Welcome to Brussels!

This is a great year for us, as we celebrate the 35th anniversary of our International Symposium on Intensive Care and Emergency Medicine. This milestone offers a perfect opportunity to look back on the last three and a half decades to see what we've learnt, and – importantly – what we have yet to. With this in mind, we will hold dedicated symposia over the coming days to shine a light on the past, present and future status of intensive care and emergency medicine, and ask: what will the next 35 years bring?

Of course, our exhilarating and informative program will feature a vast array of topics that physicians, nurses and allied healthcare professionals from all over the world will tackle head on. With symposia spanning standard presentations, plenary lectures, workshops, pro-con debates, tutorials, round tables and “Meet the expert” sessions, each type of symposium will be fine-tuned to stimulate the right balance of informative learning, interactivity and focused debate.

There will be a great deal of new information presented during the meeting, and four related papers will be published simultaneously in the New England Journal of Medicine. Interestingly, we have even more participants than last year, coming from a total of 98 countries, and we have more industry sponsors than ever!

As we begin our exciting four-day program this morning in the Henry Le Bœuf auditorium, I look forward to welcoming you with some perspectives on “Saying YES” to intensive care medicine. We must recognize we have not introduced many major therapeutic advances in the ICU. Technological advances have taken place, but are no different in the ICU than in other settings. Actually most of our multicentric, randomized, controlled trials (RCTs) have been negative, and some have shown harm. These large RCTs have often shown that ‘less is more’ (less transfusions, less caloric intake, less invasiveness, less sedation, etc.). This is largely due to the problem of heterogeneity in our patient populations, whereby some patients may benefit from – and other may be harmed by – an intervention, so that the global outcome is neutral.

Hopefully in the future we will find the tools to better identify the candidates for a new therapy. We have learned a lot from smaller, often physiological studies. Perhaps the major practical advances have been in the process of care, including better communication between the members of the ICU team. We have made enormous progress and we can be proud of it.

Starting as we mean to go on, the rest of this morning’s opening session will be a thought-provoking and expansive set of talks that will set the tone for the rest of the meeting. There are too many highlights to mention in the coming days, so we do hope you pick up a copy of ISICEM News each day, or download the electronic version from our website, to get a glimpse of just some of the exciting topics and sessions for this 35th year.

I would like to thank all of our faculty, attendees, industry and organizing committees for their continued interest and support, and I wish you an enlightening congress, and a safe journey home.

Jean-Louis Vincent
ISICEM Chairman, Dept of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles Secretary General of the World Federation of Societies of Intensive and Critical Care Medicine
It is an incredibly complicated process when someone gets a severe infection, far more so than I think even some of us who have been in the field for a long time had thought.

James A Russell

epidemic is a complicated syndrome with a paucity of positive trial data, yet there are a number of novel therapies which may have significant potential for this devastating disease, delegates will hear on Wednesday afternoon.

In rapid succession, James A Russell (University of British Columbia, Vancouver, Canada) will give two talks that will tackle the obstacles and future perspectives for sepsis, including a discussion of the complex way in which the infection takes hold. “If you give human volunteers, in an ethically-approved study, a small dose of an injected endotoxin, which is part of the gram-negative bacterial coat, it turns out that they modify the expression, i.e. the amount the RNA and protein being changed, for a third of the genes in the whole human genome,” said Dr Russell. “So it is an incredibly complicated process when someone gets a severe infection, far more so than I think even some of us who have been in the field for a long time had thought.

“Given that that is going to be thousands and thousands of genes that are up and downregulated, to then stand back and say ‘I am going to make an antibody to one of those’, and think that it might be beneficial would be probably quite naïve. Because all of these networks are so redundant that if you just block off one part of the network, others will just go around it, so this host response that injures the patient and ultimately kills them in some cases, cannot be stopped. That’s one observation I think that is important.”

As Dr Russell described, this leads to the idea of how do you then design better drug candidates, given this very incredible response, and given the potent drugs that already did not work? Referring to an intriguing paper from the cancer field, The Hallmarks of Cancer,’ he went on: “It basically showed that there are a limited number of pathways that get changed in cancer, but you need to, in any given cancer, interrupt several of those if you are going to have a chance of a cure …. So I think in sepsis it either needs to be like that, where you have multiple drugs interfering with multiple pathways to achieve success, or you have something that is hitting a really upstream node that is a key controller of the whole system, or a good part of it. And that is what our lab focuses on.”

A key question posed in one of Dr Russell’s sepsis talks held tomorrow will be whether there will ever be a positive sepsis trial? On that topic, is part of the issue actually management of expectations of what the endpoints and outcomes of a sepsis trial should be? “There are a number of us who feel that the many, many years of failed trials in sepsis were because they focused on trying to show a difference in mortality – to which all of them have failed, save one,” he said.

“The mortality of sepsis is actually going down – a number of studies have been published in the last couple of years showing that. A huge database from Australia and New Zealand showed that for the last decade, the mortality has gone from 35% to 20%, so it is great for patients, and general processes of care have improved outcomes. But what that means from a statistical point of view is to change a mortality that might be 20% now, down to 17 or 15%, is going to be very, very hard, and I would argue probably impossible, because of the sample size that is needed.

“And then the second logic is that, if you get a mortality that is down to 20%, that means that 80% of the people are now survivors, but they come out of sepsis with a lot of long-term disabilities. Ones that have been described include PTSD, depression, cognitive dysfunction, respiratory problems, a lot of neuromuscular weakness.

Continued on page 4
Alexion Satellite Symposium at the 35th International Symposium on Intensive Care and Emergency Medicine (ISICEM)

Recent advances in haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura: a critical care perspective

Tuesday, 17 March 2015
12:30–13:30, Studio (Bozar Building)

Programme

Welcome and introductions
Élie Azoulay (Paris, France)

Differentiating between sepsis, atypical haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura
Mervyn Singer (London, UK)

How patients with thrombotic microangiopathy become critically ill
Élie Azoulay

Guidelines for management of atypical haemolytic uraemic syndrome and thrombotic thrombocytopenic purpura
Marie Scully (London, UK)

Questions, answers, and closing remarks
Élie Azoulay

Please visit the Alexion Booth in the industry exhibition area

Information presented at this industry-sponsored symposium is not necessarily endorsed by ISICEM
A positive future for novel sepsis candidates?

Continued from page 2 and a slow recovery of endocrine hormone function. So what I think it means is we have to have endpoints that change acute organ dysfunction, and help decrease the risk of long-term organ dysfunction.

For Dr Russell, this has meant that focus has shifted somewhat to trying to reduce the need for dialysis or ventilation, or at least shortening the duration they are required.

“In fact you can create these kind of composite endpoints where you have, for example, vasopressor or ventilator-free days which are different between groups,” he said.

