

Case presentation

Dr J James (CT1) Prof S Chhetri (neurology)

PC & HPC

- ▶ 51 year old lady
- ▶ Presented to Chorley hospital 11/09/17
- ▶ 5/7 of left ear pain and headache
- ▶ 3/7 of left sided otorrhoea
- ▶ N+V, diarrhoea, lethargy
- ▶ Imbalance, Diplopia, confusion and reduced consciousness (GCS 12/15)

- ▶ No cough, CP, SOB, abdominal pain

PMH

11-Sep-2018	Infection ear
11-Sep-2018	Sepsis
26-May-2018	Hearing loss
26-May-2018	Chronic rhinosinusitis
17-May-2018	Infection ear
17-May-2018	Infection ear
17-May-2018	Acute bilateral otitis media
17-May-2018	Acute non suppurative otitis media
12-Apr-2018	Acute suppurative otitis media
28-Feb-2018	Streptococcal infection
26-Feb-2018	Infective otitis externa
21-Feb-2018	Conjunctivitis
21-Feb-2018	Infection ear
16-Nov-2016	Gastroenteritis
22-Sep-2016	Rheumatoid arthritis
08-Sep-2016	Rheumatoid arthritis
08-Sep-2016	Osteoarthritis NOS, of knee
29-May-2015	Chronic rhinosinusitis
13-Nov-2014	Rheumatoid arthritis
08-Aug-2014	Chronic rhinosinusitis
18-Oct-2010	Nasal polyps
13-Oct-2007	Missed abortion
10-Oct-2006	Anxiety with depression
04-Jan-2004	[X]Erosion of bone
04-Jan-2004	Rheumatoid arthritis
11-Jun-2003	Chronic sinusitis

MH

► NKDA

Last Issue	Drug / Dose / Quantity
Not yet issued	Adalimumab 40mg/0.4ml solution for injection pre-filled disposable devices, every 2 weeks SC BY herself Provided by hospital,2 pre-filled disposable injection
Not yet issued	Methotrexate 10mg/0.2ml solution for injection pre-filled disposable devices, weekly IM BY HERSELF provided by hospital ,1 pre-filled disposable injection
Repeat Medication	
06-Sep-2018	Zapain 30mg/500mg tablets (AMCo), Take One Or Two Four Times/Day,100 tablet
06-Sep-2018	Fluoxetine 20mg capsules, take two daily,60 capsule
06-Sep-2018	Folic acid 5mg tablets, one tablet to be taken weekly,8 tablet
01-Aug-2018	Beclometasone 50micrograms/dose nasal spray, 2 TWICE DAILY,2 x 200 dose
29-Jun-2018	Lansoprazole 15mg gastro-resistant capsules, One To Be Taken Each Morning,56 capsule
29-Jun-2018	Femoston 1/10mg tablets (Mylan), One To Be Taken Each Day,84 tablet
12-Apr-2018	Ferrous fumarate 210mg tablets, One To Be Taken Twice A Day,112 tablet

