

## Infections neuro-méningées sur matériels implantés

Pr Claire DAHYOT-FIZELIER  
INSERM U1070 research group  
Université et CHU de Poitiers

## Déclaration d'intérêts de 2014 à 2022

- Aucun

# Sites infectieux & contextes multiples

## Type d'infection

- Méningite
- Ventriculite
- Empyème

## Craniotomie

- Matériel de fixation
- Cranioplastie
- Electrodes de stimulation
- Boitiers

## Matériel

- DVE
- DVP
- DVA
- DLE

# Incidence variable selon le contexte...

## Diagnostic Approach to Health Care- and Device-Associated Central Nervous System Infections



Ryan M. Martin,<sup>a,b</sup> Lara L. Zimmermann,<sup>a,b</sup> Mindy Huynh,<sup>c</sup> Christopher R. Polage<sup>c,d</sup>

**TABLE 1** Rates of infection of common neurosurgical surgeries and devices

Surgery	Rate of infection (%)
Craniectomy	1–24.4
Craniotomy	0.3–12
Spine surgery with hardware	3–7
Spine surgery without hardware	<2
Diagnostic lumbar puncture	~1 in 50,000 procedures
Temporary devices	
Ventriculostomy (i.e., EVD) <sup>a</sup>	2–22 (avg. 8)
Parenchymal ICP monitor	<0.2
Lumbar drain	5
Permanent devices	
Ventricular shunt	8 (pediatric), 4–17 (adults)
Spinal cord medication pumps	<6
Deep brain stimulators	<1

DVE & DVI ~ 8 à 10%

<sup>a</sup>EVD, external ventricular drain.



# RISK FACTORS FOR ADULT NOSOCOMIAL MENINGITIS AFTER CRANIOTOMY ROLE OF ANTIBIOTIC PROPHYLAXIS

Anne-Marie Korinek MD,

Prospective, observationnelle (n=6243). Mai 1997- Déc 2003

Méningites : 1,5%

TABLE 2. Risk factors for meningitis after craniotomy (univariate analysis).

Risk factor	No meningitis N = 6148 (%)	Meningitis N = 95 (%)	P
Age (years)	51 ± 16	49 ± 16	0.20
Sex Male	3077 (50)	57 (60)	0.054
ASA score > 2 <sup>a</sup>	391 (8.6)	6 (9.1)	OR: 1.9; 95%CI: 1.2-3.0
NNIS score ≥ 1 <sup>a</sup>	1223 (27.0)	30 (45.4)	
LOS before surgery (days)	3.1 ± 11.2	4.3 ± 7.3	0.29
Emergency surgery	1308 (21.3)	16 (16.8)	0.29
Duration of surgery (min)	160 + 109	215 + 135	< 0.0001
Duration of surgery ≥ 4 h	1167 (19.6)	32 (34.0)	0.0005
Contamination class			OR: 1.7; 95%CI: 1.1-2.8
Clean	5358 (87.1)	76 (80.0)	
Clean-contaminated	687 (11.2)	18 (18.9)	0.056
Dirty	103 (1.7)	1 (1.0)	
No antibiotic prophylaxis	1023 (16.6)	17 (17.9)	OR: 28.4; 95%CI: 16.9-47.5
ABP Protocol observance	5191 (84.4)	84 (88.4)	
Cerebrospinal fluid leakage	85 (1.4)	35 (36.8)	< 0.0001
Early re-operation	364 (5.9)	20 (21.0)	< 0.0001
Incision infection	288 (4.7)	43 (45.3)	< 0.0001
Incision infection before meningitis	288 (4.7)	26 (27.3)	OR: 3.7; 95%CI:2,1-6,3

Mortalité à 3 mois : méningites vs globale 4,7% vs 13,7%

# Morbidity of Ventricular Cerebrospinal Fluid Shunt Surgery in Adults: An 8-Year Study

Neurosurgery 68:985-995, 2011

Anne-Marie Korinek MD,

**TABLE 6.** Independent Risk Factors for Shunt Revision Because of Infection, by Multivariate Analysis (Stepwise Cox Regression Model)<sup>a</sup>

Variable	Hazard Ratio (95% CI)	P Value
Previous CSF leak	3.91 (1.95-7.82)	.0001
Previous shunt revision for mechanical dysfunction	3.36 (1.76-6.38)	.0002
Surgery beginning after 10 AM	2.11 (1.15-3.89)	.016
Operating time	1.02 (1.03-1.04)	.018

1999-2006. 839 / 14275 neurochirurgies  
N = 720 patients analysés.

Infection neuroméningée : 6,1%

# Morbidity of Ventricular Cerebrospinal Fluid Shunt Surgery in Adults: An 8-Year Study

Neurosurgery 68:985-995, 2011

Anne-Marie Korinek MD,

**TABLE 6.** Independent Risk Factors for Shunt Revision Because of Infection, by Multivariate Analysis (Stepwise Cox Regression Model)<sup>a</sup>

Variable	Hazard Ratio (95% CI)	P Value
Previous CSF leak	3.91 (1.95-7.82)	.0001
Previous shunt revision for mechanical dysfunction	3.36 (1.76-6.38)	.0002
Surgery beginning after 10 AM	2.11 (1.15-3.89)	.016
Operating time	1.02 (1.03-1.04)	.018

1999-2006. 839 / 14275 neurochirurgies  
N = 720 patients analysés.

Infection neuroméningée : 6,1%

## A meta-analysis of ventriculostomy-associated cerebrospinal fluid infections

Ramanan et al. *BMC Infectious Diseases*  
2015

Mahesh Ramanan<sup>1,2\*</sup>, Jeffrey Lipman<sup>1,2</sup>, Andrew Shorr<sup>3</sup> and Aparna Shankar<sup>4</sup>

33 études. 752 infections de DVE /6681 patients

Infections de DVE : 11,3%  
11.4/1000 journées- catheter (95% CI 9.3 to 13.5)

# Quelles bactéries ?

**RISK FACTORS FOR ADULT NOSOCOMIAL  
MENINGITIS AFTER CRANIOTOMY ROLE  
OF ANTIBIOTIC PROPHYLAXIS**

---

www.neurosurgery-online.com  
VOLUME 58 | NUMBER 7 | JULY 2006

Cocci+ & BGP ~ 58%

**Morbidity of Ventricular Cerebrospinal Fluid  
Shunt Surgery in Adults: An 8-Year Study**

---

*Neurosurgery 68:985-995, 2011*

Anne-Marie Korinek MD,

Cocci + & BGP : 74%

**A meta-analysis of ventriculostomy-associated  
cerebrospinal fluid infections**

BMC infect Dis.2015.8:15-3.

Mahesh Ramanan<sup>1,2\*</sup>, Jeffrey Lipman<sup>1,2</sup>, Andrew Shorr<sup>3</sup> and Aparna Shankar<sup>4</sup>

Cocci + & BGP : 65%

Germes commensaux cutanéomuqueux

# Une morbi-mortalité élevée...

## Clinical Characteristics and Predictors of Adverse Outcome in Adult and Pediatric Patients With Healthcare-Associated Ventriculitis and Meningitis

Chanunya Srihawan,<sup>1</sup> Rodrigo Lopez Castelblanco,<sup>1</sup> Lucrecia Salazar,<sup>1</sup> Susan H. Wootton,<sup>2</sup> Elizabeth Aguilera,<sup>2</sup> Luis Ostrosky-Zeichner,<sup>1</sup> David I. Sandberg,<sup>3,4</sup> HuiMahn A. Choi,<sup>3,5</sup> Kiwon Lee,<sup>3,5</sup> Ryan Kitanawa,<sup>3,5</sup> Nitin Tandon,<sup>3,4,5</sup> and Rodrigo Hachun<sup>1</sup>

*Open Forum Infectious Diseases*

MAJOR ARTICLE

2016

**Table 3. Clinical Outcomes of 215 Adult and Pediatric Patients With Healthcare-Associated Meningitis or Ventriculitis**

Glasgow Outcome Scale	No. (%)
Death	20 (9.30)
Persistent vegetative state	31 (14.42)
Severe disability <sup>a</sup>	77 (35.81)
Moderate disability <sup>b</sup>	39 (18.14)
Good recovery	48 (22.33)

62,5% de mauvais pronostic

# Une morbi-mortalité élevée...

## Clinical Characteristics and Predictors of Adverse Outcome in Adult and Pediatric Patients With Healthcare-Associated Ventriculitis and Meningitis

Chanunya Srihawan,<sup>1</sup> Rodrigo Lopez Castelblanco,<sup>1</sup> Lucrecia Salazar,<sup>1</sup> Susan H. Wootton,<sup>2</sup> Elizabeth Aguilera,<sup>2</sup> Luis Ostrosky-Zeichner,<sup>1</sup> David I. Sandberg,<sup>3,4</sup> HuiMahn A. Choi,<sup>3,5</sup> Kiwon Lee,<sup>3,5</sup> Ryan Kitinawa,<sup>3,5</sup> Nitin Tandon,<sup>3,4,5</sup> and Rodrigo Hachun<sup>1</sup>

*Open Forum Infectious Diseases*

MAJOR ARTICLE

2016

**Table 3. Clinical Outcomes of 215 Adult and Pediatric Patients With Healthcare-Associated Meningitis or Ventriculitis**

Glasgow Outcome Scale	No. (%)
Death	20 (9.30)
Persistent vegetative state	31 (14.42)
Severe disability <sup>a</sup>	77 (35.81)
Moderate disability <sup>b</sup>	39 (18.14)
Good recovery	48 (22.33)

62,5% de mauvais pronostic

## Ventriculitis: A Severe Complication of Central Nervous System Infections

David Lunna-Paz,<sup>1,2</sup> Matthieu Rouvet,<sup>1,2,3</sup> Françoise Funàne,<sup>4</sup> Sarah Roukthir,<sup>5</sup> Loren Dainiac,<sup>5</sup> Pierre Tattavin,<sup>1,2,3</sup> and Pierre-Jean La Roca<sup>6</sup>

