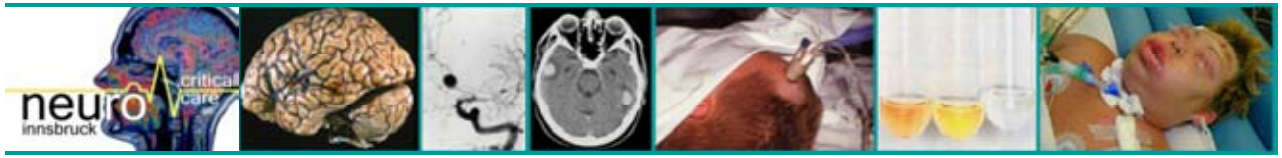

XXI WORLD CONGRESS OF NEUROLOGY
TEACHING COURSE 4:
CNS INFECTIONS AROUND THE WORLD INCL. TROPICAL NEUROLOGY

NEW DEVELOPMENTS IN
ACUTE BACTERIAL MENINGITIS

Erich Schmutzhard
Department of Neurology
Medical University Innsbruck
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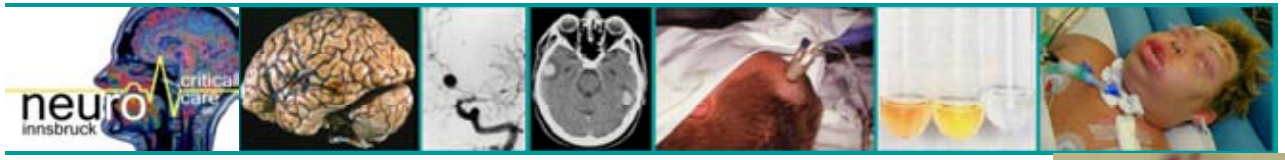
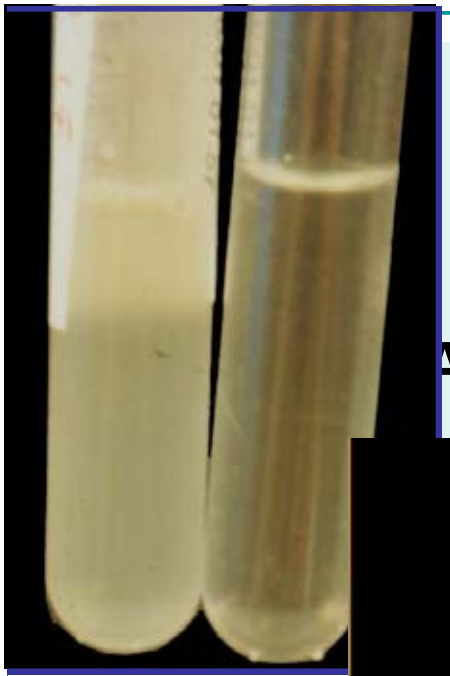
Conflict of Interest:
Phillips-Innercool, ALSIUS-Zoll, Pfizer, Bayer, Baxter, Sandoz, Novo-Nordisk, Actelion, Novartis: research grants and speaker‘s honoraria





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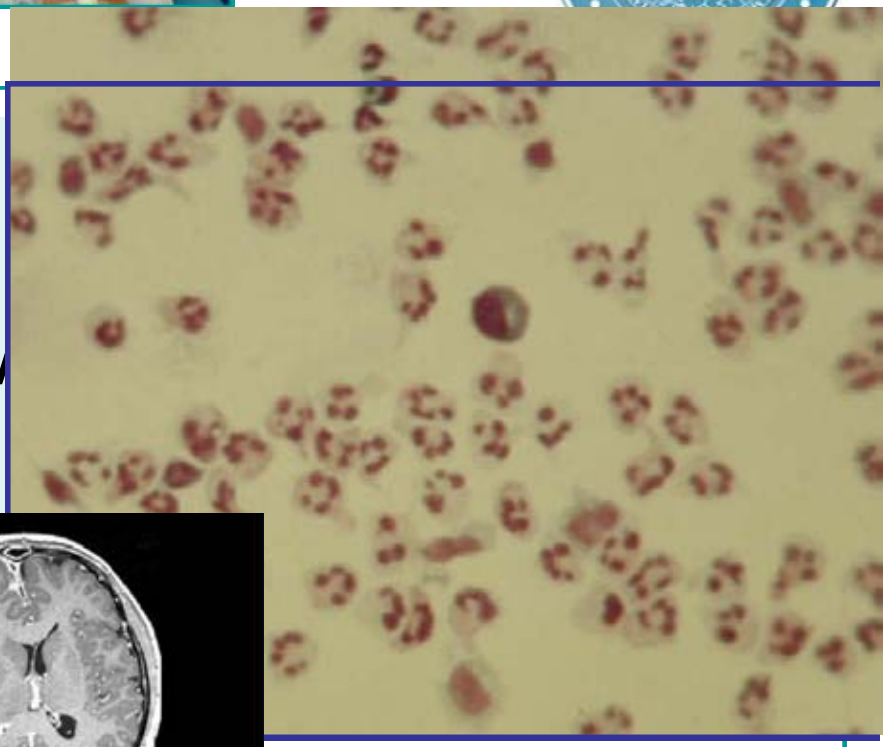

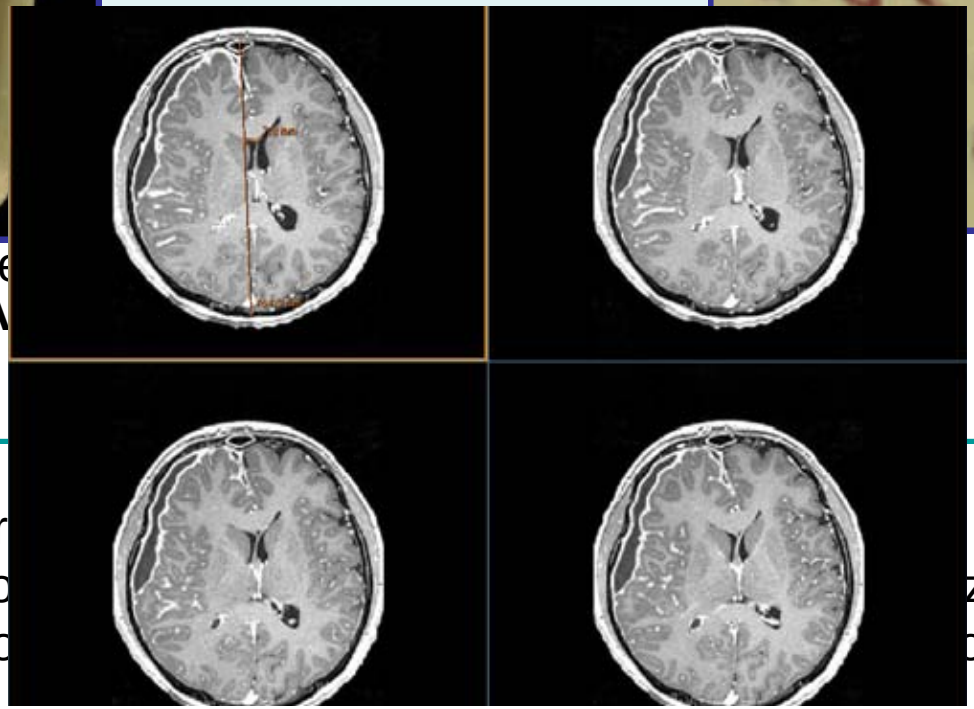

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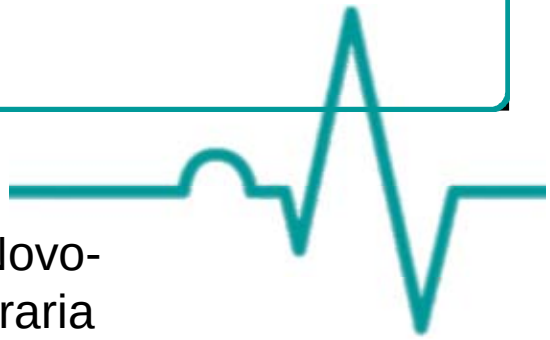
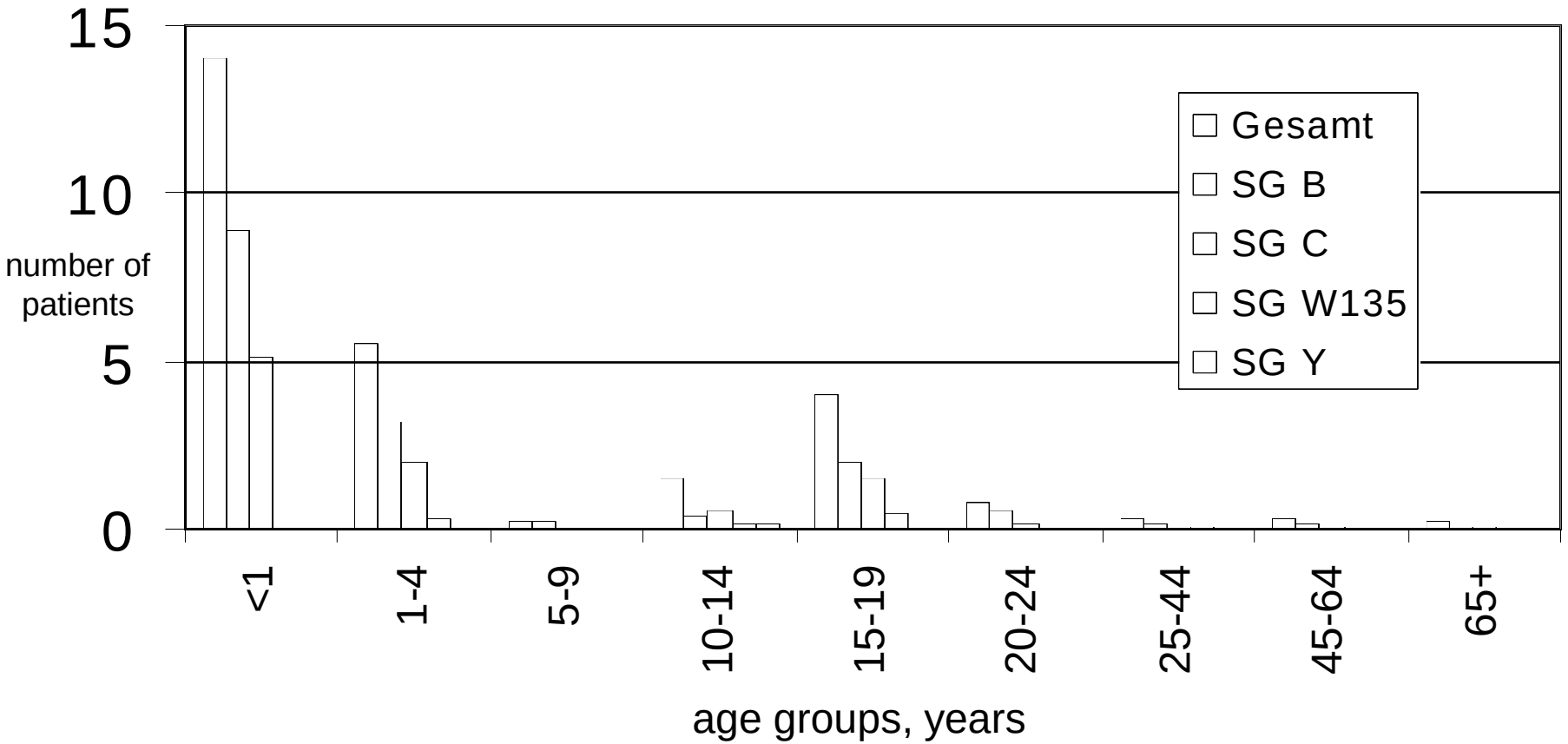


Incidence of invasive meningococcal diseases according to serogroups and age, Austria, 2012 (Heuberger 2013)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bacterial Meningitis in the United States, 1998–2007

Michael C. Thigpen, M.D., Cynthia G. Whitney, M.D., M.P.H., Nancy E. Messonnier, M.D., Elizabeth R. Zell, M.Stat., Ruth Lynfield, M.D., James L. Hadler, M.D., M.P.H., Lee H. Harrison, M.D., Monica M. Farley, M.D., Arthur Reingold, M.D., Nancy M. Bennett, M.D., Allen S. Craig, M.D., William Schaffner, M.D., Ann Thomas, M.D., Melissa M. Lewis, M.P.H., Elaine Scallan, Ph.D., and Anne Schuchat, M.D., for the Emerging Infections Programs Network

N Engl J Med 2011;364:2016-25.

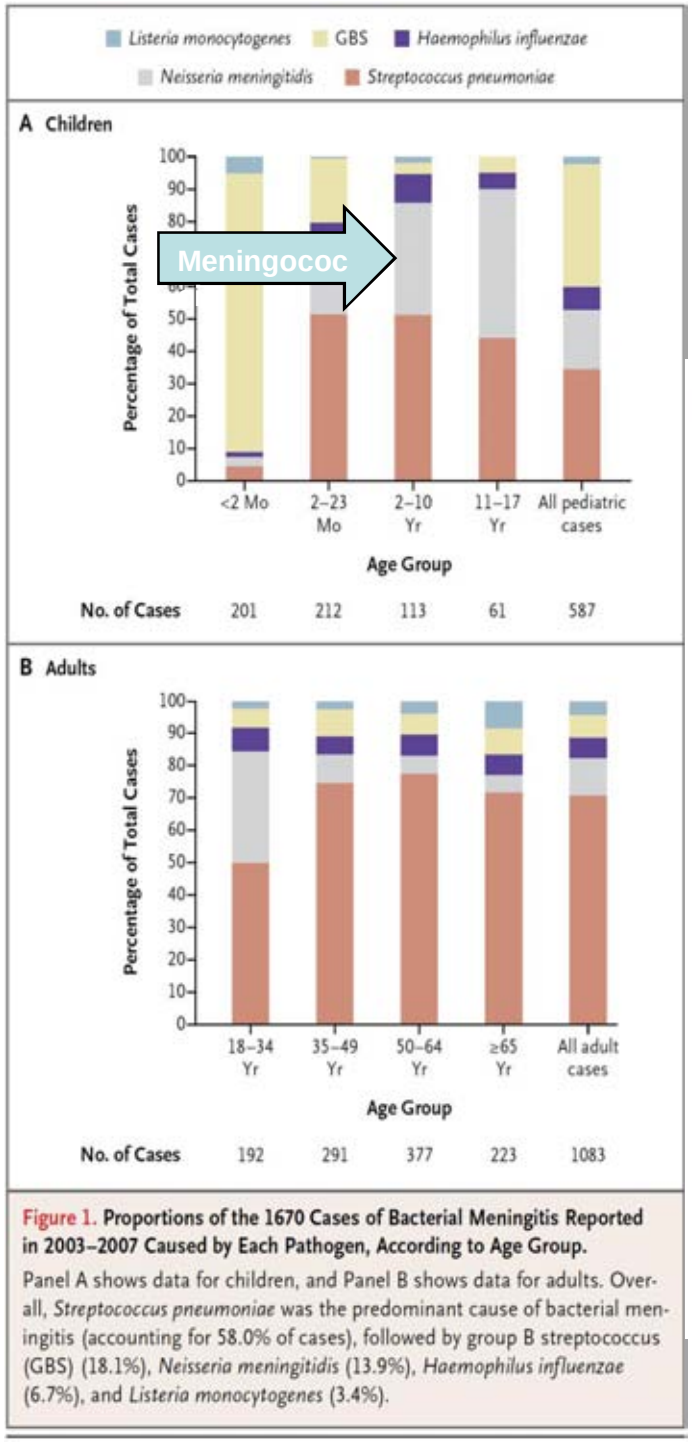


Figure 1. Proportions of the 1670 Cases of Bacterial Meningitis Reported in 2003–2007 Caused by Each Pathogen, According to Age Group.

Panel A shows data for children, and Panel B shows data for adults. Overall, *Streptococcus pneumoniae* was the predominant cause of bacterial meningitis (accounting for 58.0% of cases), followed by group B streptococcus (GBS) (18.1%), *Neisseria meningitidis* (13.9%), *Haemophilus influenzae* (6.7%), and *Listeria monocytogenes* (3.4%).

Meningococ

Li
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Adults

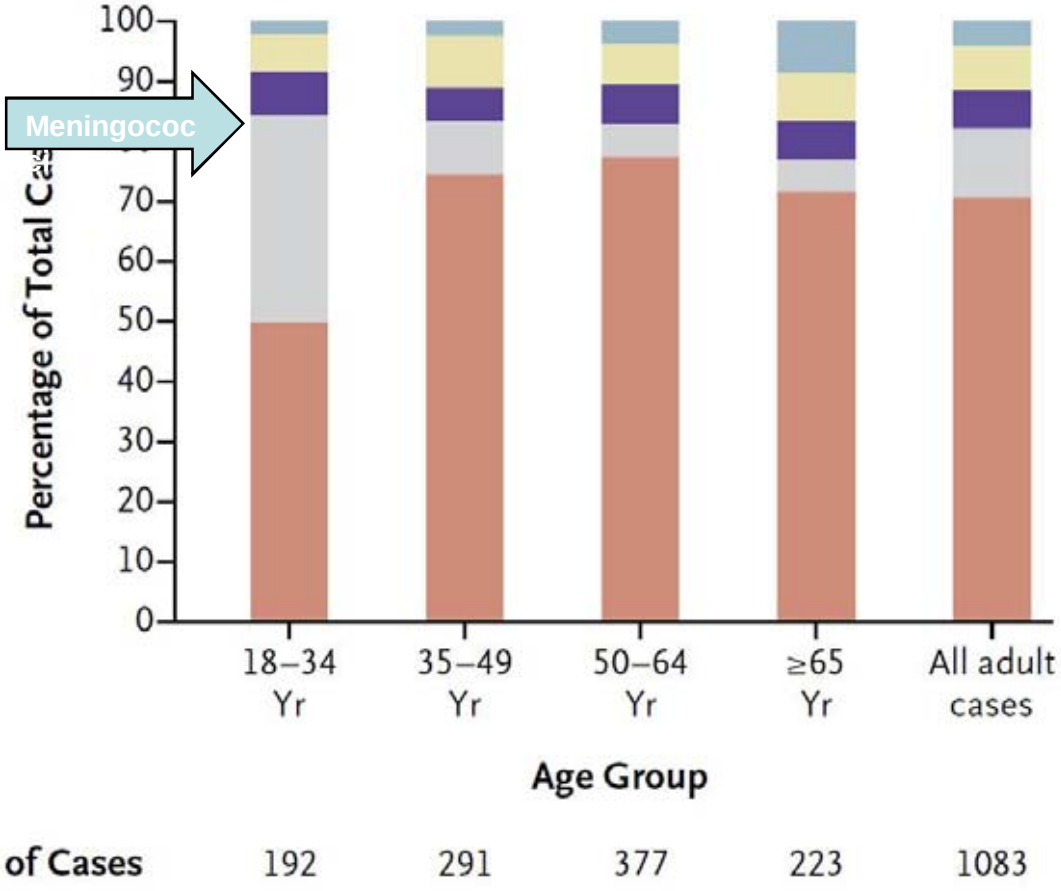

Table 1. Incidence of Bacterial Meningitis in the United States, 1998–2007, Stratified According to Age Group, Race, and Pathogen.*

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.

CONCLUSIONS

The rates of bacterial meningitis have decreased since 1998, but the disease still often results in death. With the success of pneumococcal and Hib conjugate vaccines in reducing the risk of meningitis among young children, the burden of bacterial meningitis is now borne more by older adults. (Funded by the Emerging Infections Programs, Centers for Disease Control and Prevention.)

