MMed and DCH Lectures

Weekly by Zoom

Prof Trevor Duke

MMed and DCH Lectures

Meningitis and encephalitis in children

May 25, 2020

Prof Trevor Duke


7 year old girl with fever and a seizure
Unwell only 2 days, cough, fever and ear discharge
Sleepy this morning, could not be woken by father
Seizure in COPD →

Care of any seriously ill child

- Triage
- Emergency treatment
- History and examination
- Laboratory investigations, if required
- Main diagnosis and other diagnoses
- Treatment
- Supportive care
- Monitoring
- Discharge planning
- Follow-up

Triage

- Brief history of the presenting problem
- Take temperature and weight

A. Listen for stridor or obstructed breathing
B. Look for cyanosis and for signs of respiratory distress (chest indrawing, tracheal tug), check SpO_2
C. Feel the skin temperature of the hands and feet, feel the pulse for volume, capillary refill time
D. Assess for lethargy and level of interaction.

- Bacterial meningitis
- Mastoiditis and intracranial abscess

- Viral encephalitis
- Tuberculous meningitis
- Other – intracerebral haemorrhage

Treatment

- A: positioning, NG tube to protect from aspiration
- B: oxygen, CPAP
- C: fluid bolus if signs of shock
- Antibiotics: Ceftriaxone + flucloxacillin
- Anticonvulsants

Meningitis aetiology

- Children >1 months
  - *Streptococcus pneumoniae*
  - *Haemophilus influenza* type b
    - Plasmid-mediated beta-lactamase
    - Decreased affinity to penicillin-binding proteins
  - *Neisseria meningitides*
- Neonatal meningitis (up to 2 months)
  - *E. coli*
  - Group B streptococcus

Antibiotic resistance

	1996–2000	2001–2005	*P* value
S. pneumoniae			
Penicillin	29/116 (25.0)	9/61 (14.8)	0.12
Chloramphenicol	1/115 (0.9)	3/61 (4.9)	0.09
Cotrimoxazole	9/116 (7.8)	6/60 (10.0)	0.64
Tetracycline	2/69 (2.9)	2/27 (7.4)	0.32
H. influenzae			
Ampicillin	27/104 (26.0)	27/58 (46.6)	0.01
Chloramphenicol	27/104 (26.0)	24/58 (41.4)	0.04
Cotrimoxazole	35/104 (33.7)	28/58 (48.3)	0.07

CSF specimens in children with meningitis, Goroka

Complications

Acute complications

A. Airway obstruction, aspiration
B. Breathing: Hypoxaemia, hypercarbia
C. Circulation: Shock
D. Drowsiness / disability: Seizures / coma
E. Electrolytes – hyponatraemia, acidosis
   Environment
F. Fluid overload, dehydration
G. Glucose – Hypoglycaemia
H. Haematology – coagulopathy, thrombosis

Chronic / long term complications

- Motor - ischaemic stroke, hemiplegia
- Hearing loss – neurosensory 10%
- Visual impairment
- Epilepsy
- Hydrocephalus
- Sub-dural collections

