Delegates packed into the expansive Henry Le Bœuf auditorium on Tuesday morning for the opening session of ISICEM, which saw a number of esteemed speakers take to the podium to deliver cutting-edge presentations and reports on a variety of intensive care topics.

Introducing the session, and this year’s meeting, was ISICEM Chairman Jean-Louis Vincent (Dept of Intensive Care, Erasme University Hospital, Université Libre de Bruxelles, Belgium) who first commented on the fantastic attendance already secured by day one of the meeting. Estimated at 5,990 people, Professor Vincent quipped: “We hope to find another 10 people in the street!”

During his introduction, Professor Vincent thanked all of the scientific advisors, faculty, speakers organizational teams and other contributors that work so hard to make ISICEM the success it is, with a special tribute to industry sponsors, commenting that, even in our difficult time, more sponsors than ever support this great meeting.

He also took the time to emphasize the new features of the conference this year, including the increased interactivity that has been facilitated with the exclusive use of electronic posters and emphasis on integrated social media, promoting even more collaboration between audience and speakers, and encourage more debate.

To all, he wished a great and enjoyable meeting, before closing his introduction and officially opening ISICEM 2013.

Reduced cortisol metabolism in critically ill

Following Professor Vincent’s address, and a report from the Round Table Conference on Neuroprotection (page 6), the first standalone presentation that took place during the opening session discussed novel insights into the hypothalamic–pituitary–adrenal axis – with a focus on reduced cortisol metabolism.

“When the human brain senses a stressor, it signals to the hypothalamus to release CRH [corticotropin-releasing hormone], that stimulates the pituitary glands to release ACTH [adrenocorticotropic hormone],” began presenter Greet Van den Berghe (University of Leuven, Belgium). “That drives adrenal cortisol synthesis and secretion. Then cortisol exhibits feedback inhibition on both the pituitary gland and the hypothalamus.”

In sepsis or trauma, the high cortisol levels seen are in fact present despite low levels of ACTH, leading to theories that these low levels are due to reduced cortisol metabolism. Thus there are theories of either altered ACTH sensitivity, or alternatively ACTH-independent stimuli such as adipocyte-derived factors, endothelial derived factors, immune cells and cytokines or neurons and nueropeptides.

But Dr Van den Bergh made a salient point, questioning: “If stress increases the need for cortisol in several vital organs and tissues, wouldn’t it be the most economic and logical thing to do to stop breaking it down?”

She continued, outlining the pathways for cortisol breakdown in the liver and the kidney, the most predominant pathway being the A-ring reductases (5β-reductase and 5α-reductase) in the liver. This removal is offset with regeneration of cortisol through 11β-hydroxysteroid dehydrogenase (11β-HSD) in the liver.

Crucially, in critically ill patients, elevated circulating levels of bile acids

‘Have a great meeting!’

Jean-Louis Vincent speaking at the opening session
Opening up our minds about the way ICUs are run

Open ICUs offer fundamental benefits for patients and relatives simultaneously, and we should consider closed formats a thing of the past, delegates will hear this afternoon in a session that will examine the processes of care in ICUs.

In the session, Massimo Antonelli (Università Cattolica del Sacro Cuore, Rome, Italy) will discuss a number of reasons why he believes the open format is superior. Speaking to ISICEM News, he summarized: “This way, we create an ample climate of collaboration and communication between the doctors, care givers, health workers and relatives that is fundamental for harmonization of the cure and the successful treatment of the patient in general.”

However, Professor Antonelli conceded that financial implications would be the main hindrance to this shift to an open structure. Resources are relatively scarce, with varying degree no matter where one lives or works, which can jeopardize essential core components of the system including nurse – patient ratios – a vital component.

But, for Professor Antonelli, the closed system represents an outdated model that must be changed, and it is important to note many of the skeptics that come packaged with a shift to open structures may be unfounded upon closer inspection. “A lot of physicians believe that opening the ICUs exposes them to the blame, for instance, by patients and relatives,” said Professor Antonelli. He added: “As soon as a unit decides to open to the external environment, and becomes a truly open ICU, in the beginning there may be some reluctances on behalf of the staff, fearing someone may look at them and watch what they are doing. Just in terms of control, that makes them feel uncomfortable because they feel observed and judged. This is not the case, and as soon as these things go on, they quickly realize this is an unjustified fear, and overcoming this initial obstacle, the staff is the first to strongly believe that so the relatives can come out and help in specific situations,” said Professor Antonelli, adding that this would only help bolster the relationship between the staff and the family, helping them become more comfortable and confident with such a difficult environment.

Of course, it would be idealistic to not expect relatives that is fundamental for harmonization of the cure and the successful treatment of the patient in general.”

Massimo Antonelli (Università Cattolica del Sacro Cuore, Rome, Italy)

“[Open ICUs] create an ample climate of collaboration and communication between the doctors, care givers, health workers and relatives that is fundamental for harmonization of the cure and the successful treatment of the patient in general.”

Massimo Antonelli (Università Cattolica del Sacro Cuore, Rome, Italy)

it is a real benefit for the entire unit.”

In addition, there is a perceived risk that open ICUs are more susceptible to infections, a notion which Professor Antonelli shuns as completely untrue. “The only fundamental thing that is a very essential recommendation made to all the staff and the relatives is to wash hands,” he said.

That being said, perhaps one benefit of a closed system would be 24/7 management of the unit by the in-house team? “Yes that is a good point, and probably some situations that may occur unexpectedly to severe patients in life threatening situations in the ICU in presence of relatives may create major difficulties,” commented Professor Antonelli.

However, from his observations, once relatives and friends look at the work the physicians and nurses are putting in, they immediately realize how intense is the effort that is being made to care for their loved one.

In fact, in some situations, relatives could possibly help alleviate minor issues related to staff shortages: “If there is a staff constraint, you can’t always have a nurse that stays within the room with the patient, and that complications, frustrations and even threatening behavior (be it litigious or verbal) could arise from some relatives venting their concerns and dissatisfaction when patients take a turn for the worst. However, steps can be taken to make sure this is kept to its absolute minimum, being particularly mindful that it is a very difficult time for all those involved.

“The problem is, as soon as you have a difficult case where there are some expectations coming from the family that do not correspond to the real condition of the loved one, in these cases explaining clearly with simple language, and taking the necessary time for clear explanation, being patient and insisting in the essential understandable concepts may spare a lot of mistakes and misunderstanding between the family and the doctors, and solve a lot of problems, preventing the conflict and at times also the legal problems when things go wrong,” said Professor Antonelli.

“Obviously, it is time consuming. It means the medical staff has to spend – when the family members are inside the ICU – several hours in speaking with the family one by one, not disregarding any of them.”

To formalize measures that will protect staff from any stresses and strains arising from the meshing of staff and relatives, Professor Antonelli highlighted the importance of periodic evaluation and support of staff by psychologists and other specialists, with increased support during any instances of specific conflict. “I don’t think it would be an increased cost – it simply means you have to re-engineer the composition of the staff, employing external or internal support,” he said.

Furthermore, he added that the support, comfort and community that can be offered by religion should also not be overlooked. For those of faith, such measures could be a significant boon for the patients and their families. Whether this is by harnessing existing hospital infrastructure, or with additional outside help, careful and considerate incorporation of religion could be very complementary.

