

SPECIAL SUPPLEMENT

in collaboration with CSL Behring

# Shock

Pathophysiology of endotoxic shock, *F. Forfari et al.*

Fluids in shock, *M. Cecconi et al.*

It is time for improved fluid stewardship, *M. Malbrain, T.W. Rice, M. Mythen, S. Wuyts*

Vasoactive medication and RCTs, *J. Gutteling & A.R.J. Girbes*

Advances in source control in patients with sepsis and septic shock, *J.J. De Waele & I. Martin-Loeches*

Organ cross-talk in shock and critical illness, *J.R. Prowle*

POCUS and SHOCK, *A. Wong & J. Wilkinson*

## PLUS

Xenon limits brain damage following cardiac arrest, *M. Maze & T. Laitio*

What's new in sepsis in children? *E. Esteban et al.*

Optimising sleep in the ICU, *M.C. Reade & D. Liu*

Cancer patients in the ICU, *I. Prieto del Portillo et al.*

What should we stop doing in the ICU? *F.G. Zampieri*

Caring for very old patients in the ICU, *H. Flaatten*

The sepsis box, bag and trolley, *C. Hancock & A. Hermon*

Humanizing the ICU experience with enhanced communication, *A. Rocher*

Implementing ECCO<sub>2</sub>R and vv-ECMO in non-academic centres, *K. Kogelmann*

Improving access to safe anaesthesia, *J. Mellin-Olsen*



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The primary goal of fluid stewardship is to optimise clinical outcomes while minimising unintended consequences of intravenous (IV) fluid administration. This article sets the stage for a conceptual framework for developing institutional programmes and guidelines to enhance fluid stewardship (especially in the ICU environment), an activity that includes appropriate selection, dosing, duration, de-escalation, and monitoring of fluid therapy. In patients with septic shock, haemodynamic stabilisation using fluids is a major challenge because clinicians are faced with many unresolved questions. It is clear that clinicians regard intravenous fluids like prescription drugs and should take into account the indications and

# It is time for improved fluid stewardship

A conceptual framework for developing institutional programmes and guidelines to enhance fluid stewardship (especially in the intensive care unit [ICU] environment), an activity that includes appropriate selection, dosing, duration, de-escalation, and monitoring of fluid therapy.

contraindications (Perner et al. 2012; Van Regenmortel et al. 2014; Malbrain et al. 2012; Myburgh et al. 2012; Guidet et al. 2012; Annane et al. 2013), as they may affect patient-centred outcomes (Myburgh and Mythen 2013). Clinicians should also consider not only the risk of administering too little, but also too much fluid, as the deleterious consequences of fluid overload become better established (**Figure 1**).

## 1. Definitions

It is important to precisely define the various terms commonly used in the context of fluid management to describe fluid balance, fluid overload, different dynamic phases during fluid therapy, and different types of fluids; these definitions are partially based on published conceptual models (Van Regenmortel et al. 2013; Myburgh and Mythen 2013; Hoste et al. 2014; Vincent and De Backer 2013; Malbrain et al. 2014; Vincent and Pinsky 2018).

## 2. The four Ds of fluid therapy

Many clinicians consider specific aspects when dealing with antibiotics: different classes, spectrum, toxicity, dose, compounds. Likewise, prescription of intravenous fluids should proceed with the same caution, taking into account the compounds, pharmacodynamic and pharmacokinetic properties of different fluids. Another way of conceptualising this is considering the "four Ds" of fluid therapy when treating patients with septic shock: drug, dosing, duration, and de-escalation (**Table 1**) (Malbrain et al. 2015). Fluid misuse, like antibiotic misuse, almost certainly has severe consequences for the patient.

### 2.1. Drug

#### 2.1.1. Inappropriate therapy

All resuscitation, replacement and even mainte-

nance fluids can contribute to the formation of interstitial oedema, particularly in patients with systemic inflammation associated with altered endothelial function (Myburgh and Mythen 2013). For each type of fluid, there are distinct indications: crystalloids vs colloids; synthetic vs blood-derived; balanced vs unbalanced; intravenous vs oral.

