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3

Understanding sepsis

Peter O'Donnell & Catherine Waskett

Introduction

Sepsis is a serious condition and remains the primary cause of death from infection despite advances in medicine, including antibiotic provision, vaccines and developments in acute and trauma care. Worldwide, millions of people die of sepsis every year; in the United Kingdom (UK) 102,000 cases of sepsis occur annually resulting in up to 37 000 deaths (UK Sepsis Trust, 2013). The incidence of sepsis has increased annually by 8-13% over the last decade. Reasons for this include an ageing population, increases in high-risk medical interventions and the development of drug resistant and more virulent varieties of microbes. Sustained campaigning from the UK Sepsis Trust over the past 5 years led to a publication in 2013 by the Parliamentary and Health Service Ombudsmen (PHSO) of 'Time to act: Severe Sepsis: rapid diagnosis and treatment saves lives'. This report focused on the cases of ten NHS patients who died because of failure to diagnose and rapidly treat severe sepsis. A Stage 2 Patient Safety Alert on sepsis care followed (NHS England, 2014). The alert aimed to heighten awareness of sepsis, cement existing progress such as the changes in clinical care driven by the Surviving Sepsis Campaign (SSC)(2013) and signpost health professionals to a new set of resources or toolkits developed to support prompt recognition and initiation of treatment for patients suspected of having sepsis. These toolkits included the Sepsis Six care bundle (Daniels et al, 2011) which has been associated with significant numbers of lives saved and reduced hospital stays.

Sepsis is a medical emergency. As in other medical emergencies such as heart attack, stroke or major trauma, there is a narrow window of opportunity in which timely, evidence based treatment can improve survival. It must be emphasised however, that treatment of sepsis can only begin after appropriate assessment and diagnosis have been made. Therefore the importance of a full clinical assessment, monitoring and management of a patient presenting with suspected sepsis is the focus of this chapter.

Aim and Learning Outcomes

The Aim

In this chapter the pathophysiology of sepsis, severe sepsis and septic shock will be outlined and by way of a case scenario the priorities of early, accurate assessment and management of patients presenting with suspected sepsis will be explored.

Learning Outcomes:

At the end of this chapter the reader will be able to:

- Discuss the major causes of sepsis.
- Describe the sepsis continuum.
- Identify and explain the pathophysiology of sepsis, severe sepsis and septic shock.
- Recognise the immediate assessment, specific monitoring and key investigations required to enable accurate and timely diagnosis.
- Understand and apply the Surviving Sepsis Campaign Guidelines and Surviving Sepsis Campaign Care Bundles.
- Discuss indicators of patient deterioration in sepsis.

Causes of Sepsis

Sepsis does not arise on its own; it stems from an infection in the lungs, urinary tract, skin, abdomen (such as appendicitis) or other parts of the body. Body systems most frequently affected by sepsis are respiratory, cardiovascular and renal (Dombrovskiy et al, 2007). Invasive medical procedures such as the insertion of vascular catheters, urinary catheters or surgical procedures can also introduce pathogens into the bloodstream leading to the development of sepsis. Sepsis can also be caused by neutropenia. Neutropenia is a decrease in the number of circulating neutrophils and is a common complication of systemic anti-cancer treatments such as chemotherapy (Moreau et al, 2009).It can result in a life-threatening episode of neutropenic sepsis, the risk of which is related to the degree of immunosuppression and the causative pathogen.

Any pathogenic microbe can cause sepsis, but bacteria, especially gram-negative organisms are the most common. However the incidence of gram-positive sepsis such as Methicillin Resistant Staphylococcus Aureus (MRSA) has increased. Viruses or fungi, particularly Candida, cause one-tenth of all cases (Dombrovskiy, et al, 2007).

The Continuum of Sepsis

There is evidence that early treatment for sepsis existed as far back as the early Chinese emperors but it was not until 1991 that definitions of sepsis were agreed and later published (Table 3.1)(Bone et al, 1991). These underpin more recent research and guidance from leading campaign groups such as SSC (2013) and Global Sepsis Alliance.

TABLE 3.1 ABOUT HERE

Sepsis can also be seen as a continuum progressing through stages identified above with each stage having more severe consequences, and unless treated rapidly and effectively, ultimately will result in Multi Organ Dysfunction Syndrome (MODS) (Fry, 2012.)

