

JRPI octobre 2011

Cas clinique

Weyrich P.

Interne

Service de maladies infectieuses, hôpital
Gustave Dron, Tourcoing

Cas clinique

- Patient de 59 ans admis au SAU le 28/09 de Tourcoing pour troubles de conscience.
- HDM évoluant depuis 48h, débutant par des céphalées et des nausées. Automédication par paracétamol.

A l'entrée

- Syndrome méningé avec troubles de conscience (GCS : 12). Apyrexie sous paracétamol. Hémodynamique stable. Pas d'autre foyer infectieux.
- Aggravation rapide au SAU des troubles de conscience (GCS : 6) puis de l'hémodynamique (choc septique) et transfert en réanimation

- Pas d'antécédents médico-chirurgicaux
- Habitus :
Intoxication alcoolique chronique (30g/j)
Tabagisme actif à 40 PA
Marié, 2 enfants
Pas de voyage récent
1 chat

Biologie d'entrée

**NFS: Hb=14,9 g/dl, GB=3850/mm³,
plq=64000/mm³; TP=44%, TCA=35/32**

**Créat=14 mg/l, Urée=0,64 g/l, Na=136 mmol/l,
K=4,6 mmol/l, TGO=107 UI/l, TGP=46 UI/l,
PAL=191 UI/l, GGT=94 UI/l,**

CRP=292 mg/l, PCT=21,9 ng/ml

**PL après scanner : 440 éléments/mm³ (PNN
62%, lymphocytes 29%), Glc=0,01 mmol/l,
prot=10,35 g/l, BGN au direct.**

Prise en charge

Intubation oro-trachéale, curarisation et ventilation mécanique

Support vasopressif (noradrénaline), remplissage par cristalloïdes, HSHC, insulinothérapie, transfusion plaquettaire

Antibiothérapie initiale : cefotaxime (18g/j) + amoxicilline (12g/j) + gentamycine (460mg/j) + acyclovir (3g/j)

Puis cefotaxime seul à la réception du direct (BGN)

Résultats de la culture du LCR et des hémocultures

- **Escherichia Coli BLSE**

Adaptation de l'antibiothérapie

MEROPENEM : 6 g/j

CIPROFLOXACINE : 1200 mg/j

Pour une durée de 3 semaines

- Amélioration initiale neurologique (EEG) et hémodynamique (sevrage en catécholamines) et extubation le 20/10 et transfert en service de médecine le 25/10

Le 28/10 (J8 de l'arrêt de l'antibiothérapie)

- Réascension du syndrome inflammatoire :
CRP : 212 mg/l vs nadir de 120 mg/l et
hyperleucocytose (23600 leucocytes/mm³)
- Sensibilité abdominale
- Persistance d'une confusion
- Réalisation d'un scanner TAP avec injection en urgence

