Meningitis Research Foundation

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Lessons from research for doctors in training

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Recognition and early management of meningococcal disease in children and young people

Edition 4

This handbook uses individual case histories as a basis for group discussions and learning. The clinical management points are based on "Management of Meningococcal Disease in Children and Young People" (see inside back cover) incorporating the NICE Guideline Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management CG102.

Contents

Section 1 Introduction

The *Lessons from research for doctors in training* handbook and associated algorithms have continuously been revised to incorporate updates to guidelines and practice, in particular the NICE Guideline 'Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management' CG102[1], which was last updated in February 2015.

This fourth edition continues to focus on the early recognition and management of meningococcal disease in children and young people up to 16 years of age. The algorithms 'Management of Bacterial Meningitis in Children and Young People' (edition 2A) and 'Management of Meningococcal Disease in Children and Young People' (edition 8A) agree in every particular with the NICE guidelines, and provide more 'How to' detail for busy doctors, including drugs and dosages for intubation, administration of inotropes, and managing raised intracranial pressure. Both of these algorithms can be found at the end of this handbook in Section 7.

Sepsis will be replacing the term septicaemia in our health professional resources in order to align with recommendations from national health bodies.

Meningococcal disease (MD) remains an important cause of mortality in children in the UK, and meningitis and septicaemia continue to be perceived by parents in England as the most serious vaccine-preventable diseases[2,3]. Despite a decrease in the number of cases of MD due to vaccination, early detection and management are still crucial in reducing case-fatality; improvements in initial management of patients with MD led to a 21% reduction in case-fatality rate from 1992 to 1997[4]. Additionally, two UK studies found that aggressive treatment of severe cases of MD can lead to an improvement in outcome[4,5].

Research by the Royal College of Paediatrics and Child Health (RCPCH) and the meningococcal group at St Mary's Hospital in London evaluated health care delivery for almost 500 children with MD. This study was funded by Meningitis Research Foundation (MRF), and has been the basis for the development of this handbook. The study, titled 'The role of healthcare delivery in the outcome of MD in children: case-control study of fatal and non-fatal cases', was published in the British Medical Journal in June 2005[6]. Multivariate analysis revealed three specific management failures were independently associated with an increased risk of death. These were 1) children being managed by unsupervised junior doctors, 2) children being managed by non-paediatric trained staff, and 3) a failure to use enough inotropes in septic patients (this is a marker of aggressive management).

During this study it was also seen that a few clinical errors repeatedly led to delayed or inadequate treatment of cases with MD. Complications of MD such as shock or raised intracranial pressure were often not recognised when they were present. There was also frequently a failure to appreciate how ill children were. Management of cases was often not aggressive enough given the severity of the illness and did not follow the original algorithm 'Early Management of Meningococcal Disease' which was first published in Archives of Disease in Childhood in 1999[7], with subsequent editions in that journal in 2003[8] and 2007[9].

The symptoms displayed by the children in the study prior to their admission to hospital have also been analysed and published[10]. These data shed light on the symptoms of meningococcal sepsis, which are presented in this booklet in the section *Development of Symptoms* and should make doctors aware of the importance of early signs of sepsis and help them to make an earlier diagnosis.

The importance of this research lies not only in its relevance to the correct management of MD, but also in that the complications of MD, shock and raised intracranial pressure, are also seen in other life-threatening conditions, so it is extremely important for doctors in training to be aware of the early signs as prompt action saves lives.

The aims of this handbook are:

- To use clinical examples to teach about the signs of sepsis and meningitis
- To clarify the important differences between meningococcal meningitis and sepsis
- To outline the basic management of meningococcal sepsis and meningitis in line with the algorithms
- To describe the clinical pathophysiology of meningococcal disease.

The Clinical Case Histories section of this handbook presents cases of MD from the study, which illustrate how the early signs of MD can be missed, and critical points in managing a case where lack of information (i.e. not measuring or monitoring vital signs), or not acting appropriately on the information available can adversely affect the outcome of the case. Each case illustrates a different learning point, and examples are taken from a range of settings to accurately reflect where children presenting with this disease were looked after. Not all children were managed by paediatricians. Some details have been changed in order to preserve the anonymity of children and doctors without obscuring the clinical teaching points these cases bring to light.

On the first page of each case study, the history is recounted in the left-hand column, accompanied by questions in the middle column to guide your learning and reflection. The third column gives references to relevant sections in the handbook to test your knowledge and understanding. On the reverse of each case history is the outcome for the patient and a series of discussion and learning points. We hope that these will guide individual learners and group discussions in a clinical context. The reader is also encouraged to consult the many review articles on the subject for a more in-depth understanding of pathophysiology and management of MD.

Much of the material covered in this handbook has also been developed into the interactive e-learning tool, *Bacterial Meningitis and Meningococcal Septicaemia in Children*, accessible from the RCPCH website www.rcpch.ac.uk/e-learning.

Case 1

Case history

Child of 5 years attends Emergency Department with sudden onset fever and painful right hand.

ED triage assessment:
1)? Injury soft tissue 2) unwell, pyrexia.
Sudden onset pain in right hand. No history of trauma, she is reluctant to have it touched. She is also generally unwell. Spots erupting on arm and back. Last had Calpol 2.5 hours ago.

Observation taken: temp 39.9

2 hours later - ED doctor's assessment:
Presenting complaint: right hand swollen and painful, hand painful for 4 hours, no history of trauma. Was in contact with chickenpox 5 days ago.

On examination: temp 40.1 (55 minutes after Calpol and Brufen). Small blanching spots on body. ENT / ABDO clear. No photophobia.

Diagnosis: probable early chickenpox. Child sent home with antipyretics.

Questions

What do you think of this assessment?

Is there anything else you would want to know?

Were there abnormal symptoms or signs?

Was this a timely assessment?

What do you think of the history taking?

What do you think of this examination?

What is your differential diagnosis?

Look it up

See page 48 – 'The following clinical signs must be measured and recorded to complete a full assessment'

See pages 44-45 – Symptoms of Sepsis

See pages 44-46 – Taking a History

See pages 46-56 – Examining the Patient

See page 60 – Making a provisional diagnosis

Case 1 Outcome

The child died 12 hours later of meningococcal sepsis

Discussion

ED triage assessment:

A full set of vital signs should have been measured and recorded at triage. The child may have had signs of circulatory compromise: tachycardia, tachypnoea, poor capillary refill, inadequate oxygen saturations.

No description of the spots was made, which is inadequate.

At triage, some symptoms were already abnormal, namely high fever, general unwellness, severe limb pain and new rash.

ED doctor assessment:

There was a 2 hour time delay between triage and SHO assessment. Had serial observations been done during this time, the disease trajectory may have been more obvious, and the clinician would have had more clinical information upon which to make a diagnosis.

This was an inadequate assessment:

- Full history not taken to seek explanation of painful hand.
- Lack of response to antipyretics not taken seriously.
- Two hours since child first seen, vital signs (HR, RR, BP) had still not been measured, and there had been no assessment of peripheral perfusion, O_2 sats, conscious level or pupil size / reaction.

The girl had been in contact with chickenpox 5 days previously. Chickenpox incubation period is 10-21 days so this is an extremely unlikely diagnosis.

Although limb pain is well-established as a symptom of meningococcal sepsis, the differential diagnosis includes osteomyelitis or septic arthritis.

It was too early in the disease process to specifically diagnose MD while the child was in the Emergency Department (ED). However there was sufficient cause for concern, namely an unremitting fever, a new rash, general malaise and a potential focus of infection. This child should undoubtedly have been referred to the paediatricians.

Learning points

- Measure and record vital signs.
- All febrile children must be fully assessed however well they look.
- Don't forget the less well-known symptoms such as limb pain.
- Beware 'red herrings'.
- The early rash of MD can be blanching in 30% of cases.
- Photophobia may be absent in a young child with meningitis and is not seen in pure sepsis.

Conclusion

This case history illustrates how an inadequate assessment of a child allowed a serious illness to be missed.

Case 2

Case history

Child 3 years old with short history of fever, shaking and generally unwell.

ED triage assessment:
High temperature, he looks flushed, no rash, unwell child.

Ten minutes later – ED SHO:
Febrile child, listless, irritable and drowsy.
Temp 39.7, HR 170, RR 55.
Pyrexial and drowsy: ? cause, refer to paediatric team.

Two hours later: admitted to paediatric ward.

Nursing assessment: Temp 38.4, HR 172, RR 45, BP 112/50.
Small pin prick rash on abdomen.

Ward SHO reviewed child
Sleepy but rousable, no neck stiffness or photophobia, HR 171.
No rash but few old chickenpox scars.
Chest clear.

Diagnosis: viral URTI. Child sent home.

Questions

What are the normal ranges for these vital signs? Are there any other observations you would record?

What do you think of the timing of this admission?

What do these signs tell you?

What do you think of this assessment?

Is there anything else you would want to know?

What do you think of this diagnosis? Was the appropriate action taken?

Look it up

See page 48 – Normal Values of Vital Signs Table
See pages 46-48 – Initial Assessment of Any Febrile Child

See page 49 – Clinical Signs of Septic Shock
See pages 51-56 – The Rash

See pages 46-56 – Examining the Patient
See pages 56-57 – Initial Laboratory Assessment

See page 62 – Does your diagnosis make sense?

Case 2 Outcome

The child re-presented 12 hours later in uncompensated shock, with a widespread rash and died despite full resuscitation.

Discussion

Triage assessment:
Appropriate in that this boy was given high priority to see the doctor.

ED SHO assessment:
Abnormal vital signs were noted and need to refer to paediatricians identified. However, a full assessment would have included saturation monitoring, capillary refill time (CRT), blood pressure and assessment of pupil size and reaction.

Long delay between ED and paediatric ward not explained in clinical notes. Such delays are totally unacceptable. If you assess a sick child and decide they need further assessment, it is your responsibility to ensure this happens speedily.

Paediatric ward triage assessment:
The vital signs on admission remained abnormal 2 hours after they were first recorded, indicating a problem. This is what early shock with cardio-vascular compensation looks like.

Although temperature dropped slightly, the child was still tachycardic, tachypnoeic. Drop in temperature not necessarily inconsistent with serious bacterial infection.

Paediatric SHO assessment:
A new pinprick rash was documented on the ward but was not taken seriously.

Totally inadequate assessment. Still no assessment of peripheral perfusion. This doctor was looking for meningitis and missed the early signs of sepsis.

At this stage full laboratory investigations should have been done.

To confirm presence of shock, base excess (venous blood gas) should have been measured and urine output monitored.

Diagnosis:
Very little evidence to support a diagnosis of viral URTI. Child was feverish and lethargic, but chest was clear, and no record of mucus, cough, sore throat, otitis media.

Learning points

- Children with sepsis often have rigors.
- Children in early stages of sepsis may look reasonably well and remain relatively alert.
- If you assess a sick child and decide they need further assessment, it is your responsibility to ensure this happens speedily.
- Isolated pinprick spots may appear where the rash is mainly maculopapular so it is important to search the whole body for small petechiae, especially in a febrile child with no focal cause. The early rash in MD can be very diverse in appearance.
- The septic rash does not necessarily develop at the same rate as the sepsis. Always examine the child for the clinical signs of shock.
- If an experienced nurse is concerned about a child then you should be too. Take note.
- Children with signs of shock require assessment by a senior paediatrician.
- Neck stiffness and photophobia are uncommon in a young child even if they have meningitis and their absence should not be reassuring.

Conclusion

In this case history, some clinical assessment was made. But the significance of the persistently abnormal vital signs was not understood and therefore not acted on. The doctor was confusing meningitis and sepsis: looked for neck stiffness and photophobia, and finding no signs of meningitis, dismissed signs of sepsis.

Case 3

Case history

2.5 year old boy admitted with purpura and fever.

Paediatric assessment:
Temp 39.3, Pulse 134, RR 40, CRT 6 seconds, BP unrecordable, femoral pulses present but weak.
Cyanosed, saturation 75% in air. Widespread creps.
GCS 9/15, Neck stiffness+

Purpuric rash on chest.

Bloods sent for FBC, clotting, U&E, and culture.

Diagnosis: Meningococcal meningitis.

Treatment: Antibiotics intravenously.
Fluids 40 ml/kg colloid in 2 boluses and 10 ml/kg crystalloid over 1 hour, then maintenance fluids.

Some improvement of CRT so left on the ward.

Two hours after admission:
P178, BP 112/60 RR 46.
Increasing rash, drowsy, some response to parents.
No urine output.
Results:
WCC 3.2, INR 2.2, Hb 9.5, Pl 60.
Na 132, K 3.0, Urea 8.3, Creatinine 100
Chest X-ray shows pulmonary oedema.
Frusemide given and fluids slowed down. The child has had a total of 80 ml/kg by now.

SHO review: very fast tachycardia, ? need blood gas, ? needs LP.

Six hours after admission:
HR 194, not recognising parents. Doctor reviewed child, advised that mannitol infusion be considered if further decrease CNS.

Questions

How would you interpret these signs?

What is the normal value for oxygen saturation in air?
What does purpuric rash suggest?

What do you think of these investigations?
Is there anything else you would want to know?

Meningitis or sepsis?

What do you think of the treatment given?

What would you do now?

What is this child's prognosis?

Why has pulmonary oedema developed?
How would you manage it?

What do you think of this treatment?

Is there any contraindication to a lumbar puncture in this child?

Why is this child confused?
Why is mannitol inappropriate in this situation?

Look it up

See page 48 – Normal Values of Vital Signs Table
See pages 46-48 – Initial Assessment of Any Febrile Child
See page 46 – All febrile children with haemorrhagic rashes must be taken very seriously
See pages 56-57 – Initial Laboratory Assessment
See page 43 – Disease Pathway
& pages 49-50 – Clinical Signs of Septic Shock & Clinical Signs of Meningitis

See pages 68-69 – Principles of Management of Sepsis with Shock & algorithm Management of Meningococcal Disease in Children and Young People *(inside back cover)*

See page 43 – Clinical Features of Severe Disease
See page 64 – Increased Vascular Permeability
See pages 68-69 – Principles of Management of Sepsis with Shock
See algorithm Management of Meningococcal Disease in Children and Young People *(inside back cover)*

See page 58 – Contraindications to Lumbar Puncture

See page 66 – Specific Organ Dysfunction In Shock
See algorithm Management of Meningococcal Disease in Children and Young People *(inside back cover)*

Case 3 Outcome

Six hours after admission, child had a cardiac arrest and died.

Discussion

Paediatric ward assessment:
Although there was mild meningism the predominant clinical picture was one of advanced shock. Paediatric intensive care (PICU) should have been called immediately.

Given evidence of shock, further investigations were needed: venous blood gas, biochemistry, glucose and blood for meningococcal PCR should have been done.

Treatment:
The initial bolus of fluid and administration of intravenous antibiotics were appropriate, but the treatment was too slow. Improvement in CRT alone did not mean that shock had been reversed. The continuing presence of shock after 50ml/kg showed that the child urgently required intensive care for early elective intubation, ventilation and further aggressive resuscitation.

The pulmonary oedema is the result of advanced capillary leak. The treatment is to ventilate the child, not further deplete the intravascular volume with diuretics.

Results:
Blood gas should have been done on admission to see extent of the metabolic acidosis.

There was a significant coagulopathy which needed treatment with fresh frozen plasma.

The raised urea reflects inadequate renal perfusion secondary to intravascular hypovolaemia caused by capillary leak syndrome.

There are at least three indicators of severe disease on admission: hypotension, widespread purpura and low white cell count (WCC).

SHO review:
This SHO did not understand the illness. The very fast tachycardia indicated very advanced shock. A lumbar puncture (LP) should not even have been considered. The child's deteriorating neurological state was a pre-terminal sign of shock.

A mannitol infusion was considered as the doctor was confused as to the cause of the neurological depression.

Learning points

- **Meningococcal sepsis with shock is a medical emergency.**
- In MD, extensive purpura are indicative of sepsis with coagulopathy. It is very rare for this to be accompanied by raised intracranial pressure (RICP).
- When signs of established shock are present, it is essential that early aggressive management is instituted, and protocol followed with help from experts in PICU used to dealing with children in multi-organ failure.
- If features of severe disease are present (see page 43) then seek expert help urgently.
- Mannitol is used for RICP associated with meningitis. It is not used for sepsis/shock.

Conclusion

This case history clearly demonstrates the importance of understanding the difference between sepsis and meningitis, and shows how children with advanced disease need expert care.

Case 4

Case history

15 year old boy non-specifically unwell for a day. Woke with a widespread purpuric rash and taken straight to hospital.

ED assessment:
Temp 39.0, HR 120, RR 20, BP 90/60.
Alert no meningism; purpuric rash spreading.

Diagnosis: meningococcal sepsis.
Bloods sent for FBC, glucose, biochemistry, U&E, clotting.

Results of investigations:
Hb 12.4, WCC 4.1, Platelets 48.
Na 136, K 3.5, urea 6.2, creatinine 138.
PT (prothrombin time) >180, APTT (activated partial thromboplastin time) >240, INR 12.

Please see chart on following pages for subsequent management and clinical course.

7.5 hours:
Formal referral to PICU; telephone advice given to start aggressive resuscitation as per algorithm, Management of Meningococcal Disease in Children and Young People.

8 hours:
CRT is 7 seconds. A venous gas is done: pH 7.10, PCO_2 5.16, PO_2 14.5, HCO_3 11.9,

Questions

How would you interpret these signs?
What other clinical signs are important to record?

Are there any other investigations you would undertake?

What is causing the renal impairment?
How would you interpret these results?

What test would help you establish the degree of shock?

What is this boy's prognosis?

From the chart comment on the overall fluid management.
Does this patient's good conscious level rule out shock?
Is there any contraindication to the lumbar puncture done at hour 2?
From the chart explain the significance of the fall in blood pressure at hour 5.
How would you manage this?

How would you interpret this gas?