*Open Forum Infectious Diseases*

MAJOR ARTICLE

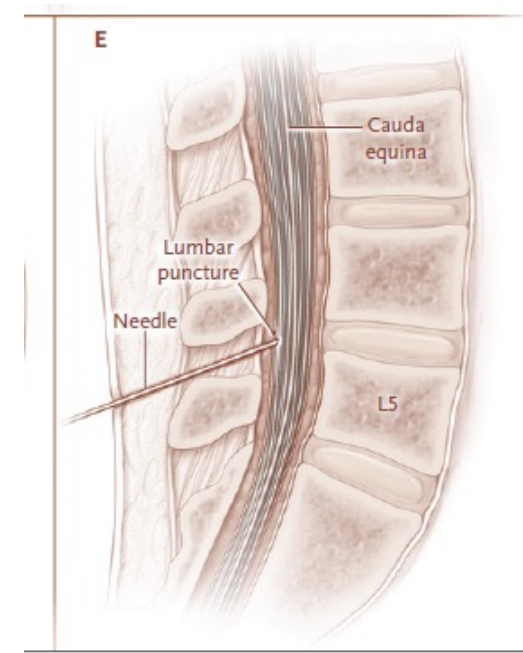
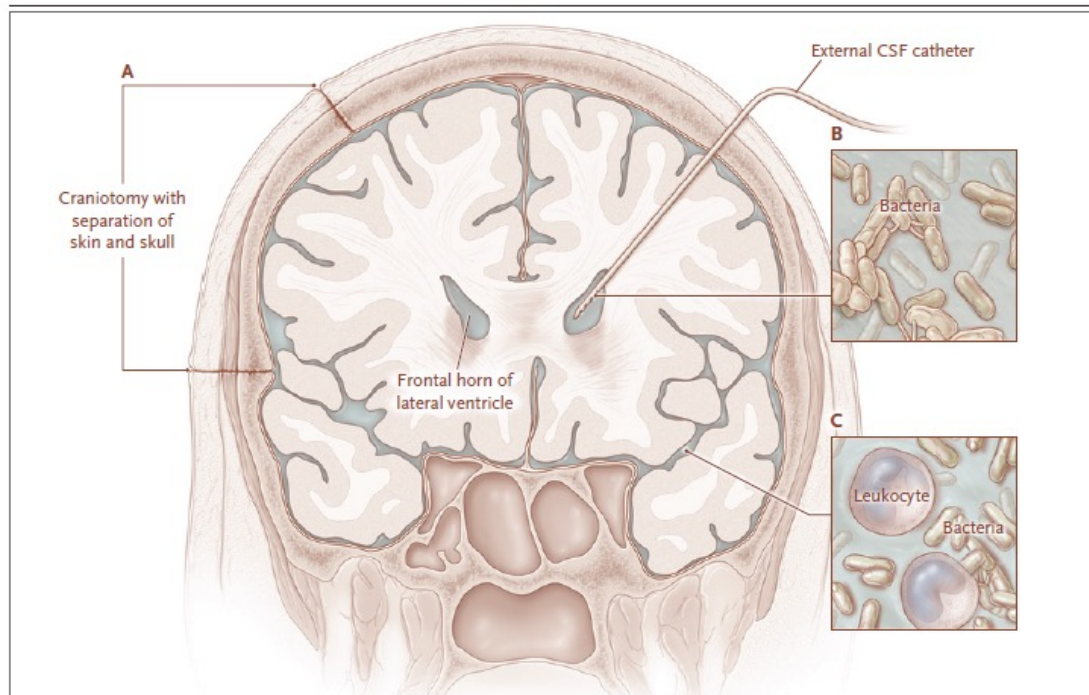
2021

Mortalité hospitalière = 30.6% (n = 30/98)  
Mortalité à 1 an = 38.8% (n = 38/98)



# Physiopathologie

- Microorganisme au niveau du site d'insertion : Défaut d'asepsie à la pose, lésions cutanées
- Migration secondaire, le long de la face interne (DVE/DVP/DLE) : contamination lors de prélèvements, brèche & écoulement LCS
- Plus rares : bactériémie, infection abdominale (DVP)





**Le meilleur traitement c'est la prévention !**



# Antibiotic or silver versus standard ventriculoperitoneal shunts (BASICS): a multicentre, single-blinded, randomised trial and economic evaluation

Conor L Mallucci\*, Michael D Jenkinson\*, Elizabeth J Conroy, John C Hartley, Michaela Brown, Joanne Dalton, Tom Kearns, Tracy Moitt, Michael J Griffiths, Giovanna Culeddu, Tom Solomon, Dyfrig Hughes, Carrol Gamble, for the BASICS Study collaborators†

Lancet 2019; 394: 1530-39

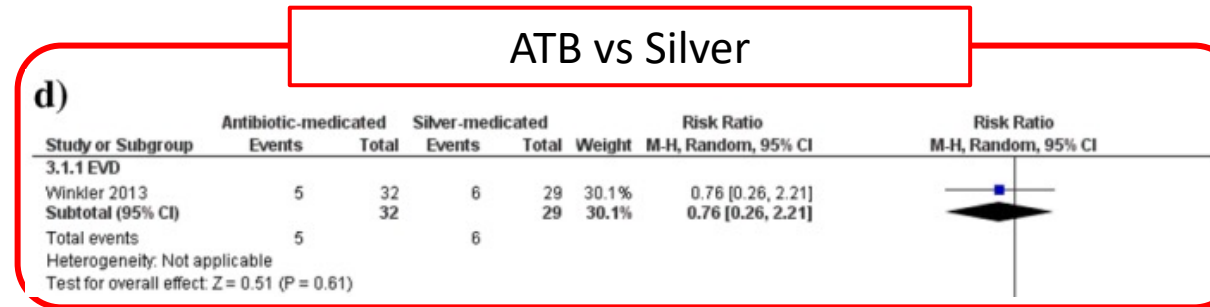
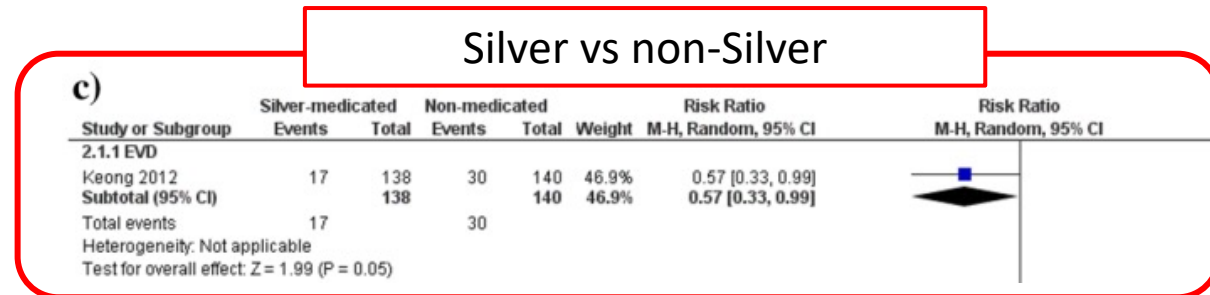
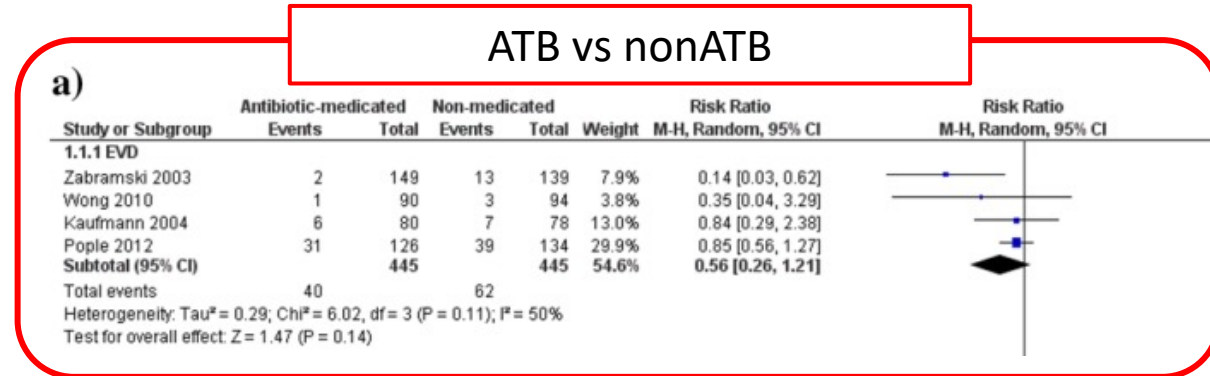
1605 patients. Standard (n=536), ATB (n=538), Silver (n=531)  
**Révision / Infection de valve : standard 6%, ATB 2%, Silver 6%**

	Events (n)	csHR (97.5% CI; p value)	sHR (97.5% CI; p value)
<b>Primary outcome*</b>			
Shunt			
Standard	32	..	..
Antibiotic	12	0.38 (0.18-0.80; 0.0038)	0.38 (0.18-0.80; 0.0037)
Silver	31	0.99 (0.56-1.74; 0.96)	0.99 (0.56-1.72; 0.95)
<b>Secondary outcomes</b>			
Time to removal of first shunt due to infection (assessed by neurosurgeon)*			
Shunt			
Standard	33	..	..
Antibiotic	15	0.45 (0.23-0.91; 0.011)	0.45 (0.23-0.91; 0.011)
Silver	30	0.93 (0.53-1.64; 0.77)	0.92 (0.53-1.61; 0.74)

Etude économique globale en faveur des DVP imprégnées d'ATB

# Efficacy of antimicrobial medicated ventricular catheters: a network meta-analysis with trial sequential analysis

Revanth Goda<sup>1</sup> · Akshay Ganeshkumar<sup>1</sup> · Varidh Katiyar<sup>1</sup> · Ravi Sharma<sup>1</sup> · Hitesh Kumar Gurjar<sup>1</sup> ·  
 Aprajita Chaturvedi<sup>2</sup> · Roshan Sahu<sup>1</sup> · Hitesh Inder Singh Rai<sup>1</sup> · Zainab Vora<sup>3</sup>



# Comment prévenir les infections de DVE?

- Eviter les poses hors du bloc

*Crit Care Med 2015; 43:1630–1637*

- Respect des règles d'asepsie de la pose à l'ablation (shampoing, tonte...)

