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The collaborative communication model for patient handover at the interface between high-acuity and low-acuity care

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Introduction Patient handovers are risky, time consuming and expensive. Patients experience multiple transitions from within and outside the ICU microsystem, as they navigate the increasingly complex and dangerous healthcare system. Safety and resilience depends on explicit communication and coordination between and among healthcare professionals [1—5]. ***Methods*** We analyzed the communications between high-acuity and low-acuity units, their content and social context, and we explored whether common conceptual ground reduced potential threats to patient safety posed by current handover practices. Common ground is essential to enable reliable interpretation of the complete handover content items existed only among selected members of the healthcare team. ***Results*** High-acuity and low-acuity units agreed about the presence of alert signs in the discharge form in 40% of the cases. The focus groups identied prehandover practices, particularly for anticipatory guidance that relied extensively on verbal phone interactions that commonly did not involve all members of the healthcare team, particularly nursing. Accessibility of information in the medical records reported by the recipient units was signicantly lower than reported by sender units. Common ground to enable interpretation of the complete handover content items existed only among selected members of the healthcare team. ***Discussion*** We describe a content and process-driven improvement strategy for redesigning and standardizing communication and coordination during patient transitions (handovers) that focuses on creating common. The limited common ground reduced the likelihood of correct interpretation and sharing of important patient signs and cues, which may contribute to adverse events. Collaborative design and use of a shared, standardized set of handover content items may assist in creating common ground. This will enable ICU teams to communicate more effectively to help increase the reliability and safety of cross-unit handovers. *European Commission funded European Handover Research Collaborative project

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Role of human factors and reliability science in preventing adverse events in ICU

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Introduction Human factors (also called ergonomics) is the study of human interactions with tools, devices, and systems with the goal of enhancing safety, efficiency, and user satisfaction. Human factors research on team decision-making in complex task environments is of relevance to trauma team performance. One must carefully consider the impact of the many "performance shaping factors" that can degrade human capabilities. ***Methods*** Overview of the relevant literature [1—5]. ***Results and main message*** Factors that influence the ICU team's effectiveness include the performance of individual team members, the equipment they use, the ICU physical environment (e.g., established care process and procedures), and the underlying organizational and cultural factors. For example, distracters such as information overload, noise, spectators, and physical obstacles can be a danger to both the patient and health care professionals. Accurate identification

of the root causes of adverse events in the ICU microsystem must precede identification and implementation of appropriate interventions. Moreover, solutions for risk associated with human behavior or active failures such as skill-based failures are different depending on the embedded hazards or latent failures in organizational process and structure. The use of sophisticated risk assessment techniques including process mapping, FMEA, and PRA can be used to identify at which point interventions are most appropriate. Once specific target risks are identified, intervention strategies can be identified or designed using a risk-informed approach to design of intervention strategies. In order for organizations to become learning organizations, they must make sense of their engineered environment and learn from safety events. The ultimate goal of sense-making is to build the understanding that can inform and direct actions to eliminate risk and hazards that are a threat to patient safety. For example, in designing features that facilitate reliable use of devices in the ICU such as infusion pumps, ventilators, etc, important features of manually operated safety devices include the overlapping attributes of intuitiveness, obviousness of activation, consistency with means of use, consistency with the environment of use, consistency with performance of primary task, and ease of use. The risks that dominate in present day ICU systems may have a different etiology than the risks that dominated one or two decades ago. This has two important ramifications. The first is that it is more difficult to understand and prevent these risks. It is harder to understand that risks may exist, at least until an accident has happened. It is harder to understand the "mechanisms", because risks can arise from non-linear interactions among normal performance variability as well as from consequences of failures and malfunctions. And because of that it is also more difficult to think of ways to reduce or eliminate the risks. In intractable systems like ICUs, risks are often associated with specific components or subsystems, or with specific actions or operations. Risk reduction can therefore be achieved by either eliminating the risk, by preventing certain actions, or by protecting against the outcomes. Eliminating or preventing performance variability may well reduce the risk, but it will also impede normal functioning. The second ramification is that many of the established risk assessment and accident investigation methods are inadequate for tightly coupled, intractable systems. Perrow who proposed that accidents could be seen as part of normal work because risk assessment and accident investigation methods naturally focus on that which is abnormal or dysfunctional highlighted this dilemma. The lesson to be learnt from that is that we must continue to evaluate critically the methods that are at our disposal to make ICUs more resilient. The development of new socio-technical systems means that new risks will emerge, and therefore that existing methods sooner or later will need to be complemented with more powerful approaches that must be lead and valued by clinicians. ***Discussion*** Sensemaking and resilience serve as conceptual frameworks to bring together well established approaches to assessment of ICU risk and hazards: 1) at the single event level using process maps and root cause analysis (RCA), 2) at the processes level using failure modes effects analysis (FMEA) and 3) at the system level using probabilistic risk assessment (PRA). The results of these separate or combined approaches are most effective when end users in conversation-based meetings add their expertise and knowledge to the data produced by the RCA, FMEA and/or PRA in order to make sense of the risks and hazards. Without ownership engendered by such conversations, the possibility of effective action to eliminate or minimize them is greatly reduced.

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Interferon in lung injury

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Learning objectives This will describe the role of adenosine in regulating capillary leak and as an anti--inflammatory agent. It will describe the controls on adenosine locally including the role of CD73 and the potential for benefit from interferon. It will discuss why the therapeutic manipulation of this has scientific rationale for lung injury. It will describe the phase 1—2 trial looking at safety and efficacy of interferon beta 1a in ARDS. ***Introduction and background*** ATP in the extracellular fluid is a pro-inflammatory agent. It is converted to ADP, then AMP and finally adenosine which is a powerful anti-inflammatory agent. Two key enzymes involved in this are CD39 which converts ADP to AMP and CD73 which does the final conversion of AMP to adenosine. There are several adenosine receptors especially the AT2 receptors and binding

adenosine to these results in reduction of inflammatory cell recruitment and reduced capillary leak. There is increasing evidence that CD73 is important in this; for example, leak into the alveolar space is dramatically reduced when CD73 is restored in animal models of acute lung injury. Interferon beta is capable of restoring CD73 expression. We looked to see if CD73 is expressed in human lungs and if interferon beta could be given safely to patients with acute lung inury. ***Methods*** Histological study of human lung tissue stained for CD73 in the presence and absence of interferon beta and co-stained with vascular and lymphatic markers to determine tissue distribution. ***Results and main message*** Interferon beta clearly CD73 expression in the human lung. Interferon beta was given to patients with ARDS in an open label safety study at four increasing doses. Fever and rigors limited use at the top dose but 22 patients were successfully treated at the second highest dose with very few side effects (one local infusion reaction). This shows that interferon can be safely administered to patients with ARDS. CD73 was shown to rise albeit slowly over a week in these patients. Excitingly the mortality for the total patient group treated with interferon beta was <10% which is very low given the APACHE score for these patients. ***Take-home message*** There is a biological rationale to promote CD73 expression in lung injury. Interferon beta can be safely administed intravenously to patients with lung injury and preliminary results suggest that further studies are warranted to investigate exciting early trends in outcome.

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Neurologic complications of critical illness

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The central and peripheral nervous systems are frequently affected as a consequence of critical illnesses in other bodily systems. Sepsis has received the most attention as a cause of neurologic problems, which include septic encephalopathy, seizures, true delirium, ischemic stroke, intracerebral hemorrhage, critical illness neuropathy, and critical illness myopathy. Other illness leading to ICU admission result in these complications less frequently. A number of ICU medications and procedures also have neurologic sequelae. The long-term cognitive and motor consequences of critical illness have recently received renewed attention. This session will briefly summarize current knowledge about these problems.

Workshop on subarachnoid hemorrhage

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Subarachnoid hemorrhage is the quintessential condition defining neurocritical care. This workshop will cover: (1) diagnosis and differential diagnosis, (2) SAH grading scales, (3) management prior to aneurysm obliteration, (4) techniques of aneurysm obliteration, (5) early complications: neurogenic stunned myocardium and Tako-Tsubo cardiomyopathy, neurogenic pulmonary edema, cerebral salt wasting and other forms of free water retention, (6) vasospasm, (7) *hydrocephalus,* (8) seizures, (9) medical complications, (10) prognosis.

ICU training in Brazil

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Learning objectives Brazil is one of the largest countries in the world and has a prominent role in Latin America, learning how intensive care training has evolved may help to understand how it is practiced and

give future directions not only on physicians' education, but also shape what will be the future of the specialty nationally. ***Introduction and Background*** Brazil is the world's fifth largest country, both by geographical area and by population. The Brazilian economy is the world's eighth largest economy by nominal gross domestic product and the ninth largest by purchasing power parity. The population of Brazil is approximately 190 million and 83.75% of the population defined as urban. Despite the political and economic stability achieved in recent years, Brazil is rated as 73th country in the Human Development Index, by the United Nations, 75th in the Corruption Perception Index, by the Transparency International, and is one of the worst countries listed in income inequality metrics, by Gini coefficients. In 1980 the Associação de Medicina Intensiva Brasileira (AMIB) was founded, but it was recognized as a distinct specialty only in 2002. Since then, AMIB was the sole responsible to define the standard curriculum for intensivists in Brazil. ***Methods*** Personal communication with experts, Associação de Medicina Intensiva Brasileira's website and Commissions (www.amib.org.br). ***Results and main message*** Intensive Care is a very young specialty in Brazil, but AMIB has been one of the most active medical associations, with nearly 6,500 active members. The pathway to become a specialist has changed over the years, and modifications in the curriculum also followed recent national regulations on duty--hours. There are three separate ways to become an intensivist in Brazil: a 2-year fellowship or specialization after an internal medicine, general surgery or anesthesiology residency (the specialization may allow other pre-requisites) or a successful proficiency test. A 4-year specialization in Intensive Care has been proposed as the unique pathway. Estimates indicate that today, 50% of the positions available in intensive care programs are not filled. Despite this, AMIB always have candidates for the Diploma in Intensive Care, possibly meaning that this is a desired title. In 2006, the AMIB co-signed the CoBaTrICE program, focusing its formation, and diploma, in a competency-based format. For 2016, candidates will no longer be able to sit for the test unless they've come from a residency program or specialization, or equivalent. ***Take-home message*** Intensive care is not the first option for many young physicians in Brazil. Future changes in the pre-requisites to sit for the AMIB's diploma may change this reality, and maybe shape the way Intensive Care is practiced in Brazil.