Because of their potential risk, **hydroxyethyl starches** are contraindicated in patients with septic shock, burns, acute or chronic kidney injury, or oliguria not responsive to fluids (Rhodes et al. 2017).

**Glucose** water should never be used as resuscitation fluid. Surprisingly, **normal saline**, which does not contain potassium, will result in higher serum potassium levels in patients with renal impairment compared to a balanced solution (lactated Ringer's), which contains 5 mmol/L of potassium, due to concomitant metabolic acidosis secondary to a reduced strong ion difference (SID) (Khajavi et al. 2008; Langer et al. 2015). In an analogy to antibiotic treatment, where inappropriate therapy may result in more organ failure, longer ICU and hospital lengths of stay, longer duration of mechanical ventilation and higher mortality (Ibrahim et al. 2000; Hoffken and Niederman 2002), (ab) normal saline as resuscitation fluid should not be administered in large amounts, as it carries the risk of hypernatraemic hyperchloraemic metabolic acidosis, acute kidney injury (AKI) and possible RRT (renal replacement therapy), and mortality (Semler et al. 2018).

### 2.1.2. Appropriate therapy

Patient risk factors (prior antibiotic use, duration of mechanical ventilation, co-morbidity, hospital length of stay above 5 days, corticosteroids, recent hospitalisation, residence in nursing home,...)

play important roles in the appropriate choice of empiric antibiotics (Kollef et al. 2006). Similarly, patient risk factors (fluid balance, fluid overload, capillary leak, acid-base status, co-morbidity, kidney function, organ function) also play an important role in empiric fluid therapy.

In patients with hypoalbuminaemia and septic shock, **albumin** may be an appropriate resuscitation fluid, especially in the late phase after the initial resuscitation (Rhodes et al. 2016; Caironi et al. 2014).

### 2.1.3. Combination therapy

Possible benefits of antibiotic combination therapy include: broader spectrum, synergy, avoidance of emergence of resistance, less toxicity,...(Tamma et al. 2012). Possible benefits of fluid combination therapy include: specific fluids for different indications (replacement vs maintenance vs resuscitation), and less toxicity.

### 2.1.4. Class

With respect to antibiotic administration, it is important to consider broad-spectrum vs specific narrower coverage classes. The choice of the antibiotic has a real impact on efficacy and toxicity. Likewise, hypotonic or hypertonic fluids, with high or low sodium or chloride level, lactate or bicarbonate buffer, glucose or not, are all equally important aspects of fluid therapy. This will have a direct impact on acid-base equilibrium, cellular hydration and electrolyte regulation.

### 2.1.5. Appropriate timing

Survival decreases 7% with each hour delay of antibiotic administration in patients with septic shock (Kumar et al. 2006). In refractory shock early fluid resuscitation has been proven beneficial in previous studies (Rivers et al. 2001). The longer the delay in fluid administration, the more microcirculatory hypoperfusion and subsequent organ damage (related to ischaemia reperfusion injury). Murphy et al. compared outcomes related to early adequate vs early conservative and late conservative vs late liberal fluid administration and found that the combination of early adequate and late conservative fluid management carried the best prognosis (Murphy et al. 2009).

## 2.2. Dosing

### 2.2.1. Poison

As Paracelsus nicely stated: "All things are poison, and nothing is without poison; only

