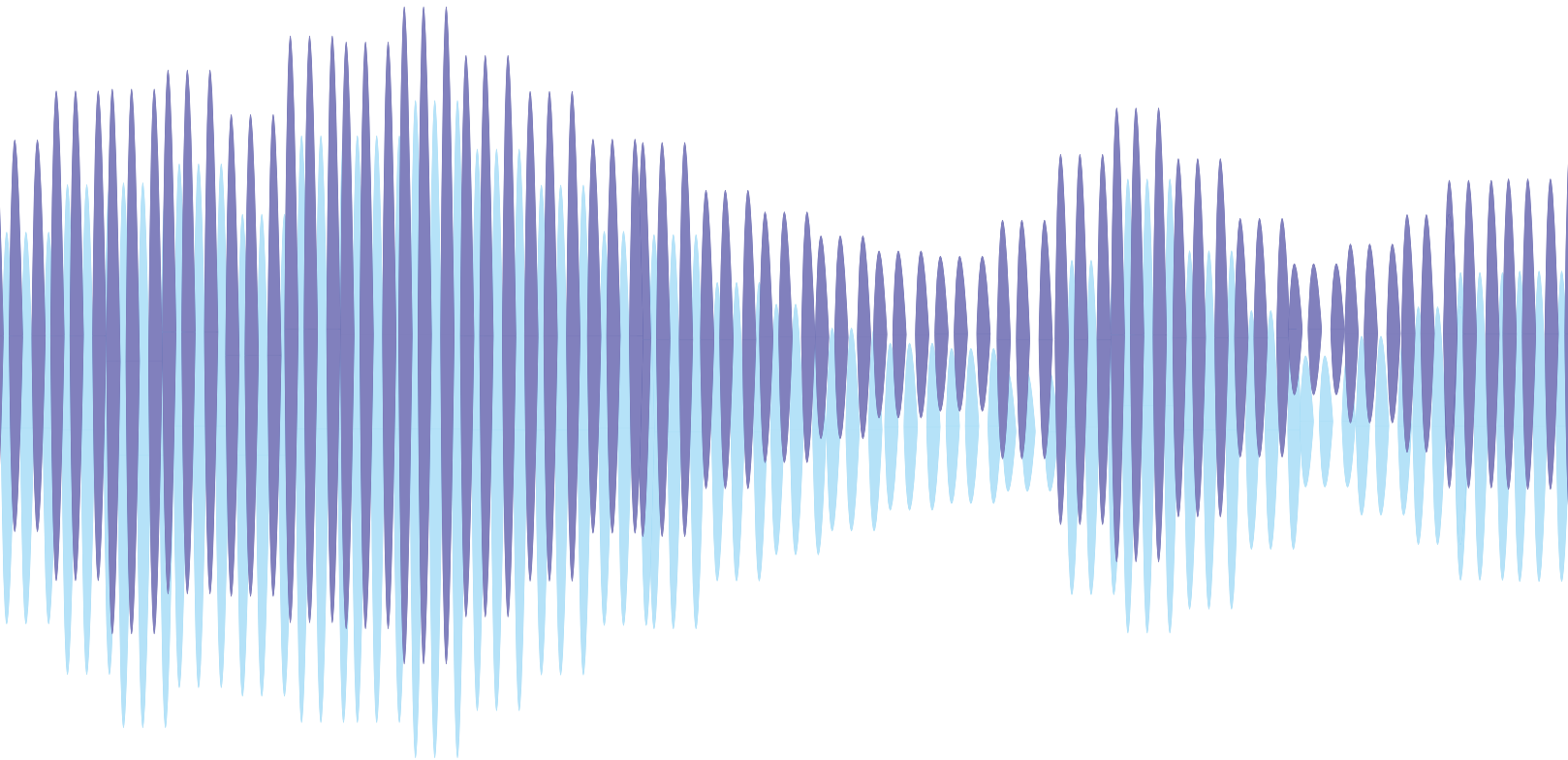
The management of children and young people with an acute decrease in conscious level

A nationally developed evidence-based Guideline for practitioners

2015 Update
Revised 2019



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RCPCH
Royal College of Paediatrics and Child Health
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Erratum: Issued August 2016

Publication: The management of children and young people with an acute decrease in conscious level, April 2015.

Items: Error in measurement units for ammonia levels (micromol/l instead of mmol/l). An insufficient explanation on how to take an ammonia sample.

Actions: To address the error in measurement units for ammonia levels, the following text has been revised in the full guideline and amended:

Page 38, 3.13.3. Hyperammonaemia - recommendations:

- Consider using a plasma ammonia threshold of >100 micromol/l to define abnormal levels. If a plasma level of >100 micromol/l or higher is found discuss immediately with a metabolic expert.

Page 39, 3.13.3. Hyperammonaemia - delphi statement - round 1:

- A plasma ammonia level of >100 micromol/l is significantly raised and needs actively treating. (22%).

Page 39, 3.13.3. Hyperammonaemia - delphi statement - round 1:

- Only a plasma ammonia level of >200 micromol/l is significantly raised and needs actively treating. (46%).

Page 39, 3.13.3. Hyperammonaemia - delphi statement - round 2:

- A plasma ammonia level of >100 micromol/l is significantly raised and needs urgent discussion and treatment.(32%).
- A plasma ammonia level of >200 micromol/l is significantly raised and needs actively treating. (64%)

Page 39, 3.13.3. Hyperammonaemia - Evidence interpretation:

- The British Inherited Metabolic Diseases Group (BIMDG) guidance75, 76 states plasma ammonia concentrations are usually above >100 micromol/l during an episode of decompensation and any patient with values above >200 micromol/l requires urgent treatment.
- They also advise that immediate treatment in the emergency setting is an intravenous infusion of glucose 200 mg/kg (2ml/kg of 10% glucose or 1ml/kg of 20% glucose) over a few minutes. The GDG decided that in an acute setting in a child with decreased conscious level a threshold for treatment of >100 micromol/l was appropriate and tested this threshold with the Delphi panel. However, neither this threshold, nor that of >200 micromol/l recommended in the 2005 Guideline had the agreement of the Delphi panel.
- On reviewing the Delphi findings the GDG decided to reword the recommendation with the >100 micromol/l threshold and with early involvement of a metabolic expert to ensure appropriate specialist advice is obtained prior to treatment being initiated and to guide further investigations.

Erratum: Issued March 2019

items: Page 38, Recommendations Notes for 3.13.3.Hyperammonaemia
Actions: The following text has been revised in the guideline and amended:

Samples that are not transported and analysed urgently are not interpretable. If ice is not readily available, transport the sample as quickly as possible at room temperature.

Even if delayed the sample should still be analysed and the result fed back urgently, with a comment from the laboratory on the possibility of an artefactual rise in ammonia, caused by the delay. If the result is >100micromol/l a repeat sample should be sent as soon as possible and without delay.

The risks posed by not analysing a screening sample for hyperammonaemia because of poor transport conditions is outweighed by delay in recognition of possible hyperammonaemia secondary to sample rejection.

Foreword

I am delighted to write the foreword of this 2015 revision of national guidance on the management of children and young people with acutely decreased conscious level. The historical context of this Guideline is of considerable interest and importance, since it represents a triumph of collaboration over more than a decade.

In 2002, following the dramatic reduction in Reye's syndrome and Reye-like illnesses, the National Reye's Syndrome Foundation UK held a workshop at which invited experts considered various aspects of Reye's syndrome and Reye-like illnesses. The main recommendation which emerged was the need to develop a formal evidence-based Guideline on the diagnosis and management of decreased consciousness. The National Reye's Syndrome Foundation UK recognised that whilst decreased consciousness is one of the common modes of presentation for children with Reye's or Reye-like conditions, it is also the endpoint of a wide range of serious illnesses which require urgent diagnosis and treatment in order to avoid secondary neurological damage or death. The initial 2005 Guideline was funded by the National Reye's Syndrome Foundation UK, produced by the University of Nottingham and subsequently endorsed by the Royal College of Paediatrics and Child Health (RCPCH) and sent to every College member.

A Guideline is only of value if it remains clinically relevant and promotes good practice, and with this in mind the National Reye's Syndrome Foundation UK went on to fund a multi-site Audit in 2010-2011, which examined some of the key recommendations of the Guideline and provided an insight into the management of children with a decreased conscious level, across the UK, highlighting areas of good practice but also deficiencies in care.

Maintaining its commitment to this important area of practice, the National Reye's Syndrome Foundation UK has since gone on to fund the creation of the updated Guideline to incorporate suggestions for improvement and correct weaknesses exposed by the audit. The update of the 2005 Guideline was considered necessary because a number of suggestions had been put forward for improving the Guideline including, for example, other common causes of decreased conscious level such as post-convulsive states, alcohol intoxication and febrile seizures. Additionally the Guideline was considered to be too long and simplification of the algorithm and the adoption of a user-friendly linear approach were needed.

The funds and work of The National Reye's Syndrome Foundation UK were incorporated into RCPCH in 2012, but the legacy of the charity is ongoing. The contribution of a relatively small charity to such an important clinical area is immeasurable, and I would thank the National Reye's Syndrome Foundation UK on behalf of the many children who are alive today because of its work.

Dr Hilary Cass
President, Royal College of Paediatrics and Child Health

Acknowledgements

The Guideline Development Group (GDG) would like to thank all stakeholders, Delphi panellists and working group members, whose hard work and effort have helped tremendously with the development of this Guideline (a full list of stakeholders can be found in the Appendices document).

Funding

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Intellectual property

Contents

1. Introduction

Decreased conscious level can be considered an acute neurological emergency characterised by significant brain impairment, necessitating a rapid and methodical approach to evaluation and treatment.

Regardless of the underlying cause, a decreased conscious level indicates a primary insult to the brain which, if left untreated, could rapidly progress to secondary damage leading to significant morbidity or even death.

The first Guideline for 'The Management of Decreased Conscious Level' was published in 2005, since when there have been significant changes in the demographics of the children and young people presenting to emergency settings with a decreased conscious level. This changing demographic was identified by a multi-centre audit carried out in 2010 with funding from the National Reye's Syndrome Foundation UK.

The continuing support of The National Reye's Syndrome Foundation UK has allowed the work required to update the Guideline.

The aim of the Guideline is to give clinicians working acutely a framework to aid the timely and safe care of children and young people presenting with a decreased conscious level of unknown cause.

Consistent with the previous Guideline, this Guideline emphasises the importance of managing this condition in a standard manner from first presentation to health services, to ensure the best outcome for patients and their families.

Population

Children aged from four weeks and up to 18 years. The term 'children' is used throughout the Guideline to include infants (over 28 days of age, excluding pre term babies still in neonatal hospital care), children and young people (up to 18 years).

Definition

A decreased conscious level is defined as being responsive only to voice, or pain, or being unresponsive on the Alert, Voice, Pain, Unresponsive Scale (AVPU), or a Glasgow Coma Score or modified Glasgow Coma Score of 14 or less.

2. Reading the Recommendations

The recommendations in this Guideline are set out in the following format:

a) The **Recommendation(s)** - There are 95 recommendations in total and they are numbered throughout (1-95).
b) An indication of the **quality of evidence** the recommendation is based on, according to Centre for Evidence-Based Medicine (CEBM) levels of evidence[1]. Some recommendations are comprised of separate parts, and each part may have a different evidence level/ recommendation grade. In these cases, the recommendations with a different grade have been asterisked (*), and their separate grade has been given.
c) **Review Question(s)** - The question the recommendation attempts to address.
d) **Evidence Summary** - A summary of the evidence the 2005 recommendation was based on, and any new evidence found.
e) **Delphi Statement(s)** - The statement(s) that were entered into the Delphi consensus.
f) **Evidence Interpretation** - An outline of the process by which the GDG arrived at the recommendation, from the evidence and/or Delphi consensus results.

Notes

1. A Guideline summary format is also available, containing just the recommendations and evidence grading, for ease of use.
2. **Due to varying level of evidence, some recommendations can be made with more certainty than others. The strength of evidence behind the recommendations has been reflected in their wording (for further information on this approach refer to the National Institute for Health and Care Excellence (NICE) Guidelines Manual[2]).**
3. 'Consider' has been used to indicate where a recommendation has been based on a Delphi consensus or weak evidence.
4. Recommendations are worded more strongly using simply a verb or the word 'should' where there is stronger evidence supporting the recommendation.
5. This method of using wording to convey the strength of the evidence underlying a recommendation has been followed throughout the guideline with two exceptions, both of which can be considered best practice. These are:
   - where a recommendation cross-refers to other related guidance, and
   - where the recommendation relates to an issue regarding child safety

   In both these instances straightforward action-based wording is used.
6. For consistency of care, where detailed information is covered in existing national guidance the GDG felt it more appropriate to refer readers to them, rather than replicate information. For topics where a cross-reference to related guidance is made in place of any other recommendations the cross-reference itself forms the recommendation. For topics where recommendations appear in this Guideline but a cross-reference is made to supplementary information this forms a note (written in bold font after the recommendations).

3. Recommendations

3.1. Assessment of airway and airway protection in children with a decreased conscious level

Recommendation(s)

1. Consider intubating a child with decreased conscious level if they have a GCS less than 8 or are non-responsive to pain on the AVPU, unless the child is showing signs of improvement
   [2005; Evidence level 5; Recommendation grade D]

Review question

What are the indications for intubation in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on the Delphi consensus. In the evidence search update two papers were retrieved; an audit of clinical Guidelines in 36 children who were administered oxygen[3] and a validation study of Guidelines[4]. The validation study found that children post Guideline implementation were successfully intubated using an oral endotracheal tube (ET) or a cuffed tracheal tube which decreased the immediate adverse effects at time of tube placements compared with children treated pre-Guideline implementation.

Evidence interpretation

The studies[3, 4] showed that Guidelines are useful to ensure standardising practice and successful intubation when followed. However, the audit was found to be biased in the selection of participants[3] and it is not possible to ensure the results of the validation study are due to the implementation of the Guideline[4]. Neither study compares the use of intubation versus non-intubation. Therefore the GDG felt the 2005 recommendation should be retained as this provides clear guidance in the circumstances intubation should be considered in children with a decreased conscious level.

3.2. Assessment of breathing and oxygen requirements in children with a decreased conscious level

Recommendation(s)

2. Treat a child with decreased conscious level with prescribed oxygen if their oxygen saturation is 95% or less, and document treatment given
   [2015; Evidence level 1a; Recommendation grade B]

Review question

What are the indications for additional oxygen therapy in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on Delphi consensus. An evidence search update was carried out and retrieved one systematic review[5]. The review[5] aimed at determining the effectiveness of acute lower respiratory tract infection management, found that nasal prongs and nasopharyngeal catheters have similar effectiveness and safety when used in patients with lower respiratory tract infection. However, there was no study that identified a single clinical sign or symptom that identified the precise level of hypoxemia that required oxygen therapy.

Evidence interpretation

The systematic review included studies where hypoxia was defined as oxygen saturation less than 90-95%. The review was well conducted and the definition of hypoxia used in the review (90-95% oxygen saturation) supported the level of oxygen saturation level used in the 2005 recommendation. The GDG felt that the original recommendation should be retained and amended to explicitly state the use of prescribed oxygen, ensuring the use of oxygen is documented in the child's records.

3.3. Assessment of capillary blood glucose in children with a decreased conscious level

Recommendation(s)

3. Consider performing a capillary glucose test within 15 minutes of presentation in a child with a decreased conscious level
   [2015; Evidence level 5; Recommendation grade D]

4. Consider performing a hypoglycaemia screen if the capillary blood glucose level is below 3 mmol/L and then immediately correct the blood glucose level
   [2015; Evidence level 5; Recommendation grade D]

   Note: for details of which investigations to perform as part of a hypoglycaemia screen refer to the British Inherited Metabolic Disease Group (BIMDG) Recurrent Hypoglycaemia Guideline[6].

Review question

In children with a decreased conscious level, how soon should a capillary (bedside) glucose measurement be performed?

Evidence summary

The 2005 evidence search retrieved studies focusing on hypoglycaemia and outcomes. However, none of these studies specifically addressed duration of hypoglycaemia and the 2005 recommendations were based on findings from the Delphi consensus survey.

The evidence search update retrieved two systematic reviews[7, 8] which addressed outcomes in hypoglycaemic and non-hypoglycaemic patients in order to validate the World Health Organisation (WHO) Guidelines[9]. One of the systematic reviews found that children with moderate hypoglycaemia or no symptoms of hypoglycaemia reached normoglycaemia within one hour if given sublingual or intravenous glucose[7], while the other[8] found that repeated doses of sublingual sugar was an effective alternative to intravenous glucose in raising blood glucose levels.

Given that the reviewed evidence did not directly address the clinical question, Delphi consensus findings from 2014 were also used to further inform the recommendations.

Delphi statements

Round 1

- Children with a decreased conscious level should have a capillary glucose test at presentation. (98%)
- In children with a decreased conscious level:
  - A capillary glucose level of less than 2.6 mmol/l is low and should be investigated further and corrected. (90%)
  - A capillary glucose of 2.6 – 3.5 mmol/l is borderline low and the result of the laboratory glucose (requested with the core investigations) should be reviewed urgently. (68%)
  - A capillary glucose level of less than 3.0 mmol/l is low and should be investigated further and corrected. (60%)
  - A capillary glucose of 3.0 – 3.5 mmol/l is borderline low and the result of the laboratory glucose (requested with the core investigations) should be reviewed urgently. (44%)
  - A capillary glucose level of less than 3.6 mmol/l is low and should be investigated further and corrected (refer to hypoglycaemia Guideline). (27%)
  - A borderline low glucose, the time to repeat the capillary glucose test and the decision to investigate and treat borderline low glucose needs to be agreed at a local level. (39%)

Round 2

- In children with a decreased conscious level:
  - A borderline low glucose (2.6 - 3.5 mmol/l) should be repeated after 15 minutes. (52%)
  - A borderline low glucose (2.6 - 3.5 mmol/l) should be repeated after 30 minutes. (52%)
  - In children with a borderline low glucose (2.6 – 3.5 mmol/l) treatment should be instigated before repeating the capillary glucose test. (48%)

Round 3

- A child with a decreased conscious level and a blood glucose below 3 should have a hypoglycaemia screen followed by immediate correction of blood sugar level. (80%)

- In a child with a decreased conscious level and a blood glucose between 3 – 3.5, a laboratory glucose should be checked, and consider treatment whilst awaiting the result. (63%)

Evidence interpretation

The systematic reviews[7, 8] include papers describing the validation of the WHO Guidelines[9], however these findings should be interpreted with caution as it is difficult to determine the exact methodology used in the reviews. Furthermore, neither review specifically addressed the duration of hypoglycemia. The 2011 audit[10] findings showed that within 15 minutes was an achievable length of time for capillary glucose to be tested following presentation, with 80.7% children less than five years old having their capillary blood glucose taken within this time.

