

# Sepsis Part 1: Possible causes and high-risk groups

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Sepsis is defined as the body's reaction to infection that results in a dysregulated, life-threatening immune response causing organs to fail (UK Sepsis Trust, 2016). Sepsis can be triggered by any infection but is most commonly the result of bacterial infections of the lungs, abdominal organs, soft tissues, skin or urinary tract (UK Sepsis Trust, 2017). Sepsis is a time-critical condition: if detected and treated early, clinical outcome is good, but if left unchecked the patient can quickly develop septic shock, which causes multi-organ failure (UK Sepsis Trust, 2017). Septic shock is a subset of sepsis with circulatory, cellular and metabolic dysfunction, and is associated with a high risk of mortality (Surviving Sepsis Campaign, 2017).

Sepsis accounts for 7–9 million deaths annually worldwide (Global Sepsis Alliance, 2019). World Sepsis Day, held on 13 September every year, aims to increase global awareness of this poorly understood condition. In May 2017, the World Health Assembly and the World Health Organization made sepsis a global health priority and adopted a resolution to prevent, diagnose, manage and improve sepsis outcome (Global Sepsis Alliance, 2017).

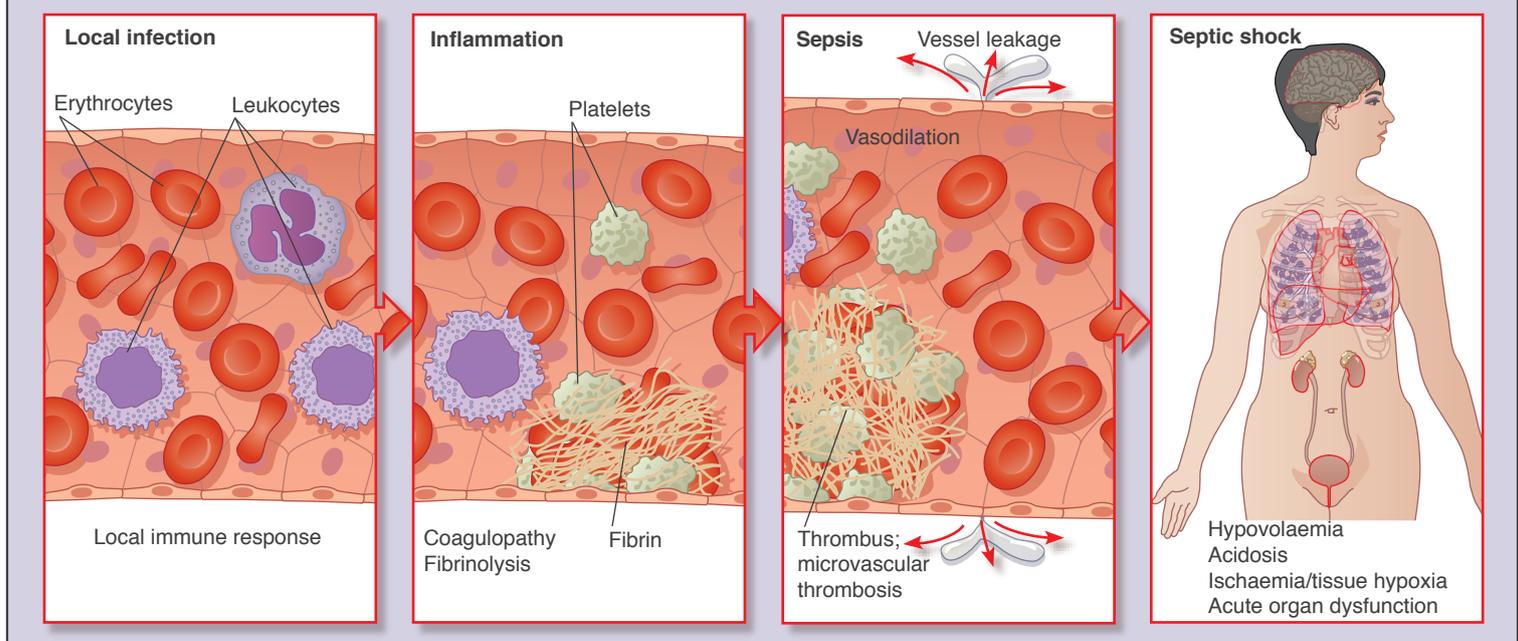
In the UK, 52,000 deaths are attributable to sepsis each year—more than lung, bowel and breast cancer combined—with a cost of £2 billion to the NHS (Nutbeam & Daniels, 2019). An estimated 65,000 patients each year survive sepsis but can be left with long-term complications, such as cognitive dysfunction, amputation and irreversible damage to the lungs, kidneys and heart, as well as post-traumatic stress disorder, often linked to their prolonged stay in intensive care units (NCEPOD, 2015).