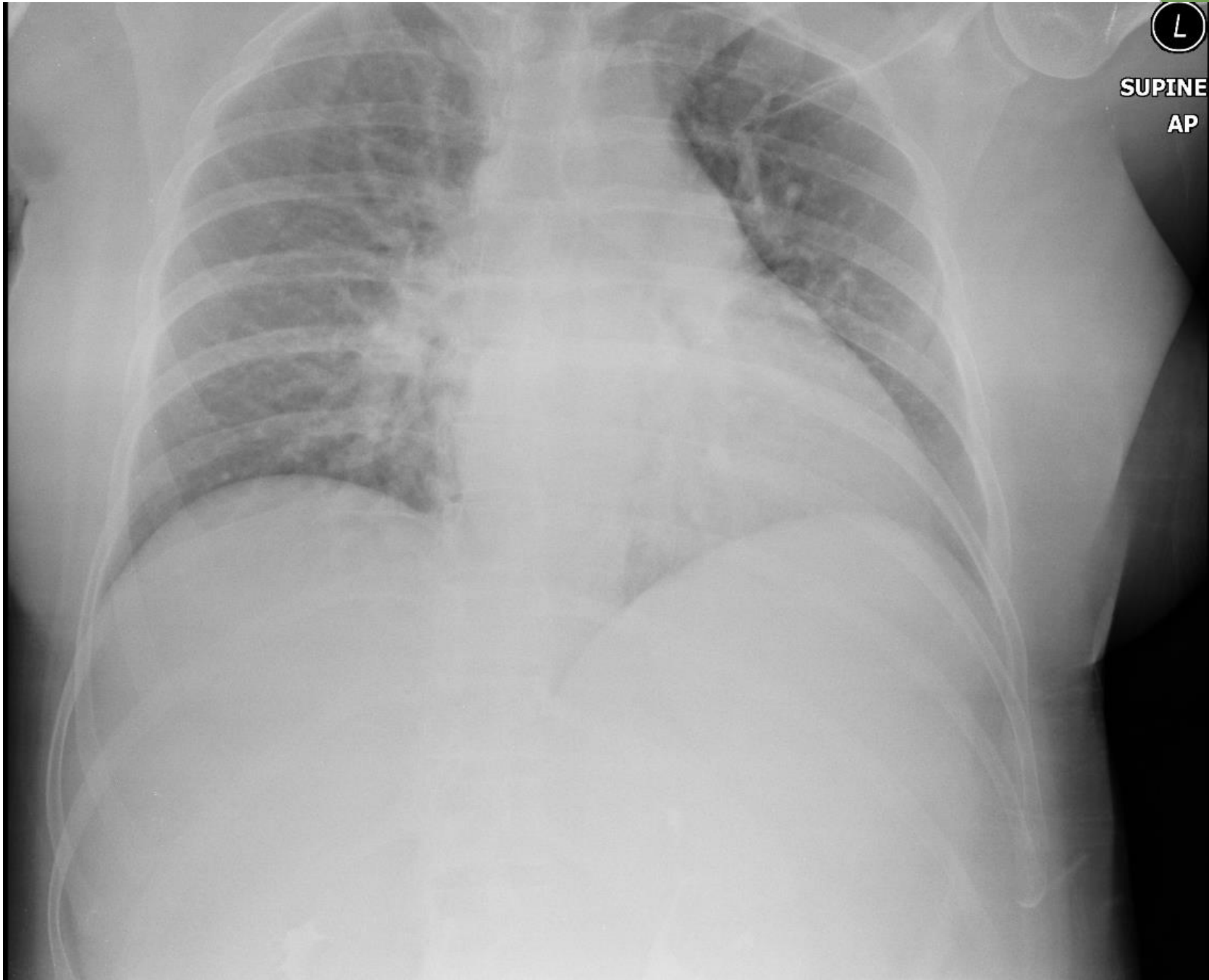
O/E

- ▶ NEWS 3- RR21 HR 110 BP 156/97 temp 37.1
- ▶ Chest clear, HS normal
- ▶ No photophobia, neck stiffness
- ▶ No facial asymmetry, normal power
- ▶ PERLA, plantars down going
- ▶ Ears: R ear and, L ear: ?perforation/retracted yellow discharge, cloudy TM

Date/Time	Sod	Pot	Urea	Creat	GFR
20Jun18 1255	136	4.3	4.2	55	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note
11Sep18 1652	<u>132</u>	4.0 Haemol...	<u>2.1</u>	<u>40</u>	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note
13Sep18 1030	136	3.8	3.4	<u>39</u>	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note
14Sep18 1007	135	3.6	2.8	45	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note
14Sep18 1154	136	3.7	2.8	49	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note
17Sep18 1037	137	3.9	5.0	<u>44</u>	>90 Estimated GFR calculations are not valid if creatinine is changing in acute disease. Please note