“I am involved in a number of studies where rather than focusing on changing mortality, what we’re trying to do is show that we can change the risk and the duration of the need for life support. That leads to some better outcomes both in terms of the patient, and the healthcare system – because all of these things cost a lot of money.”

He added: “So that’s this composite outcome theme – trying to put together a few of these things into one score, and then seeing if you can change any of them, compared to a control group.”

“In essence, quality of life is the key issue here, and Dr Russell underlined the importance of striving for long-term follow-up in every major sepsis center, with every patient coming back after survival, and then being seen by a team that includes an intensivist and, as necessary, other specialists. “I think it really needs to be run by intensive care groups that take care of these people when are acutely ill, because they know all of the problems that they have had, and then what the long-term complications of those problems could be,” he said. “We need to design interventions, rehabilitations, maybe longer-term therapy with some medications to try and prevent that progression to long-term disability.”

New candidates for sepsis

The second talk Dr Russell will be giving on sepsis will focus on three novel candidates for treatment. The first is PCSK9 (proprotein convertase subtilisin/kexin type 9), an enzyme that increases the amount of low-density lipoprotein (LDL) receptors on liver cells (and therefore LDL clearance). “It is probably the ‘hot’ molecule of the last two years for cardiovascular disease,” said Dr Russell. “There are a number of companies developing PCSK9 inhibitors for cholesterol problems and heart problems, and for people who can’t take statins.”

Moving on to discuss some of the work that he has done – along with his colleagues Keith Walley, John Boyd and the rest of his group – Dr Russell continued: “What we have discovered – and we published this a few months ago – is that PCSK9 inhibitors in animal models, and human genetic studies, could be extremely successful in sepsis. We used animal models and human studies to show that if you either knock out the gene, or inhibit it with an antibody, you can improve the outcomes in mice with models of sepsis. Humans have a natural mutation of the gene – this is how the drugs were discovered actually. If you have a mutation of the gene, and it doesn’t function, essentially you live to be 100, and when you die there is no coronary disease at autopsy.

“Similarly, if you have that same mutation, and you happen to get sepsis, you have a much better outcome than if you don’t have that mutation … so our group is very excited, and has ongoing work with PCSK9. We think it is a really, really attractive candidate.”

Crucially, the PCSK9 inhibitor works to pull endotoxins out of the circulation, and so the notion would be that, just like giving antibiotics within the first hour in the emergency room for sepsis, it may be possible to administer an antibody to PCSK9 in the first hour, and immediately pull out endotoxins, as well as the lipid molecules that come from other bacteria and form fungi. “So the aspects I like about it are: one, it is very upstream – it’s like a master switch you are turning on; two, it could be given quickly and easily; and three, because of the half-life of the antibody, you only have to give it once and then that’s it – it lasts for weeks,” said Dr Russell.

“The other thing that is important is that to date, a lot of trials have been published in the New England Journal of Medicine, and probably the first PCSK9 inhibitors will start coming on the market this year in cardiovascular disease. So they are coming in the near term, and it’s interesting.”

The second treatment that Dr Russell and colleagues are very intrigued with is selepressin – a vasopressor V1A receptor agonist. “I ran a huge trial, published a few years ago in the New England Journal of Medicine [VASSAT],” on vasopressin for septic shock,” said Dr Russell.

“It was negative, but it had a subgroup where there was a significant result, and people had less-severe septic shock. People have modified the vasopressin molecule to make it more specific to the V1a agonist, and that has better properties than vasopressin because it seems to protect against this increased ‘leakiness’ of fluid that sepsis patients get.

“A number of studies that have been published using animal models, and I had the privilege to be a lead investigator of a phase Ila trial that was presented at the Society of Critical Care Medicine over a year ago [SCCM, January 2014, Puerto Rico]. We showed in a randomized, double-blind, placebo-controlled trial that selepressin not only decreased the need for vasopressor support, it also decreased the positive fluid balance – the swelling and edema that goes into the lungs, the heart and the brains of patients.”

Dr Russell continued: “The reason I am interested in this is because if it was just a vasopressor, I’d say, ‘So what, any vasopressor is probably going to be the same as the next’. But we think this permeability protection, or this vascular leakage protection, is again one of those important upstream master switches. If that truly is what the drug is doing then that could have a really big impact on outcomes. There has really been no study of a drug that acts to decrease permeability injury … whether it is gram-positive, gram-negative or fungal sepsis.”

The final treatment that Dr Russell will discuss relates to heparin binding-protein (HBP), another molecule that has been found to increase permeability, making vessels leaky during sepsis. Along with his colleague Adam Linder, Dr Russell has been investigating the therapeutic potential of antidotes to HBP, testing fractionated, unfractionated, and even special non-anticoagulant versions of heparin.

“This is an earlier-stage idea that has not even gone into a phase II trial yet,” said Dr Russell. “The idea is that you could use either a form of heparin, or another blocker to heparin-binding protein, to try and prevent this increased permeability and injury.”

Giving his overall perspectives as to the potential of the three novel candidates, Dr Russell began by underlining their promise, when combined with biomarkers, in a personalized medicine approach to sepsis. “I am not alone in thinking that one of the reasons sepsis trials fail is because they are so heterogeneous.”

James A Russell

“I think all three candidates have a shot at going at least into the next phase, if we can get a grant or company interested in financing studies.”

James A Russell

References


“I am not alone in thinking that one of the reasons sepsis trials fail is because they are so heterogeneous.”

James A Russell

Neurotrophins: Multifunctional treatments show promise in neurotrauma and stroke

Wednesday evening plays host to a panel of eminent speakers examining neurotrophic treatment for preventing cognitive impairment after stroke and neurotrauma. Therapies for stroke and brain trauma are an unmet clinical need: the pathogenesis involves multiple cellular and molecular mechanisms, whereas present treatments tend to target a single pathogenic factor.

ISICEM News reached out to two of the key speakers before their lectures, to find out what they plan to discuss in their talks tomorrow.

Michael Chopp (Department of Neurology, Henry Ford Hospital, USA) began by describing his research using the neurotrophic drug Cerebrolysin® (EVER Neuro Pharma GmbH, Unterach, Austria) and how it stimulated neurovascular remodeling and behavioral and cognitive recovery after experimental neural injury.

“We are interested in restorative neurology in stroke and head trauma, especially in stimulating endogenous restorative processes in intact tissue to compensate for damage instead of simply treating the lesion,” said Dr Chopp.

“This can be done with stem cells and neurotrophic agents such as Cerebrolysin, we have seen these stimulate reparative processes and improve outcome.”

He added: “We have used Cerebrolysin’s restorative capacity in several different animal models: In models of mild and moderate traumatic brain injury, Cerebrolysin was given at 24 hours and one hour post-stroke, respectively, and was shown to improve outcome; In another model we used an novel embolic model of where Cerebrolysin was administered 24 hours after lesioning revealing positive results”.

