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## Message from the European Shock Society President



Dear ESS members and sympathizers, I am writing these words freshly after the Sunday World Cup finals; an epic Argentina vs. France fight (sorry, Jean-Marc!) and six days before Christmas widely celebrated in the Christian culture. Many different emotions and reflections run through my head... The dominant one being the world we have been experiencing over the recent year is a perplexing mixture of great, joyful, uplifting events counterbalanced by shameful, sad and outright tragic actions. The very same event can often trigger contrasting feelings, be it the aforementioned World Cup or the still-present COVID-19 pandemic. A well-deserved moment of athletic elation experienced by one nation is countered by a ten-month long suffering of war lived by another. *"May you live in interesting times!"* (an allegedly Chinese proverb) resonates strongly with me under the current circumstances. Yet, many before, including Sir Austen Chamberlain, Albert Camus and Robert F. Kennedy quoted it in times definitely not less turbulent than ours.

In my personal case, the upcoming 20th ESS congress in Vienna is a perfect exemplification of such an amalgamate: an (organizational) stress mixed with the (awaited) joy of bringing the ESS family back together in flesh (see the congress update below). Admitting my inability to resolve these complex emotional roller-coasters, I humbly suggest we focus on all the positive events in our lives - however tiny (or great) they might be - rather than ruminating about the hardships we live through. My great ESS-related joy has been that despite our physical separation, I have a strong feeling of a research-camaraderie (both ESS-related and beyond). I have been very much experiencing it in the recent weeks, either during assembling speakers for the conference sessions or receiving written contributions to this Newsletter. Do not miss those informative and enjoyable pieces written by our ESS colleagues. I humbly thank you all for your selfless, unpaid, time-consuming work for our society!

In the coming Christmas season (yes, my premeditated choice of "political incorrectness" with no less sincere well-wishes to any other holidays around this time), I wish you from the bottom of my presidential heart, a time of peace and professional slow-down. A time of little family and/or friendship joys, relaxing walks in a nice wintery ambience and tasty punch (or Glühwein in my geographical area) - be well, you'all!



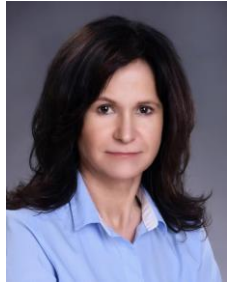
Merry Christmas & may the New Year be somewhat better than the last one!

Your President,

Marcin Osuchowski

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## Message from the General Secretary



Dear Colleagues, dear members and friends of ESS,

I trust that the pandemic has not affected your health, your daily work and your commitment to the ESS.

We previously drew attention by email to events organized by an allied organization the Global Sepsis Alliance (GSA) (see further details later in this newsletter). Please note that all the [World Sepsis Day presentations](#) are still available online, as are the [presentations of the "Celebrating 10 years of world sepsis day"](#). We are delighted that with the election of our former President Evangelos J. Giamarellos-Bourboulis, the ESS has been represented in the steering committees of both the GSA and its European affiliate the European Sepsis Alliance. Evangelos, once again we congratulate you and wish you great success in your work.

As you may be aware that the “European guideline on management of major bleeding and coagulopathy following trauma” (last published in 2019; [Crit Care 2019;23\(1\):98](#)) has received over 2600 citations. We are also delighted that ESS continues to be represented in the ABC-Trauma task force by Marc Maegele (our current treasurer) and the 6th edition of the guideline has been submitted for publication.



We are also pleased to announce that our former president Markus Huber-Lang and our current president Marcin Osuchowski will be co-organizing the Translational Trauma Research session at the [European Society of Trauma and Emergency Surgery \(ESTES\)](#) held in Ljubljana (May 7-9, 2023).

Our long-lasting member and former treasurer Ingo Marzi also informed us about the [7th CONGRESS of the European Society of Tissue Regeneration in Orthopedics and Traumatology](#) (E.S.T.R.O.T.) held in Frankfurt (July 3-5, 2023).



Once again, I would like to draw your attention to the fact that [our website](#) has many useful features and provides an excellent opportunity for networking.

Steps:

1. [Register/login](#)
2. [Browse the database](#) (with keywords for research interest/areas of other members)
3. Within your personal profile, you can also [check](#) the date of your last payment/payment period

Therefore, I would like to encourage everyone (if they have not already done so) to [join the ESS Members' database](#). An important condition for this is that the email addresses provided at the time of registration must be confirmed (this has not been done for several applicants).

Finally, I would like to wish Marcin Osuchowski a very successful 2023 congress! I look forward to participating in it in person in the beautiful Vienna. Together with our Past-President Evangelos J. Giamarellos-Bourboulis and the newly elected President-Elect Relja Borna, we support the organizational effort in any way possible.

Your Secretary,  
Andrea Szabó

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## The Treasurer's Corner



Although with less dramatic numbers and scenarios, the pandemic still reaches out into our daily lives and the ESS activities are not excluded. After being nominated and confirmed as the society's new treasurer, it took more than a year to formally hand-over and complete the transition of all responsibilities. Due to the (outdated?) Austrian bank laws, all these procedures require personal authorization with physical presence. In consequence, after many reschedules (compliments of COVID-19), finally, on Dec. 12, the current ESS president, Dr. Marcin Osuchowski and I, in my function of the new ESS treasurer, were able to set up an appointment with the society's bank, the Easybank/BAWAG in Vienna (Austria). To our joy and satisfaction (see photo), all formalities and signatures could be accomplished/provided ensuring a long-awaited transition of the treasury powers.

Of note, similar legal hurdles exist regarding the International Federation of Shock Societies (IFSS). In my capacity as the current IFSS treasurer, I am proud to say that the ESS is among the very few IFSS member societies which regularly transferred their annual membership fees over the past two years to the umbrella IFSS society. This is appreciated (and needed) given that on a regular basis the IFSS sponsors travel awards to its international meetings that are held every three years around the globe.



This again brings me to the point of sending out a gentle reminder to all ESS members (and sympathizers) not to forget to pay their bi-annual membership fees to the society. Remember that the entire membership amount (either regular or student membership fee) is deducted from the registration fee at each ESS congress. Only with this support, the income from the membership fees as

well as financial influx from alternative sources (that are currently being explored), can the society continue to increase its visibility on a larger scale and to open new windows of opportunities. We always try to view it through a prism of the society's key objective: supporting our younger and talented next generation of scientists and researchers. This is a good moment to end by mentioning the noble generosity of one of our ESS colleagues who recently donated her speaker's fee to ESS – we were touched and grateful!