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Strategies for fluid management: central role for stroke volume monitoring

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Intravenous fluid administration is one of the commonest therapeutic maneuvers in ICU and OR. Although it may sound like routine due to its daily character, fluids are associated with significant patient morbidity when insufficient or in excess. Not enough fluids may result in hypoperfusion of some territories, and subsequently in organ dysfunction or even organ failure. Too much fluid will also impair tissue perfusion because it will result in venous congestion and edema. In clinical practice, fluid administration is still mostly empirical or based on parameters such as mean arterial pressure or central venous pressure that are neither sensitive or specific to reflect the effects of fluids. Dynamic predictors of fluid responsiveness based on heart-lung interaction in ventilated patients (ΔPP, or ΔSV) suffer a number of limitations likely to be encountered in ICU patients (lack of: sinus rhythm, perfect synchrony with ventilator, tidal volume ≥7 ml/kg, etc.). Most importantly, these dynamic indices are misleading in some ICU patients who are contraindicated to fluids, i.e.: congestive right or left heart failure. Thus, the most meaningful and reliable way to guide fluid administration in ICU or in „high risk" surgical patients is titration of small volume challenges guided by stroke volume measurement. This technique has demonstrated an outcome benefit in high-risk surgical patients, by reducing postoperative morbidity, hospital length of stay, and return to oral diet in digestive surgery patients. Although no outcome benefit has been associated with stroke volume--guided fluid titration in ICU patients, it represents the safest way to avoid unnecessary infusion. Stroke volume monitoring is also the most sensitive way to detect changes in cardiovascular function.

What's new in neurocritical care

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Introduction Neurocritical care is a logical extension from multidisciplinary critical care into a specialty area requiring unique experience and expertise. Disease and injury affecting the brain transcends customary somatic hemodynamics, metabolism and cardiorespiratory function. ***Objectives*** To describe some of the new

neurocritical care issues on the horizon. ***Methods*** Review of the relevant PubMed literature ***Discussion*** New neurosurgical procedures do exist to identify and separate nerves intraoperatively, other technologies include nanomedicine technology and deep hypothermic preservation of brain tissue.

Developments in time-critical diagnostics of infection in sepsis

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Overview Sepsis diagnosis requires objective evidence for infection, which should always include an attempt at microbiological identification of pathogens from blood, and other relevant samples if available, by culture techniques. Blood culture, however, takes several days before a positive result is available and at least 5 days to determine that a specimen is negative. This temporal separation between initial clinical suspicion and confirmation of infection routinely results in the early and sustained delivery of potent broad-spectrum antimicrobials aimed at the most likely pathogens as a „safety first" strategy because delay in therapy is associated with increased mortality. The inevitable consequence is unnecessary broad-spectrum antibiotic prescription, which is associated with the development of antimicrobial resistance (eg, MRSA), *Clostridium difficile* infection as well as a range of avoidable adverse effects, and acquisition costs, of antimicrobial drug use. There is therefore an urgent need to develop and assess diagnostic techniques that could provide accurate information within hours of clinical signs appearing and so allow more informed use of antibiotic therapy at an early stage.Recent international sepsis care pathway guidelines allude to a number of rapid „non-culture-based" technologies based on PCR, miccroarray and mass spectroscopy. These core technologies may provide the capacity to improve care pathways, but there is limited clinical data to support their routine use at present. In addition, the WHO are engaging in an urgent global initiative for the growing problem of antimicrobial resistance: an important strand of this initiative is to promote the development of valid, cost effective diagnostic technologies to assist in rationalising antimicrobial drugs globally. In response to these recent international developments, I have structured my talk to help deliver the following intended learning. ***Intended learning objectives*** (1) Describe the unmet need for time-critical diagnostics of infection in the setting of sepsis. (2) Describe the key diagnostic modalities currently available for adoption in the field of rapid pathogen detection in sepsis. (3) Review the best evidence for clinical diagnostic accuracy of these modalities. (4) Outline the key challenges for future health technology assessment and implementation.

Intra-abdominal infection

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Introduction and background Abdominal infections are the second most frequent infection encountered in critically ill patients. Compared to non-abdominal infections in critically ill patients, abdominal infections present with septic shock and acute kidney injury more often, and carry a higher mortality rate. Infections originating from the colon or small bowel are more often associated with septic shock and multiple organ dysfunction compared to biliary and upper GI source of abdominal infections. Contrary to other infections, such as pneumonia and blood stream infections most of abdominal infections are acquired before patients are admitted to the ICU. In case the diagnosis was not made before admission, doing so is typically challenging and mostly relies on imaging techniques (ultrasound but most often contrast enhanced CT scan – with fine needle aspiration in selected cases) as clinical examination is often equivocal. ***Methods*** Personal interpretation of contemporary literature interlinked with personal experience. ***Results and main message*** Antibiotic therapy and source control are the cornerstones of the management of patients with abdominal infections, although the latter has a bigger impact on mortality. Microorganisms recovered from patients with abdominal infections typically are a mix of aerobic and anaerobic Gram-negative and Gram-positive bacteria, which should all be covered by the empirical antibiotic regimen selected. Empirical regimens include anti-pseudomonal beta-lactam antibiotics (piperacillin/tazobactam), carbapenems or combinations of broad-spectrum cephalosporins or quinolones combined with metronidazole. As in other infections, de-escalation based on intra-operative cultures should be considered. Duration of therapy is 5—7 days for infections with adequate source control is sufficient, longer therapies may be necessary when source control is difficult to obtain, e.g. in infected pancreatic necrosis. Unlike community-acquired disease, enterococci are considered significant pathogens and are preferably covered by the empiric antibiotic regimen. Similarly, fungi are a relatively frequent finding in critically ill, and have been associated with mortality in several studies. Selected patients may benefit from antifungal prophylaxis; when yeasts are isolated from intraoperative cultures antifungal therapy is indicated in critically ill patients. Pharmacokinetics of antibiotics may also considerably changed in the critically ill – with underdosing. Source control is essential, with timing probably equally important as for antibiotic therapy. Source control should be pursued but the method that causes the least collateral

damage to reach the goal at that moment should be preferred and open surgery may often not be the perfect solution. Percutaneous rather then surgical abscess drainage is often preferable; any intervention may cause bleeding and additional organ damage. Failed source control is a common problem in critically ill patients, but diagnosis more difficult than treatment with clinical examination unreliable. A clinical picture of persistent organ dysfunction with elevated inflammatory markers in a postoperative patient are often suggestive of failed source control. Novel biomarkers such as procalcitonin may be useful in this setting. ***Take home message*** Intra-abdominal infection remains a challenge in the critically ill. While antibiotic therapy and source control remain the cornerstone, selecting the appropriate source control procedure – which may no longer be surgery – at the right moment is equally important. Insights in diagnosis failed source control on the other hand have given new opportunities to combat this significant problem.

Workshop on acid base: the Stewart approach

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Learning objectives The Stewart approach to acid-base balance is fascinating and is increasingly being used throughout the medical community and especially in intensive care units. Invented by the late Peter Stewart around 1980, the approach completely demystifies any acid base disturbance. This workshop will explain the Stewart method. ***Introduction and background*** One of the key concepts of the Stewart approach is that bicarbonate, or HCO_3^-, does not play any role in acid-base balance. This is usually very intimidating and counterintuitive to most clinicians as the commonly used Henderson Hasselbalch dictates otherwise (1). ***Main message*** Interestingly, Stewart does not deny the value of the Henderson Hasselbalch equation. In fact, this equation is actually one of the six equations that Stewart proposes to describe acid-base equilibrium. This implies that both approaches are mathematically compatible and that the Stewart approach may provide the bigger picture. According to the Stewart approach there are only three independent variables that determine the concentration of H^+ and thus pH in any fluid, including plasma. These variables are the partial pressure of carbon dioxide (PCO_2), the total amount of not completely dissociated weak acids (Atot, mainly albumin) and the so called Strong Ion Difference (SID). The strong ion difference is the sum of all positively charged fully dissociated ions (mainly Na+) minus the sum of all negatively charged fully dissociated ions (mainly Cl-). If PCO_2 goes down, the patient will become more alkalotic. If Atot goes down, the patient will become more alkalotic. If SID goes down the patient will become more acidotic. Thus, while HCO_3^- may follow a change in one of these independent variables it can never cause a change in pH by itself. One of the most fascinating aspects of the Stewart approach is that it becomes very easy to see how fluid therapy may alter acid base status. Normal concentrations of plasma sodium and chloride are about 140 mEq/L and 100 mEq/L. This implies a normal strong ion difference of 40 mEq/L. If we now infuse normal saline, which contains 154 mEq/L of Na^+ and Cl^- with an SID of 0 mEq/L, it becomes obvious that plasma SID will go down, which causes acidosis. *Discussion* At first glance, the Stewart approach may appear difficult, especially because it involves a number of equations. However, in our workshop we will show you that the Stewart approach is actually very easy to use and understand. We will focus on a number of difficult cases and solve these interactively. We will give you the tools to apply the Stewart approach at the bedside. After the workshop you will be able to fully understand, quantify and diagnose any acid base disturbance you may encounter in daily clinical practice.

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Ultrasound – FAST, e-FAST and general ultrasound in the Intensive Care Unit

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Introduction After many years of just being a fancy gimmick for a few enthusiasts, echography is now fast moving into the mainstream teaching about almost any area of medicine, vastly extending the range of diagnostic capabilities of the dedicated bedside clinician. It is easily integrated into the clinical examination and decision making process. For some applications like the short trauma echography known as FAST (Focussed Assessment Sonography in Trauma) or e-FAST (extended FAST) the learning curve is steep, for others such as haemodynamic evaluation a larger experience base may be required. ***Objectives*** This talk is to cover the basics of ultrasound applications in the initial trauma assessment and the daily chores of an ICU physician. It is to encourage the newcomers to choose some easily learnt techniques first, while cautioning about the complexities in other applications, as in the evaluation of vena-cava-inferior-dynamics in

different haemodynamic and respiratory settings. ***Methods*** The presenter draws mainly from his collection of ultrasound images and clinical experience. While not being a researcher, he can honestly claim to have been one of the first physicians to use echography in daily ICU work, now being able to look back on almost 20 years of experience with this. ***Results*** From the point of view of an emergency room or intensive care physician, echography is an integral part of the patient assessment from the first physical examination to advanced treatment in the ICU, being an extension of his or her physical senses much like the stethoscope, and, ideally, just as naturally being carried around. Point-of-care ultrasound makes a substantial difference in daily patient care.

