HK J Paediatr (new series) 2013;**18**:105-116

Introducing the Guideline on the Management of a Child with a Decreased Conscious Level: A Nationally Developed Evidence-based Guideline for Hospital Practitioners (The Paediatric Accident and Emergency Research Group, The University of Nottingham)

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Abstract A child with decreased conscious level is a challenging medical problem to health care professionals. The present guideline was developed on an evidence based approach. It facilitate doctors in dealing the problem systemically. Easy to follow and detailed algorithms (Appendix A1-A7) were included to streamline the investigations and treatments. Latest literatures after the publication of the guideline were reviewed and no new evidence was found in subsequent reviews to justify any amendment of the original recommendations. Discussions on local adoptation are highlighted in the conclusion of the present paper.

Key words Adolescent; Child; Infant; Practice guideline; Unconsciousness

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Received August 24, 2012

*Guideline reviewed by the Working Group on Guideline and Evidence Based Practice, QA Subcommittee, COC Paediatrics, Hospital Authority, Hong Kong

Background

Children presenting with decreased conscious level can be due to a variety of reasons. It was found that about 30 children out of every 100,000 children per year would present in coma not caused by trauma. The overall mortality in this group of children could be up to 46%.[1] While some causes are obvious, others could be much more obscure. The present evidence-based guideline was developed in 2005 to help front line doctors approach the problem systematically, recognise clinically important problems, investigate and treat them.[2]

The scope of the guideline confines to any child <18 years old, with a Glasgow coma score less than 15 or not being Alert (i.e. responding only to Voice, Pain or being Unresponsive) on the AVPU score.

This guideline should not be applied to preterm infants, children with known cause of their decreased conscious level and children with a chronic abnormal conscious level state.

The guideline mainly targets on the problems that can be identified and treated within the first hours of presenting to a hospital. Specific conditions or diseases which require specific treatment protocols are not covered in detail.

The purposes of our working group in reviewing the original guideline are:

I) To review the methodology of the guideline and the appraisal summary prepared by the Royal College of Paediatrics and Child Health, UK.[3]

II) To review latest literature after the guideline was published in 2005 and to see if any major changes are required.

III) To assess the applicability of the guideline to the local Hospital Authority hospitals.

I) Introduction to Methodology of the Original Guideline

The guideline was produced by the University of Nottingham, Paediatric Accident and Emergency Research Group which included medical and nursing professionals from paediatric emergency medicine, paediatric intensive care, metabolic medicine, neurology, general paediatrics, clinical chemistry, patient and lay representatives plus input from other stakeholder subspecialty societies or associations.

Literature was electronically and hand searched between March 2004 and July 2005 for a list of clinically relevant questions drawn up according to the scope and targeted clinical conditions the guideline aimed to answer. Papers selected were then appraised on methodological quality using critical appraisal checklist developed by the Scottish Intercollegiate Guideline Network[4] and were given level of evidence according to the criteria developed by the Oxford Centre for Evidence-based Medicine.[5]

Papers which contributed to grade A and B recommendations were appraised by second member of the Guideline Development Group to ensure validity of the appraisal methodology.

When there was no published evidence found, a consensus approach was adopted. The guideline group utilised a large multi-professional Delphi panel for the Delphi Consensus process which enabled members of the panel to have their opinions registered anonymously, analysed, and then fed back to the same panel for further consideration. The whole panel results were reviewed. The group would help members to reconsider their initial position and panel members were at liberty to change their original opinion or their initial position. Consensus was aimed to achieve after one, two or three rounds of the Delphi panel discussion.[6,7] The guideline recommendation and good practice points were thus based on agreement using evidence tables or the Delphi consensus results. Disagreement on wordings was settled by discussion or consultation with stakeholder groups.

The draft guideline was then reviewed by all stakeholder groups, followed by an open forum discussion before it was finalised.

Formal appraisal process for the guideline were then performed by the Royal College of Pediatrics and Child Health and the British Association for Accident and Emergency Medicine in November 2005 using the AGREE instrument[8] to assess the methodology quality followed by independent reviewers to examine the original research papers deriving the grade A and B recommendations in the guideline. Only minor regrading of the recommendation levels was made.[3] An algorithm for the patient management was prepared (Appendix A1-A7).[9]

II) Review of the Latest Literature After the Guideline was Published in 2005

The guideline was originally planned to be reviewed 2 years after being published. Our working group thus initiated a simplified but systematic literature search for the latest evidence in the year 2005 and after.