The society and I will continue to count on your trust and support.

My best regards to all of you,

Your treasurer,  
Marc Maegele

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## Updates on the 2023 ESS Congress



Dear ESS congress participants *in spe*!

Organization of the upcoming congress in Vienna is in full swing and things are rollin' in the right direction. You are already aware about the venue - the elegant and historic University of Vienna. Definitely an appropriate location to celebrate the 40th anniversary of our ESS.

We have already created the program; see a simplified block layout below. I dare say that sessions are worth your participation and we also have a few interesting twists to spice it up some more. One of the nicest elements of the congress, in my personal opinion, will be the round table with the past ESS presidents - I am happy to say that nearly all will show up and the invites were enthusiastically responded to.

<div><div>Tentative Program: 20th Congress of the European Shock Society, Vienna, Austria</div></div>				
Wed 20-9-23		Thursday 21-9-2023	Friday 22-9-2023	Saturday 23-9-2023
ESS Summer School: Trauma Management in the ER	Found in Translation: <i>Pathomechanism of Critical Care Illness</i>		A Light in the Critical Care Tunnel: <i>Improvements in Diagnosis &amp; Therapy</i>	
	An Impactful Encounter: <i>Sepsis meets COVID-19</i>		Keynote Lecture: Alberto Mantovani, Italy	
	Poster Session I: Blast-Talks & Evaluation		40 Years ESS: Reminiscences Presidential Round Table	
	Poster Session II: Blast-Talks & Evaluation		The Lethal Trauma-Sepsis-Shock Triad: Where We Are & Where We Go	
	Parallel Session: The End is Only the Beginning: <i>Chronic Consequences of Acute Illness</i>		Parallel Session: Exosomes in Critical Illness: <i>Diagnostics, Treatment, Both?</i>	
ESS Board Meeting	Parallel Session: <i>All Models are Wrong but Some are Useful</i>		Parallel Session: It's a No-Brainer: CNS Signaling & Pathophysiology	
	ENIAC Competition: Raising Stars		Parallel Session: Coagulopathy in Trauma, Sepsis and COVID-19	
	Parallel Session: <i>Technological Palantir: in Silico Modeling</i>		Parallel Session: ESS General Assembly	
Get-together: University of Vienna		ESS Gala Dinner: Vienna City Hall		
Faculty Dinner		Organ Concert		

Another simultaneously touching and joyful support I have been receiving from our brothers/sisters-in-research (many not ESS-related), whom I invite to speak at the congress. The word "invite" is actually a semantic mis-statement given that virtually all speakers must come to the congress on their own dime (often from afar). The response to partaking in the 2023 ESS congress has been fantastic and I am proud to tell you that approx. 80% of top speakers have been already allocated. If you happen to read this, thank you so much for your contribution of expertise, time and money! This also makes me proud (you should be too!) given that it is our long-term collegial work that has made the ESS congresses into an event worth attending.

Along that line, we are lucky to have an outstanding keynote speaker, Alberto Mantovani, coming to Vienna; please see the introductory article below written by Federico Aletti. I trust it will be an inspirational experience to us but also to Dr. Mantovani.

I intend to have a live congress website at the end of January 2023, on which I will be regularly posting updates and progress of congress preparations. As always has been the case, we will

have plenty of activities specifically oriented for the junior/developing researchers. Specifically, the 2023 congress will feature:

- “Shock Summer School (1 day before the congress)”
- “European New Investigator Award Competition”
- “Students Poster Tour (with awards)”
- “Abstract Talks at parallel sessions”
- “Student Travel Awards”
- “Presidential Travel Awards”
- “Thematic Company Awards”
- “Günther-Schlag-Award”
- “All (except speakers dinner) social activities for all registered participants”

Regarding the last point above: we have been working on having an enticing social program for you. I do not want to reveal all details to whet your appetite; I will only matter-of-factly mention that the mayor of Vienna has agreed to host the ESS congress gala dinner at the most prominent Festsaal of the Viennese city hall (and also sponsor the alcoholic beverages - a significant budgetary support to the congress). Come over to Vienna to find out the rest...

Ending, my sincere gratitude goes to the AUVA organization team who has been professionally developing the technicalities of the upcoming event, our ESS council members who have gladly taken up some responsible organizational duties (e.g. Summer School) and our internal LBI Trauma staff assisting with many mundane but critical technical points.

**Vienna, 21-23 September 2023, folks... See you'all soon!**

Marcin Osuchowski

## The ESS “ZOOMosis Competiton“



The rules are simple, workload minimal and the award fantastic! This is how it goes: given that we organize/take part in plenty of online video/audio conferences with a varying level of enthusiasm and pro-active participation, we intend to boost your excitement toward these forms of digital communication. Please send us a funny piece (in any configuration) from any type of online communication (any communicator/platform)

related to your work (i.e. not with your mom/son/cousin) such as a short video, still shot, screenshot, texting screenshot. The ESS executive council will choose the top three (i.e. the winner and 2 honorable mentions). **The reward:** all three selections will be shown at the gala dinner at ESS conference to acknowledge their authors. The winner gets his registration fee to the 2023 ESS conference completely waived. Yeah, it is worth participating. Just be creative and bold.

**The fine print:** i) Executive council members may not participate, ii) you need to be an existing ESS member or sign up for the membership to have you ESS congress fee waived. Iii) it may happen that you will have faces of other zoom/webex/skype participants on the screenshot; for legal reasons, simply ask them for permission to be presented to us (in the majority of cases people agree).

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## Introducing the 2023 ESS Conference Keynote Speaker: Alberto Mantovani

Federico Aletti (ESS Council Member)

Instituto de Ciência e Tecnologia, Universidade Federal de São Paulo, Brazil



**Dr. Alberto Mantovani**

The 20th Congress of the European Shock Society in Vienna will welcome Dr. Alberto Mantovani as keynote speaker. Dr. Mantovani is one of the most distinguished contemporary Italian scientists and one of the main contributors worldwide to the remarkable advancements in the fields of immunology and oncology. Prompted by the COVID-19 pandemic, Dr. Mantovani has recently turned his interests (also) to the topics that are intrinsic to the mission of the ESS.

