

# Epidemiology of Acute Purulent Hospital-acquired Meningitis in Developed and Underdeveloped Countries

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# Nosocomial Meningitis

✓ A rare diagnosis

*(Nosocomial CNS Infections)*

1971-1974	10 /100.000
1975-1982	8.4 /100.000
Medical services	7 /100.000
Surgical services	18 /100.000

# Serious & Associated with high mortality

## ✓ Mortality;

- 16-35 % in developed countries
- 22-36 % in Taiwan
- 20-47 % in Turkey
  - 33.3% in Gazi University, Ankara

(The Netherlands ) *Weisfelt M, et al. J Hosp Infect 2007; 66:71-8*

(USA) *Durand ML, et al. NEJM 1993; 328: 21-28*

(Taiwan) *Wang KW, et al. J Clin Neurosci 2005;12: 647*

*Bulut C, et al. Turkish J Hosp Infect 2005; 9: 218-24*

*Naz H, et. ANKEM Derg 2009; 23: 82-85.*

*Dizbay M, et al. ANKEM Derg 2011;25(1): 6-11.*

*Erdem I, et al. Neurol India 2008; 56 (4): 433-7.*

# Not so rare in Neurosurgical Unit!

- ✓ 7% of all NS-ICU acquired infections
  - 0.4 % of all nosocomial infections in developed world
- ✓ In Turkey
  - 5.8 % - 19.6 % of NS-ICU acquired infections
  - 0.85% of all nosocomial infections

*Taşbakan MI, et al. Ege Tıp Dergisi 45 (2) : 127- 130, 2006*  
*Dökmetas , et al. Turkish J Hospital Infect 2002; 6: 46 – 52,*  
*Dizbay M, et al. ANKEM Derg 2011;25(1): 6-11.*

Markus Dettenkofer  
Winfried Ebner  
Thomas Els  
Regina Babikir  
Carl Lücking  
Klaus Pelz  
Henning Rüdén  
Franz Daschner

## Surveillance of nosocomial infections in a neurology intensive care unit

- ✓ 0.4 cases of meningitis/1000 patient days
- ✓ 0.8 cases of ventriculitis/1000 patient days

*J Neurol* 2001; 248:959-964

# NNIS 1992-2004

## Nosocomial Central Nervous System Infections:

- ✓ Post-craniotomy 0.91- 2.40 %
- ✓ Other interventions 1.53 %
- ✓ Shunt 4.42-5.36 %