The Delphi survey findings showed that there is little consensus on interpreting the findings of capillary glucose testing. There was clear agreement that capillary blood glucose testing should be performed at presentation. This, along with findings reported in the 2011 audit[10] meant the GDG felt it appropriate to recommend that the initial capillary blood glucose test should be performed within 15 minutes of presentation. The 2005 recommendation that a blood glucose of below 2.6 mmol/L is low and should be investigated further and corrected also received strong agreement by the Delphi panel. There was some concern amongst GDG members that a threshold of 2.6 mmol/L was too low for children with decreased consciousness and so following review of the findings from round 2 of the Delphi survey they reworded two additional statements for a third round of voting. One of these reached consensus, that a child with decreased consciousness and a blood glucose below 3 mmol/L should have a hypoglycaemia screen followed by immediate correction of blood sugar level, and was included as a recommendation. Given the lack of evidence and lack of consensus on all other Delphi statements it was not possible for the GDG to make any further recommendations. They were aware, however, that the NICE Guideline on diabetes in children and young people[11] is being updated and is due for publication in August 2015. This document will be an important source of guidance.

3.4. Observations to monitor and help manage children with a decreased conscious level

Recommendation(s)

5. Consider recording the following observations in a child with a decreased conscious level at first clinical assessment:
   - Heart rate
   - Respiratory rate
   - Oxygen saturation level
   - Blood pressure
   - Physical appearance/state
   - Temperature

   [2015; Evidence level 5; Recommendation grade D]

6. Consider recording the following observations every hour in a child with a decreased conscious level:
   - Heart rate
   - Respiratory rate
   - Oxygen saturation level
   - Blood pressure
   - Physical appearance/state
   - Temperature

   [2015; Evidence level 5; Recommendation grade D]

7. Consider continuously monitoring the following observations in a child with a decreased conscious level:
   - Oxygen saturation level
   - Continuous cardiac monitoring (ECG leads)

   [2015; Evidence level 5; Recommendation grade D]

8. Consider assessing and recording conscious level at presentation using the Glasgow Coma Score/modified Glasgow Coma Score (GCS) or AVPU scale in a child who presents with a decreased conscious level
   [2015; Evidence level 5; Recommendation grade D]

9. Consider assessing and recording the Glasgow Coma Score/modified Glasgow Coma Score (GCS) every 15 minutes in a child with a decreased conscious level if GCS is equal to or less than 12 or level V on the AVPU scale
   [2015; Evidence level 5; Recommendation grade D]

10. Consider assessing and recording the GCS/modified GCS every 30 minutes initially in a child who presents with a decreased conscious level if GCS is greater than 12 or level V on the AVPU scale
    [2015; Evidence level 5; Recommendation grade D]

11. A decrease in GCS or AVPU score indicates the need for urgent medical review
    [2015; Evidence level 5; Recommendation grade D]

Review questions

- In children with a decreased conscious level, which observations should be performed to assess their underlying diagnosis?
- In children with a decreased conscious level, which observations should be performed to monitor their clinical status?

Evidence summary

The 2005 evidence search retrieved one clinical diagnostic decision rule recommending which observations are useful in determining the diagnosis in bacterial meningitis, which is only one cause of decreased conscious level. Therefore the 2005 recommendations were based on Delphi consensus.

The evidence search update retrieved two papers for inclusion in the Guideline. A meta-analysis[12] and cohort study[13] assessed the validity of the bacterial meningitis score as a clinical prediction rule for meningitis. Both studies found that the CSF gram stain, CSF protein, blood absolute neutrophil count, seizures and spinal fluid neutrophil count are all predictors for bacterial meningitis.

In order to inform the update of the recommendations the GDG used the 2014 Delphi panel survey findings.

Delphi statements

- Consider recording the following observations every hour in a child with a decreased conscious level:
  - heart rate (95%, round 2)
  - respiratory rate (95%, round 2)
  - oxygen saturation level (95%, round 2)
  - blood pressure (98%, round 2)
  - physical appearance/state (95%, round 2)
  - temperature (77%, round 2)

- Changes in conscious level should be observed and recorded by a Glasgow Coma Score/ modified Glasgow Coma Score (GCS):
  - At presentation with a decreased conscious level (97%, round 1)
  - Every 15 minutes if GCS less than or equal to 12 (90%, round 1)
  - Every hour if GCS greater than 12 (67%, round 1)

- Changes in conscious level should be observed and recorded by a Glasgow Coma Score/ modified Glasgow Coma Score (GCS) or AVPU:
  - At presentation with a decreased conscious level (95%, round 2)
  - Every 15 minutes if GCS less than or equal to 12 (84%, round 2)
  - Every 30 minutes if GCS is 12 -14 or V on AVPU (64%, round 2)

- A decrease in GCS/AVPU indicates urgent medical review. (100%, round 2)

Evidence interpretation

The GDG reviewed the papers and due to the retrospective nature of the cohort study[13] decided it was not possible to determine if children had received treatment prior to the meningitis score being applied. The meta-analysis[12] was well conducted, however it was not possible to determine if all or some of the children had received the meningococcal vaccine, although due to the large sample reviewed this issue may be less significant.

The GDG felt that the clinical prediction rules described in these studies were applicable to meningitis only, which is only one cause of decreased conscious level, and there may be other observations that are important for children with other causes of decreased conscious level.

The GDG reviewed the 2005 recommendations and agreed that physical appearance and temperature should also be recorded by the attending clinician every hour. These items were added to the Delphi statements and tested in round 2 of Delphi panel voting.

Whilst there was clear consensus on most items in round 1 of the Delphi survey voting regarding assessment and recording of conscious level using the GCS there was disagreement about how frequently to perform this assessment when the GCS was greater than 12. The GDG felt the AVPU scale is easier to use and so the Delphi statements were modified for round 2 to include the AVPU scale and the time for assessment adjusted to every 30 minutes for when the conscious level is greater than 12 on the GCS or V on the AVPU scale. The statements still reached consensus with the addition of AVPU and so this has been retained in the recommendations. The statement recommending assessment every 30 minutes if the GCS is greater than 12 or V on AVPU scale failed to reach consensus in round 2. The GDG reviewed this statement and clarified it by adding that this recommendation refers to a child who presents with decreased conscious level. Following this amendment the recommendation was retained.

3.5. Assessment of airway and airway protection in children with a decreased conscious level

Recommendation(s)

12. Consider recording the following features when a child presents with a decreased conscious level:
    - Vomiting before or at presentation
    - Headache before or at presentation
    - Fever before or at presentation
    - Convulsions before or at presentation
    - Alternating periods of consciousness
    - Trauma
    - Ingestion of medications, alcohol or recreational drugs
    - Presence of any medications in the child‘s home
    - Any infant deaths in the family
    - Duration of symptoms

    [2005; Evidence Level, Recommendation grade D]

Review question

In children with a decreased conscious level, which features in the history should be elicited to assess the underlying diagnosis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update retrieved no new evidence.

Evidence interpretation

A list of potential causes of decreased conscious level was devised by the GDG and agreed by the 2005 Delphi panel. This list included all the causes/problems which could be identified and treated in the first hours of admission. It was based on a literature search of the aetiology of decreased conscious level in children (see the Appendices document). From this list, a search for validated Guidelines or studies validating the signs and symptoms which are suggestive of each of the causes/problems was undertaken.

There are no validated Guidelines and only one clinical diagnostic decision rule (level 2b diagnosis) to recommend which features in the history are useful in determining the diagnosis[14]. As the clinical diagnostic decision rule is only for children with bacterial meningitis, other history features may be important for children with other causes of decreased conscious level. The GDG agreed the 2005 recommendation was comprehensive and it was retained unchanged.

Recommendation(s)

13. Consider the possibility of non-accidental injury or safeguarding concerns when assessing a child with a decreased conscious level
[2005; Evidence Level 5, Recommendation grade D]

Note:

- **For further information on alerting features see NICE's When to Suspect Child Maltreatment Guideline[15]**
- **For further information on the management of self-harm in young people refer to the Royal College of Psychiatrist's Report - Managing Self Harm in Young People[16]**

Review question

In children with a decreased conscious level, which features in the history should be elicited to assess the underlying diagnosis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update retrieved no new evidence.

Evidence interpretation

The need to remind those working with children presenting with decreased conscious level to consider safeguarding concerns was felt to be important by the GDG and the recommendation was retained unchanged.

Recommendation(s)

14. Consider the following causes of decreased conscious level in children and initiate treatment within the first hour after presentation:
    - Shock* (hypovolaemic, distributive and cardiogenic)
    - Sepsis*
    - Metabolic diseases*
    - Intracranial infection*
    - Raised intracranial pressure*
    - Convulsions*
    - Intoxication / poisoning*
    - Trauma+
    - Hypertension
    - Stroke
    - Acute hydrocephalus
    - Recovering from a previous convulsion (post-convulsion/'post-ictal' state)

    [2015; Evidence level 5, *1b, +2b; Overall recommendation grade D]

    Note: for further information on stroke and hydrocephalus see the Royal College of Physicians' 'Stroke in Childhood guideline'[18]

3.6. Identifying the causes of a decreased conscious level in children

Review question

What are the non-traumatic causes of decreased conscious level in children?

Evidence summary

The 2005 evidence search retrieved a population-based prospective study from the UK[17], which identified all children presenting with coma across a region (level 1b differential diagnosis). The differential diagnosis of this population of children included infection, intoxication, epilepsy, metabolic diseases, unknown causes, non-communicating hydrocephalus, and complications of

surgery. The Delphi panel helped to extrapolate this evidence for the population covered by the Guideline and for those conditions for which there is a treatment available within the first hour from presentation to hospital.

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria. In reviewing the recommendation in order to develop Delphi statements the GDG added stroke, acute hydrocephalus and recovering from a previous convulsion. The 2014 Delphi panel voting was taken into consideration when making the recommendation.

Delphi statements

The cause(s) of decreased conscious level in children which can be suspected and for which treatment maybe initiated within the first hour after presentation include:

- shock (hypovolaemic, distributive and cardiogenic) (98%, round 1)
- sepsis (98%, round 1)
- trauma (98%, round 1)
- metabolic diseases (92%, round 1)
- intracranial infection (100%, round 1)
- raised intracranial pressure (95%, round 1)
- hypertension (92%,round 1
- stroke (79%, round 1)
- acute hydrocephalus (81%, round 1)
- intoxication/poisoning (94%, round 1)
- recovering from a previous convulsion (post-convulsion/'post-ictal' state) (76%, round 1)

Evidence interpretation

The Delphi panel reached consensus on the causes of decreased conscious level which reflects those in the original 2005 Guideline plus the additions made by the GDG for the update, hence each of these were included in the recommendation. Although stroke and hydrocephalus are not covered by the 2015 Guideline update, further information can be found in the Royal College of Physicians' Stroke in Childhood Guideline[18].

3.7. Investigating the causes of a decreased conscious level in children

Recommendation(s)

15. Consider investigating the cause of a decreased conscious level in a child using the following tests at presentation:
    - Capillary blood glucose
    - Blood gas (venous, arterial or capillary pH, pCO2, base excess, lactate)
    - Laboratory blood glucose
    - Urea and electrolytes (sodium, potassium and creatinine) Plasma lactate
    - Liver function tests (aspartate transaminase or alanine transaminase, alkaline phosphatase, albumin or protein)
    - Plasma ammonia (taken from a venous or arterial sample)
    - Full blood count and film (haemoglobin, white cell count and differential, and platelet count)
    - Blood culture
    - Urinalysis (dipstick at bedside) for ketones, glucose, protein, nitrites and leucocytes
    - 10 ml of urine to be saved for later analysis (including urine toxicology)

    [2015; Evidence level 5, Recommendation grade D]

16. Consider saving a plasma sample for future toxicology analysis if this need is suspected

    [2015; Evidence level 5, Recommendation grade D]

17. Consider implementing a technique for collecting urine for core investigations (e.g. urine bag, clean catch collecting device, catheter) as soon as the patient has had monitors attached

    [2005; Evidence level 5, Recommendation grade D]

Review question

Which investigations will screen for the causes of decreased conscious level in children?

Evidence summary

The 2005 evidence search found no evidence validating investigations or screening for causes of decreased conscious level in children, although general agreement was found in the literature as to which causes could be clinically recognised and which investigations might be useful to confirm these. Delphi panel consensus was used to draw up a list of potentially useful tests that should be

performed as part of the initial investigations, striking a balance between performing every test available to ensure not missing anything and performing the more relevant ones that were likely to pick up common important causes.

The evidence search update found seven observational diagnostic studies that were included for this review (see the Appendices document). The GDG felt these studies were of limited value for informing the recommendations as none were targeted at the population of interest i.e. children with decreased conscious level, focussing instead on children with serious bacterial or viral infection. They also noted that five of the seven included studies were examining investigations that are thought of as being still in research/not relevant to the UK NHS setting (CD64[19]; procalcitonin[20, 21]; apolipoprotein E[22]; Combur 10 reagent strips for CSF[21]). Given the lack of relevant evidence the GDG also considered the Delphi panel findings for this recommendation. For information on the addition of plasma lactate to the recommendation, see the evidence interpretation for recommendation 50.

Delphi statements

- All children with a decreased conscious level should undergo core investigations except those:
  - within one hour post-convulsion, who are clinically stable and have normal capillary blood glucose (64%, round 1; 66% round 2)
  - children involved in trauma not related to a medical collapse (58%; round 1; not voted on in round 2)
- The core investigations in children with a decreased conscious level should be:
  - capillary glucose (98%, round 1)
  - blood gas (venous, arterial or capillary pH, pCO2, base excess, lactate) (99%, round 1)
  - laboratory blood glucose (91%, round 1)
  - urea and electrolytes (sodium, potassium and creatinine) (100%, round 1)
  - liver function tests (aspartate transaminase or alanine transaminase, alkaline phosphatase, albumin or protein) (88%, round 1)
  - plasma ammonia (taken from a venous or arterial sample) (84%, round 1)
  - full blood count and film (haemoglobin, white cell count and differential, and platelet count) (99%, round 1)
  - blood culture (84%, round 1)
  - 1-2 ml plasma to be separated, frozen and saved for later analysis if required (67%, round 1; 59%, round 2)
  - 1-2 ml of acute serum to be saved for later analysis if required (64%, round 1; 59%, round 2)
  - urinalysis (dipstick at bedside) for ketones, glucose, protein, nitrites and leucocytes (94%, round 1)
  - 10 ml of urine to be saved for later analysis (75%, round 1)
- The good practice point from 2005 regarding early collection of urine for core investigations was endorsed through Delphi consensus (85%, round 1).

Evidence interpretation

The two exceptions to children who should have core investigations carried out included in the 2005 Guideline, namely children one hour post-convulsion, who are clinically stable and have normal blood capillary glucose, and those involved in trauma not related to a medical collapse were

not agreed by 2014 Delphi consensus and so were not included in the updated recommendation. Delphi panel findings on which tests should be performed to investigate the cause of decreased conscious level in children were very similar to those identified for the 2005 Guideline. There were two items from the original recommendation that failed to reach consensus on Delphi voting, separating and freezing a plasma sample and saving a serum sample for later analysis. In their discussions the GDG agreed with the findings of the Delphi survey that this need not be part of the core investigations; however they thought that this might be something worth considering if the need for future toxicology screening was anticipated, particularly given that alcohol intoxication in adolescents is the main cause of decreased consciousness in this group. They decided to make a separate recommendation that saving a plasma sample for later analysis should be considered when initial investigations are being undertaken. The GDG also agreed to retain unchanged the good practice recommendation relating to early collection of urine for core investigations.

3.8. Lumbar puncture and cranial imaging

Recommendation(s)

18. Perform a lumbar puncture, when no acute contraindications exist, if the clinical working diagnosis is:
    - Viral encephalitis, including herpes simplex encephalitis
    - Tuberculous meningitis

    [2015; Evidence level 1b; Recommendation grade B]

19. Consider performing a lumbar puncture, when no acute contraindications exist, if the clinical working diagnosis is:
    - Sepsis/bacterial meningitis
    - Cause unknown

    [2015; Evidence level 5; Recommendation grade D]

20. Analyse cerebrospinal fluid initially for:
    - Microscopy
    - Glucose (compared to plasma glucose)
    - PCR for herpes simplex*

    [2005; Evidence level 5, Recommendation grade D]

21. Consider analysing cerebrospinal fluid initially for:
    - Opening CSF pressure (if possible)
    - Gram staining
    - Culture and sensitivity
    - Protein
    - PCR for viruses other than herpes simplex
    - Mycobacterium tuberculosis when clinically suspected

    [2005; Evidence level 5, Recommendation grade D]

Note: it is also good practice to take a sample to store for possible future investigations

22. Consider analysing cerebrospinal fluid culture for mycobacterium tuberculosis when clinically suspected
[2015; Evidence level 5, Recommendation grade D]

Review questions

- When should a lumbar puncture be performed in a child with a decreased conscious level?
- What tests should be performed on a sample of cerebrospinal fluid from a child with a decreased conscious level?

Evidence summary

Evidence was included in the 2005 Guideline that showed a high diagnostic accuracy of PCR on cerebrospinal fluid for herpes simplex encephalitis (level 1b – 3c) and tuberculous meningitis (level 1b)[23-26]. Delphi panel consensus was used to add other important diagnoses – sepsis and bacterial meningitis, as well as cause unknown. The 2005 Guideline also reviewed the evidence for initial tests that should be carried out on cerebrospinal fluid, with some evidence supporting microscopy and glucose testing as useful (level 2b) when used as part of a clinical decision rule[27].

The evidence search update did not retrieve any papers and so Delphi consensus was used to inform the GDG decision-making, as well as cross-referral to the NICE Guideline on bacterial meningitis and meningococcal septicaemia[28].

Delphi statements

- A lumbar puncture should be performed, when no acute contraindications exist, if the clinical working diagnosis is:
  - sepsis/bacterial meningitis (83%, round 1)
  - viral encephalitis, including herpes simplex (84%, round 1)
  - tuberculous meningitis (83%, round 1)
  - cause unknown (76%, round 1)

- Cerebrospinal fluid investigations should include:
  - opening CSF pressure if possible (77%, round 1)
  - microscopy (94%, round 1)
  - Gram staining (94%, round 1)
  - culture and sensitivity (94%, round 1)
  - glucose (compared to laboratory plasma glucose taken just before lumbar puncture) (94%, round 1)
  - protein (94%, round 1)
  - lactate (70% round 1; 68%, round 2)
  - PCR for herpes simplex and other viruses (81%, round 1)

- sample to store for possible future investigations (73%, round 1; 73% round 2)
- culture of mycobacterium tuberculosis when clinically suspected (86%, round 1)

Evidence interpretation

The GDG noted that Delphi voting agreed with all indications for when to perform a lumbar puncture as per the 2005 Guideline, therefore this recommendation was retained with a small amendment to include viral encephalitis, including herpes simplex, as per the Delphi statement. The two cerebrospinal fluid investigations that failed to reach consensus through two rounds of Delphi voting, lactate and a sample to store for future investigations, had not been included in the 2005 Guideline and were not added to the 2015 Guideline. Following Delphi consensus voting, and in line with the rationale noted in the 2005 Guideline, the recommendations included the need for a culture of mycobacterium tuberculosis to be performed when clinically suspected, but not as part of routine investigations.