Cervical Pharyngostomy

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The cervical pharyngostomy has advantages for patients requiring long term gastric access for drainage or feeding. The NGT is associated with a complications [3], avoided by a cervical pharyngostomy. Many ICUs would replace a NGT with a percutaneous endoscopic gastrostomy (PEG). However, insertion of a PEG requires an endoscope and endoscopist, which may represent significant logistical challenges, resulting in delays, while the PEG kit adds significant expense. PEG is also associated with a small but significant risk of morbidity and mortality [5]. Cervical pharyngostomies have been performed in the Neurosurgical ICU at the Steve Biko Academic Hospital in Pretoria, South Africa since 1990. A comparison with NGTs was published in 1992 [1]. The results from 79 patients were presented in a retrospective audit from 2000-7 at the South African Critical Care Congress in 2008. There were only three minor complications: superficial bleeding, infection and minor difficulty with re-intubation after tracheostomy decannulation. The procedure was adopted in Durban in 2008. More than 30 cases have been done since in a number of hospitals. A typical procedure is illustrated below.

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Think globally, act locally: the microcirculation in sepsis

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Learning objectives The microcirculation is a critical component of the cardiovascular system that regulates substrate delivery to the tissues. This talk will first review microcirculatory physiology and the evidence for its perturbation in sepsis. We will then consider methods of evaluating microcirculatory

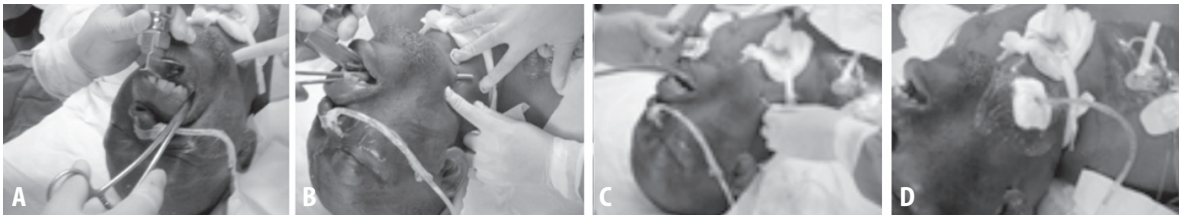

Fig. 1. Panel A: After percutaneous tracheostomy a Robert's forceps is placed in the vallecula, superior and lateral to the cricopharyngeus (upper oesophageal sphincter). Assistant palpates the tip of the forceps, ensuring the tip is medial to the carotid artery. Panel B: The assistant dissects onto the tip of the Robert's forceps, which is pushed through the skin. Panel C: The Robert's forceps is used to grip a new nasogastric tube and pull it into the pharynx. After this the tube can be advanced into the oesophagus and stomach using a laryngoscope and Magill's forceps. Panel D: The tube is help by a stay suture and the area is dressed. The tract epithelialises within a week and the tube can be exchanged for a fine bore feeding tube. Cervical pharyngostomy is a safe, cheap and simple procedure that adds no more than five minutes to the end of a percutaneous tracheostomy procedure [2]. The procedure is easy to perform without an endoscope or endosopist and should be within the scope of practice of an intensivist [4].

function, primarily using imaging technologies. Finally we will discuss a line of research aimed at testing the hypothesis that optimization of microcirculatory flow in sepsis can improve multiple organ failure. ***Introduction and background*** The ultimate goals of hemodynamic therapy in sepsis are to restore effective tissue perfusion and to maintain cellular metabolism. Patients should be resuscitated to clinical endpoints of perfusion such as capillary refill, urine output, and mental status, and also to macrocirculatory parameters of global perfusion, including heart rate, blood pressure, cardiac output, and mixed or central venous oxygen saturation. In sepsis, however, tissue hypoperfusion may result not only from decreased perfusion pressure attributable to hypotension but also from abnormal distribution of blood flow. The microcirculation is a critical regulator of distribution of flow to the tissues. Microcirculatory perturbation is a central abnormality in septic shock and represents a logical and promising therapeutic target. ***Methods*** Review of the published literature by Pubmed search, supplemented by our previous studies and preliminary data from an ongoing clinical trial. ***Results and main message*** The microcirculation is a key determinant of cellular and tissue perfusion, and the degree of microcirculatory dysfunction, particular regional heterogeneity of flow, correlates with organ dysfunction in sepsis. We will need to develop a consensus on how best to measure microcirculatory function, and what the best goals and endpoints are for microcirculatory resuscitation. We are currently testing the hypothesis that resuscitation of the microcirculation in sepsis as a component of early therapy will improve organ function. ***Take-home message*** Microcirculatory abnormalities are central to the pathophysiology of sepsis. It remains to be demonstrated, however, that resuscitation to microcirculatory endpoints will improve clinical outcomes.

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CRRT Workshop : All you Need to Know

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Learning objectives The learning objectives are multiple: 1) How to start a new CRRT programme into your ICU. 2) How to Implement Citrate without major risks into your ICU. 3) What are the Items to be looked at: Vascular access, Access location, Blood flow, Pre and post-dilution, Filtration Fraction,Timing, Dosing, Antiocoagulation, Types of Solutions and Formulations, Membranes. All these objectives will be looked at using the most recent published data [1—8]. ***Introduction and background*** Practical aspects during CRRT are of major importance. We shall review the vascular Access and location, blood flow, pre and post-dilution, filtration fraction, timing of CRRT, dosing of CRRT, anticoagulation: citrate versus heparin, which formulation of citrate to be used, how to detect citrate accumulation and intoxication, types of solutions and different types of membranes. ***Results and main message*** 1) Regarding vascular access, the right internal jugular (RIJ) approach remains the best approach before the femoral 'ones. This has been acknowledged by the KDIGO guidelines. The catheter should be 14 French and 20—25 cm for the RIJ with 1 to 2 cm in the right atrium. Regarding femoral approaches, we should go for at least 25 up 35 cm in length. 2) Blood flow will vary a lot with the type of anticoagulation used. Indeed, when using citrate, we can go for higher filtration fraction (FF) as compared with unfractionated heparin (UNH). For citrate, the blood flow will range from 150 to 250 ml/min. For UNH, the range will go from 250 up to 350 ml/min.[3]) Filtration Fraction will be running between 18—22% for UNH and between 25—30% for citrate. This has to do with the fact that citrate is better than UNH in impeding clothing and clogging. 4) Timing remains a very difficult issue as indeed many factors are affecting

this issue. We should evolve towards a composite index for timing including: door to CRRT time, SOFA score, RIFLE score, inotropic index, type of AKI (septic or non-septic). We need to agree on an acceptable definition for everyone. 5) Regarding dosing and in view of all the recent negative PRT's, the recommended delivered dose for every patient with ICU-AKI is 25 ml/kg/h. Obviously, you need to prescribe an higher dose in order to deliver 25 and probably between 30—35 ml. This delivered dose of 25 ml is also supported by the KDIGO guidelines. 6) Anticoagulation remains an hot topic and once more time, the KDIGO guideline did put in first position, citrate before UNH. On top of this, diluted citrate (0.5%) seems to be as efficient as higher dosages with less side effects. 7) Regarding solutions to be used, many solutions dedicated for citrate are now readily available on the market with reduced concentrations of bicarbonate in order to obviate the risk of metabolic alkalosis. 8) Finally, hyperadsorptive membranes (HAM) are easily available nowadays at relatively low price on the market but do carry the risk of adsorbing more antibiotics. Something that was not anticipated just a few years ago. On the other hand, those HAM membranes are promising in terms of mediator adsorption but we are lacking good data on this topic right now. ***Take home message*** Practical Guidelines for CRRT as released by KDIGO are essentials in order to minimizing the burden of early clothing and clogging of the filter. Vascular access and citrate anticoagulation do play nowadays a pivotal role into the scene. Correction implementation and continuous educational process of CRRT is a key issue for the success of this technique is every unit.

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How to set up citrate in 2013 for CRRT in your ICU

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Learning objectives This will be a more practically orientated talk aiming at showing how to set up a diluted citrate protocol into your ICU. The idea behind is to to get it run with limited number of bags (2 bags) with diluted citrate which should reduce drastically the incidence of side effect. The diluted citrate method in CVVH that we put together will be shown with a practical scheme and with the sliding scale that we are currently using in the department. The diluted citrate VUB protocol will be also compared with other types of citrate formulations been used worldwide. ***Background*** The recent KDIGO guidelines on the management of AKI have put in first position citrate anticoagulation before heparin as the first choice during CRRT. Indeed, there is a growing body of evidences showing that citrate anticoagulation do have several advantages as compared to UFH including filter lifespan, reduction of bleeding and need of transfusion and perhaps in surgical patients a reduced risk of mortality. On top of this, the wide availability of new dedicated formulations of citrate and the emergence of new diluted formulations have render a previous hazardous technique in a relatively easy procedure providing that a complete educational module have been fully implemented amongst the nursing staff but also for every attending physician. ***Methods*** Presented data are all coming from published studies in peer reviewed international journals. ***Bullet points*** (1) Diluted citrate in CVVH can be applied withy the VUB protocol for more than 95% of the ICU patients (Fig. 1). (2) Diluted citrate can also be applied in cirrhotic patients up to child B providing that are tailoring the citrate dose to the ionized calcium in the body. It is recommended with the VUB protocol to start with 50% of the citrate dose in severe liver patients. Monitoring of citrate accumulation with diluted citrate is mostly achieved by four points which are: (A) Ionized calcium in the body, (B) Rising in total calcium in the body, (C) Rapid escalation of the calcium needs of the patients and (D) increase in calcium gap. (3) Close monitoring (initially every four hours) of the ionized calcium in the body and the machine plus blood gazes and potassium plus magnesium will allow perfect titration of the citrate needs of the patient and as well will enable the clinician to detect timely a potential citrate accumulation enabling timely adaptation in order to avoid any citrate intoxication. (4) A sliding scale realized at the VUB enable the clinician and the nursing staff to adapt easily especially at night and week-end the protocol whenever needing to correct acidosis, alkalosis, dose or citrate needs. ***Conclusions and take-home message*** Diluted citrate new formulation allow nowadays the clinician to implement.

