2nd International Fluid Academy Day

Abstracts of the invited lectures: Towards the Perfect Fluid Strategy: Towards the perfect fluid strategy (Part 1); Towards the perfect fluid strategy (Part 2); Reaching the target (Part 1); Reaching the target (Part 2)

Crystalloids: What did we learn last year and what happened in the meantime?

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Learning objectives Back to Basics! In this lecture basic definitions, terminology and concepts are reviewed. What is tonicity and what are hypo-, iso- and hypertonic crystalloids? What is a balanced or unbalanced solution? What is the Strong Ion Difference (SID)? What is the Stewart approach? There is much ado about hyperchloremic metabolic acidosis caused by fluids. Where does it come from? Is it relevant, is there any animal or human data supporting this statement? How can it be avoided? Is the use of saline still acceptable, because there may be nothing "normal" about "normal saline"? Which and how much electrolyte does a patient need? Review of recent studies on the use of balanced solutions like the retrospective data by Andy Shaw and the prospective data by Lynette Scherer. ***Introduction and background*** Crystalloids are solutions, with or without glucose or dextrose that contain electrolytes dissolved in water. They are widely used as maintenance solutions, replacement solutions or resuscitation fluids. Their most important characteristics are [5] the tonicity, defining the distribution over the different body compartments and [3] the strong ion difference (SID), important for the effect on the acid-base status after administration. A balanced solution is a solution with a SID >0. There is more and more evidence that imprudent administration of crystalloids may lead to morbidity. ***Methods*** Review of the lectures of the first IFAD, Pubmed search, personal communication with experts in the field. ***Results and main message*** There are two major concerns in administering crystalloids [5]. The induction of hyperchloremic metabolic acidosis (HMA), a proven side-effect of saline. Although animal studies showed HMA can lead to kidney dysfunction and it also seemed to induce morbidity in normal volunteers, there was little data on relevant clinical parameters. This now seems to change with the retrospective data by Shaw et al. where an increase in morbidity was shown when saline vs a balanced crystalloid was used in surgical patients. There is also rising evidence that saline can lead to a delay in micturition, although the exact mechanism is unclear[3]. The induction of fluid overload. It is frequently shown that more crystalloids than colloids are needed to achieve clinical stability. Recent colloid vs crystalloid studies showed conflicting data in this matter though. Fluid overload was shown an independent risk factor of mortality in septic patients and of morbidity in the perioperative setting amongst others. ***Take-home message*** Crystalloid solutions should be prescribed with the same care and caution as we do with medication, by giving the right dose of the right fluid at the right time. When using crystalloids, avoiding HMA by using balanced solutions, seems to be important, although the critical dose for a switch from saline is not known. Fluid overload is to be avoided as it is proven to induce morbidity and mortality.

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Colloids What did we learn last year and what happened in the meantime?

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Learning objectives Review of the types of colloids (mainly starches), differences between balanced and unbalanced starches. The never-ending debate: where are we now? Is there merely a difference in cosmetics or also in outcome? What are the strengths and flaws of the actual mega-trials and meta-analyses? Are there specific situations or patient groups where colloids behave differently and may have an advantage? Which trials are still in the pipeline? This lecture will basically focus on the results of 4 recent major trials comparing the use of crystalloids vs colloids in critically ill patients: The 6S study, the CRYSTMAS trial, the CRYSTAL study and the CHEST trial. It will give a concise overview and comparison and suggest guidelines and recommendations for future use of starches. ***Introduction and background*** At the time of the First Fluid Academy Day in November 2011 the evidence base for the use of colloids vs crystalloids in critically ill patients was rather weak. Except for the SAFE and VISEP studies no randomized intervention studies were available. Crucially, neither of these addressed the use of the more recent lower molecular weight starch derivates (HES 130) or the use of "balanced" solutions. Subgroup analysis and meta-analysis indicated equipoise for most subgroups, with the exception of trauma patients where harm could be expected with the use of colloids on one side, and on the other side sepsis, cardiopulmonary bypass and malaria patients where the use of albumin might be advantageous. ***Results and main message*** The last twelve months, though, have seen an extraordinary coincidence of important fluid-therapy related studies being published, the largest ones being the "6S study" and the "CHEST trial". In both of these the colloid was one of the HES 130 solutions, and, while failing to find benefit of these solutions in critically ill patients, both trials indeed confirmed earlier suspicions of renal damage associated with them. Several other trials are under way, with results soon to be expected for two French ones investigating the use of colloids including albumin. ***Take-home message*** For the time being, at least, prudence indicates that the "Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients" is good advice, suggesting not to use 6% HES 130/0.4 or gelatin in septic patients or patients at risk of renal failure. Even the evidence for uses in other groups of patients and for other colloids is uncertain at best, with very few, specific exceptions.

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All fluids are good! Fluid strategy in the septic patient and ARDS

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Learning Objectives In this lecture the pathophysiology of acute lung injury and acute respiratory distress syndrome (ARDS) will be reviewed together with the new proposed definitions for ARDS (Berlin definition). Do we need to change the current ARDS consensus definitions? How restrictive do we have to be with regard to fluids in the patient with ARDS? Dry lungs are happy lungs but at what cost, a dry liver may be a dead liver? Do we need to sacrifice the kidneys in order to save the lungs? The issue of fluid balance and fluid overload will be discussed as well as the indications for the use of albumin in order to provide the participant with an answer to the question: "What fluids should be used in the ARDS and sepsis patient, are all fluids really good?" ***Introduction and background*** Adequate fluid administration is one of the cornerstones in the effective management of critically ill patients, and for this purpose all fluids are better than none! But many questions remain about exactly which fluid or combination of fluids to administer to which patient, how much fluid to give, and how to monitor ongoing fluid requirement needs. Sepsis and ARDS share the same complex pathophysiological process involving inflammatory mediators and various cellular components. Resultant alterations in capillary permeability can make fluid needs more difficult to assess in these patients and fluid administration more difficult to manage. ***Results and main message*** Inadequate fluid resuscitation is associated with worse outcomes, but administration of large quantities of fluid can be associated with edema formation, potentially resulting in impaired gas exchange, impaired wound healing, intolerance to feeding, and other complications. Essentially, fluids should be administered to improve microvascular blood flow by increasing plasma volume, and to increase cardiac output

by the Frank-Starling mechanism, thus maintaining oxygen delivery to the tissues. But care must be taken to avoid fluid overload and frequent re-evaluation of ongoing fluid needs is, therefore, necessary. Various methods have been developed to predict fluid responsiveness, but ongoing fluid requirements are best assessed using a repeated fluid challenge technique, in which the hemodynamic response to a predetermined amount of fluid, e.g., 1000 mL of crystalloids or 300—500 mL of colloids, administered over a short period of time, usually 30 mins, is assessed. Importantly, safety limits, such as cardiac filling pressures, need to be selected to prevent fluid overload during a fluid challenge. If the fluid challenge is successful and the hemodynamic goal is achieved, fluid administration can be stopped; if the hemodynamic goal is not reached, fluid challenges can be repeated as necessary as long as the safety limits are not exceeded. Deciding which fluid to use remains controversial, and all fluids have their own advantages and shortcomings. Less colloid than crystalloid is needed to achieve the same hemodynamic targets but colloids are more expensive and there is no evidence that one fluid type is better than the other in terms of outcomes. ***Take-home message*** Each intravenous fluid has advantages and disadvantages compared to other fluids and there is still no convincing evidence to support one type of fluid over another in all patients. Fluid choices must therefore be adapted to individual patient characteristics according to local availability; in practice, most patients will receive a combination of fluid types. Ongoing fluid requirements must be carefully monitored to ensure that fluid balance remains optimal.