Date/Time	WBC	Hb	Plt	RBC	Hct	MCV	MCH	RDW	Neut #	Lym #	Mono #	EO #	BA %	nRBC #
20Jun18 1255	6.10	118	340	4.06	<u>0.349</u>	86.0	29.1	<u>15.3</u>	2.75	2.78	0.45	0.07	0.05	0.00
11Sep18 1652	26.63!	131	400	4.43	0.386	87.1	29.6	15.8	25.05!	0.39	1.10	0.00	0.09	0.00
13Sep18 1030	16.66!	105	325	<u>3.56</u>	0.292!	82.0	29.5	<u>15.1</u>	<u>13.64</u>	1.71	<u>1.28</u>	<u>0.00</u>	0.03	0.00
14Sep18 1007	8.82	115	394	4.03	<u>0.334</u>	82.9	28.5	<u>15.3</u>	<u>7.69</u>	<u>0.94</u>	<u>0.12</u>	<u>0.00</u>	0.07	0.01
14Sep18 1154	8.55	116	414	4.04	<u>0.334</u>	82.7	28.7	<u>15.4</u>	7.36	<u>0.95</u>	<u>0.19</u>	<u>0.00</u>	0.05	0.00
17Sep18 1037	<u>11.65</u>	116	414	4.06	<u>0.340</u>	83.7	28.6	<u>15.3</u>	<u>9.94</u>	1.25	0.39	<u>0.00</u>	0.07	0.02!

20Jun18 1255	<u>2.4</u>
11Sep18 1652	263.2
13Sep18 1030	182.4
14Sep18 1007	110.5
14Sep18 1154	114.0
17Sep18 1037	<u>21.9</u>



L

SUPINE
AP

DDX?

► Plan:

- ▶ Working diagnosis: ?CNS infection 2° to mastoid/middle ear infection
- ▶ CT head
- ▶ Movement artefact
- ▶ Soft tissue opacity filling the left mastoid air cells and middle ear cavity, no erosions or gross dehiscence
- ▶ Appearance similar in right mastoid air cells of the right temporal bone likely inflammatory changes
- ▶ Soft tissue opacity of right frontal sinus , b/l frontal ethmoidal recess, b/l ethmoid left cells, left sphenoidal sinus and b/l maxillary antra
- ▶ All in keeping with inflammatory mucosal thickening
- ▶ Advised clinical correlation and ENT review

Blood Culture	
Event Time	11 Sep 18 1652
Event Status	complete
2 Blood Culture	
MICROBIOLOGY	FINAL REPORT
MICROBIOLOGY	FINAL REPORT
Specimen type:	Blood culture
Qualifier/ site:	Arm
Clinical details:	Sinusitis with new confusion and loss of balance
Current Antibiotics:	none
* Culture results:	
1	Streptococcus pneumoniae
	Detected in both bottles after <1 day of monitored incubation
	National guidance suggests testing patients with invasive S pneumoniae

Blood Culture	
Event Time	11 Sep 18 1652
Event Status	complete
2 Blood Culture	
infection for HIV.	
* Report Comment	
Pneumococcal antigen detected by latex agglutination. Organism failed to grow.	
-----end of report-----	
Unscheduled Blood Film Review	
Event Time	11 Sep 18 1652
Event Status	complete
1 Film Result	
. WBC-Marked Neutrophilia WBC-Neutrophils show cytoplasmic vacuolation RBC and Platelet morphology appears normal	

- ▶ Patient transferred to ENT RPH 11/09/18
- ▶ To treat as left mastoiditis
- ▶ On iv co-amoxiclav initially
- ▶ Patient continued to complain of left ear pain, headache, lethargy, severe phobophobia and neck pain
- ▶ Neurology review was sort due to this

13/08/19 NEURO R/W

51 years old female

PMHx

1. Rheumatoid arthritis

On DMT:

1. Humira Adalimumab injections Weekly on Wednesday
2. Methotrexate injections , once every 2 weeks

Usually independent with ADLs.

