

Sepsis

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Sepsis describes the systemic condition that is associated with infection (presumed or identified). It is a life-threatening acute illness that occurs relatively frequently in patients with palliative illnesses and at times it can be difficult to know if a patient's deterioration is due to sepsis or due to progression of their underlying illness. Sometimes this distinction is unimportant as it is clear that the person is in the last few days or weeks of life from their palliative illness, however at other times, this distinction is important because active treatment of sepsis can be very effective. Although many patients can be cured from their acute infection, some never recover to their pre-infection function, for example, sometimes some mobility or cognitive impairment remains post-treatment.

In addition to patients with palliative illnesses such as advanced cancer who develop sepsis, palliative care teams may be asked to be involved in symptom relief and psychological support for previously non-palliative patients in intensive care and critical care units who have developed multiple organ failure with little chance of recovery in the context of sepsis and where treatment is being withdrawn.

Terminology and Clinical Features

Sepsis refers to the systemic condition that occurs in association with severe infections. Some of the following features will be noted:

Signs may include
Raised temperature (e.g. temp > 38.3) or a low temperature (e.g. temp < 36.0)
Tachycardia (e.g. heart rate > 90)
Tachypnoea (e.g. RR > 20)
New confusion or drowsiness
Signs of a positive fluid balance or oedema
Raised blood sugar (> 7.7) in a non-diabetic person
Evidence of reduced tissue perfusion (e.g. decreased capillary refill)
Hypotension (systolic BP < 90 or MAP < 70 or systolic BP decrease > 40)
Blood tests of inflammation
Raised white cell count (> 12) or reduced white cell count (< 4) or > 10% precursor white cells circulating (e.g. myelocytes and metamyelocytes)
Raised CRP
Others: raised procalcitonin, raised lactate (> 1)
Features of organ failure
Hypoxaemia (low PaO ₂)
Oliguria (urine output < 0.5 ml/kg/hour despite adequate fluid resuscitation)
Creatinine increase of > 44)
Deranged coagulation with INR > 1.5 or APTT > 60)
Thrombocytopenia (platelets < 100)
Absent bowel sounds consistent with an ileus
Raised bilirubin > 70

Severe sepsis is defined as sepsis with any of the following:

- Hypotension
- Raised lactate
- Acute lung injury in the absence of pneumonia
- Renal failure with either
 - Urine output down as per the table above despite fluid resuscitation
 - Creatinine > 176
- Bilirubin > 70
- Platelets < 100
- INR > 1.5

Septic shock is defined as sepsis with hypotension despite adequate fluid resuscitation (defined as 30 ml/kg - in a 70kg man this would be 2.1 litres).

SIRS, or systemic inflammatory response syndrome, is a term used to describe the systemic inflammatory effects of any severe non-infective insult, although, because in practice, sepsis and SIRS look the same clinically, this distinction is often ignored and the terms are almost used interchangeably.

When taking a history and examining a patient with sepsis, it is very important to look for symptoms and signs that might help determine the source of infection, e.g.

- Acute red painful rash on the legs -> suggests cellulitis
- Cough productive of sputum and dyspnoea -> suggests a lower respiratory tract infection
- Suprapubic tenderness and dysuria -> suggests a UTI
- Right upper quadrant pain and fever -> suggests cholecystitis or a biliary tract infection
- Headache and vomiting -> might suggest meningitis
- Tenderness and erythema around a central or PICC line -> might suggest a line infection

Epidemiology

Sepsis is a common problem with relevant risk factors including

- Advanced age > 65 years
- Immunosuppression including comorbidities that reduce immune defences such as cancer and liver failure
- Diabetes
- Recent hospitalization

Sepsis is most commonly caused by bacteria (especially Gram positive cocci) although occasionally sepsis is caused by other organisms such as fungi.