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Dose of continuous renal replacement therapies – implications for clinical practice

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Introduction and background Clinicians instinctively think of a „dose" of any therapy or intervention. Thus antibiotics, inotropes and vaso-active drugs, sedatives, ventilation etc have their „dose" as does renal replacement therapy (RRT). RRT dose has been discussed and debated for decades and is still actively debated. ***Methods*** Review of the relevant literature. ***Results and main message*** Traditionally, for end stage kidney disease (ESKD), fractional elimination of a marker solute over time has been accepted as a measure of dose of intermittent dialysis (IHD). This is the familiar Kt/V, a dimensionless number, where *K* is the instantaneous clearance of a marker (urea in this case), *t* is the time of a dialysis session and *V* is the „pool"

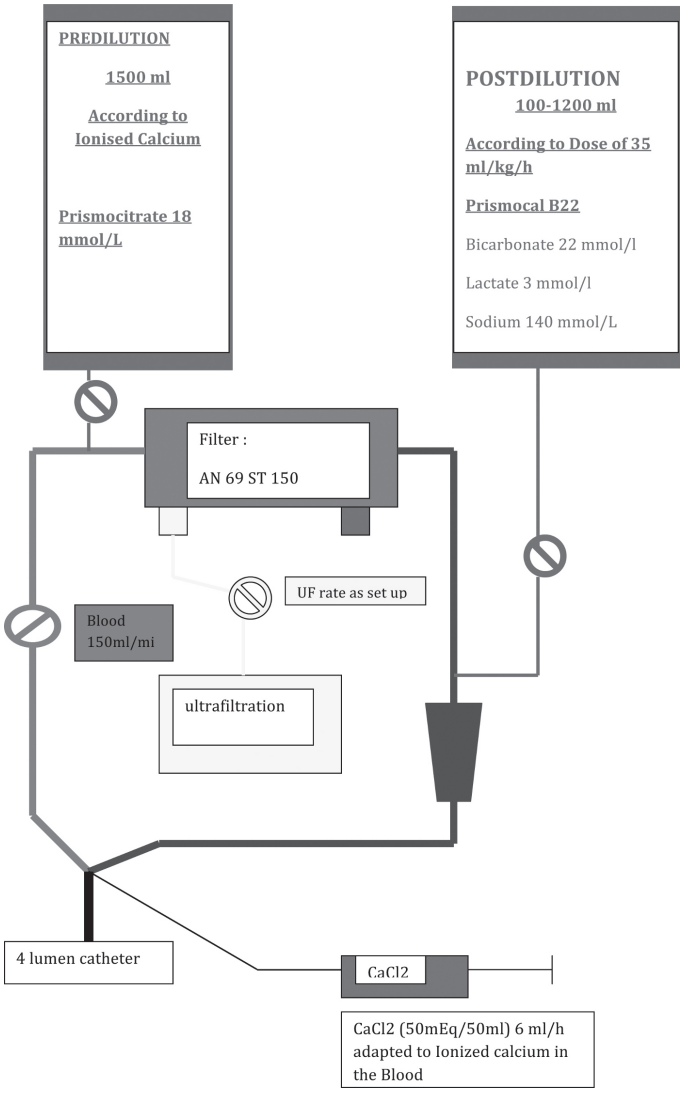

Fig. 1. Anticoagulation regimen running with citrate in predilution as established in our unit. (after Honore PM et al. unpublished data).

of the marker solute (volume of distribution of urea) thus making Kt/V applicable to individuals of various size. Urea is accepted as a traditional marker solute as it is a small molecule (molecular weight 60 Da), is easily diffusible, passes across body compartments and membranes with ease, accumulates in kidney failure, its accumulation in renal failure necessitates dialysis and has a consistent volume of distribution equal to total body water (60% of body weight). However, urea is not an ideal marker as it is not the only toxic molecule that accumulates in chronic renal failure and its elimination does not necessarily reflect elimination of other uraemic toxins. Although there are some problems with the Kt/V concept, it is, nevertheless accepted as a „measure" of dialysis dose in ESKD. For continuous forms of renal replacement therapy (CRRT), the volume of effluent (ultrafiltrate; Qf) produced is suggested as representative of the dose of RTT as it represents the clearance of small molecules (e.g. urea, creatinine) as their sieving coefficient (SC, filterability) is around 1 (i.e. they are almost completely filtered out). Thus for continuous veno-venous haemofiltration (CCVH) and continuous veno-venous haemodiafiltration (CVVHDF) it is customary to quantify the dose as Qf related to the size of the patient (ml/kg/hour). CRRT started with description of continuous arterio-venous haemofiltration by Kramer in 1973 [4]. Last three decades of 20th century engaged the clinicians' attention in descriptions of and perfecting techniques of various forms of CRRT; CVVH and CVVHDF being the only modalities practiced today with regular frequency in the critically ill with acute kidney injury, AKI, with continuous dialysis gaining ground slowly. However, the first decade of the present century has been devoted to „defining" the dose of CRRT. Daily dialysis has been shown to be beneficial in ESKD in that it gives better fluid control as well as less „swing" in biochemistry and therefore in peak uraemic toxin levels. A better survival with daily (or a higher intensity) dialysis in ESKD as shown in some studies [7], has not been universally reproduced. Similarly, an early randomised controlled trial (RCT) [5] showed that a higher CRRT dose of 35 ml/kg/hour ultrafiltrate was associated with better survival than a lower dose of 20 ml/kg/hour. This study has been criticised on various counts (a single centre study with only a small number of sepsis patients) but gave an impetuous for conduct of larger RCTs to determine the „ideal" dose of CRRT. Various other studies have been published in the past with mixed results [1, 6, 9]. Two of the largest and latest studies are worthy of closer and more critical examination. Veterans Administration/Acute Kidney Injury Network study [8] was a multi-centre study (27 US sites) which recruited 1,124 patients. Patients were randomised to receive either high RRT dose (intensive dose group) or a „conventional" RRT dose (less-intensive dose group). Once randomised, cardiovascular component of the Sepsis-related Organ Failure Score (cSOFA score) was used to determine the actual RRT mode that the patients received. Less severely ill patients (cSOFA score=0, 1 or 2) received IHD whereas more severely ill (cSOFA score=3 or 4) received CRRT or sustained low efficiency dialysis (SLED). CRRT provided was predilution CVVHDF with equal dialysate and ultrafiltrate volumes. Intensive RRT comprised of IHD or SLED six times a week (with a delivered urea Kt/V of at least 1.2) or CRRT of 35 ml/kg/hour. Less-intensive group received IHD or SLED three times a week and CRRT of 20 ml/kg/hour. This study did not show any survival advantage in intensive RRT group versus less-intensive RRT group (60 day all cause mortality being 53.6% versus 51.5% respectively; odds ratio [OR]: 1.09; 95% confidence interval [CI], 0.86—1.40; p=0.47). There were no differences in rate of renal recovery between the two groups; of the survivors, 75% were RRT dependent at day 28 (at day 90, around 50% were RRT dependent – computed figure). Patients with pre-existing renal dysfunction were excluded and patients who had one session of IHD or 24 hours of CRRT were allowed to be enrolled in the study. There was also a long time lag from ICU admission (around 6 days) to start RRT. There was a higher incidence of hypotension in patients receiving IHD in intensive RRT group. RENAL (Randomised Evaluation of Normal versus Augmented Level) RRT study [2] enrolled >1,500 patients into two groups receiving either higher intensity (Qf – 40 ml/kg/hour) versus lower intensity (Qf – 25 ml/kg/hour) post-dilution CVVHDF as the only RRT. Primary outcome was death at 90 days after randomisation. Results were reported in 1,464 patients where the primary outcomes were available. There were 322 versus 332 deaths in higher intensity group and lower intensity groups respectively (mortality of 44.7% in each group; OR, 1.00; 95% CI, 0.81—1.23; p=0.99). At 90 days, 6.8% (high intensity) and 4.4% (low intensity) of the survivors were still RRT dependant (p=0.14). *Hypophosphataemia* was more common in higher intensity group (65% vs. 54%; p=<0.001). Although earlier studies [5, 7] showed a survival benefit from an enhanced CRRT dose, these two large and properly conducted RCTs have not reproduced these earlier results. Given the results of these latest studies, the clinical community is „none-the-wiser" as to the ideal dose of CRRT. There was also less than anticipated mortality in both studies. So why have all these studies failed to show any impact of „enhanced dose" on survival? Do we now believe that „enhanced" CRRT (or RRT generally) has no place in management of patients with AKI (or ESRD)? The answers are not easy; however, some lessons can be learned from all these, especially the recent larger two studies. (1) Having due regard to the fact that VA/ATN trial was not a comparison between IHD and CRRT; it should be realised that extrapolation of concepts in ESKD to the critically ill with AKI is inappropriate as the two conditions are not comparable; critically ill with AKI are haemodynamically, biochemically and nutritionally not only unstable but also different from ESKD patients (especially from aetiology as most of AKI in the critically ill is associated with sepsis). (2) Applying Kt/V to the critically ill with AKI is inappropriate because of the uncertainty of VUREA as their body water is not constant (at least initially because of fluid resuscitation, residual urine output) nor is the urea production constant. (3) Qf as representative of CRRT dose (i.e. equ-

ivalent to Kt/V) has not been investigated in any study and may thus not represent what we think it does (i.e. Kt/V). (4) The area of focus of „dose" of any RRT is only the elimination of a single marker (urea or creatinine). Elimination of a single marker does necessarily mean that all the uraemic toxins are being eliminated. (5) During the time course of the disease there may be a window when intensity of the dose is important (e.g. early in the course of disease) and where a higher intensity may make a difference. (6) Relevant studies have used a variety of RRT techniques e.g. IHD, CVVH (post-dilution), CVVHDF (pre and post-dilution) and SLED (although very few patients were randomised to receive SLED). There have also been comparisons between CVVH and CVVHDF [6]. These variations make it difficult to draw meaningful conclusions. Studies that have used pre-dilution CRRT have not accounted for decreased efficiency that accompanies pre-dilution CRRT [10]. (7) Purely solute based concept of „dose intensity" may well be inappropriate when in most critically ill AKI is part of multiple organ dysfunction syndrome and other concepts like fluid removal, biochemical homeostasis, haemodynamic stability and nutritional and antibiotic dose adequacy may be the appropriate metrics to consider for dose adequacy/intensity. (8) „Ceiling" for „low intensity" RRT was set at Qf of 20—25 ml/kg/hr in studies. Although based on survey of clinical practice, this may well not be the actual practice but reported „ideal" practice by participating clinicians. Thus benefits of „enhanced" dose may well remain hidden in the trials. (9) Finally, none of the studies have considered processes of care. The overall holistic care of the critically ill needs to be considered in studies that investigate any therapeutic/management strategies in the critically ill. However, such studies are difficult, if not impossible, to conduct and this may well be the reason why almost all other RCTs in the critically ill have shown no benefit of individual therapies in these patients [11]. The ideal dose of CRRT is still not known with certainty. What is certain that there may well be a minimum dose below which patients will be harmed; for CRRT this dose has been suggested as Qf of about 20—25 ml/kg/hr. However, since CRRT is rarely continuous and treatment disruptions occur frequently, the delivered dose may fall short by as much as 25—30% of prescribed dose. In order to deliver adequate dose to our patients, it is reasonable to suggest a CRRT dose of 30—35 ml/kg/hr [3]. *Take home message* Different doses of RRT have been described. Prescribing such „higher" dose should ensure adequate CRRT as well as standardised therapy across ICUs and patient populations. This may then have impact on survival as concomitant therapies like antibiotics, nutrition etc can be delivered in a standardised and adequate doses.

