



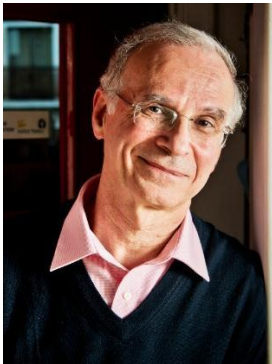
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Contents

Editorial	2
Present status of the upcoming ESS Congress (2017)	4
"I would love to be a tourist in Paris"	6
Congress Reports	9
Report from the IFSS 2016 Tokyo Meeting.....	9
Post-IFSS reflection by Soheyl Bahrami	10
Further highlights of the IFSS 2016 Meeting	11
Report from the SepsEast 2016 Meeting, Budapest.....	12
Report from the International Sepsis Forum, 6-9 December 2016, Institut Pasteur, Paris.....	13
Introducing ESS Research Groups: "Disclosing Secrets in Trauma Immunology" - Trauma and Shock Research Group led by Borna Relja (in Frankfurt).....	15
ESS joins a multi-disciplinary initiative to streamline severe trauma care pathways	17
Sepsis Awareness.....	18
Launch of the ESS Facebook page.....	20
Journal Club: What is new in shock research?.....	21
Welcome new ESS members	22
Meeting updates.....	23
Invitation to publish in Shock®	26
Advertisement (postdoc position)	27
Last words about ESS newsletter	28

Editorial



During the last congress of the International Federation of Shock Societies, I was invited, together with the other presidents of their respective Shock societies, to introduce our European Shock Society (ESS). I realized then that in contrast to all other nationally-based Societies (i.e. USA, Brazil, Japan, China, Russia, Indonesia), ours is continental: it represents either 47 countries with a total of 742.5 million inhabitants, or if one limits it to the European Union only, 27 countries with 508.2 million of inhabitants (well, before the Brexit...). Compared to the other national Societies, is ESS as strong as the continent it emerges from? The answer is no... and very far from that stance, actually. How is it possible? The ESS remains a very small society compared to some of its counterparts. Additionally, it is very poor. So poor that even its own bylaws indicate that in case of a fiscally defunct ESS congress, it is the sole responsibility of the ESS president and his/her local organizing committee to cover the potentially incurred financial loss, basically reimbursing ESS from their own money! As you can imagine, with such a proverbial sword of Damocles over someone's head, it would have been virtually impossible to recruit any members for a local (ESS congress) organization committee. Thus, I conveniently “forgot” to mention the article 18.5 of the ESS bylaws to my French colleagues, meaning that the fiscal responsibility for the congress rests with me alone right now... In the above context, an immediate question arises: how come Europe has not been playing a role proportional to its wealth, to its population? As scientists, we do not care about borders and we consider ourselves being aboard the same ship. As Louis Pasteur once said “Science has no borders because knowledge belongs to humanity”. Then, why is our common ship not bigger and stronger? In 2015; the European papers published in *Shock*, the flagship journal of all Shock societies, represented only approx. 15% of all published papers versus 79% papers from the US. Does it mean that Europeans do not investigate in the shock-related fields as actively as our American colleagues? A Web of Science™ survey of papers published in 2015 in the field of shock, trauma, sepsis, burns and hemorrhage demonstrated 11,624 articles and reviews published by the US authors, and 10,272 articles and reviews published by researchers from the European Union (i.e. 88% of the US-based papers). If we consider that with 320 million inhabitants in the US (vs. 508 million for EU), the American effort in our field of interest is proportionally higher than the one in Europe. However, the difference is not that large to explain the limited participation of European colleagues within the ESS as well as in the *Shock* journal. Thus, what are the reasons? Are European MD and MD-PhD investigators more prone to belong to purely medical Societies rather than a Society, which favors the interface between the bench and the bedside, the scientists and the physicians? Are the European MDs caught in an economic-driven patient care neglecting the importance of an academic self-reflection? Are Europeans less prone, compared to our US colleagues, to belong to a scientific association? Is this a question of money? Are there any other reasons? In any case, an extensive effort needs to be done to improve the strength of the ESS. How can we improve the situation? Let us have a dream... Let us imagine each ESS member recruiting one (or even two!) new member(s)

every year. After just few years, the ESS would increase its visibility worldwide, its influence, its role, its contribution to science (as well as its fiscal capacity). Now, let us wake up and do it!

Fortunately, a great and positive aspect of ESS, is that we have a bunch of highly dedicated, committed and motivated colleagues who do a terrific job to render the WEB site alive, who propose up-dated new way of communication (see our brand new page on Facebook), who spend time to offer you an attractive Newsletter, who actively work to support ESS and to increase its visibility, and who work hard to prepare an enjoyable congress. We just need more of these excellent people with us. Any further reasons to join ESS can be found on our WEB site:

<http://www.europeanshockociety.org/article.php?newsid=11>

Jean-Marc Cavaillon

Present status of the upcoming ESS Congress (2017)



World Alliance Against Antibiotic
Resistance

The program has been set up with the help of the international organizing committee and the French organizing committee. We will have a terrific one! Invited speakers will be soon contacted and hopefully some very prestigious colleagues should join our congress.

The list of distinguished scientists who already accepted our invitation to give a lecture:

ANNANE, Djillali (FRA),
BAHRAMI, Soheyl (AUT),
BILLIAR, Timothy (USA),
BONTEN, Marc (NDL),
CALANDRA, Thierry (CH),
CARLET, Jean (FRA),
CHAUDRY, Irshad (USA),
DALLI, Jesmond (UK),
de WAELE, Jan (BEL),
DYSON, Alex (UK),
GIAMARELLOS-BOURBOULIS,
Evangelos (GRE),
GILROY, Derek (UK),
GRAU, Georges (AUS),

HUBER-LANG, Markus (GER),
LATERRE, Pierre-François (BEL),
LIBERT, Claude (BEL),
MAEGELE, Marc (GER),
MONNERET, Guillaume (FRA),
MUNFORD, Robert (USA),
NETEA, Mihai (NDL),
NEUGEBAUER, Edmund (GER),
OSUCHOWSKI, Marcin (AUT),
PAVLOV, Valentin (USA),
PICKKERS, Peter (NDL),
RADERMACHER, Peter (GER),
RONCO, Claudio (ITA),
SINGER, Mervyn (UK),