In addition to the above Dellinger et al (2012) describe clinical indicators which can lead to early diagnosis of sepsis are recognised internationally. These terms are summarised in Table 3.2.

TABLE 3.2 ABOUT HERE

Sepsis is diagnosed when patients show two or more of these SSI and there is evidence of a new infection. In this way early treatment can be initiated before microbiological evidence of a bloodstream infection is available. It is important to note however that although sepsis is a common cause of SIRS there are non-infective triggers also such as trauma or burns.

INSERT FIRST CASE STUDY BOX HERE

The Pathophysiology of Sepsis.

The homeostatic response to infection is an inflammatory defence against the pathogen which should result in recovery. If the defensive response is unable to overcome the infection then the patient may die; also if the inflammatory response is excessive death may result. Inflammatory responses trigger the release of mediators promoting vasodilation and capillary permeability. Excessive release of these mediators is termed SIRS. It is important to note that although sepsis is a common cause of SIRS there are non-infective triggers also such as trauma or burns. If there is excessive mediator release shock will result. If sepsis is the causative mechanism then it is termed septic shock.

Once sepsis occurs an abnormal inflammatory response is likely. The presence of pathogens in the bloodstream triggers mediator release from epithelial cells lining blood vessels (Angus & Poll, 2013). These mediators include tumour necrosis factor (TNF), interleukins, nitric oxide, and platelet activating factors. The result is increased capillary permeability, activation of the clotting cascade and vasodilation. Neutrophils, a type of white blood cell are mobilised. In the case of a localised infection this process supports

homeostasis but in sepsis the systemic response results in hypotension. Severe infection increases oxygen consumption and releases radical oxide compounds which have dampening effect on cardiac output (Kumar et al, 2015). This combination of events has profound effects. Reduced cardiac output and systemic vasodilation combine to induce severe hypotension resulting in poor tissue perfusion. Triggering of the clotting cascade may lead to disseminated intravascular coagulation (DIC); a syndrome characterised by widespread coagulation and thrombus formation in small blood vessels (Wada et al, 2013). The culmination of all of these effects, if not interrupted, is the failure of organs.

Multi Organ Dysfunction Syndrome is defined as the failure of more than one organ system. Table 3.3 lists indicators of organ dysfunction. In sepsis the respiratory system frequently fails first and it is this respiratory failure which often prompts admission to intensive care units (ICU).

As a result of the above sequelae cardiac dysfunction is compounded by the reduced cardiac output associated with sepsis. Systemic hypotension inevitably reduces renal perfusion and acute kidney injury (AKI) results if this is left uncorrected (see chapter 8). Cellular injury in the affected organs releases more inflammatory mediators resulting in sustained development septic shock.

Medical Management Strategies

International guidelines exist for the management of sepsis (Dellinger et al, 2012). There are also nursing considerations to complement the guidelines (Aitken et al, 2011). A care bundle is a group of interventions which, if taken together, have been shown to improve patient outcomes. The Surviving Sepsis Campaign guidelines recommend a resuscitation bundle for severe sepsis and septic shock. This care bundle should be delivered in the first six hours after recognition of sepsis. When two or more SSIs are detected the steps outlined in table 3.4 should occur within the set time scale. The bundle contains simple tasks as well as the

more complex tasks listed. All acute NHS trusts in the UK are required to have protocols in place which meet these guidelines.

The initial 3 hour bundle, referred to as the “Sepsis Six” (BMJ, 2015), should be initiated as soon as possible within the immediate clinical environment. Oxygen can be administered and the patient should have a urinary catheter inserted. Continuous cardiac monitoring, if available, is advisable. Nursing care in the initial stages involves advocating for and implementing these interventions.

Implementation of the Sepsis Six bundle has also been promoted by the use of mnemonics such as **BUFALO** (B: Blood cultures, U: Urine output, F: Fluids, A: Antibiotics, L: Lactate and Hb,O: Oxygen) or O2 FLUID (Oxygen, Fluids IV, Lactate measurement, Urine output measurement (catheterisation), Infection screening, Drugs – antibiotics as appropriate).

