

# Infections associated with CSF shunts, and CSF drains

Diederik van de Beek | Amsterdam Neuroscience





# Disclosures

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## Conflicts of interest

Consultancies InflaRx and GSK (paid to institution)



# Nosocomial meningitis

Invasive procedures

Craniotomy

CSF catheter (shunt/drain)

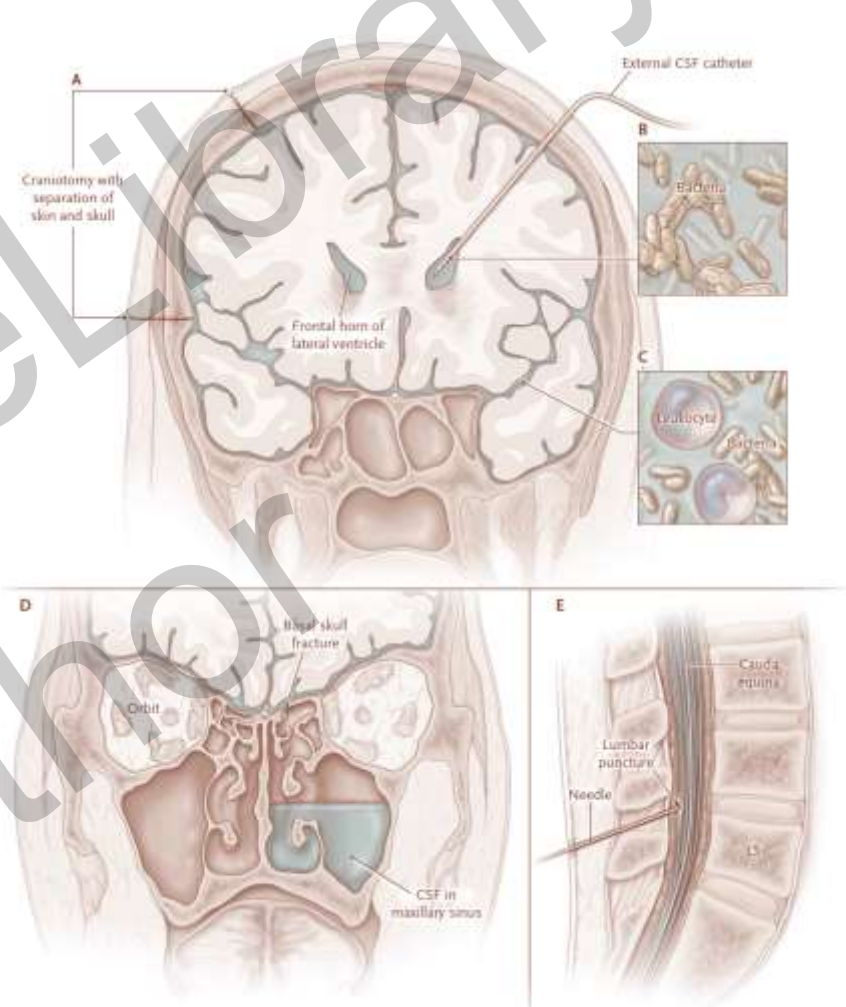
Lumbar puncture

Intrathecal infusions of medication

Complicated head trauma

Metastatic infection hospital infection

van de Beek NEJM 2010