Professor Antonelli will delve deeper into the implications and considerations for an open format ICU system during his presentation ‘Can we afford an open ICU model with limited resources?’ in the session ‘Organization: Process of care’, today at 13:45 in the Studio (Bozar).

What if the kidneys could alert you sooner?

B y the time traditional tests for acute kidney injury (AKI) detect kidney function loss, valuable time has been lost in patient treatment. With the revolutionary NephroCheCk® test, you can risk-assess patients sooner because it detects highly specific, early-rising biomarkers of kidney cell damage. Results are available in just minutes, alerting you of the patient’s risk of developing AKI.

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New Biomarkers for Early Risk Assessment of AKI: Solving the Challenge

An Educational Satellite Lunch Symposium at the 33rd ISICEM

Wednesday, March 20, 2013 | 12.30-13.30 hrs | Horta Room | Brussels, Belgium

Register at AKIAssessment.com to stay connected and receive updates about the program. You may also submit questions to the faculty which will be answered during the program. There will be additional resources on the website following ISICEM.

Minh Chawla, MD
Washington, DC, USA
Cell Cycle Arrest Biomarkers for AKI

John Kelum, MD
Pittsburgh, PA, USA
Pathogenesis of AKI

Andrew Shaw, MD
Durham, NC, USA
Implications for Management of AKI

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A special symposium exploring whether current blood gas analyzer-driven insulin administration for critically ill patients is good enough took place in front of a packed audience at Tuesday lunchtime. Leading experts examined the current clinical data and practical considerations, what the Manual vs. Automated moNitoring Accuracy of GlucosE (MANAGE) studies tell us about blood gas analyzer-driven glucose control, and the clinical use of the OptiScanner to guide the delivery of insulin (OptiScan Biomedical, Hayward, California, USA).

Opening the symposium, James Krinsley, (Stamford Hospital, Connecticut, USA) began by pointing out that the landscape of glycemic control changed considerably between the Leuven Intensive Insulin Therapy Trial (Leuven 1) of 2001,1 and NICE-SUGAR,2 which was published in 2009. In the former study, the glycemic target range of 80–110 mg/dl was more frequently achieved than in NICE-SUGAR, at a mean morning blood glucose level of 103 mg/dl versus 118 mg/dl, with ~53% versus ~25% of values in range. The NICE-SUGAR study also had a greater degree of overlap between interventional and control groups. The NICE-SUGAR investigators also found that, versus normoglycemic critically ill patients, the odds ratio for mortality was 1.41 among patients with moderate hypoglycemia and 2.10 among those with severe hypoglycemia.

Dr Krinsley emphasized these findings had been confirmed by numerous previous studies, and restated the conclusion by the NICE-SUGAR investigators that “moderate glycemic control with very low hypoglycemia rates – in NICE-SUGAR in 0.5% of patients in the control arm, is preferable to tighter control with high hypoglycemia rates, which was 6.8% of patients in the interventional arm of NICE-SUGAR”.3

He said that there are other important differences between Leuven 1 and NICE-SUGAR, with Leuven 1 using arterial blood gas analyzers exclusively and NICE-SUGAR allowed the use of hand held meters.

Citing the three domains of glycemic control: hyperglycemia, hypoglycemia, and glycemic variability, Dr. Krinsley pointed out that glycemic variability is independently associated with an increased risk of mortality, and emphasized that this “was something that wasn’t even contemplated in the designs of the interventional trials”. As Egi et al pointed out in 2009,4 tight glucose control might mean either decreasing mean blood glucose concentrations or decreasing glycemic variability, with the latter potentially an important dimension of glucose management and important management goal.

Next, Dr Krinsley asked: What about diabetic status? He showed data from a nine-center, 23-ICU study involving ~45,000 patients from four continents, published recently.5 Among non-diabetics, a mean blood glucose of 80–140 mg/dl was associated with reduced mortality risk, while a range of ≥140 mg/dl was linked to an increased mortality risk. The opposite was found in diabetics, where a mean blood glucose of 80–110 mg/dl was linked to an increased mortality, while a mean blood glucose range of 110–180 mg/dl was linked to reduced mortality.

Hypoglycemia, defined as blood glucose <70 mg/dl, was associated with increased mortality risk among patients with and without diabetes, while increased glycemic variability, defined as a coefficient of variation (CV) ≥20%, was linked to increased mortality among non-diabetics.

Dr Krinsley observed that future intervention- al trials of intensive insulin therapy in critically ill patients must manage all three domains of glycemic control. However, he said, glucometers are not up to the task, due to inadequate accuracy, too much time required by nurses to measure glucose, who should be deployed to higher value patient care and an inability to manage all three domains with intermittent monitoring. These findings were also endorsed by a round table of ICU experts at ISICEM 2012.

He continued that glycemic targets will, in future, be designated based on patient characteristics, with different ranges for diabetic versus non-diabetic patients, as well as medical versus surgical patients. He emphasized that current techniques did not provide glucose monitoring frequently enough, with the number of tests per 24 hours in the 9 center, multi-center study only 2.8–9.0. “It should be at least 24 measurements per day”, Dr. Krinsley noted. Furthermore, timely monitoring is crucial. One study showed that measurement delay was the most common contributing cause to severe hypoglycemia, in 67% of cases.6

Dr. Krinsley elaborated that even meters required up to two hours of nursing time per patient per 24 hours, with approximately twice the amount of time required for blood gas analyzers. Finally, Dr. Krinsley estimated that the cost per blood gas analyzer test in his hospital was ~$7, resulting $188 per day for 24 measurements.

He concluded: “So I asked my hospital administrators to approve the use of blood gas analyzers for blood glucose measurement, the response to me was: ‘No way, Jose!’ So we are still using strips at Stamford Hospital in the United States.”

The next speaker was Serge Brimiouille (Université Libre de Bruxelles, Brussels, Belgium), who looked at data from the MANAGE I and II studies. Dr. Brimiouille first set out what characteristics the ideal continuous glucose monitoring system should have. He said it should be rapid, be accurate [within US Food and Drug Administration accuracy guidelines], be free from interferences from disorders or drugs, be robust and suitable for a busy ICU or operating room, with no calibration required, and be cost effective compared to repeated blood gas analyzer measurements.

Using data from MANAGE I, Dr Brimiouille showed that the OptiScanner was accurate relative to the YSI plasma analyzer, that the OptiScanner can correct for interferences rapidly, and provided examples where blood gas analyzer driven insulin administration resulted in undetected hyperglycemia, variability and hypoglycemia.

Next, he looked at MANAGE II, which had the same inclusion criteria as MANAGE I, but...
Achieving glycemic control needs the right tools. 

Michele Umbrello reminded the audience that increase hepatic glucose output in critical ill patients leads to hyperglycemia, which in turn drives up muscle insulin resistance. During nutritional support, the need for insulin, which is required to maintain normoglycemia, should be planned and based on the expected degree of stress and/or infection and the presence of severe sepsis. This is therefore supported by regular, daily checks on the glucose/insulin ratio.