Look it up

See page 48 – Normal Values of Vital Signs Table
See pages 46-48 – Initial Assessment of Any Febrile Child

See pages 56-57 – Initial Laboratory Assessment

See Section 5 – Pathophysiology

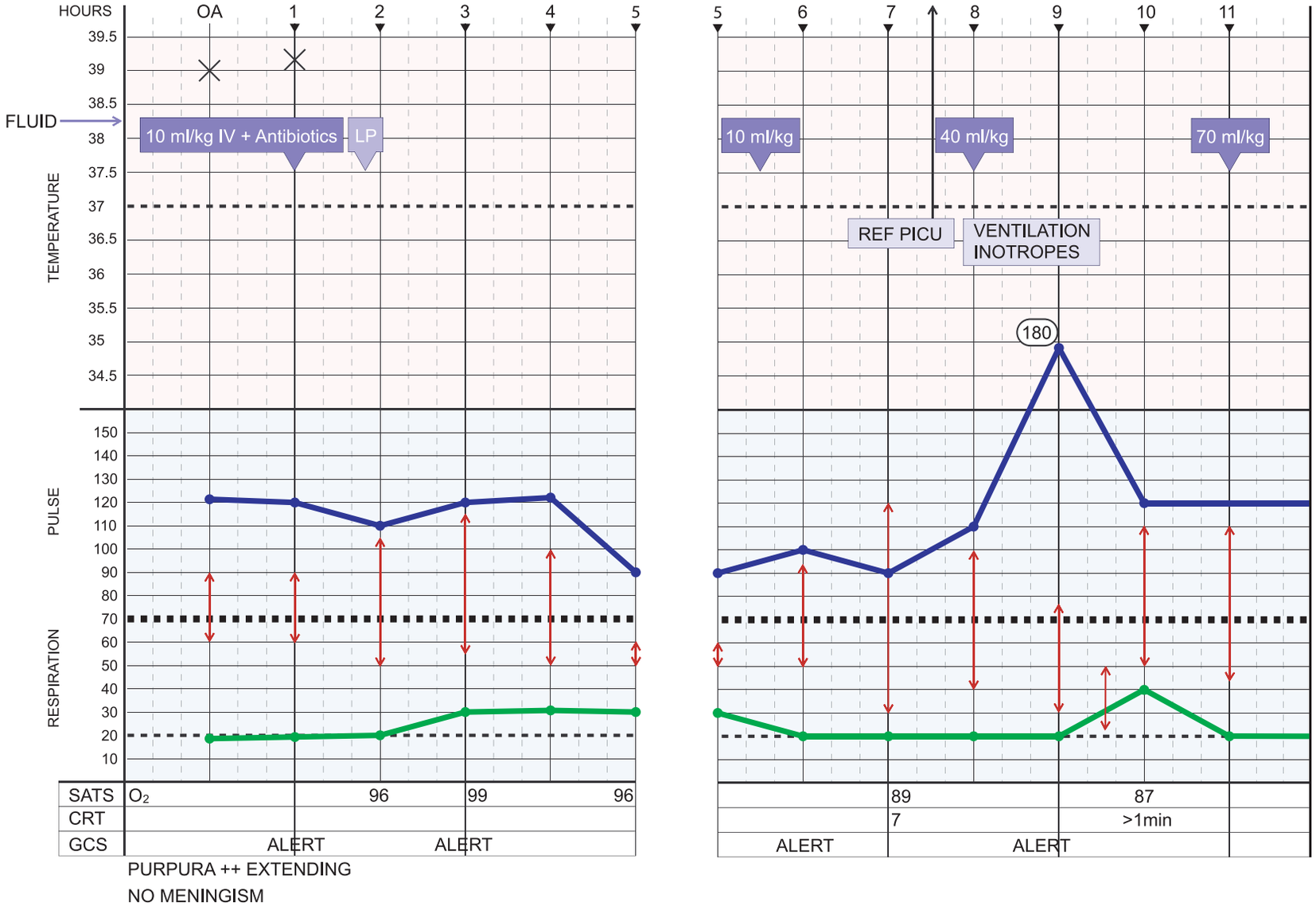
See page 49 – Clinical Signs of Septic Shock

See page 43 – Clinical Features of Severe Disease

See pages 68-69 – Principles of Management of Sepsis with Shock
See page 64 – Increased Vascular Permeability
See page 58 – Contraindications to Lumbar Puncture
See Section 5 – Pathophysiology
See algorithm Management of Meningococcal Disease in Children and Young People (*inside back cover*)

See pages 56-57 – Initial

CASE 4 CHART


HOURS
OA
1
2
3
4
5
6
7
8
9
10
11
FLUID
10 ml/kg IV + Antibiotics
LP
10 ml/kg
40 ml/kg
70 ml/kg
REF PICU
VENTILATION
INOTROPES
TEMPERATURE
39.5
39
38.5
38
37.5
37
36.5
36
35.5
35
34.5
PULSE
RESPIRATION
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
180
SATS
O2
96
99
96
89
87
CRT
7
>1min
GCS
ALERT
ALERT
ALERT
ALERT
PURPURA ++ EXTENDING
NO MENINGISM

Case 4 Outcome

At 7.5 hours after admission a PICU was called for advice. As a result, elective intubation, ventilation and aggressive fluid management commenced. Unfortunately these measures were started too late and the patient had a cardiac arrest 3 hours later.

Discussion

ED assessment:

This boy presented with meningococcal sepsis and shock. The initial medical assessment did not record the peripheral perfusion and oxygen saturation.

The results show that the patient had a low WCC, which is a marker of severe disease. There was also laboratory evidence of disseminated intravascular coagulation (DIC). Given that this child needed to be treated on PICU with central line insertion, coagulopathy should have been treated immediately with fresh frozen plasma (FFP), cryoprecipitate, or platelets, and then monitored closely. The raised urea and creatinine were the result of intravascular hypovolaemia secondary to capillary leak syndrome.

A venous blood gas would give a base excess which is a measure of the metabolic acidosis associated with shock.

The clinical and laboratory features indicated very severe disease.

ED management:

The fluid management was totally inadequate. Management should aim to maintain or restore circulating volume and optimise tissue perfusion. If the response to initial resuscitation is inadequate, and shock does not improve or progresses, then more than 60ml/kg may be required in the first hour. This patient had only 20 ml/kg in the first 6 hours after admission. No urine output was measured. By the time PICU help was sought, he was in de-compensated shock.

An LP is absolutely contraindicated in the face of widespread purpura, severe coagulopathy and cardiovascular shock

Vital signs on chart. Note that the patient remained tachycardic throughout the day. This was the result of intravascular hypovolaemia. The patient should have been catheterised to monitor the urine output on an hour-by-hour basis. By hour 3 the respiratory rate had risen to 30, most likely as a result of acidosis, pulmonary oedema and hypoxia. The teenager remained alert which is often seen in sepsis and may falsely reassure doctors as to the severity of the illness.

At hour 5 a very low blood pressure was recorded, because by this time, compensatory mechanisms were failing. Hypotension is a late and serious sign in septic shock in children and teenagers. This indicated that the patient needed much more aggressive resuscitation as per algorithm, Management of Meningococcal Disease in Children and Young People.

The blood gas done eventually at 8 hours shows a severe metabolic acidosis.

Learning points

- Meningococcal sepsis with shock is a medical emergency.
- Children who present with meningococcal sepsis in the morning may have very advanced disease as they have many hours during the night, unobserved by their parents, in which to become ill.
- If features of severe disease are present (see page 43), then seek expert help immediately.
- Children with shock may be alert until late in the illness and this may make them look less sick then they actually are.
- Hypotension is late sign of shock in children and does not need to be present to diagnose shock.
- Children with shock need assessment by a senior paediatrician
- Refer early to a regional PICU.

Conclusion

This case history shows that despite the correct diagnosis of meningococcal sepsis being made, the resuscitation was slow and inadequate. The child remained in ED for 8 hours instead of being transferred to a PICU immediately. A diagnosis of meningococcal sepsis should bring about urgent medical treatment, and expert help should be sought if there are signs of shock.

Case 5

Case history

10 month old boy. Taken to GP with h/o sudden onset of fever, vomiting and lethargy for 4 hours. Mother very anxious about child. GP referred child to walk-in clinic at hospital.

History on admission: Feverish and drowsy – sudden onset.
2 episodes of vomiting, 1 soft stool, no rash.

Assessment on admission:
Drowsy and pale, dark rings around eyes.
Temp 37.7
CVS: P 181, BP 120/52 CRT 4 secs. Child peripherally shutdown.
RS: RR 32 breathing laboured and child cyanosed.
SaO_2 100% in oxygen.
NS: GCS10 then 9, no neck stiffness.

Fine blanching rash on abdo/chest. 1 petechial spot on abdo.

Diagnosis: meningococcal sepsis

Action taken:
1. Immediately given antibiotics and 40ml/kg saline.
2. 'Crash call' put out for PICU team.
3. Full set bloods taken.

Results of investigations:
WCC 2.4, Hb 10.5, pl 70.
Glucose 3.8
Na 149, K 3.4, Ca 2.1, Mg 0.4, PO_4 1.6, Urea 10.9, Creat 121.
HCO_3 15, BE -7.
PT 30, APPT 75, INR 2.5.

Taken to PICU. Still shocked after 40ml/kg. Electively intubated and ventilated, Adrenaline started. Commenced correction of acidosis, K and Mg.

Extensive purpuric rash developed.

PICU consultant called in to supervise care.

Questions

What might sudden onset of illness in an otherwise well child suggest?

What do you think of this assessment?
What do these signs tell you?

How would you interpret the absence of hypotension in the context of other observations?
When conscious level is depressed and/or falling, is severity of disease likely to be worse when signs of meningitis are present, or when they are absent?

Does the very scanty rash rule out MD?

What do you think of this course of action?

What do you think of these results?

Is there evidence of organ failure?

Look it up

See pages 44-45 –Symptoms of Sepsis

See pages 46-48 – Initial Assessment of Any Febrile Child
See page 49 – Clinical Signs of Septic Shock
See page 64 – Increased Vascular Permeability
See page 43 – Clinical Features of Severe Disease

See pages 51-56 – The Rash &
page 61 – How much rash do you need to diagnose meningococcal disease?

See algorithm Management of Meningococcal Disease in Children and Young People(*inside back cover*)

See page 43 – Clinical Features of Severe Disease
See pages 56-57 – Initial Laboratory Assessment
See page 66 – Specific Organ Dysfunction In Shock

Case 5 Outcome

Subsequent PICU care (summary): Severe respiratory failure with pleural effusion: ventilated for total of 3 weeks. High dose inotropes required for several days. Severe coagulopathy – treated with FFP and cryoprecipitate. Renal replacement therapy needed. Peritoneal dialysis later that evening for fluid overload and renal failure – progressed to haemofiltration after several days. 3 weeks PICU, in hospital 2 months.

Discussion

Sudden onset of illness in otherwise well child. Only a short history taken but child clearly recognised to be very sick and treatment started.

Assessment very thorough and entirely appropriate. Evidence of shock. Tachycardia, cool peripheries. Note the absence of hypotension which in association with signs of shock indicates cardiac compensation.

Child has evidence of respiratory decompensation secondary to acidosis, hypoxia and capillary leak syndrome.

Depressed or falling conscious level must always be taken seriously, but it may occur quite early in meningitis. Depressed or falling conscious level in a patient with sepsis, in the absence of signs of meningitis, indicates very advanced shock.

The rash was not dramatic on admission. There was only one non-blanching spot. This shows how the typical haemorrhagic rash may only appear once the child is very ill. Do not be reassured if a child has only a scanty rash, you must try to determine how advanced the underlying sepsis is.

The results showed a low WCC, falling platelets, coagulopathy and rising urea and creatinine. These are all features of severe disease. Laboratory results outside normal ranges. There were signs of multiple organ failure.

The severity of the child's illness was appreciated immediately and aggressive resuscitation commenced. Senior help was called for and the child was admitted to an appropriate intensive care unit.

Once on PICU the aggressive management was continued following the Management of Meningococcal Disease in Children and Young People algorithm. Senior PICU help was sought to ensure this child had one to one medical attention whilst being stabilised. The typical rash of meningococcal sepsis was by then apparent. Multiorgan failure was managed in PICU.

Learning points

- Febrile illness of sudden onset = classic picture of MD, mainly affecting well children. However, respiratory illnesses, particularly flu, may predispose to MD. The less typical picture is of initially trivial symptoms suddenly becoming more serious with a high fever and other symptoms.
- Always take a parent's anxiety very seriously.
- **Meningococcal sepsis is a medical emergency.**
- Falling conscious level in a shocked child is a poor prognostic sign.
- Isolated pinprick spots may appear where the rash is mainly blanching so it is important to search the whole body for small petechiae.
- Underlying disease may be very advanced by the time a rash appears. The rapidly evolving haemorrhagic 'text book' rash may be a very late sign. It may be too late to save the child's life by the time this rash is seen. It is important to look for physical signs of serious systemic illness even if there is no rash or an unimpressive rash.
- Once shock is advanced, it can only be reversed by aggressive resuscitation and management of complications in intensive care.

Conclusion

Children with severe sepsis and multiorgan failure have a high risk of mortality especially if they are under 1 year of age. In this case all the signs of severe illness were recognised immediately and acted on appropriately. It is likely that without such rapid medical attention this child would have died.

Case 6

Case history

14 year old girl admitted to hospital with 24 hour history of fever, increasing headache associated with 6 episodes of vomiting in evening. She has developed photophobia. Also feels generally unwell with myalgia.

GP visited and gave IM penicillin as meningococcal disease considered the most likely diagnosis. GP arranged transfer to hospital by 999 ambulance.

SHO assessment on arrival:
Responsive, mild photophobia, no neck stiffness.
Temperature 39.7.
CVS: Pulse 85 regular, BP 115/75.
Heart sounds normal.
Chest clear, abdomen normal.
Pale macular rash over trunk, no purpura.

NS: Glasgow coma score 15/15.
Full power in arms and legs – all movements.
Cranial nerves intact, no papilloedema.

Differential diagnosis made of meningitis or viral illness. Given intravenous antibiotics immediately and blood tests sent.

1 hour later (registrar review):
Conscious level has deteriorated over the past hour. Now no communication, eyes open. Neck stiffness+++

BP 150/90, HR 90.
? to CT ? to do lumbar puncture.

Lumbar puncture is performed. CSF is cloudy and under very high pressure. Patient deteriorates rapidly with falling conscious level, decrease in respiratory effort.

Patient is intubated and ventilated and taken to intensive care.

Questions

What diagnosis does this history of symptoms suggest?

What do you think of the action taken by the GP?

What do you think of this assessment? What other observations would have completed the assessment?

Does the blanching rash rule out MD?

Does the absence of papilloedema rule out meningitis?

Should antibiotics be delayed until a more definitive diagnosis made? Should adjunctive treatment be considered here?

What has occurred?

What treatment does the patient need now?

Are there any contraindications to LP?

Look it up

See pages 44-46 – Taking a History

See pages 46-48 – Initial Assessment of Any Febrile Child

See pages 51-56 – The Rash & *page 61* – How much rash do you need to diagnose meningococcal disease?

See pages 50-51 – Clinical Signs of Raised Intracranial Pressure

See page 67 – Management of Sepsis and Meningitis

See pages 50-51 – Clinical Signs of Raised Intracranial Pressure

See algorithm Management of Meningococcal Disease in Children and Young People (*inside back cover*)

See page 58 – Contraindications to Lumbar Puncture

Case 6 Outcome

The patient did not recover and was found to be brain stem dead.

Discussion

This history is typical of meningitis. The patient is generally unwell with fever and myalgia but has features of CNS infection with headache, vomiting and photophobia.

Appropriate treatment from the GP.

SHO assessment:
This is a good assessment. The conscious level was recorded and signs of RICP looked for, however pupillary responses and size should also have been recorded. The SHO suspected meningitis, which was reasonable, but peripheral perfusion and oxygenation should also have been assessed.

The rash is non-specific.

Immediate administration of IV antibiotics was appropriate. If there are no signs of septic shock, a adjunctive dexamethasone should be given before, with or within 4 hours of the first dose of antibiotics, but not if more than 12 hours have elapsed. If TB meningitis is in the differential diagnosis, steroids should not be given without anti-TB therapy. Consult NICE TB Guideline (NG33) before administering steroids if TB meningitis is in the differential.

Registrar review:

LP should only be undertaken once it has been decided that the patient is stable enough to undergo this procedure.

There was a dramatic change in the patient's condition. The patient developed features of RICP. The patient urgently needed treatment to reduce the intracranial pressure.

With the dramatic change in conscious level it would have been dangerous to take the patient to the scanner without securing the airway. LP was contraindicated.

The patient unfortunately coned whilst having the LP. All efforts to resuscitate the patient after this were unsuccessful.

Learning points

- Always look for signs of RICP in all patients with evidence of meningitis.
- In cases of pure meningitis, the rash is more often scanty, absent or atypical than in meningococcal sepsis or MD with mixed presentation.
- Papilloedema does not have to be present to diagnose RICP, it is a late sign.
- Antibiotics should be given immediately if the diagnosis of meningitis is included in the differential. Consider steroids when there are no signs of septic shock.
- **RICP is a medical emergency.**
- Call for senior help and PICU immediately if there are signs of RICP.
- LP is strictly contraindicated when there is RICP, e.g. if the conscious level is deteriorating and the blood pressure is rising.

Conclusion

All patients with meningitis must have clinical signs of RICP looked for and always rechecked prior to doing an LP. Beware the patient who deteriorates after admission. If in doubt delay LP until senior advice can be sought.

Case 7

Case history

15 year old boy, 30 hours of flu-like illness. On day of presentation his mother found him febrile and confused in bed.

Assessment on admission 07:30:
Temp 38.2.
HR 103, BP 148/102
Incoherent and behaving inappropriately.
Some neck stiffness, Kernig's sign negative.
Movements almost decerebrate.
Purpuric rash noted.

Diagnosis: meningococcal meningitis
Bloods sent for FBC, clotting, U&E, and culture

Action taken:
Given intravenous antibiotics.
Admitted to ward.

On examination on ward:
Agitated, disorientated and confused with fluctuating conscious level. He had developed a convergent squint.

Sent to radiology for CT scan.

Investigations:
Hb 14, WCC 15.2, pl 190.
Urea 4.7, creatinine 54.
Na 140, K 4.2, Bicarbonate 24.
INR 1.0, PTTR 1.2.

CT scan showed no signs of raised intracranial pressure.

