make robust conclusions on the effectiveness of various treatment options. A good example is the RECOVERY trial managing to include thousands of patients from UK in RCTs giving a clear answer on the effectiveness of dexamethasone within a few months[2]. Another example is the WHO Solidarity trial that has included patients from more than 30 different countries and provided important evidence on the lack of effect on hydroxychloroquine, lopinavir, interferon beta and not least remdesivir[3], although a smaller NIH study has suggested that remdesivir may have a potential beneficial effect in those with mild or moderate[6]. Both the WHO Solidarity and the RECOVERY trials are pragmatic in their origin, were set up fast with a primary aim to quickly conclude whether a repurposed drug was beneficial or not. The WHO Solidarity trial was initially featured by slow inclusion rate, losing some of the power of the wave's first peak, which basically can be explained by delayed approvals from national drug regulators, ethical committees and/or the different countries health ministry's[7]. Bureaucracy and over-regulation combined with lack of national and international efforts to facilitate large trials can partly explain why too many small trials not able to conclude have been conducted throughout the pandemic.

Recently, both the Remap-Cap investigators and the RECOVERY trial demonstrated that the interleukin-6 receptor antagonists, toclizumab and sarilumab in critically ill patients, reduced mortality compared to standard of care[8,9]. Based on this the National Institute of Health (US) have recently launched new guidelines, recommending the use of tociluzimab together with dexamethasone to hospitalized patients in respiratory deterioration (https://www.covid19treatmentguidelines.nih.gov/statement-on-tocilizumab/). However, this is debated, and we are still awaiting viewpoints from other guideline makers, including WHO, as of today only recommend dexamethasone given to patients with severe disease dependent on oxygen[10]. Remdesivir is approved by FDA, not by EMA, and if it by any chance should exert any effectiveness, it must be administered early in the disease course. Importantly, the beneficial effects of steroids in severe COVID-19 disease were confirmed by three other RTCs[11-13]. Finally, these studies also illustrate the need for more personalized medicine; i.e., different medications for mild/moderate as compared with severe/critical COVID-19 disease.

There is still a pressing need for large scale testing of repurposed and novel agents to provide new treatment options for patients with COVID-19. EU-Solid ACT is a flexible second-generation Adaptive Platform Trial master protocol developed in accordance with relevant stakeholders including European Medical Agency, providing a modular trial network enabling

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most, if not all, European hospitals to participate at their preferred level of commitment (https://ecrin.org/node/1869). The platform is part of EU-RESPONSE and funded by the European Union's Horizon 2020. Hopefully this trial platform can bring many European centers together in a joint effort at the tale of this pandemic, additionally develop to be the architectural basement for future pandemics and research. It is, however, also of major importance these studies also embrace and involve other parts of the world, including low-income countries.

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Andreas Barratt-Due

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Animal models in the age of COVID-19 pandemic

Many milestones in medical history rest on animal modeling of human diseases. Simultaneously, many other animal studies led medical discovery astray. What is the role and place of animal experimentation during the COVID-19 pandemic? Although the overall rate of SARS-CoV-2/COVID-19 clinical publications has vastly outpaced data produced by animal-based studies (approx. 1:16 ratio in PubMed and 1:7 in medRxi; February 2021), we experience a rapid expansion of preclinical testing aiming at: i) investigating the pathophysiology of the disease, ii) testing therapeutics and iii) vaccines. Several species were tested regarding their utility in reproducing COVID-19; the World Health Organization (WHO) currently indicates four main species as reproducible COVID-19 models: non-human primates (NHP), ferrets, hamsters and mice (**Figure 1**). Except for mice, all indicated species are susceptible as wild-type (WT). WT mice are resistant to SARS-CoV-2 infection as the viral spike protein has a minimal affinity to the murine angiotensin converting enzyme-2 (ACE2) receptor, and their use requires various genetic manipulations (either in the mouse or SARS-CoV-2).