SCHULTZ, Arthur (AUT),
SHARMA, Hari Shanker (SWE),
SHARSHAR, Tarek (FRA),
SPRUNG, Charles (ISR),
TEXTORIS, Julien (FRA),
TIMSIT, Jean-François (FRA),
THIEMERMANN, Christoph (UK),
VAN DER POLL, Tom (NDL),
WANG, Ping (USA),
WARREN, Shaw (USA),
WILSON, Lindsay (UK),
WISCHMEYER, Paul (USA),
XIAO, Xian-Zhong (CHN),
YAO Yong-Ming (CHN)

Institut Pasteur

EUROPEAN SHOCK SOCIETY
1983

**Join us, Paris,
Sept. 13th-15th 2017**

15 SESSIONS

- ❖ Good or bad gases
- ❖ Hemorrhagic shock
- ❖ Non-bacterial sepsis
- ❖ Biomarkers of infection
- ❖ Resolution of inflammation
- ❖ New tracks for new therapies
- ❖ Physiopathology of sepsis and MODS
- ❖ Antibiotics and anti-microbial strategies
- ❖ Consequences of shock and sepsis on brain
- ❖ Animal models for human shock and sepsis
- ❖ Long term consequences of trauma and sepsis
- ❖ Metabolic changes during sepsis/critical illness
- ❖ Immune dysregulation during sepsis and shock
- ❖ Revisiting sepsis definitions: impact and consequences
- ❖ Role of comorbidities in the danger responses to shock

FIRST TIME An ESS Summer school on sepsis during the World Sepsis Day

A joint session with the
US Shock Society

A joint session with the
Chinese Shock Society

**XVIIth CONGRESS OF
THE EUROPEAN SHOCK SOCIETY**

<http://www.essparis2017.org>

With the help of the US and Chinese Shock Societies, we are now finalizing the common sessions. We are pleased that the World Alliance Against Antibiotic Resistance will be our partner during the session on antibiotics and anti-microbial strategies (Dr. Jean Carlet, president).

Since money is the life force to organize any congresses, we still are hunting for sponsors. At the present time, we have the positive answer from only one major Company. Accordingly, we do need your help; if you are in close contact with any companies, which would agree to support our congress, please be kind enough to convince them. A document describing the sponsorship opportunity is available at: <http://www.essparis2017.org/#sponsors>

At the present time, Prof. Benoit Vallet, French General Director for health (Ministry of Social Affairs and Health), and Prof. Christian Bréchet, General Director of Institut Pasteur, have agreed to participate in the opening ceremony.



The Entrance of the Conference Center of Institut Pasteur

Of note, at the present time, discussions are on-going to associate our meeting with the International Sepsis Forum.

Inform your students and young collaborators that a wonderful opportunity to visit Paris and to learn more on sepsis will be offered during our first ESS summer school on sepsis to be held on the 13th of September 2017. Mark your calendar!



**ESS SUMMER
SCHOOL ON
SEPSIS**

Jean-Marc Cavaillon

[Back to Contents](#)



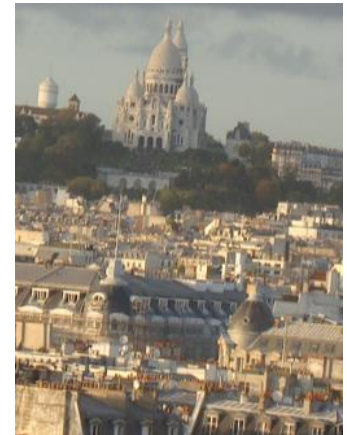
"I would love to be a tourist in Paris"

(follow up of Newsletter Summer 2016)

During your stay for the ESS conference Sept. 2017 in Paris, take the time to stroll along the river Seine (the **quays and banks** were declared by UNESCO in 1992 as part of the world heritage) and look at the "bouquinistes", these small green booths where you can buy second hand books and (more or less) old engravings. From there, you will have a wonderful sight at **Notre Dame** cathedral (built between 1163 and 1345, a masterpiece of French Gothic). Not far is, in the middle of the river Seine, **I'le Saint-Louis** with its sumptuous mansions of the XVIIth century. Don't miss the "**Quartier Latin**", the student quarter. Walk around the church **Saint-Germain des Prés**, the oldest roman abbey church in Paris, and take a drink outside the fancy cafés where the soul of Sartre and other philosophers and the shadows of Hemingway and Fitzgerald are still present.



Enjoy the **Place du Tertre**, this square in the center of the butte Montmartre retains its village atmosphere. You can have a nice diner outside and watch the numerous painters... You may even make a good deal if one of them becomes famous! On the butte, you cannot miss the **Sacré-Coeur**, this uninspired basilica because it is so big, so high, so white, but you can avoid it!



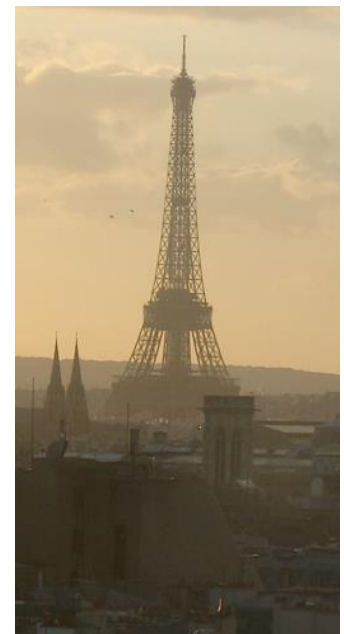
Of course you would like to walk on the **Champs-Élysées**, one of the 12 avenues, which radiate from the **Arc de Triomphe** representative of the hey-days of Napoleon's reign (You remember this ambitious little man who killed so many Europeans on so many battles fields, which finally gave their names to French or British railway stations and squares, Austerlitz, Waterloo, Trafalgar, Iena, depending on the winner). Underneath lies the Tomb of the unknown soldier marked by a permanent flame; another symbol of the deadly wars of the XXth century. Champs-Élysées, one of the most famous avenue in the world (just to say back in your country: "I have been there, look at my selfie").





sophisticated, more peaceful and romantic like **the Père Lachaise cemetery**, looking for the graves of Chopin, Balzac, Molière, Visconti, Yves Montand or Samuel Hahnemann (*you remember the guy who invented homeopathy – left picture -*).