# Internal ventricular catheter

Hydrocephalus

CSF shunt

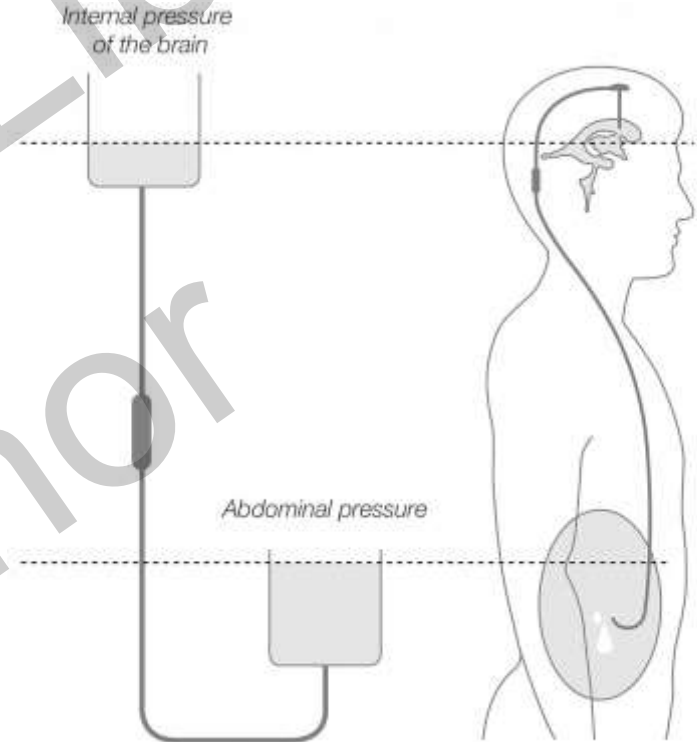
Case incidence infection 4-17%

Colonization at surgery

Infection < 1 month

Holes in surgical gloves

Double gloving decreased infection rate



van de Beek NEJM 2010, Kalkarni J Neurosurg 2001, Tulipan J Neurosurg 2006



# External ventricular catheter

Intracranial pressure monitoring or obstruction

CSF drain: infection rate 8%

Duration of drainage

Routine CSF sampling

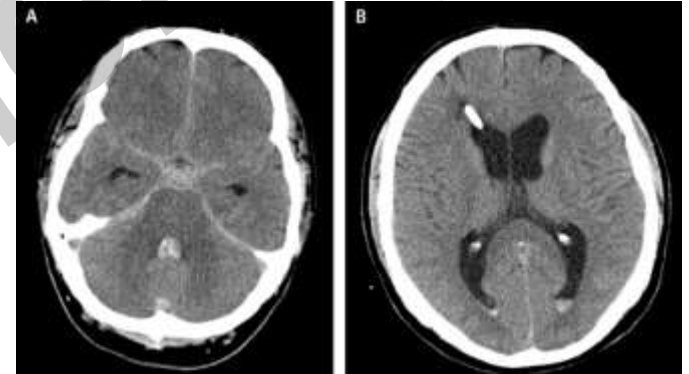
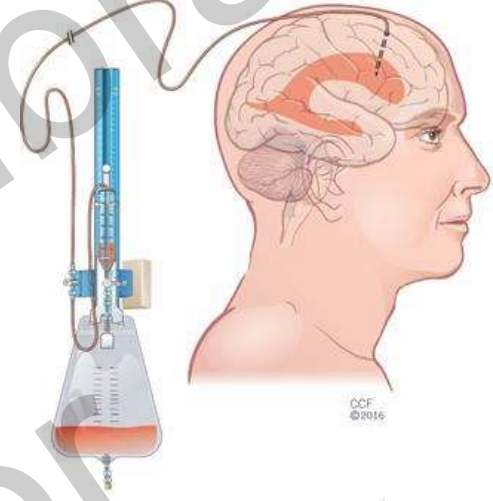
CSF leakage

