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Message from the ESS President

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

Time is flying! After the unforgotten meeting in Paris last fall (under our past-president J.M. Cavaillon), which we covered in more detail in our last newsletter, we are meanwhile in the middle of preparing our next gathering. Just as a reminder: the biannual ESS congress will be in Chania, Crete in 8th-12th October 2019. You will find more information about this exciting event, inclusive the summer school for our juniors on “hemorrhagic shock”, in the current newsletter and on our website.

An important step towards developing a common language and better understanding among clinicians, clinical scientists and scientists with classical and modern research topics of the ESS has been recently accomplished: at a joined session of ESS and ESTES (European Society for Trauma and Emergency Surgery) in Valencia, we addressed the barrier dysfunction after polytrauma. Given that this initiative was well received, we have decided to continue this important clinical dialogue at our upcoming ESS meeting with a common session entitled “Get the clinicians back to shock research”.

In this context, an interventional clinical sepsis study has been currently under way under the ESS patronage. Our president-elect, Evangelos J. Giamarellos-Bourboulis, University of Athens, is the scientific trial coordinator. We all are looking very forward to the first results which will be presented at Chania. Furthermore, as in the last years, ESS has endorsed the Survival Sepsis Campaign (led by Konrad Reinhart).

In the beginning of June, few of us (myself included) had a chance to visit the annual congress of our sister US Shock Society at Scottsdale, Arizona. Highlights of the interesting program can be found on page 5 of the newsletter.

In Europe, we have been vigorously looking for new ESS members as well as trying to inspire existing members to actively participate in various ESS affairs and activities of our lively Society. Your proactiveness in that regard will be appreciated; please encourage juniors and seniors to join our society.

Concluding, with a great team around me with special thanks to Inge Bauer, our secretary and Marcin Osuchowski, our treasurer, for their endless efforts to run and improve the ESS, I am looking very forward to our next actions and ask you to mark your calendars for our next get together, this time on the ancient Greek soil.

Enjoy reading the newsletter!
All the best,

Markus Huber-Lang
President of ESS
What is new at the new ESS Meeting 2019?

The preliminary program of the next ESS Meeting in Chania, Crete, 8th-12th October 2019 is designed in a joined effort with the IFSS and houses hot topics of high scientific impact in Shock research with several well established but also novel approaches:

For the junior ESS members and students we start with a Summer School on “Hemorrhagic Shock” on 8th October 2019. We have invited teachers with extraordinary didactical skills. We will cover shock from the first definition to the complex clinical picture, including hand on performances. This will certainly resume the great success of the summer school held in Paris. To deepen the gained knowledge, we will also offer guided poster tours (10th October) by experienced scientists for small student groups to present the latest discoveries on selected topics within the meeting – a novum!

The ESS/IFSS meeting will be supported organizationally by the Aegean Conferences. The mission of Aegean Conferences is to empower scientists to organize and participate in conferences that offer uniquely targeted content, foster high levels of scientific dialogue and provide a beautiful and relaxing environment for social interaction. In accordance to the Aegean Conference Sokrates concept all attendees will meet any time without hierarchical structure, e.g. everybody enjoys the same breakfasts, lunches and dinners or the common social event (sightseeing) without preservation or reservations to encourage discussions and scientific exchange at all levels.

The poster sessions will be a central part of the meeting and will be presented at prime times (late morning) when no parallel lecture is scheduled. The prominent New Investigator Award Competition will be also featured as the program core.

Multiple poster awards, travelling awards will be granted (provided by ESS, IFSS, and Aegean Conferences).

The corresponding shock societies under the auspices of IFSS will have their own sessions in a joined manner with ESS. A parallel session for Russian Shock SSSR will encourage Russian scientists and clinicians to present their work in their native language yet supported by a simultaneous English translation.

One session will cover European Collaborative Shock Research efforts to provide an update and also orientation of highly internationally active Shock research groups.

A Farewell dinner with common Greek dancing will close the congress!