**Table 1.** Analogy between the 4 Ds of antibiotic and fluid therapy

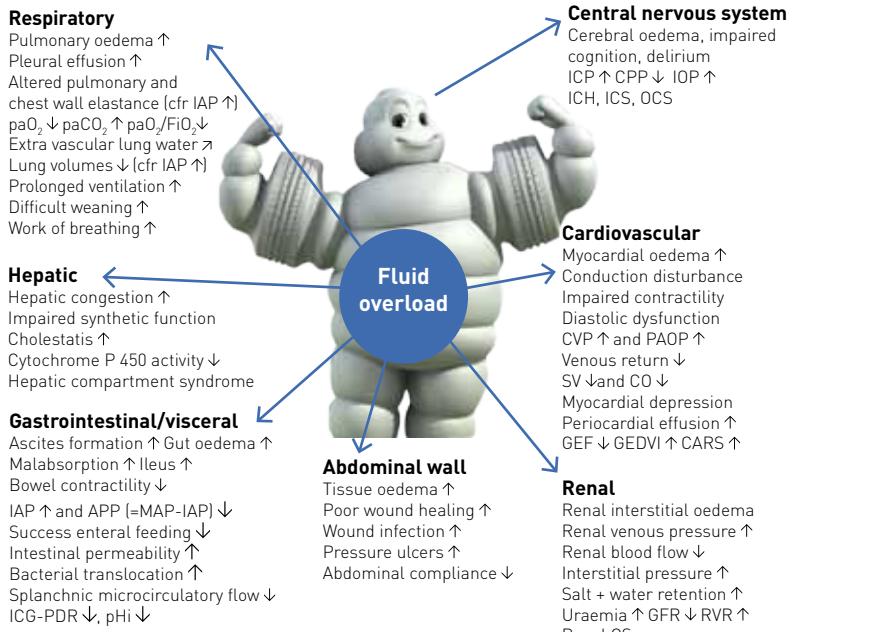
Description	Terminology	Antibiotics	Fluids
Drug	<i>Inappropriate therapy</i>	More organ failure, longer ICU LOS, longer hospital LOS, longer MV	Hyperchloraemic metabolic acidosis, more AKI, more RRT, increased mortality
	<i>Appropriate therapy</i>	Key factor in empiric AB selection is consideration of patient risk factors (e.g. prior AB, duration MV, corticosteroids, recent hospitalisation, residence in nursing home)	Key factor in empiric fluid therapy is consideration of patient risk factors (e.g. fluid balance, fluid overload, capillary leak, kidney and other organ function). Don't use glucose as resuscitation fluid
	<i>Combination therapy</i>	Possible benefits: e.g. broader spectrum, synergy, avoidance of emergence of resistance, less toxicity	Possible benefits: e.g. specific fluids for different indications (replacement vs maintenance vs resuscitation), less toxicity
Dosing	<i>Class</i>	Broad-spectrum or specific, Beta-lactam or glycopeptide, additional compounds as tazobactam. The choice has a real impact on efficacy and toxicity	Hypo- or hypertonic, high or low chloride and sodium level, lactate or bicarbonate buffer, glucose containing or not. This will impact directly acid-base equilibrium, cellular hydration and electrolyte regulation
	<i>Appropriate timing</i>	Survival decreases with 7% per hour delay. Needs discipline and practical organisation	In refractory shock, the longer the delay the more microcirculatory hypoperfusion
	<i>Pharmacokinetics</i>	Depends on distribution volume, clearance (kidney and liver function), albumin level, tissue penetration	Depends on type of fluid: glucose 10%, crystalloids 25%, vs colloids 100% IV after 1 hour, depends on distribution volume, osmolarity, oncoticity, kidney function
Duration	<i>Pharmacodynamics</i>	Reflected by the minimal inhibitory concentration. Reflected by "kill" characteristics, time (T>MIC) vs concentration (Cmax/MIC) dependent	Depends on type of fluid and desired location: IV (resuscitation), IS vs IC (cellular dehydration)
	<i>Toxicity</i>	Some AB are toxic to kidneys, advice on dose adjustment needed. However, not getting infection under control isn't helping the kidney either	Some fluids (HES) are toxic for the kidneys. However, not getting shock under control is not helping the kidney either
	<i>Appropriate duration</i>	No strong evidence but trend towards shorter duration. Don't use AB to treat fever, CRP, or chest x-ray infiltrates but use AB to treat infections	No strong evidence but trend towards shorter duration. Don't use fluids to treat low CVP, MAP, or UO, but use fluids to treat shock
De-escalation	<i>Treat to response</i>	Stop AB when signs and symptoms of active infection resolve. Future role for biomarkers (PCT)	Fluids can be stopped when shock resolves (normal lactate). Future role for biomarkers (NGAL, cystatin C, citrullin, L-FABP)
	<i>Monitoring</i>	Take cultures first, choose empiric AB and tailor when information becomes available	After stabilisation with EAFM (normal PPV, normal CO, normal lactate) stop ongoing resuscitation and move to LCFM and LGFR (=dere-suscitation)