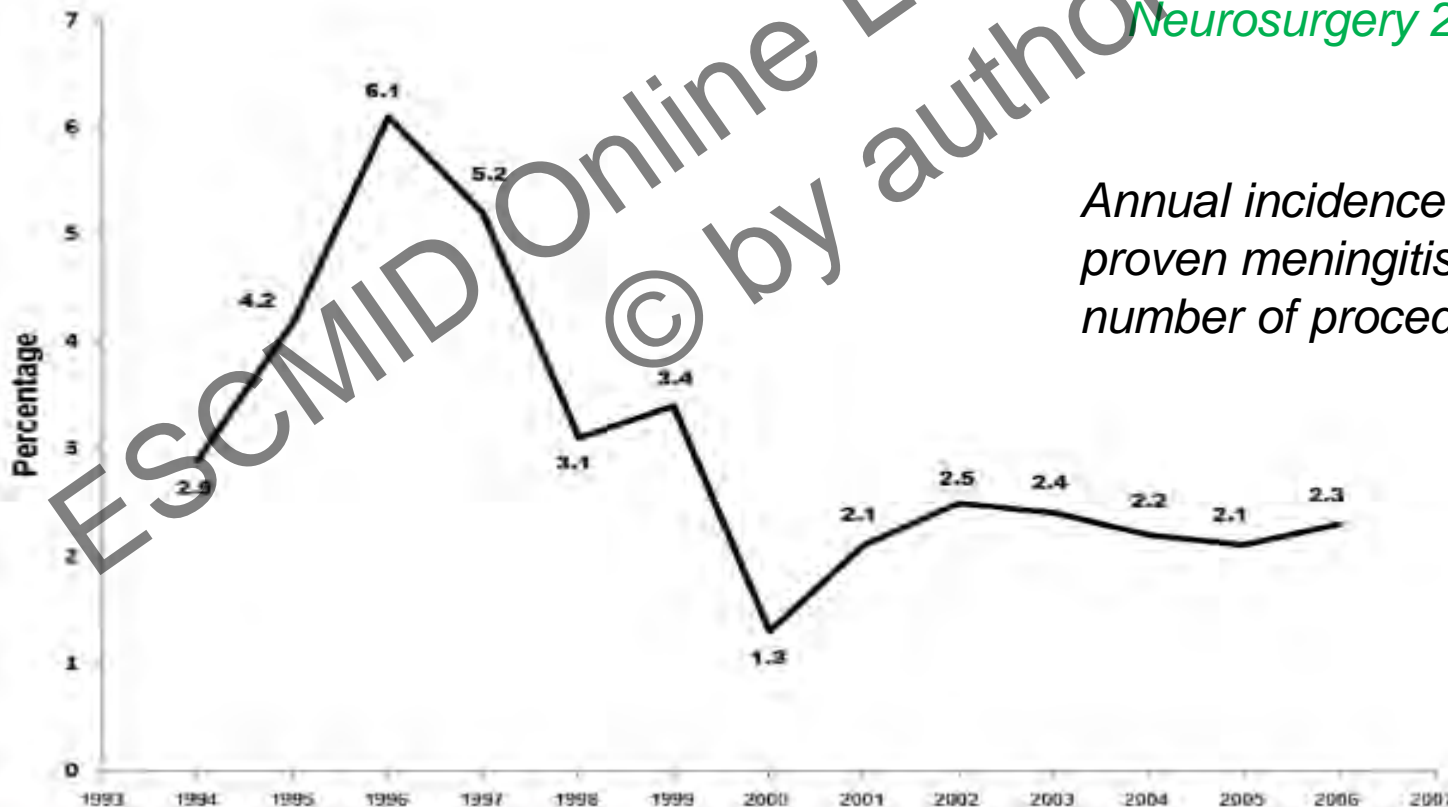
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## EFFECT OF RISK-STRATIFIED, PROTOCOL-BASED PERIOPERATIVE CHEMOPROPHYLAXIS ON NOSOCOMIAL INFECTION RATES IN A SERIES OF 31 927 CONSECUTIVE NEUROSURGICAL PROCEDURES (1994–2006)

*Neurosurgery* 2009; 64: 1123



*Annual incidence of culture-proven meningitis / total number of procedures performed*

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Department of Anesthesiology,  
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Paris, France

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

TABLE 4. Bacteriology of 95 postcraniotomy meningitis<sup>a</sup>

	No antibiotic prophylaxis, n = 17	Antibiotic prophylaxis, n = 78	Total
<i>S. aureus</i> (number meticillin resistant)	4 (1)	9 (0)	13 (1)
CNS (number meticillin resistant)	3 (0)	17 (8)	20 (8)
Streptococci	3	9	12
Enterococci	0	1	1
<i>Propionibacterium acnes</i>	3	1	4
Enterobacteriaceae	2	26	28
<i>Pseudomonas aeruginosa</i>	0	5	5
<i>Acinetobacter</i> spp	0	2	2
Anaerobes	1	0	1
Total micro organisms	16	70	86
Cutaneous micro organisms (%)	10 (62.5)	27 (38.6)	37
ABP susceptible micro organisms (%)	13 (81.2)	28 (40.0) <sup>b</sup>	41
Aseptic (%)	1 (5.9)	14 (17.9)	15

<sup>a</sup> CNS, coagulase negative staphylococci.

<sup>b</sup> *P* = 0.003. Six meningitis cases were plurimicrobial.

Antibiotic prophylaxis in entire population 9.7% → 5.8% (*p*<0.0001)  
 In low risk patients 10.0% → 4.6% (*p*<0.0001).