Of note, the second iteration of Wiggers-Bernard initiative on sepsis modelling (by invitation only) coordinated by Marcin Osuchowski will take place on Saturday, 12 October. The initiative is focused on developing guidelines for sepsis modelling to improve translational reliability and relevance of pre-clinical findings.

If you have any suggestions, please feel free to contact the ESS board any time.

Markus Huber-Lang

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ESS Meeting 2019 – Preliminary Programme

in Chania, Crete, Greece

Preliminary Programme
This year, it was the 41st time that the US Shock Society organized its annual congress. The chosen venue was a welcoming and comfortable JW Marriot Resort in Scottsdale, AZ. Although there were more than 400 participants, the meeting was a perfect occasion to meet peers and built networking. The ESS members also actively participated in that event. The program was built in majority on the abstract-selected talks which enabled the younger investigators to present their research to a wide public. Other abstracts formed a three-part breakfast poster sessions which were extremely interesting and galvanized networking. As always, there were multiple topics present. What drew my personal interest were the ‘dirty mouse’ model studies that were developed by co-housing of regular pet shop mice with their SPF inbred mates (purchased from specialized lab animal breeders). Other relatively often investigated issues include the potency of stem cell therapies, development of new models of trauma and sepsis and sepsis-induced immune dysregulations. Among the distinguished lectures virtually everyone was impressed by the talk given by Paul Kubes from Calgary. By the use of intravital multiphoton microscopy his group was able to unravel multiple new mechanisms of the host cellular response to injury (mainly liver and lungs). They also shed new light on the role of iNKT cells, macrophages and neutrophils in tissue damage. Aside from science, the conference had its fun moments with nice dinners and most of all, the Fun Run initiative (co-organized by Yoram Vodovotz and Marcin Osuchowski) which was a fun and bonding event. Next year’s 42nd Shock Society Conference will take place in Coronado (near San Diego), CA, USA, definitely worth visiting.

Tomasz Skirecki
At the recent meeting of the European Society for Trauma and Emergency Surgery (ESTES), the ESTES president, Marius Keel, Berne/Zurich, Switzerland warmly welcomed the ESS. In a common session, Ingo Marzi, Frankfurt, Germany, editor-in-chief of EJTES, introduced the ESS and chaired the joined session addressing molecular and cellular barrier dysfunction after clinical and experimental polytrauma. The session was well received and followed by a lively discussion. Of note, ESTES addresses multiple topics similar to the ESS from a more clinical point of view, which conceivably - as also shown by the common meeting – might benefit from deeper (re)translational insights and the research efforts by the ESS members. Therefore, it simply appears ideal to arrange further common sessions in the future to determine common research fields borne from clinical problems, to find a common language, and to accompany clinical studies with deeper pathophysiological rationales. In the end, the efforts of both ESS and ESTES target to improve the quality of life of the patient after trauma, shock, and sepsis.

A next common step is planned at the future ESS meeting 2019 in form of a joined ESS-ESTES session named “Socrates meets Hippocrates” or in other words, basic science meeting clinical science.

Let us work together for the benefit of the patients; right on ESTES and ESS!

Markus Huber-Lang
The PROVIDE trial

The PROVIDE trial (Validation and restoration of immune dysfunction in severe infections and sepsis; ClinicalTrials.gov NCT NCT03332225) is running in 11 study sites in Greece since December 2017 under the auspices of the ESS. PROVIDE is a randomized, double-dummy trial of personalized immunotherapy in sepsis. Using a diagnostic platform based on the measurement of circulating and HLA-DR expression on CD14-monocytes, patients are randomized into either a placebo arm or an immunotherapy arm. Circulating ferritin above 4,420 ng/ml is the diagnostic hallmark of Macrophage Activation Syndrome and HLA-DR expression below 30% in the absence of hyperferritinemia is the diagnostic hallmark of immunosuppression. Respective immunotherapy consists of Anakinra or rhIFNγ for each state. The primary endpoint is not the efficacy of each drug but of the immunotherapy strategy versus the standard of care strategy. Evangelos J. Giamarellos-Bourboulis from the National and Kapodistrian University of Athens (Greece) and Mihai Netea from the Radboud University Nijmegen (The Netherlands) are the coordinating investigators of the PROVIDE trial.