- Préférer les DVE au drains lombaires, tunnelisation des drains

*J Neurol Neurosurg Psychiatry 2009;80:1381–1385.*

- Limiter les manipulations de la ligne de drainage

*Rachel A. Williamson, Journal of Critical Care 29 (2014) 77–82*

- Durée de drainage la plus courte possible
  - Infections augmentent entre 4 et 9ème jour

- Pas de changement de DVE systématique

*Miki Katzir WORLD NEUROSURGERY, [HTTPS://DOI.ORG/10.1016/J.WNEU.2019.07.205](https://doi.org/10.1016/j.wneu.2019.07.205)*

- DVE imprégnées seulement en cas d'incidence très élevée & Cocci + prédominants

*Goda R. Neurosurgical review. 2021*

# Protocoles & formation diminuent l'incidence

## Bundle of Measures for External Cerebral Ventricular Drainage-Associated Ventriculitis\*

Maria Chatzi, RN<sup>1</sup>; Marios Karvouniaris, MD<sup>1</sup>; Demosthenes Makris, MD, PhD<sup>1</sup>;  
Eleni Tsimitrea, RN<sup>1</sup>; Charalampos Gatos, MD<sup>2</sup>; Anastasia Tasiou, MD<sup>2</sup>; Kostas Mantzarlis, MD<sup>1</sup>;  
Kostas N. Fountas, MD, PhD<sup>2</sup>; Epaminondas Zakynthinos MD, PhD<sup>1</sup>

Variables	Preintervention (n = 82)	Intervention (n = 57)	p
EVDV, n (%)	23 (28)	6 (10.5)	0.02
EVDV according to admission diagnosis			0.33
Subarachnoid hemorrhage	8 (34.8)	3 (50)	0.64
Brain trauma	3 (13.04)	1 (16.7)	1.0
Cerebral hemorrhage	9 (39.1)	2 (33.3)	1.0
Tumor surgery	3 (13.04)	0 (0)	Not applicable
Drain-associated infection rate	18	7.1	0.0001
Day of EVDV diagnosis	13.1 (9.8–16.5)	11.7 (3–20.4)	0.89
Duration of cerebrospinal fluid drainage	15.6 (13.2–18)	15.2 (12.5–18.7)	0.91
Patients with ≥ 2 external ventricular drainage catheters, n (%)	25 (30.5)	25 (43.8)	0.13
Duration of intracranial pressure monitoring	15.4 (12.9–17.8)	11.7 (9.8–13.6)	0.14
Duration of ICU stay	27.1 (22.5–31.7)	22.3 (17.4–27.3)	0.19
Unfavorable Glasgow Outcome Scale (1, 2, 3), n (%)	49 (59.8)	33 (57.9)	0.86

# Quels sont les enjeux ?

Un **diagnostic précoce** pour une **antibiothérapie précoce** dans les **objectifs thérapeutiques....**



Virginie Zarrouk,<sup>1</sup> Isabelle Vassor,<sup>1</sup> Frederic Bert,<sup>2</sup> Didier Bouccara,<sup>3</sup> Michel Kalamarides,<sup>4</sup> Noelle Bendersky,<sup>5</sup> Aimée Redondo,<sup>4</sup> Olivier Sterkers,<sup>3</sup> and Bruno Fantin<sup>1</sup>

**Table 1.** Initial presentation of patients with postoperative meningitis.

Clinical feature	All patients (n = 75)	Patients with bacterial meningitis (n = 21)	Patients with aseptic meningitis (n = 54)	P <sup>a</sup>
Age, mean years ± SD	48 ± 16	47 ± 17	49 ± 15	.7
Sex				.4
Male	45	11	34	
Female	30	10	20	
Type of disease				.08
Vestibular schwannoma	55 (73)	12 (57)	43 (80)	
Surgical approach				.81
Transpetrosal	52 (69)	12 (57)	40 (80)	
Craniotomy	15	5	10	
Other	5	1	4	
Previous neurosurgical procedure	13 (17)	7 (33)	6 (11)	.024
Duration of surgery, mean h (range)	4.1 (1–11)	3.3 (1–6)	4.2 (1–11)	.015
CSF leakage	41 (55)	13 (62)	28 (52)	.68
Time between surgery and meningitis, mean days (range)	10 (1–120)	12 (2–120)	9 (1–25)	.53
Symptom				
Headache	64 (85)	19 (90)	45 (83)	.12
Vomiting	33 (44)	8 (38)	25 (46)	.73
Meningeal stiffness	23 (31)	5 (24)	18 (33)	.26
Fever				
Temperature, >38°C	50 (67)	16 (76)	34 (63)	.28
Temperature, >39°C	21 (28)	6 (29)	15 (28)	.59
Focal neurologic defect	2	2	0	.15

**La triade méningée = sensibilité de 40 à 50%**

Virginie Zarrouk,<sup>1</sup> Isabelle Vassor,<sup>1</sup> Frederic Bert,<sup>2</sup> Didier Bouccara,<sup>3</sup> Michel Kalamarides,<sup>4</sup> Noelle Bendersky,<sup>5</sup> Aimée Redondo,<sup>4</sup> Olivier Sterkers,<sup>3</sup> and Bruno Fantin<sup>1</sup>

**Table 2. Biological findings in CSF samples from patients with bacterial or aseptic postoperative meningitis.**

Biological variable	Patients with bacterial meningitis (n = 21)	Patients with aseptic meningitis (n = 54)
Leukocyte count, mean leukocytes/mm <sup>3</sup> (range)	1560 (200–4500)	1511 (180–4200)
Erythrocyte count, mean erythrocytes/mm <sup>3</sup> (range)	2430 (20–8500)	2100 (15–6050)
Glycorrachia, mean mmol/L (range)	1.1 (0–3.8)	1.8 (0–7.3)
Proteinorrachia, mean g/L (range)	4.7 (1.6–1.7)	3.2 (1.2–12.5)

ns

**60 à 75% de méningites aseptiques en post-opératoire**



Paramètres LCS

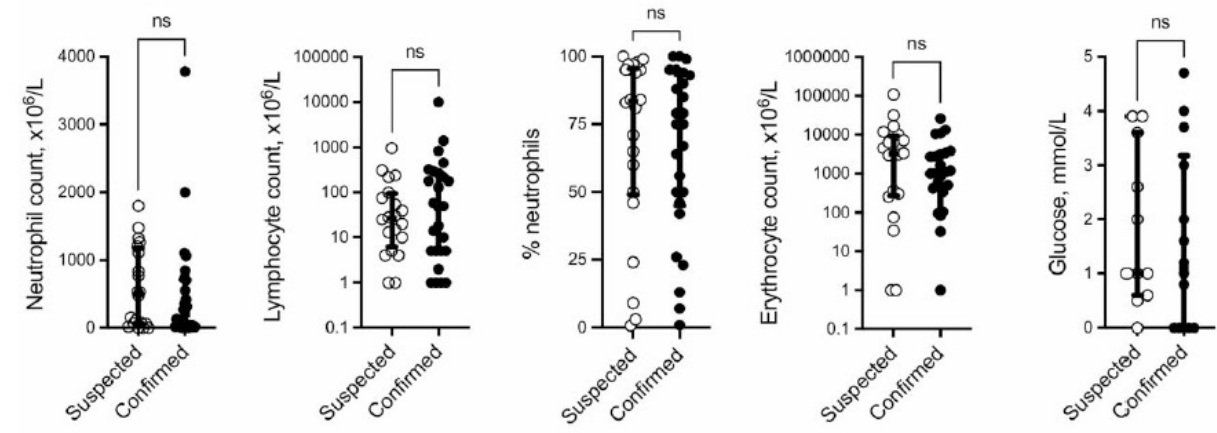
# Comparison of Suspected and Confirmed Internal External Ventricular Drain-Related Infections: A Prospective Multicenter United Kingdom Observational Study

Sei Yon Sohn,<sup>1,\*</sup> Clark D. Russell,<sup>2</sup> Aimun A. B. Jamjoom,<sup>3</sup> Michael T. Poon,<sup>3</sup> Aaron Lawson McLean,<sup>4</sup> and Aminul I. Ahmed,<sup>5</sup> on behalf of the British Neurosurgical Trainee Research Collaborative

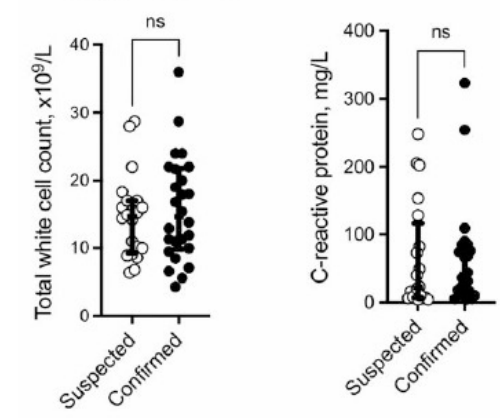
- 21 CH /GB. Cohorte 2014/2015
- iDVE : 9,3% (46/495) suspectées. 5% (n=26) confirmées.

ns

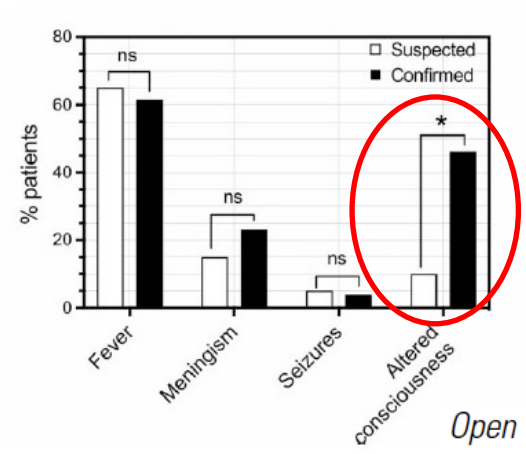
**A** CSF parameters



**B** Peripheral blood



**C** Clinical features





# 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 Bhimraj,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheld,<sup>6</sup> Diederik van de Beek,<sup>7</sup> Thomas P. Bleck,<sup>8</sup> Hugh J. L. Garton,<sup>9</sup> and Joseph R. Zunt<sup>10</sup>

## II. What are the Typical Cerebrospinal Fluid Findings in Patients with Healthcare-Associated Ventriculitis and Meningitis?