Adapted from Malbrain et al. (2014; 2018) with permission

AB antibiotic AKI acute kidney injury Cmax maximal peak concentration CO cardiac output CRP C reactive protein CVP central venous pressure EAFM early adequate fluid management EGDT early goal-directed therapy IC intracranial ICU intensive care unit IS interstitial IV intravascular LCFM late conservative fluid management L-FABP L-type fatty acid binding protein LGFR late goal directed fluid removal LOS length of stay MAP mean arterial pressure MIC mean inhibitory concentration MV mechanical ventilation NGAL neutrophil gelatinase-associated lipocalin PCT procalcitonin PPV pulse pressure variation RRT renal replacement therapy UO urine output

the dose permits something not to be poisonous." It is the dose that makes the antibiotic poisonous, and the same holds true when it comes to fluid management in the critically ill. The risk of excessive fluid administration leading to an increase in the cumulative fluid balance has been clearly demonstrated (Malbrain et al. 2014), especially in critically ill patients with septic shock (Vincent et al. 2006) and/or

acute respiratory distress syndrome (Jozwiak et al. 2013). Maintenance fluids should be used cautiously and only to cover daily needs when the patient receives no other oral or intravenous fluid intake. Their prescription should take other sources of fluids and electrolytes into account. Therefore when a patient already receives daily needs of water, glucose and electrolytes via other means (enteral or parenteral nutrition,



APP: abdominal perfusion pressure IAP: intra-abdominal pressure IAH: intra-abdominal hypertension ACS: abdominal compartment syndrome CARS: cardio-abdominal-renal syndrome CO: cardiac output CPP: cerebral perfusion pressure CS: compartment syndrome CVP: central venous pressure GEDVI: global end diastolic volume index GEF: global ejection fraction GFR: glomerular filtration rate ICG-PDR: indocyanine green plasma disappearance rate ICH: intracranial hypertension ICP: intracranial pressure ICS: intracranial compartment syndrome IOP: intra-ocular pressure MAP: mean arterial pressure OCS: ocular compartment syndrome PAOP: pulmonary artery occlusion pressure pH: gastric tonometry RVR: renal vascular resistance SV: stroke volume

medication solutions,...) specific maintenance fluids must be stopped.

### 2.2.2. Pharmacokinetics

The principle of pharmacokinetics is very well known during antibiotic administration. Pharmacokinetics (PK) describes how the body affects a drug, resulting in a particular plasma and effect site concentration (Elbers et al. 2015). PK depends on distribution volume, clearance (kidney and liver function), tissue penetration and in some situations also on albumin levels. Increased distribution volume is seen with capillary leak, hypo-oncotic states, extracorporeal circuits, surgical drains, large burns and mechanical ventilation. Pharmacokinetics of intravenous fluids depends on distribution volume, osmolality, tonicity, oncotoxicity and kidney function. Eventually, the half time depends on the type of fluid, but also on the patient's condition and the clinical context. Volume kinetics is an adaptation of pharmacokinetic theory that makes it possible to analyse and simulate the distribution and elimination of intravenous fluids (Hahn 2010). The context-sensitive half-time of crystalloids and colloids may change and vary over time depending on the patient's condition. As long as crystalloids or colloids are infused they will exert a similar volume expansion effect and their **distribution** and/

or **elimination** and excretion will be slowed in cases of shock, renal failure, sedation, or general anaesthesia (Hahn 2010; 2014). This may explain why crystalloids have a much better short-term effect on the plasma volume than previously believed. Their efficiency (i.e. the plasma volume expansion divided by the infused volume) is 50-80% as long as **infusion** continues, and even increases to 100% when the arterial pressure has dropped. Elimination is very slow during surgery, and amounts to only 10% of that recorded in conscious volunteers.