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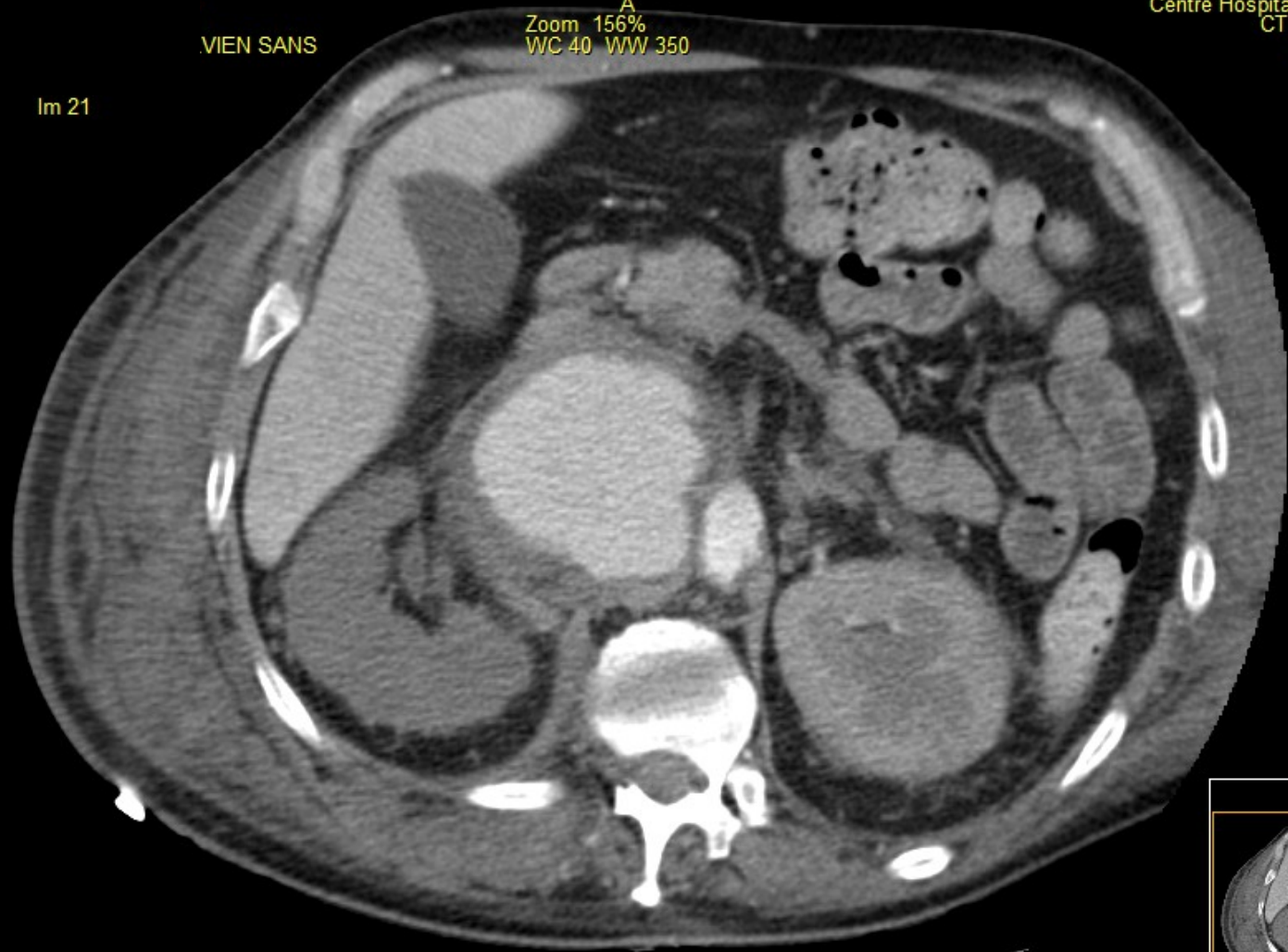