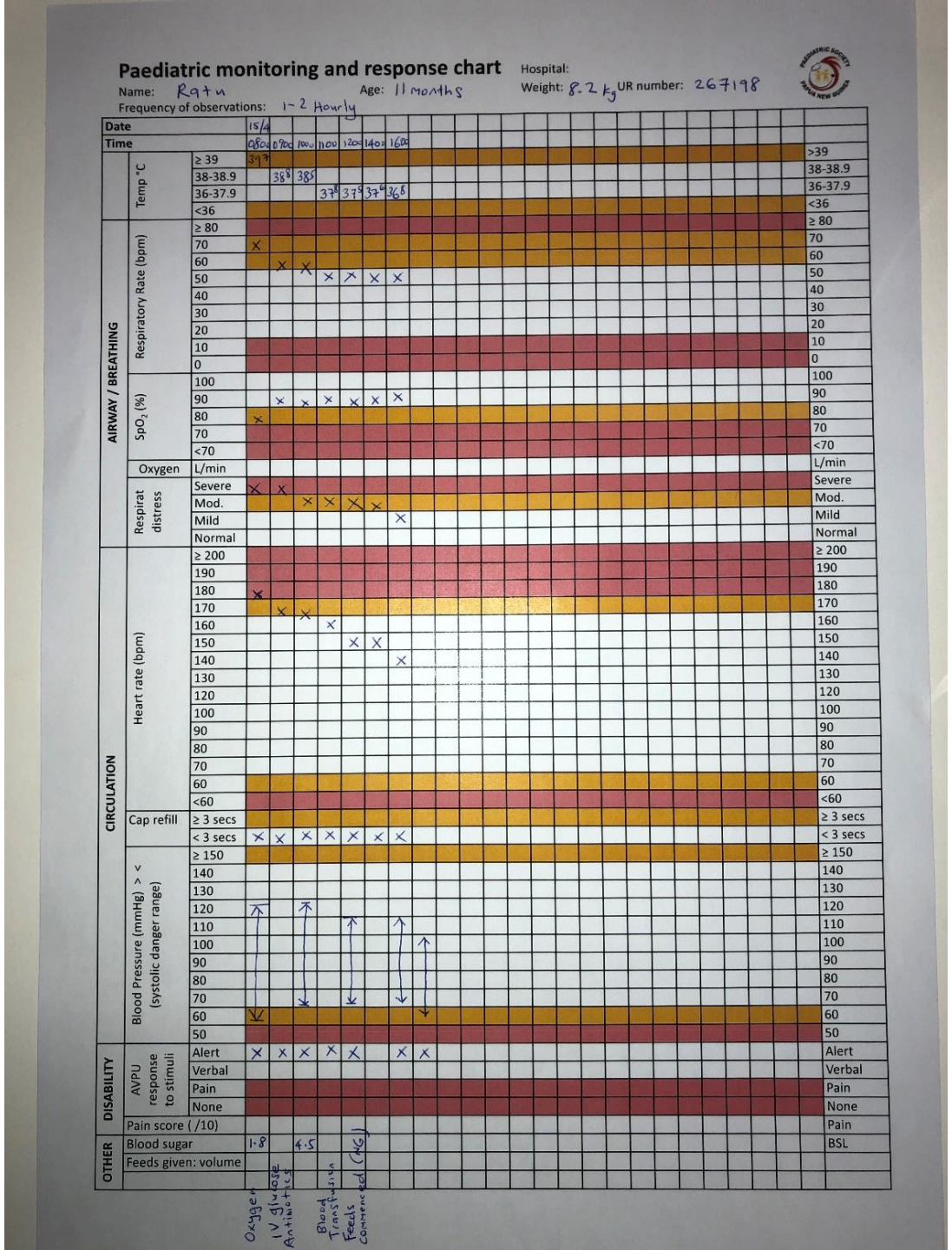
Cerebral abscess

- Gram positive
  - Streptococcus milleri, viridans
  - Staph aureus
- Gram negative aerobic
  - H. influenza
  - E. coli, Proteus
- Anaerobic
- Mastoiditis, chronic serous OM
- Cyanotic congenital heart disease
- Multi-focal Staph infection

Treatment and supportive care

- Nurse in ICU
- Supportive care
  - 30^{o} head up
  - Airway support
  - Oxygen or CPAP
  - NG feeding, careful use of IV fluids.

- Monitoring
  - Continuous / hourly, use a monitoring chart



Immunisation

- Encapsulated bacteria (polysaccharide outer covering)
  - Limited immune response to polysaccharides <2 years
  - Protein conjugate with polysaccharide
- *Haemophilus influenza* type b vaccine (Hib, Pentavalent)
  - Introduced in PNG 2008
  - Protein conjugate with Hib-polysaccharide
- Pneumococcal conjugate vaccine (PCV)
  - Introduced in PNG 2014
  - 13-valent (90+ serotypes)


2 year old boy. Previously well, unwell 2 days, cough, fever, lethargy, rash
Sleepy this morning, could not be woken by father, seizure on way to hospital

Meningococcal sepsis

- “Purpura fulminans”
  - DIC - APTT↑ PT↑ Fibrinogen↓ platelets↓
- Metabolic acidosis
- Thrombosis, tissue ischaemia
- Ceftriaxone + steroids
- Supportive care
- Prevention – meningococcal vaccine
  - Conjugate vaccines serogroups A, C, W and Y
  - Recombinant protein serogroup B

Febrile encephalopathy

- Acute onset of fever and either a change in mental state (such as confusion, disorientation, coma or inability to talk) or new onset of seizures (not including simple febrile convulsions).

