Encéphalites aiguës

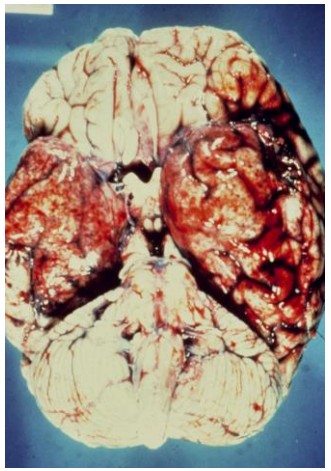
Romain Sonneville

Réanimation médicale et infectieuse
Hôpital Bichat-Claude-Bernard, AP-HP, Paris

Encéphalite aiguë

Inflammation du parenchyme cérébral ⇨ **« Dysfonction cérébrale aiguë »**

- Diagnostic histologique (Biopsie cérébrale….)
- **LCR**
- **Neuroimagerie**

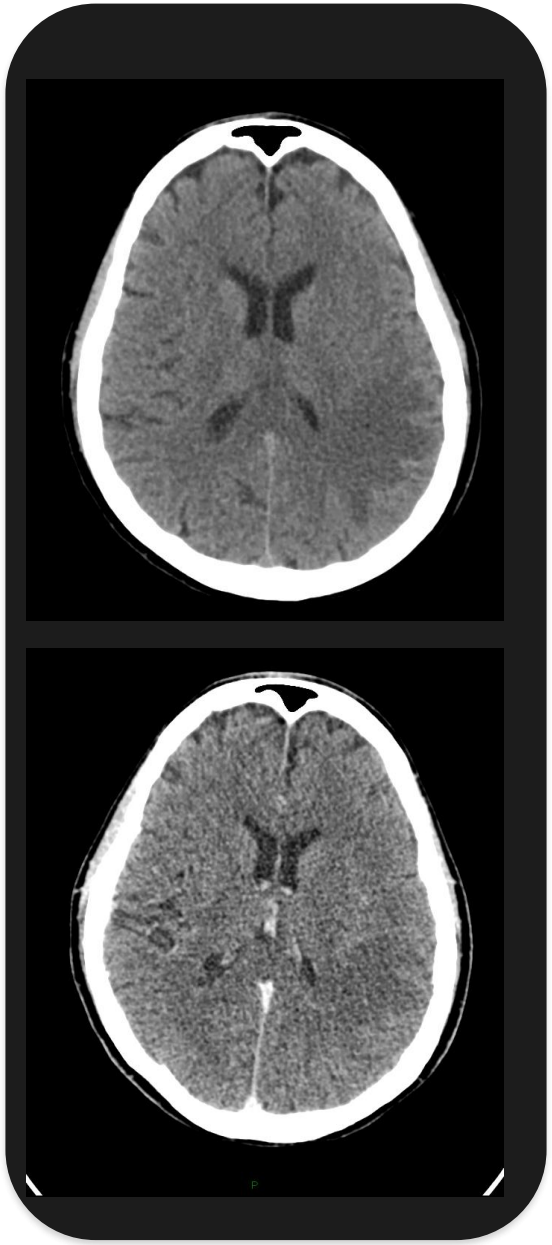


A. Venkatesan, Clin Infect Dis 2013

Le cas de Mme L …

Femme 65 ans, pas d'ATCD notable

Début aout 2015 « bronchite »



22/08 :

Troubles du langage, confusion

½ parésie droite

Fièvre

Crise tonico-clonique généralisée

Ponction lombaire :

356 éléments/mm^3 (87% PNN)

Prot. 2.2 g/l, glyco 3.3 mmol/l

ED : négatif, Ag solubles méningo et pneumo négatifs

Le cas de Mme L …

Ttt débuté :

Acyclovir IV

Cefotaxime, amoxicilline doses méningées

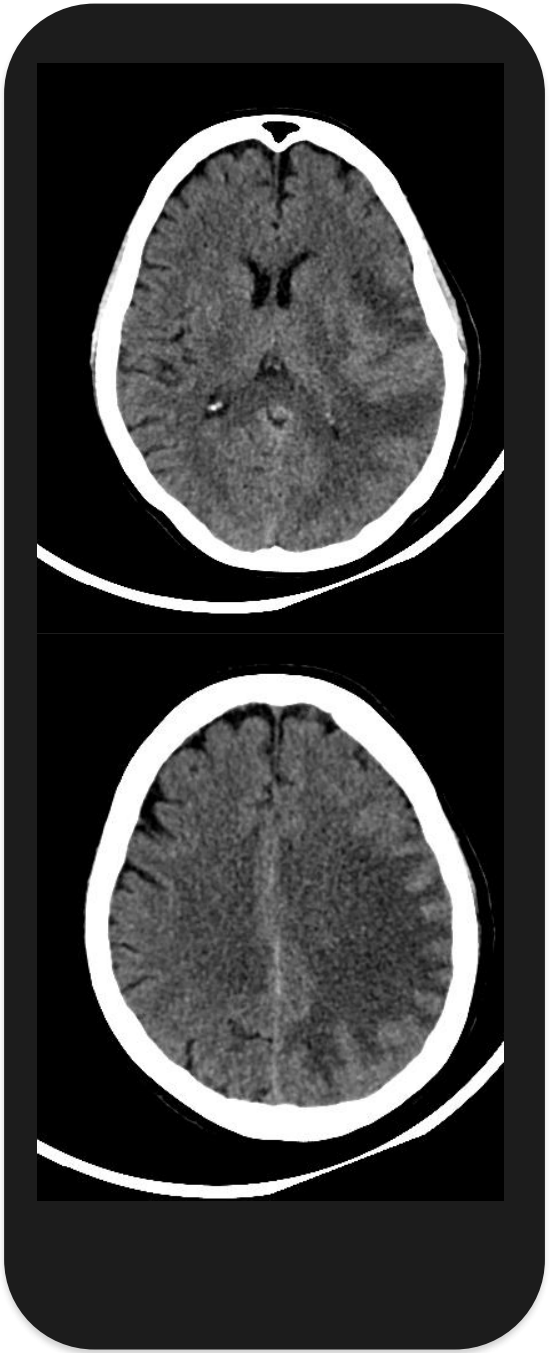
Levetiracetam

Dégradation neurologique J2

GCS 7

Transfert réanimation

PCR HSV-1, cultures LCR négatives …



Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium

•CRITERE MAJEUR : trouble de conscience, confusion, troubles du comportement (durée ≥ 24 H)

•CRITERES MINEURS (au moins 3 éléments suivants)

- Fièvre (dans les 72H encadrant l'admission)
- Convulsions "*de novo*"
- Signes focaux d'apparition récente
- LCR: ≥ 5 cellules/mm^3
- Imagerie cérébrale
- EEG

A. Venkatesan, Clin Infect Dis 2013

Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium

- **ENCEPHALITE AIGUË CONFIRMEE**

si mise en évidence:

  - d'un pathogène pourvoyeur d'encéphalite

(histologie, microbiologie, sérologie)

  - d'un "contexte dysimmunitaire" associé à encéphalite

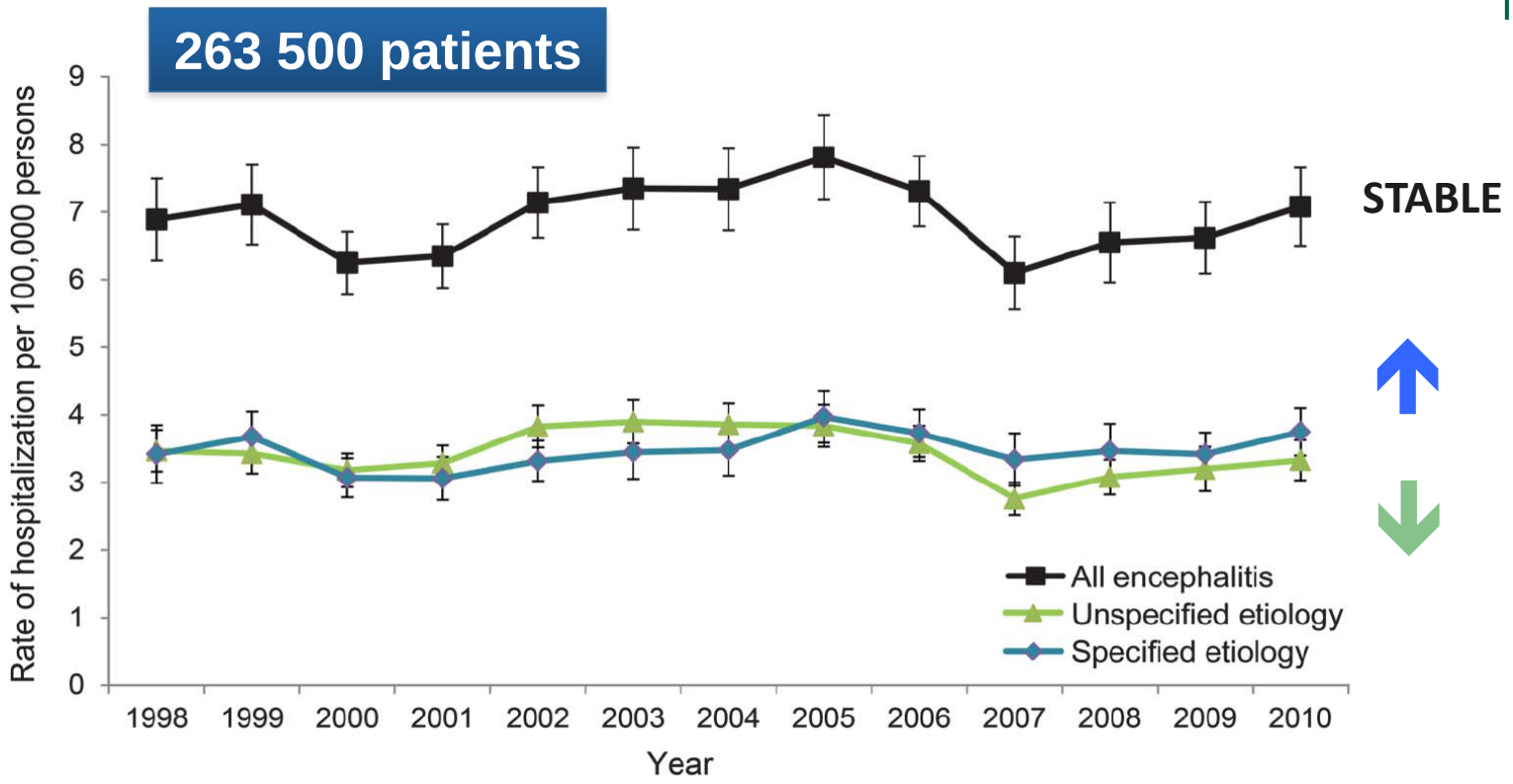
(examens immunologiques sang, LCR)

- **Encéphalite probable sinon ….**

A. Venkatesan, Clin Infect Dis 2013

Burden of encephalitis-associated hospitalisations in the United States,1998-2010

Figure 1 Annual rates of encephalitis-associated hospitalizations, United States, 1998–2010



Annual rates of overall encephalitis-associated hospitalizations varied with no apparent trend. Annual rates of encephalitis-associated hospitalizations of unspecified etiology decreased ($p = 0.01$), whereas annual rates of encephalitis-associated hospitalizations of specified etiology increased ($p = 0.01$). Error bars represent 95% confidence intervals.

NM Vora, Neurology 2013

Causes of encephalitis and differences in their clinical presentations in England: a multicentre, population-based prospective study

Julia Granerod, Helen E Ambrose, Nicholas W S Davies, Jonathan P Clewley, Amanda L Walsh, Dilys Morgan, Richard Cunningham, Mark Zuckerman, Ken J Mutton, Tom Solomon, Katherine N Ward, Michael P T Lunn, Sarosh R Irani, Angela Vincent, David W G Brown, Natasha S Crowcroft, on behalf of the UK Health Protection Agency (HPA) Aetiology of Encephalitis Study Group

203 patients
Adults > 16 yrs
18 months, 2008-2009

J Granerod, Lancet Infectious Diseases 2010

Causes of encephalitis and differences in their clinical presentations in England: a multicentre, population-based prospective study

Julia Granerod, Helen E Ambrose, Nicholas W S Davies, Jonathan P Clewley, Amanda L Walsh, Dilys Morgan, Richard Cunningham, Mark Zuckerman, Ken J Mutton, Tom Solomon, Katherine N Ward, Michael P T Lunn, Sarosh R Irani, Angela Vincent, David W G Brown, Natasha S Crowcroft, on behalf of the UK Health Protection Agency (HPA) Aetiology of Encephalitis Study Group

Infectieuses 42%

HSV-1: 38 (19%)
BK:10 (5%)
VZV: 10 (5%)

Cause inconnue 37%

Dysimmunitaires 21%

Acute Disseminated Encephalomyelitis (ADEM): 23 (11%)
NMDA-R Encephalitis: 9 (4%)
VGKC Encephalitis: 7 (3%)

J Granerod, Lancet Infectious Diseases 2010

Beyond Viruses: Clinical Profiles and Etiologies Associated with Encephalitis

Clin Infect Dis, 2006

C. A. Glaser,[1] S. Honarmand,[1] L. J. Anderson,[3] D. P. Schnurr,[1] B. Forghani,[1] C. K. Cossen,[1] F. L. Schuster,[1] L. J. Christie,[1] and J. H. Tureen[2]

- **1998-2005: 1570 patients (adultes et enfants)**
- **Admission réanimation 58%**

Infectious Encephalitis in France in 2007: A National Prospective Study

Clin Infect Dis 2009

Alexandra Mailles[1] and Jean-Paul Stahl,[2] on behalf of the Steering Committee and the Investigators Group[a]

[1]Institut de Veille Sanitaire, Saint-Maurice, and [2]Infectious Diseases Unit, University Hospital of Grenoble, Grenoble, France

- **2007: 253 patients (adultes)**
- **Admision réanimation 46%**

Clinical spectrum and outcomes of patients with encephalitis requiring intensive care

R. Sonneville[a], N. Gault[b,c,d], E. de Montmollin[a], I. F. Klein[e], E. Mariotte[a], S. Chemam[a], F. Tubach[b,c,d], B. Mourvillier[a], J. F. Timsit[a,f], M. Wolff[a] and L. Bouadma[a,f]

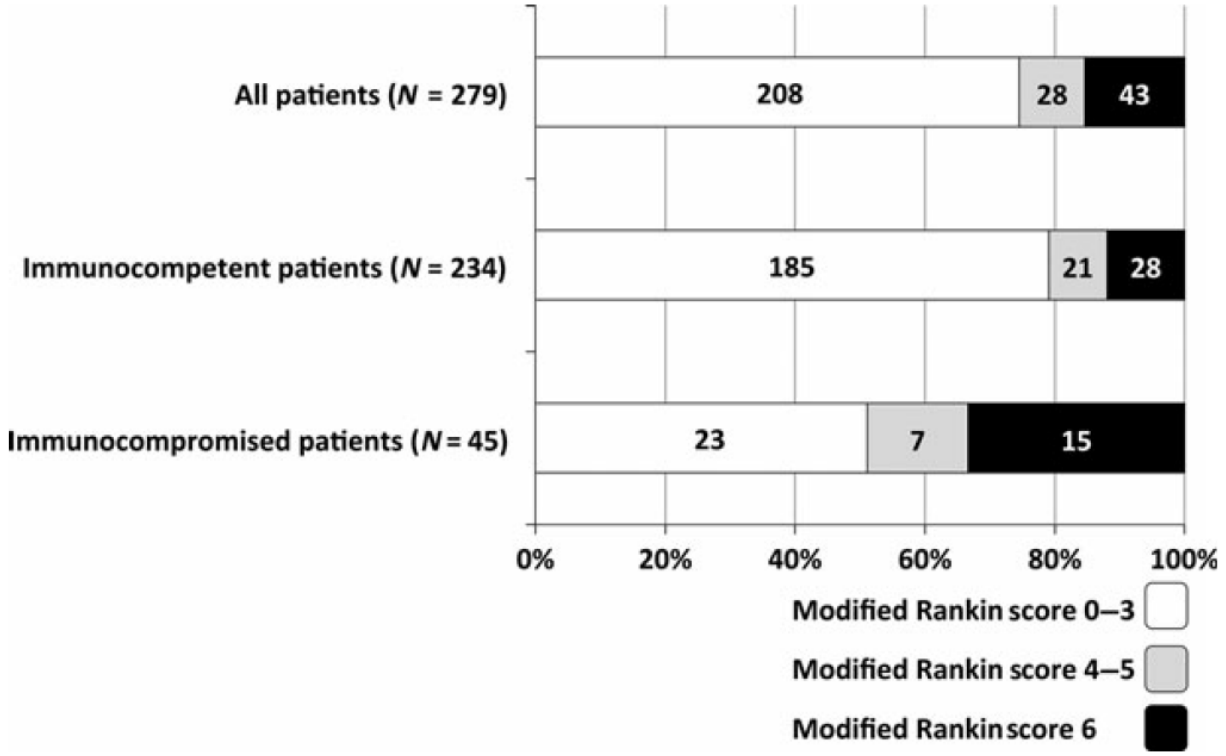


Figure 1 Modified Rankin scores 90 days after admission to the intensive care unit.