### *Cell Count, Glucose, and Protein*

#### *Recommendations*

13. Abnormalities of CSF cell count, glucose, and/or protein may not be reliable indicators for the presence of infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).
14. Normal CSF cell count, glucose, and protein may not reliably exclude infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).
15. A negative CSF Gram stain does not exclude the presence of infection, especially in patients who have received previous antimicrobial therapy (strong, moderate).

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

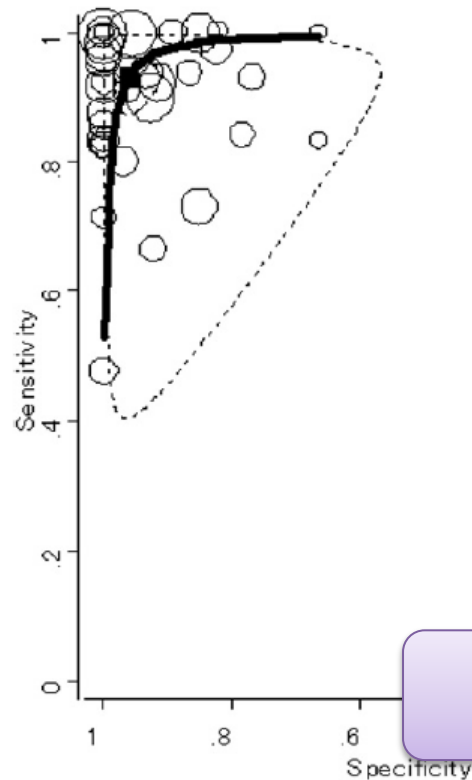
Allan R. Tunkel,<sup>1</sup> Rodrigo Hasbun,<sup>2</sup> Adarsh Bhimraj,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheld,<sup>6</sup> Diederik van de Beek,<sup>7</sup> Thomas P. Bleck,<sup>8</sup> Hugh J. L. Garton,<sup>9</sup> and Joseph R. Zunt<sup>10</sup>

- **Contamination:** An *isolated* positive CSF culture or Gram stain, with normal CSF cell count and glucose and protein concentrations and with lack of clinical symptoms suspicious for ventriculitis or meningitis.
- **Colonization:** *Multiple* positive CSF cultures or Gram stain, with normal CSF cell count and glucose and protein concentrations and with lack of clinical symptoms suspicious for ventriculitis or meningitis.
- **Infection:** Single or multiple positive CSF cultures with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis.

# Diagnostic accuracy of cerebrospinal fluid lactate for differentiating bacterial meningitis from aseptic meningitis: A meta-analysis<sup>☆</sup>

Ken Sakushima<sup>a,b,\*</sup>, Yasuaki Hayashino<sup>b</sup>, Takehiko Kawaguchi<sup>c</sup>,  
Jeffrey L. Jackson<sup>d</sup>, Shunichi Fukuhara<sup>b</sup>

33 études / méningites bactériennes & aseptiques



Cut-off lactates > 35 mg/dl (4 mmol/L)

Table 3 Summary of overall analyses and subgroup analyses.

	Sensitivity (95% CI)	Specificity (95% CI)
<b>Overall analysis</b>		
HSROC model	0.93 (0.89–0.96)	0.96 (0.93–0.98)
Random effect model	0.94 (0.92–0.96)	0.97 (0.96–0.99)
<b>Subgroup analysis</b>		
Bacteria proven BM <sup>a</sup>	0.96 (0.93–0.98)	0.97 (0.96–0.99)
Pretreated BM	0.49 (0.23–0.75)	NA <sup>b</sup>
Untreated BM	0.98 (0.96–1.00)	NA <sup>b</sup>
Cut off around 35 mg/dl	0.93 (0.89–0.97)	0.99 (0.97–1.00)
Cut off around 27 mg/dl	0.90 (0.85–0.94)	0.94 (0.90–0.98)

<sup>a</sup> Bacterial meningitis proven by culture or gram stain.

<sup>b</sup> Not available because of unabstractable data.

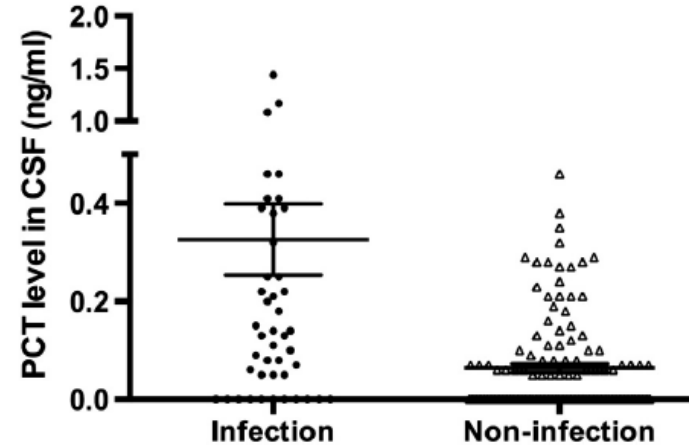
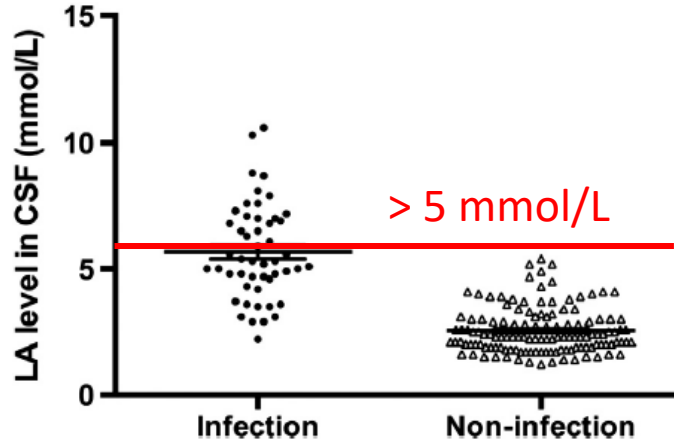
Nombreuses études contradictoires dans les infections AS !

PCT & Lactates  
dans LCS

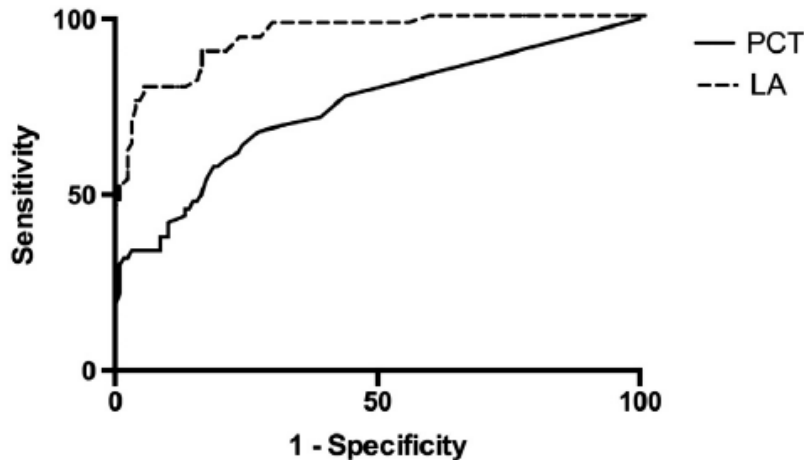
The diagnostic value of cerebrospinal fluids procalcitonin and lactate for the differential diagnosis of post-neurosurgical bacterial meningitis and aseptic meningitis<sup>☆</sup>

Youran Li<sup>a</sup>, Guojun Zhang<sup>a,b,\*</sup>, Ruimin Ma<sup>a</sup>, Yamei Du<sup>a</sup>, Limin Zhang<sup>a</sup>, Fangqiang Li<sup>a</sup>, Fang Fang<sup>a</sup>, Hong Lv<sup>a</sup>, Qian Wang<sup>a</sup>, Yan Zhang<sup>a</sup>, Xixiong Kang<sup>a,b</sup>

Rétrospective (n=178). Méningite post-op : 50/178.



ROC curve of CSF PCT and LA



The diagnostic efficacy evaluation of CSF procalcitonin and lactate for PNB.M.

