Méningites graves : quoi de neuf ?

B . Charra

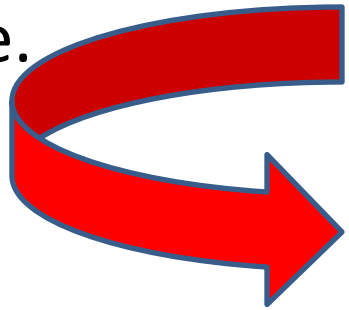
Service de réanimation médicale

CHU Ibn Rochd Casablanca

- Grave : mortalité 20 -30 %.
- Epidémiologie : stable.
- Diagnostic : méningite bactérienne
  # méningite virale
- Antibiothérapie : consensuelle .
- Corticothérapie : discutée ?

Gravité

- Purpura extensif.
- Aggravation progressive du coma .
- Trouble respiratoires ; détresse.
- Troubles neuro-végétatifs.
- Signes d'HTIC.
- Choc septique ou d'une pathologie sous jacente susceptibles de se décompenser.



Réanimation

Collège des enseignants de Neurologie 2002

Gravité

	Pneumococcal meningitis (%)	Meningococcal meningitis (%)
Coma on admission	19	7
Focal neurological deficits	65	33
Seizures	24	5
Cardio respiratory failure	38	18

D.Van de Beek, Nat Clin Pract Neurol 2006 Sep,2(9) : 504-16.

Causes de décès

Mortality rate and cause of death	
Death during hospitalisation	16- 37%
Neurological causes	39 -75%
Brain herniation	13 -75%
Cerebrovascular complications	14%
Systemic causes	24- 51%
Cardiorespiratory failure	21 -25%
Sepsis	19%
Combination of systemic and neurological causes	29 -43%

Weisfelt,Lancet Neurol 2006 Apr 5(4): 332-42

FDR évolution défavorable

Aubertin	N=80	Thrombopénie <100 PH sup à 7.47 Ventilation mécanique	32.7(3.2-332.5) 31.1(3.4-319.7) 48.8(2.6-901.5)
Van de Beek	N=696	Age avancé , otite ou sinusite ,GCS bas, tachycardie, HC+,VS augmentée, Thrombopénie ,peu d'élément dans LCR	

Auburtin M. Am J Respir Crit Care Med 2002;165:713-717

D.Van de Beek, Nat Clin Pract Neurol 2006 Sep,2(9) : 504-16.

Epidémiologie

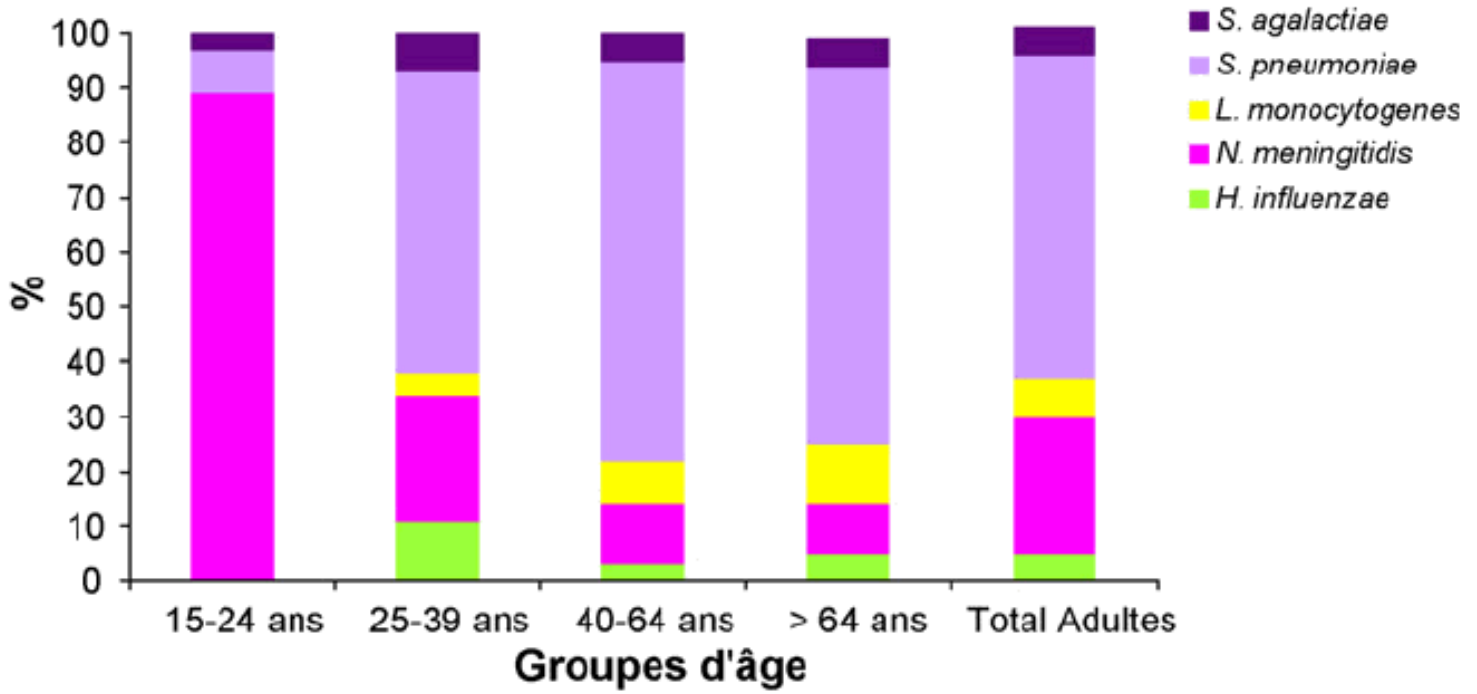
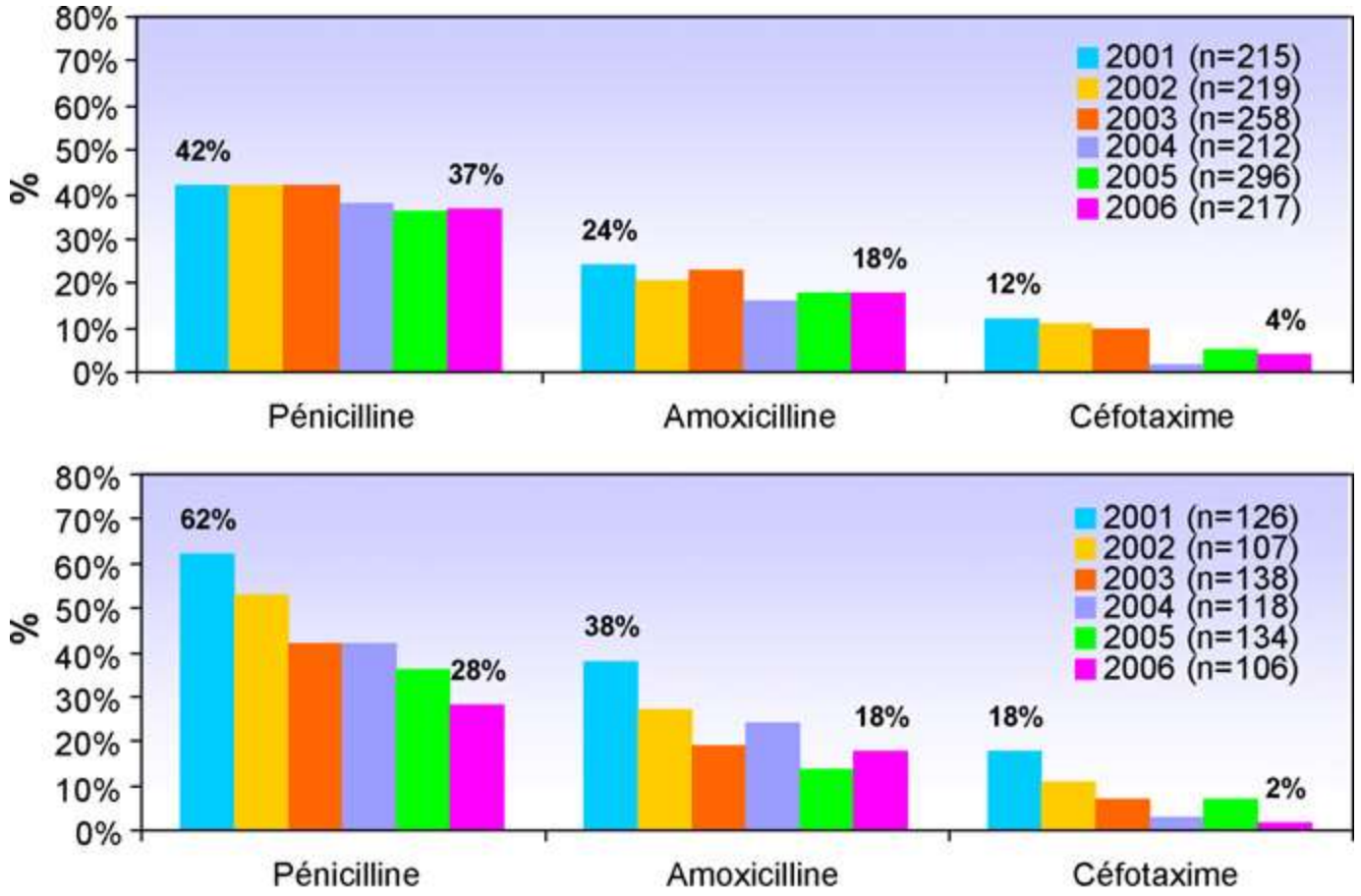