Eur J Neurol 2015

Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium

EPIDEMIOLOGICAL DATA

- Medical history
- Immunosuppression
- Medications
- Seasonal/epidemic context ?
- Recent travel ?
- Contacts:
  - animals
  - Insects
- Recent Immunization

CLINICAL EXAMINATION

- Neurological signs
- Optic nerve
- Extra-neurological signs

OTHER EXAMS

- **BRAIN MRI with gd**
- **CSF (cultures, PCR)**
- **EEG**
- Serologies
- Immunology tests

- +/- brain biopsy

A. Venkatesan, Clin Infect Dis 2013

Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium

Routine studies

CSF (unless contraindicated[b])

- Opening pressure, leukocyte count with differential, erythrocyte count, protein, glucose
- Gram stain and bacterial culture
- HSV-1/2 PCR (if test available, consider HSV CSF IgG and IgM in addition)
- VZV PCR (sensitivity may be low; if test available, consider VZV CSF IgG and IgM in addition)
- Enterovirus PCR
- Cryptococcal antigen or India ink staining
- Oligoclonal bands and IgG index
- Venereal Disease Research Laboratory

Serum

- Routine blood cultures
- HIV serology (consider RNA)
- Treponemal testing (rapid plasma reagin, specific treponemal test)

IMMUNOCOMPROMISED

PCR CMV, HHV6
PCR HIV, JC virus
PCR *Toxoplasma gondii*
M. Tuberculosis
Fungal infections

A. Venkatesan, Clin Infect Dis 2013

Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium

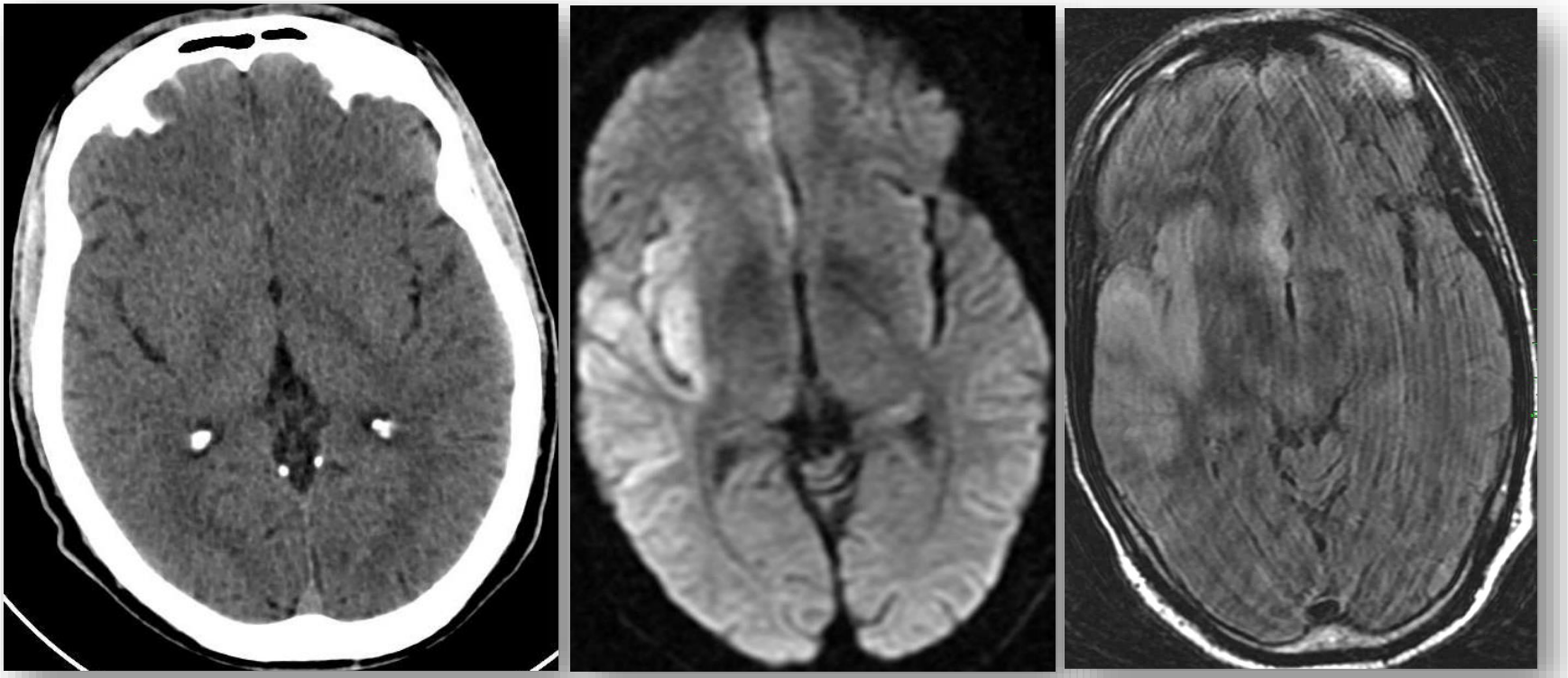
MRI is the most sensitive neuroimaging test to evaluate patients with encephalitis (A-I)

- MRI is more sensitive and specific (vs. CT)
- **Diffusion-weighted/FLAIR imaging** is superior to conventional MRI for the detection of early signal abnormalities
- **Some characteristic neuroimaging patterns** have been observed in patients with encephalitis caused by specific agents
- **ADEM & other Immune-mediated encephalitis +++**

A. Venkatesan, Clin Infect Dis 2013

HSV-1 encephalitis

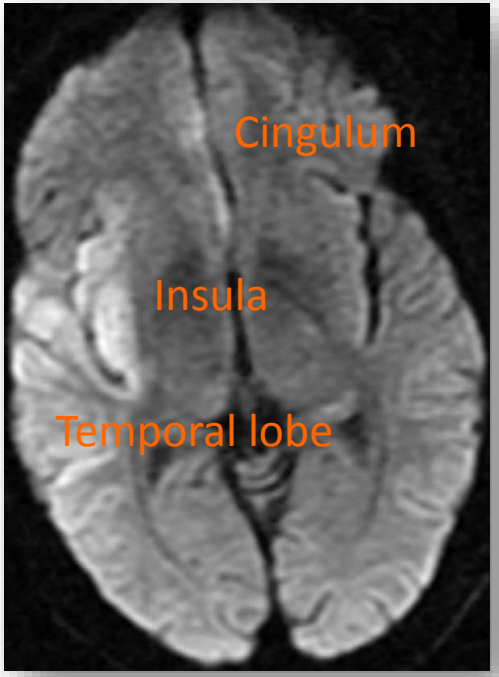
EARLY SIGNS OF BRAIN SWELLING



Use of Clinical and Neuroimaging Characteristics to Distinguish Temporal Lobe Herpes Simplex Encephalitis From Its Mimics

Felicia C. Chow,[1] Carol A. Glaser,[2,3] Heather Sheriff,[4] Dongxiang Xia,[5] Sharon Messenger,[5] Richard Whitley,[6] and Arun Venkatesan[7]

Characteristic	Model 1: HSE Compared With All Non-HSE Cases (n = 209)	
	OR (95% CI) (Total No. With MRI Characteristic)	*P* Value
Bilateral TL	0.38 (.18–.79) (n = 82)	.010
Lesions outside of TL, cingulate, or insula	0.37 (.18–.74) (n = 106)	.005
Restricted diffusion	1.62 (.75–3.50) (n = 50)	.22
Hemorrhage	1.51 (.44–5.13) (n = 15)	.51
Enhancement	0.98 (.49–1.94) (n = 86)	.95

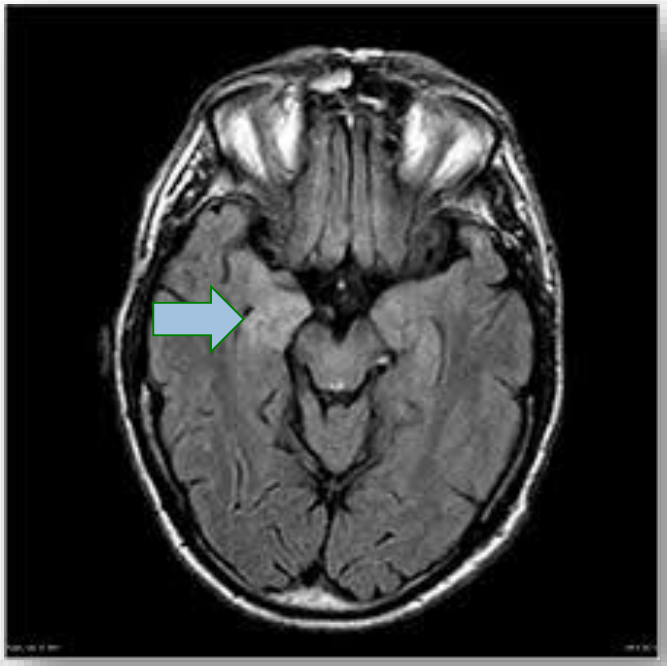


Clin Inf Dis 2015

Use of Clinical and Neuroimaging Characteristics to Distinguish Temporal Lobe Herpes Simplex Encephalitis From Its Mimics

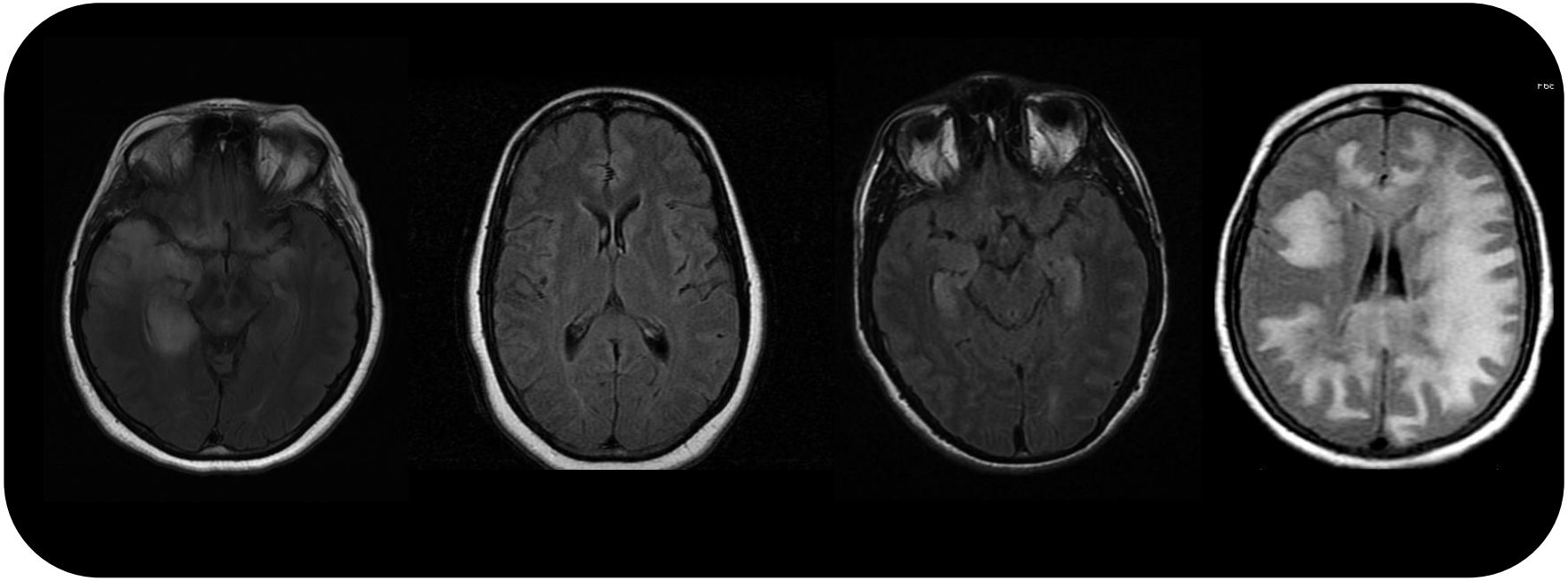
Felicia C. Chow,[1] Carol A. Glaser,[2,3] Heather Sheriff,[4] Dongxiang Xia,[5] Sharon Messenger,[5] Richard Whitley,[6] and Arun Venkatesan[7]

Characteristic	Model 3: HSE Compared With Autoimmune Cases (n = 75) OR (95% CI) (Total No. With MRI Characteristic)	*P* Value
Bilateral TL	0.24 (.06–.94) (n = 22)	.040
Lesions outside of TL, cingulate, or insula	0.36 (.10–1.35) (n = 29)	.13
Restricted diffusion	0.81 (.17–3.85) (n = 21)	.79
Hemorrhage	8.95 (.23–348.65) (n = 7)	.24
Enhancement	0.47 (.12–1.81) (n = 32)	.27



Clin Inf Dis 2015

Brain MRI patterns



Grey matter lesions

Normal MRI

Bilateral TL « Limbic »

White matter lesions

INFECTIOUS

IMMUNE-MEDIATED

Intensive Care Med
DOI 10.1007/s00134-013-2938-4

SYSTEMATIC REVIEW

Jan Claassen
Fabio S. Taccone
Peter Horn
Martin Holtkamp
Nino Stocchetti
Mauro Oddo

Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM

Recommendations for patients with infectious and non-infectious encephalitis

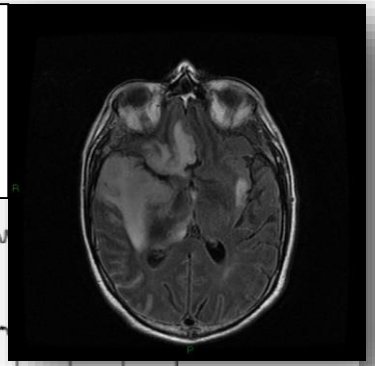
1. We recommend EEG in patients with encephalitis that are comatose or have unexplained neurological deficits to rule out NCSz (strong recommendation, low quality of evidence—grade 1C).
2. We suggest EEG in patients with encephalitis to assist with prognosis (weak recommendation, very low quality of evidence—grade 2D).

2013

Electroencephalography for diagnosis and prognosis of acute encephalitis ☆

Periodic discharges and focal slowing associated with

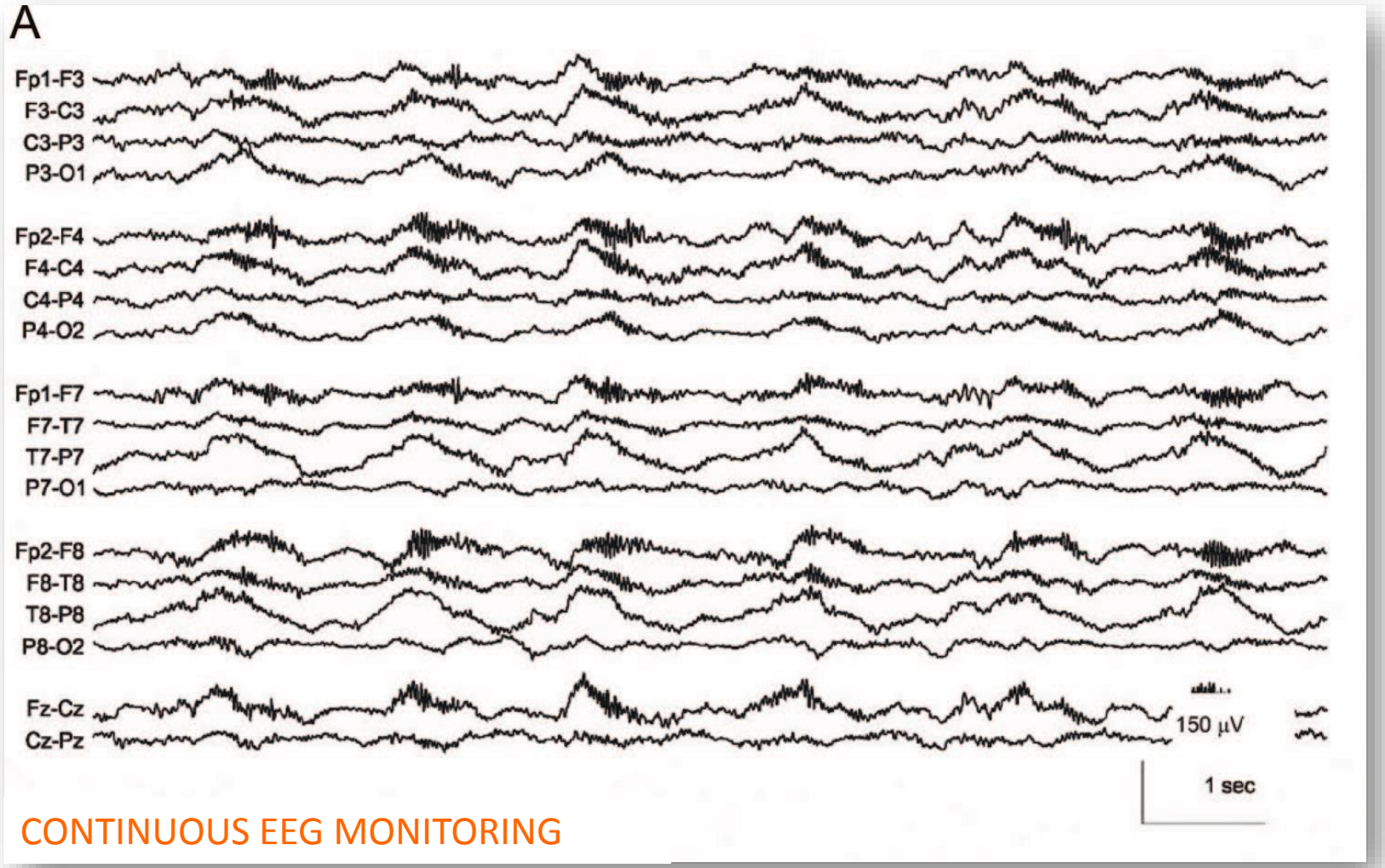
- **HSV1 encephalitis (vs. non-HSV encephalitis)**
- **Poor outcome**



R Sutter, Clin neurophysiology 2014

« Extreme delta brush »