# Post-neurosurgical Meningitis: Risk and Prognostic Factors

- ✓ 52 / 3580 meningitis (1.4%)
  - ✓ Post craniotomy 0.8%
  - ✓ Shunt or EVD 2.6%
- ✓ Independent Risk Factors
  - ✓ Duration of EVD
  - ✓ APACHE II
- ✓ Mortality %8
- ✓ Prognostic factors
  - Low CSF glucose, APACHE II, Gram negative etiology

*(Italy) Federico G, et al. Scand J Infect Dis. 2001;33(7):533-7.*

# Post-craniotomy infections

- ✓ Incidence 0.8 – 1.5 %
  - 0.28 % (35/12980) in Taiwan
- ✓ Time of onset
  - 1st week 1/3
  - 2nd week 1/3
  - > 2nd week 1/3

*Baugnon T, et al. Neurosurgery 2006;59:126-33.*  
*McClelland S III & Hall WA. Clin Infect Dis 2007;45:55-9.*  
*(Taiwan)Wang KW, et al. J Clin Neurosci 2005;12: 647*

# Risk Factors For post-Craniotomy Infection

✓ Multivariate analyses of 4578 craniotomies (OR)

- Male sex (1.6)
- Diagnostic surgery (2.7)
- Surgeon (2.3)
- No prophylaxis (2.1)
- Reintervention (1.8)
- Duration of surgery > 4h (2.1)
- CSF leakage (11.5)

# CSF leakage as a risk factor for post-craniotomy meningitis

n= 6243 patients

## CSF leakage

	+	-
Meningitis	35	60
Total	120	6123
%	29.2	0.98
p < 0.0001	OR = 28.4	

*Korinek AM, et al. Neurosurgery. 2006; 59(1):126-33.*

# Risk Factors for Meningitis After Transsphenoidal Surgery

Maarten O. van Aken, Siem de Marie,  
Aart-Jan van der Lely, Ram Singh,  
J. Herbert van den Berge, Rene M. L. Poublon,  
Wytske J. Fokkens, Steven W. J. Lamberts, and  
Wouter W. de Herder

*From the Departments of Internal Medicine, Neurosurgery,  
Otorhinolaryngology, and Bacteriology, University Hospital Rotterdam,  
Rotterdam, the Netherlands*

Risk	(+)	(-)	p
Preop. Paranasal sinus abnormalities	2/3	5/225	<.0005
Intraop CSF leakage	3/22	4/206	<.05
Postop. rhinorrhea	6/7	1/221	<.00001

# Internal Ventricular Catheter-related Infections

- ✓ Incidence 4-17 %
  - Within a month
- ✓ Risk factors
  - Holes in surgical gloves
  - Direct handling the catheter

*van de Beek D, et al. NEJM 2010; 362;2 : 146-154*  
*Conen A, et al. Clin Infect Dis 2008;47:73-82.*  
*Vinchon M, et al. Childs Nerv Syst 2006;22:692-7*  
*Kulkarni AV, et al. J Neurosurg 2001;94:195-201.*

# External Ventricular Catheter-related Infections

✓ Incidence 2 - 27%

○ 1.2 % in Taiwan

✓ Culture positive

(Meta-analyses of 23 studies)

○ 8.8 % patient

○ 8.1 % catheter

*van de Beek D, et al. NEJM 2010; 362;2 : 146-154*

*Beer, R, et al. J Neurol 2008; 255:1617-1624*

*(Taiwan) Wang KW, et al. J Clin Neurosci 2005;12: 647*

*Aucoin PJ, et al. Am J Med 1986; 80:369-376*

# Risk Factors for EVD-associated infections

- Increased duration of drainage
  - >5 days ??
- Routine sampling of CSF
- Catheter irrigation
- Intraventricular hemorrhage
- Leakage of CSF at the site
- Blockage of the drain
- Surgical technique (subcutaneously tunneled EVD, Rickham reservoir with percutaneous CSF drainage)

*van de Beek D, et al. NEJM 2010; 362;2 : 146-154*

*Beer, R, et al. J Neurol 2008; 255:1617–1624*

*Lozier AP, et al. Neurosurgery 2008;62:688-700.*

*Lyke KE, et al. CID 2001; 33: 2028-2033*

*Hoefnagel, D, et al. Acta Neurochir (Wien) 2008; 150: 209–214*



## Factors Contributing to Ventriculostomy Infection

Joon-Hyung Kim, Naman S. Desai, Joseph Ricci, Philip E. Stieg, Axel J. Rosengart, Roger Härtl, Justin F. Fraser

