



# JNI

13<sup>es</sup> Journées  
Nationales  
d'Infectiologie

Tours et le GÉRICCO

Du mercredi 13 au  
vendredi 15 juin 2012  
VINCI - Centre International  
de Congrès



## Best of 'neuro-infectieux' 2011-2012

Pierre TATTEVIN  
Maladies Infectieuses et Réanimation Médicale  
CHU Pontchaillou  
Rennes



# Déclaration de liens d'intérêts de 2010 à 2012

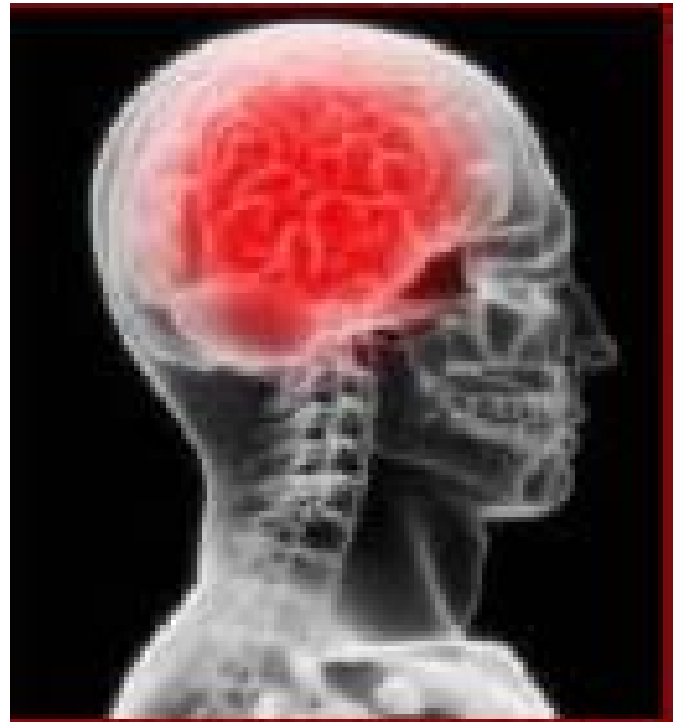
## Pierre Tattevin

- Intervenant au titre de consultant : Galderma
- Intervenant au titre d'orateur : Pfizer, Janssen, BMS, Novartis, Aventis, ViiV, Cellestis
- Participation à des groupes de travail: Astra-Zeneca, Janssen, BMS
- Invitations à des congrès ou des journées scientifiques : Astellas, Janssen, Aventis, Pfizer, Novartis, BMS, MSD



**Best of:  
Plus  
d'égalité !**

# 1. Méningites, 2011-2012





# Immunogenicity and Safety of a Meningococcal A Conjugate Vaccine in Africans

Samba O. Sow, M.D., Brown J. Okoko, M.D., M.P.H.,\*

## Rappel

- **Méningocoque A** = principal coupable, dans la ceinture méningitique
- Vaccin polysaccharidique A = efficace, mais **nécessité de rappels**
- Vaccins conjugués ACYW135 = **chers, pas très efficaces** sur méningo A

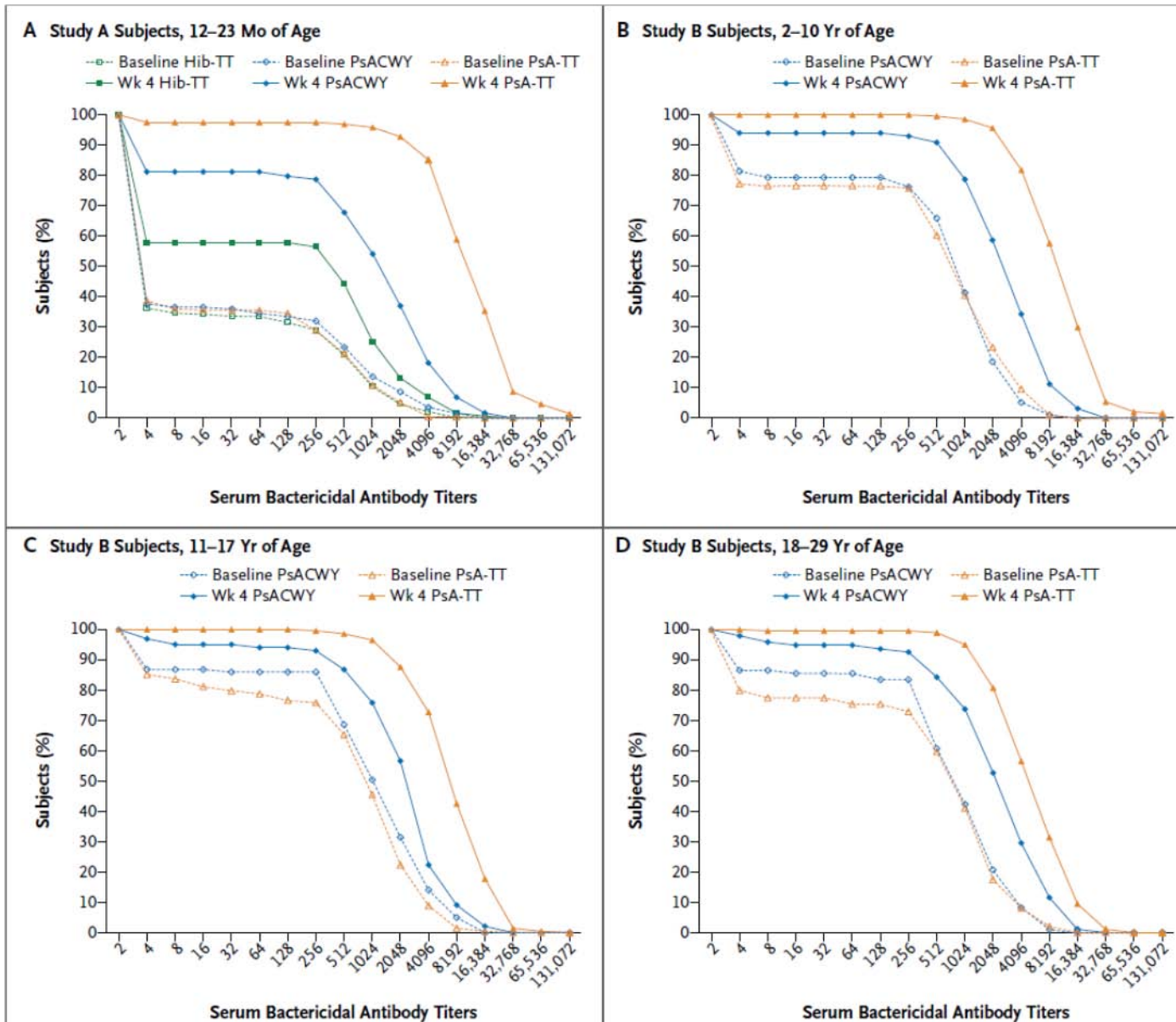
## Meningitis Vaccine Project

- Consortium OMS, PATH, Bill & Melinda Gates
- Objectif: vaccin conjugué anti-méningocoque A
- **Coût = 0,5 €/dose**
- **Efficacité > 10 ans**

=> **MenAfriVac™**

# 2 essais randomisés, Mali-Gambie-Sénégal (2006-)

- Etudes A: 601 enfants (12-24 mois) et B: 900 sujets 2-29 ans
- Comparateur: vaccins conjugués ACYW135

