A 37-year-old man presents to the emergency department with symptoms of meningitis. Gram stain of the cerebrospinal fluid reveals the presence of gram-negative diplococci. His 12-week pregnant partner should receive which one of the following as prophylaxis?

A. Ciprofloxacin.
B. Ceftriaxone.
C. Penicillin.
D. Meningococcal vaccine.
E. Erythromycin.

Reference: Infectious Diseases A clinical Approach Yung, McDonald, Spelman, Street and Johnson 2001
Therapeutic Guidelines Antiobiotics 2006
wikapeadia
http://en.wikipedia.org/wiki/Gram-negative
http://en.wikipedia.org/wiki/Gram-positive

Common clinically relevant bacteria

Gram positive: Bacillus; Listeria; Staphylococcus; Streptococcus; Enterococcus; Clostridium

Gram negative cocci: Neisseria gonorrhoea (STD); Neisseria meningitidis (meningitis); Moraxella catarrhalis (respiratory)

Gram negative bacilli: Haemophilus influenzae; Klebsiella pneumonia; Legionella pneumonia; Pseudomonas aeruginesia (respiratory) | Escherichia coli; Proteus mirabilis; Enterobacter cloacae; Serratia marcescens (urinary tract) | Helicobacter pylori; Salmonella enteritias; Salmonella typhi (GI)

80% bacterial meningitis caused by
Streptococcus pneumonia – gram positive
Neisseria meningitis – gram negative cocci
Haemophilis influenzae- gram negative bacilli

Treatment: (Therapeutic Guidelines)

If the organism or susceptibility is not known, empirical therapy should cover the most common pathogens. In patients over 3 months of age, use:

1. Ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily
   or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly
   OR
2. Cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly.

Listeria monocytogenes is resistant to cephalosporins. If the patient is immunosuppressed or Listeria infection is suspected, add to the above regimen either:

1. Benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly
   OR
2. Amoxy/ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly.

Add vancomycin if Gram-positive diplococci are seen or a pneumococcal antigen assay in CSF is positive, or if the patient has been heavily pretreated with a beta lactam (eg for recurrent ear infections). This is to ensure that Streptococcus pneumoniae isolates that display intermediate or higher resistance to penicillin and/or cephalosporins are adequately covered prior to the availability of culture and susceptibility results. Consider vancomycin also if Gram-positive cocci resembling staphylococci are seen, or if neutrophils are present but organisms are not seen, and if viral meningitis or meningococcal disease are unlikely. Use:

vancomycin 12.5 mg/kg up to 500 mg (child <12 years: 15 mg/kg up to 500 mg) IV, 6-hourly (monitor blood levels and adjust dose accordingly, slow infusion required).

Cease vancomycin if an organism likely to be susceptible to ceftriaxone/cefotaxime is isolated or if a penicillin-susceptible pneumococcus (MIC <0.125 mg/L) is isolated.

For patients with immediate penicillin or cephalosporin hypersensitivity, use:
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1  vancomycin 12.5 mg/kg up to 500 mg (child <12 years: 15 mg/kg up to 500 mg) IV, 6-hourly (monitor blood levels and adjust dose accordingly; slow infusion required).

   PLUS
ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

   OR

2  moxifloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, daily.

Choose one of the directed regimens once the organism has been identified and susceptibility results are available.

If no pathogen is isolated continue the empirical regimen for a minimum of 10 days, depending on response. Consider ceasing antibiotics if the CSF examination is consistent with viral meningitis.

For neonates and infants under 3 months, the likely organisms are *Streptococcus agalactiae*, enteric Gram-negative rods or, rarely, *Listeria monocytogenes*. Treat as for severe sepsis in children under 6 months of age in whom meningitis has not been excluded. Intravenous treatment should continue for a minimum of 2 weeks. Repeat lumbar puncture(s) are usually done to directly assess bacteriological response. Complications during therapy are not infrequent and expert advice should be sought.

**Directed Therapy**

For meningitis due to *Neisseria meningitidis* (meningococcal meningitis), use:

- benzylpenicillin 1.8 g (child: 45 mg/kg up to 1.8 g) IV, 4-hourly for 3 to 5 days.

For patients hypersensitive to penicillin (excluding immediate hypersensitivity), use:

1  ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily for 3 to 5 days

   or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly for 3 to 5 days

   OR

2  cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly for 3 to 5 days.

For patients with immediate penicillin or cephalosporin hypersensitivity, use:

- ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12 hourly for 3 to 5 days.

Prophylaxis and/or immunisation is essential for close contacts. Prophylaxis is also necessary for patients who have received only benzylpenicillin, since this does not reliably clear nasal carriage.

MICs to penicillin and ceftriaxone/cefotaxime should be determined for all *Streptococcus pneumoniae* isolates.

For strains with a penicillin MIC ≥0.125 mg/L, use vancomycin plus either ceftriaxone or cefotaxime (see Empirical therapy for doses). Specialist advice must be sought particularly if the MIC of these cephalosporins is elevated. Rifampicin or moxifloxacin are possible alternatives to vancomycin.

For penicillin-susceptible strains (MIC <0.125 mg/L), use:

- benzylpenicillin 1.8 g (child: 45 mg/kg up to 1.8 g) IV, 4-hourly for 10 to 14 days.

Very ill patients may require treatment for up to 3 weeks.

For meningitis due to *Haemophilus influenzae* type b, use:

1  ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily for 7 days

   or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly for 7 days

   OR

2  cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly for 7 days.

If the organism is proven to be susceptible, use:

1  benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly for 7 days

   OR

2  amoxy/ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly for 7 days.

