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Ten points on bacterial meningitis

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Déclaration de liens d'intérêt avec les industries de santé en rapport avec le thème de la présentation (loi du 04/03/2002) :

Intervenant : Matthijs Brouwer

Titre : 10 points on bacterial meningitis

L'orateur ne souhaite pas répondre

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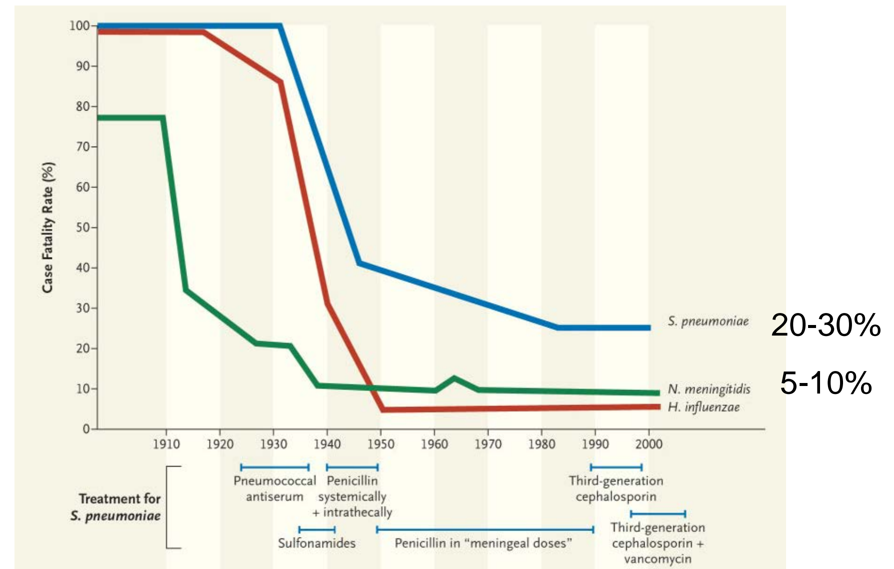
Conférencier ou auteur/rédacteur rémunéré d'articles ou documents	☐	☑
Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations	☐	☑
Investigateur principal d'une recherche ou d'une étude clinique	☐	☑

1. Bacterial meningitis kills and maims

- Mortality
  - *Streptococcus pneumoniae*
  - *Neisseria meningitidis*
  - *Listeria monocytogenes*
  - *Haemophilus influenzae*



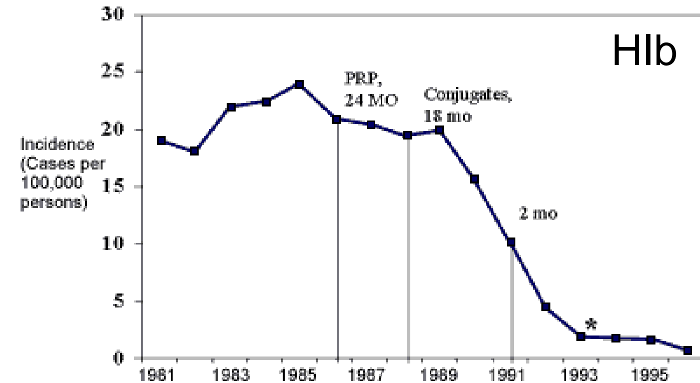
- Sequelae

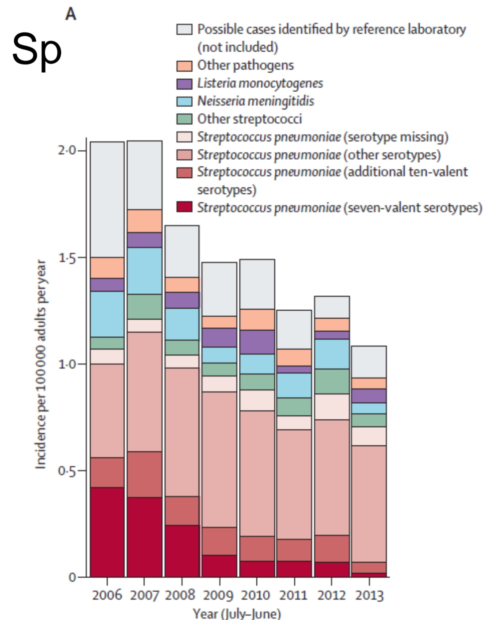
	S. pneumoniae	*N. meningitidis*
– Hearing loss	22%	5%
– Neuropsychological sequelae	32%	32%
– Focal neurologic deficits	10-30%	5%