	Infected	Non-Infected	
Concomitant systemic infection, n (%)			NS (0.12)
Present (n = 212)	10 (4.7%)	202 (95.3%)	
Absent (n = 131)	2 (1.5%)	129 (98.5%)	
Length of EVD placement, days			
Mean	20.9 ± 15.9	12.1 ± 18.2	
Median	17	10	0.005
Range	6–63	0–312	
Length of hospital stay, days			
Mean	42.1 ± 24.0	24.2 ± 21.1	
Median	36	20	0.002
Range	9–94	1–230	



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**BIAA**  
British Infection Association

[www.elsevierhealth.com/journals/jinf](http://www.elsevierhealth.com/journals/jinf)

## Characteristics of infections associated with external ventricular drains of cerebrospinal fluid

Laura N. Walti<sup>a,b,f</sup>, Anna Conen<sup>c</sup>, Julia Coward<sup>b</sup>, Gregory F. Jost<sup>d</sup>,  
Andrej Trampuz<sup>e,\*</sup>

- ✓ Switzerland, 1997-2008
- ✓ 48 cases
  - Infection within 6 days after insertion
  - In %23, 1-10 days after removal

# Prospective surveillance of drain associated meningitis/ventriculitis in a neurosurgery and neurological intensive care unit

S Scheithauer,<sup>1</sup> U Bürgel,<sup>2</sup> Y-M Ryang,<sup>2</sup> G Haase,<sup>3</sup> J Schiefer,<sup>4</sup> S Koch,<sup>5</sup> H Häfner,<sup>1</sup> S Lemmen<sup>1</sup>

- ✓ 1333 patients; 3023 DD
- ✓ 26 cases of device associated meningitis
  - 8.6 infections/1000 DD
    - LD 19.9/1000 DD
    - EVD 6.3/1000 DD
- ✓ Risk Factors
  - The presence of intraventricular blood (p=0.003)
  - Previous trauma (p=0.04)

# External Lumbar Catheter-related Infections

- ✓ Incidence ~5%\*
- ✓ Risk Factors
  - Disconnection of the external drainage system
  - Presence of infections

*\*0.8 % with strict control protocols*

*van de Beek D, et al. NEJM 2010; 362;2 : 146-154  
Governale LS, et al. Neurosurgery 2008;63:Suppl 2:379-84.*

# Lumbar Puncture-associated Infections

- ✓ Incidence 1/50.000
  - 80 cases annually in ABD

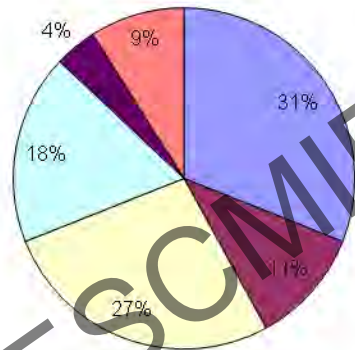
*van de Beek D, et al. NEJM 2010; 362;2 : 146-154*

Clusters of Nosocomial Meningitis  
Associated With a Single Anesthesiologist  
Claire Thénier, MD; Anne Carbonne, MD;  
Pascal Astagneau, MD, PhD

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY MARCH 2008, VOL. 29, NO. 3