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Setting goals of care in severe sepsis

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Introduction Severe sepsis is a serious worldwide healthcare condition that is associated with high mortality rates, despite improvements in the ability to manage infection. New guidelines for the management of severe sepsis were recently released that advocate for implementation of evidence based practice care for patients. While the new guidelines are focused on resuscitative measures and critical care management components, recognition of the importance of setting goals of care is also highlighted. ***Objectives*** The objective of this presentation is to review the process used to update the recommendation on setting goals of care in the Surviving Sepsis Campaign Guidelines. ***Methods*** A committee of 68 international experts representing 30 international organizations was used and groups were formed to work on individual guideline recommendations, through teleconferences, meetings, and electronic-based committee discussions.

The guidelines used the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system to establish the quality of evidence from high (A) to very low (D) and to determine the strength of recommendations as strong (1) or weak (2). GRADEpro Summary of Evidence Tables were used to synthesize the research evidence and literature review results. ***Results*** Since publication of the 2008 guidelines, the research evidence focusing on the management of severe sepsis has expanded to include a synthesis review of 21 trials of intervention studies (four of which were randomized control trials – RCTs) aimed at improving communication with family members in the ICU, a number of single center cohort studies addressing palliative care and end-of-life, a multicenter cross sectional study, a Delphi consensus study, several literature synthesis reviews, clinical practice guidelines that reviewed over 300 publications, and two additional multi--component RCTs. In-depth review of this literature resulted in changes in the recommendation previously labeled as „Consideration for Limitation of Support", to the updated recommendation „Setting Goals of Care", which identifies that the goals of care and prognosis should be discussed with patients and families (grade 1B); that goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (grade 1B); and that goals of care be addressed as early as feasible, but no later than within 72 hours of ICU admission (grade 2C).

Aiming for a negative fluid balance in patients with acute lung injury and increased intra-abdominal pressure: a pilot study looking at the effects of PAL-treatment

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Learning objectives During this lecture after a brief introduction on protocolized care will be given together with an overview on the deleterious effects of fluid overload leading to a positive cumulative fluid balance (with the results of a recent meta-analysis). The concept of the Ebb and Flow phases of shock are explained and a 3 hit model will be suggested [3, 4]. Capillary leak plays an important role in the creation of a global increased permeability syndrome (GIPS) [2]. Different methods to quantify and to measure capillary leak are suggested together with an integrated „de-resuscitation" approach in order to help those patients that do not transgress spontaneously from the Ebb to the Flow phase of shock. The abstract below is part of the open access paper with the results of a pilot study on the effects of PAL treatment (PEEP + albumin + Lasix®) in patients with acute lung injury, a positive cumulative fluid balance, poor oxygenation and increased intra-abdominal pressure [1]. ***Introduction and background*** Achievement of a negative fluid balance in patients with capillary leak is associated with improved outcome. We investigated the effects of a multimodal restrictive fluid strategy aiming for negative fluid balance in patients with acute lung injury (ALI). ***Methods*** In this retrospective matched case-control study, we included 114 mechanically ventilated (MV) patients with ALI. We compared outcomes between a group of 57 patients receiving PAL-treatment (PAL group) and a matched control group, abstracted from a historical cohort. PAL-treatment combines high levels of positive end-expiratory pressure, small volume resuscitation with hyperoncotic albumin, and fluid removal with furosemide (Lasix®) or ultrafiltration. Effects on extravascular lung water index (EVLWI), intra-abdominal pressure (IAP), organ function, and vasopressor therapy were recorded during one week. The primary outcome parameter was 28-day mortality. ***Results and main message*** At baseline, no significant intergroup differences were found, except for lower PaO2/FIO2 and increased IAP in the PAL group (174.5±84.5 *vs* 256.5±152.7, p=0.001; 10.0±4.2 *vs* 8.0±3.7 mmHg, p=0.013, respectively). After one week, PAL-treated patients had a greater reduction of EVLWI, IAP, and cumulative fluid balance (-4.2±5.6 *vs* -1.1±3.7 mL/kg, p=0.006; -0.4±3.6 *vs* 1.8±3.8 mmHg, p=0.007; -1,451±7,761 *vs* 8,027±5,254 mL, p<0.001). Repercussions on cardiovascular and renal function were limited. PAL-treated patients required fewer days of intensive care unit admission and days on MV (23.6±15 *vs* 37.1±19.9 days, p=0.006; 14.6±10.7 *vs* 25.5±20.2 days, respectively) and had a lower 28-day mortality (28.1% *vs* 49.1%, p=0.034). ***Discussion*** PAL--treatment in patients with ALI is associated with a negative fluid balance, a reduction of EVLWI and IAP, and improved clinical outcomes without compromising organ function.

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Hemodynamic monitoring anno 2013: Tips and tricks when choosing the right tool for the right patient, and how to get most out of your transpulmonary thermodilution device

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Learning objectives During this lecture an overview will be given of the different methods to measure cardiac output (CO) going from invasive (Swan-Ganz) to truly noninvasive (fingercuff). The results of a survey on the knowledge of transpulmonary thermodilution (TPTD) with PiCCO will be presented. The presentation will then focus on the possible pitfalls of the TPTD technique and will provide the participants some tips and tricks in order to get the most out of your device. ***Introduction and background*** After the publication of the negative outcome results related to the use of the pulmonary artery catheter (PAC), many ICU physicians stopped hemodynamic monitoring and returned to the basic clinical "physiological" findings like hourly urine output, skin temperature and global hemodynamic parameters like heart rate and mean arterial blood pressure (MAP) [2, 4]. However some colleagues also looked for less invasive methods to calculate cardiac output (CO). Today a variety of different techniques are available and they range from invasive to truly noninvasive, or from advanced to basic hemodynamic monitoring [7]. Going from invasive to noninvasive they are: calibrated transcardiac thermodilution (or the so-called gold standard Swan-Ganz), calibrated transpulmonary thermodilution CO with either saline as indicator (PiCCO and EV1000) or lithium-dilution (LiDCO), esophageal Doppler or ultrasound (Hemosonic, Deltex, Uscom), partial CO_2 rebreathing (NiCO), electrical impedance (Cheetah) or other uncalibrated techniques looking at arterial pulse contour obtained via a radial or femoral line like Vigileo, Flotrac, LidCo rapid, Pram, PulsioFlex, or even completely noninvasive like the Bmeye Nexfin based on fingercuff arterial waveform analysis or esCCO that calculates CO based on ECG and spO_2 curve… However every technique has its limitations and needs to be assessed on its own merits [5]. By knowing the pitfalls we can obtain new and important information [9, 10]. ***Methods*** Pubmed review of pertinent peer-reviewed articles on hemodynamic monitoring. ***Results and main message*** The different techniques currently available should be analyzed upon their merits and with respect to the patient in whom we want to use them [8]. In the emergency room (ER) and the operating room (OR) the main focus goes to the continuous measurement of MAP and the correct assessment of fluid responsiveness and the capability of correct trending, providing "continuity". As such in the ER and OR less invasive (uncalibrated) techniques based on arterial pulse contour analysis may be sufficient to provide the relevant answers [3]. However in the unstable ICU patient with ever changing conditions of preload, afterload and contractility with the use and administration of fluids, vasopressors and inotropes a more advanced accurate (and thus more likely more invasive) hemodynamic monitoring technique may be needed like the PiCCO (Pulsion Medical Systems, Munich, Germany) or EV1000 (Edwards Lifescience, Irvine, USA) or even a volumetric PAC in some conditions like ARDS or patients with pulmonary hypertension to assess a specific treatment (like NO inhalation), providing "accuracy"[1]. The use of more advanced monitoring also allows to obtain new, extra and more specific information on the fluid status (volumetric preload indicators like global enddiastolic volume index (GEDVI), right ventricular enddiastolic volume index (RVEDVI)), contractility (global and right ventricular ejection fraction (GEF and RVEF), dPmax, cardiac function and power index) and they provide information on the possible risks of fluid overload (extravascular lung water index (EVLWI), pulmonary vascular permeability index (PVPI)), in addition to the readily available information with regard to continuous CO and functional hemodynamic parameters based on pulse contour analysis like stroke volume variation (SVV) and pulse pressure variation (PPV). However any technique stands or falls with its accuracy and reproducibility. The PiCCO has gained its place in the haemodynamic monitoring field, but as with any new technique, its virtue is only fully appreciated with correct use and interpretation. A recent survey on the knowledge of Belgian and Dutch ICU nurses and doctors on the principles of TPTD showed an overall score (correct answers) of 58.3±15.1% [6]. The doctors performed better than the nurses (62.7% vs 57.0%, p=0.012), no difference was found between male and female respondents (59.4% vs 57.6%) or between Belgian and Dutch respondents (57.3% vs 59.5%). About 190 out of 252 (75.4%) scored at least 50% whereas only 45 respondents (17.9%) obtained a score of 70% or more. The amount of years of ICU experience was inversely related with the knowledge on TPTD. From this survey, we can conclude that the knowledge on the use and interpretation of the parameters obtained with TPTD, although being used regularly, is suboptimal among ICU personnel. As with all new technologies, its usefulness relies on correct understanding of the principles, a flawless measurement technique and a correct interpretation of the obtained values in different scenarios. We will therefore provide some tips and tricks for nurses and doctors listed hereafter. ***Take-home messages*** Non invasive technologies offer useful additional information. There is a learning curve with any new technology. Each technology is different and needs to be assessed on its own merits. By knowing the pitfalls we can obtain new and important information. This can eventually also alter our treatment. When performing a calibration measurement during TPTD there are 10 important things to remember for the nurses: (1) Look at arterial pressure (AP) curve; (2) Perform a rapid flush test to detect over- or underdamping response properties of the transducer system, calibration on an overdamped AP curve may afterwards lead to overestimation of continuous pul-