The steps outlined to be completed within 6 hours will usually require admission to a critical care unit. The patient will need repeated arterial blood sampling which can be made less uncomfortable if an arterial cannula is inserted; this will also allow constant and accurate blood pressure measurement. Central venous pressure and oxygen saturation measurement requires the insertion of a central venous catheter (CVC). Vasopressors are medications which act on the cardiovascular system to raise blood pressure and /or increase cardiac output. In sepsis nor-adrenaline is most commonly used; sometimes adrenaline and vasopressin are added. These drugs are usually administered using a CVC and all patients receiving them should have arterial blood pressure monitoring. Transfer to a critical care unit is usually indicated and therefore referral to the critical care unit is also indicated as an initial step.

Assessment and Reaching a Diagnosis

In practice a full systematic, preliminary assessment should have commenced on admission. However, in order to demonstrate the importance of early, accurate recognition of potential signs of deterioration and to highlight the potential to miss important clues if the practitioner lacks sufficient knowledge and awareness, the detailed assessment will be discussed here. Assessment must include simultaneous measurement of the patient's vital signs, an accurate history of presenting signs and symptoms and specific investigations in order that lifesaving interventions can be commenced immediately. In this chapter each aspect will be discussed separately; however in practice several aspects are conducted simultaneously to facilitate an accurate, prompt diagnosis, a factor that in sepsis has already been highlighted as a major factor in reducing mortality rates. Please also see table 2.4 in Chapter 2 for key signs and symptoms to be aware of.

The Preliminary Assessment

Airway

Initially Brian was conscious and talking so his airway was patent, but constant observation and assessment of his airway is vital (See chapter 1). Sepsis can cause rapid deterioration resulting in reduced conscious levels leading to airway patency problems. These problems will need immediate action and may require the use of an airway adjunct or in the seriously ill patient endotracheal intubation and mechanical intervention.

Breathing

Brian's observations reveals an elevated respiratory rate at 26 bpm. His ABGs had been taken 2 hours previously (Table 3.5) revealing low oxygen and high carbon dioxide levels. Low oxygen and high carbon dioxide levels in the blood will stimulate the respiratory centre to increase the rate of breathing to 'blow off' excess carbon dioxide. At this stage continued monitoring and documentation of Brian's respiratory rate, depth and pattern should be monitored and documented at least every 15 minutes to detect any trends or deterioration

and unless contraindicated he should receive 100 percent oxygen via a non-rebreathe mask at 10 to 15 litres per minute (British Thoracic Society, 2008). Although unlikely in Brian's case, if there was a history of chronic obstructive pulmonary disease (COPD) oxygen would need to be given with caution, with close monitoring for any reduction in his respiratory rate (see chapter 7).

Brian's pH indicates that his blood is acidotic. The pH of arterial blood can fall for a number of reasons and these are discussed in Chapters 2, 7, 8 and 10. In Brian's case the fall in arterial pH is a consequence of excess production of lactic acid associated with cellular hypoxia. Brian's lactate level is high at 5.6. Hyperlactaemia is typically present in patients with severe sepsis or septic shock and may be secondary to anaerobic metabolism due to hypoperfusion or other complex factors. The prognostic value of raised blood lactate levels has been well established in sepsis, particularly if the high levels persist. Obtaining a lactate level is essential to identifying tissue hypoperfusion in patients who are not yet hypotensive but who are at risk for septic shock (Focht et al, 2009).

Given the high risk for septic shock, all patients with elevated lactate >4 mmol/L enter the early goal-directed therapy portion of the 6-Hour Septic Shock Bundle, pressure (see table 3.4) (Dellinger et al, 2013) regardless of blood pressure.

In addition Brian's Base Excess (BE) has fallen as the body attempts to buffer the rising level of acid with a base. The level of carbon dioxide (PaO_2) is low as a consequence of Brian's increased respiratory rate. The amount of oxygen in the blood (PaO_2) and the oxygen saturation are reduced even though Brian was receiving 28% supplemental oxygen. On the sepsis continuum (Table 3.1) Brian at this point can be said to have severe sepsis.