HPI:

- Last Saturday started having headaches and left ear pain

- On Monday left work as very tired
- Tuesday noted left yellow discharge from ear
- Headache became throbbing and photophobia with neck stiffness and pain
- Then confusion and lethargic and anorexic
- No rash
- No seizures

O/E

GCS 14 E4 M6 V4

Drowsy , Photophobic ++++

Tenderness on neck movement

Fundoscopy no papilloedema

Possible right VI

Normal remaining cranial nerves

Treat as meningiensephalitis and start antibiotics as per protocol

Plan

1. Discuss with micro regarding antibiotics
2. Transfer to ward 17
3. MRI brain contrast
4. Discuss with neuroradiology if safe for LP
5. Then LP for wcc, protein, OP, paired glucose , meningiococcal and pneumococcal PCR.
6. Hold methotrexate and Humera injections

Has brisk reflexes (ULs & LLs)

Up-going plantars bilaterally

No focal weakness or sensory deficit

Negative brudzinski sign & Kernig sign

Impression

1. Bacterial meningioencephalitis

a. Initial blood cultures : +ve Cocci

LP results

- ▶ Opening pressure 22
- ▶ Glucose CSF 3 serum glucose 10.5 (3.5-6)
- ▶ Protein 1.51 (<0.5)
- ▶ CSF lactate 3.70 (<2.8)
- ▶ CSF culture and microscopy
- ▶ Clear, colourless fluid
- ▶ WCC 225- 40% neutrophil 60% lymphocytes
- ▶ Gram stain -no organism seen
- ▶ RBC <1
- ▶ Sent for viral PCR -HSV, pneumococcal and meningococcal PCR

Microbiology Discussion:	CSF collected today has raised WBC 225 with 60% polymorphs, 1 rbc and no organisms seen. However, the antigen test for S.pneumoniae was positive. Note blood culture from 11th Sept also pneumococcal antigen positive. On treatment for meningitis with ceftriaxone and dexamethasone and has clinically improved since yesterday.
Impression:	Clinical picture and results fit with Pneumococcal meningitis and bacteraemia.
Plan:	Needs minimum of 14 days of antibiotic treatment (ceftriaxone 2g BD) HIV test advised (BHIVA guidance). Stop amoxicillin - no indication for Listeria cover.

Bacterial meningitis

- ▶ Rare in adults-10 or fewer lab confirmed cases per year
- ▶ The incidence in adults was estimated to be 1.05 cases per 100,000 population
- ▶ mortality rate of community acquired bacterial meningitis is high, approximately 20% for all causes and up to 30% in pneumococcal meningitis, increasing with age
- ▶ 10% of adults die even with antibiotics due to host response to infection

Table 2 Key aetiological considerations for specific demographic groups.

Young adults	Viral meningitis more common than bacterial, especially in women in their 20s–40s.
Older adults	Second peak of meningococcal disease in late teens/early 20s Pneumococcal disease more common in over 50s <i>Listeria</i> commoner in over 60s but remains rare.
Skull fracture/CSF leak	Pneumococcal meningitis and a risk factor for recurrent meningitis
Previous lymphocytic meningitis	HSV-2 is the commonest cause of recurrent lymphocytic meningitis
Rash	Meningococcal meningitis more likely to present with a rash than pneumococcal meningitis
Co-existing upper respiratory tract infection e.g. otitis media, sinusitis	Pneumococcal meningitis is often associated with an upper respiratory tract infection
HIV Positive	Cryptococcal meningitis – commonest in those with a CD4 count $<100 \times 10^6$ but should be considered in anyone with a CD4 count of $<200 \times 10^6$ or $<14\%$. TB meningitis an important consideration at all CD4 counts Pneumococcal meningitis also increased
Other immunocompromised	Asplenic individuals are at increased risk from all encapsulated bacteria e.g. <i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> and <i>Haemophilus influenzae</i> . Complement deficiency increases risk of meningococcal disease. Risk factors for <i>listeria</i> meningitis include relative immunocompromise from alcohol dependency, diabetes and malignancy as well as overt immunocompromised from illness or medication
Travel history	An appropriate travel history may determine other rarer causes including Toscana Virus (Mediterranean), Tick Borne Encephalitis Virus (Central and Eastern Europe), other meningococcal (meningitis belt in Africa), West Nile Virus (USA), Lyme disease (appropriate exposure in Europe or USA) and parasitic meningitis (such as <i>Naegleri fowleri</i> – abundant globally occurring following visits to warm, fresh or brackish water, or trypanosomiasis – South America or parts of Africa).

