EAN-AFAN RTC IN SUBSAHARA-AFRICA

ACUTE CNS INFECTIONS
IN THE ELDERLY

Erich Schmutzhard
Univ.Klinik für Neurologie, NICU
Medizinische Universität
Innsbruck
Österreich

- **exposure**
- pre-existing **diseases**
- compromised **immunesystem**
- **age**

HISTORY

Accepted Manuscript

Title: Ongoing and emerging arbovirus threats in Europe

Author: Luisa Barzon

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DOI: https://doi.org/10.1016/j.jcv.2018.08.007
Reference: JCV 4044

To appear in: *Journal of Clinical Virology*

ARBOVIRUS THREATS IN **EUROPE**

and even more: WORLDWIDE

Table 2. Clinical syndrome associated with arbovirus infection.

Syndromes	**Viruses**
Febrile illness	Dengue, chikungunya, O'nyong-nyong, etc.
Rash	Dengue, chikungunya, Zika, O'nyong-nyong, Sindbis virus
Arthralgia and/or myalgia	chikungunya, dengue, Crimean-Congo haemorrhagic fever, sandfly viruses, O'nyong-nyong, Sindbis virus, Ross River virus
Neurological syndrome	West Nile virus, tick-borne encephalitis, Japanese encephalitis, St. Louis encephalitis, Zika virus, Powassan virus, dengue, Toscana virus, Venezuelan and other equine encephalitis viruses, Rift Valley fever, La Crosse virus and California encephalitis virus antigenic group
Haemorrhagic syndrome	dengue, yellow fever, Crimean-Congo haemorrhagic fever, Rift Valley fever
Congenital syndrome	Zika virus

Most frequent acute viral (Meningo)encephalitides

Viruses	Neurologic Manifestation	Systemic peculiarities	Diagnostics (1st/2nd choice)	Course
Adenoviruses	M, ME	fever acute pharyngitis, conjunctivitis, epidemic Keratoconjunctivitis, atypical pneumonia	1. Serology - ASI 2. virus-isolation	rarely severe course in babies children and immunocompromised
Enteroviruses	poliomyelitis	hemorrhagic conjunctivitis, bronchitis, enteritis	1. Serology 2. PCR 3. virus isolation	
Arboviruses				
-TBE	M (25%), ME (75%) after tickbite	biphasic course	1. Serology - ASI 2. RNA-PCR	mortality 0,8-2%, in up to 10% EPMS Sy or rarely polio-like course

adapted from Schmutzhard & Loescher 2016

Most frequent acute viral (Meningo)encephalitides

Viruses	Neurologic Manifestation	Systemic peculiarities	Diagnostics (1st/2nd choice)	Course
-Eastern Equine Encephalitis (EEE) -**West Nile Virus Encephalitis** **-Japanese Encephalitis** -St.Louis Enzephalitis **-Zika** **-Chikungunya** **-Dengue** -Yellow fever -CCHF	E	HISTORY: exposure – travellers / migrants to / from endemic areas, mosquito-bites	serology	mortality up to 30%
Arenaviruses				
LCM-Virus (Lympho-cytic Choriomeningitis)	ME, MM, transmission by rodents	long prodromal-Stage: fatigue backpain, muscle pains	serology, PCR	rarely severe course mortality 2,5%

Most frequent acute viral (Meningo)encephalitides

Viruses	Neurologic Manifestation	Systemic peculiarities	Diagnostics (1st/2nd choice)	Course
Herpes simplex I (II)	ME relapsing M (Mollaret)	pseudopsychotic signs and symptoms. Focal neurology, epileptic seizures	MR, EEG, PCR	w/o antiviral th: mortality: 70% **earliest possible aciclovir therapy essential**
Epstein-Barr-Virus (EBV)	M, ME (brainstem-enzephalitis, Cerebellitis) polyneuritis	infectious mononucleosis (Pfeiffer)	1. PCR 2. Serology	mostly benign mortality: 2-5%
Cytomegalovirus (CMV)	ME, Myelitis (cave: **reactivation** in **immunsuppressed**) polyneuritis	seropositivity in 50-60% of healthy population, Rarely: hepatitis, myocarditis, pneumonia	1. PCR 2. ASI and Antigen in serum	severe courses in immunosuppr. complicated courses with CMV-pneumonia, -colitis, -retinitis)