10:30: The patient's conscious level fell to 8/15 and then he suffered a respiratory arrest. The BP was 225/115. He had no respiratory effort and so was intubated and ventilated.
He was turned onto his side for a lumbar puncture, which was performed. He suffered

Questions

In teenagers, CNS symptoms and confusion are sometimes misinterpreted. What mistaken diagnosis might be reached?

What do these observations indicate?

What do you think of this assessment? What further assessment should be made?

What do you think of this treatment?

What do you think of the action taken?

What needs to be done now?

Are there signs of co-existing shock or coagulopathy?

Is CT scanning sensitive to RICP?

Are there any contraindications to LP in this situation? Is LP necessary?

Look it up

See pages 49-50 – Clinical Signs of Meningitis

See pages 49-51 – Clinical Signs of Meningitis & Clinical Signs of Raised Intracranial Pressure

See pages 46-48 – Initial Assessment of Any Febrile Child

See page 67 – Management of Sepsis and Meningitis
See pages 69-70 – Principles of Management of Meningitis with Raised Intracranial Pressure

See algorithm Management of Meningococcal Disease in Children and Young People (*inside back cover*)

See page 49 – Clinical Signs of Septic Shock, and *page 66* – Specific Organ Dysfunction in Shock

See pages 50-51 – Clinical Signs of Raised Intracranial Pressure

See page 58 – Contraindications to Lumbar Puncture

Case 7 Outcome

The pupils were noted to be fixed and dilated when examined a few hours later. The following day brain death tests were performed and the patient was declared brain dead.

Discussion

Assessment on admission:
There were signs of RICP present on admission. There was systemic hypertension, depressed conscious level and abnormal movements.

There should have been an assessment of pupil size and reactivity and examination of the fundi.

Action taken:
Antibiotics were essential but the patient should also have been given mannitol immediately and electively intubated and ventilated to try and reduce the RICP.
This patient urgently needed expert treatment in intensive care.

Investigations:
Note that even in patients with severe meningitis the investigations remain relatively normal. There was no acidosis, coagulopathy, renal dysfunction.

10:30:
There were clear clinical signs that the patient's condition was deteriorating and dangerously unstable and the RICP needed immediate action. CT scanning and waiting for test results resulted in 3 hours delay and was unacceptable.

The RICP was severe leading to respiratory arrest. There is grossly elevated systemic hypertension.

The patient coned. Clearly he had advanced disease on presentation but no efforts were made prior to his respiratory arrest to stabilise him and reduce the RICP. The LP was unnecessary for initial diagnosis and totally contraindicated after his respiratory arrest.

Learning points

- Acute confusion in a teenager may be mistaken for drug or alcohol intoxication. Meningitis and encephalitis must be included in the differential diagnosis of a teenager who is acutely confused or disruptive.
- RICP is a medical emergency. **Call for senior help and PICU immediately if there are signs of RICP.**
- Opthalmoplegia (new squint) is a further sign of RICP with herniation of supratentorial part of the brain through the tentorial opening. This must be acted on immediately.
- CT scanning is not a sensitive tool in detecting RICP. It is dangerous to put a child with fluctuating conscious level into the scanner without securing the airway first.
- It is crucial to look for the signs of RICP before attempting LP and defer if signs are present. LP is contraindicated when there are signs of RICP and neurological failure.

Conclusion

This boy presented with RICP which is a medical emergency. This was not appreciated. Inappropriate investigations were conducted and no emergency management of the condition was undertaken.

Case 8

Case history

12 year old boy referred to hospital by his GP. He was found to be febrile & drowsy with a few non-blanching spots. The GP gave a dose of intra-muscular penicillin and sent him into hospital as an emergency.

18:00 hours ED triage:
Fever for a day, generally unwell with headache, regular paracetamol during day. No urine output since very early morning. No neck stiffness or vomiting. Temperature not coming down, new rash on back, increasingly drowsy.

Observations: temp 39.5, pulse 148, RR40, Cold hands and feet. Sats 92% in air. Conscious level is V (AVPU scale). Widespread non-blanching rash on trunk.

Nursing actions: probable meningococcal disease, put out emergency call for paediatrics. High-flow oxygen started via facemask. Blood sugar done = 6.5.

18:15 hours paediatric registrar and SHO:
History taken as above; rash noted to be purpuric.
Initial examination (in oxygen): airway clear, good saturations, equal breath sounds, no crepitations. Heart rate fast at 143, capillary refill time 6 seconds at feet. Heart sounds: gallop rhythm. BP 114/72. Rash is spreading, now on legs as well. Responding to voice, no neck stiffness, equal pupils. Blood gas taken to assess the degree of metabolic acidosis: pH = 7.2, BE= - 9.

Diagnosis: meningococcal sepsis with shock.

Given ceftriaxone and 20ml/kg bolus of saline. Bloods taken for full blood count, glucose, electrolytes, biochemistry, clotting, blood culture, meningococcal PCR, blood gas to assess severity of metabolic acidosis.

Reviewed patient. Still shocked. Fluid bolus (20ml/kg saline) repeated.

19:00 hours. PICU (in same hospital) called and care taken over by intensive care team. By now patient has had 60ml/kg of fluid and shock persisting. Patient intubated and ventilated and inotropes started centrally.

Questions

What do you think of the GP's action?

What do you think of the history taken?

Are there any other observations you would record?

Has the nurse acted appropriately?

What do you think of this assessment?

How would you interpret these signs?

Were there signs of severe disease?

Why was the patient intubated and ventilated?

Look it up

See pages 44-46 – Taking a History

See pages 46-48 – Initial Assessment of Any Febrile Child

See pages 68-69 – Principles of Management of Sepsis with Shock

See pages 49-56 – Assessment of a Febrile Child with Suspected Meningococcal Disease
See page 49 – Clinical Signs of Septic Shock

See page 43 – Clinical Features of Severe Disease

See pages 68-69 – Principles of Management of Sepsis with Shock

Case 8 Outcome

The patient was ventilated for 5 days and recovered with no serious complications. He required some skin grafting for an area of skin necrosis where there had been extensive rash.

Discussion

MD was recognised in this child by the GP, who commenced treatment with parenteral penicillin and sent the child to hospital urgently.

The history-taking was thorough and relevant given the GP's actions. Oliguria identified, aiding early diagnosis of shock.

Observations were comprehensive enough to show what was wrong with this child. There were signs of circulatory insufficiency, so BP should have been taken, but nurse correctly put out a crash call and ensured that BP was measured within 15 minutes.

The nursing action was timely and appropriate. The severity of the child's condition was understood, and he was treated as a medical emergency.

The medical team completed a full assessment – thorough examination following ABC. The initial vital signs were very abnormal and remained so on repeated examination.

The assessment revealed at least 7 signs of shock: tachycardia with gallop rhythm, tachypnoea, prolonged CRP, reduced urine output, drowsiness, hypoxia (on admission), acidosis.

The medical team appreciated the patient had clinical features of severe disease: shock, absence of meningism, rapidly progressive purpuric rash, depressed conscious level. The initial laboratory investigations initiated by the medical team would have detected laboratory markers of severe disease.

Respiratory failure is common in shock. Capillary leak into lung parenchyma causes acute pulmonary oedema.

It was fortunate that there was a PICU in the hospital and that this team were able to take care of the child immediately. However, all local hospitals are able to stabilise a seriously ill child whilst waiting for a PICU to retrieve the child. Following the Management of Meningococcal Disease in Children and Young People algorithm and liaising with the PICU by telephone will ensure the correct actions are taken in the early stages of treatment.

Learning points

- All patients in septic shock should be given high flow oxygen.
- Always repeat the vital signs when you see a patient.
- Even with prompt recognition and rapid treatment of MD, patients may become shocked.
- Patients in shock may not respond to initial management, requiring aggressive resuscitation, inotropes and correction of biochemistry to stabilise.
- Involvement of PICU is vital in children with septic shock.

Conclusion

This case illustrates that even children with rapidly advancing illness can be treated successfully if the disease is recognised and fast, appropriate action taken.

Case 9

Case history

4 year old girl brought by ambulance after a prolonged seizure that began 40 minutes earlier. Parents found her in the living room shaking all of her body and unresponsive to their voices. Immediately called 999 ambulance. The paramedic team have given diazepam rectally and she is on 100% oxygen.

Non-specifically unwell for several days with a cold and irritability. Fever for 24 hours and vomited during the day – her parents have been giving her paracetamol. She has never had fits before. No family history of seizures.

Taken immediately to ED Resuscitation: Status epilepticus ? cause – possible infection.

ED SHO assessment immediately:
Airway self-maintained but Guedal airway in situ inserted by paramedics. 100% oxygen with saturations of 100%. Air entry equal bilaterally. Well-perfused centrally. Generalised tonic clonic seizure continuing. No rashes seen.

Observations: Temp 39.5, BP 130/80 (difficult to measure), Pulse 100, RR 56. Blood sugar 7.1.

Immediate intervention:
IV access obtained X 2, bloods taken for FBC, clotting, U&E, biochemistry, culture, PCR, blood gas.
IV ceftriaxone and acyclovir commenced.
Given IV lorazepam X 2 0.1mg/kg, failed to stop seizure.
Loaded with phenytoin, 20 minutes later stopped fitting.

Further clinical assessment: Only responding to deep painful stimuli (AVPU), pupils size 7 slowly reacting, normal fundi. BP 140/85, HR 90.

Diagnosis: possible meningitis or encephalitis with raised intracranial pressure.

Anaesthetic team called, child intubated and ventilated. Admitted to intensive care whilst PICU team arrives.

Results: WCC 18, Hb 9.2, Platelets 402, Na 128, K 3.3, Ur 8.0, Cr 37, bicarbonate 24, BE -1, Clotting : PT 14, APTT 32, INR 1. CRP 289.

Transferred by retrieval team to nearby tertiary PICU. Remained ventilated for 2 days on minimal settings, no inotropic support required.
Following extubation alert and appropriate. LP performed: CSF 5000 white cells predominantly polymorphs. No growth on CSF or blood. CSF PCR positive for meningococcus B. Blood cultures negative.

Questions

Appropriate initial assessment and management?

Are there any other observations you would want to record?

What do these observations indicate?

Should LP or CT scan be done to confirm the diagnosis?
What would you do now?

Are these results consistent with meningitis?

Is there any use in performing LP at this point?

Look it up

See page 79 reference 51 – CATS Clinical Guideline: Status Epilepticus. November 2005. Children's Acute Transport Service.

See pages 46-48 – Initial Assessment of Any Febrile Child

See page 50-51 – Clinical Signs of Raised Intracranial Pressure

See pages 50-51 – Clinical Signs of Raised Intracranial Pressure
See pages 69-70 – Principles of Management of Meningitis with Raised Intracranial Pressure

See pages 57-58 – Lumbar Puncture

Case 9 Outcome

This child did well post-extubation, was transferred back to local hospital and subsequently discharged home. Follow-up revealed a mild degree of sensorineural hearing loss in both ears requiring aids.

Discussion

The child was managed well in accordance with the APLS guidelines for a seriously ill child: ABC assessment with stabilisation prior to moving onto D and E. The prolonged seizure was managed correctly following the APLS seizure protocol.

Immediate assessment was comprehensive enough to enable urgent intervention. Other observations, including pupil size and reaction, fundoscopy, peripheral perfusion and examination for neck stiffness would be helpful after the fitting stops, along with repeat of blood pressure measurement, and continued vigilance for the appearance of a rash.

After fitting stopped, RICP was correctly identified through good clinical examination, vital signs measurement and pupil assessment.

Stabilisation of the child's clinical condition was the appropriate priority, and correctly, the child did not have an LP or CT scan. LP is contraindicated in patients with depressed conscious level or RICP. RICP is a clinical diagnosis and an urgent scan would only be indicated if the child had focal signs.

RICP requires management in PICU. The aim of management is to maintain oxygenation and nutrient delivery to the brain.

The results from laboratory investigations were consistent with meningitis. In cases of meningitis without sepsis, the base deficit is usually less negative than -5, and there is minimal derangement in coagulation. The slightly raised urea here was probably secondary to dehydration or vomiting.

PCR on cerebrospinal fluid (CSF) samples may be positive hours or even days after antibiotics have been given. For this child, laboratory confirmation of meningitis was important for follow up care, particularly if sequelae were later to become apparent and educational support at school was needed. Confirmation of the etiology is important for public health management of contacts as well as disease surveillance.

Learning points

- RICP is a clinical diagnosis.
- RICP is a medical emergency. **Call for senior help and PICU immediately if there are signs of RICP**.
- Patients with 'pure' meningitis may have no rash at all and often will not have any signs of shock or coagulopathy.
- LP must not be performed when contraindicated, but a delayed LP can still result in a laboratory-confirmed diagnosis.
- A laboratory-confirmed diagnosis is important for assessing the need for follow up care, for public health management of contacts, and for disease surveillance.

Conclusion

This case shows how a child with a prolonged seizure and RICP was safely managed using protocols and rapid admission to PICU.

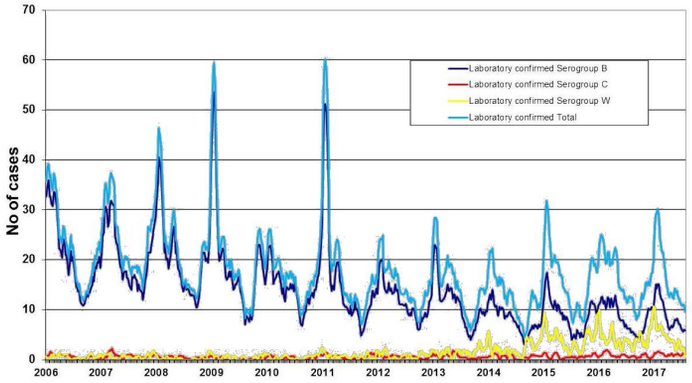
Section 3 Background to the Disease

DISEASE BURDEN

MD can kill within hours of the first symptoms and is the leading infectious cause of death in children[1]. It is not only associated with a significant risk of mortality, but also with long-term morbidity. Those who recover may be left with disabilities that dramatically alter their lives, including amputations, limb deformities, severe skin scars or tissue loss, loss of hearing or sight, intellectual impairment, motor and coordination deficits, epilepsy, and a range of less specific cognitive and psychological disorders. The meningococcus is the main cause of bacterial meningitis in children and young adults, and a common cause of sepsis and shock at these ages.

There are 12 meningococcal serogroups, determined by the chemical composition of the polysaccharide capsule of the bacteria. Serogroups A, B, C, W, X and Y cause most disease, and since the introduction of the MenC vaccine serogroup C disease has dwindled. Nearly all cases in the UK are now due to serogroups B and W. A vaccine was introduced in 2015 for babies to tackle the high proportion of endemic serogroup B infection, and a dramatic rise in a particularly virulent strain of serogroup W disease has led to the introduction of the MenACWY vaccine for teenagers.

Graph 1: Laboratory-confirmed cases of MD, England & Wales, Five-Weekly Moving Averages: 2006-2017 (week 30). Source: PHE Meningococcal Reference Unit, Manchester.



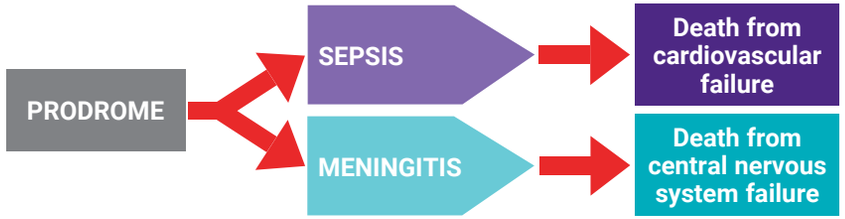
On average one in ten of us carries meningococcal bacteria in our nasopharynx and for most of us this is harmless. Carriage is unusual in young children, but the proportion of carriers increases with age, peaking in adolescents and young adults[11]. Meningococci are passed from person to person through droplets or respiratory secretions (e.g. coughing, sneezing, kissing) generally during prolonged close contact.

The disease can affect anyone of any age, but mainly affects babies, young children and adolescents. Risk factors include season (with more cases occurring in the winter months - see graph 1), exposure to smoke[12] or smokers[13], recent influenza A infection[14], and living in 'closed' communities such as university halls of residence and military barracks[15]. Individuals with a family history of MD, asplenia, splenic dysfunction, a complement disorder[16], or who are on eculizumab therapy[17] are also at increased risk of invasive MD.

CHARACTERISTICS OF MENINGOCOCCAL DISEASE

The two major clinical forms of MD are meningitis and sepsis. Most patients will have a mixed presentation. A minority will have pure sepsis and it is these patients who carry the worst prognosis and maximum effort must be made to identify them early[18]. There are important differences in the pathophysiology of meningitis and sepsis which underlie the clinical presentation and management of the two main forms of the condition (see Section 5 from page 64 Pathophysiology).

DISEASE PATHWAY



CLINICAL FEATURES OF SEVERE DISEASE

The diagram above illustrates the main causes of death from MD. In the majority of patients, one disease process predominates. Patients presenting with mixed disease will also tend, as the disease worsens, to become either profoundly septic or profoundly meningitic. A few will have combined severe sepsis with shock and severe meningitis with RICP and these need expert management. Patients presenting with septic shock without meningitis carry the worst prognosis[19]. Although a few patients with meningitis will die from RICP, most deaths from MD result from shock and multi-organ failure[20].

FEATURES WHICH PREDICT POOR PROGNOSIS AT THE TIME OF PRESENTATION INCLUDE:

- Presence of shock
- Absence of meningism
- Rapidly progressive purpuric rash
- Low peripheral WCC
- Thrombocytopenia
- Markedly deranged coagulation
- Depressed conscious level

Section 4 Making the Diagnosis

This section aims to help doctors, especially doctors in training, to avoid some of the common pitfalls in recognising and treating children with MD. It is not a fail-safe diagnostic package: since no symptom is entirely specific to this disease, many children with the symptoms described will not have MD. We hope to prompt doctors to ask "could this be meningococcal disease?" when assessing a child in the ED or on the wards where the diagnosis is in doubt.

A. TAKING A HISTORY

Meningococcal disease is extremely unpredictable. The presentation can be very varied and patients may be difficult to differentiate from those with viral illnesses during the early stages. Most children with MD present as an acutely febrile child and may not have a rash at first.