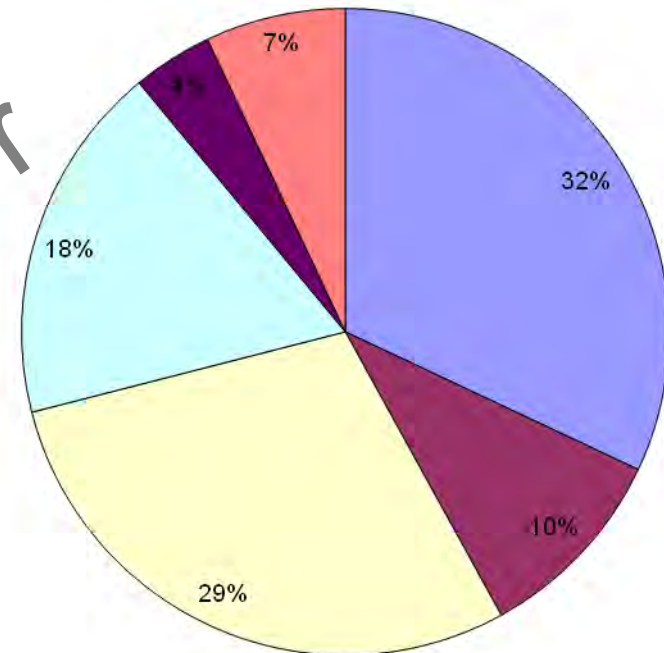
# Etiology of Nosocomial CNSI

Etiology of Nosocomial CNSI



- Coagulase Negative Staphylococci
- S. Aureus
- Gram negative bacilli
- Streptococcus spp.
- Fungus
- Other

Etiology of Nosocomial Meningitis



NNIS 1986-1992

# Etiology of Nosocomial CNS Infections

✓ Depends on

- Pathogenesis
- Timing of the infection after the predisposing event
- Differences in antibiotic usage

*van de Beek D, et al. NEJM 2010; 362;2 : 146-154*  
*Beer, R, et al. J Neurol 2008; 255:1617–1624*



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## Nosocomial bacterial meningitis in adults: a prospective series of 50 cases

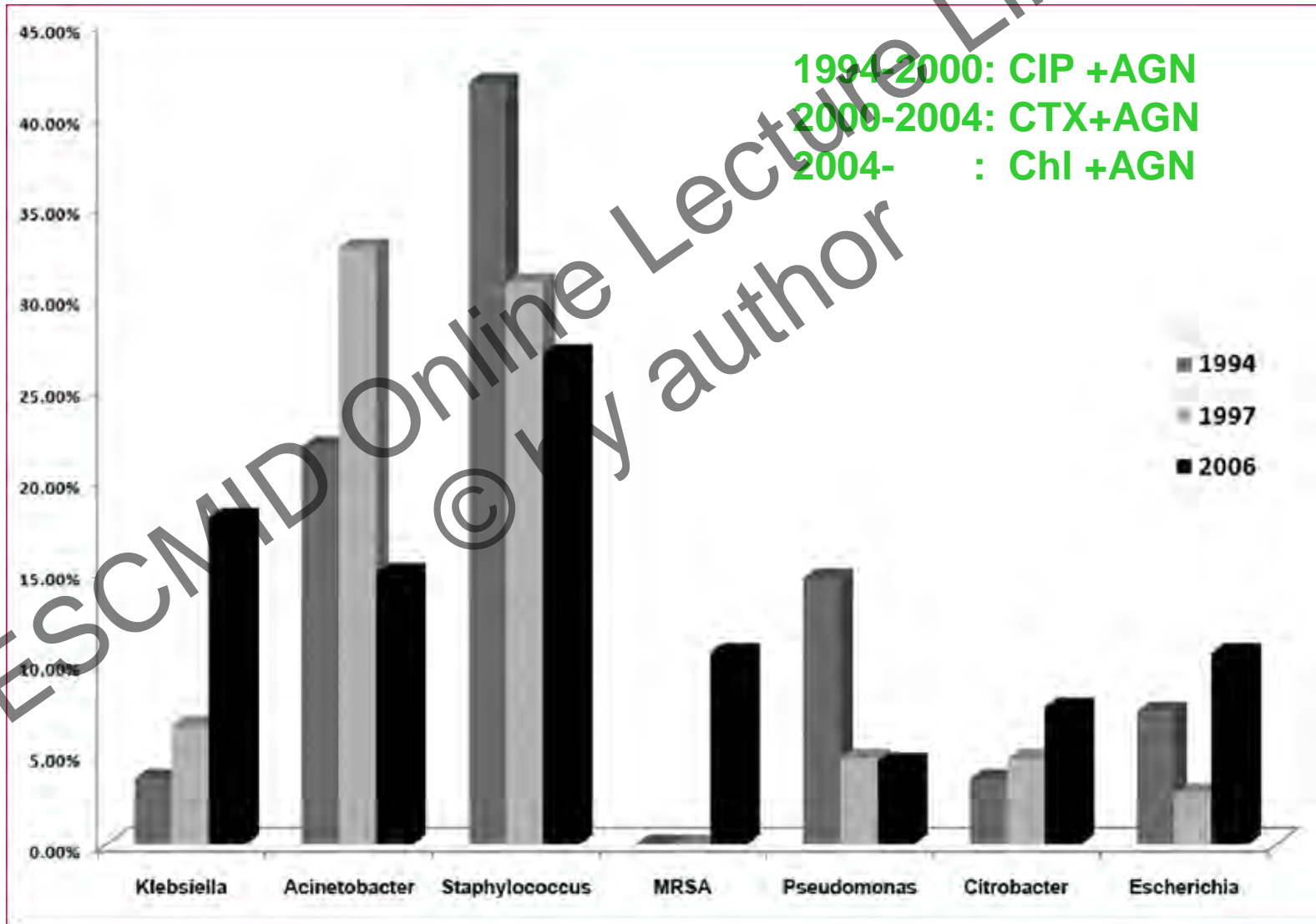
M. Weisfelt<sup>a,\*</sup>, D. van de Beek<sup>a</sup>, L. Spaniaard<sup>b</sup>, J. de Gans<sup>a</sup>