Drain blockage

Intraventricular hemorrhage

RCT: no routine replacement after 5 days

van de Beek NEJM 2010, Sørensen Br J Neurosurg 2008, Lozier Neurosurgery 2008





# External lumbar catheter

Evaluation normal pressure hydrocephalus

Infection rate 5%

Disconnection of system

Strict protocol: bundle approach

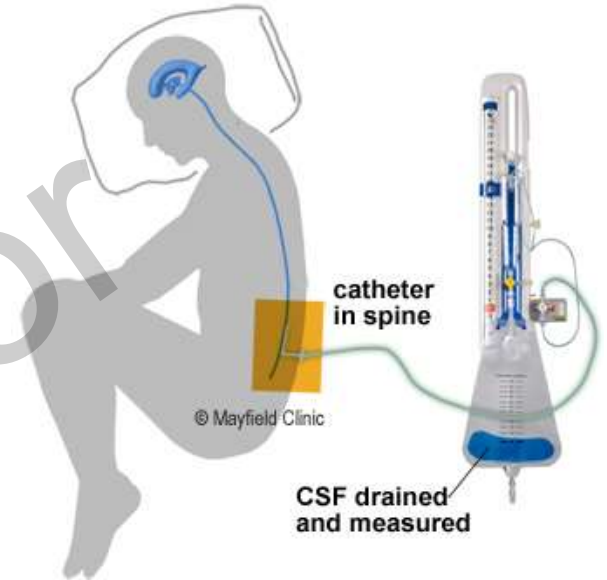
No surveillance testing

Max. 5 days

Sterile reconnection

Removal after blockage of 2<sup>nd</sup> disconnection

van de Beek NEJM 2010, Gouvernale Neurosurg 2008





# Pathogens

## Cutaneous organisms

coagulase-negative staphylococci

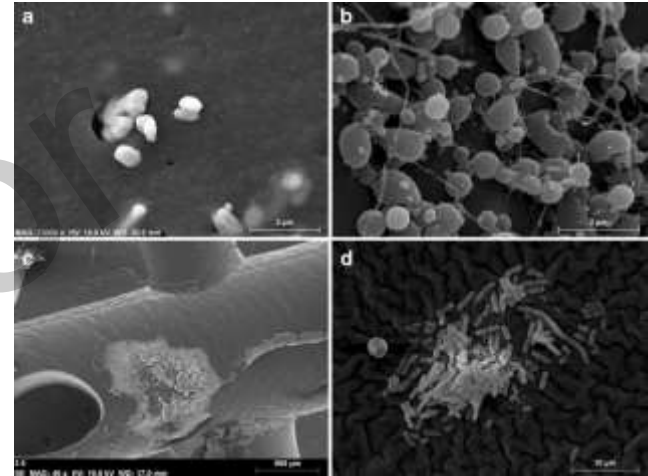
*Staphylococcus aureus*

facultative and aerobic gram-negative bacilli

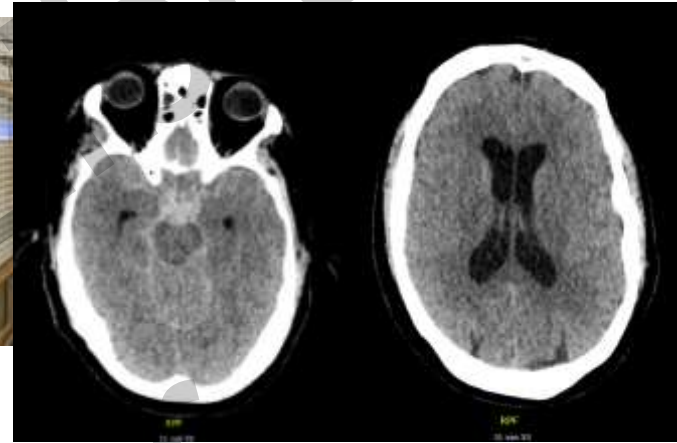
*Propionibacterium acnes*

Vancomycin plus cefepime, ceftazidime, or meropenem

Important role biofilm formation



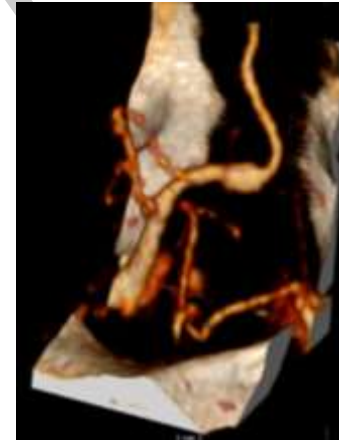




A 57-year-old man

Acute pain neck, vomiting

Neurological examination neck stiffness, otherwise normal







## Case: male, 57 years

Admitted on Acute Stroke Unit

Day 2/decreased level consciousness

ICU admission

CT: increased hydrocephalus

External ventricular catheter



## Case: male, 57 years

Day 4: fever 38.6 C, no headache

Neurological examination normal

ICU: possible aspiration pneumonia

CSF: pressure 12 cm H<sub>2</sub>O, 94400x10<sup>6</sup>/L erythrocytes, 880x10<sup>6</sup>/L leukocytes,  
protein 683 mg/L, glucose 4.28 mmol/L

What now?