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Is more (or less) better? Fluid strategy in the perioperative setting

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Learning objectives This lecture will deal with new trends in peri-operative fluid management and their proclaimed effect on outcome. Is goal-directed therapy (GDT) indicated in all high risk patients? If so, what are the reasons for the apparent discrepancy between evidence and practice concerning GDT? Is GDT always justified even if it frequently leads to a more positive fluid balance? What are the risks of GDT aimed to achieve supra-normal values? How to safely apply GDT? Is the peri-operative fluid balance important, and should we give more fluids or on the contrary less? Does the timing and the dose play a role? ***Introduction and background*** The concept of perioperative goal-directed therapy (GDT) in high-risk surgical patients has gained much support in recent years. The most common strategy advocates the administration of fluids until the (continuously measured) cardiac output (CO) is maximized ("optimized") and does not increase any further in response to fluids. Others advocate that the CO and oxygen delivery be further increased to "supra-normal" values by the use of inotropes. Although the practice of GDT has been shown to decrease the incidence of postoperative complications, shorten length of stay and even decrease surgical mortality, its penetration into clinical practice seems to be slow and out of sync with the evidence base. ***Results and main message*** Some of the not-fully resolved issues that surround the concept of perioperative GDT and that may explain its non-uniform adoption include the following: 1. GDT is usually associated with the administration of more fluids. At the same time, fluid overload is recognized as a major independent risk factor for increased postoperative morbidity. 2. Most GDT protocols are based on the response of the CO to fluid loading and do not take into account the status of fluid responsiveness. 3. Continued pursuit of hemodynamic goals in patients who do not respond may be harmful, especially when optimization to "supra-normal" values is attempted in all patients. 4. The pathophysiological rationale behind the presumed efficacy of GDT is an improvement in microcirculatory flow and tissue oxygenation. And yet, perioperative GDT have been shown to be equally effective when administered postoperatively, which puts it in contradistinction to EGDT in critically ill patients. 5. There are distinct challenges associated with the design and conduct of GDT trials. In addition, some trials have not reported positive results. ***Take-home message*** The reported benefits of perioperative GDT are too important to be disregarded or denied. And yet, there still some issues that need to be resolved. When practiced, it is essential that the GDT approach be individualized and take into account the patient's cardiac capacity. It is also important to realize that a non-critical promotion of perioperative optimization, which entails a forgiving attitude towards aggressive fluid administration, may encourage practitioners with inadequate training and experience to simply overload their patients with fluids without appropriate monitoring.

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There will be blood! Fluid strategy in trauma and hemorrhagic shock

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Learning objectives Many controversies will be dealt with regard to gelatins or starches. What are gelatins, dextrans and starches? Is molecular weight the only parameter that counts or do we need to take into account the charge? Are the smaller starches safer? Does the buffer solution in balanced solutions (lactate, acetate, malate…) matter? Is the origin of the starch (maize vs potatoes) important? Do we still have to fear for the kidneys and the coagulation with the newest starches? Should we bother about anaphylactic reactions or prior disease when using gelatins? What to use in hemorrhagic shock: colloids or crystalloids or just blood products? Some colloids are more equal than others! Our choice matters, as does the timing and the dosing. How can we limit blood loss? In this lecture, the results of meta-analyses and CRASH trial will be reviewed ***Introduction and background*** In hemorrhagic shock macrocirculation, microcirculation, and tissue perfusion are impaired due to massive blood loss. Infusion strategy aims at restoring the volume of the intravascular space and, thereby, facilitating oxygen transport. The clinical questions include indication and differential indication of crystalloidal and colloidal fluids, clinical targets, and dosing. ***Methods*** Pathophysiological considerations, pharmacological characteristics of intravenous fluids, and their relevant side effects in massive bleeding are reviewed using an unsystematic search of evidence in text books and PubMed, as well as recommendations from international guidelines on infusion management which employed systematic literature searches. ***Results and main message*** Intravenous fluids are required in order to restore microcirculation and to prevent organ dysfunction and death in massive bleeding. Deliberate hypotension is recommended in uncontrolled hemorrhage [5]. In uncontrolled hemorrhage in general pre-warmed fluids should be administered in order to prevent hypothermia-dependent coagulation disturbance [5]. In hemorrhagic shock with lactate acidosis, additional hyperchloremic acidosis due to saline-based infusions should be avoided by the use of chlorine-balanced solutions. Various crystalloidal and colloidal solutions are available. In a pathyphysiology-driven approach crystalloids are indicated to replace extravascular deficits and colloids are indicated for intravascular volume replacement. The use of crystalloids only cannot fulfill a pathophysiology-driven fluid strategy because of high volume loss into the interstitial compartment [4]. Traditionally in countries with predominant crystalloid resuscitation, coagulation management is based on a 1:1:1 ratio concept of red blood cell concentrates fresh frozen plasma (FFP) platelet concentrates. Ratio-based transfusion regimens deliver relevant amounts of volume (3 components together about 600 ml). The volume expanding capacity of the 8.5% protein solution in FFP, however, is unknown. Albumin is used in some countries as an endogenous colloidal solution in massive bleeding but both FFP and albumin also have their disadvantages, risks, and costs. Coagulation factor concentrate-based coagulation management deliver procoagulant activity in small carrier solutions (50 ml) and synthetic colloids with a context-sensitive volume expanding effect of around 100% are often used in this regimen [1]. Synthetic colloids, however, may aggravate bleeding by inducing intravascular dilutional coagulopathy [3]. Accordingly, maximum doses need to be considered. In acute bleeding the endothelial barrier is suggested to be intact. Dosing of fluids according to the targets of preload optimization and microcirculatory parameters would be useful but are often not applicable in the emergency setting of massive bleeding e.g. early in trauma management. Dosing of catecholamines and fluids according to heart rate and arterial blood pressure is clinical reality but should be supplemented by repeated blood gas analyses. Head-to-head comparisons of fluid strategies in hemorrhagic shock are scarce but a recent trial comparison showed

increased microcirculation and lactate clearance in colloid-treated trauma patients [2]. ***Take-home message*** Fluid strategy in hemorrhagic shock is heterogeneous throughout countries and continents. Studies comparing our traditional regimen are warranted. In a pathophysiology-based concept chlorine-based crystalloids plus colloids are given individualized according to metabolic (and preload) parameters with monitoring for (dilutional) coagulopathy and active avoidance of overdosing and hypervolemia.

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Towards the perfect fluid strategy (Part 2)

Answering the call of nature. Fluid strategy in traumatic brain injury

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Learning objectives Are hypertonic solutions useful or harmful? What are the possible mechanisms of action? What are the indications? What is the dose? Are there relevant side-effects? Should we use colloids or crystalloids in traumatic brain injury (TBI)? Is there a place for albumin? Is there still a place for mannitol? What is the role for triple H therapy? Should we only use it in spontaneous subarachnoid bleeding (SAB) or also in traumatic SAB? How can we treat vasospams? ***Introduction and background*** In TBI, dysfunction of the "blood-brain barrier" is a common finding, resulting in maldistribution of osmoles and water within the brain. Moreover, intravascular volume depletion due to hemorrhage from associated injuries or polyuria secondary to diabetes insipidus, are common causes of hypotension. ***Methods*** The purpose of this overview is to discuss fluid therapy in TBI by applying evidence based medicine: the most recent evidence on the use of colloids, crystalloids or hypertonic solutions is reviewed, with a specific focus on differences in safety and efficacy and how integration of monitoring parameters may be used to implement more personalized fluid treatment approaches. ***Results and main message*** The goal of fluid management is to establish and maintain adequate intravascular euvolemia to moderate hypervolemia as a negative fluid balance has been shown to be associated with an adverse effect on outcome. Inappropriate fluid administration to achieve intended CPP or MAP is however associated with fluid overload, ARDS or hyperchloremic metabolic acidosis. CVP may be used to guide fluid management while several reliable predictors of fluid responsiveness such as pulse pressure variation, systolic pressure variation have been suggested to guide fluid management. Management of electrolytes disturbances should follow complete volume restoration. Isotonic crystalloids, specifically normal saline (NS) solution are the fluid of choice for fluid resuscitation and volume replacement. Hypotonic solutions including glucose containing solutions should be avoided in the first 24 to 48 hours, unless the patient develops hypoglycemia in the absence of nutritional support. Blood and blood products may be used as appropriate. Colloids offer a number of theoretical advantages over crystalloids, but some colloids (e.g., hydroxyethyl starch solutions, dextrans) can have serious adverse effects, and albumin products entail higher costs. The results of the influential Saline vs Albumin Fluid Evaluation (SAFE) trial and a subsequent SAFE subgroup analysis indicate that colloid therapy should be avoided in patients with trauma and TBI: due to an increased mortality risk relative to crystalloid therapy. Hypertonic solutions (HSS) have been shown to decrease brain edema, reducing elevated ICP, and increasing MAP and CPP. Osmotic diuresis by using mannitol is also an effective method to decrease raised ICP after TBI but should be compensated by adequate fluid replacement with isotonic saline solution to maintain euvolemia. Unfortunately, the overall results of HSS related studies are inconsistent and further clinical trials are needed to define their role. ***Take-home message*** Hypotension is the most amenable to prevention, and should be scrupulously avoided and aggressively managed. There is no evidence that the incidence of intracranial hypertension, morbidity, or mortality is increased by the active maintenance of CPP above 60 mmHg with normalizing the intravascular volume or inducing systemic hypertension. Rather than persisting in a standardized "one size fits all" approach to fluid therapy or continuing down the separate treats of goal directed therapy, we suggest to think more in terms of "individualized therapeutic strategies" more focused on the specific requirements of each patient by using multimodality monitoring of parameters. In the context of the published literature on this topic, it appears that the osmolality of an infusion solution rather than the colloid osmotic pressure per se represents

the key determinant in the pathogenesis of cerebral edema formation. Comparison of calculated osmolarity and measured in-vitro osmolality suggests that human albumin solutions, Hartmann's solutions … are hypo-osmolar, and may, therefore, increase brain volume and intracranial pressure.