se contour CO; (3) Zero the AP curve at the level of the midaxillary line in the supine position, this should be done at least once per nurse shift; (4) Prepare the calibration bolus: the volume is based on the patient's body weight with a maximum up to 100 kgs (0.2 ml/kg), best is 20 ml in all patients and injectate temperature should be as cool as possible, best is <8°C for all patients; (5) The bolus injection site must be as close as possible to the distal CVP port and the inline sensor must be outside the normal maintenance perfusion line; (6) Injection speed must be as fast as possible and in any case at a rate of 2.5 ml/sec (or thus the 20 ml within 8 sec), whilst performing the TPTD measurement the patient must not be supine; (7) Observe the TPTD curve and check for irregularities, delete false measurements, for instance, injection of less volume than the required bolus will result in a false increase in all TPTD measurements; (8) Check the numbers, each individual TPTD measurement must not deviate more than 15% from the mean CO, if this is the case repeat 2 TPTD measurements and delete highest and lowest values, check the numbers for GEDVI and EVLWI in the same manner; (9) Check the maximal obtained cooling ΔT° after the TPTD, if this is below 0.2°C either use more bolus or cooler, in patients with induced hypothermia this can be tricky; (10) Enter the CVP value, which is just needed for automatic and continuous systemic vascular resistance calculation. When performing a calibration measurement during TPTD there are 10 important things to remember for the doctors: (1) Verify whether the injection method was correct, and in particularly check whether the injection was not interrupted or too slow, although this may only have a minor effect on the TPTD CO value it may have a huge impact on the volumetric indices; (2) Check whether a premature hump can be detected on the thermodilution curve, this can be an indicator of a cross-talk phenomenon, bolus mixing, or a right-to-left shunt, as can be seen in ARDS with pulmonary hypertension; (3) Assess the possible effect of the arterial and venous catheter positions on the TPTD values obtained, the best position is with the central venous line (CVL) in the right jugular vein and the PiCCO catheter in the femoral artery, the placement of the CVL in the femoral vein cannot be recommended due to altered bolus transit times, especially in patients with increased IAP; (4) Assess the possible effect of an extracorporeal circuit as with CVVH or ECMO, if TPTD is performed during the CVVH the values of CI and GEDVI will be decreased while EVLWI will be increased in a statistically significant manner (although this may be less relevant clinically); (5) Assess the possible effects of pre-existing valvulopathy, where a mitral regurgitation may result in consistently increased values above 1200 to 1400 ml/m^2 for GEDVI, aortic stenosis may not only increase the GEDVI values, it may also cause dramatic changes in between different TPTD measurements, therefore a baseline cardiac ultrasound may help to interpret the TPTD values; (6) Correct the GEDVI values for GEF; (7) Analyse the effect of pleural effusion, if the X-ray shows "edema" but the EVLWI is normal then the patient probably has a pleural effusion and ultrasound should be performed; (8) Index the obtained values to predicted body weight; (9) Check for hidden volumes if GEDVI is increased, like an apical aneurysm, aortic aneurysm, dilated cardiomyopathy; and finally (10) Asses the effect of prone and other body positioning. Good luck!

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PBEF/Nampt/Visfatin: a novel mediator of innate immunity

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Learning objectives To describe the biology and emerging clinical relevance of the protein PBEF in trauma, sepsis, and acute lung injury. *Introduction and background* Pre-B Cell Colony Enhancing Factor (PBEF), also known as visfatin or nicotinamide phosphoribosyl transferase (Nampt) is a highly conserved 52 kDa protein that plays an important, though still incompletely defined role in innate immunity. Originally described as a secreted cytokine-like molecule that synergized with IL-7 and Stem Cell Factor to promote

the expansion of early stage B cells (hence its name), PBEF has been recognized to play an important and ancient role in inflammation and metabolism. ***Methods*** We undertook *in vitro* studies using circulating neutrophils (PMN) from critically ill patients following trauma or sepsis, PMN from healthy donors, and a variety of transfectable cell lines. We quantified apoptosis by flow cytometry as the uptake of propidium iodide in permeabilized cells, and evaluated protein expression and protein-protein interactions by Western blot and co-immunoprecipitation respectively. Cell lines were transfected with mutant S199A PBEF that lacks the capacity to dimerize and generate NAD and with siRNA against the insulin receptor (IR). ***Results and main message*** PMN from critically ill patients show marked inhibition of their constitutive capacity to undergo apoptosis. Recombinant PBEF is anti-apoptotic in PMN, and PBEF activity is necessary for the anti-apoptotic effects of a panel of inflammatory mediators. Moreover NAD alone could delay constitutive PMN apoptosis. Patient PMN showed increased expression of PBEF. Using a variety of approaches, we confirmed that PBEF binds to the β chain of the IR, and that this interaction is necessary for the NAD-generating (Nampt) activity of the protein. Insulin could overcome the delayed apoptosis seen in trauma PMN, however PBEF competitively inhibited this activity. ***Take-home message*** PBEF contributes to prolonged PMN functional survival in trauma and sepsis through its enzymatic role in the generation of NAD. This activity is dependent upon interactions with the β chain of the IR.

Prognostication of patients with post-anoxic coma: we should wait longer

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Learning objectives To understand the limitations of prognostication in patients in coma after circulatory arrest. To understand the effect of target temperature management on the validity of prognostication. ***Introduction and background*** Sudden circulatory arrest (SCD) is a major health problem in Western Countries, which accounts for about 15% off all deaths. Most of these deaths occur immediately, often despite cardiopulmonary resuscitation (CPR), but even after recovery of spontaneous circulation (ROSC), mortality is high. About 50% of initially resuscitated patients die before hospital discharge [2]. Many of these deaths are due to post-circulatory arrest neurological sequelae [2, 10]. Prognostication of patients in coma after CPR has been investigated extensively. The American Academy of Neurology (AAN) published in 2006 a practice parameter [13]. This paper reviews data on patients not treated with therapeutic hypothermia (TH), and presents an algorithm that has been, and still is, widely used [5]. Nowadays, many comatose post-cardiac arrest patients are treated with a temperature management strategy [3], and there is a need for new data to predict the outcome in patients who remain in a coma after hypothermia treatment. Although the AAN algorithm has also been advocated to predict outcome in patients treated with TH [14], its predictive value might well be different in these patients because of the modified course of the neurological recovery or the use of sedative drugs administered during TH [1, 11, 12], suggesting that the 2006 algorithm, indeed, cannot be used anymore. ***Methods*** Short review of studies on prognostication of post-anoxic coma patients treated with target temperature management. *Results* There are no clinical neurological signs that reliably predict poor outcome less than 24 hours after cardiac arrest [9]. Some predictors, as bilaterally absent N20 SSEP have a very high accuracy, although some reports of good outcome have been published [7]. The neurological examination, as well as the EEG, is highly influenced by sedation, and TH not only often mandates sedation, but also interferes with its clearance [11]. Other predictors, as combined absence of brainstem reflexes and motor response, are biased by the risk of self-fulfilling prophecy, which is a bias occurring when the treating physicians use an outcome predictor to make a decision to withdraw treatment [6]. Biochemical markers presently have limited value in determining neurological outcome in patients in coma after circulatory arrest. The proposed cut-off value of 33 mcg/L [13] has found to be insufficiently reliable [2]. Post-hypoxic myoclonus has also been found to be a less reliable symptom then previously believed [4]. ***Main message*** Recent studies show that in comatose patients after cardiac arrest and treated with TH there is no single tests that can predict poor outcome with 100% specificity or a false positive rate (FPR) of 0. It seems warranted to wait 3—5 days after rewarming before the prognosis can be established. There are studies under way that will evaluate prognostication of outcome at 72 hours after rewarming [8]. ***Take home message*** In comatose patients after cardiac arrest who have been treated with TH there is need to wait longer before neurological evaluation can reliably be performed and the prediction of outcome can be made.

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Intelligent Ventilation in the ICU

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Learning objectives To understand the concept of "Intelligent Ventilation" where a dynamic interactive machine is used to provided closed-loop, synchroniz ed, safe and efficient ventilation with automated adjustment of the mode and level of support when the patient's respiratory needs alter; followed by timely automated weaning to reduce the ventilator time and ICU stay. ***Introduction and background*** Many forms of closed loop, automatically applied partial support protocols have been developed on many different ventilators. These include: Mandatory Minute Ventilation (MMV), Pressure Support Ventilation (PSV), Proportional Assist Ventilation (PAV), SmartCare/PS, AutoMode and Neurally Adjusted Ventilatory Assist (NAVA). The most well know, basic and effective form of closed loop control ventilation which is widely used today is Pressure support ventilation (PSV). The clinician sets a target pressure (the pressure support setting) and flow is automatically adjusted to maintain that pressure throughout inspiration. 25 years ago (1988) we started studying the clinical use of Mandatory Minute Volume Ventilation using an Ohmeda CPU 1 electronic ventilator. Thereafter (1989—1996) we started working on intelligent closed loop automatic ventilation utilizing an adaptive lung ventilation controller applied by a Mackintosh Computer mounted on an Amadeus Ventilator with a PC based analyser for on-line lung function analysis. ***Methods*** Automated, micro-processor controlled, closed loop, mechanical ventilation has been used in our Medical Intensive Care Unit (MICU) as the primary preferred ventilator modality for the past 10 years. We did a formal study of this technology over a 6 year period. Recently we introduced and started studying the IntelliVent–ASV concept in our ICU and I will report on some preliminary findings. ***Results and main message*** The development of adaptive support ventilation machines without the need for End Tidal CO_2 nor Oxygen saturation in the closed loop, has proved the reality of the least work of breathing philosophy in the optimal mechanics of ventilation of most patients. Severe forms of restrictive lung disease with severely reduced pulmonary compliance have necessitated the development of the FiO_2, PEEP and the End tidal CO_2 controllers to create the IntelliVent concept. ***Take-home message*** Most patients can be automatically ventilated optimally according to the least work of breathing fit of the measured mechanics of the lungs and chest wall. Simply by providing the maximal alveolar ventilation, for the lowest minute ventilation, and the least dead space ventilation, the resulting blood gases are likely be the best possible for the state of the lungs.