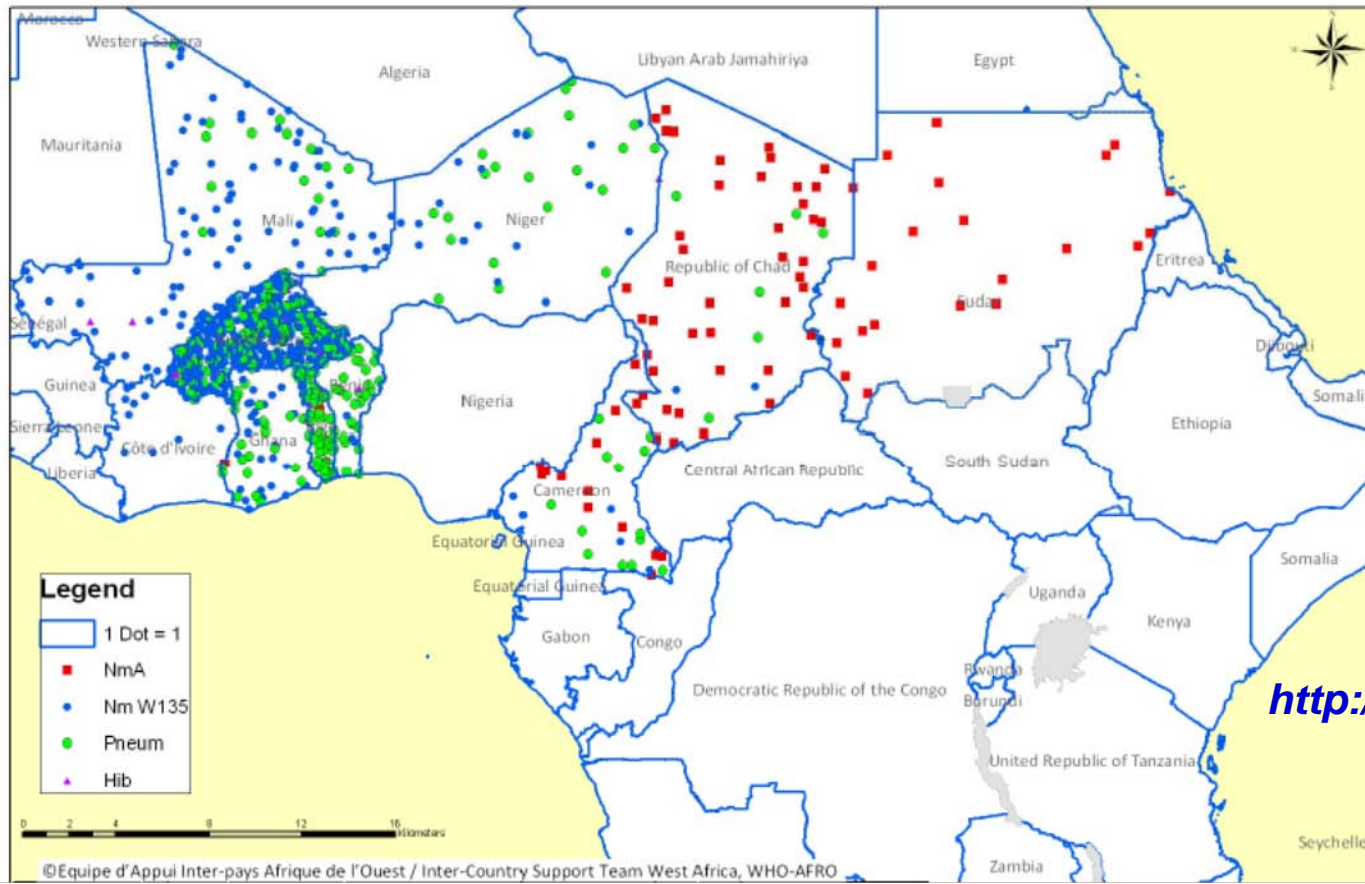


# MenAfriVac: Efficacité opérationnelle

- 55 M de sujets vaccinés (1-29 ans, 2010-11)
- Burkina, Mali, Niger
- Objectif 265 M vaccinés => stop épidémies



Figure 3 : Cartographie des principaux germes de la Méningite, Semaine 01 - 20, 2012  
*Map of Meningitis main pathogens, Week 01 - 19, 2012*

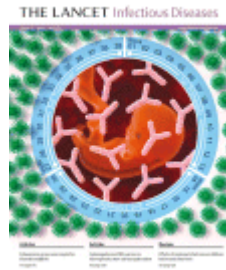


<http://www.meningvax.org>

# Slow initial $\beta$ -lactam infusion and oral paracetamol to treat childhood bacterial meningitis: a randomised, controlled trial



Lancet Infect Dis 2011;  
11: 613-21



*Tuula Pelkonen, Irmeli Roine, Manuel Leite Cruzeiro, Anne Pitkäranta, Matti Kataja, Heikki Peltola*

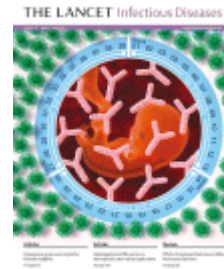
- ✓ Angola, 723 enfants (2 mois-13 ans)
- ✓ Etude randomisée, **double-aveugle, factorielle 2 x2**
- 1. **Céfotaxime, 250 mg/kg/j en perf. continue, ou en 4 fois**
- 2. **Paracétamol, 20 mg/kg x 4/j ou placebo**
- ✓ Critère principal: **mortalité ou séquelles sévères**



# Slow initial $\beta$ -lactam infusion and oral paracetamol to treat childhood bacterial meningitis: a randomised, controlled trial

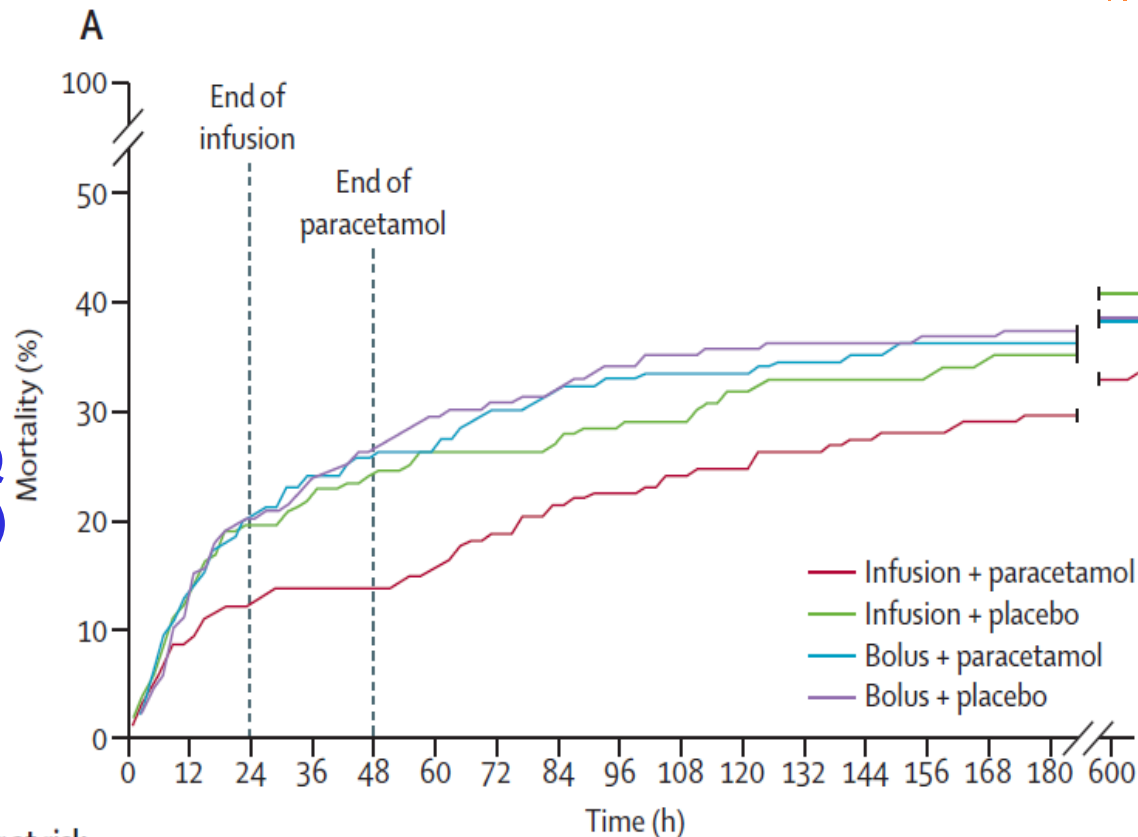


Lancet Infect Dis 2011;  
11: 613-21



Tuula Pelkonen, Irmeli Roine, Manuel Leite Cruzeiro, et al.

- ✓ Mortalité ou séquelles graves: 47%, sans impact significatif des interventions
- ✓ Perf. continue bénéfique pour les méningites à PCQ (OR 0,18 [0,03-0,9],  $P=0,04$ )
- ✓ Bénéfice bras 'céfotaxime continu + paracétamol' (post hoc => à confirmer)



	0	12	24	36	48	60	72	84	96	108	120	132	144	156	168	180	600
Number at risk																	
Infusion + paracetamol	183	167	160	158	157	154	147	142	140	137	136	133	130	129	124	123	13
Infusion + placebo	180	156	145	140	137	133	132	130	128	127	122	120	120	119	116	115	7
Bolus + paracetamol	180	157	143	137	133	132	126	123	121	120	120	118	114	112	110	110	7
Bolus + placebo	180	157	144	138	133	127	125	123	119	117	116	115	115	114	110	109	3
All	723	637	592	573	560	546	530	518	508	501	494	486	479	474	460	457	30



# 5 versus 10 days of treatment with ceftriaxone for bacterial meningitis in children: a double-blind randomised equivalence study

Elizabeth Molyneux, Shaikh Qamaruddin Nizami, Samir Saha, Khanh Truong  
Martin Willi Weber, Shamim Ahmad Qazi, for the CSF 5 Study Group\*

- ✓ Etude randomisée, **double aveugle**,
- ✓ Bangladesh, Egypte, Malawi, Pakistan, Vietnam 2001-2006
- ✓ **1004 enfants (2 mois-12 ans)**  
Âge moyen, 3 ans
- ✓ Méningite purulente
- ✓ **Stable à J5 de ceftriaxone**

	5-day treatment group (n=496)	10-day treatment group (n=508)
<b>Overall outcomes for all children</b>		
Therapy successfully completed (10 days)	469 (95%)	485 (96%)