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All fluids are bad! Fluid strategy in abdominal hypertension and liver failure

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Learning objectives Hero or Has-Been? Is there still a place for albumin? It's expensive (at least in Europe), but is it also worth the cash? Is it human or do we just hope it is? Are there still indications for iso- or even hypo-oncotic albumin? Is there an advantage of the hyperoncotic formulation to mobilize fluids? Do the kidneys like this strategy? Do we still have to measure plasma levels of albumin and is a correction of a low level necessary? What is the role of the daily and cumulative fluid balance in relation to abdominal hypertension? Is secondary abdominal compartment syndrome an iatrogenic disease related to fluid overload? How to avoid fluid overload? What are the best fluids in cirrhosis? Can we do anything else to help? What is the role for terlipressin in paracenthesis and spontaneous bacterial peritonitis (SBP)? The results of recent multicentre trials (SAFE study and ALBIOS trial) and meta-analyses will be reviewed. ***Introduction and background*** Patients with liver disease fall into 3 broad categories 1. Acute liver failure (ALF), 2. Critically ill cirrhotics (CIC) and 3. Extended hepatic surgery and resection with subsequent liver failure (HS), those with liver trauma who fall outside these categories rarely develop liver failure but are at significant risk of abdominal hypertension and biliary sepsis. These groups and the optimal fluid strategies will be discussed. ***Results and main message*** the requirements and considerations for all 3 groups are different and management needs to be individualized. Those with ALF normally present with gross volume depletion and are at least in the first days of their management in need of fluids. The optimal fluid has not been examined but no data suggests crystalloid to be worse than any other. Important is to maintain serum Na at the top of the normal range in regard of risk of encephalopathy and cerebral oedema. Hyperchloraemia may easily develop and should be looked for and avoided. Initial lactic acidosis will often resolve with adequate fluid therapy. During the period of liver regeneration these patients develop ascites and portal hypertension and clinically start to resemble a cirrhotic. In those with cirrhosis the support for use of 20% albumin exists albeit in the ward *vs* critical care environment. The fluid status of this group can be difficult to judge without supplementary monitoring. Nearly all will have a normal or increased total plasma volume but a cohort will have significant central hypovolaemia whilst others will have central volume and pressure overload with potentially right ventricular dysfunction. Splanchnic vasoconstriction may have the potential to improve central blood volume whilst avoiding excess fluid administration. Those undergoing extended hepatectomy may initially present with relative hypovolaemia and hypotension having been run with low fluids and right sided pressures peri-operatively plus a good functioning epidural. In this cohort the requirement is to give a small amount of fluid initially but utilize pressors / inotropes early. The major risk in this group is the development of small for size syndrome where portal venous inflow is excessive to the size and capacity of the remnant liver and they develop ascites and cholestasis at about day 3 onwards. Early recognition and splenic artery ligation / embolization may be considered as may the use of splanchnic vasoconstrictors / modulators of flow. ***Take-home message*** Individualize fluids and constrictors dependent upon monitoring and clinical context.

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To pee or not to pee, that is the question! Fluid strategy in acute kidney injury

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Learning objectives What is the impact of fluid balance on kidney function? Should we use crystalloids or colloids to prevent acute kidney injury (AKI)? Is there a role for albumin? Can we use diuresis and urine output as a resuscitation parameter or a clinical outcome parameter? Is there still a place for forced diuresis? When should we use renal replacement therapy and venovenous hemofiltration? Do we still have to fear for the kidneys with the newest starches? Is there a place for bioelectrical impedance analysis (BIA) to measure total body water and body composition electronically? Can I measure urine output continuously and Continuous real-time urine output monitoring for early detection of acute kidney injury. ***Introduction and background*** Fluid loading has been the cornerstone for therapy of oliguria in ICU patients. This makes sense, as in most patients, distributive or hypovolemic shock is the underlying problem for decreased urine output. This abstract will discuss the recent literature on fluid management in patients with acute kidney failure and injury. ***Results and main message*** In community acquired AKI as studied in the Grampian region in the United Kingdom, sepsis was the underlying aetiology in 47%, and hypovolaemia in 30% of AKI cases. Similarly, in the worldwide BEST Kidney study, AKI in ICU patients was attributed in 47.5% to sepsis, and in 25.6% to hypovolemic shock. Also, patients who are fluid depleted by means of diuretics are at increased risk for AKI; for instance after radio-contrast exposure. Remarkably, there are little data supporting the use of volume therapy for prevention of AKI. We should also be aware that volume therapy might be associated with decreased kidney function. Crystalloid therapy with so-called isotonic saline may lead to hyperchloremic metabiolic acidosis and is associated with AKI. Colloid therapy with synthetic colloids such as hydroxyethyl starch solutions or gelatins, is in a dose dependent manner associated with AKI. Fluid overload may also lead to decreased kidney function as a consequence of increased right ventricular pressure and venous congestion, or when more pronounced, by development of intra-abdominal hypertension. Colloid volume loading may therefore be in theory preferable to crystalloid volume therapy. However, data in large studies do not support the superiority of synthetic colloids or human albumin for preservation of kidney function. ***Take-home message*** In summary, fluid therapy is the logical cornerstone therapy in most patients with oliguria. However, the evidence for this is weak. Also, the optimal type of fluid and the endpoints that we should aim for are not yet clearly established.

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It's prime time! Fluid strategy during cardiac surgery

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Learning objectives Should we use gelatins or starches to prime? Is there a role for balanced solutions during cardiac surgery? What about the use of anticoagulation and electrolytes? Should we bother about the glycocalix? Must we keep fluid balance in equilibrium? Does the extracorporeal circuit induce a systemic inflammatory response, inflammation and capillary leak and what can we learn from it? ***Introduction and background*** Typical cardiac surgery using cardiopulmonary bypass (CPB) consists of 4 distinct phases in time: 1 pre-pump, 2 pump, 3 post-pump with surgical haemostasis/chest closure and 5 ICU. While each period has its own particularities and goals that matter, outcome mainly depends on hemodynamic stability at any time and the respective avoidance of: 1 homologous blood & its products, 2 extreme peri-operative anemia and [3] fluid overload or flood. Strategies to minimize inflammation (SIRS), coagulation disorders, acid-base derangements and, microcirculatory disturbances (glycocalix) are interrelated targets indirectly contributing to outcome. Focusing on CPB priming, it is hypothesized that fluid composition by its influence on the body's handling of such solutions can interfere with adverse phenomena. Furthermore, contact with extracorporeal circuits also triggers inflammation and blood damage to be modulated by circuit coating and some priming fluids. ***Methods*** A literature search was performed in order to detect relevant studies and meta-analyses on outcome after cardiac surgery. Additionally, there was a more specific search within subgroups for effects of pump-prime. The following key-word matrix was used:

Fluids	CPB	Priming	Goal directed
Inflammation	SIRS	CPB Circuits	Hemodynamics
Microcirculation	Glycocalix	Interstitial edema	Targets
Acid-Base	Stewart	Balanced solutions	Meta analysis
Anemia	Bleeding	Coagulation	Subgroups
Oncotic Pressure	Colloids	Fluid Balance	Survival
Outcome	Transfusion	Blood damage	Cardiac Anesthesia

Results and main message From reviewing and screening of a few hundred citations and published references the extracted evidence on the choice of CPB priming solutions is as follows [1—5]: colloids are to be preferred over crystalloids. Synthetic colloids may be good (and cheaper) alternatives to albumin. However, hydroxyl--ethyl starch increased blood loss, reoperation for bleeding, and blood product transfusion after CPB with no evidence that risks could be mitigated by lower molecular weight and substitution. Furthermore, electrically charged colloids may reduce the damage to figured blood elements during CPB. Acid-base problems of CPB can grosso modo be reduced to the problem of infusing large fluid volumes. Balanced priming solutions provide a stable acid-base status and its subsequent benefits throughout. Finally, mini extracorporeal circuits may attenuate post-bypass inflammatory response and risks of homologous transfusion. ***Take-home message*** 1. Outcome after cardiac surgery: there is more than fluids between heaven and earth; 2. Always colloids in the CPB prime; 3. Synthetic colloids are as good as albumin; 4. Charged colloids reduce blood damage during the pump; 5. Balanced solutions abolish the CPB acid-base problem;. 6. Mini extracorporeal circuits attenuates post-bypass inflammatory response.