TABLE 3.5 ABOUT HERE

Circulation

When Brian presented at A and E his blood pressure was within the normal range but the increase in his heart rate suggests that compensatory mechanisms had been activated to maintain blood pressure. His skin was warm, flushed and dry which may be opposite to what is seen in a typical 'shock picture' where cool and clammy skin is often observed. This is a result of the systemic vasodilation that occurs in sepsis and can confuse staff when assessing patients. It is usually seen before the onset of septic shock when the patient's condition is hyperdynamic. The skin is warm and flushed, pulse volume is increased, and pulse pressure is wide. At this stage monitoring of his pulse (including palpation to monitor volume and strength and blood pressure are required along with cardiac monitoring if available. After return from theatre Brian's pulse has increased to 125 bpm and his blood pressure has fallen to 90/50mmHg; his MAP now 46mmHg. This is caused by the presence of bacteria in the bloodstream triggering the release of mediators resulting in systemic vasodilation and subsequent hypotension. In addition, increased capillary permeability and vascular leakage due to the abnormal inflammatory response lead to hypovolaemia. Brian's low urine output indicates low renal perfusion.

Brian has had a subclavian Central Venous Catheter (CVC) inserted in theatre; his central venous pressure (CVP) is 4mmHg (see chapter 2 FOR CVP measurement). Ideally Brian's CVP should be maintained between 8-12mmHg so he now requires fluid replacement therapy (see Chapter 2) and should be administered 30ml/kg crystalloid to increase both his CVP and MAP. To achieve adequate fluid resuscitation the Surviving Sepsis Guidelines at least 30ml/kg of crystalloids (1.5-3 litres) to be infused for most patients in severe sepsis or septic shock. Brian may require more and fluid should be aggressively infused for as long as he continues to improve haemodynamically. If Brian remains hypotensive after fluid resuscitation, vasopressors via his CVC should be commenced to target a mean arterial pressure of 65mmHg. Nor-adrenaline should be provided as the first-line vasopressor (Dellinger et al, 2012). Adrenaline is considered the next line agent after nor-adrenaline if Brian's MAP is not maintained at 45mmHg s. Vasopressin at 0.03 units/minute is appropriate

to use with nor-adrenaline either to improve perfusion (increase MAP) or to reduce dose of nor-adrenaline (Dellinger et al, 2013).

Disability

Although awake and communicating when in A and E, three hours after he returned from theatre Brian became difficult to rouse and appeared confused. This may indicate reduced blood flow to the brain and also renal and hepatic impairment due to hypoperfusion. Brian's conscious level and confusion should be monitored at least hourly using the AVPU system (see Chapter 1) and if there is further cause for concern or should he deteriorate the Glasgow Coma Scale (GCS) will provide a more detailed evaluation of Brian's neurological status (See Chapter 4).

Brian has had occasional abdominal discomfort and bouts of diarrhoea over the past 6 months and his abdominal x-ray indicated that he had diverticular disease. Diverticular disease is a condition in which the mucosal layer of the colon herniates through the muscularis layer which is then termed a diverticulum (Porth, 2009). Most people with diverticular disease remain asymptomatic. The disease is often found when x-ray studies are completed for other purposes (as in Brian's case). When symptoms do occur, they are often attributed to irritable bowel syndrome or other causes. Ill-defined lower abdominal discomfort, a change in bowel habits (e.g., diarrhoea, constipation), bloating and flatulence are common and were some of the symptoms Brian had been having for a few months. Diverticulitis is a complication of diverticular disease in which there is inflammation and gross or microscopic perforation of the diverticulum. One of the most common complaints of diverticulitis is pain and tenderness in the lower left quadrant, accompanied by nausea and vomiting and a slight fever. These signs and symptoms were all present when Brian was admitted (Porth, 2009). Complications include perforation with peritonitis, haemorrhage and bowel obstruction. Brian's perforated bowel was a result of a perforated diverticulum and has

resulted in leakage of intestinal content into the abdominal cavity causing peritonitis and development of severe sepsis (Porth, 2009).

Due to this infection Brian was commenced on broad spectrum intravenous antibiotics after blood cultures were taken, this is in line with initial management indicated in the Surviving Sepsis Bundle (Surviving Sepsis Campaign, 2013) (see medical management section). Postoperatively, pain management should include assessment of the wound site, intensity and character of pain, along with the use of a pain assessment tool and administration of prescribed intravenous analgesia.

Exposure

Skin condition should be assessed as its integrity can be compromised during bed rest and while in the operating theatre itself. Brian's pressure areas should therefore be observed on admission and assessment undertaken to determine whether a pressure relieving mattress is required. In order to monitor urine output Brian had a urinary catheter inserted. As a result of the reduced renal perfusion and subsequent retention of water, any urine passed will be dark, concentrated and have a high specific gravity. Brian will also be nil by mouth and have a nasogastric tube passed to enable gastric decompression and drainage of gastric aspirate after surgery. Post-operatively Brian is now oliguric, tachycardic and hypotensive but his skin is still warm and flushed. These are all indications of severe sepsis.