He pointed out that the OptiScanner 5000 system uses mid infrared spectroscopy to measure glucose, and therefore does not need reagents. No calibration is needed either during use or periodically, and glucose measurements can be displayed every 15 minutes. Disposable cartridges allow for sterile blood handling circuits, and it can be used for 72 hours per patient. It is possible to program alarms to warn of hyperglycemia and hypoglycemia. In addition to data being available on either a display or via network or USB connections, it is possible to upgrade the system through software revisions.

Dr Umbrello said that his team compared the OptiScanner to central lab glucose measurements and a Radiometer (Bromshoj, Denmark) ABL blood gas analyzer at the equivalent of measurements every 15 minutes on a 200 ml blood sample over a 3-day period, at a target of 28 measurements per day. The results showed that both the OptiScanner and Radiometer devices were equivalent in accuracy, but the OptiScanner provided values every 1.5 minutes, at a far lower comparable cost, with no need for external validation. “And it does really reduce the workload,” Dr Umbrello commented.

Citing a series of cases from the study group, Dr Umbrello was able to show that patients had episodes of sudden, dramatic development of hyperglycemia, which coincided with the visit of a relative. Another particularly interesting case presentation suggested that the ability of the OptiScanner to document a sudden spike in glucose resulted in earlier identification of sepsis than otherwise achievable. He emphasized that he was showing these data not to draw a conclusion, noting “I don’t have data enough to prove causation”, but to illustrate one of the as-yet unexplored advantages of the OptiScanner. He said: “I am just suggesting we can see with this device things that we couldn’t see before.”

He went on to conclude that the OptiScanner allowed for early detection of insulin resistance, and was potentially able to detect metabolic derangements that normally would go undiagnosed. With the avoidance of hypoglycemia, patients should experience fewer adverse effects.

Finally, in one of the most telling statements of what was a fascinating and insightful symposium, Dr Umbrello commented that, after the OptiScanner, he would not want to go back to periodic testing. His closing statement was: “We think that, with the continuous monitoring of glucose in the most severe, stressed patients, we can have an earlier detection of what goes on in patients, with the possibility of detecting derangements that we otherwise wouldn’t have realized.”

Last of all, Dr Krinsley returned to the podium to summarize the technologies that underpin the OptiScanner, noting that the OptiScanner connects to the venous line, extracts ~0.1 ml of non-diluted blood, which is then centrifuged. Glucose is measured using mid-infrared spectroscopy, with glucose levels displayed with a trend every 15 minutes. He stated that this offers a number of advantages, emphasizing that it is the only glucose monitor that measures in plasma, and that the use of mid infrared spectroscopy allows “…the OptiScanner glucose measurement system not to need any calibration, over a full year, whereas other systems under development require daily calibration, another big difference.”

References
The Round Table Conference: Neuroprotection

This year’s Round Table Conference was held on March 16-18, continuing its yearly dedication to furthering a chosen field of focus by the gathering of minds and the latest insights for a three-day meeting directly preceding the ISICEM congress.

“The idea is to: one, assess the state-of-the-art in a certain area of interest; two, try to see what conclusions we can draw at this time; and then finally what are some of the future directions and recommendations for studies,” Round Table co-chair Paul E Pepe (UT Southwestern Medical Center, Dallas, USA) told ISICEM News.

The Round Table Conference takes insights from basic science and combines them in a clinical setting to help them learn the future directions that are to be taken. This year, the Round Table Conference focused on the clinical aspects of neuroprotection, with a range of sessions that explored different aspects, including ischemia and reperfusion injury, brain trauma, septic and liver encephalopathies, long-term recovery after brain damage and general concepts. It featured around 30 separate presentations, as well as many discussions.

“There has been a lot of work in the basic laboratory area but we want to make sure it is translated more to what's happening in terms of the clinical aspects of what we know in this arena,” said Dr Pepe.

Following the meeting, speakers who were in attendance are asked to provide a manuscript that will be combined in a follow-up publication that serves as a detailed report of the conference. Similarly, the report in the opening session of ISICEM served to highlight the outcomes of the Round Table Conference, offering key messages and brief glances rather than detailed accounts.

“So the intention of the session report will be to give people an overview of what's coming, but they'll get more detail in the subsequent publication that will detail all of these various presentations, and a few dozen manu-

New Study Suggests Point-of-Care Biomarker Plasma NGAL Improves Clinical Diagnosis of AKI in the Emergency Department

A new study published in Critical Care demonstrated that plasma neutrophil gelatinase-associated lipocalin (pNGAL), a biomarker that aids in the early detection of AKI, improved the diagnosis of AKI when added to clinical judgment.

Patients presenting to the ED may suffer from AKI that is not yet clinically apparent. Many of these patients develop severe AKI, leaving them dependent upon dialysis or RRT, compromising their long-term health and increasing the risk of death. Previous studies have demonstrated pNGAL's utility in the early detection of AKI, yet little research exists on the additive value of pNGAL in the ED to help reduce clinical uncertainty when assessing the risk of patients suffering from AKI.

A group of investigators led by Prf. Salvatore di Somma, M.D. (San’ Andrea Hospital, Rome, Italy), studied whether pNGAL levels could provide information that enhanced the initial clinical judgment of ED physicians when used with all other standard-of-care parameters for assessing AKI. The study included 665 patients from three clinical centers who were admitted to the hospital after presenting to the ED.

Upon initial examination, each patient received a medical history review and admission serum creatinine (SCr) was noted. SCr, while the current gold standard for detection of AKI, typically indicates AKI many hours after injury, which may delay appropriate therapy. Physicians then assigned patients to one of two categories, “AKI” or “No AKI,” and noted their levels of diagnostic confidence as a value ranging from 0% to 100%.

pNGAL concentrations were also measured at ED presentation and several other times during the patient’s hospitalization using the Alere Triage® NGAL point-of-care test. Following discharge, expert nephrologists, who were blind to any NGAL values, reviewed each patient case and made a final adjudicated diagnosis of “AKI” or “No AKI.”

Based on the ED physician’s initial clinical judgment, 218 patients (33%) were considered to have AKI, while only 49 cases (7%) were ultimately adjudicated to be true cases of AKI. AKI was over-predicted in nearly 78% of cases which were initially judged by the ED physicians to have AKI ((218-49)/218)=77.5%, suggesting that unnecessary therapies may have been administered in these instances. Additionally, the physician’s initial assessment missed AKI in 20% of cases that were ultimately adjudicated to be AKI.

Adding the pNGAL level at presentation was shown to improve the classification of patients into the “AKI” or “No AKI” categories by 32.4%. pNGAL measured on arrival was found to be the most powerful predictor of death in these patients.

“ED physicians must make critical treatment decisions that may affect the kidneys, yet it is very difficult to determine if AKI is occurring with current standard of care assessments,” said Prf. di Somma. “Having a point-of-care biomarker test can help ED clinicians promptly assess the presence of AKI to provide more timely and appropriate care for these patients.”

The study is available at: http://ccforum.com/content/17/1/R29/abstract
Visit Alere booth #2.05-2.06 or www.alere.com
Not available in the USA.
scripts,” explained Dr Pepe.

He added: “I have a terrific co-host, Nino Stocchetti, who’s really one of the world’s foremost experts, particularly in the area of head trauma. So he is very interested in neuroprotection.”