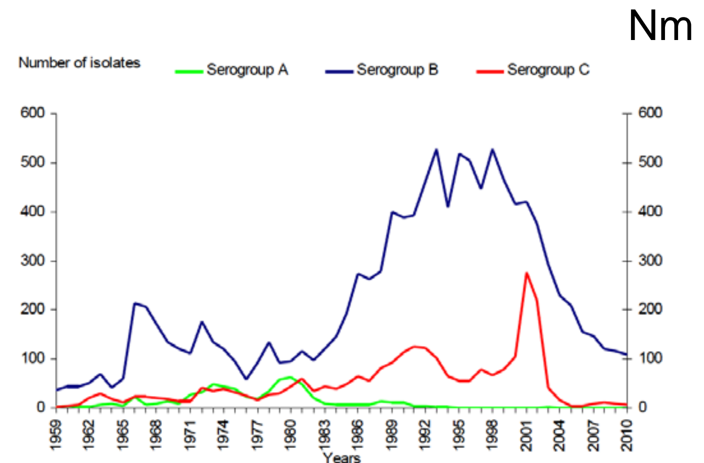
Schwartz *N Engl J Med* 2006, Lucas MJ *J Infection* 2016, Hoogman M *JNNP* 2007

2. Prevention prevails over cure

- Introduction of vaccines
  - 1990's H. influenzae type B
  - 2000 Men C
  - 2005 PCV 7
  - 2010 PCV 10-13







2. Prevention prevails over cure

- Introduction of vaccines
  - 1990's H. influenzae type B — 95-99% reduction
  - 2000 Men C — 95% reduction
  - 2005 PCV 7 — 92% reduction
  - 2010 PCV 10-13

- Patterns
  - Children first → direct protection through vaccination
  - Adults later → herd immunity

Bijlsma MW *Lancet ID* 2016, Bijlsma MW *CID* 2014, Brouwer CMR 2010

3. Diagnosis can be difficult

Suspected neurological infection: broad differential diagnosis

CNS infection

- Bacterial meningitis
- Viral meningitis or encefalitis

CNS inflammation

- Auto-immune meningitis / encephalitis

Infection outside CNS

Other neurological disease

Other systemic disease

3. Diagnosis can be difficult

Prospective study AMC 363 episodes in 3 years

All patients with suspected neurological infection on ER receiving LP.

CNS infection	24%
• Bacterial meningitis	8%
• Viral meningitis	8%
CNS inflammation	10%
• Auto-immune meningitis / encephalitis	
Infection outside CNS	31%
Other neurological disease	33%
Other systemic disease	2%

Khatib U et al, submitted

3. Diagnosis can be difficult

Clinical characteristics fail to predict neurological infection

	Sens	Spec	PPV	NPV
Headache	63%	41%	7%	94%
Fever	38%	65%	7%	93%
Altered mental status	44%	71%	11%	94%
Neck stiffness	63%	87%	28%	97%
Triad	26%	97%	44%	94%
CSF leukocyte >5	100%	57%	16%	100%
CSF leukocyte >1000	44%	100%	100%	96%