It is important to take a detailed history and ask parents about the specific symptoms of sepsis and meningitis. Beware of simply 'eyeballing' a child and assuming they have a trivial illness. This is how many mistakes are made. Make sure you have understood what exactly is worrying the parent and why they are seeking help at this point. Be careful if the child has had contact with a case of MD even if they have had prophylactic antibiotics as they can still become ill. Ask about travel to sub-Saharan Africa or contact with Hajj pilgrims[21,22]. Check for a family history of MD, asplenia or splenic dysfunction, complement deficiency and/or eculizumab treatment[16,17].

At the initial assessment look for signs and symptoms of sepsis or meningitis. Some symptoms can be subtle and must be specifically asked about when taking a history.

SYMPTOMS OF SEPSIS

- **Fever**
  - Many children become suddenly ill with a fever: the classic picture is of a disease of rapid onset. However, some children develop sepsis after a simple viral illness. In these cases the symptoms may be initially trivial and last for some time and then suddenly become more serious with a high fever and other symptoms of sepsis.
  - A history of a fever in a child presenting afebrile is important.
  - Not all children with MD (or other serious bacterial infection) have fever[23].
  - A fever that subsides after antipyretics cannot be dismissed as viral in origin.
  - Hypothermia, especially in infants, may also indicate serious infection[24].
- **Rigors** Children with sepsis often have rigors[25]. Occasionally the shaking, if very severe may be mistaken for fitting, but children having rigors will remain conscious.
- **Aches** They usually experience very bad muscle aches and joint aches making them restless and miserable.
- **Limb pain** Isolated severe limb pain in the absence of any other physical signs in that limb is a well-established phenomenon in MD[26,10]. The pain can be very severe and children have been mistakenly put into plaster to treat presumed fractures.
- **Gastrointestinal symptoms** Vomiting, nausea and poor appetite (poor feeding in babies) are common in sepsis. Abdominal pain and diarrhoea (leading to faecal incontinence in some cases) are less common but well documented[27]. This can create confusion with gastro-intestinal infections.
- **Weakness** This can become profound.
- **Rash** Ask about any new rashes or marks on the child's skin that the parents may have noticed. Note that parents may not realise that the petechiae or purpura or 'bruises' on the child's skin are a rash as they associate the word 'rash' more with a pink 'measles-like' rash. They may use other words to describe the rash, for example bruise, spot, freckle, blister, stain or mark on the skin – like chocolate, etc.
- **Decreased urine output** Ask whether the child has passed urine or had a wet nappy recently. Oliguria is one of the early signs of shock.
- **Cold hands and feet, mottled skin** As sepsis advances, cold hands and feet and mottled skin are signs of circulatory compromise that parents notice.

(Also see Clinical Signs of Septic Shock p49)

SYMPTOMS OF MENINGITIS

The main symptoms of meningitis are all due to the dysfunction of the central nervous system. Be aware that symptoms can vary according to the age of the child. Symptoms include:

- **Fever**
- **Headache**
- **Vomiting**
- **Drowsiness/confusion**
- **Fits**
- **Photophobia** (less common in young children)
- **Neck stiffness** (less common in young children)

(Also see Clinical Signs of Meningitis p49)

Young children may have fever and vomiting associated with irritability, drowsiness and confusion. **They may be very hard to assess and parent's anxieties about their state of responsiveness and alertness must always be taken seriously.**[28]

Older children are more likely to have fever, vomiting and complain of headache, stiff neck and photophobia.[10]

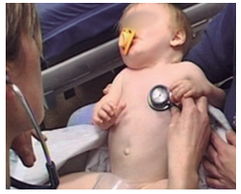
Teenagers may present with symptoms related to a change in behaviour such as confusion or aggression. These may mimic the symptoms of alcohol or drug intoxication[29].

B. EXAMINING THE PATIENT

INITIAL ASSESSMENT OF ANY FEBRILE CHILD

For all febrile children the following should be undertaken:

- Fully undress and examine systematically. Make a thorough search for a focus of infection: think about the 'hidden sites' such as meninges, urinary tract and bloodstream (sepsis). Mildly pink tympanic membranes or throat do not constitute a focus. It is best to start the examination whilst the child is not crying. It takes time to make a careful assessment.



Babies are the hardest to assess, as they are uncooperative when ill, and it is often difficult to pinpoint where the infection is coming from. When a baby is lethargic and quiet, but irritable when moved: this can be a sign of meningitis.

This child is febrile and looks ill and pale.

- If a rash is found, it is important to decide whether it is non-blanching.

MD is not the only cause of non-blanching rashes in children, but approximately one in ten children with MD dies, and most fatal cases die within 24 hours of the onset of symptoms. The window of opportunity for delivering effective treatment is therefore brief, and the consequences of waiting to confirm the diagnosis before commencing treatment can be very grave.

A child with a non-blanching rash and fever, or history of fever, requires immediate action and a senior paediatrician should be informed.

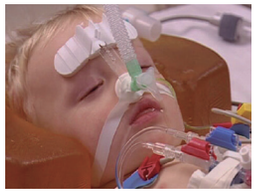
All febrile children with haemorrhagic rashes must be taken very seriously. Although many children with fever and petechiae will have viral illnesses [23, 30, 31] there is no room for complacency when assessing these children. They must all have a careful examination and their vital signs measured.

- If a child with a petechial rash has signs of meningitis or sepsis, or appears ill to you, or if the rash spreads or becomes purpuric (spots >2mm diameter), give IV antibiotics. Purpura are highly predictive of MD.
- If a child with a petechial rash has fever (or history of fever) but **does not** have signs of meningitis or sepsis, do
  - full blood count
  - C-reactive protein (CRP)
  - coagulation screen
  - blood culture
  - whole-blood polymerase chain reaction (PCR) for *N. meningitidis*
  - blood glucose
  - blood gas
  - ◆ Give antibiotics if the CRP and/or WCC (especially neutrophil count) is raised (be aware that while a normal CRP and normal WCC mean MD is less likely, they do not rule it out).
  - ◆ If CRP and WCC are not raised, assess clinical progress by monitoring vital signs, CRT, and oxygen saturations at least hourly over the next 4–6 hours (it is important to remember that severe cases of MD can present with a normal or low WCC, as well as a normal CRP due to a slow rise in CRP in the first 24 hours of illness).
  - ◆ If you are still in doubt, treat with antibiotics and admit to hospital.
- A non-spreading petechial rash without fever (or history of fever) in someone who does not appear ill is unlikely to signal MD, especially if the rash has been present for more than 24 hours.
- If you discharge a child you believe to be at low risk of MD after initial observation, advise parents to return to hospital if the child's condition gets worse, even if this is shortly after discharge.

Safety net: The NICE Fever in under 5s[32] guideline and the SIGN meningococcal disease[33] guideline highlight the importance of a safety net when a febrile child is sent home. This includes

- Encouraging the parents to trust their instincts and seek medical help again if the illness gets worse, even if this is shortly after the child was seen[10,23,32] and advising on accessing further healthcare.
- Providing information about symptoms of serious illness, including how to identify a non-blanching rash[32]. Rash is the commonest reason for parents of children with MD to seek medical help[34].

Safety net arrangements should take account of the parents' anxiety and capacity to manage the situation[32] as well as proximity to emergency care, and any individual problems with access or transport[33].



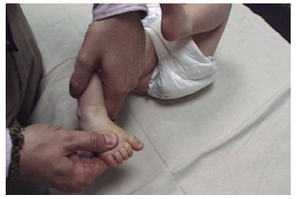
Children without a rash or with a blanching rash can still have MD[35]. The rash may appear later or not at all if the child has pure meningitis and occasionally with meningococcal sepsis.

Children without a rash can still have meningococcal disease

- Thorough clinical assessment should ascertain whether there are physical signs of serious systemic illness.
- If initial assessment of airway, breathing and circulation reveals that you are dealing with a seriously ill child, ABC should be rectified in line with APLS guidelines[36] before proceeding with the detailed examination.

The following clinical signs must be measured and recorded to complete a full assessment:

- **Temperature**
- **Heart rate**
- **Respiratory rate**
- **Blood pressure**
- **CRT or toe-core temperature gap**



Measuring capillary refill time

NORMAL VALUES OF VITAL SIGNS

Age	RR	HR/min	Systolic BP
Birth	25-50	120-170	80-90
3 m	25-45	115-160	80-90
6 m	20-40	110-160	80-90
12 m	20-40	110-160	85-95
18 m	20-35	100-155	85-95
2 y	20-30	100-150	85-100
3 y	20-30	90-140	85-100
4 y	20-30	80-135	85-100
5 y	20-30	80-135	90-110
6 y	20-30	80-130	90-110
8 y	15-25	70-120	90-110
12 y	12-24	65-115	100-120
>14 y	12-24	60-110	100-120

Adapted from Advanced Paediatric Life Support: The Practical Approach[36].

Standard technique for measurement of CRT is to press for 5 seconds on a fingertip or toe, or on the centre of the sternum, and count the seconds it takes for colour to return (shown here on dorsum of foot to facilitate capture on film).

- **Oxygen saturation measurement** (normal value is >95% in air)
- **Assessment of conscious level. AVPU** is a quick way to assess conscious level

Assess the best response patient can make:

- **A**lert? Remember, even an alert child may be very ill with sepsis.
- Responds to **V**oice? Should be seen by doctor urgently
- Responds to **P**ain? Medical emergency
- **U**nresponsive? Medical emergency

- **Pupil size and reaction**
- If **rash** present record whether it is blanching, extent of rash, speed of development and whether it is petechial or purpuric. See page 46 All febrile children with haemorrhagic rashes must be taken very seriously and The Rash on pages 51-56.

ASSESSMENT OF A FEBRILE CHILD WITH SUSPECTED MENINGOCOCCAL DISEASE

If MD is suspected, the purpose of the initial assessment should be to identify whether shock or RICP is present and the severity of the illness.

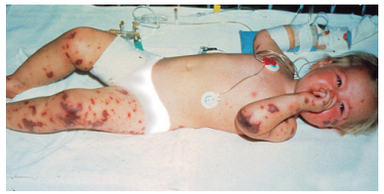
CLINICAL SIGNS OF SEPTIC SHOCK

Sepsis will lead to shock and multi-organ failure. Shock is a clinical diagnosis. The signs are a result of circulatory failure. The underlying pathophysiology of sepsis and the capillary leak syndrome leading to these signs are briefly summarised in the Pathophysiology section page 64 Section 5.

A child in early shock may still be alert and have a normal blood pressure.

The early signs of shock include:

- **Tachycardia**
- **Cool peripheries** (CRT>2 seconds) or toe-core temperature gap of >3 degrees
- **Pallor, mottling**
- **Decreased urine output** (<1ml/kg/hr)
- **Tachypnoea** – secondary to acidosis and hypoxia

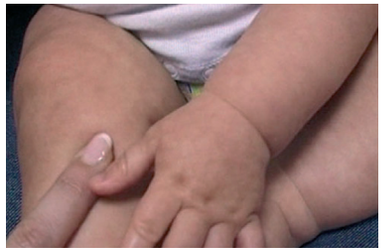


Child lucid despite advancing sepsis

(In patients with MD, signs of shock will usually co-exist with symptoms of sepsis.)

As shock progresses further signs develop:

- Metabolic acidosis with **base deficit worse than -5**
- **Hypoxia:** PaO_2 <10kPa in air or saturation < 95% in air
- **Increasing tachypnoea, tachycardia and gallop rhythm**



Mottled skin in a baby who also has prolonged CRT

Late signs of shock include:

- **Drowsiness or agitation**
- **Hypotension:** in children, blood pressure can be normal until shock is advanced.

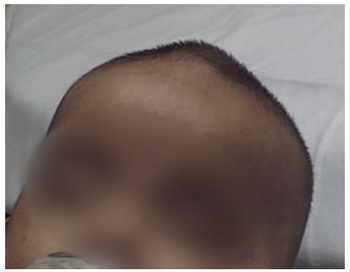
CLINICAL SIGNS OF MENINGITIS

When examining a child for signs of meningitis it is crucial to remember that the younger a child the less likely it will be to have neck stiffness or photophobia (especially those <2 years of age). Be guided by the parents as to whether the child is drowsy or behaving inappropriately. Often parents are quick to recognise that the cry of a baby has changed or they are making poor eye contact.

- Babies with meningitis may have **a full or bulging fontanelle** due to RICP.

- They may feel stiff or have jerky movements or they may be very floppy. Fits are common.
- Drowsiness or decreased conscious level (or fluctuating level) is a very important sign in children of all ages.
- Teenagers with meningitis often present in an aggressive and combative manner rather than becoming drowsy. Drug and alcohol intoxication may be suspected[29].
- Rash: can be present, but more likely to be absent, atypical, scanty or petechial than in sepsis.

(Also see Symptoms of Meningitis page 45)



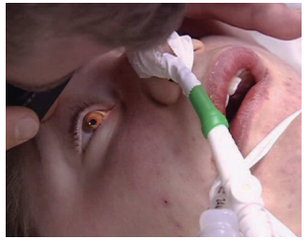
Bulging fontanelle in a baby with meningitis. Not a common sign but significant when present.

CLINICAL SIGNS OF RAISED INTRACRANIAL PRESSURE

Children and young people with meningitis are at risk of developing RICP (see Pathophysiology Section 5 page 64). RICP is a clinical diagnosis and a CT scan is unreliable for detecting it. Do not delay treatment to perform a CT scan.

Signs of RICP are:

- Reduced or fluctuating level of consciousness (GCS <9 or a drop of 3 or more)
- Abnormal posture or posturing; decorticate or decerebrate
- Unequal, dilated, or poorly responsive pupils
- Focal neurological signs
- Relative bradycardia and hypertension
- Seizures
- Cushing's triad: slow pulse, raised blood pressure and abnormal breathing pattern – late sign of RICP
- Papilloedema is a late sign, its absence does not mean there cannot be any RICP.
- Abnormal 'doll's eye' movement.



Looking for papilloedema

Note: Health care workers are encouraged to wear masks when carrying out procedures that may result in exposure to infectious respiratory droplets, for example during resuscitation[37].

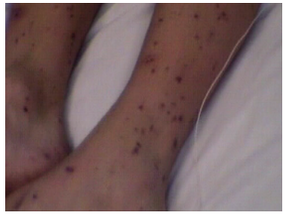
Patients with RICP may have prolonged CRT and a mild metabolic acidosis. If these signs are present in a patient with a normal heart rate or bradycardia, and a normal or high blood pressure, then they are not due to shock.

The diagnosis of RICP is a clinical one:

- Routine CT scanning is not indicated in patients with meningitis as CT scans are not sensitive in picking up signs of RICP[38, 39]. It is dangerous to put a child with fluctuating conscious level into the scanner without securing the airway first.
- LP is contraindicated in patients with signs of RICP as 'coning' can be precipitated[40, 41].

THE RASH

Most patients with meningococcal sepsis develop a rash[10, 34,42, 43] – it is one of the clearest and most important signs to recognise. A rapidly evolving petechial or purpuric rash is a marker of very severe disease.

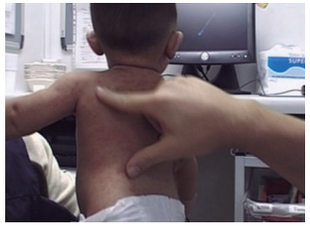


Non-blanching haemorrhagic rash

A non-blanching haemorrhagic rash is characteristic of MD, and a rapidly evolving purpuric rash is a feature of severe disease, requiring urgent, aggressive treatment. But this rash is seldom an early sign, and the underlying disease may be advanced by the time a rash appears. In MD, the rash may be absent, scanty, or it may be blanching in the early stages, especially in pure meningitis.

Early stages

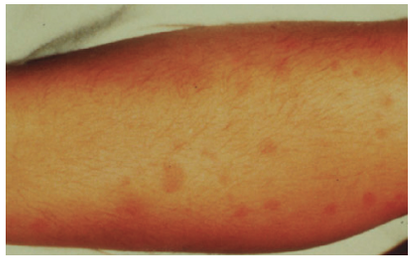
In the early stages the rash may be **blanching** and **macular** or **maculopapular**[34,35] (sometimes confused with flea bites), but it nearly always develops into a non-blanching red, purple or brownish petechial rash or purpura.



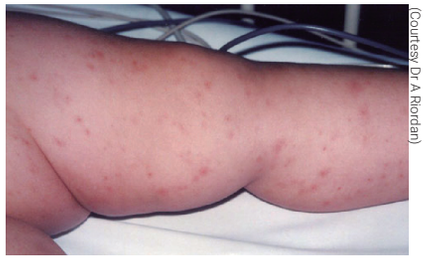
A baby with a blanching rash

***Blanching rash:** All febrile children should be checked for a rash. If rash is present, check to see if it blanches on pressure. **A non-blanching rash in a febrile child requires immediate action.** However, the rash of meningococcal sepsis can start as a blanching rash so always check that the child does not have signs of shock or meningitis.*

Isolated pin-prick spots may appear where the rash is mainly **maculopapular**[35], so it is important to search the whole body for small petechiae, especially in a febrile child with no focal cause.

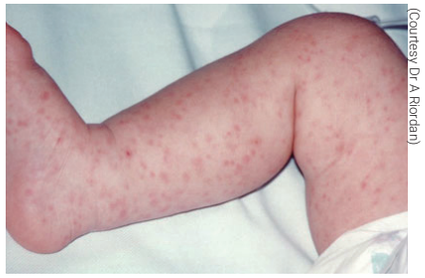


Macular rash



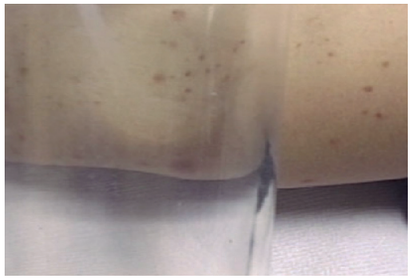
(Courtesy Dr A Riordan)

Maculopapular rash in meningococcal sepsis



(Courtesy Dr A Riordan)

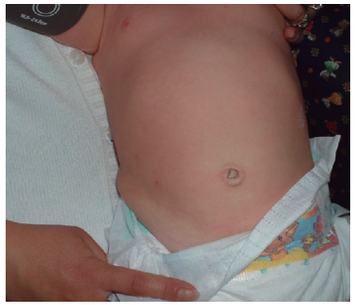
Maculopapular rash with scanty petechiae



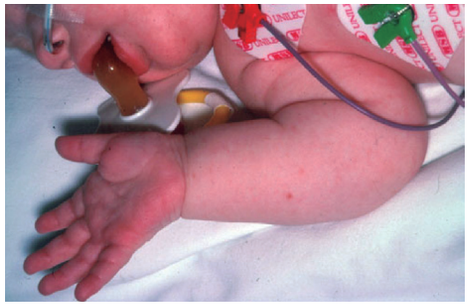
The haemorrhagic rash of meningococcal sepsis does not fade under pressure. This is nicely shown by pressing the skin with a glass tumbler

Rash in meningitis

In meningitis the rash can be scanty, blanching (macular or maculopapular), atypical or even absent.



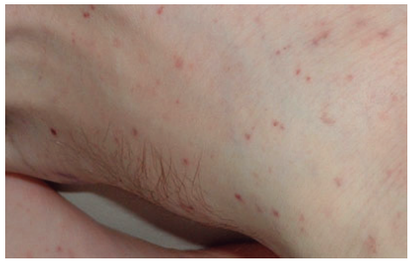
Very scanty rash: just 3 petechiae on abdomen (2) and chest (1)



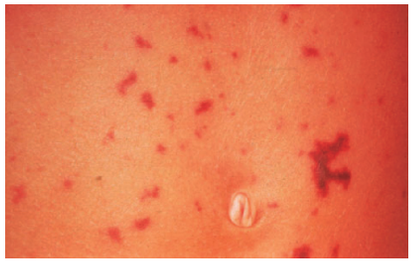
A few petechiae on mottled skin

Spectrum of meningococcal rashes

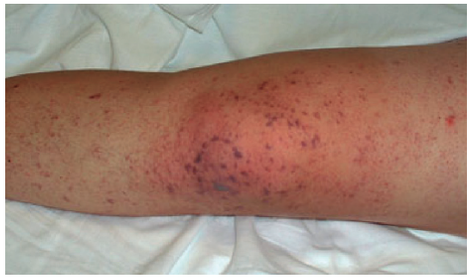
Meningococcal rashes can be extremely diverse, and look different on different skin types. The rate of progression can also vary greatly.



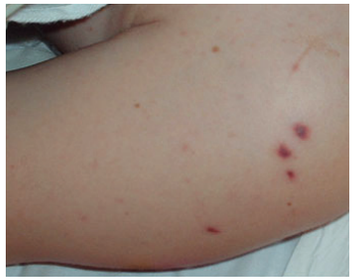
Petechial rash



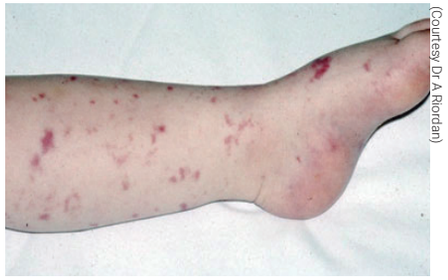
Mixed petechial/purpuric rash



Mixed petechial/purpuric rash on freckled skin

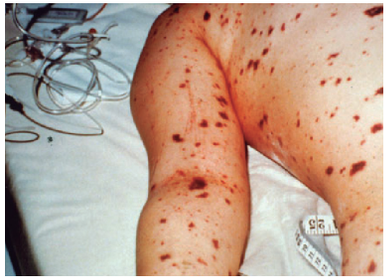


Sparse purpuric rash

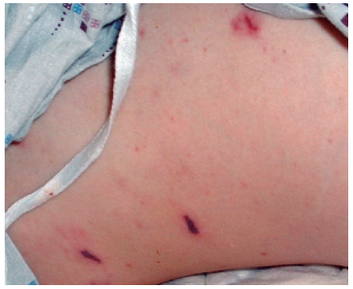


(Courtesy Dr A Riordan)

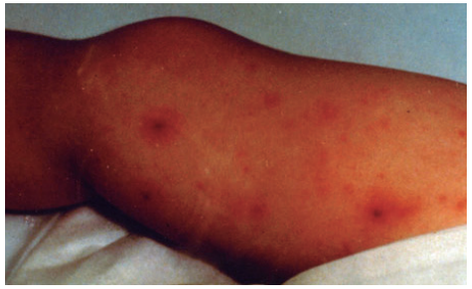
Full-blown purpuric rash of meningococcal sepsis



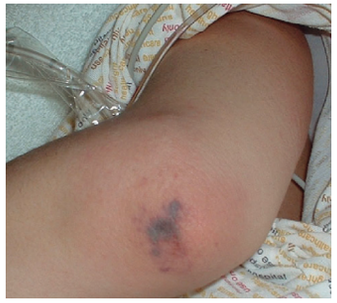
Widespread purpuric rash of meningococcal sepsis



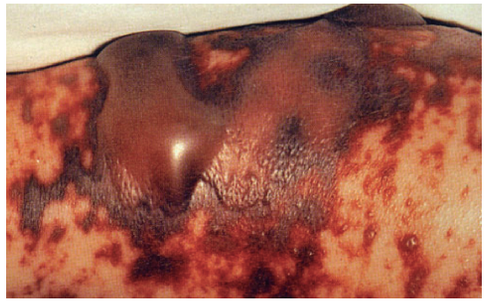
Atypical purpuric marks



Atypical purpuric spots can resemble insect bites



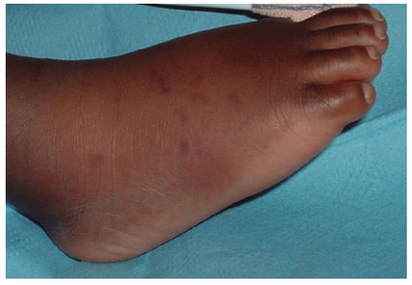
Purple blotches may be larger, resembling bruises



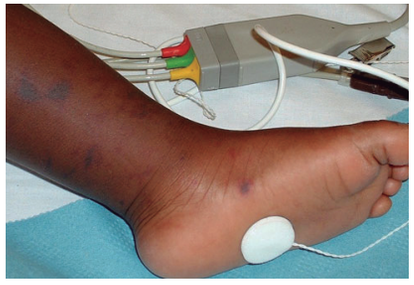
Purpuric blotches of septic rash can resemble blood blisters

Spotting the rash on dark skin

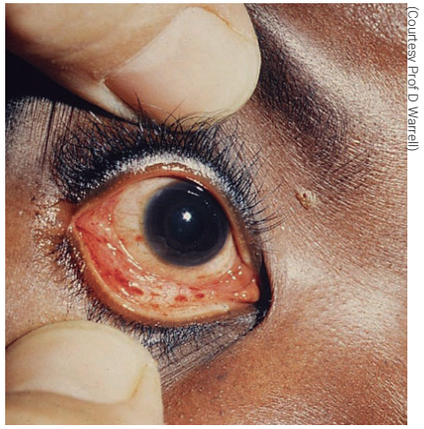
The rash can be more difficult to see on dark skin, but may be visible in paler areas, especially the soles of the feet, palms of the hands, abdomen, or on the conjunctivae or palate.



Meningococcal rash on dark skin

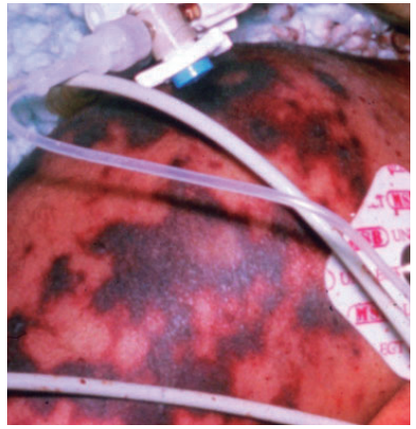


Purpuric rash on dark skin - easier to see on sole of foot



(Courtesy Prof D Warrell)

Petechial rash on conjunctivae

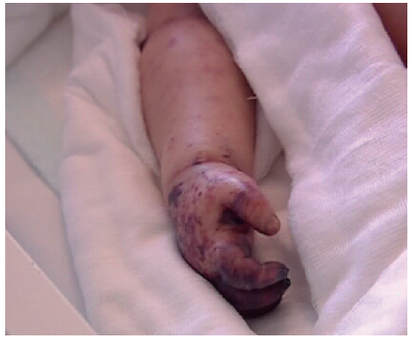


Widespread purpuric rash on dark skin

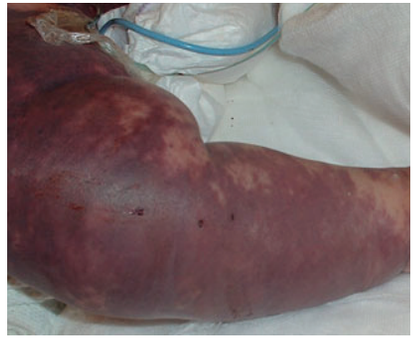
Advanced rash

Purpuric areas that look like bruises can be confused with injury or abuse.

Extensive purpuric areas are usually called 'purpura fulminans'. The extremities are normally worst affected: often the feet and hands and sometimes the ears, nose or lip. In the photo on the left, it has mainly affected the child's hands but it can extend over a whole leg or (fore)arm, as in the photo on the right.



Purpura fulminans on the hand



Purpura fulminans over the whole leg

Development of meningococcal rashes

It is crucial to remember that the underlying meningitis or sepsis may be very advanced by the time a rash appears. The rapidly evolving haemorrhagic 'text book' rash may be a very late sign, it may be too late to save the child's life by the time this rash is seen. It is very important to examine children for the signs of meningitis or sepsis (and RICP or shock) and investigate and treat if necessary based on those findings.

Although some of the causes of petechial rashes are self-limiting conditions, many others, including MD, are fulminant or life-threatening and a non-blanching rash should therefore be treated as an emergency[1, 32].

C. INVESTIGATION

INITIAL LABORATORY ASSESSMENT

The tests below should be done on all suspected cases of MD and children who are suspected of having an invasive bacterial infection:

- **Glucose**
- **Full blood count**
- **C-reactive protein**
- **Clotting studies**
- **Electrolytes and urea**
- **Calcium and magnesium** (metabolic derangements are common in sepsis and may contribute to myocardial dysfunction)
- **Phosphate**
- **Lactate**
- **Venous blood gas** to measure base excess and bicarb
- **Blood culture**
- **Meningococcal PCR** whole blood (EDTA specimen) and nasopharyngeal (throat) swab to send to reference laboratory
- **Blood group and save**

Parameter	Normal range*
Hb	10.5 to 13.5 g/dL
WCC	5.0 to 15.0 ($x10^9$)
Platelets	150 to 450 ($x10^9$)
Base Excess†	0 to -3 mmol/L
pH	7.35 to 7.45
HCO_3	22 to 26 mmol/L
PaO_2	10 to 13.5kPa or 75 to 100mmHg
$PaCO_2$	4.6 to 6kPa or 34.5 to 45 mmHg
Glucose	3.6-5.2 mmol/L
Urea	2.5 to 6.0 mmol/L
Creatinine	19 to 43 mmol/L
Na	133 to 146 mmol/L
K+	3.5 to 5.5mmol/L
Mg++	0.66 to 1.0 mmol/L
Total Calcium	2.17 to 2.44 mmol/L
PO_4	1.60-2.90 mmol/L
INR	1
PT	9.9 to 12.5 seconds
APTT	26.0 to 38.0 seconds
TT	9.2 to 15.0 seconds
Fibrinogen	1.7 to 4.0 g/L

* *Please note that normal ranges for many variables can differ among hospitals.*
† *Blood gas reports measurement of base excess (BE), which when negative indicates that there is a base deficit (acidosis).*

LUMBAR PUNCTURE

LP can be important for treatment if the clinical diagnosis is in doubt, particularly in children who are febrile without a focus. For children with obvious meningeal symptoms, microbiological confirmation is valuable for:

- duration of treatment
- decisions about prophylaxis and public health management
- follow up care of children who recover with neurological sequelae, and
- disease surveillance.

However, LP must not be performed when there are contraindications and should never delay treatment. With modern PCR techniques, CSF samples may still be positive after antibiotics have killed the organisms.

Check with a senior colleague if you are unsure.

NICE contraindications to lumbar puncture[1]

- Signs suggesting RICP (*see page 50*)
- Shock (*see page 49*)
- Extensive or spreading purpura
- After convulsions until stabilised
- Local superficial infection at LP site
- Respiratory insufficiency
- Coagulopathy

LP should also be avoided where there is any cardiovascular or respiratory compromise.

D. PITFALLS IN DIAGNOSIS

Every year children are sent home from hospital with undiagnosed MD. This leads to wasted hours in which the disease progresses and children may die unnecessarily. Simple changes to clinical practice may help prevent this. Common pitfalls in practice are explained in this section.

Contacts of cases of meningococcal disease

The risk of meningococcal disease is elevated for school contacts of cases

People who have been in contact with cases of MD are at increased risk of invasive disease. After a single case, close household contacts – usually family – are at the greatest risk, but there is an increased risk for school and nursery contacts as well[45].

Prophylactic antibiotics, usually ciprofloxacin or rifampicin, are given to reduce the risk of MD by eradicating carriage in the group of close contacts of a case who are at highest risk. They do not prevent invasive disease developing if the bacteria have already invaded the bloodstream.

Case history: Contacts of cases

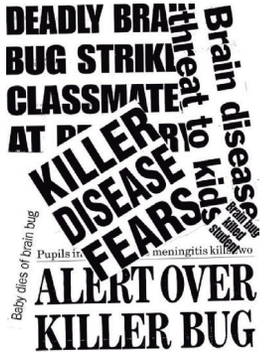
12 year old boy presented with a short history of fever, feeling dizzy and nauseated. A member of his class was then on intensive care with meningitis. His mother was concerned that he might have the same illness.

On examination he was febrile, temp 38.5, alert and orientated.

He was assessed by a doctor who found that he was alert, with no neck stiffness or photophobia. He did not have a rash and his chest was clear. The doctor diagnosed a viral illness and sent him home.

He returned 12 hours later with fulminant sepsis and died.

Guidelines for the public health management of MD are based on the statistical probability of further cases occurring and the risk/benefit balance of control measures that can be taken[44]. Wider public health action only comes into play after two or more linked cases. Although the great majority of cases of MD are sporadic and do not result in further linked cases, clusters of cases do occur. When assessing a child whose classmate has MD, consider that this could be the second case that makes the cluster.



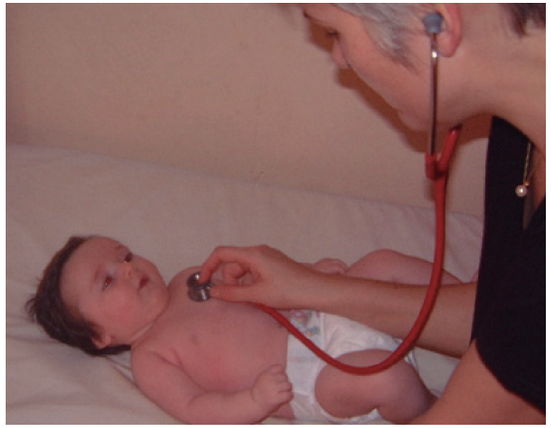
"Deadly brain bug" – common perception of meningococcal disease

Diagnosing meningitis

The media portray MD as meningitis even when the subject is a case of meningococcal sepsis. When parents bring their child to you worried that they may have meningitis they actually mean that they are worried their child has that illness they read about in the paper characterised by fever and a rash.

Parents are usually not aware that there is a difference between meningitis and sepsis and it is up to doctors to ask about the symptoms of sepsis and ensure that their clinical examination includes looking for shock.

Making a provisional diagnosis



A diagnosis based only on symptoms should be viewed as changeable until you have confirmation from investigations.

When giving a child a presumptive diagnosis like 'febrile convulsion' or 'viral illness' remember it is just that – your best guess.

Mistakes are made when doctors remain fixed with their initial diagnosis and do not think again as the case progresses

Case history: Making a provisional diagnosis

2 year old admitted with a history of fever, cough, fast breathing and fast pulse noted by the mother.

The child had experienced a 10 minute generalised convulsion at home.

On admission the child had a fever of 39.3, Pulse 220 BPM, RR 35/min, saturations 99 and no rash noted.

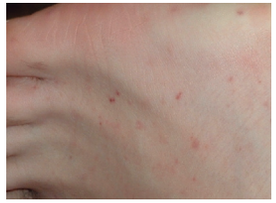
A diagnosis of febrile convulsion was made and the child was admitted to the ward.

1 hour after admission the pulse was fast at 186, BP 95/50 and respiratory rate 50. No investigations were sent.

2 hours after admission the child had a second fit for a few minutes. The medical staff decided that this was just a second febrile convulsion and did not change management or investigate. The persistent tachycardia and tachypnoea were not taken into consideration.

During the next 5 hours on the ward there were no recorded vital signs at all. Then the child was noted to have extending purpura and to be shocked. Full resuscitation was started but it was too late and the child died.

How much rash do you need to diagnose meningococcal disease?



Especially in the early stages, or when meningitis predominates, rash may be scanty, blanching or even absent.

Remember that the process of meningitis or sepsis can be quite advanced before the rash starts to appear, so if you suspect that a child may have MD then do not wait for more rash to develop, treat the child immediately.

A few petechiae

Case history: Amount of rash

2 year old boy seen by the GP: acutely unwell with high temp, vomiting, lethargy, unable to keep fluids down. Extra concern – close contact has been diagnosed as having meningococcal meningitis

GP examination: fever 38.6, pale, no rash, tachycardic but not shocked, irritable on handling.

Seen in hospital: pale and quiet temp 39.6, P 155, RR 58, no rash, thirsty

Given paracetamol, vomited immediately

SHO examination: very lethargic, sleepy but rousable, pale

RR 60, P140, No neck stiffness, 2 petechiae in nappy area

Diagnosis ? viral illness

Reviewed by registrar: diagnosis – this was likely to be a viral illness and to admit for observations, to have antibiotics if more rash appeared.

12 hours later – consultant ward round – looking worse with more rash. Investigations initiated.

Hb 10 , WCC 22.5 , Pl 244
pH 7.29 , pCO2 4.39, pO2 4.6, BE -10
INR 2.0 , APTR 1.3

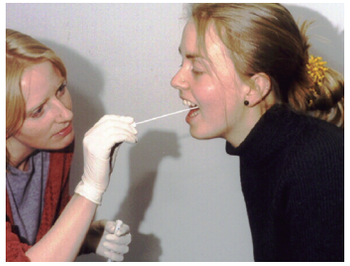
Child deteriorated quickly at this point and died.

Other rashes

If you diagnose a child as having another illness characterised by a rash, make sure that your diagnosis is likely or even possible.

You may be sure of your diagnosis, but if you decide the child is well enough to be sent home, remember to advise parents to return if their child becomes more unwell, even if this is only shortly after being seen.

Teenagers



Teenagers are most likely to carry meningococci in the nasopharynx.

Teenagers are a vulnerable group. There is a secondary peak in incidence of MD amongst young adults aged 15-20 years, with an increased risk of mortality[46]. As shown in this booklet, in the section Development of Symptoms, signs and symptoms develop later in teenagers than in younger children. Teenagers present to GPs and to hospital later than younger children do, and on average the disease is further advanced in teenagers by the time they get to hospital.

Case history: Teenagers

14 year old boy referred by the GP with diarrhoea and vomiting, abdominal pain and shivering. The GP thought the child was grey and unwell.

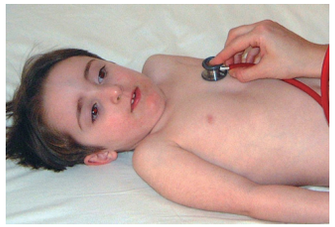
He walked into ED – no rash, alert and orientated. HR 160, RR 20, Temp 39, BP80/40, saturations 96% in air.

After 30 minutes he developed rapidly spreading purpura.

Hb 13.7, WCC 1.4, platelets 9.
Na 134, K 3.2, Urea 6.2, creat 163
PH 7.1, pCO2 4.9, pO2 4.1, BE -13.8

He was resuscitated aggressively but died.

Does your diagnosis make sense?

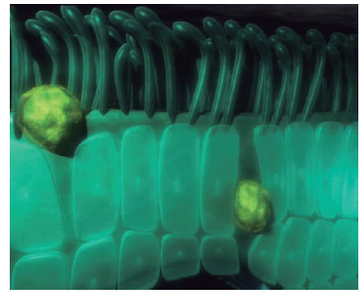


Assessing febrile children and trying to decide what is wrong with them is one of the most difficult tasks in paediatrics

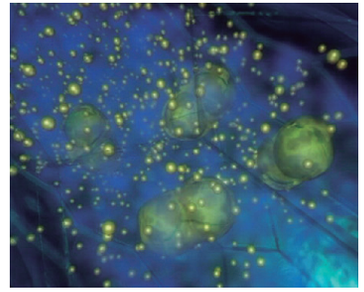
It takes time to take a good history and examine a child properly. Before you discharge the patient from your care make sure that what you have done makes sense and that you can explain your actions and decisions to anyone who may ask.

UNDERSTANDING THE PATHOPHYSIOLOGY OF MENINGOCOCCAL INFECTION AND THE PRINCIPLES OF MANAGEMENT

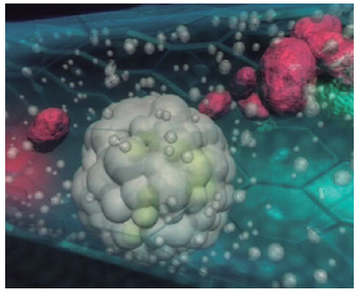
The principles of management of meningitis and sepsis are best understood by having a basic knowledge of their pathophysiology[47]. The following summary is covered in more detail in the articles listed in the references section.



Meningococci commonly colonise the human nasopharynx. About one in ten of us typically carry them in the nose and throat, and usually this is harmless. However, in some people, the bacteria are able to penetrate the defensive mucosal lining of the nose and throat to enter the bloodstream.



Once in the bloodstream, meningococci multiply rapidly, doubling their numbers every 30 minutes. In some individuals, they cross the blood-brain barrier, producing inflammation and swelling in the meninges and the brain tissue itself. This causes raised intracranial pressure, which can lead to neurological damage and death. Meningococci in the bloodstream cause sepsis. As they multiply, they shed blebs from their outer coat. These contain endotoxin. Endotoxin is the prime initiator of gram-negative bacterial septic shock. It is a lipopolysaccharide component of the bacterial outer membrane. Levels of circulating endotoxin correlate with disease severity.



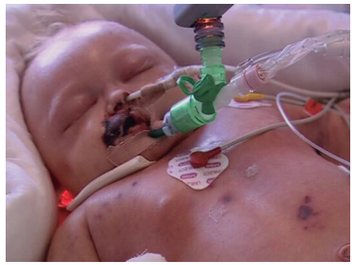
As the meningococci release endotoxin, white cells try to engulf them to overcome the infection, releasing a flood of pro-inflammatory cytokines, including IL-1, IL-6, and TNF. This damages the endothelial lining of the blood vessels. Endothelial damage activates the coagulation cascade and anti-clotting pathways are down-regulated, leading to a pro-coagulant state. Platelets rush to the site of damage to repair the endothelium. Clots start to form. Blood and other fluid haemorrhages out of the damaged vessels into the surrounding tissues. This occurs in all small vessels in the body but is most obvious in skin, hence the hallmark non-blanching rash. Widespread clotting and haemorrhaging in small vessels in fingers, toes and sometimes entire limbs can lead to necrosis and eventual amputation. The same processes in kidney, lung and other organs can cause multiple organ failure and death.

CLINICAL PATHOPHYSIOLOGY OF SEPSIS

The main processes involved in the pathophysiology of sepsis are **increased vascular permeability, myocardial dysfunction** and **disseminated intravascular coagulation**.

INCREASED VASCULAR PERMEABILITY

When meningococci invade the bloodstream, endotoxin is released from the bacteria. This triggers an inflammatory response, with release of inflammatory mediators, which is directed against the endothelial surface lining the blood vessels. One of the main functions of the endothelium is regulation of vascular permeability, and disturbance of this function causes the endothelial lining to become 'leaky', allowing increased passage of protein and water from the intravascular to extra-vascular compartments, causing a 'capillary leak syndrome'. The patient becomes hypovolaemic due to reduction in circulating volume, thus reducing cardiac output.



Severe meningococcal sepsis: this baby's body is bloated with fluid that has leaked from damaged blood vessels

Due to 'capillary leak syndrome', plasma water has leaked from damaged blood vessels into the tissues, and the baby is in shock. In severe cases, resuscitation may require giving twice a child's blood volume. Some of the fluid given to restore the circulating volume leaks into the tissues. The increased vascular permeability may continue for hours or days. Once the patient starts to recover the fluid is reabsorbed into the circulation and got rid of through the kidneys. This baby is ventilated to minimise the work of the heart and prevent her developing pulmonary oedema.

In compensation for reduced circulating volume, there is an increase in heart rate and contractility and a reduction in perfusion to skin and the splanchnic circulation. Therefore signs of hypovolaemia in sepsis include:

- **Tachycardia**
- **Tachypnoea**
- **Cool peripheries**
- **Decreased urine output**
- **Irritability or lethargy**

Note that in the early phases of septic shock, blood pressure is maintained by these compensatory mechanisms. This means that early in shock, children are alert as blood flow to the brain is being maintained at the cost of the other organs.

MYOCARDIAL DYSFUNCTION

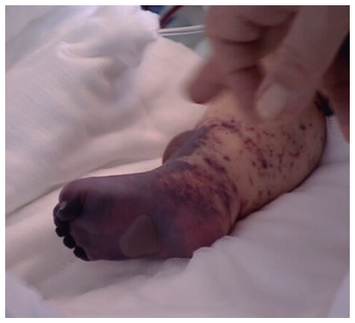
Endotoxin and inflammatory mediators (such as IL6)[48], together with other poorly-defined 'myocardial depressant factors' reduce myocardial contractility. In addition, a myocardial cytotoxic process causes myocardial cell necrosis.

Hypovolaemia and myocardial dysfunction contribute to progression of shock. In addition, nitric oxide and other vasoactive mediators cause a relative 'vasoparesis' and relative inotrope unresponsiveness.

Progression of shock leads to tissue hypoxia and capillary leak leads to pulmonary oedema resulting in tachypnoea and hypoxia.

Eventually, compensatory mechanisms fail and blood pressure falls. This is a late and serious sign in septic shock in children.

DISSEMINATED INTRAVASCULAR COAGULATION



Purpura fulminans, affecting this baby's foot

Purpura fulminans, due to damaged vessels and disseminated intravascular coagulation. There is thrombosis in the small vessels in the skin. Some of the skin has blistered like dead skin after a burn. Skin grafts will be needed to cover these black areas.

The deeper tissue is also affected: the ends of the toes are black and shrivelled. The tissues there are dead and will most likely auto-amputate. It is often not possible to know the full extent of the tissue damage at this early stage. As time progresses clear marks of demarcation between viable and dead tissue become clear.

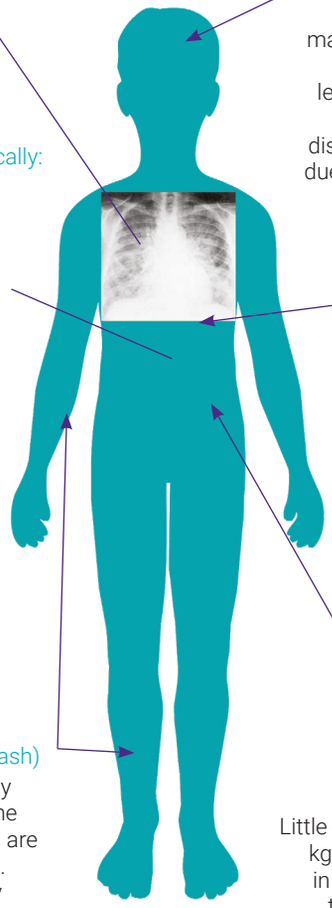
Endotoxin and the inflammatory response leads to activation of the coagulation cascade and down-regulation of anticoagulant and fibrinolytic pathways, leading to a procoagulant state. Clotting times are prolonged and thrombocytopenia occurs.

Microvascular thrombosis contributes to multiple organ failure and purpura fulminans.

Amputations:

When purpura fulminans occurs, some tissues are irreversibly destroyed due to thrombosis within the microvasculature, combined with vasoconstriction and ischaemia in peripheries. Haemorrhagic necrosis in skin and clotting in small vessels can lead to loss of skin, digits or limbs.

SPECIFIC ORGAN DYSFUNCTION IN SHOCK



Respiratory failure
(arterial PO_2 <10kPa in air or PCO_2 >6)

Common in shock. Capillary leak into lung parenchyma → acute pulmonary oedema. Clinically: tachypnoea, chest wall retraction, hypoxia.

Neurological dysfunction
In sepsis, patients may be alert until late in the illness. Falling conscious level results from impaired cerebral blood flow and disturbed brain metabolism due to hypotension, hypoxia and acidosis.

Metabolic derangement
Sepsis causes profound acidosis and derangements in metabolism, which may affect myocardial function and need correcting. Hypoglycaemia is common. Hypokalaemia, hypocalcaemia, hypomagnesaemia and hypophosphataemia all occur.

Myocardial failure
Depressed myocardial function is multifactorial, including endotoxin, cytokines, multiple metabolic derangements, hypoxia, and hypovolaemia. Clinically: tachycardia, gallop rhythm, cool peripheries and eventually hypotension.

Coagulopathy (purpuric rash)
Coagulopathy occurs early in patients with sepsis. The laboratory findings of DIC are common in such patients. Coagulopathy is generally associated with the presence of a purpuric rash, but significant coagulopathy may infrequently occur in the absence of purpura.

Renal failure
Little or no urine output (<1ml/kg/hour) is a very early sign in septic shock, initially due to hypovolaemia. If shock persists then renal failure may occur. Serum creatinine ≥2 times upper limit of normal for age or 2-fold increase in baseline creatinine indicates renal dysfunction.

CLINICAL PATHOPHYSIOLOGY OF MENINGITIS

Meningococcal meningitis generally has a better prognosis than sepsis. Meningococci reach the brain from the bloodstream, implying that the patient's immune response has prevented bacterial proliferation in the blood and not suffered overwhelming sepsis. This is because organisms are handled differently in these patients, which is probably due to differences in their inflammatory response to infection as well as different bacterial characteristics.

Deaths do occur, however, due to the severity of the inflammatory process within the brain.

Once bacteria enter the CSF, endotoxin and inflammatory mediators initiate a CSF inflammatory response, causing leakage of protein and fluid out of the cerebral vasculature. In addition, the processes delineated in sepsis occur in brain blood vessels, causing cerebral oedema and cerebral vascular thrombosis. As a consequence there is an increase in brain water content and an increase in intracranial pressure. Both the increased pressure and thrombosis may lead to a reduction in cerebral perfusion, and consequently cerebral infarction and sometimes brain death.

MANAGEMENT OF SEPSIS AND MENINGITIS

The aim of this section is to outline the principles of management of sepsis and meningitis which are based on understanding the pathophysiology. A fuller explanation of the management of MD can be found in section 1.4 of the NICE guideline Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management[1]. The Guideline Development Group (GDG) for this guideline, together with authors of the original St Mary's/MRF algorithm **'Early Management of Meningococcal Disease in Children and Young People'**, revised this algorithm to incorporate the NICE guideline, and devised an additional algorithm summarising the Management of Bacterial Meningitis in Children and Young People, both of which are published at the back of this handbook. This section of the booklet and the section which follows provide a narrative description of the management plan outlined in both algorithms. The algorithms are also available in poster format from MRF.

Give antibiotics (ceftriaxone*) to the following:

- All children with a petechial rash, if
  - petechiae start to spread
  - the rash becomes purpuric
  - the child appears ill to you
  - there are signs of bacterial meningitis
  - there are signs of meningococcal sepsis

**Do not use ceftriaxone in premature babies; neonates <1 month old; in babies with jaundice, hypoalbuminaemia or acidosis; or those receiving concomitant treatment with IV calcium. In these situations use cefotaxime (50mg/kg qds).*

- Children with an unexplained petechial rash and fever (or history of fever) but without signs of meningitis or sepsis if the CRP and/or WCC (especially neutrophil count) is raised, as this indicates an increased risk of having MD.
- Children with shock with or without a rash.
- Children with clinical evidence of meningitis. If LP is contraindicated (see page 58), treat immediately with antibiotics and perform LP when safe (but a full set of bloods for culture and PCR should be taken if not already done). Give adjunctive dexamethasone before, with, or within 4 hours of the first dose of antibiotics, but not if more than 12 hours have elapsed, and not in children <3 months of age. If TB meningitis is in the differential diagnosis, steroids should not be given without anti-TB therapy. Consult NICE TB Guideline (NG33) before administering steroids if TB meningitis is in the differential.

Door to needle time[49]

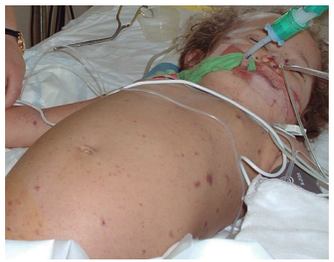
Once the decision to give antibiotics has been taken, ensure they are written up and given within 30 minutes. Unacceptable delays in giving antibiotics can occur when responsibility for this is delegated without personal follow-up.

PRINCIPLES OF MANAGEMENT OF SEPSIS WITH SHOCK

This section provides a narrative description of the management plan outlined in the algorithm Management of Meningococcal Disease in Children and Young People.

Children with evidence of shock need immediate resuscitation:

- Assess airway for patency.
- Give high-flow oxygen to all patients even if oxygen saturations are normal in order to optimise tissue oxygenation.
- Secure good venous access. The goal of circulatory support in shock is the maintenance of tissue perfusion and oxygenation. Remember in shocked children the intraosseous (IO) route may be the most effective way of giving large volume replacement.



Bloated appearance due to capillary leak syndrome. Fluids given during volume resuscitation contribute to this at first.

- Rapid fluid resuscitation should be initiated. Give an immediate bolus of 20ml/kg of 0.9% Saline over 5-10 minutes and reassess immediately (HR, RR, BP, CRT, O_2 sats, urine output, conscious level). If the clinical response is short-lived or absent, and shock does not improve or progresses, large volumes may be required (over 60ml/kg in the first hour). There is evidence from adults that early goal-directed resuscitation of patients with septic shock is associated with an improvement in outcome[50].
- Hypoglycaemia (glucose <3 mmol/l) is common and should be corrected: 5ml/kg 10% dextrose bolus IV, then check glucose hourly and correct if necessary.
- If shock persists immediately give a second bolus of 20ml/kg of 0.9% Saline or of 4.5% Human Albumin over 5-10 minutes and reassess immediately. Observe closely for response/deterioration. Consider urinary catheter to monitor output.
- If signs of shock persist after 40 ml/kg of fluid resuscitation, immediately give a third bolus of 20ml/kg of 0.9% Saline or 4.5% Human Albumin over 5-10 minutes and reassess immediately.
- There is now significant risk of pulmonary oedema, so elective tracheal intubation and mechanical ventilation should be initiated even if there are no signs of respiratory failure. This will optimise oxygenation, reduce the work of breathing, and improve cardiac function. Call for anaesthetist assistance for urgent tracheal intubation and mechanical ventilation and contact PICU.
- Invasive monitoring and central venous access will be required to guide fluid therapy and optimise support.
- Start inotropes to optimise tissue perfusion and improve myocardial function.

PRINCIPLES OF MANAGEMENT OF MENINGITIS WITH RAISED INTRACRANIAL PRESSURE

See algorithms Management of Meningococcal Disease in Children and Young People and Management of Bacterial Meningitis in Children and Young People.

The main objective in managing patients with RICP is to maintain oxygen and nutrient delivery to the brain. **Call for senior help and PICU immediately if there are signs of RICP**.

- Patients with GCS <9 or drop of 3 points in last hour, or fluctuating level of consciousness should have their airway secured by tracheal intubation and mechanical ventilation.
- Optimise ventilation to ensure normocapnia and avoid hypoxia. Cautious fluid resuscitation. Maintenance of circulating volume and adequate blood pressure is the goal. Overaggressive fluid resuscitation will exacerbate cerebral oedema. Only patients with shock require aggressive fluid resuscitation to ensure cerebral perfusion. Patients **without** shock require close monitoring and judicious fluid replacement depending on heart rate, blood pressure, urine output and metabolic acidosis.