Dr. Mantovani earned his M.D. degree at his *alma mater*, the Università degli Studi di Milano, Italy, in 1973. Following his residency in oncology at the Università di Pavia, Italy, he undertook a long journey in immunology and cancer research that brought him first to the UK and then to the NIH in the USA to complete his postgraduate training. He then moved back to his home country and became a successful researcher at the renowned Istituto di Ricerche Farmacologiche “Mario Negri” in Milan, where he remained for about 25 years. During that time, he divided his efforts between his research lab at “Mario Negri” and his academic appointments first at the Università di Brescia and subsequently at his *alma mater* in Milan. In 2005, he moved to the Istituto Clinico Humanitas on the outskirts of Milan, as its scientific director and president of the research foundation of the Humanitas Institute, as well as professor emeritus at the Humanitas University. Since 2017, while he remained at Humanitas, he has also been a professor and chair of Inflammation and Therapeutic Innovation with the William Harvey Research Institute at the Queen Mary University in London, UK.

Dr. Mantovani’s achievements have included discoveries of important molecular mechanisms that characterize inflammatory processes and of crucial aspects of the role of innate immunity in cancer. The impact of his contributions, ever since his early career in the ‘70s, has been defined by innovative paradigms that he has introduced, for instance the now well-known idea of tumor-associated macrophages acting as “corrupt policemen” that promote tumor progression (rather than helping in the fight against cancer). The impact of these discoveries has earned him not just a strong scientific reputation but also several prestigious awards such as the Triennial OEI Award from the Organization of the European Cancer Institutes, the Robert Koch Award, the American-Italian Cancer Foundation (AICF) Prize for Excellence in Medicine, the American Association for Cancer Research International Pezcoller Award for Extraordinary Achievement in Cancer Research and the Association for Cancer Immunotherapy’s (CIMT) Lifetime Achievement Award.

Apart from his work on cancer, Dr. Mantovani has also been active in the field of acute illness; recently, he contributed to the identification of genetic profiles associated with COVID-19 and identified severity biomarkers of the disease. As a person at the crossroads of cancer and critical illness, Dr. Mantovani is uniquely equipped to cast two-directional bridges between those two fields. His outstanding body of knowledge generated by his multi-tier research activity makes him a qualified liaison able to transplant successes from the cancer field to address the most complex and unresolved problems in the field of various acute critical care conditions such as sepsis, shock and trauma.

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Dr. Mantovani has also dedicated significant efforts to communicating with the lay public to further awareness of science and medicine and to provide balanced and competent advice during the COVID-19 pandemic. He wrote several books and articles on immunology, vaccines and health to educate the general public.

We look forward to Dr. Mantovani's keynote lecture in Vienna next September, confident that his talk will provide the ESS congress participants with new and valuable food-for-thought. Welcoming among our ranks one of the most accomplished European biomedical scientists is a unique gateway to novel ideas and solutions that we can put to a good use in our various fields of expertise.

## ESS Summer School: "Trauma Management in the ER"

Organized by Markus Huber-Lang, Germany, and Christoph Schlimp, Austria  
(ESS Council Members)



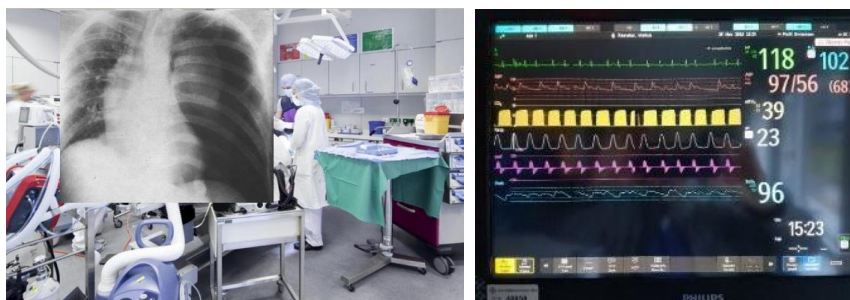
**Markus Huber-Lang**

This exciting workshop is offered to every student and junior researcher/clinician irrespective of the educational background and actual research field. The workshop will take place one day before the official ESS meeting begins (i.e. Wednesday, 20 September 2023). The main intention of the course is to give participants an all-around understanding of a real-life decision-making that must be taken in a modern Emergency Room.



**Christoph Schlimp**

The workshop will be run by the experts-in-the-field and will feature chosen simulated emergency settings on polytrauma and associated complications. After a theoretical input, principles of the initial anesthesiological and surgical management will be demonstrated and repeated by the participants in a hands-on manner. In addition, monitoring methods and imaging of the polytrauma patients will be demonstrated and diagnostic strategies applied under realistic time-pressure. We expect an exciting training session for all participants.



*ESS practical course at the ESS meeting 2019 in Chania (Copyright: MHL)*

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**Important:** The workshop is free for participants registered to the 2023 ESS congress!

The workshop will take place at the Lorenz Böhler Trauma Hospital and Ludwig Boltzmann Institute for Traumatology, Donaueschingenstrasse 13, Vienna. Coffee breaks and meal will be served. Pre-registration is required just by an email to the ESS secretary: [szabo.andrea.exp@med.u-szeged.hu](mailto:szabo.andrea.exp@med.u-szeged.hu).

Workshop size is limited: the first 25 applications will be accepted (a waiting list will be available). Use this excellent opportunity to expose yourself to new knowledge and get to know your peers!

## 1822 - 2022: Bicentenary of the birth of Louis Pasteur

### Pasteur and sepsis

Jean-Marc Cavaillon (ESS Past-President)  
National Research Agency, Paris, France



**Jean-Marc  
Cavaillon**

Next to the Poland-born Marie Curie-Skłodowska, Louis Pasteur (1822-1895) is the most famous French scientist (Figure 1 & 2). A true French hero having his face on stamps in numerous countries, his statues in many cities; three of them in Paris, one in Mexico, Chicago, Conoor, Bogota, and Montreal. More than 3300 French cities have a « rue Pasteur » and similar is true in few other places across the world. An institute bearing his name was created in 1887 and an international Institut Pasteur Network exists around the globe. While the institution did not compete in the race for a COVID-19 vaccine, the network has been highly efficient to provide SARS-CoV-2 tests in developing countries and screening the populations.

Louis Pasteur has not always been a precursor. In its obituary “Science” wrote: “Pasteur is considered as the father of modern bacteriology, but we must remember that he was not a pioneer in these lines of work. There was hardly a problem that he studied which had not been already recognized, and even studied to a greater or less extent by his predecessors [...] Others discovered facts, Pasteur determined laws” [1].

Jean Rostand (1894-1977), a French biologist and writer, wrote: « It is commonly believed in the public that it was Pasteur who discovered the role of microbes in the production of infectious diseases. In truth, this considerable discovery does not belong to him; it belongs to another French scientist: Davaine [...] who was the first to dared to affirm and was able to demonstrate by the experimental method that a microscopic organism is the agent responsible for a disease » (namely anthrax).