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Designing clinical trials in the critically ill

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Learning objectives Gain an improved understanding of the challenges of clinical trial design in the critical care setting. Identify potential reasons for the recent lack of positive clinical trials in the critically ill and understand how this might be improved. ***Introduction*** Many time consuming, expensive and negative phase 3 clinical trials involving many thousands of patients have been undertaken in critical care, and continue to be funded. Furthermore, phase 3 studies frequently fail to achieve their planned recruitment target. Often such studies are based on small pilot studies with inadequate phase 2 trial data and limited mechanistic data to provide a sound scientific rationale. ***Methods*** Literature review. ***Results and main message*** Prior to undertaking a large phase 3 clinical trial in the critically ill, the following should be considered. 1) The intervention should have biological plausibility and there should be a body of evidence from in vitro experiments using human cells where possible. 2) There should be supportive data from animal studies. There should be evidence that the intervention can modulate mechanisms important in the pathogenesis of the disease or improve surrogate outcomes in more than one model of the disease and both as a preventative and therapeutic agent. 3) Observational studies should support a clinical effect in patients with the disease. 4) Data from healthy volunteers studies should demonstrate that the intervention can modulate mechanisms important in the pathogenesis of the disease. 5) Proof of concept data from a pilot study in patients with the disease should show that the intervention improves surrogate clinical outcomes and is well tolerated (ideally underpinned by investigations to examine if the intervention modulates important biological mechanisms). 6) A well designed phase 2 clinical trial in patients of an appropriate size to be adequately powered to: a) confirm efficacy for a clinically important endpoint; b) determine the treatment effect size; c) provide data that the intervention has beneficial effects on biological mechanisms important in the disease process in addition to clinical efficacy and d) accurately inform the sample size required to provide sufficient power to assess mortality as the primary outcome in a phase 3 trial. Importantly such a phase 2 trial should also inform feasibility and safety. An important consideration is defining what is a clinically important endpoint in studies in the critically ill and the link to outcome should be clear. If phase 2 study confirms safety but is negative for the clinically important primary endpoint while showing a trend to improvements in surrogate clinical outcome measures and underlying biological mechanisms, it may be appropriate to undertake a further phase 2 study. The design of a second phase 2 study should be necessarily different and informed by the initial phase 2 study. 7) The phase 3 trial should reflect the design of the positive phase 2 trial in terms of population studied and intervention (eg for a drug the dose and duration of treatment). A systemic review should also be undertaken [1]. ***Take-home message*** A step-wise approach to the body of evidence required to inform clinical trial design may be needed in order to successfully identify new therapies for the critically ill.

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Pharmacological treatment of ALI

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Learning objectives Provide a state-of-the-art update on recent and ongoing trials, as well as promising potential future pharmacological therapies in ARDS. ***Introduction*** Despite its high incidence and devastating outcomes, acute respiratory distress syndrome (ARDS) has no specific treatment, with effective therapy

currently limited to minimising injurious ventilation and avoiding a positive fluid balance. Since it was first described in 1967, and despite over 40 years of research, few pharmacological therapies have emerged for ARDS. ***Methods*** Literature review. ***Results and main message*** The data on the following will be reviewed. ***Neuromuscular blockade*** A multi-centre, randomised, placebo-controlled trial showed that infusion with cisatracurium besylate within 48 hours of mechanical ventilation to patients with moderate ARDS improved 90-day survival [2]. This finding needs to be confirmed in a further phase 3 trial. β adrenergic agonists Data suggests beta-adrenergic agonists could accelerate alveolar fluid clearance, as well as providing cytoprotection, increased surfactant secretion and decreased endothelial permeability. ALTA (Albuterol Treatment for Acute Lung Injury) failed to demonstrate a difference in ventilator-free days between those receiving inhaled β-agonist therapy and those given placebo [6]. BALTI-2 was a multi-centre study investigating intravenous salbutamol in patients with ARDS, but was terminated early due to excess mortality in the IV salbutamol group [5]. On the basis of these larger trials, β-agonists should be avoided in patients with ARDS. **Corticosteroids** Despite a systematic review and meta-analysis [3], the role of steroids in ARDS remains unclear, and in light of ongoing uncertainty, further trials are both planned and ongoing. *Statins* HMG CoA-reductase inhibitors (statins) have a range of effects on mechanisms implicated in the development of ARDS [1, 4]. Two larger trials are presently recruiting in the UK and Ireland (HARP-2) and in the USA, investigating simvastatin and rosuvastatin respectively. Data to support the need for clinical trials of aspirin, stem cell therapy, keratinocyte growth factor will be briefly discussed. ***Take-home message*** Despite many therapies being studied to date there has been little success in developing effective pharmacological therapies for the management if ARDS. However, given the high associated morbidity and mortality, pressure remains to continue efforts to improve outcomes. Increasing numbers of pharmacological therapies are being investigated, and with encouraging pre-clinical and early clinical results, it is expected that over the coming years some will develop into useful agents for the prevention and treatment of ARDS.

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Myocardial dysfunction in sepsis

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Objective The aim of this short presentation is highlight the role of silent myocardial ischemia in the aetiology of sepsis related cardiac dysfunction. Other humoral factors that may cause myocardial dysfunction in sepsis will also be discussed. ***Main data sources*** In addition to published work [1] currently available in public domain clinical records/images of a young patient – managed in the critical care unit at Manchester Royal Infirmary, with a normal coronary circulation and no cardiac risk factors who developed an inferior myocardial infarction during a severe septic illness will be used. The underlying message, pertaining to reversible myocardial ischemia in the above patient, is reinforced using a case series of seven patients who underwent Tc-99 myocardial perfusion scans during the acute stage of septic shock at our in-house nuclear cardiology facility (Cairo University Hospital). ***Data extraction and data synthesis*** The Manchester patient underwent coronary angiography 5 weeks after the septic illness, which showed a normal coronary circulation. The seven Cairo patients underwent one Tc-99 perfusion scans within 72 hours after admission to the ICU and a repeat scan 5—7 days later. Both Tc-99 scans were performed at rest and an objective 20-segment scoring system was used to grade the severity of perfusion defects. All seven patients had reversible perfusion defects either within a single well-defined coronary territory or with a more patchy distribution that did not correlate to a single coronary territory. The perfusion defects were reversible to varying degrees in all seven patients with two patients showing complete reversibility (the mean±SD perfusion defect scores for all seven patients were 17.7±5.7 on the first scan and 7±5.9 on the repeat scan). ***Conclusions*** Reversible myocardial perfusion defects – possibly due to microvascular thrombosis, is an important component of septic shock.

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Are we ready for protocolized hemodynamic management in severe sepsis?

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A large number of trials have demonstrated that protocol-based strategies can reduce variation and cost of ICU medicine and improve morbidity and mortality of critically ill patients. These include protocols for ventilator-weaning, sedation and analgesia, transfusion, and the prevention of ventilator-associated pneumonia and catheter – related blood stream infections. Several protocolized cardiovascular management algorithms have also been proposed for the care of hemodynamically unstable patients, mainly those who have severe sepsis or septic shock. These include the SCCM's practice parameters for hemodynamic support of sepsis in adult patients [1], a pulmonary artery catheter-based algorithm [2], and the Surviving Sepsis Campaign (SSC) „bundle" for the initial hemodynamic resuscitation which has been recently updated (CCM February 2013). These noble efforts to standardize care of patients in septic shock need to be carefully examined because, due to the complexity of hemodynamics in sepsis, the goals of therapy are much more difficult to define with certainty than in other forms of shock. A central element in all the above mentioned protocols is the reliance on specific values of filling pressure (either CVP or PAOP). This is especially true for the SSC bundle, which recommends aggressive fluid administration until a value of CVP of 8—12mm Hg (12—15 in ventilated patients) is reached as a first step in the management of shock. However, there is a vast evidence-based consensus that filling pressures are inadequate for the determination of the patient's need for fluids, and that reliance on these parameters may lead to either incomplete fluid resuscitation or to detrimental fluid overload. The second parameter that plays a major role in 2 of these algorithms is the central venous oxygen saturation ($ScvO_2$), which is regarded as „the gold standard for defining global adequacy of cardiovascular performance". The $ScvO_2$ is indeed an important cardiopulmonary parameter, and yet, especially in septic shock when oxygen extraction is notoriously low, it may be misleadingly normal or high in the presence of inadequate tissue oxygenation. The SSC resuscitation bundle is based on a 2001 single--center study which included an unusual subject pool and which has never been replicated. Additionally, while the SSC guidelines have significantly increased, both in volume and in the number of references that they cite, from 2004, through 2008 until 2012, the section devoted to hemodynamic resuscitation has been only slightly changed and its references have not been updated at all. The SSC claims that the reported improved survival following the adoption of its guidelines provides the necessary evidence for the efficacy of the hemodynamic resuscitation bundle. However, as administered and studied to date, only the early administration of appropriate antibiotics was found to be independently associated with survival benefit, while the attainment of the CVP and $ScvO_2$ goals did not influence survival. The sepsis bundles of the SSC include only recommendations that can be converted into data elements that can be precisely defined, with clearly identified failure modes, and that could be measured by retrospective chart audit. According to the Institute of Healthcare Improvement, with whom the SSC partnered in order to promote the Campaign, „a bundle must be followed for every patient, every single time…There should be no controversy involved, no debate or discussion of bundle elements…Addition of other strategies not found in the bundles is not recommended". This approach seems to be in line with other attempts to turn consensus statements into performance measures, pay-for-performance and other tools to critique the quality of physician care. In conclusion, hemodynamically unstable septic patients should not be treated by over-simplistic protocols which rely on physiologically inadequate parameters and which may lead to critical mistakes. Any attempt to protocolize care in septic patients has to use more comprehensive hemodynamic monitoring and has to leave room for individualized clinical judgment.