Causes of febrile encephalopathy
12 studies, n=2077

- India (4)
- PNG (3)
- Nepal (1)
- Kenya (1)
- Cambodia (1)
- China (1)
- Vietnam (1)

Causes of febrile encephalopathy	Total N (%)
Total	2077
Viruses	297 (14.3)
Bacterial meningitis	262 (12.6)
Cerebral malaria	203 (9.8)
Tuberculous meningitis	108 (5.2)
Septicaemia	13
Disordered electrolytes	6
Hepatic encephalopathy	3
DKA	3
Reyes syndrome	3
Acute Disseminated Encephalomyelitis	2
Cryptococcus neoformans	1
Shigellosis	1
Enteric fever	1
Prolonged coma after seizure	1
Intracranial bleed	1
Known causes	905 (44%)
Unknown	1172 (56%)

Viruses	**297 (14.3)**
Japanese Encephalitis	156 (7.5)
Enterovirus	58 (2.8)
Dengue	31 (1.5)
Cytomegalovirus	19
Herpes Simplex Virus	15
Mumps	13
HHV-7 (Roseola, febrile seizures)	12
HHV-6 (Roseola: fever, diarrhoea, rash)	11
Influenza	9
Rubella	7
Measles	4
Varicella zoster	3
Epstein-Barr Virus	1

Steroids in meningitis

- Effective in:
  - Reducing sensorineural hearing loss in Hib meningitis
  - Reducing mortality in adults with pneumococcal meningitis
- If given at the same time or 15 minutes before the first dose of antibiotics (ceftriaxone)
- Dose
  - Dexamethasone: 0.15mg/kg IV Q6 x 48 hours
  - Methylprednisolone: 1mg/kg Q6 x 48 hours

Fluids in meningitis

Duke T et al. Ann Trop Paeds

346 children with bacterial meningitis randomised to: Oral /NG milk at 60% maintenance or IV half-normal saline + 5% dextrose at 100% maintenance

	Restricted enteral	**Intravenous (100%)**
Number	172	174
Died during admission	31 (18.0%)	28 (16.1%)
Survived, but severe sequelae	26	15
Poor outcome (death or severe neurological sequelae)	57 (33.1%)	43 (24.7%)

Sunken eyes or poor skin turgor risk factor for adverse outcome: OR 5.7 (2.8-11.3)

Eyelid oedema also risk factor for adverse outcome: OR 2.5 (1.4-4.8)

100% maintenance fluids iv will cause oedema in ¼ of all children

Use an isotonic fluid Hartmann solution

Fluids in meningitis

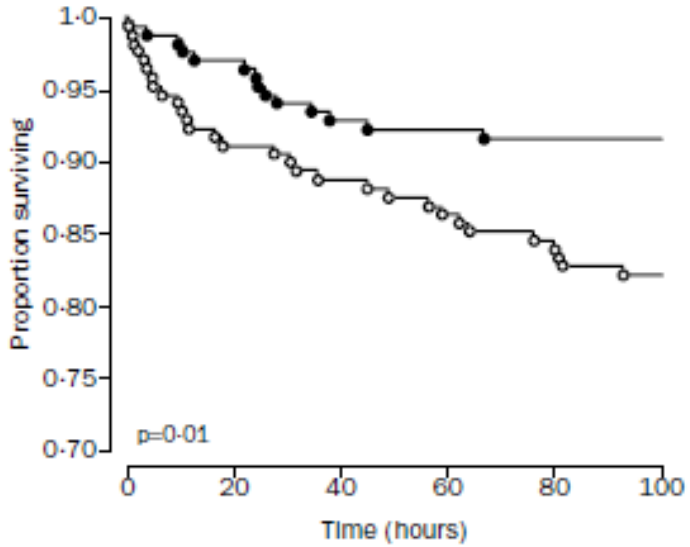
- Correct signs of dehydration
- Give 50% of maintenance IV using an isotonic fluid (Hartmann solution with 5% glucoise ideal)
- Monitor each day for signs of over-hydration or oedema
- If oedema develops reduce IV fluid rate or start frusemide
- (remember oedema may be due to fluid overload, hypoalbuminaemia, immobility, anaemia).
- Commence NG feeds as soon as it is possible (or if the child is awake allow breast feeding).