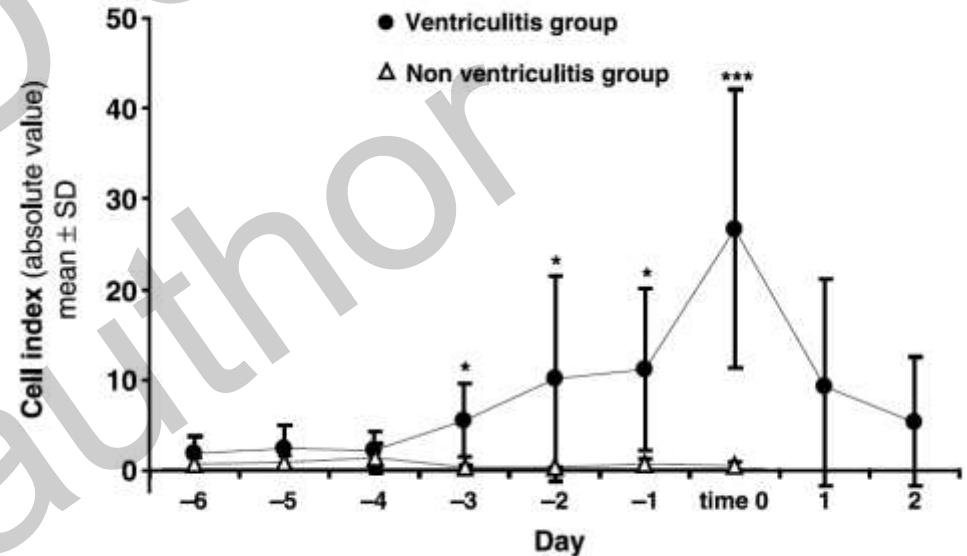
## Case: male, 57 years

- A. Wait-and-see
- B. Rx aspiration pneumonia
- C. Rx bacterial meningitis
- D. Use “cell index” to re-calculate CSF leukocytes



# Cell index

$$\frac{\text{leucocytes (CSF)}/\text{erythrocytes (CSF)}}{\text{leucocytes (blood)}/\text{erythrocytes (blood)}}$$



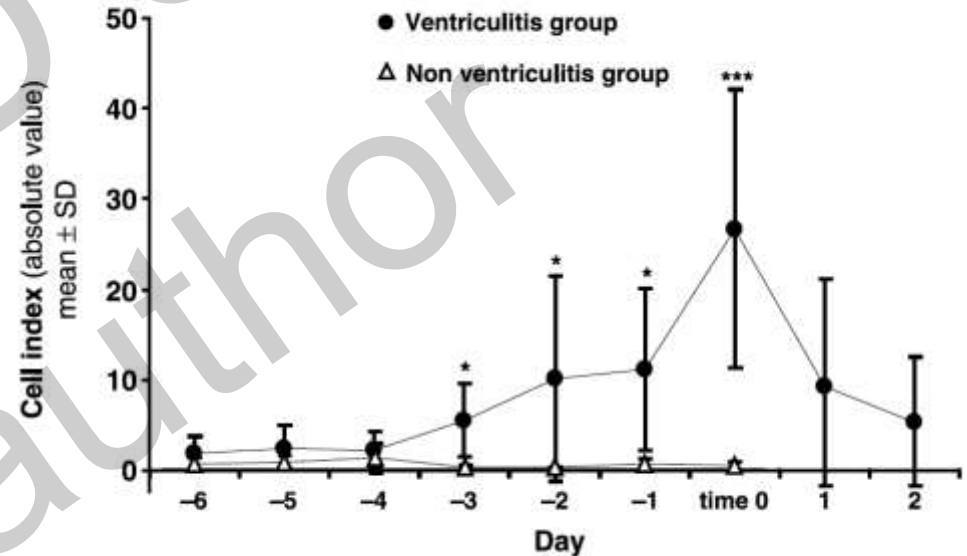


# Cell index

$$\frac{888/94,400}{12/5,230} = 4$$

No studies of diagnostic accuracy

$$\frac{\text{leucocytes (CSF)/erythrocytes (CSF)}}{\text{leucocytes (blood)/erythrocytes (blood)}}$$





# Classification IDSA

1. Contamination: An isolated positive Gram stain, with normal CSF cell count and glucose and protein, and no clinical symptoms suspicious for ventriculitis.
2. Colonization: Multiple positive Gram stains, with normal CSF cell count and glucose and protein, and no clinical symptoms suspicious for ventriculitis or meningitis.
3. Infection: Single or multiple positive Gram stains, leukocytosis and/or hypoglycorrhachia, or an increased protein, and clinical symptoms suspicious for ventriculitis or meningitis.