Papers were searched electronically via the Hospital Authority eKG platform using database: Embase, Medline, and all All EBM Reviews – Cochrane DSR, ACP Journal Club, DARE, CCTR, CMR, HTA, and NHSEED and employing keywords: altered consciousness or consciousness disorder and the disease or clinical condition categories of the original guideline.[2] Search was done around May 2009 for review articles and with patient age less than 18 year old and later search was repeated in early November 2009 to include additional keywords: meta analysis, systematic review, unconsciousness, transient loss of consciousness, coma, stupor, drowsiness, obtundation and delirium. Additional searches were done in 2010 on selected topics, especially on those with no Delphi consensus reached in the original guideline (investigation of borderline hypoglycaemia and management of raised intracranial pressure – fluid regime, use of mannitol or hypertonic saline and indication of invasive monitoring device)

After the searches, systematic reviews or evidence based guidelines were identified on the topics of herpes simplex encephalitis,[10] bacterial meningitis[11-16] and meta analysis from Cochrane Database and Systemic Review on use of steroid in tuberculosis meningitis[17,18] and use of mannitol for acute traumatic brain injury.[19]

a) Herpes simplex encephalitis – A review article by De Tiege et al was published in 2008.[10] The content of the review was in line with the recommendations made by the Guideline on Herpes simplex encephalitis.
b) Bacterial meningitis – The source articles of the review published in 2009 by Prasad et al[11] concerning the use of corticosteroid were already included in the reference list of the original guideline. Another meta-analysis of individual patient data extracted from recent randomised, double-blind, placebo-controlled trials was published in March 2010.[12] Though adjunctive dexamethasone treatment does not seem to significantly reduce death, dexamethasone seemed to reduce hearing loss among survivors.[12,13] This is line with the finding of another meta-analysis[14] and the latest review from the Cochrane collaboration review finding that corticosteroid dexamethasone leads to a reduction in hearing loss.[15] The recent NICE guideline[16] also confirmed the beneficial effect of early (before or with the first dose antibiotics) steroid treatment on long term neurological sequelae. The beneficial effect on reducing severe hearing loss can also be observed when steroid is given shortly after the first dose of antibiotics (5 RCTs involving 501 children, RR 0.29, 95% CI 0.14 to 0.63, p = 0.002). A steroid regime was thus proposed in the NICE guideline for patients older than 3 months old with high likelihood of bacterial meningitis.
c) Use of steroid in tuberculous meningitis – The original guideline does not cover the treatment of the tuberculous meningitis. In a systematic review by Prasad et al[17] involving seven trials, 1140 participants (including 411 deaths) with all having used dexamethasone or prednisolone, corticosteroids reduced the risk of death (RR 0.78, 95% CI 0.67 to 0.91). Data on disabling residual neurological deficit from three trials showed that corticosteroids reduce the risk of death or disabling residual neurological deficit (RR 0.82, 95% CI 0.70 to 0.97). Hence, corticosteroids are recommended in HIV-negative people with tuberculous meningitis to reduce death and disabling residual neurological deficit. The use of steroid with concomitant anti-tuberculous treatment is included in the NICE guideline.[18]
d) Use of mannitol for acute traumatic brain injury – In the review by Wakai and Robert,[19] four trials published in 1984 to 2003 were reviewed but there was no articles included after the present guideline was published. Thus there is no new reliable evidence to make recommendations on the use of mannitol in the management of patients with traumatic brain injury. During the literature search, latest articles possibly related to guideline grade A or B recommendations were then appraised on their methodological quality similar to the approach as stipulated in the original guideline and discussed in the Working group meetings. After rounds of discussions, it was finally concluded that there are no new evidence to justify any amendment of the original grade A and B recommendations of the guideline.