Until recently, although all tested species displayed respiratory symptoms (including COVID-19-like pneumonia), they generally lacked hypoxemic respiratory failure, extrapulmonary

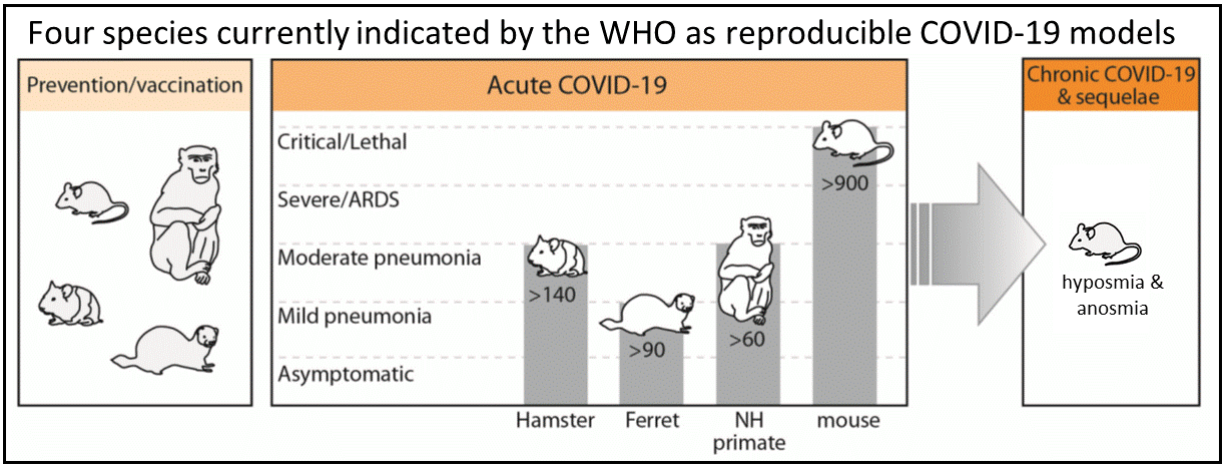

Figure 1. The number overlaid on bars depicts an approximate count of the PubMed-listed studies (including prevention, vaccination and disease model) utilizing a given species (PubMed queried in February 2021). Figure modified from Winkler et al. 2021 EBioMedicine – in press.

organ dysfunction and lethality observed in patients. This has created a translational dissonance given that the key investigative efforts have been focused on saving lives of the most severely sick COVID-19 patients – a phenotype non-existent in animals until summer of 2020. In July 2020, Jiang et al. published the first study reporting a lethal model of COVID-19 in a mouse expressing human ACE2 receptor (PMID: **32516571**). This severe phenotype was soon after repeated (by using different SARS-CoV-2/ACE2 biding adaptation approaches) in four other mouse studies (PMID: **33031744; 33257679; 32841215; 33465158**). Generation of the lethal phenotype (and some neurological sequelae) has positioned the mouse as a

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translationally attractive model for COVID-19 given that this is currently the only species covering the entire range of the disease severity (i.e. from mild to lethal). NHP (e.g. aged Rhesus macaque) that are most closely related to humans display moderate COVID-19 severity at best.

While a seemingly superb achievement, it simultaneously creates a potential investigative risk as the mouse is generally an inferior model of human airway diseases (e.g. murine monopodial vs. human trichotomous airway branching system) and this limitation is additionally aggravated with a practical inability to employ a long-term ventilatory support - the hallmark of severe COVID-19 treatment. Thus, a reflexive over-reliance on a single-species disease model may produce misleading findings that are rapidly propagated until contradicted in other species. It is therefore imperative to continue developing other non-mouse models of COVID-19 across a range of species. The tree shrew constitutes an apt example; it is a species that is phylogenetically much closer to human compared to any rodent and there is substantial evidence demonstrating its capacity to effectively model human diseases including viral infections (PMID:**28585435; 30116606; 12823622**). It is therefore not an overstatement that researchers from the developed countries (including the undersigned) tend to be biased toward species that are easily available and most commonly used (such as the mouse). While not lambasting rodent-based research it is possible that the tree shrew (and other less commonly used species) might emerge as a superior species in recapitulating various human sequelae. Upon a robust technological and organizational development to facilitate their experimental applicability (and of other non-common animals) data generated in such models might actually surpass the translational gains stemming from the mouse studies.