# Clinical findings

Clinical suspicion: workup and treatment

Fever & decrease level of consciousness

Underlying disease masks symptoms

<50% neck stiffness

Low grade infection: malaise

Distal portion shunt: peritonitis, bacteremia







# Diagnostic workup

1. Neuroimaging: malfunction shunt, masses
2. Cerebrospinal fluid: cell counts, Gram's staining, glucose, protein, cultures

20% CSF culture positive drain infections: no cells!

3. Blood cultures

Aerobic and anaerobic culturing techniques

Some use: CSF lactate, C-reactive protein, procalcitonine, PCR



# Cohort 230 consecutive patients

External CSF drain: lumbar 54%, ventricular 42%, >1 type 4%

Daily sampling and Gram stain

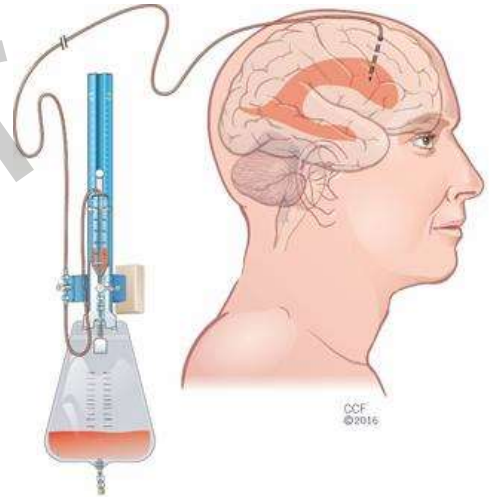
Drain infection 22 patients (10%)

CSF characteristics

Not predictive for infection

Sensitivity and specificity < 60%

Schade J Neurosurg 2006





# CSF lactate

Post-neurosurgery: sensitivity 88%

Drain infection conflicting with

65 episodes

Non-specific symptoms

Lactate normal in 19



	Finding
(%) of episodes	48/60 (80)
cells/L (range)	61 (0.3–5010)
(%) of episodes	46/60 (77)
cells/L (range)	32 (0–3006)
(%) of episodes	34/42 (81)
mmol/L (range)	4 (1–14)
level	
g/L, no. (%) of episodes	36/62 (58)
Median value, g/L (range)	0.8 (0.1–36)
CSF-to-blood glucose ratio	
<0.5, no. (%) of episodes	16/31 (52)
Median value (range)	0.4 (0.1–1)



# Antimicrobial treatment

**Table 2.** Recommended Empirical Antimicrobial Therapy for Nosocomial Bacterial Meningitis, According to the Pathogenesis of the Infection.

Pathogenesis	Common Bacterial Pathogens	Antimicrobial Therapy*
Postneurosurgical infection	Facultative and aerobic gram-negative bacilli (including <i>Pseudomonas aeruginosa</i> ), <i>Staphylococcus aureus</i> , and coagulase-negative staphylococci (especially <i>S. epidermidis</i> )	Vancomycin plus cefepime, ceftazidime, or meropenem†
Ventricular or lumbar catheter	Coagulase-negative staphylococci (especially <i>S. epidermidis</i> ), <i>S. aureus</i> , facultative and aerobic gram-negative bacilli (including <i>P. aeruginosa</i> ), <i>Propionibacterium acnes</i>	Vancomycin plus cefepime, ceftazidime, or meropenem†
Penetrating trauma	<i>S. aureus</i> , coagulase-negative staphylococci (especially <i>S. epidermidis</i> ), facultative and aerobic gram-negative bacilli (including <i>P. aeruginosa</i> )	Vancomycin plus cefepime, ceftazidime, or meropenem†
Basilar skull fracture	<i>Streptococcus pneumoniae</i> , <i>Haemophilus influenzae</i> , group A $\beta$ -hemolytic streptococci	Vancomycin plus a third-generation cephalosporin (i.e., ceftriaxone or cefotaxime)