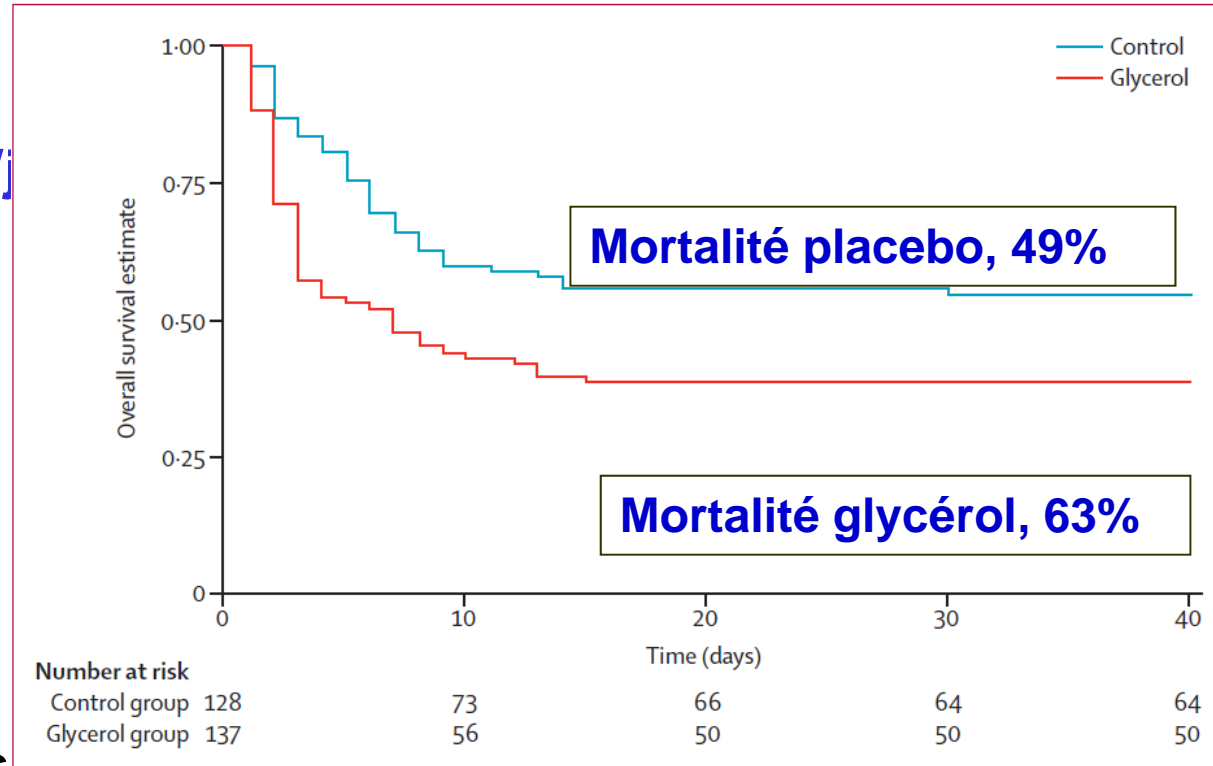
<b>Study outcomes by cause</b>		
<i>Streptococcus pneumoniae</i>	n=154	n=181
Death due to any reason after cure (all deaths)	12	9
Survival with sequelae (all)	54	72
Antibiotic therapy modified after random assignment or therapy failure	2	3
<i>Haemophilus influenzae</i>	n=134	n=132
Death due to any reason after cure (all deaths)	4	5
Survival with sequelae (all)	33	31
Antibiotic therapy modified after random assignment or therapy failure	6	5
<i>Neisseria meningitidis</i>	n=46	n=27
Death due to any reason after cure (all deaths)	1	0
Survival with sequelae (all)	6	3
Antibiotic therapy modified after random assignment or therapy failure	1	0

# Glycerol adjuvant therapy in adults with bacterial meningitis in a high HIV seroprevalence setting in Malawi: a double-blind, randomised controlled trial



Katherine M B Ajdukiewicz, Katharine E Cartwright, Matthew Scarborough, James B Mwambene, Patrick Goodson, Malcolm E Molyneux, Eduard E Zijlstra, Neil French, Christopher J M Whitty, David G Lalloo

- ✓ Etude randomisée, **double aveugle**, Malawi 2006-8
- ✓ **oral glycérol, 75 mL x 4/j** vs placebo, x 4 j
- ✓ **265 adultes, 83% VIH+**  
46% ATB avant inclusion  
médiante symptômes, 5 j
- ✓ Essai stoppé après analyse intermédiaire planifiée **aOR pour décès 2,4 [1,3-4,2],  $p=0,003$**

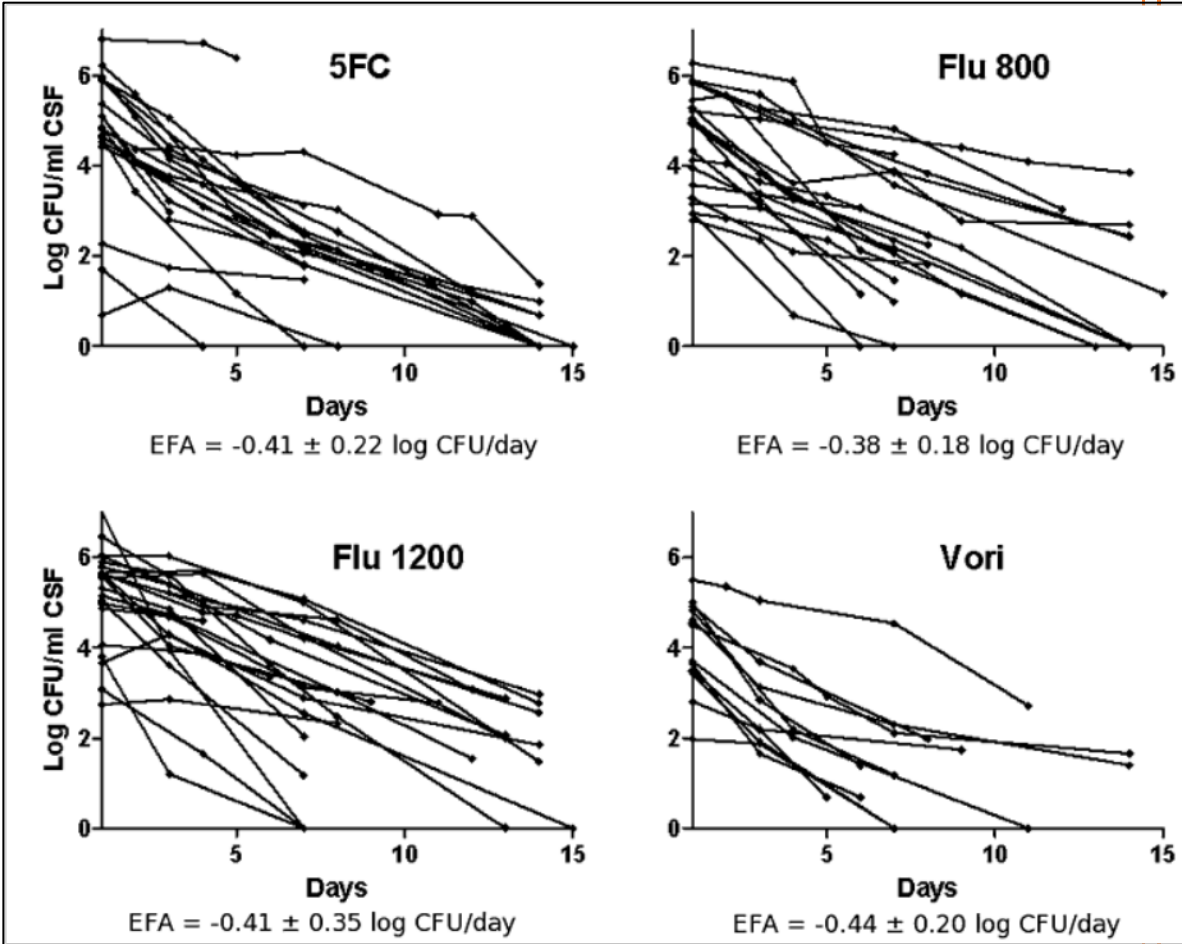




# Comparison of the Early Fungicidal Activity of High-Dose Fluconazole, Voriconazole, and Flucytosine as Second-Line Drugs Given in Combination With Amphotericin B for the Treatment of HIV-Associated Cryptococcal Meningitis

Angela Loyse,<sup>1,2,3,4</sup> Douglas Wilson,<sup>3</sup> Graeme Meintjes,<sup>1,5,6</sup> Joseph N. Jarvis,<sup>4</sup> Tihana Bicanic,<sup>4</sup> Leesa Bishop,<sup>3</sup> Kevin Rebe,<sup>1,5</sup> Anthony Williams,<sup>1</sup> Shabbar Jaffar,<sup>7</sup> Linda-Gail Bekker,<sup>2</sup> Robin Wood,<sup>2</sup> and Thomas S Harrison<sup>4</sup>