Political and healthcare organisations have increased focus on better care and outcomes for patients with sepsis. Sepsis is a clinical priority in the UK (NHS England, 2015). It is now linked to the Commissioning for Quality and Innovation (CQUINs) payments framework, which focuses on preventing avoidable cases of sepsis, increasing awareness of sepsis among both public and professionals, improving standards, reporting mechanisms and the identification and treatment of sepsis, and highlighting appropriate and timely antibiotic use and antimicrobial stewardship. In the UK, many NHS trusts have implemented local and regional initiatives to improve outcomes for patients including the use of sepsis pathways.

The National Confidential Enquiry into Patient Outcome and Death (NCEPOD, 2015) recommends introducing a clinical lead for sepsis who will champion best practice, take responsibility for the clinical governance of management of sepsis and liaise with staff responsible for antimicrobial stewardship in their hospital. The National Institute for Health and Care Excellence (NICE, 2017) has published guidelines and recommendations on the recognition, diagnosis and early management of sepsis. Reports from the Parliamentary and Health Service Ombudsman (2013), the NCEPOD (2015) and Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries Across the UK (MBRRACE-UK, 2014) highlight failings in identifying sepsis and promote best practice in the assessment and timely initiation of treatment for sepsis.

This procedure explains the pathophysiology of sepsis, its possible causes and vulnerable patient groups.