Specific Investigations

The following specific investigations to detect a clinically suspected focal infection, the presence of a clinically occult focal infection, and complications of sepsis and septic shock are indicated and would have been completed both pre and post operatively:

- Full blood count (FBC) with differential leukocyte count

- Blood group, save and cross matching for potential blood transfusion
- Coagulation studies (prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen levels)
- Serum Lactate
- Electrolytes (sodium, chloride, magnesium, calcium, phosphate, glucose,)
- Renal and hepatic function tests (creatinine, blood urea nitrogen, bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, albumin, lipase)
- Blood cultures
- Urinalysis and urine cultures
- Gram stain and culture of secretions and tissue

The following radiological studies may also be undertaken to evaluate patients with suspected severe sepsis and septic shock although in Brian's case as he had an abdominal focus to his presenting symptoms only a chest and abdominal x-ray was necessary:

- Chest, abdominal, or extremity radiography
- Abdominal ultrasonography
- Computed tomography of the abdomen or head

INSERT BOX 3 CASE SCENARIO ABOUT HERE

Brian's vital signs indicate he is now at the septic shock stage of the sepsis continuum (see table 3.1 and 3.2); he has persistent hypotension despite adequate volume resuscitation, requiring vasopressors to maintain cardiac output and tissue perfusion. Septic shock is far easier to recognise, as by this time patients are very unwell and usually present as pale, cold and clammy rather than the warm and flushed appearance that can manifest in earlier stages of sepsis. The survival rate for patients in septic shock is very low with estimates of between 40-60% mortality rates despite critical care support (McPherson et al, 2013. Further management strategies in severe sepsis and septic shock focus upon the restoration and

maintenance of adequate tissue perfusion to prevent multiple organ dysfunction. Haemodynamic support in severe sepsis and septic shock is provided by:

- Restoring the adequate circulating blood volume.
- Optimising perfusion pressure and cardiac function with vasoactive and inotropic support to improve tissue oxygenation by reversing inappropriate vasodilation and improving cardiac output.

Please refer to chapter 2 for further detail regarding fluid resuscitation and the use of vasoactive and inotropic drugs in the management of all types of shock.

Ongoing care issues and the role of the nurse

Although the Surviving Sepsis Campaign Guidelines (Dellinger et al, 2012) provide a comprehensive review of the medical management of patients with sepsis and septic shock essential nursing care for optimal outcomes is not identified. Expert nursing knowledge and skills are required for the early recognition of SSI as well as both the identification of the patient deteriorating as a result of developing sepsis and the ongoing implementation of competent care for the known severe sepsis patient. In addition many of the sepsis bundle recommendations involve aspects of nursing care. Nurses can play an important role in promoting implementation of the guidelines. The guidelines include prevention measures addressing education, accountability, surveillance of nosocomial infection, hand hygiene and prevention of respiratory, central catheter related, surgical site and urinary tract infections with infection management recommendations focused on both focused control of the infection source and transmission based precautions. In addition consideration needs to be given to the patient's family and carers. Open and frank discussions with the patient and family about treatment and possible outcomes will help them understand the severity of the condition and its expected outcome. Please also refer to Chapter 2 for further detail regarding ongoing care issues and the role of the nurse when caring for patients in shock.

Summary

Sepsis is a systematic response to overwhelming infection and is a serious condition carrying a high risk of mortality. The hallmarks of severe sepsis and septic shock are changes that occur at the microvascular and cellular level and may not be clearly manifested in recorded vital signs or on clinical examination. The nurse is often the closest to the patient and in a key position to identify any subtle changes at their earliest onset and is therefore able to advocate early intervention. Knowledge of the signs of symptoms of SSI, SIRS, sepsis and septic shock is key to this. Once sepsis is diagnosed, early and aggressive treatment in accordance with the Surviving Sepsis Campaign guidelines can begin, which greatly reduces mortality rates associated with sepsis.

Further Reading

Daniels, R., Nutbeam, T. (eds) *ABC of sepsis.* (Oxford : Wiley-Blackwell, 2010).
McClelland H, Moxon A (2014) Early identification and treatment of sepsis. *Nursing Times*; 110: 4, 14-17.