While the lethal and most severe COVID-19 models are a focal point, the mild-to-moderate phenotype (that currently predominates in all species) should not be reflexively rejected as inadequate. In contrast, such “light” phenotypes are investigatively very valuable given that they well-facilitate a detection of any adverse effects of tested therapeutics. In highly lethal disease models, the study design is primarily set toward observing hypothesized benefits rather than undesired complications. In the context of the animal use justification and wide awareness that in vivo findings should be interpreted with caution (especially given the infancy of the COVID-19 modeling), the emerging SARS-CoV-2/COVID-19 animal data are relatively compatible with the findings from the largest clinical trials. For example, CQ/HCQ demonstrated neither preventive nor therapeutic benefit in non-critical pneumonia in NHP (PMID: **32698191**), ferrets (PMID: **33037151**) and hamsters (PMID: **33037151**). Furthermore, remdesivir demonstrated some potential benefit in NHP (PMID: **32516797**) and mice (PMID: **32643603; 33523654**) and the same holds true for convalescent plasma and neutralizing monoclonal Abs tested (pre-and post-infection) in mice (PMID: **32643603; 32553273; 33166988**) and hamsters (PMID: **32540903**). Given the clinical uncertainty regarding the latter therapeutics, the positive animal findings should not be dismissed as unreliable but rather explored to gain knowledge why they were successful and utilize this information in optimization of subsequent human trials including endpoints, cohort selection, qualitative antibody enrichment, application routes and more.

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Animal models have also shown their great value in the development process of anti-COVID-19 vaccines. Some of the most advanced/approved including Janssen-Cilag (PMID: **32731257**), Sinovac (PMID: **32376603**), Oxford/AstraZeneca (PMID: **32731258**), Moderna (PMID: **32722908**), Pfizer/BioNTech (PMID: **33301246**) and Sinopharm (PMID: **32778225**) heavily depended on animal testing. While the key pre-clinical step typically involved vaccine efficacy testing in NHP, in at least four of those studies, immunization with the vaccine candidates was also performed in BALB/c (Sinovac, Oxford/AstraZeneca, Pfizer/BioNTech, Sinopharm), CD1 mice (Oxford/AstraZeneca) and in Wistar (Sinovac) and Sprague Dawley rats (Sinopharm). Some postulate to omit animal-based safety testing and to directly transition vaccine candidates to phase-1 trials to save time. Such an accelerated development, however, is considered very controversial by many experts as it risks exposing human recipients to: i) potential adverse effects and ii) to non-toxic but no/low-efficacy vaccines. As in case of drug testing, to increase a possibility of detecting any adverse effects during the preclinical vaccine safety testing, it is advisable to employ more than a single species.

Design of animal research for translational COVID-19 purposes should be largely aimed at supporting the preparation and execution of clinical trials. This should be done by using the entire available pre-clinical armamentarium including pathomechanistic investigations, preselection of therapeutics, identification of non-and responder subgroups, identification and optimization of endpoints. To achieve desired synergy, such a process requires knowledge on the limitations and advantages of a given model and intricacies of proper study design that maximally synchronizes with the stringent demands of the clinical-level research. Given the pressing need for a rapid understanding of COVID-19 and improvement of patient outcomes, such converging areas should be rapidly developed in a form of existing pre-clinical networks of expert-consortia with a pro-active support from funding agencies/governments (to ensure sufficient financial means) as well as ethical/regulatory committees (for expedited assessment/approval of animal studies). It appears prudent to perform a standardized multivariate testing across mild, moderate and severe phenotypes as such an approach has the best potential to assess safety and to advise on the clinical trial decision-making.