Do not rely on CRT to guide fluid management as this may be falsely prolonged in patients with RICP. Rely instead on the other markers of organ perfusion and circulatory status as described.

Consider the use of mannitol or hypertonic saline for acute changes in RICP as suggested by pupillary changes or sudden onset hypertension and bradycardia.

Nurse patient in head-up position, 20-30 degrees from horizontal. Avoid inserting central venous lines into the internal jugular vein as this impedes venous drainage of the head and the insertion of the line may exacerbate RICP.

PUBLIC HEALTH

- Doctor immediately notifies any suspected case of meningitis or meningococcal sepsis by phone to the local Health Protection Team or on-call Public Health Specialist. This is the legal duty of the doctor who makes or suspects the diagnosis – usually the hospital doctor notifies even if the case was referred by a GP.
- After a single confirmed or probable (i.e. where MD is the most likely clinical diagnosis) case of MD, only close contacts living in the same household as the case in the 7 days before disease onset or kissing contacts need antibiotic prophylaxis[44].
- Healthcare staff only require prophylaxis if their mouth or nose has been splattered (clearly felt) with large particle droplets/secretions from the respiratory tract of a patient with confirmed or probable MD, or if conjunctivitis develops within 10 days of exposure[51]. This is unlikely to occur except when using suction during airway management, inserting an oro/nasopharyngeal airway, intubating, or if the patient coughs in your face. Healthcare workers should reduce the possibility of exposure by using face masks and using closed suction[45].
- Public Health arranges for prophylactic antibiotics to be prescribed to contacts as necessary. Ciprofloxacin and rifampicin are both licensed for use in preventing secondary cases of MD. Ciprofloxacin is now recommended due to a number of advantages, including the requirement of only a single dose and its recommended use in pregnancy[45]. Rifampicin interferes with the oral contraceptive pill and stains body fluids red, including urine and saliva, and permanently stains soft contact lenses. Some individuals may experience rash or stomach upset. Ceftriaxone and azithromycin are alternatives which may also be used for pregnant contacts.
- Antibiotic prophylaxis should eliminate carriage, but if the contact is already incubating the bacteria, he or she can still get the disease. Close contacts of a case need to understand that they are at increased risk of meningitis and sepsis, and should be alerted to the symptoms and given a leaflet on meningitis and sepsis.
- The local Health Protection Team will:
  - arrange for the next of kin to be interviewed to establish other close contacts and will arrange prophylaxis for them, and for later immunisation of all close contacts if indicated
  - ensure information is disseminated to appropriate local schools, work places and GPs
  - be responsible for early detection of clusters and outbreaks of disease.

The study which provided the clinical cases for this learning tool also collected data on the pre-admission symptoms of 448 children aged less than 17 years. Parents were asked to report the time the illness first started, the initial symptoms and all subsequent symptoms until hospital admission.

There has been very little information in the recent literature on this subject to guide doctors – published information about the development of symptoms generally relies on data collected from hospital patients. The results of this study provide the first description of the time course of the clinical features of MD in children and adolescents prior to hospital admission.

Recognition of MD can be difficult especially for doctors unfamiliar with the infection. Doctors may rely on the text book image of advanced MD or look for symptoms more often reported in adults like neck stiffness and photophobia. It also does not help that doctors, parents and the media call this disease meningitis and so the importance of sepsis is ignored or forgotten.

The full paper describing the pre-admission symptoms of the patients can be read in full in the Lancet[10]. A summary of the important findings is shown below.

CLINICAL FEATURES OF DISEASE

Table 1 (below) shows all the symptoms reported by parents and the median time it took for those symptoms to appear from the start of this illness. The children are grouped into 4 age bands as children within each age band have similar case fatality rates. The red lines in each column show the median time it took parents to take their child to a GP. From the figure it can be seen that it takes longer for older children to be taken to the doctor. This could be because their symptoms take longer to manifest or that their parents are less worried about them and respond less quickly.

EARLIEST SYMPTOMS

The earliest features were common to many self-limiting viral illnesses. Fever was the first symptom to be noticed in children aged under 5 years, headache in the older children and adolescents. Virtually all children (95%) developed fever at some point and most young children were miserable and irritable. Anorexia, nausea and vomiting were relatively early features at all ages, with many children also exhibiting upper respiratory symptoms (sore throat and coryza). This non-specific phase lasted for about 4 hours in younger children but as long as 8 hours in adolescents.

SEPSIS SYMPTOMS

The next symptoms to develop in all age groups were signs of sepsis and circulatory shut-down – limb pain, abnormal colour, cold extremities and, in older children, thirst. Parents of younger children also reported drowsiness and breathing

Section 6 Development of symptoms

Table 1: Median times of onset of clinical features of meningococcal disease prior to hospital admission.

Hours from onset	Age < 1 year	Median (IQR)*	Age 1 - 4 years	Median (IQR)	Age 5 - 14 years	Median (IQR)	Age 15 - 16 years	Median (IQR)
0 - 4	Fever	0 (0, 6)	Fever	0 (0, 3)				
	Miserable/irritable	0 (0, 7)			Headache	0 (0, 12)	Headache	0 (0, 2)
	Poor feeding	1 (0, 9)	Miserable/irritable	2 (0, 10)			Sore throat/coryza	0 (0, 9)
	Nausea/vomiting	1 (0, 11)	Nausea/vomiting	3 (0, 11)				
	Coryza	2 (0, 13)	Decreased appetite	3 (0, 13)	Nausea/vomiting Fever	2 (0, 12)	Thirst	4 (1, 39)
	Drowsy	4 (0, 14)	Drowsy	4 (0, 11)		3 (0, 13)		
5 - 8	Diarrhoea	5 (0, 9)			Abnormal colour	5 (0, 29)		
	Abnormal colour	5 (0, 18)	Leg pain	6 (0, 13)	Decreased appetite	6 (1, 17)		
	Breathing difficulty	5 (0, 19)			Thirst	6 (2, 16)	General aches	6 (0, 20)
	Leg pain	7 (0, 15)	Headache	6 (1, 17)	Sore throat/coryza	7 (0, 16)	Fever	6 (1, 16)
	Floppy tone	8 (1, 19)	Sore throat/coryza	7 (1, 19)	Leg pain	7 (0, 15)		
	Rash	8 (4, 18)	Breathing difficulty	7 (1, 17)	General aches	7 (1, 18)		
9 - 12				9 (3, 18)				
			Abnormal colour General aches	9 (4, 18)				
			Rash	9 (6, 18)				9 (3, 21)
			General aches	9 (4, 18)	Drowsy	9 (1, 21)	Decreased appetite	
			Seizure	9 (1, 18)				10 (3, 19)
			Diarrhoea	10 (6, 14)				
	Cold extremities	9 (1, 20)					Nausea/vomiting	
	General aches	9 (4, 22)						
					Miserable/irritable	12 (2, 22)		
			Cold extremities	11 (2, 17)	Confusion/delirium	12 (8, 24)	Leg pain Miserable/irritable	
			Confusion/delirium	11 (5, 17)				12 (5, 23)
			Neck stiffness Photophobia	11 (8, 17)				12 (3, 25)
				12 (6, 27)				
13 - 16	Photophobia	13 (5, 17)					Drowsy	14 (6, 27)
	Unconscious	15 (6, 17)			Cold extremities	13 (7, 26)	Breathing difficulty	15 (13, 17)
	Bulging fontanelle	15 (3, 20)	Floppy	13 (8, 20)	Rash	14 (8, 21)	Diarrhoea	16 (8, 26)
	Neck stiffness	15 (2, 27)			Neck stiffness	15 (6, 25)	Neck stiffness	16 (6, 30)
	Seizure	16 (14, 31)					Cold extremities	16 (6, 32)
17 - 20	Thirst	17 (7, 27)			Photophobia	17 (5, 39)	Photophobia	17 (5, 29)
							Abnormal colour	18 (4, 29)
							Rash	19 (11, 26)
21 - 24					Diarrhoea	22 (20, 25)		
			Unconscious	23 (17-42)			Confusion/delirium	23 (13, 30)
					Seizure	24 (9, 79)	Unconscious	24 (19, 41)
>24					Breathing difficulty	34 (10, 57)		
					Unconscious	34 (11, 52)	Seizure	26 (25, 27)

*Notes: * IQR = inter-quartile range.*

difficulty (usually described as rapid or laboured breathing) at this stage and occasionally diarrhoea.

Three symptoms were fairly frequent: cold extremities (35-47%), limb pain (31 -63% excluding infants) and abnormal colour (17-21%), usually described as pallor or mottling. Thirst, diarrhoea and breathing difficulty presumably also reflect sepsis but were less common.

RASH

The first classic symptom to emerge was rash, although at onset this was sometimes non-specific and only evolved to a petechial and then grossly haemorrhagic rash over a period of hours. Although it was the most common classic feature of disease it was certainly not always present. (see Table 2). In infants a haemorrhagic rash was present in less than half of cases by hospital admission. The rash was also not an early symptom occurring a median of 8 hours after the start of the illness in babies, 9 hours in 1-4 year olds, 14 hours in 5-14 year olds and 19 hours in the 15 and 16 year olds.

Table 2: Age-specific frequency of clinical features of meningococcal disease prior to hospital admission.

	<1 year %	1 to 4 years %	5 to 14 years %	15 to 16 years %
Early features				
Leg pain	5.1	30.6	62.4	53.3
Thirst	3.4	6.4	11.4	12.6
Diarrhoea	9.9	7.8	3.1	5.5
Abnormal colour	20.6	16.8	18.5	19.0
Breathing difficulty	16.2	9.7	7.1	12.1
Cold extremities	44.0	46.7	34.9	44.4
'Classic' features				
Haemorrhagic rash	42.3	64.2	69.8	65.9
Neck pain or stiffness	15.5	28.1	45.9	52.9
Photophobia	24.5	24.1	26.4	35.5
Bulging fontanelle	11.5	n/a	n/a	n/a
Late features				
Confusion or delirium	n/a	42.8	49.4	47.6
Seizure	8.9	12.8	7.8	7.3
Unconscious	7.0	9.1	5.9	15.1

Notes: 1. Percentages given are standardised to UK case-fatality - see text
2. Age-specific data on frequency of other symptoms are available from the authors.

SYMPTOMS OF MENINGITIS

Meningism was more common in older children, about half the children aged over 5 years had symptoms of meningism and half of these had photophobia. These are not reliable signs in children below 5 years of age.

The median time of onset of specific symptoms suggestive of meningitis (neck stiffness, photophobia, bulging fontanelle) was later, around 12-15 hours from illness onset. The very late stage signs (such as unconsciousness, delirium, or seizures) occurred at a median of 15 hours in infants, about 24 hours in older children.

Fig 1. Time course of development of symptoms.

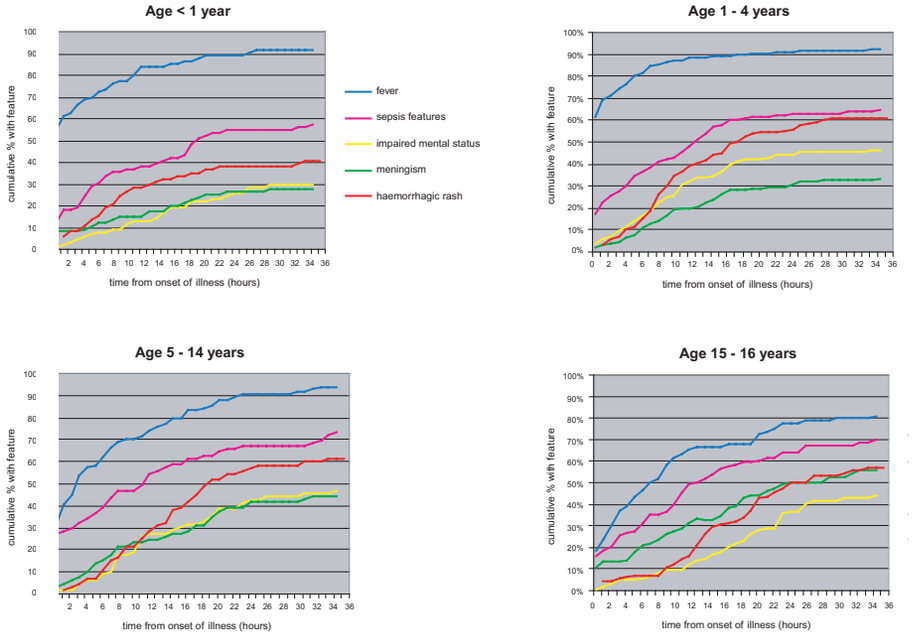


Figure 1 displays graphically by age group the proportion of children developing specific groups of symptoms over the 36 hours from onset of illness. It shows that few children develop new symptoms after 24 hours from onset. The order of progression at all ages is fever, sepsis symptoms and then the classic symptoms of haemorrhagic rash, impaired mental state and meningism. The slower progression of illness in the oldest children is clear; they are also the only age group in which meningism is an earlier and more frequent feature than haemorrhagic rash and impaired consciousness.

SUMMARY OF IMPORTANT POINTS

- Most children with MD will become ill enough to require hospital admission within 24 hours of the start of their symptoms. This means there is a narrow window for diagnosis and doctors must be aware of the early symptoms of meningococcal infection to maximise their opportunity to make the diagnosis.
- The symptoms children present with vary with increasing age.
- Younger children tend to be brought to hospital earlier in their illness.
- We have identified three important clinical features – limb pain, cold extremities and abnormal colour – which are early sepsis symptoms of MD in children and adolescents. We recognise that these symptoms may occur in other febrile illnesses and are not specific to MD, but doctors are urged to consider a possible diagnosis of MD whenever these symptoms are seen.
- The median times of onset of the early sepsis symptoms were within 7-12 hours. The parents of three-quarters (76.1%) of children identified one or more of these early symptoms before hospital admission. Fewer than 10% of children presented with the classic signs of meningism or impaired consciousness without parents having previously recognised a haemorrhagic rash, or other specific sign of sepsis.
- The rash of MD is not an early sign and may not always be present before hospital admission.
- The 'classic triad' of symptoms of rash, meningism and impaired consciousness generally occur later in the pre-hospital illness. Do not be reassured by the absence of these 'classic' features if you see a child within 12 hours of the start of their illness.

The order of progression at all ages is fever, sepsis symptoms and then the classic symptoms of haemorrhagic rash, impaired mental state and meningism.

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Section 7 Abbreviations

ABC	Airway, Breathing, Circulation
APLS	Advanced Paediatric Life Support
APTR	Activated partial thromboplastin time ratio
APTT	Activated partial thromboplastin time
AVPU	Alert, Voice, Pain, Unresponsive
BE	Base excess
BP	Blood pressure
BPM	Beats per minute
CNS	Central nervous system
CRP	C-reactive protein
CRT	Capillary refill time
CSF	Cerebrospinal fluid
CT	Computed tomography
CVS	Cardiovascular system
CXR	Chest x-ray
DIC	Disseminated intravascular coagulation
ECG	Electrocardiogram
ED	Emergency Department
EDTA	Ethylenediaminetetraacetic acid
ENT	Ear, nose and throat
ETT	Endotracheal tube
FBC	Full blood count
FFP	Fresh frozen plasma
GCS	Glasgow Coma Scale
GDG	Guideline Development Group
Hib	*Haemophilus influenzae* type b
HR	Heart rate
HSV	Herpes simplex virus
ICP	Intracranial pressure
INR	International normalised ratio
IO	Intraosseous
IV	Intravenous
LP	Lumbar puncture
MD	Meningococcal disease
MRF	Meningitis Research Foundation
NG	Nasogastric
NICE	National Institute of Health and Care Excellence
PCR	Polymerase chain reaction
PEEP	Positive End Expiratory Pressure
PHE	Public Health England
PICU	Paediatric Intensive Care Unit
PR	Prothrombin ratio
PT	Prothrombin time
RCPCH	Royal College of Paediatrics and Child Health
RICP	Raised intracranial pressure
RR	Respiratory rate
SIGN	Scottish Intercollegiate Guidelines Network
TB	Tuberculosis/tuberculous
TT	Thrombin time
URTI	Upper respiratory tract infection
WCC	White blood cell count

Notes

Management of Bacterial Meningitis in Children and Young People

Incorporates NICE Bacterial Meningitis and Meningococcal Septicaemia Guideline CG102. Distributed in partnership with NICE

Edition 2A

Meningitis Research Foundation

Endorsed by RCPCH Royal College of Paediatrics and Child Health — Leading the way in Children's Health

Meningococcal Disease Algorithm
www.meningitis.org

Symptoms and signs of bacterial meningitis?

YES

Check airway, breathing and circulation; gain vascular access

YES

Signs of raised intracranial pressure (RICP) or shock?

NO

Perform diagnostic tests BM1 Correct any dehydration

Contraindication to Lumbar Puncture? BM2

NO

Perform Lumbar Puncture
Do not await CSF results before starting antibiotics

YES

<3 months old?

YES

Empiric antibiotics for suspected meningitis
IV Cefotaxime + either Amoxicillin or Ampicillin (can replace Cefotaxime with Ceftriaxone if no contraindication BM3)
DO NOT DELAY ANTIBIOTICS

NO

Empiric antibiotics for suspected meningitis
IV Ceftriaxone unless contraindicated BM3
DO NOT DELAY ANTIBIOTICS

Add Vancomycin if recently overseas, or prolonged or multiple antibiotic exposure within last 3 months.

LP results available?

NO

YES

NO

Lumbar puncture suggests meningitis?
- In neonates (<28 days old), ≥ 20 cells/µl ■ In older children > 5 cells/µl or > 1 neutrophil/µl
(if lower cell count, still consider bacterial meningitis if other symptoms and signs suggest the diagnosis especially in neonates).

YES

NICE Fever in under 5s guideline CG160
www.nice.org.uk/guidance/cg160

- **Consider TB meningitis** If raised CSF WCC and risk factors for TB. If TB meningitis in differential diagnosis refer to NICE TB NG33 for appropriate antibiotic treatment
- **Consider Herpes simplex meningoencephalitis**. If HSV in differential diagnosis give Aciclovir.