- ✓ Etude randomisée ouverte, Afrique du Sud 2006-8
- 80 VIH+, naïf ARV
- ✓ 4 bras 'd'attaque' (14 j)
- AmB 0,7-1 mg/kg/j i.v. +
- 5-FC 100 mg/kg/j, ou
- Fluco 800 mg/j, ou
- Fluco 1200 mg/j, ou
- Vorico 600 mg/j
- Traitement entéral (P.O. ou SNG)
- Décès 12% (J14), 29% (J70)



## 2. Encéphalites, 2011-2012

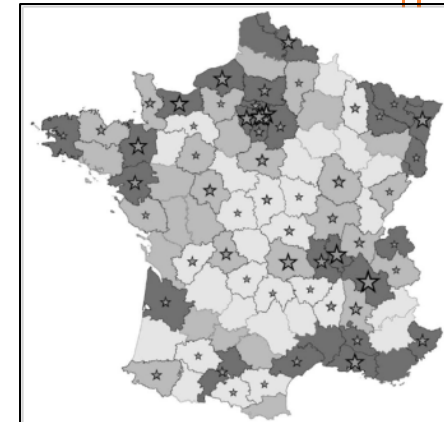
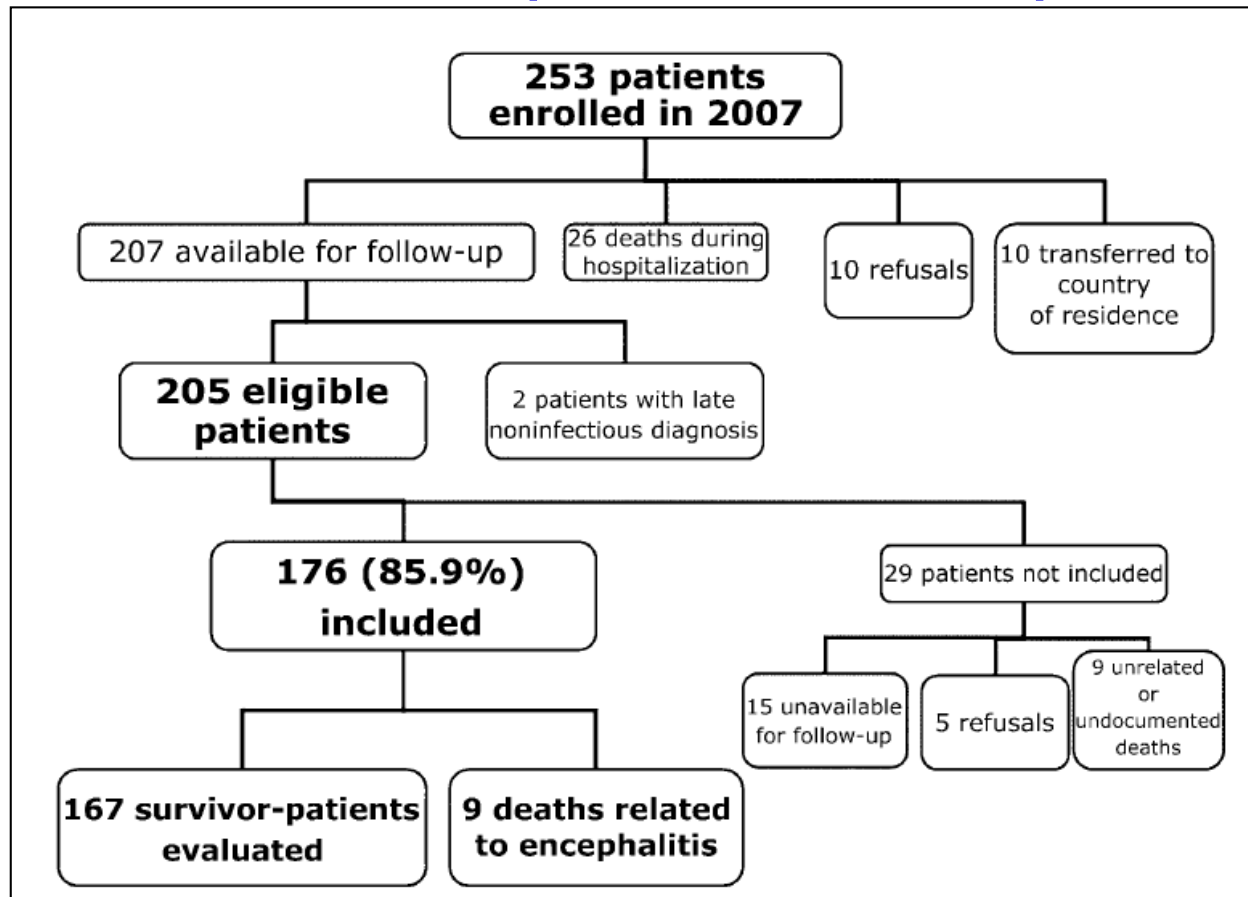


# Long-term Outcome of Patients Presenting With Acute Infectious Encephalitis of Various Causes in France



Alexandra Mailles,<sup>1</sup> Thomas De Broucker,<sup>2</sup> Pascale Costanzo,<sup>3</sup> Laurent Martinez-Almoyna,<sup>4</sup> Véronique Vaillant,<sup>1</sup> Jean-Paul Stahl,<sup>5</sup> on behalf of the Steering Committee and Investigators Group

Que sont devenus les rescapés de l'étude 'encéphalite 2007' 3 ans + tard ?



# Long-term Outcome of Patients Presenting With Acute Infectious Encephalitis of Various Causes in France



Alexandra Mailles,<sup>1</sup> Thomas De Broucker,<sup>2</sup> Pascale Costanzo,<sup>3</sup> Laurent Martinez-Almoyna,<sup>4</sup> Véronique Vaillant,<sup>1</sup> Jean-Paul Stahl,<sup>5</sup> on behalf of the Steering Committee and Investigators Group

## ✓ Principaux troubles

Concentration (42%)

Comportement (27%)

Langage (20%)

Mémoire (19%)

## ✓ FDR évolution à 3 ans

- Favorables

Ni HSV, ni VZV

Education

- Défavorables

Âge

Co-morbidités

**Table 1. Glasgow Outcome Scale (GOS) Categories and Outcomes in Patients Included in Follow-up Study**

GOS Score	Clinical Meaning	Outcome	Patients, No. (%)
1	Death	Poor	9 (5)
2	Neurovegetative state; patient unresponsive and speechless for weeks or months	Poor	3 (2)
3	Severe disability; patient dependent for daily support	Poor	25 (14)
4	Moderate disability; patients independent in daily life	Poor	31 (18)
5	Good recovery; resumption of normal life with minor neurological and psychological deficits	Favorable	108 (61)

# The Frequency of Autoimmune N-Methyl-D-Aspartate Receptor Encephalitis Surpasses That of Individual Viral Etiologies in Young Individuals Enrolled in the California Encephalitis Project



Mary S. Gable,<sup>1</sup> Heather Sheriff,<sup>1</sup> Josep Dalmau,<sup>2,3</sup> Drake H. Tilley,<sup>4</sup> and Carol A. Glaser<sup>1</sup>

⏏ 1<sup>ère</sup> cause de méningo-encéphalite avant 30 ans

⏏ 30 cas sur 79 documentés (HSV1, n=7)

⏏ Femme jeune avec troubles mnésiques, psychose, convulsions, mouvements anormaux

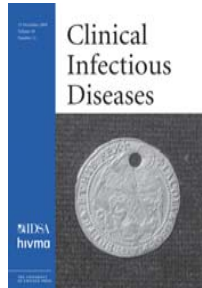
⏏ Association avec tumeur de l'ovaire

⏏ Traitement

⏏ Exérèse tumeur (même si bénigne)

⏏ Immunosuppresseurs

- IgIV, voire plasmaphérèse
- + corticothérapie à dose 'de cheval' (bolus 1 g/j)