Marcin Osuchowski

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A Personalized Randomized Trial of Validation and Restoration of Immune Dysfunction in Severe Infections and Sepsis (PROVIDE): Implications for the COVID-19 pandemic

Findings on the heterogeneity of the immune responses of sepsis led to the understanding that despite similarities of clinical phenotypes, not all septic patients should receive the same treatment but this should be individualized. This personalized approach becomes even more important when it comes to adjunctive treatments that modulate the dysregulated response of the host. We traditionally believe that patients with sepsis may be divided into three types of immune responses: 1) those with overwhelming hyper-inflammatory responses (a situation mimicking macrophage activation syndrome 2) those with predominating hypo-inflammatory responses (or immunoparalysis), and 3) those with mixed features. In the context of therapeutic benefits, this classification needs to be first proven in a prospective clinical trial.

The PROVIDE trial (ClinicalTrials.gov registration NCT03332225) is the first clinical trial to cover the unmet need described above. The trial is sponsored by the Hellenic Institute for the Study of Sepsis and it is under the auspices of the European Shock Society. The trial was conducted between December 2017 and December 2019 at 14 study sites in Greece (EudraCT 2017-002171-26; approval by the National Ethics Committee 78/17; approval by the National Organization for Medicines IS 75-17). The trial had one screening step aiming to develop immune classification criteria and one intervention step aiming to deliver immunotherapy targeting the immune dysfunction pattern of participants. Adults with septic shock (by the Sepsis-3 definition) due to lung infection (community-acquired, hospital-acquired and ventilator-associated), primary bacteremia and acute cholangitis were screened for eligibility. In the first step, patients were screened on two consecutive days in order to be classified by laboratory traits into macrophage activation-like syndrome (MALS) or sepsis-induced immunoparalysis or mixed phenotype. The screening tools were serum ferritin for MALS and HLA-DR/CD14 co-expression for sepsis-induced immunosuppression. Patients diagnosed with MALS and immunoparalysis were randomized in the second intervention step into double-blind, double-dummy immunotherapy arm or standard-of-care. Patients assigned into the immunotherapy arm received treatment with either intravenous anakinra (IL-1 receptor antagonist; targeting MALS) or subcutaneous recombinant IFNγ (targeting immunosuppression). Patients assigned into the standard-of-care arm received intravenous and subcutaneous placebo treatment. Main exclusion criteria were primary and secondary immunodeficiencies and solid and hematologic malignancies.

Until June 30 2019, 240 patients were screened for eligibility. Results proved that classification into MALS may rely on ferritin; and into sepsis-induced immunosuppression on the number of HLA-DR molecules on CD-14 monocytes. MALS, immunosuppression and mixed phenotype were strata of immune activation accompanied by different outcomes. Using this classification system, we compared at the beginning of COVID-19 pandemic the immune classification of patients with community-acquired pneumonia of the PROVIDE trial with the classification of

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patients with COVID-19. We concluded that contrary to bacterial sepsis, all patients with COVID-19 who developed acute respiratory distress syndrome are classified either into MALS or into complex immune dysregulation. Patients with complex immune dysregulation resemble patients with sepsis-induced immunosuppression since they have similarly low expression of HLA-DR on circulating CD14-monocytes. However, monocytes from patients with complex immune dysregulation by COVID-19 are characterized by excessive production of pro-inflammatory cytokines whereas CD14-monocytes from patients with sepsis-induced immunosuppression are down-regulated for the production of pro-inflammatory cytokines. These findings are published in the June issue of Cell Host and Microbe (https://pubmed.ncbi.nlm.nih.gov/32320677).