TABLE 7-1 Empiric Antimicrobial Therapy Based on the Predicted Meningeal Pathogen

Predisposing Condition	Bacterial Pathogen	Antibiotic
Children and adults; community acquired	<i>Streptococcus pneumoniae</i> and <i>Neisseria meningitidis</i>	Third- or fourth-generation cephalosporin plus vancomycin
Otitis, mastoiditis, sinusitis	Streptococci species, gram-negative anaerobes (eg, <i>Bacteroides</i> species, <i>Fusobacterium</i> species), <i>Staphylococcus aureus</i> , <i>Haemophilus</i> species, Enterobacteriaceae	Third- or fourth-generation cephalosporin plus vancomycin plus metronidazole
Adults over the age of 55 and people with chronic illness	<i>S. pneumoniae</i> , gram-negative bacilli, <i>N. meningitidis</i> , <i>Listeria monocytogenes</i> , <i>Haemophilus influenzae</i>	Third- or fourth-generation cephalosporin plus vancomycin plus ampicillin
Endocarditis	Viridans streptococci, <i>S. aureus</i> , <i>Streptococcus bovis</i> , HACEK group, enterococci	Third- or fourth-generation cephalosporin plus vancomycin
Immunosuppressed	<i>S. pneumoniae</i> , <i>L. monocytogenes</i> , <i>H. influenzae</i>	Third- or fourth-generation cephalosporin plus vancomycin plus ampicillin
Postneurosurgical	Staphylococci, gram-negative bacilli	Vancomycin plus meropenem or vancomycin plus ceftazidime
Intraventricular device	Staphylococci, gram-negative bacilli, anaerobes	Vancomycin plus meropenem or vancomycin plus ceftazidime plus metronidazole

HACEK = *Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*.
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Symptoms

- ▶ The 'classic triad' of neck stiffness, fever and altered consciousness present in less than 50% of cases
- ▶ More unwell/ reduced GCS-bacterial
- ▶ When a rash was present in the context of meningitis, the causative organism was *Neisseria meningitidis* in 92% of cases
- ▶ 37% of cases of meningococcal meningitis patients did not have a rash
- ▶ Kernig's and Brudzinski's signs are not helpful in the clinical diagnosis of suspected meningitis; they have been reported to have high specificity (up to 95%) but the sensitivity can be as low as 5%

Immediate Action

- **Airway**
- **Breathing** - Respiratory rate & O₂ saturation
- **Circulation** - Pulse; capillary refill time; urine output; blood pressure (hypotension occurs late)
- **Disability** - Glasgow coma scale; focal neurological signs; seizures; papilloedema; capillary glucose
- **Senior review +/- Critical Care review** if any **Warning Signs** are present

Suspected Meningitis

(meningitis without signs of shock, severe sepsis or signs suggesting brain shift)

- Blood cultures
- Lumbar puncture
- Dexamethasone 10mg IV
- Ceftriaxone OR Cefotaxime 2g IV immediately following LP*
(see also **alternative initial antibiotics**)
- CT scan normally not indicated
- Careful fluid resuscitation (avoid fluid overload)

*If LP cannot be done in the first hour, antibiotics must be given immediately after blood cultures have been taken

Suspected meningitis with signs suggestive of shift of brain compartments secondary to raised intracranial pressure

- Get Critical Care input
- Secure airway, high flow oxygen
- Take bloods including Blood Cultures
- Give Dexamethasone 10mg IV
- Give Ceftriaxone OR Cefotaxime 2g IV immediately after blood cultures taken
- **Delay LP**
- Arrange neurological imaging (once patient is stabilised)

Signs of severe sepsis or a rapidly evolving rash

(with or without symptoms and signs of meningitis)