Evangelos J. Giamarellos-Bourboulis
President-Elect of ESS
Editorial: Sepsis-3

A debate to be continued
(please feel free to let us know your opinion)

SEPSIS is “a life-threatening organ dysfunction caused by a dysregulated host response to infection”. [JAMA 2016]

Jean-Marc Cavaillon (Paris)
According to the best experts in the world, the innate immunity (the host response to infection) of individuals dealing with a severe infection is abnormal or impaired or failing (cf definition of the word “dysregulation”). This is a rather surprising view, because perfectly healthy people can develop sepsis, suggesting that sepsis can occur in patients with a normal immune system. Probably, the most appropriate word would have been “maladaptive”, since it is rather the intensity of the host response which can be deleterious and lead to organ dysfunction, and also to a modification of the immune system. The most provocative example is given by this paper (Kalil Clin Infect. Dis 2015, 60, 216) of which the conclusion is: “Our findings suggest that the immuno-suppression associated with transplantation may provide a survival advantage to transplant recipients with sepsis through modulation of the inflammatory response.”

Jean Carlet (Paris)
I agree that maladaptive is better than dysregulated. You know that I never really liked those terms because I do not see anything dysregulated or maladaptive or excessive in the body's response to infection. Its reactions are just perfectly suited to virulence factors or toxins, very violent, sometimes depending on the importance of the inoculum. When the patients produce very serious shocks for paronychia, or ear infections without mastoiditis, I will gladly revise this provocative position.

Didier Payen (Paris)
First, thanks for stimulating on such a major concept that requires large knowledge of very contradictory published data. Second, I am supportive to this statement, and as we recently discussed with Jean-Marc in Pasteur Institute, it is amazing to see the modest incidence and severity of inflammation in HIPEC surgery, despite long and major surgery, the tissue damage corresponding to organ removals, etc... The difference is the presence almost simultaneously to chemotherapy leading to DNA damage and histone damage, which impairs the inflammatory response. Then, "maladaptive" sounds more adequate considering the necessary response, the downregulation viewed as an adaptive response. However, pre-acute injury status (co-morbidity) and per-injury treatment may change the inflammatory response and tolerance. Third, timing should then be considered very carefully since it is during the first days (acute phase) that around 50% of the deaths occur, the other 50% occurring after, over a large period interval (months or years), and for different context and reasons.

Tarek Sharshar (Paris)
The two words refer to specific status.
Maladaptive seems appropriate if we know to what. But do we know to what?
Dysregulated might mean not controlled, term used in economy for the free market, if we can image any uncontrolled physiologic system. We can imagine that a system is badly controlled if we have any clues about its control. But not sure that we have any (clue)...
So to me, the two terms are little bit "loose" but what do we have instead...

**Benoit Misset (Rouen)**
Hmm ... I do not see any abnormality of immunity in sepsis. Immunity has the right to be overtaken by events. To me, SEPSIS is "a life-threatening organ dysfunction caused by an infection". Sometimes it goes, sometimes it does not, because the microbe is too bad or are too many, because the caregiver is too slow or awkward, because the patient is coming late, because the basic immunity is bad. Indeed, some ischemia-reperfections kill or heal in the same way, and without infection, and for the same reasons (too strong, too late ... etc.) if we had an anomaly of the immunity, it should be a little homogeneous and we would have already detected signs a little reproducible it’s a little fatalistic and not very exciting as a position, but...