If you want to have an overview of the city, of course you will think to get to the top of the **Eiffel Tower** (317 m high) but I will recommend the top of the **tour Montparnasse** (209 m high), at least a place from where you don't see this ugly late tower ! You can also get to the top of the **Centre Georges Pompidou**, this strange, freshly repainted refinery-like museum of modern art, close to the historical **Marais quarter**. Finally, you could also climb on the top of the **Grande Arche** in the business center of La Défense. Of course this list of monuments would not be complete without mentioning the **Conciergerie**, an important stronghold of Capetians and witness of the remarkable civilian architecture of the XIVth century, la **Sainte Chapelle** with its boast radiant stained-glass and rose windows from the XVth century, **l'Hôtel des Invalides**, standing on the huge esplanade, founded by Louis XI for wounded soldiers, **l'Hôtel de Ville**, a very nice neo-renaissance style building, Paris town hall, **l'Opéra Garnier**, built in 1860, its ceiling was decorated later by Chagall, le **Panthéon**, a old church transformed to house the ashes of illustrious men who fought for France's freedom; there are also the tomb of famous writers (Voltaire, Rousseau, Hugo, Zola, Dumas) and scientists (Pierre & Marie Curie, Langevin and Braille).



Don't forget to appreciate these last days of the summer in some of the nice parks and gardens. From the most recent one created in 1996, the **Parc André Citroën** (on the former site of Citroën automobile plant) with its huge green houses to the **Parc de Bagatelle**, a lovely place with its rose garden, a real digest of the art of gardening over the last three centuries. Have a look of the **Jardin du Luxembourg**, a romantic garden adjoining the Sénat and of course enjoy the **Jardin des Tuileries**, a magnificent formal French garden designed by Le Nôtre (The famous gardener who drew the Park of Versailles) where you could visit the Nymphaea of Monet in the Orangerie Museum. With pools, flower beds and ramps its spreads in a single expanse from the Pyramid du Louvre to the **Place de la Concorde**.

Don't miss the view on this wonderful square built in 1755-75 by Louis XVth's architect Gabriel, famous for the obelisk of Louqsor, offered by the viceroy of Egypt, which dominates the place since 1836. It is there that the king Louis XVIth lost his head during the French revolution. Indeed the "guillotine", invented by a medical doctor, Dr. J-I. Guillotin, cut efficiently some 1100 heads on that square! Nowadays, the "Grande Roue" offers a far more peaceful atmosphere... although there is a fight between the Mayor of Paris which wishes to remove it and its owner! So not that sure it will be still there on September 2017!



How the artiste JR got rid of the pyramid of the Louvre!



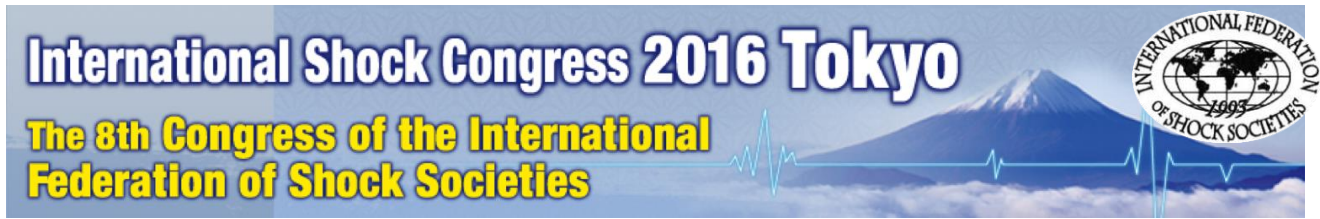
A window over Paris

To be continued (next time we will talk about Paris' museums)

Jean-Marc Cavaillon

Congress Reports

Report from the IFSS 2016 Tokyo Meeting



held in the Dome Hotel in Tokyo, October 3-5, 2016 under the presidency of Prof. Hiroyuki Hirasawa. The Congress gathered 50 invited speakers and 160 registered participants from 21 countries.

After a presidential address of Prof. Hirasawa, the congress started with a session devoted to a presentation of the different Shock Societies present in Tokyo (Ping Wang-president of the US Shock Society, Reinaldo Salomao-president of the Brazilian Shock Society, Yong-Ming Yao-president of the Chinese Society, Shigeto Oda-president of the Japanese Shock Society, and Viktor Moroz-president of the Russian Society for Shock Studies). Jean-Marc Cavaillon presented the ESS, paying tribute to the ESS founders (see the Spring ESS Newsletter) and some of the most recent past-presidents and the places where the ESS biennial congresses were held: Jean-Louis Vincent (La hulpe, 1998); Jan Goris (Nijmegen, 2000); Ansgar Aasen (Oslo, 2002); Heinz Redl (Vienna, 2005); Uwe Brückner (Ulm, 2006); Christoph Tiemerman (Lisbon, 2009); Salvatore Cuzzorea (Taormina, 2011); Soheyl Bahrami (Vienna, 2013); Edmund Neugebauer (Cologne, 2015). Dr. Cavaillon also paid tribute to some key leaders and friends of the ESS (Günther Schlag, Eugen Faist, Irshad Chaudry). He mentioned the outstanding work of the present team (Inge Bauer, Marcin Osuchowski and Markus Huber-Lang). Finally, Dr. Cavaillon concluded by inviting the participants to attend the next 2017 ESS congress in Paris.



Two excellent plenary lectures were delivered. One was given by **Shizuo Akira** (Osaka University, Japan). After recalling the Toll-like receptors properties, he presented his recent investigations on three different RNases induced by TLR ligands, namely, Regnase-1, Zc3h12a, and Roquin. These enzymes cleave mRNAs of inflammatory genes such as IL-6 and IL-12p40, and negatively regulate cellular inflammatory responses. Regnase-1 deficient T-cells produce enhanced levels of cytokines (IFN γ , IL-4, IL-17). Zc3h12a KO mice undergo spontaneous death, splenomegaly, and lymphadenopathy associated with large amount of auto-antibodies. Regnase is present during the early phases of inflammation whereas Roquin is expressed during the late phase (*Mino et al., 2015, Cell 161, 1058–1073*).



The second plenary lecture was given by **Kevin Tracey** (Feinstein Institute, Manhasset, USA). In 2016, Kevin Tracey was awarded by the US Shock Society with the Scientific Achievement Award, and by the International Endotoxin and Innate Immunity Society with the Bang Award. Kevin Tracey recounted his amazing odyssey, which started in 1985 with his fight to save Janice, a one year-old child who died of sepsis, to his demonstration of the deleterious properties of TNF (a paper published in Science, 1986, cited more than 2500 times, and a paper published in Nature, 1987 cited

more than 2280 times), until his most recent discoveries on the cross-talk between the immune system and the central and peripheral nervous system which controls an exacerbated inflammatory response. His last results concern the successful use of an implanted vagus nerve stimulator in patients with rheumatoid arthritis (*Koopman et al. PNAS 2016;113(29):8284-9*) and the role of choline acetyltransferase T-cells that control arterial blood pressure (*Olofsson et al. Nature Biotech. 2016*).

by Jean-Marc Cavaillon

Post-IFSS reflection by Soheyl Bahrami

When I was approached by the president of IFSS Dr. Hirasawa and the Congress committee in May 2015 to propose and organize a session on behalf of the ESS without financial travel support for speakers, I had serious concerns to find colleagues, who would accept the financial burden in addition to the scientific challenge. Considering the hot topic of coagulopathy as a potential session, I simply called the experts in the field, expecting many refusals. To my pleasant surprise, all colleagues immediately agreed to contribute. Thanks to all those speakers we successfully organized the Symposia 2 entitled “Sepsis & Trauma Associated Coagulopathy” as the ESS Contribution to the IFSS. This collegial spirit was a wonderful experience to me.

