

What are the useful clinical features of bacterial meningitis found in infants and children?

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The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at:

http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: *What are the useful clinical features of bacterial meningitis found in infants and children?*

The WHO Pocketbook of Hospital Care for Children states that the following are indicative of Bacterial meningitis (BM) in children: "A history of; vomiting, inability to drink or breastfeed, headache or pain in the back of the neck, convulsions, irritability, recent head injury. On examination; a stiff neck, repeated convulsions, lethargy, irritability, bulging fontanelle, a petchial rash or purpura, evidence of head trauma and signs or raised intracranial pressure i.e. unequal pupils, rigid posture, focal paralysis, irregular breathing[1]".(Pocketbook Ch 6.3, pg 148)

INTRODUCTION

Bacterial Meningitis (BM) is a serious illness in which the dural layers of the central nervous system become infected and inflamed. Each year it claims many lives and is associated with a high incidence of disability and long term health implications[2]. Mortality levels of 5% are recorded in children in the developed world[2], but these rise to approximately 30% in the developing world[2],[3].

Hib vaccination programmes have almost eradicated H. Influenzae meningitis in the Western world and pneumococcal and meningococcal vaccines have been recently developed[2]. Bacterial meningitis may soon be nearly eradicated in some countries but in the developing world vaccination programmes are still patchy and bacterial meningitis is likely to be a significant cause or morbidity and mortality for years to come. Hence the correct interpretation of the clinical features of BM still plays a critical role in the management of the disease particularly in the developing world.

METHODOLOGY

Electronic searches were carried out using PubMed, the Cochrane Library, Medline, Embase and Global Health from 1966 to present. 874 abstracts were identified and read. 11 prospective cohort studies of children with suspected BM and 4 retrospective cohort studies of children with confirmed BM in developing countries were reviewed. All articles were appraised using criteria defined by the Scottish Intercollegiate Guidelines Network[4]. A quality assessment was performed using the

levels of evidence recommended by the Oxford Centre of Evidence Based Medicine[5].

RESULTS AND DISCUSSION

1. Fever is the single most common presenting complaint for patients with BM. Fever is a sensitive indicator in children over the age of one (35-97%[3],[6-11],[13],[15],[17],[23], mean 83%) but as would be expected of a single physical finding common to many disorders it has a low specificity and is only reported in four studies (mean 44.5% range 23-73%[3],[13],[15],[17]). Twelve cohort studies reported fever and all failed to demonstrate that elevated temperature alone was a statistically significant indicator of BM[3],[6-11],[13],[15],[17],[23]. Fever is less frequent in infants (1-12 months of age) with a mean sensitivity of 67.8%[6],[10],[14] although fever can also be absent in older children. Reporting of fever across the studies was variable; in addition none of the studies recorded the length of time from onset of illness to assessment which makes it difficult to assess fever as an early indicator of BM.

2. Seizure is a reasonably specific sign of BM (range 53-94%[3],[13],[17] mean 88.5% only reported in 3 studies), but lacks sensitivity (range 11-83%[3],[6-11],[13-17] mean 55%). Two studies stated that seizure is only a reliable predictor of BM outside the febrile convulsion age range [6 months to 6 years]10,11 or if the seizure is focal (RR= 3.49 [1.02-11.87][10],[11], and it is therefore argued that routine lumbar puncture or empirical treatment for meningitis after apparently uncomplicated febrile convulsion alone is unjustified[1],[10],[11]. Studies that focused on meningococcal meningitis reported lower frequency of seizures[11],[12]. There is a wide discrepancy in the prevalence of the sign between the studies and it is a difficult sign to evaluate because cerebral malaria complicates some of the studies, therefore the results should be treated with caution.

3. Altered Consciousness ranging from confusion to coma has a mean sensitivity of 47% and specificity of 69%. Again there is a broad range of results (20-98% sensitive[3],[6],[7],[11],[13-17] and 76-98% specific[3],[13],[17]), which makes it difficult to rely on the stated figures. This range of findings can be partly explained by the different methods used between the studies to assess consciousness. Some studies use standard scales such as the Glasgow or Blantyre Coma scale and others use more descriptive terms as 'unrousable' or 'lethargic'[11],[19],[20]. According to one study older children are more likely to present with coma than young children or infants, and it is suggested that this is because parents consult earlier with unwell infants than older children.[6]The lack of consensus in results highlights the need for research using standardised methods for assessing consciousness such as the Glasgow Coma Scale or AVPU score. Altered consciousness is the final common pathway

for many illnesses and needs rapid assessment and treatment. The sign is most useful in diagnosing BM when seen in combination with other signs and symptoms.

4. Meningeal Signs include neck stiffness, Brudzinski's sign, Kernig's sign and in infants a bulging fontanelle. These are considered the most specific of meningeal signs. Considering the signs of meningeal irritation have been in use for over 100 years, assessment of their accuracy has been limited. A well designed prospective study is necessary to definitively establish the accuracy of meningeal signs. Neck stiffness was reported as 15-88% sensitive[3],[6],[8-11],[16],[17] and 81-98% specific[3],[17]. Molyneux et al found that neck stiffness became a more predominant feature with age with; 44% of infants, 63% 1-5-year olds and 86% of children older than 5 years affected and this is supported by Salih et al who found the absence of neck rigidity at diagnosis was significantly associated with young age (<2 months) ($p=0.05$)[11]. One study reported that neck stiffness was less frequently reported by parents than was found on examination of a child, 56% compared to 88% ($p<0.001$)[11]. It is essential therefore to thoroughly examine for the sign if there is any suspicion of BM. Brudzinski's sign[8] was only reported in one study by Chotpitayasundh who found it to be 75% sensitive and Kernig's sign was reported in to be 73% sensitive in children older than one year[6]. Bulging fontanelle has a sensitivity of 16-70%[3],[6],[8],[9],[13],[15],[17] and a specificity of 83-98%[3],[17] for children under the age of one. It is not a sign recorded in older children. More than 80% of BM occurs in the first year of life[14] and infants often have ambiguous signs so bulging fontanelle is a valuable sign for this age group.

5. Respiratory Tract Infection (RTI) coincides with laboratory samples positive for *H. influenzae*[1],[15],[18] in two studies. Akpede et al found 40.6%[14] and Chotpitayasundh et al found 50.1%[8] of patients to have upper RTI. Berkley 2004 reported chest signs frequently with respiratory distress in 27% (CLR 1.11), and crepitations in 17% (CLR 1.1) of patients but found no statistical evidence that these signs, compatible with lower respiratory tract infection are good predictors of BM[13]. Chest in-drawing was present in 34% of participants in Lehmann et al's study (OR 0.4 [0.3-0.7])[3]. However, Weber et al produced results contrary to the above reporting upper RTI to be a negative predictor of BM[17]. This is probably because children who were admitted with respiratory symptoms in Weber's study had been vaccinated against Hib making it unlikely that respiratory illnesses caused by Hib would lead to BM[17].

6. Gastrointestinal Abnormalities were reported in a number of studies. Vomiting was observed as a common symptom in a number of studies: occurring in 40-70% of patients[7],[8],[14-16],[18]. Diarrhoea is reported by Akpede et al to affect 41.5%[14] and by Berkley et al to affect 28% (CLR 0.39 ALR 0.41) of patients[16]. Other studies found approximately 25% of patients with BM to have co-existing diarrhoea[8],[11]. Diarrhoeal symptoms and malnutrition are associated with salmonella meningitis with 67% presenting with diarrhoea compared to 48% in patients with BM caused by other infective agents ($p=0.05$)[6].

7. Rash There is a paucity of data on the value of rash as the presenting sign in BM. Petechiae/ ecchymosis was only reported in one study, it was highly sensitive 98% and specific 100%[15] but these results came from a small cohort of patients. In the other study that discussed rash four children with BM presented with papular lesions but none had the purpuric rash associated with high mortality in BM[11]. The lack of evidence makes it difficult to draw any conclusions nevertheless any child

presenting with a non blanching rash needs careful investigation.

8. Lack of signs were reported in some studies where children had a diagnosis of BM based on findings from lumbar puncture and blood culture but who presented with no clinical signs. Pulickal et al reported 40% of patients lacking signs[10]. Akpede et al found that 30.3% patients lacked signs ($p<0.001$)[15]. One study found the majority without clinical signs to be under the age of two years (80% <2 $P=0.005$)[14]. It is important to recognise that young children have ambiguous signs of illness so there is a risk of under diagnosis if undue reliance is placed on clinical signs. However this does not mean that examination should be any less thorough because missing the signs of bacterial meningitis has severe consequences.

9. Combined signs Only three prospective studies, Weber et al 2002, Berkley et al 2004 and Akpede et al 1994, looked at the diagnostic value of symptoms in combination. Weber uses the signs specified by the WHO-IMCI (Integrated Management of Childhood Illness) to produce a model that is 98% sensitive and 72% specific[17]. Weber also produced a model based on all independent predictors of BM producing a model which is 96% sensitive and 52% specific[17] and of particular interest is the negative predictive value of >99% in these combination models; children without any of the identified signs were unlikely to have BM[17]. Berkley et al also tested the WHO-IMCI model finding it to be 85% sensitive and 59% specific and then combined the following independent signs of BM; bulging fontanelle, neck stiffness, cyanosis, seizure (outside febrile seizure age range) partial seizure, impaired consciousness, fever (excluding malaria or parasitaemia) and found the model to be 79% sensitive and 80% specific[13]. Akpede et al found infants with a triad of symptoms; seizure, fever and meningeal irritation to be highly discriminatory for BM (RR 4.22, 1.48-12.54 χ^2 9.93 $p=0.002$)[14].

CONCLUSION

BM is a serious illness that is responsible for considerable morbidity and mortality, particularly in the developing world. No single clinical feature emerges as sufficiently distinctive to make a robust diagnosis of BM. However, across the sixteen studies, fever, seizures, meningeal signs and altered consciousness are consistently associated with BM. This supports the advice given in the WHO Pocket Book of Health Care for Children and even when these signs are seen in isolation they should alert practitioners to the possibility of BM. The evidence available suggests that when signs are observed in combination, they provide a discriminatory screening tool which is both sensitive and specific.

An awareness of these key clinical signs, combined with a thorough history and examination, can identify a large proportion of children with BM. However, the serious consequences of missed diagnosis, the prevalence of malaria (a disease that can mimic BM) and the possibility of absent signs in infants and young children should urge caution. In such circumstances a strong case can be made for a high index of suspicion and routine use of lumbar puncture and empirical treatment when there is any doubt of diagnosis.

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