Figure 1. Pasteur in the French press. From left to right: As an immortal icon depicted after his death on September 28th, 1895; At his jubilee when received at the Sorbonne, accompanied by Sadi Carnot, the president of France; As a fighter going back to the infectious diseases battlefield, namely cholera.

Nevertheless, Louis Pasteur made a few key pioneer works as well. He discovered molecular chirality and the great German chemist, Eilhard Mitscherlich (1794-1863) while he was received in Paris to be acknowledged as a foreign member of the French Academy of Sciences, said to Pasteur: « You saw what I could not find ». In 1861, he discovered the anaerobic life for certain bacteria. In 1877, Pasteur and Jules Joubert (1834-1910) reported that the bacterium of anthrax could not develop when associated with other microorganisms: “life prevents life”. That was the first report on antibiosis. In 1887, he proposed the first bacteriologic war, using *Pasteurela multocida* to kill rabbits who were endangering the cellars of Champagne of Mrs Pommery. He then sent his nephew, Adrien Loir (1862-1941) in Australia to help the country to eradicate the rabbits, but he failed and thus did not receive the £25 000 which would have been awarded for a successful mission. He co-discovered certain germs, *Streptococcus* with Theodor Billroth (1829-1894), *Pneumococcus* (*Streptococcus pneumoniae*) with George M. Sternberg (1838-1915) and *Staphylococcus* with Alexander Ogston (1844-1929).

His works on fermentation were in the paths of Antonie van Leeuwenhoek (1632-1723), Adamo Fabroni (1748-1816), Louis Jacques Thénard (1777-1857), Theodor A.H. Schwann (1810-1882), Friedrich T. Kützing (1807-1893), Pierre Jean François Turpin (1775-1840), Charles Cagniard de Latour (1777-1859) and Pasteur failed to recognize what Antoine Béchamp (1816-1908) had claimed, i.e. fermentation is the consequence of action of enzymes (zymases) released by yeast. Yet, his contributions were key for wine, vinegar makers and breweries to improve their products. Of note, the so-called “pasteurization” was first applied to wine, as first reported by Nicolas Appert (1749-1841) in 1831. Only in 1886, a German chemist, Franz von Soxhlet (1848-1926) applied the process to milk.

His works on the refutation of the spontaneous generation and the germ theory were in the paths of many scientists who had the intuition, while some (Francesco Redi (1626-1697), Louis Joblot (1645-1723), Lazzaro Spallanzani (1729-1799), Theodor Schwann (1810-1882), Franz Schulze (1815-1921)) had made the appropriate demonstration. He entered the field of infectious diseases when he was called to study silk worm diseases. After initially refuting the claim of Béchamp that it was an infectious disease, he subsequently admitted it and proposed

an appropriate way to sort infected eggs as earlier suggested in 1856 by Emilio Cornalia (1824-1882) an Italian naturalist.



*Figure 2. Pasteur in the art. From left to right: Painting by Lucien Laurent-Gsell, his nephew showing Pasteur welcoming rabid patients who were vaccinated by Dr. Joseph Grancher; Sculpture by Paul Dubois at the Carlsberg brewery in Copenhagen to thank for his works on beer; Commemorative plate by Max Claudet to whom Pasteur complained to have been represented too serious.*

Pasteur moved to the field of vaccination and developed three veterinary vaccines against fowl cholera, anthrax and pig erysipelas. His work on anthrax vaccine followed that of Henri Toussaint (1847-1890), and his work on rabies vaccine followed Victor Galtier (1846-1908), who had also shown that rabies could be transferred from dogs to rabbits. It was the seminal work of Pierre-Henri Duboué (1834-1889), who first identified the nervous system as the path followed by the virus to reach the brain; Pasteur was initially looking for the culprit pathogen within the bloodstream. Pasteur achieved his effective vaccine preparation based on the dried spinal cord from sick rabbits - an original idea from Emile Roux (1853-1933) that Pasteur further improved. After successful development of the rabies vaccine, an institute was created with help of his closest collaborators to offer rabies vaccinations to the public, research in microbiology and teaching [3]. After Emile Roux and Alexandre Yersin (1863-1943) had demonstrated that diphtheria was due to a toxin, the research on toxins and endotoxins was also performed by the pasteurians [4].

The most frequent source of sepsis by the mid XIX<sup>th</sup> century was puerperal fever (in addition to the nosocomial infections acquired by wounded soldiers from the battle field). In the General Hospital of Vienna, in 1847, Ignaz Semmelweis (1818-1865) demonstrated that the hands of the medical students were responsible of the contamination of the parturients after having participated to autopsies of cadavers [2]. Carl Mayrhofer (1837-1882) was invited by the head of the maternity department, Carl Braun (1822-1891) to demonstrate that the disease was in fact due to an environmental miasma. In 1865, Carl Mayrhofer observed « vibrions » in the uterine tissues and could transmit the death to rabbits. In 1869, in Strasbourg, Victor Feltz (1835-1893) and Léon Coze (1819-1896) observed deadly bacteria in the blood of a woman who died of puerperal fever. The injection of this blood could kill a rabbit. The report was published in the "Gazette Médicale de Strabourg". Ten years later, Feltz republished on March 17<sup>th</sup> 1879 in the Comptes Rendus de l'Académie des Sciences, a similar observation, and he named the observed bacterium *Leptothrix puerperalis*. On the 18<sup>th</sup> of March 1879, Pasteur published his own similar observation of bacteria in the lochias, the blood and the uterus of two patients who died of puerperal fever. He proposed to use diluted boric acid to wash the genital tract. Pasteur contacted Dr. Feltz for some patient blood samples with an aim to demonstrate that his patient had died of anthrax. He injected one guinea-pig with the blood sample, and two guinea-pigs with anthrax. The animals were sent

by train from Paris to Nancy; by the time of arrival, the animals were already severely ill, close to die. Because of the aura of the master, Feltz recognized that his female patient (who died post-partum) had died of anthrax, a disorder he had never encountered before. This is how a chemist convinced a medical doctor that his initial diagnosis was wrong! This work was further pursued by one of Pasteur's pupils, Dr. Jacques Amédée Doléris (1852-1938). Doléris examined more than forty women with puerperal fever, identifying a diplococcus, named later as *Streptococcus* by Theodor Billroth (1829-1894), a famous German surgeon.