Khatib U et al, submitted

3. Diagnosis can be difficult

Clinical characteristics fail to predict bacterial meningitis

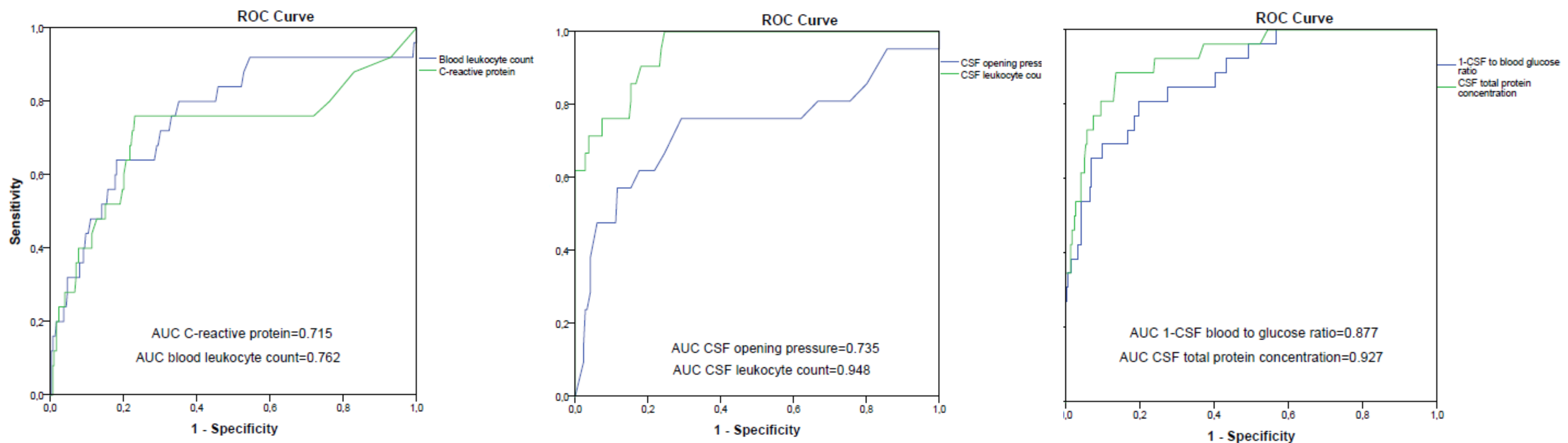
- Meningeal signs: 3 studies, 441 patients

	Sens	Spec	PPV	NPV
Neck stiffness	31%	71%	41%	61%
Kernig's sign	11%	95%	60%	60%
Brudzinksi's sign	9%	95%	50%	62%

Brouwer MC, *Lancet* 2012

3. Diagnosis can be difficult

Best diagnostic accuracy: CSF leukocyte count

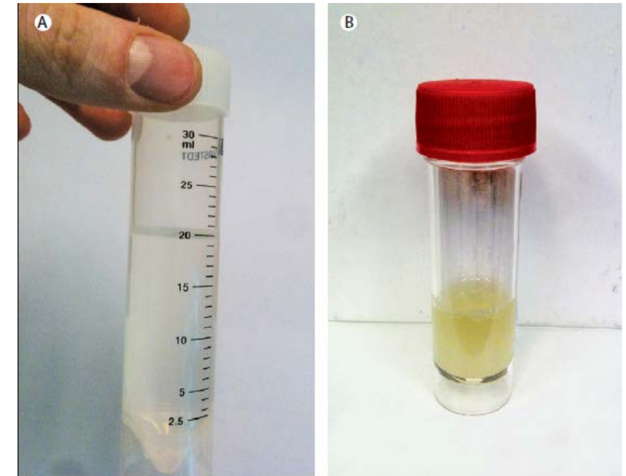


Khatib U et al, submitted

4. Everyone needs a lumbar puncture

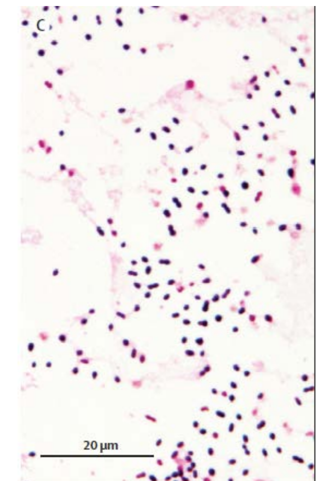
CSF examination needed to

- Confirm the diagnosis
- Identify pathogen
- Perform susceptiblity testing



Diagnosis

- CSF leukocytosis
- High protein
- Positive culture
- Low glucose
- Positive gram stain
- PCR



Brouwer MC, *Lancet* 2012

5. Not everyone needs a CT

Risk of cerebral herniation due to LP (1-2%)