**Table II** Cerebrospinal fluid culture results according to underlying conditions in adults with nosocomial bacterial meningitis

Cerebrospinal fluid culture results	All episodes (N = 50)	History of neurosurgery (N = 32)	Distant focus of infection (N = 9)	Immunocompromised state <sup>a</sup> (N = 14)
<i>Streptococcus pneumoniae</i>	13 (26)	4 (13)	6 (67)	4 (29)
<i>Staphylococcus aureus</i>	12 (24)	10 (31)	2 (22)	2 (14)
<i>Haemophilus influenzae</i>	4 (8)	3 (9)	1 (11)	1 (7)
<i>Staphylococcus epidermidis</i>	3 (6)	2 (6)	0	0
<i>Escherichia coli</i>	3 (6)	2 (6)	0	0
<i>Klebsiella pneumoniae</i>	2 (4)	2 (6)	0	1 (7)
<i>Pseudomonas aeruginosa</i>	2 (4)	2 (6)	0	2 (14)
Other bacterial pathogens <sup>b</sup>	11 (22)	7 (22)	0	4 (29)



# Etiology of CNS infections in Taiwan



# Superinfections!!

## A series of 21 cases

Case	Gender	Age (years)	Underlying condition	Initial pathogen (s)	Antibiotics	Management	Interval* (days)	New presentation	New pathogen(s)	Antibiotics	Management	Survived
More than 7 days interval*												
Gram (+) → G (-) or G (-) → G (+)												
1	M	55	Infarct, craniectomy, EVD	<i>Staphylococcus aureus</i> <sup>S</sup>	LZD+EPM	Removed EVD → new EVDs	61	Fever, leukocytosis, CSF pleocytosis	ESBL- <i>Escherichia coli</i>	MEP	Removed EVD	No
2	F	48	SICH, craniectomy, EVD	<i>Staphylococcus aureus</i> <sup>S</sup>	VA+CAZ	Removed EVD → craniotomy, new EVDs	34	Fever, hydrocephalus	<i>Stenotrophomonas maltophilia</i> <sup>F</sup>	MOX+TMP + TIG+ ATM	Removed EVD → New EVD → removed EVD → VP shunt	Yes
3	F	55	DM, SICH, craniotomy, VPS	<i>Staphylococcus aureus</i> <sup>S</sup>	VA	Removed VPS, debridement → new EVD	11	Fever, CSF pleocytosis	<i>Acinetobacter baumannii</i>	LZD+MEP	New EVD → ventriculo-pleural shunt	Yes
4	F	41	SICH, craniectomy, EVD	<i>Staphylococcus epidermidis</i> <sup>S</sup>	VA	Craniotomy, EVD → VPS	4	No	<i>Enterobacter cloacae</i> + <i>Pseudomonas aeruginosa</i>	CAZ	Removed VPS	No
5	M	73	TICH, craniectomy, EVD (removed)	Coagulase-negative staphylococci <sup>S</sup>	VA	New EVD	9	Fever, seizure, altered consciousness	<i>Enterobacter cloacae</i>	ROC	Removed EVD → VP shunt	Yes
6	M	46	TICH, craniectomy, VPS	Coagulase-negative staphylococci <sup>S</sup>	VA	Externalisation VPS → removed VPS → new EVDs	46	Fever	Coagulase-negative staphylococci <sup>S</sup> + <i>Acinetobacter baumannii</i>	MEP	Removed EVD → new EVDs → VP shunt	Yes
7	M	34	Hydrocephalus, VPS	<i>Staphylococcus epidermidis</i> <sup>S</sup>	VA	Removed VPS, New EVDs	28	Fever, CSF pleocytosis	<i>Acinetobacter spp</i>	CEF	Removed EVD → New EVD → removed → VPS	Yes
8	F	45	Lung cancer, meningeal metastasis, Omayo implant, infection	Coagulase-negative staphylococci <sup>S</sup>	VA	Debridement, removed Omayo implant	42	Fever	<i>Acinetobacter spp</i>	CAZ		Yes
9	F	48	Brain tumor, SICH, craniectomy	<i>Pseudomonas aeruginosa</i>	CEF	New EVD	14	No	<i>Enterococcus spp</i>	AMP+CEF	New EVD → Removed EVD	Yes
10	M	67	DM, SICH, VPS, craniotomy, EVD	<i>Acinetobacter baumannii</i>	MEP	Removed VPS, new EVDs	41	Fever	<i>Staphylococcus aureus</i> <sup>S</sup>	VA	Removed EVD	No