During the Round Table report in the opening session of this year’s ISICEM, co-chair Nino Stocchetti (University of Milan, Italy) was the first to speak, reiterating some of the matters the neuroprotection the meeting hoped to address. These included traumatic brain injury and spinal chord injury, as well as subarachnoid hemorrhage, ischemic stroke, ischemic reperfusion, liver encephalopathy and sepsis.

“We started with some general concepts of trial design, animal models the time window for protection,” he said. “When you deal with the brain, this window is very short, and also we dealt with the concept of what really neuroprotection is about. And of course we started with a review of what we know works.”

While Professor Stocchetti took more of a look at where we are today, for Dr Pepe, his task was to look to the future, and how we can understand the mechanisms of what we’re experiencing in the clinical arena.

“Part of my job today is to say that the future looks bright, as far as I’m concerned,” he said. But before looking to the next steps in the field, Dr Pepe first looked back at the literature thus far, underscoring that many techniques that were thought to have promise for neuroprotection never really panned out. As such, he commented that many look at the field of neuroprotection as a ‘glass half empty’, suffering from skewed data.

“But what I’ve heard over this last couple of days is that there is no better neuroprotection that all of you in this room who take care of patients,” he added. While the time for highlights was short in the Round Table session at ISICEM, the publication that will follow in due course will offer detailed discussion of a great number of topics that Dr Pepe himself stressed the importance of. These include preventative measures and aggressive treatments for stroke, the best ways to deliver hypothermia, vasospasm and the comparison of intravenous versus inhalation sedation. “But there are other interesting aspects of neuroprotection too,” said Dr Pepe.

“For example, let’s say that when someone is severely burned, we often see that they have altered mental status. This has been an interesting observation, and it turns out what we think now is that there is a lot of inflammatory mediators involved.”

He added: “What we’re... Continued on page 17

“We’re going to try and address specialty areas such as pediatrics, sepsis and serious other things along those lines. And some new really innovative strategies for neuroprotection, including new ways to prevent reperfusion injuries as we call them.”

Paul E Pepe (UT Southwestern Medical Center, Dallas, USA)
Postoperative cardiac comfort: Dexmedetomidine as a platform for success

The emergence and postoperative phase after cardiac surgery represents a singular challenge in achieving the combined goals of hemostasis, hemodynamic stability, rewarming, ventilatory weaning, tracheal extubation and ongoing patient comfort.

One could consider three broad groups of patients, each representing different challenges with regard to patient comfort. The first is the uncomplicated, lower risk procedure, e.g. coronary artery bypass grafting (CABG) in a relatively healthy patient. These patients can be “fast tracked” through the postoperative phase and may bypass the intensive care unit altogether. The second is the more complex procedure, which implies a sicker patient, e.g. combined valve and CABG, aortic reconstruction or heart transplant, or a lower risk procedure in a high risk patient who has substantial comorbidity. These patients will require a period of postoperative ventilation and management, and then careful weaning and post-extubation support. The third and most challenging group are those patients who undergo highly complex surgery, e.g. pulmonary endarterectomy, urgent or emergent ventricular assist device placement, or those who suffer an intra-operative critical event, requiring massive support with or without extracorporeal membrane oxygenation.

The second and third groups of post-cardiac surgery patients may require a prolonged sedation and analgesia regimen that preserves hemodynamic stability, followed by a protracted recovery phase. The primary goal is to achieve adequate analgesia - the most common cause of anxiety and agitation is inadequately treated pain. However, analgesia should not cause excessive respiratory depression that might delay tracheal extubation. The goals of sedation can be separated into [a] anxiety - desirable in all patients and situations; [b] hypnosis (induction of sleep) - desirable in some patients, especially those who are acutely ill and on high levels of ventilatory support; and [c] anterograde or retrograde amnesia for pain and discomfort, but not so much that results in confusion and disorientation.

Traditional approaches utilized intermittent dosing of longer-acting opioids and benzodiazepines, with the advent of shorter-acting drugs (fentanyl, midazolam, propofol), continuous infusion techniques have become prominent. Limitations include the need for drug discontinuation prior to extubation, excessive somnolence, emergence and post-extubation anxiety, agitation and pain, delirium, and tolerance, accumulation of active metabolites and withdrawal syndromes.

Dexmedetomidine, a selective parenteral alpha-2 agonist, has properties that make it uniquely suited to achieving patient comfort after cardiac surgery. It provides dose-dependent central anxiolysis and suppresses the adrenergic response to stress. It enhances analgesia without any respiratory depression. It provides unique “cooperative sedation”, i.e. patients arouse easily in a calm, cooperative state even when intubated, and go back to their former level when left alone. Dexmedetomidine appears to induce a more natural sleep, which may account for a lower incidence of perioperative delirium. It also has airway drying and anti-shivering effects that may be helpful.

Dexmedetomidine has no known toxicity, and its adverse effects are consistent with its sympatholytic action. These can be prevented by avoiding concomitant vagotonic drugs or stimuli in patients without pacing backup, and by appropriate patient selection.

Professor Robert Sladen will discuss in greater detail the evidence basis for the use of dexmedetomidine in the postoperative cardiac patient in his tutorial as part of the session ‘Therapeutic strategies to facilitate cardiac postoperative care in the ICU’. Wednesday 20 March 2013 at 18:15 – 19:45 Copper Hall
You are most welcome to attend the Satellite Symposium held during the ISICEM 2013, Brussels, Belgium.

**Therapeutic strategies to facilitate cardiac postoperative care in the ICU**

Wednesday 20 March 2013 at 18:15 – 19:45
Copper Hall, The Square
Light snack will be served at 18:00 at the entrance of the room

**CHAIRS**
Jean Mantz, Paris, France
Robert Sladen, New York, USA

**INTRODUCTION**
Dan Longrois, Paris, France

**POSTOPERATIVE CARDIAC FUNCTION – THE ROLE OF LEVOSIMENDAN**
Sonja Fruhwald, Graz, Austria

**POSTOPERATIVE CARDIAC COMFORT – DEXMEDETOXOMINE AS A PLATFORM FOR SUCCESS**
Robert Sladen, New York, USA

**DISCUSSION & QUESTIONS**

**Welcome!**
Putting the value of novel renal biomarkers under the microscope

The importance and relevance of new biomarkers for renal injury will be questioned from a variety of angles by a leading expert on Wednesday afternoon as part of a session dedicated to the examination of renal biomarkers.

Amongst a series of presentations on, among others, subclinical renal impairment, new cell-cycle arrest biomarkers, and the application of recent findings to clinical practice, Matthieu Legrand (Université Paris 7 Denis Diderot) will ask the question: What's wrong with these new biomarkers?

Setting out the central aspects of his presentation, Dr Legrand spoke to ISICEM News. He began by saying: "I will refer mainly to biomarkers of renal injury. There are many of them, and on the frontline of that is NGAL [neutrophil gelatinase-associated lipocalin]." He explained that recent studies have indicated that NGAL is a promising biomarker because the expression of NGAL in renal tissue increases dramatically after ischemia-perfusion injury, but not in cases of pure pre-renal failure.