A unique EEG pattern in adults with anti-NMDA receptor encephalitis



CONTINUOUS EEG MONITORING

SE Schmitt, Neurology 2012

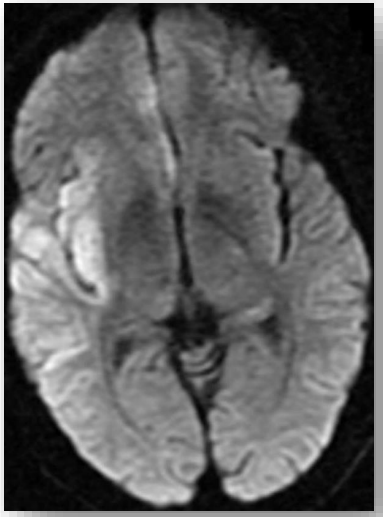
Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Herpes simplex encephalitis

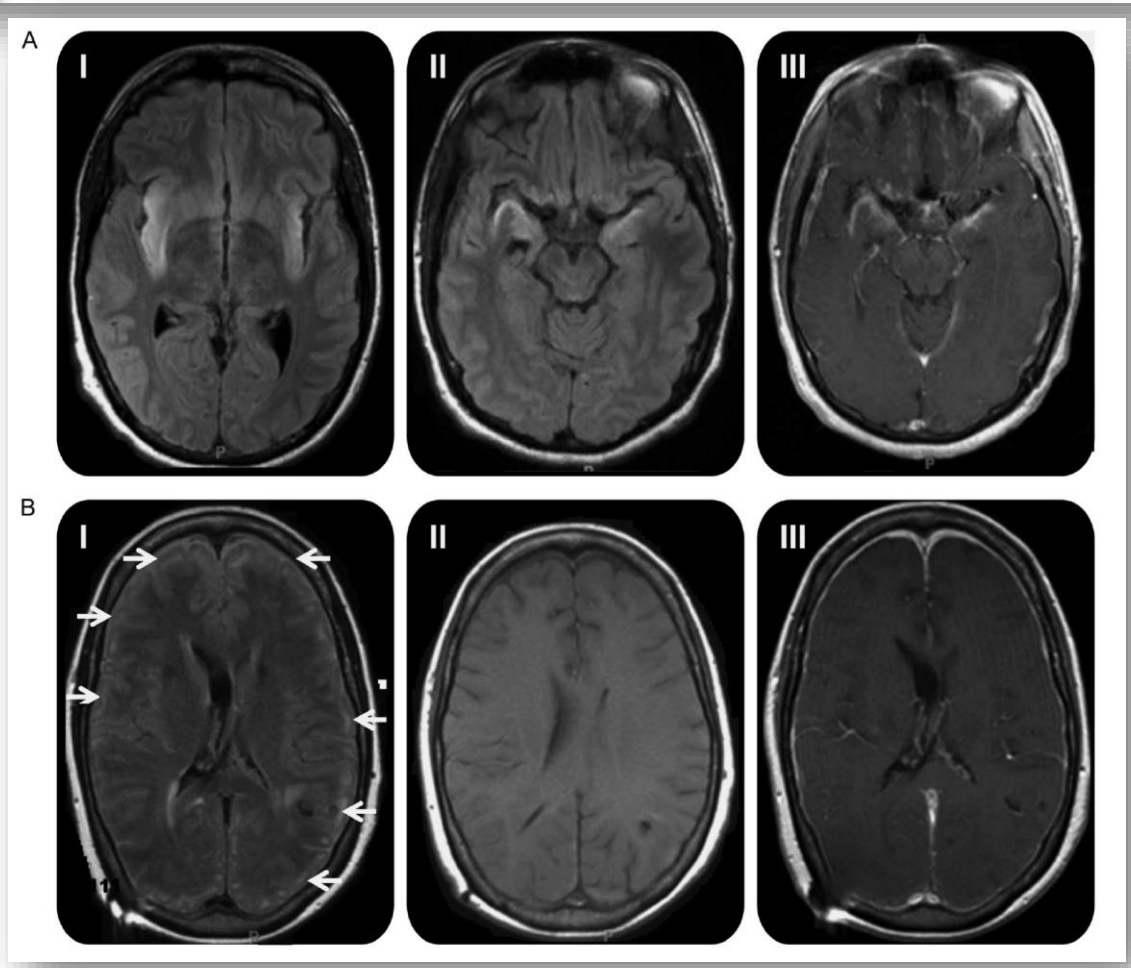
Why is it missed?

- Signes neurologiques frustres chez ID et sujets agés
- Absence de fièvre (10-15%)
- LCR : absence de méningite (10-15%)
- TDM initial normal (33% des patients avt J7)
- PCR HSV négative au début des symptômes



M Sabah, BMJ 2012

Atypical manifestations and poor outcome of herpes simplex encephalitis in the immunocompromised



I Than, Neurology 2012

Outcome of and Prognostic Factors for Herpes Simplex Encephalitis in Adult Patients: Results of a Multicenter Study

Franck Raschilas,[1,2] Michel Wolff,[2] Frédérique Delatour,[3] Cendrine Chaffaut,[4] Thomas De Broucker,[5] Sylvie Chevret,[4] Pierre Lebon,[1] Philippe Canton,[6] and Flore Rozenberg,[1] for the French Herpes Simplex Encephalitis Study Group[a]

Table 4. Multivariate analysis of factors associated with poor outcome at 6 months for 85 patients with herpes simplex encephalitis.

Parameter	OR (95% CI)	*P*
SAPS II >27 at hospital admission	3.7 (1.3–10.6)	.014
More than 2 days between hospital admission and initiation of acyclovir therapy	3.1 (1.1–9.1)	.037

Clin Infect Dis 2002

Vidarabine versus Acyclovir Therapy in Herpes Simplex Encephalitis

Richard J. Whitley, M.D., Charles A. Alford, M.D., Martin S. Hirsch, M.D., Robert T. Schooley, M.D., James P. Luby, M.D., Fred Y. Aoki, M.D., Daniel Hanley, M.D., Andre J. Nahmias, M.D., Seng-Jaw Soong, P.D., and The NIAID Collaborative Antiviral Study Group*

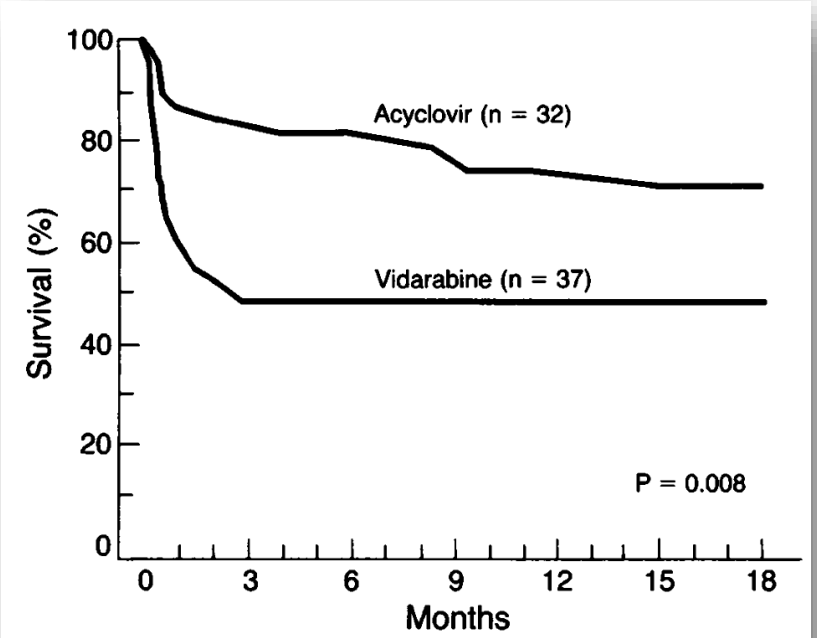
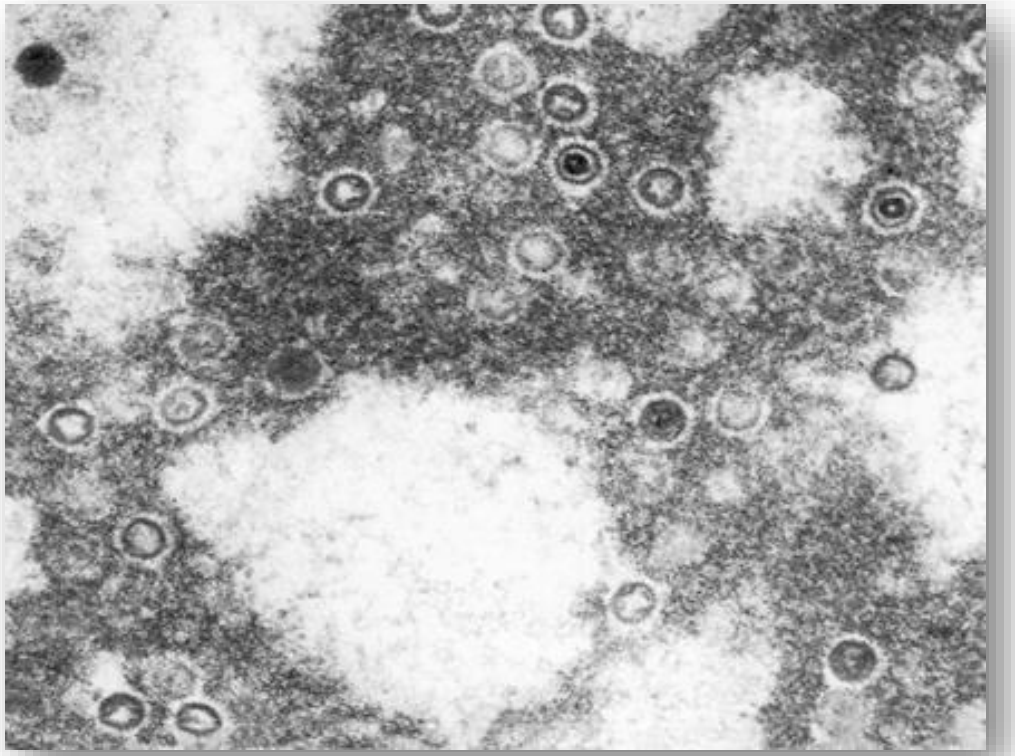


Figure 3. Comparison of Survival in Patients with Biopsy-Proved Herpes Simplex Encephalitis Treated with Vidarabine or Acyclovir.



Acyclovir IV 10mg/kg/8H

Durée 10 jours

N Engl J Med 1986

Encéphalite HSV-1

- Acyclovir IV : 10 mg/kg/8h IVL

(fonction rénale normale)

- Durée ACV : 14 à 21 jours CAR
  - Existence de rechutes à l'arrêt à J10
  - Persistence de PCR + au delà de 10 jours chez certains patients

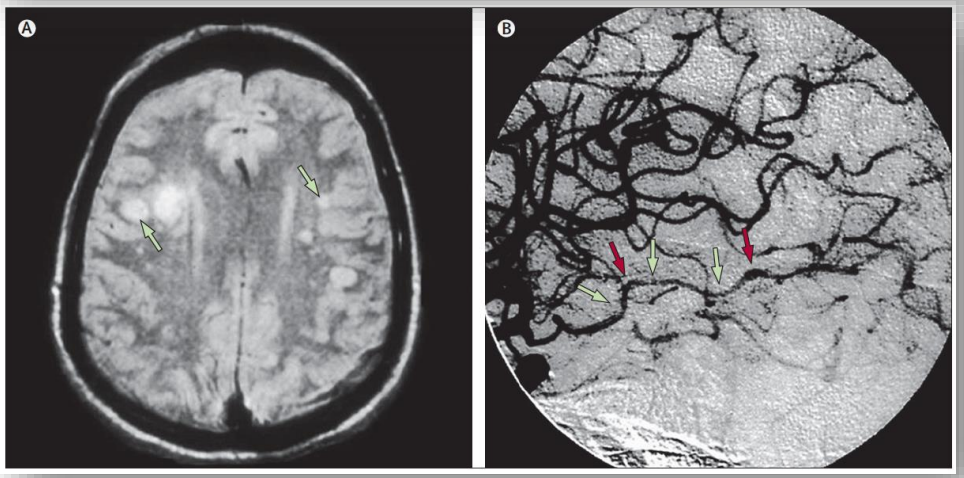
- PCR de contrôle à l'arrêt du traitement

(+++ si évolution clinique imparfaite sur le plan neurologique)

- Pas de bénéfice au traitement d'entretien par valacyclovir en entretien

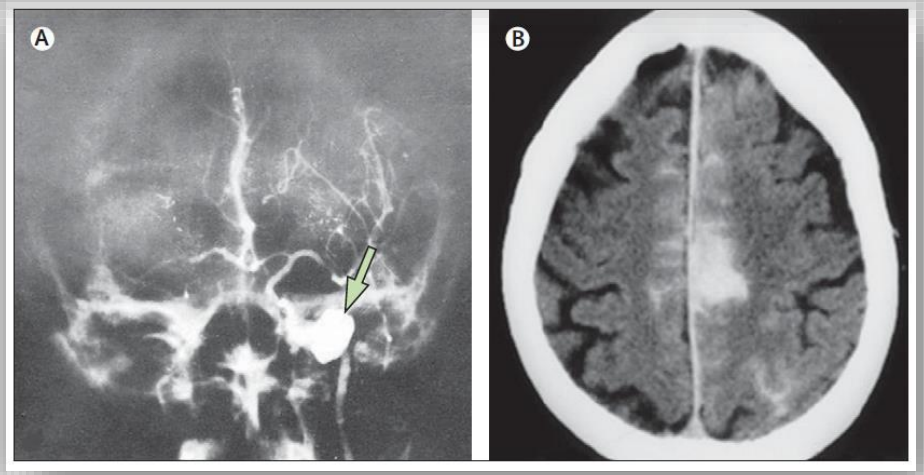
A Venkatesan, Clin Inf Dis 2013
Gnann JW Jr, Clin Inf Dis 2015

Varicella zoster virus vasculopathies: diverse clinical manifestations, laboratory features, pathogenesis, and treatment



SMALL VESSEL MULTIFOCAL VASCULOPATHY

LARGE VESSEL GRANULOMATOUS ARTERITIS



MCA ANEURYSM AND SAH

- CSF pleocytosis can include increased red blood cells
- CSF pleocytosis absent in a third of cases
- Detection of VZV antibody superior to that of VZV DNA for diagnosis

D Gilden, Lancet Neurol 2009

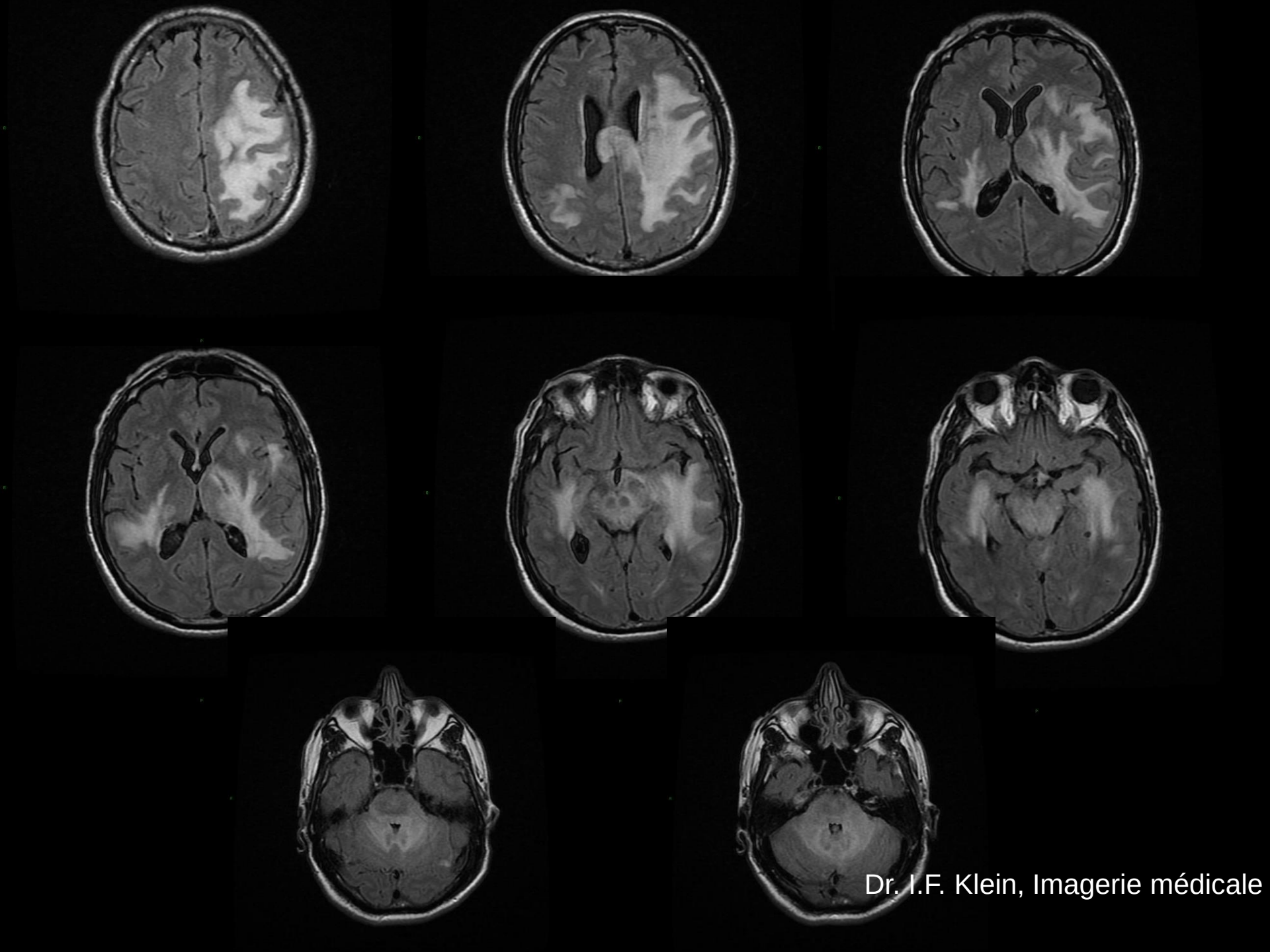
Intensive Care Med (2008) 34:528–532
DOI 10.1007/s00134-007-0926-2