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Micro particles contamination: Innocent bystander or real threat?

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Learning objectives With modern imaging techniques it is possible to document the presence of multiple particles related to transfusion and infusion therapy like precipitates, glass, air bubbles, microbes, plastic and rubber. Is this problem and what is the solution? During this lecture a literature overview will be given on the use of in-line filters to retain these micro particles and on possible negative effects of particles for our patients. But are they cost-effective? What is the clinical importance and are there any outcome studies? ***Introduction and background*** Particulate contamination due to infusion therapy is a known problem [5] and carries a potential health risk for intensive care patients. Particles induce thrombogenesis [1, 4], deteriorate the microcirculation and modulate immune responses [3]. ***Methods*** This single-centre, prospective, randomized controlled trial assessed the effects of in-line filtration on the reduction of major complications in critically ill children. 807 subjects were randomly assigned to either a control (n=406) or filter group (n=401), the latter receiving in-line filtration. The primary endpoint was reduction in the rate of overall complications, which included the occurrence of systemic inflammatory response syndrome (SIRS), sepsis, organ failure (circulation, lung, liver, kidney) and thrombosis. Secondary objectives were length of stay in the pediatric intensive care unit (PICU) and overall hospital stay. Duration of mechanical ventilation and mortality rates were analyzed as well [2]. ***Results and main message*** Analysis demonstrated a significant reduction in the overall complication rate (n=166 [40.9%] *vs* n=124 [30.9%]; P=0.003) for the filter group. In particular, the incidence of SIRS was significantly lower in the filter group (n=123 [30.3%] *vs* n=90 [22.4%]; P=0.01). Length of stay on the PICU (3.89 days [95% CI 2.97-4.82] *vs* 2.98 days [2.33-3.64]; p=0.025) and duration of mechanical ventilation (840 minutes [95% CI 335-1345] *vs* 658 minutes [425-891]; p=0.028) were significantly reduced in the filter group. No severe adverse effects of in-line filtration occurred [3]. ***Interpretation*** Contaminations with micro particles seem to have an important impact on intensive care patients. In-line filtration is effective in reducing severe complications in critically ill patients. The overall

complication rate during the PICU stay was significantly reduced. In-line filtration was most effective in reducing SIRS. Therefore, in-line filtration improves the safety of intensive care patients and represents a preventive strategy resulting in significant reductions in the length of stay and duration of mechanical ventilation (ClinicalTrials.gov number; NCT00209768). ***Funding*** Research Fund of Hannover Medical School; unrestricted grant from Pall Corporation, Dreieich, Germany and B. Braun Corporation, Melsungen, Germany

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Reaching the target (Part 1)

Respect your goals and change your targets! Interactive case discussion

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Learning objectives Is fluid overload a cosmetic issue or just bad medicine? Oedema and derailed cumulative fluid balances: are they just collateral damage or do they put the patient in additional danger? What is best: restrictive *vs* liberal fluid strategies? What is the Ebb and Flow phase of shock? Is anasarc edema just of cosmetic concern or is it harmful for the organs and eventually the patient? Maybe we need to rethink the 2 hit ischemia-reperfusion model and replace it by a 3 hit model, where unresolved shock will lead to the third hit, the global increased permeability syndrome? We need to move our targets and adapt our goals. Is there an additional effect of early removal of fluids or should we go from early goal directed treatment to late conservative treatment, to late goal directed fluid removal. How should we guide our fluids, should we use barometric or volumetric preload indices? Is there a place for PAL in the de-resuscitation phase? How can we get the right answers to the 4 basic questions: 1. when do I start giving fluids (this about the safety of fluids), 2. when do I stop giving fluids (this is about the risks of fluids), 3. when do I start to empty the patient (this is about the safety of removing fluids), and finally 4. when do I stop emptying the patient (this is about the risks of removing to much fluids)? Old habits die hard but does the good old central venous and capillary wedge pressures still hold against the new volumetric armamentarium? When are barometric indices of preload not working? Why are static filling pressures useless as resuscitation endpoint since they may lead to under- or futile over-resuscitation? Why are volumetric indices better in conditions of increased intrathoracic pressure? ***Introduction and background*** During the 1st iFAD we learned about preload and fluid responsiveness as being two different things [16—18]. In certain situations like increased intrathoracic pressure or increased intra-abdominal pressure (IAP) our traditional barometric filling pressures like the central venous pressure (CVP) or pulmonary artery wedge pressure (PAWP) are erroneously increased [1, 8]. In those circumstances volumetric preload indices like global enddiastolic volume index (GEDVI), right ventricular enddiastolic volume index (RVEDVI) or left ventricle enddiastolic area index (LVEDAI) better reflect the true preload conditions of the patient. Since increased IAP has an impact on the global ejection fraction (GEF), correction of GEDVI in relation to the GEF may further improve the predictive value of this preload parameter [12]. Fluid management in these patients can be very tricky because adequate early initial resuscitation is mandatory however in order to prevent secondary abdominal hypertension one must avoid ongoing futile (crystalloid) fluid loading [4, 5, 9, 14, 15]. We will illustrate opposite changes between CVP and GEDVI in a patient with increased IAP [11]. In order not to do any harm to the patient we need to find answers to the 4 basic questions: 1. when do I start giving fluids, 2. when do I stop giving fluids, 3. when do I start to empty my patient, and finally 4. when do I stop emptying? ***Patient history*** A 55 year old man with a previous history of acute myeloid leukemia was admitted to the ICU because of acute respiratory failure. He had gained 7kg in weight the previous week on the ward where he was diagnosed as having a gastro-enteritis related to the chemotherapy (cytosar). His CVP measured on the ward was 32 cmH_2O. The tentative diagnosis hence was acute lung oedema and a bolus of 40 mg frusemide was administered intravenously. ***Initial clinical course*** On admission to the ICU he was in distress with a respiratory rate of 34 breaths per minute. Further examination of his vital signs showed a core temperature of 34.4°C, a mean arterial pressure (MAP) of 59 mmHg and a sinus tachycardia of 140 beats per minute. Because of clinical exhaustion and failure of noninvasive mechanical ventilation, he was intubated