The symposium covered different aspects of pathophysiology and treatment strategies of sepsis- and trauma-induced coagulopathy (DIC & TIC). The presentation by Dr. Toshiaki Iba (Juntendo University Tokyo, Japan) focused on the role of histones in inflammation, particularly on histones-induced endothelial activation and coagulopathy. In this respect the inhibitory effect of some plasma proteins such as albumin, activated protein C, and pentaxin 3 towards histones toxicity and the therapeutic potential of pharmaceutical agents such as heparins were addressed by Dr. Iba.

The cross-talk between the complement and coagulation systems, contributing to coagulopathy and immune dysfunction after trauma and during sepsis was in focus of the second presentation entitled “Molecular management in trauma” given by Dr. Markus Huber-Lang. His talk addressing some immunological phenomena following trauma such as neutrophil dysfunction, the blockade of key elements of complement activation (C3, C5a) was suggested as a potential therapeutic approach.

The management of the low fibrinogen concentration as potential risk factor in bleeding trauma patients was the subject of the talk by Dr. Heinz Redl. A theragnostic approach based on specific ROTEM and TEG assays has been introduced to be implemented in the treatment of trauma-induced coagulopathy. The presentation was followed by an intense discussion regarding various clinical aspects.

Dr. Marc Maegele (Cologne-Merheim Medical Center/University Witten-Herdecke, Cologne, Germany) presented an update on the 2016 European guidelines for the management of the trauma related coagulopathy. He specifically addressed potential concerns regarding the limitation of blood products and the 1:1:1 transfusion strategy. In addition, Dr. Maegele discussed the advantages of the viscoelastic test methods in the early detection of hemostatic disorders but also the limitation of their availability in the point of care guided therapy.

The impact of age in sepsis and pancreatitis related coagulopathy was nicely presented by Dr. Hiroshi Saito (University of Kentucky, Lexington, KY, USA). Based on his experimental data, it appears that in contrast to the young mice, aged mice cannot efficiently produce activated protein C (aPC). In this respect, the age-associated low level of thrombomodulin has been suggested by Dr. Saito to be the underlying mechanism for

the reduced aPC in aged individuals. Finally, the presentation by Dr. Wenjun Matini (US Army Institute of Surgical Research, Houston, TX, USA) aimed at experimentally approaching the trauma-induced coagulopathy by comprehensively reviewing experimental data that explore potential contributors of TIC, including hypothermia, acidosis, shock, fibrinogen, and fluid resuscitation.

I would like to express my sincere thanks to all of the speakers for making this symposium possible and successful. I would also like to take this opportunity to congratulate Prof. Hirasawa and his team for organizing the IFSS congress in a perfect way; it included not only the top scientific program but was also enriched by many social events that promoted interaction among participants and offered an insight into the local culture. Another very joyful element of the IFSS congress was the strong participation of junior scientists, not only from Japan but also from many overseas countries – the strong Travel Award support was certainly a helpful factor.

Soheyl Bahrami
President of the IFSS

Further highlights of the IFSS 2016 Meeting

In a great talk at the session „Microcirculation and endothelial damage“, Dr. Motomu Shimaoka (Mie University Graduate School of Medicine, Japan) demonstrated that we begin to understand the deregulated interplay between inflammation and coagulation which plays a pivotal role in the pathogenesis of sepsis. Apart from the well-known integrins, the expression of coagulation-regulating molecules on the surface of endothelial cells such as thrombomodulin (TM) or activated protein C (APC) participates in the process of leukocyte adhesion to endothelium. As demonstrated by Dr. Shimaoka, binding of the lymphocyte function-associated antigen-1 (LFA-1) to the membrane-proximal part of thrombomodulin indicates that TM potentially functions as a new ligand for leukocyte integrins, thus, it may be involved in the dynamic regulation of leukocyte adhesion with endothelial cells. In this context, a new generation of potent therapeutic small-molecules targeting both inflammation and coagulation in sepsis/septic shock may hold great promise.

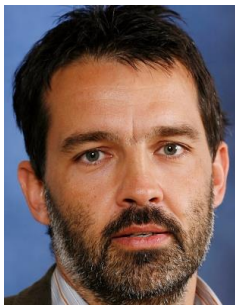
Another excellent talk at the same late session was presented by Dr. E. Christiaan Boerma (Academic Medical Center Amsterdam, The Netherlands). Dr. Boerma presented an innovative approach of using in-vivo microscopy at the bedside of critically ill sepsis patients to monitor total vessel density (TVD, recruitment of capillaries), which may be used as a stop-sign for fluid administration. As the microcirculation disturbance plays a central pathophysiological role in the development of organ failure (and considering that microcirculatory alterations are more severe in non-survivors than in survivors), the maximum TVD might denote a promising tool for monitoring microcirculation and support personalization of the therapeutic strategies in critically ill patients.

Despite several questions still to be answered (hopefully at the next Shock Meetings), several innovative goal directed strategies/therapies have been introduced at the International Shock Congress.

A warm regards and my sincere thanks to Prof. Hirasawa, all organizers, attendees, members and mentors.

by Borna Relja

Report from the SepsEast 2016 Meeting, Budapest



The remarkably popular (>500 participants) SepsEast Forum (<http://sepseast2016.com/>) was organized by Zolt Molnár (professor of Anesthesiology, University of Szeged, Hungary) for the 3rd time in Budapest, on November 10-12, 2016. The name of this congress refers to the fact that (1) sepsis is a dedicated common field of interest for the attending anesthesiologists and intensivists and (2) that this conference intends to be a meeting point for clinicians and researchers from different Central and Eastern European countries, also serving as a melting pot of ideas originating from the Western Europe, US and Japan.