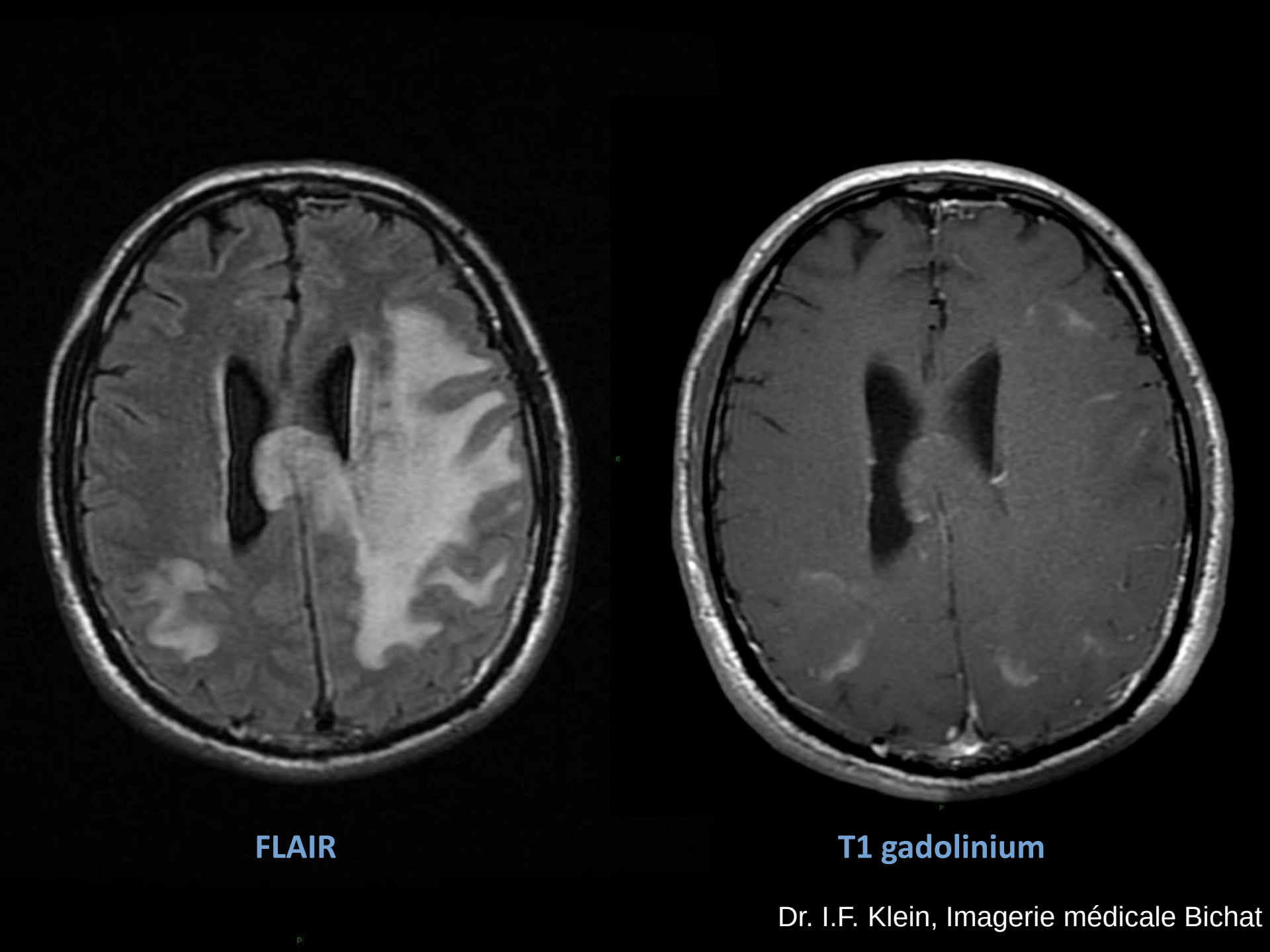
BRIEF REPORT

Romain Sonneville
Sophie Demeret
Isabelle Klein
Lila Bouadma
Bruno Mourvillier
Juliette Audibert
Stéphane Legriel
Francis Bolgert
Bernard Regnier
Michel Wolff

Acute disseminated encephalomyelitis in the intensive care unit: clinical features and outcome of 20 adults

Parameter	All patients ($n = 20$)
Age, years	37 (27–51)[a]
Fernale sex, *n* (%)	11 (55)
Preceding infectious disease, *n* (%)	14 (70)
Latency period, days	8 (6–14)
SAPS II	33 (15–45)
MV, *n* (%)	14 (70)
Temperature, °C	39 (38–39)
Neck stiffness, *n* (%)	10 (50)
GCS	7 (4–13)
Seizures, *n* (%)	6 (30)
Motor deficit, *n* (%)	17 (85)

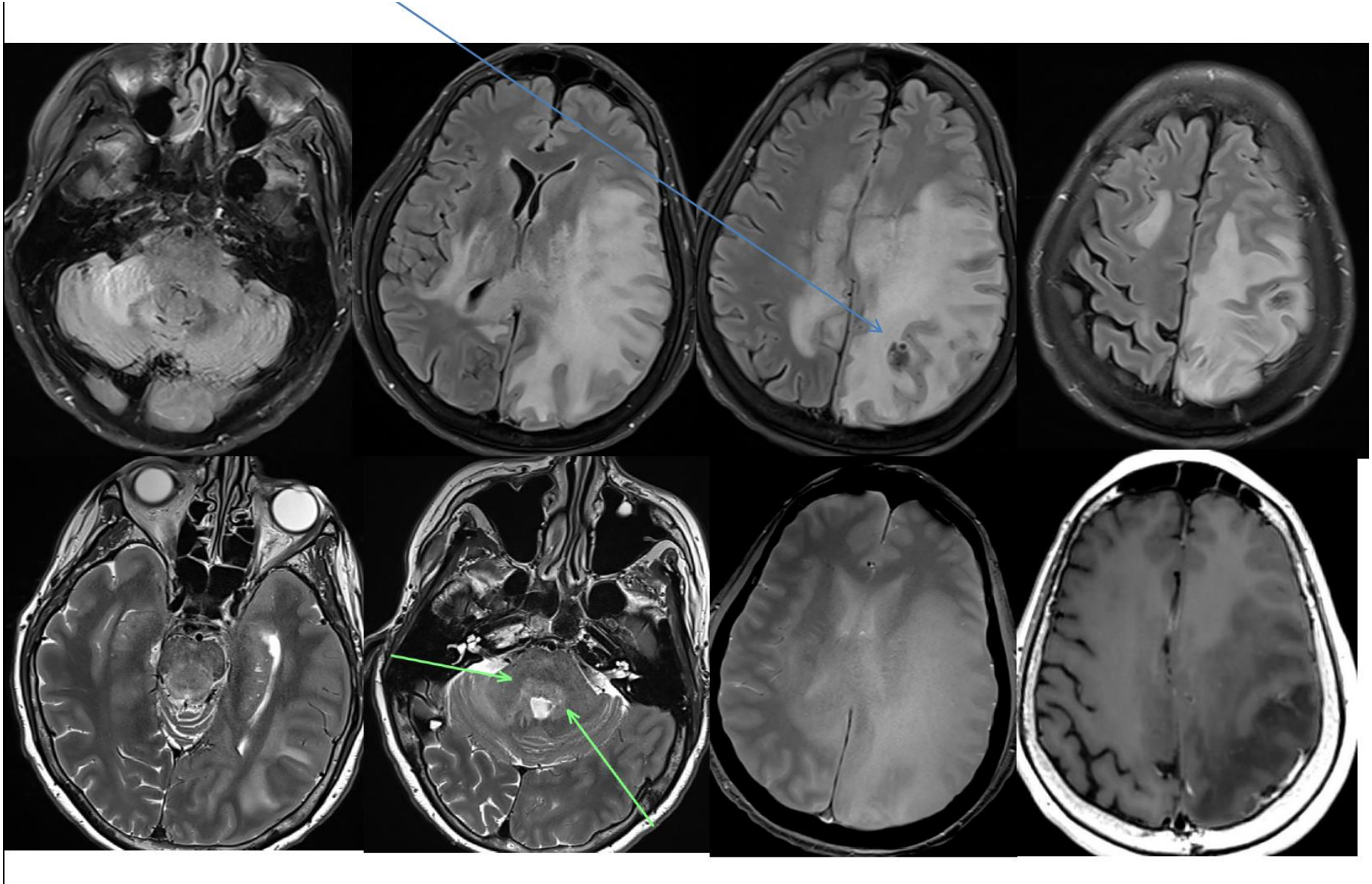

Dr. I.F. Klein, Imagerie médicale



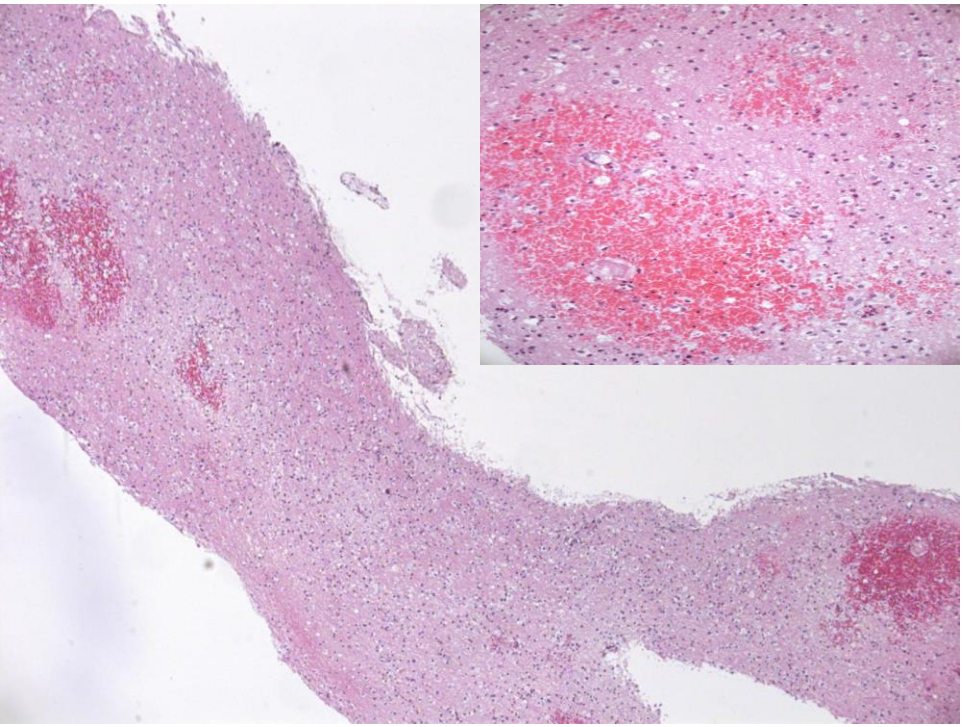
Dr. I.F. Klein, Imagerie médicale Bichat

Mme L

IRM … BIOPSIE CEREBRALE…

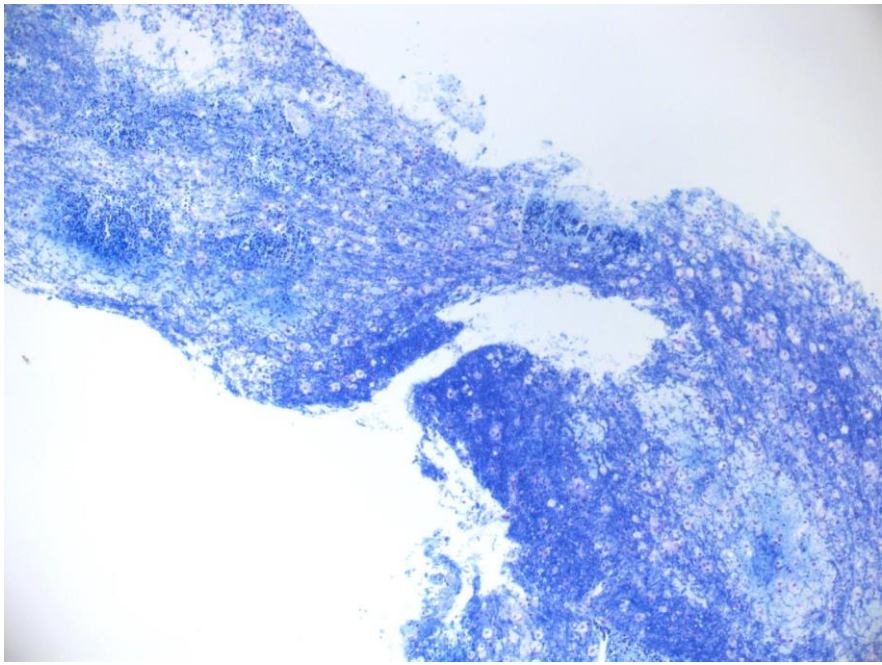


Mme Le V….



Inflammation périvasculaire
Pâleur substance blanche

Composante hémorragique

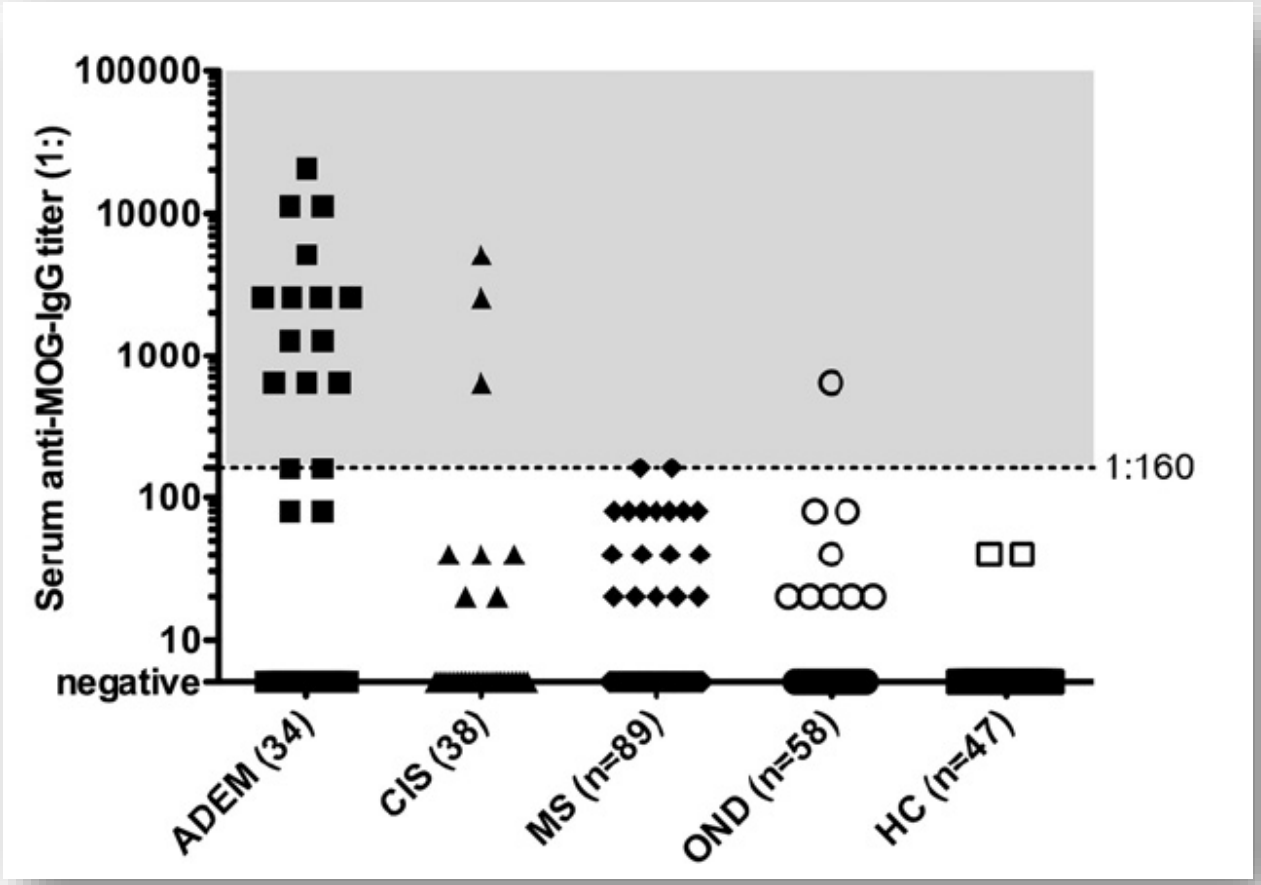


Démyélinisation
(Kluver Barrera)