### 2.2.3. Pharmacodynamics

Pharmacodynamics (PD) relates plasma concentrations to a specific effect, i.e. how the antibiotic affects the body and the bacteria. As previously described, antibiotic plasma concentrations are determined by dosing strategy, volume of distribution (Vd) and clearance (CL) (Elbers et al. 2015). Volume dynamics depends on the type of fluid used and desired location: intravascular (resuscitation), interstitial vs intracellular (cellular dehydration). Volume kinetics and dynamics depend on underlying conditions.

### 2.3. Duration

#### 2.3.1. Appropriate duration

The duration of fluid therapy is equally impor-

tant and the volume must be tapered when shock is resolved. However, many clinicians use certain triggers to start, but are less aware of triggers to stop fluid resuscitation, hence carrying the potential of fluid overload and all its detriments (Malbrain et al. 2014; Benes et al. 2015). As with duration of antibiotics, there is no strong evidence but a trend towards benefit from shorter duration of IV fluids (Hjortrup et al. 2016). Clinicians should not use fluids to treat low central venous pressure, mean arterial pressure, or urine output per se, but to treat shock instead. For fluids, the Frank-Starling relationship between cardiac output and cardiac preload is the equivalent of the dose effect curve for standard medications. Because of the shape of the Frank-Starling relationship, the response of cardiac output to the fluid-induced increase in cardiac preload is not constant (Monnet et al. 2017).

#### 2.3.2. Treat to response

Clinicians should stop antibiotics when signs and symptoms of active infection resolve. Likewise, fluids should be stopped when shock is resolved (e.g. normal lactate). As with antibiotics (e.g. CRP or procalcitonin), the future role for biomarkers (e.g. neutrophil gelatinase-associated lipocalin, cystatin C, citrullin, or liver-type fatty acid binding protein) needs to be established. After the very initial fluid administration, only one half of patients with circulatory failure respond to continued intravenous fluid administration with an increase in cardiac output (Bentzer et al. 2016).

### 2.4. De-escalation

#### 2.4.1. Withholding or withdrawing

The final step in fluid therapy is to consider withholding or withdrawing resuscitation fluids when they are no longer required (Malbrain et al. 2014; Benes et al. 2015; O'Connor and Prowle 2015). Along with conditioning fluid administration on the presence of fluid responsiveness, this contributes to reducing overall cumulative fluid balance. A positive cumulative fluid balance should be avoided by all means as studies have shown that fluid overload is an independent predictor for increased morbidity and mortality (Malbrain et al. 2014; Silversides et al. 2017). Eventually, active fluid removal may be indicated in some patients with global increased permeability syndrome (GIPS) and volume overload, and this is referred to as de-resuscitation. As

**Table 2.** The ROSE concept avoiding fluid overload

	<b>Resuscitation</b>	<b>Optimisation</b>	<b>Stabilisation</b>	<b>Evacuation</b>
<b>Hit sequence</b>	First hit	Second hit	Second hit	Third hit
<b>Time frame</b>	Minutes	Hours	Days	Days to weeks
<b>Underlying mechanism</b>	Inflammatory insult	Ischaemia and reperfusion	Ischaemia and reperfusion	Global Increased Permeability Syndrome
<b>Clinical presentation</b>	Severe shock	Unstable shock	Absence of shock or threat of shock	Recovery from shock, possible Global Increased Permeability Syndrome
<b>Goal</b>	Early adequate goal-directed fluid management	Focus on organ support and maintaining tissue perfusion	Late conservative fluid management	Late goal-directed fluid removal (de-resuscitation)
<b>Fluid therapy</b>	Early administration with fluid boluses, guided by indices of fluid responsiveness	Fluid boluses guided by fluid responsiveness indices and indices of the risk of fluid administration	Only for normal maintenance and replacement	Reversal of the positive fluid balance, either spontaneous or active
<b>Fluid balance</b>	Positive	Neutral	Neutral to negative	Negative
<b>Primary result of treatment</b>	Salvage or patient rescue	Organ rescue	Organ support (homeostasis)	Organ recovery
<b>Main risk</b>	Insufficient resuscitation	Insufficient resuscitation and fluid overload (e.g. pulmonary oedema, intra-abdominal hypertension)	Fluid overload (e.g. pulmonary oedema, intra-abdominal hypertension)	Excessive fluid removal, possibly inducing hypotension, hypoperfusion, and a "fourth hit"