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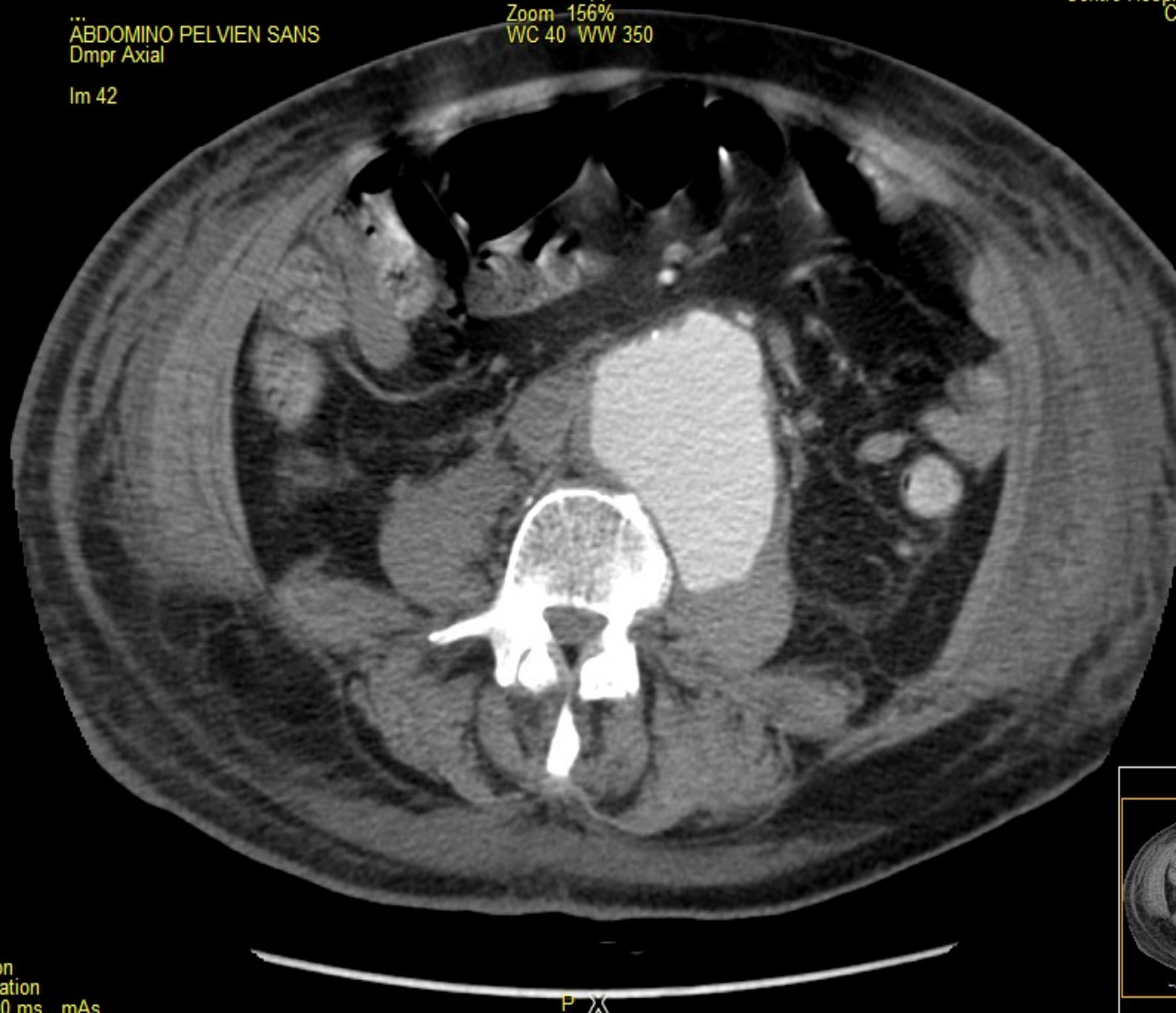
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