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## Systemic dissemination of viral material in COVID-19: innocent bystander or pathogenic actor?

Jesús F. Bermejo-Martin and Ana P. Tedim

Institute of Biomedical Research of Salamanca

Centro de Investigación Biomédica en Red en Enfermedades Respiratorias (CiberES)

University of Salamanca, Spain



**Jesús F. Bermejo-Martin**

Although SARS-CoV-2 causes mainly a respiratory infection, the dissemination of viral material to the blood (both viral RNA and/or antigens) has been extensively evidenced to represent a signature of critical illness and mortality [1-3]. Persistence of SARS-CoV-2 RNA in the blood (RNAemia) is correlated to fatal outcome [4]. Moreover, presence of viral material in blood, determined either by real-time RT-PCR (RT-qPCR) or by droplet digital PCR (ddPCR), is associated to the presence of

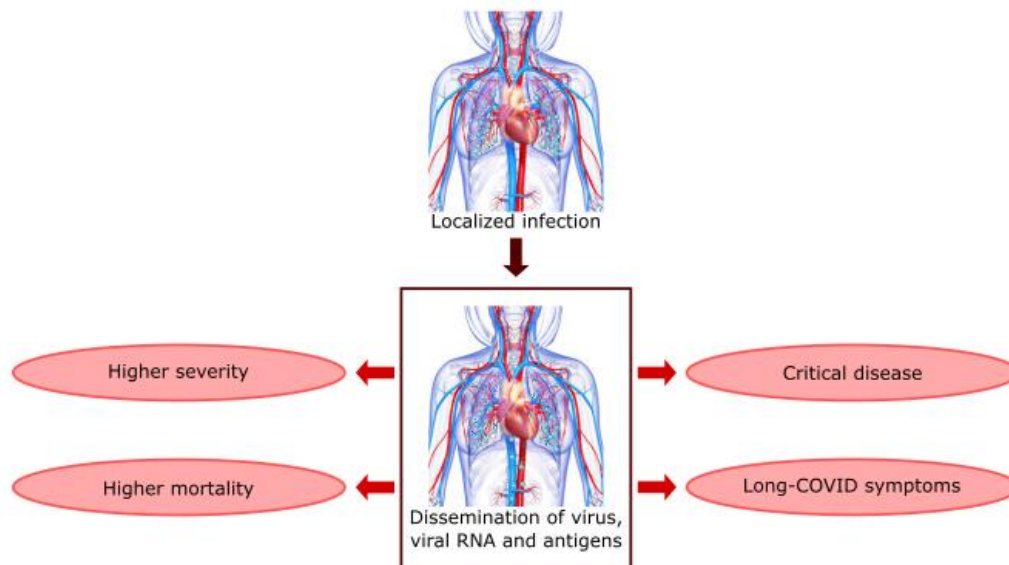


**Ana P. Tedim**

a “sepsis-like” dysregulated host response to the infection, characterised by the simultaneous presence of elevated levels of biomarkers of pro and anti-inflammatory responses, endothelial dysfunction and tissue damage [1].

While the pathogenic role of the presence of viral material in the blood remains to be elucidated, an uncontrolled viral replication represents a major event in severe COVID-19. Recent works showed that viral RNA levels in plasma represent a surrogate of the degree of viral replication in the lungs [5]. Thus, large amounts of viral material in the blood indirectly reflects an underlying defect of the host response to effectively control the virus.

Whether the presence of viral RNA and antigens corresponds or not to the presence of live virus in blood is not known, but this material represents a stimuli per se to the innate immune response, and may also be mediating direct endothelial or tissue injury. Recently, viral RNAemia has been described to be associated with worse quality of life and the presence of more long-COVID symptoms at six months after hospital admission [6]. Altogether, available evidence linking systemic dissemination of SARS-CoV-2 material with COVID-19 severity and its long-term consequences support vaccines as a strategy to prevent uncontrolled viral replication, as well as the early treatment with antivirals or (active) monoclonal antibodies in already infected patients at risk of poor outcome. Whether the removal of viral material from blood, with hemofilters, could alleviate the acute and chronic consequences of COVID-19 is an interesting avenue of research.



#### *Local vs. disseminated virus infection*

Finally, the monitorization of viral RNA load and/or the detection of viral antigens in the blood should be routinely implemented in the management of patients with signs of severe COVID-19, in order to early identify those at risk of clinical deterioration. This quantification of viral RNA load in blood can be routinely performed in diagnostic laboratories using the same RT-qPCRs that are used to diagnose SARS-CoV-2 infection in nasal swabs [5]. Nevertheless, when available it is better to use ddPCR to quantify SARS-CoV-2 RNA in blood, as this method is more sensitive, less affected by PCR inhibitors and performs direct quantification without the need for standard curve [1]. SARS-CoV-2 antigen detection tests can also be used to detect SARS-CoV-2 material in the blood and could be used as a point-of-care method at the bedside of severe COVID-19 patients. Including viral RNA load quantification and antigen detection in blood in clinical practise could drastically improve the management of COVID-19 patients.

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## Emergency Use Authorization of Anakinra for COVID-19 by Food and Drug Administration

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**Evangelos J.  
Giamarellos-  
Bourboulis**

As already presented in our Winter 2022 newsletter, an early anakinra treatment of COVID-19 pneumonia in adults guided by circulating suPAR (soluble urokinase plasminogen activator receptor) was registered by the European Medicines Agency (EMA) in December 2021 for hospitalized patients [1]. More precisely, this registration is based on the favorable results of the double-blind randomized clinical trial SAVE-MORE [2], which showed that the cornerstone of management relies on the early recognition of the patients at risk for progression into severe respiratory failure (SRF). The patients presenting with suPAR concentration  $\geq 6$  ng/mL were subjected to treatment with anakinra. The treatment was accompanied by an overall 64% change for better outcomes compared to patients receiving placebo treatment, as this is defined by the World Health Organization Clinical Progression Scale at day 28. The study SAVE-MORE was run at 37 study sites (29 in Greece and 8 in Italy) and it was led by Evangelos Giamarellos-Bourboulis, the past ESS president. On 8 November 2022, the Food and Drug Administration of the United States provided an Emergency Use Authorization of early anakinra treatment in adults with COVID-19 pneumonia at risk for progression into SRF.