Adapted from Malbrain et al. (2014; 2018) with permission

for antibiotics (**Table 1**), the duration of fluid therapy must be as short as possible, and the volume (i.e. dose) must be the lowest amount effective in treating shock.

#### 2.4.2. Monitoring

While antibiotic de-escalation may not help individual patients, it could benefit the ICU as a whole by reducing the selection pressure for resistance. Similarly, after stabilisation (normal pulse pressure variation, normal cardiac output, normal lactate) clinicians need to stop ongoing (futile) fluid resuscitation and move to de-escalation (late conservative fluid management) and de-resuscitation (late goal-directed fluid removal) (see **Table 2** for explanation). However, too aggressive de-resuscitation may result in new hypoperfusion and increase in end-organ damage.

### 3. The four phases of fluid therapy

Recently a conceptual model of septic shock was proposed with four distinct dynamic phases of fluid therapy (Cordemans et al. 2012; Malbrain et al. 2018): **Resuscitation**, **Optimisation**, **Stabilisation**, and **Evacuation** (de-resuscitation) (R.O.S.E.) (**Table 2**). Specifics of the four phases are: "When to start intravenous fluids?", "When to stop intravenous fluids?", "When to start de-resuscitation or active fluid removal?" and finally "When to stop de-resuscitation?"

et al. 2014). A multidisciplinary collaboration is an alternative approach, as has been described for antibiotic stewardship (MacDougall and Polk 2005; Paterson 2006; Doron and Davidson 2011; Schuts et al. 2016).

A comparable strategy could be used for IV fluids, by implementing '**fluid stewardship**'. There is no clear definition yet, but one preliminary example could be "a series of coordinated interventions, introduced to select the optimal fluid, dose and duration of therapy that results in the best clinical outcome, prevention of adverse events and cost reduction" (Dellit et al. 2007; Goff 2011). Similar to antibiotic stewardship, the purpose is threefold. First, the most appropriate, individualised therapy has to be chosen. It is crucial that the right fluid is prescribed in the right dose and duration and that there is a timely evaluation to start de-escalating fluid therapy (Malbrain et al. 2018). Second, early detection and prevention of inappropriate fluid administration is necessary to avoid adverse events (Bates et al. 1995). Finally, cost containment should be achieved through implementation of preventive quality improvement measures (Etchells et al. 2012).

#### 4. Fluid stewardship

##### 4.1. Conceptual framework

The multifaceted nature of fluid stewardship will need collaboration between different disciplines such as emergency medicine, critical care, anaesthesiology, nephrology, as well as general medicine, surgery and clinical pharmacy (Malbrain et al. 2018; Dellit et al. 2007). If the primary goal of fluid stewardship is to optimise clinical outcomes while minimising unintended consequences as detailed above, then the bedside clinician needs to understand fluid physiology. The combination of effective fluid stewardship with a comprehensive fluid bundle and organ function monitoring programme should limit the deleterious effects of inappropriate fluid prescription.