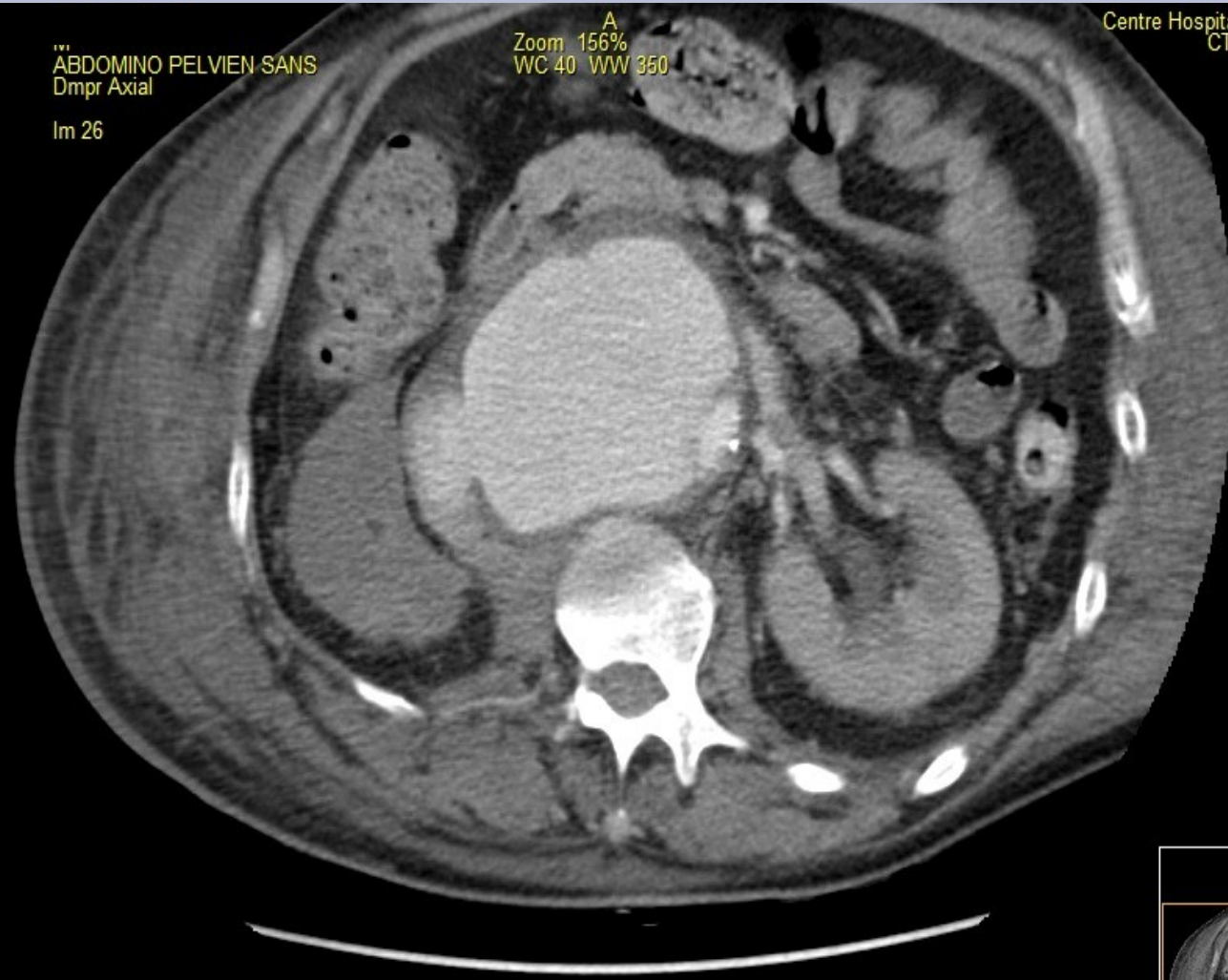
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WC 40 WW 350