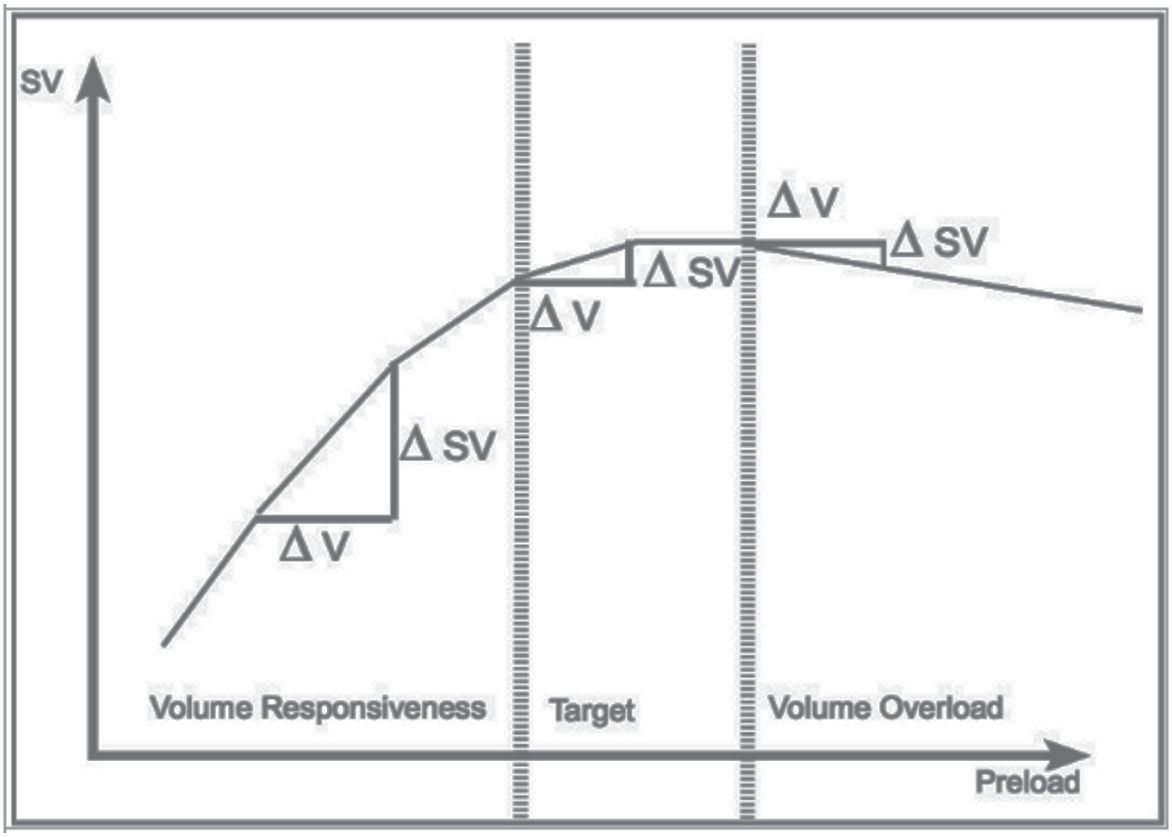

Fig. 1. Relation between preload and stroke volume in different fluid loading conditions

and mechanically ventilated (ventilator rate set at 24×500ml tidal volume, inspiration: expiration ratio 1:1 and a PEEP of 15 cmH_2O) however oxygenation was poor with a pO2/FiO2 ratio of only 115. Breaths sounds were diminished and fine crackles were heard over both lungs. The abdomen was tender, firm and distended with an IAP of 26 mmHg. Neurological and extremities examination were unremarkable, however, the patient was oliguric. A femoral PiCCO catheter (Pulsion Medical Systems, Munich, Germany) was inserted and confirmed the diagnosis of septic shock with a cardiac index (CI) of 5.1 l/min/m2 (normal range 3.0—5.0) and low systemic vascular resistance index (SVRI). The CVP measured invasively was 24 mmHg with a stroke volume variation (SVV) and pulse pressure variation (PPV) of 16% and 18% respectively and a GEDVI of 650 ml/m2, confirming intravascular underfilling and fluid responsiveness, despite the high CVP. Blood cultures grew *Enterococcus faecalis* and *Clostridium difficile* toxins were positive on a recent stool sample. The patient's MAP was initially responsive to fluids together with inreasing doses of noradrenaline up to 1μg/kg/min and dobutamine up to 15 μg/kg/min, however he soon became anuric and the cumulative fluid balance was positive for another 12 l. Due to ongoing fluid resuscitation and profound capillary leak his pO2/FiO2 ratio further deteriorated to 75. At that time CVP was 29 mmHg, MAP 65 mmHg, both SVV and PPV were 14%, GEDVI was 780 ml/m2, IAP 28 mmHg, but extravascular lung water index (EVLWI) had increased from 12 initially to 19 ml/kg predicted body weight (PBW). ***Further clinical course*** The patient was diagnosed having an abdominal compartment syndrome (ACS) due to abdominal sepsis related to the toxic megacolon caused by diffuse clostridium difficile pseudomembraneus colitis. According to the consensus definitions report of the World Society on Abdominal Compartment Syndrome (WSACS, www.wsacs.org) ACS is defined as an acute increase in IAP above 20 mmHg with new onset organ failure [2]. On abdominal CT scan the caecum diameter was 18 cm with wall thickening up to 3.5 cm, the whole colon was infiltrated and dilated. In fact the whole colon was one huge abscess. Therefore the option was taken to perform a total colectomy and decompressive laparotomy with temporal abdominal vacuum assisted fascial closure. After decompression, despite the good CI and SVV and PPV parameters the patient was put on continuous venovenous hemofiltration (CVVH) with aggressive ultrafiltration combined with hyperoncotic albumin 20% substitution because of the high EVLWI and low pO2/FiO2 ratio. Within this regard it is important to notice that higher opening pressures are needed to recruit the lungs and higher PEEP values are needed to prevent collapse at endexpiration [20]. Over the following days his condition improved with a decrease in IAP to 16 mmHg and EVLWI to 13 ml/kg and a concomitant rise in pO2/FiO2 ratio to 175. The CVP remained stable at 18 to 22 mmHg while SVV and PPV normalised to values ranging from 9 to 12%. The abdomen was primarily closed on day 9 and the patient could be weaned from the ventilator and was extubated on day 13. The patient was

discharged alive from the ICU after 22 days. ***Take-home messages*** Traditional filling pressures are erroneously increased in situations of high intrathoracic pressures (related to IAP or PEEP). In this situation enddiastolic volumes are better preload indicators. Normal values of GEDVI and EVLWI in surgical and septic patients have been described in a recent meta-analysis [6]. The PPV and SVV are not indicators of preload but rather markers of fluid responsiveness (in fully ventilated patients with a tidal volume above 6ml/kg and in regular sinus rhythm). Pay attention to the fact that increased IAP may increase baseline values of SVV and PPV, so higher thresholds may be needed in order to define fluid responsiveness [10]. Therefore one can start to give fluids when GEDVI (and GEF-corrected GEDVI) is low and PPV and SVV are high. However, before giving any fluids one must always assess fluid responsiveness with the passive leg raising (PLR) test or the end-expiratory occlusion (EEO) test taking into account that IAP may also have an impact on the interpretation of these tests [7, 13, 19]. Figure 1 illustrates the relationship between preload and stroke volume (SV) in different loading conditions. Measurement of flow (CI) alone does not allow you to discriminate between over- and underfilling. One must stop filling when GEDVI (or GEF corrected GEDVI), SVV and PPV return to normal or when EVLWI starts to increase above 10 ml/kg PBW. After the initial resuscitation phase an even more important question that needs to be answered is: "when to stop filling?" EVLWI can guide you to get rid of the excess fluids by initiating diuresis with frusemide or starting CVVH with ultrafiltration as was recently shown [3]. So I start emptying my patient when IAP or EVLWI increase and when the daily or cumulative fluid balance is positive. Finally one must stop emptying the patient when IAP and EVLWI normalise, when cumulative fluid balance gets close to zero, or hen central venous oxygen saturation (ScvO2) decreases. Off course if hepatosplanchnic perfusion is compromised (as evidenced by a low plasma disappearance rate of indocyanine green) one must stop emptying the patient since a dry liver leads to a dead patient!

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What's all that dancing about? Measuring fluid responsiveness

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Learning objectives What are the tools we have at our disposal to keep the fluid therapy in control? Is the patient really in need for extra fluid? How can you tell? What defines a fluid responder? Why can a fluid challenge be dangerous for the patient? Can we always trust the passive leg raising test? Is there any difference in the prognostic value between SVV, PPV or SPV? Can we use the respiratory systolic variation test at the bedside? When do we use them? What about noninvasive, noncalibrated devices to measure cardiac output? How less invasive can one go in a septic patient under vasopressors? Can we use new techniques like electric impedance or finger cuff pressure in ICU patients? Do we need a specific device for a specific patient? How can we assess fluid responsiveness? How can we avoid fluid overload? Low preload ≠ give fluids Fluid responsiveness ≠ low preload, fluid responsiveness ≠ give fluids! How can I assess whether the patient needs fluids anyhow? What are the limitations for using functional hemodynamics? Can I use it in a patient with right heart failure, arrythmias, low tidal volume, spontaneous breathing? Do we need new thresholds for fluid responsiveness in conditions of increased intrathoracic or intraabdominal pressure? What is there beyond PPV, SVV and SPV? Can we use PVI or FRI? Has a low SVV any meaning in patients with atrial fibrillation? Should I perform a passive leg raising test and tele- or endexpiratory occlusion test in all patients and what are the limitations? ***Introduction and background*** Predicting which patients with an acute circulatory failure will respond to fluid by a significant increase in cardiac output is a daily challenge, in particular in the setting of intensive care units. This challenge has become even more crucial since evidence is growing that administering excessive fluid amounts is at risk in critically ill patients, in particular in patients with lung injury. However, some tests and indices allow to predict fluid responsiveness before deciding to administer volume expansion. ***Methods*** PubMed review. ***Results and main message*** The analysis of respiratory variation of stroke volume has received the largest level of evidence, but heart-lung interaction indices cannot be used in cases of spontaneous breathing activity, cardiac arrhythmias, low tidal volume and low lung compliance. Some more recently developed tests, such as the end-expiratory occlusion test, the "mini" fluid challenge and the passive leg raising test. These tests can be used as alternative methods solving the problem of prediction of volume responsiveness in cases of spontaneous breathing activity and/or cardiac arrhythmias. The ideal management of fluid therapy should also include a precise assessment of the effects of volume expansion on cardiac output and tissue oxygen consumption. It should also take into consideration indices alerting about the risk of fluid overload, like extravascular lung water estimated by transpulmonary thermodilution. ***Take-home message*** There is a growing corpus of evidence suggesting that overzealous fluid administration is deleterious in critically ill patients, particularly in cases of sepsis and/or lung impairment. During the past years, several tests have been developed to detect volume responsiveness before administering fluid.

