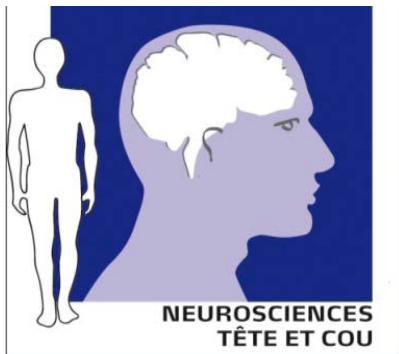


Infections neuro-méningées post opératoires: comment faire le diagnostic ?, comment traiter ?

PF Perrigault

DAR C, Pôle Neurosciences Tête et Cou

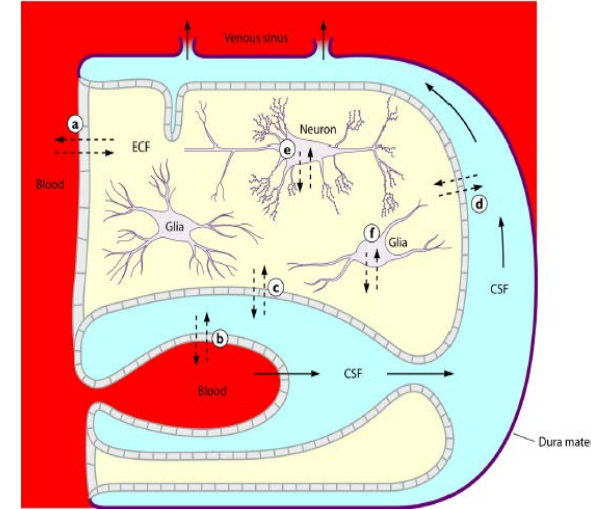
CHU Montpellier



Déclaration d'intérêts

- **Intervenant au titre d'orateur**
MSD
- **Participation à des groupes de travail**
MSD, Pfizer
- **Invitation congrès/journées scientifiques**
MSD, Pfizer, Astellas, Sanofi

Physiopathologie



- **LCR dépourvu de défense immunitaire**
 - Paucicellulaire < 5 leuco/mm³
 - Concentration en complément et IgG = 2 à 5 % du plasma
 - Pouvoir de phagocytose et bactéricidie faible en l'absence d'activité opsonisante du LCR
 - Souvent comparé à un sérum de patient neutropénique
- **La dure mère et la barrière hémato-méningée sont d'extraordinaire moyens de défense contre l'infection**
- **Leur rupture (chirurgie, traumatisme, valve) permet la colonisation bactérienne du LCR**
- **Le risque est proportionnel à la durée**

Epidémiologie

Incidence: études prospectives multicentriques françaises

- **2944 patients. 4 % infections,**
Korinek Neurosurgery 1997
 - **1,5 % infections superficielles**
 - **2,5 % infections profondes dont 1,2 % méningites, autres (abcès, empyème)**
- **4578 craniotomies, 6,6% d'infections**
Korinek neurosurgery 2005
- **Grande variabilité parmi les centres et différences avec d'autre études**
0,8 % (0.3% méningites). 1587 interventions. Pas de facteur de risque...

McClelland CID 2007

Méningites nosocomiales

- **Post opératoires**
- Incidence varie en fonction du type d'intervention
- Post craniotomie: 0.3 à 1,5 %
- Dérivation ventriculaire interne: 4 à 21 %. *Conen CID 2008*
- **Post Traumatisme crânien**
 - 860 patients: 1,4 %. *Baltas Neurosurgery 1994*
 - 2 à 11 % en cas de fractures complexes. *Bullock Neurosurgery 2006*
 - Jusqu'à 15 % si fuite LCR. *Choi Br J Neurosurg 1996*
- **Cas particulier capteur de PIC**
 - Ventriculostomie 7,3 % / 6,7 %
 - Capteur intra parenchymateux 0,4 % / 1,9 %
 - » *Guyot Acta Neuroch 1998, Kahn Acta Neuroch 1998*

Facteurs de risque de méningite post craniotomie hors dérivation

- **6243 patients surveillés prospectivement**
- **1,52 % méningites, 13,7 % mortalité** *Korinek neurosurgery 2006*
- **Analyse multivariée**
 - **Fuite de LCR, RR: 28,4**
 - **Infection superficielle, RR: 3,7**
 - **Sexe masculin, RR: 1,9**
 - **Durée de la chirurgie > 4 h, RR 1,7**
- **Sur les 120 patients avec fuite de LCR, 35 vont développer une méningite soit 29,2%**
- **Sur les 6123 patients sans fuite, 60 vont développer une méningite soit 0,98 % (p<0,0001)**

Microbiologie hors dérivations du LCR

- 1/3 de positivité au gram direct, 2/3 en culture (72 h) *Zarrouk CID 2007*
- Bactériologie *Korinek Neurosurgery 1997*
 - 117 infections / 2944 patients

	Scalp Infections	Bone Flap Osteitis	Meningitis/ Abscess	Total (%)
Meti-S <i>S. aureus</i>	7	8	17	32 (33)
Meti-R <i>S. aureus</i>	5	0	12	17 (18)
<i>S. epidermidis</i>	1	0	3	4 (4.2)
<i>Streptococci</i>	2	0	4	6 (6.3)
Other GPC	1	0	4	5 (5.2)
Enterobacteriaceae S ^b	0	0	4	4 (4.2)
Enterobacteriaceae R ^b	2	0	11	13 (13.5)
<i>Acinetobacter</i> spp.	5	1	2	8 (8.3)
<i>P. aeruginosa</i>	1	0	2	3 (3.1)
Others	1	0	3	4 (4.2)
Total	25	9	62	96
GPC/AGNB	16/9	8/1	40/22	64/32

^a *S. aureus*, *Staphylococcus aureus*; *S. epidermidis*, *Staphylococcus epidermidis*. GPC, gram-positive cocci; *P. aeruginosa*, *Pseudomonas aeruginosa*; AGNB, aerobic gram-negative bacilli.

^b Enterobacteriaceae S, wild enterobacteriaceae sensitive to usual antibiotics; R, hospital-acquired enterobacteriaceae resistant to antibiotics.

