# CLINICAL DIAGNOSIS AND INVESTIGATION OF BACTERIAL MENINGITIS IN ADULTS

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## INTRODUCTION

Bacterial meningitis constitutes a medical emergency and continues to engender serious anxiety in sufferer, carer and relative alike. Meningococcal disease, in either its meningitic or septicaemic form, accounts for the vast majority of adult cases of meningitis in the UK. There have been significant advances in the understanding of the pathogenesis of this condition over the last decade. The mortality rate in adults, however, has remained relatively unchanged over the last 20 years at 5% for the purely meningitic presentation and 15-40% for those with meningococcal sepsis/septicaemia with or without meningitis. The British Infection Society has recently published a consensus statement on the management of this frightening condition and it is appropriate that the College addresses this topical subject.[1]

## DIAGNOSIS IN PRIMARY CARE

The rapidity of development of severe clinical illness determines the continued need for vigilance with regard to the potential diagnosis of meningitis and for urgent treatment of the condition. The Department of Health in the UK has issued the directive that any case of suspected meningitis should be given antibiotics, preferably parenterally at the earliest opportunity,[2] by the diagnosing physician. Hence the recommendation that GPs should administer '1200mg benzylpenicillin without delay ideally by the intravenous route'.[1]

To hospital clinicians, the recognition of acute meningitis may appear a relatively straightforward procedure. Critical analysis of the literature, however, demonstrates a lack of data on the presentation of meningococcal disease in primary care settings. Most reports detail findings at the time of hospital presentation and are composed of retrospective case record reviews. Table 1 shows presenting symptoms from a recent study in Iceland.[7] Attempts have been made to identify, through meta analysis of these reports, discriminatory features for meningitis.[3,4] Combinations of symptoms and signs including fever, vomiting and neck stiffness suggest serious disease, but taken individually they are poor discriminators for meningitis.[4] The lack of fever, neck stiffness and altered mental state have been suggested to effectively exclude meningitis,[3] however the quality of retrospective studies used in such analyses remains a considerable concern. Generally clinical signs lack both sensitivity and specificity in the diagnosis of meningitis, particularly at the extremes of age.[5] Recently only one study has detailed the presentation in general practice. The primary care physician must therefore maintain a high index of suspicion for possible meningitis, being aware of the need to follow febrile cases with no clear diagnosis and to consider action in the form of administration of antibiotics and urgent hospital admission if concern continues. The most important symptoms/signs remain the combination of fever, neck stiffness, vomiting and clouding of consciousness without other obvious cause.

Table 1
Clinical signs and symptoms in 1,332 adults with community acquired bacterial meningitis in Iceland.

| Clinical sign/symptom | Percentage affected |
|---|---|
| • Fever (>38°C) on admission | 97 |
| • Fever > one day | 12 |
| • Neck stiffness | 82 |
| • Abnormal mental states | 66 |
| - confused or lethargic | 45 |
| - only responsive to pain | |
| - unresponsive to pain | 11 |
| • Triad of fever, neck stiffness, impaired consciousness | 51 |
| • Seizures | 10 |
| • Rash, petechial, purpuric/ ecchymotic or maculopapular | 52 |

## INDICATIONS FOR HOSPITAL ADMISSION

Urgent hospital admission is mandatory in any adult who may have meningitis. The recent working party recommendation advises this in any patient with one or more of the following:

- signs of meningeal irritation
- impaired conscious level
- petechial or purpuric rash
- febrile or unwell and suffered a recent fit
- any illness, especially headache, or any of the above in contacts of established cases of meningitis.[1]

The lack of rash, particularly a petechial or purpuric one, does not exclude meningitis. Forty-eight percent of cases in the Icelandic study[7] and 60% in a recently published British review did not have rash present at admission.[8]

Neck stiffness has been reported as absent in 18% of cases and this feature often indicates more severe disease of the septicaemic form.

Papilloedema was recorded present in 4% of cases in the cited study. Cranial nerve palsies occur reasonably frequently in 10-30% of cases, and seizures have been recorded in approximately 30% of cases.