	Procalcitonin	Lactate	Procalcitonin + lactate	Procalcitonin/ lactate
AUC	0.746	0.943	-	-
Cut-off point	0.075	3.450	-	-
p value	<0.001	<0.001	-	-
NLR (%)	0.44	0.12	0.39	0.06

**Cut-off dans le LCS :**  
Lactates : 3,45 mmol/L (Se:90%, Spe:84%)  
PCT : 0,075 ng/mL (Se:68%, Spe:73%)



PCT sang vs LCS

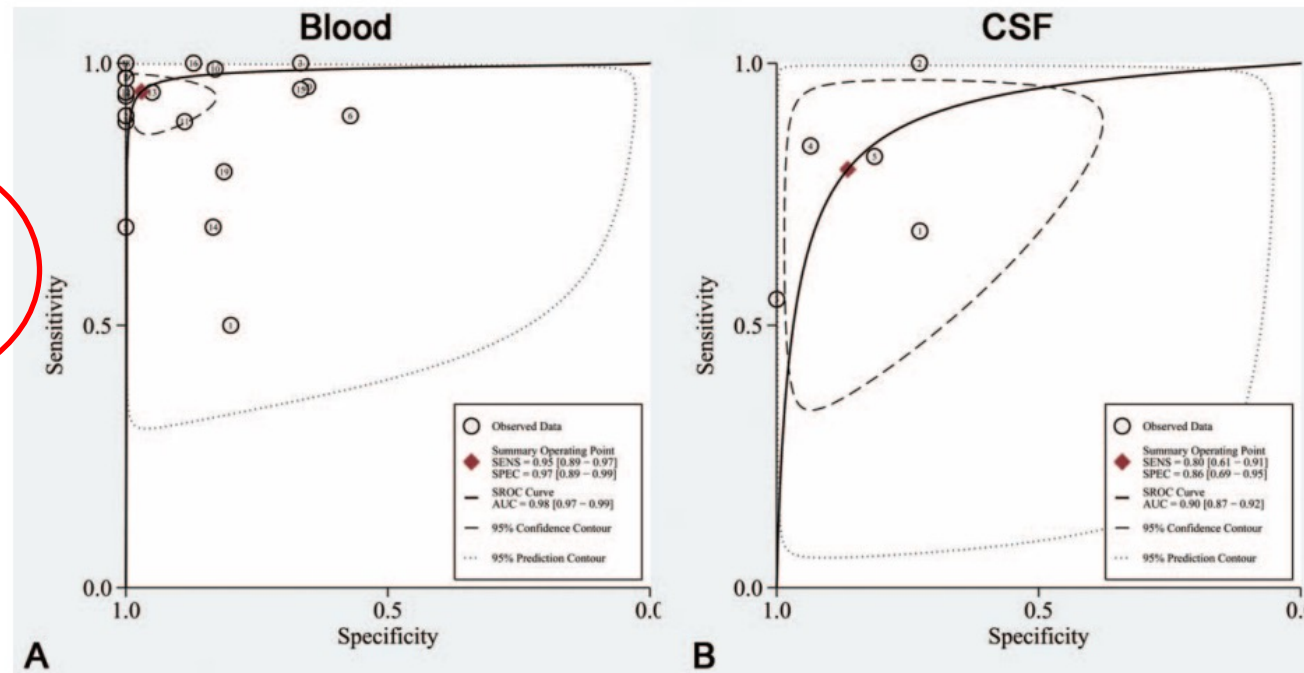
# Diagnostic Accuracy of Procalcitonin in Bacterial Meningitis Versus Nonbacterial Meningitis

*A Systematic Review and Meta-Analysis*

Ting-Ting Wei, MM, Zhi-De Hu, MM, Bao-Dong Qin, MM, Ning Ma, MM, Qing-Qin Tang, MM, Li-Li Wang, MM, Lin Zhou, MD, PhD, and Ren-Qian Zhong, MD, PhD

22 études / 2058 patients

**PCT sang**  
-Se : 0,95  
-Sp : 0,97



**PCT LCS**  
-Se : 0,80  
-Sp : 0,86

FIGURE 2. The SROC AUC of PCT in BM diagnosis. The overall diagnostic efficiency of PCT in BM is summarized by the regression curve. AUC = area under curve, BM = bacterial meningitis, PCT = procalcitonin, SROC = summary receiver operating characteristic.

Quid des infections associées aux soins ?

# 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 Bhimraj,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheld,<sup>6</sup> Diederik van de Beek,<sup>7</sup> Thomas P. Bleck,<sup>8</sup> Hugh J. L. Garton,<sup>9</sup> and Joseph R. Zunt<sup>10</sup>

## III. What Specific Tests of Cerebrospinal Fluid can be used to Confirm the Patient has Healthcare-Associated Ventriculitis and Meningitis?

### Recommendations

30. An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of healthcare-associated bacterial ventriculitis and meningitis (weak, moderate).
31. An elevated serum procalcitonin may be useful in differentiating between CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection (weak, low).
32. Nucleic acid amplification tests, such as polymerase chain reaction, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low).
33. Detection of  $\beta$ -D-glucan and galactomannan in CSF may be useful in the diagnosis of fungal ventriculitis and meningitis (strong, moderate).

# Diagnostic difficile...

- Gold standard = Culture de LCS
  - 23 à 78% des cultures négatives / infections AS
  - 20 % de faux négatifs / méta-analyse 2019

*Dorresteijn K. Neurology 2019*

*Martin RM. J Clin Microbiol. 2018. 56 (11)*

- LCR stérile : infection décapitée / ATB
  - Jusqu'à 50% d'ATB avant prélèvement de LCS
  - ARN 16S/PCR (Se 80%, Spé 98%). Peu d'études / infection AS

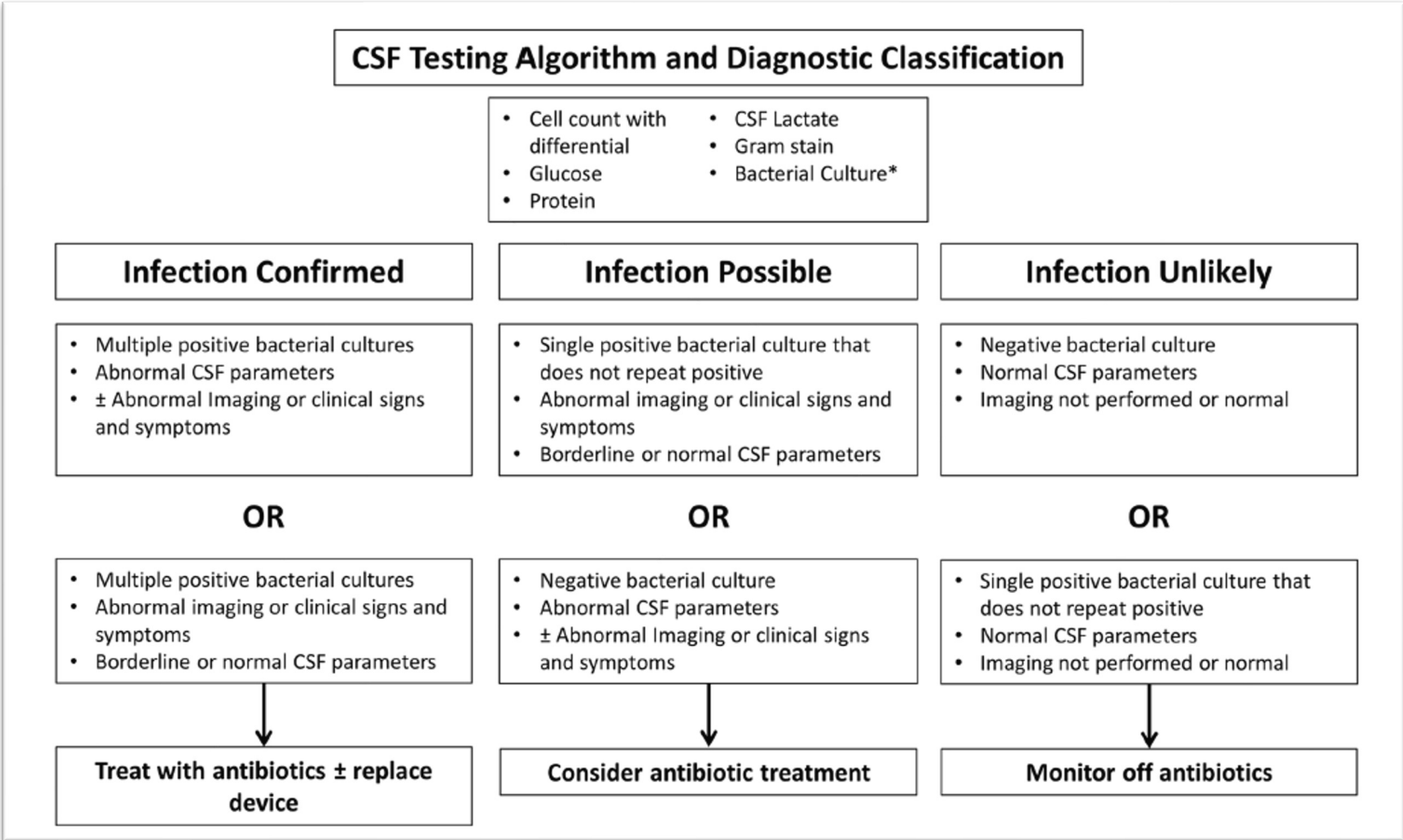
*Srihawan C. Open Forum Inf Dis 2016.*

*Martin RM. J Clin Microbiol. 2018. 56 (11)*

- Aspécificité des résultats biochimiques & hématologiques du LCS
- Réaction inflammatoire systémique aspécifique / Lésion initiale

Ryan M. Martin,<sup>a,b</sup> Lara L. Zimmermann,<sup>a,b</sup> Mindy Huynh,<sup>c</sup> Christopher R. Polage<sup>c,d</sup>

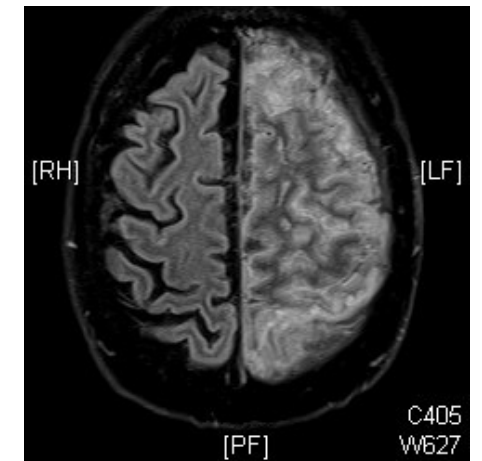
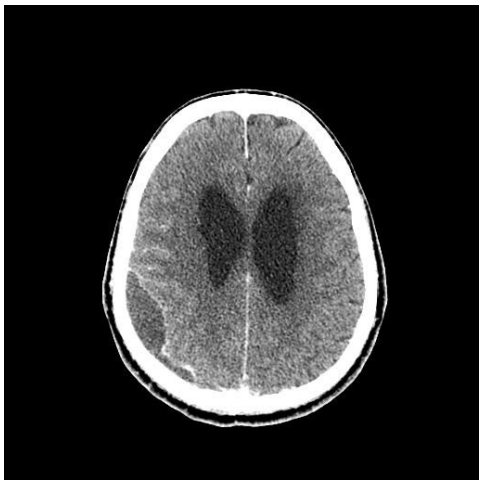
## Le diagnostic repose sur un faisceau d'arguments...