Members of the Hellenic Sepsis Study Group

Evangelos Giamarellos-Bourboulis

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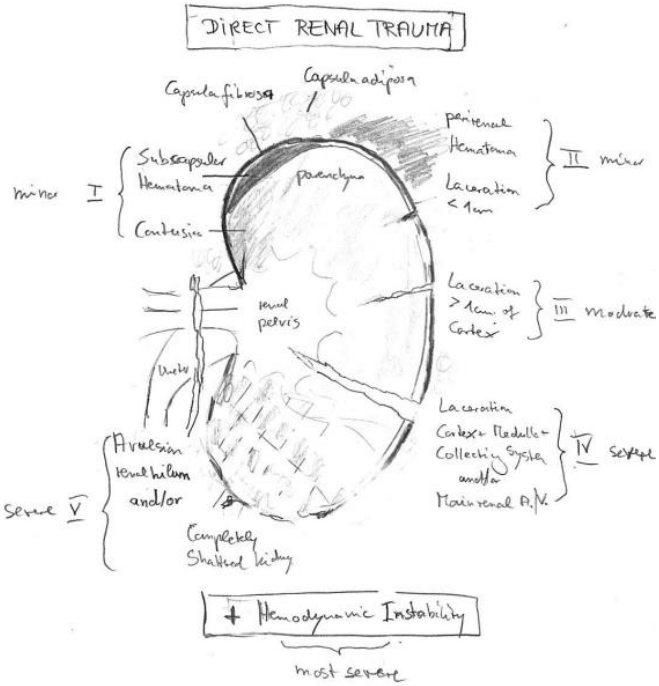
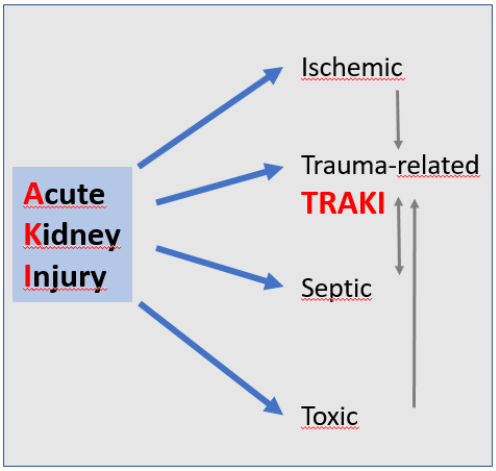
Recently published in the context of shock – TRAKI: Trauma-Related Acute Kidney Injury

by Messerer et al. Nat Rev Nephrol. 2021 Feb;17(2):91-111.

Physical trauma can hit anybody at any time. Although direct kidney injury is infrequent, development of acute kidney injury (AKI) after trauma is often seen after severe tissue trauma. Major risk factors for initiation and progression of AKI are accompanying abdominal or brain injury, (hemorrhagic) shock, rhabdomyolysis, nephrotoxic drugs, or infectious complications. Multiple immunopathophysiological mechanisms are involved; some of them are covered in the above mentioned, comprehensive review. Of note, besides the established types of AKI, here an additional subtype has been defined which may be of special interest for the ESS-members: TRAKI, meaning trauma-related AKI. Furthermore, the complex innate immunological consequences for the kidneys and their intense organ-cross-talking and potential role in development of multiple organ dysfunction syndrome (MODS) is also described. Finally, novel exciting therapeutic approaches are introduced which certainly will evoke future research efforts within and beyond the European Shock Society.
Hope you will enjoy reading.





