In July, NICE issued a guideline on the recognition, diagnosis and early management of sepsis, in response to the publication of evidence showing significant shortcomings in care. This article summarises the main recommendations of the new guidance.

In 2013, the Parliamentary and Health Service Ombudsman published Time to Act, a review of NHS management of 10 patients who died from sepsis. The report catalogued the errors associated with each of these deaths and made recommendations to improve the initial assessment and treatment of sepsis, avoid delays in admission and treatment, and improve staff training. The first among these was improving recognition of the condition through new guidance from NICE that would “support GPs, ambulance staff and hospital clinicians to recognise severe sepsis in people at an early stage, so enabling earlier treatment, which is known to improve outcomes”.

Two years later, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) published a wide-reaching review of the care delivered to patients with sepsis, based on an appraisal of 551 cases. Of the 543 cases with sufficient data for assessment, it found that there was room for improvement in clinical and/or organisational care in almost two-thirds of cases (see Figure 1). There was delay in identifying sepsis in 36 per cent of all cases, in 51 per cent of cases of severe sepsis, and in 33 per cent of cases of septic shock. The median delay in identifying sepsis was nine hours (see Figure 2). Investigations considered essential in the diagnosis of sepsis were missed in 39 per cent of patients and delayed in a further 39 per cent. Most patients did not have an early assessment by a consultant and half of cases lacked input from a microbiologist. Based on these findings, NCEPOD made 21 recommendations on improving the care process and its delivery.

Aims of the NICE guideline
The origin of the new NICE guideline, Sepsis: Recognition, Diagnosis and Early Management, therefore differs from most because it was driven by overwhelming evidence and recognition at all levels of significant shortcomings in care. The Guideline Development Group (GDG) found little reliable epidemiological evi-
dence about sepsis but NICE cites statistics from the UK Sepsis Trust suggesting there may be 150,000 cases per year in the UK, with 44,000 deaths. If sepsis was not high on the agenda for CCGs and NHS trusts, it will be now.

The guideline includes no fewer than 137 recommendations in 12 categories covering three broad areas: recognition and diagnosis; management of sepsis; and staff training and patient education. The GDG recognised that there are already many management guidelines available, so the NICE guideline “aims to ensure healthcare systems in all clinical settings consider sepsis as an immediate life-threatening condition that should be recognised and treated as an emergency. The guideline outlines the immediate actions required for those with suspicion of sepsis and who are at highest risk of morbidity and mortality from sepsis. It provides a framework for risk assessment, treatment and follow-up or ‘safety-netting’ of people not requiring immediate resuscitation.”

Recognising the importance of early involvement of a consultant, NICE even goes as far as specifying the seniority of the clinicians (with supporting definitions) who should carry out particular roles.

Recognition and diagnosis

These topics are covered by four categories: identifying people with suspected sepsis; risk factors; assessment; and stratifying risk of severe illness or death.

NICE echoes the UK Sepsis Trust’s social media campaign by recommending: “Think ‘could this be sepsis?’ if a person presents with signs or symptoms that indicate possible infection.” Very detailed recommendations are made for face-to-face assessment of different age groups. The online version of the guideline provides links to algorithms and risk stratification tools for assessing children and young people, and adults in and out of hospital (available at www.nice.org.uk/guidance/ng51/resources). It emphasises the nonspecific nature of symptoms and the importance of listening to concerns expressed by the individual or the family, and the need for care when talking to people whose first language is not English or who have other difficulties with communication. Neutropenic sepsis should be suspected in people receiving treatment for cancer (covered by the 2012 NICE guideline CG151).

NICE lists risk factors for sepsis in neonates (covered by the 2012 neonatal infection guideline CG149), women who are pregnant or who have recently given birth or have had a termination or miscarriage, and others (including the very young and very old, people who are immunosuppressed, have had recent invasive procedures, have indwelling lines or other breaches of skin integrity, or who misuse drugs).