Dr Legrand continued: "Another central point of my presentation will be that biomarkers of renal injury are the opposite of biomarkers of kidney function. While biomarkers of function are serum creatinine and urine output, there are many biomarkers of kidney injury, although mainly NGAL, KIM-1 [Kidney Injury Molecule-1] and L-FABP [Liver Fatty Acid Binding Protein]. For my talk, I will mainly focus on one because it's the one that is most advanced on the commercial journey, and already available in many hospitals, which is NGAL."

It's a very attractive idea to have biomarkers, what is the primary problem with them in kidney injury? Dr Legrand commented: "The main issue is that we have not yet, I think, explored the true meaning of difference between biomarkers of kidney injury and biomarkers of kidney function. Of course, we 'know' the difference, but even in knowing that, we still confuse biomarkers of kidney injury and biomarkers of kidney function. Therefore, maybe we are not looking at the right outcomes when we look at the clinical studies."

As an example, Dr Legrand pointed out that urinary NGAL levels have been linked to long-term cardiovascular mortality in older adults with no history of clinical cardiovascular disease, at a median level of 192ng/ml, which is higher than the 150ng/ml most commonly proposed for the detection of acute kidney injury, which suggests a high noise/signal ratio for renal failure diagnosis.

Noting that the concept that a single biomarker could capture the mechanisms of a disease and could accurately predict loss of function, as well as stage kidney injury in the many conditions that can promote AKI is clearly flawed, Dr Legrand made a comparison with the field of cardiology, in which the main biomarker of cardiac injury is troponin. He said: "No cardiologist will use troponin to predict the decrease of cardiac function and, if we apply the same principle to the kidney, biomarkers of kidney injury are not likely to be very powerful predictors of prognosis of kidney function."

He continued: "Another aspect is that, in certain settings and in very specific populations, there is a very good relationship between injury and function, but there is not one here in most conditions of kidney injury in adults patients. "Here, the relationship between function and injury is very, very complex. It depends on baseline kidney function, and it depends on the nature of the injury. By this I mean that sepsis is not cardiopulmonary bypass, is not toxic shock, is not gentamycin, and so on."

Furthermore, Dr Legrand stated: "When it comes to talking of a good outcome, the problem is: Which outcome should we look at? Maybe the mid-term prognosis of this biomarker may be a good way to validate it."

He added: "There are a lot of potential issues but, in my opinion, the main issue is the way we try to use NGAL. If we know it is a biomarker of kidney injury, we are trying too much, in my opinion, to correlate it with biomarkers of kidney function."

"Another issue is the specificity of NGAL in cases of systemic inflammation. Of course, NGAL increases in kidney injury, but it can also increase in many other organs and therefore we lose the specificity for the kidney, and the extent of the kidney injury may not be completely related to the amount of NGAL found in the blood or in the urine because of extra-renal secretion. This is clearly a point we have to work on."

Dr Legrand said: "The third issue is, like any other biomarkers, an analytical one. The meaning of the NGAL urine level depends on the form of the protein that we are detecting. Levels can also differ between the different assays being used, including with commercial kits. We published last month a short report in Intensive Care Medicine, which showed that, when measuring the same urine sample with three different techniques of NGAL measurements, we found quite different results, probably because we were not exactly looking at the same form of NGAL."

In response to that assessment, does Dr Legrand think, therefore, that we need to be looking for more biomarkers, or we should be looking at a different approach for assessing kidney injury? He replied: "I definitely think that we should still be looking at new biomarkers, but the main question we have to address is which biomarker for which situation."

"We have to look further into what are we trying to understand when we see an increased level of one biomarker over another. Maybe increased NGAL levels will mean one thing, and levels of another biomarker will mean something different. With a multi-biomarker approach, we will probably get a further insight into the pathophysiology and understanding of acute kidney injury in critical conditions. But we have really to go further in trying to detect acute kidney injury – in its real meaning, i.e. tissue renal damage. After that, we will gain insights into the relationship between renal damage and loss of function."

References
Improvements in the management of ventilator-associated pneumonia (VAP) have helped reduce reported hospital rates, but despite the development of new, more objective (albeit surrogate) definitions, present-day ventilation-associated infection management is fighting against increased antibiotic resistance and controversial new characterizations, delegates will hear this morning.

Giving presentations that will explore both updated management and new definitions in VAP during the session, Michael S Niederman (Winthrop-University Hospital, Mineola, USA) offered a glimpse of his main messages to ISICEM News, beginning with how the updates for VAP definition were born: “A lot of this started in the United States several years ago, when the Institute for Healthcare Improvement (IHI) started urging everyone to use ventilator bundles and told everyone that it was possible to get zero VAP, and all of a sudden hospitals that were not academic hospitals, and had never been noteworthy before, suddenly reported zero VAP,” he said.

After reports from these hospitals of going even more than a year without incidences of VAP, concerns mounted that the information was not genuine, and that, within the framework of the VAP definitions, there had been subjective manipulation to reach these conclusions. “So nobody was really sure if this was real or people were manipulating the definition,” said Dr Niederman.

“And somewhat in support of the latter is the fact that the mortality rates in the ICUs and the use of antibiotics didn’t disappear as dramatically as the incidence of pneumonia, which it should have.”

That being said, Dr Niederman was quick to underline that the new ventilator bundles are a promising tool for at least reducing the rates of VAP, perhaps by as much as 50%.

In direct response to the somewhat easily-manipulated VAP definitions that were at the forefront of these suspiciously low-rate VAP reports, the Centers for Disease Control and Prevention (CDC) in the US responded with a definition that they hoped would be more objective and less manipulable. The resultant definition, Ventilator-Associated Conditions (VAC), and its infectious variant (IVAC).

“Those new definitions are controversial, because they require objectivity but they don’t require a chest radiograph, which has always been a standard for defining pneumonia,” said Dr Niederman. “And they heavily weight changes in oxygenation during mechanical ventilation to define a ventilator-associated condition. If that change occurs for a sustained period — usually it’s two days after a period of stability that defines ventilator-associated condition — and if you’re antibiotic has started, then it defines an infectious ventilator-associated condition. And they’ve argued that this is a surrogate for ventilator-associated pneumonia — it’s not the same, but it’s a surrogate.”

Dr Niederman added that, while there have been large retrospective studies showing that the overall prognosis for patients with VAC and IVAC is similar for the prognosis of patients with ventilator-associated pneumonia, the caveat is that the frequency of VAC has VAP gone?

Has VAP gone? Silver Hall Wednesday 20 March 10:40–12:00

The latest updates for ventilator-associated pneumonia

Continued on page 13

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The many variables in how we organize care

ICU organization can have a profound effect on patient outcomes, but the sheer variability in practices and design between each institution makes it difficult to pinpoint which approaches are best, delegates will hear this afternoon in a session dedicated to organizational issues in the ICU.

“Variability tells us that we don’t really have a clear message as to what is the best way to have either an organizational structure or more of a process structure,” Greg S Martin (Emory University School of Medicine, Atlanta, USA) told ISICEM News.

“There’s a variety of pieces that go into the things that we want our patients to receive or to respond to or benefit from while they are receiving ICU services.”

He added: “We want people to have a good experience in terms of avoiding some of the adverse things that we hear about, such as neuro-muscular complications, musculoskeletal complications and cognitive complications; all those sorts of things. So there are all these things that go into what you want as a quality outcome at the end of an ICU stay, and how we define ‘quality’ obviously varies quite a bit. And one of the things that we are realizing is that of all these moving pieces, some of them relate to the way we organize and run our ICU.”