- Get Critical Care input
- Secure airway and give high flow oxygen
- Fluid resuscitation
- Blood Cultures
- Ceftriaxone OR Cefotaxime 2g IV immediately after blood cultures taken
- **Delay LP**

Follow Surviving Sepsis Guidelines at:
<http://www.survivingsepsis.org/guidelines>

TABLE 1		Initial Management for suspected bacterial meningitis		
	Antibiotics	Corticosteroids (Stop if non-bacterial cause identified)	Lumbar Puncture	Other actions
<u>WITH</u> severe sepsis or a rapidly evolving rash (with or without symptoms and signs of meningitis ¹)	See Table 2 for antibiotics and ADD: Gentamicin** 5mg/kg based on ABW/CBW (max 500mg) IV stat dose	Do not give Dexamethasone if non-blanching rash is present, i.e. possible meningococcal septicaemia	Delay LP	Blood Cultures Critical Care input Senior review Follow <u>sepsis</u> pathway
<u>WITH</u> signs suggestive of shift in brain compartment ²	See Table 2 for antibiotics	Dexamethasone* 8.25mg IV 6 hourly for 4 days (start with or just before first dose of antibiotics)	Delay LP	Bloods cultures Critical Care input Senior review Urgent CT scan If HSV encephalitis is possible add IV Aciclovir
<u>WITHOUT</u> signs of shock, severe sepsis or signs suggesting shift of brain injury ²	See Table 2 for antibiotics	Dexamethasone* 8.25mg IV 6 hourly for 4 days (start with or just before first dose of antibiotics)	Perform LP If LP cannot be done in the first hour, antibiotics must be given immediately after blood cultures taken	Blood cultures
¹ Signs and symptoms of meningitis Headache/Fever /Neck Stiffness/Rash/Shock ² Signs suggestive of shift in brain compartment Focal neurological signs/Presence of papilloedema/Continuous or uncontrolled seizures/GCS ≤12				

TABLE 2		Initial therapy for suspected bacterial meningitis		
The table outlines the initial empirical treatment to be used pending the identification of a causative organism. Once an organism has been identified, therapy can be targeted following discussion with a microbiologist.				
	No recent travel/No risk of penicillin resistant pneumococci		Recent travel/Risk of penicillin resistant pneumococci	
	1st Line No known allergy to beta-lactams or non-severe penicillin allergy	2nd Line Penicillin Allergy (anaphylaxis/severe reaction)	1st Line No known allergy to beta-lactams or non-severe penicillin allergy	2nd Line Penicillin Allergy (anaphylaxis/severe reaction)
16 to ≤59 years, not immunosuppressed	Ceftriaxone 2g IV 12 hourly	Chloramphenicol ^b 25mg/kg IV 6 hourly	Ceftriaxone 2g IV 12 hourly AND Vancomycin ^d dose as per guidelines	Chloramphenicol ^b 25mg/kg IV 6 hourly AND Vancomycin ^d dose as per guidelines
≥ 60 years old or immunosuppressed or pregnant	Ceftriaxone 2g IV 12hourly AND Amoxicillin ^a 2g IV 4hourly	Chloramphenicol ^b 25mg/kg IV 6hourly AND Co-trimoxazole ^c 120mg/kg IV in 4 divide doses	Ceftriaxone 2g IV 12 hourly AND Amoxicillin ^a 2g IV 4hourly AND Vancomycin ^d dose as per guidelines	Chloramphenicol ^b 25mg/kg IV 6hourly AND Co-trimoxazole ^c 120mg/kg IV in 4 divide doses AND Vancomycin ^d dose as per guidelines
Doses assume normal renal and hepatic function. For further advice on dosing, speak to microbiology.				
Discuss all immunocompromised and pregnant patients with microbiology.				

Table 4 Classical CSF Features of the different causes of meningitis.