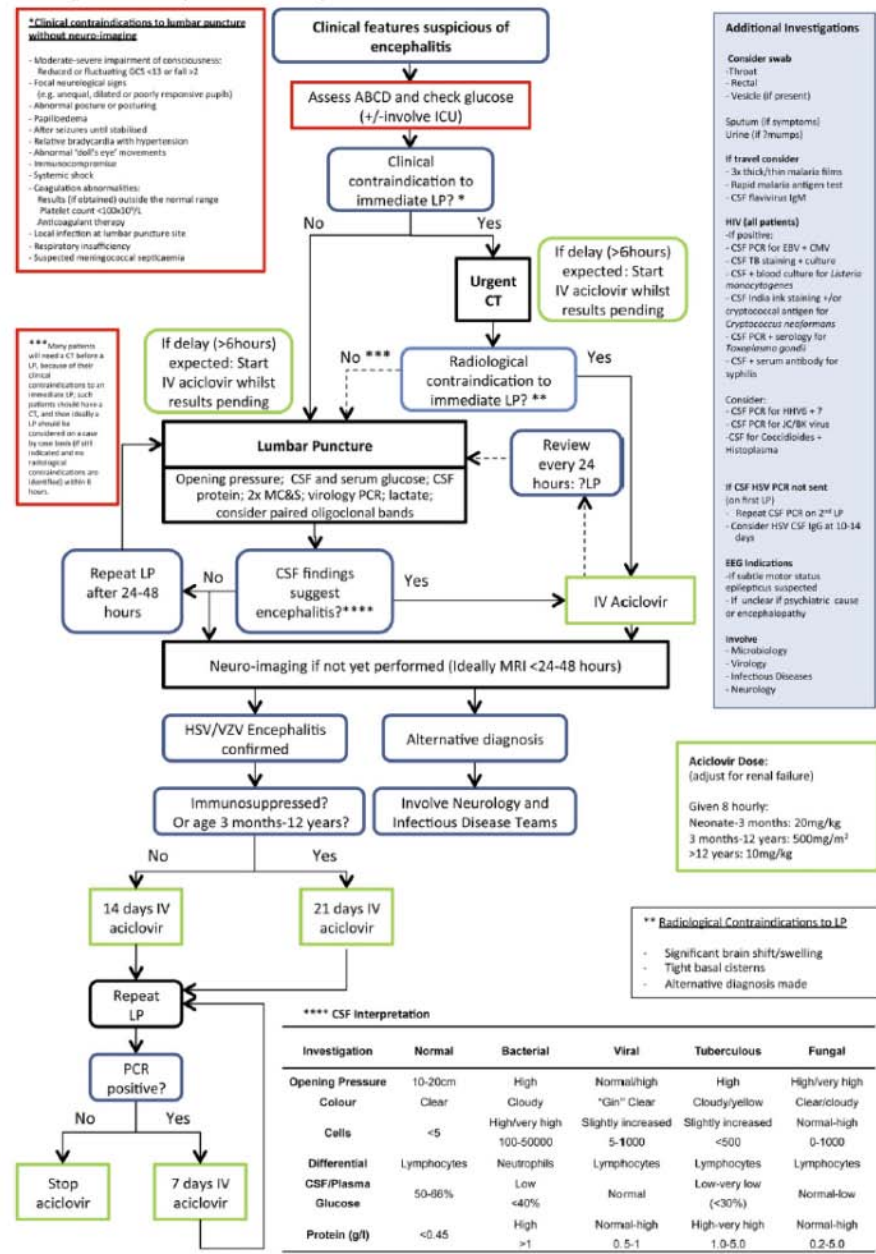


# Management of suspected viral encephalitis in adults – Association of British Neurologists and British Infection Association National Guidelines

T. Solomon <sup>a,b,\*</sup>, B.D. Michael <sup>a,b,l,u</sup>, P.E. Smith <sup>c,m</sup>, F. Sanderson <sup>d,n</sup>, N.W.S. Davies <sup>e,o</sup>, I.J. Hart <sup>f,p</sup>, M. Holland <sup>g,q</sup>, A. Easton <sup>h,r</sup>, C. Buckley <sup>i,s</sup>, R. Kneen <sup>j,t</sup>, N.J. Beeching <sup>k,p</sup>, On behalf of the National Encephalitis Guidelines Development and Stakeholder Groups



## Management of suspected viral encephalitis



Patients (when conscious level permits) and their next-of-kin should be made aware of the support provided by voluntary sector partners such as the Encephalitis Society ([www.encephalitis.org/](http://www.encephalitis.org/))

Abbreviations: ABCD Awake Breathing Circulation and Disability; CMV Cytomegalovirus; CSF cerebrospinal fluid; CT computed tomography; EBV Epstein Barr virus; EEG Electroencephalograph; GCS Glasgow coma score; HIV Human Immunodeficiency virus; IV intravenous; MC+S Microscopy culture and sensitivity; MRI Magnetic resonance imaging; PCR Polymerase chain reaction; TB Tuberculosis; VZV Varicella zoster virus

Figure 1 Algorithm for the management of patients with suspected encephalitis.

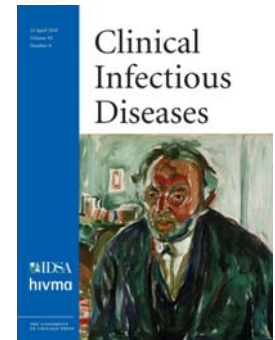
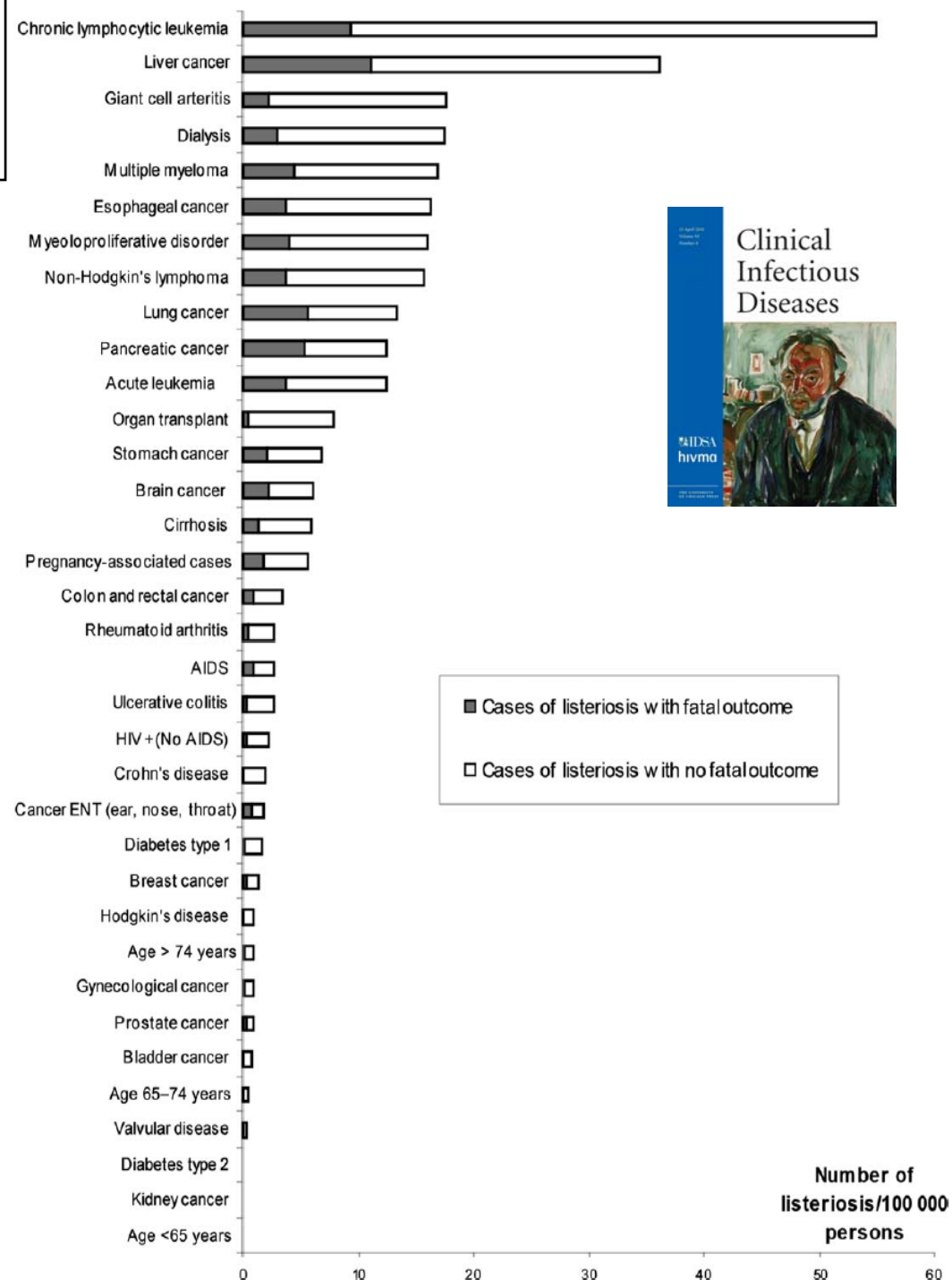
# Incidence of Listeriosis and Related Mortality Among Groups at Risk of Acquiring Listeriosis

Véronique Goulet,<sup>1</sup> Marjolaine Hebert,<sup>1</sup> Craig Hedberg,<sup>2</sup> Edith Laurent,<sup>1</sup> Véronique Vaillant,<sup>1</sup> Henriette De Valk,<sup>1</sup> and Jean-Claude Desenclos<sup>1</sup>