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ORIGINAL ARTICLE

## Clinical characteristics, pathogens implicated and therapeutic outcomes of mixed infection in adult bacterial meningitis

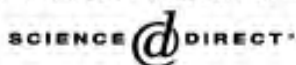
Wan-Chen Tsai<sup>a</sup>, Shu-Fang Chen<sup>a,1</sup>, Wen-Neng Chang<sup>a</sup>, Cheng-Hsien Lu<sup>a</sup>, Yao-Chung Chuang<sup>a</sup>, Nai-Wen Tsai<sup>a</sup>, Chiung-Chih Chang<sup>a</sup>, Chun-Chih Chien<sup>b</sup>, Chi-Ren Huang<sup>a,\*</sup>

- ✓ nosocomially-acquired
- ✓ post-neurosurgical (86 %)
- ✓ **hydrocephalus (p = 0.002)**
- ✓ lower level of CSF WBC, protein & lactate

***Increasing incidence of Pseudomonas spp. and Acinetobacter spp. infections***



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Turkey

## Nosocomial meningitis in a university hospital between 1993 and 2002

I. Palabiyikoglu\*, E. Tekeli, F. Cokca, O. Akan, N. Unal, I. Erberktas, S. Lale, S. Kiraz

**Table V** Causative agents for consecutive years (in descending order)

1993-1998	1999	2000	2001	2002
CNS	CNS	MRSA	MRSA	NFGNB
MSSA	MRSA	NFGNB	NFGNB	MRSA
<i>Klebsiella</i> spp.	NFGNB	<i>Enterococcus</i> spp.	<i>Klebsiella</i> spp.	<i>Candida</i> spp.
<i>Pseudomonas</i> spp.	<i>Candida</i> spp.	<i>Escherichia coli</i>	<i>Pseudomonas</i> spp.	CNS
<i>Escherichia coli</i>	<i>Pseudomonas</i> spp.	<i>Pseudomonas</i> spp.	<i>Escherichia coli</i>	<i>Klebsiella</i> spp.
NFGNB	<i>Enterococcus</i> spp.	<i>Candida</i> spp.	<i>Candida</i> spp.	<i>Pseudomonas</i> spp.
<i>Candida</i> spp.	<i>Escherichia coli</i>	CNS	<i>Enterococcus</i> spp.	<i>Escherichia coli</i>

CNS, coagulase-negative staphylococci; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S. aureus*; NFGNB, non-fermentative Gram-negative bacilli.