**Frank Brunkhorst (Jena)**
I personally prefer the PIRO system (predisposition, insult, response, organ dysfunction), proposed by John Marshall in 2014: "PIRO is a template proposal for a staging system for acute illness that incorporates assessment of pre-morbid baseline susceptibility (predisposition), the specific disorder responsible for acute illness (insult), the response of the host to that insult, and the resulting degree of organ dysfunction" (Virulence. 2014 Jan 1; 5(1): 27–35).

**Manu Shankar-Hari (London)**
As someone who was part of the group that defined Sepsis-3, the words “dysregulated”; “maladaptive”; “non-homeostatic”; “abnormal” were debated a lot. There is no right or wrong word here - I think.
The goal is to convey the message that the host responses (immune and non-immune responses) are neither normal nor homeostatic, at least initially.
Second, this ‘dysregulated’ represents a transition point between infection and sepsis. In my humble opinion, our energy is better spent defining the immune system abnormalities in sepsis and what that means.
Choice of rewording this may be reserved for the immune part of the host response. The protection against infections by the immune system involves four interlinked tasks: danger signal surveillance and recognition from non-self, effector functions in response to sensing danger signals, homeostatic regulation, and generation of immunological memory in certain situations.

Jean-Marc Cavaillon
Year 2018: Bicentenary of the birth of Ignác Semmelweis

Opening of the Bicentenary of the birth of Ignác Semmelweis took place on the 5th of June, 2018 in the building of the Hungarian Academy of Sciences in Budapest (with following invited lectures):

Zsuzsanna Jakab (the Regional Director for Europe of the World Health Organization) marked Ignac Semmelweis “as a man who saved more lives than any other physician in the history of humanity combined” and highlighted his impact on the global health priorities of the 21st century. She mentioned that the incidence of healthcare associated infections remains to be a global problem (with the overall mortality of nearly 10% worldwide), leading to 110,000 deaths per year also in Europe. It could be learnt that improving hand hygiene in healthcare can reduce pathogen transmission by 50% also in these days and that infection prevention is also associated with reduced antimicrobial resistance (due to reduced need of antibiotics). Current status of maternal and infant mortality as well as the importance of children vaccination was also highlighted in the lecture.

Our Past-President Jean-Marc Cavaillon (Institut Pasteur, Paris) also gave a lecture entitled “Hygiene versus contagiosity: the legacy of Ignaz Semmelweis” (see highlights of the lecture below, next page)

Wolfgang Graninger (General Hospital, Vienna) demonstrated a sequence from discovering the role of cadaverous poisoning in maternal mortality (discovery of Semmelweis) to recognition of the more general state sepsis and also presented historical aspects of asepsis. He did not miss to mention “Semmelweis Reflex” which was termed by RA Wilson (in 2004) as: “Innovation in science is often not followed by honors, but by punishment because existing paradigms and behavioral patterns are questioned and attacked”.

Bernard Charpentier, (Federation of European Academies of Medicine, president) held a lecture about historical aspect of recognition of the discovery of Semmelweis by the French Academy of Medicine and discovery of streptococcus by L. Pasteur as a cause of sepsis. Thomas Schnalke also held a lecture about the legacy of Ignaz Semmelweis in the Berlin Museum of Medical History at the Charité.