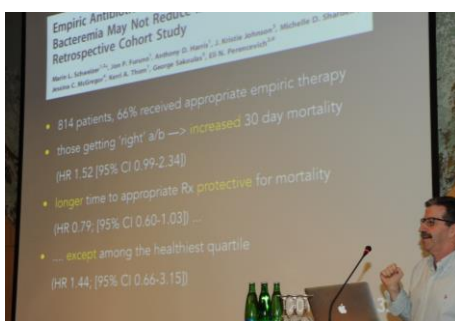
The congress comprised of 14 symposia and 4 poster sessions and pre-congress workshops (hands-on ultrasound workshop, simulation course on bronchoscopy, workshop on hemeostasis).

Sepsis was a targeted topic and it assumed various formats. A “Special Issue” round table discussion with participation of several top scientists including Mervyn Singer: “Sepsis-3” (recommended link: <http://jamanetwork.com/journals/jama/fullarticle/2492881>), Anand Kumar: “Optimizing antimicrobials - Speed of source control in septic shock”, Frank Brunkhorst: “Measures to improve incidence and outcome of nosocomial infections”, Axel Nierhaus: “Immunological interventions in sepsis...” and the congress president Zolt Molnár: “Sepsis and Love”.

This latter presentation wittily compared the similarities of sepsis and



Konrad Reinhart



Mervyn Singer

love in hemodynamic (and many more) respects. The above was followed by sessions about infection control at ICUs (chaired by Anand Kumar), results of cytokine absorption (chaired by Takashi Tagami) and relevance of biomarkers (chaired by Zoltán Pető) and Pro-Con debates on early percutaneous tracheostomy and evidences in sepsis (by Konrad Reinhart and Mervyn Singer). There were further sessions focusing on ECMO therapy, respiratory dysfunction and mechanical ventilation, hemodynamics, monitoring and other intensive care-related topics.



A concert was given by a band called “OnCall” in which the congress president himself was the guitarist/singer while the head of the Dept. of Emergency Medicine, (University of Szeged, Hungary) served as the drummer (similarly to concerts in the past 2 years).

by Andrea Szabó



Report from the International Sepsis Forum, 6-9 December 2016, Institut Pasteur, Paris

Once again, the reputable buildings of the Institut Pasteur hosted the International Sepsis Forum (ISF) meeting. This is an annual conference centered on an international collaborative effort between industry and academia and gathers the most recognized experts from both fields. The primary goal of the ISF is to reduce the mortality and morbidity of sepsis worldwide. ISF is presently chaired by Dr. Derek Angus, Professor and Chair of the Department of Critical Care Medicine at the University of Pittsburgh, USA. The congress held a series of plenary sessions with lectures by invited experts who addressed the diagnosis, epidemiology, science and clinical treatment of sepsis. Additionally and with no less attention, a poster session was organized (with best abstract awards granted), where younger researchers could present results of their work.

What made this conference special was the fact that the new definitions of sepsis as well as the new Surviving Sepsis Campaign Guidelines have been released this year and the authors of both attended the meeting. Mervin Singer who was the first author of the new Sepsis-3 consensus definitions summarized them and presented the philosophy that stood behind them. This lecture was followed by a vigorous discussion by a panel of experts and members of the audience. Several concerns regarding the bedside application of the new definitions were raised. Also, the use of SOFA score as a diagnostic tool was questioned. In turn, the authors of the consensus tried their best to clarify the novel paradigm in the context of the new sepsis definitions and highlighted that the diagnostic accuracy of proposed scores needs a prospective validation. Interestingly, several reports from different countries from Greece to Japan showed a good accuracy of the new definitions in their retrospective cohorts. The new treatment guidelines, which are planned to be published around March 2017, also provoked many questions, especially the guidelines on the initial resuscitation and lack of specific hemodynamic goals (other than decreasing circulating lactates). However, such guidelines shift the concern on the individualization of treatment by frequent evaluation of the patients' clinical status rather than just achieving given parameters which may be misleading (e.g. central venous pressure for all patients).

Unfortunately, none of the clinical sepsis trials presented at the meeting unequivocally succeeded, but they provide many pieces of interesting information, especially from the observational trials. John Marshall spoke about several promising on-going clinical trials (corticosteroid, vasopressor, fluid, antibiotic, heparin, Ringer's lactate, gut decontamination, probiotic). This provoked a response from Jean-Louis Vincent who rose the point that in none of those on-going studies, the study design has been improved based on the failures of the past trials. Next, Philip Dellinger (Camden, USA) reported the failures of the EUPHRATES trial (Evaluating the Use of Polymyxin B Hemoperfusion in a Randomized controlled trial of Adults Treated for Endotoxemia and Septic shock). The study aimed to eliminate circulating endotoxin with polymyxin B cartridges by a two-hour treatment performed twice over 24h appeared under-designed (given that most endotoxin in the blood stream is bound to red blood cells, platelets, and leukocytes). Jean-Louis Vincent convincingly presented thrombomodulin as a valuable target of an on-going phase II clinical trial. Another study sponsored by Bristol-Myers Squibb aimed to target PDL-1 to limit the alteration of the immune system in sepsis patients is currently recruiting participants.

In the latter context, it is definitely worth mentioning the work of Tom van der Poll's team showing the low contribution of secondary infections on the mortality in sepsis patients. Van der Poll and his colleagues also performed an impressive genome-wide transcription assay in a huge group of patients comparing the genomic response to community-acquired versus hospital-acquired pneumonia. Even though they did not

[Back to Contents](#)

find many differences on the gene expression level between these two conditions, they elegantly showed the potential of such an assay approach (*van Vught et al. JAMA 2016, 315, 1469*).

What is also worth mentioning, more and more leaders in the field pay attention to different endotypes of sepsis patients revealed by gene polymorphisms (as that mentioned by Thierry Calandra regarding MIF (*Savva et al. Proc. Natl Acad Sci USA 2016, 29, 113*) (see also *Davenport et al. Lancet Respir Med. 2016, 4, 259-71*), or by epigenetic imprinting, and the compartment specific cellular changes during sepsis. Appreciation of all of those factors will hopefully help to better design clinical trials in the near future.

by Tomasz Skirecki
Jean-Marc Cavaillon

Introducing ESS Research Groups: “Disclosing Secrets in Trauma Immunology” - Trauma and Shock Research Group led by Borna Relja (in Frankfurt)