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Hemodynamic monitoring – accuracy vs. continuity

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Cardiac output (CO) is the main determinant of oxygen delivery and may be compromised or inadequate

in many disease states. It is therefore that many of our therapeutic efforts are aimed at improving low- or inadequate-flow states. The two main reasons for monitoring of CO in clinical practice include the identification of patients who have low (or high) CO values that are not evident clinically, and the quantification of the response to diagnostic and therapeutic interventions. The monitoring of CO is therefore very useful for proper decision-making in critically ill patients. The fact that this statement is not supported by evidence--based medicine tells us more about the shortcomings of EBM than those of the measurement of CO. By analogy, speedometers in cars and similar devices in airplanes have not been introduced following randomized controlled trials. Thus it is high time to consider the CO as an additional vital sign in critically ill and high risk surgical patients.The introduction of uncalibrated continuous CO monitors into clinical practice has been associated with questions about their accuracy in comparison with CO measured by the pulmonary artery catheter (PAC). Although considered the „gold standard", thermodilution CO has its own limitations with a reported precision of ±10—20%. The current convention is that any new method for measuring CO (e.g. pulse contour) should achieve a 30% agreement with bolus thermodilution, although the relevance of these arbitrary limits may need to be reassessed. When evaluating the role of new CO devices in clinical care, the fundamental question is whether the new device can replace thermodilution CO measurement as a guide to clinical decisions.Many of the new CO monitors provide a real-time continuous measurement. The continuity of measurement of physiological parameters is a powerful tool. A continuous real-time CO may be more useful and informative than CO measured by intermittent thermodilution, especially in assessing the response to therapeutic or diagnostic events with short time constants, such as fluid loading, passive leg raising (PLR), and the immediate response to inotropes. What is therefore of most importance is the ability of these monitors to reliably track changes in CO. Many of these monitors may be successfully used for perioperative optimization but may perform less adequately in the presence of significant changes in vascular tone. When striving to achieve specific „supra-normal" goals for CO and oxygen delivery, it is mandatory to use techniques with proven accuracy. Even when reliably and accurately measured, the interpretation of CO may not be straightforward, since a „normal" or even high CO does not preclude the presence of inadequate regional and microcirculatory flow while a low CO does not tell us what to do. In order to correctly use the CO value we need to integrate in the decision making process other parameters like fluid-responsiveness, preload, and indicators of the (in)adequacy of the CO. The realization that all hemodynamic parameters have limitations and confounding factors should serve as an incentive to adopt decision-making strategies that take this uncertainty into account. This is especially true during a therapeutic conflict, i.e., a situation where each of the possible therapeutic decisions carries some potential harm. Therapeutic conflicts are commonly found in critical care and present the biggest challenge for protocolized cardiovascular management. A therapeutic conflict should be solved by an a-priori assessment of the possible harm that each of the respective potential decisions may cause when found to be wrong. For example, it has recently been suggested that when the pulse pressure variation (PPV) is in a range in which fluid responsiveness cannot be reliably predicted (the „gray zone") and in a situation where fluid overload may be particularly deleterious, higher-than-normal PPV values should serve as indication for fluid administration. In conclusion, we have to recognize that all our measurements may be less accurate and less informative than we may want (or think). We have to face this challenge rather than become passive or even nihilistic. A reliable continuous measurement of vital physiological parameters, a multi-parametric approach, and more reliable decision-making strategies are some of the means that would allow us to correctly use new technologies for the benefit of our patients.

Appropriateness of care in ICU

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Learning objectives ICU professionals who perceive the care they provide as inappropriate experience moral distress and are at risk for burnout. This situation can jeopardize the quality of care and increase staff turnover [2]. ***Introduction and background*** The number of published studies related to burnout, conflicts, stressful conditions in ICU, is dramatically increasing and this is also true for interventions related to improving team working in the ICU [1, 3—5]. Nevertheless, no intervention has ever been tested with the aim of improving or avoiding the mentioned conditions. ***Methods*** Survey submitted to Intensive Care Unit (ICU) Healthcare providers investigating perceived appropriateness of care [2]. ***Results and main message*** ICU healthcare providers were surveyed and inappropriate care was perceived for at least one patient on the day of the survey in 27% of ICU staff interviewed [2]. ***Take-home message*** Inappropriate care is perceived by healthcare providers in the field of critical care. The work in the Intensive Care Unit (ICU) is extremely hard and stressful. Stress, conflicts and burnout are proven to impair communication among the ICU staff [4, 5]. There is evidence in the medical and non-medical literature suggesting that the burn out leads to low performance and concentration. Good teamwork and an emphasis on clarifying ethical issues are associated with lower perception of inappropriateness of care.

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ICM resources in Europe

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Learning objectives Intensive Care Medicine (ICM) is a multidisciplinary medical specialty which trains doctors from a variety of backgrounds (anesthesia, internal medicine, surgery, cardiology, etc) to care for patients with life-threatening diseases. The discipline of critical care is not the same across Europe. As a matter of fact, it could be considered as a mother speciality, a sub-speciality or a supra-speciality, according to the training charts recognised by the national law [3,4]. Accreditation in ICM may be given by a Royal College, a Society or a University. Some regions require trainees to demonstrate their knowledge by passing an examination, producing a thesis or both, while other authorities do not require any specific accreditation [3]. Unfortunately, inappropriate use of medical interventions is widespread, and non-adherence to established standards of care has been related to elevated rates of hospital mortality and readmission [1]. One prospective study, published in 2004, estimates that 1 in 5 citizens will die in Western countries in an Intensive Care Unit [1]. This is emphasizing the need for increasing resources and specialists in ICM. ***Introduction and background*** Costs related to the training in CCM are high, the necessity of linking skills and knowledge with a systematic training, provides an important opportunity for proposing specific accreditation [1, 2, 6, 7]. In Europe several projects have been implemented and are consistent with the European Directive of 2005 to facilitate the free movement of doctors and mutual recognition of their diplomas, certificates, and other evidence of formal qualifications. In 2012 this directive should have been modified to match new laws and needs [6]. ***Methods*** We followed work performed by the European Board of Intensive Care promoting ICM in Europe. ***Results and main message*** The UEMS has not a section representing ICM. Nevertheless, a new board has been recently created in the section of Anaesthesia and a road map has been approved by the UEMS. The new directive in 2012 will not recognize ICM as a mother specialty. Therefore, equivalence will be the only way junior specialist will be able to move from one to another European country. New networks should be created on a National level to encourage and support specialists and their free movement in Europe. The number of ICU beds is variable in Europe and resources are limited in some countries compared to others [5]. ICM is a new discipline still looking for European identity. ***Take-home message*** ICM is not a mother specialty and there are significant variations among training and accreditation in Europe. ICU beds are variable regardless increasing needs for ICU and increasing number of admissions.

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Do probiotics work in the critically ill?

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Gram-negative sepsis is a real and growing threat within the intensive care unit, compounded by increasing antimicrobial resistance. Whilst the incidence of infection can be decreased in part by improved infection control, other therapeutic strategies are urgently needed. With escalating antibiotic resistance, particularly to

„last resort" antibiotic agents, it is time to look for alternatives in treating infection. Studies of probiotics and sepsis are in their infancy, still in vitro and in animal models but the results are encouraging and suggest that translation to bedside is well worthwhile. Recent animal studies have shown that the probiotic exerts systemic anti-inflammatory effects, which could offer a novel adjunctive treatment for sepsis caused by Gram-negative bacteria. It is plausible that probiotics may calm the sepsis cytokine cascade triggered by pathogenic Gram--negative bacteria and hence reduce the associated morbidity and mortality. Local effects at the level of the gastrointestinal tract may reduce colonisation of critically ill patients with Gram-negative bacteria and hence reduce the incidence of ventilator associated pneumonia. How to get research grants? In this tutorial, I'll give some thoughts and tips from a grant reviewer's perspectives for research and fellowship grants.

21st century thinking

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Learning objectives Stimulation of thought and discussion about moral issues in intensive care medicine and related fields and their interaction with 21st Century technology, clinical care and research. ***Introduction and background*** When viewed in retrospect, events in history may appear to follow a linear and logical progression which seems readily understandable and almost inevitably determined. However, the unmoderated interaction of moral, technological and social factors, some of which are seldom made explicit, underlies these changes. Medicine, including intensive care medicine, is not insulated from these broader forces and intensivists do not often take an opportunity to consider such issues. This presentation has given us such an opportunity. ***Methods*** Personal reflections on 35 years in intensive care medicine and related fields, supplemented by selective review of medical and other scientific literature, discussion with colleagues and some ephemera. A few significant themes are presented in a dialectical framework, including disclosure of my emotional commitments where these are not immediately obvious. ***Results and main message*** The excellence of our clinical practice is threatened by the appeal of strident calls to action in the face of need (e.g. in organ donation) [1, 15], by our hopes, fears and prejudices (e.g. intensive insulin therapy (11), hormonal treatment in organ donation [10, 17], decompressive craniotomy [2, 8, 16]), by perverse economic incentives and marketing (colloidal fluid therapy [3—7, 12—14,18]) and by our own gizmo idolatry (9) (being 'guided by the beauty of our weapons'). We can resist these influences by steadfastly retaining our intellectual and moral integrity and using these strengths to act forthrightly in our practice. ***Take-home message*** All of us share a moral responsibility for our own behaviour and for the way that this shapes the society we live in. Intensivists work at the nexus of medical technology and human tragedy and have responsibility for moral leadership in that peculiarly fluid and nuanced world. Explicit discussion of relevant issues other than the merely technical can only enhance our ability to look after our patients and their families and thereby contribute to the greater societal good.

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Intensive Care over Nations - the ICON audit

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Learning objectives To understand the importance of international epidemiological data in providing insight into intensive care unit (ICU) characteristics and patient populations in different countries and regions around the world.***Introduction and background*** There is considerable variability in ICU provision, types of patients, and patient outcomes among ICUs, but there are relatively few international data of this topic. The Intensive Care over Nations (ICON) audit was, therefore, launched by the World Federation of Societies of Intensive and Critical Care Medicine (WFSICCM) to collect data on various aspects of ICUs and ICU patients worldwide. ***Methods*** In this prospective observational study, all adult (>16 years) patients admitted to a participating ICU over a 10-day period were included, except for planned ICU admissions for routine postoperative surveillance. Data on basic diagnoses, hemodynamic and laboratory variables allowing calculation of SAPS II and SOFA scores, microbiological results, lengths of ICU and hospital stay and outcomes were collected. ***Results and main message*** More than 700 centers contributed to the ICON audit, with data on over 10,000 patients from more than 80 countries. In this session, we will discuss some of the early results. ***Take-home message*** This study demonstrates how worldwide collaborative initiatives can be effective. The data collected will provide an important insight into patterns of intensive care patient populations in different countries and regions, helping to improve the planning of current and future critical care in individual countries and on a more global scale.