Centre Hospitalier Gustave Dron
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Im 35

R



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FFS Pat. Position
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120 kV mA 700 ms mAs

P X



667741-MIAE
15/12/1951
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VIEN SANS

H
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WC 40 WWV 350

Centre Hospitalier Gustave Dron
CT LightSpeed VCT
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A

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3.0 mm Thk
FFS Pat. Position
-21.5 Slice Location
120 kV mA 700 ms mAs

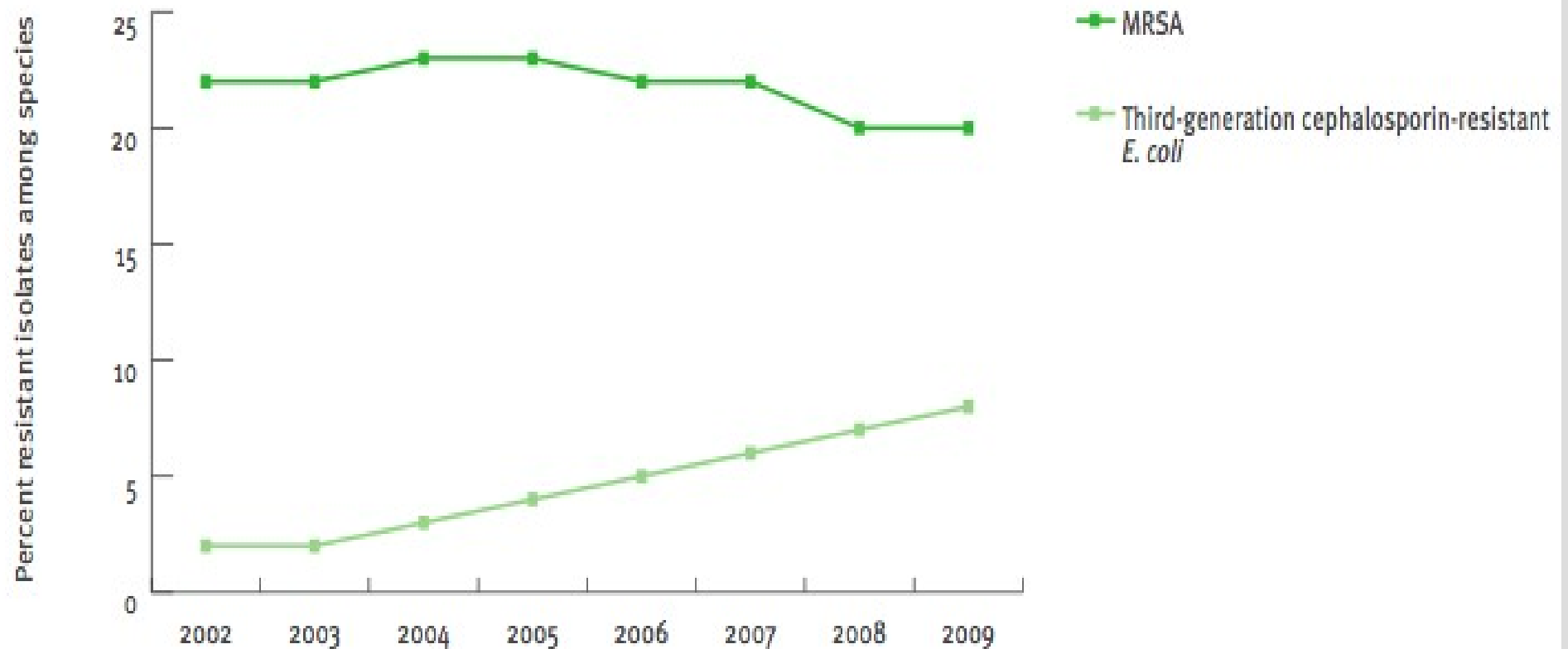
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Une méningite à E. Coli BLSE communautaire

Figure 2.2: Proportion of third-generation cephalosporin-resistant *Escherichia coli* (CREC) and methicillin-resistant *Staphylococcus aureus* (MRSA). EARSS/EARS-Net 2002–2009 (22 countries/198 laboratories)



Only laboratories reporting susceptibility results for specific antimicrobials continuously during the period 2002–2009 are included in the analysis.

Table 1. Predisposing Factors in 404 Single Episodes of Bacterial Meningitis.

FACTOR	COMMUNITY- ACQUIRED (N = 253)	NOSOCOMIAL (N = 151)
	percent	
Acute otitis media	19	1
Chronic otitis media	7	0
Sinusitis	12	4
Pneumonia	15	8
Endocarditis	7	1
Head injury*		
Recent	5	13
Remote	4	0
Recent neurosurgery*	0	68
Neurosurgical device†	1	32
Altered immune state	19	31
Diabetes mellitus	10	6
Alcoholism	18	5
Cerebrospinal fluid leak	8	13
None of the 13 factors	25	8

*Recent denotes head injury or neurosurgery within one month of the onset of meningitis; remote, more than one month before the onset of meningitis.

†Neurosurgical devices included ventriculostomy, ventriculo-peritoneal or ventriculoatrial shunt, lumbar epidural catheter, lumboperitoneal catheter, and dorsal-column stimulator.