The specific IV fluid need depends on the indication: whether it is intended to replace lost fluids, maintain basic metabolic needs or restore circulating volume (Malbrain et al. 2018). To determine the right type of fluid therapy for the individual patient, the clinician must choose based on the clinical exam, laboratory results and the characteristics of the available IV fluids. Though commonly prescribed, intravenous fluids are not always appropriate (Gao et al. 2015). Prescription of intravenous fluids is often done by junior doctors using either an experience-based approach, or by habit, with limited input from senior colleagues (McCrory et al. 2017; Lobo et al. 2001; Lewis

##### 4.2. Assessment

First, measure baseline fluid dosing, duration, costs and use patterns; second, study indications for fluid administration (resuscitation, maintenance, replacement, nutrition); and finally, identify clinician indications for prescriptions.

##### 4.3. Goals of desirable fluid use

Goals need to be formulated and 'appropriate', and rational IV fluid use needs to be defined for the institution and individual patients. Empiric versus goal-directed IV fluid treatment needs to be defined for the four indications (resuscitation, maintenance, replacement, nutrition). Treatment guidelines for clinical syndromes need to be established. The appropriateness of IV fluid therapy should be assessed during the audit process. Therefore, the process of an IV fluid treatment is divided into four stages (**Table 3**), based on an audit framework developed by the UK National Institute for Health and Care Excellence (NICE) (Sansom and Duggleby 2014; Padhi et al. 2013).

First, the physician has to assess the patient's IV fluid needs and decide on the right treatment (indication). Only the three major indications

need to be examined thoroughly for the purpose of a clinical audit: resuscitation, maintenance and replacement or redistribution. Second, every IV fluid prescription has to be detailed in order to ensure a proper administration and a fluid management plan is available to enable continuity of care. Third, the information in the hospital's fluid guideline or bundle is used to create different quality standards. Finally, these standards represent the necessary elements to do a full and qualitative check of appropriateness (see **Table 3**). If all standards are met, the therapy will be classified as appropriate for that patient.

#### **4.4. Interventions on IV fluid prescribing**

IV fluid prescribing consists of numerous elements. The day-to-day work of the core fluid stewardship members is to screen patients' medical records for appropriateness of IV fluid administration.

Further tasks may lie in the automatic review of the medical record after empiric use, fluid balance results, other laboratory data (urea and electrolytes, kidney function, albumin levels,...), and to provide advice on appropriate duration of fluid therapy. Finally, the fluid stewardship team could write an annual report to the hospital administration with calculation of clinical benefits and cost savings, if any.

#### **4.5. Provide feedback, continuing education**

The fluid stewardship team should organise a survey to test the prescriber's knowledge about composition of fluids, indications and monitoring of fluid status. The team can provide targeted education about particular fluid composition, or one specific fluid at a time, as well as empiric versus goal-directed treatment.

#### **4.6. Implement Fluid Stewardship**

Analogous to antibiotic practice in critically ill patients, it is time to introduce **fluid stewardship** in the ICU, through a few simple steps. Start with a snapshot: First, check what intravenous fluids are commonly used and for what indications. Next, perform a survey of knowledge (of the nurses, doctors, pharmacists, etc). Finally, perform a clinical audit of patient records (surgical vs medical). This should be followed by a **Plan-Do-Check-Act** (PDCA) cycle: set up guidance (introduce fluid bundle); perform education (including tailored lectures