III) The Applicability of the Guideline to the Local Hospital Authority Hospitals

Our working group acknowledges that certain recommendations of the original guideline may need local modifications or considerations.

a) Core laboratory investigations for metabolic causes of reduced conscious level and hypoglycaemia in children with no other clear explanation.[20]
   - Local surveys were done covering all Hospital Authority paediatric departments with emergency admissions. All the core investigations are available within their own cluster hospitals. However, some of the investigations for hypoglycaemia are not available locally, like plasma insulin, growth hormone, free fatty acid, plasma beta-hydroxybutyrate, acyl-carnitine profile and urine organic acid. After some follow up arrangements, they can now be accessed through the two university hospitals (Prince of Wales and Queen Mary Hospitals) or through Princess Margaret and Queen Elizabeth Hospitals.

b) Service arrangements like timing of consultation of experienced paediatrician, paediatric subspecialist or specialist of other discipline.
   - While recruiting subspecialist or experts in other fields early in the patient care process is the trend, our working group found these service arrangement recommendation being beyond the scope of our working group review. Differences in medical systems and variations in the settings and organisations of individual hospitals may imply some local adaptation being required before adoption of these recommendations.

c) Conditions identified in the guideline requiring management protocol agreed at a local level.
   - Specific conditions like the management of raised intracranial pressure are recommended to have local guidelines. On the other hand, though the guideline recommends the NICE guideline for the management of diabetes ketoacidosis, it is envisaged that there could also be minor variation among local departments in fine tuning the management of the diabetes ketoacidosis patients.

d) Peri-arrest arrangement or investigations taken at post mortem.
   - The original guideline has grade D recommendations on certain tests to be performed based on grade 5 evidence (expert opinions). While these are useful references, it is worth noting that Hospital Authority has also issued a Guidance note on Perimortem / Postmortem Specimen Collection for Paediatric Patients suspected of unknown infectious diseases in July 2009.[21] In the local guidance notes, tests for toxicology and inborn errors of metabolism are also included. Individual hospitals are advised to review the local guidance note and to liaise with the local pathology department accordingly.

Overall Guideline Review Summary

The present guideline together with the appraisal summary from Royal College of Paediatrics and Child Health and British Association for Emergency Medicine provide concise information and an easy to follow algorithm based on available evidence and consensus of a large representative group of different disciplines. Though the guideline was due for revision in 2007, we could not find new evidence (focused systematic search up to 2009) to justify any amendment of the grade A and B recommendation of the guideline. Additional evidences were noted on the use of steroid in tuberculous meningitis and meningitis likely of bacterial origin. Laboratory investigations for unclear causes of altered conscious are now streamlined in all Hospital Authority paediatric departments after local surveys and follow up actions. Recently, some has advocated including the investigation of poisoning, especially on carbon monoxide poisoning in the use of the guideline[22] Individual departments are encouraged to explore and consolidate the consultation mechanism of subspecialists and the peri-arrest arrangement of investigations in their local setting if required.

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Appendix

(A1-A7) Algorithm. The management of a child (aged 0-18 years) with a decreased conscious level (http://www.nottingham.ac.uk/paediatric-guideline/Guideline%20algorithm.pdf (With kind permission from Dr Richard Bowker, lead author of the Paediatric Accident and Emergency Research Group which developed the guideline and algorithm).

Appendix A1 Guideline for the management of a child aged 0-18 years with a decreased conscious level.

Explanatory notes
Recommendations marked with the symbol Ⓐ or Ⓑ are based on the highest quality of evidence

Entry criteria
The following algorithm should be used for children aged 0 – 18 years who present to hospital with a reduced level of consciousness. This is defined as scoring <15 on the Glasgow Coma Scale (GCS) modified for children or responding only to voice, pain or being unresponsive on the AVPU scale. Ensure the child is maximally roused from sleep before recording conscious level.