The risk of severe illness or death should be graded on the basis of the person’s history and physical examination using criteria stratified by age (under five years, 5–11 years and ≥12 years). These recommendations are presented as three downloadable tables defining high, moderate to high, and low risk, according to history, respiratory signs and symptoms, blood pressure, circulation and hydration, temperature and skin appearance. In children of any age, behaviour, eg crying, wakefulness, activity, leg pain and cold hands or feet, should also be taken into account. These criteria are very specific in places – for example, precise thresholds are given for raised respiratory rate at age five years, 6–7 years and 8–11 years at different levels of risk, with similar information for heart rate and temperature. Such detail means the downloadable algorithms will be essential near-patient tools.

The tables are complemented by notes on interpreting temperature, heart rate, blood pressure, cognitive state and oxygen saturation. These emphasise the context in which the measurement is made (eg heart rate may be lower in adults who are fit and normal blood pressure does not exclude sepsis in children); the need to avoid over-reliance on temperature (fever may be absent); the difficulty of measuring oxygen saturation in cases of peripheral shock; and awareness that changes in cognitive state may be subtle or indirect (irritability in children, impaired functional ability in older people).

Management

This section includes managing suspected sepsis outside and within acute hospital settings, antibiotic treatment, the use of IV fluids and oxygen, and finding the source of infection.

There are three criteria for referral for emergency care:

- The presence of any of the high risk criteria
- Age under 17 years with impaired immunity and the presence of moderate to high risk criteria

![Figure 2. Cumulative percentage delay in diagnosing sepsis, severe sepsis and septic shock among 505 cases assessed in the 2015 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) review](image-url)
Sepsis is associated with a wide range of pathogens (see Figure 3).² Antibiotic treatment should be consistent with other NICE guidance on antimicrobial stewardship (NG15, 2015), the treatment of meningococcal disease in the under-16s (CG102, 2010), fever in the under-5s (CG160, 2013) and early-onset neonatal infection (CG149, 2012). The aim is to administer the antibiotic within an hour for anyone at high risk; if a transfer is likely to take longer, there should be mechanisms in place to do so in the community. For inpatients, it is important to take a blood sample for culture before the antibiotic is given.

The choice of antibiotic is determined by age. Neonates presenting in the community should receive ceftriaxone or ceftaxime (depending on gestational age) whereas those in hospital and up to 72 hours old should be treated with benzylpenicillin and gentamicin. Children under three months old should also receive an agent active against *Listeria* spp, eg amoxicillin. Up to age 17 years, the drug of choice is ceftriaxone for community-acquired sepsis but inpatients should be treated according to the local antimicrobial formulary. The choice for adults should be guided by the local formulary except that suspected meningococcal disease should be treated with benzylpenicillin (in the community) or ceftriaxone (inpatients).

Guidance on the selection and use of intravenous fluids is drawn from NICE guidelines for adults (CG174, 2013) and children and young people (NG29, 2015) in hospital. Crystalloid fluids are recommended (glucose-free for all except adults) when fluid resuscitation is indicated, the rate and electrolyte concentration depending on age. A consultant should attend if there is no improvement after two boluses.

Oxygen is indicated to achieve a target saturation of 94–98 per cent in adults (88–92 per cent for patients at risk of hypercapnic respiratory failure) and for children who have signs of shock or oxygen saturation of <91 per cent when breathing air. Oxygen should also be considered for children in whom oxygen saturation is >92 per cent if clinically indicated.

The initial assessment should include a thorough examination to search for sources of infection, informed by the patient’s history, clinical findings, lab results and including consideration of imaging of the chest, abdomen and pelvis. The guideline lists contraindications to a lumbar puncture (unless instructed by a consultant) but, in their absence, this procedure may be indicated for infants under one month, or aged one to three months who appear unwell or whose white cell count is <5×10⁹/L or >15×10⁹/L.

**Patient information and staff training**

A member of the team should be nominated to provide information to patients and their families, particularly in an emergency. This should include an explanation that the person has sepsis and what this means, and information about the management plan and the investigations to be carried out. Families should also be given timely and regular updates on treatment, care and progress, and they should be able to ask questions about diagnosis, treatment options, prognosis and complications. Information should be jargon free and it is important to

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**Figure 3.** Distribution of pathogens in the 198 patients with sepsis in whom a pathogen was identified in the 2015 National Confidential Enquiry into Patient Outcome and Death (NCEPOD) review²

- Not reaching a definitive diagnosis or the inability to offer treatment safely outside an acute hospital setting.