Diagnostic clinique des méningites

- **Habituellement précoce 8 à 15 post op**
- **Tableau clinique idéal n'existe pas (vs méningite communautaire)**
 - **Céphalées fréquentes > 80 %**
 - **Vomissements**
 - **Raideur de nuque**
 - **Fièvre fréquente mais peu spécifique en post op**
 - **Dégradation neurologique**
 - **Tous ces signes sont inconstants et souvent pas évaluable chez patient sédaté en réanimation**

Clinical parameters do not predict infection in patients with external ventricular drains: a retrospective observational study of daily cerebrospinal fluid analysis

J Clin Neurosc 2008

Sharmini Muttaiyah,¹ Stephen Ritchie,² Arlo Upton¹ and Sally Roberts¹

Diagnostic clinique

Méningites post op hors dérivation LCR

Zarrouk CID 2007

Concept de méningite aseptique +++

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)	<i>P</i> ^a
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)	
Supratentorial tumor	9	4	5	
Spine disease	5	3	2	
Arnold-Chiari	3	1	2	
Other	3	1	2	
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

Diagnostic clinique

infections post dérivation LCR

Conen CID 2008

Variable	Episodes (n = 78)
Temperature >38°C	61 (78)
Neurological signs and symptoms	
Headache	16 (21)
Nausea	11 (14)
Neck stiffness	35 (45)
Decrease in GCS from baseline, points	
Any decrease	24 (31)
1	8
2	4
3	2
4	5
≥5	5
No neurological signs or symptoms	28 (36)
Local signs and symptoms	
Erythema	23 (29)
Local pain	15 (19)
Swelling	10 (13)
Purulent wound discharge	10 (13)
No local signs or symptoms	40 (51)
No fever or neurological or local signs or symptoms	2 (3)
Duration of symptoms before diagnosis of infection, median days (range)	5 (0–21)
Time between implantation or last surgery and manifestation of infection	
<1 month	48 (62)
1–12 months	22 (28)
>12 months	8 (10)

Diagnostic biologique LCR

- **Les critères classiques ne sont pas discriminants**
 - Protéïnorrhée, hypoglycorachie (rapport < 0,4), GB > 100/mm³
 - Même normal avec authentique méningite *Mayall NEJM 1984*
 - si GB > 7500/mm³ et glycorachie < 0,1 g/l *Forgacs CID 2001*
- **Problème des méningites « aseptiques »**

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

Zarrouk CID 2007

Autres paramètres

- **Dans le LCR**
 - **Index de cellularité**
 - **Lactate LCR**
 - **PCR 16 S**
- **Dans le sang**
 - **Procalcitonine**

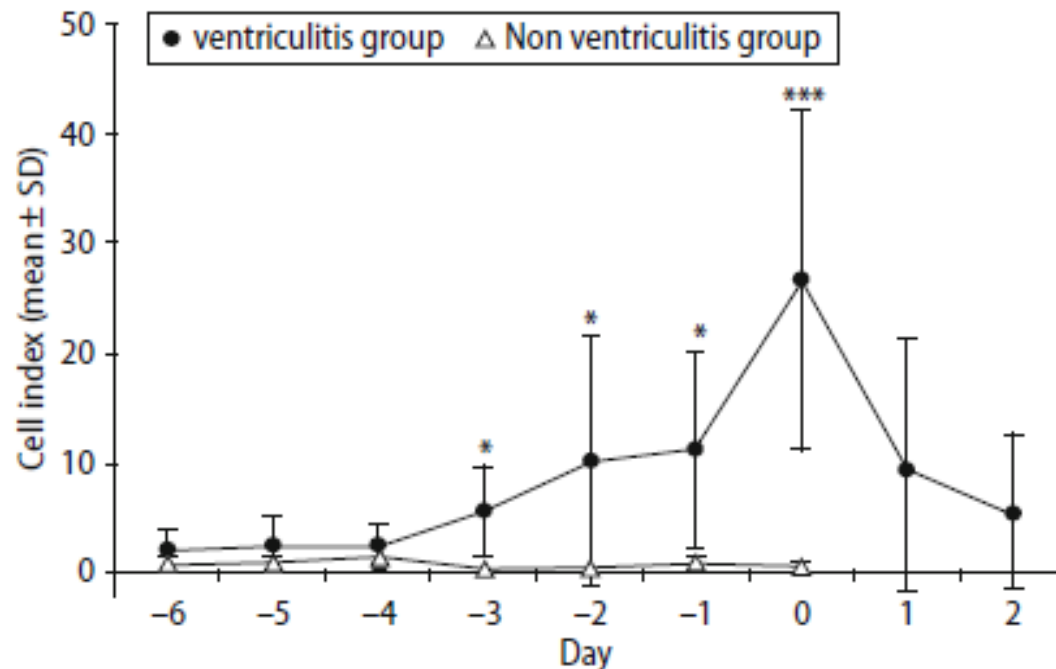
Index de cellularité

Cell index – a new parameter for the early diagnosis of ventriculostomy (external ventricular drainage)-related ventriculitis in patients with intraventricular hemorrhage?

Acta Neurochir (Wien) (2004) 146: 477–481

B. Pfausler¹, R. Beer¹, K. Engelhardt¹, G. Kemmler², I. Mohsenipour³, and E. Schmutzhard

- **Rapport GB / GR dans LCR divisé par GB / GR dans sang = 1 si contamination sanguine du LCR. Infection si IC x 5, précède l'infection**
- **13 patients ! 7 infectés !**
- **Prélèvements tous les jours !**