Anticonvulsants in meningitis

- Safer anticonvulsant drugs than diazepam, phenobarbitone, paraldehyde and phenytoin, especially if monitoring limited and no ICU support
- Levetiracetam
- Sodium valproate

Effect of phenobarbital on seizure frequency and mortality in childhood cerebral malaria: a randomised, controlled intervention study

Jane Crawley, Catherine Waruiru, Sadik Mithwani, Isiah Mwangi, William Watkins, David Ouma, Peter Winstanley, Timothy Peto, Kevin Marsh



	Placebo (n=170)	Phenobarbital (n=170)	Unadjusted analyses		Adjusted analyses	
			Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Seizures						
Three or more of any duration	46 (27%)	18 (11%)	0·32 (0·18–0·58)	<0·001	0·34 (0·19–0·62)*	<0·001
Any lasting 5 min or longer	43 (25%)	20 (12%)	0·39 (0·22–0·70)	0·002	0·42 (0·24–0·76)*	0·004
Any episode of status epilepticus†	23 (14%)	9 (5%)	0·36 (0·16–0·78)	0·01	0·38 (0·17–0·85)*	0·02
Death	14 (8%)	30 (18%)	2·39 (1·28–4·64)	0·01	2·49 (1·19–5·23)‡	0·02
Neurological sequelae						
At discharge	33/156 (21%)	18/140 (13%)	0·55 (0·30–1·02)	0·06	0·56 (0·30–1·05)*	0·07
3 months after discharge	15/144 (10%)	9/131 (7%)	0·63 (0·27–1·47)	0·39	0·69 (0·29–1·65)*	0·40

*Adjusted for seizures before admission.
†Lasting >30 min or more than six within 2 h.
‡Adjusted for factors associated with increased mortality (Blantyre score, respiratory distress, base excess, glucose, urea, creatinine).

Table 2: **Clinical outcome**

Greatest risk of death when diazepam combined with phenobarbitone

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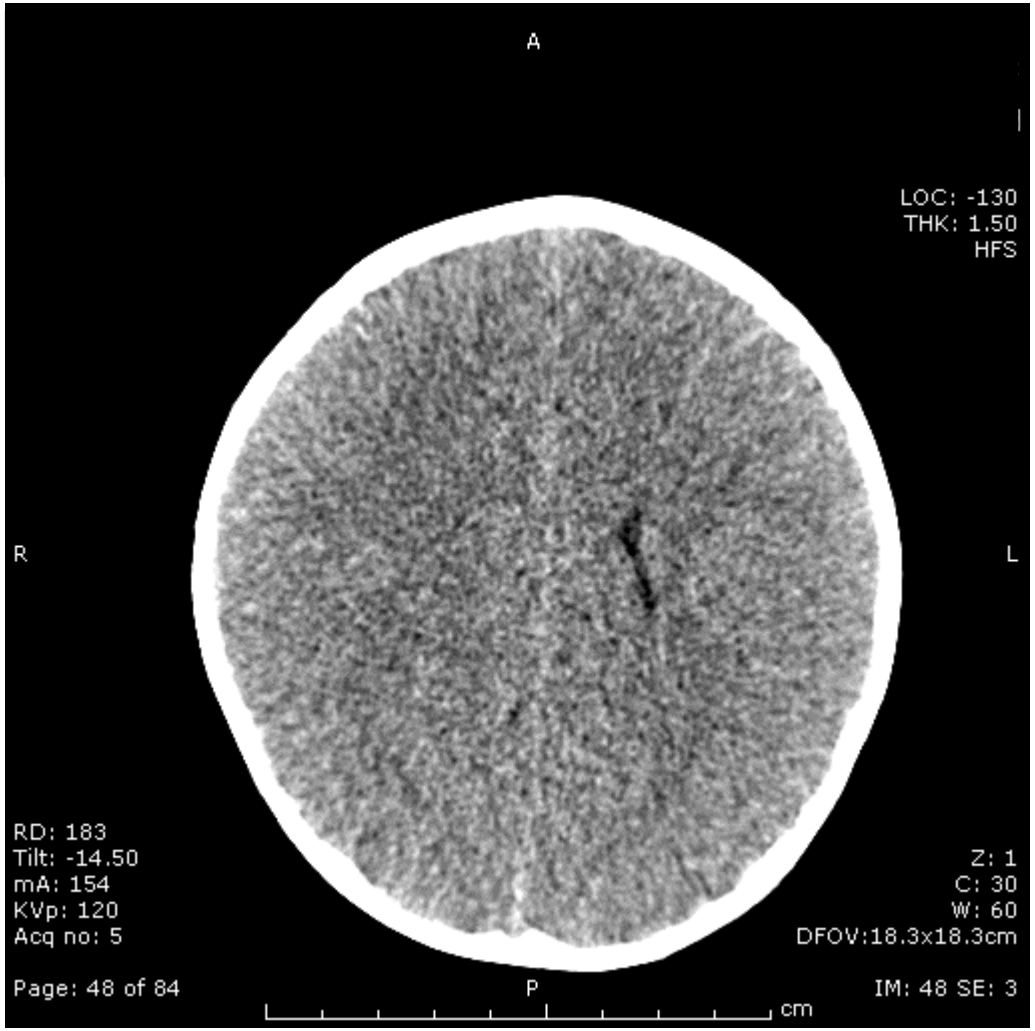
Diazepam doses	Placebo	Phenobarbital	Odds ratio (95% CI)	p
<3 doses	13/150 (9%)	25/162 (15%)	1·9 (0·9–3·9)	0·07
⩾3 doses	1/20 (5%)	5/8 (62%)	31·7 (1·2–814)	0·001