Individuals at moderate to high risk should be assessed to obtain a definitive diagnosis and to decide whether they can be treated without admission. Those with suspected sepsis but no high or moderate to high risk criteria should be given information about monitoring symptoms and how to access medical care if they are concerned.

Management after admission is determined by age and risk factors with little room for ambiguity about what is to be done. For patients with at least one high risk factor, the guideline details what lab work to do immediately and how to act on the results. Everyone at high risk should have their case reviewed by a consultant and be treated within one hour with a broad-spectrum antibiotic at maximum dose. The response to a moderate to high risk level depends on the number of risk factors present – one vs two or more – both require prompt review and hourly monitoring but the presence of more risk factors mandates earlier, more comprehensive action. A similarly graded response is recommended for children with different thresholds for intervention.
check that these explanations have been understood.

Information should also be provided for individuals who have been assessed but not diagnosed with sepsis, and their families. They should be informed about what sepsis is, why it was suspected and what investigations were carried out, what symptoms to look out for and what to do if they develop. People who are at increased risk of sepsis – for example, when discharged after surgery – should also understand how to recognise the symptoms and how to get prompt medical attention.

People who actually did have sepsis should be fully informed of the diagnosis, what was done about it, what further care might be needed, how their recovery will proceed and what complications they might expect. This phase of management should be consistent with NICE’s 2009 guideline Rehabilitation after Critical Illness in Adults (CG83) and its recommendations on follow-up after meningococcal disease (CG102).

Everyone in whom sepsis was suspected or diagnosed should be provided with details of national charities and support groups providing information about sepsis and its causes, for example the UK Sepsis Trust (sepsistrust.org).

Compared with the fine detail of NICE’s clinical recommendations, its advice on staff training is succinct. Everyone in primary or secondary care, the community and in care homes involved in assessment, including students, should regularly undergo training in how to identify people who might have sepsis. All health professionals involved in triage or early management should have regular training in risk stratification strategies, local protocols for early treatment (including antibiotics and intravenous fluids), and criteria and pathways for escalation.

Summary

Sepsis has, perhaps, not received the attention it needs. When NICE published this guideline, its publicity emphasised that sepsis should be treated as seriously as myocardial infarction. The GDG noted that the mortality associated with sepsis is greater than that of cancers of the breast, bowel and prostate combined. This very detailed guideline provides the blueprint to redress the balance.

References


Declaration of interests

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics and recommendations. July 2016.

Are there improved outcomes with early invasive strategy for acute coronary syndrome?  

Clinical question: Does an early invasive strategy for acute coronary syndrome improve short-term outcomes?

Bottom line: According to this real-world observational study, an early invasive strategy – coronary angiogram within 72 hours of presentation – is associated with lower risks of short-term cardiac death and rehospitalisation for myocardial infarction (MI). However, this inference may not be valid because of a lack of key clinical information that may have influenced the data. (LOE = 2b)

Study design: Cohort (retrospective).

Synopsis:
Using data from a Danish national registry, these investigators included patients aged 30 to 90 years who were hospitalised with a first episode of unstable angina or acute MI. Patients were identified as having had an early invasive strategy (diagnostic coronary angiogram within 72 hours of hospitalisation) or a conservative invasive strategy (coronary angiogram after 72 hours or no angiogram). The primary outcome was cardiac death or rehospitalisation for MI within 60 days. The investigators used propensity score matching to balance the baseline characteristics of the two groups in the initial cohort of 54,000 patients, resulting in 9852 matched patient-pairs. Notably, 42 per cent of the conservative-strategy patients in the propensity-matched cohort received no cardiac catheterisation. Overall, treatment with an early invasive strategy was associated with lower risks of cardiac death (5.9 vs 7.6 per cent; number needed to treat [NNT] = 59; p<0.001), all-cause death (7.3 vs 10.6 per cent; NNT=30; p<0.001), and rehospitalisation for MI (3.4 vs 5 per cent; NNT=63; p<0.001). However, as an accompanying editorial suggests, the causal inference is not necessarily valid. Given the use of an administrative database, the investigators lacked important clinical information. As such, the validity of this study is questionable.

POEMs

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