Describing his molecular studies, Dr Chopp explained: “We have closely studied the molecular basis of how Cerebrolysin functions, and discovered that it turns on endogenous processes by stimulating transcription factors, amongst many other molecules – Sonic hedgehog (SHH). We believe that SHH may mediate its effect though preproenkephalin A’s restorative effect. Furthermore when SHH is inhibited, Cerebrolysin treatment fails.”

In describing Cerebrolysin’s pleiotropic positive effects, Dr Chopp continued: “Cerebrolysin also facilitates neurovascular remodeling via SHH by promoting trophic factors from the vasculature, as well as increasing myelination and astrogliogenesis. Ex vivo data have revealed increased levels of endothelial factors, restorative factors, and gliogenesis and neurogenesis.”

Dr Chopp finished by explaining his behavioural data: “We have used a plethora of behavioural tests (modified water maze, adhesive removal and novel object recognition) to show that Cerebrolysin improved cognitive performance, learning and memory and motor skills after experimentally induced brain trauma.”

Also speaking during the session will be Natan Bornstein (Department of Neurology, Tel Aviv Medical Center, Israel), who told ISICEM News about his stimulating research into early mobilization therapy, post-stroke. Dr Bornstein began by highlighting the present objective regarding stroke outcome, saying: “The goal of reducing patient mortality incidence to that of survival with severe disability is not enough, ideally we’d like to see negligible disabilities or full recovery.

“One Early Mobilization (VEM) rehabilitation after stroke decreases mortality and improves the outcome for patients. In particular, if patients are mobilized within 24 hours of infarct, they have far fewer complications and a substantially improved outcome.”

He then described AVERT (A Very Early Rehabilitation Trial), a phase III trial lead by Julie Bernhardt and Peter Langhorne: “This randomized trial, currently being conducted across 50 centers worldwide, compares the effects of early mobilization and physiotherapy to that of standard stroke unit care. It involves more than 2000 patients and tests whether mobilization within 24 hours of stroke onset improves outcome at three months post-stroke. These exciting results will be analyzed and presented later this year.”

He elaborated: “This is an extended version of the Phase II AVERT trial by the same group that showed significant benefit for patients.”

The use of a combination of early mobilization and neurotrophins – such as Cerebrolysin – in stroke recovery may be a way forward, as Dr Bornstein stressed: “There are several studies that have demonstrated that the use of Cerebrolysin in acute ischemic stroke may improve functional outcome in the early period after stroke onset.”

Of course the critical time window in stroke patients is well known – tissue plasminogen activator is only effective if administered within 4.5 hours of insult; however Dr Bornstein believes that if this rapid response was applied to other stroke treatments, then the outcome would be even more favorable. In his concluding remarks to ISICEM News, Dr Bornstein commented: “To build upon these pieces of existing data, combined therapy of Cerebrolysin, early mobilization and physiotherapy within 24 hours of onset of stroke may have a beneficial outcome.”

Drs Chopp and Bornstein will be speaking during the satellite symposium ‘Neurotrophic treatment for the prevention of complications and cognitive impairment after stroke and neurotrauma’, held Wednesday evening at 18:15–19:45 in 100 Hall. Dr Muresanu will also be presenting on ‘How to manage the burden of cognitive impairment after TBI’.

**References**

Immunotherapy in sepsis

Knowledge of the immune system’s reaction to different diseases has evolved considerably over the past few decades. As part this afternoon’s session dedicated to the latest in this field, Tom van der Poll (Academic Medical Centre, Amsterdam, the Netherlands) discusses the dynamic and multifaceted immune response in sepsis, giving his insights into the current candidate therapies and as-yet unanswered questions.

Sepsis is an infection that cannot be controlled by the normal immune mechanisms’ attempts to return the body to homeostasis, creating many secondary issues along the way. It is now appreciated that the body responds via a complex interaction of both pro-inflammatory and concurrent anti-inflammatory pathways.

Studying these pathways has brought many candidate therapies to the fore, all of which aim at modulating the immune response to optimize the balance of pro- and anti-inflammatory mechanisms to combat invading pathogens. In an interview with ISICEM News, Dr van der Poll described how far we have come, what the current targets are, and how best to approach a broad field such as sepsis.

“In the old days, it was believed that sepsis produced a hyper-inflammatory response, and that that was it,” he began. “We were all going to inhibit this hyper-inflammation, and thereby we would rescue our patients. What we know now is that there is a lot more going on.”

Indeed, the original sepsis trials that took place during the 1980s sought to influence the host response by way of high-dose corticosteroids. Following this, a slew of other, more targeted interventions emerged, all seeking to inhibit excessive inflammation.

Tumor necrosis factor (TNF), for example, emerged as the first targeted anti-inflammatory candidate from a sepsis animal model in which it was found in elevated levels in the circulation following intravenous bolus administration of high-dose bacteria.

In this model, animals were found to survive by antibody-blocking of the endogenous TNF. Following TNF-inhibitory clinical trials, this target was found to confer no benefit, and this was the case for the many that followed this path.

“At that stage, it was perceived that sepsis was basically the graveyard of industrial companies seeking to develop sepsis therapies directed at the host response,” noted Dr van der Poll. “But over the past decade, it has become clearer that hyperinflammation is not driving the entire sepsis response per se.

“Probably in a subset of patients hyperinflammation is a main factor, pathophysiological-ly-wise. But there are also a lot of anti-inflammatory mechanisms and a dysfunction of cells in general. We don’t know exactly what the course of that is yet.”

That patients react differently has lent a crucial shift in the perception of sepsis in general, but it should also be guiding our therapy, as Dr van der Poll explained: “Over the past decades we have approached sepsis patients as a well-defined entity, but we now know that sepsis patients as a group are very heterogeneous. They are all captured by the word ‘sepsis’, yet not all patients have the same pathologies or driving pathophysiological mechanisms.”

“The future that lies ahead of us should also focus on making subgroups within that definition that might benefit from certain interventions – this could be anti-inflammatory or pro-inflammatory. At the moment we try to treat the whole group in the same way, and probably that is not the best way to go.”

Moreover, treating sepsis successfully will not be a simple case of finding the right target for the right patient; its dynamic nature means that a given immune therapy will be appropriate only at specific immune phases of the sepsis course. From these factors and the influence of others such as patient comorbidities and genetics, and pathogen virulence and load, a highly heterogeneous picture emerges.

As well as identifying candidates to dampen hyperinflammation, Dr van der Poll explained that several trials have aimed at restoring the responsiveness of cells in patients that are in a state of so-called ‘immunoparalysis,’ which is thought to leave the host vulnerable to secondary infection.