Andrea Szabó
The first recorded epidemic of puerperal fever occurred at the Hôtel Dieu Hospital in Paris in 1646. Since many epidemics happened around the world at that time, particularly in the UK some famous British doctors [Alexander Gordon (1795); Johm Thomas Ingleby (1838); Robert Storrs (1842)] (supported by an American physician Oliver Holmes, 1843) claimed that it was a contagious disease. It was shortly thereafter, in 1847, that a demonstration of the veracity of this contagion was made. However, this does not mean that the demonstration was immediately accompanied by adequate measures. We are at the General Hospital in Vienna, Austria, where a Hungarian doctor, named Ignaz Semmelweis (1818-1865), used to work. He had been appointed an assistant under the authority of the Head of the Maternity Department, Johann Klein (1788-1856), who was reluctant to accept new ideas. Semmelweis was troubled by the death of one of his friends, Dr. Jakob Kolletschka (1803-1847), who died of sepsis after being wounded by a scalpel that had been used during the autopsy of a corpse. Semmelweis noted that the clinical manifestations that preceded the death of his friend were quite similar to the events that accompany the death of women after childbirth. The large Vienna General Hospital where Semmelweis worked, had two delivery clinics. The two maternities were side by side and received the patients alternately every other day. There, as elsewhere, women might die of puerperal fever. Until 1838, mortality was the same in both clinics, ranging from 4.94% to 8.29% depending on the year. From 1840, mortality increased significantly in one of the maternity wards. According to Louis Ferdinand Céline, a French writer and an MD whose medical thesis focused on the life of Semmelweis, Semmelweis would have swapped staff from each clinic to the other clinic. Then death would have moved from one clinic to another, according to the staff. It is obviously not true, Celine had probably made a little romance history. It is difficult to imagine that a young Hungarian doctor could have so much authority over the Viennese establishment. But what is true is that Semmelweis realized that there was a major difference between the two clinics. Since 1839, one part of the staff had been midwives, while the other was medical students. But what did students make before helping women to give birth? They learnt anatomy by dissecting human corpses, an activity initiated and greatly supported by Dr. Klein. Then, without washing their hands, they went to the maternity to practice childbirth. After the death of his friend, Semmelweis made the connection, while realizing that the foul smell of death followed the students from the autopsy room to the delivery room. Its aim was therefore to eliminate the foul odors of putrefaction from cadavers carried by the medical students. Semmelweis recommended the use of a solution of calcium hypochlorite for washing hands and brushing nails. Semmelweis was then convinced that these deadly smells were the reflection of the
presence of a cadaverous poison from which one must get rid of. It was in May 1847 that Semmelweis introduced its new rules of hygiene. The result was breathtaking, and mortality went down from almost 16% to less than 1%. One could have expected an admiring look, a warm welcome or at least benevolence for this vital observation and for the demonstration of those convincing result ... which saved lives! Disappointingly, it did not happen. Semmelweis was a foreigner in Vienna, and he seemed to consider the young Austrian students responsible to convey death. Shame on him. His contract was not renewed by Johann Klein. Back in Hungary, in Budapest, he had not have received any more attention from the Hungarian medical corps than in Vienna. Yet, at St Rochus Hospital in Pest where he worked and applied his hygiene rules, he again reduced mortality to less than 1% of deliveries. Semmelweis was slow to publish his work, and did so only eleven years later in a Hungarian-language newspaper; and he waited another two years before publishing in German in 1860. However, as early as 1848, Semmelweis communicated his observation in France after having transmitted a note read in front of the Academy of Sciences and published on February 21st, 1848 in the weekly reports of the sessions of the said academy. It sounds like a snippet that seems to have gone almost unnoticed:

M. SEMMELWEIS, Head of Clinic at the Vienna General Hospital, gives a note on puerperal fever, and on a cause, which he regards as very frequently presiding over the development of this disease. “The frequency of puerperal fever, in some hospitals, has led several practitioners to consider this condition to be of an epidemic nature. The author of the Note does not share this opinion. He thinks that the disease does not reign equally in all delivery services, but that it predominates in those where are working medical students who are involved in dissections. Formerly, he says, medical and midwifery students were distributed in the two delivery clinics that exist at the Vienna Grand Hospital; the disease reigned in both departments with equal intensity. From 1836, the first clinic was assigned to
medical students, the second reserved exclusively for student midwives. From that day there was an enormous difference between the two services in mortality, and this difference was maintained until May, 1847, when measures were prescribed. The success of which seemed to prove that the true cause of evil had been well recognized. The author notes that, in the nine months since then, the lowest mortality figures have been observed during the worst winter months, those when students handle more dissections. In fact, he regards the puerperal fever of the hospices as being, in many cases, the result of a contagious infection produced by cadaveric elements. According to him, the use of simple water or soap water is not sufficient to completely destroy the deleterious substances that remain attached to the epidermis of the hands; but ablutions performed with a concentrated solution of lime chloride protect from any chance of infection.”