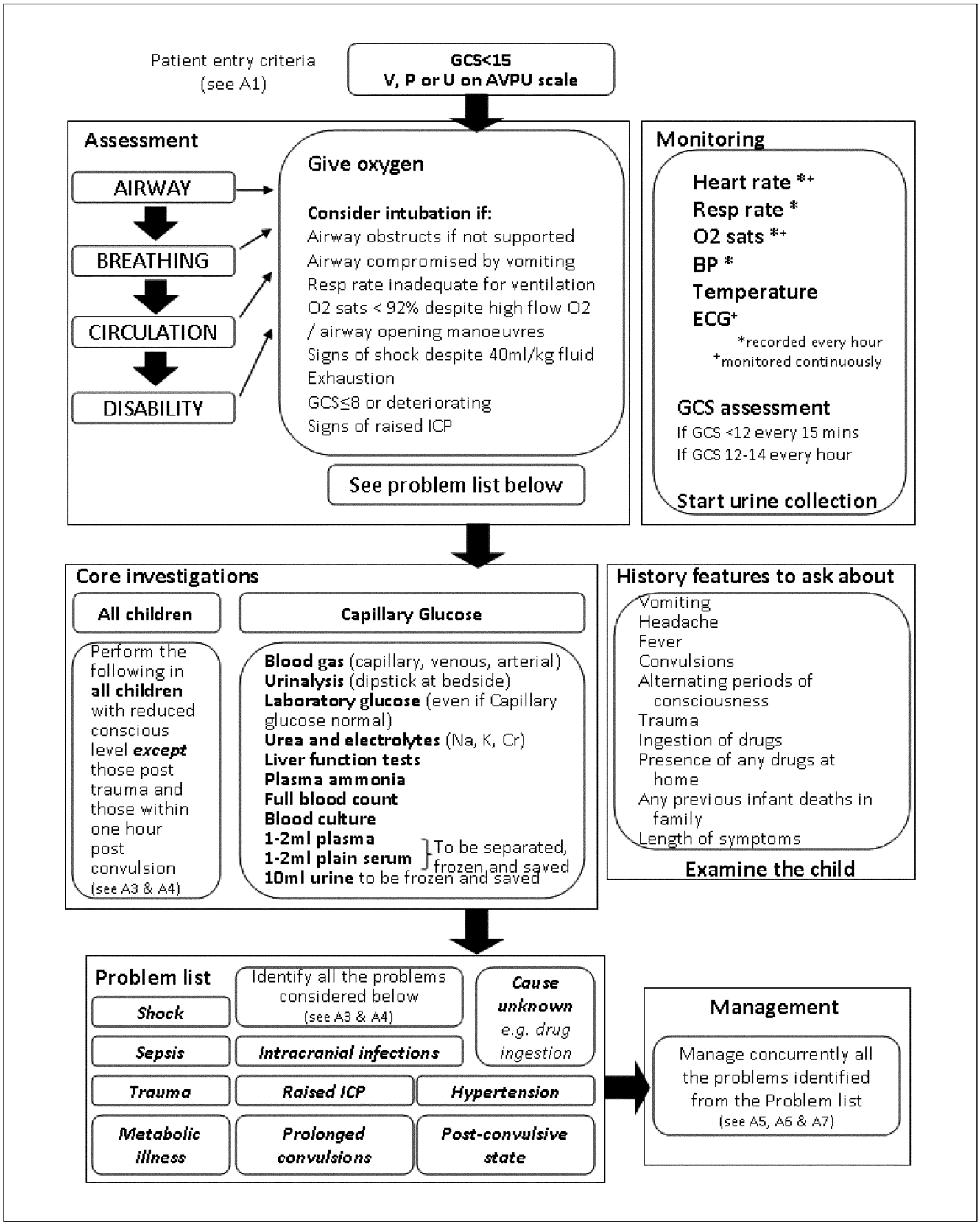
Exclusion criteria
Infants on a neonatal intensive care unit.
Children with a known condition for episodes of reduced conscious level (e.g. epilepsy, diabetes) where a management plan is already agreed upon.
Children with learning disabilities, whose score on the GCS is < 15 when they are healthy.

In certain children with reduced conscious level, it may be appropriate to watch and wait. However, if a decision is made to stick a needle into a child to investigate the cause, take all the samples listed as "core investigations" at the first opportunity.