Identifying which state a patient might be in – if such a simplistic view can be taken at all given the complex interactions at play – is achieved by a variety of methods: “The most commonly used method is to look at HLA-DR expression, at circulating immune cells and particularly monocytes,” said Dr van der Poll. “Patients that have immune suppression have a downregulated HLA-DR expression.”

“And another way of looking at it is by the capacity of circulating cells that produce cytokines upon restimulation. You can take peripheral blood mononuclear cells, or whole blood leukocytes, and expose them again to, for example, endotoxin (lipopolysaccharide) – cells from patients are less capable of releasing pro-inflammatory cytokines. That is a read-out of immune suppression that has been used frequently. There are other read-outs, but those are the two main.”

Such markers, along with clinical measures, are an increasingly appreciated part of targeted immune therapy. Discussing the current candidates looking to boost immunity during the immunoparalytic phase, Dr van der Poll noted interferon-gamma, granulocyte macrophage colony stimulating factor (GM-CSF), and interleukin-7 as currently under investigation, adding: “But none of these interventions have been implemented in clinical practice. It is simply too early, and we are not yet sure that these will be beneficial in patients with sepsis.”

Dr van der Poll will address the feasibility of immunotherapy in sepsis during the session, “New insights into the immune response,” taking place today at 13:45 in 400 Hall.

References
Does vitamin D have a role in the ICU?

Today's closing plenary lecture will be given by Kenneth Christopher (Brigham and Women's Hospital, Boston, USA), who will be speaking about recent and future studies on the potential benefits of vitamin D in the ICU population. While it has garnered increasing research interest over the past few years, a clear picture is yet to develop, with many trials in the pipeline hoping to explain if and where the supplement might find a home as an adjunct immune therapy.

The correlation between vitamin D and immunity in, for example, acute kidney injury (AKI) and sepsis, has long been evident, sparking the hypothesis that one might improve outcomes by prescribing it. In addition to publishing observationally on these topics, Dr Christopher was involved in an interventional RCT in Graz, Austria, in which 475 ICU patients were given a high dosage of vitamin D, and which hinted that mortality might be improved with supplementation.

The Graz trial did not identify a difference in its primary outcome – length of stay – but a difference was found in its secondary outcome of mortality, which is encouraging. However, in an interview with ISICEM News, Dr Christopher remained sceptical: "This is not definitive," he said. "The RCT was not designed with the particular outcome of mortality in mind. There appears to be a suggestion that vitamin D status is important for ICU outcomes based on observational data, and it looks like there might be something beneficial in vitamin D administration in the ICU. But what that 'something' is needs to be studied further."

In order to pin down the role that vitamin D might have, a more targeted approach must be adopted, Dr Christopher explained. Thus, he is currently planning a trial that looks at mortality as a primary endpoint, that will be more selective in terms of recruitment: "The Austrian trial was done on patients with vitamin D levels of less than 20 ng/ml – so a subset of all ICU patients. But, as with any particular medication, there is probably a target audience that it might work on. From the Austrian trial it looks as though it is those that have a very low level of vitamin D that could potentially benefit."

And this will be the first of many steps that, if proven to be of clinical benefit, could lead to big changes in the way that ICU patients are managed. But at this early stage, many uncertainties remain, such as how best to administer vitamin D, in terms of formulation, dosage and frequency of dosing.

Going on to give an idea of where the greatest benefit might lie should the trials show an outcome difference, Dr Christopher said: "In my opinion the outcomes may be different not based on what's happening in healing, but what is happening over the course of the patient's stay in the hospital. Vitamin D – if it is going to work – could potentially prevent future problems of infection, it could help patients wean off ventilation better, or help them with their longer term recovery. I think that is really where the mechanism will be in terms of better outcomes."

The majority of patients in the ICU have deficient levels of vitamin D, which Dr Christopher defined as a serum concentration of lower than 30 ng/ml. But this definition may have different implications for individual patients. On top of this, the distinct lack of conformity in assays used in measuring serum concentrations – an issue not unique to vitamin D – introduces another source of variation that ought to be controllable.

"That is a little troublesome because you cannot necessarily compare all of the studies to each other," said Dr Christopher. "But there is an interesting policy question in terms of what vitamin D deficiency is, and what assay should be used to define it – none of those concepts are clear."

The reality of contemporary urban lifestyles means that most people spend the majority of their time indoors, which can take a toll on vitamin D levels, especially in areas where sunlight is weaker or during times of the year when daylight hours are limited. And this idea serves to turn the vitamin D-immunity causal hypothesis on its head: "In some deficient patients, the deficiency will just be reflective of the fact that they are homebound so are not active and going outside, because they are chronically ill. In observational studies you don’t know if comorbidities are associated with or exacerbated by vitamin D deficiency."

It is impossible to separate out these factors until results begin to emerge from interventional studies. Until then, what approach does Dr Christopher take with his ICU patients in whom vitamin D deficiency is noted? "I am very conservative in recommending vitamin D to my ICU patients, unless I have a level that I know is really low," he said. "This is because, although I am confident in the data, it is not at the point where policy can be made on what should be done in the ICU."

"Vitamin D is essentially non-toxic. Even at high doses, the trials essentially haven't shown consistent toxicity problems. We do have some mild increase in calcium, but this is self-limiting and it hasn’t been reported to lead to problems in the ICU setting. So it is probably safe to give, but we don’t completely know for sure. And no drug is ever truly benign; we don’t know enough information to be confident enough to give high dose vitamin D to every single patient that walks in the ICU. It is time to talk about it, and time to study a targeted approach, but it is not time to say that all patients should be supplemented."

Amid a boom in research on vitamin D, sceptics – including Dr Christopher – patiently await the arrival of robust data from well-designed RCTs. “In many ways, I am agnostic,” he said. “Nobody pays me to say that vitamin D is good. I just go by what the data shows me. I believe that it is certainly a marker for poor outcome – I think people will accept that. Whether supplementation can actually change outcome is still up in the air."

"Vitamin D is cheap and it is a ‘natural’ substance, and levels are easy to modify. So it is in many ways a tantalising substance to go after! People already know what it is, so people in the community will understand it and the buy-in will be large if it works. Hopefully it is something that will make a difference. There is a lot of great work that is going on right now, and the next two to five years will be fairly exciting in terms of the trial results that will come out."

"The next two to five years will be fairly exciting in terms of the trial results that will come out."

Kenneth Christopher
Germany’s prospective, controlled epidemiological trial looking at the relative safety of a patient-focused, evidence-based patient blood management (PBM) program, is set to complete in the second half of this year, at which point over 100,000 patients will have been enrolled. An update on this trial, together with practical procedural and organizational tips that have emerged from it, will be presented by Kai Zacharowski (University Hospital, Frankfurt, Germany), forming the conclusion of today’s session dedicated to transfusions in intensive care and emergency medicine.