One example is the timing of admissions. Specifically, Dr Martin outlined that data points to weekends as having poorer patient outcomes overall, in part due to aspects such as staff turnover and ancillary services being absent until the start of the following Monday. But there other staffing issues as well. “We see data that says nurses who have more patients to care for or different responsibilities during their time when they are working their shift are more at risk of anxiety and stress, even some symptoms of what seems to be posttraumatic stress disorder,” said Dr Martin.

To address the variables and gray areas in the way care is structured, organized and delivered, Dr Martin commented that it was clear that more understanding was needed. To that end, a network of close to 50 sites around the US (roughly 70–75 ICUs) were rallied, all of whom were willing to participate in gathering data on their ICU, both in terms of its organization and also its patients.

“The first thing we really tried to understand was what is the structure of intensive care delivered in ICUs around the US,” said Dr Martin. “In the US, critical care is somewhat different than Europe and other places around the world, so for instance we have a lot of specialty ICUs: medical, surgical, trauma, burn, cardiac, neurologic, respiratory – they certainly exist in different places but the subspecialization within the United States has really grown dramatically in the 5, 10, 15 years or so.”

For this first area of interest, focus was really placed on how these subspecializations affect outcomes, being as there is some data that points towards adverse outcomes when patients are moved to an inappropriate specialized ICU (a medical ICU patient moved to a surgical ICU, for example).

In terms of staffing, data was collected on a wide-ranging array of aspects including whether intensivists were staffing the ICUs, and how nurses, respiratory therapists, physiotherapists and other rehabilitation specialists were staffed.

Dr Martin continued: “Part of it is how large is your ICU, how large is your hospital, is it a teaching hospital or a community hospital, is it a urban hospital or a rural hospital, is it a for-profit hospital or a non-profit hospital (which is obviously a big difference in the US), and then we sort of get into more granular patient information.”

Protocols were a large focus, not only in terms of which of them are effective and which are not, but also the mechanisms of how they are put into action. “We wanted to understand if the protocols were something that the hospital had in place to be implemented and used automatically, or were they something that a physician had to recognize the patient might benefit from…and then order it on their own,” explained Dr Martin.

“And those are very different things, because you can imagine in the first scenario, if a patient comes in and is someway identified as having a certain condition – and it could be identified simply as someone on a ventilator – everyone can see it, it’s obvious the patient is on a ventilator, and then there might be a protocol attached to that which can be implemented automatically simply because the patent is in the ICU on a ventilator.”

“Then there are things that are a lot more difficult where you might say well the patient has severe sepsis or septic shock, and that is a more physician-driven protocol where that physician has to identify the disease or the condition and then not only recognize that but then be aware that there is a protocol for managing that, and that they should implement it.”

In total, about 40–50 different types of protocol were collated from the study, and during analysis particular focus was paid to determining the benefits and pitfalls of each one, and whether they were automated or physician-driven.

During the study, the participating centers were also concurrently tasked with collecting data on the next 100 patients that came through the ICU, recording basic demographic details (age, race, gender, etc.) but also ascertaining who was responsible for their care, whether this was changing from day to day, and what conditions, diseases and supporting needs the patients had. All of this was then tied in with the protocols, examining whether, for example, an acute respiratory distress syndrome patient or sepsis patient was actually exposed to appropriately-designated protocols and so on. “We ended up having about 6500 patients enrolled in this study to try and understand this,” said Dr Martin.

For his presentation at ISICEM, Dr Martin will summarize some of the insights from the study in more detail, the first point being the differences between mortality rates in the dif-
The many variables in how we organize our ICUs

The latest updates for ventilator-associated pneumonia

Continued from page 11

Variability tells us that we don’t really have a clear message as to what is the best way to have either an organizational [ICU] structure or more a process structure.

Greg S Martin (Emory University School of Medicine, Atlanta, USA)

The same degree of impact on ventilator-associated conditions. So I think those will be the controversies that will be discussed.

In terms of management, Dr Niederman stressed that the issues are somewhat different. Management has always heavily relied on the use of antibiotics, and the challenge today is that the organisms causing VAP are becoming increasingly antibiotic resistant. There are even carbapenemase-producing enterobacteriaceae which have raised a level of international concern. “But, at the same time, there aren’t really any great new antibiotics in development,” he said.

And there are a lot of reasons for that. Part of it is that there hasn’t been a lot of innovation, but mostly there is not a lot of motivation for innovation in the pharmaceutical industry because what we have been doing is to use antibiotics judiciously, and for the shortest course possible, and so that is all responsible management.

“However, if you are an investor in a pharmaceutical company, you’d much rather invest in a drug for a chronic condition that the patient will take every day for 20 years and never re-evaluate that use. The return on investment will be huge, whereas an antibiotic may be used for a week or two weeks at most, perhaps once in your life.”

Without significant pharmaceutical investment and innovation, the mounting concerns that surround antibiotic resistant pathogens will thus have to be tackled with more current solutions. Whether this is with better understanding of pharmacokinetics, pharmacodynamics or changing the dosing and infusion methods for antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be mobilized. For instance, topical application of antibiotics, solutions need to be
Managing pregnancy in the ICU

The most up-to-date knowledge, and the gaps in our current understanding, of how to manage the pregnant patient in the ICU were explored on Tuesday morning in front of a packed audience in the Horta Room.

Kees Polderman (University of Pittsburgh, Pennsylvania, USA) explained that one of the problems is that physiological studies and drug safety tests are usually performed in healthy male volunteers, and drug safety and efficacy studies usually exclude pregnancy, while large clinical trials almost always exclude pregnant patients.

Therefore, Dr Polderman said the question then becomes: "Can we simply translate and apply our knowledge from the literature, and use our regular ICU experience with ICU treatments, when acting for clinically ill pregnant patients?"

The first problem is that you are caring for two patients, who sometimes have conflicting interests, and both of which need monitoring. The second is that the usual parameters and normal reference values that usually guide therapy have changed. In addition, the patient is often awake, very worried, and perhaps agitated. This, Dr Polderman commented, doesn’t include the worried spouse and the worried relatives.

Looking at the basic principles of ICU care in pregnancy, he said that the largest risk of injuring the fetus is during the first 8–10 weeks of pregnancy gestation. After 12 weeks, the placenta has fully formed, after which the chorionic villi ‘float’ in the maternal blood, gathering oxygen and nutrients and excreting waste products. There is no direct contact between maternal and fetal blood, but substances and drugs with a diameter ≤ 500 Dalton will freely pass across the placenta, as will certain larger molecules.

During pregnancy, women experience cardiovascular, respiratory, renal, gastrointestinal, and metabolic changes. Cardiovascular changes include increases in blood volume and plasma volume, increases in cardiac output, regional changes in circulation and blood supply, and possible obstructions in venous return with increased preload. The purpose of these changes is to increase blood supply to the placenta and increase the chance of maternal survival during and after labor. The consequences for the ICU are ‘abnormal’ values on hemodynamic measurement, systolic murmur, decrease in hematocrit, a strong influence of body position on circulatory parameters, and severe hampering of resuscitation and CPR.