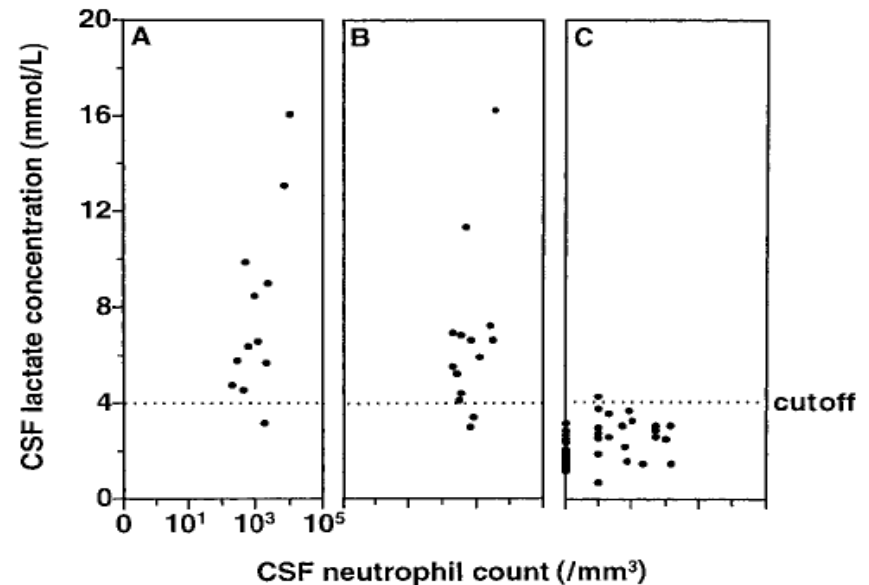
Lactates LCR

- *Bien discriminant pour les méningites communautaires seuil 3,5 mmol/l*

Sakushima J Infect 2011

- **Moins pertinent en post opératoire**

- Seuil 4 mmol/l *Leib CID 1999*
- VPP 98 %
- VPN 94 %



- **Post dérivation interne**

- *Conen CID 2008*

Lactate level	
>1.9 mmol/L, no. (%) of episodes	34/42 (81)
Median value, mmol/L (range)	4 (1-14)

- **Post op neurochirurgie (PL)**

- *Grille neurocirugia 2012* seuil à 5,9 mmol/l chez 10 méningites....
- *Maskin Clin Neurol Neurosurg 2013* seuil 4 mmol/l VPN 97 %, VPP 76 %

PCR 16 S

- **Détection ADN bactérien dans le LCR, intérêt petit inoculum ou ATB ?**
- ***Banks Neurosurgery 2005***
 - Infections sur dérivation 28 pts
 - 86 prélèvements
 - Propionibacterium acnes
 - Staphylocoque doré
 - Pas de BG –
 - Pas de faux négatifs
- ***Deutch Neurosurgery 2007***
 - 350 prélèvements chez 86 patients post drainage ventriculaire

TABLE 3. Summary of PCR and culture correlation^a

	Positive	Negative
PCR (+)	18/86	43/86
PCR (-)	0/86	24/86

^a PCR, polymerase chain reaction.

TABLE 3. Distribution of culture and polymerase chain reaction results for 10 of 16 episodes of ventricular drainage-related bacterial meningitis due to gram-positive bacteria

PCR result, no. of episodes	Culture result, no. of episodes		Total, no. of episodes
	Positive	Negative	
Positive	3	1	4
Negative	6	6	12
Total	9	7	16

TABLE 4. Distribution of culture and polymerase chain reaction results for 8 of 16 episodes of ventricular drainage-related bacterial meningitis due to gram-negative bacteria

PCR result, no. of episodes	Culture result, no. of episodes		Total, no. of episodes
	Positive	Negative	
Positive	4	4	8
Negative	0	8	8
Total	4	12	16

PCR 16 S

- **Zarrouk J Clin Microbiol 2010**

- 26 méningites aseptiques
- 6 méningites confirmées

Finding	No. of CSF samples with indicated result for culture		Total no. of specimens
	Positive	Negative	
Positive	2	0	2
Negative	4	26	30
Total	6	26	32

- **Rath, Infection 2014**

- *Septifast*
- *Résultat le jour même*

	CSF +	CSF -	total
PCR +	17	1	18
PCR -	4	40	44
total	21	41	62

	Culture +	Culture -	Total
PCR +	0	0	0
PCR -	8	51	59
Total	8	51	59

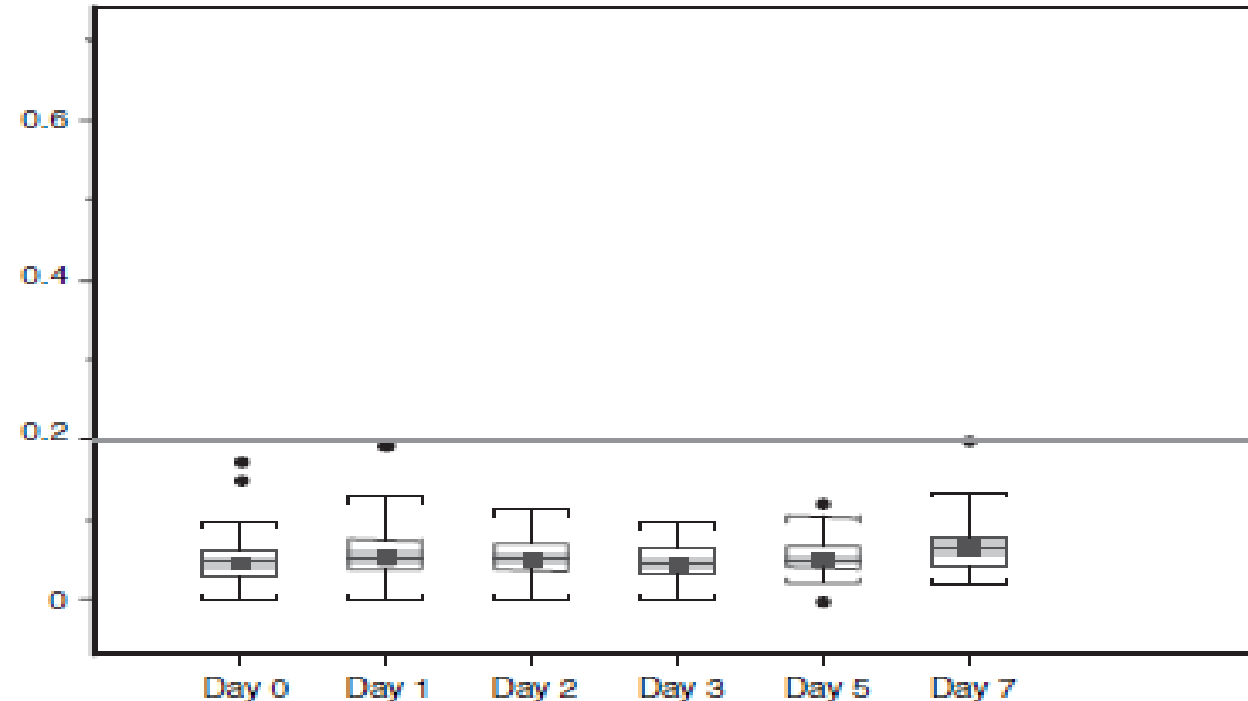
Données service SFAR 2013

Procalcitonine

50 patients post opératoire de neurochirurgie sans complication

- À J 3**
- 25 % augmentation CRP
 - 56 % augmentation GB
 - fièvre à J1
 - pas d'augmentation PCT

Procalcitonin (ng/mL)



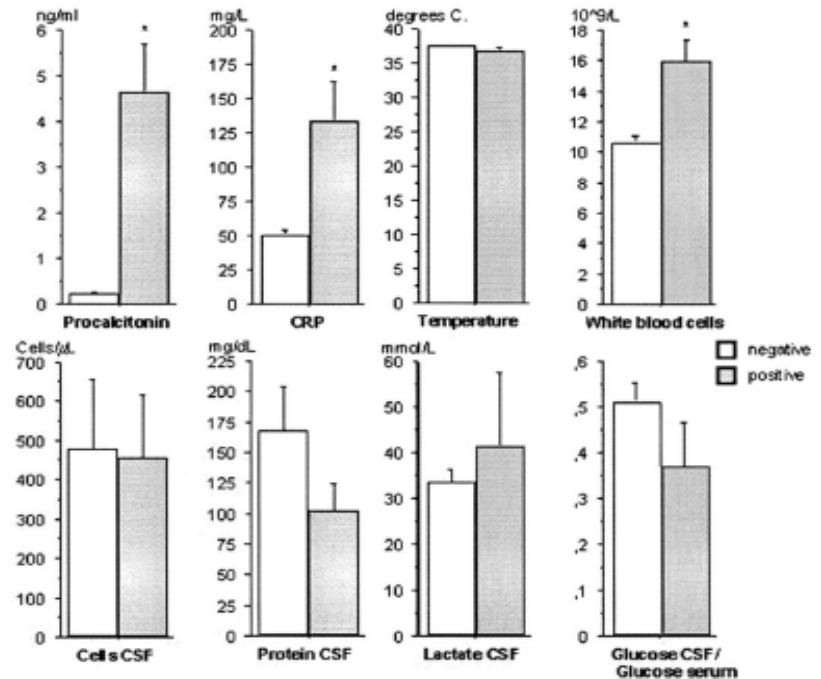
*Laifer Clin Microbiol Infect
2005*

Procalcitonine

- **Etudes contradictoires**

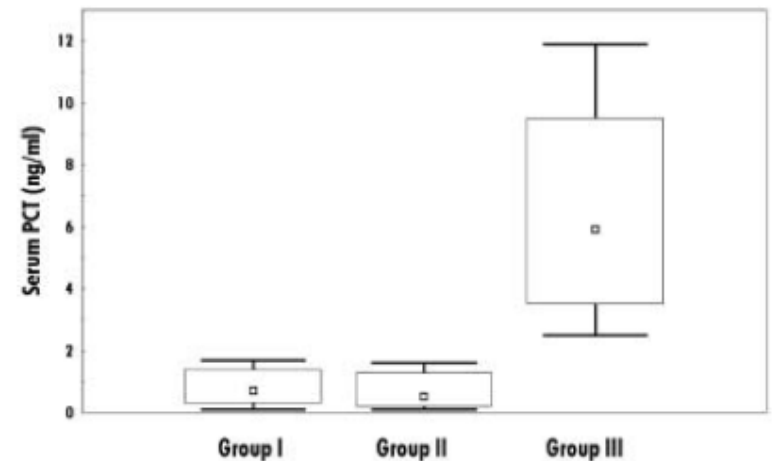
- ***Berger Crit Care Med 2002***

- 34 patients avec DVE
- 5 ventriculites
- Seuil 1 mg / L. $p < 0,00001$



- ***Martinez Intensive Care Med 2002***

- I: Ventriculite aseptique 11
- II: Ventriculite confirmée 4
- III: Méningite communautaire 10

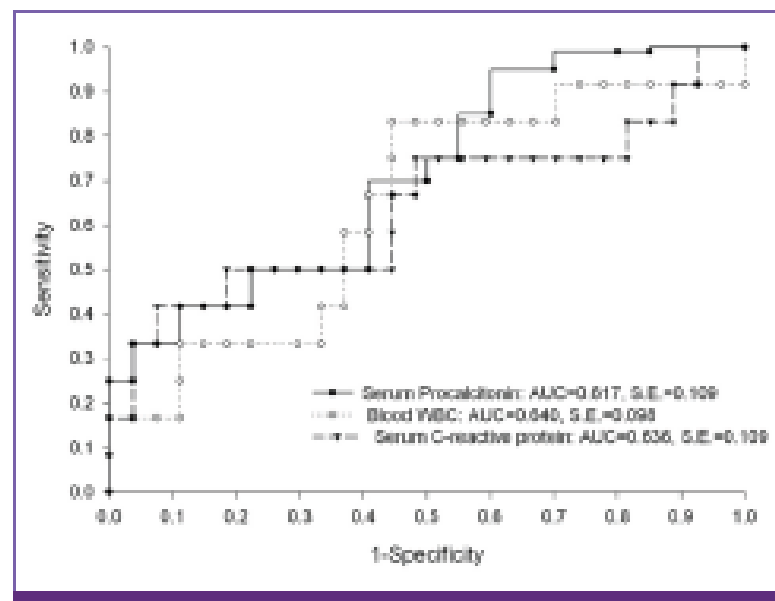


Predictive Performance of Serum Procalcitonin for the Diagnosis of Bacterial Meningitis after Neurosurgery

Choi, Infect Chemoter 2013

Comparaison méningites: septique (14) aseptique (64)

CSF markers	septique (14)	aseptique (64)	
CSF WBC count /mm ³ , median (IQR)	765 (62 to 4,212)	130 (22 to 822)	0.86
CSF RBC count /mm ³ , median (IQR)	1,090 (37 to 16,750)	1,265 (55 to 37,250)	0.35
CSF protein, mg/dL, median (IQR)	115 (62 to 258)	100 (55 to 215)	0.42
CSF glucose, mg/dL, median (IQR)	50 (4 to 98)	57 (46 to 80)	0.15
CSF LDH, IU/L, median (IQR)	148 (72 to 476)	102 (48 to 204)	0.67
CSF ADA, U/L, median (IQR)	3.2 (2.1 to 4.5)	3.3 (1.9 to 6.1)	0.51



Aspect scannographique



Non injecté



injecté

- Présence d'un dépôt de pus en intraventriculaire avec réhaussement de l'épendyme à l'injection

Traitement empirique des méningites post-opératoires

- Recommandations françaises *Portier.presse Méd. 1987 !!!*

Association de céfotaxime - fosfomycine qui permet de traiter les staphylocoques méti S, les BGN et certains staphylocoques méti R (synergie entre les 2 antibiotiques).

Avenir de la ceftaroline ?

- Recommandations anglo-saxonnes

Morris Infect Dis Clin North Am. 1999

Céfotaxime ou association de ceftazidime - vancomycine si contexte épidémique

Recommandations mais influence de l'épidémiologie du pays et de l'unité +++ prévalence de BMR ++

2010

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.

En fait recommandations IDSA 2004

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 β -hemolytic streptococci	Vancomycin plus a third-generation cephalosporin (i.e., ceftriaxone or cefotaxime)



ELSEVIER

Contents lists available at ScienceDirect

Journal of Microbiology, Immunology and Infection

Journal homepage: <http://www.e-jmii.com>

Original Article

Influence of Third-generation Cephalosporin Resistance on Adult In-hospital Mortality From Post-neurosurgical Bacterial Meningitis

Chia-Jung Chang, Jung-Jr Ye, Chien-Chang Yang, Po-Yen Huang, Ping-Cherng Chiang, Ming-Hsun Lee*

Table 3. Antimicrobial resistance of the causative organisms from the cerebrospinal fluid of 60 patients with post-neurosurgical meningitis^a

Antimicrobial agent ^b	Gram-negative organisms					Gram-positive organisms
	<i>Serratia marcescens</i> (n=7)	<i>Klebsiella pneumoniae</i> (n=6)	<i>Enterobacter cloacae</i> (n=4)	Glucose non-fermenting GNB ^c (n=15)	Total (n=43)	
Ceftriaxone ^d	0 (0)	1 (16.7)	4 (100)	15 (100)	25 (58.1)	–
Ceftazidime	0 (0)	1 (16.7)	4 (100)	5 (33.3)	15 (34.9)	–
Cefepime	0 (0)	1 (16.7)	4 (100)	3 (20.0)	12 (27.9)	–
Carbapenems	0 (0)	0 (0)	0 (0)	5 (33.3)	5 (11.6)	–
Oxacillin	–	–	–	–	–	13 (65.0) ^e
Vancomycin	–	–	–	–	–	0 (0.0) ^f

Traitement antibiotique *De Bels Acta neurochirg 2002*

Table 2. *Bacterial Epidemiology and Micro-organism Susceptibility to Different Antibiotic Regimen in 41 Patients^a Without CSF Shunting Material*

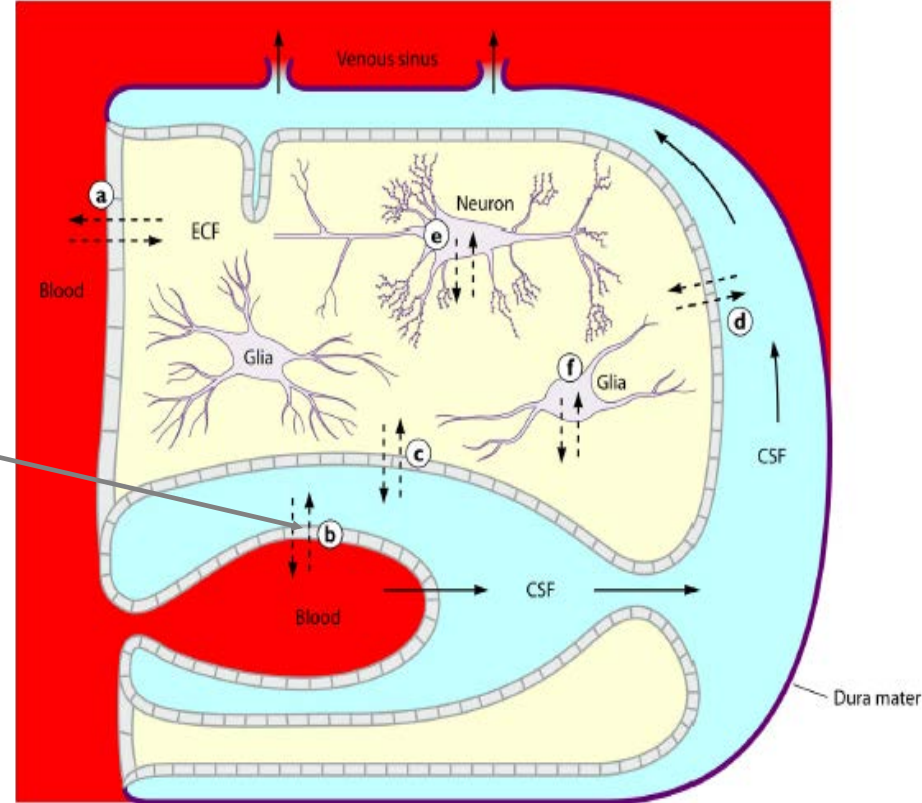
Bacteria	Total	CTX	VAN	CTX-FOS	CTX-VAN
<i>MSSA</i>	11	11	11	11	11
<i>MRSA</i>	0	0	0	0	0
<i>MSCNS</i>	5	5	5	5	5
<i>MRCNS</i>	1	0	1	0	1
<i>Other cocci</i>	5	3	5	3	5
<i>Enterobacteriaceae</i>	13	13	0	13	13
<i>Pseudomonas spp</i>	2	0	0	0	0
<i>Acinetobacter spp</i>	0	0	0	0	0
<i>Corynebacteria spp</i>	3	3	3	3	3
<i>Anaerobes spp</i>	1	1	1	1	1
Total	41	36 (87.8%)	26 (63.4%)^b	36 (87.8%)	39 (95.1%)

Table 3. *Bacterial Epidemiology and Micro-organism Susceptibility to Different Antibiotic Regimen in 65 Patients^a with CSF Shunting Material*

Bacteria	Total	CTX	VAN	CTX-FOS	CTX-VAN
<i>MSSA</i>	9	9	9	9	9
<i>MRSA</i>	5	0	5	3	5
<i>MSCNS</i>	18	18	18	18	18
<i>MRCNS</i>	10	0	10	5	10
<i>Other cocci</i>	7	2	7	2	7
<i>Enterobacteriaceae</i>	9	9	0	9	9
<i>Pseudomonas spp</i>	5	0	0	0	0
<i>Acinetobacter spp</i>	2	0	0	0	0
<i>Corynebacteria spp</i>	0	0	0	0	0
<i>Anaerobes spp</i>	0	0	0	0	0
Total	65	38 (58.5%)	49 (75.4%)^{b-c-d}	46 (70.8%)^e	58 (89.2%)^{f-g}

Traitement documenté

- Dépend de la bactérie
- Diffusion de l'ATB
- En cas de méningite
 - Ouverture des « tight junctions »
 - Diminution production-élimination LCR
 - diminution élimination active ATB (efflux)
- IV fortes posologies
- Contrôle LCR 48-72 H si mauvaise amélioration clinique.
- Durée
 - Staph blanc 10 j
 - Staph doré et entérobactérie 15 (21) j
 - Sur DVP 15 j
- Si culture négative: arrêt des ATB++
 - Si pas ATB préalable !
 - Sinon à discuter en fonction de la clinique et de la biologie



Nau Cin Microbiol Rev 2010

Bonne (≈ 50%)	Moyenne* (≈ 30%)	Mauvaise (< 10%)
Phénicolés Quinolones Rifampicine Fosfomycine Imidazolés Sulfamides Linézolide	Péni G et A Céphalo 3 Carboxy Péni Uréido Péni Carbapénem Vancomycine	Péni M Céphalo 1 et 2 Aminosides Teicoplanine Fucidine Cyclines Macrolides Lincosamides Polymyxines
	* Améliorée en cas d'inflammation des méninges	

Pénétration méningée

Lancet nov 2012

Bacterial Meningitis 2

Advances in treatment of bacterial meningitis

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

	CSF penetration (CSF:plasma)* in uninfamed meninges	CSF penetration (drug in CSF:plasma)* in inflamed meninges	Comments on use of antibiotic class for meningitis treatment
β-lactams			Poor CSF penetration, but high systemic doses are well tolerated and attain CSF concentrations that greatly exceed the MIC of susceptible bacteria. 40% of cefotaxime vs 90% of ceftriaxone is protein bound. Avoid imipenem because it could lower the seizure threshold. <u>Continuous infusions could enhance bacterial killing</u>
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	
Aminoglycosides			Poor CSF penetration and toxicity limits increases in systemic doses. Consider intraventricular/intrathecal delivery if needed
Gentamicin	0-01	0-1	
Amikacin	No data	0-1	
Glycopeptides			Poor CSF penetration and toxicity limits increases in systemic doses. Continuous infusions could enhance bacterial killing. Limited data for intraventricular/intrathecal delivery
Vancomycin	0-01	0-2	
Teicoplanin	0-01	0-1	
Fluoroquinolones			Good CSF penetration. Moxifloxacin is an alternative agent for the treatment of penicillin-resistant pneumococcal meningitis
Ciprofloxacin	0-3	0-4	
Moxifloxacin	0-5	0-8	
Levofloxacin	0-7	0-8	
Others			
Chloramphenicol	0-6	0-7	Excellent CSF penetration, although toxicity concerns limit its use
Rifampicin	0-2	0-3	80% protein bound; <u>CSF concentrations greatly exceed MIC of susceptible bacteria</u>
Newer agents			
Cefepime	0-1	0-2	Effective against penicillin-resistant pneumococcal meningitis
Linezolid	0-5	0-7	Case report/series suggest effectiveness for pneumococcal, staphylococcal, and enterococcal meningitis, although high interindividual variability in CSF pharmacokinetics suggests therapeutic drug measurements could be needed
Daptomycin	No data	0-05	Poor penetration, but CSF concentrations exceed MIC of susceptible bacteria; case reports/series suggest efficacy in staphylococcal and enterococcal meningitis
Tigecycline	No data	0-5	Good CSF penetration, but concentrations achieved at current standard doses could be insufficient to ensure bacterial killing

CSF=cerebrospinal fluid. MIC=minimum inhibitory concentration. *Based on calculated area under the curve (AUC)_{CSF}/AUC_{plasma}, when possible, but data are limited for most antibiotics and AUC cannot be calculated on the basis of single CSF measurements. In these circumstances, CSF penetration is estimated from paired plasma and CSF measurements.

Bacterial Meningitis 2

Advances in treatment of bacterial meningitis

Van de Beek Lancet nov 2012

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

Staphylococcus aureus

Meticillin sensitive

Nafcillin or oxacillin

Vancomycin, linezolid, daptomycin

Meticillin resistant||

Vancomycin

Trimethoprim-sulfamethoxazole, linezolid, daptomycin

Staphylococcus epidermidis||

Vancomycin

Linezolid

Enterobacteriaceae**

Cefotaxime or ceftriaxone

Aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole, meropenem, ampicillin

Pseudomonas aeruginosa

Ceftazidime or cefepime¶¶

Aztreonam, meropenem, ciprofloxacin¶¶

*Acinetobacter baumannii***

Meropenem

Colistin (usually formulated as colistimethate sodium), polymyxin B††

Staph résistant ou blanc: possible association avec rifampicine (matériel +++)

Un certain nombre d'équipes françaises si staph meti S:

Quinolone-rifampicine ou Cotrimoxazole-rifampicine

Choix du carbapénem

Management of meningitis due to antibiotic-resistant
Acinetobacter species

Lancet Infect Dis 2009

Boek-Nam Kim, Anton Y Peleg, Thomas P Lodise, Jeffrey Lipman, Jian Li, Roger Nation, David L Paterson

IMIPENEM NON: risque d'épilepsie
moins bonne pénétration



MEROPENEM OUI: 2 gr x 3 probablement en perfusion de 2-4 h

linezolid

**Bonne diffusion LCR mais variations interindividuelles (augmenter dose ?)
Bactériostatique. Pas d'étude contrôlée, option pour entérocoque vanco R ?**

Linezolid in the central nervous system: Comparison between cerebrospinal fluid and plasma pharmacokinetics

BRUNO VIAGGI¹, ANTONELLO DI PAOLO², ROMANO DANESI²,
MARIALUISA POLILLO², LAURA CIOFI², MARIO DEL TACCA² & PAOLO MALACARNE¹

SJID 2011

Infection 2007

**Treatment of Meningitis
Caused by Methicillin-Resistant
Staphylococcus aureus with Linezolid**

A.T. Kessler, A.P. Kourtis

Plasma and cerebrospinal fluid concentrations of linezolid in neurosurgical critically ill patients with proven or suspected central nervous system infections

Int J Antimicrob Agents 2014

AAC 2007

Pharmacokinetics of Intravenous Linezolid in Cerebrospinal Fluid and Plasma in Neurointensive Care Patients with Staphylococcal Ventriculitis Associated with External Ventricular Drains^v

Serum and Cerebrospinal Fluid Concentrations of Linezolid in Neurosurgical Patients^v

AAC 2006

Daptomycine

JAC 2008

Treatment of external ventricular drain-associated ventriculitis caused by *Enterococcus faecalis* with intraventricular daptomycin

Bactériode, diffusion 6%

Actif sur le biofilm, intraventriculaire possible

Possibilité d'augmenter les doses IV 10 mg / kg

Eviter la monothérapie (selection de résistances)

Juliet Elvy¹, David Porter² and Erwin Brown^{1*}

Successful Treatment of Methicillin-Resistant *Staphylococcus aureus* Meningitis with Daptomycin

CID 2008

Journal of Antimicrobial Chemotherapy (2006) 57, 720–723
doi:10.1093/jac/dkl007
Advance Access publication 3 February 2006

JAC

**Daptomycin is more efficacious than vancomycin against a
methicillin-susceptible *Staphylococcus aureus* in
experimental meningitis**

Peter Gerber¹, Armin Stucki², Fernando Acosta³, Marianne Cottagnoud³
and Philippe Cottagnoud^{2*}

Cerebrospinal Fluid Penetration of High-Dose Daptomycin in Suspected *Staphylococcus aureus* Meningitis

*Annals
pharmacotherapy
2010*

Tigécycline

Serum, tissue and body fluid concentrations of tigecycline after a single 100 mg dose

Keith A. Rodvold^{1*}, Mark H. Gotfried¹⁻³, Michael Cwik⁴, Joan M. Korth-Bradley⁵, Gary Dukart⁵ and Evelyn J. Ellis-Grosse⁵

Peu de données

Diffusion 10 % dans LCR

Intérêt: parfois seul ATB avec Coli pour carbapénemase

Cerebral Spinal Fluid Penetration of Tigecycline in a Patient with *Acinetobacter baumannii* Cerebritis

Leslie Ray, Kimberly Levasseur, David P Nicolau, and Marc H Scheetz

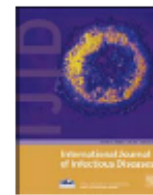
Ann Pharmacotherapie 2010



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid



Case Report

2010

Tigecycline use in two cases with multidrug-resistant *Acinetobacter baumannii* meningitis

E. Ediz Tutuncu*, Ferit Kuscu, Yunus Gurbuz, Baris Ozturk, Asli Haykir, Irfan Sencan

Colistine



International Journal of Antimicrobial Agents 29 (2007) 9–25

INTERNATIONAL JOURNAL OF
**Antimicrobial
Agents**

www.ischemo.org

Review

Intraventricular or intrathecal use of polymyxins in patients with Gram-negative meningitis: a systematic review of the available evidence

Matthew E. Falagas^{a,b,*}, Ioannis A. Bliziotis^a, Vincent H. Tam^c

ORIGINAL ARTICLE

INFECTIOUS DISEASES

Intrathecal colistin for drug-resistant *Acinetobacter baumannii* central nervous system infection: a case series and systematic review

T. Khawcharoenporn¹, A. Apisarnthanarak¹ and L. M. Mundy²

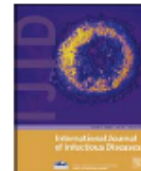
Clin Microbiol Infect 2010;



Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid



Review

Post-neurosurgical multidrug-resistant *Acinetobacter baumannii* meningitis successfully treated with intrathecal colistin. A new case and a systematic review of the literature

Antonio Cascio^{a,*}, Alfredo Conti^b, Luca Sinardi^c, Chiara Iaria^d, Filippo Flavio Angileri^b,
Giovanna Stassi^e, Teresa David^c, Antonio Versaci^c, Maurizio Iaria^f, Antonio David^c

2010

Posologies intraventriculaires

Nau Cin Microbiol Rev 2010

Pas d'AMM

Clamper la sonde pendant 1 h

Dosages si possible de la résiduelle. Tant que C > 10 à 20 fois CMI, pas de réinjection

Van de Beek NEJM 2010

TABLE 2. Intraventricular application of antibiotics to reach effective concentrations within the CNS^a

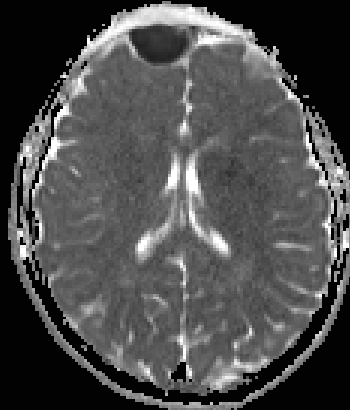
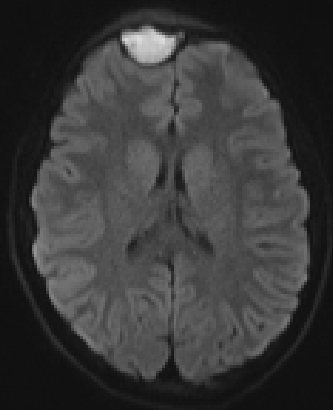
Antibiotic	Dose for adults	Severe reported side effect(s)
Gentamicin	5 mg every 24 h	Hearing loss (temporary), epileptic seizures, aseptic meningitis, eosinophilic CSF pleocytosis
Tobramycin	5 mg every 24 h	Similar to those of gentamicin
Amikacin	30 mg every 24 h	Similar to those of gentamicin
Streptomycin	Up to 1 mg/kg every (24–)48 h	Hearing loss (temporary), epileptic seizures, radiculitis, transverse myelitis, arachnoiditis, paraplegia
Vancomycin	5–20 mg every 24 h	Hearing loss (temporary)
Colistin (polymyxin E) methanesulfonate (12,500 IU = 1mg)	10 (1.6–20) mg every 24 h	Meningeal inflammation; with high doses, epileptic seizures, loss of appetite, agitation, eosinophilia, edema, pain, albuminuria
Daptomycin	5–10 mg every 72 h	Fever
Amphotericin B	0.1–0.5 mg every 24 h	Tinnitus, fever, shivering, Parkinson syndrome

Conclusion

- Infections pas très fréquentes
- Méningites post op # méningites communautaires
- Staphylocoque ++/ BG –
- Diagnostic difficile
- Problème des méningites aseptiques
- Traitement moins consensuel
- Problème des BMR

Abcès et empyème post-opératoires

- Incidence 2,7 %, survient au cours du premier mois.
- Clinique: réapparition des signes initiaux: épilepsie, détérioration neurologique et fièvre modérée
- Méningite associée 14 %
- Dg: Imagerie +++ TDM ou IRM. Attention PL !!
- Ponction collection



Bactériologie abcès / empyème

- Polymicrobien dans 14,4 % des cas
- Propionibacterium acnes 37 %
- Staphylocoques dorés 20 %
- Staphylocoques coag neg 17 %
- Entérobactéries 15 %
- P Aeruginosa 3 %
- Streptocoques 3 %

Korinek, neurosurgery 2005

Brain Abscess

Matthijs C. Brouwer, M.D., Ph.D., Allan R. Tunkel, M.D., Ph.D.,
Guy M. McKhann II, M.D., and Diederik van de Beek, M.D., Ph.D.

2014

Table 2. Antimicrobial Therapy in Patients with Brain Abscess.

Treatment	Therapy*
Empirical treatment	
Standard	Cefotaxime or ceftriaxone plus metronidazole; alternatively, meropenem (add vancomycin if infecting pathogen may be <i>Staphylococcus aureus</i> , pending organism identification and in vitro susceptibility testing)
For transplant recipients	Cefotaxime or ceftriaxone plus metronidazole, voriconazole, and trimethoprim-sulfamethoxazole or sulfadiazine
For patients with HIV infection	Cefotaxime or ceftriaxone plus metronidazole, pyrimethamine, and sulfadiazine; consider isoniazid, rifampin, pyrazinamide, and ethambutol to cover possible tuberculosis infection
Treatment based on isolated pathogen	
Bacteria†	
Actinomyces species‡	Penicillin G
Bacteroides fragilis‡	Metronidazole
Enterobacteriaceae‡	Cefotaxime or ceftriaxone
Fusobacterium species‡	Metronidazole
Haemophilus species‡	Cefotaxime or ceftriaxone
Listeria monocytogenes	Ampicillin or penicillin G§
Mycobacterium tuberculosis	Isoniazid, rifampin, pyrazinamide, and ethambutol
Nocardia species	Trimethoprim-sulfamethoxazole or sulfadiazine
Prevotella melaninogenica‡	Metronidazole
Pseudomonas aeruginosa	Ceftazidime or ceftipime‡
<i>S. aureus</i>	
Methicillin-sensitive	Nafcillin or oxacillin
Methicillin-resistant	Vancomycin
Streptococcus anginosus group, other streptococcal species‡	Penicillin G
Fungi	
Aspergillus species	Voriconazole
Candida species	Amphotericin B preparation¶
Cryptococcus neoformans	Amphotericin B preparation¶
Mucorales	Amphotericin B preparation
Scedosporium apiospermum	Voriconazole
Protozoa	
T. gondii	Pyrimethamine plus sulfadiazine

Infections sur dérivations internes

- Sur une série prospective incluant 839 procédures
incidence infection 6, 1 % *Korinek neurosurgery 2011*
- FDR: fuite LCR antérieure, dysfonction mécanique antérieure, durée chirg, ne pas être programmé en 1ère position
- **Diagnostic:** dysfonction valve et contexte fébrile, Sd d'irritation péritonéale, écoulement purulent trajet cathéter, cultures positives valve ou cathéter
- Cas particulier car possiblement à distance (1 mois à 1 an)

Conen CID 2008

Pathogen	Overall (n = 78)	Infection onset		
		Early ^a (n = 48)	Delayed ^b (n = 22)	Late ^c (n = 8)
Coagulase-negative staphylococci ^d	29 (37)	19	9	1
<i>Staphylococcus aureus</i> ^d	14 (18)	9	5	...
<i>Propionibacterium acnes</i>	7 (9)	5	2	...
Viridans group streptococci	3 (4)	2	1	...
Enterobacteriaceae ^e	3 (4)	3
Nonfermenters ^f	2 (3)	...	1	1
<i>Enterococcus</i> species	1 (1)	...	1	...
Polymicrobial ^g	12 (15)	4	2	6
Culture negative	7 (9)	6	1	...

Infections sur dérivation internes

Recommandations IDSA

Tunkel CID 2004

- **Ablation de la valve de dérivation interne**
- **Mise en place de DVE**
- **Traitement ATB**
- **Si staphylocoque coag - et LCR normal et stérilisé, la réimplantation peut se faire dès J3**
- **Si staphylocoque coag- et LCR anormal, la réimplantation ne peut se faire avant J7 sous réserve cultures négatives et protéinorachie < 2g/l**
- **Dans les autres cas une stérilisation de 10 à 14 j est nécessaire avant réimplantation. Une période d'arrêt des ATB de 3 j peut aussi être proposé avant réimplantation**