Recommendation(s)

23. Consider deferring or not performing a lumbar puncture as part of the initial acute management of decreased consciousness in a child who has:
    - Signs of raised intracranial pressure (pupillary dilation (unilateral or bilateral), pupillary reaction to light impaired or lost, bradycardia (heart rate less than 60 beats per minute), hypertension (mean blood pressure above 95th centile for age), abnormal breathing pattern, abnormal posture)
    - A GCS of less than or equal to 8
    - A deteriorating GCS
    - Focal neurological signs
    - Had a convulsion (seizure) lasting more than 10 minutes and has a GCS equal to or less than 12
    - Shock
    - Clinical evidence of systemic meningococcal disease
    - A CT or MRI scan suggesting blockage or impairment of the cerebrospinal fluid pathways e.g. by blood, pus, tumour or coning

    [2015; Evidence level 5; Recommendation grade D]

    Note: Beware performing a lumbar puncture in children with abnormal clotting

Review question

Which clinical features in a child with a decreased conscious level should be considered as contraindications to performing a lumbar puncture?

Evidence summary

The list of contraindications included in the 2005 Guideline was based on Delphi panel consensus, supported by studies of risk factors associated with death in children who had had a lumbar puncture performed[29-32].

There was no evidence identified in the evidence search update to answer this question in relation to contraindications to lumbar puncture and so Delphi consensus was used to inform the GDG decision-making as well as cross-referral to the NICE Guideline on bacterial meningitis and meningococcal septicaemia[28].

Delphi statements

- A lumbar puncture should be deferred and not performed as part of the initial acute management in a child who has:
  - a GCS equal to or less than 8 (84%, round 1)
  - a deteriorating GCS (88%, round 1)
  - new focal neurological signs (76%, round 1)
  - had a convulsion (seizure) lasting more than 10 minutes and has a GCS equal to or less than 12 (81%, round 1)
  - shock (81%, round 1)
  - clinical evidence of systemic meningococcal disease (81%, round 1)
  - dilated pupil (unilateral) (87%, round 1)
  - dilated pupils (bilateral) (75%, round 1)
  - impaired or lost pupillary reaction to light (81%, round 1)
  - bradycardia (heart rate less than 60 beats per minute) (81%, round 1)
  - hypertension (mean blood pressure above 95th percentile for age) (78%, round 1)
  - abnormal breathing pattern (79%, round 1)
  - abnormal posture (79%, round 1)
  - signs of raised intracranial pressure (83%, round 1)
  - a CT or MRI scan suggesting blockage or impairment of the cerebrospinal fluid pathways e.g. by blood, pus, tumour or coning (84%, round 1)

Evidence interpretation

Contraindications for performing a lumbar puncture listed in the 2005 Guideline all reached consensus in the Delphi survey and the majority were retained. In order to reflect current practice the GDG added a statement to the list relating to the finding on cranial scan suggesting blockage or impairment of cerebrospinal fluid pathways. This statement reached consensus too and so has been added to the recommendation. In order to simplify the recommendation and make it easier to refer to in practice the most common contra-indication of raised intracranial pressure has been moved to the top of the list and signs of this then listed in brackets. The loss of doll's eye response has been removed as the GDG felt its inclusion was an unhelpful distraction.

Recommendation(s)

24. Be aware, a normal CT scan does not exclude raised intracranial pressure and should not influence the decision to perform a lumbar puncture if other contraindications are present.
[2005; Evidence level 5; Recommendation grade D]

25. Be aware, the decision to perform a lumbar puncture in a child with a decreased conscious level should be made by an experienced paediatrician or consultant with paediatric experience who has examined the child.
[2015; Evidence level 5; Recommendation grade D]

Review question

Can a cranial scan (CT scan, MRI scan or ultrasound scan) rule out raised intracranial pressure to allow for a lumbar puncture to be performed?

Evidence summary

Evidence reviewed for the 2005 Guideline included a study (evidence level 1b) that demonstrated the sensitivity of CT scan to detect raised intracranial pressure was 99.1%, with a specificity of 78.1%[33].

There was no new evidence identified in the evidence search update to answer this question on intracranial scanning and so Delphi consensus was used to inform the GDG decision-making as well as cross-referral to the NICE Guideline on bacterial meningitis and meningococcal septicaemia[28].

Delphi statements

- A normal CT scan does not exclude raised intracranial pressure and should not influence the decision to perform a lumbar puncture if other contraindications are present. (90%, round 1)
- The decision to perform a lumbar puncture in a child with a decreased conscious level should be made by a consultant paediatrician who has examined the child. (75%, round 2)

Evidence interpretation

Whilst the evidence reviewed found a very high sensitivity for detection of raised intracranial pressure using a CT scan, this was limited to one study involving children with traumatic brain injury[33]. The GDG felt it was not appropriate to extrapolate from this finding to all children with decreased consciousness and endorsed the opinion of the Delphi panel reminding clinicians that a normal CT scan does not exclude raised intracranial pressure. This recommendation was therefore retained as per the 2005 Guideline. Similarly the recommendation stating who should make the decision to perform a lumbar puncture was retained, although the Delphi statement's wording was amended to say 'consultant' paediatrician rather than an 'experienced' paediatrician. Although this statement was supported by 75% of the panel (a borderline agreement) a number of the comments received indicated that this wasn't feasible in all settings and so the GDG adjusted the recommendation to include both an experienced paediatrician and a consultant with paediatric experience in order to ensure it was appropriate across all settings.

Recommendation(s)

26. Carry out an urgent cranial CT or MRI scan when the child is stable if the working diagnosis is raised intracranial pressure
[2015; Evidence level 1b; Recommendation grade A]

27. Consider carrying out an urgent CT or MRI scan when the child is stable if the working diagnosis is:
    - Intracranial abscess
    - Cause unknown

[2015; Evidence level 5; Recommendation grade D]

28. Consider performing a cranial MRI scan within 48 hours if possible, if not carried out at presentation, if the diagnosis is still uncertain
[2015; Evidence level 5; Recommendation grade D]

Note: For information on cranial imaging and raised intracranial pressure refer to recommendations 69 - 70

Review question

Can a computerised tomography (CT) or magnetic resonance imaging (MRI) scan demonstrate raised intracranial pressure?

Evidence summary

A study reviewed in the 2005 Guideline showed that if the intracranial pressure is greater than 25 mmHg then the sensitivity of a CT scan was 97.7% and the specificity 60.6% for diagnosing the raised pressure (level 1b)[33].

No new evidence was identified to answer this question in relation to intracranial imaging and so Delphi consensus was used to inform the GDG decision-making as well as cross-referral to the NICE Guideline on bacterial meningitis and meningococcal septicaemia[28].

Delphi statements

- An urgent cranial CT or MRI scan should be carried out when the child is stable if the working diagnosis is:
  - raised intracranial pressure (94%, round 1)
  - intracranial abscess (86%, round 1)
  - cause unknown (83%, round 1)

- A cranial MRI scan should be performed within 48 hours if possible, if not carried out at presentation, if the diagnosis is still uncertain. (83%, round 1)

Evidence interpretation

The GDG suggested adding MRI scanning as an alternative to CT scanning to the 2005 recommendation on when to perform intracranial scanning, and performing an MRI scan within 48 hours if diagnosis remains uncertain. These additions were endorsed by Delphi consensus.

3.9. Managing the causes of decreased conscious level in children

Recommendation(s)

29. Consider starting concurrent management strategies in a child with a decreased conscious level to treat the potential different causes, whilst waiting for test results to confirm the most likely diagnosis. **[2005; Evidence Level 5, Recommendation grade D]**

Review question

Which cause of decreased conscious level in children should be treated first to improve clinical outcome?

Evidence summary

The 2005 Guideline found no studies validating the treatment of decreased conscious level in children, therefore there was no evidence that prioritising the treatment of one suspected cause over another would improve outcomes. The Delphi panel agreed (91%, round 1) that treating all the likely causes concurrently at the beginning of the clinical course was the best management strategy.

No new evidence was found by the evidence search update. Given the lack of relevant literature to guide current clinical practice, Delphi panel findings were taken into consideration.

Delphi statement

In children with a decreased conscious level, concurrent management strategies need to be started to treat the potential different causes, and keep the child safe, while waiting for test results to confirm the diagnosis. (98%, round 1)

Evidence interpretation

The evidence search update did not retrieve any additional evidence, so the GDG decided to retain the original recommendation, as supported by the findings from the 2014 Delphi panel.

3.10. Circulatory Shock

3.10.1. Recognition

Recommendation(s)

30. Consider circulatory compromise and refer for further investigations if one or more of the following are present in a child with a decreased conscious level:
    - Mottled, cool extremities
    - Diminished peripheral pulses

    [2015; Evidence level 5; Recommendation grade D]

31. Consider circulatory shock if one or more of the following are present:
    - Systolic blood pressure is less than 5th percentile for age
    - Decreased urine output less than 1 ml/kg/hour

    [2015; Evidence level 5; Recommendation grade D]

    Note: For triage of such children refer to the criteria defined in the paediatric sepsis six[36]

Review question

What clinical features determine the presence of circulatory shock in a child with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update retrieved one cohort study[34] validating septic shock guidance in the USA. The study found that the implementation of the Guideline increased the identification of septic shock and overall decreased the length of a patient's hospital stay. The Guideline used the recognition of visual signs (hypotension, tachycardia, fever/hypothermia, tachypnoea) and clinical status (capillary refill time, mental status changes, peripheral pulse quality, skin appearance) in the diagnosis of septic shock in patients.

Delphi statements

- Shock can be recognised clinically if one or more of the following signs are present in a child with decreased conscious level:
    - capillary refill time greater than two seconds (72%, round 1; 61% round 2)
    - plasma lactate greater than 2mmol/l (61%, round 1; 41% round 2)
    - mottled, cool extremities (79%, round 1)
    - diminished peripheral pulses (81%, round 1)
    - systolic blood pressure is less than 5th percentile for age (82%, round 1)
    - decreased urine output less than 1 ml/kg/hour (78%, round 1)

Evidence interpretation

The GDG had concerns about the retrospective nature of this study and in light of the poor quality of evidence the GDG extrapolated the information from this study[34] and the original recommendation to form the Delphi statements. In addition, they considered the structure of the original recommendation to be confusing and so separated the features into those signs that suggest shock and observations that can confirm it. Plasma lactate greater than 2 mmol/L and capillary refill time over two seconds did not receive consensus in the Delphi survey and so have been removed from the recommendation. For ongoing management of shock clinicians are signposted to the Surviving Sepsis Campaign[35] and Sepsis Six care pathway[36].

3.10.2. Diagnosis

Recommendation(s)

32. Consider looking for signs of the following, if shock is present in a child with a decreased conscious level:
    - Sepsis
    - Trauma (blood loss, tension pneumothorax, cardiac tamponade)
    - Anaphylaxis (urticarial rash, wheeze, stridor, swollen lips/tongue)
    - Heart failure (enlarged liver, peripheral oedema, distended neck veins, heart murmur

    [2015; Evidence level 5; Recommendation grade D]

Review question

What are the causes of circulatory shock in children with a decreased conscious level?

Delphi statements

- If shock is present in a child with decreased conscious level, look for signs of:
  - sepsis (94%, round 1)
  - trauma (blood loss, tension pneumothorax, cardiac tamponade) (97%, round 1)
  - anaphylaxis (urticarial rash, wheeze, stridor, swollen lips/tongue) (97%, round 1)
  - heart failure (enlarged liver, peripheral oedema, distended neck veins, heart murmur) (93%, round 1)

Evidence Summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria, and so again Delphi consensus was used to inform the recommendation.

Evidence interpretation

The 2005 recommendation was agreed by the Delphi panel and retained.

Recommendation(s)

33. Consider requesting core investigations to determine the cause of shock in a child with a decreased conscious level, because shock is not a diagnosis in itself
[2015; Evidence level 5; Recommendation grade D]

Note: for a list of core investigations refer to recommendations 15-17

Review question

What tests should be performed in the presence of circulatory shock in children with a decreased conscious level to determine the underlying diagnosis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Delphi statement

Shock in a child with a decreased conscious level is not a diagnosis in itself and so the core investigations should be requested to determine the cause. (94%, round 1)

Evidence interpretation

The GDG endorsed the recommendation based on Delphi panel consensus.

3.10.3. Treatment

Recommendation(s)

34. Administer a fluid bolus of 20 mL/kg of isotonic fluid if shock is present in a child with decreased conscious level
[2005; Evidence level 1b; Recommendation grade A]

35. Consider administering a fluid bolus of 10 ml/kg of isotonic fluid if shock is present in a child with ketoacidosis or signs of raised intracranial pressure and a decreased conscious level. Repeat the fluid bolus if necessary
[2015; Evidence level 5; Recommendation grade D]

Review question

What fluid therapy should be initiated in the presence of circulatory shock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on three systematic reviews[37-39] where there was found to be no clear evidence in the preferential use of crystalloid or colloids. Therefore the 2005 recommendation promoted the use of either fluid.

The evidence search update found four studies which demonstrated no preferential use of colloids or crystalloids for shock[40-43]. One systematic review found that less fluid was needed when using hypertonic saline[44] and one systematic review found that administering no fluid bolus had significantly better mortality outcomes in children with general septic shock[42], but this does not seem to be the case in other studies. Three studies[40,41,45] administered 20 ml/kg of fluid bolus, and the titration of fluids varied over 10-20 minutes.

Delphi statement

- If shock is present in a child with a decreased conscious level, a fluid bolus of 20 ml/kg of crystalloid should be given, unless the child has diabetic ketoacidosis or signs of raised intracranial pressure, where a bolus of 10 ml/kg of crystalloid may be used and repeated if necessary. (78%, round 1)

Evidence interpretation

All of the studies found indicated no difference between colloid and crystalloid treatments. However, the GDG felt there were certain issues concerning the methodology of the studies. The GDG was also concerned about the heterogeneity of the population samples used between the studies, mainly due to varying underlying conditions. Given this uncertainty the GDG did not feel it appropriate to specify crystalloid or colloid fluid. This is in line with guidance provided in the NICE Bacterial meningitis and meningococcal septicaemia Guideline[28]. They did, however, have concerns about the amount of fluid administered and felt it appropriate to amend the Delphi statement to reflect circumstances where a smaller bolus should be considered. The amended statement received consensus from the Delphi panel and so a recommendation was added to highlight the circumstances where a smaller fluid bolus should be considered.

Recommendation(s)

36. Consider assessing and monitoring the response to a fluid bolus, by looking for one or more of the following clinical signs:
    - A reduction in tachycardia
    - A reduction in prolonged capillary refill time
    - An improvement in the level of consciousness
    - An increase in blood pressure (to normal level for age)
    - A reduction in lactate concentration and/or improvement in base excess as measured by blood gas analysis
    - An increase in urine output

    [2015; Evidence level 5; Recommendation grade D]

Review question

What monitoring should be initiated in the presence of circulatory shock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found two studies which showed that a higher shock index (heart rate: systolic blood pressure) is related to increased mortality[46, 47]. One retrospective chart analysis found that lactate levels higher than 5 mmol/l were associated with a higher mortality rate, and concluded that lactate is a feasible and useful predictor of outcome in children with septic shock[48].

Delphi statements

- The response to a fluid bolus should be monitored by detecting a positive response as defined as one or more of:
  - a reduction in tachycardia (90%, round 1)
  - a reduction in prolonged capillary refill time (82%, round 1)
  - an increase in urine output (75%, round 1)
  - an improvement in the level of consciousness. (85%, round 1)
  - a reduction in lactate concentration and/or improvement in base excess as measured by blood gas analysis (75%, round 1)

- The response to a fluid bolus should be monitored by plasma lactate levels. (25%, round 2)

Evidence interpretation

The GDG noted that the new evidence, although of low quality, provided support for the inclusion of heart rate, blood pressure and lactate levels when monitoring response to a fluid bolus which

is in line with the Surviving Sepsis Campaign Guideline[35]. The Delphi panel survey findings also supported the use of heart rate measurement and reduction in lactate concentration and/or improvement in base excess as well as the other parameters listed in the original recommendation and thus these were retained in the updated recommendation.

Recommendation(s)

37. Consider administering fluid boluses of up to and over 60 mL/kg, as guided by clinical response
[2015; Evidence level 5; Recommendation grade D]

Review question

How much fluid is required for the treatment of circulatory shock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

Due to the lack of relevant evidence, the GDG consulted the Surviving Sepsis Campaign: 'International Guidelines for Management of Severe Sepsis and Septic Shock' Guideline[35], which recommends that treatment with fluid boluses up to and over 60 ml/kg. The GDG therefore decided to update the previous recommendation accordingly. However, the GDG felt the previous recommendation was unclear, and wanted to emphasise that the level of fluid administered should be based on clinical response.

Recommendation(s)

38. Consider intubation and ventilation if more than 40 mL/kg of fluid bolus has been given, to prevent uncontrolled pulmonary oedema developing
[2005; Evidence level 5; Recommendation grade D]

Review question

When should intubation and ventilation be initiated for the treatment of circulatory shock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

In light of no new evidence the GDG retained the 2005 recommendation which is in line with current NICE guidance on bacterial meningitis and meningococcal septicaemia[28].

Recommendation(s)

39. Consider starting drug treatment to support the circulation and refer to paediatric intensive care if more than 40 mL/kg of fluid has been given with little clinical response
[2015; Evidence level 5 diagnosis; Recommendation grade D]

Review question

When should specific circulatory support (including vasopressor, inotropic and vasodilator treatments) be initiated for the treatment of circulatory shock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update retrieved a randomised controlled trial[45] which compared the impact of 40 mL/kg of fluid over 40 minutes followed by dopamine and further titration of therapy with, 20 mL/kg over 20 minutes up to a maximum of 60 mL/kg over one hour followed by dopamine in treating septic shock. There was no significant difference in overall mortality, rapidity of shock resolution or intubation rates between the two groups. The cumulative survival at 72 hours was similar in the two study groups; 72.5% (95% CI 58.9 - 86.1) in the 20 mL/kg group and 77.6% (95% CI 66.0 – 89.2) in the 40 mL/kg group. In addition, the study demonstrated that treatment with 40 mL/kg of fluid followed by dopamine required more fluid to be administered overall than treatment with 20 mL/kg over 20 minutes up to a maximum of 60 mL/kg over one hour followed by dopamine.

Evidence interpretation

The GDG reviewed the randomised controlled trial[45] and found some inherent biases in the conduct of the study in that the principle investigator for the study was not blinded. Furthermore the study was conducted in a resource-poor setting with limited access to invasive monitoring and life support technology. The GDG also noted that the study did not explore any harm that may arise from using dopamine and focused more on the volume of fluid administered in the analysis, as opposed to the drug administration. Therefore, the GDG decided to retain the 2005 recommendation based on Delphi consensus. This recommendation was cross-referenced with the NICE 'Bacterial meningitis and meningococcal septicaemia in children' Guideline[28], to ensure that they were consistent with each other.

Recommendation(s)

40. Consider monitoring children on an intensive care or high dependency unit if they have been unresponsive to 40 mL/kg of fluid
[2005; Evidence level 5; Recommendation grade D]

Review question

What monitoring should be initiated in the presence of circulatory sock in children with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update retrieved no papers which met the inclusion criteria.

Evidence interpretation

As no new evidence was found, the GDG decided to retain the 2005 recommendation, which is in line with NICE Guidelines[28].