These manifold changes are reflect in the impact on the respiratory, renal, and gastrointestinal system, which Dr Polderman summarized for the attentive audience. He continued on to the problems associated with drug use during pregnancy, including teratogenic effects, changes in blood/plasma volumes, serum albumin, etc. He said that drugs fall into one of three categories: safe, not sure, and unsafe. These are further delineated in the US Food and Drug Administration categories of A, B, C, D, and X.

After looking at certain drug categories in particular, Dr Polderman restated that "the most important thing is to avoid and prevent complications of our treatments". He did note that mortality rates among pregnant women on ICU are 2.3% per year in developed and 10%–25% in developing countries. The prognosis for the mother is usually very good, he said, although mortality is increased among those admitted for non-obstetric reasons, while, for the child, mortality is fair to good, at around 10%.

He ended by saying: "Better understanding of [the] basic concepts, and carefully weighing our therapeutic options, can help us improve maternal and neonatal outcome in our pregnant patients."
Update on Renal Replacement Therapy

Rome, Italy, December 8-11, 2013
(Ambasciatori Palace Hotel)
Exploring the differences in intensive care bed provisions across Europe

The heterogeneity of European intensive care provision, and the implications for outcomes and future healthcare planning, was explored by a leading expert during an in-depth session on intensive care around the globe on Tuesday afternoon.

Andrew Rhodes (St George’s Healthcare NHS Trust, London, UK) spoke to ISICEM News ahead of his presentation, explaining initially how the number of intensive care beds varies between European countries. He said: “We did a study last year looking at how many intensive care beds there are around Europe, and there big differences between some of the countries. For example, Germany has more than virtually every other country in Europe, and there quite large differences, up to five- and six-fold.”

Specially, Dr Rhodes and colleagues collected prospective data on critical care bed numbers in Europe from July 2010 to July 2011, identifying 2,068,892 acute care beds and 73,595 critical care beds. On average, there were 11.5 critical care beds per 100,000 head of population, which ranged from a mean of 29.2 beds in Germany through 15.9 beds in Belgium, 11.6 in France, and 6.6 in the UK, to a low of 4.2 in Portugal. The number of critical care beds per count was positively correlated with gross domestic product (GDP), but were not correlated with the proportion of GDP spent on healthcare.

Dr Rhodes explained: “There are limitations in some of this data, in that there isn’t a consistent definition between countries in terms of what we are describing as an intensive care bed. Some of those inconsistencies are kept for artificial purposes because it’s in some people’s interests to say they have got lots of beds or few beds, depending on what side of the argument they want. That is dictated in some ways by funding mechanisms. So if you get funded by saying you have got more intensive care beds, then clearly you are likely to say that you have got more than less.”

He continued: “One of the points to make is that, actually, not having a consistent definition across Europe hampers our ability to understand the differences, but even saying that, the differences we have found are really quite staggering. For example, there is about a five-fold difference between the UK and Germany.”

What does Dr Rhodes think the reasons are for those sorts of huge differences? He replied: “Well, the reasons are a bit more difficult and are very subjective, clearly. I suspect that Germany is a bigger, richer country, although we weren’t able to match just to finance in terms of GDP and the economic strength of the country. I suspect it’s more political reasons, such that some specialties have developed at different rates in different countries, as have people’s perceptions of what they want from healthcare. The UK has got a very socialist healthcare system, where we provide probably very good healthcare at a slightly lower level for a very wide number of patients, whereas Germany has got a different kind of mechanism for finance. So if you get funded by saying you have got more intensive care beds, and 8% were admitted to critical care after surgery, with a mean length of stay of 1.2 days. Of patients who died before discharge, 73% were not admitted to critical care at any stage.

Crude mortality rates varied from 1.2% in Iceland to 21.5% in Latvia, with rates of 3.2%, 2.5%, and 3.6% in Belgium, France, Germany, and the UK, respectively. Odds ratios relative to the UK, adjusted for age, American Society of Anesthesiologists’ score, urgency of surgery, grade of surgery, surgical specialty, and the presence of either metastatic disease or cirrhosis, for Belgium, France, Germany, Iceland, and Latvia were 1.65, 1.36, 0.85, 0.47, and 7.44, respectively.

Dr Rhodes said: “Now, you can’t directly relate that to the fact that they have got different numbers of intensive care beds, so it’s not a cause of funding, and they provide more of the high-end care. So it’s a bit difficult to understand it. You can make a whole series of assumptions but you don’t know for sure.”

He commented: “The more interesting thing is what impact it has. Clearly, if you have got five times the number of beds, there are two implications: Either the UK has got too few beds, and therefore patients aren’t able to get that level of care, and perhaps won’t be doing so well, or Germany has got too many beds, at which point they are saying that perhaps may not be needed, which is costing them a vast amount of money.”

Does this have an impact on the relative outcomes data between, say, the UK and Germany? “Well that’s where it becomes muddy,” Dr Rhodes commented. “You see, it is very difficult to determine that. We looked at some data last year for outcomes following surgery, and the outcomes in Germany did seem to be better.”

Looking at mortality after surgery among 46,539 patients undergoing inpatients noncardiac surgery in 498 hospitals across 28 European countries, the researchers found that 4% died before hospital discharge, and
and effect, but there are relationships that can be seen. "You make some interesting hypotheses and assumptions, and you can suggest, actually, there seems to be a relationship between the number of intensive care beds, the number of patients following surgery coming through them, and outcome. But it's definitely by no means so straightforward. Nevertheless, when you start asking those questions, it stimulates other areas and avenues of research to better understand the differences between countries."

In general, does Dr Rhodes feel that, in terms of overall healthcare assignment of resources, there is enough emphasis on intensive care in Europe? He replied: "Just on that data, in the UK, there is not enough beds, and it definitely feels like that practicing in the UK anyway. You could almost argue that Germany is probably gone to the other end, in the sense that they may have slightly too many beds. "It depends on how you are going to fund these things. So clearly if we were to double the number of beds, we double the amount of money required. Is the UK population willing to afford that in terms of healthcare, are we willing to prioritize healthcare being spent in that direction as opposed to primary care or other aspects of care?"

Andrew Rhodes (St George’s Healthcare NHS Trust, London, UK)

The Round Table Conference: Neuroprotection

Continued from page 7

finding out is that actually those mediators are probably transmitted systemically through the blood stream and go to other organs... we found that the brain was becoming inflamed, even though the initial injury is from a remote site."

With this in mind, it seems there are obvious mediators of inflammation that can travel and cause damage elsewhere, and one of the topics Dr Pepe himself is involved in is in the role of sex hormones to offer protection.

Indeed, women of child bearing age have been shown to have better in-hospital cardiac arrest survival outcomes than equal-aged men. "Sex hormones might be protective or even therapeutic," said Dr Pepe. "The other thing I think is very interesting to discuss now is that it’s not just a matter of treatment but when you treat," he continued. "What are the time windows? Is it too early to do it? Should you treat someone immediately, or later? Is it actually harmful to do it immediately or later with certain therapies?"

He added that we should think beyond guidelines - with goals to not just meet but surpass them. Similarly, he stressed that we must begin to be more adaptive in our trials designs, examining the mechanisms – and associated possibilities – that surround the latest insights in neuroprotection.