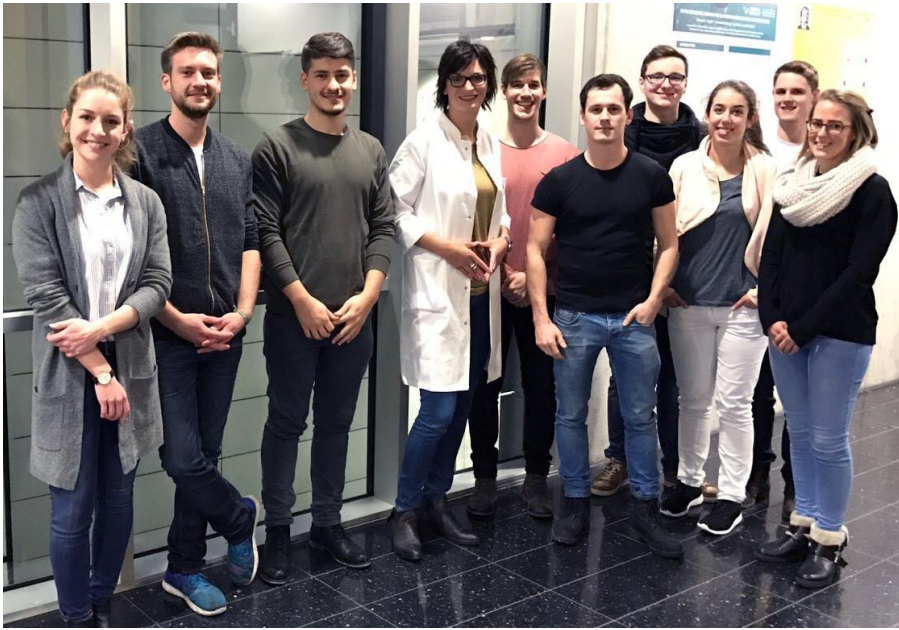
With a long-standing interest in the mechanisms involved in trauma-induced injury, inflammation and regeneration, Borna Relja, a graduate of Biology from the Goethe University Frankfurt, joined Dr. Ingo Marzi's lab more than ten years ago to address trauma and shock research. Dr. Marzi, who became head of the Department of Trauma, Hand and Reconstructive Surgery nearly 15 years ago, successfully brought up basic trauma research ideas to the Goethe University. Within the last decade, Dr. Relja, funded by the German Research Foundation (DFG) from the beginning of her work, investigated the pathophysiology behind trauma- and shock-induced inflammation and organ failure. By studying multiply traumatized patients in parallel to experimental *in vivo* studies, Dr. Relja put strong emphasis on the clinical relevance of her research in terms of potential translational diagnostic and/or therapeutic approaches.



After her research fellowship in 2009 at the Mie University in Japan, in Dr. Takei's lab, Dr. Relja returned to Frankfurt. Since then, under her supervision, her young team took a leading role in alcohol-related trauma research in Germany, and became a prime example of a productive and well-funded lab. With both PhDs and MDs working together, Dr. Relja's team primarily focuses on the dual role of alcohol misuse with regard to regeneration, inflammation and outcome. Her research projects are coordinated by several excellent clinical residents. Dr. Nils Wagner's work deals with the experimental investigation of the clinical "drink and drive" scenario, identifying potential therapeutic options. The research work of Dr. Katharina Mörs concentrates on the profound analysis of the underlying mechanisms, especially the role of NFkappaB-mediated pathways.

In a close collaboration with renowned researchers and clinicians, Drs. Pape, Hildebrand, van Griensven, Huber-Lang and other experts, Frankfurt's team constitutes the mainstay of the *TREAT* Research Group, which successfully established a promising long-term pig model of polytrauma. Dr. Relja's group already achieved auspicious results with regard to pulmonary and hepatic complications as well as systemic inflammatory deregulation of the innate and acquired immune system in this valuable and complex model. The direct translational clinical relevance is addressed not only in experimental but also in clinical studies in Frankfurt by other young talented residents within the Trauma and Shock Research Group. There are numerous further current national and international research cooperations, e.g. with Dr Takei's and Dr. Eguchi's lab at the Mie University in Japan or Dr. Billiar's and Dr. Vodovotz's lab at the University of Pittsburgh in the US.

Moreover, together with other members of the national German Trauma Research Network (NTF), notably Drs. Huber-Lang and Marzi, Dr. Relja has set up a national biobank for sera obtained from multiply traumatized patients. With valuable support of the German Society for Trauma Surgery, a nationwide database for clinical and experimental immune-monitoring accomplishing the biobank is established and coordinated under their primary responsibility. For the pursuit of knowledge and the advancement of science by providing this “tool”, the acute critical illness in the clinical scenario will be monitored prospectively, allowing high-quality “immune-monitoring” of multiply traumatized patients as well as the adequate therapy approaches in the future.



Visitors and new members are always welcome to our Trauma and Shock Research Group in Frankfurt!

By Nils Wagner, Katharina Mörs and Borna Relja

ESS joins a multi-disciplinary initiative to streamline severe trauma care pathways

ESS is joining forces with other medical societies to streamline severe trauma care pathways. Under the leadership of Professor Jean-Louis Vincent, the ambitious initiative aims to interface pre-hospital emergency care with the intra-hospital medical and surgical teams for patients with major trauma. Ultimately the project will develop of a tool to share the minimum essential information to support emergency transport decisions using innovative telemedicine solutions.

The project was conceived by the European Critical Care Foundation (ECCF), an independent foundation established to improve the care of critically ill patients.

Introducing the project in September to representatives from European Society for Anaesthesiology (ESA), European Society for Emergency Medicine, European Society for Paediatric and Neonatal Intensive Care and ESS, Prof Vincent said “Faster, more reliable information about hospital capacity and capabilities and relevant practical information is needed to ensure that patients arrive at the most appropriate facility in the shortest possible time. Greater information about the emergency in pre-hospital settings is needed to trigger the activation of intra-hospital teams responsible for further diagnostic tests, anaesthesia, surgery, intensive care and other processes of care. We can only address this through collaboration between our different disciplines, as well as with other key players in pre-hospital systems – local government, the emergency services, payers, hospital administrators and industry partners”.

ESS Councilor Professor Dr Marc Maegele (Cologne/Germany) is currently co-writing a paper with Professor Dan Longrois (ESA) and others that will develop these themes and propose a patient-centred integrated care model for severe trauma. A number of cities and regions have expressed an interest in collaborating on the topic and it is expected that a two-year pilot project will lead to framework for sharing data and information. In parallel, ECCF will showcase the project and promote project findings and recommendations to EU and national policymakers as the project evolves.

The European Critical Care Foundation acts as a neutral platform for multi-disciplinary discussion and collaboration between medical societies and other critical care stakeholders, and provides visibility at a political level for diverse issues in the care of acutely ill patients. Further information about the work of the Foundation can be found at www.euroccf.org

HELEN BREWER, European Critical Care Foundation, Brussels 30 November 2016.



by Marc Maegele

Sepsis Awareness

1st World Sepsis Congress



The **1st World Sepsis Congress** took place *completely online* on September 8th and 9th, 2016. The congress was endorsed by the ESS:

According to the program chairs, Simon Finfer and Konrad Reinhart, 15.000 people from 146 countries registered for the **1st World Sepsis Congress**:

“This was the first time we have organized a congress on such a scale, but given the resounding success and enthusiastic feedback from registrants for this first congress, we plan to repeat the congress in two years”.