Markus Huber-Lang

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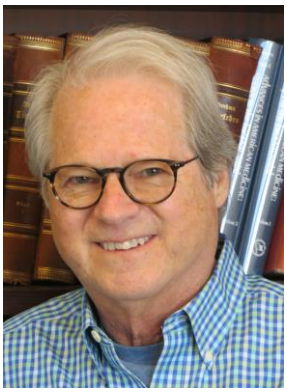
Vision of the Editor-in-Chief of Shock®



It is an honor and a privilege to assume the role of Interim Editor-in-Chief of SHOCK, but also a challenge to try to fill the shoes of Irshad Chaudry who has led SHOCK so successfully for 26 years. During this time SHOCK has served as the official journal of multiple Shock Societies throughout the world, but the affiliation with the European Shock Society is the oldest, and arguably, the strongest of these. If anything, I would like to see the connection and collaboration with the ESS strengthened even more. The European Editorial Office under the leadership of Mihály Boros continues to serve a critical function and I look forward to continuing to work closely with the European Office.

As Interim Editor-in-Chief, I see my task as primarily one of sustaining the level of excellence the journal now enjoys. As such, I do not intend to make any major changes in the journal. However, there are a few initiatives that have arisen from the subcommittee on journal enhancement as part of the Strategic Planning initiative led by President Marc Jeschke that I would like to enact during this year.

The first is the introduction of Graphical Abstracts. These will provide succinct visual communication of the key points of published papers in a format that is easily shared via social media such as Twitter. With the help of Melanie Scott and Meihong Deng we have developed guidelines for the construction of graphical abstracts and I am now working with the publisher to begin publishing these with our accepted manuscripts.

We are also developing a feature of “Special Topic” issues. These would be clusters of manuscripts on a focused and timely topic anchored by a review article accompanied by 2-4 original research articles on that topic. These would be integrated with a more proactive process of soliciting review articles. I would like to see these features be tightly focused on topics of emerging importance. This serves not only to increase citation rates (and impact factor) but also to make SHOCK more valuable to readers.

Since assuming the Editor-in-Chief role in October, I have become acutely aware of the “reviewer fatigue” experienced by many of our Editorial Board members. We received about 830 manuscripts last year to be reviewed compared to 700 the previous year. To help address the heavy reviewing load, I have solicited recommendations from our Editorial Board for guest reviewers to help spread the workload and also to develop a pipeline for new Editorial Board members. If you would like to serve as a guest reviewer, please do send me an email along with your area of expertise with key words.

Finally, a change in Editor-in-Chief is an excellent time to reflect on the mission of the Journal. This is a time when the nature of Shock research is changing rapidly. SHOCK has served us very well for the past 26 years. Now is a good time to consider how it can be even better looking forward. I have constructed a survey which will shortly be sent to Editorial Board members as well as Executive Council of the Shock Society and the European Shock Society. This survey

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addresses the types of submissions that we are receiving (and may receive in the future) and asks for prioritization. SHOCK is currently accepting fewer than 30% of submissions, so there is an opportunity to be selective not only with regard to the technical quality of research, but also with respect to impact and alignment with our mission. I will share the results of this survey once they are compiled. This information should be of value to the new Editor-in-Chief in leading SHOCK into the future.

This is a time of great opportunity to raise the stature of SHOCK to the next level and to position the Journal to be a leader in publishing important shock research in the future. If you have thoughts regarding strategies or priorities in accomplishing this goal, I am always very happy to hear them.

Mark G. Clemens
The Editor-in-Chief of SHOCK®, Interim

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Invitation to publish in Shock®

Shock is a monthly journal that publishes the results of investigations in the field of injury, inflammation and sepsis; of clinical and laboratory origin alike (current IF=2.96). It is the official Journal of all international Shock Societies, including ESS. Thanks to its efficient reviewing process, you will typically have your submitted paper reviewed within 15 days.
So do not hesitate, submit your next best results to SHOCK!
http://www.editorialmanager.com/shock.