… rates of bacterial meningitis have decreased …

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Vaccine 24 (2006) 6232–6239
Vaccine
www.elsevier.com/locate/vaccine

The impact of routine infant immunization with *Haemophilus influenzae* type b conjugate vaccine in Malawi, a country with high human immunodeficiency virus prevalence

Paul Daza [a], Richard Banda [b], Keystoxe Misoya [c], Agnes Katsulukuta [d], Bradford D. Gessner [e,*], Reggis Katsande [f], Bekithemba R. Mhlanga [f], Judith E. Mueller [e], Christopher B. Nelson [g,1], Amos Phiri [h], Elizabeth M. Molyneux [i], Malcolm E. Molyneux [h]

[a] *Mzuzu Central Hospital, Mzuzu, Malawi*
[b] *World Health Organization, Lilongwe, Malawi*
[c] *Queen Elizabeth Central Hospital, Blantyre, Malawi*

[d] *National EPI Programme, Ministry of Health, Lilongwe, Malawi*
[e] *Agence de Médecine Préventive a l'Institut Pasteur, 28 rue du Docteur Roux, 75015 Paris, France*
[f] *African Regional Office, World Health Organization, Harare, Zimbabwe*
[g] *World Health Organization, Geneva, Switzerland*
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[i] *Paediatrics Department, College of Medicine, Blantyre, Malawi*

Received 20 April 2006; received in revised form 20 May 2006; accepted 23 May 2006
Available online 9 June 2006

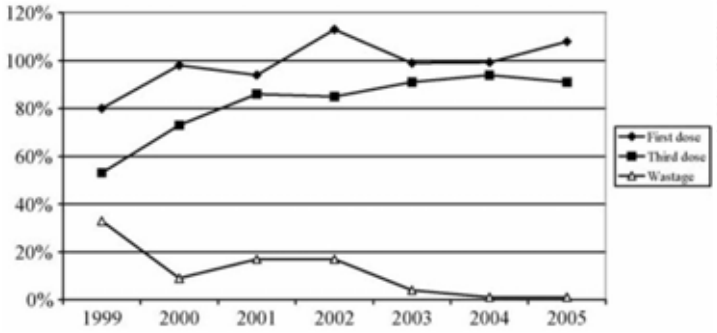


Fig. 1. Administrative vaccine coverage and wastage for diphtheria/tetanus/pertussis vaccine (through January 2002) and diphtheria/tetanus/pertussis/hepatitis B/*Haemophilus influenzae* type b conjugate vaccine (from February 2002) used in routine infant immunization; Blantyre District, Malawi, 1999–2005.

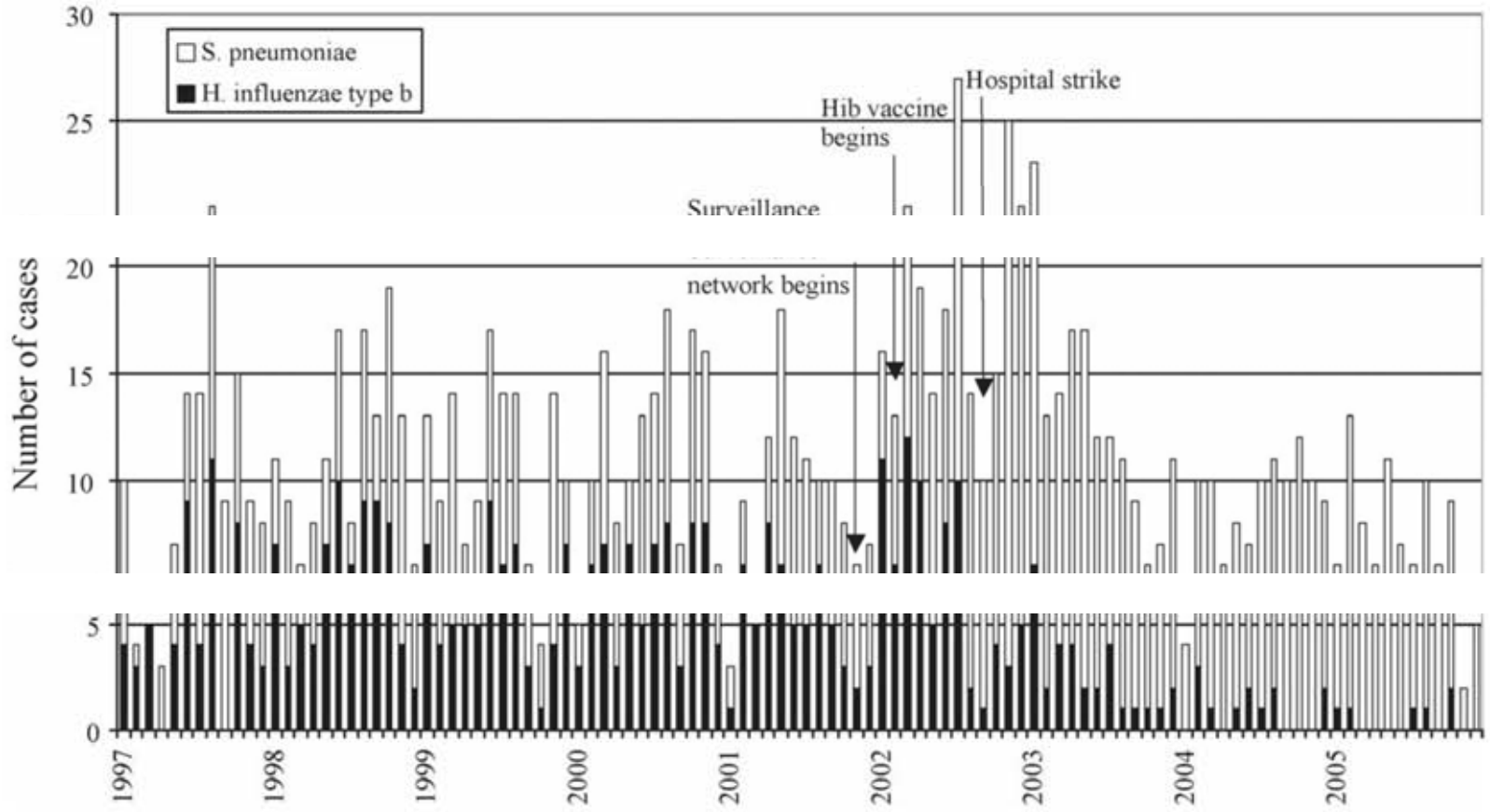


Fig. 2. Number of *Haemophilus influenzae* type b and *Streptococcus pneumoniae* meningitis cases, by month and year, among children <60 months of age; Queen Elizabeth Central Teaching Hospital, Blantyre, Malawi, 1997–2005.

Global Alert and Response (GAR)

Meningococcal Disease: situation in the African Meningitis Belt

25 March 2009 - During the first 11 weeks of 2009 (January 1- March 15), a total of 24 868 suspected cases, including 1 513 deaths (1), have been reported to WHO by countries of the meningitis belt.

Meningococcal disease in Chad

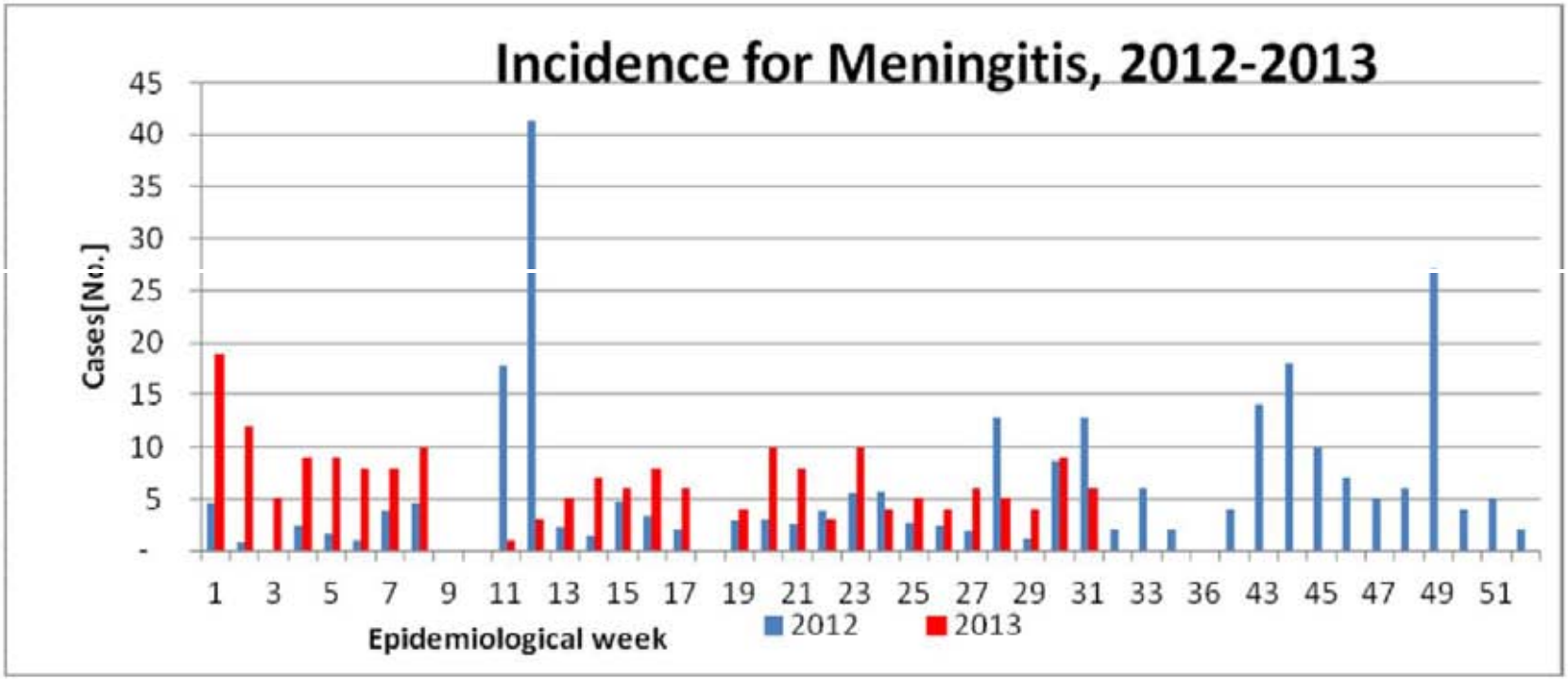
8 March 2011 - From 1 January to 6 March 2011, the Ministry of Health of Chad reported 923 suspected cases of meningococcal disease including 57 deaths (case-fatality rate: 6.2%).

Ministry of Health Uganda

Weekly Epidemiological Bulletin

Epidemiological week 31 of 2013 [29 July – 4 August 2013]

Meningitis: Only sporadic cases of meningitis are being reported; with six (6) cases including two (2) deaths reported from the five (5) districts of Amuria, Kibuku, Mubende, Oyam, & Soroti during the current week. The figure below shows the number of meningitis cases reported by week for 2012 & 2013 [annex 1 for district specific reports].



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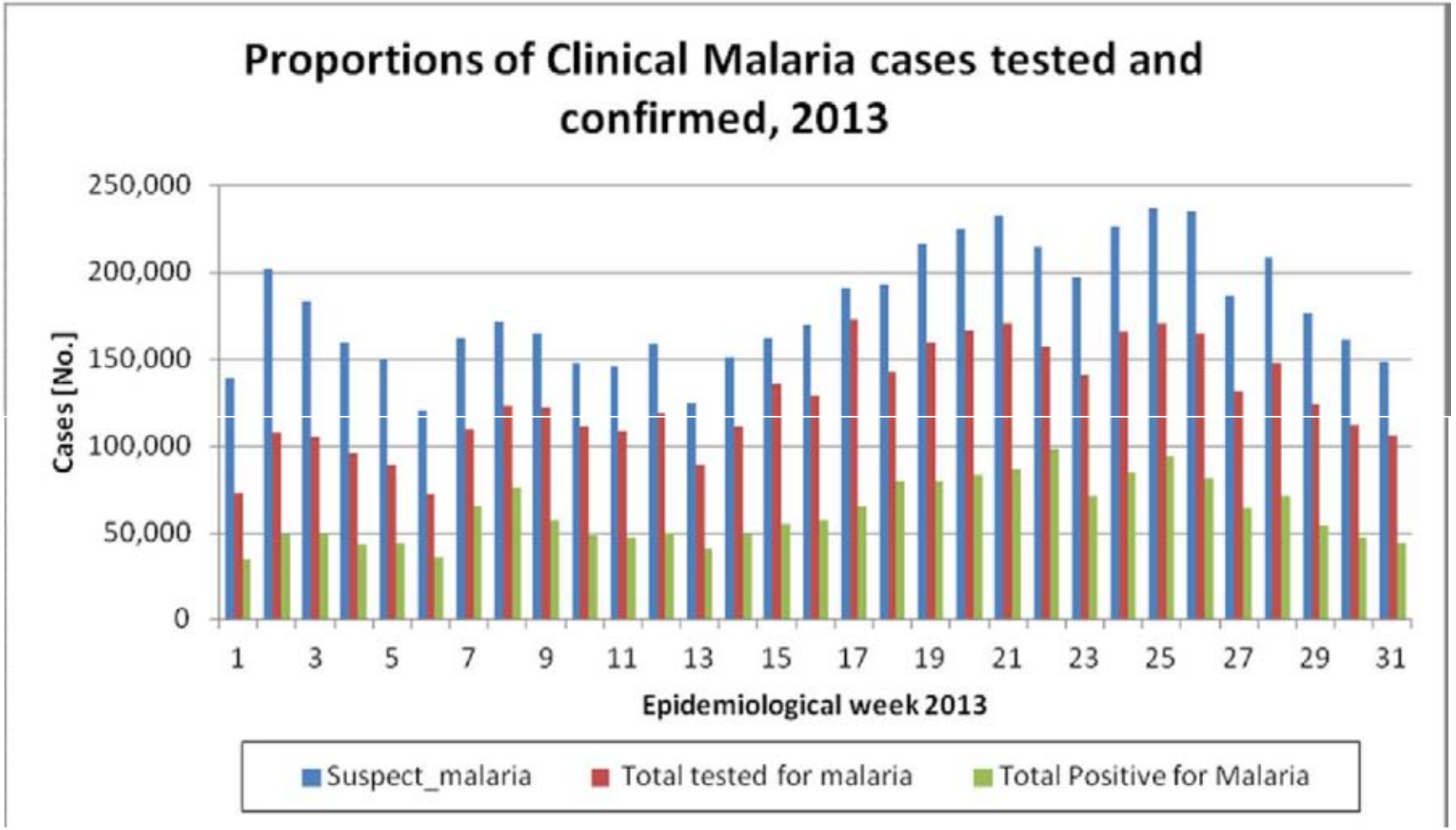

Journal of Infection (2008) 57, 449–454

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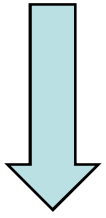
Antibiotic treatment delay and outcome in acute bacterial meningitis

Rasmus Køster-Rasmussen [a,*], André Korshin [b], Christian N. Meyer [c]

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data



Diederik van de Beek, Jeremy J Farrar, Jan de Gans, Nguyen Thi Hoang Mai, Elizabeth M Molyneux, Heikki Peltola, Tim E Peto, Irmeli Roine, Mathew Scarborough, Constance Schultsz, Guy E Thwaites, Phung Quoc Tuan, A H Zwinderman

Lancet Neurol 2010; 9: 254–63

Published Online February 4, 2010

Summary

Background Dexamethasone improves outcome for some patients with bacterial meningitis, but not others. We aimed to identify which patients are most likely to benefit from dexamethasone treatment.

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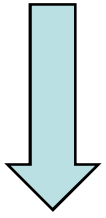

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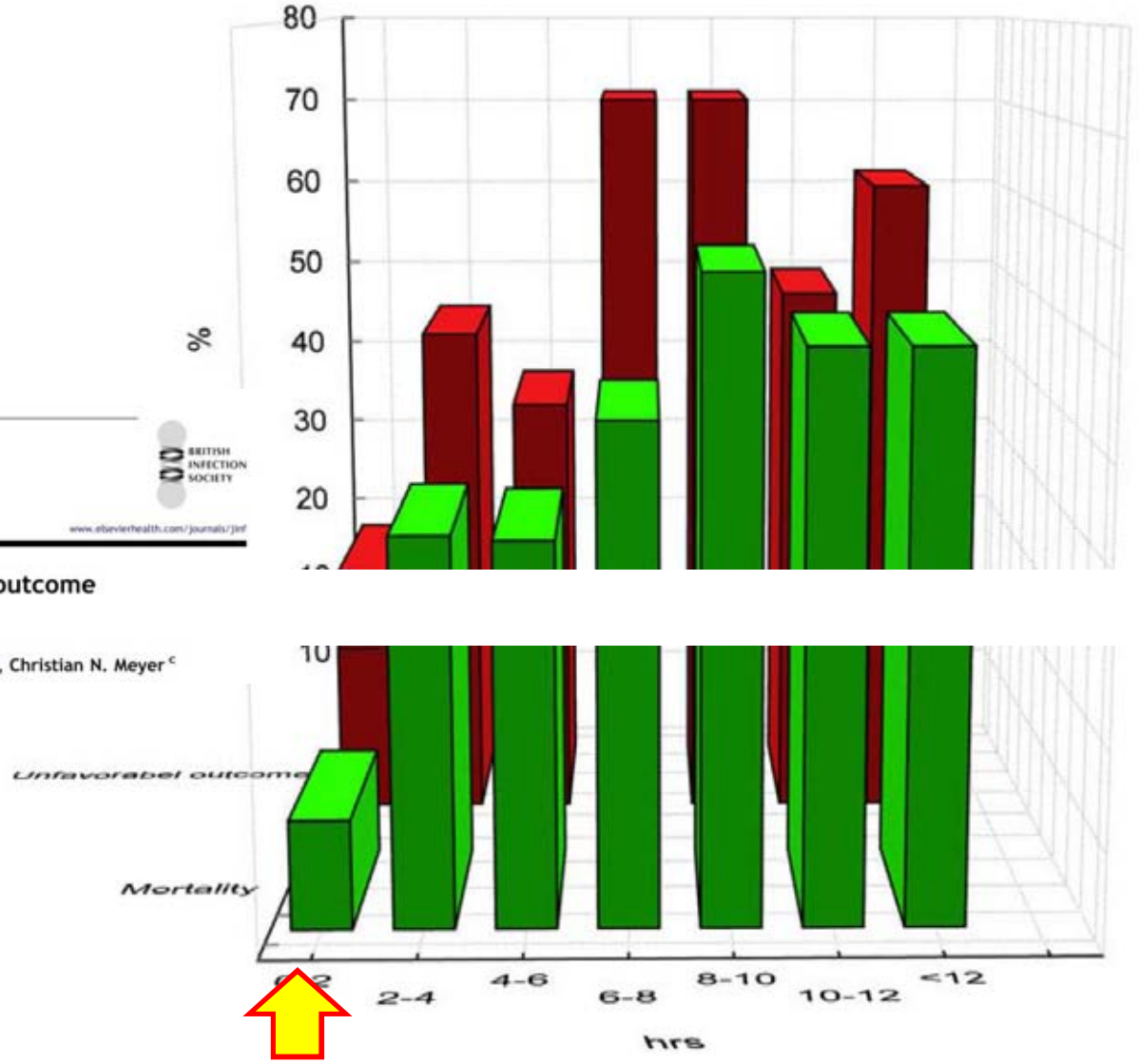

Figure 2 Rate of mortality and unfavourable outcome according to the treatment delay in time interval in acute bacterial meningitis.

Journal of Infection (2008) 57, 449–454

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BRITISH INFECTION SOCIETY

Antibiotic treatment delay and outcome in acute

Rasmus Kø

- **family physicians,**
- **general practitioners,**
- **emergency medical personnel**

Figure 2 Rate of mortality and unfavourable outcome according to the treatment delay in time interval in acute bacterial meningitis.