All talks are freely available. Please visit www.worldsepsiscongress.org to find more information and the link to the talks.

What L'Oréal and Starfish Have to Do with Sepsis

Do you know what 'L'Oréal' and 'Starfish' have to do with awareness for sepsis?

L'Oréal:

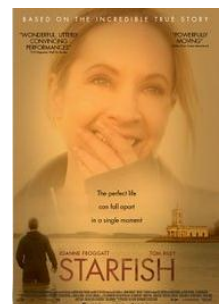


Orlaith Staunton speak at the L'Oréal Women of Worth Gala

L'Oréal honors extraordinary women who selflessly volunteer their time to serve their communities. Orlaith Staunton is one of these remarkable women. Orlaith and her husband Ciaran founded the Rory Staunton Foundation For Sepsis Prevention after losing their son Rory to Sepsis in 2012.

Starfish:

Starfish is the title of a critically acclaimed British independent film that depicts the true story of a family whose life falls apart when Tom, husband and father, is struck by sepsis.



“We are incredibly happy that sepsis is picking up steam in the media, and that the [several books](#) about sepsis are now joined by a movie. However, we still have a long way to go until everyone knows about sepsis — thanks for your continued support in this fight!” (Konrad Reinhart & the World Sepsis Day Head Office)

CHEST Journal: Special Article Collection

A new *Special Article Collection* was provided by the [CHEST Journal](#).



The collection focused on sepsis, drawing together a selection of recently published articles from **CHEST** in recognition of [Sepsis Awareness Month](#).

Please submit the [form](#) to access the CHEST Sepsis Article Collection.

by Inge Bauer

Launch of the ESS Facebook page

On January 2017, ESS started its Facebook page, the aim of which is to raise awareness of our society and the events that it organizes as well as link up its existing (and potential) members. ESS sincerely encourages all current members to 'like' our page. That way, you will be continuously up-dated with the society's life and activities. By 'liking' our page, we will be able to keep reminding you about all upcoming deadlines related to the ESS congress.



See you in the virtual space!

<https://www.facebook.com/europeanshock/>



Journal Club: What is new in shock research?

Highlights of remarkable findings recently published in shock research

Occurrence of early danger signals in trauma patients

Source: Timmermans K et al. Plasma levels of danger-associated molecular patterns are associated with immune suppression in trauma patients. *Intensive Care Med.* 2016 Apr; 42(4): 551-61. doi: 10.1007/s00134-015-4205-3. Epub 2016 Feb 24. ([link to paper](#))

Main important messages:

The release of danger signals occurs extremely early after a sterile inflammation, and the consequences on the immune system are also happening very rapidly after the insult. The group of Peter Pickkers (Nijmegen, The Netherlands) analyzed blood samples obtained on the trauma scene, in the emergency room and during the following days. The highest levels of damage associated molecular patterns (DAMPs) (i.e. circulating nuclear DNA, mitochondrial DNA and HSP70) were measured in samples harvested from the trauma scene. Significant amount of pro- and anti-inflammatory cytokines were already measurable in the emergency room. The peaks of IL-6 and IL-8 were observed on day one, but IL-10 reaches its peak when assessed in the emergency room. Markers of the reprogramming of circulating leukocytes (i.e. reduced HLA-DR mRNA, ex vivo TNF, IL-6 & IL-10 production in response to LPS) were already noticeable in samples obtained on the trauma scene. This very nice investigation illustrates that the two wave curve (SIRS followed by CARS) propagated by some tenors in the field for more than a decade is wrong, and that the alteration of the immune system is occurring concomitantly with the inflammatory response.

Written by: Jean-Marc Cavaillon, Institut Pasteur Paris

Welcome new ESS members

We cordially welcome our new members who joined the ESS in 2016:



Claude Libert, PhD; Belgium

Ashham Mansur, MD; Germany

Viktoria Weber, PhD; Austria

Fabienne Venet, PharmD, PhD; France

Theodoros Xanthos MD, Pg Dip (Ed), MSc, MRes (EdD), PhD, FHEA, FAcadMEd, FCP, FERC, ERT, FESC, Cyprus

Meeting updates

Dear reader of the newsletter,

If you give a talk at any of the following congresses, please advertise our ESS 2017 Congress in Paris. A slide will be provided by Jean-Marc Cavaillon (jean-marc.cavaillon@pasteur.fr).

46th Critical Care Congress

January 21-25, 2017

Honolulu, Hawaii, USA

<http://www.sccm.org/Education-Center/Annual-Congress/Pages/default.aspx>



22nd International Symposium on Infections in the Critically Ill Patients and Infection and Sepsis Symposium

February 08-10, 2017

Porto, Portugal

<http://www.ichs.org/event-2293932>



37th International Symposium on Intensive Care and Emergency Medicine

March 21-24, 2017

Brussels, Belgium

<http://www.intensive.org/>



ESICM Euroasia

April 6-8, 2017

Hong Kong, China

<http://www.esicm.org/events>



18th European Congress of Trauma & Emergency Surgery

May 7-9, 2017

Bucharest, Romania

<http://www.estesonline.org/estes-congress-2017/>



40th Annual Conference on Shock

Mariott Harbor Beach

June 3-6, 2017

Fort Lauderdale, Florida



40th Annual Conference on Shock

Mariott Harbor Beach
Fort Lauderdale, Florida
June 3 - 6, 2017

<http://shocksociety.org/Meetings/Annual-Meeting-Schedule.aspx>

8th World Congress of the Abdominal Compartment Society WSACS

June 15-17, 2017

Banff, Alberta, Canada

<http://www.wcacs2017.org/>



30th Annual European Congress on Surgical Infections

June 8 -9, 2017

Hamburg, Germany

<http://sis-e.org/2017/>



2017 RDCR SYMPOSIUM

June 26-28, 2017

Bergen, Norway

<http://rdcr.org/>



17th Congress of European Shock Society: numerous "premières"