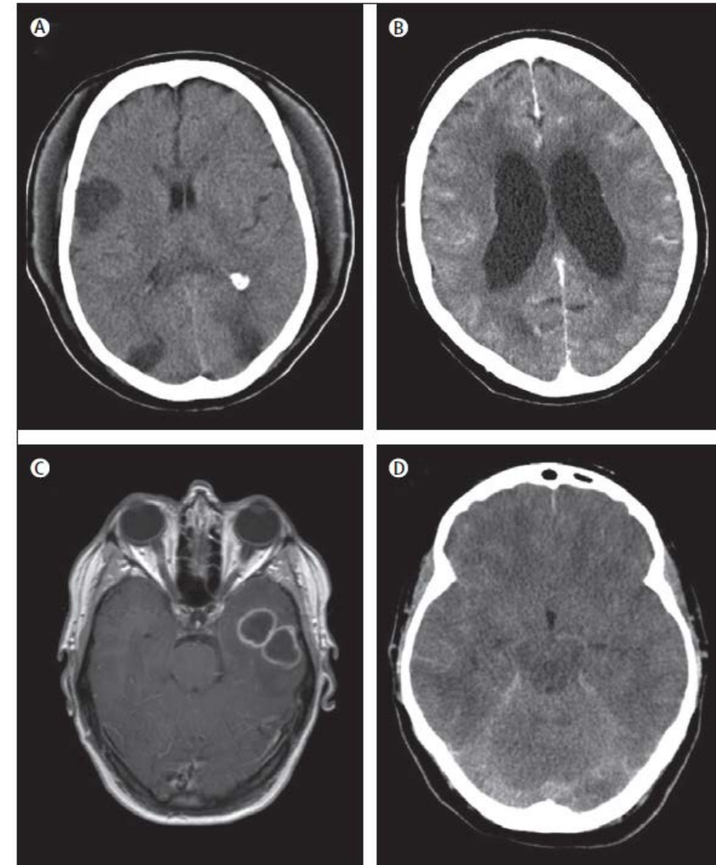
Brain shift on CT predicts herniation

Clinical characteristics predict CT abnormalities

- Focal neurologic deficits
- Score Glasgow Coma Scale <10
- Severe immunocomprose (e.g. HIV)
- Seizures on presentation

