INTRODUCTION
Sepsis, the systemic maladaptive response to an infection manifested as complex immunological, metabolic and cardiovascular disorders that progress gradually. Increase in venous and arteriolar dilatation and cardiac depression lead to tissue hypo-perfusion. Organ dysfunction can be represented as an acute change in total qSOFA score ≥ 2 points consequent to the infection [quick SOFA = respiration rate > 22/min, altered mental status, systolic blood pressure < 100mmHg; each carries one point]. Septic shock is the state where vasopressor is required to maintain mean arterial pressure (MAP) > 65mmHg, and serum lactate level > 1.5 mmol/L in the absence of hypovolemia.

PATHOGENESIS
Sepsis is the culmination of complex interactions between the infecting microorganisms and the host immune, inflammatory, and coagulation responses. Both the host responses and the characteristics of the infecting organism influence the outcome of sepsis. The innate immune system responds rapidly by means of pattern-recognition receptors (e.g., toll-like receptors [TLRs]). Binding of TLRs to epitopes on microorganisms stimulates intracellular signalling, increasing transcription of pro-inflammatory molecules. Activated neutrophils release mediators that increase vascular permeability. Activated endothelial cells release nitric oxide, a potent vasodilator that acts as a key mediator of septic shock. These processes like intravascular volume depletion, peripheral vasodilatation, myocardial depression, and increased tissue metabolism lead to an imbalance between systemic oxygen delivery and oxygen demand, resulting in global tissue hypoxia or shock.

DIAGNOSIS
Diagnosis of septic shock is based on clinical, hemodynamic and biochemical changes. i.e.

1. Clinical signs of tissue hypo-perfusion; cold and clammy skin, cyanosis, decreased urine output (less than 0.5ml/kg body weight per/hr) and altered mental status (obtundation, disorientation, and confusion).
2. Systemic arterial hypotension i.e. systolic blood pressure (SBP) < 90mmHg or MAP < 70mmHg, with associated tachycardia.
3. Increase in serum lactate level (more than 1.5mmol/L).

TREATMENT
Fluid resuscitation and early antibiotic therapy is the rule in treatment of septic shock. Aim is to administer antibiotics within one hour. In the mean time the patient has to be resuscitated, a diagnosis is made and microbiological specimens are taken. In emergency department (ED), patient to be resuscitated quickly according to VIP rule: ventilate (oxygen administration), infuse (fluid resuscitation) and pump (administration of vasoactive agents).

VENTILATION
Oxygen has to be given quickly, either by mask or if required endotracheal intubation and mechanical ventilation.

INFUSION
Patient is ideally given crystalloids (NS/RL) at the rate of 20-30 ml/kg in first hour and after that fluid to be infused accordingly. After each 250ml of fluid given, the patient’s chest has to be examined to avoid volume overload. Passive leg rising test may be done to ascertain the fluid requirement but this needs meticulous examination and sophisticated instruments like PICCO etc. Central venous pressure (CVP) has to be maintained between 8-12 cmH2O. In resource poor settings, thorough clinical examinations like heart rate, MAP, chest examinations and hourly urinary output can be done to judge fluid requirement.

PUMP
If still, MAP is not in optimal level vasopressors and inotropes are to be given. Nor-adrenalin is the vasopressor of choice followed by adrenalin, vasopressin, and dopamine at a dose given in the table 1. Dopamine has limited role as a vasopressor in septic shock, as there is risk of arrhythmias or if given, only in bradycardiac septic shock patients. The role of steroid is minimal in septic shock management. If given, it is hydrocortisone as continuous IV infusion totalling 200 mg/24 hours in patients where BP is poorly responsive to fluid...
resuscitation and vasopressor therapy. Ionotropic agents like dobutamine can be given by itself or in addition to vasopressors to the patients with cardiac dysfunction as evidenced by high-filling pressures and low cardiac output. Levosimendan, as an inotrope, is more expensive and acts primarily by binding to cardiac troponin C and increasing the calcium sensitivity of myocytes. However this agent is having a very long half-life, which limits the practicality of its use in acute shock states.

**OTHERS**

**Antibiotics**

With resuscitation of the patients, early appropriate antibiotics in the recommended doses to be given within first hour of arrival. Two or more antibiotics can be given according to micro-organism susceptibility patterns in the hospital or community. Once the culture or microbiologic identification is done, the antibiotic may be given according to the culture sensitivity report (De-escalation of antibiotic therapy).

The care must be given to achieve the goals of therapy like;

a. CVP 8-12 cmH₂O
b. Mixed venous oxygen saturation (Svo₂) > 65%
c. MAP ≥ 65 mm Hg
d. Urine out-put > 0.5 ml/kg/hr
e. Normalization of serum lactate level i.e. less than 1.5 mmol/L where Svo₂ measurement is not available.

In resource poor settings like distant peripheral hospitals, achieving MAP ≥ 65 mm Hg and urine output > 0.5 ml/kg/hr justifies treatment.

**Source Control**

Control of source of infection in the form of drainage, debridement, and device removal gives better outcome.

**Hand Hygiene**

Hand hygiene of the health care personnel, before and after touching the patients is very much crucial.

**Nutrition**

Early feeding is always beneficial, which prevents gut translocation of bacteria. Calorie requirement is 20-30 Kcal/kg/day, where carbohydrate source is 60%, proteins 20% and Lipids 20%. Electrolyte corrections, micro nutrients has definite role in sepsis management.

**Organ Support**

Organ support such as ventilator and renal replacement therapy often required at the time of respiratory failure and renal failure respectively.

**Other Parameters**

Other parameters to be optimized are like, blood and blood products are to be administered according to need (eg: to maintain haematocrit 30%). Albumin may be given in hypoalbuminemic patients. Glycemic control-keeping blood sugar between 110-180 mg/dl, preferably by intravenous insulin infusion. Care must be taken to avoid hypoglycaemia. Proton pump inhibitors (PPI) and H₂ receptor blockers are to be given for stress ulcer prophylaxis. Heparin, low molecular weight heparin (LMWH) and pressure stockings for deep vein thrombosis (DVT) prophylaxis. Head of bed should be elevated to 30-45 degrees to prevent aspiration.

**CONCLUSION**

Septic shock is a life threatening condition, associated with high fatality rate. Prompt identification and appropriate treatment is mandatory for better outcome. Treatment should include airway management, hemodynamic stabilization and appropriate antibiotics in first hour of arrival of patients. Monitoring the response to therapy is crucial by careful clinical evaluation and blood lactate measurements.

**REFERENCES**