3.11. Sepsis

3.11.1. Recognition

Recommendation(s)

41. Sepsis should be suspected and treated in a child with a decreased conscious level if two or more of the following four are present:
    - A body temperature of greater than 38°C or less than 35.5°C*
    - Tachycardia*
    - Tachypnoea*
    - A white cell count greater than $12x10^9$ /L or less than $4x10^9$ /L

    or if there is a non-blanching petechial or purpuric skin rash*
[2015; Evidence level 5, *2b; Recommendation overall grade D]

Review question

What clinical features determine the presence of sepsis in a child with a decreased conscious level?

Evidence summary

The 2005 recommendation was based on several studies (level 1b – 2b)[49-57] performed to investigate whether infants and young children with fever will have a serious bacterial infection grown on culture. A number of studies were also included that described the development and validation of scoring systems designed to predict serious bacterial infection (level 4). Studies looking at children with petechiae or purpura have shown that being described as being 'ill' has a sensitivity of between 79-100% and a specificity of 81-88% for diagnosing sepsis (level 2b). Being lethargic was one of the stated criteria for being described as 'ill', which is consistent with a decreased conscious level. The GDG used this evidence when drafting the 2005 recommendation, extrapolating from the study populations to the population of children with a decreased conscious level, hence the recommendation was downgraded to C overall (although the section pertaining to a non-blanching petechial or purpuric rash was considered grade B).

The evidence search update yielded three studies for inclusion in the update (level 1b – 2b) (see the Appendices document). Unfortunately none of the studies were focused on the population of interest, children with decreased conscious level. Furthermore, two were investigating biochemistry, felt by the GDG to be not relevant to the question of initial diagnosis (brain natriuretic peptide levels[58]; C-reactive protein, cholesterol, high density lipoprotein and CD64 expression[59]) and one was looking at differential diagnosis in an area not felt to be relevant (septic arthritis vs. transient synovitis of the hip[60]).

Given the lack of relevant recent evidence the GDG looked to the Surviving Sepsis Campaign: International Guideline for management of severe sepsis and septic shock[35], the NICE Feverish illness in children Guideline[61] and findings from the Delphi consensus survey to ensure the recommendation is up to date. The Surviving Sepsis Campaign Guideline - Surviving Sepsis[35] was used to update the original 2005 recommendation and inform the Delphi statements.

Delphi statements

- Sepsis can be defined as the systemic response to infection. In a child with a decreased conscious level, sepsis should be suspected and treated if two or more of the following are present:
  - a body temperature of greater than 38°C (84%, round 1)
  - a body temperature of less than 36°C (67%, round 1)
  - a history of fever at home (63% round 1; 72% round 2)
  - tachycardia (81%, round 1)
  - tachypnoea (81%, round 1)
  - a change in white blood cell count to greater than $12x10^9$ /L (67%, round 1; 81%, round 2)
  - a change in white cell count to less than $4x10^9$ /L (81%, round 1)

  or if there is a non-blanching petechial or purpuric skin rash. (90%, round 1)

Evidence interpretation

The GDG agreed to adopt the international consensus definition of sepsis as reported in the Surviving Sepsis Campaign Guideline Surviving Sepsis[35].

The GDG amended the 2005 recommendation on when to suspect sepsis in line with Delphi consensus voting, which endorsed the new thresholds for white blood cell count reported in the Surviving Sepsis Campaign Guideline[35], and removed a history of fever at home. The lower temperature threshold of 36°C failed to reach consensus in round 1 of voting. In round 2 there was an error in the Delphi statement which included the threshold greater than 36°C instead of less than 36°C. In light of this the GDG decided to retain the original lower threshold of less than 35.5°C. This is in line with the Surviving Sepsis Campaign Guideline[35] which uses a threshold of less than 35°C measured rectally.

3.11.2. Diagnosis

Recommendation(s)

42. Consider performing the core investigations in a child with a decreased conscious level and suspected sepsis as there could be another underlying cause
[2005; Evidence level 5; Recommendation grade D]

43. Consider the following additional investigations in a child with a clinical diagnosis of sepsis and decreased conscious level:
    - Chest X-Ray
    - Urine culture if urinalysis positive for leucocytes and/or nitrites
    - Blood polymerase chain reaction (PCR) for meningococcus and pneumococcus
    - Coagulation studies if clotting abnormality suspected
    - Skin swab if areas of inflammation are present
    - Joint aspiration if signs of septic arthritis are present
    - A thick and thin film for malarial parasites if foreign travel to endemic area

[2015; Evidence level 5; Recommendation grade D]

Note: for a list of core investigations refer to <u>recommendations 15-17</u>

Review question

What investigations should be sent in a child with sepsis and a decreased conscious level to determine the cause and any predisposing factors?

Evidence summary

The 2005 recommendations regarding investigations for a child with sepsis and decreased conscious level was based on a Delphi consensus. The evidence search update retrieved no papers which met the inclusion criteria for this question and so the original recommendations were tested again using the Delphi survey.

Delphi statements

- A child with a decreased conscious level and suspected sepsis could have another underlying diagnosis and should have the core investigations requested. (82%, round 1)

- A child with a clinical diagnosis of sepsis should be considered for the following additional investigations:
  - chest X-ray (85%, round 1)
  - throat swab (69%, round 1; 72% round 2)
  - urine culture if urinalysis positive for leucocytes and/or nitrites (91%, round 1)
  - lumbar puncture (87%, round 1)
  - PCR from blood for meningococcus and pneumococcus (91%, round 1)
  - coagulation studies (activated partial thromboplastin time, prothrombin time, fibrinogen, fibrinogen degradation products) if clotting abnormality suspected (93%, round 1)
  - skin swab if areas of inflammation are present (79%, round 1)
  - joint aspiration if signs of septic arthritis are present (76%, round 1)
  - a thick and thin film for malarial parasites if foreign travel to endemic area (82%, round 1)
  - intracranial imaging if no other source of infection determined (85%, round 1)

Evidence interpretation

The 2005 recommendation on performing core investigations was endorsed by Delphi consensus and retained. The additional investigations recommended in 2005 were amended slightly to reflect 2014 Delphi panel voting and throat swab removed. In order to reduce duplication and potential confusion lumbar puncture was also removed as this is recommended as a core investigation and so does not need to be included here as an additional investigation. Intracranial imaging was removed from this list as it is dealt with under the sections core investigations and intracranial abscess. The additional information on coagulation studies from the Delphi statement (i.e. 'activated partial thromboplastin time, prothrombin time, fibrinogen, fibrinogen degradation products') was removed from the recommendation as different laboratories have different coagulation screens, and the GDG considered this information too detailed to be universally applicable.

3.11.3. Treatment

Recommendation(s)

44. Consider initiating broad spectrum antibiotics intravenously after appropriate cultures have been taken in a child with a decreased conscious level and suspected sepsis.
[2005; Evidence level 5; Recommendation grade D]

45. Consider review by an experienced paediatrician within the first hour of presentation, for a child with a decreased conscious level and suspected sepsis
[2005; Evidence level 5; Recommendation grade D]

46. Refer to the Surviving Sepsis Campaign Guideline[35] and the Sepsis Six care pathway[36] for ongoing treatment of sepsis
[2015; Evidence level 5; Recommendation grade D]

Review question

Which antibiotics should be started in children with sepsis and a decreased conscious level?

Evidence summary

The 2005 Guideline included studies comparing different antibiotics for bacteraemia and sepsis (level 1b)[62-64], however none were able to demonstrate a clear benefit of one antibiotic over another and the Delphi panel agreed that broad spectrum antibiotics should be started, with the precise antimicrobial agent being decided locally.

The evidence search update retrieved no new papers which met the inclusion criteria for this question and so the original recommendations were tested again using the Delphi survey.

Delphi statements

- In a child with a decreased conscious level and suspected sepsis, broad spectrum antibiotics should be started intravenously after appropriate cultures have been taken. (91%, round 1)
- A child with a decreased conscious level and suspected sepsis should be reviewed by an experienced paediatrician within the first hour of presentation. (93%, round 1)

Evidence interpretation

Delphi panel voting showed a clear endorsement of the two recommendations for starting a broad spectrum antibiotic and early review within the first hour of presentation by an experienced paediatrician. The recommendation for a broad spectrum antibiotic is also in line with the Surviving Sepsis Campaign Guideline[35] which recommends that antimicrobial treatment is started within an hour of presentation. Both 2005 recommendations were retained unchanged.

The 2005 recommendation relating to the use of second line antibiotics if there is a poor response to treatment was removed by the GDG as this is outside the scope of the Guideline which is focussed on diagnosis and initial management of decreased consciousness in children.

For ongoing treatment of sepsis the GDG felt it most appropriate to signpost clinicians to the Surviving Sepsis Campaign Guideline Surviving Sepsis[35] and the Sepsis Six care pathway[36].

3.12. Trauma

Recommendation(s)

47. Record a child's history for evidence of trauma in a child with decreased conscious level
[2005; Evidence level 5; Recommendation grade D]

Evidence summary

The 2005 recommendation was based on the results from the Delphi consensus.

Delphi Statement

In a child with decreased conscious level, evidence of trauma should be elicited from the history and examination. (100%, round 1)

Evidence interpretation

Traumatic causes of decreased conscious level in children were determined to be outside the scope of the Guideline. However, for completeness the Delphi panel agreed that identifying injury should be part of the evaluation of the child with decreased consciousness.

Recommendation(s)

48. Examine a child with decreased conscious level for evidence of trauma from a collapse and request the core investigations to detect any underlying medical cause
[2005; Evidence level 5; Recommendation grade D]

Evidence summary

The 2005 recommendation was based on the results from the Delphi consensus.

Delphi Statement

In a child with a decreased conscious level and evidence of trauma from a collapse, the core investigations should be requested to detect an underlying medical cause in the child. (87%, round 1)

Evidence interpretation

The Delphi panel agreed that trauma could be secondary to a medical condition (e.g. the child became unconscious and fell out of a tree). Therefore the core investigations would be appropriate to perform in these cases.

Recommendation(s)

49. Manage a child with a decreased conscious level and evidence of trauma according to Advanced Paediatric Life Support[65] and the NICE Head injury Guidelines[66]
[2005; Evidence level 5; Recommendation grade D]

Evidence summary

The 2005 recommendation was based on the results from the Delphi consensus.

Delphi Statement

A child with decreased conscious level and evidence of trauma should be further managed according to Advanced Paediatric Life Support and the NICE Head injury Guidelines. (79%, round 1)

Evidence interpretation

The 2014 Delphi panel agreed following the Advanced Paediatric Life Support (APLS)[65] and NICE Head Injury Guidelines[66] would be an appropriate step to take after the patient has left the scope of this Guideline.

3.13. Metabolic illness

3.13.1. Hypoglycaemia

Recommendation(s)

50. Consider requesting the following tests from the saved samples taken with the core investigations in a child with a laboratory glucose of less than 3 mmol/L and a decreased conscious level:
    - Plasma insulin
    - Plasma cortisol
    - Plasma growth hormone
    - Plasma free fatty acids
    - Plasma beta-hydroxybutyrate
    - Acyl-carnitine profile (on Guthrie card or from stored frozen plasma)
    - Urine organic acids
    - Plasma amino acids

    [2015; Evidence level 5; Recommendation grade D]

    Note: for details of which investigations to perform as part of a hypoglycaemia screen refer to the British Inherited Metabolic Disease Group (BIMDG) Recurrent Hypoglycaemia Guideline[6]

Review question

In children with a decreased conscious level and hypoglycaemia, what further investigations will diagnose the underlying cause?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Delphi Statement

- A child with a decreased conscious level and laboratory glucose of less than 2.6 mmol/l should have the following tests requested from the saved samples, which were taken with the core investigations:
  - plasma lactate (90%, round 1)
  - plasma insulin (88% ,round 1)
  - plasma cortisol (87%, round 1)
  - plasma growth hormone (75%, round 1)
  - plasma free fatty acids (75%, round 1)
  - plasma beta-hydroxybutyrate (76%, round 1)
  - acyl-carnitine profile (on Guthrie card or from stored frozen plasma) (78%, round 1)
  - urine organic acids (82%, round 1)
  - plasma amino acids (82%, round 1)

Evidence interpretation

The 2014 Delphi panel agreed the tests that should be carried out to diagnose the underlying causes of hypoglycaemia. Following expert advice the GDG decided to remove plasma lactate from this section and add it to the list of core investigations (recommendation 15). The freezing and thawing process causes artefactual elevation, meaning plasma lactate must be tested within 20 minutes of blood being taken.

Recommendation(s)

51. Consider administering an intravenous bolus of 2 mL/kg of 10% dextrose in a child with hypoglycaemia
    [2015; Evidence level 5; Recommendation grade D]

    Note: It is good practice to re-check the blood sugar after the IV administration of dextrose

Review question

In children with a decreased conscious level and hypoglycaemia, what treatment will improve their hypoglycaemia?

Evidence summary

The 2005 recommendation was based on Delphi consensus. The evidence search update retrieved one randomised controlled trial[67] which compared the efficacy of sublingual and intravenous administration of sugar. Similar outcomes were reported with intravenous and sublingual sugar, however the authors concluded it was important to highlight the use of sublingual sugar and its ability to restore normoglycemia rapidly among moderately hypoglycaemic children.

Evidence interpretation

The GDG considered the study[67] and found that sublingual sugar had the benefit of ease of administration compared to intravenous glucose. However the study did find that sublingual sugar resulted in additional doses being administered and the children's hypoglycaemia in the study was caused by fasting and would be difficult to translate into clinical practice. Furthermore, the study was found to hold some bias as there was no mention of blinding to children, parents, nurses or researchers in the study or how children were randomly allocated to treatment groups. Therefore the GDG felt that the study was not conclusive enough to form the basis of a recommendation. The GDG were aware of Advanced Life Support Group (APLS) guidance[65] which states that 2 ml/kg of 10% dextrose should be used in all children. After considering this evidence and current guidance the 2005 recommendation was amended to follow the APLS guidance.

Recommendation(s)

52. Consider administering an infusion of 10% dextrose solution to maintain a child's blood glucose between 4 and 7 mmol/L
    [2015; Evidence level 5; Recommendation grade D]

53. Consider seeking urgent support from an endocrinologist and metabolic medicine physician to determine subsequent management
    [2015; Evidence level 5; Recommendation grade D]

Review questions

In children with a decreased conscious level and hypoglycaemia, what treatment will improve their hypoglycaemia?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Delphi statements

- An infusion of 10% dextrose solution should be administered to maintain the blood glucose between 4 and 7 mmol/L (79%, round 1)
- Hypoglycaemia is not a diagnosis in itself, therefore urgent support from an endocrinologist and

metabolic medicine physician should be obtained to determine the subsequent management (75%, round 1)

Evidence interpretation

The Delphi panel agreed the use of intravenous dextrose in the maintenance of blood glucose level and the need for metabolic and endocrinology support for subsequent management.

3.13.2. Diabetic ketoacidosis

The care of children with diabetic ketoacidosis, and other hyperglycemic hyperosmolar nonketotic comas, are outside the scope of this Guideline. For guidance on diabetic ketoacidosis please refer to the NICE Guideline on Diabetes in Children and Young People[11] and the British Society of Paediatric Endocrinology and Diabetes DKA Guideline[68]. The GDG were also aware that an update of the NICE Guideline on Diabetes in Children and Young People is due for publication in August 2015 along with a new NICE Guideline on Diabetic Ketoacidosis in Children, and noted that these would be important sources of guidance for clinicians.

3.13.3. Hyperammonaemia

Recommendation(s)

54. Consider using a plasma ammonia threshold of >100micromol/l to define abnormal levels. If a plasma level of >100micromol/l or higher is found discuss immediately with a metabolic expert.
[2015; Evidence level 5; Recommendation grade D]

Note: A plasma ammonia sample from a free-flowing venous (or arterial) sample should be taken immediately to the laboratory, which should be informed in advance of its pending arrival. If any delay longer that 10 minutes is expected before analysis, then the sample should be transported on ice. If ice is not readily available, transport the sample as quickly as possible at room temperature.
Even if delayed the sample should still be analysed and the result fed back urgently, with a comment from the laboratory on the possibility of an artefactual rise in ammonia, caused by the delay. If the result is >100micromol/l a repeat sample should be sent as soon as possible and without delay.
The risks posed by not analysing a screening sample for hyperammonaemia because of poor transport conditions is outweighed by delay in recognition of possible hyperammonaemia secondary to sample rejection.

Review question

In children with a decreased conscious level and hyperammonaemia, what plasma ammonia level should prompt treatment?

Evidence summary

The 2005 evidence search found six studies looking at the prognosis of children with a variety of conditions which cause a rise in the plasma ammonia level[69-74]. They all agreed that the plasma concentration of ammonia is related to outcome, i.e. the higher the peak or the longer the level remains high the worse the prognosis (level 4 prognosis). Two studies[69, 71] found that the level of peak

plasma ammonia at which prognosis deteriorates is between 180 micromol/L and 350 micromol/L. The 2005 Delphi panel agreed that a level of 200 micromol/L should be taken as the cut-off level for action.

The evidence search update did not retrieve any papers matching the inclusion criteria, therefore a Delphi panel was again used to test the recommendations.

Delphi statements

Round 1

- A plasma ammonia sample should be taken from a free-flowing venous (or arterial) sample and be taken immediately to the laboratory, which should be informed in advance of its pending arrival. If any delay longer that 10 minutes is expected before analysis, then the sample should be transported on ice. Samples that are not transported and analysed urgently are not interpretable.
  - A plasma ammonia level of >100micromol/l is significantly raised and needs actively treating. (22%)
  - Only a plasma ammonia level of >200micromol/l is significantly raised and needs actively treating. (46%)
  - As soon as a significantly raised plasma ammonia level is detected, contact the nearest metabolic medicine centre for advice. (81%)

Round 2

- A plasma ammonia sample should be taken from a free-flowing venous (or arterial) sample and be taken immediately to the laboratory, which should be informed in advance of its pending arrival. If any delay longer than 10 minutes is expected before analysis, then the sample should be transported on ice. Samples that are not transported and analysed urgently are not interpretable.
  - A plasma ammonia level of >100 micromol/l is significantly raised and needs urgent discussion and treatment. (32%)
  - A plasma ammonia level of >200 micromol/l is significantly raised and needs actively treating. (64%)

Evidence interpretation

The British Inherited Metabolic Diseases Group (BIMDG) guidance[75, 76] states plasma ammonia concentrations are usually above >100 micromol/l during an episode of decompensation and any patient with values above >200 micromol/l requires urgent treatment[77]. They also advise that immediate treatment in the emergency setting is an intravenous infusion of glucose 200 mg/kg (2ml/kg of 10% glucose or 1ml/kg of 20% glucose) over a few minutes. The GDG decided that in an acute setting in a child with decreased conscious level a threshold for treatment of >100 micromol/l was appropriate and tested this threshold with the Delphi panel. However, neither this threshold, nor that of >200 micromol/l recommended in the 2005 Guideline had the agreement of the Delphi panel. On reviewing the Delphi findings the GDG decided to reword the recommendation with the >100 micromol/l threshold and with early involvement of a metabolic expert to ensure appropriate specialist advice is obtained prior to treatment being initiated and to guide further investigations. This recommendation was felt to be the safest in light of the lack of evidence to guide practice and the wide degree of variation in current opinion. This replaces recommendations in the 2005 Guideline describing the treatment regimes for raised ammonia levels which failed to reach consensus in two rounds of Delphi voting (see the Appendices document for details of Delphi consensus statements and voting).