# L'imagerie

- Indiquée pour :
  - Éliminer une ventriculite
  - Éliminer une vasospasme / ischémie associée
  - Diagnostiquer un empyème (IRM > TDM)
  - Éliminer une TVC associée
  - TDM abdo / DVP



# Antibiothérapie précoce dans les objectifs thérapeutiques....



# 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.

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

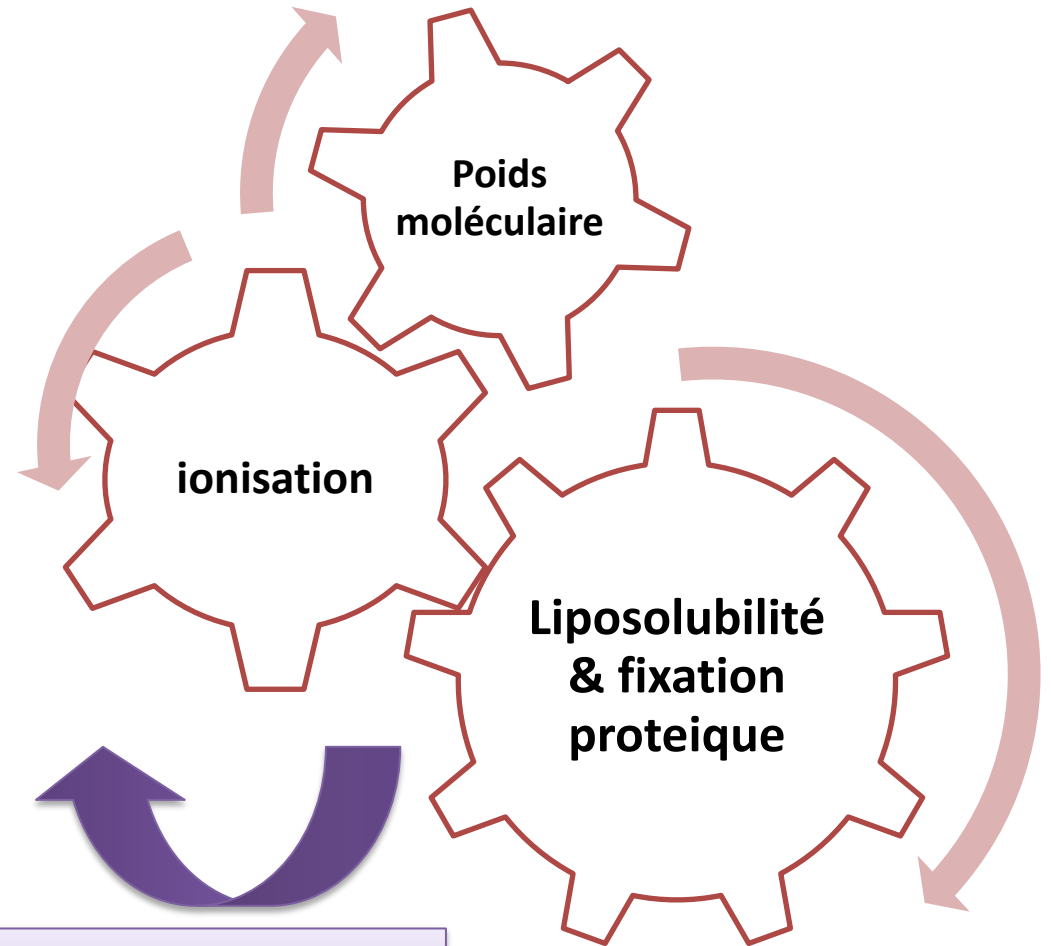
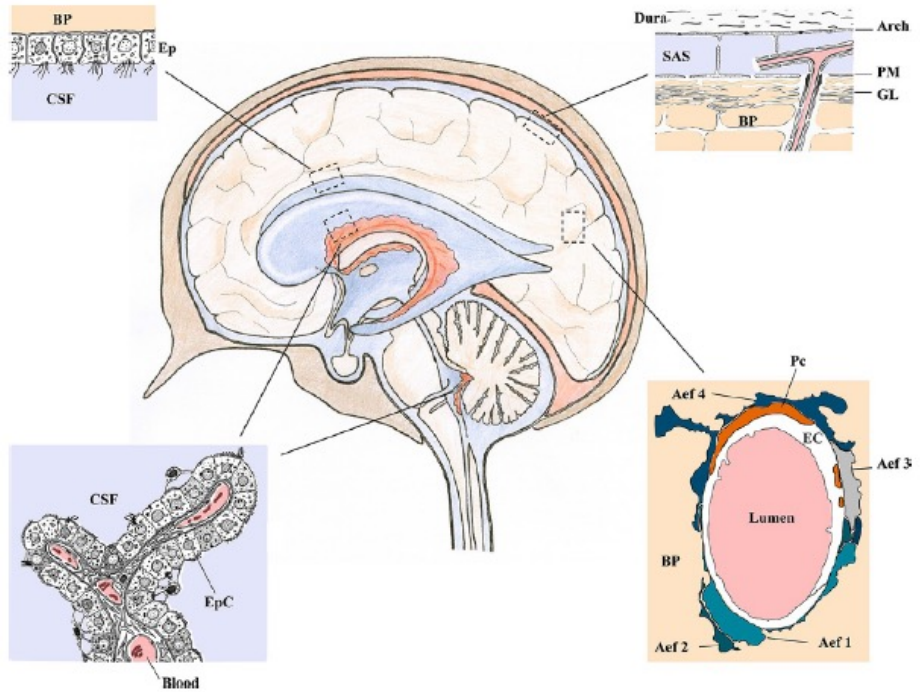
Allan R. Tunkel,<sup>1</sup> Rodrigo Hasbun,<sup>2</sup> Adarsh Bhimraj,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheld,<sup>6</sup> Diederik van de Beek,<sup>7</sup> Thomas P. Bleck,<sup>8</sup> Hugh J. L. Garton,<sup>9</sup> and Joseph R. Zunt<sup>10</sup>

**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)

Adapter à l'écologie du service ....

# Diffusion des antibiotiques



Transporteurs d'efflux (Pg-p, MRP4, OAT3...)

# Advances in treatment of bacterial meningitis

Diederik van de Beek, Matthijs C Brouwer, Guy E Thwaites, Allan R Tunkel

< 10%

30 à 70%

	CSF penetration (CSF:plasma)* in uninflamed meninges	CSF penetration (drug in CSF:plasma)* in inflamed meninges
<b>β-lactams</b>		
Benzylpenicillin	0.02	0.1
Amoxicillin/ampicillin	0.01	0.05
Cefotaxime	0.1	0.2
Ceftriaxone	0.007	0.1
Meropenem	0.1	0.3
<b>Aminoglycosides</b>		
Gentamicin	0.01	0.1
Amikacin	No data	0.1
<b>Glycopeptides</b>		
Vancomycin	0.01	0.2
Teicoplanin	0.01	0.1
<b>Fluoroquinolones</b>		
Ciprofloxacin	0.3	0.4
Moxifloxacin	0.5	0.8
Levofloxacin	0.7	0.8
<b>Others</b>		
Chloramphenicol	0.6	0.7
Rifampicin	0.2	0.3
<b>Newer agents</b>		
Cefepime	0.1	0.2
Linezolid	0.5	0.7
Daptomycin	No data	0.05
Tigecycline	No data	0.5

# Advances in treatment of bacterial meningitis

Diederik van de Beek, Matthijs C Brouwer, Guy E Thwaites, Allan R Tunkel

	CSF penetration (CSF:plasma)* in uninfamed meninges	CSF penetration (drug in CSF:plasma)* in inflamed meninges
<b>β-lactams</b>		
Benzylpenicillin	0.02	0.1
Amoxicillin/ampicillin	0.01	0.05
Cefotaxime	0.1	0.2
Ceftriaxone	0.007	0.1
Meropenem	0.1	0.3
<b>Aminoglycosides</b>		
Vancomycin	0.01	0.2
Teicoplanin	0.01	0.1
<b>Fluoroquinolones</b>		
Ciprofloxacin	0.3	0.4
Moxifloxacin	0.5	0.8
Levofloxacin	0.7	0.8
<b>Others</b>		
Chloramphenicol	0.6	0.7
Rifampicin	0.2	0.3
<b>Newer agents</b>		
Cefepime	0.1	0.2
Linezolid	0.5	0.7

**Objectif PD atteint ?  
Bactéries peu sensibles**

Facteur 2 à 10 pour les molécules peu diffusibles

Peu d'effet sur les molécules à bonne diffusion

# PK-pop LCR



Etude PK/PD de population de 9 agents anti-infectieux à large spectre dans le liquide céphalo-rachidien (LCR), chez des patients cérébro-lésés porteurs d'une dérivation ventriculaire externe (DVE).