# Antimicrobial treatment

Microorganism	Standard Therapy	Alternative Therapies
<b>Staphylococci<sup>a</sup></b>		
Methicillin sensitive	Nafcillin or oxacillin	Vancomycin
Methicillin resistant	Vancomycin	Daptomycin, trimethoprim-sulfamethoxazole, or linezolid
<i>Propionibacterium acnes</i>	Penicillin G	Third-generation cephalosporin, <sup>b</sup> vancomycin, daptomycin, or linezolid
<b><i>Streptococcus pneumoniae</i></b>		
Penicillin MIC $\leq 0.06$ $\mu\text{g/mL}$	Penicillin G	Third-generation cephalosporin <sup>b</sup>
Penicillin MIC $\geq 0.12$ $\mu\text{g/mL}$		
Cefotaxime or ceftriaxone MIC $< 1.0$ $\mu\text{g/mL}$	Third-generation cephalosporin <sup>b</sup>	Cefepime or meropenem
Cefotaxime or ceftriaxone MIC $\geq 1.0$ $\mu\text{g/mL}$	Vancomycin plus a third-generation cephalosporin <sup>b,c</sup>	Moxifloxacin <sup>d</sup>
<i>Pseudomonas aeruginosa</i>	Cefepime, ceftazidime, or meropenem	Aztreonam or ciprofloxacin
<i>Haemophilus influenzae</i>		
$\beta$ -lactamase negative	Ampicillin	Third-generation cephalosporin, <sup>b</sup> cefepime, or a fluoroquinolone
$\beta$ -lactamase positive	Third-generation cephalosporin <sup>b</sup>	Cefepime, aztreonam, or a fluoroquinolone
Extended spectrum $\beta$ -lactamase-producing gram-negative bacilli	Meropenem	Cefepime or a fluoroquinolone
<i>Acinetobacter baumannii</i>	Meropenem	Colistin (usually formulated as colistimethate sodium) <sup>a</sup> or polymyxin B <sup>a</sup>
Other Enterobacteriaceae <sup>f</sup>	Third-generation cephalosporin <sup>b</sup>	Meropenem, aztreonam, trimethoprim-sulfamethoxazole, or ciprofloxacin
<i>Candida</i> species <sup>g</sup>	Lipid formulation of amphotericin B $\pm$ flucytosine	Fluconazole or voriconazole
<i>Aspergillus</i> species	Voriconazole	Lipid formulation of amphotericin B or posaconazole



# Intraventricular treatment

Insufficient evidence for routine use

Retrospective case series

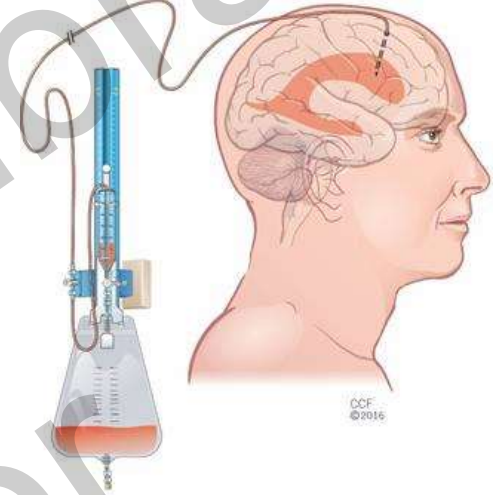
Poor response to systematic treatment

Vancomycin & gentamycin

Administer antimicrobial therapy: clam drain 15-60 minutes

Dose and interval: 10-20 times MIC, ventricular size, daily output drain

Tunkel CID 2017, Tamber J Neurosurg Pediatr 2014, Lewin Neurocrit Care 2018





# Intraventricular treatment

Antimicrobial Agent	Daily Intraventricular Dose
Amikacin	5–50 mg <sup>a</sup>
Amphotericin B deoxycholate <sup>b</sup>	0.01–0.5 mg in 2 mL of 5% dextrose in water
Colistin (formulated as colistimethate sodium)	10 mg
Daptomycin	2–5 mg <sup>c</sup>
Gentamicin	1–8 mg <sup>d,e,f</sup>
Polymyxin B	5 mg <sup>g</sup>
Quinupristin/dalfopristin	2–5 mg
Tobramycin	5–20 mg
Vancomycin	5–20 mg <sup>e,f,h</sup>