Most frequent acute viral (Meningo)encephalitides

Viruses	Neurologic Manifestation	Systemic peculiarities	Diagnostics (1st/2nd choice)	Course
Influenza-A- and –B-Virus	ME and parainfectious EM, including hemorrhagic encephalopathy	flu, bronchitis pneumonia myalgia,	1.Serology 2. PCR	usually benign course, in the elderly: with organ involvement: mortality 10%
Mumps-virus	M, ME	In up to 50% meningitis after the start of parotitis, orchitis, pancreatitis, Oophoritis	1.Serology 2. ASI	
Measles-virus	(para)infectious **Encephalitis SSPE**	5th to 9th day (up to 33rd) day after start of exanthema, bronchopneumonia laryngitis, enteritis	1.Serology 2. ASI	mortality 1-20% in encephalitis: 50% longterm sequelae

Most frequent acute viral (Meningo)encephalitides

Viruses	Neurologic Manifestation	Systemic peculiarities	Diagnostics (1st/2nd choice)	Course
Pox-virus	EM, parainfectious	cyclic course	1. PCR, Serology 2. virus-risolation	cerebral manifestation in up to 5%
Rubella-Virus	parainfectious EM cave: embryopathy	exanthema, nuchal lymph-adenopathy	ASI, PCR	
Rhabdoviruses	**Rabies – encephalitis 80% radiculomyelitis: 20%**	„furious“ rabies „dumb“ rabies	1. PCR 2. surface sample from cornea 3.skin-biopsy (nuchal region)	mortality 100%

Most frequent acute viral (Meningo)encephalitides

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Viral encephalitides:
You **MUST** recognize:
Herpes simplex I encephalitis
and
Rabies

Current Infectious Disease Reports (2018) 20:34
https://doi.org/10.1007/s11908-018-0641-x

NEUROLOGICAL INFECTIOUS DISEASES

Acute Flaccid Paralysis and Enteroviral Infections

Ari Bitnun[1] · E. Ann Yeh[2]

NMO: transverse myelitis: sensory **plus** motor
Polio: grey matter: motor, **no** sensory

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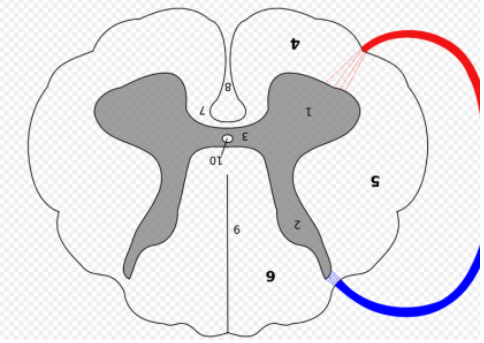
Abstract

Purpose of Review The focus of this review is on enterovirus (EV)-associated acute flaccid paralysis (AFP) due to spinal cord anterior horn cell disease. Emphasis is placed on the epidemiology, pathogenesis, diagnosis, treatment, and outcome of AFP caused by polioviruses, vaccine-derived polioviruses, EV-D68, and EV-A71.

These are all viruses causing poliomyelitis

Poliomyelitis (Greek: πολιός = ‚grey', μυελόν =‚spinal cord', -itis = inflamm.)