## Nosocomial meningitis due to *Acinetobacter calcoaceticus* in 10 children after ventriculoperitoneal shunt insertion

Sir, *Filka J, et al. J Hosp Infect 2000*  
*Slovak Republic*

*Acinetobacter calcoaceticus* is an uncommon cause of nosocomial meningitis.<sup>1</sup> This organism may be multiply antibiotic resistant<sup>2</sup> and outbreaks of infection have been reported, notably from intensive care units.<sup>3,4</sup>

Journal of Hospital Infection (2009) 71, 176–180



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*USA*

## Neurosurgically related nosocomial *Acinetobacter baumannii* meningitis: report of two cases and literature review

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*Infectious Disease Division, Winthrop-University Hospital, Mineola, NY, USA and State University of New York School of Medicine, Stony Brook, NY, USA*

*Turkey*

## ACINETOBACTER BAUMANNII'YE BAĞLI BİR MENENJİT OLGUSU

Dr. Mustafa SÜN BÜL, Dr. Cafer EROĞLU, Dr. Zeynep AKÇAM  
Dr. Hakan LEBLEBİCİOĞLU

*Üniversitesi Tıp Fakültesi, Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Anabilim  
Dr. SAMSUN*

Journal of Hospital Infection (2004) 57, 300–307



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## Outbreak of nosocomial meningitis caused by *Acinetobacter baumannii* in neurosurgical patients

M.M. Wroblewska<sup>a,b,\*</sup>, L. Dijkshoorn<sup>c</sup>, H. Marchel<sup>b</sup>, M. van den Barselaar<sup>c</sup>,  
E. Swoboda-Kopec<sup>a,b</sup>, P.J. van den Broek<sup>c</sup>, M. Luczak<sup>a,b</sup>

Research article

Open Access

## **Nosocomial outbreak of neonatal *Salmonella enterica* serotype Enteritidis meningitis in a rural hospital in northern Tanzania**

Hogne Vaagland<sup>\*1,2</sup>, Bjørn Blomberg<sup>2,3</sup>, Carsten Krüger<sup>4,5</sup>, Naftali Naman<sup>4</sup>, Roland Jureen<sup>3</sup> and Nina Langeland<sup>3,6</sup>

# *Acinetobacter* spp. meningitis

## ✓ Incidence

- Adult                    %3.6
  - Children                %11
  - Leading cause of postneurosurgical meningitis in Turkey
- } ranked 5<sup>th</sup> in USA & Taiwan

## ✓ Mortality

- ≥ 15%
- 72.7 in Brazil

*Kim BN, et al. Lancet Infect Dis 2009; 9:245-55*  
*Metan G, et al. Int J Antimicrob Agents 2007;29: 112–13.*  
*Sacar S, et al. BMC Infect Dis 2006; 6: 43.*  
*Tuon FF, et al. Braz J Infect Dis 2010;14(5):437-440*

## Summary of 76 patients reported with acinetobacter meningitis (1980–July 2008)

### Primary neurosurgical diagnosis

Spontaneous intracranial haemorrhage	25 (32.9)
Traumatic head injury	18 (23.7)
Brain tumour	16 (21.1)
Others	6 (7.9)
No neurosurgical disease	11 (14.5)

### Prior procedure(s)

Craniotomy	37 (48.7)
Insertion or exchange of external ventricular drain (EVD)	33 (43.4)
Ventriculoperitoneal shunt	11 (14.5)
Insertion of lumbar drain	3 (3.9)
Others	3 (3.9)
No neurosurgical procedure	15 (19.7)



**Molecular epidemiology and the clinical significance of *Acinetobacter baumannii* complex isolated from cerebrospinal fluid in neurosurgical intensive care unit patients**

G. Bayramoglu · S. Kaya · Y. Besli ·  
E. Cakir · G. Can · O. Akmeden · F. Aydin ·  
I. Koksal

- ✓ 21 / 30 isolates were clinically significant
- ✓ The prolonged (>7 days) use of cephalosporins was more common in patients with clinically significant ABC isolates ( $p = 0.049$ ).

# Take home message,

- ✓ Epidemiologic data is increasing
  - But still limited for underdeveloped countries
  - Varying incidence of meningitis/infection after various interventions of CNS
  - Mortality is higher in developing countries
  - In order to compare, device-associated rates are needed

✓ Etiology is changing

- Acinetobacter infections have a role as well as other gram negatives
- Mixed & superinfections are being reported

✓ Mortality is higher with gram negatives