van de Beek NEJM 2010, Tunkel CID 2017





# Multidrug resistant Gram-negative bacilli

Acinetobacter species

3rd- and 4th-generation cephalosporins

Intravenous meropenem +/- aminoglycoside IV or IT

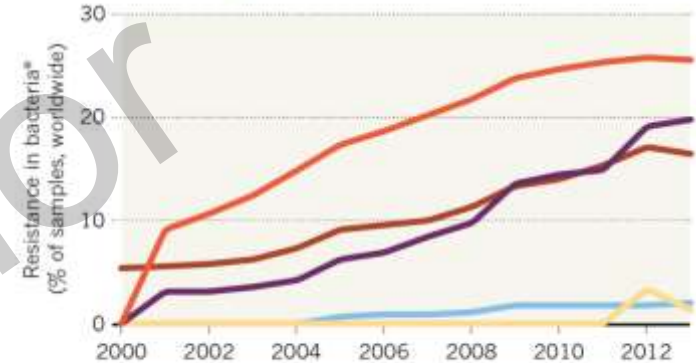
Carbapenem resistance: colistin IV or IT

Last resort: colistin plus tigecycline

## THE SPREAD OF ANTIBIOTIC RESISTANCE

An increasing proportion of bacteria display resistance to common antibiotics.

— Fluoroquinolones — Cephalosporins (3rd gen) — Aminoglycosides  
— Carbapenems — Polymyxins



\*Enterobacterias, including *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* and *Salmonella*

©nature



# Removal of catheters

Infection: removal catheter

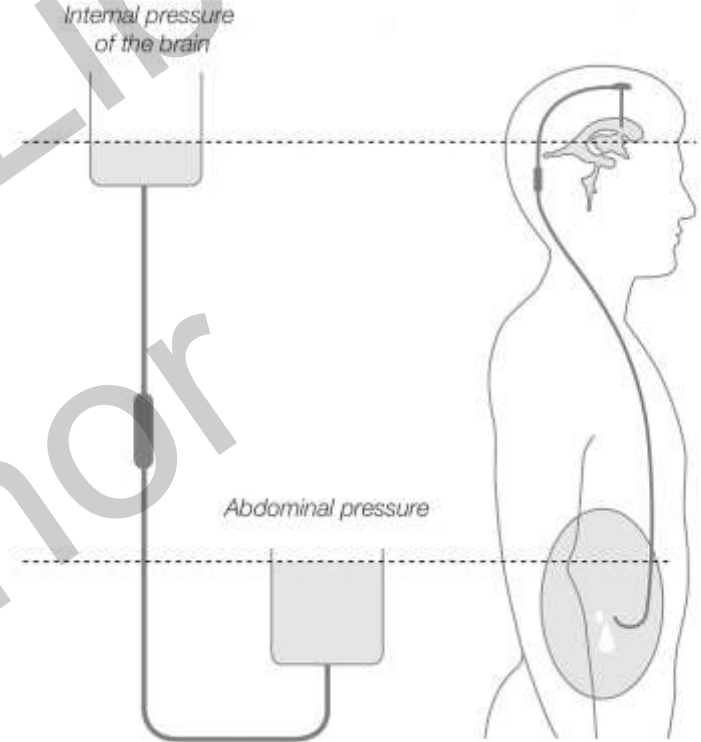
Externalization catheter if needed

Reimplantation: 7-10 days negative cultures

Observational study 42 patients

84% cured with IV and IT antimicrobials

Non *S. aureus* infections





# Prevention of infection

Surgical techniques

Protocols

Double gloving

Prophylactic antimicrobial therapy

Cochrane review

OR infection was 0.52 (95% CI, 0.36-0.74)