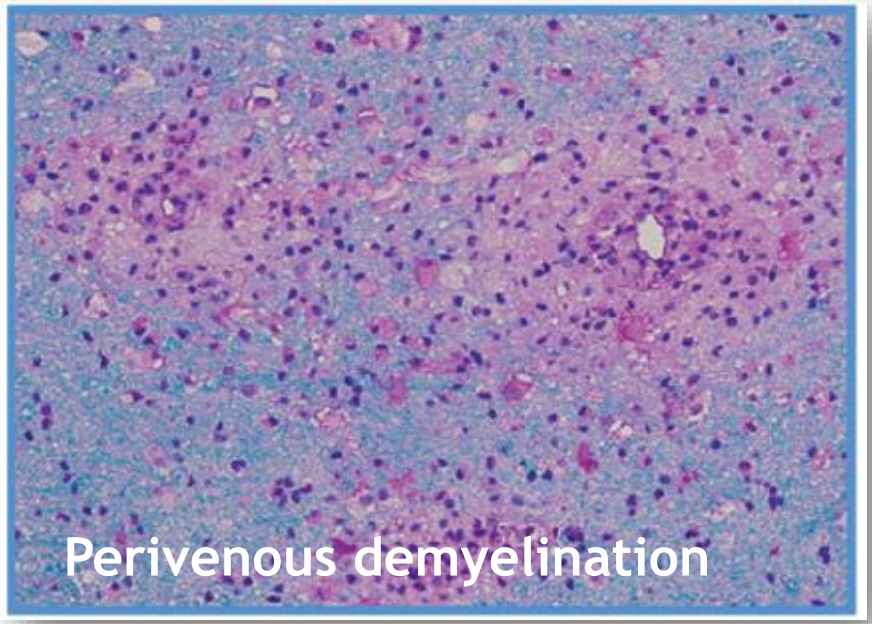
Remerciements H Adle-Biassette

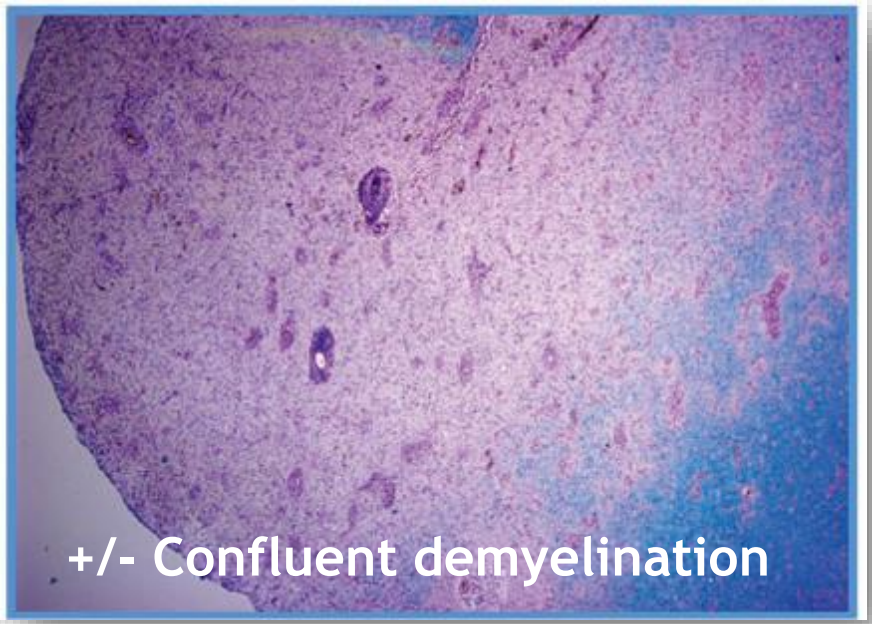
Temporal dynamics of anti-MOG antibodies in CNS demyelinating diseases

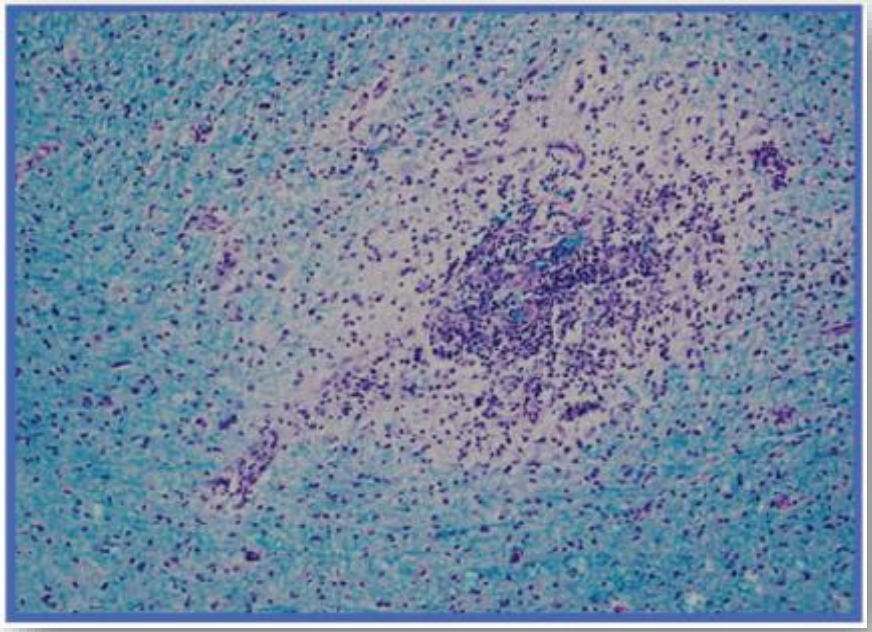
Franziska Di Pauli[a,1], Simone Mader[a,1], Kevin Rostasy[b], Kathrin Schanda[a], Barbara Bajer-Kornek[c], Rainer Ehling[a], Florian Deisenhammer[a], Markus Reindl[a], Thomas Berger[a,*]



Clinical Immunology, 2010







- Lésions périveinulaires
- Substance blanche
- Infiltrat lymphocytaire
- Démyélinisation
- Axones et artères épargnés
- Lésions du « même âge »

NP Young, Brain 2010

The Management of Encephalitis: Clinical Practice Guidelines by the Infectious Diseases Society of America

IDSA GUIDELINES

ADEM

Although not fully assessed in randomized, placebo-controlled trials **high-dose intravenous corticosteroids (methylprednisolone, 1 g IV/day, 3–5 days) are generally recommended for ADEM**

Reports of successful treatment with PLEX have also been documented, although no data from randomized trials are available.

PLEX should be considered in patients who respond poorly to corticosteroids

Tunkel Clin Inf Dis 2008

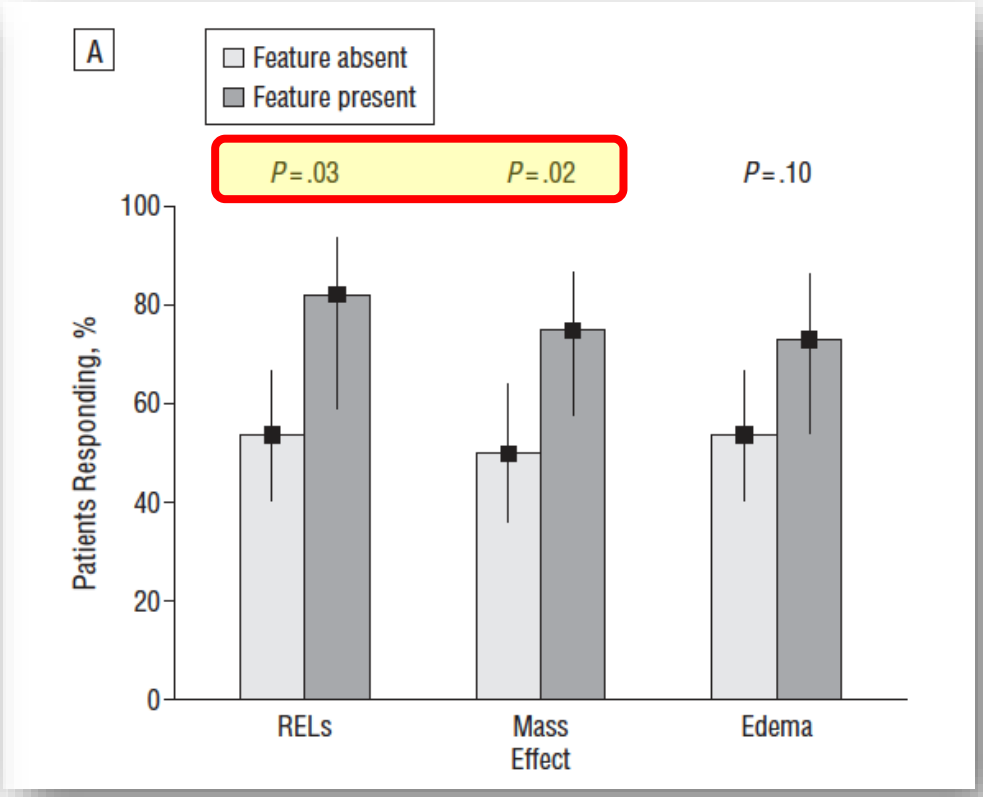
Beneficial Plasma Exchange Response in Central Nervous System Inflammatory Demyelination

Setty M. Magaña, BS; B. Mark Keegan, MD; Brian G. Weinshenker, MD; Bradley J. Erickson, MD, PhD; Sean J. Pittock, MD; Vanda A. Lennon, MD, PhD; Moses Rodriguez, MD; Kristine Thomsen, BA; Stephen Weigand, MS; Jay Mandrekar, PhD; Linda Linbo, RN; Claudia F. Lucchinetti, MD

153 patients with acute steroïd-refractory CNS inflammatory demyelinating diseases

Table 3. Unadjusted Logistic Regression Models of Clinical Features Associated With Plasma Exchange Response Among All 153 Patients

Feature	PLEX Response Rate, %	OR (95% CI)	*P* Value
Sex			.68
Female	58	1 [Reference]	
Male	61	1.16 (0.58-2.32)	
Time from index attack to PLEX, d			.89
≤20	60	1 [Reference]	
21-60	60	1.03 (0.51-2.07)	
>60	55	0.81 (0.31-2.14)	
EDSS score at index attack			.98
<8	59	1 [Reference]	
≥8	58	0.99 (0.51-1.94)	
Deep tendon reflexes			.001
Flaccid or absent	31	1 [Reference]	
Brisk or normal	66	4.28 (1.78-10.26)	

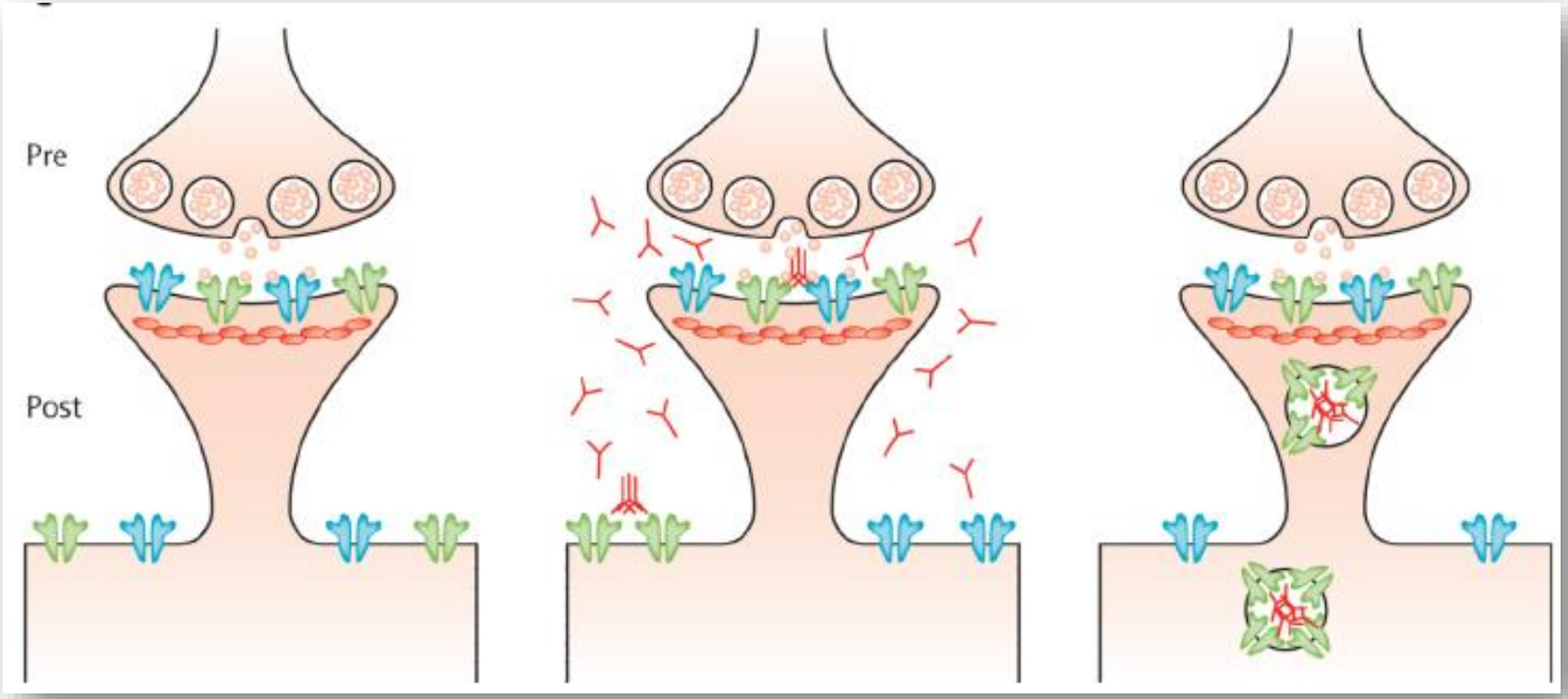


REL: ring enhancement lesions

Arch Neurol. Published online March 14, 2011.

Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis

Josep Dalmau, Eric Lancaster, Eugenia Martinez-Hernandez, Myrna R Rosenfeld, Rita Balice-Gordon



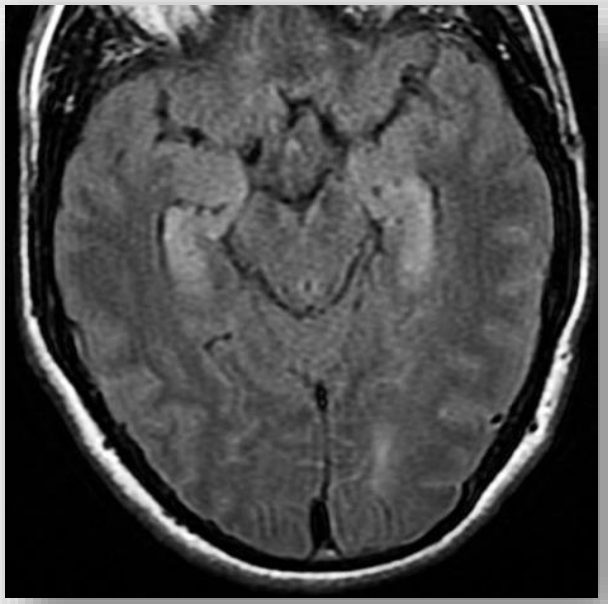
Ac anti NMDA-R dirigé contre récepteur au glutamate

CORRELATION Tx Ac ⇔ SYMPTOMES

Lancet Neurol 2011

Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies

100 patients	Patients
Women and girls	91
Median age, range (years)	23, 5–76
Prodromal symptoms (information available for 84 patients)	72
Symptom presentation	
Psychiatric (first seen by psychiatrist)	77
Neuropsychiatric (first seen by neurologists)	23
Seizures	
Any type	76
Generalised tonic-clonic	45
Partial complex	10
Other*	30
Dyskinesias and movement disorders	
Any type	86
Orofacial	55
Choreoathetoid and complex movements with extremities, abdomen or pelvis	47
Abnormal postures (dystonic, extension), muscle rigidity, or increased tone	47
Other†	25
Autonomic instability‡	69
Central hypoventilation	66



Brain MRI	
Total with abnormal findings	55
Medial temporal lobes	22
Cerebral cortex	17
Cerebellum	6

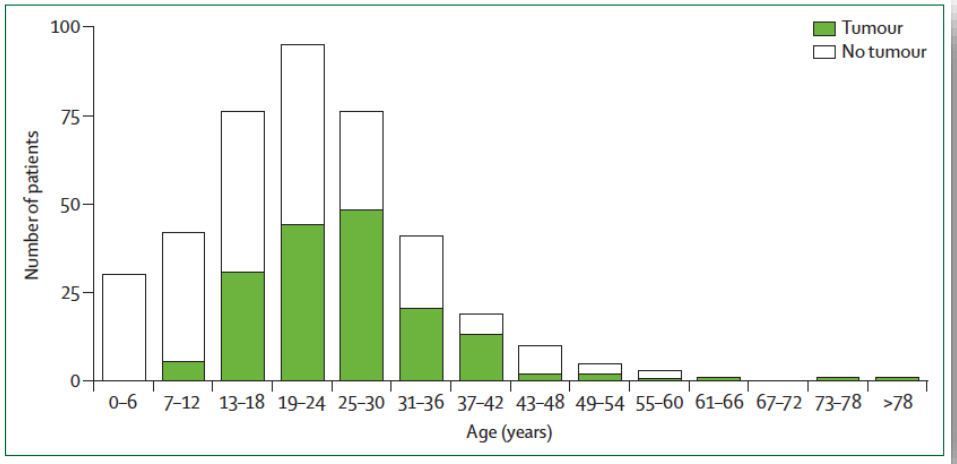
Normal MRI in 45% of patients

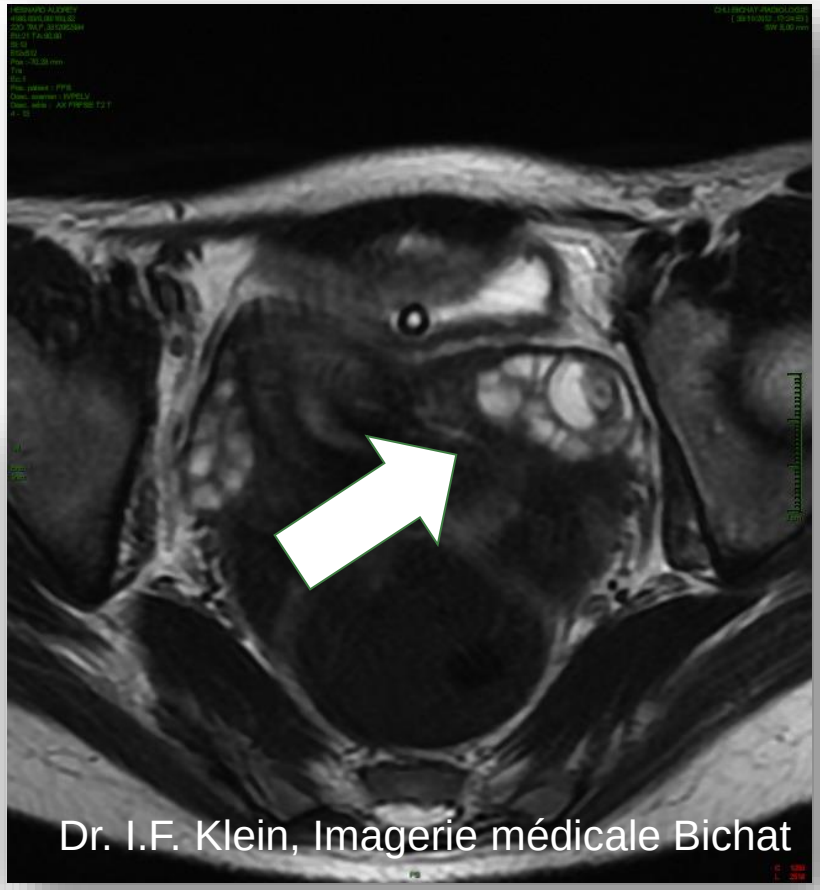
Dalmau Lancet Neurol 2008

Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis

Josep Dalmau, Eric Lancaster, Eugenia Martinez-Hernandez, Myrna R Rosenfeld, Rita Balice-Gordon