## Pathology of sepsis

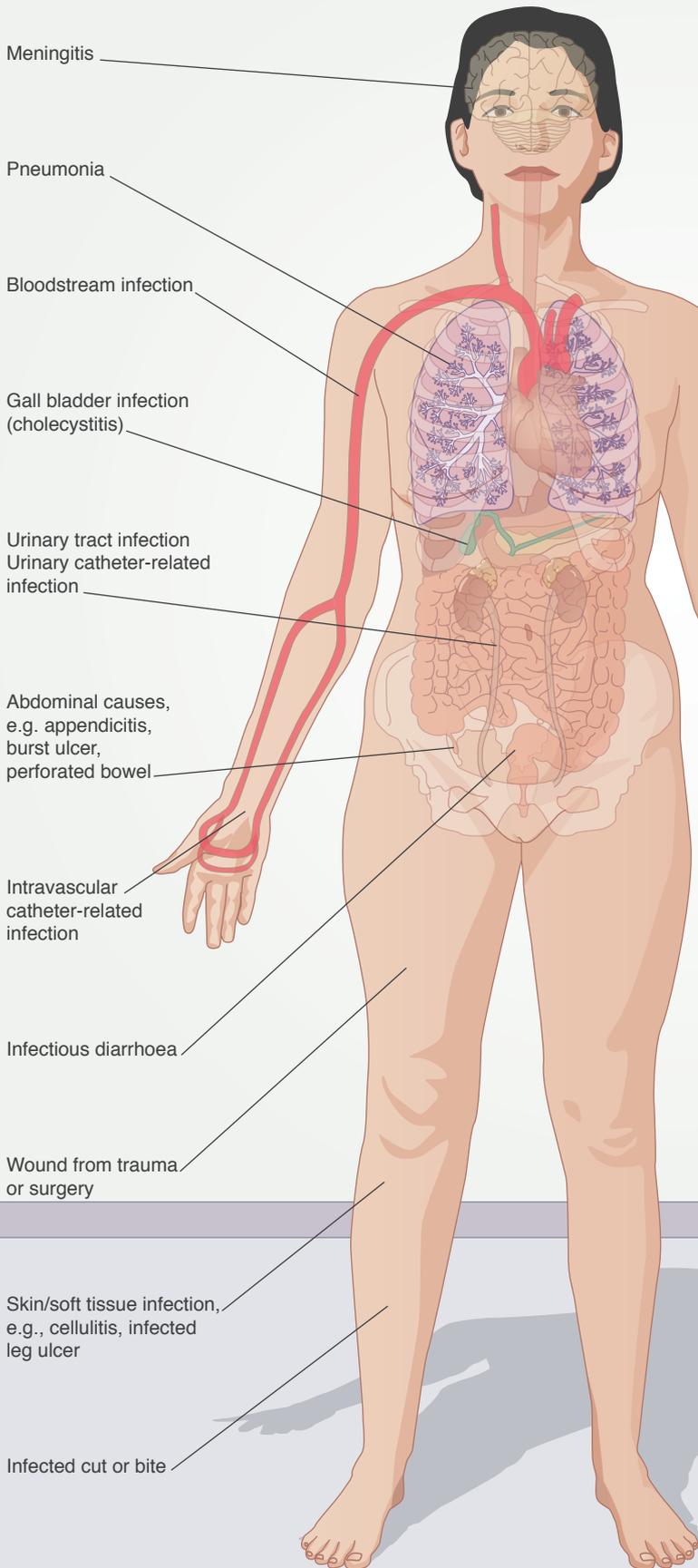


The pathogenesis of sepsis is complex and remains poorly understood (Annane *et al.*, 2005). During sepsis, pathogens interact with the products released by the immune system as a response to infection (Rello & Restrepo, 2008). The goal of the immune system is to achieve homeostasis and destroy the pathogens, but if a local immune response is unable to do this, a systemic (whole body) inflammatory response occurs (McCormick, 2009), with the immune system releasing large amounts of leukocytes (white blood cells) and chemicals such as chemokines, cytokines and coagulation factors (Ward & Levy, 2017). This abnormal and dysregulated immune response causes complex changes in the body's inflammatory and coagulopathy function and leads to vasodilation, vessel leakage and an increase in metabolic function. The resultant increase in oxygen demand to the organs, coupled with intravascular loss of fluid into the interstitial space due to vasodilation and vessel leakage, causes tissue hypoperfusion, acidosis and ischaemia at the cellular level (McClelland & Moxon, 2014).

Do not undertake or attempt any procedure unless you are, or have supervision from, a properly trained, experienced and competent person. Always first explain the procedure to the patient and obtain their consent, in line with the policies of your employer or educational institution.

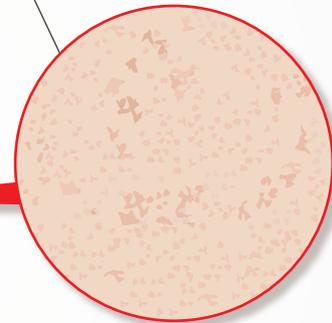
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Some common causes of sepsis



Signs of sepsis in adults (UK Sepsis Trust, 2019)

- S**lurred speech or confusion
- E**xtrême shivering or muscle pain or fever
- P**assing no urine (in a day)
- S**evere breathlessness
- I**t feels like you are going to die
- S**kin mottled or discoloured



Signs of sepsis in children (UK Sepsis Trust, 2019)

A child who is unwell with a fever (or who has had a fever in the last 24 hours) or low temperature and who has any of the following symptoms requires urgent medical attention:

- Breathing very fast
- A "fit" or convulsion
- Skin that looks mottled, bluish, or pale
- A rash that does not fade when you press it
- Very lethargic or difficult to wake
- Feels abnormally cold to touch.

If a child shows any of the following symptoms, seek advice:

- Temperature over 38°C in babies under 3 months, or over 39°C in babies aged 3–6 months
- Any high temperature in a child who cannot be encouraged to show interest in anything
- Low temperature (below 36°C: check three times in a 10-minute period)
- Finding it much harder to breathe than normal
- Can't say more than a few words at once (for older children who normally talk)
- Not passed urine or had a wet nappy for 12 hours
- New baby under 1 month old with no interest in feeding
- Not drinking for more than 8 hours (when awake)
- Bile-stained (green), bloody or black vomit/sick
- Fontanelle on a baby's head is bulging
- Eyes look "sunken"
- Child cannot be encouraged to show interest in anything
- Baby is floppy
- Weak, "whining" or continuous crying in a younger child
- Confusion in an older child
- Not responding or very irritable
- Stiff neck, especially when trying to look up and down.