Pathophysiology

The normal response to infection begins with innate immune cells such as macrophages recognizing and binding to the pathogen which results in release of cytokines and neutrophils being activated. When the inflammatory response becomes widespread beyond the site of infection, then damage can occur at these tissues. This is sepsis and no-one knows why this occurs in some patients and circumstances, but not in others. Some of the features of this damage at a microscopic level might

include:

- Endothelial damage / capillary lesions due to the imbalances in the coagulation and fibrinolytic systems causing local tissue ischaemia
- Vasodilation with hypotension
- Endothelial injury in the lungs with pulmonary oedema
- Cytokine induced renal vasoconstriction plus poor perfusion from hypotension causing acute tubular necrosis and renal failure
- Inflammatory mediators causing cell signalling abnormalities within the central nervous system causing a delirium

Management

Investigations and treatment of suspected sepsis in the palliative care population will vary greatly from patient to patient. For patients who have a very advanced terminal illness, then investigations and treatment is inappropriate. In patients who have a good quality of life and who might, would it not be for the current sepsis, have many months or even years to live, then aggressive treatment is usually appropriate. The management described below is for these patients:

Oxygen and Respiration

Oxygen is important as sepsis is often associated with increased work of breathing. In palliative patients with severe sepsis and respiratory failure, intubation and mechanical ventilation is usually not appropriate, however it would be standard treatment when necessary in other patients. A chest x-ray +/- a blood gas may be helpful in identifying source of infection and severity of sepsis, although again, in the hospice setting this will often not be appropriate.

Fluid resuscitation and Perfusion

Where there is evidence of poor perfusion or hypotension is present, an IV line should be inserted and rapid IV fluids given. The amount of fluid to give is not well defined, but obviously severely hypotensive patients need urgent fluid in large amounts (e.g. an initial 500 ml bolus followed by 2-3 litres over 6 hours) whereas patients without hypotension need less. When giving rapid fluids, signs of fluid overload such as a raised JVP and pulmonary oedema should be watched for. Studies have not shown benefit of one fluid over another and so a crystalloid (e.g. normal saline) is a good option.

For patients whose blood pressure does not response to IV fluids, standard treatment in non-palliative patients includes vasopressors such as noradrenaline (norepinephrine) in intensive care. This is unlikely to be appropriate for palliative patients, although there might be the occasional time it is.

Antibiotics

Blood and other cultures appropriate to symptoms should be taken.

Urgent antibiotics directed at the likely source of infection are very important. Most hospitals have local protocols that should guide therapy. The likely site of infection and patient allergies are key

factors in determining the most appropriate antibiotics but in general broad spectrum antibiotics should be used until the infecting organism is known, for example:

Tasozin 4.5 g IV three times a day

VTE prophylaxis

Patients with sepsis are at high risk of DVTs and prophylaxis should usually be given if active treatment is being contemplated.

Discussion with patient and family

An honest discussion with the family and patient is almost always helpful and required. A discussion will help make clear what the patient and family wish and it is a chance to prepare the family for the death of their loved one.

Symptom Relief Medications

Patients with sepsis and a palliative illness can have symptom relief treatment (e.g. opioids for pain) in addition to active treatment. Active treatments and all they entail (e.g. blood tests and IV lines) can be quite distressing for patients near the end of their life and sometimes a pragmatic approach involves starting with active treatment for a few days but withdrawing if no improvement or deterioration is occurring. Like all things in palliative care, this is an art-form as much as a science.

Prognosis

In the palliative care setting, sepsis often is the final event leading to death. Even in the non-palliative patient population, well treated sepsis has a high mortality rate with perhaps up to 1 in 2 people dying where there is multi-organ dysfunction.

One of the key prognostic factors is how the patient's own system responds. Some negative prognostic indicators for patients with sepsis (not specifically palliative care patients) are:

- Hypothermia (3 times more likely to die in one study)
- Leukopaenia (2 times more likely to die in one study)
- Coagulopathy (6 times more likely to die in one study)

The site of infection is also an important prognostic factor. Pulmonary, gastrointestinal or unknown source infections carry a worse prognosis than urinary source infections. The presence or absence of a positive blood culture does not appear to influence prognosis.

Early treatment is an important prognostic factor. Early antibiotics has a major effect on reducing mortality, as does aggressively restoring vascular perfusion (e.g. fluid resuscitation).

In a patient who recovers from sepsis, they will often return to their baseline, or near baseline, function before they became acutely unwell. Some patients however never recover to their pre-infection function, for example sometimes some mobility or cognitive impairment remains post-

treatment.

[condition, microbiology](#)

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