Global emergence of enterovirus D68: a systematic review

Charlotte Carina Holm-Hansen, Sofie Elisabeth Midgley, Thea Kølsen Fischer

Lancet Infect Dis 2016; 16: e64–e75

Published Online February 23, 2016

Since its discovery in California in 1962, reports of enterovirus D68 have been infrequent. Before 2014, infections were confirmed in only 699 people worldwide. In August, 2014, two paediatric hospitals in the USA reported increases in the number of patients with severe respiratory illness, with an over-representation in children with asthma. Shortly after, the authorities recognised a nationwide outbreak, which then spread to Canada, Europe, and Asia. In 2014, more than 2000 cases of enterovirus D68 were reported in 20 countries. Conc paralysis of unknown cause were reported in several US states and in l in some of the paralysed children, but not all. Complications in pa resemble those caused by poliomyelitis. In this paper we systematica its global epidemiology and its ability to cause respiratory infections a data from 70 papers to report on prevalence, symptoms, hospitalisatio D68, both before and during the large outbreak of 2014. The magnitu underscores a need for improved diagnostic work-up of paediatric re use of antibiotics, but also to ensure better surveillance of diseases. Ex terms of capacity and ability to detect and report any upsurge of respi manner, and focus should be paid to development of preventive mea have potential for severe disease.

Introduction

most we

Acute flaccid paralysis

Acute flaccid paralysis is a complex clinical syndrome with sudden onset of limb weakness in one or more limbs or the respiratory and bulbar muscles as a result of damage of the lower motor neurons.[63,66] Acute flaccid paralysis is one of the most devastating and disabling complications of poliovirus and other non-polio enteroviruses, and surveillance for acute flaccid paralysis is the gold standard for m itoring of polio.[75] Monitoring includes finding and orting children with acute flaccid paralysis, collect stool samples for analysis, and isolating and mapp wild poliovirus and vaccine-derived poliovirus.[75,76] 60 231 cases of acute flaccid paralysis were reported to WHO in 2014 (data from Aug 26, 2015); the incidence of non-poliomyelitis acute flaccid paralysis is 5·0 cases per year per population

Encephalitis - Management

In case of a clinical syndrome suggestive for an **Encephalitis,**

➔ immediate empiric **antiviral therapy** with Acyclovir essential

➔ proper history: exposure (vectors?), epidemic situation

➔ if available: imaging (MR)
EEG
(spinal tap)
(neuro-)critical care monitoring and management

Encephalitis - Management

In case of a clinical syndrome suggestive for an **Encephalitis,**

➔ immediate empiric **antiviral therapy** with Acyclovir essential

➔ if available: **(neuro)critical care monitoring and management**

Most frequent causes for critical care :

- qualitative or/and quantitative impairment of consciousness
- seizures
- impairment of breathing
- impairment of swallowing

- increased intracranial pressure
- status epilepticus
- optimal temperature management
- nutrition

Jouan et al. Critical Care (2015) 19:345
DOI 10.1186/s13054-015-1046-y

CRITICAL CARE

RESEARCH Open Access

Long-term outcome of severe herpes simplex encephalitis: a population-based observational study

Youenn Jouan[1,3*†], Leslie Grammatico-Guillon[2,3†], Fabien Espitalier[3,4], Xavier Cazals[5], Patrick François[3,6] and Antoine Guillon[1,3]

Key messages

•The hospital incidence of adult herpetic encephalitis was 10 times higher than previously reported.

•Morbidity and mortality remain high during the acute phase, so **(neuro-) intensive care** specialists should promptly take charge of these patients.

•In the most **severe cases**, patients may have **high intracranial pressure** with temporal herniation.

•**Initial brain images** are **not predictive** of the risk of **brain herniation**.

•In life-threatening situations with intractable high intracranial pressure and temporal herniation of the brain, **decompressive hemicraniectomy** appears to be a **useful salvage therapy** that could be considered

Intensive Care Med
https://doi.org/10.1007/s00134-019-05684-0

ORIGINAL

Functional outcomes in adult patients with herpes simplex encephalitis admitted to the ICU: a multicenter cohort study

P. Jaquet[1], E. de Montmollin[1,2], C. Dupuis[1,2], C. Sazio[3], M. Conrad[4], V. Susset[5], S. Demeret[6], J. M. Tadie[7], L. Argaud[8], F. Barbier[9], B. Sarton[10], R. Chabane[11], D. Daubin[12], N. Brulé[13], N. Lerolle[14], M. Alves[15], D. Da Silva[16], A. El Kalioubi[17], S. Silva[10], P. Bailly[18], M. Wolff[1], L. Bouadma[1,2], J. F. Timsit[1,2], R. Sonneville[1,19*] and ENCEPHALITICA study group

…. in the multivariate analysis ….

- **high age**
- high body temperature
- **early admission to a (N)ICU**

…. strongest **predictors** of outcome (**poor** / **good**)…..

Intensive Care Med. 2019 Aug;45(8):1103-1111

acute bacterial meningitis

incidence ↓
age ↑

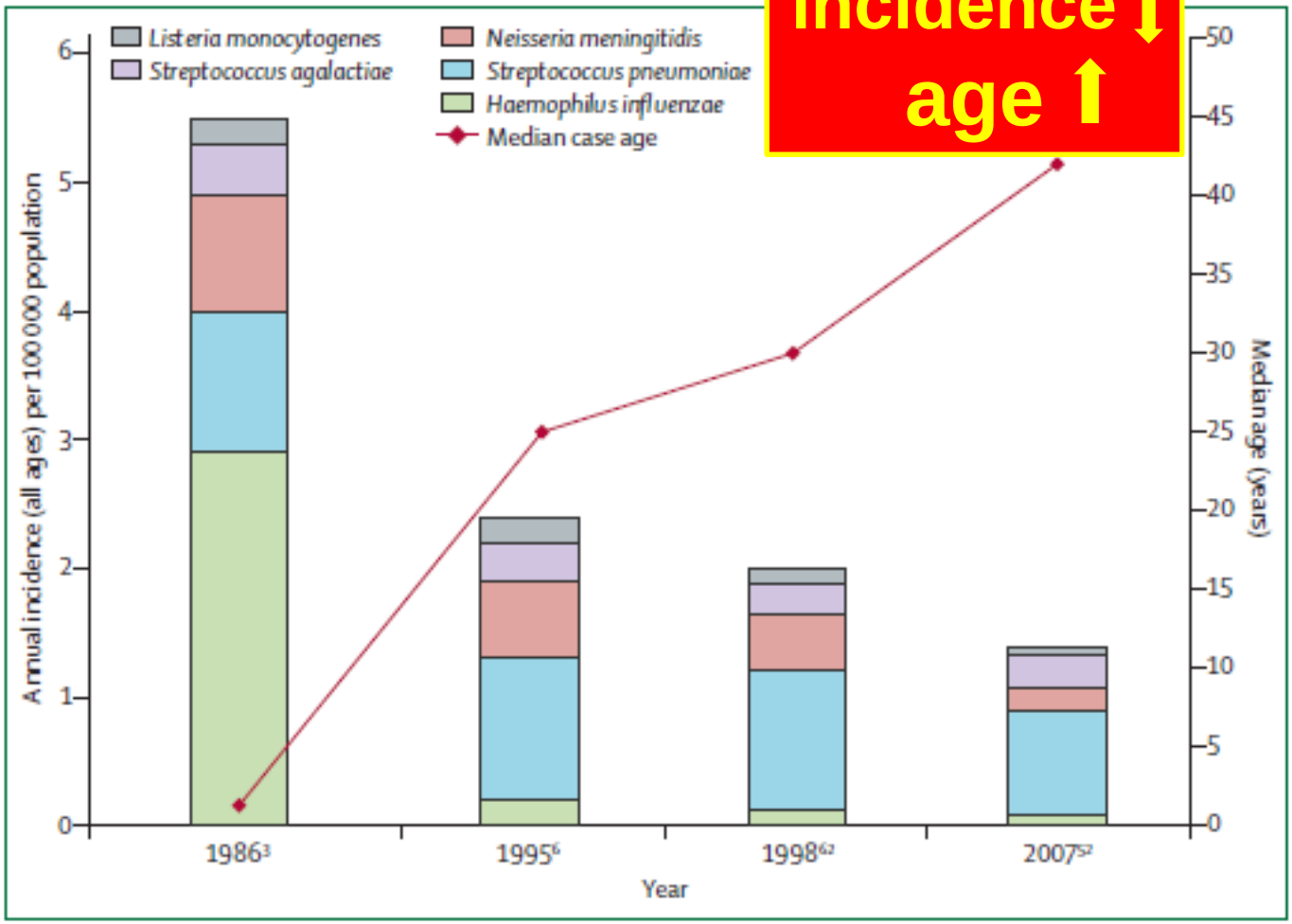


Figure 2: Prevalence of bacterial meningitis in the USA attributable to *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Streptococcus agalactiae*, and *Listeria monocytogenes*, 1986–2007[3,4,52]

Modified from McIntyre et al, Lancet 2012

REVIEW ARTICLE

CONTINUUM AUDIO INTERVIEW AVAILABLE ONLINE

Acute Bacterial Meningitis

By Larry E. Davis, MD, FAAN

ABSTRACT

PURPOSE OF REVIEW: While acute bacterial meningitis is becoming less common in developed countries because of the widespread use of vaccines against *Streptococcus pneumoniae, Neisseria meningitides,* and *Haemophilus influenzae*, bacterial meningitis still occurs worldwide, with

CONTINUUM (MINNEAP MINN) 2018;24(5, NEUROINFECTIOUS DISEASE):1264-1283.

Address correspondence to Dr Larry E. Davis, New Mexico VA Health Care System, 1501 San Pedro Dr SE, Albuquerque, NM 87108, *Larry.Davis@VA.gov*.

TABLE 1-3

Risk Factors for Acute Bacterial Meningitis in Adults and the Elderly

WORLD WIDE

major public health issue in urban areas
Gram negatives
➔ multi-drug **resistance**
➔ **MRSA, 3MRGN, 4MRGN**

immuno-
senescence
multi-
morbidity

Living in groups or retirement homes

Pulmonary disease

- Concurrent pneumonia
- Chronic obstructive pulmonary disease
- Asthma
- Smoking

Malignancy

- Melanoma
- Chronic lymphocytic leukemia
- Advanced cancers
- Chemotherapy
- Metastatic cancers

Chronic sinus or middle ear disease

Diabetes mellitus

Autoimmune disease

- Rheumatoid arthritis
- Systemic lupus erythematosus

Immune deficiency

- Human immunodeficiency virus (HIV) infection
- Primary immunodeficiency, complement C3 deficiency
- Organ transplants
- Asplenia
- Severe anemia
- Alcoholism

Chronic renal disease dialysis, urinary tract infection, or kidney infect
renal stones

Chronic liver disease, cirrhosis

Positive blood cultures

Shock or hypotension

Recent cranial neurosurgery

Indwelling catheters or central venous lines, especially into CSF spac

CONTINUUM (MINNEAP MINN) 2018;24(5, NEUROINFECTIOUS DISEASE):1264–1283.

Address correspondence to Dr Larry E. Davis, New Mexico VA Health Care System, 1501 San Pedro Dr SE, Albuquerque, NM 87108, *Larry.Davis@VA.gov*.

Clinical features of bacterial meningitis in adults

- Fever
- Neck stiffness
- Altered level of consciousness

44%

Van de Beek 2004, Bijlsma 2016

- **Headache**
- Fever
- Neck stiffness
- Altered level of consciousness

2 out of 4: 95%

95% have at least **two of the four signs and symptoms** of headache, fever, neck stiffness and altered mental status

Curr Opin Infect Dis. 2017 Feb;30(1):135-141. doi: 10.1097/QCO.0000000000000335.

Community-acquired bacterial meningitis.

Costerus JM[1], Brouwer MC, Bijlsma MW, van de Beek D.

[1]Department of Neurology, Centre of Infection and Immunity Amsterdam (CINIMA), Academic Medical Centre, Amsterdam, the Netherlands.

SUMMARY:

➔ The incidence of bacterial meningitis has been decreasing after the implementation of effective vaccines.

➔ Treatment should be administered **as soon as possible** and time to treatment should **not exceed 1 h !**

you need the **history**:
preceding diseases (otitis, sinusitis, broncho-pneumonia), immune status
TBI, asplenia, previous hospital admissions
exposure, epidemics, vaccination status,
local, regional AB-resistance pattern

TABLE 4.1. Empiric antibiotic in-hospital treatment for community-acquired bacte

Patient group	Standard treatment	
	Reduced *Streptococcus pneumoniae* antimicrobial sensitivity to penicillin	*S. pneumoniae* susceptible to penicillin
Neonates <1 month old	Amoxicillin/ampicillin/penicillin plus cefotaxime, or amoxicillin/ampicillin plus an aminoglycoside	
Age 1 month to 18 years	Cefotaxime or ceftriaxone plus vancomycin or rifampicin	Cefotaxime or ceftriaxone
Age >18 and <50 years	Cefotaxime or ceftriaxone plus vancomycin or rifampicin	Cefotaxime or ceftriaxone
Age >50 years, or Age >18 and <50 years plus risk factors for *Listeria monocytogenes*[a]	Cefotaxime or ceftriaxone plus vancomycin or rifampicin plus amoxicillin/ampicillin/penicillin G	Cefotaxime or ceftriaxone plus amoxicillin/ampicillin/ penicillin G

[a]Diabetes mellitus, use of immunosuppressive drugs, cancer and other conditions causing immunocompromise.

ESCMID Cuidelines 2016, Clin Microbiol Infect 2016; 22: S37–S

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 years of age
(pneumococci !!!)

Bacterial Meningitis

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 resource-poor regions, where the disease burden is highest, dexamethasone is ineffective. 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

Gudina *et al. BMC Neurology* (2016) 16:153
DOI 10.1186/s12883-016-0678-0

BMC Neurology

RESEARCH ARTICLE Open Access

Adjunctive dexamethasone therapy in unconfirmed bacterial meningitis in resource limited settings: is it a risk worth taking?

Esayas Kebede Gudina[1,2*], Markos Tesfaye[2,3], Aynishet Adane[4], Kinfe Lemma[5], Tamiru Shibiru[6], Andreas Wieser[7,8,9], Hans-Walter Pfister[10] and Matthias Klein[10]

Listeria monocytogenes, Listeria ivanovii

Gram-positive, facultatively anaerobe rod

17 Species
- only ***Listeria monocytogenes*** and ***Listeria ivanovii*** **human-pathogen**

survive and grow at
-0,4° to +45°C, **pH 4,4 - 9,4**, even
with high salt concentration,
and with competitive flora (cheese)

Infection occurs through **contaminated food**
e.g. meat, cheese, fruits, vegetable

~10^9 bacteria needed in the immuno-competent

~10^2 – 10^4 in the elderly, old and immuno-compromised,

Incubation period up to 14 days,
in the elderly and pregnant: up to 65 days reported

Infected persons may shed the bacteria in the feces over months

Neurolisteriosis *(„MONALISA Studie“, Charlier C et al, Lancet Inf Disease 2017)*

Meningitis (13%)

Meningoencephalitis (87%)

Rhombencephalitis (17%)

brain abscess (2%)

Neurologic sequelae 44%

case fatality in meningitis 9%

in brain abscess or encephalitis 33%

higher mortality if patient is initially treated with steroids

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

OPEN ACCESS Freely available online

PLOS | ONE

Neuro-Intensive Treatment Targeting Intracranial Hypertension Improves Outcome in Severe Bacterial Meningitis: An Intervention-Control Study

Martin Glimåker[1]*, Bibi Johansson[2], Halla Halldorsdottir[3], Michael Wanecek[3], Adrian Elmi-Terander[4], Per Hamid Ghatan[5], Lars Lindquist[2], Bo Michael Bellander[4]*

1 Unit for Infectious Diseases, Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden, **2** Unit for Infectious Diseases, Department of Medicine Huddinge, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden, **3** Department of Anesthesiology, Karolinska University Hospital, Stockholm, Sweden, **4** Department of Clinical Neuroscience, Section for Neurosurgery, Karolinska University Hospital, Stockholm, Sweden, **5** Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Key points: Adults with acute bacterial meningitis and severely impaired consciousness, showed decreased mortality (30% to 10%) and significantly improved overall outcome when subjected to neuro-intensive care with intracranial pressure-targeted treatment and cerebrospinal fluid drainage (N=52) compared to conventional intensive care (N=53).

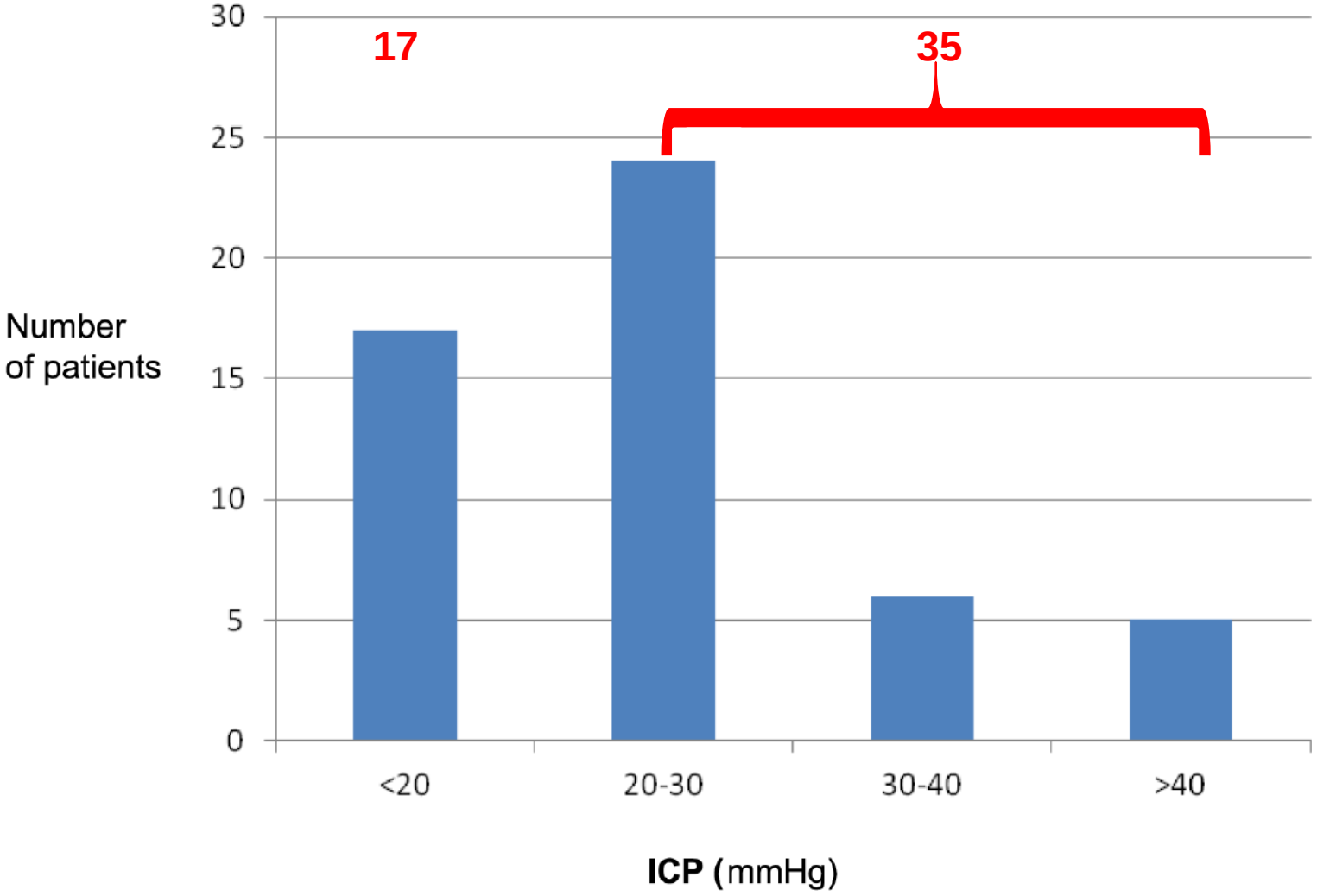
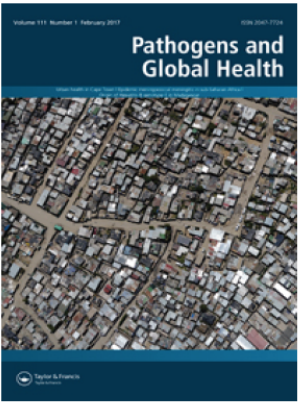


Figure 3. The highest levels of intracranial pressure (ICP), as observed continuously during episodes of more than 5 min, in the neuro-intensive care unit after initial cerebrospinal fluid drainage at operation; n = 52 (external ventricular drainage; n = 48, parenchymal ICP-monitor; n = 4).

doi:10.1371/journal.pone.0091976.g003



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Pathogens and Global Health

ISSN: 2047-7724 (Print) 2047-7732 (Online) Journal homepage: http://www.tandfonline.com/loi/ypgh20

Emergence and control of epidemic meningococcal meningitis in sub-Saharan Africa

Idris Mohammed, Garba Iliyasu & Abdulrazaq Garba Habib

To cite this article: Idris Mohammed, Garba Iliyasu & Abdulrazaq Garba Habib (2017) Emergence and control of epidemic meningococcal meningitis in sub-Saharan Africa, Pathogens and Global Health, 111:1, 1-6, DOI: 10.1080/20477724.2016.1274068

To link to this article: http://dx.doi.org/10.1080/20477724.2016.1274068

Accepted author version posted online: 20 Dec 2016.
Published online: 12 Jan 2017.

Country	Year	Number of cases	CFR	Serotype
Before MenAfriVac Campaign				
Nigeria[15]	1977	1257	8.3	A
Rwanda[16]	1978	1182	4.8	A
Burkina Faso[17]	1979	538	10.2	C
Côte d'Ivoire[18]	1983	414	NA	A
	1985	251	8.5	A
	1985	367	8.5	A
Chad[19]	1988	4542	9.5	A
Sudan[20]	1988	32,016	NA	A
Ethiopia[21,22]	1981	50,000	2.0	A
	1989	41,139	3.9	A
Kenya[23]	1989	3800	9.4	A
Burundi[24,25]	1992	1615	8.0	A
Burkina Faso[26]	1996	42,129	10.0	A
	1997	22,305	11.3	A
Mali[25]	1996	7254	11.5	A
	1997	11,228	10.1	A
Niger[27,28]	1995	41,930	8.7	A
	1996	16,145	9.9	A
After MenAfriVac Campaign				
Burkina Faso[32]	2012	2825	16.9	W
Chad[32]	2012	5808	4.4	A
Nigeria[33]	2015	6394	5.0	C
Niger[34]	2015	8500	6.7	C