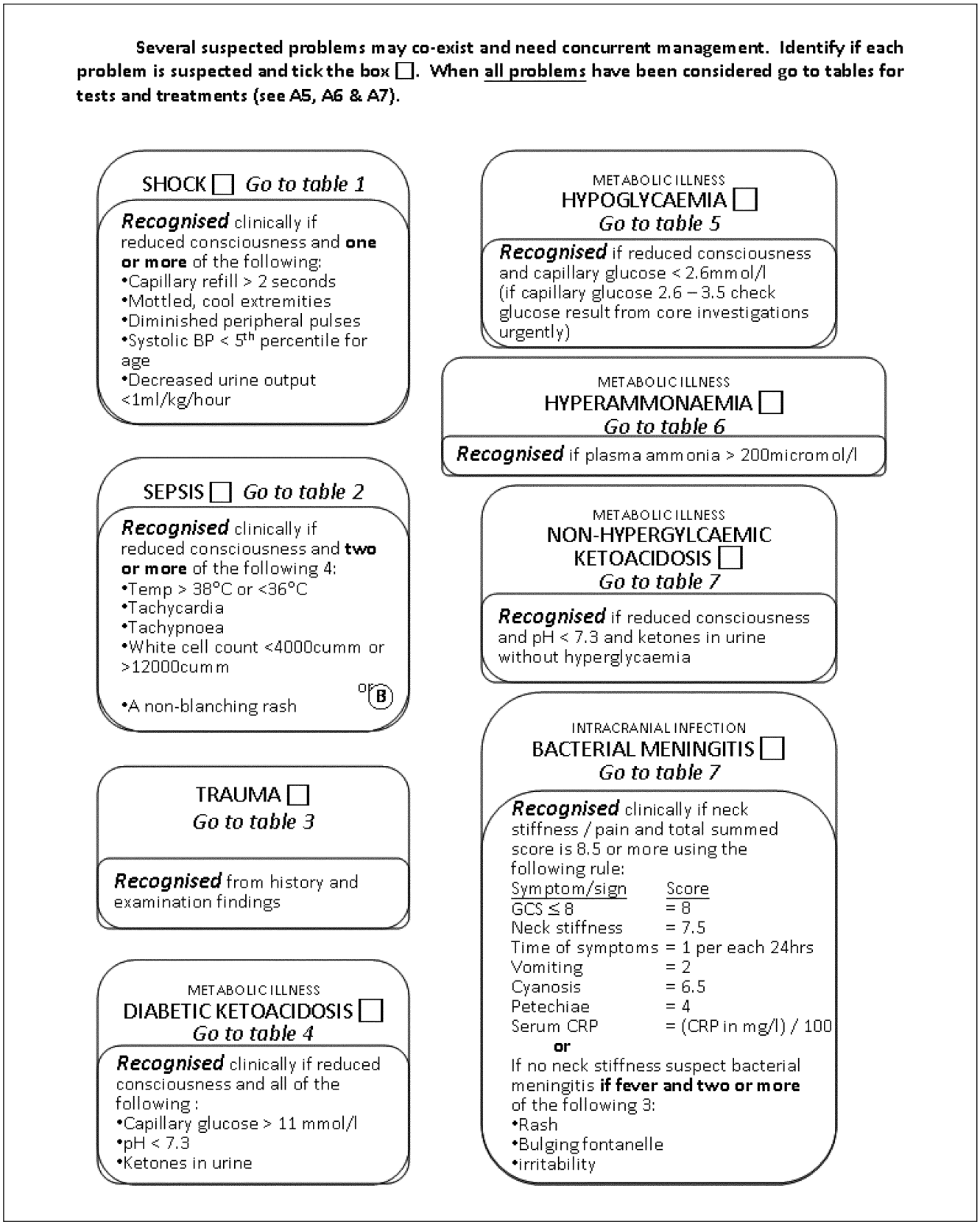
Glasgow coma scale with modification for children			
Best eye response			
1.	No eye opening		
2.	Eye opening to pain		
3.	Eye opening to verbal command		
4.	Eyes open spontaneously		
Best verbal response (use one of the following)			
	Adult version (aged 5+)	***Children's modification***	***Grimace response for preverbal or intubated patients***
1.	No verbal response	No vocal response	No response to pain
2.	Incomprehensible sounds	Occasionally whimpers and/or moans	Mild grimace to pain
3.	Inappropriate words	Cries inappropriately	Vigorous grimace to pain
4.	Confused	Less than usual ability and/or spontaneous irritable cry	Less than usual spontaneous ability or only response to touch stimuli
5.	Orientated	Alerted, babbles, coos, words or sentences to usual ability	Spontaneous normal facial / oromotor activity
Best motor response			
1.	No motor response to pain		
2.	Abnormal extension to pain		
3.	Abnormal flexion to pain		
4.	Withdrawal to painful stimuli		
5.	Localises to painful stimuli or withdraws to touch		
6.	Obeys commands or performs normal spontaneous movements		