**Table 3.** Four stages of evaluation of IV fluid therapy

<i>Stage of evaluation</i>	<i>Audit standard</i>
1. Assessment	<ul style="list-style-type: none"> <li>Patient fluid balance is assessed on admission in the hospital</li> <li>Patient's fluid and electrolyte needs are assessed as part of every ward review</li> <li>Assessment includes the use of an appropriate clinical parameter for evaluation of the fluid balance</li> <li>Recent lab result with urea and electrolytes (within 24 hours of fluid prescription)</li> </ul>
2. Indication	<p>A) <b>RESUSCITATION</b></p> <ul style="list-style-type: none"> <li>For patients in need of fluid resuscitation:           <ul style="list-style-type: none"> <li>the cause of the fluid deficit is identified</li> <li>an assessment of shock or hypoperfusion is made</li> <li>a fluid bolus of 500mL of crystalloids is given</li> </ul> </li> <li>Patients who have received initial fluid resuscitation are reassessed</li> <li>Care is upgraded in patients who have already been given &gt;2000mL of crystalloids and still need fluid resuscitation after reassessment</li> <li>Patients who have not had &gt;2000mL of crystalloids and who still need fluid resuscitation after reassessment receive 250–500 mL of crystalloids and have a further reassessment</li> </ul> <p>B) <b>MAINTENANCE</b></p> <ul style="list-style-type: none"> <li>Patients should be assessed for maintenance IV fluids needs at least daily</li> <li>If patients need IV fluids for routine maintenance alone, the initial prescription is restricted to:           <ul style="list-style-type: none"> <li>25–30 mL/kg/day (1 mL/kg/hr) of water and</li> <li>approximately 1 mmol/kg/day of potassium (<math>K^+</math>) and</li> <li>approximately 1–1.5 mmol/kg/day of sodium (<math>Na^+</math>) and</li> <li>approximately 1 mmol/kg/day of chloride and</li> <li>approximately 50–100 g/day (1.1–1.5 g/kg/day) of glucose to limit starvation ketosis</li> </ul> </li> <li>Definition of inappropriateness in case of electrolyte disturbances           <ul style="list-style-type: none"> <li>Solutions not containing adequate amount of sodium in case of hyponatraemia (<math>Na &lt; 135 \text{ mmol/L}</math>)</li> <li>Solutions not containing adequate amount of potassium in case of hypokalaemia (<math>K &lt; 3.5 \text{ mmol/L}</math>)</li> <li>Solutions containing too much sodium in case of hypernatraemia (<math>Na &gt; 145 \text{ mmol/L}</math>)</li> <li>Solutions containing too much potassium in case of hyperkalaemia (<math>K &gt; 5 \text{ mmol/L}</math>)</li> </ul> </li> </ul> <p>C) <b>REPLACEMENT AND REDISTRIBUTION</b></p> <ul style="list-style-type: none"> <li>If patients have ongoing abnormal losses or a complex redistribution problem, the fluid therapy is adjusted for all other sources of fluid and electrolyte losses (e.g. normal saline may be indicated in patients with metabolic alkalosis due to gastro-intestinal losses)</li> </ul>
3. Prescription	<ul style="list-style-type: none"> <li>The following information is included in the IV fluid prescription:           <ul style="list-style-type: none"> <li>the type of fluid</li> <li>the rate of fluid infusion</li> <li>the volume of fluid</li> </ul> </li> <li>The IV fluid prescription is adapted to current electrolyte disorders and other sources of fluid administration</li> </ul>
4. Management	<ul style="list-style-type: none"> <li>Patients have an IV fluid management plan, including a fluid and electrolyte prescription plan over the next 24 hours</li> <li>The prescription for a maintenance IV fluid is evaluated at least every 24 hours and changes after a clinical exam, a change in dietary intake or evaluation of laboratory results</li> </ul>

to all junior doctors) and ward-based opportunistic teaching; and regularly re-evaluate the situation and keep increased awareness (with flyers, screen-savers, etc.).

#### **Conclusions**

There are only four major **indications** for fluid administration in the critically ill: resuscitation, maintenance, replacement and nutrition (enteral or parenteral).

In this review, a conceptual framework is presented looking at fluids as drugs by taking into account the four **Ds** (drug selection, dose, duration and de-escalation) and the four phases of fluid therapy within the ROSE concept (resuscitation, optimisation, stabilisation, evacuation). This framework will provide answers to the four

basic questions surrounding fluid therapy: 1) when to start IV fluids?; 2) when to stop fluid administration?; 3) when to start fluid removal and finally 4) when to stop fluid removal? Answering these **questions** for each patient can provide the basis for fluid stewardship (like antibiotic stewardship) in the ICU. This **fluid stewardship** can be promulgated through a three-pronged attack for fluid safety: namely educating, changing prescribing habits, and increasing awareness. Good luck! ■

For conflict of interest statement and full references see <https://iii.hm/o1y>

#### **Abbreviations**

ICU intensive care unit  
IV intravenous