For patients with immediate penicillin or cephalosporin hypersensitivity, use:

1  chloramphenicol 1 g (child: 20 to 25 mg/kg up to 1g) IV, 6-hourly for 7 days

   OR

1  ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly for 7 days

For meningitis due to *Listeria monocytogenes*, penicillin and amoxy/ampicillin appear equally efficacious. Use:
1. benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly
   OR
2. amoxycillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly.

In patients hypersensitive to penicillin, trimethoprim+sulfamethoxazole may be used alone:
trimethoprim+sulfamethoxazole 160+800 mg (child: 4+20 mg/kg up to 160+800 mg) IV, 6-hourly.

There is limited evidence that combination therapy with beta lactam plus trimethoprim+sulfamethoxazole improves outcomes. The value of adding an aminoglycoside is not clear.
The usual duration of therapy is 3 weeks, with extension to 6 weeks in immunocompromised patients.
Oral therapy with trimethoprim+sulfamethoxazole may be used to complete the course after initial 3 weeks if there has been a good response to IV therapy.

**Streptococcus agalactiae** is the commonest cause of meningitis in the newborn. Use:
benzylpenicillin 60 mg/kg up to 2.4 g IV, 4-hourly for 14 to 21 days.

**Cryptococcal meningitis** is caused either by **Cryptococcus neoformans** (particularly in immunocompromised patients) or **Cryptococcus gattii** (previously known as **C. neoformans var. gattii**). Monitoring of CSF pressure is a critical part of management to ensure that communicating hydrocephalus does not develop and cause permanent neurological sequelae. Consultation with those experienced in the management of this condition is strongly recommended.
The standard treatment for cryptococcal meningitis is:
amphotericin B desoxycholate 0.7 mg/kg IV, daily (dosage to be adjusted according to tolerance) for 6 to 10 weeks
PLUS
flucytosine 25 mg/kg IV or orally, 6-hourly for 6 to 10 weeks (monitor plasma levels),

Patients infected with **Cryptococcus gattii** may be slower to respond and require a longer treatment course. Alternatively, if the CSF is culture negative after 2 weeks of therapy, cease the amphotericin B desoxycholate and flucytosine and commence:
fluconazole 800 mg (child: 20 mg/kg up to 800 mg) orally or IV for the first dose, then 400 mg (child: 10 mg/kg up to 400 mg) orally, daily for at least 10 weeks of therapy.

Itraconazole has been successfully used when fluconazole cannot be used.
In HIV-infected patients, the regimen as outlined above has been shown to be successful, without the need for culture negativity at 2 weeks.
In the immunocompromised, long-term suppressive therapy may be required. If there has been a successful response after 10 weeks of fluconazole at the above dose, reduce the dose to:
fluconazole 200 mg (child: 5 mg/kg up to 200 mg) orally, daily indefinitely as secondary prophylaxis.

**Note 1:** Lipid or liposomal formulations of amphotericin have been successfully used when toxicity from amphotericin B desoxycholate has become a problem; however, there is limited data in the literature to guide dose and duration of therapy.

**Note 2:** Oral flucytosine is not registered for use in Australia; available via Special Access Scheme.

**Chemoprophylaxis for meningitis**

**Introduction**
Chemoprophylaxis for meningitis or other infections caused by **Neisseria meningitidis** (meningococcus) and the now much less common **Haemophilus influenzae** type b (Hib) is offered to close (usually household) contacts of the index case. Among close contacts there will be a person or persons asymptptomatically carrying the organism which caused the index infection. Chemoprophylaxis aims to eradicate asymptomatic carriage in the network of contacts so that susceptible members of the group do not acquire the organism and get an invasive infection.
The **Guidelines for early clinical and public health management of meningococcal disease in Australia** provide definitions of a close contact, and appropriate prophylactic regimens. See also the Australian Immunisation...
Handbook. Prophylaxis outside the immediate family should be initiated and coordinated by public health authorities. Despite prophylaxis, disease can still occur. Parent education regarding frequent, careful observation and the need for examination by a medical practitioner at the first signs of any unexplained illness is essential.

*Neisseria meningitidis* (meningococcus)

Suitable regimens for *Neisseria meningitidis* (meningococcus) prophylaxis are:

1. **Ceftriaxone** 250 mg (child: 125 mg) IM as a single dose (preferred option during pregnancy)
   OR

2. **Ciprofloxacin** (adult and child ≥12 years) 500 mg orally, as a single dose (preferred option for women taking oral contraceptives)
   OR

3. **Rifampicin** 600 mg (neonate <1 month: 5 mg/kg; child: 10 mg/kg up to 600 mg) orally, 12-hourly for 2 days (preferred option for children).

Rifampicin is associated with multiple drug interactions and is contraindicated in pregnancy, alcoholism and severe liver disease.

*Haemophilus influenzae* type b (Hib)

A suitable regimen for *Haemophilus influenzae* type b (Hib) prophylaxis is:

- Rifampicin 600 mg (neonate <1 month: 10 mg/kg; child: 20 mg/kg up to 600 mg) orally, daily for 4 days.

Alternatively, although data are limited, if rifampicin is considered unsuitable, use:

- Ceftriaxone 1 g (child: 25 mg/kg up to 1 g) IM, daily for 2 days.

Where the index case is under 2 years of age, commence a full course of Hib vaccination as soon as possible after recovery, regardless of any previous Hib immunisation. Unvaccinated contacts under 5 years of age should be immunised as soon as possible.


**Answer B. Ceftriaxone.**