AVPU Scale Record the condition which best describes the patient
Alert Responds to Voice Responds to Pain Unresponsive

Appendix A2 Algorithm for the management of a child aged 0-18 years with a decreased conscious level.



Appendix A3 Indentify all problems.



Appendix A4 Indentify all problems (continued from A3).

Several suspected problems may co-exist and need concurrent management. Identify if each problem is suspected and tick the box ☐. When all problems have been considered go to tables for tests and treatments (see A5, A6 & A7).

INTRACRANIAL INFECTION
HERPES SIMPLEX ENCEPHALITIS (HSE) ☐
Go to table 9

Recognised clinically if reduced consciousness and **one or more** of the following:
- Focal neurological signs
- Fluctuating GCS > 6 hours
- The child has or has been in contact with herpetic lesions

INTRACRANIAL INFECTION
ABSCESS ☐
Go to table 10

Recognised clinically if reduced consciousness level and focal neurological signs +/- signs of infection and / or signs of raised ICP

INTRACRANIAL INFECTION
TB MENINGITIS ☐
Go to table 11

Recognised clinically if reduced consciousness and signs of meningitis and / or contact with pulmonary TB

RAISED ICP ☐
Go to table 12

Recognised clinically if **papilloedema** or **two or more** of the following 5:
- Reduced consciousness (U on AVPU or GCS ≤ 8)
- Abnormal pattern of respiration
- Abnormal pupils
- Abnormal posture
- Abnormal doll's eye / caloric response

HYPERTENSION ☐
Go to table 13

Recognised if systolic BP > 95th centile for age on two separate readings

PROLONGED CONVULSION ☐
Go to table 14

Recognised clinically if convulsion lasts > 10 minutes

POST-CONVULSIVE STATE ☐
Go to table 15

Recognised clinically if reduced conscious level within one hour post convulsion **and** a normal capillary glucose

