

## Editorial

**Fluid Therapy in Critically Ill - New Perspective**

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Fluid administration in critically ill patients must be titrated for each patient because either too much or too little can have negative impact on patient outcome. The salvage, optimization, stabilisation, de-escalation (SOSD) mnemonic should be used as a general guide to fluid resuscitation and fluid administration

Fluid administration is a cornerstone of treatment of critically ill patients. Despite the ubiquitous use, it carries significant risks associated with under or over-administration. Hypovolemia is associated with decreased organ perfusion, ischemia, and multi-organ failure. However, hypervolemia and volume overload are associated with organ dysfunction, delayed liberation from mechanical ventilation, and increased mortality. Despite appropriate provision of intravenous fluid therapy, adverse drug effects such as electrolyte abnormalities and acid-base disturbances may occur. The management of volume status in critically ill patients is both dynamic and tenuous, a process that requires frequent monitoring and high clinical insight. As patient-specific considerations for fluid therapy evolve across the continuum of critical illness, a standard approach to the assessment of fluid needs and prescription of intravenous fluid therapy is necessary. Use of intravenous fluids is challenging in critically ill patients because of predisposing factors that result in altered fluid distribution and accelerated volume losses. These complexities are perpetuated by the dynamic nature of critical illness, in which fluid requirements can change frequently and rapidly.

Fluids are drugs used in patients with shock to increase the cardiac output with the aim to improve oxygen delivery to the cells. Fluid administration is integrated into the complex management of pressure and flow “macro” hemodynamic variables, coupled to the “micro” local tissue flow distribution and regional metabolism. Macro-variables are managed by measuring systemic blood pressure and evaluating the global cardiac function. The critical threshold of oxygen delivery to the cells is difficult to estimate, however, several indexes and clinical signs may be considered as surrogate of that, and integrated in a decision-making process.

There are three main indications of fluid therapy: resuscitation, replacement, and maintenance. Moreover, the impact of fluid administration as drug diluent or to preserve catheter patency, i.e., fluid creep, should also be considered. As for antibiotics, intravenous fluid administration should follow the four Ds: drug, dosing, duration, de-escalation. Fluids are drugs with indications, contraindications, and side effects. Different indications need different types of fluids, e.g., resuscitation fluids should focus on rapid restoration of circulating volume; replacement fluids must mimic the fluid that has been lost; maintenance fluids must deliver basic electrolytes and glucose for metabolic needs. However, timing and administration rate are equally important for fluids. Whereas, in contrast to most drugs, there is no standard therapeutic dose for fluids. The duration of fluid therapy is also crucial and volume must be tapered when shock is reversed. However, while “starting triggers” for fluid resuscitation are quite clear, clinicians are less aware of “end points” of fluid resuscitation. The final step in fluid therapy is to withhold/withdraw fluids when they are no longer required, thus reducing the risk of fluid overload and related deleterious effects.

The strategy of fluid administration fundamentally changes along with the time course of septic shock. Recently a three-hit, or even four-hit model of septic shock was suggested trying to answer four basic questions, in which we can recognize four distinct dynamic phases of fluid therapy: resuscitation, optimization, stabilization and evacuation (de-resuscitation) (the acronym ROSE)

**First phase: Resuscitation**

After the first hit which can be sepsis, but also burns, pancreatitis or trauma, the patient will enter the “ebb” phase of shock. This life-threatening phase of severe circulatory shock can occur within minutes and is characterized by a strong vasodilation leading to a low mean arterial pressure and microcirculatory impairment. At this initial phase, usually during the first 3–6 h after the initiation of therapy, fluid resuscitation is commonly administered according to an early, adequate, goal-directed, fluid management strategy. In fact, rather than infusing a predefined given amount of fluid, the goal should be

individualized for every patient, based on the evaluation of the need for fluids and on the patient's premorbid conditions. A fluid challenge is a dynamic test to assess fluid responsiveness by giving a fluid bolus and simultaneously monitoring the hemodynamic effect.

**Second phase: Optimization**

The second hit occurs within hours and refers to ischemia and reperfusion.

The optimization phase starts when the patient is no longer in overt absolute/relative hypovolemia, but remains hemodynamically unstable. The aim of this phase is to optimize and maintain adequate tissue perfusion and oxygenation in order to prevent and limit organ damage. Fluid challenges must be conducted carefully, bearing in mind the four essential components: Type of fluid (e.g., a balanced crystalloid-like PlasmaLyte); Rate (@100–200 mL over 10 min); Objective (e.g, normal arterial pressure or heart rate); and Limits (e.g, high central venous pressure level).

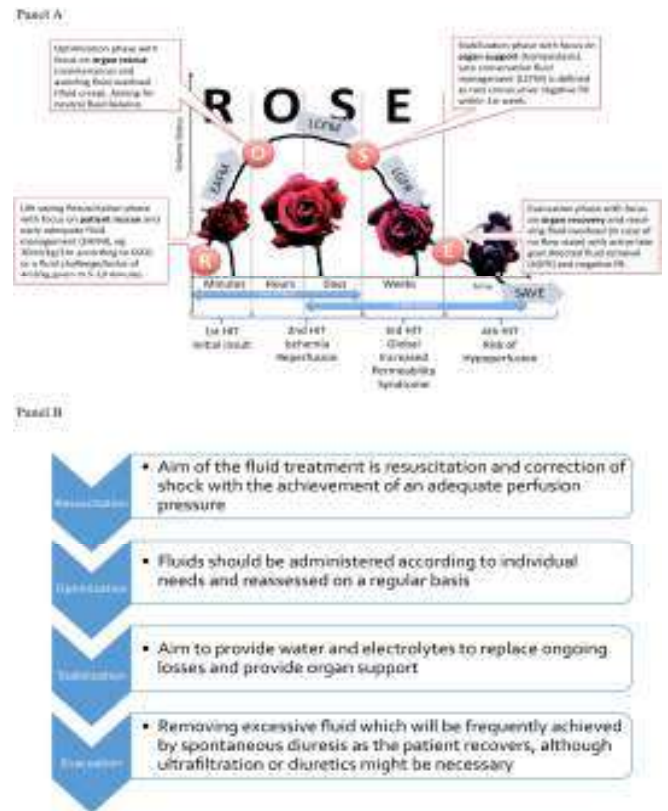
**Stabilization phase (S)**

Once the patient is stable, the stabilization phase begins and evolves over days. In this phase, the aim of fluid management is to ensure water and electrolytes to replace ongoing losses and provide organ support. Since persistence of a positive daily fluid balance over time is strongly associated with a higher mortality rate in septic patients, clinicians should also be aware of the hidden obligatory fluid intake, as it may contribute more than a litre daily. Hence, the target should be a zero or slightly negative fluid balance.

**Fourth phase: Evacuation**

After the second hit, the patient may either further recover, entering the "flow" phase with spontaneous evacuation of the excess fluids that have been administrated previously, or, as is the case in many critically ill patients, the patient remains in a "no-flow" state followed by a third hit, usually resulting from global increased permeability syndrome with ongoing fluid accumulation due to capillary leak. In this de-resuscitation phase, we try to find an answer to the third and fourth question: "When to start fluid removal?" and "When to stop fluid removal?" in order to find the balance between the benefits (reduction in second and third space fluid accumulation and tissue edema) and risk (hypoperfusion) of fluid removal. Obviously, the risk at this phase is to be too aggressive with fluid removal and to induce hypovolemia, which may trigger a

"fourth hit" for hemodynamic deterioration and hypoperfusion



**Conclusion -** The prescription of fluid therapy is one of the most common medical acts in hospitalized patients but many of the aspects of this practice are surprisingly complex. Fluids should be prescribed with the same care as any other drug and every effort should be made to avoid their unnecessary administration. The bottom line is "Give the right fluid in the right dose to the right patient at the right time"

**References -**

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## How to start AMSP in your hospital?

Building process of AMS program <sup>[11,12]</sup> can be split into following components:

1. Gathering prerequisites
2. Setting out goals of AS program
3. Selection of strategies to achieve the set goals
4. Monitor and evaluate the AS program

### 1. Prerequisites:

For understanding what all prerequisites are required to start ASP; one needs to be familiar with core elements of AS program. The know-how of these elements could be gained either through literature review or visiting and collaborating with established AS teams in other hospitals or a combination of both. In general, building an AMSP team in your own hospital is most important. AMSP team is typically multi disciplinary in composition. It brings together various stakeholders such as hospital administrators, infectious disease physicians, clinical pharmacists/ pharmacologists, microbiologists and clinicians with common interest in improvising antimicrobial use. Some of the other prerequisites include existence of antimicrobial standard treatment guidelines, adequate diagnostic support among available human and IT resources.

### 2. Delineating goals of ASP

Local situation SWOT analysis (strengths, weakness, opportunities and threats) needs to be conducted first. This helps identify priority problem areas and thus aids in setting out clear ASP goals in the given facility.

### 3. Selection of AMSP Strategies:

AMSP strategies or interventions can be broadly classified as active and supplemental strategies. <sup>[11,12]</sup> They can be employed separately as well as in combination depending upon available resources and expertise in the given healthcare setting. Commonly employed active strategies include Prospective audit and feedback and Preauthorization.

a) Prospective audit and feedback: This approach involves concurrent review of antimicrobial prescription orders by the AMSP team. Feedback is provided to the prescribing physician regarding the suitability of antibiotic use with respect to selection,

dose, dosing regimen and duration of antibiotic therapy based on diagnostic workup and clinical condition of the patient. This approach mainly focuses on rapid de-escalation of antimicrobial therapy.

b) Formulary restriction/ Preauthorization: This strategy involves pre-prescription restrictions on use of certain selected antibiotics. Prior authorization or approval is required from designated AMSP team members before prescribing these antibiotics. This approach has the advantage of targeting specific antimicrobials based on local resistance patterns.

In addition to above; there are various supplemental strategies for AMSP. These include organising didactic education events; developing facility specific standard treatment guidelines for infectious syndromes; antibiotic cycling; antibiotic time outs; dose optimization; timely de-escalation and employing computer assisted decision support systems.

### 4. Monitoring and evaluating ASP:

Development of ASP infrastructure and selection of strategies for implementation are just not enough. It is equally important to evaluate the impact of selected interventions in achieving ASP goals. If the goals are not met-analyse the barriers and enablers; review the strategies and adapt accordingly.

### Conclusion:

Growing AMR represents global health emergency. Antimicrobial Stewardship programs represent core components of many national action plans to combat AMR and optimize healthcare outcomes in multiple ways. Therefore, building and implementing ASPs across hospitals is the need of the hour. We are hopeful that this article would encourage interested healthcare professionals to take their first step in the fight against antimicrobial resistance.

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