**Table 1. Neurosurgical Techniques to Minimize the Risk of Postoperative Meningitis.**

## Before surgery

- Wash scalp hair, remove dirt or debris, and cover open wounds with a clean dressing
- Clip, but do not shave, hair
- Use chlorhexidine or an iodine-based skin preparation
- Drape the surgical site with adhesive drapes and transparent adhesive film to prevent implantable hardware from coming in contact with exposed skin
- Maintain sterile field with careful aseptic techniques
- Administer prophylactic antibiotics to achieve adequate tissue concentrations before incision

## During surgery

- Minimize blood loss and tissue trauma; avoid hypothermia unless it is deliberately induced
- Remove devitalized and grossly contaminated tissue and small bone fragments
- Use a double layer of gloves when handling implantable devices
- Irrigate the operative field with warmed sterile physiologic solution
- Perform careful hemostasis to avoid postoperative wound hematomas
- Position the cerebrospinal fluid drainage devices carefully to maintain a continuous flow of cerebrospinal fluid; ensure that the exit site is fashioned so that there is no leakage around the cerebrospinal fluid drain; ensure that the catheter is tunneled from the insertion site and secured to the skin so that it cannot be dislodged and that it is connected securely to a sterile drainage system; sample the cerebrospinal fluid under sterile conditions
- Close the skin carefully, with wound edges secured to prevent leakage of cerebrospinal fluid but with good skin perfusion; avoid passing hardware directly beneath the incision

## After surgery

- Use percutaneous drains to collect postoperative hemorrhage; ensure that the drains are tunneled so that they will not leak and secured so that they cannot be dislodged
- Apply a barrier dressing where necessary, particularly to prevent the patient from inadvertently opening the wound
- Avoid putting pressure on the wound in the postoperative period; take measures to prevent pressure sores in other areas



# Antimicrobial-impregnated catheters

Minocycline or clindamycin combined with rifampin

RCT 110 patients CSF shunt (internal catheter)

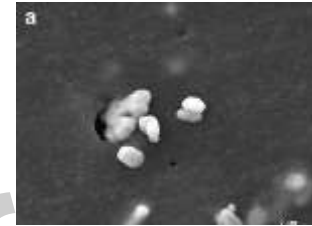
17% vs 6% infections ( $p=0.084$ )

Systematic review 2613 shunt procedures

3% vs. 7% ( $p<0.00001$ )

Regardless of hospital size, shunt volume, location, patient risk factors

Govender J Neurosurg 2003, Thomas Br J Neurosur 2012, Jenkinson Trials 2014



STUDY PROTOCOL

Open Access

The British antibiotic and silver-impregnated catheters for ventriculoperitoneal shunts multi-centre randomised controlled trial (the BASICS trial): study protocol



## Case: male, 57 years

Start vancomycine 2 dd 1000 mg plus ceftazidime 2 dd 2000 mg

Bloodcultures negative

CSF cultures negative

Removal catheter

Stop antibiotics after 5 days



**Amsterdam UMC**  
University Medical Centers



# Conclusions

Strict protocols decrease infection risks

CSF parameters do not rule out meningitis

Clinical suspicion: start antimicrobial treatment

Intraventricular treatment = last resort

RCT antimicrobial impregnated catheters



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# Further reading

THE NEW ENGLAND JOURNAL OF MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

## Nosocomial Bacterial Meningitis

Diederik van de Beek, M.D., Ph.D., James M. Drake, M.B., B.Ch.,  
and Allan R. Tunkel, M.D., Ph.D.

Clinical Infectious Diseases

IDSA GUIDELINE



2017 Infectious Diseases Society of America's Clinical  
Practice Guidelines for Healthcare-Associated Ventriculitis  
and Meningitis\*

Allan R. Tunkel,<sup>1</sup> Rodrigo Hasbun,<sup>2</sup> Adarsh Bhatnagar,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheldt,<sup>6</sup> Diederik van de Beek,<sup>7</sup>  
Thomas P. Block,<sup>8</sup> Hugh J. L. Gertsen,<sup>9</sup> and Joseph R. Zaccaro<sup>10</sup>



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