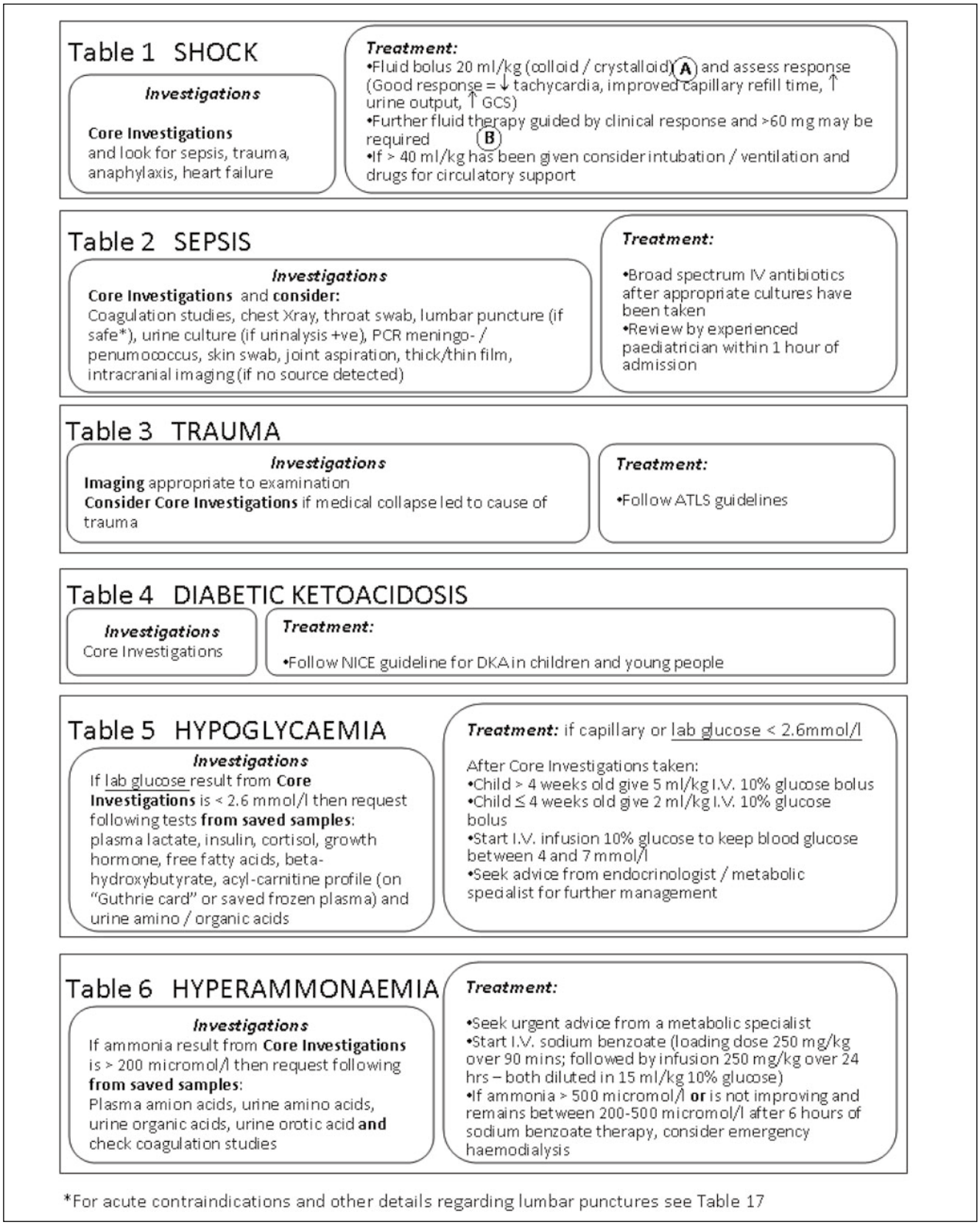
CAUSE UNKNOWN ☐
Go to table 16

No clinical clues to the cause after core investigations reviewed, consider drug ingestion, non-convulsive status, metabolic encephalopathy not presenting with hyperglycaemia / hypoglycaemia / hyperammonaemia / non-hyperglycaemic ketoacidosis, other infectious agents, inflammatory conditions – see Table 16

Have you identified all the suspected problems?

Only move on to the tables for further tests and treatments (A5, A6 & A7) when ALL PROBLEMS have been considered.

Appendix A5 Management of all 16 identified problems.



Appendix A6 Management of all 16 indentified problems (continued from A5).

Table 7 NON-HYPERGLYCAEMIC KETOACIDOSIS

Investigations	*Treatment:*
If pH< 7.3, ketones in urine and a normal or low capillary glucose noted from Core Investigations then request following from saved samples: Plasma lactate, plasma amino acids, urine amino acids, urine organic acids	•Seek urgent advice from a metabolic specialists if child has non-hyperglycaemic ketoacidosis or plasma lactate > 15 mmol/l •Carefully monitor fluid balance due to risk of raised ICP •Nutrition should be re-started early to prevent catabolism

Table 8 BACTERIAL MENINGITIS

Investigations	*Treatment:*
Core Investigations and lumbar puncture (if safe*)	•Give I.V. dexamethasone 0.15 mg/kg before / with antibiotics (A) •Broad spectrum antibiotics (A) - Don't delay if lumbar puncture contraindicated*

Table 9 HERPEX SIMPLEX ENCEPHALITIS (HSE)

Investigations	*Treatment:*
Core Investigations and **consider** : MRI scan, EEG, lumbar puncture (if safe*) for HSV PCR (A)	•Give I.V. aciclovir 10 mg/kg (or 500 mg/m2 if aged 3 months to 12 years) TDS (A) - Don't delay if lumbar puncture contraindicated* •Treatment should continue for 14 days if HSE highly suspected •If no ongoing clinical suspicion of HSE aciclovir can be stopped before 14 days