He continued, summing up other areas that will be seen in the report: "We’re going to try and address specialty areas such as pediatrics, sepsis and serious other things along those lines. And some new really innovative strategies for neuroprotection, including new ways to prevent reperfusion injuries as we call them." Tying back to his comments earlier, he commented: "Maybe the glass isn’t half empty. Maybe it’s always full. Because we also have to keep our minds open that there is more beyond what see in the laboratory or what we think are biases."

In his final comments, Dr Pepe said as the ‘glass fills’ in the field of neuroprotection, come the 22nd century, he is confident that the lessons we are learning – and new approaches we are urging towards – will mean we will be able to offer neuroprotection for patients we hitherto have never even been able to consider likely of saving.

References


An in-depth look at prognosis after cardiac arrest

A n informative and fascinating Round Table discussion on prognosis after cardiac arrest will take place on Wednesday morning, when a panel of leading experts from across Europe will discuss the latest issues in this important area of intensive care.

ISICEM News spoke to the chair of the Round Table, Niklas Nielsen (Helsingborg Hospital, Sweden), and panel member Mauro Oddo (CHUV-University Hospital, Lausanne Switzerland), ahead of the session to examine the impact of recent studies on the current best-practice in prognosis after cardiac arrest, and future prospects.

Dr Nielsen explained: “During the last 10 years, there has been an increase in interest in the cardiac patient population after the introduction of therapeutic hypothermia in 2002. This is also now recommended in guidelines from the European Resuscitation Council and the American Academy of Neurology,1,2 and almost every national resuscitation guideline throughout the world.”

He continued: “More and more, it was realised that the moment when you make your prognosis – when you decide on whether to continue care or withdraw life-supporting therapies – is a very decisive moment. It has a great impact on the patient in terms of what will happen, eventually, so it’s extremely important that this prognostication is made at the right moment, and using the right tools.

“It is also the case that, in 2006, when the American Academy of Neurology published guidelines for prognostication,3 they proposed an algorithm for how to look at different aspects of prognostication. They were quite strict and dogmatic in the way that you could use this algorithm and, in the last couple of years, almost every aspect of these guidelines has been challenged in the era of therapeutic hypothermia.

“None of these different sub-components of the algorithm is really applicable any more, so I think that one of the main objects of the Round Table discussion is to inform the audience that you cannot rely on the 2006 American Academy of Neurology guidelines right now.”

If that is the case, what does Dr Nielsen believe people should be looking to, and how does he see the next few years in terms of new guidelines? Dr Nielsen said: “The sub-components that are mentioned in the guidelines have been tested again and again in the era after therapeutic hypothermia was introduced, and we believe that they are valid if you combine them, if you have a multimodal approach to your prognostication. We will discuss delay prognosis, compared with what was done previously, until about four and a half or five days after cardiac arrest in the general population.

Then we will try to give a picture of which patients we really believe will have a poor prognosis, and how you can identify those using the different aspects of prognostication. These are neurophysiological modalities, clinical imaging, such as CT and MRI, different biomarkers, and then of course the mainstay is still clinical examination.

“After that, we will try to identify patients in whom the clinician should be really cautious, and realise that this is a patient with a potentially good outcome who should be subject to extended care and to prolonged observation.”

People who will be on the panel for the Round Table will be from quite different areas of Europe. Does that reflect differences in European practice or are we quite unified or consistent? Dr Nielsen commented: “I talked to the panel in the last couple of days, and we are pretty much unified. You should realise that there is a very great span on how prognostication is performed in different countries in Europe, and also on an international level. However, the group here are all quite into this subject, and I think we are pretty much agreed on how to do it. The different experts might stress different modalities more or less, but all in all, I think we are quite unified on how we look at this.”

He added: “One more thing is that there is a large, recently-completed, trial on almost 1000 cardiac arrest patients. It is a randomised, multicenter, international trial, where a lot of aspects of prognostication will be investigated in-depth. Therefore, in a couple of years, we will know much more about this question.”

Dr Nielsen ended by saying: “Another problem with the previous work on this subject is that, for many of the modalities that have been tested, the clinicians have known about the thing that is being tested during the trial or the study. Consequently, it hasn’t been blinded,

“Since neurological examination may give rapid predictions, it is important to remember that, in several studies, neurological examination may give false predictions in up to 20% or 25% of patients.”

Mauro Oddo (CHUV-University Hospital, Lausanne Switzerland)
An in-depth look at prognosis after cardiac arrest

Prognosis after cardiac arrest

Gold Hall

Wednesday 20 March
11:20–12-30

Journal,1,2 and hypothermia was then introduced. The first seminal studies were published in the New England Journal,1,2 and hypothermia was then increasingly applied. I think that, for the last five years, many centres have used hypothermia, and hypothermia and sedation is being used to keep patients cool after neurological examination.”

He continued: “This was a major change, because hypothermia changes outcomes and has increased the number of patients who survive and awake with good recovery. However, these increasing numbers mean it becomes very important to assess the prognosis early on.”

The paradox, Dr Oddo, explained is that assessing that prognosis has now become a challenge due to the hypothermia itself and because the patients are sedated. He added that this is also because, prior to the introduction of hypothermia, there was the so-called self-fulfilling prophecy mentioned above by Dr Nielsen, in which it is assumed that a comatose patient is not going to wake up and therapy is therefore withdrawn.

Dr Oddo continued: “Now, there have been several studies, including some from our group in Lausanne,3–7 that have shown that this is no longer the case. There are patients who may stay comatose for a few days, even experience epilepsy, and still wake up and have a reasonable outcome. Therefore, for these main reasons, if you look at several meetings, also at the European Resuscitation Council, and many other meetings where cardiac arrest is discussed, the issue about prognosis and the prediction of outcome is examined. What does Dr Oddo believe is a good outcome? He said: “A reasonably good outcome is the patient going back home, and being able to manage himself or herself, without help. He or she may have some loss of memory, or impairment of function, but that may come back and many of these patients can even go back to work.”

What does Dr Oddo think the other Round Table members’ perspectives are going to be and the main issues that will be discussed? He explained: “Well, I think that the main issues are those related to how we can improve prognostication and how available the tools are that we may use, because even for neurological examination we should have quantitative tools.”

a very systematic way. Right now, we only have presence or absence. But I have an abstract at ISICEM showing very exciting data on how we are using a new tool for the quantitative assessment of one important element in neurological examination, which is fundamental. A complete neurological assessment should be performed by intensivists and neurologists. Even this is, I think, not necessarily available everywhere, or rather it is available but it’s not necessarily performed in the capillary reflex.”

Another important point, Dr Oddo said, is: “Since neurological examination may give rapid predictions, it is important to remember that, in several studies, neurological examination may give false predictions in up to 20% or 25% of patients. Therefore, it’s not necessarily reliable if you predict outcome only based on neurological examination, as you may be wrong in up to 25% of cases, which of course is not acceptable.

“The issue is therefore that we add electrophysiology, and electro-physiology means basically EEG, with assessment of reactivity and evoked potentials. These tools are not necessarily available everywhere. There also needs to be a very good relationship between intensivists and neurologists, and we need to be aware that this is very important.”

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