Since suPAR is not commercialized in the United States, the at-risk patient population to receive anakinra treatment is identified by the presence of three out of the following eight measurable [3]:

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**Clinical/laboratory endpoints:**

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Age  $\geq 75$  years  
 Need for oxygen supplementation  
 Current/previous smoking status  
 SOFA (sequential organ failure assessment) score  $\geq 3$   
 Neutrophil-to-lymphocyte ratio  $\geq 7$   
 Hemoglobin  $\leq 10.5$  g/dL  
 Medical history of ischemic stroke  
 Blood urea  $\geq 50$  mg/dL and/or medical history of renal disease

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## SEPSIS Challenges in TUNISIA

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*«General Hannibal: I will either find a way or make one...»*



**Mouna Ben Azaiz**

Bacterial and viral sepsis continue to be an emergent threat to our society with 50 million cases per year worldwide. In this context, encouraged by the European Shock Society and Global Sepsis Alliance initiative we began celebrating the World Sepsis Day in Tunisia since 2018. Our aim was to afford a scientific update for health care providers and to raise general awareness about this disease in my home country. To meet this goal, we organized presentations such as **“The different faces of sepsis, COVID-19 infection: a challenging new viral sepsis and SEPSIS challenges”** discussing various aspects of sepsis pathophysiology also including COVID-19 as its viral manifestation (see photos).

At the beginning of the COVID-19 pandemic, inspired by our works on sepsis and following the recommendations of WHO and NIH, we hypothesized a link between severe COVID-19 cases and bacterial sepsis. As a consequence of that work, we established the first in-house protocols dealing with SARS-CoV-2 and published our reflections as well as early data regarding COVID-19 pathophysiology and treatment [1-3]. We explored the possibility of

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monitoring and predicting outcomes by using circulating cytokine (IL-6 and IL-10) and/or lymphocyte measurements as a simplified «immune signature» of the COVID-19 patients.

Our vision for the management of sepsis in Tunisia is that we have to gain a thorough understanding of the challenges and to deal with them in a strategic and holistic manner. All this keeping the «education is the key point» lead-phrase identified by the Global Sepsis Alliance in mind. This education approach is especially relevant and applicable in a developing country with limited resources. Thus, we will continue to celebrate the World Sepsis Day by mainly focusing on raising awareness regarding preventing antibiotic resistance, and highlighting the need for an early diagnosis of sepsis using easily available biomarkers and diagnostics methods.

In conclusion, I wish the best to our society and I am proud to share with you our «Tunisian touch» while we continue our fight against sepsis to save lives around the world. I strongly believe that as scientists we must learn from our great scientists of the past like Charles Nicolle and Louis Pasteur. Their past statements on the importance of collaboration and the fact that viruses do not recognize borders resonate well in the current global situation and underline the need to work together. Finally, I leave with you this positive statement by L. Pasteur: “Science has no borders, because knowledge belongs to humanity”. See you in Vienna in 2023!



*Photos from Sepsis Days*

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## Artificial Intelligence in shock research: an ongoing journey from the computer to the bedside

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**Federico Aletti**

Translational research in the field of circulatory shock has always strived to make a tangible impact on the treatment and survival of patients in the intensive care unit (ICU). Over the last decades, major medical and technological achievements have significantly enhanced the array of "weapons" that intensive care physicians, nurses and physical therapists can deploy to reduce mortality and help acutely ill patients fight the disease and recover towards a "good" standard of life following ICU discharge.

Recently, the multi- and inter-disciplinary nature of shock research that the European Shock Society embraces, promotes, and advocates for, has been further emphasized by a stronger bond between biomedical engineering, computational/data sciences, and health sciences. Besides the progress achieved by the improvement of the medical equipment currently available in the ICU (and for cutting-edge preclinical research), novel data analysis and modeling approaches, based on machine learning (ML) and artificial intelligence (AI), have been introduced to the field of critical care as highlighted in the 2020 ESS review on the COVID-19 pandemic [1].

The ICU environment is characterized by a significant level of complexity and a unique wealth of data. Vital signs such as hemodynamic and respiratory signals can be collected from ICU monitors that receive continuous or intermittent high-fidelity measurements (and estimates generated by algorithms embedded in the monitors) from electrocardiogram electrodes, blood pressure transducers, mechanical ventilators, pulse oximeters, etc. Laboratory tests of biological fluids and tissues provide discreet, coarse data on fundamental biochemical parameters and markers. When available, offline, high-throughput measurements (that currently have limited point-of-care value) add knowledge on the disruption of crucial biological processes by the disease onset and progression and convey information about their restoration throughout the course of treatment.

Such a massively dense data space that is *in theory* available both in hospital and animal ICUs requires the most refined data analysis tools to extract as much information as possible about acute illness and the critical management of ICU patients. Cutting-edge AI and ML algorithms provide powerful computational solutions to this problem. As highlighted in an interesting

editorial from Mamdani and Slutsky published in *Intensive Care Medicine* [2], the deployment of AI and ML to the ICU requires an appropriate strategy for their clinical translation, though (Figure 1). In particular, the preliminary verification of the quantity, quality, availability, and accessibility of the data “alone” is not sufficient to ensure that state-of-the-art algorithms will extract valuable information without specific, well-defined clinical and scientific questions and appropriately formulated and validated models.



*Figure 1. Strategy for the deployment of AI tools to the ICU (from [2]).*

Although AI and ML could play a key role in disentangling the complexity of acute patient monitoring, one of the key issues affecting any data analysis strategy is: “*how good are my data?*” Thus, it is particularly important to consider what type of contribution is expected from the utilization of sophisticated statistical and modeling techniques. If a description of the pathophysiological cascades underlying shock remains elusive, especially when dealing with the interpretation of symptoms, individual patient trajectory prediction, response to treatment and cohort stratification in the ICU, AI and ML can significantly help in the recognition of patterns in specific types of data.

As discussed in another recent review by Young, Pinsky and Clermont [3], among the several possible contributions of AI, promising results have been achieved in i) the identification of disease (e.g., the impact of COVID-19-related pulmonary injury benefiting from the image analysis via AI algorithms), ii) the prediction of features characterizing acute disease progression (e.g., the risk for sustained tachycardia and hypotensive crises) and iii) the classification of different disease phenotypes (e.g., the data-driven identification of the vital signs dynamics and inflammatory states). However, despite the excitement of the research community for a greater contribution of state-of-the-art algorithms to the solution of complex biomedical problems in this “big data” era, we should remain cautiously realistic about the actual goals of AI and ML. For instance, it is still debatable that purely data-driven modeling strategies could be suitable to guide ICU doctors in the choice of the most appropriate therapeutic protocols.