3.14. Intracranial infections

3.14.1. Bacterial meningitis

3.14.1.1. Recognition

Recommendation(s)

55. Think about bacterial meningitis in children who present with one or more of the signs and symptoms detailed below:
    - Non-blanching rash
    - Stiff neck
    - Altered mental state / Unconsciousness
    - Shock
    - Back rigidity
    - Bulging fontanelle
    - Photophobia
    - Kerning's sign
    - Brudzinski's sign
    - Toxic/moribund state
    - Paresis
    - Focal neurological deficit including cranial nerve involvement and abnormal pupils sizes

    [2015; Evidence level 2b; Recommendation grade A]

    Note: For a more detailed list of non-specific symptoms see the NICE guidance on Bacterial Meningitis and Meningococcal Septicaemia[28]

Review question

In children with a decreased conscious level, what are the clinical signs of bacterial meningitis?

Evidence summary

The 2005 recommendation utilised a clinical decision rule to aid the diagnosis of bacterial meningitis[78-81]. The evidence search update retrieved eight relevant papers, six of which validated clinical diagnostic rules[12-13, 82-85] the sensitivity and specificity of which are summarised in table 2. The other two papers[86, 87] were systematic reviews evaluating clinical features of bacterial meningitis in children (and as such have not been included in table 1). Both reviews found evidence of clinical signs fever, seizures, altered consciousness, bulging fontanel, toxic/moribund appearance and abnormal crying all to be presenting clinical features of bacterial meningitis.

Table 1: summary of diagnostic rules

Study	Diagnostic rule	Specificity	Sensitivity
Bonsu 2008[13]	Peripheral blood test to determine leukocyte count vs Gram stain test of CSF from lumbar puncture	Not provided	Not provided
Nigrovic 2012 (meta-analysis)[12]	Bacterial meningitis score	62.1% (95% CI 60.5-63.7)	99.3% (95% CI 98.7-99.7)
Dubos 2010[84]	Meningitest vs Bacterial meningitis score	36% (95% CI 27-46) 52% (95% CI 42-62)	100% (95% CI 96-100) 100% (95% CI 96-100)
Dubos 2008[83]	Bacterial meningitis score distinguish from bacterial and aseptic meningitis	73% (CI not provided)	100% (95% CI 84-100)
Chavanet 2007 (retrospective chart analysis)[82]	Meningitest	85% (CI not provided)	100% (CI not provided)
Tuerlinckx 2012 (retrospective cohort)[85]	Bacterial meningitis score	61.5% (95% CI 53.6-69.3)	92.3% (95% CI 82.1-100)

Evidence interpretation

The GDG reviewed the validation studies of the clinical decision rules which were all found to have high sensitivity and most also had high to moderate specificity. The bacterial meningitis score (BMS) was found to be effective in the diagnosis of bacterial meningitis and would be useful in assisting other clinical decision rules. The quality of the evidence was varied with the meta-analysis providing strong evidence for the use of the BMS[12]. However, two studies[83, 84] used secondary analysis of data to validate the use of the BMS and another was a retrospective cohort study[85], thus displaying bias in the selection and classification of patients included in the analysis. Although these studies displayed bias they did support the conclusion from the meta-analysis[12]. The two systematic reviews[86, 87] extracted the clinical signs of bacterial meningitis, which supports the WHO[9] and NICE Guidelines[28]. The GDG felt that the BMS was a useful tool to use for the detection of bacterial meningitis but it was based on investigations rather than clinical signs. Therefore the 2015 recommendation states the specific signs and symptoms validated by these two systematic reviews[86, 87] and adjusted in line with NICE guidance[28]. The GDG felt it was important to note that there is not enough evidence that a single clinical feature is distinctive of bacterial meningitis and clinicians should refer to the NICE guidance[28] for additional non-specific signs of bacterial meningitis.

3.14.1.2. Diagnosis

Recommendation(s)

56. Consider carrying out the core investigations and a lumbar puncture in a child with a decreased conscious level and suspected bacterial meningitis, if no acute contraindications exist
[2015; Evidence level 5; Recommendation grade D]

Note:

- **For a list of core investigations refer to recommendations 15-17**
- **For further information on the contraindications for performing a lumbar puncture refer to recommendation 23**
- **For a list of which tests to perform on the CSF refer to recommendations 20-22, and the NICE guidance on Bacterial Meningitis and Meningococcal Septicaemia[28]**

Review question

In children with a decreased conscious level, which rapid investigations help screen for or diagnose bacterial meningitis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus.
Six papers were retrieved in the evidence search update. One retrospective study[13] showed the likelihood of bacterial meningitis increased directly with the total protein concentration and neutrophils in the white blood cell count. Two prospective cohort studies were retrieved[88, 89] which examined CSF to determine the diagnosis of aseptic meningitis and bacterial meningitis. One study[88] analysed the use of B7-H3 levels in plasma and CSF for differential diagnosis between aseptic meningitis and bacterial meningitis in children in China. Children with bacterial meningitis were found to have significantly higher B7-H3 levels in CSF and plasma than aseptic meningitis children ($p=0.004$ and $p<0.0001$ respectively) and the control group ($p=0.004$ and $p<0.0001$ respectively). Another study[89] examined children with aseptic meningitis and bacterial meningitis to determine pattern of distribution of LDH isoenzymes in cerebrospinal fluid of patients. Children with bacterial meningitis were found to have significantly higher LDH levels (944053 +/- 11203 U/L) than children with aseptic meningitis (33053+/- 5075 U/L).

One study[90] found that certain clinical signs (loss of consciousness, prolonged capillary refill time, decreased alertness, respiratory effort and the physician's illness assessment) had strong positive likelihood ratios for the diagnosis of BM, although these had wide confidence intervals. Certain clinical prediction rules had poor positive likelihood ratios, including the NICE traffic light system, the modified Yale Observation Scale and the Paediatric Advanced Warning

Score. Another study[91] found that PCR of CSF performed well as a diagnostic measure for BM, with a sensitivity of 100%, specificity of 93.8%, positive predictive value of 75% and negative predictive value of 100%. A final study[92] demonstrated that a gram probe PCR of CSF was more effective than CSF culture at detecting bacterial meningitis. The positive detection of bacterial meningitis using GP-PCR was significantly higher than the positive detection of bacterial meningitis using CSF culture (6.64% compared to 4.77%, p<0.001).

Evidence interpretation

The evidence demonstrated the importance of undertaking a lumbar puncture in a child with suspected bacterial meningitis to ascertain CSF total protein concentration and neutrophil count in the diagnosis of bacterial meningitis in a child. The GDG felt that with no substantial harms demonstrated from the use of lumbar puncture in determining meningitis it was important that clinicians carry out the core investigations and perform a lumbar puncture to investigate a possible diagnosis of bacterial meningitis in child with a decreased conscious level. The recommendation supports current NICE guidance[28] which also states that CSF should be examined for white blood cell count, total glucose concentration and microbiological culture. The GDG felt was important to ensure there was consistency across national guidance to ensure there was no confusion amongst clinicians.

Whilst most of the studies reviewed compared different tests on CSF in determining the diagnosis of bacterial meningitis the GDG felt this topic was already comprehensively covered in the NICE Guideline[28] and again for consistency decided to cross-refer here.

3.14.1.3. Treatment

Recommendation(s)

57. Treat a child with suspected bacterial meningitis according to the NICE bacterial meningitis and meningococcal septicaemia guidance[28]
    [2005; Evidence level 5; Recommendation grade D]

Review questions

- In children with a decreased conscious level and suspected bacterial meningitis, which antibiotics should be started?
- In children with a decreased conscious level and suspected bacterial meningitis, does adjuvant treatment with steroids improve survival or neurological morbidity?

Evidence summary

The 2005 recommendation was based on four meta-analyses looking at the effects of steroid treatment with antibiotics for bacterial meningitis[93-96] and a systematic review which demonstrated that no single antibiotic regime is better than any other for bacterial meningitis[97].

The evidence search update retrieved three randomised controlled trials that met the inclusion criteria. Two studies[98, 99] tested the effectiveness of ceftriaxone in children with bacterial meningitis. Ceftriaxone was found to have no significant effect on death or clinical failure compared to the use of only intramuscular chloramphenicol[98]. Molyneux[99] compared children receiving ceftriaxone for 5 days and 10 days and found there to be a no significant difference in neurological outcomes between the two groups.

One randomised controlled trial[100] conducted in 10 centres throughout Latin America comparing dexamethasone and glycerol found there were significantly poorer outcomes in the placebo group. However, there was no difference in profound hearing loss in all treatment groups and the addition of glycerol to dexamethasone did not significantly improve outcomes.

Evidence interpretation

The GDG reviewed the evidence, however due to thorough and detailed NICE guidance[28, 101] already available in the area of bacterial meningitis, the GDG felt that replicating this information in the decreased conscious level guidance was not appropriate and clinicians should refer to the NICE guidance for treatment regimes.

3.14.2. Viral Encephalitis

3.14.2.1. Recognition

Recommendation(s)

58. Consider the possibility of viral encephalitis, including herpes simplex encephalitis (HSE), if a child with a decreased conscious level has one or more of the following:
    - Focal neurological signs
    - Fluctuating conscious level, for 6 hours or more
    - Previous contact with herpetic lesions
    - A prolonged convulsion with no obvious precipitating cause
    - No obvious clinical signs pointing towards the cause

    [2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what are the signs of viral encephalitis?

Evidence summary

The previous recommendation was based on a Delphi consensus. The evidence search update found no new evidence and so Delphi survey was again used to test the recommendations. The

Delphi statements were developed using information from the Association of British Neurologists, British Paediatric Allergy Immunology and Infection Group's Guideline[102] on viral encephalitis in children.

Delphi statements

- Viral encephalitis, especially herpes simplex encephalitis (HSE), should be suspected clinically in a child with decreased conscious level if the child has had two or more of the following:
  - a prolonged convulsion with no obvious precipitating cause (70%, round 1; 73% round 2)
  - focal neurological signs, including a focal convulsion (84%, round 1)
  - a fluctuating conscious level for 6 hours or more (88%, round 1)
  - contact with herpetic lesions (88%, round 1)

Evidence interpretation

There are no validated clinical diagnostic decision rules to help identify children with viral encephalitis, including herpes simplex encephalitis (HSE), from those with bacterial meningitis or other causes of decreased conscious level. Several neurologists on the 2014 Delphi panel commented that HSE is a diagnosis of exclusion. The Delphi panel were given several options to decide who to give intravenous aciclovir to in the acute situation. As well as being a diagnosis of exclusion ('—no obvious signs pointing towards the cause') the Delphi panel agreed to some inclusion criteria which form the basis of the recommendation. Although the criterion of a 'prolonged convulsion with no obvious precipitating cause' just failed to meet the 75% threshold for Delphi panel consensus, the GDG decided that it was safer to include this within the recommendation as well as adding 'no obvious clinical signs pointing towards the cause' to ensure this potential diagnosis is not overlooked.

There has been debate amongst the virologist stakeholders about the relevance of contact with herpetic lesions, as this is rarely the route of transmission for the primary infection of HSE. However, the Guideline developers felt that, in the situation of a child with a decreased conscious level and the knowledge that there had been contact with herpetic lesions (i.e. cold sores), it would be reasonable to treat with aciclovir on that basis alone.

3.14.2.2. Diagnosis

Recommendation(s)

59. Confirm the clinical suspicion of herpes simplex encephalitis by a positive CSF PCR result for herpes simplex virus DNA
[2015; Evidence level 1b; Recommendation grade A]

Review question

In children with a decreased conscious level, which investigations help screen for or diagnose viral encephalitis?

Evidence summary

The 2005 recommendation was based on a two studies comparing the use of a PCR of CSF (evidence level 1b) to a brain biopsy[23, 25], and one study investigating the use of MRI and EEG for the diagnosis of HSE[103]. The evidence search update retrieved no new evidence.

Delphi statements

- The clinical suspicion of HSE can be strengthened by:
  - A magnetic resonance image scan with non-specific features if HSE is suspected (61%, round 1; 34%, round 2)
  - An abnormal EEG with nonspecific features of herpes simplex encephalitis (66%, round 1; not voted on in round 2)
  - A positive CSF PCR result for herpes simplex virus DNA (84%, round 1)

Evidence interpretation

The GDG agreed with the findings from the Delphi panel voting that supported the use of CSF PCR to confirm the presence of the herpes simplex virus. Magnetic resonance imaging cannot precisely diagnose HSE, whilst a normal MRI will be reassuring abnormal findings are not specific enough to rule out other diagnoses[103]. Similarly electroencephalogram (EEG) features of HSE are not specific enough to rule out other diagnoses, but a normal EEG would be reassuring[103].

The gold standard for herpes simplex encephalitis had in the past been considered to be brain biopsy. As PCR of CSF is a less invasive test and has been demonstrated to be highly sensitive and specific this is now the standard for early diagnosis and was proved to be as accurate as brain biopsy in comparative studies[23, 25] (level 1b Diagnosis). The GDG decided to update the previous recommendation to reflect that a PCR of CSF is considered a highly specific test, and altered the wording of the recommendation accordingly.

3.14.2.3. Treatment

Recommendation(s)

60. If HSE is clinically suspected in a child with decreased conscious level, administer intravenous aciclovir (20 mg/kg every 8 hours for children aged 1-3 months; 500 mg/m^2 three times a day if aged 3 months to 12 years; 10 mg/kg every 8 hours for children aged over 12 years). If a lumbar puncture is contraindicated, do not delay giving treatment
[2015; Evidence level 1b; Recommendation grade A]

Note: For further information refer to the most current version of the British National Formulary for Children (BNFC)[104]

Review question

In children with a decreased conscious level, what is an effective treatment for viral encephalitis?

Evidence summary

The original recommendation was based on two studies which demonstrated that aciclovir is an effective treatment for HSE. The first[105] investigated vidaribine (an early antiviral treatment) against placebo in children and adults. In the placebo arm 70% of patients died (this high figure is consistent with other survival data at the time), whereas only 28% of patients died in the treatment arm. A second study[106] compared vidaribine with aciclovir. This study found that risk of dying from HSE was more than halved by using aciclovir compared to vidaribine (RR = 0.4). Vidaribine is better than placebo and aciclovir is better than vidaribine for the treatment of HSE. If the fatality rate of untreated HSE is still 70% then the NNT with aciclovir to prevent one death is 2.

The evidence search update found one relevant study, investigating the effect that recombinant interferon ß in combination with aciclovir, as opposed to aciclovir alone. It was found that there was no difference in neurological outcome at 21 days or three months after the onset of symptoms between the two groups[107].

Delphi statement

If viral encephalitis is suspected clinically then intravenous aciclovir 10 mg/kg (or 500 mg/m^2 if aged 3 months to 12 years) three times a day should be administered, without waiting to perform a lumbar puncture if a lumbar puncture is contraindicated. (85%, round 1)

Evidence interpretation

The new study[107] supports the current recommendation to use aciclovir in the treatment of HSE over aciclovir plus recombinant interferon ß in combination with aciclovir; although the GDG noted that the very small sample size undermines the validity of these findings. The Delphi panel strongly agreed with the previous recommendation, which was based on level 1b evidence reviewed for the 2005 Guideline. The GDG therefore decided to retain this recommendation, updating the dosages in line with children's BNF guidance[104].

Recommendation(s)

61. Decide the duration of treatment (usually up to 21 days) in consultation with local experts in paediatric infectious diseases and neurology, if herpes simplex encephalitis is confirmed or highly suspected
[2015; Evidence level 5; Recommendation grade D]

Note: For further information refer to the most current version of the British National Formulary for Children (BNFC)[104]

Review question

In children with a decreased conscious level and suspected viral encephalitis, how long should treatment be administered for?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found no new evidence.

Delphi statements

- If HSE is confirmed or highly suspected then intravenous aciclovir should continue for:
  - 14 days (36%, round 1; 34% round 2)
  - 21 days (37%, round 1; 32% round 2)
- Intravenous aciclovir can be stopped before 14 days of treatment if there is no ongoing clinical suspicion of HSE (negative CSF and blood samples) (52%, round 1; 50% round 2)

Evidence interpretation

Reviewing the 2005 evidence the GDG noted that there are no comparative studies comparing length of course of aciclovir with outcome. The randomised controlled trials[106, 108] used a 10 day course. Various case reports have suggested relapses after a 10 day course. There are studies to determine the length of time to clear herpes simplex viral DNA from CSF, which conclude that there is still DNA detectable after 14 days in a large proportion of patients (International Herpes Management Forum 2004)[109]. However, there are no studies which show whether patients with detectable HSV DNA at two weeks relapse more frequently than those who do not have residual DNA.

There was a lack of consensus in the Delphi panel voting regarding duration of treatment. The BNF for children states that children aged 1-3 months should receive treatment with aciclovir for at least 21 days (up to 21 days for children over three months). This, plus the fact that longer term treatment is outside the scope of this Guideline, meant the GDG felt it appropriate to recommend the involvement of a local specialist in deciding treatment regimens.

3.14.3. Intracranial abscess

3.14.3.1. Recognition

Recommendation(s)

62. Consider intracranial abscess in a child with a decreased conscious level if there are:
    - Focal neurological signs +/- signs of sepsis
    - Signs of raised intracranial pressure

    [2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what are the clinical signs of an intracranial abscess?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found no new evidence.

Evidence interpretation

There are no diagnostic decision rules to aid the diagnosis of an intracranial abscess clinically. The gold standard test to diagnose an intracranial abscess is neuroimaging (usually CT initially with MRI being employed in specific cases). The Delphi panel agreed that in the presence of focal neurological signs or signs of raised intracranial pressure then a CT should be performed to rule in or out an intracranial abscess.

3.14.3.2. Diagnosis

Recommendation(s)

63. Consider using cranial imaging to diagnose an intracranial abscess

    [2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what investigations help screen or diagnose intracranial abscess?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found no new evidence.

Evidence interpretation

Cranial imaging is considered to be the gold standard investigation for a suspected intracranial abscess. Although there are many studies reporting CT as a useful test for an intracranial abscess[110-112], none of them blindly compared CT to a reference test of aspiration of the abscess, autopsy or intraoperative findings in children. The determination that cranial imaging is the gold standard is therefore based on expert opinion, and was endorsed by the GDG who agreed to retain the 2005 recommendation that cranial imaging be considered for use in diagnosing intracranial abscess.

3.14.3.3. Treatment

Recommendation(s)

64. Consider administering broad spectrum antibiotics after blood cultures have been taken, if an intracranial abscess is diagnosed in a child with a decreased conscious level, and obtain advice urgently from a paediatric neurosurgeon
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and suspected intracranial abscesses, which treatments should be started?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found no new evidence.