	Normal	Bacterial	Viral	Tuberculous	Fungal
Opening Pressure (cm CSF)	12–20	Raised	Normal/mildly raised	Raised	Raised
Appearance	Clear	Turbid, cloudy, purulent	Clear	Clear or cloudy	Clear or cloudy
CSF WCC (cells/uL)	<5	Raised (typically >100) ^a	Raised (typically 5–1000) ^a	Raised (typically 5–500) ^a	Raised (typically 5–500) ^a
Predominant cell type	n/a	Neutrophils ^b	Lymphocytes ^c	Lymphocytes ^d	Lymphocytes
CSF protein (g/L)	<0.4	Raised	Mildly raised	Markedly raised	Raised
CSF glucose (mmol)	2.6–4.5	Very low	Normal/slightly low	Very low	Low
CSF/plasma glucose ratio	>0.66	Very low	Normal/slightly low	Very low	Low

CSF – cerebrospinal fluid; WCC – white cell count.

Local laboratory ranges for biochemical tests should be consulted and may vary from these quoted here.

A traumatic lumbar puncture will affect the results by falsely elevating the white cells due to excessive red cells. A common correction factor used is 1:1000.

^a Occasionally the CSF WCC may be normal (especially in immunodeficiency or tuberculous meningitis).

^b May be lymphocytic if antibiotics given before lumbar puncture (partially treated bacterial meningitis), or with certain bacteria e.g. *Listeria monocytogenes*.

^c May be neutrophilic in enteroviral meningitis (especially early in disease).

^d May be neutrophils early on in the course of disease.

Notify!

- ▶ All cases of meningitis (regardless of aetiology) should be notified to the relevant public health authority.
- ▶ The Consultant in Communicable Disease Control (CCDC) or Consultant in health protection in the Public Health England health protection team should be contacted early
- ▶ Prophylaxis of contacts should be initiated by the CCDC/Consultant in health protection and not the admitting clinicians
- ▶ Ciprofloxacin should be given to all close contacts of probable or confirmed meningococcal meningitis: 500 mg stat for adult contacts
- ▶ Rifampicin as alternate
- ▶ All meningitis patients should be screened for HIV

Immunosuppression

- ▶ Pneumococcal meningitis -review patients history for immunosuppression
 - ▶ Asplenia, splenic dysfunction/ectomy (sub optimal response to vaccine)
 - ▶ Complement deficiency
 - ▶ On DMARDS (esp Eculizumab/solaris)
- ▶ Should be vaccinated and take prophylactic antibiotics
- ▶ Precautions in meningitis
 - ▶ Respiratory isolated and until meningococcal meningitis or sepsis is excluded, or thought unlikely, or they have received 24 h of Ceftriaxone or a single dose of Ciprofloxacin
 - ▶ Droplet precautions should be taken until a patient has had 24 h of antibiotics.
 - ▶ Antibiotic chemoprophylaxis should be given to healthcare workers who have been in close contact with a patient with confirmed meningococcal disease ONLY when exposed to their respiratory secretions or droplets for example during intubation or as part of CPR when a mask was not worn

Box 10. Complications of acute meningitis and meningococcal sepsis.

	Complication	Warning signs	Action
Meningitis	Subdural empyema	Persistent fever New neurology	Urgent imaging WITH contrast Neurosurgical opinion
	Seizures (generalised tonic-clonic or subtle motor) Hydrocephalus	Abnormal movements Reduced consciousness	EEG monitoring
	Cerebral venous sinus thrombosis	Reduced consciousness New focal neurological signs Failure to improve	Neuroimaging and neurosurgical opinion MR venogram
Meningococcal Sepsis	Purpura fulminans	Rapidly progressive rash	Ensure on appropriate antibiotics Involve critical care and infection specialist as soon as possible
	Septic shock	Cold peripheries Refractory hypotension	Ensure on appropriate antibiotic therapy Involve critical care and infection specialist as soon as possible

► Any questions ?

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Suresh
Chhetri

Suresh's 22 mile/35 km walk P2B4MND page

Fundraising for Lancashire Teaching Hospitals NHS Foundation Trust Charity

📅 Event: Suresh's 22 mile/35 km walk P2B4MND, 29 Sep 2018

👥 Team: P2B4MND raising funds for MND Care & Research centre (new local charity covering Lancashire & South Cumbria) and the MNDA