Femme jeune
Associée à tumeur dans 50% des cas
Tératome ovarien > 50% +++





Lancet Neurology 2011

N-Methyl-D-Aspartate Receptor Antibodies in Herpes Simplex Encephalitis

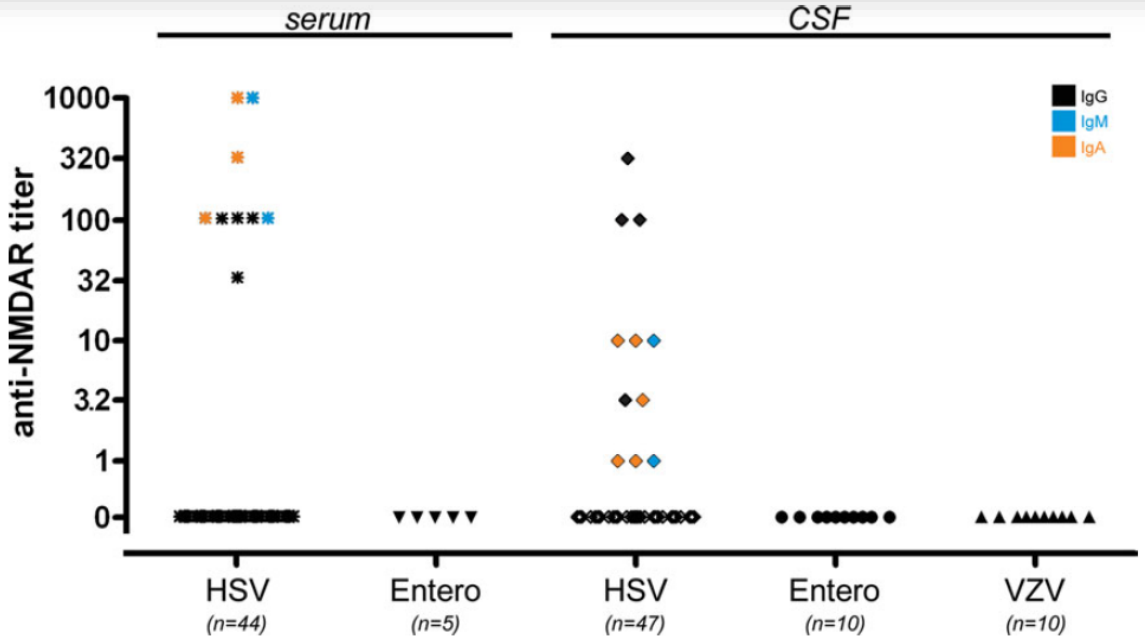
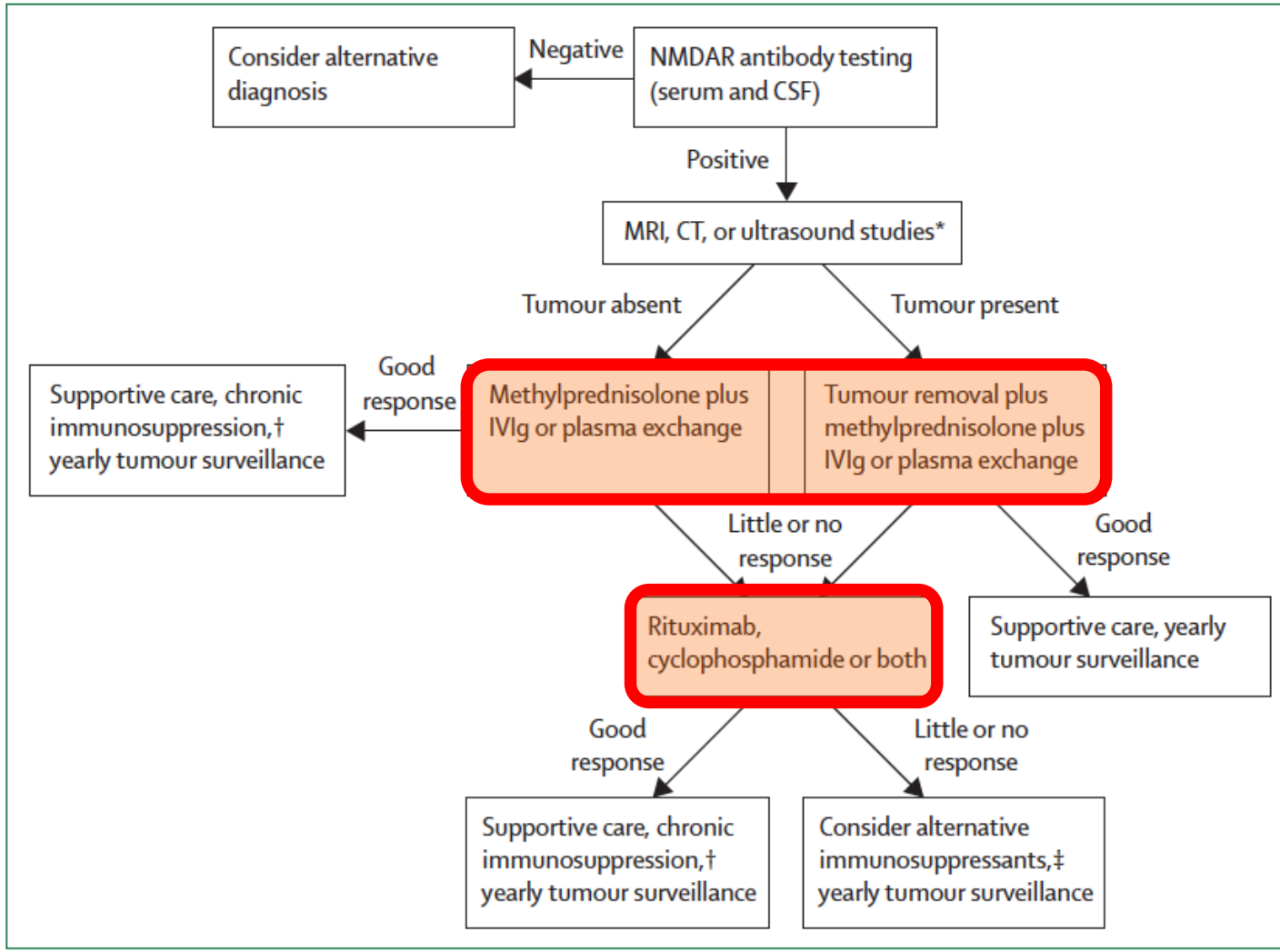


FIGURE 4: N-Methyl-D-aspartate receptor (NMDAR) antibodies in encephalitis patients. Of patients with herpes simplex virus (HSV) encephalitis, 20.5% had immunoglobulin (Ig)G, IgM, or IgA NMDAR antibodies in serum and 23.4% in cerebrospinal fluid (CSF), whereas no antibodies were detected in the CSF and serum of patients with enterovirus encephalitis or CSF of varicella zoster virus (VZV) encephalitis (serum of VZV cases not available). [Color figure can be viewed in the online issue, which is available at annalsofneurology.org.]

Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis

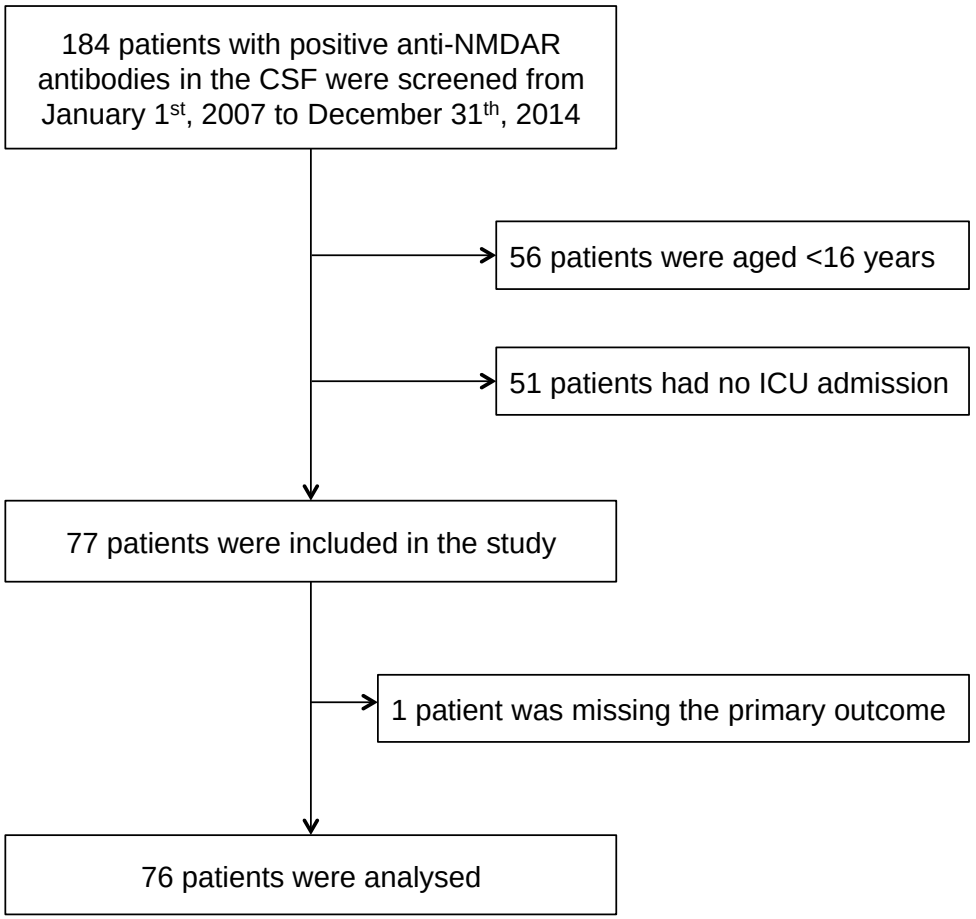
Josep Dalmau, Eric Lancaster, Eugenia Martinez-Hernandez, Myrna R Rosenfeld, Rita Balice-Gordon



Lancet Neurology 2011

Impact of early immunomodulating treatment on outcome of adult patients with anti-N-methyl-D-aspartate receptor encephalitis requiring intensive care: a multicentre study with prospective long-term follow-up

E. De Montmollin (1) ; S. Demeret (2) ; N. Brule (3) ; M. Conrad (4) ; F. Dailler (5) ; N. Lerolle (6) ; JC. Navellou (7) ; C. Schwebel (8) ; M. Alves (9) ; M. Cour (10) ; N. Engrand (11) ; JM. Tonnelier (12) ; S. Ruckly (13) ; G. Picard (14) ; V. Rogemond (14) ; JF. Timsit (15) ; J. Honnorat (14) ; R. Sonneville (15) ; ENCEPHALITICA study group



E. de Montmollin, Abstract SRLF 2016

Impact of early immunomodulating treatment on outcome of adult patients with anti-N-methyl-D-aspartate receptor encephalitis requiring intensive care: a multicentre study with prospective long-term follow-up

E. De Montmollin (1) ; S. Demeret (2) ; N. Brule (3) ; M. Conrad (4) ; F. Dailler (5) ; N. Lerolle (6) ; JC. Navellou (7) ; C. Schwebel (8) ; M. Alves (9) ; M. Cour (10) ; N. Engrand (11) ; JM. Tonnelier (12) ; S. Ruckly (13) ; G. Picard (14) ; V. Rogemond (14) ; JF. Timsit (15) ; J. Honnorat (14) ; R. Sonneville (15) ; ENCEPHALITICA study group

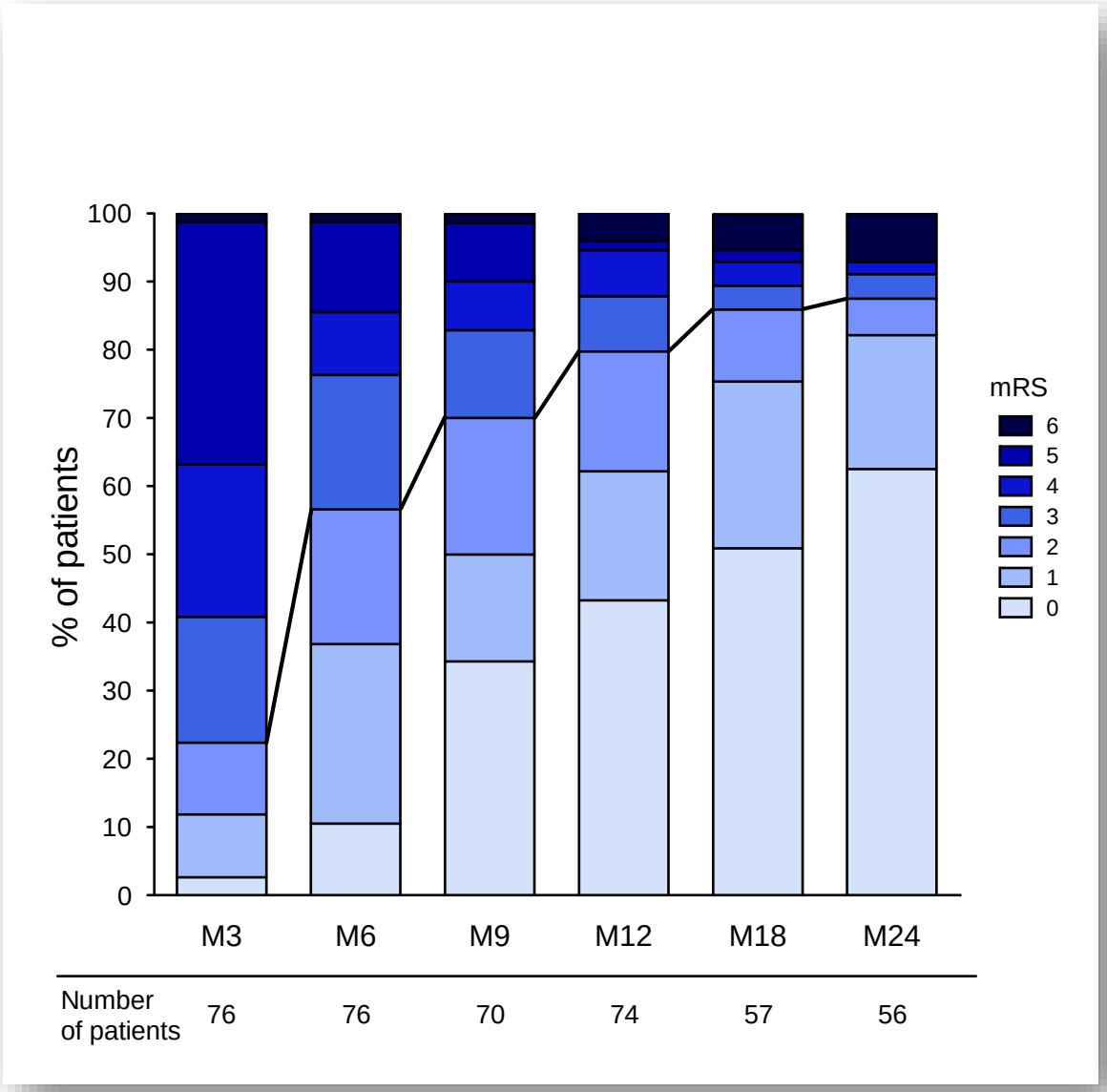
Multivariate analysis of prognostic factors of good neurological outcome at 6 months (mRS < 2)

N= 76 ICU patients with NMDAR encephalitis

Variable	Odds ratio (95% CI)	p
First line immunomodulating treatment		
Early intravenous immunoglobulins	2.26 (0.54–9.35)	0.26
Early steroids	3.26 (0.62–17.19)	0.16
Early combined treatment	8.42 (2.11–33.57)	0.003
Late treatment	Reference	0.03
White blood cells in first CSF (cells/mm^3)		
<10	6.88 (1.58–29.92)	0.01
10-50	3.60 (1.03–2.65)	0.05
>50	Reference	0.03