Despite the unfavorable opinion of the medical "establishment", some of Semmelweis' colleagues and friends contributed to the dissemination of his work. In December 1847, the year of his observation, his friend Ferdinand von Hebra (1816-1880), a dermatologist at the General Hospital, told the Society of Physicians in Vienna: “Dr. Semmelweis realized ... pregnant women in childbirth may be infected by the birth attendant himself ... puerperal fever was nothing more than cadaveric infection.” Charles Henry Felix Routh (1822-1909), his former pupil sends a communication that was read in London in front of the medical-surgical society in November 1848. Interestingly, he recalled that similar situations have been reported in the maternity hospitals in Prague and Strasbourg. In Kiel, the problem was so acute that Prof. Gustav Adolf Michaelis (1798-1848), after considering the closure of his maternity ward, applied with great success the rules enacted by Semmelweis (one single death over a period of several months). However, the hypothesis was that inflammation was more likely to be the result of harsher manipulations by male doctors than by midwives. Moreover, the absence of contagiousness was corroborated by the fact that midwives never caught the disease and that the unhealthier, less clean environment of some maternities necessarily had to explain the occurrence of puerperal fevers. Except that in Vienna, the care of the premises and the immediate environment were strictly identical for the two maternities.

For his part, Joseph Skoda (1805-1881), a great patron of medicine in Vienna, charged at the time by the Minister of Education to reorganize medical education, presented on 18 October 1849 the work of Semmelweis before the Vienna Academy of Sciences. His communication does not appear totally in support, and it is more for him the opportunity to settle accounts with Johann Klein, the head of the maternity ward, with whom he was at war of power.
Much more favorable were the presentations made by Franz Hector Arneth (1818-1907). The latter was a former head of clinic of the maternity of Vienna that he left in November 1850. He communicated successively in front of the French Academy of Medicine on January 7, 1851, and the Medico-Surgical Society of Edinburgh on April 16, 1851. Arneth spoke of Semmelweis as a "wise observer," and presented the actions required to eliminate cadaver miasma. He also recalled the similarities of situation observed in Strasbourg but also in Pavia, and mentioned the successes obtained in Kiel by Prof. Michaelis after introducing the rules developed by Semmelweis.

Thus, in the years following his discovery, Semmelweis himself contributed very little to the dissemination of his own ideas, except perhaps this communication that he himself transmitted to the French Academy of Sciences. On the other hand, his colleagues and friends made it possible to make known his works before that in 1861, Semmelweis gathered his works, his analyzes, his statistics, his figures in a book in German language, thus accessible to a greater number of readers. The analysis of this book was reported the following year by the Drs. Eugène Follin (1823-1867) and Charles Lasègue (1816-1883) in their journal, "The General Archives of Medicine". Unconvinced by the demonstration, they wrote:

"Here is an informative and curious book less because of what it teaches us about puerperal fever than because it teaches us about the differences in medical statistics. [...] This time, it's a doctor, authorized by his position, by his special knowledge [...] which compiles the figures, combines them, and interprets them, and who, in the name of their autocracy, promulgates a new theory of puerperal fever. "If afterwards our good doctors report factually the contents of the book, to conclude, they carry the final thrust in a subtle language little practiced nowadays: "Our formal opinion, based on a sad experience of the disease, is far from favorable to the exclusive theory that does not propose, but affirms Dr. Semmelweis [...] We do not hesitate to take rank among the criticisms to which the honorable professor widely blames. Like all the writers of fiery controversies, he calls the discussion, but when it has come, he does not tolerate or refute it, his defense of his doctrines resembles the pamphlets of the Middle Ages, where the use of Latin excuses the most violent apostrophes ".