Table 2. Causative Organisms in Single Episodes of Meningitis, 1962 through 1988.*

ORGANISM	COMMUNITY- ACQUIRED (N = 253)	NOSOCOMIAL (N = 151)
	no. (%)	
<i>Strep. pneumoniae</i>	97 (38)	8 (5)
Gram-negative bacilli†	9 (4)	57 (38)
<i>N. meningitidis</i>	35 (14)	1 (1)
Streptococci‡	17 (7)	13 (9)
Enterococcus	0	4 (3)
<i>Staph. aureus</i>	13 (5)	13 (9)
<i>L. monocytogenes</i>	29 (11)	5 (3)
<i>H. influenzae</i>	9 (4)	6 (4)
Mixed bacterial species	6 (2)	10 (7)
Coagulase-negative staphylococci	0	13 (9)
Other§	4 (2)	5 (3)
Culture negative	34 (13)	16 (11)

*Percentages do not always total 100 because of rounding.

†In community-acquired meningitis, the causative organisms were *Escherichia coli* (4 episodes), *klebsiella* (3), *enterobacter* (1), and *proteus* (1); in nosocomial meningitis, *E. coli* (17), *klebsiella* (13), *pseudomonas* (6), *acinetobacter* (6), *enterobacter* (5), *serratia* (5), *citrobacter* (2), *proteus* (1), "coliform" bacteria (1), and "nonenteric gram-negative rods" (1).

‡In community-acquired meningitis, the causative organisms were group A (4 episodes), group B (1), nonenterococcal group D (3), group D, not further identified (1), other groups (5), and nonhemolytic, nongrouped (3); in nosocomial meningitis, the causative organisms were group B (4), nonenterococcal group D (3), other groups (2), alpha-hemolytic, nongrouped (3), and non-hemolytic, nongrouped (1).

§In community-acquired meningitis, the causative organisms were anaerobes (3 episodes) and diphtheroids (1); in nosocomial meningitis, the causative organisms were micrococci (2), *neisseria* species (1), *propionibacteria* (1), and diphtheroids (1).

Table 1. Demographic characteristics, clinical features and predisposing factors upon hospital admission (patients may have one or more underlying diseases or predisposing factors)

Characteristics	Episodes of meningitis (n = 40)
Age, years, median (Q1; Q3)	56 (41; 76)
Males/females, n	20/20
African or Caribbean origin, n (%)	5 (12.5)
McCabe and Jackson classification, n (%)	
Non-fatal underlying disease	24 (60)
Ultimately fatal underlying disease	7 (17.5)
Rapidly fatal underlying disease	9 (22.5)
Underlying disease, n (%)	30 (75)
Chronic alcoholism	13 (33)
Cirrhosis	9 (23)
Immunosuppressive therapy	4 (10)
Infection with human immunodeficiency virus	3 (7.5)
Agammaglobulinaemia or hypogammaglobulinaemia	2 (5)
Asplenia	1 (2.5)
Malignancy	7 (18)
Diabetes mellitus	7 (18)
Remote head trauma	4 (10)
Previous episode of bacterial meningitis	3 (7.5)
Signs and symptoms upon presentation	
Body temperature, °C, median (Q1; Q3)	38.6 (37.8; 39.4)
Triad of fever, neck stiffness and change in mental status, n (%)	24 (60)
Altered consciousness, n (%)	36 (90)
Score on Glasgow Coma Scale ^a , median (Q1; Q3)	12 (9; 14)
< 8 (indicating coma)	6 (15)
Focal neurological deficit, n (%)	12 (30)
Hemiparesis, n (%)	12 (30)
Cranial nerve palsy, n (%)	2 ^b (5)
Generalised seizures, n (%)	12 (30)
SAPS II ^c , median (Q1; Q3)	40 (30; 56)
Mechanical ventilation, n (%)	28 (70)
Inotropic support for septic shock, n (%)	16 (40)

^aGCS: Glasgow coma scale [17].