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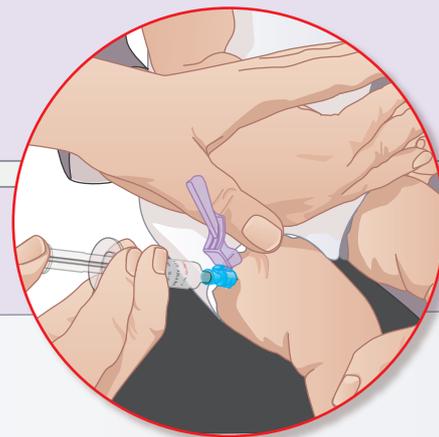
### Recognising sepsis

Anyone can be affected by sepsis, and it remains unclear why some people who get an infection develop sepsis and others do not. People are more likely to develop sepsis after a viral illness, such as a cold, or a minor injury (UK Sepsis Trust, 2019). Evidence suggests that early recognition of sepsis can be improved. The very young, the very old, patients who are immunosuppressed and pregnant women are at particular risk (NHS England, 2015).

### Vulnerable groups: (a) Children and babies

Sepsis is the leading cause of death in children worldwide and an estimated 3 million neonates and 1.2 million children develop sepsis annually (Fleischmann-Struzek *et al.*, 2018; WHO, 2018). Children often present with atypical or vague signs and symptoms, which can lead to delayed or inappropriate treatment (UK Sepsis Trust, 2019). The immune system of a child is not the same as that of an adult, and the immune system does not reach full maturity until adolescence. Neonates are most compromised as their immune system is poor and their immune response is less reactive to pathogens (Randolph & McCulloh, 2014).

The UK vaccination programme has contributed to the prevention of sepsis. Childhood vaccinations against *Haemophilus influenzae* type B, meningococcal serogroup C and pneumococcal infection has both protected the vaccinated children and reduced the circulation of these organisms in the wider community (NHS England, 2015).



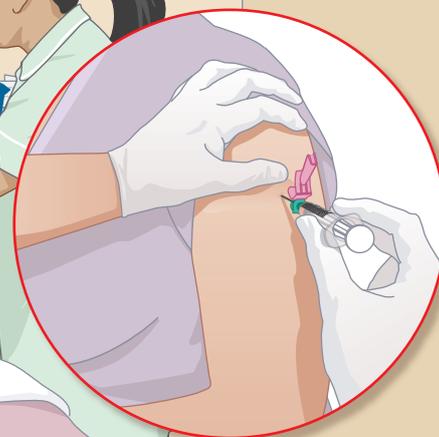
Ensuring that childhood vaccinations are kept up to date will help protect children against sepsis



### (b) Older patients

Due to existing comorbidities, reduced immunity, limited function and the effects of aging, older people are particularly vulnerable to developing sepsis (Nasa *et al.*, 2012), in particular from respiratory and urinary tract infections (UTI) (NCEPOD, 2015). Liver disease and malnutrition increase the risk of developing sepsis (Martin *et al.*, 2017; Yan *et al.*, 2014; Foreman *et al.*, 2003).

The influenza and pneumococcal vaccine programme can help to prevent some cases of pneumonia and taking preventative measures, such as ensuring adequate nutrition and hydration and effective management of incontinence, can help reduce the chance of UTI (NHS England, 2015).



Some vaccination programmes for older people reduce the risk of infections that can result in sepsis