Doubtless, the cantankerous Semmelweis’ character did not help him to pass his message peacefully. He blamed all his colleagues, felt attacked and misunderstood by all, finally he lost his mind. I would like to believe Céline who considers his death as a suicide following a deliberate inoculation of the cadaveric poison from a scalpel used during the dissection of a corpse. In fact, with the complicity of his wife and a Viennese doctor, Semmelweis was interned in an insane asylum while he was passing through Vienna en route to the spa water..."
town of Gräfenberg. From his passage in this asylum, no precise medical information exists in the archives. Except an injury to a finger of the right hand. It worsened so much, and, ironically, at the age of 47, Semmelweis died, on the evening of August 13, 1865, from sepsis, this pathology he had fought against much of his life. He was autopsied at the Vienna General Hospital, where he had practiced, and his death by blood poisoning was confirmed. He was buried in Vienna. They were few to attend his burial. Even his wife was not present, and only a friend from Budapest made the trip. But his best enemy Carl Braun, attended the funeral. Subsequently, his body was transferred to Budapest's Kerepesi Cemetery in 1891, before being transferred again in 1964 to Taban in the courtyard of his birthplace.
A European Group for promoting basic and translational research in Sepsis Immunology

Immunologists, infectious diseases and intensive care medicine specialists with a shared primary research interest in sepsis immunology. Our overarching goal is to develop and foster collaborative research by working in partnership with groups with similar interests, Medical and Scientific Societies, Academia and the Industry. Sepsis was recently redefined by the SEPSIS-3 task force as a life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction is currently defined by an increase in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more. The underlying mechanisms leading to organ dysfunction involve pro- and anti-inflammatory responses, along with major modifications in non-immunologic pathways such as cardiovascular, neuronal, autonomic, hormonal, bioenergetic, metabolic, and coagulation, all of which have prognostic significance. In our view, the immune alterations in sepsis as well as their role in the development and progression of organ dysfunction deserve more attention.

EGIS aims to address a number of open questions, including but not limited to the following issues:

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<td>The immunological status post-sepsis (protracted immunosuppression / PICS syndrome) and long-term consequences.</td>
<td>Studies evaluating immunological alterations in the convalescence phase of sepsis and beyond.</td>
<td>The long-term consequences of immunotherapies: autoimmunity induction</td>
<td>Studying these consequences in animal models. Documentation of autoimmune phenomena in the trials.</td>
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<td>Emergence, causes and evolution of lymphopenia</td>
<td>Additional work evaluating causes and effects of apoptosis, endothelial adhesion and tissue homing.</td>
<td>What are good immunological biomarkers in sepsis?</td>
<td>Development of a biomarker panel valid for diagnosis, severity stratification, mortality prediction and guidance of immunological interventions.</td>
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<td>The role of hitherto neglected immune cells (e.g. B cells, others)</td>
<td>More preclinical studies using cellular and animal models.</td>
<td>Insufficient exploitation of the differential blood count</td>
<td>Retrospective/prospective studies evaluating the value of immature granulocyte count, delta neutrophil index, individual cell subpopulations.</td>
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<td>Lack of standardization of animal sepsis models</td>
<td>Creating guidelines for animal sepsis models</td>
<td>Lack of standardization of immune monitoring.</td>
<td>Standardization of quantitative and functional immunological tests (PCR-based test, FACS, and others)</td>
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<td>Is there a common denominator of immune cell alterations, and what is the heterogeneity of immune cell dysfunction?</td>
<td>Evaluating shared alterations in immune cell function, e.g. metabolic switch, mitochondrial dysfunction, as well as cell-specific changes using single cell measurement technologies</td>
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<td>Prospective studies recruiting patients with infection who will develop sepsis.</td>
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These issues must be addressed by conducting respective basic and translational immunology studies in sepsis. At the inaugural meeting held on 23 and 24 May 2018 in Berlin, EGIS defined as its major task to provide a platform for fostering the exchange of ideas and tools, gaining better access to shared research resources, and providing practical advice and assistance in the development of research studies and clinical trials related to sepsis immunology. EGIS will also develop an educational program for students, researchers and health professionals interested in this field.