**1959 listérioses documentées en France (2001-2008)**

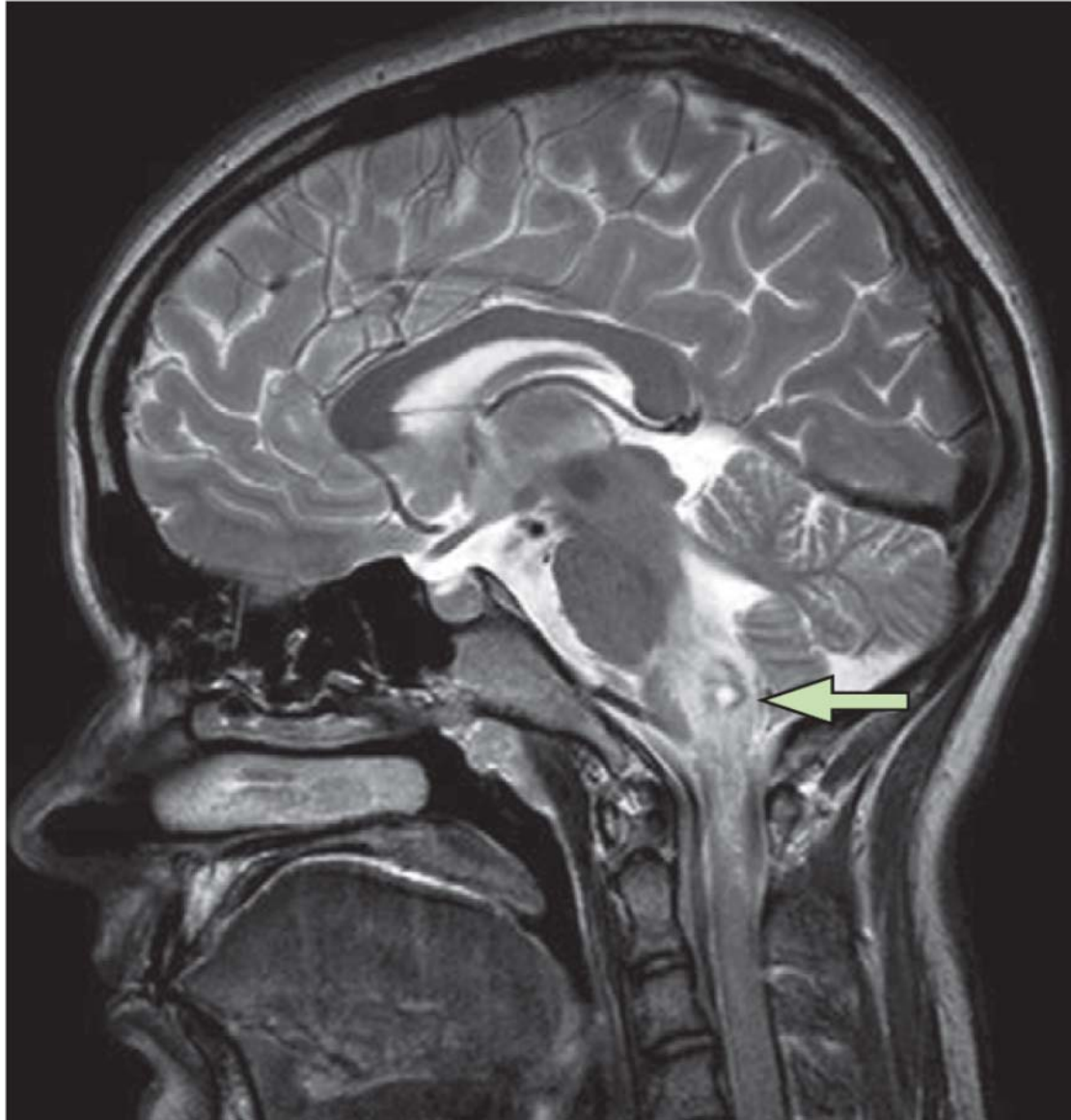
**Estimation incidence selon groupes à risques**

**11 maladies cancéreuses parmi les 'top 15'**



# A strange case of waitress headache

*Dacia Dalla Libera, Bruno Colombo, Giulio Truci, Paolo Rossi, Donatella De Feo, Simon Tiberi, Vittorio Martinelli, Giancarlo Comi*



Doctors strike: "The BMJ's long list of 'Standing up for doctors'. The BMA has, directly speaking, done its job well. In doing so it may have lost the respect and goodwill of a large section of the British public, especially those who are affected by the strike action."

# Rhombencephalitis

## A Series of 97 Patients

Mireia Moragas, MD, Sergio Martínez-Yélamos, MD, Carles Majós, MD, Pedro Fernández-Viladrich, MD, Francisco Rubio, MD, and Txomin Arbizu, MD

**TABLE 1.** Etiologic Spectrum of Rhombencephalitis in 97 Patients

<b>Etiology</b>	<b>Patients</b>
Unknown cause	31
Multiple sclerosis	28
Behçet disease	10
<i>Listeria monocytogenes</i>	9
Paraneoplastic syndrome	6
Anti-Yo antibodies	3
Anti-Tr antibodies	3
Epstein-Barr virus	4
Tuberculosis	2
Pneumococcal infection	2
Systemic lupus erythematosus	1
Lymphoma	1
<i>Brucella</i>	1
JC virus	1
Relapsing polychondritis	1
Total	97