PBM comprises a system of measures intended to reduce perioperative blood loss, minimizing transfusion necessity and optimizing outcomes. The program is in debt to an increasing awareness of the relatively high prevalence of anemia (either idiopathic, acquired or exacerbated), associated with increased rates of morbidity, mortality, and length of hospital stay. As a modifiable risk factor amid blood supply shortage and in sight of the complications that can occur around transfusions, the World Health Organisation is pressing countries to implement PBM programs as the new standard of care to limit unnecessary blood transfusion.

Professor Zacharowski, along with fellow PBM project...
leaders Patrick Meybohm and Dania Fischer, designed the trial that takes place in four German university hospitals, in Frankfurt, Bonn, Kiel and Münster, including all patients undergoing surgical procedures falling within inclusion criteria. A control group consists of those treated before the implementation of the PBM program, with an expanding data set of post-PBM patients. The primary endpoint is a composite of in-hospital myocardial infarction, stroke, acute renal failure, death of any cause, pneumonia and sepsis until discharge from hospital in patients before and after implementation of the PBM program.1-2

In an interview with ISICEM News, Professor Zacharowski explained that his talk will focus mainly upon sharing the implemented strategies that appear to be reducing blood wastage and transfusions. “A few simple changes enabled us to reduce our patients’ blood loss for diagnostic purposes by roughly 2,000 liters per year – helping us to prevent iatrogenic anemia,” he said.

Noting some of these changes, he went on: “We have changed central laboratory practice so that we now have smaller blood vials. We have also exchanged the way we take blood from patients on the ICU. This used to be done in a way where you take a sample which is diluted with saline and blood; you then throw this one away, and then you take a real sample for clinical laboratory or for blood analysis or whatever. “We have developed a system which now has been sold by several companies (we are not the owners of it). It is a flush system, where you take the patient’s blood out, which is diluted but you keep it in the circuit and then you take a blood sample, and then you flush the patient’s own blood back into the body so the patient is not losing much. We have a lot of other things to share in terms of what improves patient outcomes on the ICU.”

Professor Zacharowski will also be giving an up-to-date evaluation of clinical trials on anemia in ICU patients that have been carried out over the past few years, with an eye to making recommendations and further practical hints on how to implement these regardless of healthcare systems’ limitations.

The trial combines bundles of measures, each bundle with a particular objective directed towards the overarching goal of reducing the need for transfusion. “It is also open to implement more bundles,” explained Professor Zacharowski. “You could implement more bundles if they are improving patient blood management.”

Professor Zacharowski will be presenting references that evidence that Professor Zacharowski will be presenting reflects the ethos of the PBM program: “We try to take evidence into clinical practice, which is one of the most difficult things to do.”

Such steps need to be taken to shake up a status quo that, as Prof Zacharowski explained, relies too heavily on allogeneic transfusion. And this brings with it an economic benefit, too: “When you do proper patient blood management you are talking about millions in savings, which you can basically re-invest in other patient safety measures.”

References


“When you do proper patient blood management you are talking about millions in savings, which you can basically re-invest in other patient safety measures.”

Kai Zacharowski

“Brainstorming: ‘Big Questions for the Experts’”

Parador de Alcali de Henares, Madrid, Spain, May 3-6, 2015
Nephrotoxicity key component in renal failure

The ins and outs of renal failure will be placed on the chopping block today at ISICEM, with one talk arguing that the most prominent cause in renal failure is in fact the doctors themselves. “I will be really reminding people of the kinds of things which cause acute kidney injury – and many of those are controlled by the physicians,” explained John Kellum (Center for Critical Care Nephrology, University of Pittsburgh, PA, USA).

More specifically, Dr Kellum will be discussing the nephrotoxic effects of treatments administered to patients, be they drugs, or other sources such as fluids that are not necessarily understood to be nephrotoxic, but have adverse renal effects. “Patients in the ICU are complicated and have multiple issues going on,” continued Dr Kellum. “So it is quite common for them to receive lots of different medications, some of which can influence different functions.

“We often have to balance those adverse effects with the positive things we are trying to affect with the medications and the treatments. So my talk is really about trying to focus people’s attention to the degree of which various drugs can cause nephrotoxicity. And the other part of it is that some of these relationships are potentially modifiable, meaning that we can choose certain medications that are less nephrotoxic if we recognize how big of a problem it could be.”

With this in mind, what reference material does the average ICU doctor have to hand in order to assess what drugs may be appropriate to use?

“I think that is part of the problem because at least some of this issue is related to drug combinations, which are not easy to look up,” said Dr Kellum.

“You don’t necessarily have a resource to identify which combinations of drugs are likely to produce nephrotoxicity. In North America there is still a rampant use of normal saline, primarily for fluid resuscitation, which is problematic. There are potential roles for fluids like albumin, etc., so maybe there is a nephrotoxicity and renal injury, Dr Kellum touched upon the concept of protocolized care, saying: “There is quite a lot of interest of late in trying to automate a protection system.”

With this in mind, a recent publication by Wilson et al. in The Lancet examined how outcomes would be affected if an automated electronic alert for acute kidney injury was used for patients in a hospital setting, ostensibly attracting earlier attention to AKI by attending physicians.1 However, results from the randomized, controlled trial showed that the alert system did not improve clinical outcomes.

“They showed, basically, that if you told physicians there was an acute kidney injury, it wouldn’t really change their management,” said Dr Kellum. “There wasn’t anything they did that really influenced outcomes. So the real issue is should we tell people before they develop acute kidney injury or, once they develop acute kidney injury, give them more specific advice about what medications might be causing it etc? Just telling the doctor that, in case they didn’t notice, their patient has acute kidney injury, isn’t really helpful.”

Conversely, a study that focused on systematic serum creatinine (SCr) screening in children receiving nephrotoxins showed a 42% reduction in AKI intensity, lending credence to the notion that focusing on the drugs themselves is a valuable alternative to reduce AKI.2

“Having a system which can detect potential toxic combinations or give physicians advice as to which medications may be less toxic would be perhaps be more useful,” said Dr Kellum in closing.

References
Don’t miss!

ISICEM 2015’s ePoster sessions – packed with interesting and innovative accounts from centers all over the world.

For even more, make sure you attend the poster award ceremony, held at 10:15 on Thursday in the Gold Hall.
Should we be paying more attention to monitoring and reversal of NOACs?

The novel (non-vitamin K antagonist) oral anticoagulants (NOACs) have brought a wealth of choice in managing thrombotic and embolic risk in patients with atrial fibrillation or venous thromboembolism. The choices that clinicians make in this regard depend upon a keen understanding of the data surrounding both suitability and risk – topics under discussion today in a plenary lecture by Peter Verhamme (University Hospitals Leuven, Belgium).