On behalf of all EGIS participants (in alphabetical order): Michael Bauer, Frank Brunkhorst, Jean-Marc Cavaillon, Evangelos J. Giamarellos-Bourboulis, Matthijs Kox, Marius Moebius, Christian Meisel, Guillaume Monneret, Axel Nierhaus, Mihai G. Netea, Joerg C. Schefold, Manu Shankar-Hari, Antoni Torres, Tom Van Der Poll, Fabienne Venet, Martin Winkler.

EGIS management coordinators: Jesus F Bermejo-Martin, Ignacio Rubio.

Any members of ESS interested in joining this group can directly get in touch with Jesus Bermejo Martin (jfbermejo@saludcastillayleon.es) and Ignacio Rubio (IGNACIO.RUBIO@med.uni-jena.de).

Jean-Marc Cavaillon
Journal Club: What is new in shock research?

Recent highlights of remarkable findings published in shock research


Main important messages:
Existence of sepsis endotypes as a patterns of transcriptomic response have been proposed some time ago to explain the heterogeneity of sepsis patients. In this paper, authors took data of the whole blood transcriptome of early sepsis patients from 14 dataset (7000 patients) and used a novel approach to normalize the original results to the transcriptomes of healthy controls (assuming similar transcriptome among control studies). After performing series of bioinformatic pathway analyses, the authors found out that the data could be split into 3 clusters: ‘inflammopatic’ (high activation of innate immunity), ‘adaptive’ (high adaptive response signal) – with the lowest mortality, and ‘coagulopathic’. These clusters differed in terms of clinical data (shock status, WBC, age, mortality) however neither of them could assign patients to a given pattern. Next, the authors selected a 33-gene classifier that was used to validate the clustering in another cohort of patients (n=600). This tool presented 83% accuracy in reassigning patients to their same clusters. In conclusion, this study suggests that early response to sepsis can be classified into one of the major clusters which have distinct molecular and clinical characteristics. Such approach creates a new opportunity to identify specific treatment-responding endotypes.

Written by: Tomasz Skirecki, Center of Postgraduate Medical Education, Warsaw
ESS Membership

Dear ESS members,
please kindly pay your ESS membership for 2018/19. Currently, a fixed 2-year membership fee of EUR 100 for regular members and EUR 50 for student members applies.

We sincerely appreciate your contribution; please do not ignore this important commitment. We are happy to receive your funds at:

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

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

Thank you!
Upcoming events

2018 TERMIS World Congress: TERMIS (Tissue Engineering & Regenerative Medicine International Society) September 4-7, 2018 (Kyoto, Japan)
https://www.termis.org/meetings_worldcongress.php

31st Annual Congress ESICM (European Society of Intensive Care Medicine): October 20-24, 2018 (Paris, France)
https://www.esicm.org/events/31st-esicm-annual-congress-paris/

42nd Annual Conference on SHOCK: June 8-11, 2019 (Coronado, CA, USA)
http://shocksociety.org/Meetings/Future-Meetings.aspx

18th ESS Congress/ 9th IFSS Congress October 8-12, 2019 (Chania, Crete, Greece)

World Federation of Societies of Intensive and Critical Care Medicine: 14th World Congress: October 14-18, 2019 (Melbourne, Australia)
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Invitation to publish in Shock®

Shock is a monthly journal that publishes the results of investigations in the field of injury, inflammation and sepsis; of clinical and laboratory origin alike (current IF=3.113). 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!

Last words about the ESS newsletter

Dear present ESS member,

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

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

Dear past ESS member,

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

Markus Huber-Lang
## ESS Membership application form

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

![European Shock Society Membership Application Form](http://www.europeansonshockssociety.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

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Area(s) of research interest:

Expertise and/or facilities:

Publications: