ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

This is a medical emergency. Consult early with an Senior Emergency Medical Officer or Paediatrician if meningitis suspected.

For further information see NSW Health policy directive PD2013_044 (2.12.2013) Infants and Children: Acute Management of Bacterial Meningitis or CEC Sepsis Kills neonatal and paediatric first dose empirical parenteral antibiotic guidelines.

CLINICAL PRESENTATION

Can be variable—see PD2013_044 for detailed information.
High index of suspicion if any signs of sepsis, particularly if there is no focus or there is altered mental status.
Parental anxiety should not be discounted. It is often of significance even if the child does not appear especially unwell.
History and examination (in addition to usual) should include:-

- **Age** (approximately 90% of bacterial meningitis occurs at age < 5 years)
- **Vaccination history**
- **Predisposing factors**:-
  - Recent infections (75% have had a preceding or concurrent URTI).
  - Known contact with someone with meningitis.
  - Recent travel.
  - Head trauma or cranial surgery.
  - Maternal obstetric history if child < 3 months including maternal group B streptococcus status.
- **Recent use of antibiotics** (may modify clinical presentation and CSF findings).
- **Drug allergies.**

INITIAL MANAGEMENT: Resuscitation then timely administration of antimicrobials are the priorities

- **Assess ABCDEFG** and resuscitate as required:
  - **Airway**
  - **Breathing**
  - **Circulation** (fluid restriction is not an issue in the initial stabilisation of children with meningitis. Treat shock with 20mL/kg of 0.9% sodium chloride and reassess)
  - **Disability** (level of consciousness, look for signs of cerebral oedema). Manage cerebral oedema if present. See local guideline: **Control of ICP.**
  - **Exposure** (presence of rash, temperature control).
  - **Fluids** (monitor input and output to maintain adequate hydration).
  - **Glucose** (must be checked early in management process and correct as necessary).
- **Manage seizures** (see table 1) if they occur:
  - Meningitis must be considered in any child presenting with seizures in association with fever, particularly in children < 12 months or if fever is prolonged or refractory to management.
  - **BUT** not all children with fever and convulsions will have meningitis.
- **Investigate**: (see table 2A, 2B, 3A, 3B & 4)
  - **Routine investigations** for all patients with suspected bacterial meningitis (table 2A).
  - Possible **additional tests** based on clinical presentation (table 2B).
  - **Lumbar puncture** (see table 3A & 3B).
  - **Gram stain** (see table 4).
- **Corticosteroids** (see table 5).
- **Antibiotic management** (see table 6, 7 & 8).
- **Notify Public Health Department** if suspected or confirmed bacterial meningitis.

REMEMBER
START ANTIBIOTICS IMMEDIATELY IF LP WILL BE DELAYED or CSF IS TURBID ON LP or EXTREMELY HIGH CLINICAL SUSPICION

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TABLE 1: MANAGEMENT OF SEIZURES

- Seizures should be treated immediately.
  - IV midazolam 0.15mg/kg.
    - Alternative
      - IM midazolam 0.15mg/kg or
      - Buccal or intranasal midazolam 0.5mg/kg or
      - Rectal diazepam 0.5mg/kg (not kept in The Tweed Byron HSG)
    - Doses repeat at least once if needed
  - If seizures continue consider
    - IV phenytoin 20mg/kg (loading dose) - first choice or
    - IV Phenobarbitone 20mg/kg (is sedating compared to phenytoin but more commonly used in neonates).
  - If seizures continue notify senior emergency medical officer or paediatrician urgently and consult NSW Health PD 2009_065 (16.10.2009): Acute management of seizures in Infants and Children for further information.

TABLE 2A: INVESTIGATIONS

Routine investigations for all patients with suspected bacterial meningitis		
Category of TEST	**TEST**	**Comments**
Microbiology	Blood culture	Valuable, particularly if CSF analysis is not possible.
	CSF for MCS	Microscopy includes Gram stain and WCC and differential (for urgent analysis – communicate this with pathology lab).
Haematology	FBC, WCC differential and film	A low or normal WCC does not exclude meningitis. Thrombocytopenia can occur in DIC.
Biochemistry	Urea, Creatinine, Electrolytes, BGL, LFTs	Monitor Na^+ to detect SIADH. Renal and hepatic impairment can occur with sepsis and should be monitored.
	CSF protein, glucose	See table 3B for expected CSF protein and CSF: blood glucose ratios.

ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

TABLE 2B: INVESTIGATIONS		
Possible additional tests based on clinical presentation		
IN THE CONTEXT OF ED CARE, SAMPLES MAY BE TAKEN AND MARKED FOR STORAGE (PARTICULARLY CSF) FOR LATER ADDITION OF RELEVANT STUDIES TO AVOID HAPHAZARD ORDERING OF TESTS.		
Haematology	Coagulation profile including FDP	Indicated in patients with clinical evidence of a coagulopathy.
Biochemistry	CRP, ESR	Inflammatory markers like CRP (preferred) or ESR may be useful markers of a bacterial infection but lack specificity for meningitis.
	Urinary Osmolality and Na	Indicated if patient has hyponatraemia and SIADH is possible.
	Plasma Osmolality	Indicated if patient has hyponatraemia and SIADH is possible.
Radiology	Neuroimaging (Head CT +/- contrast or MRI)	Indicated if clinical evidence of raised ICP e.g. significantly altered mental state, bradycardia, hypertension or focal neurological signs or in those who may have an alternative diagnosis (e.g. trauma, SAH). Neuroimaging does not reliably exclude raised ICP. Patients should be clinically stable to be considered for neuroimaging.
Microbiology Virology Serology	CSF – bacterial antigen detection	Limited sensitivity. Only occasionally indicated e.g. if previous antibiotics used (discuss with senior staff or clinical microbiologist).
	Viral culture (largely superseded by PCR)	Indicated if CSF pleocytosis and viral meningitis is suspected.
	Neissiera meningitides PCR	Helpful if prior antibiotics used.
	Streptococcus pneumonia PCR	Helpful if prior antibiotics used.
	Enterovirus PCR Herpes simplex PCR	Indicated if viral meningitis is suspected.
	Mycobacterium tuberculosis (MTB) stain, PCR and culture	Indicated if MTB suspected. Adequate volumes should be obtained for mycobacterial culture (important for determining resistance)-aim for 5-10mL CSF minimum.
	Cryptococcal stain and antigen	Usually in immunocompromised patients, particularly HIV infected patients, but not exclusively (NB: discuss with senior staff or clinical microbiologist).
	Cytology	Indicated if CNS leukaemia is possible. Ask lab to send to haematology for cytology if eosinophilic meningitis is suspected, as eosinophils are labile.
	Skin scrapings of skin lesions for MCS (largely superseded by PCR for meningococcus)	MCS: Gently de-roof the skin lesion with a needle. Roll a sterile swab over the base of the lesion and then onto a glass slide (for Gram stain). Collect another swab and place in Stuart's transport media for culture.
	Throat Swab	
	Serum Neisseria meningitides IgM serology	Helpful in aiding diagnosis. Utility for immediate diagnosis limited. May require convalescent serology.
	Cryptococcal antigens	Indicated if cryptococcal meningitis suspected.
	Enteroviral serology Herpes simplex serology	Indicated if viral meningitis suspected.

ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

TABLE 3A: LUMBAR PUNCTURE (LP)

LP should be performed once the diagnosis is suspected and the patient is stabilised.
Antibiotics SHOULD ONLY BE GIVEN prior to LP - if LP is to be delayed and bacterial meningitis is clinically suspected.
CT scan before LP delays diagnosis.
CT scan cannot rule out raised ICP.

SPECIFIC INDICATIONS TO DELAY LUMBAR PUNCTURE (LP)	
Local site for LP	• Skin infection at site of LP. • Anatomical abnormality at the LP site.
Patient instability	• Respiratory or cardiovascular compromise. • Continuing seizure activity.
Suspicion of space occupying lesion or raised ICP	• Focal seizure. • Focal neurological signs. • Reduced conscious state (some suggest a GCS <8) and especially if the patient is comatose. • Decerebrate or decorticate posturing. • Fixed dilated or unequal pupils. • Absent dolls eye movement. • Papilloedema. • Hypertension or bradycardia. • Irregular respirations.
Haematological	• Coagulopathy.

TABLE 3B: LUMBAR PUNCTURE—INTERPRETING THE CSF

	Polymorphs (PMN) x10^6/L	Lymphocytes x10^6/L	Protein[d] g/L	Glucose[b] mmol/L	Glucose CSF: Blood Ratio[c]
Normal ≤1 month of age	0[a]	<20	< 1.0	≥ 2.5	≥ 0.6
Normal > 1 month of age	0	≤ 5	< 0.4	≥ 2.5	≥ 0.6
Bacterial Meningitis	100-10,000 but may be normal	Usually < 100	> 1.0 (but may be normal)	Usually decreased	< 0.4[c] (but may be normal)
Viral Meningitis	Usually < 100	10-1,000 (but may be normal)	0.4-1 (but may be normal)	Usually normal	Usually normal

[a] the presence of PMN cells in a neonate is unusual and should **ALWAYS** raise concerns for bacterial meningitis.
[b] low CSF glucose (<2.2mmol/L) is found in two thirds of patients with bacterial meningitis **but a normal glucose does not exclude bacterial meningitis.**
[c] **blood glucose levels obtained at the time of LP** enable proper interpretation of the CSF glucose as changes in CSF glucose follow changes in blood glucose by ≥ 30 minutes.
[d] 90% of patients with bacterial meningitis will have elevated protein but protein levels may be elevated in a traumatic tap. There will be 0.01-0.15g/L increase in protein for every 1000 RBC in uncentrifuged CSF.

RBC in CSF. **Guide to distinguishing a traumatic tap from CSF pleocytosis.** The safest strategy is to use the un-adjusted WCC and treat for bacterial meningitis if the WCC is greater than the normal range. The simple guide that is often used is the ratio 1 WBC:500 RBC in the CSF, however this can vary depending on the peripheral WCC and RBC and so is not reliable.

ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

TABLE 4: GRAM STAIN RESULT OF COMMON CAUSES OF COMMUNITY ACQUIRED BACTERIAL MENINGITIS

Best test for rapid diagnosis. Will identify bacteria in 60-90% of cases

ORGANISM	GRAM STAIN
Group B streptococcus	Gram positive cocci resembling streptococci.
Streptococcus pneumoniae	Gram positive diplococci or GPC resembling streptococci.
Neisseria meningitides	Gram negative diplococci or gram negative cocci.
Haemophilus influenzae	Gram negative cocco-bacillus.
Enterobacteriaceae e.g. E. coli	Gram negative rods.
Listeria monocytogenes	Gram positive rods or Gram variable rods. L. monocytogens is resistant to cephalosporins but sensitive to benzylpenicillin. **Discuss with microbiologist.**

TABLE 5: CORTICOSTEROIDS

- In suspected or confirmed acute bacterial meningitis, **COMMENCE STEROIDS if:**
  - **≥ 3 months of age.** (Note: there is not enough evidence to recommend < 3 months of age)
  - **Not pre-treated with parenteral antibiotics.**
- Current evidence suggests that early steroids (first dose given before, with or just after antibiotics) in children with acute bacterial meningitis reduce the risk of hearing loss and neurological sequelae.
- **REGIMEN**
  - **Dexamethasone 0.15mg/kg/dose (maximum dose 10mg), IV, 6 hourly for 4 days**
  - **Give as a "push" followed by first dose of antibiotics for practical purposes.**
  - If dexamethasone is not available, hydrocortisone 4mg/kg up to 200mg IV used for initial dose.
  - The decision to continue steroids for 4 days should be reviewed after laboratory and microbiological information becomes available over the next ≥ 48 hours. If CSF results are not consistent with bacterial meningitis and the child is clinically improving, the recommendation is to stop steroids but continue antibiotics for at least 48 hours until negative CSF cultures are confirmed.

TABLE 6: EMPIRIC INTRAVENOUS ANTIMICROBIAL DOSES
See table 7 for empiric antimicrobial selection

Antimicrobial	Dose	Frequency of dose by age		
		First week of life	Weeks 2-4 of age	Age > 4 weeks
Aciclovir	See separate columns	20mg/kg/dose 8 hourly	20mg/kg/dose 8 hourly	1 month to 5 years 20mg/kg/dose, 8 hourly 5-12 years 15mg/kg/dose, 8 hourly >12 years 10mg/kg/dose, 8 hourly
Benzylpenicillin	60mg/kg/dose (max 2.4g)	12 hourly	6-8 hourly	4 hourly
Ampicillin	50mg/kg/dose (max 2g)	8 hourly	6 hourly	4 hourly
Cefotaxime	50mg/kg/dose (max 2g)	12 hourly	8 hourly	6 hourly
Ceftriaxone	50mg/kg/dose (max 2g)	N/A	N/A	12 hourly
Ciprofloxacin	10mg/kg/dose (max 400mg)	N/A	N/A	12 hourly
Moxifloxacin	10mg/kg/dose (max 400mg)	N/A	N/A	12 hourly
Vancomycin	15mg/kg/dose (max 750mg)	12 hourly	8 hourly	6 hourly

ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

TABLE 7: EMPIRIC ANTIMICROBIAL SELECTION

Antimicrobial therapy should be initiated immediately after LP results or immediately after LP if clinical suspicion for meningitis is high or the CSF is turbid.

Note: this table differs from the NSW Health (Clinical Excellence Commission) "Sepsis Pathway" antibiotic regimes for neonates (≤28 days) and paediatric patients (> 28 days and ≤ 16 years) and some of the antimicrobial doses and frequency of administration is slightly different. Do not delay giving antimicrobials because of this. Use one of the guidelines and **seek expert advice from FACEM or paediatrician early.**

Once the organism has been identified and susceptibility results are available, choose the appropriate directed regimen.

AGE GROUP	COMMON ORGANISMS	ANTIMICROBIAL
0 - 3 months	Group B streptococcus Escherichia coli Listeria monocytogens (Note: PD2012_044 indicates that if HSV encephalitis is suspected in newborns administer aciclovir but CEC neonatal sepsis pathway recommends it as standard treatment for neonatal (≤28 days) meningitis/ encephalitis.	**Ampicillin (or benzyl penicillin)** **PLUS** **Cefotaxime** (Ceftriaxone is contraindicated in newborns). **PLUS** **Aciclovir** (if child ≤ 28 days of age or HSV encephalitis is suspected)
> 3 months - 16 years	N. meningitides H. influenzae (now rare with Hib vax) (Note: PD2012_044 indicates to add vancomycin to third generation cephalosporin if Streptococcus pneumoniae is suspected but CEC paediatric sepsis pathway indicates it be used for all patients when meningitis is suspected in severe sepsis. Vancomycin is not mentioned in the CEC neonatal sepsis pathway)	**Cefotaxime or ceftriaxone** **PLUS** **Vancomycin** (see indications below) Note: When meningitis is suspected in severe sepsis in CEC paediatric sepsis pathway, vancomycin is recommended empirically. This is because the patient is most likely too unstable for an immediate LP and protocol for delayed LP in place.
Indications to add vancomycin	Suspicion of Streptococcus pneumoniae • CSF with gram positive diplococci or Gram positive cocci resembling streptococci seen on Gram stain. • CSF negative by gram stain but clinical features highly suspicious of bacterial meningitis. • High clinical suspicion of bacterial meningitis but a LP is contraindicated. • Severe sepsis as per CEC sepsis pathway and suspicious of meningitis.	Note: vancomycin must always be used in combination with a third generation cephalosporin for penicillin resistant Streptococcus pneumonia meningitis, **and NEVER as a sole agent.** 28% of Streptococcus pneumoniae strains in Australia have reduced susceptibility to penicillin and also reduced susceptibility to third generation cephalosporins.

Notes on paediatric and neonatal patients

- If unable to gain IV access -> use IO (or umbilical vein-neonate) or give IM antibiotics.
- See CEC neonatal or paediatric sepsis pathway for further information on vascular access.

Notes on paediatric patients

- If signs of encephalitis - **ADD aciclovir**
- If history of penicillin anaphylaxis - **use moxifloxacin or ciprofloxacin instead of third generation cephalosporin**.

Whilst prevention strategies like intrapartum antibiotics for group B streptococcus and routine childhood immunisations against Haemophilus influenza type b, Neisseria meningitides type c and Streptococcus pneumonia are effective, the differential diagnosis of acute bacterial meningitis should still include these organisms.

ACUTE MANAGEMENT OF BACTERIAL MENINGITIS

TABLE 8: DURATION OF ANTIMICROBIAL THERAPY	
BACTERIA	DURATION OF THERAPY
Group B streptococcus	14 days
Gram negative rods	21 days
Listeria monocytogens	21 days
Neisseria meningitides	7 days
Haemophilus influenzae type b	10 days
Streptococcus pneumoniae	14 days
"Culture negative" but significant CSF pleocytosis present	Minimum of 7 days recommended and seek clinical microbiologist advice.

OTHER ISSUES

- All cases of suspected bacterial meningitis should be isolated initially in a single room until 24 hours after a third generation cephalosporin has been administered.
- Ongoing isolation requirements should be determined by the hospital infection control team and is based on the suspected or confirmed organism.
- Transfer to tertiary referral centre—contact:
  - QCC (Queensland) - first option 1300799127 or
  - NETS (New South Wales) 1800 10 NETS (6387).
- Notification of Public Health Unit
  - Remember that Haemophilus influenzae type b and Neisseria meningitides must be reported to the local Public Health Unit on clinical suspicion alone.
  - In proven Haemophilus influenzae type b and Neisseria meningitides liaise with the Public Health Unit in regards to chemoprophylaxis of contacts.

REMEMBER — START ANTIBIOTICS IMMEDIATELY IF:-

- **LP WILL BE DELAYED**
- **CSF IS TURBID ON LP**
- **EXTREMELY HIGH CLINICAL SUSPICION**

REFERENCES:-

- NSW Health PD2013_044: Clinical Practice Guidelines Infants and Children: Acute Management of Bacterial Meningitis, 2.12.2013.
- CEC paediatric sepsis pathway first dose empirical parenteral antibiotic guideline v2.1
- CEC neonatal sepsis pathway first dose empirical parenteral antibiotic guideline v2.1
- Communicable Diseases Network Australia: Guidelines for the early clinical and public health management of meningococcal disease in Australia, October 2007
- Therapeutic guidelines: Meningitis: empirical therapy accessed online 17 December 2013