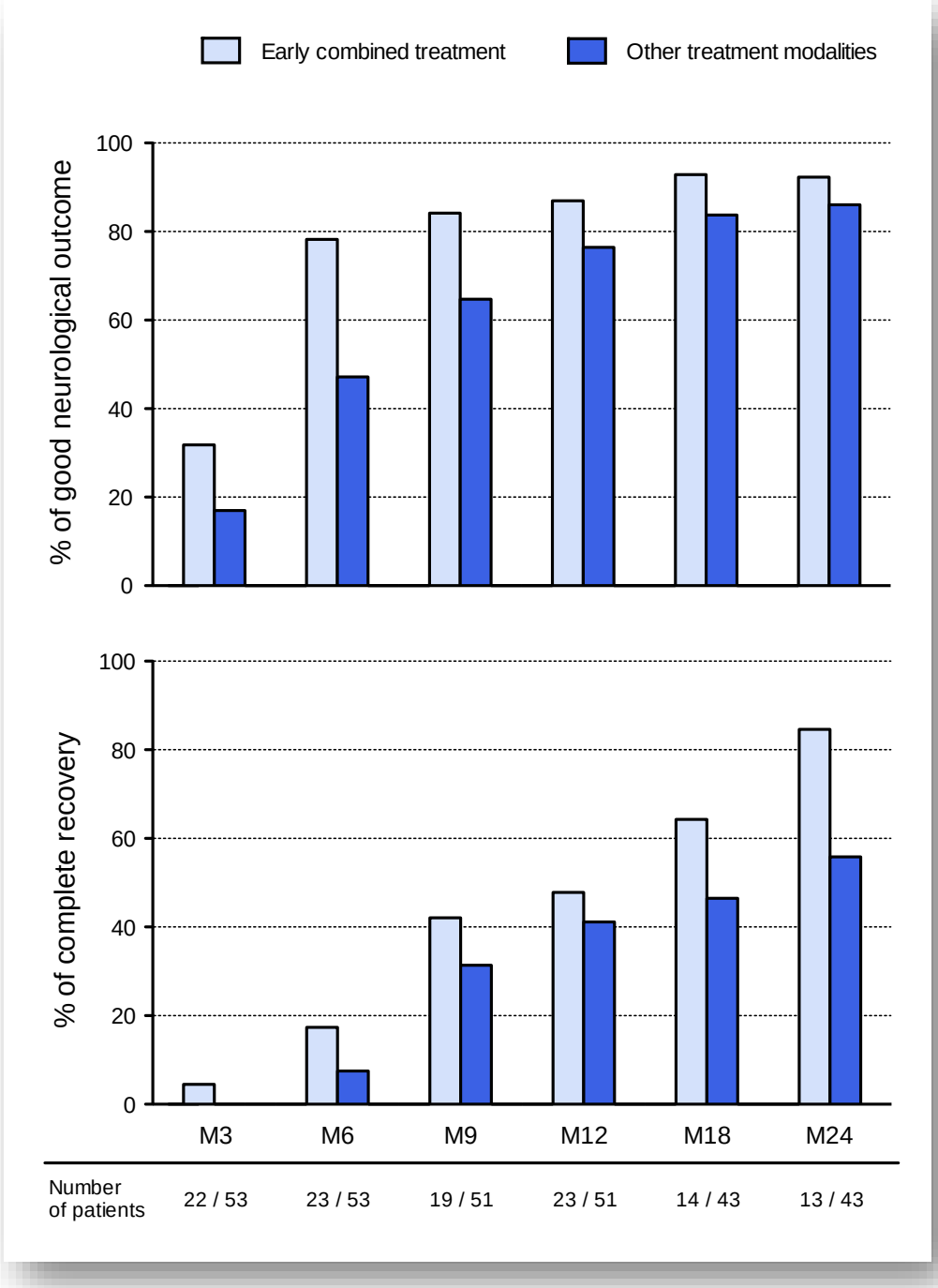
E. de Montmollin, Abstract SRLF 2016

Modified Rankin scale scores



E. de Montmollin, Abstract SRLF 2016

Outcomes



E. de Montmollin, Abstract SRLF 2016

Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Antiepileptic drugs for the primary and secondary prevention of seizures in viral encephalitis (Review)

Pandey S, Rathore C, Michael BD

THE COCHRANE COLLABORATION®

Authors' conclusions

There is insufficient evidence to support the routine use of antiepileptic drugs for the primary or secondary prevention of seizures in viral encephalitis. There is a need for adequately powered randomised controlled trials in viral encephalitis patients to assess the efficacy and safety of antiepileptic drugs for the primary and secondary prophylaxis of seizures, which is an important clinical problem.

2012

Early-onset status epilepticus in critically ill patients with encephalitis

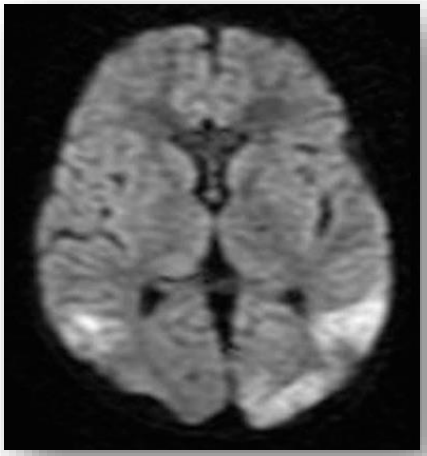
N=290 patients with encephalitis

Bichat medical ICU, Paris, France (1991-2013)

STATUS EPILEPTICUS = 20%

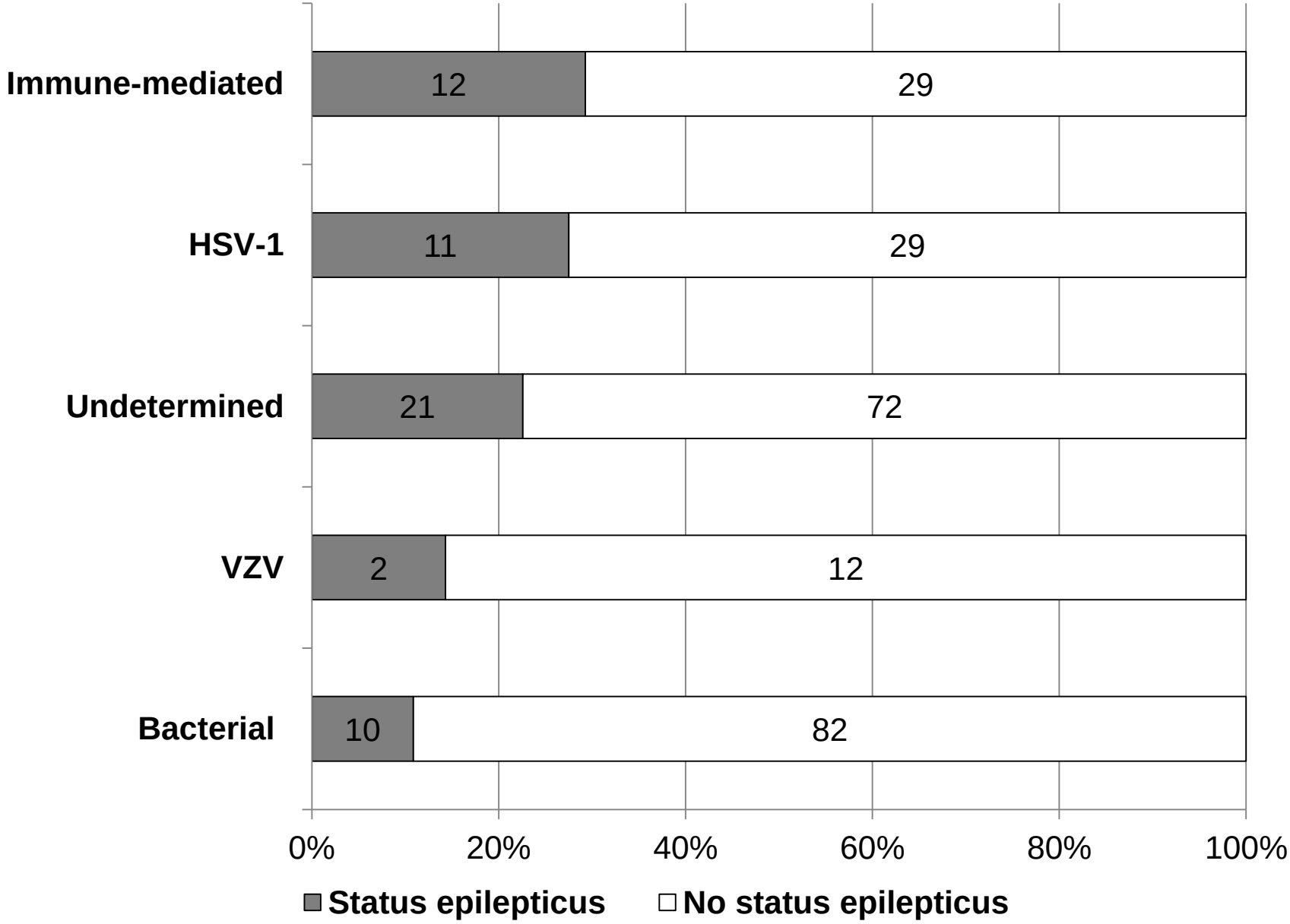
MULTIVARIATE ANALYSIS

Variable	Adjusted OR	95% CI
GCS < 8, indicating coma	3.1	1.5-6.3
Cortical involvement (neuroimaging)	3.7	1.8-7.8
N of non-neurologic organ failures		
0	1.0	
1	13.6	4.9-37.7
More than one	3.1	0.7-13.7
Bacterial etiology (vs. non-bacterial)	0.3	0.1-0.7

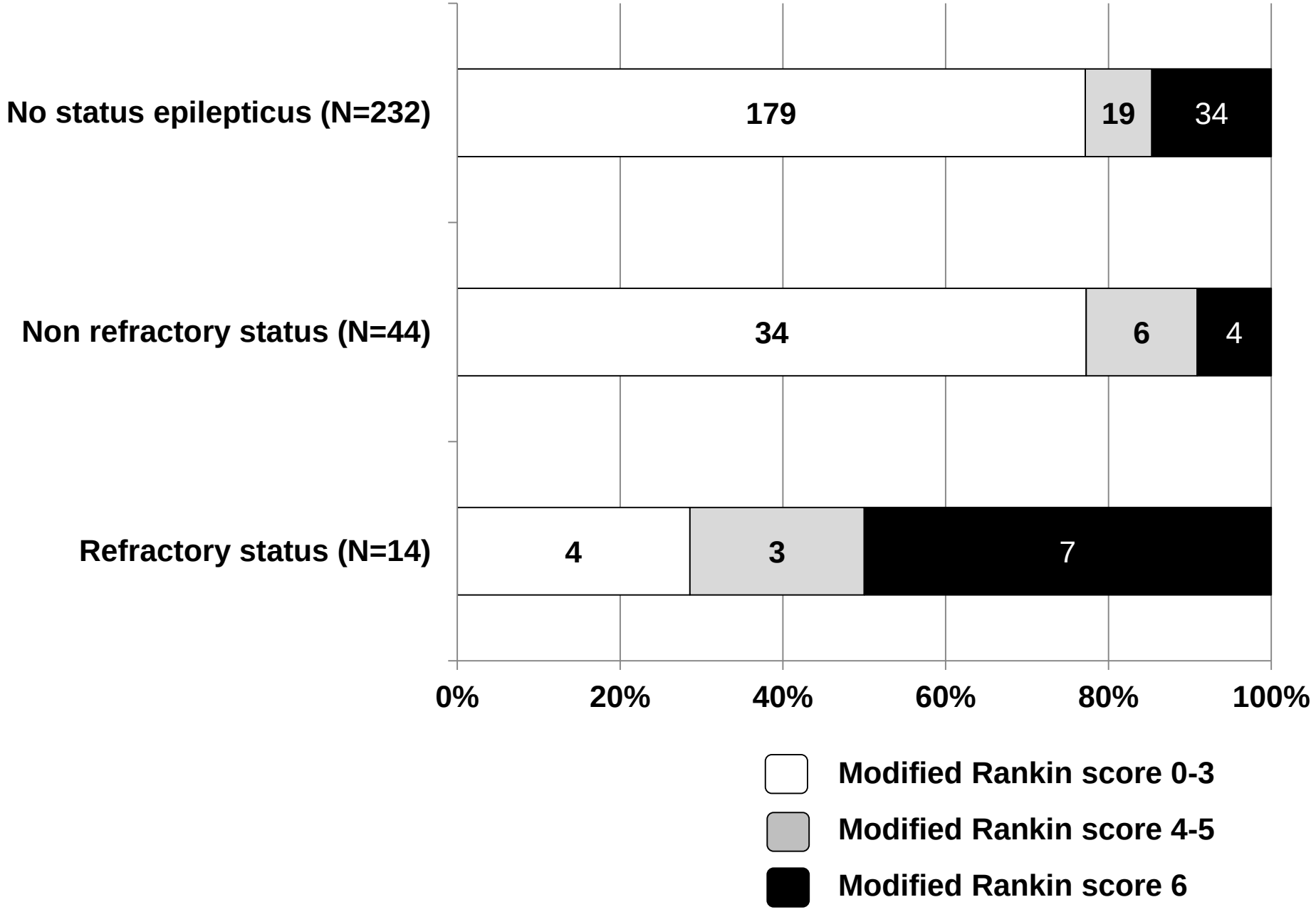


CORTICAL INVOLVEMENT

under revision



under revision



under revision

Corticoïdes ?

Study protocol

Open Access

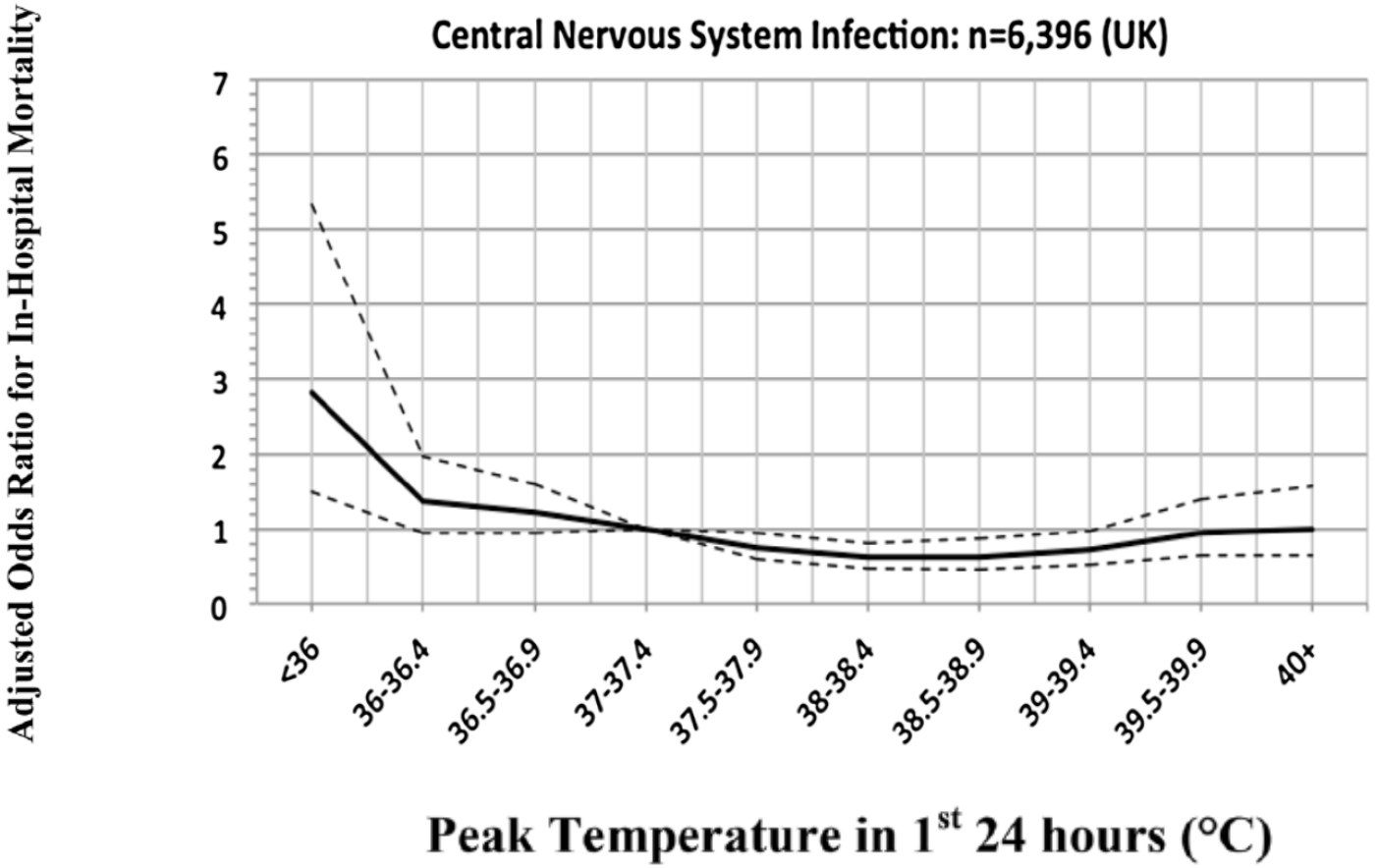
Protocol for German trial of *A*cyclovir and corticosteroids in *H*erpes-simplex-virus-encephalitis (GACHE): a multicenter, multinational, randomized, double-blind, placebo-controlled German, Austrian and Dutch trial [ISRCTN45122933]

Francisco Martinez-Torres[†1,9], Sanjay Menon[†1,2], Maria Pritsch[3], Norbert Victor[3], Ekkehart Jenetzky[3], Katrin Jensen[3], Eva Schielke[4], Erich Schmutzhard[5], Jan de Gans[6], Chin-Hee Chung[7], Steffen Luntz[8], Werner Hacke[1], Uta Meyding-Lamadé[*1,2] for the GACHE Investigators

DexEnceph

BrainInfectionsUK.org

Early temperature and mortality in critically ill patients with acute neurological diseases