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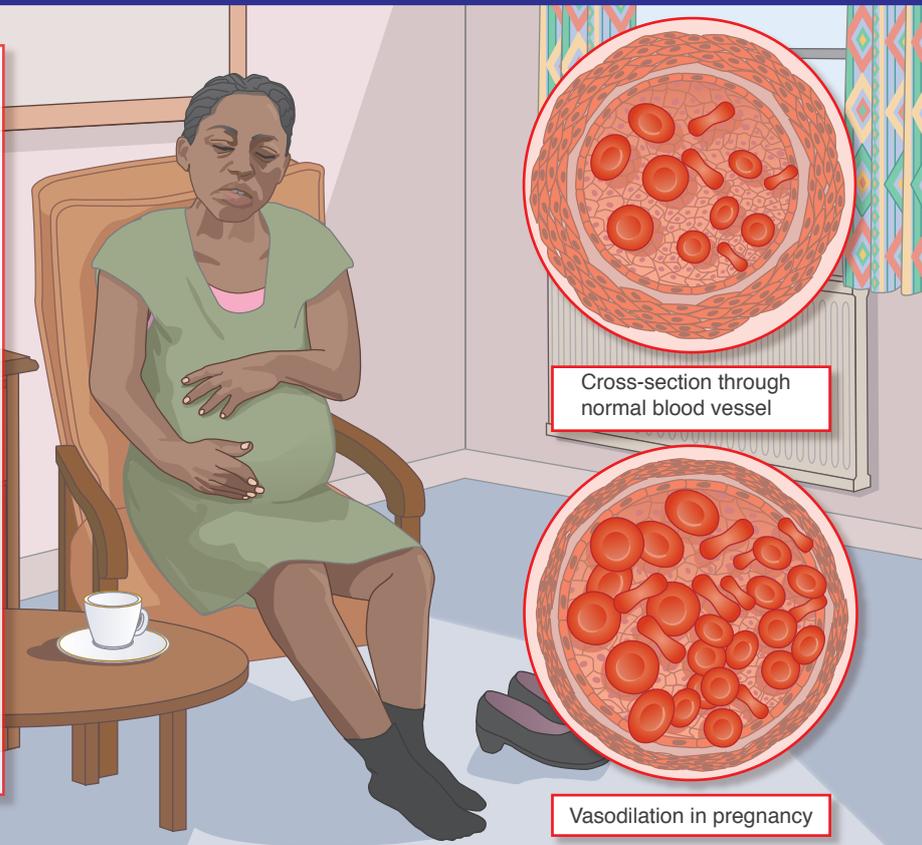
## (c) Pregnancy

Sepsis is a major cause of morbidity and mortality in pregnant women and their babies in low- and middle-income countries, due to lack of access to safe and affordable healthcare (WHO, 2018). During pregnancy, significant physiological changes occur that make pregnant women more vulnerable. Vasodilation of arterial and venous smooth muscle occurs to accommodate the increase in blood volume (see inset), making pregnant women vulnerable to dyspnoea, palpitations, tiredness and pulmonary oedema. Changes to respiratory physiology increase the respiratory rate.

Changes to the coagulation of the blood, increased body weight and a reduction in cardiorespiratory reserve increase complications during infection (Joseph *et al.*, 2009).

The ureters can become obstructed by the expanding uterus leading to urinary stasis and increasing the incidence of developing a UTI.

Measure pulse, temperature, respiratory rate and blood pressure in any pregnant woman who presents feeling unwell. Preventing influenza during pregnancy is important and pregnant women are offered influenza immunisation for this reason (NHS England, 2015).



## (d) People who are immunosuppressed

Patients may be immunosuppressed due to radiotherapy, chemotherapy, long-term steroid therapy or anti-rejection drugs following organ transplant, autoimmune conditions, diabetes or vascular disease. Prevention and treatment of sepsis can be challenging in patients with a poor immune response to infection (Kalil & Opal, 2015).

The bone marrow continuously produces white blood cells called neutrophils, which help to provide immunity, but chemotherapy suppresses this function and prevents these white blood cells from maturing. As a result, their number in the bloodstream decreases; this is called neutropenia (Vioral & Wentley, 2015). Cancer patients receiving chemotherapy are therefore prone to neutropenic sepsis, which is a significant cause of cancer treatment-related mortality (Ford & Marshall, 2014). Patients who are on long-term immunosuppressant therapy likewise require regular monitoring of their white blood cell counts.

Advise vulnerable patients about relevant immunisations. For example, offer the pneumococcal vaccine to patients with respiratory conditions, such as chronic obstructive pulmonary disease (COPD). Give information to patients and carers about how to recognise the signs and symptoms of sepsis and what to do if they feel unwell. The UK Sepsis Trust has excellent resources for patients: <https://sepsistrust.org/>