## IMMEDIATE INVESTIGATION OF CASES

The potential for rapid deterioration in possible meningitis cases requires that admitting teams are able to react rapidly and decisively on admission of a case. By necessity a clinical diagnosis must be made and acted upon, and appropriate and safe investigations undertaken that will hopefully confirm the diagnosis and guide further management during the subsequent course of the illness.

It is recommended[1] that on arrival blood should be taken for:

- blood culture
- coagulation studies
- routine renal, hepatic and haematological assessment
- a throat swab, and samples from a purpuric lesion should be sent for microscopy and culture[9]
- an appropriate sample should be taken at the time of first blood sampling for polymerase chain reaction studies.

Thereafter, and without further delay, empirical antibiotic therapy should be commenced.*

It is appropriate that the consultant with responsibility for the patient's management is notified of the admission and the Consultant in Communicable Disease Control (CCDC) contacted without delay. Prophylaxis of close contacts and community contacts should be coordinated by the CCDC and admitting clinicians should apply themselves to the management of the acute case.[10,11]

### INDICATIONS FOR LUMBAR PUNCTURE

Essentially, meningitis is by definition a pathological diagnosis, determined by the presence of abnormal cellular pleocytosis and biochemistry of the Cerebrospinal Fluid (CSF). A lumbar puncture (LP) to obtain CSF is therefore a very important diagnostic test in this condition. Two to three decades ago LP was standard practice in the management of suspected meningitis. The potential danger of mid-brain and cerebral herniation in the presence of raised intra-cranial pressure has, however, been well documented[12] and has led to the strong recommendation that LP should be avoided in the presence of any signs of raised intracranial pressure, deteriorating conscious level or focal neurological signs.[1] In these circumstances management must be guided by clinical parameters.[3] A normal CAT scan in these circumstances may allow safe LP to be performed; however it must be recognised that this does not rule out the risk of complications completely.[13]

The advantages of LP are in the pathological confirmation of the diagnosis, the isolation of the causative pathogen and the considerable epidemiological benefit that such information brings. The recommendation that prior antibiotics be given to all suspected cases of meningitis has significantly reduced the likelihood of isolation of the causative pathogen. Two published retrospective studies concluded that the microbiological aetiology would have remained unconfirmed in 48-63% of cases with clinical meningitis if blood culture alone was relied upon for pathogen isolation;[7,14] one further study indicated even lower rates of culture positivity.[29] Prior antibiotics should not contraindicate attempt at LP. CSF PCR in this situation can be positive when CSF is culture negative (see below).[15] The availability of vaccines against group A and C meningococcal disease and the introduction of the very effective Group C conjugate vaccine gives added urgency to the need for rapid and accurate demonstration of the causative organism in order that appropriate prophylactic policy decisions may be made by the CCDC or designated officer. The public reaction to a case of meningitis only adds to this stress. LP is a potentially dangerous investigation whose benefits are nevertheless calculated to outweigh its disadvantages in the management of cases of meningitis. The caveat remains that the procedure should never be undertaken when clear contraindication exists or where the patient is shocked and requires immediate resuscitation such that valuable time would be lost in the care of the case by undertaking the test. The additional recommendation of the BIS working party[1] that LP is unnecessary if the patient has a 'confident clinical diagnosis of meningococcal infection with a typical meningococcal rash' recognises that valuable epidemiological information may be lost if this advice is followed. The responsible clinician must be prepared to make a careful clinical judgement in each individual case and this should be endorsed in cases of difficulty by the consultant with overall responsibility for the case. Whatever course of action is followed antibiotic therapy must be administered as soon as the diagnosis is suspected, and must never be delayed in order to allow LP to take place.[1] Serial LPs are only ever indicated when there is unsatisfactory clinical progress or serious doubt arises as to the accuracy of the initial diagnosis. Every LP must be deemed to be safe by the exclusion of contraindications before it is undertaken. LP is thus useful to make and confirm the diagnosis of bacterial meningitis and may enable informed review of antibiotic therapy when sensitivities are available. It remains a very useful source of epidemiological information if organisms are recovered. The increasing use of PCR may replace LP/CSF examination in the future, but the reliability of molecular techniques has not yet become sufficient to allow this at present.

### USE OF CT SCANNING IN MENINGITIS

CT scanning should not be seen as a routine emergency investigation in suspected bacterial meningitis.[16] It has a role as a 'pre LP' investigation in those with evidence of focal neurology, depressed conscious level, seizures or papilloedema.[17] However it should be noted that a normal CT scan does not completely negate the risk of coning post LP.[13] There are no CT features pathognomonic of bacterial meningitis but abnormalities can be seen reflecting complications such as cerebral collections or abscess formation. Recent evidence has demonstrated the need for clinical vigilance with regard to the possibility of cerebral abscess formation in patients presenting with features of possible meningitis. Early contrast enhanced CT scanning or Magnetic Resonance Imaging is very important in this condition.[18] Treatment should never be delayed while waiting for radiological investigation. Repeat CT scanning may be a vital component in the ongoing management of difficult cases.

### PROGNOSTIC SCORING SYSTEMS

In bacterial meningitis there are established clinical and laboratory prognostic indicators.[19] In addition some have attempted to quantify these into scoring systems which may aid the clinician in decisions regarding intensive care management.[19-21] As a guide to management of individual adults with suspected bacterial meningitis these are currently limited. There have been no large trials to evaluate the scoring systems on a prospective basis in the UK. Paediatric scoring systems have been validated and some work has

*Further information regarding this can be found in Dr Wood's paper *Antimicrobial treatment of community acquired meningitis in adults* which is due to be published in the November issue of *Proceedings.*

been done in adult disease to attempt to match this;[22] however, there is currently no universally accepted adult system to give prognostic evaluation of presenting features. To help validate newer, sometimes experimental therapies it is important to have a simple effective system based mainly on initial clinical assessment, perhaps including basic laboratory parameters. This important area needs further development to ensure 'evidence based' practice in an emotive field.

### IDENTIFICATION / ISOLATION OF MENINGOCOCCI FROM SKIN

Petechiae are characteristically associated with meningococcal septicaemia but have been described with *Strep. pneumoniae*, staphylococcal, *Haemophilus influenzae* and viral infections. Isolation and/or demonstrations of meningococci from petechial skin lesions is well recognised. Three methods have recently been evaluated; aspiration, punch biopsy or simply scraping the epithelial surface of the lesion until a small amount of blood can be directly spotted onto a slide.[23-25] Gram stain can provide a rapid confirmation of clinical diagnosis and culture can confirm this. This should be regarded as an adjunct to CSF analysis but in cases where LP result is unhelpful or unavailable it may provide the only microbiological confirmation of meningococci. Gram stain can still be positive up to 45 hours later in patients who have already been treated with antibiotics. Clearly examination of purpuric lesion blood is less invasive than LP and there are few - if any - complications if a sterile technique is adopted.

### POLYMERASE CHAIN REACTION IN THE DIAGNOSIS OF MENINGITIS

PCR is now becoming an important investigation in the attempt to secure the diagnosis in acute bacterial meningitis. It can be performed on CSF, whole blood and serum.[15,26-28] With the introduction of early antibiotic therapy the likelihood of positive blood cultures in this condition has reduced significantly and has been reported as low as 5%.[29] PCR for meningococcal components in peripheral blood has been reported to exhibit sensitivity and specificity of over 90% as a diagnostic test.[15] As further experience is obtained in the use of PCR, it may, in future, not be necessary to perform LP. PCR is a relatively rapid test compared with serological investigations which require the time taken to mount an immune response, and it can be used for non-culture-based subtyping of meningococcal strains as an epidemiological tool.[29] The main drawback preventing widespread use of PCR techniques is the poor reproducibility of these results and the disconcerting incidence of false-negative results even in experienced hands.[30] Refinements in this technique promise the most important development in diagnostic capabilities over the next decade.

The diagnosis of acute bacterial meningitis requires clinical vigilance and appropriate use of both established and developing diagnostic techniques. Improvements in the sensitivity and specificity of these techniques have permitted diagnostic accuracy and early appropriate therapy to progress without mutual compromise.

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