NOACs share the efficacy of warfarin, while exceeding its safety profile in terms of life-threatening and intracranial hemorrhage. “Their increased convenience is important,” explained Dr Verhamme in an interview with ISICEM News, “Because no routine monitoring of coagulation laboratory parameters is needed.”

“Importantly, also the perioperative management is much more convenient with these new agents. However, NOACs are not the answer to all our needs. NOACs should not be used in critically ill patients and in patients with mechanical heart valves. There are also questions on their use in peritoneal dialysis patients and in patients with mechanical heart valves.”

He continued: “In the last years, guidance on the management of patients on NOACs in frequent clinical scenarios has become available. Many institutions have now implemented these guidelines, which has surely facilitated the more optimal use of NOACs in various clinical scenarios.”

While the predictable pharmacodynamics and pharmacokinetics of the NOACs remove the necessity for laboratory testing, a recent report by Vanden Daelen et al. (of which Dr Verhamme is a contributing author) surmised that this might be useful in the emergency setting and in improving the management of severe bleeding.

“The more predictable onset and offset of NOACs (compared to vitamin K antagonists) is an advantage for the pre-operative management,” said Dr Verhamme, adding: “However, some caution is needed with respect to resuming NOACs in the postoperative phase, where a few days of ‘bridging’ therapy with a prophylactic dose of low-molecular weight heparin may be appropriate, especially in patients with major surgical procedures.”

Dr Verhamme explained that, upon the introduction of the NOACs, many physicians were uncomfortable with the notion of suspending routine monitoring without witnessing NOAC activity on a per-case basis – despite this practice being validated in large-scale trials, such as RE-LY.

As such, some continued ongoing monitoring, albeit in a greatly limited capacity, it being justifiable in extraordinary circumstances only.

The work by Vanden Dalen et al. makes recommendations on assay choice in NOAC monitoring, based on a review of current data on both management and reversal. With most data emerge from preclinical study, healthy volunteers, or in vivo or ex vivo study, more evidence is set to emerge in the coming years. In cases of bleeding, current recommendations center on stopping anticoagulation and employing standard resuscitation procedure. This includes: assuring hemodynamic stability, assessing time since last NOAC dose, determining creatinine, blood formula, and assessing NOAC activity.

The latter points are determined by laboratory assay, with active partial thromboplastin time in the case of dabigatran, and prothrombin time in rivaroxaban, proving to be sensitive qualitative measures in certain assays. With respect to specific quantitative assays, Vanden Dalen et al. deemed that diluted thrombin time for dabigatran and chromogenic anti-Xa assay for all Xa inhibitors (which includes rivaroxaban and apixaban) are highly sensitive.

A distinct dearth of reversal agents has similarly been a source of ferment, although specifically-designed antidotes are certainly in the pipeline. This nevertheless presents a clinical challenge in the interim period, explained Dr Verhamme, demanding particular attention to the assessment of risk factors, as well as possible dose-adjustment in individual patients, to minimize the risks associated with bleeding, overdose or emergency surgery.

On the topic of reversal agents, Dr Verhamme continued: “Importantly, it now has become clear that PCCs (prothrombin complex concentrates) do support hemostasis in case of major bleeding in patients on the thrombin inhibitor dabigatran or on factor Xa-inhibitors. Some recent insights on the impact of (activated) PCCs, and the more specific reversal agents under development, will also be presented at ISICEM.

“This is reassuring for many physicians, since even though NOACs reduce life-threatening bleeding and intracranial bleeding, many physicians remain confronted with bleeding such as gastrointestinal bleeding. Guidance to support hemostasis has now been validated in appropriate preclinical models, and more and more ‘real life’ data is currently being registered. Importantly, these real life data also support the efficacy and the safety benefit of NOACs.”

References
A plenary lecture held on Thursday morning will focus on venous thromboembolism (VTE) prevention, with Robert Fowler (Sunnybrook Health Sciences Centre, University of Toronto, Canada) speaking on the current state of detection and treatment, along with the latest from the PROTECT (Prophylaxis for Thromboembolism in Critical Care Trial) and E-PROTECT studies that aim to find the most cost-effective means to prevent and reduce the economic burden of VTE in the ICU.

VTE covers a spectrum of diseases, from the asymptomatic to fatal. The most common venous thrombi for critically ill patients occur in the deep veins of the leg and pelvis and pose a risk of traveling to the lungs as a pulmonary embolism (PE). With diagnosis not always being straightforward, a keener eye on preventative strategies has become an important priority in many healthcare systems across the world.

Speaking to ISICEM News, Dr Fowler explained that VTE is a common complication of acute and critical illness, with deep vein thrombosis (DVT) and PE being associated with an increased risk of death. Describing the work he has been doing on preventative strategy, he said: “A recent multicenter, blinded, randomized trial (PROTECT) compared the effectiveness of the two most common pharmacoprevention strategies: administration of low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH).

“Drug acquisition costs have historically been higher for LMWH than for UFH. However, if the effects of these drugs differ substantially, paying more may be worth it. This highlights the need for comparative economic and clinical effectiveness research to inform practice. Past work by our group has shown that it is likely not economical to perform routine screening to detect DVTs, but instead, prevention is the key to reducing costs and improving outcomes.”

Robert Fowler

Continued on page 14
Weighty decisions: Heparin choice for VTE prevention

“From a health care payer perspective, VTE prophylaxis with the LMWH dalteparin in critically ill medical-surgical patients was more effective and had similar or lower costs than the use of UFH.”

Robert Fowler

E-PROTECT was funded by the Heart and Stroke Foundation (Ontario, Canada), the University of Toronto, and the Canadian Intensive Care Foundation. PROTECT was funded by the Canadian Institutes of Health Research, the Heart and Stroke Foundation (Canada), and the Australian and New Zealand College of Anesthetists Research Foundation.

These two tandem studies, carried out over the past 10 years, have demonstrated the necessity of cost-effectiveness analyses beyond face-value daily drug costs, in order to make sound treatment decisions. The group is now focused on translating these findings to ICU clinicians and hospital administrators.

In his conclusions, Dr Fowler stressed the hidden burden that uninformed choices can bring: “If an ICU with 1,000 medical-surgical admissions per year uses UFH instead of LMWH for prevention of VTE, the annual incremental cost may be between $1,000,000 and $1,500,000 with similar or worse clinical outcomes, despite the individual drug cost of UFH being $4 to $5 less per day.”

Thursday’s plenary lecture marks the second of two for Dr Fowler at this year’s ISICEM meeting. His first lecture will take place this afternoon at 13:45 in the Tent, titled ‘Ebola virus disease: Lessons for the intensivist’.

References
This morning’s dedicated nosocomial infection session will explore a number of aspects of prevention, one being the incredible importance of hand washing, as Didier Pittet (University Hospital of Geneva, Switzerland) will stress for those in attendance.

