The relationship between VO2 & DO2 in cardiogenic, hypovolaemic & septic shock.

- Hypovolaemic shock due to other intravascular pathology may also require surgery; however, in these cases correcting hypovolaemia, hypoxia & anaemia preoperatively can significantly reduce perioperative mortality.

**Major Pathophysiology**

**NB:** Supply independence refers to the initial stages where oxygen uptake of tissues stays constant by tissues extracting more oxygen per unit of blood; below critical DO2, in some trauma patients outcome may be improved if fluid resuscitation is delayed until bleeding is controlled.

**General Measures**

- Traditionally, hyperlactataemia in critically ill patients and particularly those in shock was normally interpreted as a marker of secondary anaerobic metabolism.
- A number of papers have suggested that lactate formation during sepsis is not due to hypoxia but rather to metabolic processes.
- Arterial lactate concentration is dependent on the balance between its production and consumption.
- In general, this concentration is less than 2 mmol/l, although daily production of lactate is actually 1500 mmol/l.
- In physiological conditions, lactate is produced by muscles (25%), skin (25%), brain (20%), intestine (10%) and red blood cells (20%), which are devoid of mitochondria.
- Lactate is essentially metabolized by liver and kidney.

**Antibiotics**

- It is vital to select an appropriate antibiotic and to ensure that the dosing regimen is optimal.
- Spectrum should be narrowed and directed at the identified organisms.
- Lactate is produced in the cytoplasm according to the following reaction:
  \[
  \text{Pyruvate} + \text{NADH} + \text{H}^+ \rightarrow \text{lactate} + \text{NAD}^+
  \]
- This reaction favours lactate formation, yielding a 10-fold lactate/pyruvate ratio.
- Pyruvate is essentially metabolized by the mitochondrial aerobic oxidation pathway via the Krebs cycle.
  \[
  \text{Pyruvate} + \text{CoA} + \text{NAD} \rightarrow \text{acetyl CoA} + \text{NADH} + \text{H}^+ + \text{CO}_2
  \]
- Lactate is produced during this reaction, but it is also required to maintain ATP synthesis.
- Lactate can be utilized directly by periportal hepatocytes (60%) to produce glycogen and glucose (neoglucogenesis and the Cori cycle). A number of papers have suggested that lactate formation during sepsis is not due to hypoxia but rather to metabolic processes.

**Steroids**

- Large doses of steroids (eg 30-120mg/kg) given within 24 hours of septic shock result in haemodynamic improvement but not increased survival.
- While low dose steroids in patients with septic shock who had a sub-normal rise in synacthen appeared to improve outcome in one study, a larger follow-up study has not confirmed this benefit.
- The addition of an intravenous infusion of vasopressin (0.04U/min) can increase blood pressure, SVR & urinary output, provided vasopressin levels are low.
- Vasopressin also has the potential to reduce VO2 by the respiratory muscles.
- Intubation will facilitate insertion of lines and monitoring which may be difficult in a confused, agitated patient.

**Oxygen & Mechanical Ventilation**

- All shocked patients should be given high flow oxygen via a facemask with the aim of improving arterial oxygen saturation and DO2 to the tissues.
- Mechanical ventilation has much to commend it in the patient with high work of breathing as it will reduce VO2 by the respiratory muscles.

**Fluid Therapy**

- Optimising preload and restoring circulating volume are fundamental aspects of correcting tissue hypoxia in patients with shock.
- In patients with severe sepsis, aggressive volume replacement within 6 hours of presentation in conjunction with targeting an SvO2 of 70-75 can reduce hospital mortality by up to 16%.
- It is logical to replace the fluid which is lost; however, a restrictive transfusion strategy with a transfusion threshold of 70 appears to reduce in hospital mortality in patients with critical illness.
- The benefit of a restrictive transfusion strategy appears to be greatest for patients with APACHE scores of 20 or less and those aged less than 55 years.
- Human albumin has been shown to be safe in a large clinical trial and in the subgroup of patients with leaky capillaries it appears to restore circulating volume more efficiently; however, it is associated with increased morbidity and mortality in patients with traumatic brain injury.
- MMW-HES 200kDa and HMW-HES 450kDa have been associated with renal impairment & clotting abnormalities respectively.
- Hypertonic crystalloids have been studied in initial resuscitation of head injured patients; however, no benefits have been demonstrated.

**Hypovolaemic Shock**

- Altered haemodynamics may precipitate by increased systemic & pulmonary vascular resistance.

**Specific Measures in Septic Shock**

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**General Measures**

- Activated Protein C: an endogenous protein capable of promoting fibrinolysis and inhibiting thrombosis and inflammation; in sepsis the conversion of protein C from an inactive form to an active form is impaired due to downregulation of thrombomodulin by inflammatory cytokines.
- In patients with severe sepsis and APACHE-II >25, infusion of APC at 24ug/kg/hr for up to 96 hours reduces absolute risk of death by 6%. This effect was not seen in patients on heparin & it has subsequently been shown to increase mortality in patients with severe sepsis with low risk of death and in children.

**Hydroxyethyl Starch**

- Numerous studies have demonstrated that haemodynamic status often improves following commencement of haemofiltration & it is postulated that this is due to cytokine removal in the ultrafilter & by adsorption onto the filter.
- In patients with severe sepsis, there is some evidence that higher dose haemofiltration (45ml/kg/hr) may improve outcome; however, a rigorous, randomised trial has yet to be performed.

**Specific Measures in Septic Shock**

- It is usual to initiate high dose haemofiltration (45ml/kg/hr) to correct hypovolaemia, hypoxia & anaemia preoperatively.
- The use of vasopressin in this circumstance has not been well studied & potential concerns about tissue ischaemia and cardiac function exist.
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**High Volume Haemofiltration**

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**IABP**

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