Criteria present in 40% of patients

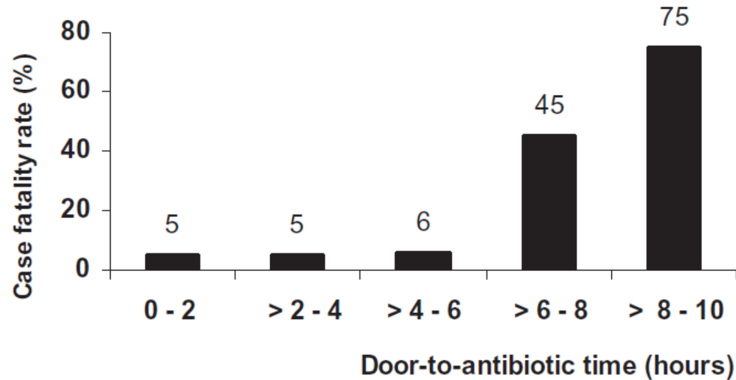
CT performed in 80%

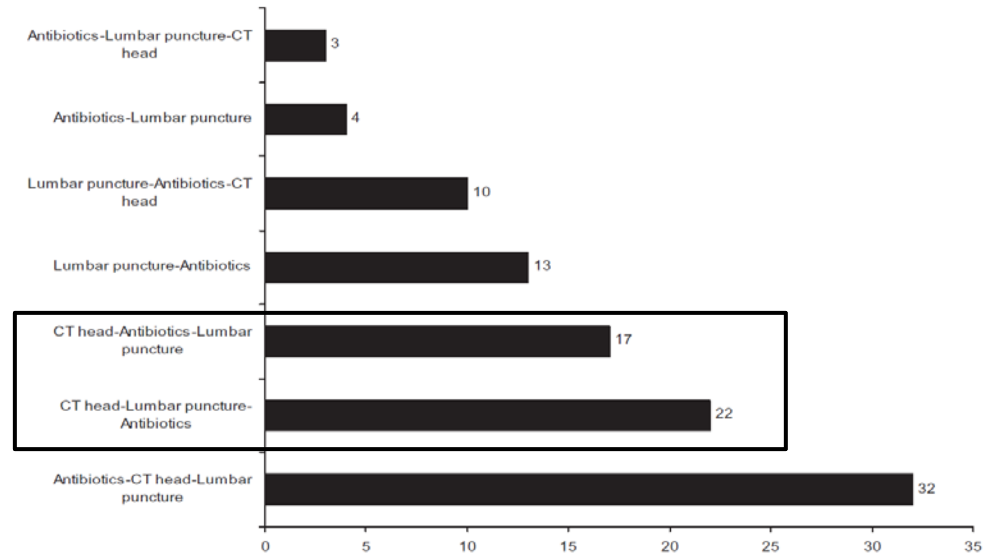


Hasbun, NEJM 2001; van de Beek NEJM 2006

6. Time is brain

CT prolongs time to treatment





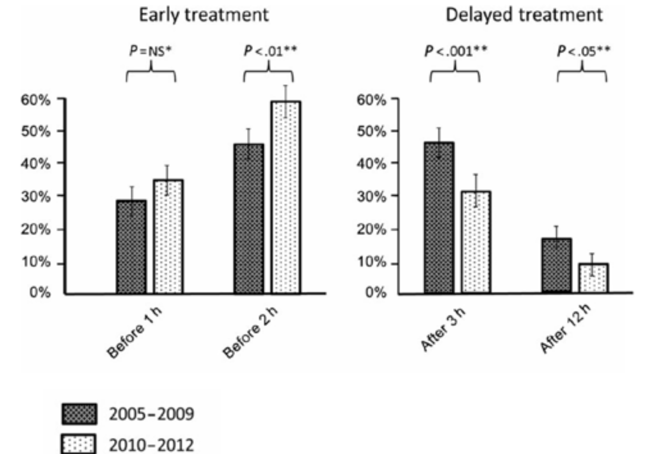
	No. of cases			Crude OR (95%CI)
	Total	Alive	Dead	
Door-to-antibiotic time >3.8 h (study median)	59	48	11	4.3 (1.1–16.2)*
CT of the head followed by lumbar puncture, followed by antibiotics	24	18	6	3.8 (1.1–12.7)*

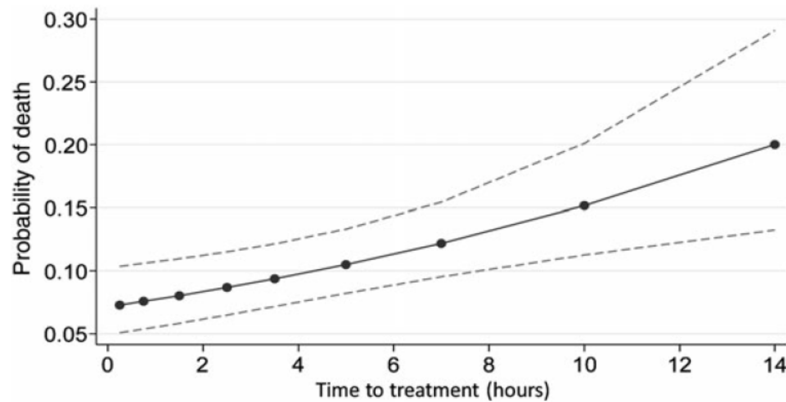
Proulx,QJM 2005

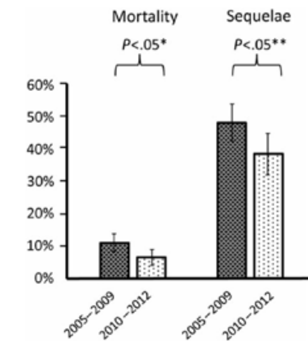
6. Time is brain

Changed practice Sweden 2010:

Better outcome if CT is not routinely performed







Glimaker, *CID* 2015

6. Time is brain

ESCMID guideline bacterial meningitis 2016:

- Start treatment within 1 hour of arrival of the patient

Van de Beek et al, *CMI* 2016

7. Treat what you expect

- Empiric antibiotic treatment based on:
  - Epidemiology
  - Risk factors patients
  - Local resistance patterns

ESCMID guideline	No risk factors listeria		Risk factors listeria
	Age <50 years	Age >50 years	
S. pneumoniae susceptible to penicillin	3rd gen ceph	3rd gen ceph + amoxicillin	3rd gen ceph + amoxicillin
Reduced sensitivity *S. pneumoniae* to penicillin	3rd gen ceph + vancomycin	3rd gen ceph + amoxicillin + vancomycin	3rd gen ceph + amoxicillin + vancomycin