“Healthcare-associated infections (HAI) are a universal problem, killing 16 million individuals worldwide each year,” he told ISICEM News.

Professor Pittet is the lead of the World Health Organization’s (WHO) ‘Clean Care is Safer Care’ campaign, which was initiated in October 2005. “We established a multimodal five-element strategy to improve practice [‘5 Moments for Hand Hygiene’]: replacing soap and water hand washing by alcohol-based hand rubs; education campaigns; monitoring and feedback of performance to healthcare workers; reminders in the work place; and changing safety culture,” he explained.

The strategy is currently active in 179 of the 194 United Nations country member states, and Professor Pittet shared that it is estimated the impact of the global campaign will be the prevention of more than 8 million deaths per year, worldwide.

With MRSA and other severe infection risks being a significant concern, encouraging hospitals to adopt hand-washing strategies is a crucial part of the battle. “There is still a lot to do,” said Professor Pittet. “Compliance with hand hygiene practices is still quite low in many hospitals, and in many wards around the world. Compliance used to be around 20%, and is nowadays around 40 to 50% according to large recent studies, but there is still a long way to go until compliance can reach at least 80%, as according to the 5 Moments for Hand Hygiene strategy, delineated as indications for hand hygiene during healthcare by the WHO.”

While results are far from instantaneous, Professor Pittet emphasized that successful hand hygiene promotion programs are associated with MRSA reduction within 6 months to 1 year, and still represent the most important parameter in the control of MRSA in places such as the UK, and in many other nations with national surveillance.

But is there a ceiling to how much hand hygiene can improve MRSA rates? “Hand hygiene is obviously not all we need, but it is the most impactful strategy – comparable to the impact of vaccination on some infectious diseases,” said Professor Pittet.

He concluded: “The difficulty in hand hygiene promotion is to change the behavior in a sustained way. We have succeeded in establishing a system change, which is replacing soap and water hand washing by alcohol-based hand rubs. Work remains to be done, but we have come really far. The rest will be to instill behavioral change, and then sustain it.”
ARDS and sepsis: Incidences and outcomes  Salle M (Bozar)  Tuesday  15:05

‘Who cares’ about ARDS definitions?

ARDS and sepsis will take center stage this afternoon, with a comprehensive session that will explore the incidences and outcomes of both conditions. Speaking during the session will be Gordon Rubenfeld (Sunnybrook Health Sciences Centre, Toronto, Canada) who will pose the question of ‘ARDS definitions: Who cares?’. Professor Rubenfeld spoke to ISICEM News to explain what he means by this, beginning by commenting: “Diagnosing a disease only matters if it changes therapy or prognosis,” he said.

“We have some data that shows lung-protective ventilation is at least safe for everyone on a ventilator, and does not require a diagnosis of ARDS. The diagnosis of ARDS is not needed for rescue therapy for hypoxemia (ECMO, iNO), and overall it is not clear that the diagnosis of ARDS changes prognosis.

“It is very important for researchers, but perhaps not crucial for clinicians.”

Professor Rubenfeld went on to stress that the most important question would not be whether to treat everyone on a ventilator the same way, rather it should be that, for patients who have acute hypoxic respiratory failure (not from cardiac failure), does it actually matter if they meet the criteria for ARDS or not, for clinical purposes? “The doctor has lots of important decisions that do not rely on diagnosing ARDS,” he said.

“Why is the patient hypoxic? Do they need antibiotics? Is this a non-infectious pulmonary disease that might need steroids? What is the patient’s volume status? What are the goals of care in this case? For patients who have acute hypoxic respiratory failure that is not primarily from cardiac disease, the factor that separates ‘ARDS’ from ‘non-ARDS’ is the chest X-ray. And the chest X-ray is a big problem.”

But what does Professor Rubenfeld feel is essential going forward in terms of how we manage ARDS? “I think that it is unlikely that we will find a ventilator strategy that improves mortality compared to ARDSnet lung protective ventilation,” he said. “The effect sizes of a ventilator intervention compared to this control arm are likely to be small enough that thousands of patients will be required.

“I think that there will be a lot of ongoing interest in rescue strategies for patients dying of hypoxemia. The problem with this area of investigation is that, outside of a flu epidemic, the number of these cases is likely small. As the technology gets easier, we will have safer extracorporeal life support for severe hypoxic respiratory failure, expanding beyond the rescue scenario. But this will need to be carefully evaluated.”

Professor Rubenfeld also noted that pharmacologic interventions remain of interest, but the barrier there would be accurate surrogate Phase 2 endpoints to guide drug development. He concluded: “General care of the ICU patient (sedation optimization, early mobilization if it works, weaning) has a lot of promise, and we will continue to improve these areas, but they are not specific to ARDS.”

“Overall it is not clear that the diagnosis of ARDS changes prognosis.”

Gordon Rubenfeld

“General care of the ICU patient (sedation optimization, early mobilization if it works, weaning) has a lot of promise, and we will continue to improve these areas, but they are not specific to ARDS.”

Gordon Rubenfeld

Professor Rubenfeld will deliver his presentation ‘ARDS definitions: Who cares?’ during the session ‘ARDS and sepsis: Incidences and outcomes’, held at 15:05 this afternoon in Salle M (Bozar).
Red blood cell (RBC) transfusions are one of the most frequent procedures in every hospital and can increase risk to patients and costs to hospitals. Many transfusions are considered unnecessary, so there is a growing recognition of the need to reduce RBC transfusions. Laboratory hemoglobin values are used as a primary indicator for RBC transfusions, are only available intermittently, and are often delayed — leading to suboptimal transfusion decisions.

Masimo has invented noninvasive and continuous hemoglobin (SpHb®) monitoring, which helps clinicians optimize transfusion decisions by providing real-time trending in hemoglobin status. SpHb has been shown to help clinicians reduce blood transfusions in both low and high blood loss surgery,¹ ² and has demonstrated its lifesaving potential to help clinicians detect occult bleeding in places like intensive care units and labor and delivery wards.³

With the growing recognition of the need to reduce transfusions, noninvasive and continuous hemoglobin (SpHb) can be a key tool to help overcome the limitations of existing approaches.