## 9 antibiotiques

- **Cocci +**: Vancomycine, daptomycine, linézolide.
- **BGN** : Céfépime, Ceftazidime, colistine, méropénème, pipéracilline-tazobactam, ceftaroline.

## Population

- Patients **cérébro-lésés** avec **DVE**
- **25 patients/antibiotique**
- 4 à 7 points PK/patient
- **175 patients / 3 ans**

**Résultats préliminaires de Meropénème & Linézolide :**  
**Posologies recommandées insuffisantes / antibiothérapie probabiliste**

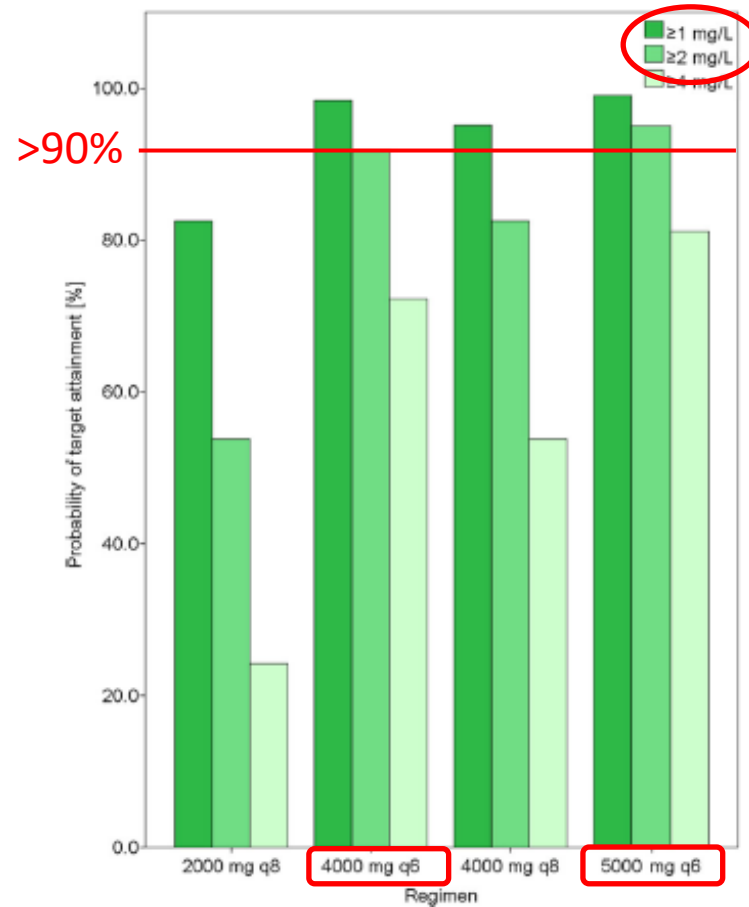




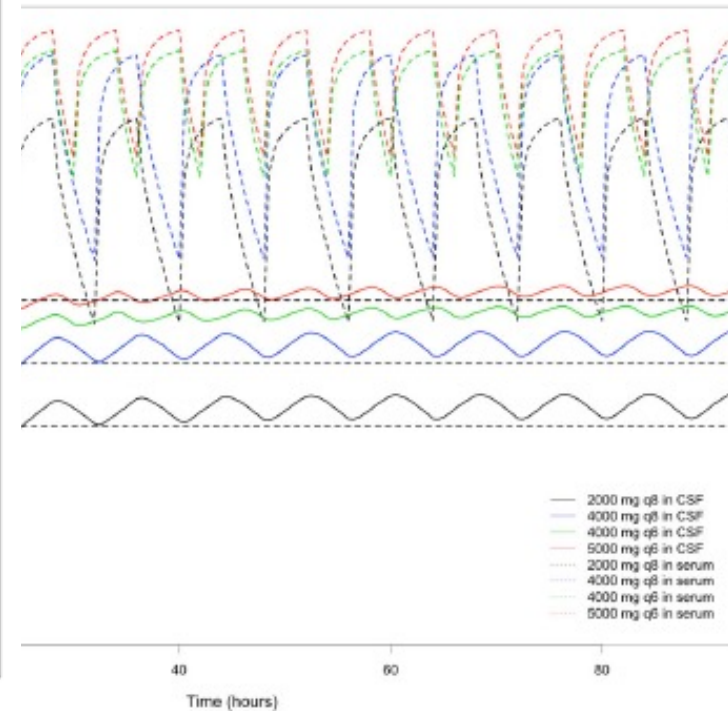


# Cerebrospinal fluid penetration of meropenem in neurocritical care patients with proven or suspected ventriculitis: a prospective observational study

Ute Blassmann<sup>1\*</sup>, Anka C. Roehr<sup>2</sup>, Otto R. Frey<sup>2</sup>, Cornelia Vetter-Kerkhoff<sup>1</sup>, Niklas Thon<sup>3</sup>, William Hope<sup>4</sup>, Josef Briegel<sup>5</sup> and Volker Hugel<sup>5</sup>



Diffusion : AUC CSF/pl = 9% [3-16]



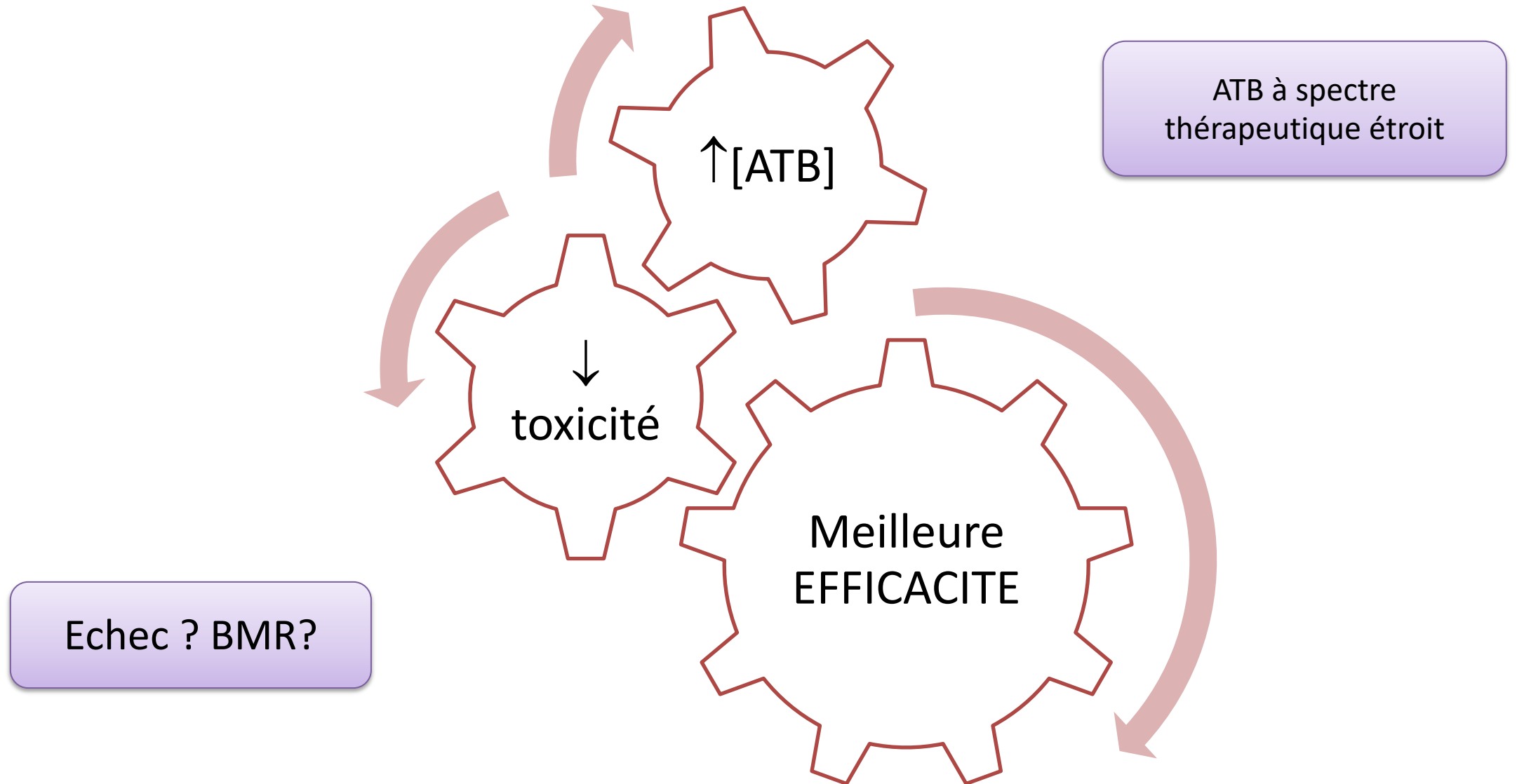
Risque de toxicité !





En cas d'échec : ATB intra-ventriculaires ?  
Associer pour améliorer l'efficacité ?