^bTwo patients had both hemiparesis and cranial nerve palsy.

^cSAPS II: simplified acute physiology score [18].

Q1, 25th percentile; Q3, 75th percentile.

Quel traitement proposer ?

Tableau 1

Paramètres pharmacocinétiques. Synthèse concernant les principaux antibiotiques utilisés dans le traitement des infections du système nerveux central, en relation avec leur activité in vitro. Sur base de deux revues [3,4] avec mise à jour sur base de références récentes [49] et des données pharmacocinétiques disponibles dans les notices correspondantes.

Pharmacokinetic parameters. Summary for the main antibiotics used in the treatment of central nervous system infections, in relation with their in vitro activity. Based on two reviews [3,4] updated with recent references [49] and on pharmacokinetic data available in the package inserts of the corresponding marketed products.

Antibiotiques	Posologie		Paramètres pharmacocinétiques sériques						CMI typiques des germes sensibles responsables d'infections du SNC ^{b,c} [mg/L]								
	Dose journalière	Intervalle (h)	Pic sérique (mg/L)	t _{1/2} (h)	AUC ^a (mg L ⁻¹ h)	Liaison prot (%)	Conc. LCR (mg/L)	% pénétration	S.p	H.i	N.m	S.a	L.m	E.c.	P.a	B.f	B.B.
<i>β-lactames</i>																	
Pénicilline G	24 10 ⁶ U	4	115	1	700	55	0,8–10	8	0,01	0,8	0,05		0,5				0,5
Ampicilline	12 g	4	48	1	1000	17	0,3–38	4–65	0,02	0,5	0,05		0,5				
Céfotaxime	8–12 g	4–6	214	1–1,7	750	35	1–83	4–55	0,01	0,06		2		0,12	16		0,06
Ceftazidime	6 g	8	160–185	1,5–2	780	17	2–30	14–45	0,25	0,06		8		0,25	2		
Ceftriaxone	4 g	12–24	216–280	5–10	2400	90	2–7	1,5–7	0,01	0,01		2		0,25	16		0,06
Méropénème	6 g	8	110	0,8–1	410	2	1–32	11	0,03	0,1	0,01	0,03	0,3	0,03	2		0,25
Aztréonam	6–8 g	6–8	204–255	1,3–2		30–60	2–28	17		0,12				0,25	16		
<i>Glycopeptides</i>																	
Vancomycine	2–3 g ^d	8–12	25	4–6	450	10–55	0,1–5	0–22	0,5			1					
<i>Phénicolés</i>																	
Chloramphénicol	4–6 g	6	10	4	394	25–50	2–23	20–66	1,6	0,8	0,8	8		6			
<i>Oxazolidinones</i>																	
Linézolide	600 mg	12	13	4,5	160	31	6	80	2	32		2	4				
<i>Aminoglycosides</i>																	
Gentamicine	3–5 mg/kg	24	12–20	2–3	74	<10	0–3	0–2,5		4		4	1	4			
Amikacine	15–mg/kg	24	34–50	2–3	240	<10	0,4–6	20–34		12				1	6		
<i>Sulfamidés</i>																	
Sulfaméthoxazole/triméthoprim	10–20 mg/kg	6–12		11	1200	70	50–150	0,5/0,3–93/19	8	4	0,25	0,12	4	8			
<i>Ansamycines</i>																	
Rifampicine	600 mg	24	17	2–5	41	80	0,3–5	4–21	0,06	1	0,03	0,02	0,12				
<i>Tétracyclines</i>																	
Doxycycline	100 mg	12	2,5	20		90	0,6–8,6	13–26	0,5	8	8			64			0,25
<i>Fluoroquinolones</i>																	
Ciprofloxacine	800 mg	12	9	3,5	70	15–30	0,4–3	26–37	2	<0,6	<0,1	2	2	0,25	0,5		
Lévofloxacine	500 mg	12	5	6	94	24–38		16	1	0,03	0,02	0,25		0,12	2		
Moxifloxacine	400 mg	24	4	11	48	30–50	3–4		0,25	0,06	0,03	0,25		0,12	4	1	
<i>Nitroimidazoles</i>																	
Métronidazole	30 mg/kg	6	25	8	320	11	6–27	42–90									4

^a Calculé pour un patient de 1 m 75, 70 kg, avec une clairance à la créatinine de 100 ml/min.