Table 3: **Mortality in phenobarbital and placebo groups, according to number of doses of diazepam**

Non-febrile encephalopathy

- Trauma
- Haemorrhage
- Toxins / drugs
- Metabolic – Ammonia
- Hypertensive
- Epilepsy syndrome
- Acute on chronic encephalopathy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THK: 1.50
HFS
R
L
RD: 183
Tilt: -14.50
mA: 154
KVp: 120
Acq no: 5
Z: 1
C: 30
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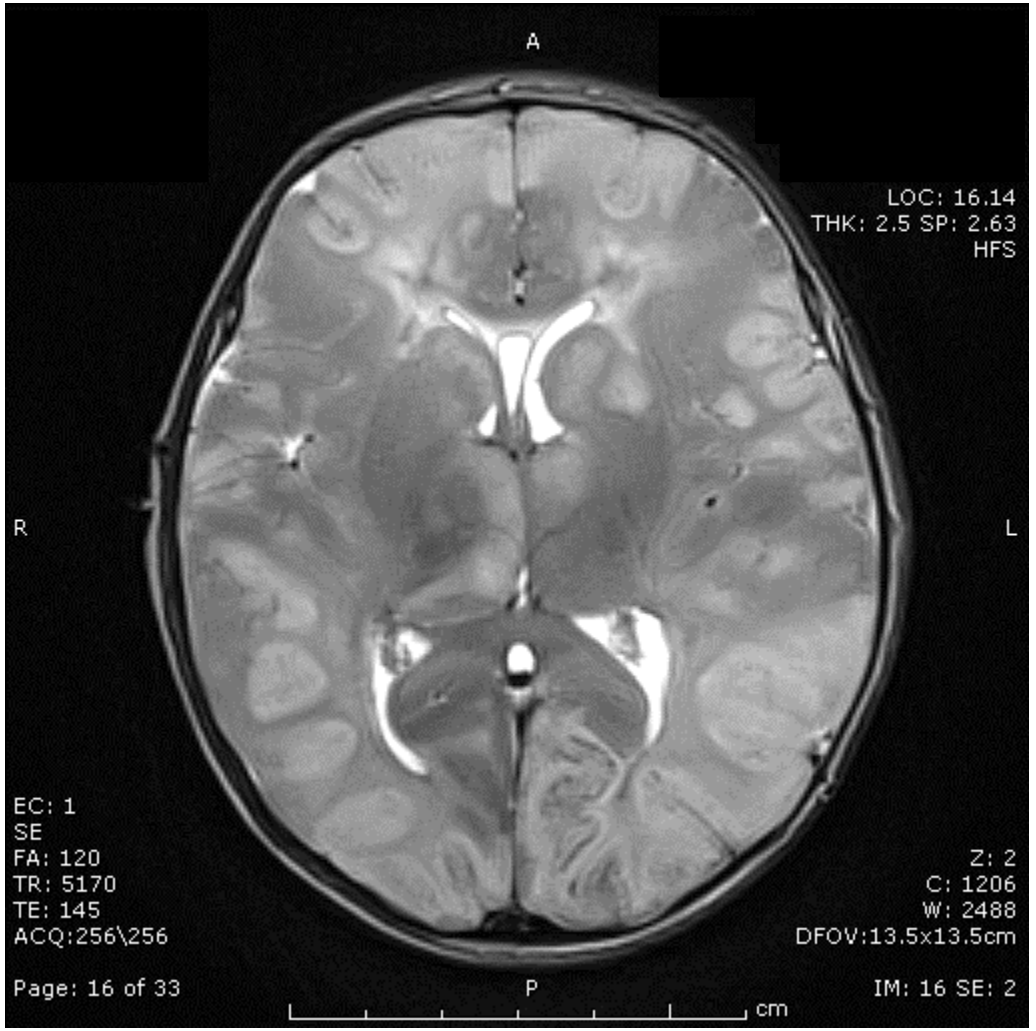
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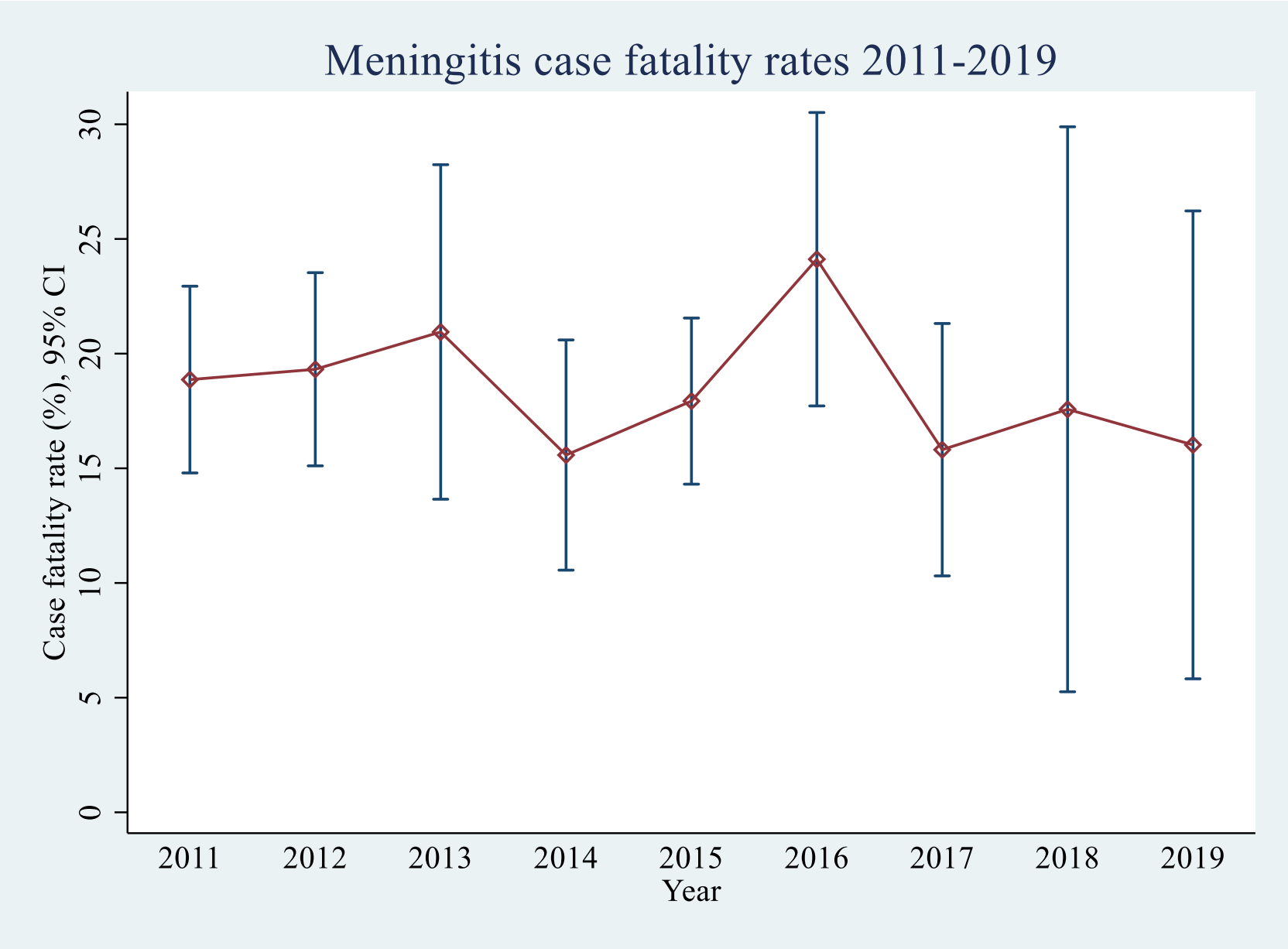
Meningitis case fatality rates 2011-2019
Case fatality rate (%), 95% CI
0
5
10
15
20
25
30
2011
2012
2013
2014
2015
2016
2017
2018
2019
Year