Evidence interpretation

There are no validated Guidelines for the management of intracranial abscesses. The majority are caused by bacterial infections[113]. It is important to identify the causative agent so that antibiotic therapy can be tailored. However, because of the location of the abscess, antibiotics penetrate the abscess poorly and therefore are often insufficient to treat the abscess in isolation. The GDG agreed that broad spectrum antibiotics should be started early but the choice should be determined by local resistance patterns and microbiology advice.

3.14.4. Tuberculous Meningitis

3.14.4.1. Recognition

Recommendation(s)

65. Consider tuberculous meningitis in a child with decreased conscious level if:
    - There has been contact with a case of pulmonary tuberculosis
    - The CSF opening pressure is high, the CSF is cloudy or yellow, contains slightly increased cells (less than 500), which are lymphocytes, with a low or very low CSF/plasma glucose ratio (less than 0.3), and a high or very high protein (1-5 g/L)

    [2015; Evidence level 5; Recommendation grade D]

66. Treat a child with suspected tuberculous meningitis according to the NICE Tuberculosis Guideline[114]

    [2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what are the clinical signs of tuberculous meningitis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Delphi statements

- Tuberculous meningitis should be suspected in a child with a decreased conscious level if:
    - There are clinical features of meningitis (60%, round 1; not voted on in round 2)
    - There has been contact with a case of pulmonary tuberculosis (87%, round 1)
    - The CSF opening pressure is high, the CSF is cloudy or yellow, contains slightly increased cells (less than 500), which are lymphocytes, with a low or very low CSF/plasma glucose ratio (less than 0.3), and a high or very high protein (1-5 g/L). (79%, round 1)

Evidence interpretation

The 2014 Delphi panel agreed that tuberculous (TB) meningitis should be suspected, but not treated until further information was available, if the child had been in contact with TB or the opening CSF pressure was high. They also felt it important to cross-refer to the NICE Guideline[114] for treatment of tuberculous meningitis.

3.14.4.2.Diagnosis

Recommendation(s)

67. Consider performing core investigations and a lumbar puncture for a child with a decreased conscious level and suspected tuberculous meningitis if no acute contraindications exist
[2005; Evidence level 5; Recommendation grade D]

Note:

- **For a list of core investigations refer to recommendations 15-17**
- **For further information on the contraindications for performing a lumbar puncture refer to recommendation 23**
- **For a list of which tests to perform on the CSF refer to recommendations 20-22**

Review question

In children with a decreased conscious level, which investigations help screen for or diagnose TB meningitis?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update found three relevant studies. Two studies compared interferon gamma tests with the gold standard tuberculin skin test, one found that specificity of interferon gamma tests was 100%, and sensitivity was greater than 75%[115]. The other found that the T-SPOT.TB performed similarly to the tuberculin skin test for diagnosing TB[116]. Another study identified particular signs on CT scans which were associated with TB meningitis[117].

Evidence interpretation

The GDG decided not to base their decision-making on the study examining CT scans because it was retrospective and only looked at a very small sample. The GDG also felt that interferon gamma tests and tuberculin skin test would not be performed in an acute setting, and are therefore not relevant to this question. The GDG therefore decided to retain the 2005 recommendation.

3.15. Raised Intracranial Pressure

3.15.1. Recognition

Recommendation(s)

68. For the recognition and management of raised intracranial pressure refer to the NICE Bacterial meningitis and meningococcal septicaemia Guideline[28]
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what are the clinical signs of raised intracranial pressure?

Evidence summary

The 2005 recommendation was based on the Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

As no new evidence was found, the GDG decided to refer to the NICE Bacterial meningitis and meningococcal septicaemia Guideline[28] for further information.

3.15.2. Investigations

Recommendation(s)

69. Consider requesting core investigations, and request urgent cranial imaging for a child with a decreased conscious level and suspected raised intracranial pressure, after the child's acute management has been discussed with paediatric intensive care
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and raised intracranial pressure, what tests should be performed to determine the level of raised intracranial pressure?

Evidence summary

The 2005 recommendation was based on the Delphi consensus, and one study showing that CT scans are as effective for detection of raised intracranial pressure as intracranial pressure monitoring, with a sensitivity of 99.1% and specificity of 78.1%[33]. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

The GDG noted that the study included in the 2005 review[33] was carried out with children following head injury thus there is a likelihood of a high incidence of raised intracranial pressure amongst the study population which undermines the validity of the findings. The GDG were clear the study was based on a population which is outside the scope of the 2015 guideline and should not be used as the basis for any recommendations. They also reiterated that it is important to recognise that a normal CT scan cannot be used to rule out raised intracranial pressure. However, the GDG agreed with the original Delphi panel findings that CT scans can provide useful information when there is a suspicion of raised intracranial pressure and are worth performing. They also felt that some institutions may have access to urgent MRI scanning, which may give a better indication of the level of intracranial pressure in comparison to a CT scan. The recommendation has therefore been updated to reflect the fact that either CT scan or MRI can be used.

Recommendation(s)

70. Consider reviewing the results of all the investigations performed, and consider further tests of the cause of the raised intracranial pressure if not diagnosed
[2005; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and raised intracranial pressure, what tests should be performed to determine the underlying cause of raised intracranial pressure?

Evidence summary

The 2005 recommendation was based on a Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

As new no evidence was found, the GDG decided to retain the previous recommendation.

Recommendation(s)

71. Consider the following head positions to prevent coning in a child with raised intracranial pressure:
    - Position the patient's head in the midline
    - Angle the patient's head up at 20 degrees above the horizontal

    [2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and raised intracranial pressure, what head position should be maintained to reduce the raised intracranial pressure?

Evidence summary

The previous recommendation was based on a Delphi consensus. The evidence search update found one study which found that raised intracranial pressure returned to baseline when the head of bed elevation was increased to 30 degrees[118].

Evidence interpretation

The study found was based on a small sample of traumatic brain injury patients, who are outside the scope of this Guideline. The study also only recorded initial changes in intracranial pressure observed following head of bed elevation, which may not reflect the maximum amplitude or duration of the effect. Therefore the GDG felt it best to retain the 2005 recommendation.

Recommendation(s)

72. Whilst treating a child with a confirmed diagnosis of raised intracranial pressure:
    - Avoid inserting central venous lines in the neck
    - Maintenance fluids should not be hypotonic (maintenance fluids need to be agreed at a local level)

    [2015; Evidence level 5; Recommendation grade D]

73. Consider forming local level agreements about the decision to give mannitol or hypertonic saline and their doses

    [2015; Evidence level 5; Recommendation grade D]

Review questions

- In children with a decreased conscious level and raised intracranial pressure, what maintenance fluid strategy should be used?

- In children with a decreased conscious level and raised intracranial pressure, what are the indications for mannitol or hypertonic saline?

Evidence summary

For the first review question, the 2005 recommendation was based on a Delphi consensus. The evidence search update found one study[119] comparing cerebral perfusion-targeted approach (CP) with the conventional intracranial pressure-targeted approach (IC) to treat raised ICP. The 90-day mortality was higher in the group treated with a CP approach than in the group treated with an IC approach.

For the second review question, the 2005 recommendation was based on a Delphi consensus. The evidence search update found a retrospective chart analysis which showed that children with sustained (longer than 72 hour) serum sodium levels above 170 mEq/L had a significantly higher occurrence of complications[120]. Another retrospective study was found that demonstrated that hypertonic saline was more effective than mannitol in the treatment of cerebral oedema[121].

Evidence interpretation

For the first review question, findings from the one small included study supported the continued use of the conventional intracranial pressure targeted approach to treat raised intracranial pressure. The GDG retained the 2005 recommendation stating that hypotonic intravenous fluids should be avoided. For the second review question, the GDG was concerned that both studies were retrospective, as only associations could be drawn from them. Therefore, the GDG decided not to base a new recommendation on these studies. The GDG did consult the NICE Guideline[122] and APLS[32], to ensure the recommendation reflected these Guidelines.

Recommendation(s)

74. Consider sedation, intubation and ventilation to maintain the $PaCO_2$ between 4.5 and 5.0 kPa in a child with a clinical diagnosis of raised intracranial pressure, before imaging
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and raised intracranial pressure, what are the indications for sedation and ventilation?

Evidence summary

The 2005 recommendation was based on the Delphi consensus. The evidence search update did not retrieve any papers matching the inclusion criteria.

Evidence interpretation

As no new evidence was found the GDG retained the original recommendation, however the $PaCO_2$ range was amended in line with the NICE Guideline[122].

3.16. Hypertensive encephalopathy

Recommendation(s)

75. Consider the following in a child with hypertension and a decreased conscious level:
    - Signs of raised intracranial pressure
    - Papilloedema

    and check a four limb blood pressure
    [2005; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what are the clinical signs of hypertensive encephalopathy?

Evidence summary

The 2005 recommendation was based on GDG consensus. The evidence search update found no new evidence.

Evidence interpretation

In a child with a decreased conscious level, hypertension is defined as the systolic blood pressure greater than 95th centile for age on two separate readings. Hypertension may be caused by raised intracranial pressure, in which case a reduction in blood pressure may lead to a clinical deterioration due to the concomitant fall in cerebral perfusion pressure. However, if the cause of the decreased conscious level is hypertension itself then it is important to reduce this in a controlled way. Therefore, distinguishing between hypertensive encephalopathy and hypertension secondary to raised intracranial pressure is crucial to making the correct management decisions. Hypertensive encephalopathy is often caused by a renal problem and the high blood pressure will have been present for some time. This is not usually the case with raised intracranial pressure, as the raised blood pressure is often a transient phenomenon responding to changes in cerebral perfusion pressure.

There are no validated clinical decision rules for either raised intracranial pressure or hypertensive encephalopathy. The GDG agreed with comments received from the Delphi panel that trying to differentiate raised intracranial pressure from hypertensive encephalopathy was an important part of the management of these cases. The 2005 recommendation was retained.

Review question

In children with a decreased conscious level, what investigations screen for or diagnose the causes of hypertensive encephalopathy?

Evidence summary

The 2005 recommendation was based on GDG consensus. The evidence search update retrieved no new evidence.

Evidence interpretation

As hypertensive encephalopathy is often caused by an acute or chronic renal problem, the GDG in discussion with stakeholders agreed that reviewing the screening tests of renal function may help differentiate hypertensive encephalopathy from raised intracranial pressure. The 2005 recommendation was retained.

Recommendation(s)

77. Consider seeking urgent help from a paediatric nephrologist or intensivist when presented with a child with hypertension and no other cause for decreased conscious level
[2005; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and hypertension, what treatments should be started to reduce morbidity associated with hypertensive encephalopathy?

Evidence summary

The 2005 recommendation was based on GDG consensus. The evidence search update retrieved no new evidence.

Evidence interpretation

There are no randomised controlled trials for the treatment of hypertensive encephalopathy and therefore treatments vary according to experience. A published Guideline for treating hypertension in children states that — 'severe, symptomatic hypertension should be treated with intravenous drugs'[123]. The GDG agreed that the decision to treat should be made with the involvement of a nephrologist or intensivist with experience of hypertensive encephalopathy and retained the 2005 recommendation.

3.17. Prolonged convulsion

Recommendation(s)

78. Consider treating a child with a convulsion lasting longer than five minutes
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level, what is the neurological outcome after a prolonged convulsion?

Evidence summary

The 2005 recommendation was based on the Delphi consensus statement that a convulsion needs treating if it has not stopped after 10 minutes. The evidence search update retrieved one validation of Guidelines study[124] which found the time taken to administer treatment following the implementation of the Guidelines improved, with a decreased need for invasive procedures.

Evidence interpretation

There were some concerns over a potential self-fulfilling bias being displayed by healthcare professionals involved in the research and whether the same results could be attributed if health professionals were unaware of the study. With the lack of strong evidence and to reduce confusion the GDG felt that it was important the recommendation reflected NICE epilepsy guidance[101] and APLS[65] guidance which state that treatment should be commenced at 5 minutes. It was agreed the recommendation should be updated to reflect this guidance. The GDG felt that healthcare professionals should not rush treatment but should be aware that waiting 10 minutes before treating a convulsion would be too long.

Recommendation(s)

79. Follow the APLS[32] and NICE guidance[101] to treat a child with a prolonged convulsion (i.e. lasting longer than five minutes)
[2015; Evidence level 5; Recommendation grade D]

Review question

In children with a decreased conscious level and a prolonged convulsion, what treatment is required to stop the convulsion?

Evidence summary

The 2005 Guideline found no validated Guidelines for the treatment of a convulsion and the Delphi panel agreed that APLS and status epilepticus working party guidance should be followed in this instance. The evidence search update found strong evidence to suggest that midazolam and diazepam were effective treatments in treating prolonged convulsions[125, 126]. Diazepam was reported to be more socially awkward to administer and related to respiratory depression. On the other hand, diazepam was found to reduce convulsion time by 1.3 minutes (p=0.09) when compared to intranasal midazolam[127]. A study by Kaputu et al[128] conducted in Sub-Saharan Africa suggested that although rectal diazepam is more effective, sublingual lorazepam is easier to use, so may be preferred in areas where diazepam is not readily administered.

Evidence interpretation

The GDG felt the setting, and therefore management, of the children in the study by Kaputu et al[128] would have been different from that in the UK and that it was therefore inappropriate to generalise these findings to a UK setting. The evidence from the study by O'Dell et al, Holsti et al, and McIntyre et al[125-127] was in line with the APLS[32] and NICE guidance[101] and the GDG felt that this guidance should be followed in the event of a prolonged seizure in a child and made a recommendation signposting clinicians to this information.

Recommendation(s)

80. Consider performing core investigations at first clinical assessment in a child with a prolonged convulsion (i.e. lasting longer than five minutes) who is not known to have epilepsy
[2015; Evidence level 5; Recommendation grade D]

81. In addition to checking the core investigation, consider checking the plasma calcium and magnesium levels when a child presents with a prolonged convulsion (i.e. lasting longer than five minutes)
[2015; Evidence level 5; Recommendation grade D]

82. Consider discussing treatment with a paediatric intensivist if a child has:
    - plasma sodium level less than 125 mmol/l
    - ionized calcium level less than 0.75 mmol/l or plasma calcium level less than 1.7 mmol/l
    - a plasma magnesium level less than 0.65 mmol/l

    and the convulsion is ongoing despite anticonvulsant treatment
    [2015; Evidence level 5; Recommendation grade D]

Review questions

- In children with a decreased conscious level and a prolonged convulsion, what tests screen for or diagnose the underlying treatable cause?
- In children with a decreased conscious level and a prolonged convulsion secondary to hyponatraemia, what treatment is required to stop the convulsion?
- In children with a decreased conscious level and a prolonged convulsion secondary to hypocalcaemia, what treatment is required to stop the convulsion?
- In children with a decreased conscious level and a prolonged convulsion secondary to hypomagnesaemia, what treatment is required to stop the convulsion?

Evidence summary

The evidence search update found two epidemiological studies[129, 130]. These two studies found that aetiology of a seizure was related to mortality in children. However, these studies did not provide an indication of tests that should be used.

The evidence search update found no evidence to support the change of recommendations 81 and 82. Previous recommendations were based on Delphi consensus and one cohort and case series study that the GDG felt showed it was reasonable to check the calcium and magnesium in children with a prolonged convulsion. In light of the lack of evidence the recommendations were tested again through the 2014 Delphi survey.

Delphi statements

- If the convulsion is prolonged the core investigations should be sent at first presentation. (81%, round 1)

- If the convulsion is prolonged and the child is under a year of age, the plasma calcium and magnesium should be requested as well as the core investigations.
  - at the first presentation (85%, round 1)
  - at every presentation (35%, round 1; not voted on in round 2)

- If the child is on regular antiepileptic drugs (AEDs) and has had a prolonged convulsion, or cluster of more severe or frequent convulsions than usual, take a serum sample to send for their specific, named AED blood levels at every presentation. (52%, round 1; not voted on in round 2)

- If the plasma sodium is less than 125 mmol/l and the convulsion is ongoing despite anticonvulsant treatment, an infusion of 5 ml/kg of 3% saline should be given over one hour. (40%, round 1; 61% round 2)

- If the ionized calcium is less than 0.75 mmol/l or plasma calcium is less than 1.7 mmol/l and the convulsion is ongoing, an infusion of 0.5 mmol/kg of 10% calcium gluconate should be given over five minutes (note that this precipitates if given simultaneously in the same IV line with ceftriaxone). (48%, round 1; 68%, round 2)

- If the plasma magnesium is less than 0.65 mmol/l and the convulsion is ongoing, an infusion of magnesium sulphate 50 mg/kg (0.2 mmol/L) should be given over 1 hour. (48%, round 1; 57% round 2)

Evidence interpretation

The 2005 recommendation to performance investigations originally based on Delphi consensus and re-validated by the 2014 Delphi consensus. The GDG felt the wording of the recommendation was ambiguous and amended the recommendation to state the core investigations are to be carried out at first clinical assessment.

Very little evidence exists to inform recommendations 81 and 82. Delphi consensus showed that the panel agreed with the retention of the first recommendation to perform additional tests when the convulsion is prolonged (now defined as lasting longer than five minutes). There was no consensus however on either of the thresholds to define, or treatments to correct, abnormal findings. In light of this, and in the absence of any internationally recognised guidance, the GDG decided it would be appropriate and safe to refer to a local paediatric intensivists for advice if sodium, calcium or magnesium levels are found to be abnormal. When defining abnormal levels the GDG decided it would be safest to introduce conservative levels to facilitate faster referral where it was needed.

The GDG made the decision to remove the reference to children under one from recommendation 81 (as seen in the Delphi Statement); this criteria was from evidence in the 2005 Guideline, which was based on a population outside of the scope of the 2015 Guideline.

3.18. Post-convulsive state

Recommendation(s)

83. Consider performing a detailed history and examination in a child during the first hour of the post-convulsive state
[2005; Evidence Level 5; Recommendation grade D]

84. Consider observing a child with a normal capillary glucose and not performing any further tests during the first hour of the post-convulsive state
[2005; Evidence Level 5; Recommendation grade D]

85. Consider reassessing a child following a convulsion if they have not awoken from the post-convulsive state within one hour
[2005; Evidence Level 5; Recommendation grade D]

Note: for further information on the assessment of airway and airway protection, and breathing and oxygen requirements refer to recommendations 1-2

Review question

In children after a convulsion, what tests should be performed to determine the underlying cause of the convulsion?

Evidence summary

The 2005 recommendations were based on Delphi panel consensus. There was no evidence retrieved in the evidence search update.

Delphi statement

- All children with a decreased conscious level should undergo core investigations, except those:
  - Within one hour post-convulsion, who are clinically stable and have a normal capillary blood glucose. (66%, Round 2)

Evidence interpretation

The 2015 Delphi panel did not reach consensus. The GDG therefore decided to retain the 2005 recommendations, amended with the addition of the word 'consider' to reflect the fact they are based on consensus rather than evidence.

Recommendation(s)

86. Consider carrying out and recording the core investigations after the first hour of the post-convulsion state if the child has not recovered normal consciousness
[2005; Evidence Level 5; Recommendation grade D]

Review question

In children after a convulsion, what treatment is required?

Evidence summary

The 2005 recommendations were based on Delphi panel consensus. There was no evidence retrieved in the evidence search update.