References – Sepsis Chapter

Aitken, LM, Williams, G, Harvey, M et al (2011) Nursing considerations to complement the surviving Sepsis Guidelines. *Critical Care Medicine* 39 (7): 1800-18.
Angus D, van der Poll T., (2013) Severe Sepsis and Septic Shock, *N Engl J Med* 369:840-851 August 29.
Bone, RC (1991)Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest*, 101 (6): p 1644-1655.
British Medical Journal (2015) Sepsis in Adults, *BMJ* Best practice monograph 245.
Daniels, R, Nutbeam, T, McNamara, G. Galvin, C (2011) the sepsis six and the severe sepsis resuscitation bundle: a prospective observational cohort study. *Emerg Med* 28 (6):507-12.
Dellinger R., Levy M., Carlet J., Bion J., Parker M. , Jaeschke R. , Reinhart K., Angus D., Brun-Buisson C., R Beale, Calandra T., J Dhainaut J, Gerlach H., Harvey M., Marini J., JMarshal J., Ranieri M., Ramsey G., Sevransky J, ThompsonT., Townsend S., Vender J, Zimmerman J., Vincent J, (2008) Surviving sepsis Campaign: International guidelines for management of severe sepsis and septic shock: *Crit Care Med.* 36: 296–327
Dellinger, R., Levy M., Rhodes A, Annane D., Gerlach H., Opal S., Sevransky J., (2012) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, *Critical Care Medicine* (2013) 41 (2): 580-637.

Dombrovskiy, VY, Martin,AA, Sunderram, J and Paz, HL (2007) Rapid increase in hospitalization and mortality rates for severe sepsis in the United States: A trend analysis from 1991 to 2003. *Critical Care Medicine,* 35 (5): 1244-1250.
Focht A, Jones AE, Lowe TJ. (2009) Early goal-directed therapy: improving mortality and morbidity of sepsis in the emergency department. *Jt Comm J Qual Patient Saf*. 35:186-91.
Fry, D. E. (2012). Sepsis, systemic inflammatory response, and multiple organ dysfunction: the mystery continues. *The American Surgeon*, 78(1), 1-8.
Intensive Care National Audit & Research Centre (ICNARC) (2011) *Number of admissions receiving advanced respiratory support,* ICNARC:London
Kumar D., Kumar A., Singh S., Tilak R., (2015) , Candidemia-induced pediatric sepsis and its association with free radicals, nitric oxide, and cytokine level in host , *Journal of Critical Care,* Volume 30, Issue 2, Pages 296–303
McPherson, D., Griffiths, C,. Williams, M,. Baker, A,. Klodowski, E,. Jacobson, B, and Donaldson, L. (2013) Sepsis associated mortality in England: an analysis of multiple cause of death data from 2001 to 2010. BMJ Open, Vol 3 (8).
Moreau, M, Kiastersky, J, Schwarzbold, A et al (2009) A general chemotherapy myelotoxicity score to predict febrile neutropenia in haematological malignancies. *Annals of Oncology*, 20 (3): 513-519.
NHS England (2014) Stage two: *Resources to support the prompt recognition of sepsis and the rapid initiation of treatment.* http://tinyurl.com/k5lenqt
Parliamentary and Health Service Ombudsman (2013) *Time to act. Severe sepsis: rapid diagnosis and treatment saves lives.* http://tinyurl.com/q31oc4u
Society of Critical care Medicine, 2013, Surving Sepsis Campaign-Sepsis Care Bundles, London
Wada H, Thachil J, Di Nisio, M, Mathew P, Kurosawa S, Gando S, Kim HK, Nielsen JD, Dempfle C-E, Levi M, Toh C-H., (2013)Guidance for diagnosis and treatment of disseminated intravascular coagulation from harmonization of the recommendations from three guidelines. *J Thromb Haemost* 11: 761–7.

Additional resources

Sepsis Six Saving Lives video (15 minutes of content) can be accessed at: http://www.youtube.com/watch?v=CrUHnYIZbpM
ICNARC Intensive care national audit and research centre. Can be accessed at: https://www.icnarc.org/Our-Audit/Audits/Cmp/Our-National-Analyses/Reason-For-Admission
The UK Sepsis Trust can be accessed at: http://sepsistrust.org/

Table 3.1 Clinical Indicators of Sepsis (Dellinger et al.)