Table 10 INTRACRANIAL ABSCESS

Investigations	*Treatment:*
Core Investigations and **CT SCAN**	•Broad spectrum antibiotics after blood cultures taken •Seek urgent advice from a paediatric neurosurgeon

Table 11 TB MENINGITIS

Investigations	*Treatment:*
Core Investigations and **lumbar puncture** (if safe*) (B)	•If CSF microscopy is abnormal seek urgent advice from microbiology department

Table 12 RAISED ICP

Investigations	*Treatment:*
Core Investigations and **consider CT scan** (A)	•Position patient's head in midline •Tilt patient head-up 20 degrees and avoid neck lines •Maintenance fluids should not be hypotonic (B) •Rate of maintenance fluids to be agreed locally •Consider intubation and maintain $PaCO_2$ between 4.0 – 4.5 kPa •Mannitol or 3% saline indications and dose to be agreed locally

Table 13 HYPERTENSION

Investigations	*Treatment:*
Core Investigations especially reviewing urinalysis, creatinine and urea, look for raised ICP, papilloedema, and check four limb BP	•Seek urgent advice from a paediatric nephrologist or intensivist

*For acute contraindications and other details regarding lumbar punctures see Table 17

Appendix A7 Management of all 16 indentified problems (continued from A5 & A6).

Table 14 PROLONGED CONVULSION

Investigations

Core Investigations if child not known to have epilepsy

If child under 12 months old request plasma calcium and magnesium (B)

Treatment:

- Follow APLS guidelines for anticonvulsant therapy
- If the **convulsion is ongoing** despite anticonvulsants, consider specific treatments or electrolyte imbalance, e.g.
- Plasma sodium < 115 mmol/l, give 5 ml/kg of 3% saline I.V. over one hour
- Plasma calcium is < 1.7 mmol/l or ionized calcium < 0.75 mmol/l, give 0.3 ml/kg of 10% calcium gluconate I.V. over 5 mins
- Plasma magnesium < 0.65 mmol/l, give 50 mg/kg of magnesium sulphate I.V. over one hour

Table 15 POST CONVULSIVE STATE

Investigations

- It may be appropriate to closely observe the child if normal capillary glucose, without performing any further tests, in the first hour
- Detailed history and exam
  If still reduced GCS after one hour perform **Core Investigations** and investigations for "**Cause unknown**" (Table 16)

Treatment:

- Treat according to history and examination findings
- If after 1 hour child has not recovered to their normal conscious level, treat as "**Cause unknown**" (Table 16)

Table 16 CAUSE UNKNOWN

Investigations

- Core Investigations and if after reviewing these results the cause of reduced consciousness remains unknown request / perform the following: **CT scan, lumbar puncture** (if safe*), **urine toxicology screen, urine organic and amino acids, plasma lactate**

If the cause is still unknown after reviewing Core Investigations results, CT scan and initial CSF results, consider the following: EEG (? Non-convulsive status); acyl-carnitine (on Guthrie card or from saved plasma); ESR and autoimmune screen (? Cerebral vasculitis); thyroid function test and thyroid autoantibodies (? Hashimoto's encephalitis)

Treatment:

- Support treatments to protect airway, breathing and circulation
- Start broad spectrum antibiotics and I.V. aciclovir
- Discuss with paediatric neurologist within 6 hours of admission

*For acute contraindications and other details regarding lumbar punctures see Table 17

Table 17 LUMBAR PUNCTURE

A lumbar puncture should be deferred or not performed as part of the initial acute management in a child who has:

- GCS ≤ 8
- Deteriorating GCS
- Focal neurological signs
- Had a seizure lasting more than 10 mins and still has a GCS ≤12
- Abnormal breathing pattern
- Abnormal doll's eye response
- Abnormal posture
- Shock
- Bradycardia (heart rate < 60)
- Hypertension (BP > 95th centile for age)
- Clinical evidence of systemic meningococcal disease
- Pupillary dilatation (unilateral / bilateral)
- Pupillary reaction to light impaired or lost
- Signs of raised ICP

A normal CT scan does not exclude acutely raised ICP (A)

If a lumbar puncture is performed, CSF should be sent for **microscopy** (B), **gram staining, culture and sensitivity, glucose** (B), **protein, PCR for HSE** (B) **and other virus**