Delphi statements

- During the first hour of the post-convulsion state, a detailed history and examination should be performed, but if the capillary blood glucose is normal, and there are no other indications, other tests, including the core investigations may be deferred. (No consensus achieved: strongly agree 68%)

- After the first hour of the post-convulsion state, if the child has not recovered to a normal conscious level the core investigations should be performed. (No consensus achieved: strongly agree 71%)

Evidence interpretation

The 2014 Delphi panel did not reach consensus. The GDG therefore decided to retain the 2005 recommendation.

3.19. Alcohol intoxication

Recommendation(s)

87. Consider carrying out a blood alcohol test in a child with a decreased conscious level with suspected alcohol intoxication
[2015; Evidence level 3b; Recommendation grade C]

Review question
What investigations/tests should be undertaken in a child with alcohol intoxication and a decreased conscious level?

Evidence summary

One retrieved study[131] found using serum alcohol concentration and physician's clinical judgment to determine a child's alcohol intoxication severity, led to an average of 67.7% accuracy; whereas using blood alcohol concentration and clinical judgment lead to an average 61.1% accuracy in diagnosing the correct acute alcohol intoxication. The child's level of consciousness was found to be the most useful clinical sign in diagnosing alcohol intoxication.

A study by Barnett[132] found that patients who had an alcohol related diagnosis in medical records tended to have higher blood alcohol concentration, however only 36% patients identified as having either an alcohol related discharge diagnosis or positive blood test were found to have both. The study also used saliva tests to determine alcohol intoxication, however only one confirmed case was identified using this method.

Evidence interpretation

The evidence retrieved in the search should be used with some caution as it investigates participants at one point in time, and in the Tonisson study[131] two different selection methods were used depending on how intoxicated the child was. Whilst the studies show that serum and blood alcohol concentration are effective in determining severity of alcohol intoxication, findings also suggest that clinicians are often able to reach an accurate diagnosis using clinical examination alone. The GDG agreed with this finding and felt that the use of blood alcohol tests, whilst potentially beneficial, were not always necessary. They recommended therefore that the use of blood alcohol testing should be considered and its use based on individual clinical judgement.

Recommendation(s)

88. Consider following the ABCD system (as in APLS)[32] and carry out the core investigations in a child with alcohol intoxication.
[2005; Evidence level 5; Recommendation grade D]

89. Consider the need to treat the following in a child with a decreased conscious level and suspected alcohol intoxication:
- Hypoglycaemia with intravenous (IV) glucose and maintenance dextrose/saline
- Respiratory failure and or aspiration pneumonia
- Hypotension
- Other drugs ingested at the same time, e.g. opiates, or benzodiazepines, or paracetamol

And avoid emetics (in case of aspiration)
[2005; Evidence level 5; Recommendation grade D]

90. Consider identifying all likely substances or drugs that may be contributing to the child's decreased conscious level and call your local regional poisons unit for advice
[2005; Evidence level 5; Recommendation grade D]

Note: For further information refer to the Royal College of Psychiatrist's Practice standards for young people with substance misuse problems[133]

Review question

What treatment should be undertaken in children with alcohol intoxication?

Evidence summary

The evidence search did not retrieve any papers matching the inclusion criteria.

Delphi statements

- The commonest cause of acute intoxication leading to a child or young person having a decreased conscious level is excessive alcohol (ethanol) ingestion. Care should follow the usual ABCD system (as in APLS), and include the core investigations. Look especially for and treat:
  - Hypoglycaemia with IV glucose and maintenance dextrose/saline (87%, round 1)
  - Respiratory failure and or aspiration pneumonia (84%, round 1)
  - Hypotension (77%, round 1)
  - Other drugs ingested at the same time, e.g. opiates, or benzodiazepines, or paracetamol

(87%, round 1)

- Avoid emetics (in case of aspiration) (75%, round 1)
- Identify all likely substances or drugs that may be contributing and call your local regional poisons unit if in doubt about the best treatment. (87%, round 1)

Evidence interpretation

Due to the lack of evidence relevant to this clinical question the recommendations were based on Delphi consensus.

3.20. Cause unclear

Recommendation(s)

91. Consider performing additional tests in discussion with a specialist (e.g. neurologist or metabolic expert depending on the clinical picture) after reviewing core investigations if the cause of decreased conscious level remains unknown. The additional tests are:
    - Cranial CT or MRI scan
    - Lumbar puncture
    - Urine toxicology
    - Urine organic and plasma aminoacids
    - Plasma lactate

    [2015; Evidence level 5; Recommendation grade D]

92. Consider performing an electro-encephalogram (EEG) after reviewing core investigations, CT or MRI scan results or initial CSF results

    [2015; Evidence level 5, Recommendation grade D]

    Note: for further information on the contraindications for performing a lumbar puncture refer to recommendation 23

Review question

In children with a decreased conscious level and no clinical clues to the cause, what tests should be performed to determine the diagnosis?

Evidence summary

The 2005 recommendation was based on Delphi panel and GDG consensus. The Delphi panel agreed that the core investigations should be sent initially. If after reviewing these screening tests no further clues emerged (e.g. hyperammonaemia or hyponatraemia), then the list of additional tests should be requested. Some of these tests can be requested from the saved samples taken

with the core investigations. No new evidence was found in the evidence search update and so again Delphi survey was used to update this recommendation.

Delphi statements

- The following additional tests should be requested if, after reviewing the core investigations results, the cause of a child's decreased conscious level remains unknown:
  - cranial CT scan (87%, round 1)
  - lumbar puncture (84%, round 1)
  - plasma lactate (87%, round 1)
  - urine toxicology screen (87%, round 1)
  - urine organic acids (84%, round 1)
  - plasma amino acids (86%, round 1)

- In a child with a decreased conscious level with an unknown cause after reviewing the core investigations, CT scan and initial CSF results, the following tests should be considered:
  - an EEG, organised as soon as possible, to exclude non-convulsive status epilepticus (77%, round 1)
  - urine amino acids, in children less than five years old (68%, round 1)
  - acyl-carninite profile (on Guthrie card or from stored frozen plasma) (67%, round 1)
  - ESR and autoimmune screen for cerebral vasculitidies (54%, round 1)
  - carbon monoxide tests (blood carboxyhaemoglobin/haemoglobin should be less than 6%; use finger clip pulse-CO-oximeter monitor, not a normal pulse-oximeter which misreads CO-Hb as oxi-Hb) (57%, round 1)
  - breath alcohol level (27%, round 1)
  - blood alcohol level (57%, round 1)
  - thyroid function tests and thyroid antibodies for Hashimoto's encephalitis (57%, round 2)

Evidence interpretation

All of the tests listed in the first recommendation were agreed by the Delphi panel and retained in the recommendation. The GDG added MRI scan to this recommendation so that either CT or MRI can be performed depending upon local protocols and availability. The GDG, after reviewing comments made by the Delphi panel, added plasma amino acids to this group of tests rather than the next group of tests listed in the second Delphi statement. The reason for this decision was that plasma amino acids may be diagnostic and the interpretation of the organic acid profile is helped by knowledge of the amino acid profile. Therefore, in everyday laboratory practice the two tests need to be looked at together. Following stakeholder consultation the GDG also agreed to add that there should be discussion with a relevant specialist when deciding which tests to perform.

The tests listed in the second Delphi statement based on the 2005 recommendation received little support from the Delphi panel, with only electro-encephalogram reaching consensus, therefore only this has been retained as a recommended second line of testing.

The GDG thought it would be beneficial to mention the following other conditions which could be considered in the differential diagnosis:

- **Deliberate harm/injury** (safeguarding concerns) e.g. shaking

- **Overdose**
  - sedation/anaesthesia/analgesia (including unusual reactions)
  - Carbon monoxide
  - Deliberate/self-harm (safeguarding concerns)

- **Other**
  - Hashimoto Encephalopathy (suggest check thyroid antibiotics and thyroid function tests)

- **Note for further information refer to:**
  - The NICE Guideline - When to Suspect Child Maltreatment[15]
  - The Royal College of Psychiatrist's Report - Managing Self Harm in Young People[16]
  - The Royal College of Psychiatrist's Practice Standards - Young people with substance misuse problems[133]

3.21. Good practice points

A separate Delphi process was carried out for children and young people for the 2015 Guideline. Unfortunately there was not sufficient feedback or consensus on any of the statements to reliably update any of the good practice points. The GDG therefore retained this section from the 2005 Guideline.

Recommendation(s)

93. During resuscitation and initial management of a child with a decreased conscious level, the parents/carers should be allowed to stay with the child if they wish
[2005; Recommendation grade, Good practice point]

Evidence interpretation

The 2005 GDG sought testimonies from parents of children who had had an acute illness which resulted in a decreased conscious level. The responses received from parents were positive about the experiences when they had been able to stay with their child. The Delphi panel which included patient/parent representation agreed that with enough staff support parents should be allowed to stay with their child.

Recommendation(s)

94. During resuscitation and initial management of a child with a decreased conscious level, the parents/carers should be kept informed of the possible underlying diagnoses and treatments required
[2005; Recommendation grade, Good practice point]

Evidence interpretation

The 2005 GDG sought testimonies from parents of children who had had an acute illness which resulted in a decreased conscious level. The responses received from parents were positive about the experiences when they had been kept informed of the management of their child's illness. The Delphi panel which included patient/parent representation agreed that parents should be kept informed and the information given should be tailored to each individual case.

Recommendation(s)

95. During resuscitation and initial management of a child with a decreased conscious level, the parents/carers should be kept informed of the possible prognosis of their child if it is known
[2005; Recommendation grade, Good practice point]

Evidence interpretation

The 2005 GDG sought testimonies from parents of children who had had an acute illness which resulted in a decreased conscious level. The responses received from parents were positive about the experiences when they had been kept informed of the seriousness of their child's condition. The Delphi panel which included patient/parent representation agreed that with parents should be kept informed of their child's prognosis on a case-by-case basis.

4. Methodology for the 2015 Guideline

This Guideline update has been funded by the National Reye's Syndrome Foundation UK. The RCPCH in collaboration with the University of Nottingham and the GDG have carried out this update, in accordance with the RCPCH standards for development of clinical Guidelines in paediatrics and child health.

While the Guideline assists the practice of healthcare professionals, it does not replace their own clinical knowledge and skills.

For further information on the methodology used for the 2005 Guideline see the Appendices document.

4.1. Scope

4.1.1. Population covered

Children aged from four weeks and up to 18 years who have a decreased conscious level, defined as being responsive only to voice, or pain, or being unresponsive on the AVPU scale or a Glasgow Coma Score or modified Glasgow Coma Score of 14 or less.

4.1.2. Target audience

Any healthcare professional in an acute situation who is presented with a child with a decreased conscious level.

4.1.3. Healthcare setting

Any setting where a health professional may be presented with a child with a decreased conscious level.

4.1.4. What this Guideline covers

This is an update of the 2005 'The Management of a Child with Decreased Conscious Level' Guideline. Including:

- Assessment of airway and airway protection in children with a decreased conscious level
- Assessment of breathing and oxygen requirements in children with decreased conscious level
- Assessment of capillary glucose in children with a decreased conscious level
- Observations to monitor and help manage children with a decreased conscious level
- Managing the causes of decreased conscious level in children
- Circulatory shock
- Sepsis
- Trauma
- Metabolic illness (Hypoglycaemia, Hyperammonaemia)
- Intracranial infections (Bacterial meningitis, encephalitis, Intracranial abscess, Tuberculosis (TB) meningitis)

- Raised intracranial pressure
- Prolonged convulsion
- Post convulsion state
- Alcohol intoxication
- Cause unclear
- Good practice points

4.1.5. What this Guideline does not cover

The Guideline does not cover:

- Neonates (28 days or younger)
- Pre-term infant survivors on neonatal intensive care units
- Children with a previously diagnosed condition which may decompensate causing a decreased conscious level (e.g. epilepsy, ventriculo-peritoneal shunt, previously diagnosed metabolic condition), who already have an agreed management plan for acute illness
- Children who on a day to day basis score 14 or less on the Glasgow Coma Scale or Modified Glasgow Coma Scale (e.g. children with epileptic encephalopathy, minimally responsive state following acquired brain injury)
- The following conditions were considered outside of the scope of the Guideline, and are already addressed by existing Guidelines:
  - Non-ketotic hyperglycaemia
  - Peri-arrest management

Note

For consistency of care, where detailed information is covered in existing National Guidance the GDG felt it more appropriate to refer readers to them, rather than replicate information. For topics where a cross-reference to related guidance is made in place of any other recommendations the cross-reference itself forms the recommendation. For topics where recommendations appear in this guideline but a cross-reference is made to supplementary information this forms a note (written in bold font after the recommendations).

4.2. Developers and conflicts of interest

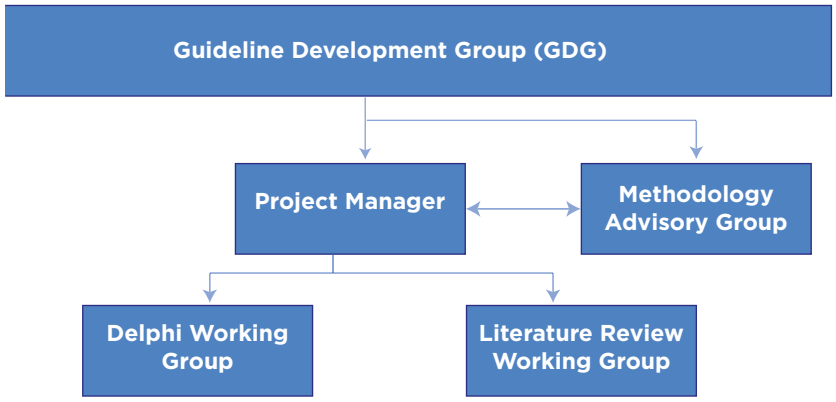
A Guideline Development Group (GDG) was appointed to oversee the Guideline update process. The group agreed the scope, search questions, finalised references for inclusion and provided the rationale for interpreting evidence into recommendations. The RCPCH project manager led and carried out the literature searches, abstract screening and critical appraisal work, as well as coordinating the development of the Delphi process and Guideline update. In addition three groups were set up to support the development of the Guideline update (figure 1).

a) A **Methodology Advisory Group** was established to provide methodological advice to the project manager and GDG, thus ensuring AGREE II criteria[134] were met.

b) A **Literature Review Working Group** was established to support the project manager in identifying evidence, through carrying out abstract screening and critical appraisal work.
c) A **Delphi Working Group** was established to guide the development of the Delphi questionnaire.

This update was drafted in consultation with GDG which met every three months during the development of Guideline. The GDG and all other working groups declared all conflicts of interest which were recorded. None were declared, with the exception of the funder whose role on the GDG was to maintain oversight of the project's progress; the funder did not have any influence over the clinical questions or systematic review strategy used in the Guideline.

Figure 1: Organisational structure of Guideline



4.3. Aims and objectives

The Guideline aims to provide healthcare professionals with guidance on the identification and management of decreased conscious level in children. In order to:

- Improve and standardise assessment, investigation and treatment of the child presenting with a decreased conscious level
- Reduce the risk of misdiagnosis and delay of lifesaving treatment

4.4. Developing the clinical questions

The scope of this Guideline was to carry out an update of the original 2005 Guideline and include alcohol intoxication as a cause of decreased conscious level. The GDG reviewed clinical questions used in the 2005 Guideline and amendments were made or questions excluded as appropriate in order to bring them up to date with current practice. For the area of alcohol intoxication review questions were formed based on the scope and a protocol prepared for each review question. Review questions were developed in a framework of population, intervention, comparison and outcome for reviews of management of alcohol intoxication. This was to guide the literature searching process, critical appraisal and synthesis of evidence, and facilitated the development of recommendations. The project manager worked with a sub-set of members of the literature review working group to form the review questions.

4.5. List of review questions

Assessment of airway and airway protection in children with a decreased conscious level

- What are the indications for intubation in children with a decreased conscious level?

Assessment of breathing and oxygen requirements in children with a decreased conscious level

- What are the indications for additional oxygen therapy in children with a decreased conscious level?

Assessment of capillary glucose in children with a decreased conscious level

- In children with a decreased conscious level, how soon should a capillary (bedside) glucose measurement be performed?

Observations to monitor and help manage children with a decreased conscious level

- In children with a decreased conscious level, which observations should be performed to assess their underlying diagnosis?
- In children with a decreased conscious level, which observations should be performed to monitor their clinical status?

History of illness

- In children with a decreased conscious level, which features in the history should be elicited to assess the underlying diagnosis?

Identifying the causes of decreased conscious level in children

- What are the non-traumatic causes of decreased conscious level in children?

Investigating the causes of decreased conscious level in children

- Which investigations will screen for the causes of decreased conscious level in children?

Lumbar puncture and cranial imaging

- When should a lumbar puncture be performed in a child with a decreased conscious level?
- What tests should be performed on a sample of cerebrospinal fluid from a child with a decreased conscious level?
- Which clinical features in a child with a decreased conscious level should be considered as contraindications to performing a lumbar puncture?
- Can a cranial scan (CT scan, MRI scan or ultrasound scan) rule out raised intracranial pressure to allow for a lumbar puncture to be performed? Can a computerised tomography (CT) or magnetic resonance imaging (MRI) scan demonstrate raised intracranial pressure?

Managing the causes of decreased conscious level in children

- Which cause of decreased conscious level in children should be treated first to improve clinical outcome?

Circulatory shock

- What clinical features determine the presence of circulatory shock in a child with a decreased conscious level?
- What are the causes of circulatory shock in children with a decreased conscious level?
- What tests should be performed in the presence of circulatory shock in children with a decreased conscious level to determine the underlying diagnosis?
- What fluid therapy should be initiated in the presence of circulatory shock in children with a decreased conscious level?
- What monitoring should be initiated in the presence of circulatory shock in children with a decreased conscious level?
- How much fluid is required for the treatment of circulatory shock in children with a decreased conscious level?
- When should intubation and ventilation be initiated for the treatment of circulatory shock in children with a decreased conscious level?
- When should specific circulatory support (including vasopressor, inotropic and vasodilator treatments) be initiated for the treatment of circulatory shock in children with a decreased conscious level?

Sepsis

- What clinical features determine the presence of sepsis in a child with a decreased conscious level?
- What investigations should be sent in a child with sepsis and a decreased conscious level to determine the cause and any predisposing factors?
- Which antibiotics should be started in children with sepsis and decreased conscious level?

Metabolic illness

Hypoglycaemia

- What level of hypoglycaemia should be investigated?
- In children with a decreased conscious level and hypoglycaemia, what further investigations will diagnose the underlying cause?
- In children with a decreased conscious level and hypoglycaemia, what treatment will improve their hypoglycaemia?

Hyperammonaemia

- In children with a decreased conscious level and hyperammonaemia, what plasma ammonia level should prompt treatment?
- In children with a decreased conscious level and hyperammonaemia, what tests should be

performed to diagnose the underlying cause?
- In children with a decreased conscious level and hyperammonaemia, what treatments should be performed to reduce the plasma ammonia level?