Indeed, physiological modeling should also be revived to motivate a systematic approach to a deeper understanding of the actual pathophysiological mechanisms. In the field of circulatory shock research, a comprehensive, multiscale interpretation of the disease pathways and mechanisms could have important translational implications. AI and ML provide tools to process the abundance of the high-throughput data and high-fidelity signals that are accessible in the ICU and in the lab by recognizing patterns more efficiently and therefore identifying the most important features for improved, physiologically meaningful models of the disease. In turn, such models could help define new therapeutic targets and biomarkers, eventually leading to tangible improvements at the bedside.

However, rather than just emphasizing the current limitations of AI and ML in the ICU, the critical care community will benefit from working side-by-side with bioengineers and data scientists to overcome them. A “roadmap” can be traced to identify the future tasks required to enhance the translational potential of AI and ML. Among these needs, the most pressing

ones include [3] i) the improvement of data standardization, de-identification and sharing strategies, ii) the implementation of ever more robust quality control protocols to ensure that the data are of adequate quality for use in AI and ML-based analytical tools, and iii) the design of *in silico* clinical trials to maximize the usefulness of modeling when limited resources hamper the viability of large scale preclinical and clinical trials.

In summary, it is crucial to keep leveraging the outstanding potential of highly complex algorithms from AI and ML. At the same time, the effort to combine data-driven and hypothesis-driven modeling should be encouraged to overcome the limitations of physiological and biophysical models. Increasing the impact of AI and ML in the clinical setting will be the challenge of the next several years. The beginning of this new “digital era” of critical care has shown promise. We only need to wisely harness it.

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## Introducing the [www.sepsiswissen.de](http://www.sepsiswissen.de) project

Edmund A.M. Neugebauer (ESS Past-President) and Silke Piedmont  
Brandenburg Medical School Theodor Fontane (MHB) Germany



**Edmund A.M.  
Neugebauer**

The project “Sepsis-Wissen”(“Sepsis-Knowledge”) aims to strengthen the health competency of patients-at-risk to improve prevention and early diagnosis of sepsis. This is necessary as sepsis-associated awareness and knowledge remains rather low across Europe including Germany. Yet, about 11 million people die from sepsis each year worldwide; sepsis causes more deaths than myocardial infarction and stroke combined.

To raise sepsis awareness, the project Sepsis-Wissen is both a campaign informing about sepsis as well as a research project. The project is run by Prof. Konrad Reinhart from Charite` as the leader of the consortium

and other healthcare partners including the undersigned. The ongoing project relies on two German federal states as intervention regions. As knowledge on sepsis is too low in both laypersons and health professionals alike, the campaign targets both groups. For example, there had been street campaigns consisting of posters and videos shown in



**Campaign SepsisWissen out on the street**

public areas such as train and bus stops and in public use vehicles. The team placed printed material and advertisements in popular magazines with access to wide lay audiences. A large TV station broadcasted sepsis information. Various cooperation agreements with, e.g., associations of physicians, pharmacists and nurses further increased the outreach.

The campaign also focused on high-maintenance patients and their relatives, e.g. by developing guidelines on how laypersons can support sepsis-prevention and aftercare. Hospitals present sepsis videos on the screens at patients' beds and in waiting areas. As of today, our team trained more than 600 health professionals in sepsis knowledge and communication. The project also identified needs in daily practice; one result is a sepsis checklist to guide laypersons in early sepsis detection: <https://www.sepsis.science/checklist>.

The research part of the project consists of a trial on "risk communication on sepsis early detection and prevention" (RICOSEP) with already available results ([Debbeler et al. \(2022\)](#)). In addition, two survey rounds of risk groups were completed; the third one is about to start. Those surveys plus analyses of vaccination rates are key elements in measuring the campaign's effects. As part of the process evaluation, the Brandenburg Medical School (MHB) and Charité University Berlin currently conduct qualitative interviews and quantitative surveys with health care professionals. Our overarching goal is to aid future sepsis campaigns worldwide.

The SepsisWissen project is funded by the Innovationsfonds of the German Federal Joint Committee (01VSF19020). More information and campaign material can be found here: [www.sepsiswissen.de](http://www.sepsiswissen.de). The "Sepsis-Wissen" project was also presented in a session of the World Sepsis Day Symposium on September 16, 2022.

## World Sepsis Day and Global Sepsis Alliance: Update

Evangelos J. Giamarellos-Bourboulis (ESS Past-President)

4th Department of Internal Medicine, ATTIKON University Hospital, Athens, Greece



September 13 – World Sepsis Day  
[worldsepsisday.org/wsd2022](http://worldsepsisday.org/wsd2022)

### September 16 – "Making Sepsis a National and Global Health – Celebrating 10 Years of World Sepsis Day"

[10yearswsd.org](http://10yearswsd.org)

The year 2022 is the 10-year anniversary of the World Sepsis Day (WSD) event with its first iteration that took place in 2012. WSD is a global initiative to raise awareness about sepsis among both health care providers and the public. The 10-year anniversary celebration took place on 16 September 2022 in Berlin with an international hybrid event attracting several thousand participants.

The anniversary was endorsed by the General Director of the WHO Dr. Tedros Adhanom Ghebreyesus and by the German Federal Minister of Health Prof. Dr. Karl Lauterbach. Two

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main sessions addressed the burden of sepsis and learning-by-exchange on the scientific fields. This was accompanied by two panel discussions on i) how to boost the implementation of the WHO sepsis resolution and ii) the challenges and lessons learnt from the COVID-19 pandemic.

### **September 20 – 5th ESA Annual Meeting – Sepsis Management, an Indicator of Quality of Care in Europe**

The European Sepsis Alliance (ESA) is a subsidiary of the Global Sepsis Alliance. In September 2022, the elections for the Steering Committee of ESA took place. The past ESS president, Evangelos J. Giamarellos-Bourboulis was re-elected as ESA chairman. The annual meeting of the ESA featured four main highlights:

- Address by the European Commissioner for Health and Food Safety, Stella Kyriakides. During her talk she defined sepsis as a “top-killer” illness in the world.
- Presentation by Adam Linder (University of Lund, Sweden) on the importance of increasing sepsis awareness through national public campaigns. Prof. Linder emphasized the fact that the real incidence of sepsis remains unknown due to the facts that a) ICD coding for sepsis is very poor and the quality of healthcare differs among the European countries; b) 90% of sepsis patients are treated outside the intensive care units; and c) the impact/prevalence of antimicrobial resistance in/upon sepsis remains undetermined.
- Presentation of the first results of the European Sepsis Care Survey (ESCS) by Christian S. Scheer (University Medical Center Greifswald, Germany). The ESCS is one of the ESA initiatives endorsed by the following societies: European Shock Society, European Society of Intensive Care Medicine, European Society of Anesthesiology and Intensive Care, European Society of Clinical Microbiology and Infectious Diseases, European Society of Emergency Medicine, European Society of Paediatric and Neonatal Intensive Care and International Fluid Academy. The survey was done in 25 EU countries using an online questionnaire capturing information on the level of sepsis care in Europe. Main results showed i) lack of a bundle for sepsis management in the general ward compared to the Intensive Care Unit (ICU) and ii) an earlier information on positive blood culture results in academic hospitals providing continuous service (24 hours a day for 7 days).
- Panel discussion on how anti-sepsis measures can be effectively integrated and operationalized across the European health systems.