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The Black Box Revelation: What's new in neuromonitoring?

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Learning objectives There are many critical care conditions in which the brain is not working properly. Whatever the underlying cause, determining precisely which aspects of brain function are affected and how best to manage the neurological dysfunction can often be difficult. Invasive and non-invasive methods monitor different aspects of the brain function. Neuromonitoring have evolved considerably in recent years and now play an important role in the care of patients with brain injury. In this lecture we will review different neuromonitors available today. ***Introduction and background*** No monitor will improve outcome by itself. Neuromonitoring will contribute to enhanced recovery only if the physiologic data are integrated into a patient care plan. The aims of "neuromonitoring" can be considered to be: 1. Improving pathophysiological understanding of cerebral disease in critical illness; 2. Identification of deteriorating neurological function and secondary insults that may benefit from specific treatments; 3. Providing clear physiological data to guide and individualize therapy; 4. Assisting with

prognostication. ***Results and main message*** Different technologies are available and each monitor will measure one or more parameter (pressure inside the skull, cerebral blood flow, oxygen availability or consumption, electrical activity, metabolites…). There is no "ideal" single brain monitor. A combination of monitoring techniques, selected accordingly to the pathophysiological derangement, may provide better insight into brain function than a single monitor used alone. If an increased intracranial content is suspected clinically and after neuroimaging, intracranial pressure is the adequate monitoring system Although non-invasive evaluation of ICP is possible using the transcranial Doppler (TCD)-derived pulsatility index or optic nerve sonography, the only methods for continuous on-line monitoring of ICP remain invasive. ICP is generally accepted as a relatively low-risk, and high-value, monitoring in severe cases with abnormal CT scan. In neurocritical care patients we need to take also cerebral perfusion pressure (CPP) into account. Using an ultrasound probe, flow velocity (rather than flow itself) can be measured non-invasively. Recently, continuous measurement of regional CBF is now possible using a thermal diffusion probe inserted into the brain parenchyma and may help identify and possibly prevent brain ischemia. Several techniques can be used to measure brain oxygenation, the most common in the ICU being jugular venous bulb oximetry and direct $PbtO_2$ measurement. Computerized system will allow the clinician to integrate information coming from different devices and to have a better understanding of the cerebral conditions. ***Take-home message*** 1. Monitoring of brain function should be considered in all comatose patients in the ICU. 2. No monitor will improve outcome itself and will only contribute to enhanced recovery if the output physiologic data are integrated into a beneficial patient care plan. 3. There is no "ideal" single brain monitor; a combination of monitoring techniques may provide better insight into brain function than a single monitor used alone.

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Magic is in the air. Monitoring the respiratory system

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Open questions The respiratory system is fascinating, however in the critically ill many questions remain unanswered: How can we assess and quantify lung function, ventilation and oxygenation? What is the importance of extravascular lung water (EVLWI) and pulmonary vascular permeability (PVPI) at the bedside? How can I measure work of breathing? Do I need trans-diaphragmatic pressures? Should I titrate my PEEP based on esophageal pressure or gastric pressure or both? What about transpulmonary pressures? How can I measure lung and chest wall compliance at the bedside? Is there a place for bioelectrical-impedance analysis (BIA) or bioreactance or bicore? Promising techniques for the future like electrical impedance tomography (EIT): are they an interesting tool or just another gizmo? What are the indications for chest ultrasound? When will I have a portable CT? How can we monitor lung oedema and is it of any importance? Do clinical parameters like chest X-ray or P/F ratio correlate with lung water? What is the gold standard for measurement of increased permeability? Is EVLWi increased in patients with pleural effusions or atelectasis? Can we integrate different monitoring tools, eg ventilator and hemodynamic monitor? How do the different body compartments interact? How to deal with therapeutic dilemmas: kidney *vs* lung; lung *vs* liver; brain *vs* lung; heart *vs* lung? Can we measure lung recruitment or ventilation/perfusion (mis)match at the bedside? What are the indications for ECMO or extracorporeal CO_2 removal?***Learning objectives*** Whereas EVLWI is frequently recommended to titrate volume management in patients with acute respiratory distress syndrome (ARDS), recently esophageal pressure and intra-abdominal pressure (IAP) have been recommended to titrate ventilator settings. Electrical impedance tomography of the thorax has now been introduced as a new imaging and monitoring technology of the lungs. The purpose of this lecture is to review and discuss methodological and clinical aspects of esophageal pressure, IAP, EVLWI, and EIT. This includes a review on the working principle of EIT, the validity of measurements of pulmonary aeration and ventilation, pulomary perfusion and cardiac stroke volume, and the use of EIT and

esophageal pressure and abdominal pressure guiding ventilatory settings. ***Background*** Functional electrical impedance tomography (EIT) of the lung noninvasively measures relative impedance changes in the lung tissue during tidal breathing and creates images of the local ventilation distribution at bedside. In addition, there is increasing evidence that EIT may even be capable of assessing regional pulmonary perfusion. Hence, it is expected to become a valuable tool to individually improve ventilatory settings. However, EIT provides complex regional information which is difficult to interpret. Consequently, current research focuses on novel approaches to analyze and quantify EIT data in the spatial as well as in the temporal domain. ***Methods*** Based on recent literature, we will review and discuss methodological and clinical aspects of esophageal pressure and abdominal pressure EVLWI, EIT when used as monitoring tools in the intensive care unit (ICU) [1—6]. ***Results and main message*** EIT is well validated to determine regional ventilation in healthy and injured lungs. New approaches, such as the regional ventilation delay index, focus on analyzing and interpreting the complex information in the spatial as well as in the temporal domain. Promising findings suggest that EIT can be used to monitor regional lung mechanics, collapse, recruitment and probably even overdistension. Whereas indicator-free EIT measurements might be sufficient for the continuous measurement of cardiac stroke volume, data on the assessment of regional lung perfusion are currently limited. Currently, no large scaled studies tested if esophageal pressure and abdominal pressure EVLW, EIT are advantageous to titrate fluid management or mechanically ventilation in critically ill patients. ***Take-home message*** EIT has the potential to play an important role in individually optimizing ventilator settings in critically ill patients. Clinical studies are necessary to evaluate the role of EIT in routine care of critically ill patients.

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Looking beyond heart and kidney! Solving the cardiorenal dilemma...