The Joint Commission has introduced Patient Blood Management Measures that encourage hospitals to evaluate appropriateness of transfusions as a continuous quality indicator.¹¹ The American Medical Association and The Joint Commission also recently identified RBC transfusions as one of the top five overused procedures in medicine, defining overuse as “circumstances where the likelihood of benefit is negligible or zero, and the patient is exposed to the risk of harm”.¹⁰

How SpHb Monitoring Helps with Transfusion Decisions
Masimo’s solution provides hemoglobin both noninvasively and continuously. The noninvasive aspect makes the technology easy to apply to the patient, and the continuous aspect assists RBC transfusion decision making. While SpHb monitoring is not intended to replace blood draws, it identifies significant changes in hemoglobin and lack of significant changes in hemoglobin between invasive blood sampling and laboratory analysis.¹⁴

Continuous hemoglobin means you can determine the directional trend of hemoglobin — whether it is stable, rising, or falling. This can help avoid unnecessary transfusions when the SpHb trend is stable and the clinician may otherwise perceive hemoglobin is dropping, or when the SpHb trend is rising and the clinician may otherwise perceive it is not rising fast enough. Inside and outside the operating room, a dropping SpHb trend may also allow clinicians to identify internal bleeding and permit earlier interventions.

Cost Savings Model from Capgemini
Capgemini, a leading supplier of global consulting and technology services, released a study showing that a typical 500 bed hospital incorporating Masimo rainbow® Pulse CO-Oximetry into its clinical standards and care pathways could generate nearly $500,000 in net annual cost savings and financial gains. Capgemini reported that significant financial benefits could be derived from incorporating noninvasive total hemoglobin (SpHb) by helping clinicians prevent unnecessary blood transfusions, identify internal bleeding, and increase patient throughput. The study concluded that “whether considered on a per-patient, department, or hospital-wide analysis, there are significant clinical and financial benefits to implementing Pulse CO-Oximetry technology.”

References
3. Case studies at www.masimo.com/guarantee
Zero Tolerance for resistant organisms

A session probing the issue of multiorganism resistance takes place this afternoon, defining the problems and possible solutions both now and in the future. Miguel Sánchez García (Hospital Clínico San Carlos, Madrid, Spain), who will be arguing that we can control bacterial resistance in the ICU, spoke to ISICEM News in advance of the meeting to discuss his perspectives.

Amid a decline in the rate of newly-approved drugs to treat resistant organisms, a rise in multidrug-resistant (MDR) infections over the past few decades poses a significant threat to public health, especially in vulnerable populations. The nature of ICU practices equate to a significant risk, not least because of the typical condition of patients increasing the risk of patient-to-patient transmission.

For Dr Sánchez García, the phenomenon of bacterial resistance, which is of course experienced by all who work in intensive care, is not something to be met with apathy. "Occasional cases tend to be accepted as ‘normal’, particularly in complicated patients with prolonged hospital or ICU stay and broad-spectrum antimicrobial therapy,” he said.

“When several simultaneous cases accumulate, with the same resistant microorganism being identified in cultures, cross-colonization due to breaches in hygiene should be investigated and an endogenous source such as the patient’s gastrointestinal tract, or common environmental sources like tap water, should be investigated.”

With increasing number of simultaneous cases, measures such as barrier precautions and the cohorting of cases are usually implemented by preventive medicine services or hospital epidemiologists, he explained, adding: “The approach to ‘prevention’ and ‘therapy’ of resistance aims at control of endogenous sources, like with selective decontamination of the digestive tract and reduction of selection pressure by antimicrobial stewardship, and exogenous reservoirs through decontamination of surfaces and devices.”

Dr Sánchez García is a member of the Spanish Scientific Expert Committee for the ‘Zero Resistance’ project, which follows two previous programs aimed at targeting ICU-acquired infections. The program includes a web-based teaching module, and its implementation, which is ongoing, is described in full in this year’s Annual Update in Intensive Care and Emergency Medicine 2015.

In the same vein, the ongoing ‘Zero Resistance’ project looks at another aspect of minimizing ICU infection by way of prevention and management. Nine nominated intensivists with expertise in the field of prevention and management of infection were appointed to a special Scientific Expert Committee, along with one intensive care nurse, a microbiologist, an epidemiologist, an infectious disease specialist, and two technicians from the Spanish Ministry of Health with broad knowledge in the field.

In the literature, bundles were developed with the aim of reducing ICU-acquired MDR infections by 20%, and with the secondary objective of studying the epidemiology of MDR infections in Spanish ICUs. The program includes a web-based teaching module, and its implementation, which is ongoing, is described in full in this year’s Annual Update in Intensive Care and Emergency Medicine 2015.

Commenting on the increasing relevance of MDR organisms over the last few decades that spurred ‘Zero Resistance’ into being, Dr Sánchez García said: “What used to be an uncommon resistance pattern has become the predominant phenotype for many bacteria. In addition, many regions of the world face the threat of resistant bacteria being more and more prevalent in the community and no longer exclusively in hospitals.”

And while he is positive that changes can be made to combat resistance, he commented on the different opinions in the clinical and scientific community with regard to how best we should overcomin it: “The reservoir is investigated and cross-transmission reinforced, and in addition antibiotic therapy stewardship aims at reducing the development of resistance by prudent use of antibiotics. Here, two antagonistic approaches exist, either restricting broad-spectrum or last-resort antimicrobials, or following a strategy called ‘diversity’, which proposes that different classes of antibiotics are used simultaneously.

“The first aspect to consider should certainly be the prudent use of antimicrobials. Subsequently, ICUs should consider measures to prevent development and dissemination of resistance. A matter of substantial debate is the degree of surveillance, i.e. performance of scheduled cultures, as well as at ICU admission, to detect carriers of multi-drug resistant bacteria.”

Dr Sánchez García will discuss strategies of improving ICU rates of MDR infection during the session, ‘Multiresistant organisms’, which takes place today from 13:45 in 100 Hall.

Miguel Sánchez García

References

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Beyond Pulse Oximetry: The Future of Non-Invasive Monitoring

Location: Room Gold Hall, Brussels Meeting Center (SQUARE)
Date and Time: Tuesday, March 17 • 12:30 – 13:30, Lunch will be provided
Chairperson: Michael Pinsky
Please register at www.masimo.com/ICUFuture

Presenters

Can We Monitor Everything Non-Invasively?

Michael R. Pinsky, MD, CM, Dr hc, FCCP, FCCM
Professor of Critical Care Medicine, Bioengineering, Anesthesiology, Cardiovascular Diseases, and Clinical & Translational Sciences
Vice Chair for Academic Affairs UPMC, Pittsburgh, Pennsylvania

Functional Hemodynamic Monitoring to Drive Resuscitation and Improve Outcomes

Maxime Cannesson, MD, PhD
Professor of Anesthesiology and Vice Chair – Research Director, Cardiac Anesthesia Department of Anesthesiology & Perioperative Care
University of California Irvine

Oxygen Reserve and Early Warning

Michael Ramsay, MD, FRCA
Chairman Department of Anesthesiology and Pain Management, Baylor University Medical Center and Research Institute
President Baylor Research Institute, Dallas, Texas

Interactive Session, please ask any questions to our Faculty now! For more information, please stop by Stand #2.23.
Please register and ask your questions at www.masimo.com/ICUFuture