Van de Beek et al, *CMI* 2016

7. Treat what you expect

17e CONFERENCE DE CONSENSUS EN THERAPEUTIQUE ANTI-INFECTIEUSE

Prise en charge des méningites bactériennes aiguës communautaires (à l'exclusion du nouveau-né)

Suspected pathogen (Gram stain)	*S. pneumoniae*	*N. meningitidis*	*L. monocytogenes*	*H. influenzae*
Antibiotics	Ceftriaxon / cefotaxim	Ceftriaxon / cefotaxim	Amoxicillin + gentamycin	Cefotaxim

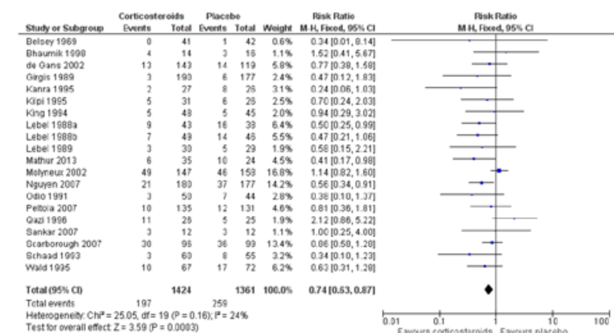
Negative Gram stain	No risk factors for listeria	Risk factors Listeria
Antibiotics	Ceftriaxon / cefotaxim	Ceftriaxon / cefotaxim + amoxicillin + gentamycin

8. Dexamethasone is for everyone

- European dexamethasone trial (301 pts)

	Death		Unfavorable outcome	
	DXM	Placebo	DXM	Placebo
All patients	11/157 (7%)	21/144 (15%)	23/157 (15%)	36/144 (25%)
S. pneumoniae	8/58 (14%)	17/50 (34%)	15/58 (26%)	26/50 (52%)

- Cochrane meta-analysis (4121 pts)
  - No effect mortality
  - Decrease hearing loss, neurological sequelae corticosteroid group



De Gans *NEJM* 2002, Brouwer, *Cochrane* 2015

8. Dexamethasone is for everyone

- Follow-up studies

1. **Comparison nation-wide cohorts Netherlands pneumococcal meningitis**

– 1998-2002 (352 pts) vs. 2006-2009 (357 pts)

– DXM prescription 7% → 92%

– Mortality 30% → 20%

2. **Nationwide cohort 2006-2014 (1412 pts), all bacterial meningitis**

– Pneumococcal OR poor outcome 0.55 (CI 0.38-0.80)

– Non-pneumococcal OR poor outcome 0.44 (CI 0.23-0.85)

– No harm DXM detected

Therefore: also continue DXM in (most) non-pneumococcal meningitis patients

Brouwer, *Neurology* 2010; Bijlsma *Lancet Inf Dis* 2016

9. Ask other specialists

- Often other foci of infection

Pathogen	Infection focus	Ask whom?	What to do?
S. pneumoniae, *H. influenzae*	Otitis / Sinusitis (40%)	Ear-, nose-, throat specialis	Nettoyage
Staph. aureus	Endocarditis (56%)	Cardiology	Cardiac US
S. pneumoniae	Pneumonia (18%)	(Pulmonology)	Chest X-ray
S. pyogenes	Subdural empyema (35%)	(Neurosurgeon)	Cranial MRI
Risk factor			
Alcoholism	Endocarditis (10%), pneumonia (30%)	Cardiology, (Pulmonology)	Cardiac US Chest X-ray

Lucas *Circulation* 2013; Lucas Jinf 2015

10. Follow your patients

- Hearing evaluation in all patients before discharge
  - Early detection facilitates cochlear implant
  - Consult ENT specialist

- Neuropsychological evaluation in selected patients
  - Frequent complaints of concentration loss
  - Neuropsychological evaluation and rehabilitation consultation when interfering with daily living

Hoogman JNNP 2007

11. Merci pour l'attention

ESCMID Study Group for Infectious Diseases of the Brain – ESGIB

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