Steroids: Dexamethasone 0.15 mg/kg to a max dose of 10 mg, qds x 4 days for children ≥ 3 months old IF ≤ 12h from first antibiotics and LP shows:
- frankly purulent CSF ■ CSF WCC > 1000/µl ■ raised CSF WCC and protein > 1 g/L ■ bacteria on Gram stain.

Steroids should not be used in developing countries.
If TB meningitis in the differential diagnosis, refer to NICE NG33 before administering steroids.

Reduced or fluctuating conscious level or focal neurological signs? BM4

YES

Perform CT Scan

NO

- Full-volume maintenance fluids: enteral feeds if tolerated or isotonic IV fluids e.g. 0.9% Saline or 0.9% Saline with 5% Glucose
- Do not restrict fluids unless there is evidence of increased anti-diuretic hormone secretion or RICP
- Monitor fluid administration, urine output, electrolytes and blood glucose
- See Meningococcal Disease Algorithm to treat seizures.

- Close monitoring for signs of Raised ICP, Shock & repeated review
Go to Meningococcal Disease Algorithm if signs are found and consult a paediatric intensivist, anaesthetist, or intensivist
- Perform delayed LP if no longer contraindicated BM2
- If LP contraindicated, perform delayed LP when no longer contraindications.

Antibiotics for confirmed meningitis
- Meningococcus: IV Ceftriaxone for 7 days
- *H influenzae*: IV Ceftriaxone for 10 days
- *S pneumoniae*: IV Ceftriaxone for 14 days, add Vancomycin if resistant strain.
- Group B Strep: IV Cefotaxime for ≥ 14 days
- *L monocytogenes*: IV Amoxicillin or Ampicillin for 21 days in total, plus IV Gentamicin for at least the first 7 days
- Gram-negative bacilli: IV Cefotaxime for ≥ 21 days (unless alternative directed by local antimicrobial resistance patterns or specific sensitivities)

Unless directed otherwise by antibiotic sensitivities. Duration may be dictated by clinical response – discuss with infectious disease specialist.

YES

Specific pathogen identified?

NO

Antibiotics for unconfirmed meningitis

<3 months old?

YES

NO

IV Cefotaxime (or Ceftriaxone unless contraindicated BM3) + either Amoxicillin or Ampicillin IV for ≥ 14 days.

IV Ceftriaxone for ≥10 days.

Notify public health, prophylaxis see MD11 on Meningococcal disease algorithm; Long-term management BM7

BM1 Diagnostic and other laboratory tests:
Take bloods for Blood gas (bicarb, base deficit), Lactate, Glucose, FBC, U&E, Ca++, Mg++, PO_4, Clotting, CRP, Blood cultures, Whole blood (EDTA) for PCR, X-match. Take Throat swab. If limited blood volume, prioritise blood gas, lactate, glucose, electrolytes, FBC, clotting.

BM2 Contraindications to Lumbar Puncture
- Clinical or radiological signs of raised intracranial pressure
- Shock
- After convulsions until stabilised
- Coagulation abnormalities
  - Clotting study results (if obtained) outside the normal range
  - Platelet count below 100 x 10^9/L
  - on Anticoagulant therapy
- Local superficial infection at LP site
- Respiratory insufficiency.

Perform delayed LP in children with suspected bacterial meningitis when contraindications no longer present

BM3 Contraindications to Ceftriaxone
Premature neonates with corrected gestational age < 41 weeks and other neonates <1 month old, particularly those with jaundice, hypoalbuminaemia, or acidosis; or receiving concomitant treatment with intravenous calcium.

BM4 Indications for CT scan in children with suspected bacterial meningitis
CT scan cannot reliably detect raised intracranial pressure. This should be assessed clinically.
Perform a CT scan to detect other intracranial pathologies if GCS ≤8 or focal neurological signs in the absence of an explanation for the clinical features.
Do not delay treatment to undertake a CT scan.
Clinically stabilise the child before CT scanning.
Consult a paediatric intensivist, anaesthetist, or intensivist.

BM5 Indications for tracheal intubation and mechanical ventilation
Threatened or actual loss of airway patency (e.g. GCS <9, response to pain only).
- Need for any form of assisted ventilation e.g. bag–mask ventilation.
- Clinical observation of increased work of breathing
- Hypoventilation or Apnoea
- Features of respiratory failure, including
  - Irregular respirations (e.g. Cheyne–Stokes breathing)
  - Hypoxia (saturation <94% in air, PaO_2 < 13 kPa or 97.5mmHg), hypercapnoea ($PaCO_2$ > 6 kPa or 45 mmHg)
- Continuing shock following 40ml/kg of resuscitation fluid
- Signs of raised intracranial pressure
- Impaired mental status
  - GCS drop of ≥ 3, or score <9, or fluctuation in conscious level
  - Moribund state
- Control of intractable seizures
- Need for Stabilisation for brain imaging or for transfer to PICU.

Should be undertaken by a health professional with expertise in paediatric airway management, Consult PICU. (See MD4)

BM6 Repeat LP in neonates after starting treatment if:
persistent or re-emergent fever, new clinical findings (especially neurological findings), deteriorating clinical condition, or persistently abnormal inflammatory markers

BM7 Long-term management: Before discharge consider need for after care, discuss potential long-term effects with parents, arrange hearing test. Refer children with severe or profound deafness for cochlear implant assessment ASAP. Use MRF discharge checklist **http://www.meningitis.org/assets/x/55764.** Provide 'Your Guide' and direct to meningitis support organisations **www.meningitis.org/recovery** or **www.meningitisnow.org/recovery.** Offer further care on discharge as needed. Paediatrician to review child with results of their hearing test 4-6 weeks after discharge from hospital considering all potential morbidities and offer referral. Inform GP, health visitor or school nurse.

Based on NICE CG102 www.nice.org.uk/guidance/CG102
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MD1 Estimate of child's weight (1–10 yrs)
Weight (kg) = 2 x (age in years + 4)

MD2 Observe HR, RR, BP, perfusion, conscious level
Cardiac monitor & pulse oximetry.

Conscious Level	Normal Values			
Alert	Age	RR/min	HR/min	Systolic BP
Responds to **V**oice	Birth	25-50	120-170	80-90
Responds to **P**ain	3 m	25-45	115-160	80-90
Unresponsive	6 m	20-40	110-160	80-90
	12 m	20-40	110-160	85-95
	18 m	20-35	100-155	85-95
	2 y	20-30	100-150	85-100
	3 y	20-30	90-140	85-100
	4 y	20-30	80-135	85-100
	5 y	20-30	80-135	90-110
	6 y	20-30	80-130	90-110
	8 y	15-25	70-120	90-110
	12 y	12-24	65-115	100-120
N.B. Low BP is a pre-terminal sign in children	>14 y	12-24	60-110	100-120

MD3 Take bloods for Blood gas (bicarb, base deficit), Lactate, Glucose, FBC, U&E, Ca++, Mg++, PO_4, Clotting, CRP, Blood cultures, Whole blood (EDTA) for PCR, X-match. Take Throat swab. If limited blood volume, prioritise blood gas, lactate, glucose, electrolytes, FBC, clotting.

MD4 Intubation (call anaesthetist and consult PICU) see **BM5**
Consider using: Atropine 20 mcg/kg (max 600 mcg) AND Ketamine 1-2 mg/kg in shock or Thiopental (thiopentone) 3-5 mg/kg in RICP AND Suxamethonium 2 mg/kg (caution, high potassium). ETT size = age/4 + 4, ETT length (oral) = age/2 + 12 (use cuffed ETT tube if possible). Then: Morphine (100 mcg/kg) and Midazolam (100 mcg/kg) every 30 min.

MD5 Inotropes
Dopamine at 10-20 mcg/kg/min. Make up 3 x weight (kg) mg in 50 ml 5% dextrose and run at 10 ml/hr = 10 mcg/kg/min. (These dilute solutions can be used via a peripheral vein).
Start Adrenaline via a central or IO line only at 0.1 mcg/kg/min.
Start Noradrenaline via a central or IO line only at 0.1 mcg/kg/min. for 'warm shock'.
Adrenaline & Noradrenaline: Make up 300 mcg/kg in 50 ml of normal saline at 1 ml/hour = 0.1 mcg/kg/min.

MD6 Hypoglycaemia (glucose < 3 mmol/l) 2 ml/kg 10% Dextrose bolus IV.

MD7 Correction of metabolic acidosis pH < 7.2
Give half correction bicarb IV.
Volume (ml) to give = (0.3 x weight in kg x base deficit ÷2) of 8.4% bicarb over 20 mins, or in neonates, volume (ml) to give = (0.3 x weight in kg x base deficit) of 4.2% bicarb.

MD8 If K+< 3.5 mmol/l
Give 0.25 mmol/kg over 30 mins IV with ECG monitoring.
Central line preferable. Caution if anuric.

MD9 If total Calcium < 2 mmol/l or ionized Ca_{++}< 1.0
Give 0.1 ml/kg 10% $CaCl_2$ (0.7 mmol/ml) over 30 mins IV (max 10 ml) or 0.3 ml/kg 10% Ca gluconate (0.22 mmol/ml) over 30 mins IV (max 20 ml). Central line preferable.

MD10 If Mg++< 0.75 mmol/l
Give 0.2 ml/kg of 50% $MgSO_4$ over 30 mins IV (max 10 ml).

MD11 Urgently **notify** public health of any suspected case of meningitis or meningococcal disease
Prophylaxis of household contacts of MD (goo.gl/1NTbck)
- Preferred: Ciprofloxacin single dose <5yrs 30 mg/kg up to max 125 mg; 5-12yrs 250 mg; >12yrs 500 mg or
- Rifampicin bd for 2 days: <1yr 5 mg/kg; 1-12yrs 10 mg/kg; >12yrs 600 mg *or*
- Ciprofloxacin, ceftriaxone *or* azithromycin may be used for pregnant and breast-feeding contacts of cases

For index case not treated with Ceftriaxone, prophylaxis when well enough.
Hib: prophylaxis may be indicated – consult public health

MD12 Antibiotics for confirmed and unconfirmed (but clinically suspected) meningococcal disease: IV Ceftriaxone for 7 days unless contraindicated **BM3** (see bacterial meningitis algorithm for antibiotics against other pathogens)

Based on Early Management algorithm, Dost Paediatrics, Imperial College at St Mary's Hospital as described in Arch Dis Child 1990;80:290 & 2007;92:283 & on NICE CG102
www.nice.org.uk/guidance/cg102
Authors AJ Pollard (GDG chair), A Ceske, SN Faust, L Glennie, C Haines, PT Heath, JS Kroll, M Levin, I Maconochie, S McQueen, P Monk, S Nadel, N Ninis, MP Richardson, MJ Thompson, AP Thomson, D Turner.
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Management of Meningococcal Disease in Children and Young People

Incorporates NICE Bacterial Meningitis and Meningococcal Septicaemia Guideline CG102. Distributed in partnership with NICE

Edition 8A

Meningitis Research Foundation

Endorsed by RCPCH Royal College of Paediatrics and Child Health — Leading the way in Children's Health

RECOGNITION

May present with predominant **SEPTICAEMIA (with shock), MENINGITIS (with raised ICP)** or **both. Purpuric/petechial non-blanching rash is typical.**
Some may have neither shock nor meningitis. Rash may be atypical or absent in some cases.

Call consultant in Emergency Medicine, Paediatrics, Anaesthesia or Intensive Care
Initial assessment looking for shock/raised ICP
Do not perform Lumbar Puncture yet

Give IV Ceftriaxone (80 mg/kg od) without delay **BM3**
Do not use Ceftriaxone at the same time as calcium-containing solutions: in this situation use Cefotaxime (50 mg/kg qds)

SIGNS OF SHOCK? MD2
- Tachycardia
- Capillary refill time > 2 seconds
- Cold hands/feet; pale or blue skin
- Respiratory distress/ oxygen saturation <95% in air
- Altered mental state/decreased conscious level
- Decreased urine output (<1 ml/kg/hr)
- Hypotension (late sign)
- Hypoxia on arterial blood gas
- Base deficit (worse than -5 mmol/l)
- Increased lactate (>2 mmol/l)

NO

YES

Do not perform Lumbar Puncture; Nil by mouth

- ABC & High flow Oxygen (minimum 10 l/min) by face mask
- Insert 2 large IV cannulae (or IO); Take bloods, see **MD3**
- Take blood gas (including lactate). Measure glucose.

VOLUME RESUSCITATION
- Immediate bolus of 20 ml/kg of 0.9% Saline over 5-10 minutes and reassess immediately
- If shock persists immediately give second bolus of 20 ml/kg of 0.9% Saline or of 4.5% Human Albumin over 5-10 minutes and reassess immediately
- Observe closely for response/deterioration
- Consider Urinary catheter to monitor output

After **40 ml/kg fluid** resuscitation – **STILL SIGNS OF SHOCK?**

NO — Repeated review

YES

WILL REQUIRE URGENT ELECTIVE INTUBATION AND VENTILATION MD4
D/W Paediatric intensivist and Call anaesthetist
- Immediate bolus of 20 ml/kg of 0.9% Saline or 4.5% Human Albumin over 5-10 minutes and reassess immediately; Continue boluses if necessary with repeated clinical and laboratory assessments including blood gas measurements. Fluid resuscitation should be guided by lactate, tachycardia, perfusion, hypoglycaemia to avoid fluid overload and determine need for inotropes.
- Start peripheral inotropes (Dopamine); if IO access start Adrenaline **MD5**
- ET Tube (Cuffed if possible) and CXR
- Anticipate pulmonary oedema ensure adequate PEEP (≥5cm H_2O)
- Central venous access
- Urine catheter to monitor urine output
- Start Adrenaline infusion (central) if continuing need for Volume resuscitation & Inotropes
- For warm shock: warm peripheries, bounding pulses and low diastolic pressure, give Noradrenaline (central)

Anticipate, monitor and correct:
- Hypoglycaemia **MD6**
- Acidosis **MD7**
- Hypokalaemia **MD8**
- Hypocalcaemia **MD9**
- Hypomagnesaemia **MD10**
- Anaemia
- If bleeding or performing invasive procedure (i.e.central line insertion) treat coagulopathy with FFP/Cryoprecipitate/platelets

RAISED INTRACRANIAL PRESSURE?
- Reduced or fluctuating level of consciousness (GCS <9 or a drop of 3 or more)
- Relative Bradycardia and Hypertension
- Focal neurological signs
- Abnormal posture or posturing
- Seizures
- Unequal, dilated or poorly responsive pupils
- Papilloedema (late sign)
- Abnormal 'doll's eye' movements

YES

Do not perform Lumbar Puncture; Nil by mouth

- ABC & High flow Oxygen (minimum 10 l/min) by face mask
- Insert 2 large IV cannulae (or IO); Take bloods, see **MD3**
- Take blood gas (including lactate). Measure glucose.
- Give 0.25g/kg bolus of 20% Mannitol or 3ml/kg Hypertonic Saline (3% or 2.7% as available) over 5 minutes
- Treat shock if present

Call anaesthetist and contact PICU
- Intubate and ventilate to control $PaCO_2$ (4–4.5 kPa)
- Urinary catheter and monitor output, NG tube

Do not perform Lumbar Puncture

NEUROINTENSIVE CARE
- 30° head elevation, midline position
- Avoid internal jugular lines
- Repeat Mannitol or hypertonic Saline (3% or 2.7% as available) if indicated
- Sedate (muscle relax for transport)
- Cautious fluid resuscitation (but correct coexisting shock)
- Monitor pupillary size and reaction
- Avoid hyperthermia
- Once patient is stabilised, consider CT scan to detect other intracranial pathology if GCS<9, fluctuating conscious level or focal neurological signs

Do not restrict fluids unless there is evidence of:
- raised intracranial pressure, or
- increased antidiuretic hormone secretion

STEPWISE TREATMENT OF SEIZURES
- IV Lorazepam (0.1 mg/kg) or Midazolam (0.1 mg/kg) bolus
- Consider Paraldehyde (0.4 ml/kg PR)
- Phenytoin (18 mg/kg over 30 min IV with ECG monitoring)

If persistent seizures:
- Thiopental (thiopentone) 4 mg/kg in intubated patients (beware of hypotension)
- Midazolam/Thiopental infusion

Perform delayed LP when stable and no contraindications

GO TO BACTERIAL MENINGITIS ALGORITHM

Bacterial meningitis algorithm
www.meningitis.org

YES

NO

CLINICAL FEATURES OF MENINGITIS?

NO

Take bloods, see **MD3**
Close monitoring for signs of
- Raised ICP
- Shock

Perform LP if no contraindication
DO NOT DELAY ANTIBIOTICS

Repeated Review
Children with MD can deteriorate rapidly.
Deterioration detected?

Transfer to Intensive Care by Paediatric Intensive Care Retrieval Team

Notify public health, prophylaxis see; MD11 Long-term management: see BM7 on Bacterial Meningitis Algorithm

Section 7 Acknowledgements

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How Meningitis Research Foundation can help

For information and support call our free helpline

UK **080 8800 3344**

Ireland **1800 41 33 44**

helpline@meningitis.org

www.meningitis.org

Our vision is for a world free from meningitis and septicaemia. That's why we fund research into the prevention, detection and treatment of the diseases, promote education and awareness amongst the public and health professionals, and provide support to those affected.

Our Helpline staff respond to calls from people who want help and information. An interpretation service is available if required.

NICE and SIGN guidelines also advise doctors to signpost patients and their families to meningitis charities for support and information.

Head office

Bristol
Tel 0333 405 6262
info@meningitis.org

Offices also in Edinburgh, Belfast and Dublin.

We can help by providing the following:

- **Your Guide** provides in-depth information for parents about recovery and potential after effects of meningitis and septicaemia.
- **My Journal** is a place for parents and children to keep a personal record of the illness and their recovery, available online.

Your Guide and My Journal have been produced jointly with Meningitis Now.

- **Neonatal e-Tool** with an accompanying algorithm detailing the management of bacterial meningitis in infants <3 months. These arose from MRF-funded research which identified delays in treatment and national differences in management of bacterial meningitis in young infants. CPD credits are available on completion of the eTool, available at neonatal.meningitis.org.
- **Vital Signs** cards for front line nurses to aid in the early recognition of meningitis and sepsis.
- **Algorithms** at the back of this handbook detailing the management of bacterial meningitis and meningococcal disease are also available as posters.

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