Term	Definition
Systemic inflammatory response syndrome (SIRS)	The systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: • Temperature >38°C or <36°C Heart rate >90bpm • Respiratory rate >20 breaths/min or PaC0 <32mmHg • White blood cell count >12,000/mm3 • <4,000/mm3, or >10% immature (band) forms
Sepsis	The systemic response to infection, manifested by two or more of the following, as a result of infection: • Temperature >38°C or <36°C Heart rate >90bpm • Respiratory rate >20 breaths/min or PaC0 <32mmHg and white blood cell count >12,000 cells/mm3 • <4,000 cells/mm3 or >10% immature (band) forms
Severe sepsis	Associated with organ dysfunction, hypo-perfusion or hypotension. Hypo-perfusion and perfusion abnormalities may include but are not limited to: • Lactic acidosis • Oliguria • Acute alteration in mental status
Septic shock sepsis	Induced with hypotension despite adequate fluid resuscitation, along with the presence of perfusion abnormalities that may include - but are not limited to - lactic acidosis, oliguria or an acute alteration in mental status. Patients receiving inotropic or vasopressor agents may not be hypotensive at the time that

	perfusion abnormalities are measured
Sepsis-induced hypotension	A systolic blood pressure <90mmHg or a reduction of 2:40mmHg from baseline in the absence of other causes for hypotension
Multiple organ dysfunction syndrome (MODS)	The presence of altered organ function in an acutely ill patient such that homoeostasis cannot be maintained without intervention

Table 3.2 Signs and Symptoms of Serious Infection

Term	Clinical Indicator
Signs of serious infection (SSI)	Temperature: <36^{0}C or >38 ^{0}C Heart rate: >90 bpm Respiratory rate: >20 White cell count: <4000 or > 12000 add units
Sepsis	Bloodstream infection
Severe Sepsis	Sepsis with evidence of organ failure
Septic Shock	Sepsis with shock
SIRS	Systemic inflammatory response syndrome

Table 3. 3 – Signs of Acute Organ Failure

Cardiovascular System	Pulse > 100 beats per minute Dysrhythmias Systolic Blood Pressure , 90mmHg or 40 point drop from baseline Mean Arterial Pressure< 65 add units
Respiratory System	Respiratory rate > 24 breaths per minute O_2 Sat <90% with new/more oxygen
Renal System	Creatinine >177µmol/L or urinary output <0.5ml/kg/hr for 2 hrs
Coagulation	International normalised ratio >1.5 or partial thromboplastin time >60 seconds
Gastrointestinal System	Ileus
Hepatic System	Bilirubin >34µmol/L
Central Nervous System	Altered level of consciousness Confusion Psychosis
Hypoperfusion	Lactate >2mmol/L

TABLE 3.4 Sepsis six care bundle (Society of Critical Care Medicine, Surviving Sepsis Campaign)

To be completed within 3 hours	• Give oxygen • Measure lactate level • Obtain blood culture sample before administering antibiotics • Administer broad spectrum antibiotics • Administer 30ml/kg crystalloid for hypotension or if lactate ≥ 4mmol/L • Monitor hourly urine output • Referral for critical care advice/ transfer
To be completed within 6 hours	• Administer vasopressors if hypotension does not respond to fluid resuscitation. Attempt to raise Mean Arterial Pressure (MAP) ≥ 65mmHg • Measure Central Venous Pressure if hypotension is persistent or if lactate ≥ 4mmol/L (target 8 mmHg) • Measure Central Venous Oxygen saturation if hypotension is persistent or if lactate ≥ 4mmol/L (target 70%) • Repeat lactate measurement if

	initial lactate is raised

Table 3.5 Arterial blood gases

	Normal range of ABG values on air	**Brian's ABG results 8 hours after his return from theatre on 28% oxygen**
pH	**7.35-7.45**	**7.32**
PaO_2 (kPa)	**11-13.3**	**10.5**
$PaCO_2$ (kPa)	**4.8-6.0**	**3.9**
HCO_3 (mmol/L)	**21-28**	**17.8**
BE	**-2 to +2**	**-4**
SaO_2 (%)	**95-100**	**94**
Lactate (mmol/L)	**0.5 to 2.2**	**5.0**