Welcome new ESS members

Amy Tsurumi
Boston, USA

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Please visit our updated, mobile-friendly website

https://europeanshocksociety.org/

- Images of the life of our society (NEW)
- Historical background of our society
- Bylaws of ESS
- Previous newsletters
- Education materials
- … and many other interesting topics

Representative images from our website

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Upcoming events

ESTES 2021: 21th[h] European Congress of Trauma & Emergency Surgery
April 26–30, 2021, ***Digital***
https://www.estes-congress.org/

The Society for Cardiovascular Angiography and Interventions (SCAI)
April 28-May 1, 2021, ***Virtual Scientific Sessions***
https://scai.org/scai-2021-scientific-sessions

33rd European Congress on Surgical Infections (SIS-E)
June 9-11, 2021, ***Virtual***
http://sis-e.org/

ESOT Congress 2021
August 29 –September 1, 2021, Milan, Italy
https://www.esotcongress.org/

ISICEM 2021 - 40th International Symposium on Intensive Care and Emergency Medicine
August 31-September 3, 2021, Brussels, Belgium
https://www.intensive.org/index.asp

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ESICM LIVES, 34th Annual Congress
October 2-6 2021, Copenhagen, Denmark
https://www.esicm.org/events/34rd-annual-congress-copenhagen/

44th Annual Conference on Shock
October 12-15, 2021, Portland, Oregon
https://www.shocksociety.org/meetings

ESICM LIVES Forum, Major Trauma & Brain Injury: From assessment to treatment
2022, Athens, Greece
https://www.esicm.org/events/livesforum-athens2021/

Tissue Engineering and Regenerative Medicine International Society (TERMIS) European Chapter Meeting
Postponed to March, 2023, Manchester, UK
https://www.termis.org/eu-2020

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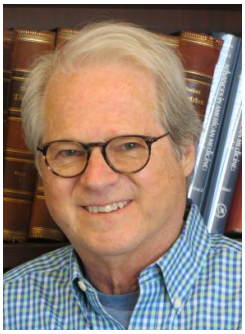

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ESS Membership

Dear ESS members,
please kindly pay your ESS membership for 2020/21. Currently, a fixed 2-year membership fee of EUR 100 for regular members and EUR 50 for student members applies.

We sincerely appreciate your contribution; please do not ignore this important commitment.
We are happy to receive your funds at:
European Shock Society
IBAN: AT13 1420 0200 1093 6552
BIC: EASYATW1
Please identify your transfer with your first/last name and a "full/student ESS membership fee" annotation.
Thank you!

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Last words about the ESS newsletter

Dear present ESS member,

If you like your ESS Winter/Spring Newsletter, please feel free to share it with your colleagues in the lab, department and/or institute. Perhaps, you could use this opportunity to suggest them to join us (a registration form can be found at the end of this Newsletter). Do not forget that we need you to keep improving our society so it stands proud and strong among other international Shock Societies.

This Newsletter, put together by your peers, belongs to you! We invite you to identify with it as members of the ESS. Moreover, we ask you to help us make it even better. Accordingly, we would be delighted to publish in our next issue any input you might be wishing to share with us (e.g. discussion on a given research/popular science topic, announce available positions in your lab, a contribution to the journal club corner, historical memories, comments about sepsis 3.0 etc.)

Dear past ESS member,

Please do not forget to renew your membership. We need all colleagues, junior and senior alike, to enable the ESS to host in its ranks the best representatives of the European Shock research - at the bedside and/or at bench alike.

Jean-Marc Cavaillon
our Past-President

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ESS Membership application form

(http://www.europeanshocksociety.org/register)

Please send completed form to Andrea Szabó (ESS General Secretary):

e-mail: **szabo.andrea.exp@med.u-szeged.hu**

fax: **+36 62 545 743**

Form fields shown in italics are optional

Title	
First Name(s)	
Last Name	
Country	
Position	
Institution	
e-mail	
Phone	
Research ID	
Area(s) of research interest	
Expertise and/or facilities	
Publications	

Two-year membership fee:

regular members: 100 €
student members: 50 €

Please transfer the membership fee to

European Shock Society
IBAN: AT13 1420 0200 1093 6552
BIC: EASYATW1

and please identify your transfer with your first/last name and a "regular/student ESS membership fee" annotation.

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