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data

Diederik van de Beek, Jeremy J Farrar, Jan de Gans, Nguyen Thi Hoang Mai, Elizabeth M Molyneux, Heikki Peltola, Tim E Peto, Irmeli Roine, Mathew Scarborough, Constance Schultsz, Guy E Thwaites, Phung Quoc Tuan, A H Zwinderman

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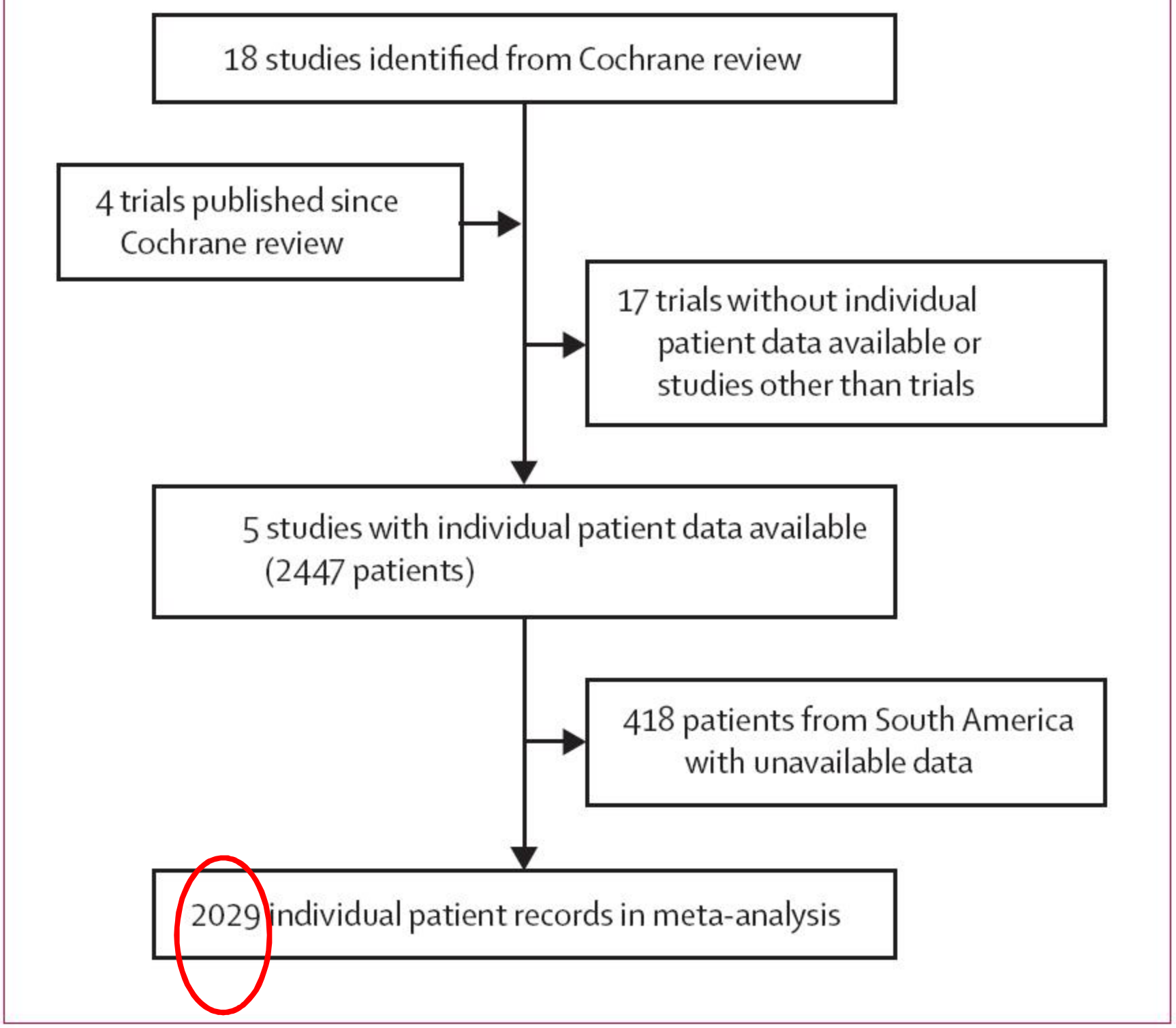
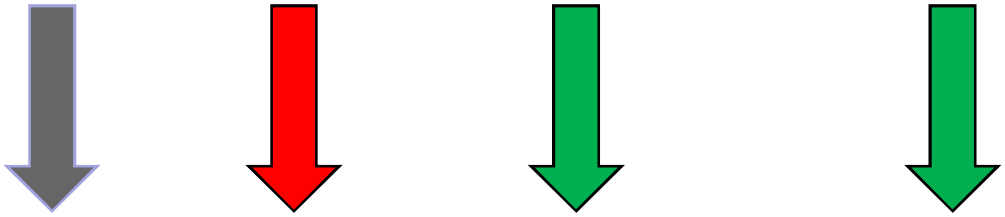

18 studies identified from Cochrane review
4 trials published since Cochrane review
17 trials without individual patient data available or studies other than trials
5 studies with individual patient data available (2447 patients)
418 patients from South America with unavailable data
2029 individual patient records in meta-analysis



	Study period	Patients (n)	Age	Inclusion criteria	Dexamethasone dose	Empirical antibiotic*	Primary outcome
Europe[16]	1992–2001	301	>16 years	Clinically suspected BM plus CSF criteria	10 mg four times daily for 4 days	Intravenous amoxicillin 2 g every 4 h (77% of patients†)	Unfavourable outcome (defined by a Glasgow outcome score of 1–4) at 8 weeks
Malawi (child)[15]	1997–2001	598	2 months to 13 years	Clinically suspected BM plus CSF criteria	0·4 mg/kg twice daily for 2 days	Intravenous benzylpenicillin 200 000 IU/kg every 24 h plus chloramphenicol 100 mg/kg every 24 h	Death at 1 month
Vietnam[13]	1996–2005	429	>14 years	Clinically suspected BM plus CSF criteria	0·4 mg/kg twice daily for 4 days	Intravenous ceftriaxone 2 g every 12 h	Death at 1 month
Malawi (adult)[14]‡	2002–2005	465	>15 years	Clinically suspected BM plus CSF criteria	16 mg twice daily for 4 days	Intravenous or intramuscular ceftriaxone 2 g every 12 h	Death at 1 month
South America[12]§	1996–2003	236	2 months to 16 years	Clinically suspected BM plus CSF or blood criteria	0·15 mg/kg four times daily for 2 days	Intravenous ceftriaxone 80–100 mg/kg every 24 h	Death, severe neurological sequelae, or audiological sequelae at hospital discharge

BM=bacterial meningitis. *Dexamethasone was given before or with the first dose of per-protocol parenteral antibiotic in all five studies. †23% of patients received other antibiotic treatment. ‡2×2 design with patients randomly assigned to dexamethasone or placebo and to intravenous or intramuscular ceftriaxone. §2×2 design with patients randomly assigned to dexamethasone plus glycerol, dexamethasone plus placebo, placebo plus glycerol, or placebo plus placebo; patients assigned to receive glycerol with either dexamethasone or placebo were excluded from the individual patient data meta-analysis; data from this trial were analysed as two strata according to randomisation schedule.

Table 1: **Characteristics of the five studies included in the analysis**

Metaanalysis

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data

Diederik van de Beek, Jeremy J Farrar, Jan de Gans, Nguyen Thi Hoang Mai, Elizabeth M Molyneux, Heikki Peltola, Tim E Peto, Irmeli Roine, Mathew Scarborough, Constance Schultsz, Guy E Thwaites, Phung Quoc Tuan, A H Zwinderman

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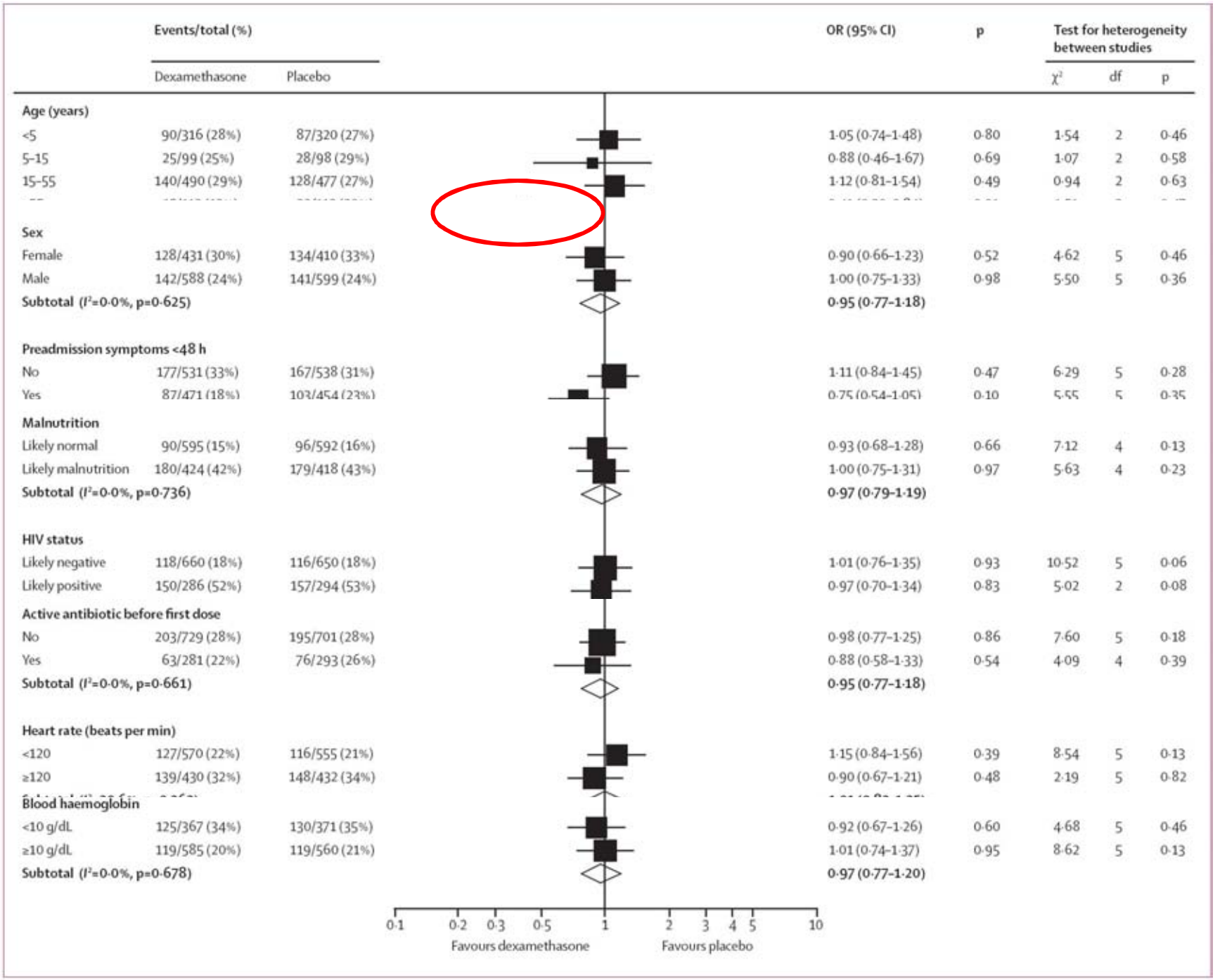


Figure 2: **Subgroup analyses for death**
BM=bacterial meningitis. OR=odds ratio.

	Events/total (%)		OR (95% CI)	p	Test for heterogeneity between studies		
	Dexamethasone	Placebo			χ^2	df	p
Consciousness level							
Normal	33/288 (11%)	25/305 (8%)	1·39 (0·78–2·46)	0·26	2·76	4	0·60
Mild impairment	67/349 (19%)	79/350 (23%)	0·82 (0·55–1·21)	0·32	1·92	5	0·86
Moderate impairment	80/220 (37%)	87/212 (41%)	0·83 (0·53–1·28)	0·41	12·59	5	0·03
CSF white cell count (cells per µL)							
0–99	42/76 (55%)	34/64 (53%)	1·09 (0·53–2·25)	0·82	2·00	4	0·74
100–999	101/284 (36%)	104/280 (37%)	0·96 (0·66–1·37)	0·80	3·31	5	0·65
1000–9999	80/450 (48%)	91/487 (19%)	0·92 (0·65–1·30)	0·64	8·19	5	0·15
≥10 000	39/187 (21%)	41/162 (25%)	0·80 (0·47–1·34)	0·39	2·66	5	0·75
Subtotal (I^2=0·0%, p=0·911)			**0·93 (0·75–1·15)**				
CSF glucose							
CSF protein							
<250 mg	36/283 (13%)	25/250 (10%)	1·39 (0·80–2·43)	0·24	2·81	5	0·73
≥250 mg	184/588 (31%)	196/607 (32%)	0·95 (0·73–1·23)	0·68	5·99	5	0·31
Subtotal (I^2=32·3%, p=0·224)			**1·02 (0·80–1·29)**				
Pyogenic organism seen on microscopy							
No	87/240 (36%)	81/210 (39%)	0·97 (0·66–1·42)	0·88	5·22	5	0·39
Causative organism							
Unknown	55/176 (31%)	45/164 (27%)	1·29 (0·75–2·21)	0·36	5·80	5	0·33
S pneumoniae	131/383 (34%)	146/376 (39%)	0·82 (0·60–1·11)	0·20	9·15	5	0·10
N meningitidis	4/122 (3%)	4/117 (3%)	0·87 (0·23–3·27)	0·84	4·27	3	0·23
H influenzae	28/135 (21%)	37/162 (23%)	0·86 (0·49–1·51)	0·60	1·39	2	0·50
S suis	0/72 (0%)	3/65 (5%)	0·12 (0·01–2·43)	0·07	..	..	..
Aerobic gram-negative bacilli	31/51 (61%)	17/37 (45%)	2·03 (0·76–5·40)	0·15	0·86	2	0·65
Other	9/52 (17%)	14/67 (21%)	0·54 (0·19–1·54)	0·24	2·59	4	0·63
BM confirmation							
Confirmed	203/815 (25%)	221/824 (27%)	0·90 (0·72–1·14)	0·4	9·87	5	0·08
Probable	55/176 (31%)	45/164 (27%)	1·29 (0·75–2·21)	0·36	5·80	5	0·33
Subtotal (I^2=30·8%, p=0·229)			**0·95 (0·77–1·17)**				

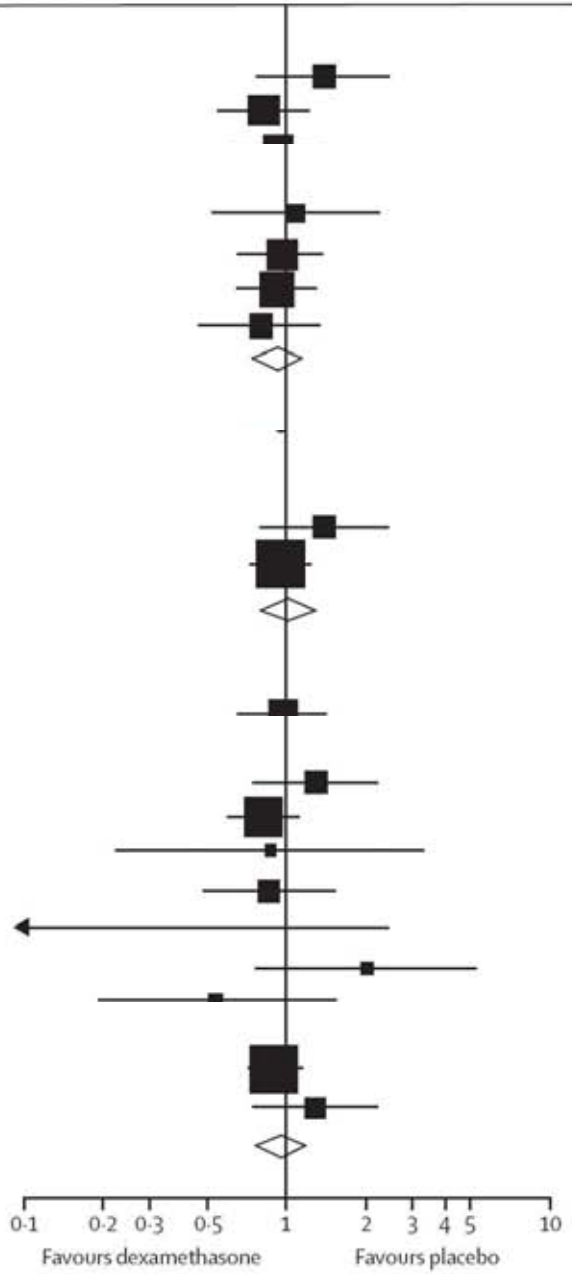


Figure 3: **Subgroup analyses for death**
BM=bacterial meningitis. OR=odds ratio.

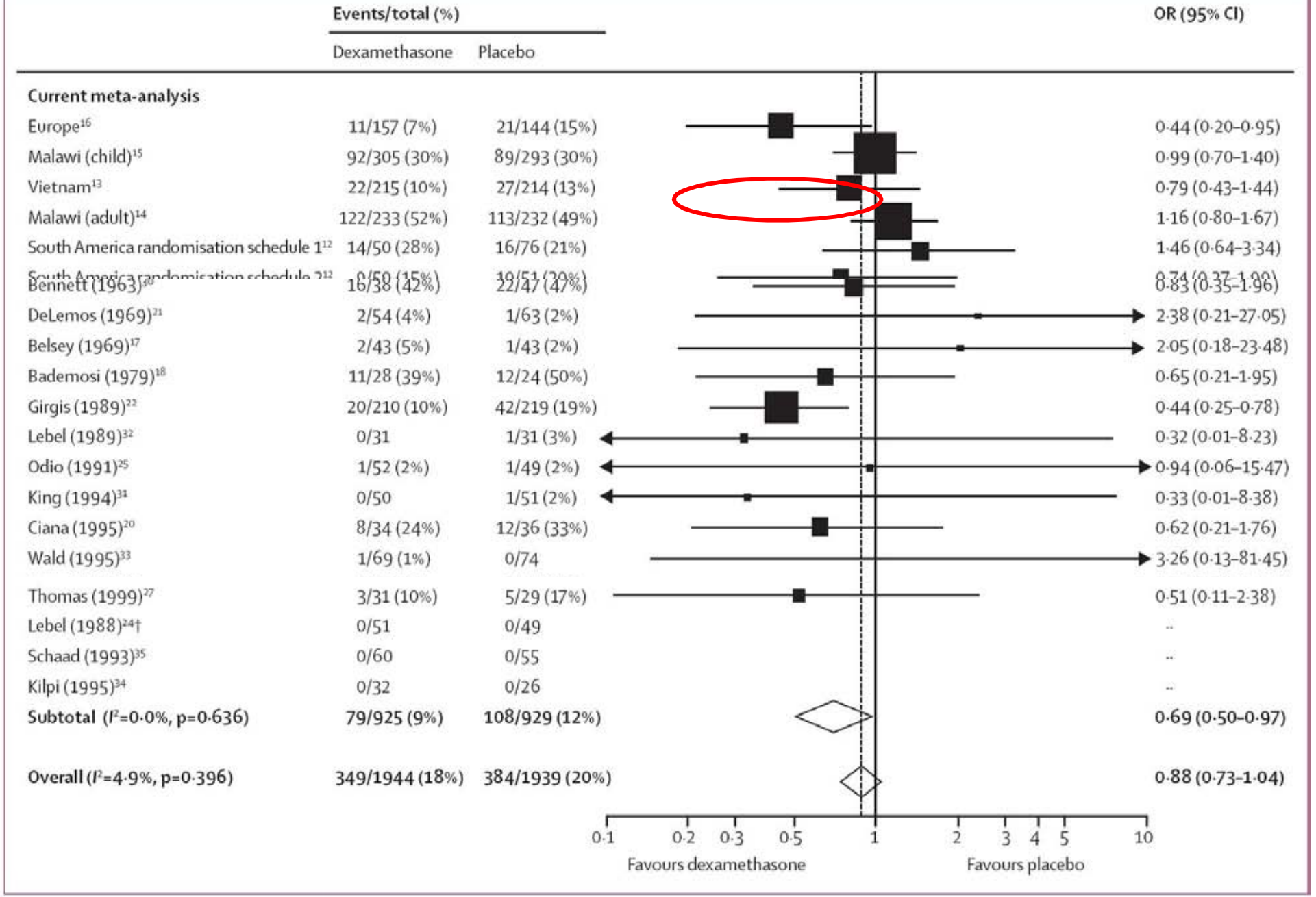


***Figure 4*: Effect of adjunctive dexamethasone therapy on death**

Trials included in the rest of this study[12–16] and other studies[17,27,30–35] included in the Cochrane systematic review[8] are shown. OR=odds ratio. *Study 1 in Lebel.[24] †Study 2 in Lebel.[24]

Metaanalysis

Adjunctive dexamethasone in bacterial meningitis: a meta-analysis of individual patient data

Diederik van de Beek, Jeremy J Farrar, Jan de Gans, Nguyen Thi Hoang Mai, Elizabeth M Molyneux, Heikki Peltola, Tim E Peto, Irmeli Roine, Mathew Scarborough, Constance Schultsz, Guy E Thwaites, Phung Quoc Tuan, A H Zwinderman

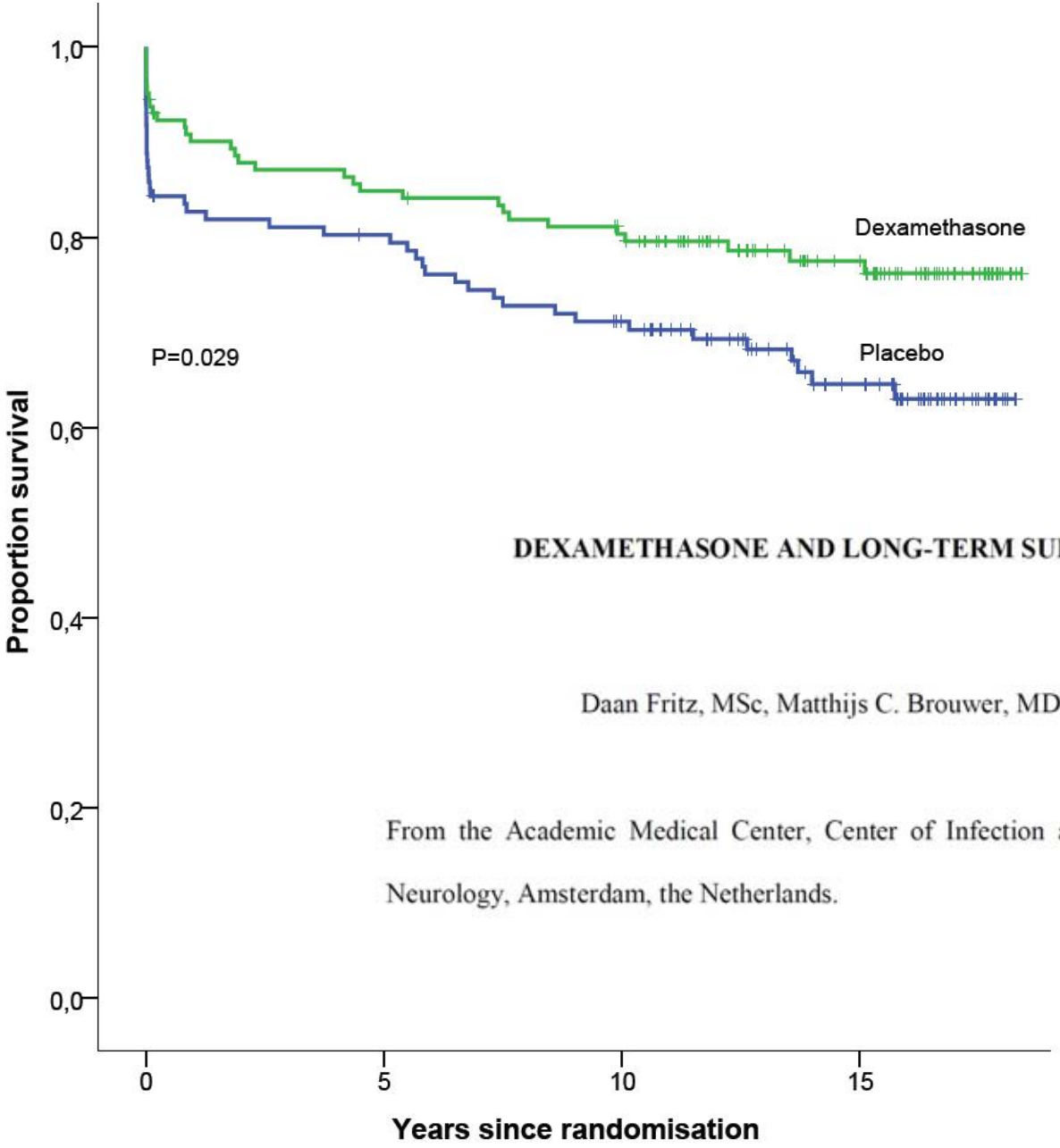
Lancet Neurol 2010; 9: 254–63
Published Online
February 4, 2010

Summary

Background Dexamethasone improves outcome for some patients with bacterial meningitis, but not others. We aimed to identify which patients are most likely to benefit from dexamethasone treatment.

Europeans

> 55 y



NEUROLOGY/2012/453324 Fritz *et al*

DEXAMETHASONE AND LONG-TERM SURVIVAL IN BACTERIAL MENINGITIS

Daan Fritz, MSc, Matthijs C. Brouwer, MD PhD, Diederik van de Beek, MD PhD

From the Academic Medical Center, Center of Infection and Immunity Amsterdam (CINIMA), Department of Neurology, Amsterdam, the Netherlands.

Neurology Nov. 14th, 2012

Neurology. 2012 Oct 9;79(15):1563-9
Adjunctive dexamethasone in adults with meningococcal meningitis.
Heckenberg SG, Brouwer MC, van der Ende A, van de Beek D; Academisch Medisch Centrum; Atrium Medisch Centrum.
From the Departments of Neurology (S.G.B.H., M.C.B., D.v.d.B.), Medical Microbiology (A.v.d.E.), Center of Infection and Immunity Amsterdam (CINIMA), and The Netherlands Reference Laboratory for Bacterial Meningitis Academic Medical Center (A.v.d.E.), University of Amsterdam, Amsterdam; and Department of Neurology (S.G.B.H.), Kennemer Gasthuis, Haarlem, the Netherlands

This study provides Class III evidence that adjuvant dexamethasone in adults with meningococcal meningitis does **not increase negative** outcomes such as deafness, death, or negative Glasgow Outcome Scale measures

Neurology. 2012 Oct 9;79(15):1563-9

Adjunctive dexamethasone in adults with meningococcal meningitis.

Heckenberg SG, Brouwer MC, van der Ende A, van de Beek D; Academisch

Bone RC, Fisher CJ Jr, Clemmer TP, *et al*. A controlled clinical trial of high-dose methylprednisolone in the treatment of severe sepsis and septic shock. *N Engl J Med* 1987;**317**:653–8.

(CINIMA), and The Netherlands Reference Laboratory for Bacterial Meningitis Academic Medical Center (A.v.d.E.), University of Amsterdam, Amsterdam; and Department of Neurology (S.G.B.H.), Kennemer Gasthuis, Haarlem, the Netherlands

This study provides Class III evidence that adjuvant dexamethasone in adults with meningococcal meningitis does **not increase negative** outcomes such as deafness, death, or negative Glasgow Outcome Scale measures

Bacterial Meningitis [redacted]

Advances in treatment of bacterial meningitis

Diederik van de Beek, Matthijs C Brouwer, Guy E Thwaites, Allan R Tunkel

Lancet 2012; 380: 1693–702

November 10, 2012

Bacterial meningitis kills or maims about a fifth of people with the disease.

support this notion are scarce. Additionally, whether or not adjunctive anti-inflammatory therapies (eg, dexamethasone) improve outcomes in patients with bacterial meningitis remains controversial; in [redacted], where the disease burden is highest, [redacted]. Other adjunctive therapeutic strategies, such as glycerol, paracetamol, and induction of hypothermia, are being tested further. Therefore, bacterial meningitis is a substantial and evolving therapeutic challenge. We review this challenge, with a focus on strategies to optimise antibiotic efficacy

J Neural Transm (2013) 120:343–346
DOI 10.1007/s00702-012-0939-z

Controversies in neurology, Vienna, 2012: Steroids in bacterial meningitis: no

Bettina Pfausler · Erich Schmutzhard

1. Adjunctive dexamethasone treatment has—for the time being—no clearly proven clinical benefit in children with acute bacterial meningitis.
2. Adjunctive dexamethasone treatment may be beneficial (with respect to mortality) in pneumococcal meningitis in elderly (>55 years), European patients.
3. Adjunctive dexamethasone has no effect onto mortality or long-term morbidity in resource poor countries, the region where acute bacterial meningitis still plays and will continue to play an important role in community/public health.
4. Dexamethasone should not be given to patients who have received prior antibiotic therapy.

5. In view of the changing epidemiologic features in old and elderly patients with bacterial meningitis, it needs to be stressed that so far dexamethasone has never been evaluated in a sufficient way to prove its benefit in patients with bacterial meningitis due to gram negatives, staphylococci, i.e., in nosocomial meningitis, posttraumatic meningitis, post-neurosurgical meningitis or meningitis in newborns, etc.
6. Dexamethasone might be deleterious in patients with deranged glucose levels, so glucose variability needs to be avoided by any means.
7. Dexamethasone might be potentially dangerous in deranging coagulation homeostasis, thus potentially be responsible for delayed onset ischemic stroke.
8. The widespread implementation of vaccination programs (Haemophilus influenzae type B, pneumococci and meningococci, mainly serotype C) has led and will further lead to a significant change in epidemiology.

Viallon *et al. Critical Care* 2011, **15**:R136
http://ccforum.com/content/15/3/R136

CRITICAL CARE

RESEARCH Open Access

Meningitis in adult patients with a negative direct cerebrospinal fluid examination: value of cytochemical markers for differential diagnosis

Alain Viallon[1*], Nicolas Desseigne[1], Olivier Marjollet[1], Albert Birynczyk[1], Mathieu Belin[1], Stephane Guyomarch[1], Jacques Borg[2], Bruno Pozetto[3], Jean Claude Bertrand[1] and Fabrice Zeni[1]

Key messages

- Identification of bacterial meningitis on direct examination had low sensitivity
- Identification of bacterial meningitis with classic biomarkers is insufficient
- Models for predicting the acute bacterial origin of meningitis are not easy to use
- Cerebrospinal fluid lactate and procalcitonin are easy to determine
- Cerebrospinal fluid lactate and procalcitonin are the best markers for differentiating between bacterial and viral meningitis

Am. J. Trop. Med. Hyg., 88(1), 2013, pp. 127–131
doi:10.4269/ajtmh.2012.12-0447

Handheld Point-of-Care Cerebrospinal Fluid Lactate Testing Predicts Bacterial Meningitis in Uganda

Albert Majwala, Rebecca Burke, William Patterson, Relana Pinkerton, Conrad Muzoora, L. Anthony Wilson, and Christopher C. Moore*

Department of Internal Medicine, Mbarara Regional Referral Hospital, Faculty of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda; Department of Medicine, Duke University School of Medicine, Durham, North Carolina; Department of Laboratory Medicine, University of Virginia School of Medicine, Charlottesville, Virginia; Division of Infectious Diseases and International Health, Department of Medicine, University of Virginia, Charlottesville, Virginia

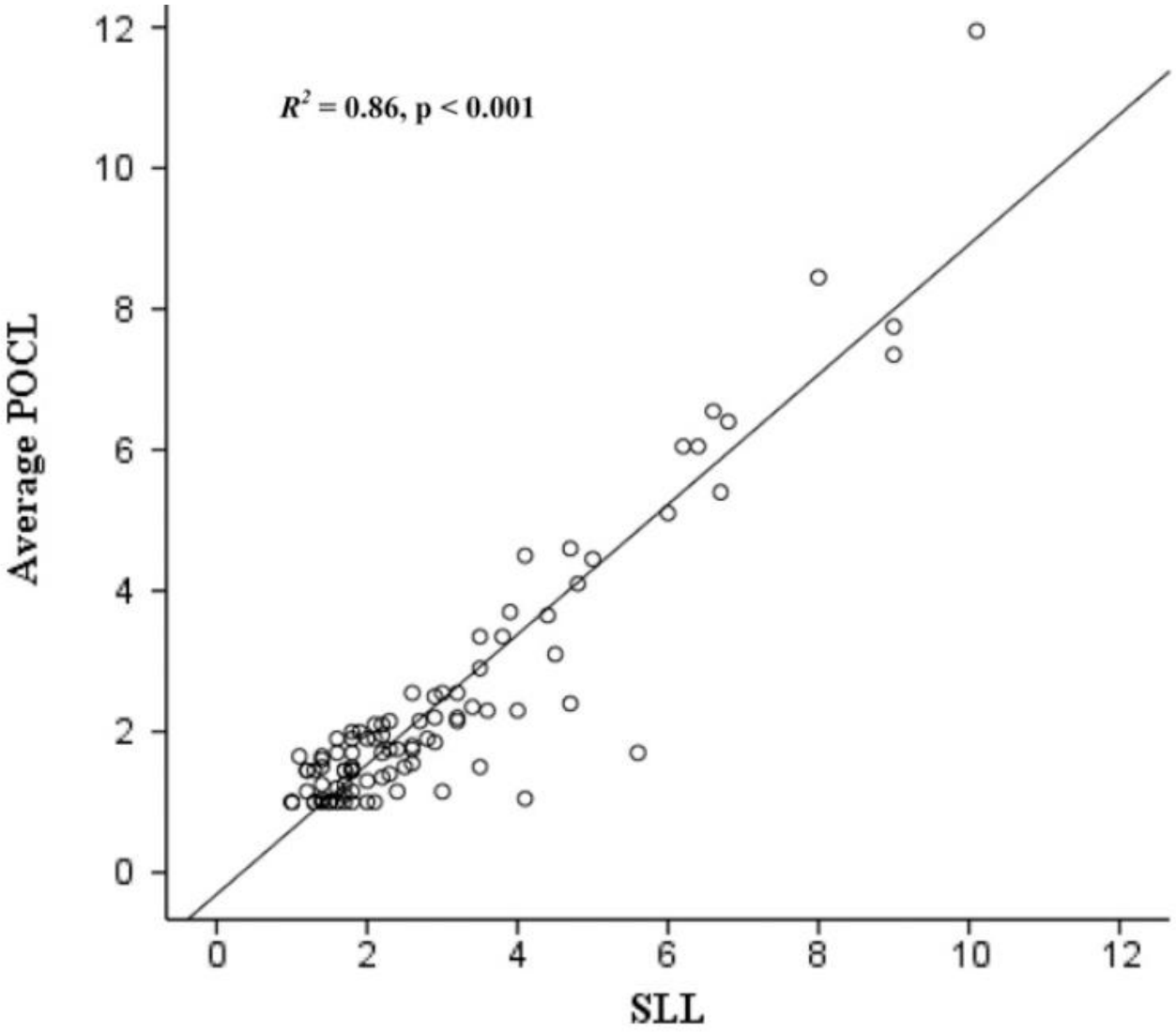
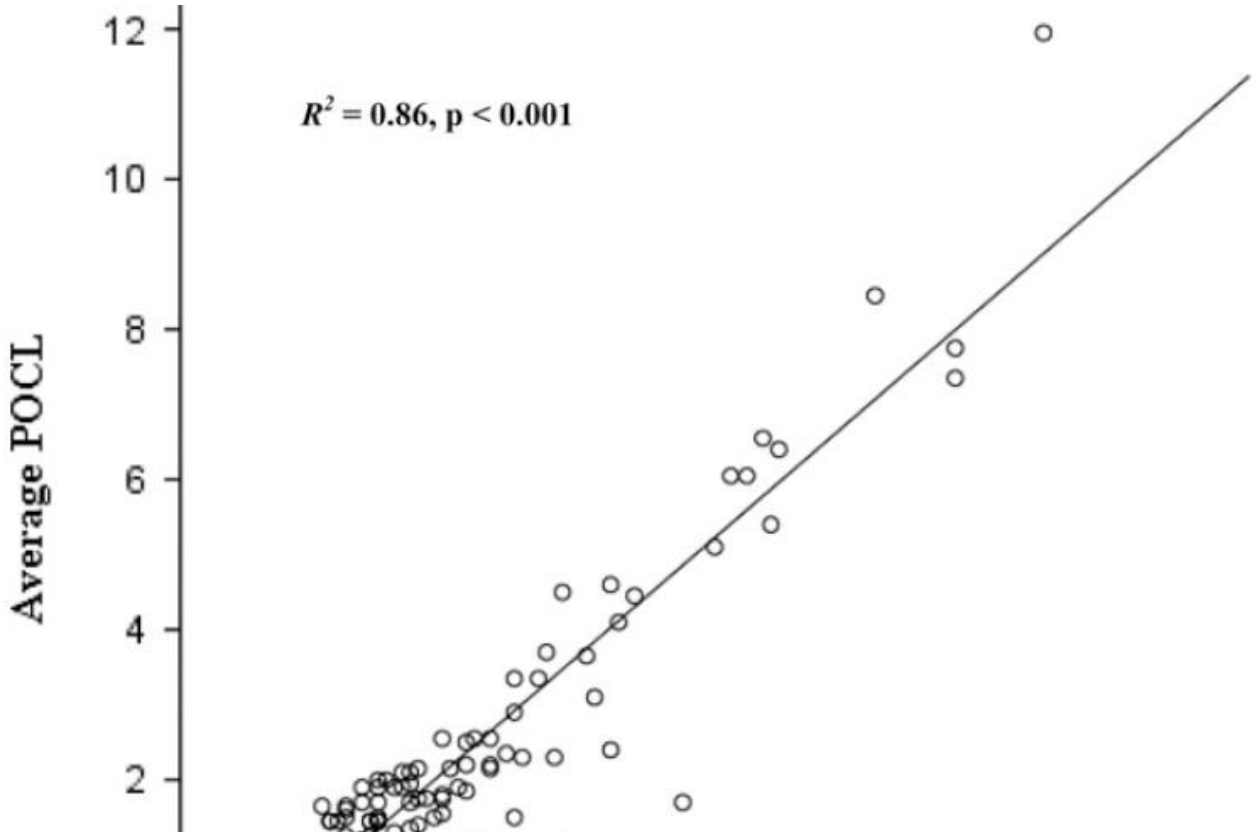


FIGURE 1. Scatter plot with regression line of average POCL and SLL results (in millimoles per liter) for CSF samples submitted to the clinical laboratory at the University of Virginia.



in only 60 seconds, and testing can be done by anyone after a brief training session. In such settings, discrimination of bacterial versus non-bacterial meningitis could be greatly augmented by CSF POCL testing, which could result in a reduction of already limited expenditures and antibiotics.

OPEN ACCESS Freely available online

PLoS one

Incorporation of Real-Time PCR into Routine Public Health Surveillance of Culture Negative Bacterial Meningitis in São Paulo, Brazil

Claudio T. Sacchi[1]*, Lucila O. Fukasawa[1], Maria G. Gonçalves[1], Maristela M. Salgado[1], Kathleen A. Shutt[2], Telma R. Carvalhanas[3], Ana F. Ribeiro[3], Brigina Kemp[4], Maria C. O. Gorla[5], Ricardo K. Albernaz[3], Eneida G. L. Marques[6], Angela Cruciano[7], Eliseu A. Waldman[8], M. Cristina C Brandileone[5], Lee H. Harrison[2], São Paulo RT-PCR Surveillance Project Team[¶]

1 Division of Medical Biology, Department of Immunology, Instituto Adolfo Lutz, São Paulo, Brazil, **2** Infectious Diseases Epidemiology Research Unit, University of Pittsburgh Graduate School of Public Health and School of Medicine, Pittsburgh, Pennsylvania, United States of America, **3** Center for Epidemiologic Surveillance, São Paulo, Brazil, **4** Center for Epidemiologic Surveillance, Campinas, Brazil, **5** Division of Medical Biology, Department of Bacteriology, Instituto Adolfo Lutz, São Paulo, Brazil, **6** Bacteriology Area, Department of Medical Biology, Instituto Adolfo Lutz Regional Laboratory of Campinas, Campinas, Brazil, **7** Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America, **8** Faculdade de Saúde Pública, Universidade de São Paulo, São Paulo, Brazil

Table 4. Multivariable analysis of risk factors for being a RT-PCR positive, culture-negative case-patient, using culture positive patients as controls.

Risk Factor	OR	95% CI	p-value
Hospital 3, 6, or 1	4.3	2.1–8.6	<0.0001
Antibiotic in CSF	12.2	5.9–25.0	<0.0001
Age ≥18 years	2.8	1.3–5.8	0.006
N. meningitidis	3.3	1.5–7.7	0.005

There were a total of 103 case-patients and 142 controls.
OR, odds ratio; CI, confidence interval; CSF, cerebrospinal fluid.
doi:10.1371/journal.pone.0020675.t004

BMC Infectious Diseases

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Research article

Open Access

Hyperglycemia in bacterial meningitis: a prospective cohort study

Ewout S Schut[†1], Willeke F Westendorp[†1], Jan de Gans[1], Nyika D Kruyt[1], Lodewijk Spanjaard[2,3], Johannes B Reitsma[4] and Diederik van de Beek*[1]

Address: [1]Department of Neurology, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Medical Microbiology, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands, [3]Netherlands Reference Laboratory for Bacterial Meningitis, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands and [4]Department of Clinical Epidemiology and Biostatistics, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands

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* Corresponding author †Equal contributors

Published: 8 May 2009

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Accepted: 8 May 2009

This article is available from: http://www.biomedcentral.com/1471-2334/9/57

Conclusion: The majority of patients with bacterial meningitis have hyperglycemic blood glucose levels on admission. Hyperglycemia can be explained by a physical stress reaction, the central nervous system insult leading to disturbed blood-glucose regulation mechanisms, and preponderance of diabetics for pneumococcal meningitis. Patients with diabetes and bacterial meningitis are at high risk for unfavorable outcome.

BMC Infectious Diseases

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Address: [1]Department of Neurology, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Medical Microbiology, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands, [3]Netherlands Reference Laboratory for Bacterial Meningitis, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, the Netherlands and [4]Department of Clinical Epidemiology and Biostatistics, Center of

GENERAL RULE in intensive care medicine:

Avoid by any means and in every patient HYPO- and HYPERGLYCEMIA!!!

Conclusion: The majority of patients with bacterial meningitis have hyperglycemic blood glucose levels on admission. Hyperglycemia can be explained by a physical stress reaction, the central nervous system insult leading to disturbed blood-glucose regulation mechanisms, and preponderance of diabetics for pneumococcal meningitis. Patients with diabetes and bacterial meningitis are at high risk for unfavorable outcome.

BMC Infectious Diseases

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Hyperglycemia in bacterial meningitis: a prospective cohort study

Ewout S Schut[†1], Willeke F Westendorp[†1], Jan de Gans[1], Nyika D Kruyt[1], Lodewijk Spanjaard[2,3], Johannes B Reitsma[4] and Diederik van de Beek[*1]

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GENERAL RULE in intensive care medicine:

Avoid by any means and in every patient i.e. GLUCOSE VARIABILITY!!!

Conclusion: The majority of patients with bacterial meningitis have hyperglycemic blood glucose levels on admission. Hyperglycemia can be explained by a physical stress reaction, the central nervous system insult leading to disturbed blood-glucose regulation mechanisms, and preponderance of diabetics for pneumococcal meningitis. Patients with diabetes and bacterial meningitis are at high risk for unfavorable outcome.

BMC Infectious Diseases

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Research article

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Hyperglycemia in bacterial meningitis: a prospective cohort study

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and even more in severe bacterial meningitis:

Avoid by any means and in every patient HYPO- and HYPERGLYCEMIA!!!

Conclusion: The majority of patients with bacterial meningitis have hyperglycemic blood glucose levels on admission. Hyperglycemia can be explained by a physical stress reaction, the central nervous system insult leading to disturbed blood-glucose regulation mechanisms, and preponderance of diabetics for pneumococcal meningitis. Patients with diabetes and bacterial meningitis are at high risk for unfavorable outcome.

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

Summary

Background S … lence of bacterial meningitis in … co-infection. Mo… …ids.

Department of Medicine, College of Medicine, Chichiri, Blantyre, Malawi (K M B Ajdukiewicz MRCP, K E Cartwright MRCP, M Scarborough PhD, J B Mwambene Dip Med Sci, P Goodson Dip Med Sci, M E Molyneux Dip Med Sci, E E Zijlstra PhD); **Monsall Unit, Department of Infectious Diseases and Tropical Medicine, North Manchester General Hospital, Delaunays Road, Manchester, UK** (K M B Ajdukiewicz); **Microbiology, Leicester Royal Infirmary, Infirmary Square, Leicester, UK** (K E Cartwright); **Microbiology, John Radcliffe Hospital, Headington, Oxford, UK** (M Scarborough); **Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK** (M E Molyneux, D G Lalloo FRCP); **Department of Internal Medicine, Erasmus Medical Centre, Rotterdam, The Netherlands** (E E Zijlstra); **Karonga Prevention Study, Chilumba, Malawi** (N French FRCP); **Department of Clinical Research, London School of Tropical Medicine and Hygiene, Keppel St, London, UK** (N French, C J M Whitty FRCP)

Correspondence to: Katherine Ajdukiewicz, Monsall Unit, Department of Infectious Diseases and Tropical Medicine, North Manchester General Hospital, Delaunays Road, Manchester M8 5RB, UK
katherineaz@doctors.org.uk

Lancet Infect Dis 2011; 11: 293–300

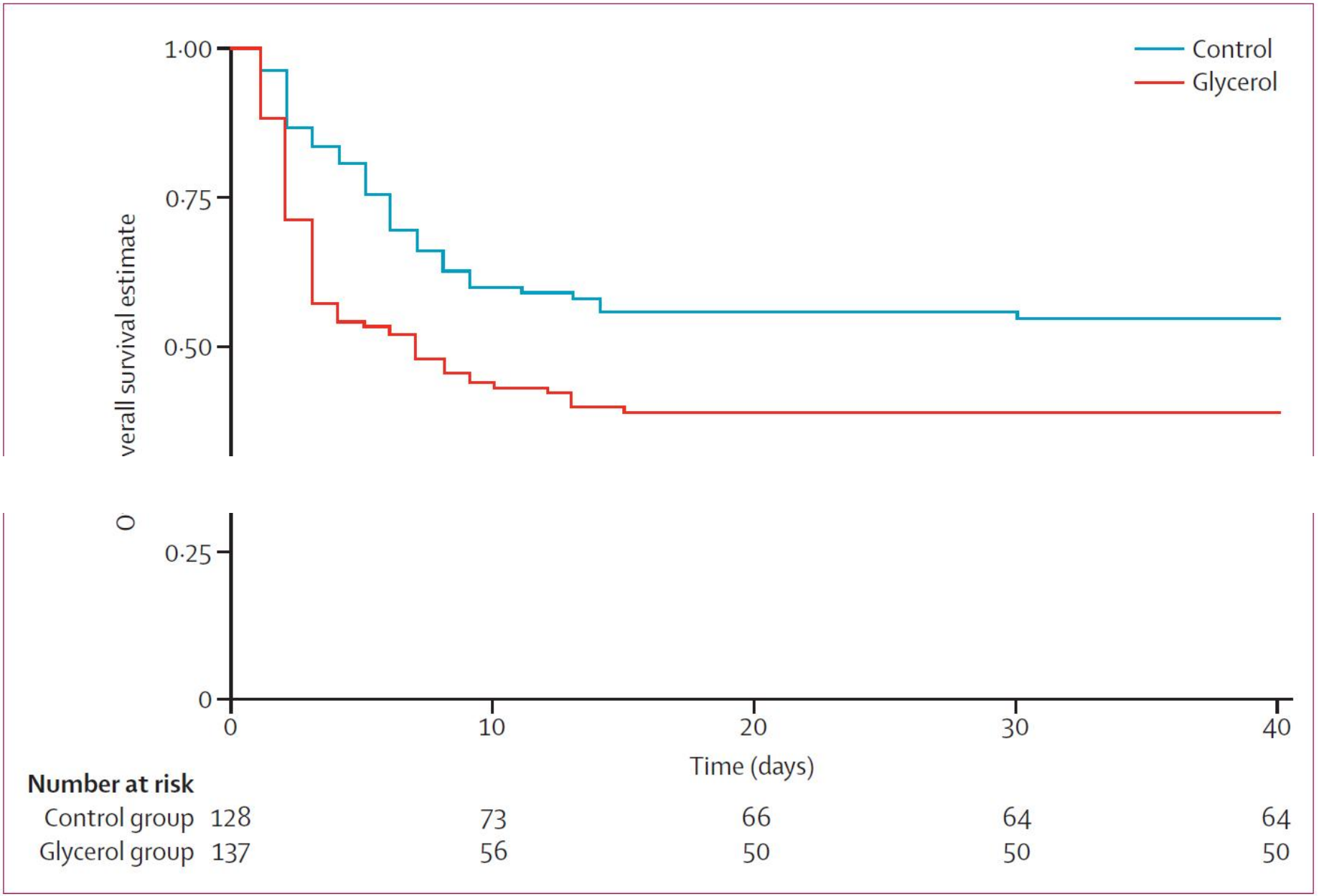


Figure 2: **Kaplan-Meier survival estimates for glycerol *vs* control**

	Placebo	Glycerol	Odds ratio (95% CI, p)	Adjusted odds ratio (95% CI, p)*
Died before day 40	61/125 (49%)	86/136 (63%)	1·8 (1·1–3·0) p=0·02	2·4 (1·3–4·2, p=0·003)
Died or disability before day 40†	75/124 (60%)	93/135 (69%)	1·4 (0·87–2·4) p=0·2	1·7 (0·97–3·1, p=0·07)
Died by day 10	53/126 (42%)	80/136 (59%)	2·0 (1·2–3·2) p=0·007	2·7 (1·5–4·8, p=0·001)
Per-protocol analysis death to day 40	57/106 (54%)	77/118 (65%)	1·6 (0·9–2·8) p=0·08	2·2 (1·2–4·1) p=0·01
Died by day 40 restricted to proven bacterial disease	21/53 (40%)	43/63 (68%)	3·3 (1·5–7·0) p=0·002	5·5 (1·9–15·4, p=0·0011)
Died by day 40 restricted to pneumococcal disease	20/51 (39%)	31/45 (69%)	3·4 (1·5–8·0) p=0·004	8·2 (2·4–28·5, p=0·0006)

Data are n (%) unless otherwise stated. *Prespecified factors: HIV status, age, organism in blood or cerebrospinal fluid, antiretroviral treatment, pre-treatment antibiotics, fits prior to admission, Glasgow coma score, duration of symptoms, sex, prior AIDS-defining events. †No day 40 data for two patients.

Table 3: **Primary and secondary outcome data**

In our study in adults, which was stopped early by the data safety monitoring board due to futility, glycerol was associated with significantly higher mortality within 40 days than was placebo. Glycerol was also associated with worse outcomes in all major secondary analyses, except deafness, at day 40. This trial therefore does not support the use of glycerol as adjunctive treatment for bacterial meningitis in adults in Malawi.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2010, p. 1323–1326 Vol. 54, N
0066-4804/10/$12.00 doi:10.1128/AAC.00812-09

Attenuation of Cerebrospinal Fluid Inflammation by the Nonbacteriolytic Antibiotic Daptomycin versus That by Ceftriaxone in Experimental Pneumococcal Meningitis[▽]

Denis Grandgirard, Kevin Oberson, Angela Bühlmann, Rahel Gäumann, and Stephen L. Leib*

Laboratory for Experimental Neuroinfectiology, Institute for Infectious Diseases, University of Bern, Bern, Switzerland

Received 17 June 2009/Returned for modification 4 October 2009/Accepted 29 December 2009

Antibiotic-induced bacteriolysis exacerbates inflammation and brain damage in bacterial meningitis. Here the quality and temporal kinetics of cerebrospinal fluid (CSF) inflammation were assessed in an infant rat pneumococcal meningitis model for the nonbacteriolytic antibiotic daptomycin versus ceftriaxone. Daptomycin led to lower CSF concentrations of interleukin 1β (IL-1β), IL-10, IL-18, monocyte chemoattractant protein 1 (MCP-1), and macrophage inflammatory protein 1 alpha (MIP-1α) ($P < 0.05$). In experimental pneumococcal meningitis, daptomycin treatment resulted in more rapid bacterial killing, lower CSF inflammation, and less brain damage than ceftriaxone treatment.

Slow initial β-lactam infusion and oral paracetamol to treat childhood bacterial meningitis: a randomised, controlled trial

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

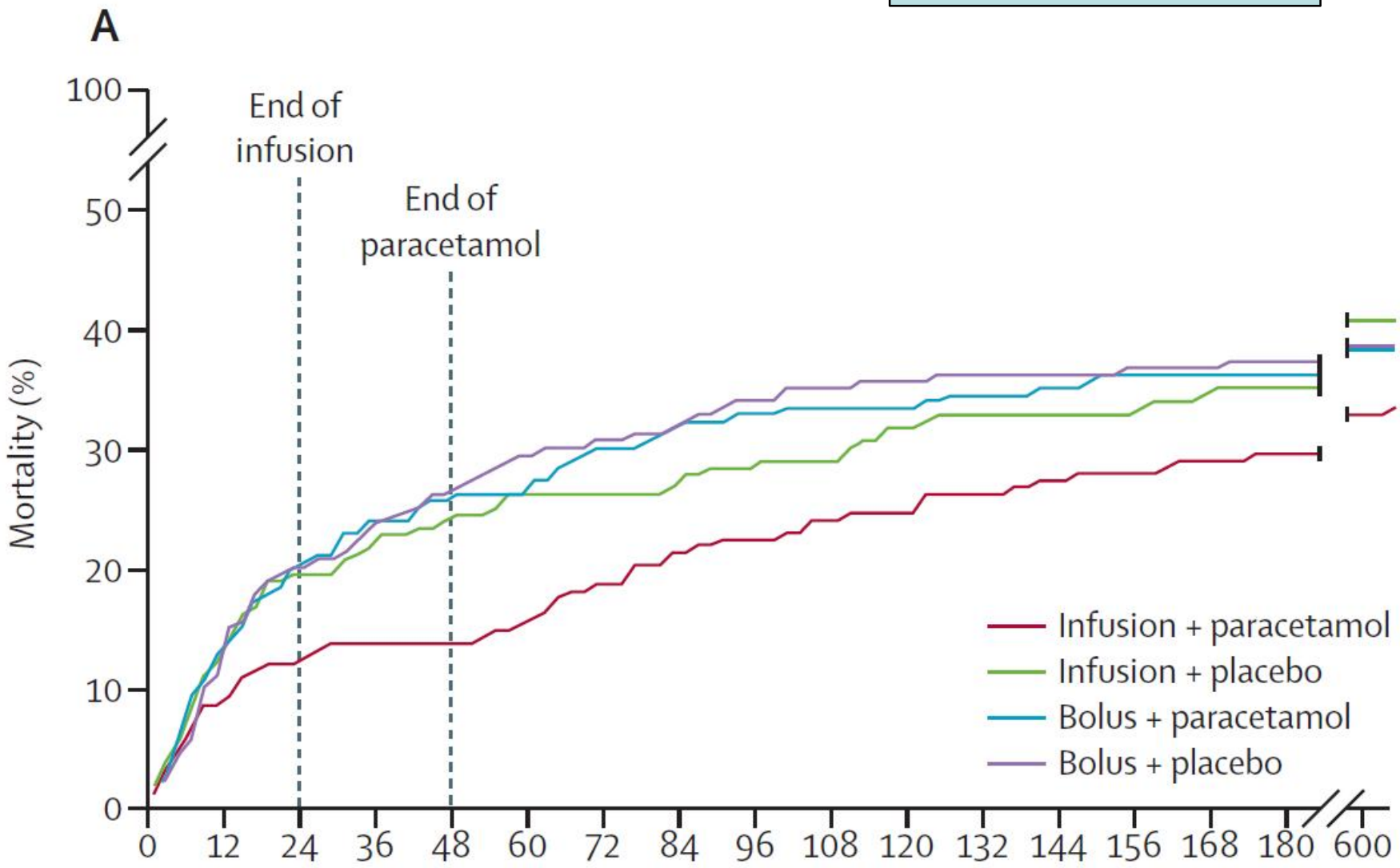
Summary

Background New antimicrobials or adjunctive treatments have not substantially reduced mortality from acute childhood bacterial meningitis. Paracetamol seems to have beneficial effects in bacteraemic adults and some experts recommend initial slow β-lactam infusion. We investigated whether these treatments had benefits in children with bacterial meningitis.

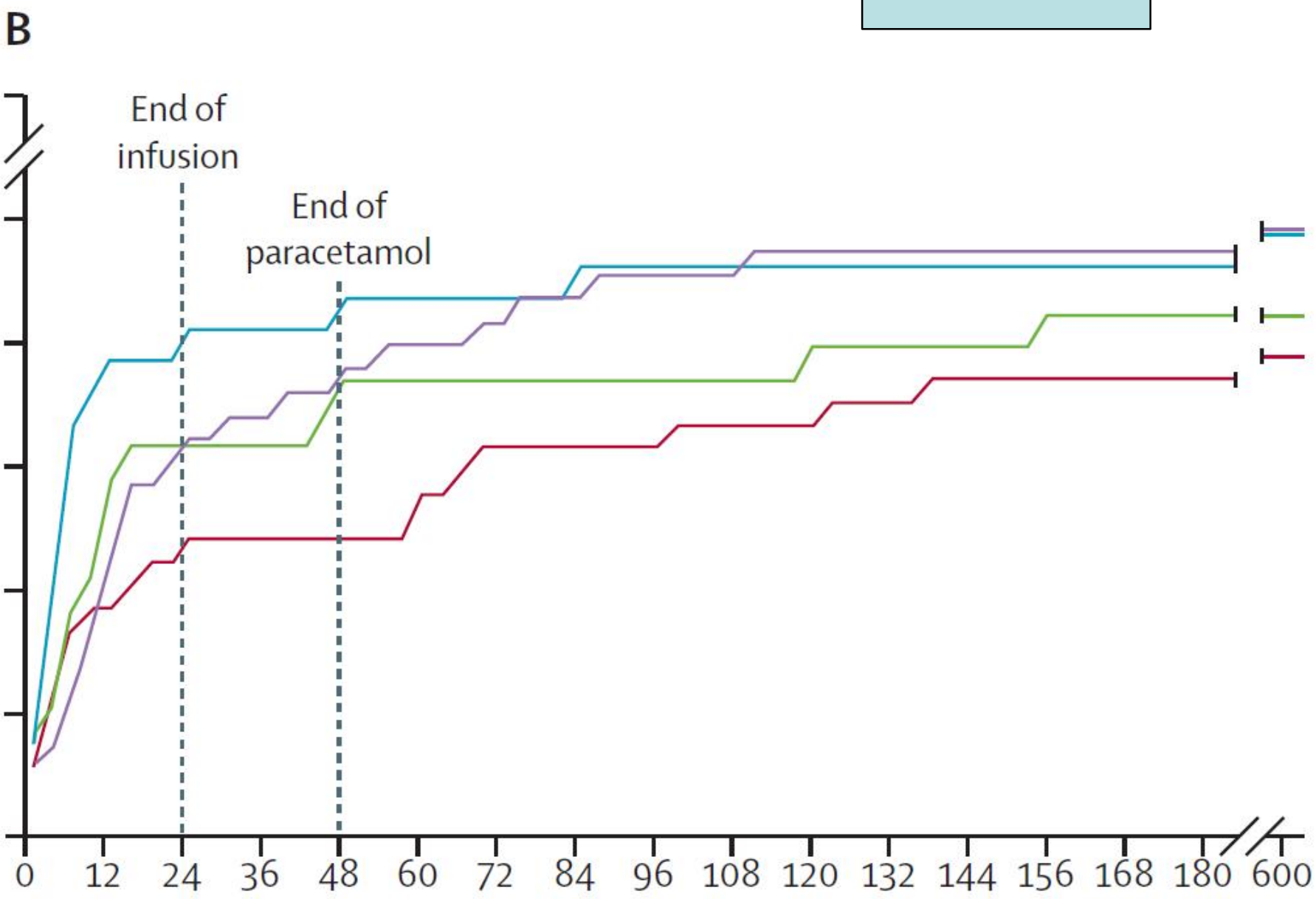
Lancet Infect Dis 2011; 11: 613–21

Published Online May 6, 2011 DOI:10.1016/S1473-

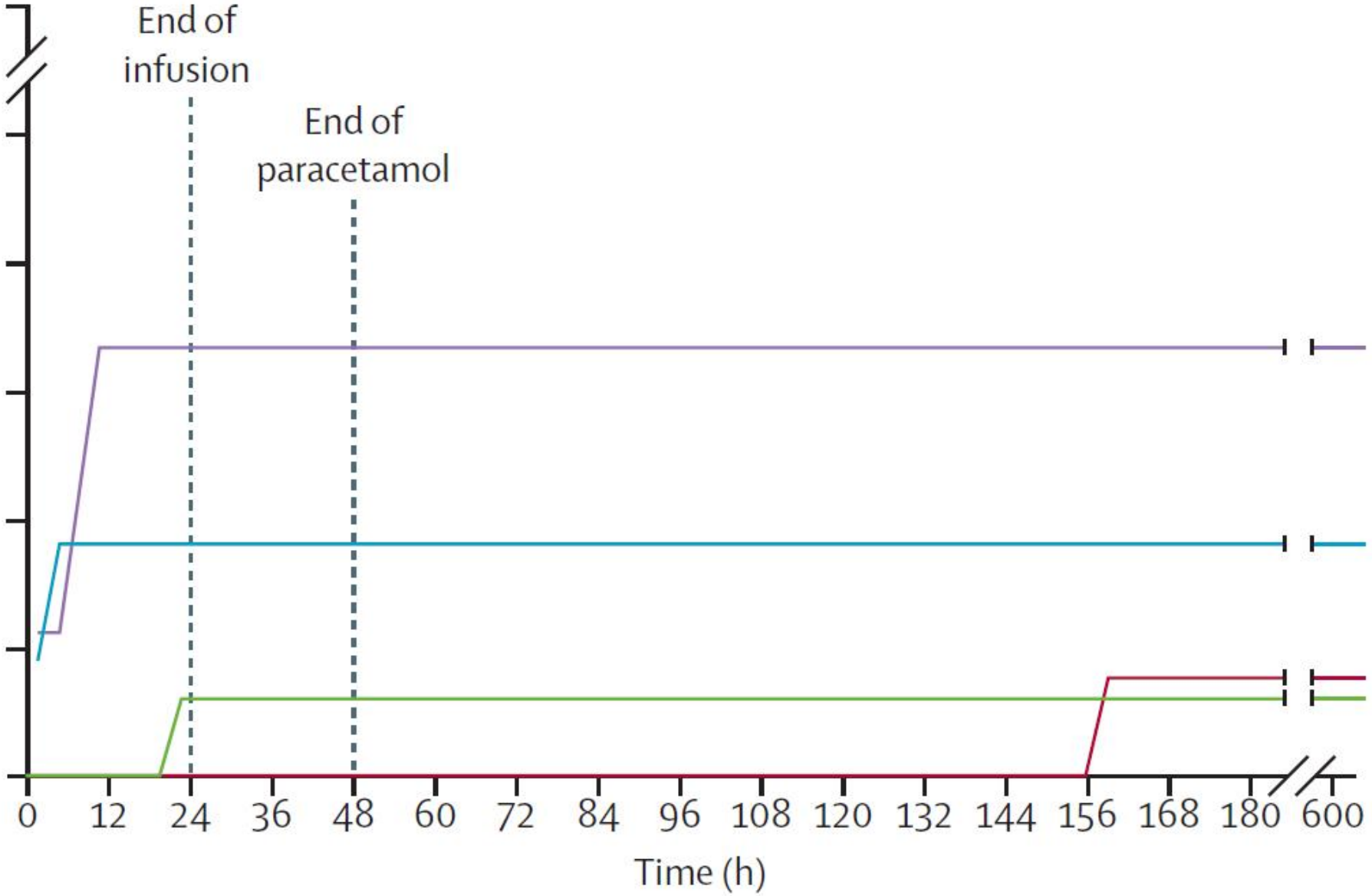
all bacterial species



pneumococci



meningococci



Slow initial β-lactam infusion and oral paracetamol to treat childhood bacterial meningitis: a randomised, controlled trial

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Lancet Infect Dis 2011; 11: 613–21

Published Online May 6, 2011

DOI:10.1016/S1473-

YES, SHOULD BE STRONGLY CONSIDERED

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 Huu, Matloob Azam, Zulfiqar Ahmad Bhutta, Ramadan Zaki, Martin Willi Weber, Shamim Ahmad Qazi, for the CSF 5 Study Group**

Summary

Background Bacterial meningitis is an important cause of m

University of Malawi Medical School Department of Paediatrics, Queen Elizabeth Central Hospital, Blantyre, Malawi (Prof E Molyneux FRCPCH); **Division of Maternal and Child Health, Aga Khan University, Karachi, Pakistan** (Prof S Q Nizami FCPS, Prof Z A Bhutta FRCPCH); **Department of Microbiogy, Dhaka Shishu Hospital, Dhaka, Bangladesh** (Prof S Saha PhD); **Children Hospital No 1, Ho Chi Minh City, Vietnam** (Prof K T Huu MD); **Department of Paediatrics, Wah Medical College, Islamabad, Pakistan** (Prof M Azam FRCPCH); **Department of Paediatrics, Abbasia Fever Hospital, Cairo, Egypt** (Prof R Zaki MD); **and Department of Child and Adolescent Health and Development, World Health Organization, Geneva, Switzerland** (M W Weber DrMedHabil, S A Qazi MD)

countries, but the

Lancet 2011; 377: 1837–45

Findings We included 1004 of 1027 children randomly assigned to study groups in our analyses; 496 received treatment with ceftriaxone for 5 days, and 508 for 10 days. In the 5-day treatment group, two children (one infected with HIV) had a relapse; there were no relapses in the 10-day treatment group and there were no bacteriological failures in either study group. Side-effects of antibiotic treatment were minor and similar in both groups.

Interpretation In children beyond the neonatal age-group with purulent meningitis caused by *S pneumoniae*, *H influenzae* type b, or *N meningitidis* who are stable by day 5 of ceftriaxone treatment, the antibiotic can be safely discontinued.

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

Journal of Infection (2011) 62, 172–177

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CASE REPORT

Induced hypothermia in adult community-acquired bacterial meningitis — more than just a possibility?

Dragan Lepur*, Marko Kutleša, Bruno Baršić

Department of Neuroinfections and Intensive Care Medicine, University Hospital for Infectious Diseases "Dr. Fran Mihaljević", Zagreb 10000, Croatia

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

Therapeutic hypothermia in bacterial meningitis

This study presents a series of 10 patients with **severe bacterial meningitis:**

nine patients: pneumococci,
one patient: Escherichia coli

with an **initial median GCS of 6** (range 3 to 9),
APACHE II ranging from **22 to 34** (median 31).

A protocol of **non-invasive ICP monitoring** (using transcranial Doppler sonography, optic nerve sheath diameter sonography and jugular bulb oxymetry) was employed.

Hypothermia was induced by intravenous infusion of cold isotonic saline and maintained with continuous venovenous hemofiltration at 32 to 34°C.

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

Therapeutic hypothermia in bacterial meningitis

This study presents a series of 10 patients with **severe bacterial meningitis:**

Table 1 Demographic and clinical data of patients with community-acquired bacterial meningitis treated with hypothermia-Part one.

Patient no.	Age/sex	Day of disease[a]	Coexisting conditions	Seizures	Etiology	APACHE II	GCS at admission	GCS at discharge from ICU	GOS[f]	Karnofsky score (%)[g]
1	82/F	1	Otitis	Yes	*S. pneumoniae (PSSP)*[d]	31	8	15	4	50
2	63/M	3	Otitis	No	*S. pneumoniae (PRSP)*[e]	22	4	15	3[b]	60
3	47/F	2	Immunocompromised[c]	No	*S. pneumoniae (PSSP)*	23	6	15	5	90
4	71/F	2	Rectal adenocarcinoma	No	*S. pneumoniae (PSSP)*	32	7	14	4	50
5	76/M	1	Otitis	No	*S. pneumoniae (PSSP)*	24	9	NA	2	NA
6	78/F	2	Immunocompromised	Yes	*S. pneumoniae (PSSP)*	33	3	NA	2	NA
7	61/F	1	Acute renal failure	No	*E. coli*	33	3	NA	1	NA
8	68/F	2	Immunocompromised, Pneumonia	No	*S. pneumoniae (PSSP)*	34	3	NA	1	NA
9	70/M	1	Immunocompromised	No	*S. pneumoniae (PSSP)*	26	8	15	5	90
10	75/F	1	Immunocompromised	No	*S. pneumoniae (PSSP)*	33	4	14	3	40

[a] Day of disease on which hypothermia was started.
[b] Paraplegia caused by severe myelitis.
[c] Immunocompromised - the use of immunosuppressive drugs or the presence of diabetes mellitus, chronic renal failure or alcoholism.
[d] PSSP = penicillin-susceptible *Streptococcus pneumoniae*.
[e] PRSP = penicillin-resistant *Streptococcus pneumoniae*.
[f] Score on Glasgow Outcome Scale – at discharge from ICU [1(death), 2(vegetative state), 3(severe disability), 4(moderate disability), 5(mild or no disability)].
[g] Karnofsky performance score – at discharge from ICU.

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

Table 2 Demographic and clinical data of patients with community-acquired bacterial meningitis treated with hypothermia-Part two.

Patient no.	CSF cell count[a] (cells/mm^3)	CSF-blood glucose ratio[b]	CSF protein concentration (mg/L)[c]	CSF lactate concentration (mmol/L)[d]	BHI_m[e]	Vasopressor support	Adjuvant dexamethasone treatment	Duration of hypothermia (hours)	Meningitis-related complications	Hypothermia/CVVHF -related complications
1	36 000	0,0	7450	18,0	N/A	Yes	Yes	72	none	none
2	200 000	0,0	12 100	15,9	0.876	Yes	Yes	72	severe myelitis	none
3	9216	0,47	1843	8,6	0.610	No	No	72	none	none
4	2560	0,0	9447	20,4	0.644	No	Yes	72	none	none
5	1160	0,03	11 936	25,9	0.350	No	Yes	72	refractory brain edema	none
6	1633	0,03	1790	25,4	0.090	Yes	Yes	96	ischemic stroke	none
7	12 997	0,39	7348	18,7	0.210	Yes	Yes	48	refractory brain edema	none
8	19 200	0,02	7273	—	0.342	Yes	Yes	48	ventriculitis, refractory brain edema	none
9	4437	0,23	8533	19,3	0.495	No	No	96	none	moderate amylase increase
10	4266	0,0	6031	12,4	0,0	Yes	No	96	ischemic leukoencephalopathy	none

[a] CSF white cell count (normal value: <5 cells/mm^3).
[b] CSF-blood glucose ratio (normal value: >0,4).
[c] CSF protein concentration (normal range: 150–450 mg/L).
[d] CSF lactate concentration (normal range: 1,58–2,03 mmol/L).
[e] Mean breath-holding index - at admission to ICU.

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

Nothing is said about

- **rewarming,**
- **rewarming speed and**
- **duration of hypothermia**.

Two patients died within 48 hours from admission because of **refractory intracranial hypertension**,
two more patients with severe **residual neurological deficits** (GOS 2) **died later on**, after discharge from the ICU, because of late-onset nosocomial sepsis; in total, a rather **high mortality rate**

TEMPERATURE MANAGEMENT IN CENTRAL NERVOUS INFECTION

The surviving six patients had a mean ICU stay of 22 days (range 8 to 36),

two had a severe and two a moderate residual neurologic deficit.

Two of the entire group of **10 patients** with **bacterial meningitis** had **complete neurological recovery (GOS 5).**

Factors Associated with the Occurrence of Hearing Loss after Pneumococcal Meningitis

Lise Worsøe,[1] Per Cayé-Thomasen,[1,5] Christian Thomas Brandt,[3,4] Jens Thomsen,[1,5] and Christian Østergaard,[2]

[1]Department of Oto-rhino-laryngology, Head and Neck Surgery, Copenhagen University Hospital Gentofte, Hellerup, [2]Department of Clinical Microbiology, Copenhagen University Hospital Herlev, Herlev, [3]Department of Infectious Diseases, Copenhagen University Hospital Hvidovre, Hvidovre, [4]Copenhagen HIV Programme, Faculty of Health Sciences, University of Copenhagen, and [5]Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark

Clinical Infectious Diseases 2010; 51(8):917–924

Hearing loss is common after pneumococcal meningitis, and audiometry should be performed on all patients. Important risk factors for hearing loss are advanced age, female sex, severity of meningitis, and the presence of a certain bacterial serotype.

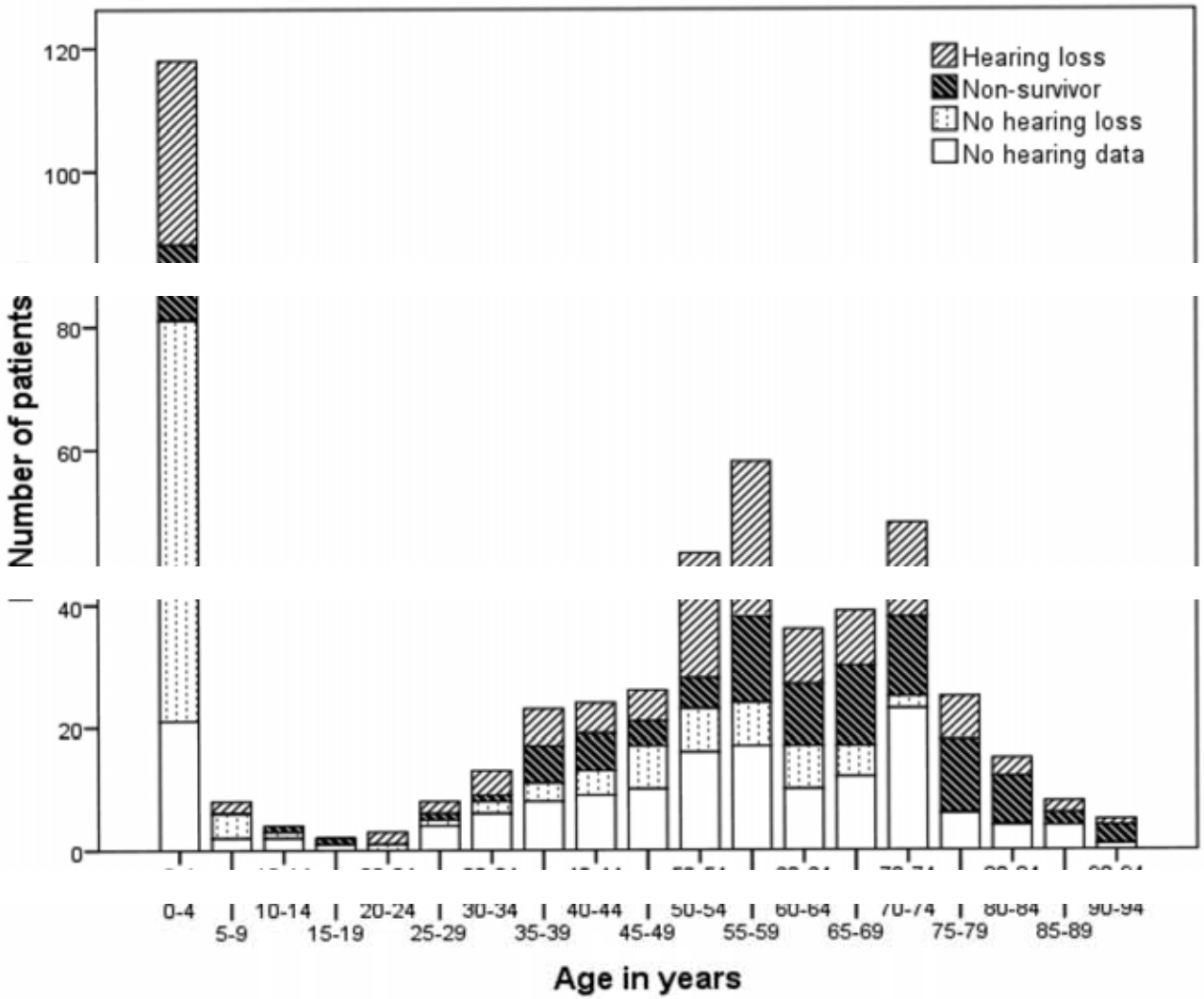


Figure 2. Age distribution, survival, and hearing outcome for meningitis due to *Streptococcus pneumoniae* in Denmark from 1999 to 2003 ($N = 505$). The hearing loss was determined by audiometric testing. Adult patients had a higher mortality and a higher occurrence of hearing loss, compared with pediatric patients ($P < .001$).

BE AWARE of this disease
KNOW the EPIDEMIOLOGY, epidemiologic trends

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

COMMUNICABLE DISEASE THREATS REPORT

CDTR

Week 5, 27 January-2 February 2013

Each year, approximately 1.2 million cases of invasive meningococcal disease are recorded worldwide.

In Europe, group B is the most prevalent meningococcal serogroup, with 3,406-4,819 cases reported annually between 2003 and 2007, according to a surveillance report published by the European Centre for Disease Prevention and Control.

WHO, 2010

16th of November 2012

European Medicines Agency

recommends approval of first vaccine for meningococcal meningitis serogroup B

16th of November 2012:

European Medicines Agency

recommends approval of first vaccine for meningococcal meningitis serogroup B

Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials

Timo Vesikari, Susanna Esposito, Roman Prymula, Ellen Ypma, Igor Kohl, Daniela Toneatto, Peter Dull, Alan Kimura, for the EU Meningococcal B Infant Vaccine Study group

www.thelancet.com Published online January 14, 2013

NEW DEVELOPMENTS IN ACUTE BACTERIAL MENINGITIS

Be ready to employ - with all precautions - also in acute bacterial meningitis:

-neurocritical care medicine
-general/systemic critical care medicine
(e.g. for concomitant/accompanying sepsis syndrome)
-all monitoring methods and devices

Nosocomial meningitis is different from community acquired meningitis

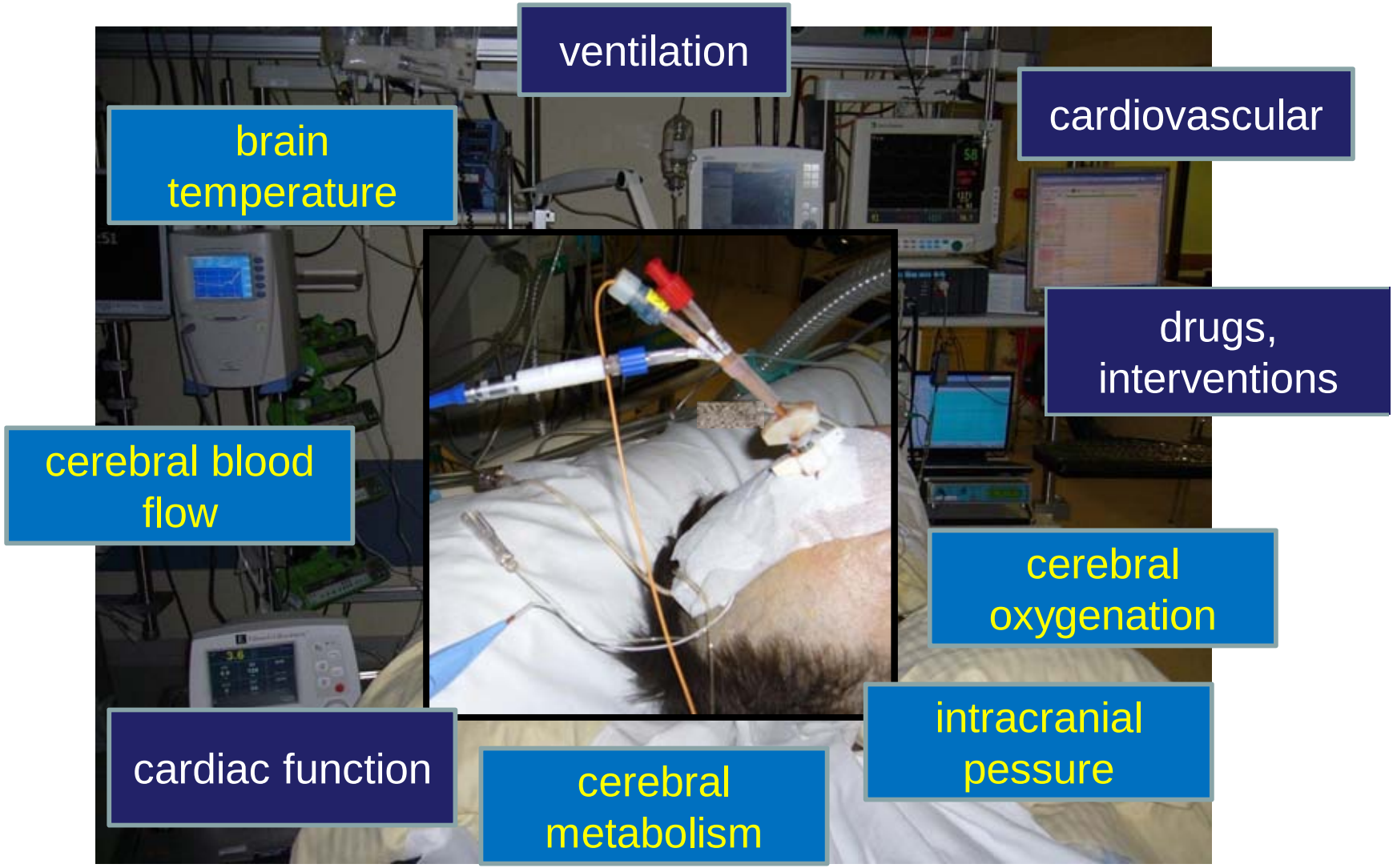
and do not forget epidemiology and epidemiological trends

What is the impact of extended neuromonitoring in routine intensive care?

- Guidance of CPP
- Guidance of optimal blood and brain glucose values
- Guidance of haematocrit and transfusion requirements
- Guidance of decompressive craniectomy

J.Stover, 2011

Invasive Neuromonitoring Innsbruck



NEW DEVELOPMENTS IN ACUTE BACTERIAL MENINGITIS

è BUT DO NOT FORGET YOUR CLINICAL SKILLS

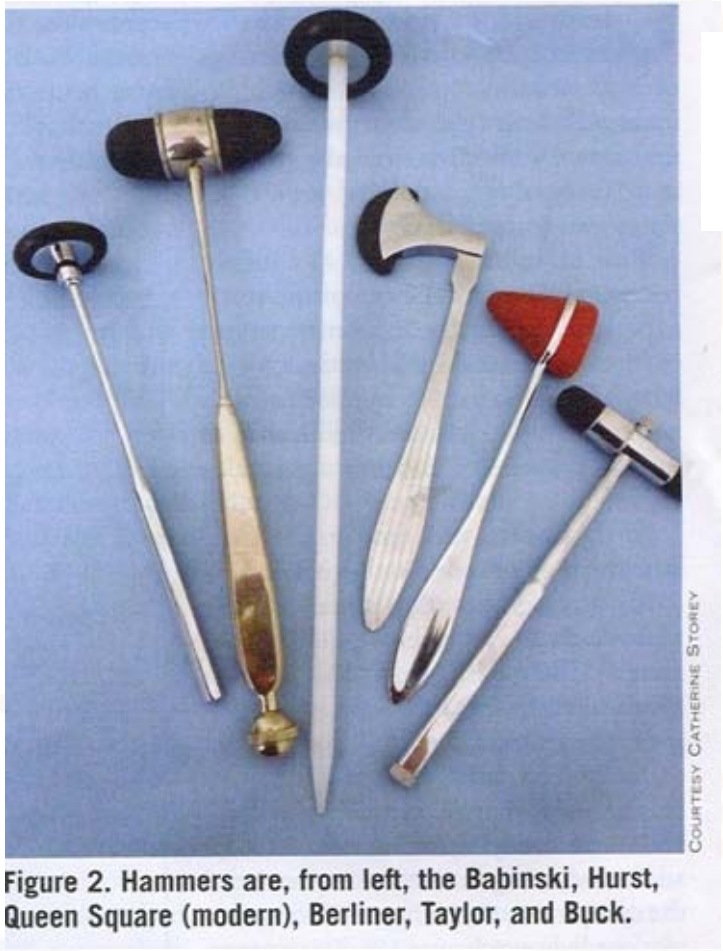


Figure 2. Hammers are, from left, the Babinski, Hurst, Queen Square (modern), Berliner, Taylor, and Buck.

Courtesy: Catherine Storey

WCN 2013

SAVE THE DATE

XXI WORLD CONGRESS OF NEUROLOGY

Vienna, Austria, **21-26** September **2013**

many thanks for your attention

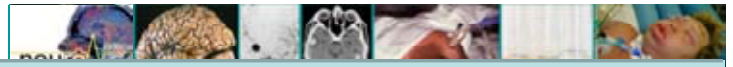
WFN

ÖGNH AUSTRIAN SOCIETY OF NEUROLOGY

EFNS EUROPEAN FEDERATION OF NEUROLOGICAL SOCIETIES

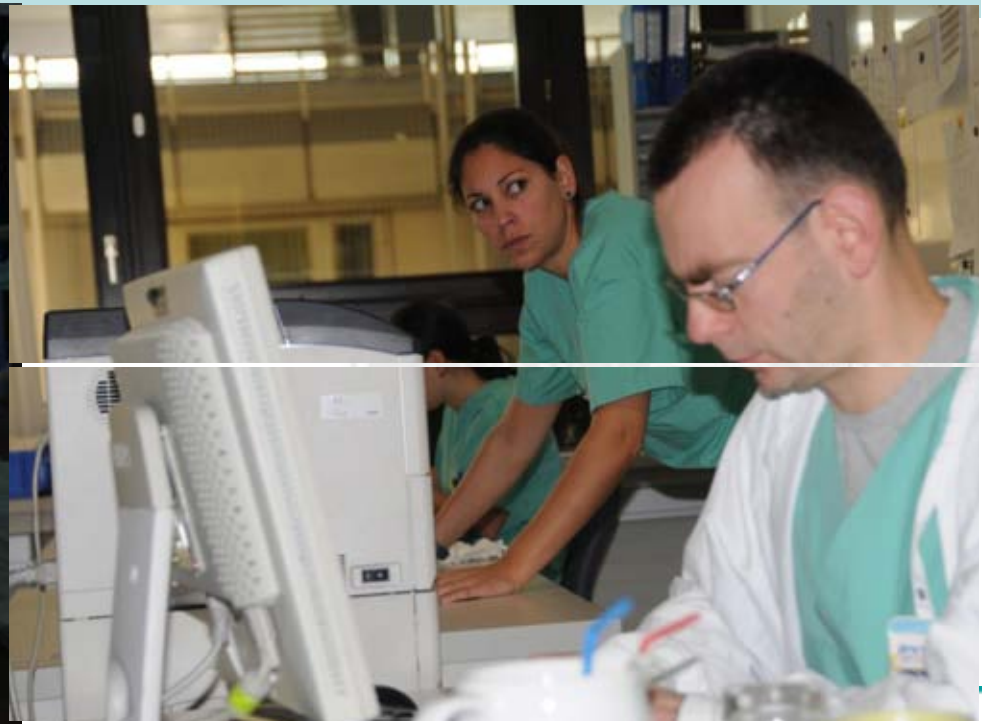
NEUROLOGY IN THE AGE OF GLOBALIZATION

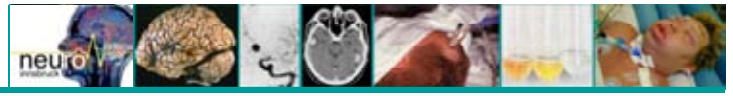
www.wcn-neurology.com



and many thanks to all my co-workers

Bettina Pfausler: **CNS Infections**, Prognosis and complications in Critical Care Neurology
brain death, Ethics in Critical Care Neurology, Nodding Syndrome
Ronny Beer: TBI, cerebral Hypoxia, **Antibiotics PK/PD,** SyNAPSE, INTERACT 2, CINCH, NOSTRA
Raimund Helbok: Multimodal Monitoring, COSBID, NOSTRA, Neurorobotics
Gregor Broessner: Th.Hypothermia, prophylactic Normothermia, CINCH, IcTUS 2, Eurohyp
Peter Lackner: Translational neurocritical care: murine cerebral malaria, Sepsisencephalopathy,
microdialysis in murine model, murine SAH
Marlene Fischer: Neurovascular Compartment and brain temperature, IcTUS 2
Alois Schiefecker: Multimodal Monitoring, COSBID
Monika Wallnöfer, Franziska Di Pauli, Anna Hotter, Bettina Künz-Steininger



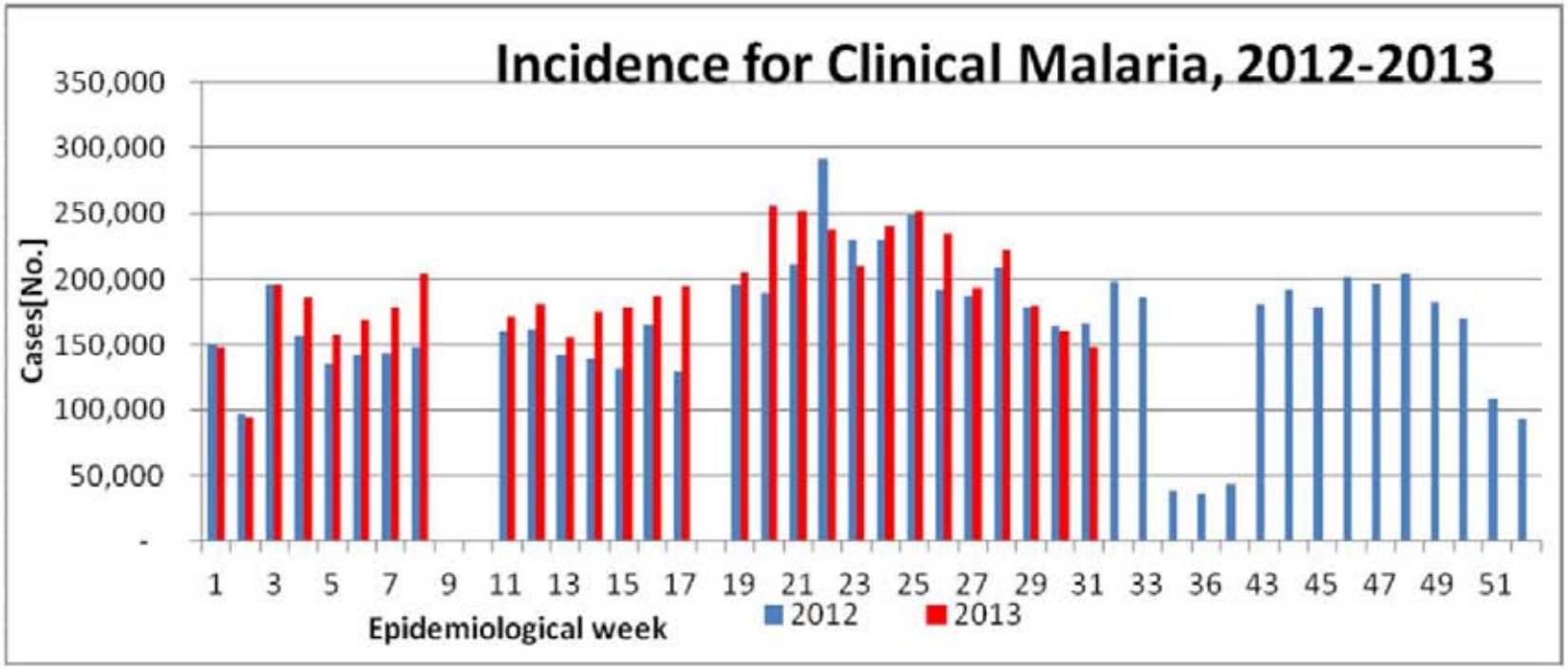

neuro

Ministry of Health Uganda

Weekly Epidemiological Bulletin

Epidemiological week 31 of 2013 [29 July – 4 August 2013]

Malaria: Is the commonest cause of morbidity and mortality in the country; thus this week, 148,948 clinical malaria cases including 42 deaths were reported from the 102 districts that submitted weekly reports. This translates into a national weekly incidence of 469 clinical malaria cases per 100,000. The top 10 districts [Tororo, Abim, Isingiro, Moyo, Ibanda, Otuke, Kiruhura, Buliisa, Koboko, & Lyantonde] had an incidence of 1,001-1,552 clinical malaria cases per 100,000 this week. The figure below shows the number of clinical malaria cases reported to the MoH by week for 2012 & 2013 [annex 1 for district specific reports].



Glycerol in bacterial meningitis: one strike and out?

Matthijs C Brouwer, Diederik van de Beek
Department of Neurology and Department of Infection and Immunity, Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands

www.thelancet.com/infection Vol 11 April 2011

glycerol was harmful as an adjunctive therapy in adults with bacterial meningitis in this setting.

The mechanism of harm of oral glycerol remains unclear. Few data on clinical complications were recorded,

Glycerol in bacterial meningitis: one strike and out?

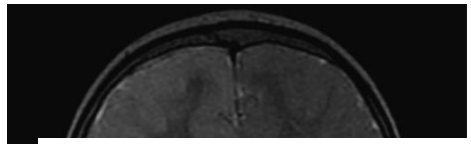
Matthijs C
Department
Immunity, C
(CINIMA), A
Amsterdam

Glucose!!!!!

Osmolytes!! è
Never give hyperosmolar substances **continuously,** if at all,only as **bolus**

glycerol v
with bact

The mechanism of harm of oral glycerol remains unclear. Few data on clinical complications were recorded,



Published April 19, 2012 as 10.3174/ajnr.A3035

ORIGINAL RESEARCH

Acute Brain MRI Findings in 120 Malawian Children with Cerebral Malaria: New Insights into an Ancient Disease

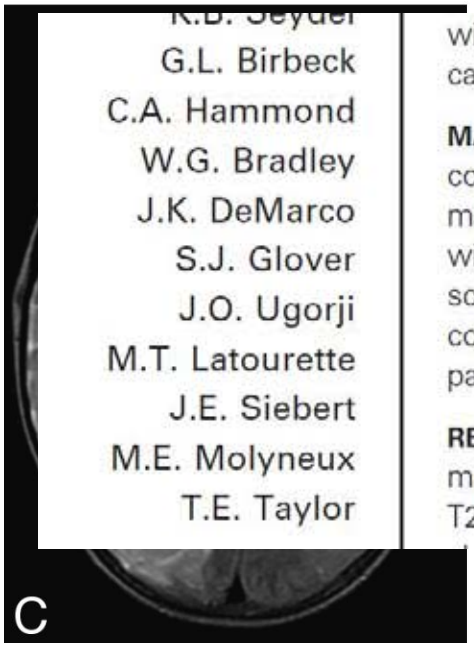
M.J. Potchen
S.D. Kampondeni
K.B. Seydel
G.L. Birbeck
C.A. Hammond
W.G. Bradley
J.K. DeMarco
S.J. Glover
J.O. Ugorji
M.T. Latourette
J.E. Siebert
M.E. Molyneux
T.E. Taylor

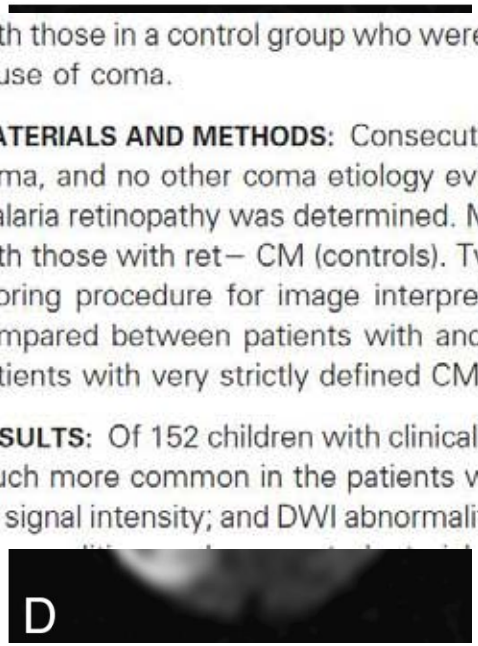
BACKGROUND AND PURPOSE: There have been few neuroimaging studies of pediatric CM, a common often fatal tropical condition. We undertook a prospective study of pediatric CM to better characterize the MRI features of this syndrome, comparing findings in children meeting a stringent definition of CM with those in a control group who were infected with malaria but who were likely to have a nonmalarial cause of coma.

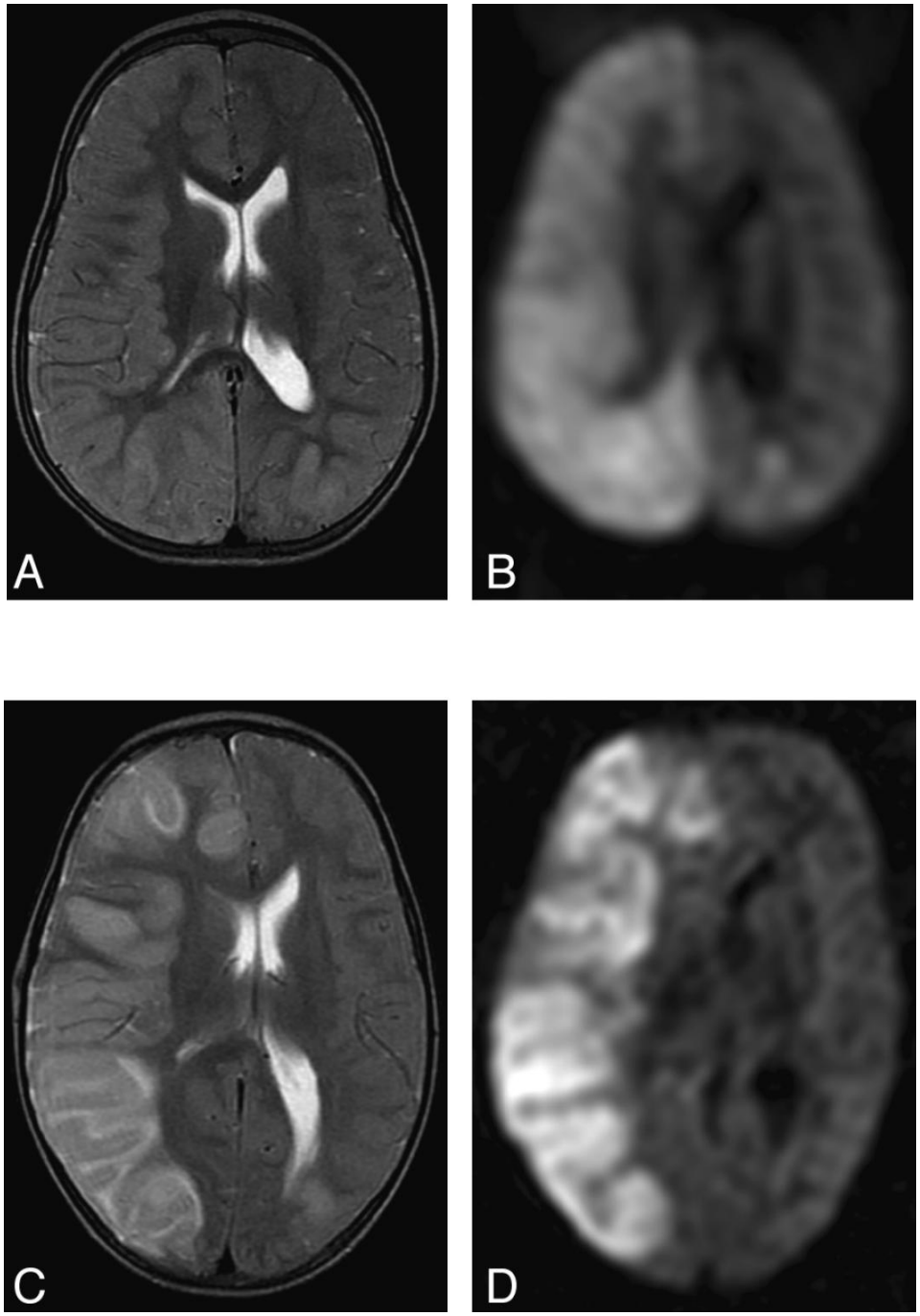
MATERIALS AND METHODS: Consecutive children admitted with traditionally defined CM (parasitemia, coma, and no other coma etiology evident) were eligible for this study. The presence or absence of malaria retinopathy was determined. MRI findings in children with ret+ CM (patients) were compared with those with ret− CM (controls). Two radiologists blinded to retinopathy status jointly developed a scoring procedure for image interpretation and provided independent reviews. MRI findings were compared between patients with and without retinopathy, to assess the specificity of changes for patients with very strictly defined CM.

RESULTS: Of 152 children with clinically defined CM, 120 were ret+, and 32 were ret−. Abn
much more common in the patients with ret+ CM were markedly increased brain volume
T2 signal intensity; and DWI abnormalities in the cortical, deep gray, and white matter structure

Brain edema






A
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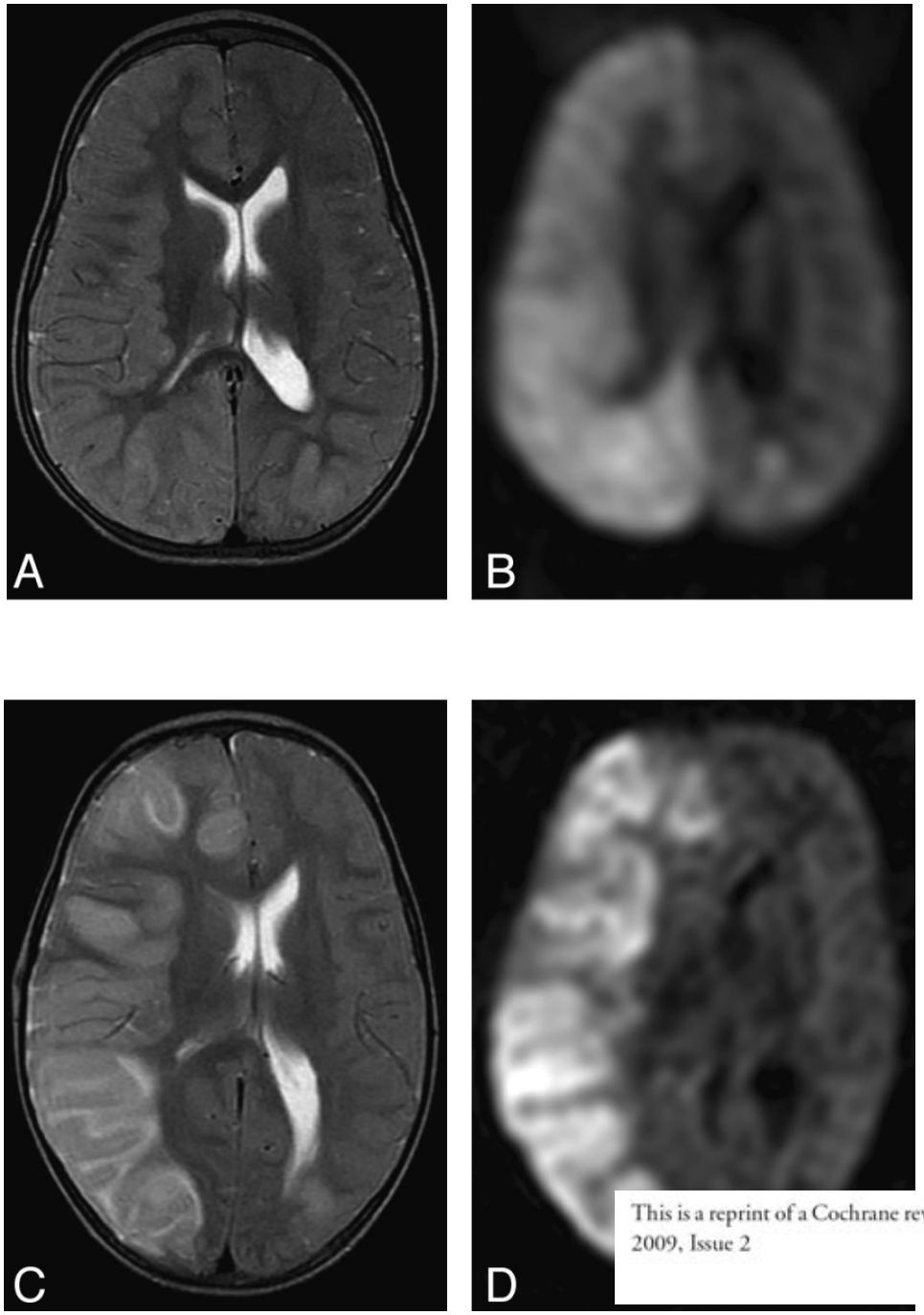
C
D



Brain edema è steroids, osmotherapy

Steroids for treating cerebral malaria (Review)

Prasad K, Garner P

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2009, Issue 2

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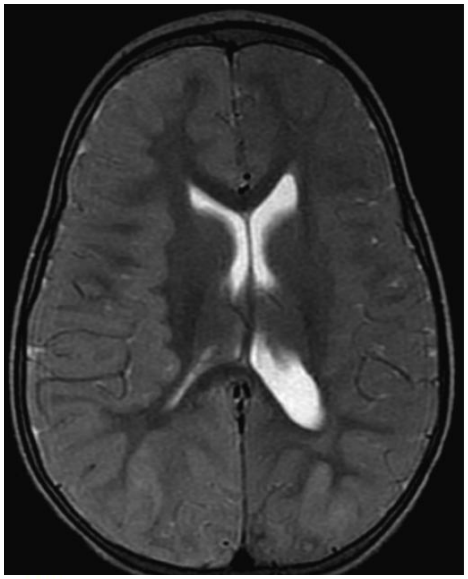
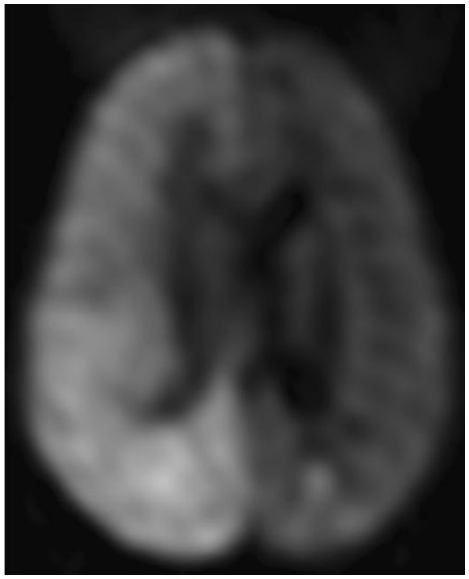




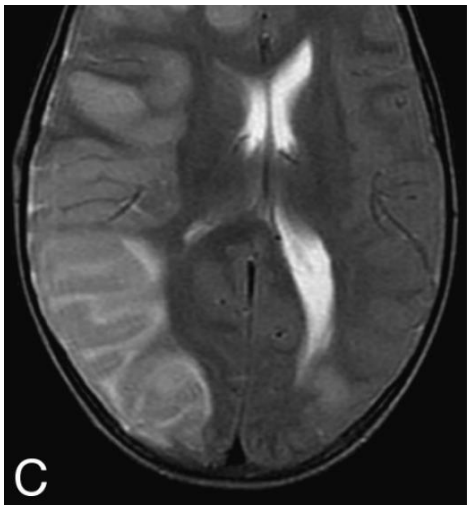
Brain edema è steroids, osmotherapy

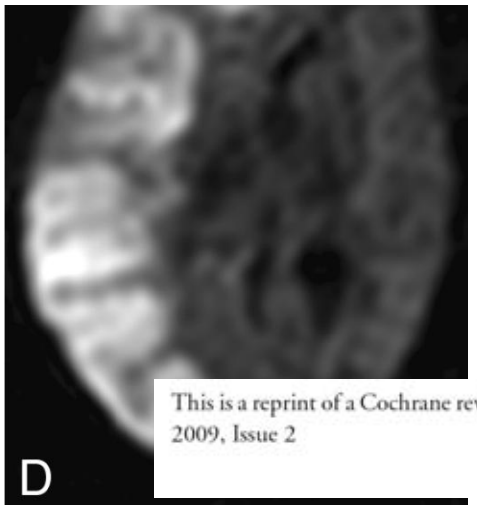
Steroids for treating cerebral malaria (Review)

Prasad K, Garner P

This review assesses the effects of corticosteroid drugs given for cerebral malaria, on death, life-threatening complications, and residual disability in survivors.

The authors included two trials with a total of 143 patients (both adults and children). There were no significant differences in the number of deaths between the corticosteroid and control groups, and data on clinical complications were difficult to assess. Neither trial examined disability.





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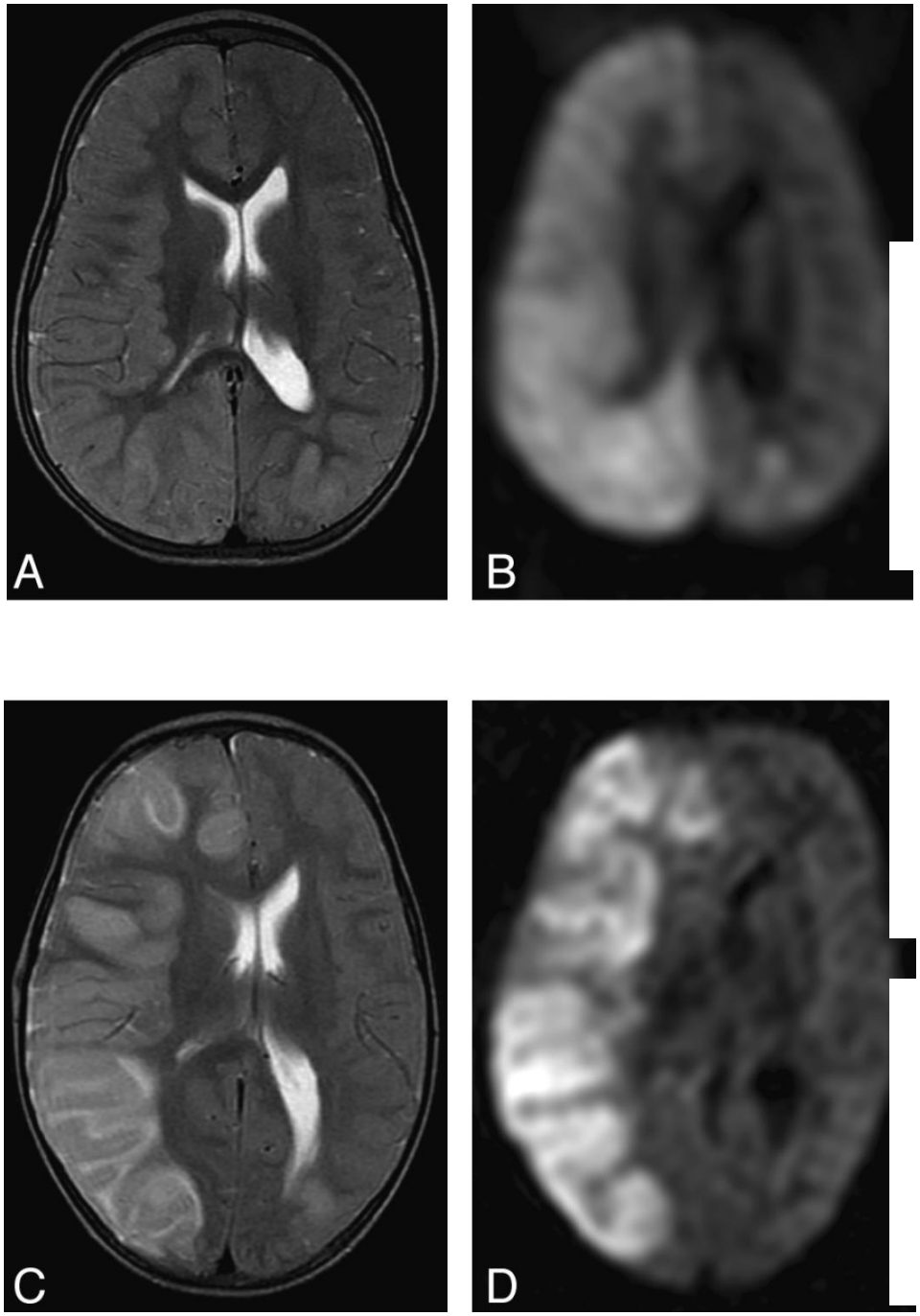

Brain edema è steroids, osmotherapy ??

Mannitol and other osmotic diuretics as adjuncts for treating cerebral malaria (Review)

Okoromah CAN, Afolabi BB, Wall ECB

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Mannitol and other osmotic diuretics as adjuncts for treating cerebral malaria (Review)

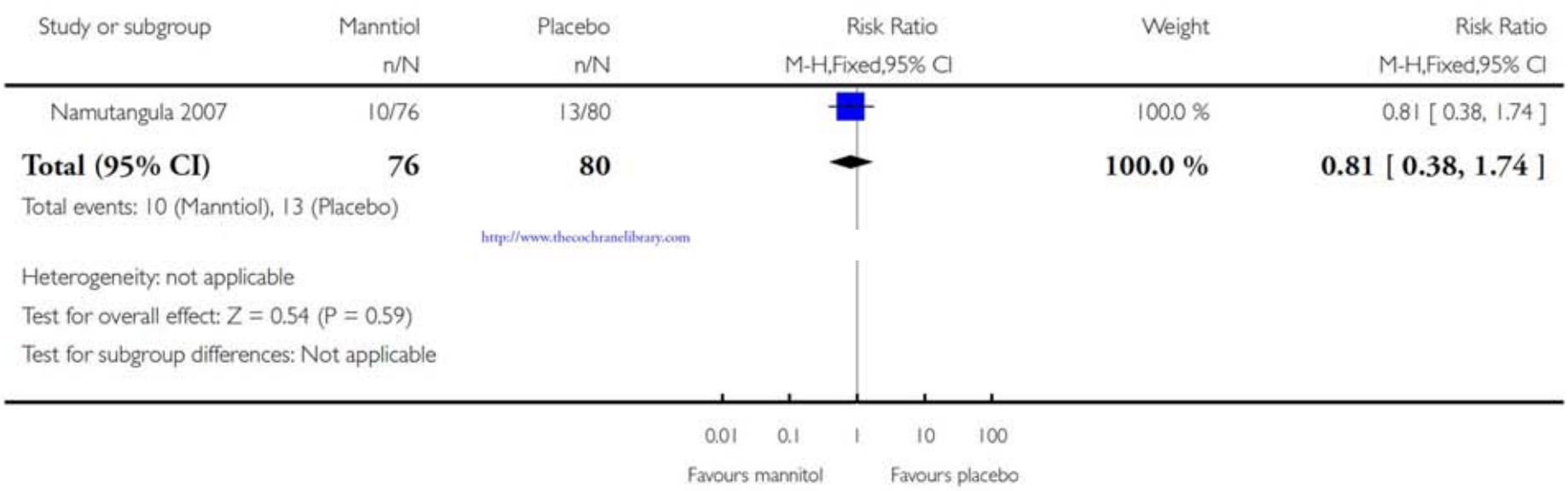
Okoromah CAN, Afolabi BB, Wall ECB

Analysis 1.1. Comparison 1 Mannitol versus placebo, Outcome 1 Death.

Review: Mannitol and other osmotic diuretics as adjuncts for treating cerebral malaria

Comparison: 1 Mannitol versus placebo

Outcome: 1 Death



Mannitol and other osmotic diuretics as adjuncts for treating cerebral malaria (Review)

Okoromah CAN, Afolabi BB, Wall ECB

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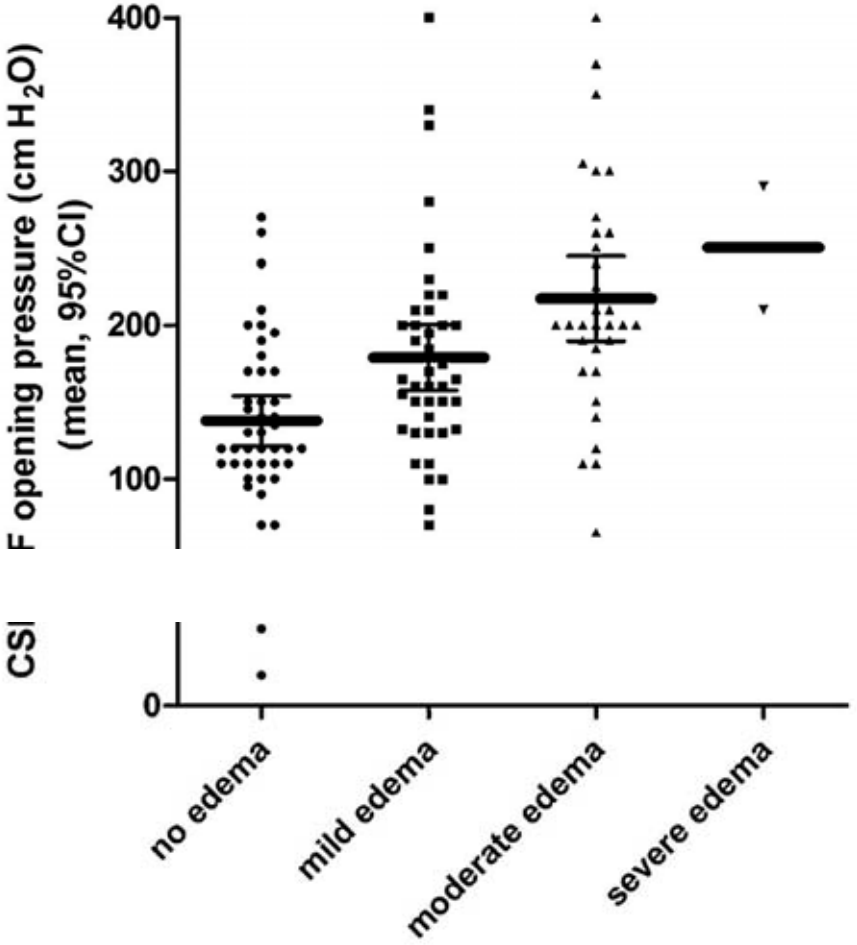
Brain Swelling and Mannitol Therapy in Adult Cerebral Malaria: A Randomized Trial

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

[1]Depatment of Medicine and Radiology, Ispat General Hospital, Rourkela, Orissa, India; [2]Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and [3]Centre for Tropical Medicine, Churchill Hospital, Oxford, United Kingdom



Brain Sw y in Adult Cerebral al

Figure 2. Relation between severity of cerebral edema on computed tomographic scan and opening pressures on lumbar puncture in adult patients with slide-proven cerebral malaria; *P* value for trend = .001. CI, confidence interval; CSF, cerebrospinal fluid.

Sanjib Mohanty,[1] Sar dhan,[1] Bhabanisankar Das,[1] Jayakrushna Patnaik,

[1]Depatment of Medicine and Radiology, Ispat General Hospital, Rourkela, Orissa, India; [2]Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and [3]Centre for Tropical Medicine, Churchill Hospital, Oxford, United Kingdom

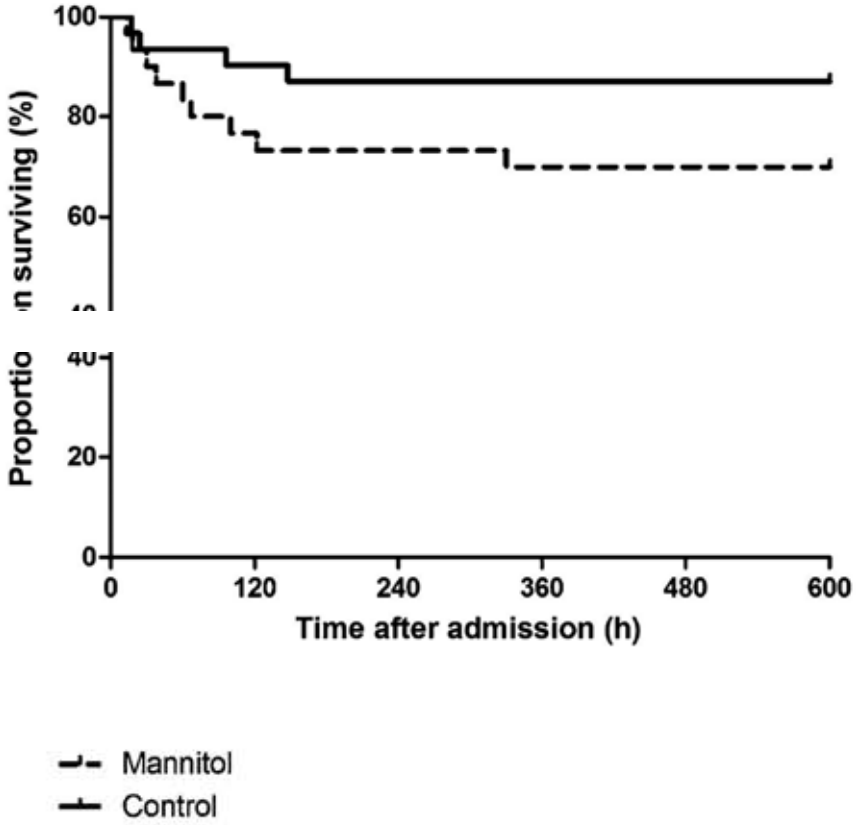


Figure 3. Survival curves for patients treated with (*dashed line*) or without (*solid line*) mannitol as adjunctive treatment for cerebral malaria with cerebral edema identified on computed tomographic scan. Log-rank test χ^2: 2.58; $P = .11$.

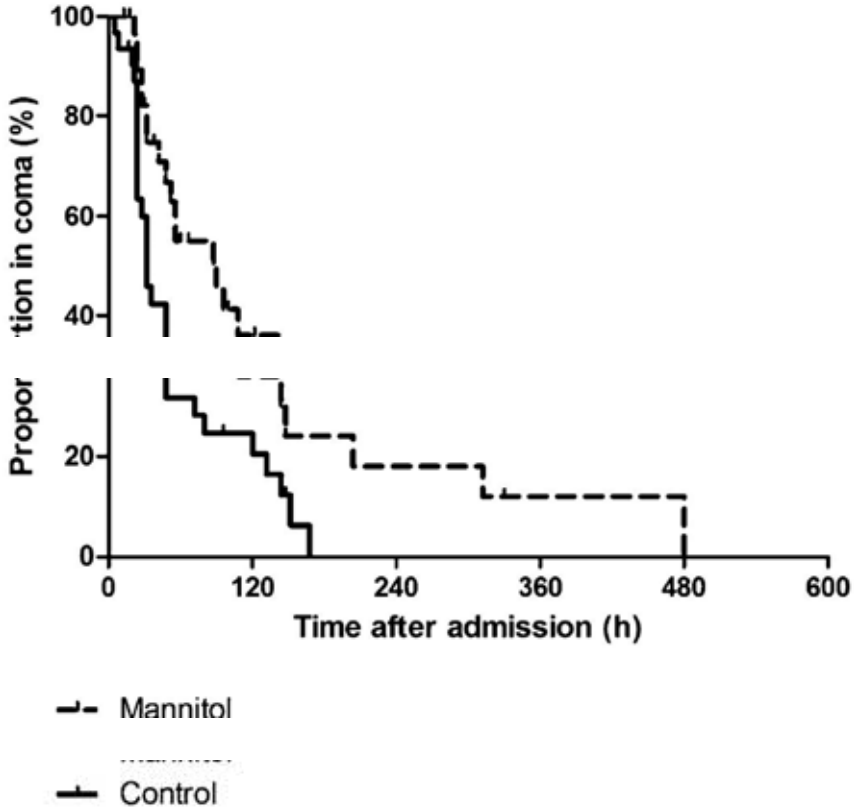


Figure 4. Kaplan–Meier curves for the proportion of patients still in coma after start of treatment with (*dashed line*) or without (*solid line*) mannitol as adjunctive therapy for cerebral malaria with cerebral edema identified on computed tomographic scan. Data from patients who died were censored at the moment of death. Log-rank test χ^2: 6.37; $P = .01$.

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

[1]Depatment of Medicine and Radiology, Ispat General Hospital, Rourkela, Orissa, India; [2]Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; and [3]Centre for Tropical Medicine, Churchill Hospital, Oxford, United Kingdom