### 3. Divers neuro-infectieux, 2011-12

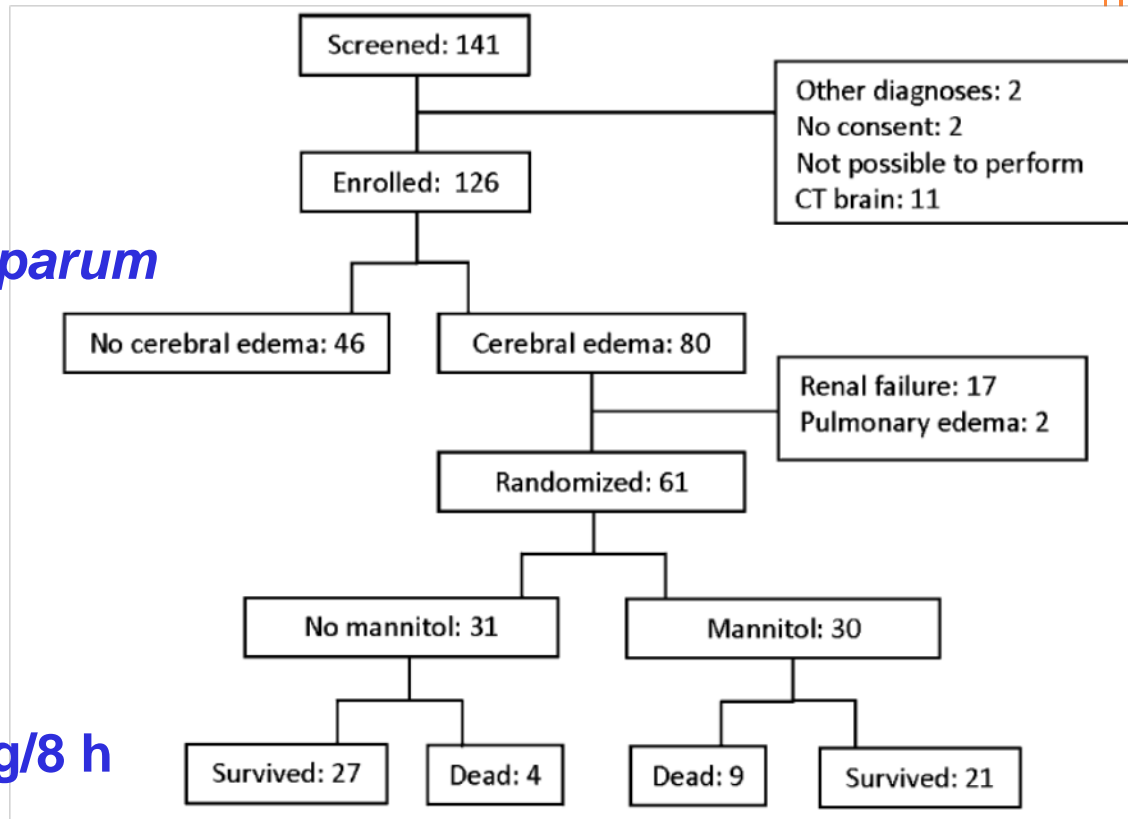




# Brain Swelling and Mannitol Therapy in Adult Cerebral Malaria: A Randomized Trial

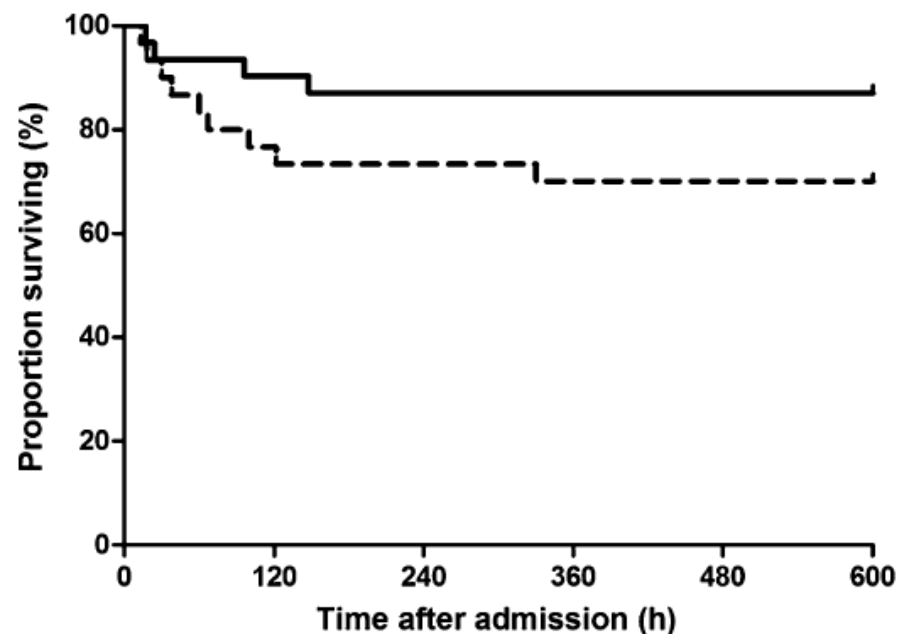
Sanjib Mohanty,<sup>1</sup> Saroj Kanti Mishra,<sup>1</sup> Rajyabardhan Patnaik,<sup>1</sup> Anil Kumar Dutt,<sup>1</sup> Sudhir Pradhan,<sup>1</sup> Bhabanisankar Das,<sup>1</sup> Jayakrushna Patnaik,<sup>1</sup> Akshaya Kumar Mohanty,<sup>1</sup> Sue J Lee,<sup>2,3</sup> and Arjen M. Dondorp<sup>2,3</sup>

- ✓ Etude monocentrique, Inde
- ✓ 141 patients avec coma (GCS<11) + paludisme *P. falciparum*
- ✓ 126 TDM cérébraux
- ✓ 80 (63%) œdème cérébral
- ✓ 61 patients randomisés
- ✓ Mannitol 1,5 g/kg puis 0,5 g/kg/8 h



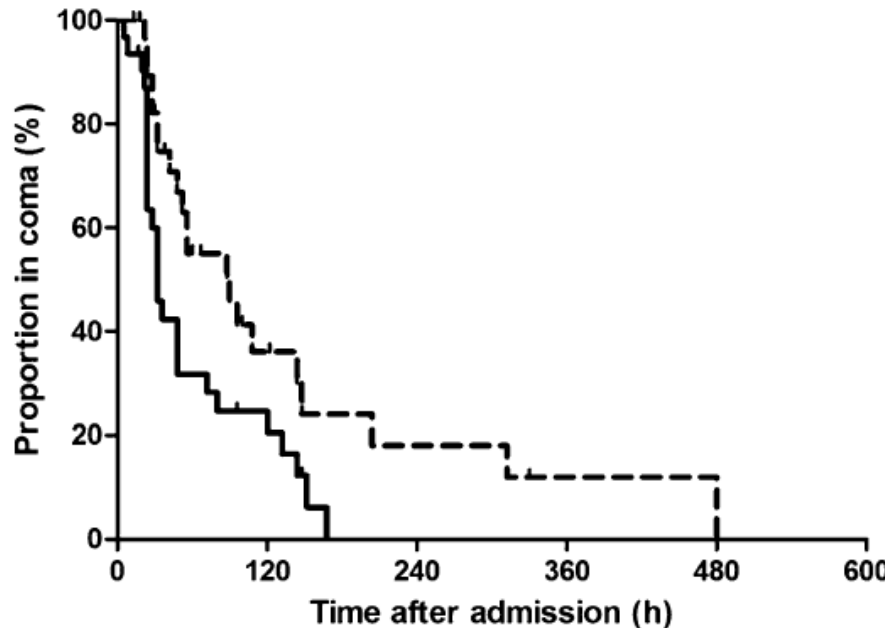
# Brain Swelling and Mannitol Therapy in Adult Cerebral Malaria: A Randomized Trial

Sanjib Mohanty,<sup>1</sup> Saroj Kanti Mishra,<sup>1</sup> Rajyabardhan Patnaik,<sup>1</sup> Anil Kumar Dutt,<sup>1</sup> Sudhir Pradhan,<sup>1</sup> Bhabanisankar Das,<sup>1</sup> Jayakrushna Patnaik,<sup>1</sup> Akshaya Kumar Mohanty,<sup>1</sup> Sue J Lee,<sup>2,3</sup> and Arjen M. Dondorp<sup>2,3</sup>



--- Mannitol  
— Control

**Mortalité 30% vs. 13% ( $p=0,11$ )**



--- Mannitol  
— Control

**Médiane coma 90 h vs. 32 h ( $p=0,02$ )**

# Iatrogenic Creutzfeldt-Jakob Disease, Final Assessment

Paul Brown, Jean-Philippe Brandel, Takeshi Sato, Yosikazu Nakamura, Jan MacKenzie, Robert G. Will, Anna Ladogana, Maurizio Pocchiari, Ellen W. Leschek, and Lawrence B. Schonberger



## Trois groupes

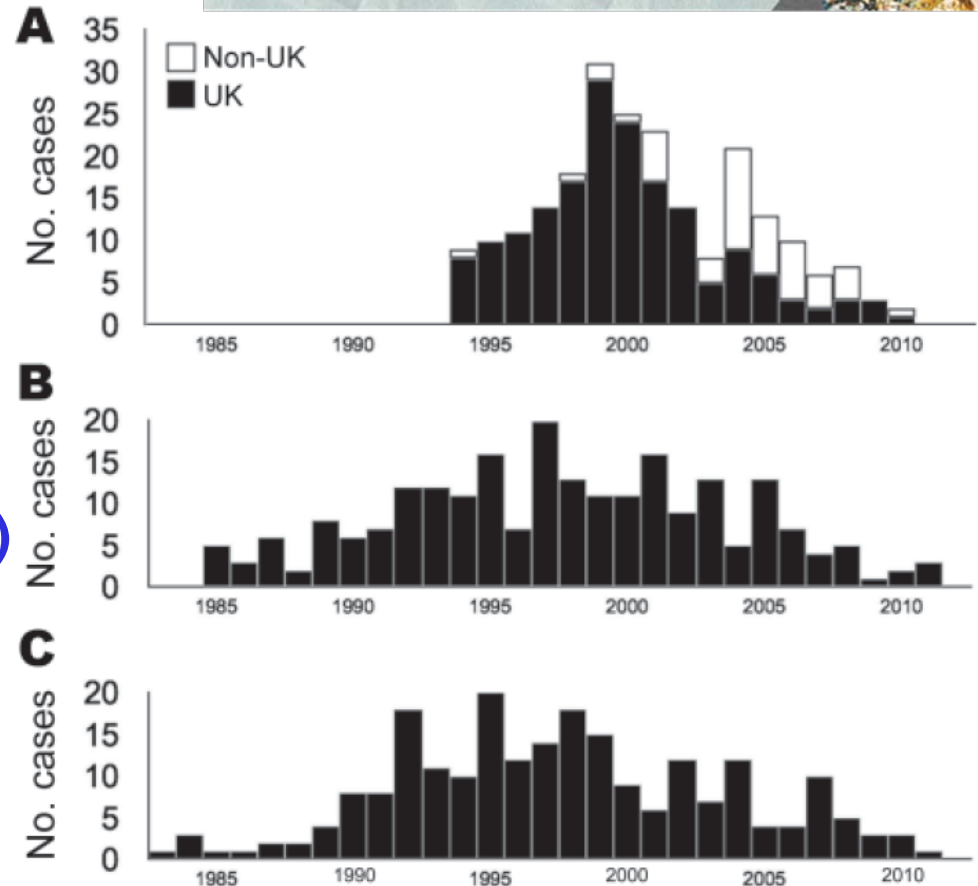
### A. Viande bovine

### B. Hormone de croissance (n=226)

- Incubation moy. 17 ans (5-42)
- **France, n=119 (attaque 6,3%)** contamination 1983-1985
- Royaume Uni, n=65

### C. Greffe dure-mère (n=228)

- Incubation moy. 12 ans (1-30)
- **Japon, n=142**





# Central nervous system involvement in dengue

A study in fatal cases from a dengue endemic area

F.M.C. Araújo, PhD  
M.S. Araújo, MD  
R.M.R. Nogueira, MD, PhD  
R.S.N. Brilhante, PhD  
D.N. Oliveira, MD  
M.F.G. Rocha, PhD  
R.A. Cordeiro, PhD  
R.M.C. Araújo, MD  
J.J.C. Sidrim, MD, PhD

*Epidémie dengue, état de Ceara Nord-Est Brésil*

## 150 décès suspects d'infections

✓ 84 dengues confirmées

✓ Dont 41 LCR +

Encéphalite (n=19), méningo-encéphalite (n=14) et méningite (n=8)

**Table 1** Dengue laboratory confirmation according to the diagnosis hypothesis at the moment of necropsy

Patients	DENV +, n (%)	DENV -, n (%)	Total, n (%)
Suspected of dengue	65 (43.3)	30 (20.0)	95 (63.3)
Not suspected of dengue	19 (12.7)	36 (24.0)	55 (36.7)
Total	84 (56.0)	66 (44.0)	150 (100)

**Table 2** Results of 84 fatal dengue cases according to available specimens and methodologies

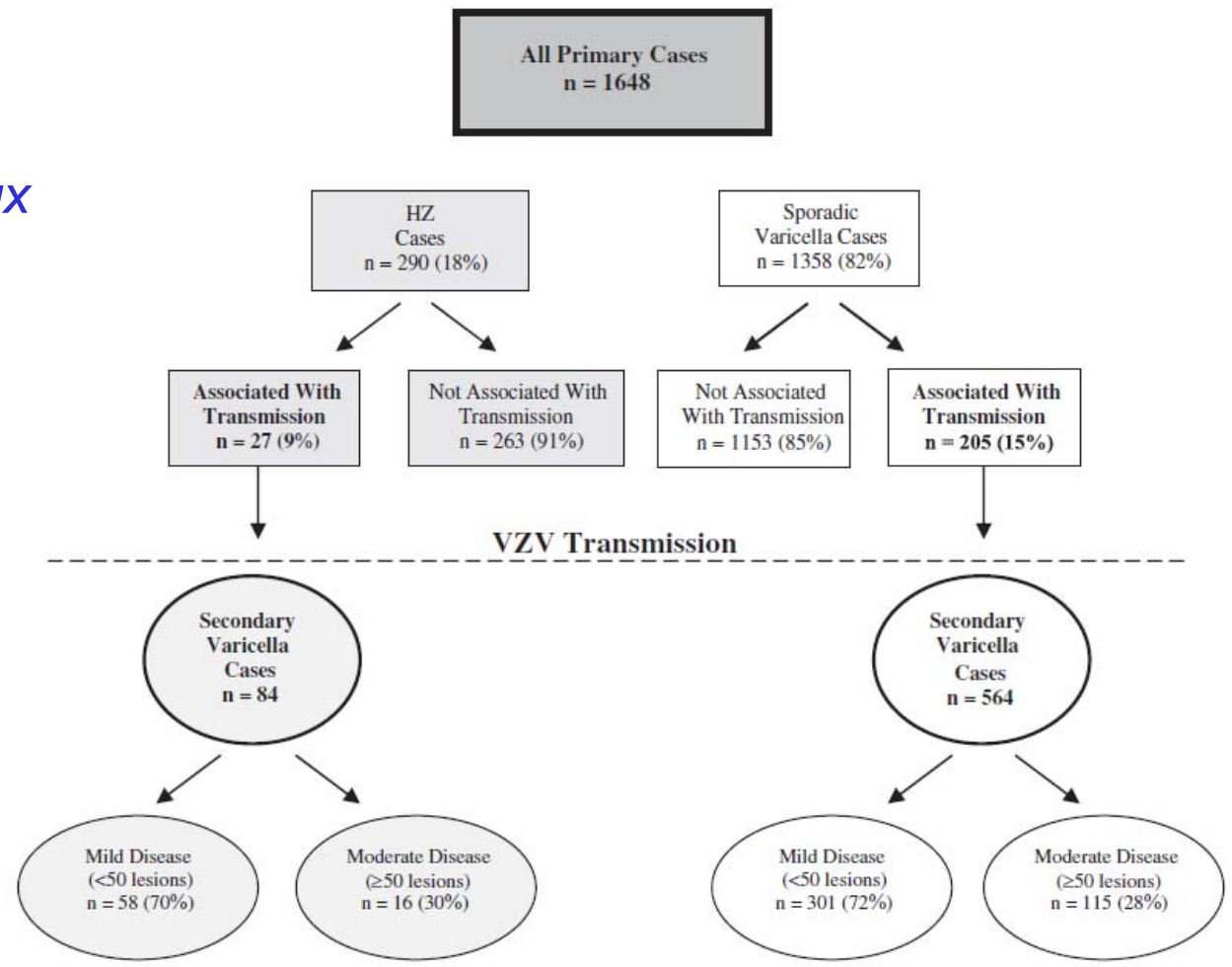
Clinical sample	RT-PCR, P/T (%)	Virus isolation, P/T (%)	Serotype detected	IgM, P/T (%)	IgG, P/T (%)	NS1Ag, P/T (%)	IHC, P/T (%)
CSF	7/84 (8.3)	1/84 (1.2)	3 DENV-2; 5 DENV-3	27/84 (32.1)	34/84 (40.5)	22 /84 (26.2)	ND
Sera	2/29 (6.9)	0/29 (0.0)	2 DENV-3	13/29 (44.8)	13/29 (44.8)	ND	ND
Blood	ND	1/80 (1.2)	1 DENV-3	ND	ND	ND	ND
Liver tissues	ND	ND	ND	ND	ND	ND	57/84 (67.9)
Total	9/113 (8.0)	2/193 (1.0)	3 DENV 2; 8 DENV 3	40/113 (35.4)	47/113 (41.6)	22/84 (26.2)	57/84 (67.9)

# Transmission of Varicella Zoster Virus From Individuals With Herpes Zoster or Varicella in School and Day Care Settings



Kendra Viner,<sup>1</sup> Dana Perella,<sup>1</sup> Adriana Lopez,<sup>2</sup> Stephanie Bialek,<sup>2</sup> Claire Newbern,<sup>1</sup> Rodrerica Pierre,<sup>1</sup> Niya Spells,<sup>1</sup> and Barbara Watson<sup>1</sup>

*Zona aussi contagieux que varicelle ?*



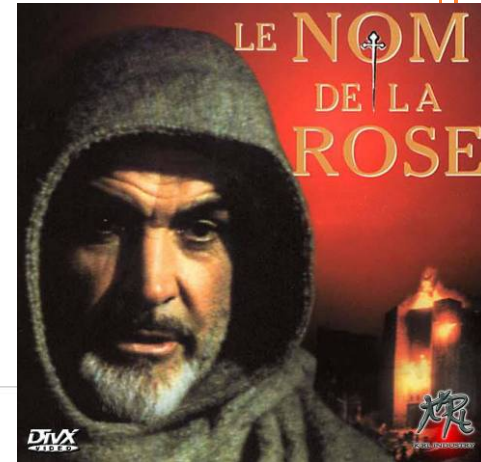


# Does Monastic Life Predispose to the Risk of Saint Anthony's Fire (Herpes Zoster)?

Jacques Gaillat,<sup>1,a</sup> Vincent Gajdos,<sup>2,3,a</sup> Odile Launay,<sup>4,5</sup> Denis Malvy,<sup>6</sup> Bruno Demoures,<sup>7</sup> Lucie Lewden,<sup>8</sup> Sybil Pinchinat,<sup>9</sup> Tarik Derrough,<sup>8</sup> Claudine Sana,<sup>8</sup> Evelyne Caulin,<sup>8</sup> and Benoît Soubeyrand<sup>8</sup>

*Hypothèse: l'absence d'entretien de l'immunité anti-VZV par des contacts avec la population générale (enfants) favoriserait le zona*

*=> Hypothèse réfutée*



**Table 3. Frequency of Zoster**

	Groups		Total	P	OR [95% CI]
	Monks/ nuns	General population			
Principal analysis population (n)	920	1533	2453		
Frequency % (n)	16.2 (149)	15.1 (231)	15.5 (380)	$\chi^2 P = .27^b$	1.14 [.91–1.44]
Subgroup analysis (n) <sup>a</sup>	824	1387	2211		
Frequency % (n)	6.4 (53)	6.1 (85)	6.2 (138)	$P = .54^b$	1.12 [.78–1.6]

**NOTE.** <sup>a</sup> Analysis of events occurring during the last 10 years before the study.

<sup>b</sup> P adjusted for sex and age.

# Neuro-infectieux 2012: Qu'a t'on appris ?

- **Vaccin conjugué méningocoque A**
  - Marche bien, et longtemps (> 10 ans)
  - < 0,5 €/dose
  - Gros espoirs pour la ceinture méningitique
- **Céfotaxime continue dans les méningites bactériennes**
  - Semble mieux, chez l'enfant
- **Traitement méningites purulentes de l'enfant: stop à J5 si stable**
- **Compagnon de l'AmB en tt d'attaque cryptococcose SNC**
  - Fluconazole 800-1200 ou vorico 600 mg/j aussi fongicides que 5-FC
- **Anti-oedémateux: bof !**
  - Pas de glycérol si méningite adulte
  - Pas de mannitol si oedème cérébral palud
- **Rescapés d'encéphalites**
  - Évolution favorable 2/3 des patients
  - Troubles idem post-trauma crânien
- **Encéphalite Ac anti-NMDAr**
  - 1ère cause encéphalite avant 30 ans
  - Femme jeune, troubles psy, mouvements anormaux, tumeur ovaire
  - Traitement spécifique efficace
- **FDR listériose mieux quantifiés**
- **Encéphalites dengue**
- **Variants Creutzfeldt-Jakob: la fin?**
- **Nouvelles données transmission et immunité VZV**