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Learning objectives Should I use NGAL and cystatine C or troponine I and BNP? What is the pathophysiology of cardiorenal dilemma or should I call it cardio-abdomino-renal syndrome (CARS)? What are the treatment options? Is there a place for diuretics or do I need aggressive ultrafiltration? Is urine output important or just a by-product? What is the role of the right heart, the CVP and the IAP? How to diagnose and what are the best imaging tools for CARS? ***Introduction and background*** Historically, poor forward flow – i.e. low cardiac output – resulting in unrestrained neurohumoral upregulation, has been considered as the main culprit mechanism of congestive heart failure (CHF). However, growing evidence has emphasized the concurrent importance of backward failure – i.e. systemic congestion – both in pathophysiology and disease progression. Coexisting renal dysfunction often complicates the treatment of advanced CHF and is more frequent in patients with elevated cardiac filling pressures. Nevertheless, current pathophysiological models unsatisfactorily explain the detrimental link between congestion and cardiorenal function. ***Results and main message*** Abdominal congestion, i.e. splanchnic venous and interstitial congestion, manifests in a substantial amount of patients with advanced heart failure. Compromised capacitance function of the splanchnic vasculature, impaired abdominal lymph flow resulting in interstitial edema, dysfunction of congested abdominal organs, impaired intestinal barrier function and endocrine effects of gut derived hormones or toxins could all be implied in subsequent disease progression and the pathophysiology of cardio renal dysfunction. Several important features of abdominal congestion contribute to the impaired natriuretic capacity of the kidneys in congestive heart failure. Decreased renal blood flow, resulting in excessive fractional reabsorption of sodium in the proximal tubules of the nephron might partly explain diuretic resistance, secondary hyperaldosteronism, and loss of response to endogenous natriuretic peptides. Therefore, a more thorough understanding of abdominal congestion, and traditional concepts on renal physiology should lead

to better treatment strategies to break the vicious cycle of abdominal congestion leading to impaired sodium excretion and further systemic congestion in heart failure. ***Take-home message*** Understand potentially important derangements in the abdominal compartment affecting cardiorenal efficiency in advanced CHF. Importantly, get a good understanding that abdominal congestion might account for the state of impaired natriuresis that is characteristic for advanced CHF and "CardioRenal Syndrome". Provide insights into compelling arguments to explain diuretic resistance, secondary hyperaldosteronism and loss of response to endogenous natriuretic peptides, which might lead to alternative – more pathophysiologically based – treatment strategies, aiming to relieve congestion while preserving renal function.

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The future of monitoring starts today: Capturing capillary leak

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Learning objectives What is the place for Orthogonal Polarization Spectral (OPS) Imaging or should I use Sidestream Dark Field (SDF) Imaging instead? How can we monitor the microcirculation? Is there an edema meter or should I use Glycocheck? How can we quantify capillary leak at the bedside? How to measure increased permeability? Should I use scintigraphy or is there a lab parameter that I can use like the capillary leak index (CRP divided by albumin?)***Introduction and background*** The administration of fluids resulting in hemodilution, although highly affective in increasing intravascular volume under conditions of hypovolemia may result in many alterations in the determinants of microcirculatory function and tissue oxygenation all of which can be regarded as deleterious. These include changes in oxygen content, viscosity, flow redistribution, sheer stress, oxygen consumption, altered red blood cell deformability, coagulation and in the activation of inflammatory and oxidative stress pathways. These properties of fluids indeed classify fluids as drugs in the same way as insulin and steroids are regarded. The various properties of fluids affect the homeostasis of oxygen transport at the microcirculatory level necessary to maintain optimal tissue oxygenation leading to cell and organ dysfunction. ***Results and main message*** We performed investigations using techniques aimed at measuring the perfusion and oxygenation of the microcirculation in various organ systems in clinically relevant animal models. Here we found that hemodilution, although giving the impression from the macrocirculation that oxygen transport is well maintained, causes diffusional shunting and regional dysoxia. This response was found to be organ dependent with the heart being most resilient to hemodilution and the kidney most sensitive [1]. In fact hemodilution in the kidney was found to result in enhanced oxygen consumption and cause the kidney to go into oxygen supply dependency already on the first step of isovolemic hemodilution. In addition fluids caused degradation of the glycocalyx layer, induced oxidative stress and inflammatory activation irrespective of the type of fluids [2]. In clinical investigations we performed in cardiac surgery and anemic hematological patients using direct observation of the perfusion of the sublingual microcirculation using hand held microscopes and measurement of the microcirculatory oxygen availability by use of sublingual spectrophotometry, we studied the reaction of the microcirculation to hemodilution and blood transfusions [3]. In the scenario of hemodilution we found a massive reduction in the functional capillary density associated with capillary fall out, together with a rise in oxygen content of the remaining red blood cell filled capillaries to occur. Thus hemodilution causes regional hypoxia in the microcirculation associated with increase in diffusion distances to the cells. Fluids with increased viscosity such as starches are much better in recruiting the microcirculation than less viscous fluids such as crystalloids [4]. Blood transfusions being such a viscous fluid causes a recruitment of previously unfilled capillaries [3]. Indeed we showed in experimental studies that even though fluids can improve systemic hemodynamic variables, blood is essential for realization of tissue oxygenation especially in the kidney [5]. In conclusion fluids although affective in increasing circulating volume if administered in inappropriate volumes cause hypoxemia, induce oxidative

stress and inflammation. ***Take-home message*** We suggest that the monitoring of the microcirculation provide the optimal monitor for titrating fluids as both convection (hypovolemia) and diffusion (hypervolemia) limitation of the circulation can be quantified thereby providing suitable optimal end-points for fluid administration. Newly introduced computer controlled hand held bedside microscopic monitoring devices is expected to bring closer this technology from research tool to a clinical monitoring device [6].

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Reaching the target (Part 2)

From eyeballing to closed loops! Perioperative fluid optimization

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Learning objectives What are our tools to guide fluid therapy during the peri-operative period? Should I use minimal invasive hemodynamic monitoring in all patients? Should I use volumetric or barometric indices and what about Doppler or echo? Should I still use a Swan-Ganz or rather transpulmonary thermodilution? What outcome parameter should I use to assess my performance? ***Perioperative fluid management: from gut feeling to closed loops*** In the Sceptic's Medical Dictionary [1] – an iconoclastic book I highly recommend – Michael O'Donnell defines clinical experience as "Making the same mistakes with increasing confidence over an impressive number of years". Although very provocative, this statement is sometimes not so far from reality when considering intra- and post-operative fluid management. For decades, the decision to give fluid was based on clinical examination, heart rate and blood pressure (a high heart rate and a low blood pressure often triggering a fluid bolus), when not simply on the gut feeling of the good doctor. Unfortunately, tachycardia and hypotension are not specific and sensitive markers of hypovolemia nor of fluid responsiveness. ***The value of dynamic parameters*** Dynamic parameters (PPV, pulse pressure variation & SVV, stroke volume variation) are today available on almost all bedside and haemodynamic monitors and have dramatically changed the way clinicians think and give fluid. Several studies have demonstrated that their intra-operative measurement and optimization was useful to improve post-operative outcomes. However, dynamic parameters have limitations precluding their use in several clinical situations. The main limitations to the use of dynamic parameters in surgical patients have been recently summarized as "SOS" [2]. The first "S" stands for Small tidal volume and Spontaneous breathing activity; the "O" stands for Open chest. The second "S" stands for Sustained cardiac arrhythmias. Other limitations do exist but are less frequently encountered such as right ventricular failure and a high respiratory rate. Finally, questions remain regarding the usefulness of dynamic parameters in other clinical situations such as laparoscopic procedures (they may still be valuable but likely with different cut-off values). A recent study based on the analysis of more than twelve thousand patients showed that dynamic parameters are usable in 39% of all surgical patients, and in 53% of patients with an arterial line (a common scenario for high-risk procedures where optimal fluid management is key). ***The future of peri-operative fluid therapy*** When dynamic parameters cannot be used, alternatives do exist. The simplest one consists in administering a fluid bolus of 200-250 ml and in quantifying the effect on stroke volume. If stroke volume does increase in response to the bolus, the patient is obviously fluid responsive (his SVV and PPV values would be high if they were usable). In the UK, this approach is now recommended by the National Institute for Clinical Excellence (NICE) to guide fluid therapy in high-risk surgical patients. Similar recommendations have been made in October 2011 by the French Society of Anaesthesiology (SFAR) and we can reasonably assume that other scientific societies will follow. These recommendations are based on multiple single centre randomized controlled trials and on several meta-analyses [3]. Whether clinicians will quickly adopt peri-operative fluid optimization strategies is another story. The availability of new and less/non invasive technologies facilitating stroke volume monitoring, such as oesophageal Doppler and pulse contour methods, should help but may not be sufficient [4]. Indeed, despite the existing body of scientific evidence,

uncertainty remains for some clinicians. Large scale clinical studies as well as quality-improvement programs confirming the benefits of such strategies may help to resolve their uncertainty (5). Another challenge will be the adherence to treatment protocols in a very busy environment where priority is given to anaesthesia and analgesia (6). Teaching and training will play a major role and the use of (paper or electronic) checklists may further help. Ultimately, the development of closed-loop systems may unload anaesthesiologists from this task and ensure an optimal compliance to fluid optimization treatment protocols (6).