Fig. 1. Fréquence relative des bactéries à l'origine de méningites chez l'adulte en France métropolitaine en 2006 (D'après les données du réseau Epibac, InVS [4]).

Relative frequency of bacteria responsible for adult meningitis in metropolitan France in 2006 (according to Epibac network, InVS data [4]).

E. Varon. Méd Mal Inf . 39 (2009) 432–444



Adulte

Enfant

Méningites : évolution des souches de *S. pneumoniae de sensibilité diminuée* (pourcentage de I + R) aux bêta-lactamines chez l'adulte (en haut) et chez l'enfant (en bas) de 2001 à 2006 [17].

E. Varon. Méd Mal Inf . 39 (2009) 432–444

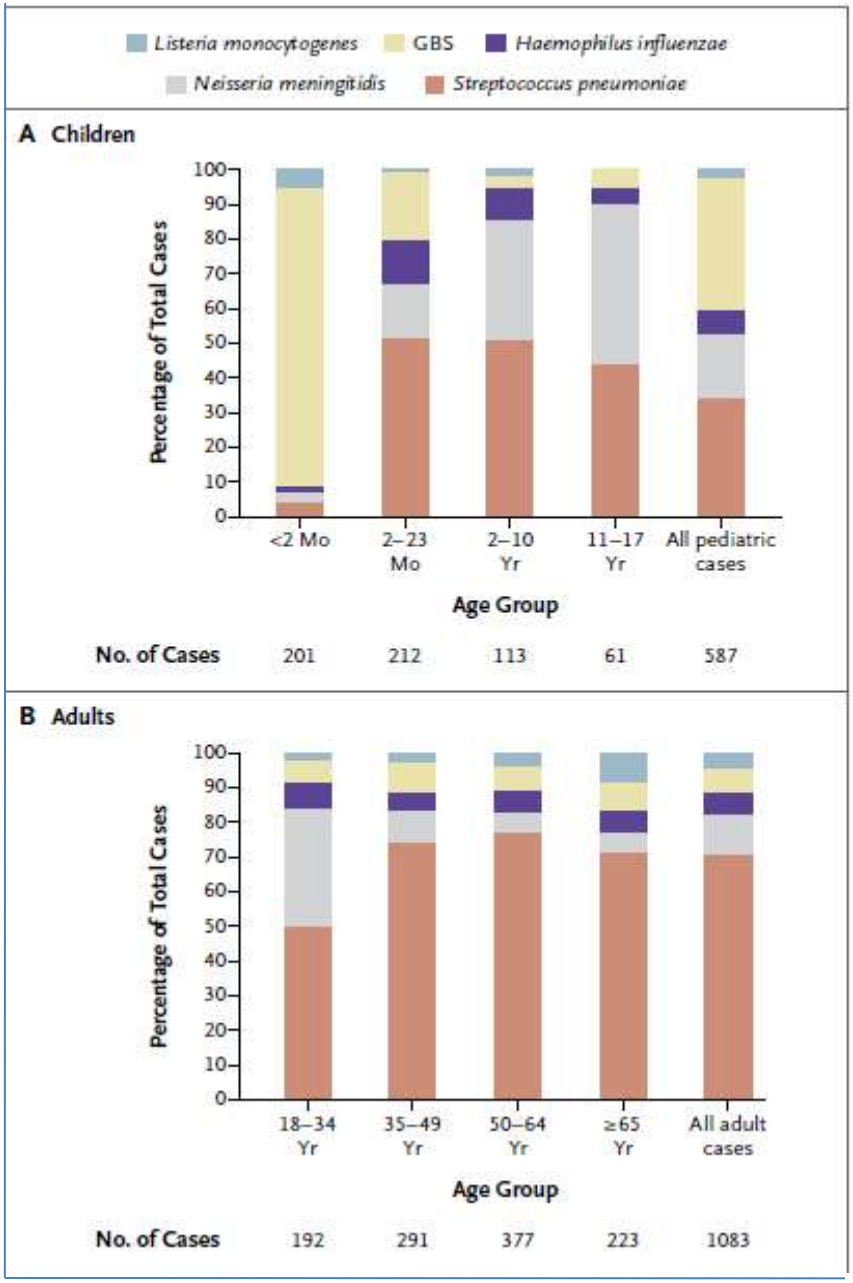
Table 1. Incidence of Bacterial Meningitis in the United States, 1998–2007, Stratified According to Age Group, Race, and Pathogen.*

Characteristic	1998–1999	2000–2001	2002–2003	2004–2005	2006–2007	Percent Change, 2006–2007 vs. 1998–1999 (95% CI)
	no. of cases per 100,000 population (95% CI)					
Age group						
<2 Mo	73.46 (56.45 to 94.35)	88.28 (69.69 to 109.95)	56.59 (42.13 to 74.45)	77.27 (60.58 to 96.90)	80.69 (63.53 to 101.42)	10 (1 to 20)
2–23 Mo	14.20 (11.85 to 16.91)	11.49 (9.45 to 13.92)	6.56 (5.06 to 8.38)	6.95 (5.47 to 8.89)	6.91 (5.30 to 8.77)	–51 (–55 to –48)
2–10 Yr	1.55 (1.20 to 1.96)	1.48 (1.16 to 1.88)	0.94 (0.68 to 1.27)	1.07 (0.79 to 1.43)	0.56 (0.36 to 0.82)	–64 (–68 to –59)
11–17 Yr	1.03 (0.71 to 1.43)	0.87 (0.60 to 1.22)	0.62 (0.39 to 0.94)	0.56 (0.34 to 0.86)	0.43 (0.25 to 0.71)	–58 (–64 to –51)
18–34 Yr	0.99 (0.79 to 1.22)	0.86 (0.68 to 1.07)	0.70 (0.54 to 0.89)	0.76 (0.59 to 0.97)	0.66 (0.50 to 0.86)	–33 (–38 to –27)
35–49 Yr	1.23 (1.01 to 1.48)	1.30 (1.08 to 1.55)	1.08 (0.89 to 1.31)	0.91 (0.74 to 1.13)	0.95 (0.76 to 1.16)	–23 (–29 to –17)
50–64 Yr	2.15 (1.75 to 2.57)	1.83 (1.49 to 2.21)	2.09 (1.75 to 2.48)	1.79 (1.49 to 2.14)	1.73 (1.44 to 2.06)	–19 (–25 to –14)
≥65 Yr	2.64 (2.13 to 3.16)	2.20 (1.76 to 2.72)	2.21 (1.78 to 2.71)	1.51 (1.16 to 1.94)	1.92 (1.53 to 2.38)	–27 (–32 to –22)
All ages	2.00 (1.85 to 2.15)	1.82 (1.69 to 1.97)	1.49 (1.38 to 1.62)	1.41 (1.30 to 1.54)	1.38 (1.27 to 1.50)	–31 (–33 to –29)
Race†						
White	1.71 (1.55 to 1.87)	1.58 (1.43 to 1.73)	1.28 (1.15 to 1.42)	1.27 (1.14 to 1.41)	1.28 (1.14 to 1.40)	–25 (–28 to –23)
Black	4.07 (3.57 to 4.62)	3.85 (3.40 to 4.35)	3.12 (2.72 to 3.57)	2.62 (2.28 to 3.03)	2.41 (2.13 to 2.84)	–41 (–44 to –37)
Other	1.55 (0.98 to 2.23)	0.68 (0.37 to 1.18)	0.76 (0.44 to 1.25)	0.67 (0.39 to 1.14)	0.46 (0.25 to 0.86)	–70 (–75 to –64)
Pathogen						
Streptococcus pneumoniae	1.09 (0.98 to 1.20)	1.03 (0.93 to 1.13)	0.93 (0.83 to 1.03)	0.76 (0.68 to 0.85)	0.81 (0.72 to 0.90)	–26 (–29 to –23)
Neisseria meningitidis	0.44 (0.37 to 0.51)	0.37 (0.31 to 0.44)	0.23 (0.19 to 0.29)	0.22 (0.17 to 0.27)	0.19 (0.14 to 0.24)	–58 (–61 to –54)
Group B streptococcus	0.24 (0.20 to 0.30)	0.30 (0.25 to 0.36)	0.21 (0.17 to 0.26)	0.27 (0.22 to 0.32)	0.25 (0.21 to 0.31)	4 (–3 to 12)
Haemophilus influenzae	0.12 (0.09 to 0.17)	0.10 (0.07 to 0.14)	0.10 (0.07 to 0.13)	0.10 (0.07 to 0.14)	0.08 (0.05 to 0.11)	–35 (–42 to –27)
Listeria monocytogenes	0.10 (0.08 to 0.16)	0.03 (0.01 to 0.05)	0.03 (0.01 to 0.05)	0.05 (0.04 to 0.10)	0.05 (0.03 to 0.08)	–46 (–53 to –39)

* CI denotes confidence interval.

† Race was obtained from medical records. "Other" includes American Indian or Alaska Native, Asian or Pacific Islander, or other race. Within a site and age group, cases with missing data for race were assumed to have a distribution of race similar to that among cases with available data.

Michael C et all . NEJM 2012.

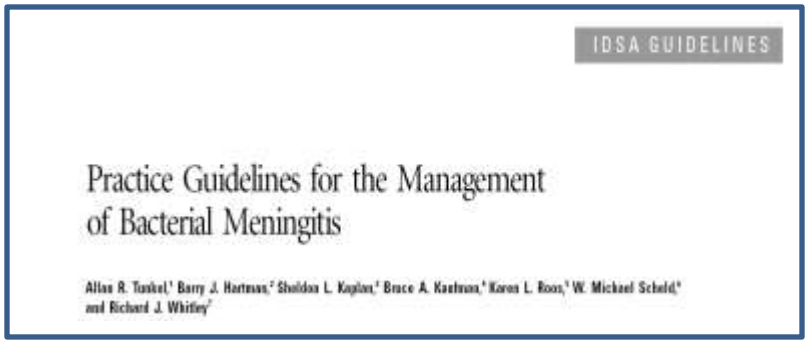


Michael C et all . NEJM 2012.

Table 3. Characteristics of Patients with Bacterial Meningitis Identified by the Emerging Infections Programs Network, 2003–2007.

Characteristic	*Neisseria meningitidis*	*Haemophilus influenzae*	Group B Streptococcus	*Listeria monocytogenes*	*Streptococcus pneumoniae*	All
			percent of patients			
Pediatric patients	**N=107**	**N=42**	**N=222**	**N=13**	**N=203**	**N=587**
Male sex	62.6	61.9	49.5	46.2	54.7	54.5
Race*						
White	69.2	71.4	47.3	30.8	59.1	56.7
Black	17.8	16.7	42.3	38.5	25.6	30.2
Other	2.8	9.5	3.2	0.0	3.0	3.4
Underlying medical condition†						
Immunocompromising condition	1.3	6.5	0.0		6.9	3.0
Chronic condition	8.8	9.7	3.6		9.1	6.7
Prematurity only	1.3	3.2	11.9		2.3	5.9
None	88.8	80.6	84.5		81.7	84.4
Case fatality rate						
All pediatric patients	3.8	0	7.3	7.7	9.4	6.9
Pediatric patients <2 yr	2.5	0	7.5	0	7.7	6.3
Adult patients	**N=125**	**N=69**	**N=80**	**N=44**	**N=765**	**N=1083**
Male sex	48.8	46.4	40.0	56.8	49.9	49.1
Race*						
White	52.8	62.3	45.0	70.5	54.5	54.8
Black	20.8	24.6	33.8	11.4	29.8	28.0
Other	4.8	2.9	2.5	6.8	2.0	2.6
Underlying medical condition or risk group†						
Immunocompromising condition	11.3	15.0	22.7		25.0	22.5
Chronic condition	18.6	36.7	36.4		35.1	32.7
Smoking	14.4	8.3	7.6		8.4	8.7
Age ≥65 yr only	2.1	8.3	4.5		7.0	7.4
None	53.6	31.7	28.8		24.5	28.7
Case fatality rate						
All adult patients	10.4	7.2	20.8	20.5	17.5	16.4
Adult patients ≥50 yr	9.1	5.1	30.0	24.2	18.3	18.0

Michael C et all . NEJM 2012.



Clin. Infect. Dis 2004;39:1267-84

Pneumocoque péni I	**: 12.7% → 17.9%**
Pneumocoque péni R	**: 21.5% → 14.6%**
Pneumocoque C3G I	**: 10.3%**
Pneumocoque C3G R	**: 6%**

Richter CID 2009

Diagnostic

Scanner ou PL?

➢ Facteurs associés à un retard à l'antibiothérapie :

- Absence d'antibiothérapie avant transfert.
- Séquence scanner-PL-ATB.
- Absence de la triade clinique classique.

Proulx, QJM.2005Apr;98(4) :291-8

Scanner ou PL ?

Table 2. Recommended criteria for adult patients with suspected bacterial meningitis who should undergo CT prior to lumbar puncture (B-II).

Criterion	Comment
Immunocompromised state	HIV infection or AIDS, receiving immunosuppressive therapy, or after transplantation
History of CNS disease	Mass lesion, stroke, or focal infection
New onset seizure	Within 1 week of presentation; some authorities would not perform a lumbar puncture on patients with prolonged seizures or would delay lumbar puncture for 30 min in patients with short, convulsive seizures
Papilledema	Presence of venous pulsations suggests absence of increased intracranial pressure
Abnormal level of consciousness	...
Focal neurologic deficit	Including dilated nonreactive pupil, abnormalities of ocular motility, abnormal visual fields, gaze palsy, arm or leg drift

Indications d'une TDM cérébrale avant la PL

1. Signes de localisation neurologiques
2. Troubles de vigilance mesures par un score de Glasgow inferieur ou égal à 11.
3. Crises épileptiques récentes ou en cours, focales ou généralisées.
4. Signes d'engagement (mydriase unilatérale, hoquet, instabilité hémodynamique, trouble ventilatoire, mouvements d'enroulement).

L'examen du fond d'oeil avant réalisation de la ponction lombaire n'est pas indispensable.

Conférence de consensus SPLF 2008

En pratique en réanimation

- Tous les patients admis en réanimation ont une indication à réaliser un scanner avant la PL
- Donc la séquence proposée est

- 2 Hémocultures
- Dexamethasone ? ? ?
- Antibiothérapie
- Scanner
- PL

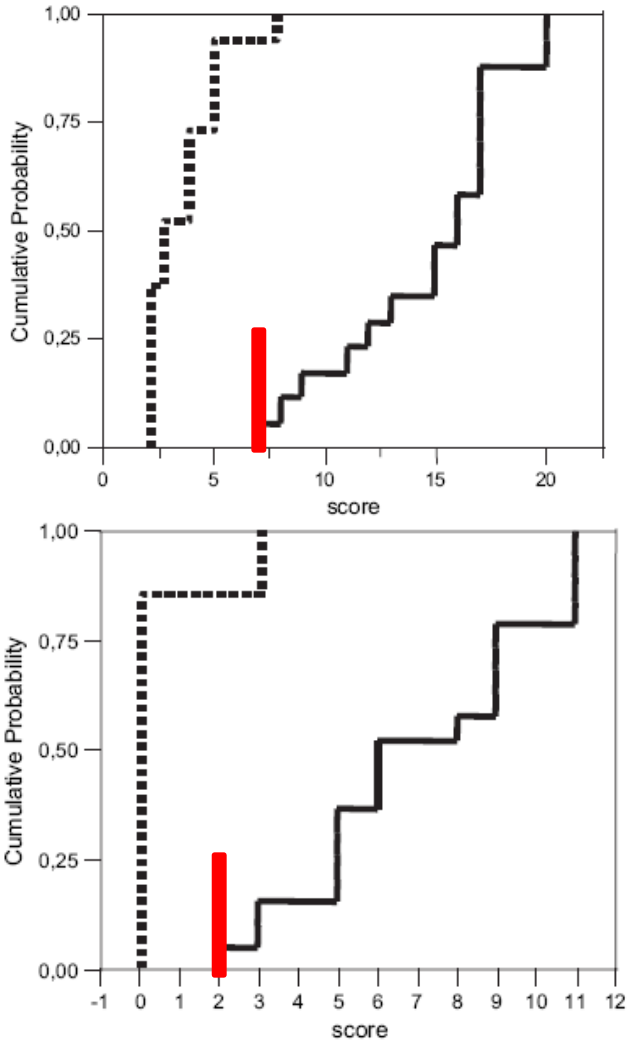
The "Dijon" score

Categorical analysis regression tree (CART) method

Parameter	Value of category			
	Adult		Children	
	Breakpoint	Value	Breakpoint	Value
Leucocytosis (cells/ml)	>15 000	3	–	–
CSF leucocytes count (c/ml)	>1700	4	≥1800	2
	<1700	2		
	≤250	1		
CSF PMNs (%)	>90	4		
	>80	2	>80	3
	>25	1		
CSF protein level (g/l)	>2.3	5	>1.2	3
	>0.8	2		
CSF/Blood glucose ratio	≤0.35	4	≤0.3	3

ADULTS

CHILDREN



VM

BM

Discriminant cutoff values

- Adults 6
- Children 2

Chavanet P, J Infect 2007; 54: 328-336

The "Dijon" score

Categorical analysis regression tree (CART) method

Des scores/modèles performants d'aide au diagnostic différentiel ont été validés et peuvent être proposés pour l'utilisation clinique quotidienne, notamment dans les SAU, aussi bien d'adultes que d'enfants, pour identifier les patients ayant une très faible probabilité d'avoir méningite bactérienne, chez lesquels l'antibiothérapie peut ainsi être évitée

The "Dijon" score

Categorical analysis regression tree (CART) method

- Ces modèles fournissent:

  une probabilité de méningite bactérienne assortie d'une bonne valeur prédictive négative

- Leur utilisation ne doit pas se substituer au raisonnement diagnostique et à l'analyse rigoureuse de chaque cas

- Il faut les considérer un examen complémentaire performant, un élément d'aide au diagnostic

La place de PCT

Tableau 1
Indices de performance de la PCT sérique dans le diagnostic des méningites bactériennes – synthèse des principales études.
Performance index for serum PCT used to diagnose bacterial meningitis– summarized data from the major studies.

	Étude Année (réf)	Effectifs	Valeurs PCT (ng/ml) MB[a]		Valeurs PCT (ng/ml) MA[a]		Valeur seuil proposée[b]	VPN (%)	VPP (%)	ASC ROC
Enfants	Gendrel et al.	23 MB	Moyenne	60,9	Moyenne	0,32	2	100	100	ND[d]
	1998 [8]	51 MA	Extrêmes	4,8–335	Extrêmes	0–1,7				
	Prat et al.	25 MB	Médiane	12,1	Médiane	0,55	2	100	100	0,87
	2004 [29]	18 MA	5–95 percentiles	2,4–207	5–95 percentiles	0,1–1,7				
	Dubos et al.	18 MB	Moyenne	20,5	Moyenne	0,3	0,5	ND	ND	0,95
	2006 [30]	134 MA	Extrêmes	0,2–107	Extrêmes	0,1–4,4				
Adultes	Viallon et al.	32 MB	Moyenne	10,03	Moyenne	0,08	0,93	100	100	1
	2000 [6]	90 MA	Extrêmes	0,93–104	Extrêmes	0,07–0,15				
	Jereb et al.	20 MB	Médiane	6,45	Médiane	0,27	0,5	93	100	ND
	2001 [13]	25 MA[c]	Extrêmes	0,25–44	Extrêmes	0,05–0,44				
	Ray et al.	8 MB	Médiane	3,75	Médiane	0,07	2,13	99	100	0,98
	2007 [10]	55 MA	Extrêmes	0,1–6,16	Extrêmes	0–0,08				

[a] MB = méningite bactérienne, MA = méningite aseptique (méningite virale ou non bactérienne).
[b] Valeur seuil déterminée à l'aide de la courbe ROC ou de la méthode de Youden.
[c] Toutes les méningites sont dues au virus TBE.
[d] Non déterminée.

Van de Beek, Med mal inf, 2009

Serum-PCT and CSF-lactate, an update

	Bacterial meningitis n = 35	Viral meningitis n = 218	p
Glucose level (mmo l/ L)	8,4 ± 2,7	6,1 ± 1,8	0,03
(min – max)	(4,9-14,6)	(4-18)	
Lactate (mmol / L)	3 ± 1,8	1,8 ± 1,7	0,0001
(min – max)	(1-8)	(1-7)	
Procalcitonin (ng / mL)	17 ± 45	0,09 ± 0,03	0,0001
(min – max)	(0,2-257)	(0,07-0,1)	
C-reactiv protein (mg / L)	159 ± 148	42 ± 39	0,0001
(min – max)	(19-660)	(3-152)	
CSFparameters			
leucocyte count / mm^3	1515 ± 2000	257 ± 520	0,0001
(min – max)	(25-10320)	(23-6500)	
Neutrophil count / mm^3	1003 ± 2000	75 ± 160	0,0001
(min – max)	(22-10000)	(15-1188)	
Glucose level (mmol / L)	2,5 ± 1,5	3,4 ± 1	0,0001
(min – max)	(0,1-5)	(2,1-14)	
CSF / serum glucose ratio	0,24 ± 0,3	0,51 ± 0,15	0,01
(min – max)	(0,1-0,5)	(0,3-1,8)	
Lactate (mmol / L)	9 ± 5	2,6 ± 1,6	0,0001
(min – max)	(3,2-25)	(0,5-3,7)	
CSF / serum lactate ratio	3,7 ± 2,7	1,5 ± 1,4	0,0001
(min – max)	(1,5-8,4)	(1-1,9)	
Protein level (g / L)	4,9 ± 4,6	1 ± 0,6	0,0001
(min – max)	0,5-24	0,3-4	

Viallon A., Crit Care Med, 2011.

Serum-PCT and CSF-lactate, an update

	CSF parameters				Serum parameters	
	Neutrophil /mm^3	Protéïn g/L	Glucose mmol/l	Lactate mmol/l	PCT ng/mL	CRP mg/L
AUC	0,86	0,93	0,69	0,96	0,99	0,92
[IC 95%]	[0,86-0,94]	[0,92-0,98]	[0,69-0,76]	[0,95-1]	[0,99-1]	0,92-0,98]
Optimal cut-point	118	1,88	2,2	3,8	0,28	37
Sensitivity	0,80	0,89	0,97	0,94	0,97	0,86
Specificity	0,85	0,93	0,49	0,97	1	0,84
Positive predictive Value	0,47	0,67	0,92	0,82	0,97	0,46
Négative predictive Value	0,96	0,98	0,71	0,99	1	0,97
Global value	0,84	0,92	0,9	0,96	0,99	0,84

Viallon A., Crit Care Med, 2011.

PCT/Lactate

- la PCT sérique est un marqueur performant pour discriminer entre MB et MV
- mais peut être pris en défaut dans les 2 sens dans des cas individuels,
- la mesure du lactate dans le LCR
- bon prédicteur de MB si lactate LCR > 3,5 mmol/l
- MB exclue si lactate LCR < 3 mmol/l

ginal Article
ical Microbiology

Lab Med 2012;32:44-49
//dx.doi.org/10.3343/alm.2012.32.1.44

2234-3806 eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

luation of the Seeplex® Meningitis ACE Detection for the Detection of 12 Common Bacterial and al Pathogens of Acute Meningitis

n Shin, M.D.[1,2], Kye Chul Kwon, M.D.[1], Jong Woo Park, M.D.[1], Ji Myung Kim, M.D.[1], So Young Shin, M.D.[3], n Hoe Koo, M.D.[1]

ent of Laboratory Medicine[1], College of Medicine, Chungnam National University, Daejeon; Department of Laboratory Medicine[2], Asan Medical Center, y of Ulsan College of Medicine, Seoul; Department of Laboratory Medicine[3], College of Medicine, The Catholic University of Korea, Daejeon, Korea

Background: Bacterial meningitis is an infectious disease with high rates of mortality and high frequency of severe sequelae. Early identification of causative bacterial and viral pathogens is important for prompt and proper treatment of meningitis and for prevention of life-threatening clinical outcomes. In the present study, we evaluated the value of the Seeplex Meningitis ACE Detection kit (Seegene Inc., Korea), a newly developed multiplex PCR kit employing dual priming oligonucleotide methods, for diagnosing acute meningitis.

Methods: Analytical sensitivity of the kit was studied using reference strains for each pathogen targeted by the kit, while it's analytical specificity was studied using the human genome DNA and 58 clinically well-identified reference strains. For clinical validation experiment, we used 27 control cerebrospinal fluid (CSF) samples and 78 clinical CSF samples collected from patients at the time of diagnosis of acute meningitis.

Results: The lower detection limits ranged from 10^1 copies/μL to 5×10^1 copies/μL for the 12 viral and bacterial pathogens targeted. No cross-reaction was observed. In the validation study, high detection rate of 56.4% was obtained. None of the control samples tested positive, i.e., false-positive results were absent.

Conclusions: The Seeplex Meningitis ACE Detection kit showed high sensitivity, specificity, and detection rate for the identification of pathogens in clinical CSF samples. This kit may be useful for rapid identification of important acute meningitis-causing pathogens.

Antibiothérapie

Antibiothérapie

Référence	[10]	[11]	[12]	[13]	[14,15]
Société savante – Pays	Spilf – France	Recommandations nationales – Pays-Bas	États-Unis	Consensus British Infection society	Algorithme British Infection society
Année	1996	1997	1997	1999	2003
Recommandations	*Examen direct négatif selon orientation étiologique et/ou en présence de signe de gravité* : Suspicion de *S. pneumoniae* : C3G de préférence Suspicion de PSDP et/ou signe de gravité : C3G + vancomycine Suspicion de *Listeria* : amoxicilline en association avec gentamycine ou cotrimoxazole Suspicion de *N. meningitidis* : amoxicilline ou C3G Absence d'orientation et signes de gravité : amoxicilline et C3G	*Âge 16–60 ans* : pénicilline *Âge > 60 ans* : amoxicilline + C3G *Âge > 16 ans et facteur de risque (alcoolisme, altération du statut immunitaire, traumatisme crânien, fuite de LCR)* : amoxicilline + C3G *Neurochirurgie récente et âge > 16 ans* : vancomycine + C3G	*18–50 ans* : C3G (*S. pneumoniae*, *N. meningitis*) *50 ans* : ampicilline + C3G (*S. pneumoniae*, *L. monocytogenes*, BGN) *Déficit immunitaire cellulaire* : ampicilline + ceftazidime (*L. monocytogenes* ou BGN) *Traumatisme crânien, neurochirurgie ou fuite LCR* : vancomycine + ceftazidime (Staphylocoque, bacille Gram négatif, *S. pneumoniae*)	*Présence d'un rash méningococcique typique* : benzylpénicilline ou ampicilline *Absence de rash typique et âge 18–50 ans* : C3G *Nécessité de différer la PL, et ce, en absence de rash typique ou provenance de zone de prévalence élevée du PSDP* : C3G + vancomycine ou rifampicine *Si diplocoque Gram négatif* : benzylpénicilline ou ampicilline *Si diplocoque Gram positif* : C3G ± vancomycine (si suspicion PSDP) ou rifampicine *Si BGN* : ampicilline + gentamycine	*C3G de première intention* + ampicilline chez sujets âgés avec suspicion de *Listeria* + vancomycine ± rifampicine si suspicion PSDP

Van de Beek, Med mal inf, 2009

Antibiothérapie

Table 4. Recommendations for empirical antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition (A-III).

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
Age		
<1 month	*Streptococcus agalactiae, Escherichia coli, Listeria monocytogenes, Klebsiella* species	Ampicillin plus cefotaxime or ampicillin plus an aminoglycoside
1–23 months	*Streptococcus pneumoniae, Neisseria meningitidis, S. agalactiae, Haemophilus influenzae, E. coli*	Vancomycin plus a third-generation cephalosporin[a,b]
2–50 years	*N . meningitidis, S. pneumoniae*	Vancomycin plus a third-generation cephalosporin[a,b]
>50 years	*S. pneumoniae, N. meningitidis, L. monocytogenes,* aerobic gram-negative bacilli	Vancomycin plus ampicillin plus a third-generation cephalosporin[a,b]
Head trauma		
Basilar skull fracture	*S. pneumoniae, H. influenzae,* group A β-hemolytic streptococci	Vancomycin plus a third-generation cephalosporin[a]
Penetrating trauma	*Staphylococcus aureus,* coagulase-negative staphylococci (especially *Staphylococcus epidermidis),* aerobic gram-negative bacilli (including *Pseudomonas aeruginosa)*	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
Postneurosurgery	Aerobic gram-negative bacilli (including *P. aeruginosa), S . aureus,* coagulase-negative staphylococci (especially *S. epidermidis)*	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
CSF shunt	Coagulase-negative staphylococci (especially *S. epidermidis), S. aureus,* aerobic gram-negative bacilli (including *P. aeruginosa), Propionibacterium acnes*	Vancomycin plus cefepime,[c] vancomycin plus ceftazidime,[c] or vancomycin plus meropenem[c]

[a] Ceftriaxone or cefotaxime.
[b] Some experts would add rifampin if dexamethasone is also given.
[c] In infants and children, vancomycin alone is reasonable unless Gram stains reveal the presence of gram-negative bacilli.

Clin. Infect. Dis 2004 .

Antibiothérapie

Microorganism, susceptibility	Standard therapy	Alternative therapies
Streptococcus pneumoniae		
Penicillin MIC		
<0.1 μg/mL	Penicillin G or ampicillin	Third-generation cephalosporin,[a] chloramphenicol
0.1–1.0 μg/mL[b]	Third-generation cephalosporin[a]	Cefepime (B-II), meropenem (B-II)
≥2.0 μg/mL	Vancomycin plus a third-generation cephalosporin[a,c]	Fluoroquinolone[d] (B-II)
Cefotaxime or ceftriaxone MIC ≥1.0 μg/mL	Vancomycin plus a third-generation cephalosporin[a,c]	Fluoroquinolone[d] (B-II)
Neisseria meningitidis		
Penicillin MIC		
<0.1 μg/mL	Penicillin G or ampicillin	Third-generation cephalosporin,[a] chloramphenicol
0.1–1.0 μg/mL	Third-generation cephalosporin[a]	Chloramphenicol, fluoroquinolone, meropenem
Listeria monocytogenes	Ampicillin or penicillin G[e]	Trimethoprim-sulfamethoxazole, meropenem (B-III)
Streptococcus agalactiae	Ampicillin or penicillin G[e]	Third-generation cephalosporin[a] (B-III)
Escherichia coli and other Enterobacteriaceae[g]	Third-generation cephalosporin (A-II)	Aztreonam, fluoroquinolone, meropenem, trimethoprim-sulfamethoxazole, ampicillin
Pseudomonas aeruginosa[g]	Cefepime[e] or ceftazidime[e] (A-II)	Aztreonam,[e] ciprofloxacin,[e] meropenem[e]
Haemophilus influenzae		
β-Lactamase negative	Ampicillin	Third-generation cephalosporin,[a] cefepime, chloramphenicol, fluoroquinolone
β-Lactamase positive	Third-generation cephalosporin (A-I)	Cefepime (A-I), chloramphenicol, fluoroquinolone
Staphylococcus aureus		
Methicillin susceptible	Nafcillin or oxacillin	Vancomycin, meropenem (B-III)
Methicillin resistant	Vancomycin[f]	Trimethoprim-sulfamethoxazole, linezolid (B-III)
Staphylococcus epidermidis	Vancomycin[f]	Linezolid (B-III)
Enterococcus species		
Ampicillin susceptible	Ampicillin plus gentamicin	…
Ampicillin resistant	Vancomycin plus gentamicin	…
Ampicillin and vancomycin resistant	Linezolid (B-III)	…

Clin. Infect. Dis 2004 .

Antibiothérapie

Table 3. Recommendations for antimicrobial therapy in adult patients with presumptive pathogen identification by positive Gram stain.

Microorganism	Recommended therapy	Alternative therapies
Streptococcus pneumoniae	Vancomycin plus a third-generation cephalosporin[a,b]	Meropenem (C-III), fluoroquinolone[c] (B-II)
Neisseria meningitidis	Third-generation cephalosporin[a]	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam
Listeria monocytogenes	Ampicillin[d] or penicillin G[d]	Trimethoprim-sulfamethoxazole, meropenem (B-III)
Streptococcus agalactiae	Ampicillin[d] or penicillin G[d]	Third-generation cephalosporin[a] (B-III)
Haemophilus influenzae	Third-generation cephalosporin[a] (A-I)	Chloramphenicol, cefepime (A-I), meropenem (A-I), fluoroquinolone
Escherichia coli	Third-generation cephalosporin[a] (A-II)	Cefepime, meropenem, aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole

NOTE. All recommendations are A-III, unless otherwise indicated. In children, ampicillin is added to the standard therapeutic regimen of cefotaxime or ceftriaxone plus vancomycin when *L. monocytogenes* is considered and to an aminoglycoside if a gram-negative enteric pathogen is of concern.

[a] Ceftriaxone or cefotaxime.

[b] Some experts would add rifampin if dexamethasone is also given (B-III).

[c] Gatifloxaxin or moxifloxacin.

[d] Addition of an aminoglycoside should be considered.

Clin. Infect. Dis 2004 .

Antibiothérapie

Table 8. Duration of antimicrobial therapy for bacterial meningitis based on isolated pathogen (A-III).

Microorganism	Duration of therapy, days
Neisseria meningitidis	7
Haemophilus influenzae	7
Streptococcus pneumoniae	10–14
Streptococcus agalactiae	14–21
Aerobic gram-negative bacilli[a]	21
Listeria monocytogenes	≥21

Clin. Infect. Dis 2004 .

17e Conférence de Consensus en Thérapeutique Anti-Infectieuse

organisée par la Société de Pathologie Infectieuse de Langue Française

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

Mercredi 19 novembre 2008

ASIEM, Paris

Traitement de1er intention des Méningites purulentes avec ED positif

Examen direct	antibiotique	dosage
CG + pneumocoque	Cefotaxime Ou Ceftriaxone	➢300mg/kg/j en iv, en 4 perfusions, ou en iv continue avec dose de charge de 50/mg/k en une heure ➢100mg/kg/j en iv en 1 ou 2 perfusions
CG - meningocoque	Cefotaxime Ou Ceftriaxone	➢200mg/kg/j en iv, en 4 perfusions, ou en iv continue avec dose de charge de 50/mg/k en une heure. ➢ 75 mg/kg/j en iv en 1 ou 2 perfusions
BG + Listeriose	Amoxicilline + gentamicine	➢200mg/kg/j en iv en 4-6 perfusions, ou perfusion continue ➢3-5 mg/kg/j en une perfusion unique journaliere
BG - *H influenzae* *E coli*	Cefotaxime Ou Ceftriaxone	➢200mg/kg/j en iv, en 4 perfusions, ou en iv continue avec dose de charge de 50/mg/k en une heure. ➢75 mg/kg/j en iv en 1 ou 2 perfusions

Traitement de1er intention des Méningites purulentes avec ED négatif

Examen direct négatif	antibiotique	dosage
Sans arguments en faveur d'une listeriose Si enfant de moins de 3 mois	Cefotaxime Ou Ceftriaxone +gentamicine	➢300mg/kg/j en iv, en 4 perfusions, ou en iv continue avec dose de charge de 50/mg/k en une heure ➢100mg/kg/j en iv en 1 ou 2 perfusions ➢3-5 mg/kg/j en une perfusion unique journalière
Avec arguments en faveur d'une listeriose	Cefotaxime Ou Ceftriaxone + Amoxicilline +Gentamicine	➢300mg/kg/j en iv, en 4 perfusions, ou en iv continue avec dose de charge de 50/mg/k en une heure ➢100mg/kg/j en iv en 1 ou 2 perfusions ➢ 200mg/kg/j en 4 perfusions ou iv continue ➢3-5 mg/kg/j en une perfusion unique journalière

European Journal of Neurology 2008, **15:** 649–659 doi:10.1111/j.1468-1331.2008.02193.x

EFNS GUIDELINES/CME ARTICLE

EFNS guideline on the management of community-acquired bacterial meningitis: report of an EFNS Task Force on acute bacterial meningitis in older children and adults

A. Chaudhuri[a], P. M. Martin[b], P. G. E. Kennedy[c], R. Andrew Seaton[d], P. Portegies[e], M. Bojar[f] and I. Steiner[g] for the EFNS Task Force

ii. Pneumococcus with reduced susceptibility to penicillin or cephalosporins;
Ceftriaxone or Cefotaxime plus Vancomycin ± Rifampicin [IV]. Alternative therapy Moxifloxacin, Meropenem or Linezolid 600 mg combined with Rifampicin [IV]

2008

Corticothérapie

Corticothérapie dans les méningites bactériennes

- Méningite bactérienne supposée et/ou confirmée avant ou simultanée à la 1ère dose d'ATB 10 mg x 4/j IV Pendant 4 jours .
- Interruption du traitement si méningite non à pneumocoque, à reconsidérer si méningocoque.

Conférence de consensus SPLF 2008

Corticothérapie dans les méningites bactériennes

- DXM non recommandée si:
  - ATB thérapie antérieure
  - Choc septique associé
  - Immunodépression, VIH+
  - Méningite post neurochirurgie, nosocomiale
  - ATCD de dérivation du LCR

Conférence de consensus SPLF 2008

Corticothérapie dans les méningites bactériennes: **Adultes**

Dexamethasone 10 mg (4 times daily, 4 days) before or with first dose of antibiotic in:

1. Adults with bacterial meningitis
2. Adults with suspected bacterial meningitis

No dexamethasone:

1. Pre-treatment with parenteral antibiotics
2. Hypersensitivity to steroids
3. Recent head injury
4. CSF shunt

No dexamethasone, but consider low dose corticosteroids if:

1. Adults with septic shock with bacterial meningitis
2. Adults with septic shock and suspected bacterial meningitis

Fig. 2. Recommendations for adjunctive corticocorticosteroid treatment in adults with (suspected) bacterial meningitis in high-income countries.

Van de Beek, Med mal inf, 2009

DXM et méningites

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data.
De Beek. Lancet Neurol. 2010;9:254-263

- Aucun effet bénéfique de la DXM
  - Mortalité
  - Surdité
  - Séquelle neurologique
- Ni même en sous groupe (Age , bactérie, moment d'administration, VIH)

Méningite grave et DXM?

~Peu d'études sur le sujet Méningite/Sepsis

Pneumococcal meningitis in the intensive care unit. Prognostic factors of clinical outcome in a series of 80 cases.

Auburtin M. Am J Respir Crit Care Med 2002;165:713-717

⇨ Tendance effet protecteur de la DXM

Seulement 2 patients avaient une défaillance HD

Méningite grave et DXM?

- Score de Glasgow < 8

TABLE 4. UNFAVORABLE OUTCOME AT EIGHT WEEKS ACCORDING TO THE SCORE ON THE GLASGOW COMA SCALE ON ADMISSION.*

COMA SCORE AND CULTURE RESULTS	DEXAMETHASONE	PLACEBO	RELATIVE RISK (95% CI)	P VALUE
	no./total no. (%)			
Score of 12 to 14				
All patients	8/80 (10)	8/80 (10)	1.00 (0.40–2.53)	1.00
Streptococcus pneumoniae	1/15 (7)	2/11 (18)	0.37 (0.04–3.55)	0.56
Neisseria meningitidis	3/27 (11)	4/34 (12)	0.94 (0.23–3.87)	1.00
Score of 8 to 11				
All patients	7/52 (13)	14/41 (34)	0.39 (0.18–0.89)	0.03
S. pneumoniae	6/27 (22)	12/23 (52)	0.43 (0.19–0.95)	0.04
N. meningitidis	1/17 (6)	0/9 (0)	—	1.00
Score of 3 to 7				
All patients	8/25 (32)	14/23 (61)	0.53 (0.27–1.02)	0.08
S. pneumoniae	8/16 (50)	12/16 (75)	0.67 (0.38–1.17)	0.27
N. meningitidis	0/6	1/4 (25)	—	0.40

*Higher scores indicate a better level of consciousness. CI denotes confidence interval.

Dexamethasone in adults with bacterial meningitis.
De Gans. N Engl J Med 2002;347:1549-1556

Volet réanimation

Osmothérapie

- Mannitol
  - Effet surtout rhéologique probable
  - Peu d'études au cours méningite
- Glycérol
  - Pas d'étude chez l'adulte
  - Une étude chez enfant avec effet bénéfique associé à DXM
- Sérum salé hypertonique

Ventilation

- → Hyperventilation
  - → Hypocapnie
    - → Vasoconstriction cérébrale
      - → Diminution DSC
        - → Diminution PIC
- → Restauration autorégulation cérébrale après courte hyperventilation modérée

Moller, Stroke 2000;31:1116-1122

Hémodynamique

- Maintenir volémie correcte
- Aucun rationnel justifiant la restriction hydrique
- Drogues vasoactives pour maintenir PAM entre 70 et 100 mmHg

Convulsions

- Incidence des convulsions

Characteristic Clinical course	All Episodes of Meningitis (N =696)	Episodes of pneumococcal Meningitis (N=352)	Episodes of Meningococcal Meningitis (257)
Seizures	(107) 15	85(24)	12(5)

- Pas de traitement prophylactique indiqué à priori

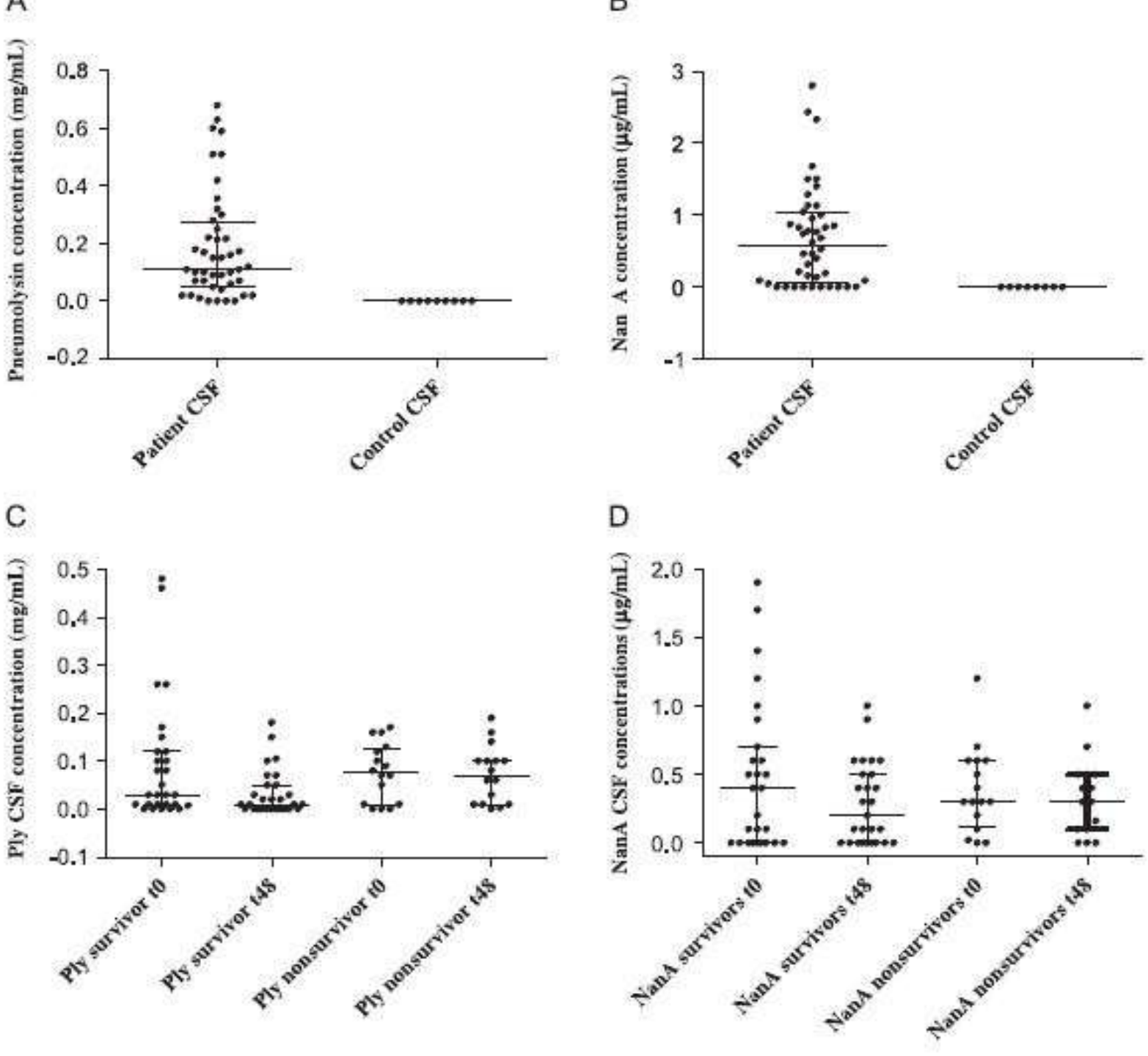
D.Van de Beek, Nat Clin Pract Neurol 2006 Sep,2(9) : 504-16.

Perspectives

Persistence of Pneumolysin in the Cerebrospinal Fluid of Patients With Pneumococcal Meningitis Is Associated With Mortality

Emma C. Wall,1,a Stephen B. Gordon,1,a Samia Hussain,2
Upali R. S. Goonetilleke,1 Jenna Gritzfeld,1 Matthew Scarborough,3 and
Aras Kadioglu2
1Clinical Research Group, Liverpool School of Tropical Medicine, 2Institute of
Infection and Global Health, University of Liverpool; and 3Nuffield Department
of
Medicine, John Radcliffe Infirmary, Oxford, United Kingdom

CID.2012:54


A
Pneumolysin concentration (mg/mL)
0.8
0.6
0.4
0.2
0.0
-0.2
Patient CSF
Control CSF
B
Nan A concentration (µg/mL)
3
2
1
0
-1
Patient CSF
Control CSF
C
Ply CSF concentration (mg/mL)
0.5
0.4
0.3
0,2
0.1
0.0
-0.1
Ply survivor t0
Ply survivor t48
Ply nonsurvivor t0
Ply nonsurvivor t48
D
NanA CSF concentrations (µg/mL)
2.0
1.5
1.0
0.5
0.0
NanA survivors t0
NanA survivors t48
NanA nonsurvivors t0
NanA nonsurvivors t48

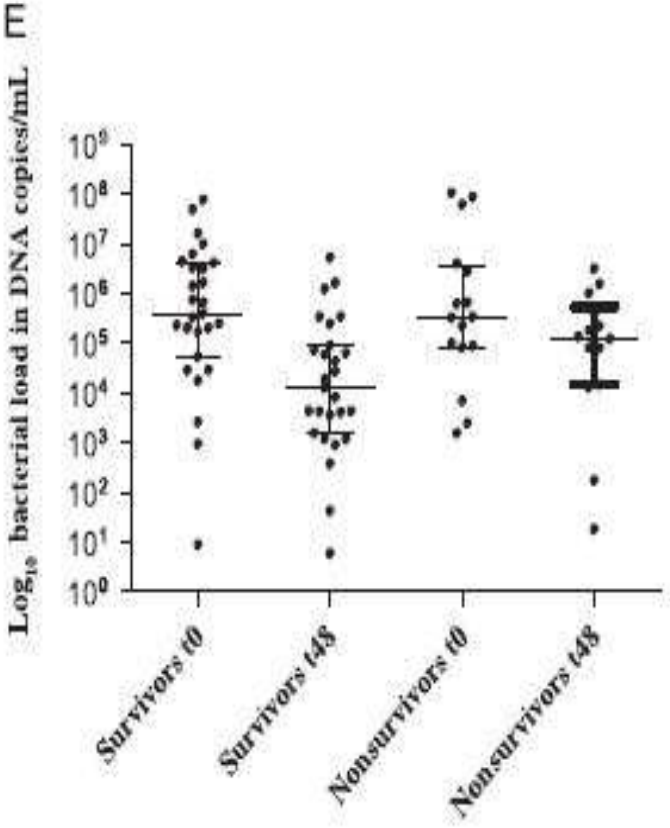


Figure 1. *A* and *B*, Concentrations of pneumococcal proteins pneumolysin (Ply) and neuraminidase A (NanA) in the cerebrospinal fluid (CSF) of patients with proven meningitis compared with controls. The lower limit of detection was 2 ng/mL for Ply and 10 ng/mL for NanA. *C* and *D*, Concentrations of pneumococcal proteins Ply and NanA in the CSF of patients with proven meningitis comparing samples taken from survivors and nonsurvivors at admission and 48 hours. The lower limit of detection was 2 ng/mL for Ply and 10 ng/mL for NanA. *E*, Bacterial load of *Streptococcus pneumoniae* in the CSF of patients with proven meningitis comparing survivors and nonsurvivors at admission and 48 hours.

pneumococcal meningitis.

In conclusion, we found that all pneumococcal meningitis patients had greater levels of Ply and NanA than those expected from extrapolated animal models. The persistence of high levels of Ply in nonsurvivors despite falling numbers of bacteria suggests that this protein is involved in severe pathogenesis. Blocking or inhibiting pneumolysin during acute meningitis may represent a future therapeutic option to improve mortality.

Conclusion

- Mortalité lourde.
- ATB : Consensuelle.
  Nouveaux ATB.
- Corticoïde : DXM discutée.
  HSHC / sepsis : oui.
- Nécessité des études +++