Intracranial infections

Bacterial meningitis

- In children with a decreased conscious level, what are the clinical signs of bacterial meningitis?
- In children with a decreased conscious level, which rapid investigations help screen for or diagnose bacterial meningitis?
- In children with a decreased conscious level and suspected bacterial meningitis, which antibiotics should be started?
- In children with a decreased conscious level and suspected bacterial meningitis, does adjuvant treatment with steroids improve survival or neurological morbidity?

Viral encephalitis

- In children with a decreased conscious level, what are the clinical signs of herpes simplex encephalitis?
- In children with a decreased conscious level, which investigations help screen for or diagnose herpes simplex encephalitis?
- In children with a decreased conscious level and suspected herpes simplex encephalitis, is aciclovir an effective treatment?
- In children with a decreased conscious level and suspected herpes simplex encephalitis, how long should aciclovir be continued for?

Intracranial abscess

- In children with a decreased conscious level, what are the clinical signs of an intracranial abscess?
- In children with a decreased conscious level, which investigations help screen for or diagnose intracranial abscess?
- In children with a decreased conscious level and suspected intracranial abscess, which treatments should be started?

Tuberculous (TB) meningitis

- In children with a decreased conscious level, what are the clinical signs of tuberculous (TB) meningitis?
- In children with a decreased conscious level, which investigations help screen for or diagnose TB meningitis?

Raised intracranial pressure

- In children with a decreased conscious level, what are the clinical signs of raised intracranial pressure?

- In children with a decreased conscious level and raised intracranial pressure, what tests should be performed to determine the level of raised intracranial pressure?
- In children with a decreased conscious level and raised intracranial pressure, what tests should be performed to determine the underlying cause of raised intracranial pressure?
- In children with a decreased conscious level and raised intracranial pressure, what head position should be maintained to reduce the raised intracranial pressure?
- In children with a decreased conscious level and raised intracranial pressure, what maintenance fluid strategy should be used?
- In children with a decreased conscious level and raised intracranial pressure, what are the indications for mannitol or hypertonic saline?
- In children with a decreased conscious level and raised intracranial pressure, what are the indications for sedation and ventilation?
- In children with a decreased conscious level and raised intracranial pressure, what are the indications for paralysing agents?
- In children with non-traumatic decreased conscious level and raised intracranial pressure, what are the indications for invasive intracranial pressure monitoring?

Hypertensive encephalopathy

- In children with a decreased conscious level, what are the clinical signs of hypertensive encephalopathy?
- In children with a decreased conscious level and hypertension, what investigations screen for or diagnose the causes of hypertensive encephalopathy?
- In children with a decreased conscious level and hypertension, what treatments should be started to reduce morbidity associated with hypertensive encephalopathy?

Prolonged convulsion

- In children with a decreased conscious level, what is the neurological outcome after a prolonged convulsion?
- In children with a decreased conscious level and a prolonged convulsion, what tests screen for or diagnose the underlying treatable causes?
- In children with a decreased conscious level and a prolonged convulsion, what treatment is required to stop the convulsion?
- In children with a decreased conscious level and a prolonged convulsion secondary to hyponatraemia, what treatment is required to stop the convulsion?
- In children with a decreased conscious level and a prolonged convulsion secondary to hypocalcaemia, what treatment is required to stop the convulsion?
- In children with a decreased conscious level and a prolonged convulsion secondary to hypomagnesaemia, what treatment is required to stop the convulsion?

Post convulsion state

- In children after a convulsion, what is the duration of a decreased conscious level (post convulsion state)?
- In children after a convulsion, what tests should be performed to determine the underlying cause of the convulsion?

- In children after a convulsion, what treatment is required?

Alcohol intoxication

- What clinical features determine the presence of alcohol intoxication in a child with a decreased conscious level?
- What investigations/tests should be undertaken in a child with alcohol intoxication and a decreased conscious level?
- What treatment should be undertaken in children with alcohol intoxication?

Cause unclear

- In children with a decreased conscious level and no clinical clues to the cause, what tests should be performed to determine the diagnosis?
- In children with a decreased conscious level and no clinical clues to the cause, what treatments should be started empirically to improve the long term neurological prognosis?

Good practice points

- This subject was based on patient/carer testimonies and Delphi consensus. No evidence searches were undertaken.

4.6. Identifying the evidence

The review questions formed the starting point for systematic reviews of relevant evidence. A total of 71 review questions were searched. All searches were conducted on core databases, MEDLINE, Embase, AMED, Cochrane library and CINAHL. Searches were limited by English language. There was no searching of grey literature, nor was hand searching of journals undertaken.

All searches were updated and re-executed within eight weeks of the start of the stakeholder consultation to ensure the reviews were up-to-date. The search process was completed by 1 September 2014 and no papers published after this date have been considered. All searches were carried out on literature published from 1 January 2004 to 1 September 2014, with exception of the alcohol intoxication questions which were undertaken from 1 January 1990 to 1 September 2014.

4.7. Reviewing and synthesising the evidence

Evidence relating to the review questions was identified by the project manager and literature review working group by title screening and abstract screening papers against review questions' inclusion criteria. Full papers were then obtained. Each paper was reviewed by one reviewer and information extracted. A proportion of papers (8.4%) were reviewed by two reviewers for quality assurance purposes. Full papers were reviewed against pre-specified inclusion and exclusion criteria to identify studies that addressed the review questions in the appropriate population and reported outcomes of interest. Papers were critically appraised using checklists developed by SIGN[135] (RCT, Case Control and Cohort Studies) and key information about the study's population,

methods and results were extracted using a pro-forma. Extracted data was then placed into an evidence table and used by the project manager to develop evidence statements for the GDG to consider and discuss in order to develop recommendations (see the Appendices document).

In line with the RCPCH standards manual for development of clinical Guidelines[136] the type of clinical question determined the highest level of evidence that may be sought. In assessing the quality of the evidence; each study received a quality rating using the Oxford Centre for Evidence-based Medicine – levels of evidence[137].

4.8. Developing and grading recommendations

The GDG and literature review working group were split into groups by topic and meetings were held to discuss the evidence and formulate recommendations (a process referred to as 'interpreting evidence into recommendations').

Recommendations for clinical care were derived and explicitly linked to the evidence that supported them. In the first instance, the project manager developed short clinical evidence statements which were presented to each topic group alongside the evidence tables. Statements summarising the topic group's interpretation of the evidence and any extrapolation from the evidence used when making recommendations were also written to ensure transparency in the decision-making process. The criteria used for interpreting evidence into recommendations can be seen in figure 2.

Figure 2: Criteria for interpreting evidence to recommendations

- **Relative value on the main objective of the clinical question**
- **Consideration of the clinical benefits and harms**
- **Consideration of the net health benefits and resource-use**
- **Quality of evidence**
- **Other considerations**

Recommendations were graded A – D to reflect the strength and applicability of the underlying evidence, with A representing recommendations based on systematic reviews (with homogeneity) of the most robust evidence possible depending upon the type of underlying clinical question (e.g. randomised controlled trials for effectiveness studies) and D representing a recommendation based on consensus, expert opinion, case series or studies with 'troublingly inconsistent or inconclusive' findings[137]. In line with the 2005 Guideline where a recommendation has a number of bullet points with differing levels of evidence supporting the different points, the overall grade for the recommendation reflects the lowest grade of related evidence, with points based on higher evidence levels indicated as such using an asterisk*.

The GDG also identified areas where evidence to answer their review questions was lacking and used this information to formulate recommendations for future research (see the Appendices document).

In areas where the 2005 recommendation was retained the recommendation wording was updated and brought in line with standard NICE guideline wording and the 2015 recommendations.

Note

Due to varying level of evidence, some recommendations can be made with more certainty than others. The strength of evidence behind the recommendations has been reflected in their wording (for further information on this approach refer to the NICE Guidelines Manual[2]).

- 'Consider' has been used to indicate where a recommendation has been based on a Delphi consensus or weak evidence.
- Recommendations are worded more strongly using simply a verb or the word 'should' where there is stronger evidence supporting the recommendation.
- This method of using wording to convey the strength of the evidence underlying a recommendation has been followed throughout the guideline with two exceptions, both of which can be considered best practice. These are:
    - where a recommendation cross-refers to other related guidance, and
    - where the recommendation relates to an issue regarding child safety

  In both these instances straightforward action-based wording is used.

4.9. Delphi process

For areas in the Guideline where there was no substantial evidence found, and the GDG agreed that the 2005 recommendation might need amending as part of the update, a two round Delphi consensus method was used to derive recommendations. This involved the participation of 67 healthcare professionals from specialities including general paediatricians, paediatric neurologists, emergency medicine physicians, paediatric intensive care physicians, metabolic physicians and children's nurses. For details of how Delphi Panel members were recruited see the Appendices document.

Participants rated a series of statements developed by the Delphi working group using a 1-9 Likert scale (1 being strongly disagree, 9 strongly agree), and an option to select 'not in my area'. Delphi statements were based on the 2005 recommendations and amended as appropriate by the Delphi working group. Consensus was defined as 75% of ratings falling in the 1-3 or 7-9 categories. Results and comments from each round were discussed by the working group and final recommendations were made according to predetermined criteria (figure 2). In addition the Delphi panel were given the opportunity to add comments during the survey. These comments were reviewed by the GDG and used to aid decision-making.

The defining rules of the Delphi consensus process were as follows:

- The panel must be multidisciplinary and include at least five representatives from each speciality
- A nine point Likert scale will be used for panellists to provide their responses to statements
- Consensus disagreement will be defined as 75% of panellists who responded selecting 1,2, 3 on the Likert scale
- Consensus agreement will be defined as 75% of panellists who responded selecting 7, 8, 9 on the Likert scale

- Consensus agreement and consensus disagreement was calculated based on the total number of respondents for that round, and includes respondents who did not answer individual statements or who answered 'not in my area'
- There will be no literature sent to participants as any evidence sent out could bias responses
- There will be a minimum of two rounds
- Any recommendations whose underpinning Delphi statements fail to reach consensus will be made explicit in final Guideline and all Delphi voting included in the Guideline appendices

The Delphi panel survey was conducted online with panellists being contacted via email. The Delphi panel voted on a total of 228 statements in round 1. Because this number was so large the first round of the Delphi survey was divided into two parts in an attempt to maximise the response rate. The Delphi panel voting is summarised in Table 2 below:

Table 2: Delphi panel voting

Delphi round	Number of statements	Number of respondents	Response rate
Round 1 part 1	107	63	50.4%
Round 1 part 2	121	67	47.5%
Round 2	70	44	69.8%
Round 2 - sepsis	5	21	17.4%
Round 3	3	44	31.4%

Following round 1 voting any statements that reached consensus (75% or more votes indicating strong disagreement or agreement) were used to form the Guideline recommendations. Where there was no consensus, Delphi panel voting and comments were reviewed by the GDG and statements sent out again for voting in round 2. Statements were revised following round 1 in order to improve clarity or to bring in line with current practice as suggested by Delphi panel comments before sending out for round 2 voting. Due to an error with the sepsis Delphi statements in round 2 leading to a 0% response rate, these statements were sent out again separately. The GDG reviewed the Delphi findings from round 2, accepting as recommendations statements that received consensus. For statements which did not reach consensus the GDG considered the Delphi findings and comments and consensus was agreed within the group. In instances where no consensus could be achieved the GDG felt it was inappropriate to provide a recommendation in this area. Details of Delphi voting and GDG decision-making underpinning consensus recommendations are described for each recommendation under the sub-heading 'Delphi statements' and in the evidence interpretation. Voting for the Delphi statements is given as a percentage of panellists strongly agreeing with the statement (voting 7, 8 or 9).

Two exceptions were agreed to the original list of Delphi rules. For three statements relating to metabolic illness the GDG felt it would be preferable to include guidance if consensus could be reached and so these were sent out as a third round of voting. Also, in round 1 part 2 and round 2 of Delphi voting fewer than five metabolic specialists participated. The GDG agreed to continue with the Delphi process as they felt the Delphi panel remained sufficiently robust to deliver useful consensus for the majority of statements. However, this did disadvantage the Delphi process in the specific areas relating to the treatment of metabolic disorders. A number of statements in this section failed to reach consensus, with a large proportion of panellists responding that they felt unable to vote as this was not their area of expertise. The GDG made recommendations in these

instances referring clinicians to local experts. Full details of Delphi statements and voting are given in the Appendices document.

4.10. Economic evidence

The economic evaluation was removed from the Guideline update, as a cost-effectiveness analysis was beyond the scope of the Guideline. The cost comparison of the incurred marginal costs associated with sending the recommended core investigations would differ regionally throughout the UK.

4.11. Good practice points

Parents, carers and young people were invited to take part in a Delphi consensus survey. The 2005 Guideline included good practice points which were developed using a Delphi process. The GDG felt that it was important to obtain parents, carers and young people's opinions in the update of the good practice point recommendations.

4.12. Guideline consultation details

A stakeholder consultation took place between 27 October and 14 November 2014. During this time stakeholders were given the opportunity to comment on the Guideline. All comments were collated and assigned to GDG members for comment and discussion.

4.13. Parent, carer and patient participation

The Guideline sought to embed involvement from parents, carers and patients from the outset. At every development stage of the Guideline the RCPCH children and young people advocacy team were consulted to consider the ethical and meaningful involvement of young people, parents and carers into the Guideline development. This involved the RCPCH advocacy team attending GDG meetings as well as a lay representative sitting on the GDG.

The views and opinions of parents, carers and young people were sought in the development of the 2015 Guideline outputs.

4.14. Stakeholder involvement

The Guideline sought to involve stakeholders in all stages of the Guideline development. Due to the breadth of the scope, input from a wide variety of specialities was required. The GDG included representation from stakeholders and stakeholders were invited to comment on the draft Guideline scope and draft recommendations. For a full list of stakeholders see the Appendices document.

4.15. Funding

The funding body, the National Reye's Syndrome Foundation UK, did not influence the GDG's decisions or the Guideline recommendations other than through its role as a stakeholder.

5. Implementation of the 2015 Guideline

5.1. Guideline update

It is recommended that this Guideline is updated within the next five years so that clinical recommendations take into account important new information. The evidence should be checked three years after publication, and healthcare professionals and patients views should be sought to assess whether all or part of the guidance requires updating. If important new evidence is published at other times it may be decided that a more rapid update of some recommendations is necessary.

5.2. Editorial independence

All Guideline group and working group members declared all conflicts of interests prior to the Guideline development starting.

5.3. Implementation

The full Guideline will be hosted on the following websites:

- Royal College of Paediatrics and Child Health (Clinical Standards Section)
- The College of Emergency Medicine
- The National Reye's Syndrome Foundation UK
- University of Nottingham

In addition, all confirmed stakeholders will be approached for direct publication on their website, or link to the RCPCH site.

5.4. Implementation advice

To implement this guidance into your practice we suggest that this Guideline is read by healthcare professionals in all Acute Care Settings, as well as Pre-Hospital Providers.

The RCPCH in collaboration with the University of Nottingham are developing the following resources, in addition to the full Guideline, to aid implementation of the guide across the healthcare profession:

- Guideline summary format
- Algorithm for the management of care
- Public and patient resource material

5.5. Resource implications

It is not envisioned these recommendations will have a substantial impact on local resources. The purpose of the recommendations is to aid healthcare professionals in the identification, diagnosis and treatment of children with a decreased conscious level.

It should be noted, where performance of a cranial MRI is recommended, this may necessitate transfer to a tertiary level paediatric centre with the required facilities.

For pathways to specialised services refer to NHS England's Specialised Service Specifications.

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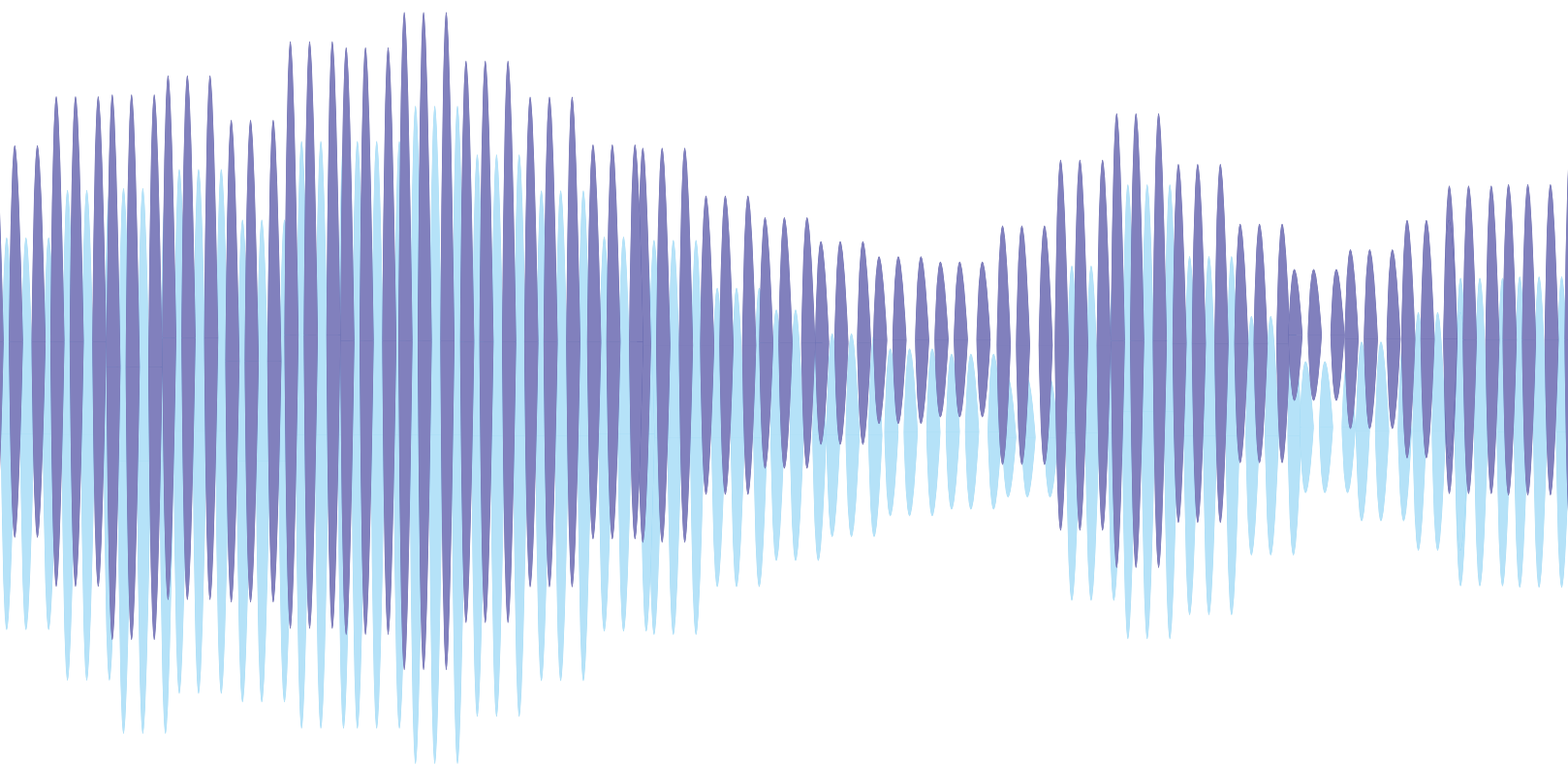

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