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Measuring the gut feeling! Latest news on abdominal pressure monitoring

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Learning objectives When should I measure intraabdominal pressure (IAP)? What is the right target for abdominal perfusion pressure (APP=MAP-IAP) in my patient? How can I measure abdominal compliance and do I need it? What is a tensiometer? Is clinical examination or the use of an abdominal perimeter accurate and useful? What is the impact of body mass index, body positioning and PEEP on IAP? Is intra-abdominal volume important? Is the abdomen a hydraulic container that follows Pascal's law? What is the place for ultrasound and CT. In this lecture an overview will be given of the different direct and indirect techniques, from basics (with foleymanometer) to advanced microchip transducers. What is the role of the polycompartment syndrome in assessing compartmental pressures?***Introduction and background*** Intra-abdominal hypertension has been recognized as a source of morbidity and mortality in many different settings. Intra-abdominal pressure monitoring is the method of choice to diagnose, quantify and follow up patients at risk for and diagnosed with abdominal compartment syndrome. Tools for IAP monitoring are becoming standard tools in critical care, and proper knowledge of the essentials of IAP monitoring is key to allow appropriate treatment decisions, also in more difficult situations.***Methods*** Review of contemporary literature on IAP monitoring and integration in clinical practice as seen through the eyes of the bedside clinician, resulting in physiology-based IAP measurement guidelines. ***Results and main message*** Awareness of IAH as a cause of organ dysfunction has greatly increased, as was demonstrated in recent questionnaires.Gold standard for IAP measurement remains the transvesicular method, with 20mL of saline as standard instillation volume. Newer methods have focused largely on ways to measure IAP via the stomach using both conventional and more advanced technology such as wireless remote capsules or pressure transducers incorporated into nasogastric tubes. The gastric route remains controversial as most studies found considerable differences between the transgastric route and conventional measurement, limiting the use of the stomach for IAP measurement based on the available evidence. The latter could not be said from direct intraperitoneal measurement. Although this requires surgical inserted catheters, in patients on continuous peritoneal dialysis the peritoneal catheter can be used for reliable IAP measurement. Other interesting advances include the use of microdialysis catheters inserted in the rectus abdominis muscle to early detect subclinical organ dysfunction; clinical implications at this stage remain elusive.Femoral pressures cannot be used as a surrogate for IAP.Positioning can affect IAP measurement, especially when the head-of-bed (HOB) is elevated for 30 degrees or more as shown in several large clinical studies. It remains unclear to what extent this is a measurement effect with limited clinical consequences due to changes in hydraulic forces, or really increases the IAP with the potential to affect organ function.Proning also has consequences for IAP measurement, but probably even more relevant is the effect of releasing the abdomen when putting the patient in prone as this may result in decrease abdominal compliance. PEEP only minimally affects IAP and should not be considered as contributing significantly to IAH.Obesity and pregnancy are conditions in which patients have a higher baseline IAP; in obesity there is a more or less linear relation with BMI and IAP of 15mmHg may be perfectly normal in these subjects.As IAP is used more widely in different settings, knowledge of the pitfalls in IAP measurement is most relevant. These include conditions in which IAP measurement is not reliable such as space occupying lesions in the pelvis such as fracture, hematoma, among others. Care should also be taken that IAP is measured at end expiration, in conditions without any spontaneous abdominal muscle activity, which can be impossible in a critically ill patient. Patients who respiratory insufficient may use their abdominal muscles as secondary muscles for respiration resulting in a high IAP of which the clinical relevance is uncertain. Routine IAP measurement in all ICU patients or all mechanically ventilated patients is probably not necessary. Selective IAP measurement in subgroups such as patients with the need for vasoactive drugs, PEEP >10 cmH_2O, PaO_2/FiO_2 ratio <300, pancreatitis, hepatic disease with ascites, GI bleeding, burns (BSA>40%), large volume

resuscitation or after emergency laparotomy will allow early detection of clinically relevant IAH or ACS in most circumstances. Obviously, in case of clinical deterioration even in not ICU admitted patients (e.g. hypotension, oliguria, respiratory insufficiency) the presence of IAH should be considered, and IAP measured when the risk for IAH is deemed pertinent.***Take-home message*** IAP measurement has evolved from an illustre technique using self-assembled measurement kits to a readily available, reliable and reproducible tool in modern critical care units. Several conditions may affect baseline IAP; similarly, treatment modalities in the ICU can also results in IAP measurement changes. Risk factors for IAH have now better been described allowing for selective IAP measurement with maximal efficiency.

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Should we only think green? Update on hepatosplanchnic monitoring

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Learning objectives Is there still a place for gastric tonometry? When to use echo-doppler to assess the liver and portal veins? Is the indocyanine green plasma disappearance test (ICG-PDR) a measure of liver function or just an indicator of hepatosplanchnic flow? Do I need to know the cardiac output when assessing ICG-PDR? Is there a place for citrulline or I-FABP measurements? What is the place of standard liver function tests and venous ammonia? Is there anything new on the horizon? ***Introduction and background*** Tissue hypoxia in the gastrointestinal tract may occur even under circumstances of normal indices of global perfusion and oxygenation. Mucosal hypoxia will lead to loss of gastrointestinal barrier function and increased risk of bacterial translocation and distant organ failure. Monitoring of various aspects of liver function in the critically ill is usually limited to static blood test. However, dynamic tests may reveal otherwise hidden hepatocellular dysfunction. At present, conventional monitoring does not maximize timely or differential detection of liver or GIT dysfunction and does not allow for short-term monitoring of selective therapeutic targets. The present talk will evaluate the current state of options for hepatosplanchnic monitoring. ***Methods*** Pubmed review of pertinent peer-reviewed articles. ***Results and main message*** Imaging techniques for monitoring of the hepatosplanchnic region include Duplex Doppler ultrasound (DDUS), MRI, CT scanning and the still experimental endoluminal laser Doppler flowmetry. For the critically ill patient, only DDUS is of practical use but limited to static evaluations of patency of hepatic artery and portal vein. Monitoring of the gastrointestinal tract may include (cumbersome) repetitive measurements of intestinal permeability and serial determinations of biomarkers of enterocyte mass or dysfunction. The former still rely mainly on urinary determinations of orally delivered disaccharides and are of very limited clinical value outside research protocols given the lack of directed intervention to ameliorate increased intestinal permeability. Low levels of plasma citrulline and high levels of intestinal fatty acid binding protein seem promising for diagnosing enterocyte necrosis. Beyond this potential diagnostic utility, increasing levels of citrulline may also serve as dynamic marker for therapeutic interventions. Potential monitoring in the ICU of various aspects of hepatocellular liver function include tests for elimination capacity (galactose), for metabolite formation (Lidocaine) and of perfusion and function (indocyanine green clearance). Each of these has drawbacks. Short-term changes in the plasma disappearance rate of ICG (ICG-PDR) reflect change in blood flow rather than hepatocellular function and as such is the only test that allows for true interventional monitoring. ***Take-home message*** There is still a lack of evidence-based, dynamic methods to monitor therapeutic interventions aimed at improving the function the hepatosplanchnic region. The combination of Citrulline and I-FABP hold promise as diagnostic biomarkers for enterocyte dysfunction or necrosis, IGC-PDR is at present the only technique that allows dynamic, short-term evaluation of hepatic blood flow.

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The Honorary IFAD Closing Lecture: Engineering the Superfluid

Mythen M

Learning objectives What's in the pipeline in fluid management? Pushing the Boundaries! What's beyond the Final Frontier? The fluid therapy of the future! Do the newer fluids have additional properties beyond correcting volume deficits? Can they avoid or even treat capillary leak with a so-called sealing effect? Are there relevant anti-inflammatory effects? Do we have to shift our attention from the macro- to the microcirculation? What will the ideal fluid look like? Should it be a balanced crystalloid solution with a SID of 24 to avoid hyperchloremic metabolic acidosis? Should it be a hypertonic or hyperoncotic solution like albumin 20% to avoid a positive cumulative fluid balance? Should it be a colloid to remain in the plasma for a longer time? Should the ideal fluid be seen as a drug, with the least possible side effects on liver and kidney function and coagulation? Is blood the ideal fluid since it is the only fluid available that carries oxygen and promotes oxygen transport to the tissues? Is the ideal fluid, the fluid that is not administered to the patient? Or are we stuck with saline forever?