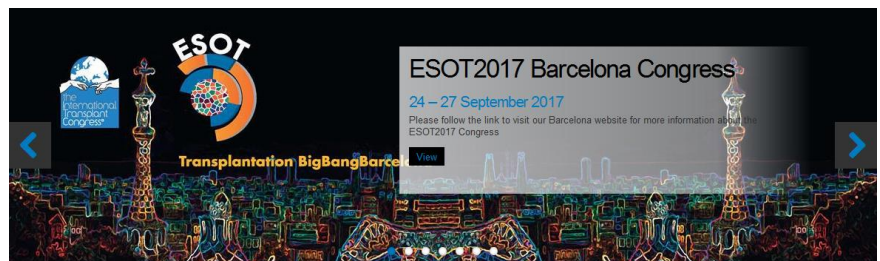
September 13-15, 2017

Paris, France

<http://www.essparis2017.org>**18th Congress of the European Society for Organ****Transplantation**

September 24-27, 2017

Barcelona, Spain

<http://esot2017.esot.org/>**13th World Congress of Intensive and Critical Care Medicine/XXII Brazilian Congress of Intensive Care Medicine**

November 8-11, 2017

Rio de Janeiro, Brazil

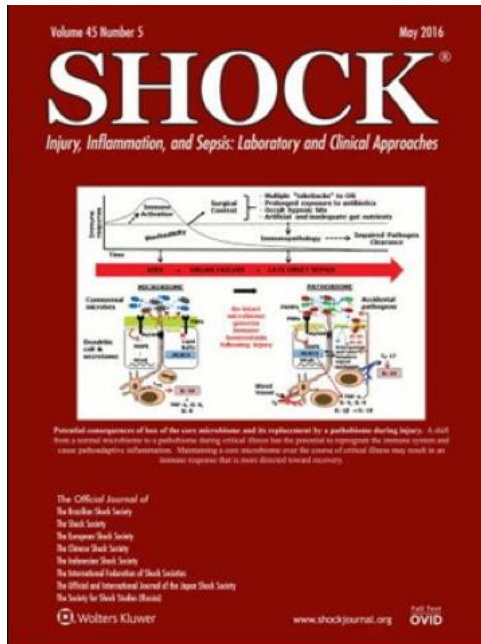
<http://www.criticalcare2017.com.br/ingles/>**41st Annual Conference on Shock**

June 9 - 12, 2018

JW Marriott Camelback Inn Resort and Spa
Scottsdale, Arizona<http://shocksociety.org/Meetings/Future-Meetings.aspx>

Invitation to publish in Shock®

REMINDER



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=3.048). 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>.

Advertisement (postdoc position)



Sepsis, defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection, represents a major healthcare challenge with high incidence and mortality. A recent reappraisal in sepsis pathophysiology has led to a significant gain of interest for the central role of acquired immunosuppression in this clinical context. Indeed, sepsis and in particular septic shock are associated with the development of immune dysfunctions affecting both innate and adaptive immune responses. Importantly, intensity and duration of sepsis-induced immune alterations are associated with increased risk of secondary infections and mortality, therefore identifying sepsis-induced immune alterations as a novel therapeutic target in this hitherto deadly disease.

The research unit EA 7426 PI3 “Pathophysiology of Injury-Induced Immunosuppression” (Université Claude Bernard LYON 1 - Hospices Civils de Lyon – bioMérieux) headed by Pr Monneret is dedicated to the study of injury-induced immunosuppression. This multidisciplinary group is composed of more than 20 researchers and clinicians with strong expertise in Immunology, Intensive Care Medicine, Transcriptomics, Computational Biology and Bioinformatics. In a translational research approach combining observational studies in clinic and physiopathologic evaluations in ex vivo and in vivo models, the group led by Dr Venet is focusing on injury-induced lymphocyte alterations (e.g, inhibitory immune checkpoints, bioenergetics, IL-7 as lymphocyte rejuvenator).

Within this research unit, Dr Venet is seeking for a highly motivated post-doctoral fellow with strong experience in cellular biology and immunology as well as excellent interpersonal skills. Excellent publication record in relevant scientific areas would be a plus. This post-doctoral position will be financed through an application to the Marie Skłodowska-Curie actions – Individual European Research Fellowship. This research program initiated by the UE (Horizon 2020 program) is opened to researchers either coming to Europe or moving within Europe and finances 2-year individual fellowships. Once the candidate is identified, research proposal will be prepared in close collaboration with EA 7426 research team.

Applications with CV, contact information for three references and a description of the candidate's past research experience should be sent to fabienne.venet@chu-lyon.fr.

Recent publications:

- Peronnet E, Mouillaux J, Monneret G, Gallet-Gorius E, Blein-Henry S, Lepape A, Textoris J, Venet F; MIP Réa Study Group. Elevated soluble IL-7 receptor concentration in non-survivor ICU patients. *Intensive Care Med.* 2016;42(10):1639-40.
- Restagno D, Venet F, Paquet C, Freyburger L, Allaouchiche B, Monneret G, Bonnet JM, Louzier V. Mice Survival and Plasmatic Cytokine Secretion in a "Two Hit" Model of Sepsis Depend on Intratracheal *Pseudomonas Aeruginosa* Bacterial Load. *PLoS One.* 2016;11(8):e0162109.
- Hotchkiss RS, Monneret G, Payen D. Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy. *Nat Rev Immunol.* 2013;13(12):862-74.
- Venet F, Foray AP, Villars-Méchin A, Malcus C, Poitevin-Later F, Lepape A, Monneret G. IL-7 restores lymphocyte functions in septic patients. *J Immunol.* 2012;189(10):5073-81
- Venet F, Lukaszewicz AC, Payen D, Hotchkiss R, Monneret G. Monitoring the immune response in sepsis: a rational approach to administration of immunoadjuvant therapies. *Curr Opin Immunol.* 2013;25(4):477-83.

LAST WORDS ABOUT



NEWSLETTER

Dear present ESS member,

If you like your ESS Winter 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).

The annual membership fee is 50 EUR for regular members and 25 EUR for student members.

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



European Shock Society Membership Application Form

Sign up online at www.europeanshocksociety.org/register

Please post completed form to:
ESS General Secretary, Dept of Anaesthesiology, Heinrich Heine University Duesseldorf, Duesseldorf, Germany
or fax to:
+49 211 81 015 12053

Form fields shown in italics are optional

Title	<input type="text"/>
First Name(s)	<input type="text"/>
Last Name	<input type="text"/>
<i>Researcher ID</i>	<input type="text"/>
Country	<input type="text"/>
Job Title	<input type="text"/>
Company/ Institution	<input type="text"/>
Email Address	<input type="text"/>
<i>Web Address</i>	<input type="text"/>
Phone No.	<input type="text"/>

Area(s) of research interest:

Expertise and/or facilities:

Publications:

<http://www.europeanshocksociety.org/register>