# La voie intra-ventriculaire...



# Quels objectifs PK-PD dans le SNC ?

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 Bhimraj,<sup>3</sup> Karin Byers,<sup>4</sup> Sheldon L. Kaplan,<sup>5</sup> W. Michael Scheld,<sup>6</sup> Diederik van de Beek,<sup>7</sup> Thomas P. Bleck,<sup>8</sup> Hugh J. L. Garton,<sup>9</sup> and Joseph R. Zunt<sup>10</sup>

### Quotient inhibiteur (QI)

$$QI = [ATB_{CSF}] / CMI$$

$$QI > 10-20$$

$$[ATB_{CSF}] > 10-20 \times CMI$$

### VII. What is the Role of Intraventricular Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis?

#### Recommendations

55. Intraventricular antimicrobial therapy should be considered for patients with healthcare-associated ventriculitis and meningitis in which the infection responds poorly to systemic antimicrobial therapy alone (strong, low).
56. When antimicrobial therapy is administered via a ventricular drain, the drain should be clamped for 15–60 minutes to allow the agent to equilibrate throughout the CSF (strong, low).
57. Dosages and intervals of intraventricular antimicrobial therapy should be adjusted based on CSF antimicrobial concentrations to 10–20 times the MIC of the causative microorganism (strong, low), ventricular size (strong, low), and daily output from the ventricular drain (strong, low).

# Pour quels antibiotiques ?

Antibiotiques	Indications	Doses / jour
Gentamicine	BGN / Cocci	5 mg (4 à 10 mg)
Amikacine	BGN / Cocci	10-20 mg (5 à 40 mg)
Colistine	Acinetobacter baumannii / Pseudomonas aeruginosa	62500 UI -125 000 UI (40 000 à 400 000 UI)
Vancomycine	Staphylococcus / Enterococcus/ Streptococcus / Listeria	10-20 mg (5 à 50 mg)

Durée : 3 à 7j,  
jusqu'à LCR stérile (→ >50j)

Ng K. *Neurocrit Care* 2014. 20:158-171  
Cascio A. *Int J Infect Dis* 2010. 572-579  
Wang JH. *J Microbiol Immunol Inf* 2014. 47, 204-210

# Treatment of staphylococcal ventriculitis associated with external cerebrospinal fluid drains: a prospective randomized trial of intravenous compared with intraventricular vancomycin therapy

BETTINA PFAUSLER, M.D., HEINRICH SPISS, M.D., RONNY BEER, M.D.,  
 ANDREAS KAMPFL, M.D., KLAUS ENGELHARDT, M.D., MARIA SCHOBER, M.D.,  
 AND ERICH SCHMUTZHARD, UNIV. PROF.

• N=10 ventriculites / DVE

**Vanco IV : 500mg x 4/j)**

**Vanco IVR : 10 mg/j**

Sampling Time (hrs)	No. of Samples	Concentration (mean ± SD)	
		CSF (µg/ml)	Serum (µg/ml)
1	34	1.25 ± 0.35	25.94 ± 1.44
5	34	1.10 ± 0.25	13.29 ± 2.22
9	34	1.73 ± 0.40	16.60 ± 2.23
13	34	1.41 ± 0.32	23.70 ± 1.60
17	34	1.56 ± 0.41	14.90 ± 2.76
21	32	1.39 ± 0.30	18.86 ± 2.58

Sampling Time (hrs)	No. of Samples	Concentration (mean ± SD)	
		CSF (µg/ml)	Serum (µg/ml)
1	33	565.58 ± 168.71	3.64 ± 1.48
5	33	59.00 ± 34.08	0.44 ± 0.39
9	33	13.46 ± 1.60	0.15 ± 0.09
13	33	8.34 ± 1.17	0.07 ± 0.07
17	33	5.61 ± 0.84	0.05 ± 0.05
21	33	3.74 ± 0.66	0.12 ± 0.08

**[vanco ] < 5 µg/mL**

**[vanco ] > 5 µg/mL pendant > 17h**

# Treatment of staphylococcal ventriculitis associated with external cerebrospinal fluid drains: a prospective randomized trial of intravenous compared with intraventricular vancomycin therapy

BETTINA PFAUSLER, M.D., HEINRICH SPISS, M.D., RONNY BEER, M.D.,  
 ANDREAS KAMPFL, M.D., KLAUS ENGELHARDT, M.D., MARIA SCHOBER, M.D.,  
 AND ERICH SCHMUTZHARD, UNIV. PROF.

• N=10 ventriculites / DVE

**Vanco IV : 500mg x 4/j)**

**Vanco IVR : 10 mg/j**

Sampling Time (hrs)	No. of Samples	Concentration (mean ± SD)		Sampling Time (hrs)	No. of Samples	Concentration (mean ± SD)	
		CSF (µg/ml)	Serum (µg/ml)			CSF (µg/ml)	Serum (µg/ml)
1	34	1.25 ± 0.35	25.94 ± 1.44	1	33	565.58 ± 168.71	3.64 ± 1.48
5	34	1.10 ± 0.25	13.29 ± 2.22	5	33	59.00 ± 34.08	0.44 ± 0.39
9	34	1.73 ± 0.40	16.60 ± 2.23	9	33	13.46 ± 1.60	0.15 ± 0.09
13	34	1.41 ± 0.32	23.70 ± 1.60	13	33	8.34 ± 1.17	0.07 ± 0.07
17	34	1.56 ± 0.41	14.90 ± 2.76	17	33	5.61 ± 0.84	0.05 ± 0.05
21	32	1.39 ± 0.30	18.86 ± 2.58	21	33	3.74 ± 0.66	0.12 ± 0.08

**[vanco ] < 5 µg/mL**

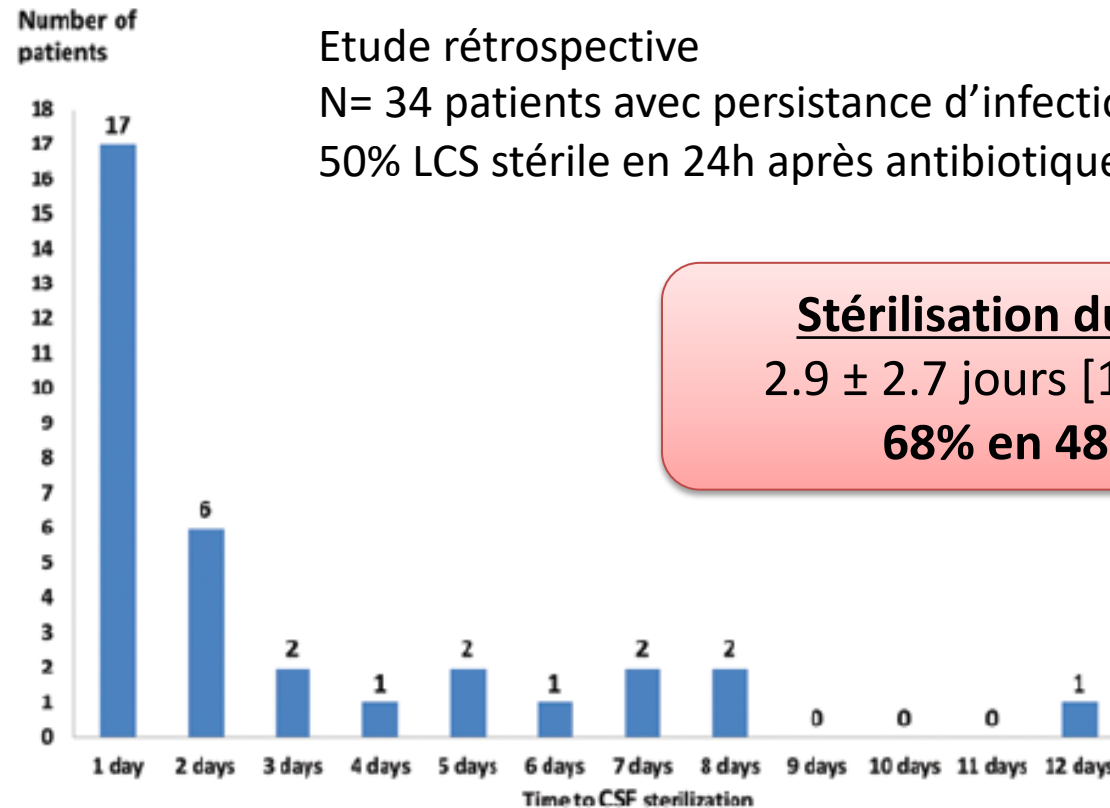
**[vanco ] > 5 µg/mL pendant > 17h**



# Intraventricular and lumbar intrathecal administration of antibiotics in postneurosurgical patients with meningitis and/or ventriculitis in a serious clinical state

Clinical article

FRANTIŠEK REMEŠ, M.D.,<sup>1</sup> ROBERT TOMÁŠ, M.D., PH.D.,<sup>1</sup> VLASTIMIL JINDRÁK, M.D.,<sup>2</sup>  
VÁCLAV VANIŠ, M.D.,<sup>2</sup> AND MICHAL ŠETLÍK, M.D.<sup>1</sup>



Etude rétrospective

N= 34 patients avec persistance d'infection à J5-J8/ ATB IV

50% LCS stérile en 24h après antibiotique IVT/IT

**Stérilisation du LCR**

**2.9 ± 2.7 jours [1–12 j]**

**68% en 48h**

# Que faut-il retenir ?

- **Forte morbi-mortalité**
- **Diagnostic difficile / peu spécifique**
- **La prévention est la clé** de ces infections
  - Protocole de soins stricts
  - Education des équipes, suivi de l'incidence
- **Ablation du dispositif infecté**
- **En probabiliste : posologies insuffisantes / germes les moins sensibles**
  - Adaptation individuelle indispensable
  - Suivi thérapeutiques de la PK
- **En cas d'échec ou de résistance : Penser à la voie intra-ventriculaire**





Limiter la morbi-mortalité

Prévention

&

Approche individuelle de  
l'adaptation posologique





**INSERM U1070 "Pharmacology of Antimicrobial Agents and antibioResistance"**

$H_2N$

$HN$

$NH_2$

$NH_2$

$\frac{dG}{dt} = k_{growth} \times G - k_{death}$

$\frac{dP}{dt} = k_{OP} \times G - k_{...}$