## Upcoming events



### 2023 Critical Care Congress

January 21-24, 2023,

San Francisco, California

<https://www.sccm.org/Annual-Congress/critical-care-conference>



### 1st EuroAfrica

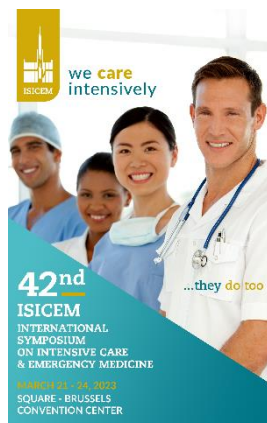
### Conference Cairo

February 9–13, 2023,

Cairo, Egypt



<https://www.esicm.org/events/euroafrica-2023/>



### ISICEM 2023 – 42nd International Symposium on Intensive Care and Emergency Medicine

March 21-24, 2023, Brussels, Belgium

<https://www.isicem.org/1/Home.asp>

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 SCIENCE TO  
 PRACTICE:  
 FROM  
 COLLEAGUES  
 TO FRIENDS

Illustration: © Adobe Stock, gregor27

## 22nd European Congress of Trauma & Emergency Surgery

May 7–9, 2023, Ljubljana, Slovenia

<https://www.estes-congress.org/>



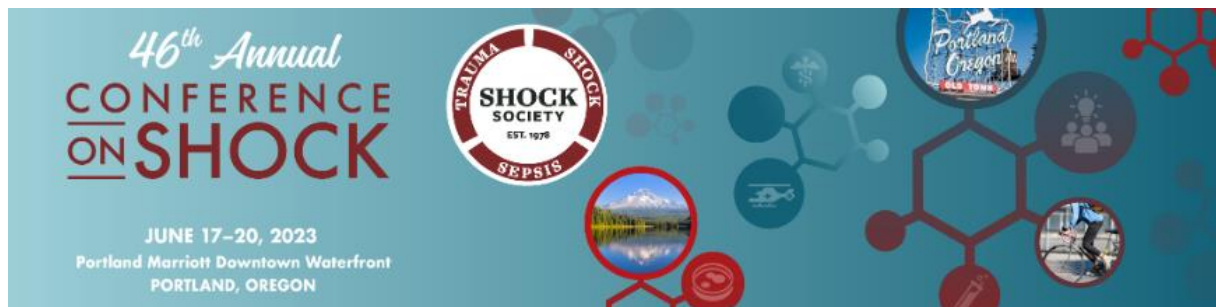
**2023**  
*Phoenix*  
 MAY 18-20  
**Scientific Sessions**

The Society for Cardiovascular Angiography and Interventions (SCAI)

SCAI 2022 Scientific Sessions

May 18–20, 2023, Phoenix, Arizona

<https://scai.org/scai-2023-scientific-sessions>



## 46th Annual Conference on Shock

June 17–20, 2023, Portland, Oregon

<https://www.shockociety.org/annual-conference-on-shock-2023>



**7th E.S.T.R.O.T. CONGRESS**  
 European Society of Tissue  
 Regeneration in Orthopedics and  
 Traumatology

July 3-5, 2023, Frankfurt, Germany

<https://www.estrot.org/seventh-estrot-congress-23.php>



**SEPSIS 11<sup>th</sup> UPDATE 2023 (German Sepsis Society)**  
 September 6-8, Weimar, Germany  
<https://sepsis-update.de/>



**ESOT Congress 2023**  
 September 17–20, 2023, Athens, Greece  
<https://esot.org/esot-events/esot-congress-2023/>



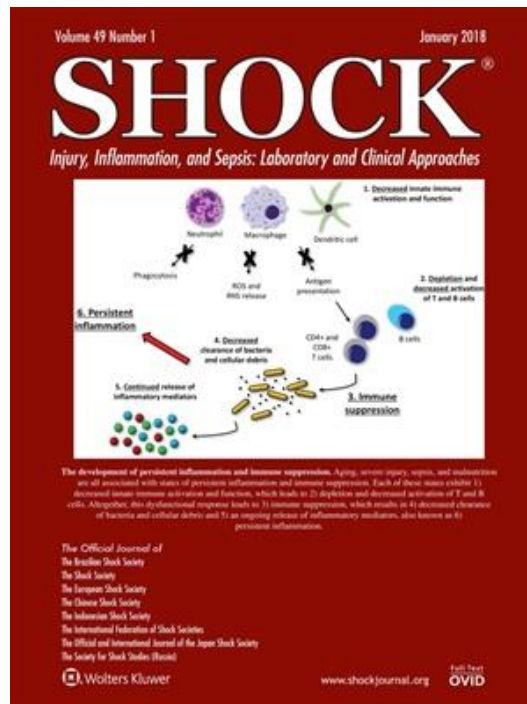
**20<sup>th</sup> Congress of ESS**  
 September 21–23, 2023, Vienna, Austria



**European Congress on Surgical Infections (SIS-E)**  
 NOT announced yet, 2023,  
<https://sis-e.org/>

by Andrea Szabó

## 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=3.553). 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.

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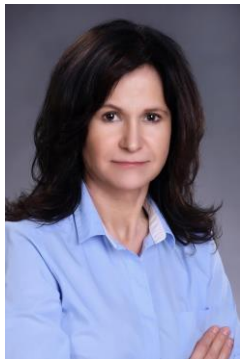


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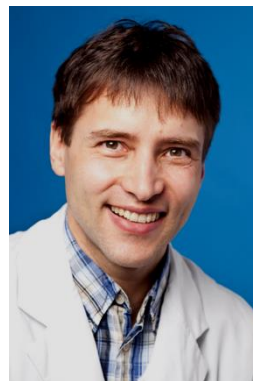
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