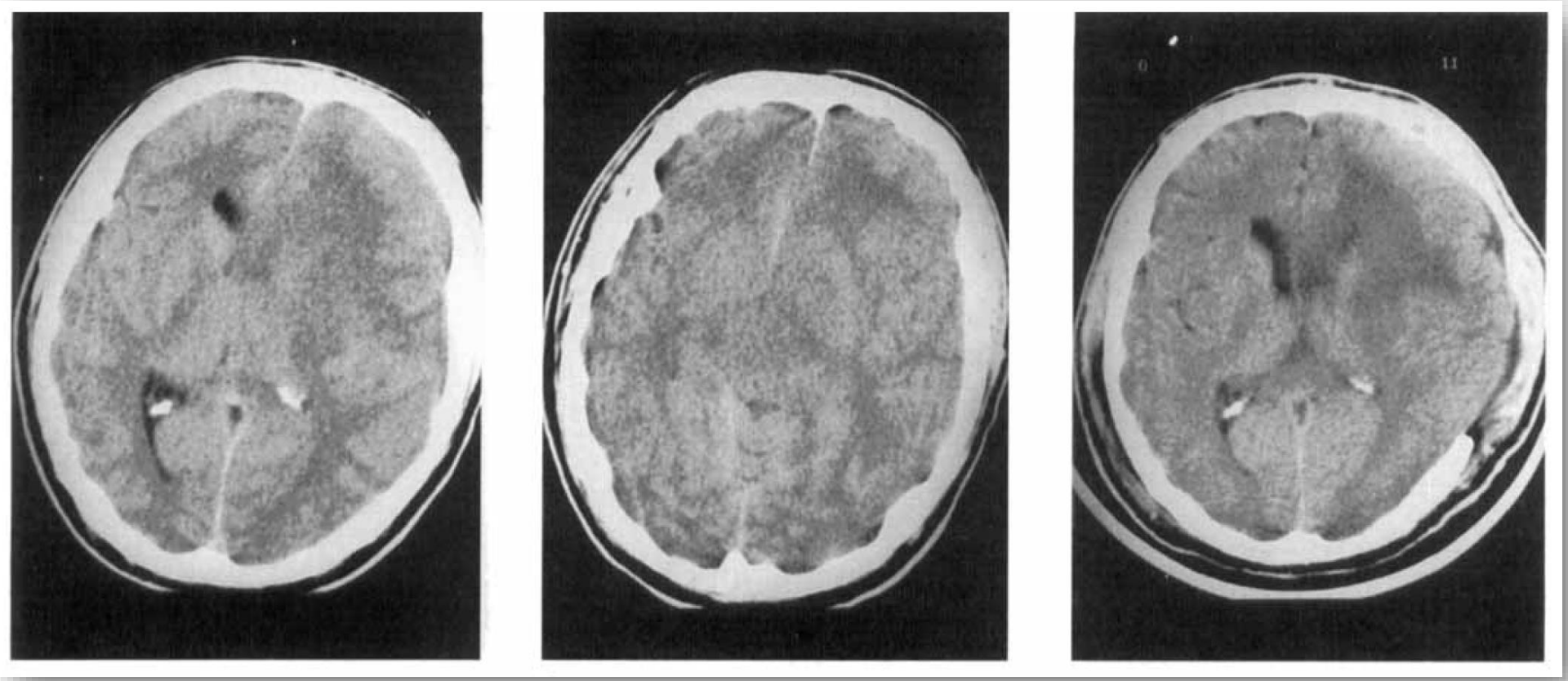


M Saxena, Intensive Care Med 2015

Craniectomy:

An aggressive treatment approach in severe encephalitis

S. Schwab, MD; E. Jünger, MD; M. Spranger, MD; A. Dörfler, MD; F. Albert, MD; H.H. Steiner, MD; and W. Hacke, MD



Neurology 1999

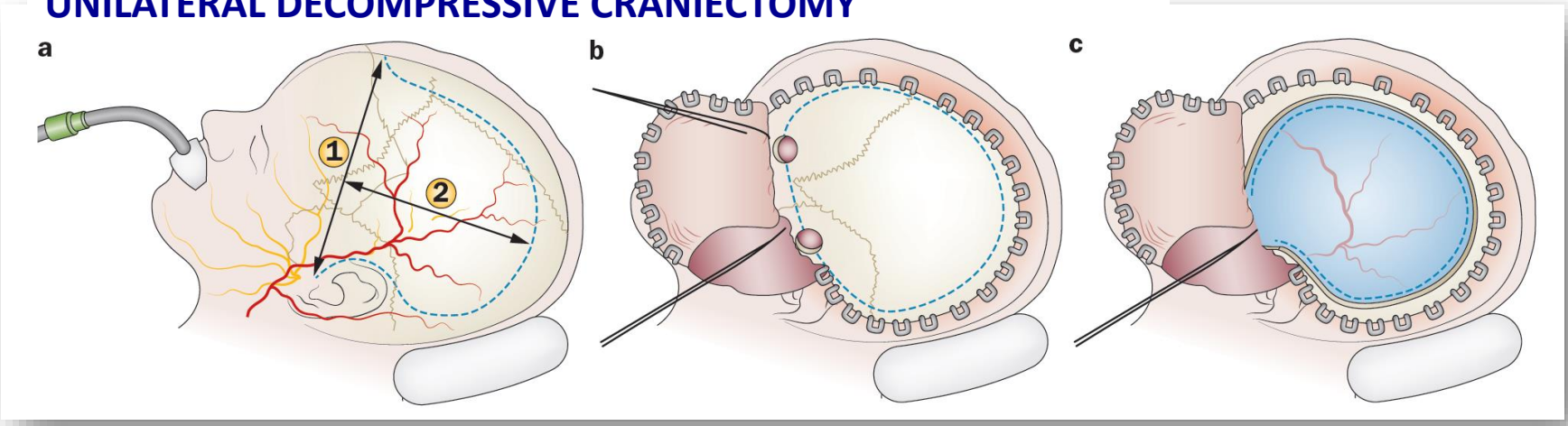
Acta Neurochir (2012) 154:1717–1724
DOI 10.1007/s00701-012-1323-3

REVIEW ARTICLE

Decompressive craniectomy for encephalitis with brain herniation: case report and review of the literature

N=48 patients
Literature review of published cases
39 (81%) had a favorable functional recovery

UNILATERAL DECOMPRESSIVE CRANIECTOMY



J Perez Bovet, Acta Neurochirurgica 2012
A Kolias, Nat Rev Neurol 2013

Encéphalites aiguës

- Définitions et épidémiologie en 2015
- Evaluation initiale et algorithme diagnostique
- Reconnaitre les causes justifiant un traitement spécifique
- Traitement symptomatique
- Peut-on améliorer le pronostic ?

Clinical spectrum and outcomes of patients with encephalitis requiring intensive care

R. Sonneville[a], N. Gault[b,c,d], E. de Montmollin[a], I. F. Klein[e], E. Mariotte[a], S. Chemam[a], F. Tubach[b,c,d], B. Mourvillier[a], J. F. Timsit[a,f], M. Wolff[a] and L. Bouadma[a,f]

N= 279 ICU patients with encephalitis

Factors associated with a poor outcome (mRS=4-6 at day 90)

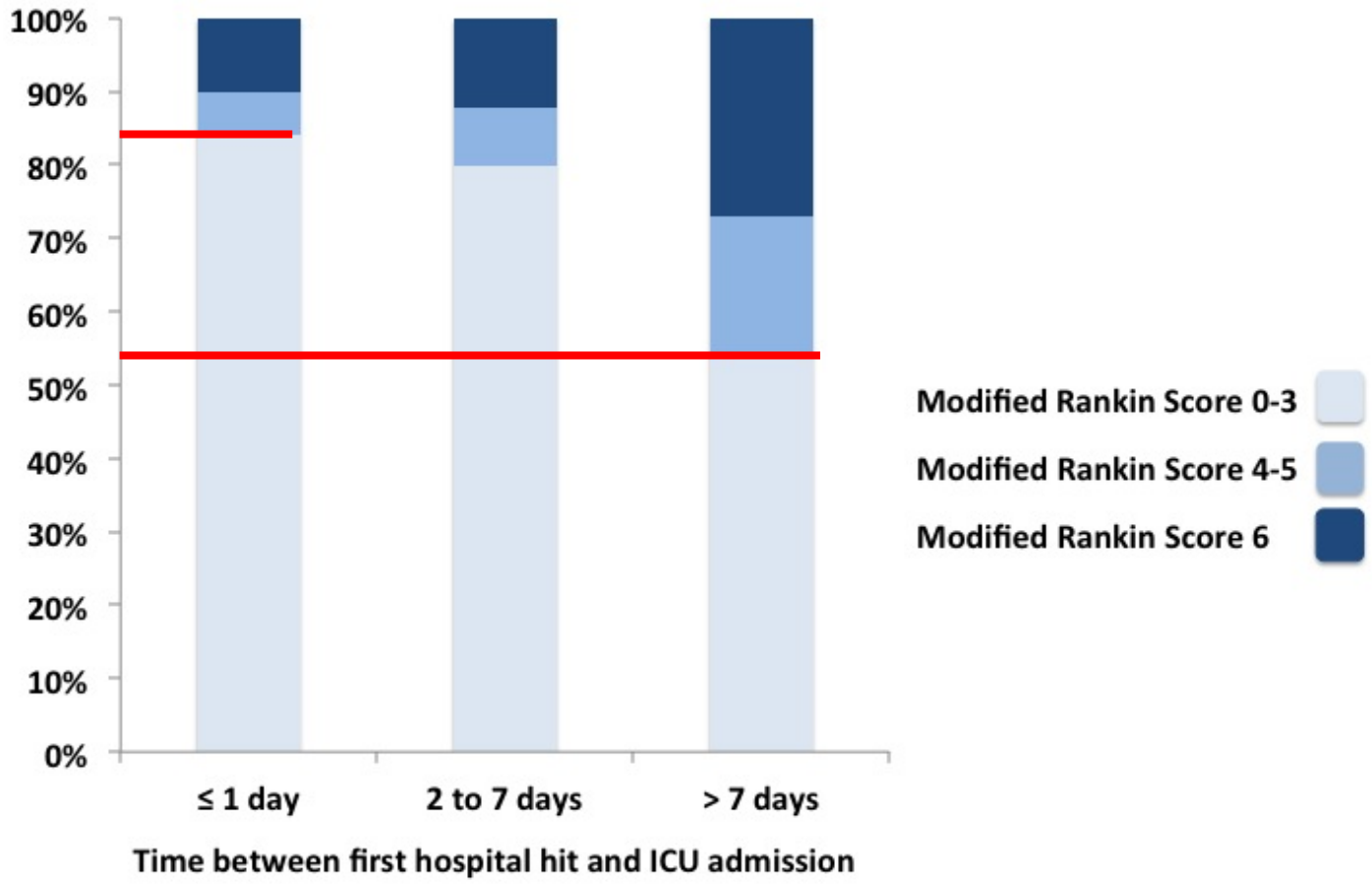
=> 71 (25%) patients

Variable	**Odds Ratio**	**95% CI**
KNAUS score 3-4	6.3	2.0-21.2
Coma	7.1	3.1-17.0
Temperature (per ° C)	0.7	0.5-0.9
Aspiration pneumonia	4.0	1.5-11.0
CSF protein levels, per 1 g/l	1.6	1.2-2.1
Time between hospital and ICU admission, days	1.04	1.01-1.07

Eur J Neurol 2015

Clinical spectrum and outcomes of patients with encephalitis requiring intensive care

R. Sonneville[a], N. Gault[b,c,d], E. de Montmollin[a], I. F. Klein[e], E. Mariotte[a], S. Chemam[a], F. Tubach[b,c,d], B. Mourvillier[a], J. F. Timsit[a,f], M. Wolff[a] and L. Bouadma[a,f]



Eur J Neurol 2015

Outcomes of patients with acute encephalitis

Table 3 Multivariate analysis of factors associated with death in patients with all-cause encephalitis[a]

Died before discharge (n = 19)	OR	95% CI	Average marginal effects, %	*p* Value
Age ≥65 y	2.10	0.44–10.02	7.47	0.35
Male	3.63	0.97–13.54	13.00	0.04
Thrombocytopenia	6.28	1.41–28.03	18.54	0.01
Cerebral edema	18.06	3.14–103.92	29.20	<0.01
Status epilepticus	8.16	1.55–43.10	21.19	0.01
Immunosuppression	1.86	0.27–12.6	6.28	0.50
Charlson comorbidity	1.16	0.84–1.60	1.49	0.37

A Venkatesan, Neurology 2013

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

A Mailles, Clin Inf Dis 2012

- 2007: 253 patients (adultes)
- Mortalité 9 (5%)
- Survie sans aucune séquelles : 71 (40%) patients

Table 2. Demographic Features of Patients Enrolled in Follow-up, by Causative Agent

Causative Agent	Patients, No. (%)	Age, Median (Range)	Age <16 y	Male-Female Ratio	Favorable Outcome: (GOS Score, 5)	Full Recovery	Encephalitis-Related Deaths
All patients	176 (100)	53.5 y (1 mo to 89 y)	23 (13)	1.6	108 (61)	71 (40)	9 (5.1)
HSV[a]	43 (24)	58 y (1 mo to 85 y)	1 (2)	1.3	18 (42)	6 (14)	3 (7.0)
VZV	15 (9)	63 y (6 mo–to 86 y)	3 (20)	4	7 (47)	5 (33)	1 (6.7)
M. tuberculosis	10 (6)	64 y (17–75 y)	0	1	7 (70)	5 (50)	1 (10.0)
Other cause[b]	23 (13)	51 y (6 mo to 87 y)	8 (35)	2.8	16 (70)	12 (52)	1 (4.3)
Unknown	85 (48)	43 y (1–89 y)	11 (13)	1.4	60 (71%)	43 (51)	3 (3.5)

Data are No. (%) of patients unless otherwise indicated.

Abbreviations: GOS, Glasgow Outcome Scale; HSV, herpes simplex virus; *M. tuberculosis, Mycobacterium tuberculosis*; VZV, varicella-zoster virus.

[a] In 2007, all adult patients with HSV encephalitis were treated with acyclovir for 2 or 3 weeks at a dosage of 10–15 mg/kg/8 hours. The 1-month-old patient received 20 mg/kg/8 hours for 3 weeks. Acyclovir was started 0–10 days after onset (mean, 1 day) [19].

[b] Causative agents included *Listeria monocytogenes* (n = 4), tick-borne encephalitis (n = 3), *Mycoplasma pneumoniae* (n = 2), Epstein-Barr virus (n = 2), cytomegalovirus (n = 2), enterovirus (n = 2), *Legionella pneumophila* (n = 1), influenza A (n = 1), *Borrelia burgdoferi* (n = 1), *Rickettsia coronii* (n = 1), *Francisella tularensis* (n = 1), *Cryptococcus neoformans* (n = 1), and Toscana virus (n = 2).

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

Table 4. Factors Associated With Favorable Outcome, Final Logistic Regression Model (n = 128)

Variable	Favorable Outcome	Poor Outcome	Multivariate Analysis	
			OR (95% CI)	*P*
Comorbid conditions[a]	14 (18)	19 (37)	0.25 (.08–.73)[a]	.01
Age, mean (range), years (OR for 5-y increase)[b]	50 (19–89)	63 (28–85)	0.83 (.72–.96)	.01
Level of education, years				.02
None	3 (4)	9 (17)	Reference	
<6 (stopped before high school)	16 (21)	16 (31)	4.0 (.73–22.22)	.11
6–9 (high school)	13 (17)	16 (31)	1.4 (.25–8.34)	.69
10–13 (college)	21 (28)	5 (10)	10.5 (1.5–74.2)	.02
>13 (university)	23 (30)	6 (12)	6.4 (.99–40.77)	.05
Causative agent				.05
Herpes simplex virus	15 (19)	21 (40)	Reference	
Varicella-zoster virus	5 (6.5)	5 (9)	1.9 (.3–11.1)	.5
M. tuberculosis	6 (6.9)	3 (6)	6.0 (1.1–33.6)	.04
Other	9 (10)	3 (6)	8.4 (1.6–44.1)	.01
Unknown	41 (54)	20 (38)	3.2 (1.2–9.0)	.03

The final model was obtained by a step-by-step descending procedure. Data are No. (%) of patients unless otherwise indicated.

Abbreviations: CI, confidence interval; *M. tuberculosis*, *Mycobacterium tuberculosis*; OR, odds ratio.

[a] Equivalent to comorbid conditions associated with poor outcome with OR = 4 (1.4–12.0).

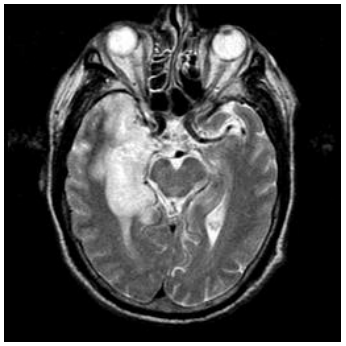
[b] Equivalent to age associated with poor outcome with OR = 1.5 (1.1–1.9) for an increase of 10 years.

Mailles, CID 2012

Les encéphalites, en conclusion ….

- **Un syndrome neurologique aigu,** des étiologies très variées
  - infectieuses
  - dysimmunitaires
- **Evaluation précoce, algorithme diagnostique**
- **IRM CEREBRALE ++++**
- **Le retard à l'instauration du traitement spécifique est associé à un mauvais pronostic**
- **Amélioration du pronostic**
  - Admission précoce en réanimation ?
  - Traitements adjuvants ?
  - Prévention des complications non-spécifiques

  (inhalation, œdème cérébral, convulsions)



EncephalitICa

***Encephalit**is in Intensive **Ca**re*

- **Pronostic neurologique des encéphalites admises en réanimation,(soumis PHRC-IR 2015)**
- Cohorte prospective multicentrique
- 50 centres de réanimation en France + EUROPE
- En association avec cohorte ENCEI

(JP Stahl, P Tattevin)

ESICM EUROPEAN SOCIETY OF INTENSIVE CARE MEDICINE

SOCIETE DE PATHOLOGIE INFECTIEUSE DE LANGUE FRANCAISE Spilf

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES