Convegno Nazionale

La Gestione Appropriata delle Infezioni in Riabilitazione: indicazioni strategiche

Cona (Fe) 20 Giugno 2019

Aula Congressuale

Nuovo Arcispedale S. Anna, Via A. Moro n. 8

Le infezioni post-neurochirurgiche: come affrontarle

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Disclosures

Research grants
- Pfizer
- Angelini

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- MSD
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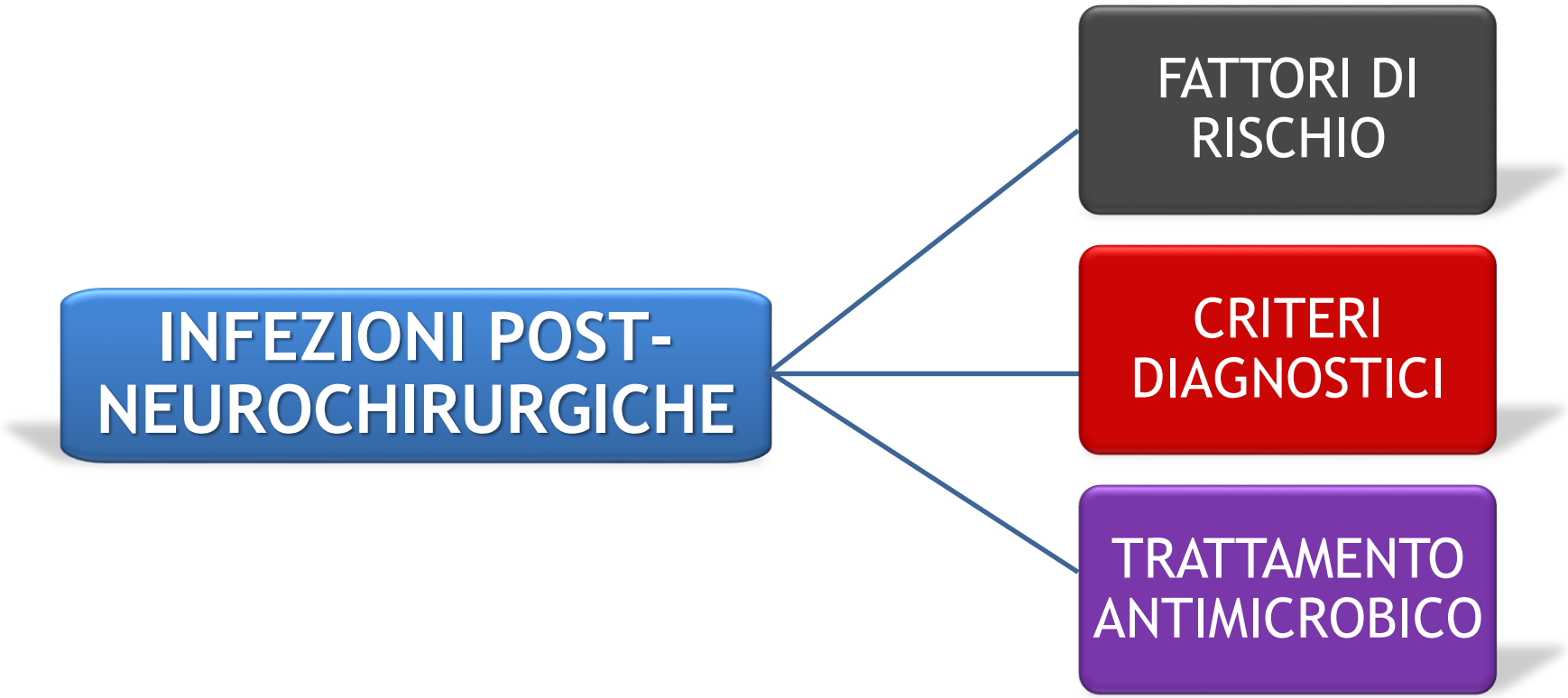
INFEZIONI POST-NEUROCHIRURGICHE
FATTORI DI RISCHIO
CRITERI DIAGNOSTICI
TRATTAMENTO ANTIMICROBICO

Risk factors of neurosurgical site infection after craniotomy: A systematic review and meta-analysis

C. Fang et al. American Journal of Infection Control 2017; 45: e123-e134

Risk factors associated with SSI after craniotomy, increased risk of SSI

- Other infection,
- CSF leakage
- CSF drainage
- venous sinus entry
- duration of operation (>4 hours) (as for retrospective cohort studies)
- number of operations (>1)
- surgical reasons (nontraumatic)
- ASA score (>2)

No relationship was found between hair removal, age, operative sites, emergency procedures, antibiotic prophylaxis, material type of the implant, surgical wound classification, intracranial pressure monitors, foreign body placement, hypertension, diabetes, steroid use, and SSI occurrence

Risk factors for surgical site infections after neurosurgery: A focus on the postoperative period

N. Cassir et al. / American Journal of Infection Control 43 (2015) 1288-91

Factors associated with SSI after cranial surgery

Factors	SSI (N 25) N (%)	No SSI (N 501) N (%)	Univariate *p* Value *	Multivariate *p* Value *
NNIS score ≥2	16 (64)	61 (12.2)	<.0001	<.001
Previous surgery same site	6 (24)	33 (6.6)	.008	.01
Length of postoperative stay in ICU ≥7 d	11 (44)	39 (7.8)	<.0001	<.005
Duration of drainage ≥3 d	9 (36)	91 (18.2)	.04	.04
CSF leakage	3 (12)	10 (2)	.02	.04

* *P* <.05

Risk factors for surgical site infections after neurosurgery: A focus on the postoperative period

N. Cassir et al. / American Journal of Infection Control 43 (2015) 1288-91

Factors associated with SSI after spinal surgery

* *P* <.05

Factors	**SSI (N 25) N (%)**	**No SSI (N 501) N (%)**	**Univariate *p* Value ***	**Multivariate *p* Value ***
NNIS score ≥2	7 (38.9)	26 (6.4)	<.0001	<.002
Emergency	15 (83.3)	162 (40)	<.001	.10
Traumatic	15 (83.3)	130 (32.1)	<.0001	.08
Foreign body	16 (88.9)	178 (44)	<.0001	.50
Osteosynthesis	16 (88.9)	167 (41.2)	<.0001	NA
Length of postoperative stay in ICU ≥7 d	7 (38.9)	7 (1.7)	<.0001	<.01
Duration of drainage ≥3 d	14 (77.8)	86 (21.2)	<.0001	.01
Other infection	8 (44.4)	10 (2.5)	<.0001	.002

Risk factors for surgical site infections after neurosurgery: A focus on the postoperative period

N. Cassir et al. / American Journal of Infection Control 43 (2015) 1288-91

Causative microorganisms of the 43 surgical site infections

Microorganisms	Brain surgery (n = 25)	Spinal surgery (n = 18)	Total (N = 43)
Staphylococcus aureus	6 (24)	4 (22.2)	10 (23.2)
CoNS	0 (0)	2 (11.1)	2 (4.6)
Enterococcus spp	2 (8)	0 (0)	2 (4.6)
Enterobacteriaceae	3 (12)	6 (33.3)	9 (20.9)
Pseudomonas aeruginosa	2 (8)	0 (0)	2 (4.6)
Propionibacterium acnes	4 (16)	1 (5.5)	5 (11.6)
Other anaerobes	1 (4)	3 (16.6)	4 (9.2)
Multibacteria	4 (16)	1 (5.5)	5 (11.6)
Undocumented	3 (12)	1 (5.5)	4 (9.2)

NOTE. Values are n (%).
ConS, coagulase-negative staphylococci.

Implementation of a care bundle and evaluation of risk factors for surgical site infection in cranial neurosurgery

B.M. Davies et al. / Clinical Neurology and Neurosurgery 144 (2016) 121–125

'Bundle compliance' required administration of antibiotics <60 min of induction, maintenance of intraoperative blood sugar (BM) <11 mmol and temperature at >36°C.

In this study only the use of an implant(s) was recognised as an independent risk factor for SSI and the bundle of care had no impact. These findings highlight that untailored interventions will not always be successful.

Cultured Microorganisms.

Organisms Cultured	(%)
Staphylococcus Aureus	31 (47.0)
Coagulase Negative Staphylococcus	7 (10.3)
Enterobacter Species	5 (7.4)
Coliforms	2 (3.0)
Klebsiella Species	2 (3.0)
Other[*]	5 (7.4)
No growth	16 (23.5)

[*] VRE, Diphtheria species, *Pseudomonas aerginosa*, gram +ve Baccillus, gram +ve Cocci.

Implementation of a care bundle and evaluation of risk factors for surgical site infection in cranial neurosurgery

B.M. Davies et al. / Clinical Neurology and Neurosurgery 144 (2016) 121–125

Univariate analysis baseline characteristics and the development of SSI.

Univariate Analysis			
Variable	*SSI*	*No SSI*	*P Value*
Age (years, IQR)	51 (23)	52 (25)	0.39
ASA (%)			0.98
Good [I–III]	61 (89.7)	1062 (89.6)	
Poor [IV–V]	7 (10.3)	123 (10.4)	
Length of Operation (min, IQR)	122 (108)	115 (126)	0.47
Elective procedure (%)	47 (69.1)	796 (67.2)	0.74
Altemier Wound Classification (% of group)			0.43
Clean	68 (100)	1156 (97.6)	
Clean contaminated	0 (0)	5 (0.4)	
Contaminated	0 (0)	0 (0.0)	
Dirty	0 (0)	24 (2.0)	
Category of Surgery (% of group)			<0.0005
Oncology	26 (38.2)	487 (41.1)	
Vascular	2 (2.9)	64 (5.4)	
Skull Base	7 (10.3)	146 (12.3)	
Cranioplasty	10 (14.7)	44 (3.7)	
Other Implant	12 (17.6)	146 (12.3)	
Trauma/Miscellaneous	11 (16.2)	298 (25.1)	
Grade of Principal Surgeon (% of group)			0.46
Consultant	34 (50.0)	578 (48.8)	
Trainee (Consultant Present)	14 (20.6)	188 (15.9)	
Trainee	20 (29.4)	419 (35.4)	
Neurosurgery within last 1 month (%)	9 (13.2)	73 (6.2)	0.022
Temperature >36 °C (%)	61 (89.7)	1098 (92.7)	0.21
Sugar <11 mmols (%)	68 (100)	1175 (99.2)	0.57
Antibiotics given <60 min of induction (%)	65 (95.6)	1143 (96.5)	0.43

Risk factors associated with death or neurological deterioration among patients with Gram-negative postneurosurgical meningitis

A. Neuberger et al. Clin Microbiol Infect 2016; 22: 573.e1-573.e4

TABLE 2. Multivariate analysis and prognostic score for death or neurological deterioration[a]

Variable[b]	Odds ratio [c]	95% CI	Categories	Regression coefficient	Score
Time from admission to meningitis (days)	1.05 (per day)	1.02–1.09	0–6	0.048971	0
			7–14		1
			15–21		2
			≥22		4
Decreased level of consciousness at diagnosis	2.69	0.99–7.31	Yes	0.99104	3
			No		0
Blood glucose >180 mg/dL	3.70	1.27–10.77	Yes	1.309041	4
			No		0
Blood creatinine (mg/dL)	4.07 (per 1 mg/dL)	1.50–11.08	≤1.2	1.404554	0
			>1.2		4
Cerebrospinal fluid glucose <50 mg/dL at diagnosis	5.02	1.71–14.77	Yes	1.613369	5
			No		0

[a]Neurological deterioration was defined as any decrease on a clinical score of 1–5 (alert, responsive to voice, responsive to pain only, unresponsive, and dead) from the onset of meningitis until discharge or death.
[b]Charlson's Score and cerebrospinal fluid protein were entered into the multivariate regression analysis but not retained in the final model.
[c]Hosmer and Lemeshow p 0.35.

No significant differences between groups in co-morbid conditions, infecting bacteria, the positivity of first and second CSF Gram stains or concurrent bacteraemia.

Procalcitonin in cerebrospinal fluid in meningitis: a prospective diagnostic study

Alons IME et al. *Brain and Behavior* 2016; 6: e00545

	Bacterial meningitis (n = 26)	CAM (n = 16)	PNM (n = 10)	Viral meningitis (n = 14)	Non-infectious (n = 14)
CSF leukocyte count × 10^6 per liter ave	5,998	7,551	3,514	267	1
Polynuclear cells × 10^6 per liter ave	5,589	7,428	2,832	28	0.1
Mononuclear cells × 10^6 per liter ave	616	576	677	239	0.7
Erythrocytes × 10^6 per liter ave	23,649	12,892	408,597	180	287
CSF glucose mmol L^{-1} ave	1.6	1.0	2.6	3.5	3.4
CSF protein g L^{-1} ave	3.3	3.9	2.4	1	0.4
PCT in CSF ng mL^{-1} Average (95% CI)	0.61 (0.29–0.90)	0.81 (0.31–1.31)	0.29 (0.10–0.45)	0.10 (0.08–0.12)	0.08 (0.05–0.09)
PCT in plasma ng mL^{-1} Median (IQR)	0.5 (4.36)	1.28 (6.82)	0.05 (0.08)	0.02 (0.02)	-
PCT ratio CSF:plasma Median (IQR)	0.86 (2.79)	0.18 (0.27)	5.18 (4.69)	3.00 (1.38)	-
Mean difference PCT in CSF versus non infectious (95% CI)	0.74 ng mL^{-1} (0.20–1.28)	0.73 ng mL^{-1} (0.20–1.27)	0.21 ng mL^{-1} (0.05–0.37)	0.30 ng mL^{-1}	-
Mean difference PCT in CSF versus Viral meningitis (95% CI)	0.73 ng mL^{-1} (0.19–1.27)	0.71 ng mL^{-1} (0.18–1.25)	0.18 ng mL^{-1} (0.02–0.34)		

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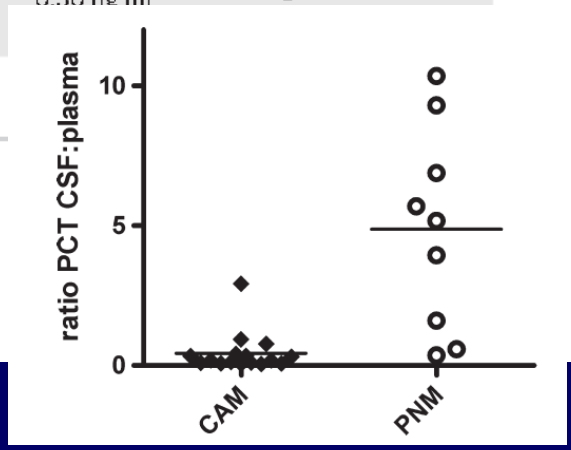


Procalcitonin in cerebrospinal fluid in meningitis: a prospective diagnostic study

Alons IME et al. *Brain and Behavior* 2016; 6: e00545

Study limitations

- ✓ study size is relatively small
- ✓ difference in PCT levels in CSF in patients diagnosed with bacterial meningitis with a positive and negative bacterial CSF culture is not statistically significant
- ✓ there are no reference values for PCT in CSF available

Clinical application

- ✓ These results show a good sensitivity and negative predictive value for PCT in CSF
- ✓ The use of PCT in CSF in determining the need for and possibly duration of antibiotic treatment

Impact of surgical site infection surveillance in a neurosurgical unit

S. Buffet-Bataillon et al. / Journal of Hospital Infection 77 (2011) 352–355

Univariate analysis of surgical site infections, 2008 ($N = 1471$)

Variables	No SSI ($N = 1444$)	SSI ($N = 27$)	P
Age (years)[a]	50.1 ± 20.7	47.7 ± 16.6	NS
Length of hospitalisation (days)[a]	13.8 ± 18.6	22.7 ± 18.6	0.01
Length of preoperative stay (days)[a]	2.2 ± 4.6	2.7 ± 2.9	0.01
Type of operative procedure			NS
Cranial surgery	854 (59.1%)	17 (63%)	
Cerebrospinal fluid derivation, spinal surgery, peripheral nerves surgery, stimulation	590 (40.9%)	10 (37%)	
Duration of operative procedure (min)[a]	112.2 ± 81.9	132 ± 84.1	NS
Surgical wound classification			NS
Clean	1353 (93.7%)	25 (92.6%)	
Clean-contaminated, contaminated, dirty-infected	91 (6.3%)	2 (7.4%)	
Prosthetic implant used	444 (30.7%)	12 (44.4%)	NS
Emergency surgery	464 (32.1%)	8 (29.6%)	NS
ASA severity score			NS
1, 2	1120 (77.6%)	22 (81.5%)	
3, 4, 5	324 (22.4%)	5 (18.5%)	

Univariate analysis of surgical site infections (SSIs), 2009 ($N = 1410$)

Variables	No SSI ($N = 1394$)	SSI ($N = 16$)	P
Age (years)[a]	52.5 ± 18.6	50.4 ± 17.4	NS
Length of hospitalisation (days)[a]	11.7 ± 16.6	9.8 ± 5.5	NS
Length of preoperative stay (days)[a]	2.3 ± 7.1	1.3 ± 1.1	NS
Type of operative procedure			NS
Cranial surgery	812 (58.2%)	10 (62.5%)	
Cerebrospinal fluid derivation, spinal surgery, peripheral nerve surgery, stimulation	582 (41.8%)	6 (37.5%)	
Duration of operative procedure (min)[a]	108.5 ± 77	131.8 ± 97.7	NS
Surgical wound classification			NS
Clean	1337 (95.9%)	15 (93.8%)	
Clean-contaminated, contaminated, or dirty-infected	57 (4.1%)	1 (6.2%)	
Prosthetic implant used	418 (30%)	9 (56.3%)	0.03
Emergency surgery	481 (34.5%)	4 (25%)	NS
ASA severity score			NS
1, 2	1095 (78%)	11 (68.8%)	
3, 4, 5	299 (21.4%)	5 (31.2%)	

Management of post-neurosurgical meningitis: narrative review

K. Hussein et al. / Clinical Microbiology and Infection 23 (2017) 621–628

Post-neurosurgical meningitis occurs after craniectomy, craniotomy or following the insertion of internal or external ventricular and lumbar catheters. In addition, post-neurosurgical inflammatory processes often have a noninfectious aetiology.

Meningitis following craniotomy occurs in 0.3% - 8.6% of all patients. Actual rates probably depend on the different indications for surgery, underlying medical conditions, and local implementation of infection-control measures.

The incidence of PNM following the insertion of cerebrospinal fluid (CSF) draining devices also ranges widely between 4% and 17% (internal ventricular catheters), 0% and 22% (external ventricular drains) and 0.8% and 7% (external lumbar catheter)

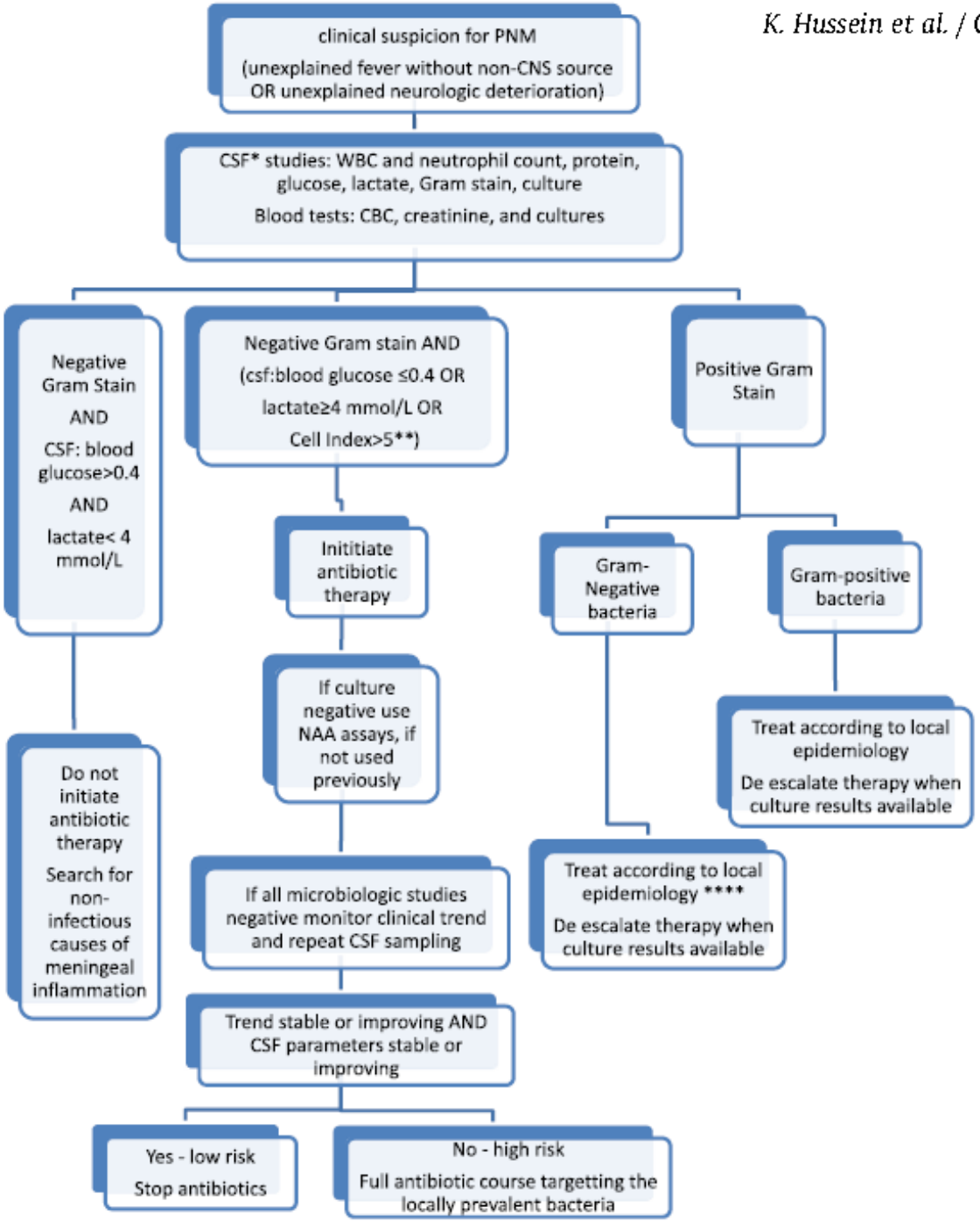
Management of post-neurosurgical meningitis: narrative review

K. Hussein et al. / Clinical Microbiology and Infection 23 (2017) 621–628

PNM diagnosis, namely CSF culture, has important limitations. A negative CSF culture in a patient with PNM is often the result of previous antibiotic therapy, and rarely the result of meningitis caused by fastidious bacteria, fungi or mycobacteria.

Prolonged incubation of at least 10 days is necessary for the isolation of some bacteria such as *P. acnes*. Nucleic acid amplification tests are useful in providing amore rapid identification of bacteria in the CSF or for difficult-to-grow bacteria. In some studies, PCR did not improve culture sensitivity , whereas in others sensitivity improved mainly for patients pretreated with antibiotics .

These data point to a possible complementary advantage of culture and NAAT in the diagnosis of PNM meningitis. Assays that test simultaneously for multiple pathogens or broad-range 16S rRNA PCR are available commercially or as in-house assays



Antibiotic prophylaxis, recommended for neurosurgery, is directed mainly against Gram-positive bacteria.

Antibiotics used in impregnated catheters (minocycline, rifampin, clindamycin) and silver coating are active mainly against Gram-positive bacteria.

These approaches shift remaining infections to a Gram-negative spectrum.

The contemporary bacteriological profile of PNM is further complicated by increasing rates of infections caused by multidrug-resistant Gram-negative bacteria, with the emergence of *Acinetobacter baumannii*

GRAM-POSITIVE THERAPY

Linezolid has very good CNS penetration (AUCCSF/AUCserum of 0.8e1)
Tedizolid has a broader spectrum of activity, but lower CNS penetration than linezolid
Daptomycin is bactericidal, but has poor CNS penetration
Telavancin CNS 0.1% in non-inflamed meninges and 2% in inflamed meninges
Fosfomicina
Oritavancin 2%-5% in rabbit models of meningitis
Ceftaroline 3% in non-inflamed meninges and 14%e15% in inflamed meninges
Ceftobiprole 2% and 16%, respectively

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Nau R et al. Clin Microbiol Rev 2010;23:858e83.
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Stucki A, et al. Antimicrob Agents Chemother 2006;50:770e3.
Ambrose PG, et al. Clin Infect Dis 2012;54(Suppl. 3):S220e8.
Cottagnoud P, et al. Antimicrob Agents Chemother2013;57:4653e5.
Stucki A, et al. Antimicrob Agents Chemother 2013;57:5808e10.
Stucki A, et al. Antimicrob Agents Chemother 2012;56:921e5.
Cannon JP, Lee TA, Clark NM, Setlak P, Grim SA. The

GRAM-NEGATIVE THERAPY

Meropenem
Colistin
Cefoperazone
Cefepime
Fosfomicina
Ceftolozano/tazobactam
Combinations with avibactam might prove beneficial, as avibactam seems to have better penetration than other β-lactam inhibitors
Intrathecal administratino of anti-Gram negative bacteria menigitis

Cannon JP, et al. J Antimicrob Chemother 2014; 69: 2043e55.
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Post craniotomy extra-ventricular drain (EVD) associated nosocomial meningitis: CSF diagnostic criteria

Breakpoints to diagnose EVD associated nosocomial meningitis:

- ✓ marked CSF pleocytosis (>50 WBCs/mm^3) in
- ✓ high lactic acid levels (>6 nmol/L),
- ✓ positive Gram stain (same morphology as the CSF culture isolate) and
- ✓ positive CSF culture of a neuropathogen (same morphology as the Gram stained organism)

Only if all four diagnostic criteria were present, was EVD associated nosocomial meningitis diagnosed

External ventricular drain (EVD) associated acute bacterial meningitis (ABM): CSF profiles & microbiologic data.

Patients with EVDs	Disorder requiring an EVD	CSF Lactate acid levels (mmol/L)	CSF WBC counts (K/mm^3)	CSF RBC counts (K/mm^3)	CSF glucose levels (ng/dL)	CSF protein levels (ng/dL)	CSF Gram stain	CSF culture
1	ICH	1.7	0	0	72	16	Negative	CoNS
2	ICH	3.6	40	30,000	97	56	Negative	CoNS
3	SAH	2.9	1	600	56	172	GNB	*E. cloacae*
4	ICH	18.3	50	52,000	240	459	Negative	Negative
5	ICH	6.8	8200	60,000	84	63	Negative	*Enterobacter aerogenes*
6	SAH	3.4	123	30,000	75	41	Negative	VSE, *C bifermentans*
7	SAH	2.7	47	17,281	78	22	Negative	*Streptococcus Viridans*, *Lactobacillus* sp.
8	SAH	5.5	400	50,000	68	69	GNB	CoNS
9	SAH	6.5	40	2480	109	97	Negative	Negative
10	ICH	11.7	19,100	130,000	125	309	Negative	Negative
11	SDH	9.2	40	2726	103	308	Negative	Negative
12	SAH	7.7	31	90,000	47	99	Negative	CoNS
13	ICH	6	500	80,000	63	175	Negative	Negative
14	SAH	2.2	37	5000	40	62	Negative	CoNS
15	ICH	7.2	1100	190,000	98	313	Negative	Negative
16	Brain tumor	6.3	317	7000	112	284	Negative	Negative
17	ICH	6.8	500	66,894	27	238	Negative	Negative
18	Brain tumor	18.8	106	8805	114	324	Negative	Negative
19	ICH	6.5	4344	267,556	51	181	Negative	Negative
20	Brain tumor	3.6	104	25,500	37	200	Negative	Negative
21	SAH	6.4	194	75,000	90	291	Negative	Negative
22	**SAH**	**10.6**	**99**	**3428**	**21**	**147**	**GNB**	***E. cloacae***

WORLD NEUROSURGERY 98: 525-531, FEBRUARY 2017

Evaluation of Meropenem Penetration into Cerebrospinal Fluid in Patients with Meningitis After Neurosurgery

Yuyi Zhang[1,2], Jing Zhang[1,3], Yuancheng Chen[1,3], Jicheng Yu[1,3], Guoying Cao[1,3], Xiaojie Wu[1,3], Mingyu Chen[4], Jufang Wu[1,3], Xu Zhao[1,3]

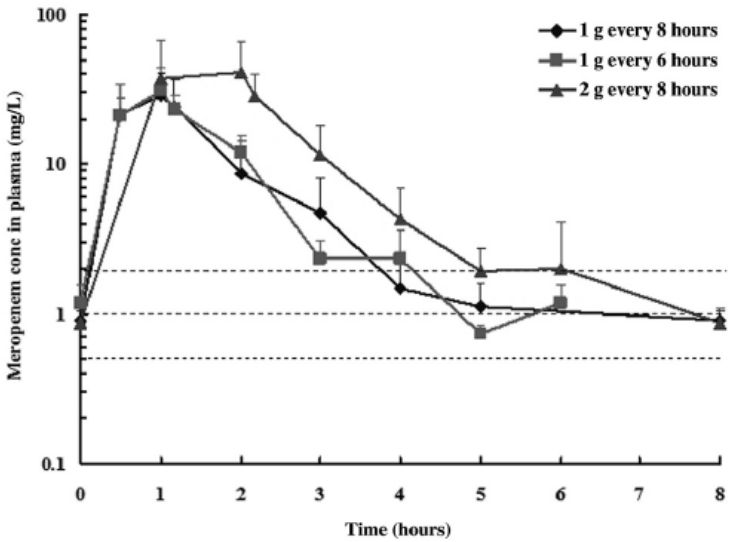


Figure 1. Mean plasma concentration time curve at steady state after intravenous infusion of multiple doses of meropenem (mean ± standard deviation, n — 7–24). The dotted lines from top to bottom indicate 2 mg/L, Clinical and Laboratory Standards Institute breakpoint for *Acinetobacter baumannii;* 1 mg/L, Clinical and Laboratory Standards Institute breakpoint for *Escherichia coli;* and 0.5 mg/L (i.e., limit of quantification), respectively. The data below limit of quantification were not included in this analysis. The value at time point 0 is the value at the last time point. Meropenem is eliminated rapidly from the body. It reaches steady state at the fourth sampling point. The trough concentration of meropenem before the fifth dose is comparable with the concentration immediately before administration of the fourth dose.

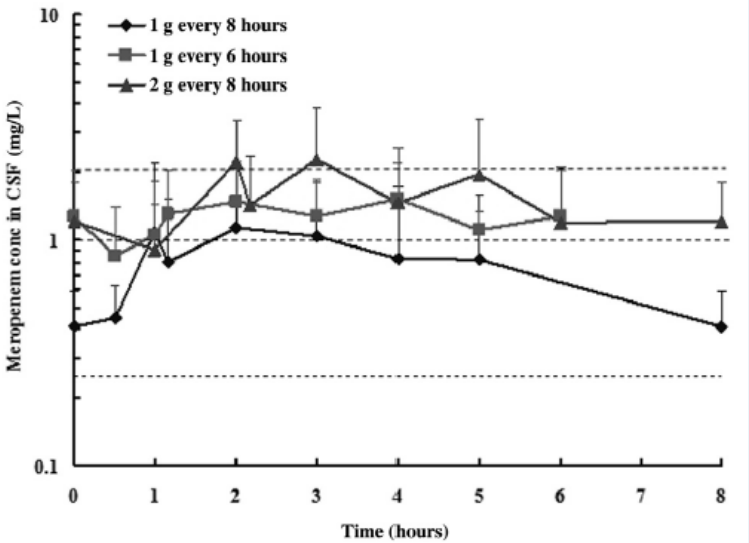


Figure 2. Mean cerebrospinal fluid (CSF) concentration time curve at steady state after intravenous infusion of multiple doses of meropenem (mean ± standard deviation, *n* — 7–24). The dotted lines from top to bottom indicate 2 mg/L, Clinical and Laboratory Standards Institute breakpoint for *Acinetobacter baumannii;* 1 mg/L, Clinical and Laboratory Standards Institute breakpoint for *Escherichia coli;* and 0.5 mg/L (i.e., limit of quantification), respectively. The data below limit of quantification were not included in this analysis. The value at time point 0 is the value at the last time point. Meropenem is eliminated rapidly from the body. It reaches steady state at the fourth sampling point. The trough concentration of meropenem before the fifth dose is comparable with the concentration immediately before administration of the fourth dose.

Evaluation of Meropenem Penetration into Cerebrospinal Fluid in Patients with Meningitis After Neurosurgery

Yuyi Zhang[1,2], Jing Zhang[1,3], Yuancheng Chen[1,3], Jicheng Yu[1,3], Guoying Cao[1,3], Xiaojie Wu[1,3], Mingyu Chen[4], Jufang Wu[1,3], Xu Zhao[1,3]

Table 3. Pharmacokinetic Parameters of Meropenem in the Patients with Meningitis After Multiple Intravenous Infusion

		Plasma			Cerebrospinal Fluid		
Parameter	**Unit**	**1 g Every 8 Hours**	**1 g Every 6 Hours**	**2 g Every 8 Hours**	**1 g Every 8 Hours**	**1 g Every 6 Hours**	**2 g Every 8 Hours**
C_{max}	mg/L	28.9 ± 2.7	31.5 ± 3.4	43.2 ± 5.3	1.2 ± 0.2	1.6 ± 0.2	2.4 ± 0.3
T_{max}	Hours	1.0 ± 0.1	1.0 ± 0.1	1.7 ± 0.5	2.4 ± 1.0	2.5 ± 1.1	2.6 ± 0.8
C_{min}	mg/L	0.3 ± 0.03	0.4 ± 0.06	0.5 ± 0.07	0.3 ± 0.03	0.6 ± 0.1	0.7 ± 0.1
AUC_{0-8}	mg·hours/L	47.9 ± 2.3	49.3 ± 2.5	94.2 ± 8.4	5.4 ± 0.5	6.7 ± 0.4	10.7 ± 0.7
$AUC_{0-\infty}$	mg·hours/L	48.6 ± 2.3	50.2 ± 2.6	95.1 ± 8.4	6.9 ± 0.8	15.5 ± 12.1	16.6 ± 6.6
$T_{1/2}$	Hours	1.4 ± 0.4	1.0 ± 0.2	1.3 ± 0.4	3.3 ± 1.0	5.5 ± 5.3	4.6 ± 4.1
MRT_{0-8}	Hours	1.6 ± 0.04	1.5 ± 0.05	2.0 ± 0.09	3.5 ± 0.1	2.9 ± 0.1	3.8 ± 0.1
CL_t	L/hour	20.6 ± 1.0	20.0 ± 1.0	21.2 ± 1.9	NA	NA	NA
V_d	L	40.5 ± 11.1	27.6 ± 6.3	38.8 ± 12.7	NA	NA	NA
$R_{AUC\ 0-t}$	%	NA	NA	NA	11.3 ± 1.2	13.7 ± 1.2	11.4 ± 1.2
$R_{AUC\ 0-\infty}$	%	NA	NA	NA	14.3 ± 1.7	30.9 ± 24.2	17.6 ± 7.3
$R_{C\ max}$	%	NA	NA	NA	4.1 ± 0.7	5.1 ± 0.8	5.6 ± 1.0

Parameters were obtained using bootstrap method. Results are reported as mean ± standard deviation (n = 200). $R_{AUC\ 0\ t} = AUC_{0\ t}$(CSF)/$AUC_{0\ t}$(plasma) × 100%. $R_{AUC\ 0\ \infty}$ and $R_{C\ max}$ were obtained by a similar method.

C_{max}, maximal concentration; T_{max}, the time when concentration reaches C_{max}; C_{min}, minimal concentration; AUC, area under the curve; $T_{1/2}$, half life; MRT, mean residence time; CL_t, clearance; NA, not available; V_d, distribution volume.

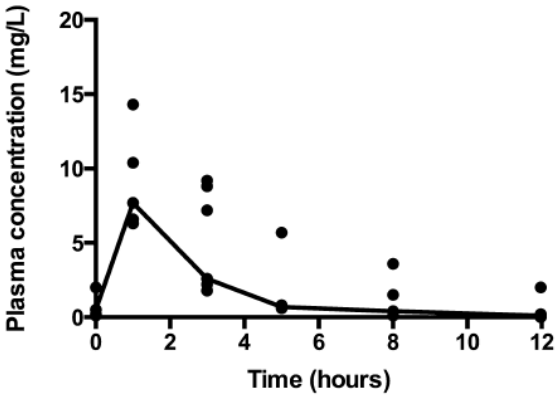
Plasma and cerebrospinal fluid concentrations of linezolid in neurosurgical critically ill patients with proven or suspected central nervous system infections

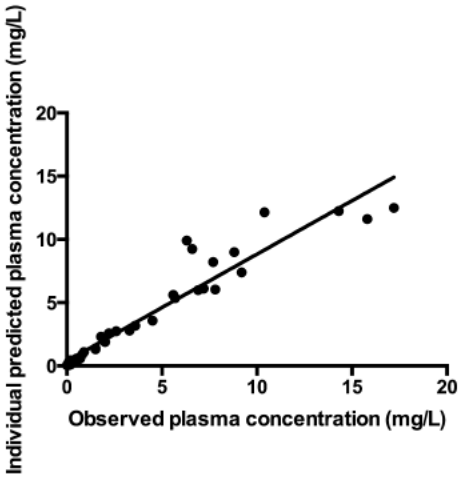
Individual pharmacokinetic results in plasma and cerebrospinal fluid (CSF) and values of the AUC_{0-24h}/MIC of linezolid in plasma and CSF calculated for different MICs.

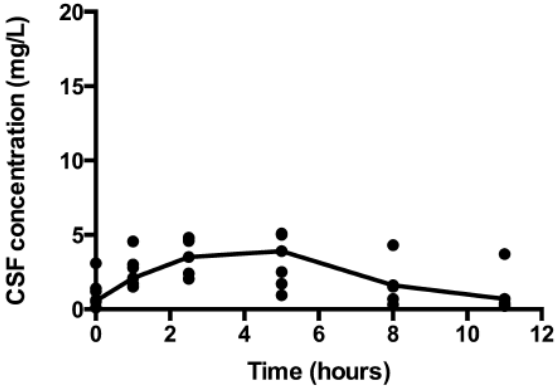
Patient	Plasma AUC_{0-12h} (mg h/L)	CSF AUC_{0-12h} (mg h/L)	Ratio CSF AUC_{0-12h} to plasma AUC_{0-12h}	Plasma AUC_{0-24h}/MIC ratio			CSF AUC_{0-24h}/MIC ratio		
				MIC (mg/L)			MIC (mg/L)		
				1	2	4	1	2	4
1	57.6	21.1	0.37	115.2	57.6	28.8	42.2	21.1	10.6
2	61.5	47.4	0.77	123.0	61.5	30.8	94.8	47.4	23.7
4	18.7	17.0	0.91	37.40	18.7	9.4	34.0	17.0	8.5
5	59.5	28.7	0.48	119.0	59.5	29.8	57.4	28.7	14.4
6	17.1	14.2	0.83	34.2	17.1	8.6	28.4	14.2	7.1
7	47.6	32.0	0.67	85.2	47.6	23.8	64.0	32.0	16.0
8	16.3	20.6	1.26	32.6	16.3	8.2	41.2	20.6	10.3
Median	47.6	21.1	0.77	85.2	47.6	23.8	42.2	21.1	10.6
IQR	17.9–58.6	18.8–30.4	0.58–0.87	35.8–117.1	17.9–58.6	9.0–29.3	31.2–60.7	18.8–30.4	9.4–15.2

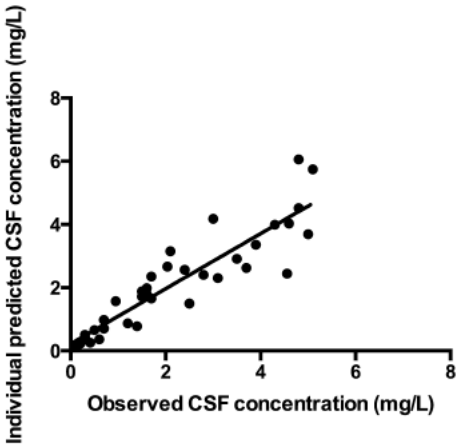
AUC_{0-12h}, area under the drug concentration–time curve from time 0 to 12 h; AUC_{0-24h}, area under the drug concentration–time curve from time 0 to 24 h (calculated as $AUC_{0-12h} \times 2$); MIC, minimum inhibitory concentration; IQR, interquartile range.

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



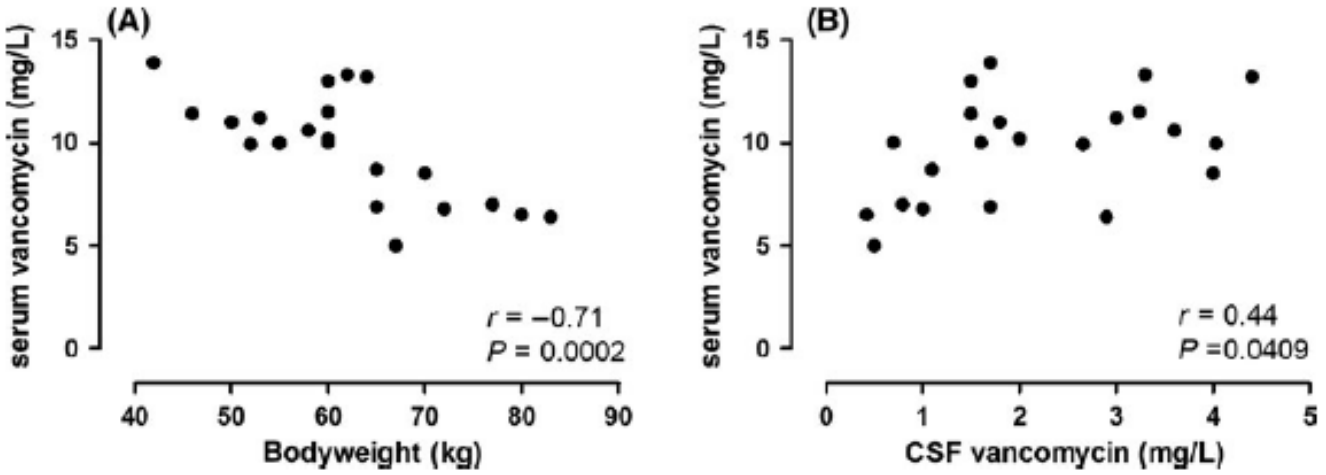




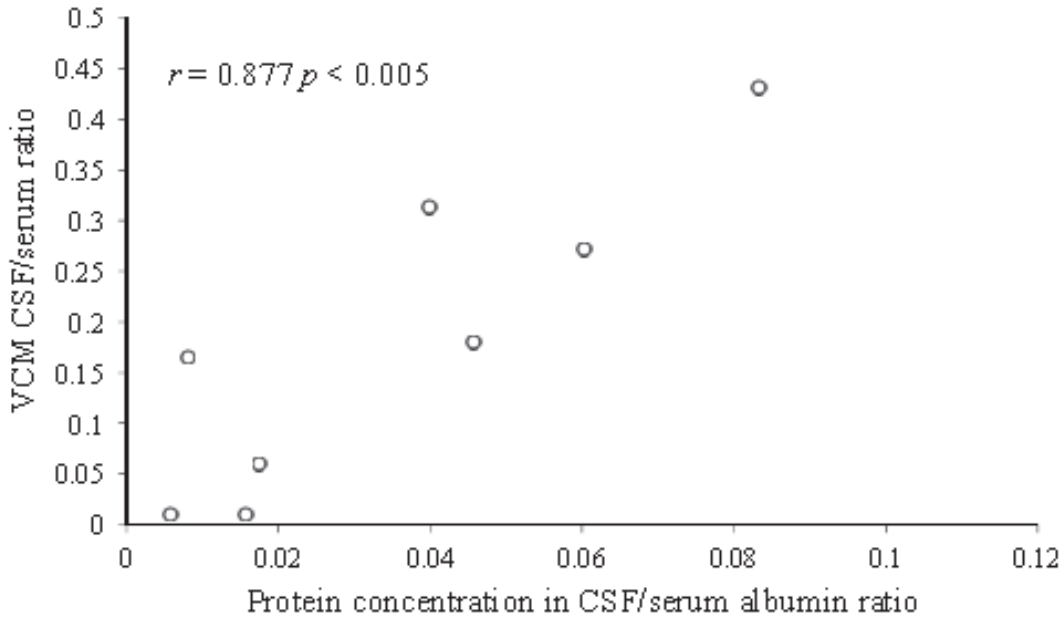


Journal of Clinical Pharmacy and Therapeutics

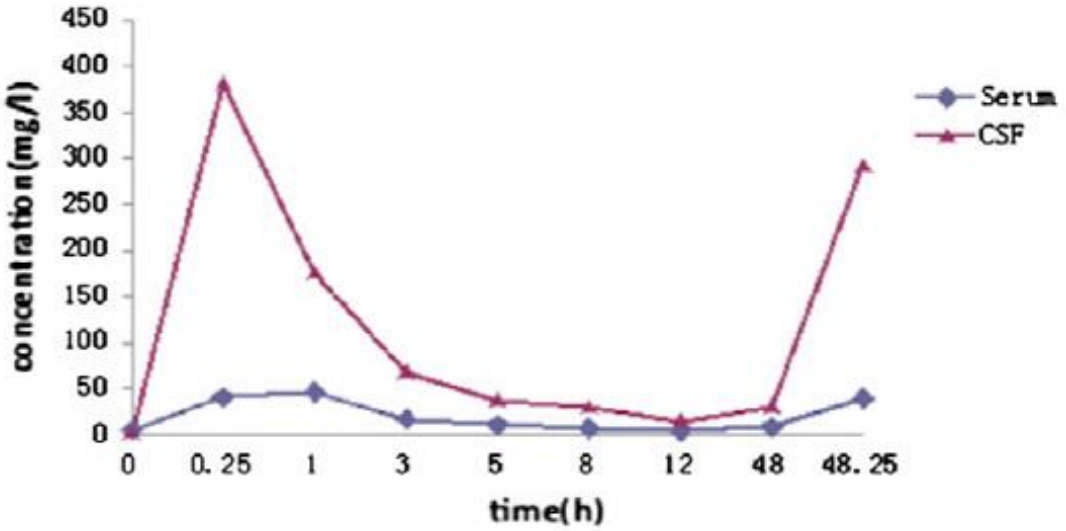
Comparation of vancomycin penetration into cerebrospinal fluid in postoperative intracranial infection and community-acquired meningitis patients



Correlation between vancomycin penetration into cerebrospinal fluid and protein concentration in cerebrospinal fluid/serum albumin ratio☆



The methodology and pharmacokinetics study of intraventricular administration of vancomycin in patients with intracranial infections after craniotomy☆



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A Translational Pharmacokinetic Rat Model of Cerebral Spinal Fluid and Plasma Concentrations of Cefepime

Sean N. Avedissian,[a,b] Gwendolyn Pais,[a,b] Medha D. Joshi,[b,c] Nathaniel J. Rhodes,[a,b] Marc H. Scheetz[a,b,d]

The median CSF/blood percentage of penetration was 19%.
Cefepime transit to the CSF is rapid and predictable in the rat model.
This model will be highly useful for understanding the therapeutic window for cefepime and neurotoxicity.

Intraventricular versus intravenous colistin for the treatment of extensively drug resistant *Acinetobacter baumannii* meningitis

European Journal of Neurology 2016, **23:** 68–75

P. De Bonis[a,b,*], G. Lofrese[a,*], G. Scoppettuolo[c], T. Spanu[d], R. Cultrera[e], M. Labonia[f], M. A. Cavallo[b], A. Mangiola[a], C. Anile[a] and A. Pompucci[a]

doi:10.1111/ene.12789

International Journal of Antimicrobial Agents 41 (2013) 499–508

Intraventricular and intrathecal colistin as the last therapeutic resort for the treatment of multidrug-resistant and extensively drug-resistant *Acinetobacter baumannii* ventriculitis and meningitis: a literature review

Ilias Karaiskos, Lambrini Galani, Fotini Baziaka, Helen Giamarellou*

International Journal of Antimicrobial Agents 49 (2017) 389–390

Intrathecal or intraventricular administration of colistin, vancomycin and amikacin for central nervous system infections in neurosurgical patients in an intensive care unit

A.Tsimogianni, P. Alexandropoulos, V. Chantziara, A. Vassi, G. Micha, F. Lagiou, E. Chinou, G.Michaloudis, S. Georgiou

A case report of intraventricular tigecycline therapy for intracranial infection with extremely drug resistant *Acinetobacter baumannii*

Antibiotics susceptibility tests for *Acinetobacter baumannii* in CSF.

Antibiotics	Susceptibility	MIC
Tigecycline	Susceptible	2
Amoxicillin–clavulanic acid	Resistant	>=32
Tobramycin	Resistant	>=16
Ampicillin	Resistant	>=32
Ciprofloxacin	Resistant	>=4
Ceftriaxone	Resistant	>=64
Amikacin	Resistant	>=64
Cefazolin	Resistant	>=64
Cefepime	Resistant	>=64
Cefoxitin	Resistant	>=64
Gentamicin	Resistant	>=16
Imipenem	Resistant	>=16
Levofloxacin	Resistant	>=8
Trimethoprim–sulfamethoxazole	Resistant	>=320
Ceftazidime	Resistant	>=64
Ertapenem	Resistant	>=8

TAKE HOME MESSAGE

- ✓ La prevenzione è sempre la migliore misura da attuare per limitare il rischio infettivo postchirurgico
- ✓ Indagare i possibili quadri di immunosoppressione prima dell'intervento neurochirurgico
- ✓ Conoscere l'epidemiologia locale
- ✓ Prelievi di campioni da sedi differenti e loro differenziazione
- ✓ Giusta interpretazione dei risultati delle indagini di laboratorio secondo il quadro clinico
- ✓ Attuare il miglior trattamento antimicrobico possibile per efficacia
- ✓ I tempi di terapia antimicrobica devono essere ben definiti
- ✓ Consultarsi con gli specialisti infettivologo

Convegno Nazionale

La Gestione Appropriata delle Infezioni in Riabilitazione: indicazioni strategiche

Cona (Fe) 20 Giugno 2019

Aula Congressuale

Nuovo Arcispedale S. Anna, Via A. Moro n. 8

Le problematiche infettivologiche nel paziente SM trattato

GRAZIE