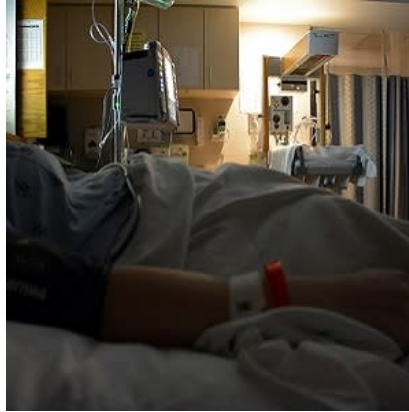




## Managing patients with refractory septic shock



The Surviving Sepsis Guidelines provide a specific framework to treat patients with septic shock. These guidelines include the use of antimicrobial therapy, source control, fluid therapy and targeted vasopressors. However, there is still a small proportion of patients that does not respond to these measures and consequently deteriorates into refractory shock and progressive multi-organ failure. Specific guidelines to manage such patients do not exist.

Refractory septic shock, defined as the presence of hypotension with end-organ dysfunction, often requires high-dose vasopressor support and has an associated mortality of up to 60%. Patients with vasopressor requirements greater than 1  $\mu\text{g}/\text{kg}/\text{min}$  norepinephrine or equivalent have mortality as high as 80-90%. Microcirculatory failure and ischaemic consequences have been frequently observed in such patients. There is thus a need to improve outcomes in this small, critically ill patient population.

This article presents an overview of different interventions that were used in a specialist Severe Respiratory Failure centre in the UK to manage patients with confirmed or suspected toxin-producing bacteria.

These interventions include:

**Albumin:** Balanced crystalloids were used for initial volume replacement followed by 20% human albumin solution in case ongoing fluid resuscitation was required. While the role of albumin in septic shock still remains unclear, clinical studies do suggest a certain benefit.

**Hydrocortisone:** Corticosteroids have been frequently studied for managing septic shock. While clinical trials have yet to demonstrate a clear survival benefit related to the use of hydrocortisone, beneficial effects may be seen in patients with the highest illness severity scores. At this special centre, patients with refractory shock were administered a hydrocortisone infusion (8mg/h following a 50-mg bolus).

**Femoral arterial access:** This was routinely used for invasive blood pressure monitoring in patients with refractory septic shock. The subsequent increase in target mean arterial blood pressure (MAP) resulted in a reduction in vasopressor dosing among these patients.

**Lower the MAP target:** In the specialist referral centre, MAP target in patients with refractory septic shock was reduced to 50-55 mmHg to allow a reduction in vasopressor requirements which in turn led to improved tissue perfusion and reduction of hyperlactaemia. Use of vasopressin was avoided in these patients as it is associated with an increased risk of peripheral and mesenteric ischaemia in patients with refractory septic shock. In

addition, early enteral nutrition was avoided in patients on high-dose vasopressors. Parenteral nutrition was preferred until the shock state was resolved.

**Minimise sedation:** Current guidelines recommend minimising sedation in mechanically ventilated patients with sepsis. However, this approach is not always adhered to. Patients with refractory septic shock often have a reduced level of consciousness and therefore, sedation requirements for this patient segment tends to be lower as compared to the general ICU sepsis population. Also, altered hepatic metabolism and reduced renal clearance in shocked patients could lead to the accumulation of sedative agents. That is why minimum sedation is used in patients with refractory septic shock. The first-line strategy if sedation is required is to use an opiate-based regimen in conjunction with low-dose propofol.

**Replacement of thiamine and vitamin C:** Levels of vitamin C are generally low in critically ill patients. In septic shock patients, vitamin C deficiency and absolute or relative thiamine deficiency is also common. In the centre, patients with refractory shock were given combined vitamin C (4.5 g/day) and thiamine (2.25 g/day) three times per day until the shock state was resolved. Combination therapy was used because it appears to be more effective due to the synergistic effect between the two agents.

**Adjunctive antimicrobial therapy:** Clindamycin was administered to patients with refractory septic shock until microbiological analysis excluded toxin-producing pathogens or until stabilisation of organ dysfunction.

**Intravenous immunoglobulin (IVIG):** Current guidelines recommend against the use of IVIG in septic shock but patients with refractory septic shock were treated with IVIG because early administration is likely to offer benefit.

**Levosimendan:** Improved cardiac function in patients with refractory septic shock can be achieved using levosimendan in conjunction with the maintenance of ionised calcium levels. That is why patients with echocardiographic features of moderate to severely impaired left ventricular systolic function and impaired end-organ perfusion were given levosimendan.

**Epoprostenol and heparin:** Patients with refractory septic shock with peripheral mottling were administered low-dose epoprostenol infusion to improve microcirculatory flow and to prevent the occurrence of peripheral thrombotic events. When titrated slowly, prostacyclin infusion can reduce peripheral ischaemic complications. In case of disseminated intravascular coagulation and suspicion of end-organ microthrombosis, low-dose intravenous heparin infusion may also be initiated.

**Renal replacement therapy:** Early haemodiafiltration with doses of 40-60 mg/kg/h was initiated in patients with refractory septic shock to facilitate rapid temperature control and correction of metabolic acidosis.

**Extracorporeal support:** Extracorporeal technology provides respiratory and cardiac support in highly selected patients with refractory septic shock. It also helps achieve stability and buys time for other therapeutic interventions to have an impact. Extracorporeal support also improves global oxygen delivery, reduces intrathoracic pressures, improves carbondioxide clearance and acid-base management and improves myocardial performance.

The fact is that management of patients with refractory septic shock continues to be a challenge. Established conventional interventions have failed to deliver and that is why it is important to implement a different approach that uses pragmatic strategies whenever necessary. Even though many of the interventions that have been discussed may lack conclusive evidence, they are relatively inexpensive, widely accessible and may help in achieving haemodynamic stability and reversing progressive deterioration in this small patient population with a very high mortality.

Source: [Critical Care](#)  
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