NICE National Institute for Health and Care Excellence

2018 surveillance of meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (NICE guideline CG102)

Surveillance report

Published: 4 October 2018
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Contents

Surveillance decision

We propose to update the NICE guideline on bacterial meningitis.

The following table gives an overview of how evidence identified in surveillance might affect each area of the guideline.

Section of the guideline	New evidence identified	Impact
1.1 Symptoms, signs and initial assessment		
Investigation and management in children and young people with suspected bacterial meningitis	Yes	No
1.2 Pre-hospital management		
Pre-hospital management of suspected bacterial meningitis and meningococcal septicaemia	Yes	No
1.3 Diagnosis in secondary care		
Investigation and management in children and young people with petechial rash	Yes	No
Investigation and management in children and young people with suspected bacterial meningitis	Yes	Yes
Polymerase chain reaction (PCR) tests for bacterial meningitis and meningococcal disease	Yes	No
Skin samples for meningococcal disease	Yes	No
Performing lumbar puncture and interpreting cerebrospinal fluid parameters for suspected bacterial meningitis	Yes	Yes
Cranial computed tomography in suspected bacterial meningitis	No	No
1.4 Management in secondary care		
Antibiotics for suspected bacterial meningitis or meningococcal disease	Yes	No
Treatment for specific infections in confirmed bacterial meningitis	No	No
Treatment of unconfirmed bacterial meningitis	Yes	No

Treatment of meningococcal disease	No	No
Other aspects of management in bacterial meningitis and meningococcal septicaemia	No	No
Corticosteroids	Yes	No
Adjunctive therapies	Yes	No
Monitoring for deterioration for meningococcal disease	Yes	No
Retrieval and transfer to tertiary care	No	No
1.5 Long-term management		
Long-term effects of bacterial meningitis and meningococcal septicaemia	Yes	No
Immune testing	Yes	Yes

Reasons for the decision

This section provides a summary of the areas proposed to be updated and the reasons for the decision to update.

Diagnosis in secondary care

Procalcitonin

New systematic review and observational evidence supports the use of both serum and cerebrospinal fluid (CSF) procalcitonin (PCT) in the diagnosis of bacterial meningitis, including differential diagnosis between bacterial and viral meningitis. NICE guideline CG102 did not identify any evidence that examined the diagnostic accuracy of PCT for differentiating bacterial meningitis from other infections. Further new systematic review evidence indicates that PCT in addition to standard testing may be more cost effective than standard testing alone.

The new evidence identified through the surveillance review strengthens the evidence base for including PCT alongside other variables in diagnosis in secondary care. There is therefore a potential impact on recommendations 1.3.7 and 1.3.17, which advise that a C-reactive protein and white blood cell count should be performed, but do not include PCT testing.

Age-specific reference values

Topic expert feedback and new evidence indicates that up to date age-specific reference values, including those published by Public Health England (PHE), are available. The reference values cover normal ranges for blood test results or CSF findings to help interpret the test results in children (especially neonates) and young people with suspected bacterial meningitis. There is a potential impact to review section 5.5 of the full guideline on performing lumbar puncture and interpreting CSF parameters for suspected bacterial meningitis, specifically the text concerning normal ranges for CSF variables. Because of a lack of evidence on neonates at the time of guideline development, the normal CSF values presented in NICE guideline CG102 reflect those for the adult population for total protein concentration, and for children over 1 year old and adults for glucose concentration. The related research recommendation (4.2) should also be reviewed, to assess whether a new recommendation is needed.

Long-term management

New intelligence indicates a potential impact on recommendations 1.5.8–1.5.10, to take account of the MenB vaccine that has been introduced since publication of NICE guideline CG102. A review of the wording of these recommendations should be considered, so that any child who has received meningococcal vaccination and subsequently develops meningococcal disease should be tested for complement deficiency. The current recommendations for testing exclude children who have had meningococcal disease caused by serogroup B, based on the lower likelihood of complement deficiency in this subgroup at the time of guideline development.

For further details and a summary of all evidence identified in surveillance, see appendix A.

Overview of 2018 surveillance methods

NICE's surveillance team checked whether recommendations in meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (NICE guideline CG102) remain up to date.

The surveillance process consisted of:

- Initial feedback from topic experts via a questionnaire.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations and deciding whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the decision with stakeholders.
- Considering comments received during consultation and making any necessary changes to the decision.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Search and selection strategy

We searched for new evidence related to the whole guideline.

We found 59 studies in a search for systematic reviews, randomised controlled trials and observational studies published between October 2014 and April 2018.

We also included 41 studies identified by a search in previous surveillance in 2015, including any studies suggested during consultation.

From all sources, we considered 100 studies to be relevant to the guideline.

See appendix A: summary of evidence from surveillance for details of all evidence considered, and references.

Selecting relevant studies

Methodological search filters for systematic reviews and randomised controlled trials were not used in the surveillance search, in order to capture observational studies of relevance to sections on signs, symptoms and diagnosis.

Ongoing research

We checked for relevant ongoing research. Of the ongoing studies identified, 5 studies were assessed as having the potential to change recommendations; therefore we plan to check the publication status regularly, and evaluate the impact of the results on current recommendations as quickly as possible. These studies are:

- ISRCTN11369832: Using procalcitonin to guide duration of antibiotics.
- ISRCTN48274252: Analysis of water and electrolyte balance during osmotherapy in meningitis/encephalitis.
- NCT02308982 and ISRCTN15791925: IGNITE: Immunoglobulin in the treatment of encephalitis.
- Assessing the potential benefits of group B Streptococcus (GBS) vaccines.
- Listeria infection in infants: Traditionally, pregnancy-associated *L. monocytogenes* has been considered capable of causing meningitis and sepsis in infants aged up to 3 months.

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guideline. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to NICE guideline CG102.

We sent questionnaires to 11 topic experts and received 6 responses. The topic experts either:

- participated in the guideline committee who developed the guideline or
- were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty.

The potential triggers for updating were considered to be:

- New sepsis guidelines, including NICE guideline NG51, which need alignment with NICE guideline CG102.
- Changes in epidemiology and diagnosis after introduction of MenB vaccine for all infants in 2015.
- Emergency management to incorporate any critical management evidence.
- New guidelines from PHE have been issued on testing that should be undertaken to monitor vaccine impact.
- New data on immunological testing should be reviewed in view of new research in this area.
- Recent epidemiological data which suggest antibiotic choice especially for infants under 3 months should be revised.
- Choice of antibiotic, including for penicillin-allergic patients.

Other sources of information

We considered all other correspondence received since the guideline was published.

Administration of pre-hospital antibiotics

An enquiry was received from the coroner's office relating to the potential administration of pre-hospital antibiotics. However, Chief Medical Officer guidance and NICE guideline CG102 recommendation 1.2.2 advise against administering pre-hospital antibiotics without a non-blanching rash. No new evidence was identified in the current or previous surveillance review to direct a change in practice and the research recommendation on this topic therefore remains ongoing.

Serogroup B vaccination

There was a query about whether the surveillance of NICE guideline CG102 would consider a new meningococcal group B vaccination. However, prevention of meningitis is outside the remit of the guideline so this area would not be considered in the surveillance review. The Joint Committee on Vaccinations and Immunisations sets the national policy for vaccinations in the UK.

Diagnostic algorithms

Through the surveillance of NICE's guideline on fever in under 5s, topic experts highlighted a study which compared 2 algorithms devised to help identify which children with non-blanching rash had meningococcal disease. The study revealed that the Birmingham-Liverpool algorithm had a similar sensitivity but higher specificity than the NICE algorithm. This study is included in the evidence summary.

Views of stakeholders

Stakeholders are consulted on all surveillance decisions except if the whole guideline will be updated and replaced. Because this surveillance decision was to update part of the guideline, we consulted on the decision.

Overall, 14 stakeholders commented, of whom 12 agreed with the decision to update the guideline and 2 noted that they had no comments on the proposals. The stakeholders included royal colleges, charities, NHS trusts and pharmaceutical companies.

The following issues were raised about the proposal to update:

Duration of follow-up

Stakeholders commented that the recommended 6-week follow-up in infants recovering from bacterial meningitis would fail to detect significant cognitive and neuromotor sequelae. A review of the timeframes for follow-up particularly for young infants recovering from meningitis was suggested. The evidence submitted will be passed on to the developer for consideration in the update and this area may be explored as part of the scoping process. Clinical feedback also highlighted ongoing research that includes duration of follow-up, which will be monitored for potential future impact.

Safety netting information

A stakeholder commented that the provision of safety netting information is not fully addressed in the guideline and that it should be aligned with the related quality standard in this area. The NICE Pathway on bacterial meningitis and meningococcal septicaemia in under 16s includes both NICE guideline CG102 and NICE quality standard 19, and thereby incorporates the additional guidance on safety netting.

Signs and symptoms

A stakeholder suggested a review of symptoms information to ensure this section of the guideline remains up to date. No evidence was identified in the surveillance review to impact section 1 on symptoms, signs and initial assessment. However, the section includes table 1 covering symptoms and signs of bacterial meningitis and meningococcal septicaemia. The proposed restructuring of the table will be reviewed by the update committee to include consideration of the column entries for bacterial meningitis and meningococcal septicaemia.

Overlap with other guidelines

Stakeholders commented on the need to align NICE guideline CG102 with related guidelines on sepsis and fever in under 5s, as well as the related quality standard. The surveillance review proposal includes an amendment to the introductory text to the guideline to cross refer to the subsequently published NICE guideline on sepsis. The NICE Pathway on bacterial meningitis and meningococcal septicaemia in under 16s includes both NICE guideline CG102 and NICE quality standard 19, and thereby links to the related quality statements.

Procalcitonin

Stakeholders expressed mixed views on the proposal to review the evidence on the diagnostic accuracy of PCT. One stated that it is an expensive test and not widely available in the NHS, another highlighted the evidence of its diagnostic value. The potential impact of PCT testing will be considered in the update process in the context of cost effectiveness and availability in NHS secondary care.

Fluid resuscitation

A stakeholder highlighted evidence to support the use of balanced crystalloid solutions rather than normal saline for resuscitation to avoid hyperchloremic acidosis. Although the submitted evidence did not meet the surveillance eligibility criteria, this area may be explored as part of the scoping process for the update.

Interleukin-6

A stakeholder highlighted the need to include interleukin-6 (IL-6) as a biomarker for the differential diagnosis of bacterial meningitis. Evidence for CSF cytokines, including IL-6, was considered in the surveillance review. The new evidence showed potential diagnostic value, but no impact on the

guideline is anticipated until the findings are substantiated by further prospective, larger studies in UK settings.

Duration of antibiotics

A stakeholder highlighted new evidence to support a shorter duration (30 days or less) of antibiotic treatment for infants under 90 days of age. The evidence submitted will be passed on to the developer for consideration in the update and this area may be explored as part of the scoping process. The ongoing study Listeria infection in infants aims to establish the incidence of proven and possible listeria, age, geographical and ethnic distribution, management and outcome at diagnosis and at 1 year follow-up. This data is expected to provide stronger and more conclusive evidence to inform a potential future impact on NICE guideline CG102.

Polymerase chain reaction testing

A stakeholder suggested that polymerase chain reaction (PCR) testing should be done on receipt of CSF if there is a high suspicion of bacterial meningitis based on clinical presentation and the gram stain is negative. However, the surveillance review did not identify any evidence to warrant a change in this recommendation. Further evidence in this area may be explored as part of the scoping process for the update.

See appendix B for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Editorial amendments

During surveillance of the guideline we identified the following issues with the NICE version of the guideline that should be corrected.

NICE guideline introduction

Paragraph 3 of the introduction should be amended to take account of the introduction of the MenB vaccine into the schedule in 2015. The text should be amended to:

The epidemiology of bacterial meningitis in the UK has changed dramatically in the past 2 decades following the introduction of vaccines to control Hib, serogroups B and C meningococcus and some types of pneumococcus.

Text to be removed:

As no vaccine is currently licensed against serogroup B meningococcus, this pathogen is now the most common cause of bacterial meningitis (and septicaemia) in children and young people aged 3 months or older.

Additional text should be considered for addition to this paragraph by the update committee to take account of the MenACWY vaccination programme for teenagers, including routine vaccination at 13–15 years of age, which was introduced into the schedule in 2015.

In the introductory text to the guidance section 1, the cross referral to feverish illness in children (NICE clinical guideline 47) should be amended to cross refer to the NICE guideline on fever in under 5s: assessment and initial management. The guideline number and hyperlink should be amended.

Immediately after this paragraph, a cross referral should be added to the subsequently published NICE guideline on sepsis. The text should state:

This guideline assumes that if a child presents with signs or symptoms that indicate possible infection, the child will be managed according to NICE's guideline on sepsis: recognition, diagnosis and early management until bacterial meningitis or meningococcal septicaemia is suspected.

Patient-centred care

The patient-centred care section of the short version of NICE guideline CG102 will be replaced with the following box as per newer NICE guidelines:

> People have the right to be involved in discussions and make informed decisions about their care, as described in your care.
>
> Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Symptoms, signs and initial assessment

Table 1: More specific symptoms/signs

In the note column, a statement may need to be added to the line "Focal neurological deficit including cranial nerve involvement and abnormal pupils" qualifying the "X" entry for meningococcal septicaemia. The proposed text is: "Cerebral oedema may occur without meningitis, and in these circumstances there may be abnormal pupil reactions". This additional text should be reviewed by the committee as part of the update.

Table 1 column headings should also be amended to address an overarching ambiguity, where meningococcal meningitis and meningococcal septicaemia are included in 2 columns. The following suggested structure should be reviewed by the committee as part of the update:

Symptom/ sign	Bacterial meningitis (non-meningococcal)	Meningococcal disease		Notes
		Meningococcal meningitis	Meningococcal septicaemia	

Cross referral to other guidelines

Footnotes 3 and 4 from recommendations 1.1.3 and 1.1.4 should be amended to cross refer to the updated NICE guideline on fever in under 5s.

Editorial corrections are needed to the hyperlinks of footnotes 6 and 7, which direct to the Health Protection Agency. Footnote 6 should direct to the Health Protection (Notification) Regulations 2010.

Recommendation 1.1.19 should state:

Meningococcal disease: guidance on public health management (March 2018) Public Health England

in place of:

Guidance for Public Health Management of Meningococcal Disease in the UK (Health Protection Agency Meningococcus Forum, 2006)

and Footnote 7 should direct to Meningococcal disease: guidance on public health management.

Diagnosis in secondary care

Cross referral to NICE guideline on tuberculosis

Recommendation 1.3.24 should be amended to cross refer to the updated NICE guideline on tuberculosis. The guideline number and hyperlink should be amended.

Management in secondary care

Antibiotics for suspected bacterial meningitis or meningococcal disease

Based on topic expert feedback, recommendation 1.4.5 wording should be amended for clarity with the following revised text:

Where calcium-containing infusions are being administered, do not use ceftriaxone, instead use cefotaxime.

Cross referral to NICE guideline on tuberculosis

Recommendations 1.4.7 and 1.4.41 should be amended to cross refer to the updated NICE guideline on tuberculosis. The guideline number and hyperlink should be amended in the existing cross reference.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we decided that an update is necessary.

ISBN: 978-1-4731-3113-2