^b Les concentrations minimales inhibitrices (CMI) indiquées en gras correspondent à celles qui sont susceptibles d'entraîner un échec thérapeutique.

^c S.p. : *Streptococcus pneumoniae*; H.i. : *Haemophilus influenzae*; N.m. : *Neisseria meningitidis*; S.a. : *Staphylococcus aureus*; L.m. : *Listeria monocytogenes*; E.c. : *Escherichia coli*; P.a. : *Pseudomonas aeruginosa*; B.f. : *B. fragilis*; B.b. : *Borrelia burgdorferi*; AUC : Area Under the Curve.

^d Certains auteurs recommandent des doses jusque 60 mg/kg [32].

Randomized Comparison of Meropenem with Cefotaxime for Treatment of Bacterial Meningitis

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Medical Research Council Pneumococcal Diseases Research Unit, Department of Medical Microbiology, University of Witwatersrand and South African Institute for Medical Research, Johannesburg, South Africa,¹ and Pediatric Infectious Disease Unit, Soroka University Medical Center and the Faculty of Health Sciences, Ben Gurion University of the Negev, Beer-Sheva, Israel²

TABLE 5. Clinical outcome and pathogens isolated in CSF culture-proven meningitis

Outcome or pathogen	No. (%) of patients with preexisting neurological abnormalities ^a prior to antibiotic therapy		No. (%) of patients without neurological abnormalities prior to therapy	
	Meropenem	Cefotaxime	Meropenem	Cefotaxime
Outcome				
Cure ^b	8 (47)	3 (60)	46 (79)	49 (83)
Cure with audiological sequelae	1 (6)	1 (20)	9 (16)	7 (12)
Cure with neurological sequelae	6 (35)	0	2 (3)	1 (2)
Cure with audiological and neurological sequelae	2 (12)	1 (20)	1 (2)	0
Death	0	0	0	2 (3)
Total	17 (100)	5 (100)	58 (100)	59 (100)
Pathogens isolated from CSF				
<i>H. influenzae</i>	7 (41)	0	27 (47)	32 (54) ^c
<i>N. meningitidis</i>	7 (41)	2 (40)	22 (38)	19 (32)
<i>S. pneumoniae</i>	3 (18)	3 (60)	9 (16)	6 (10)
<i>E. coli</i>				1 (2)
<i>Salmonella</i> species				1 (2)
Total	17 (100)	5 (100)	58 (100)	59 (100)

^a Preexisting neurological abnormalities were as follows. For 17 patients randomized to meropenem: 7 patients, seizures in past 24 h; 1 patient, head injury; 2 patients, seizures in past 24 h plus head injury; 3 patients, seizures in past 24 h plus coma; 1 patient, cerebrovascular accident; 1 patient, positive Babinski reflex; 1 patient, jittery; 1 patient, hypertonic and jittery. For 5 patients randomized to cefotaxime: 3 patients, seizures in past 24 h; 1 patient, stupor; 1 patient, coma and head injury.

^b Includes 13 patients treated with meropenem and 12 patients treated with cefotaxime who had no neurological sequelae, but for whom auditory analysis was complicated at the follow-up assessments by the presence of an effusion or was not done.

^c Two isolates were identified only as *Haemophilus* species.

Conclusion

- Faible prévalence des méningites à Escherichia Coli BLSE, souvent dans un contexte nosocomiale ou neurochirurgicale
- Traitement basé sur les carbapénèmes (en particulier meropenem)
- Encore plus faible prévalence des anévrysmes mycotiques à Escherichia Coli BLSE