Encéphalites

Dr Marion Le Maréchal

Infectiologie, CHU de Grenoble

16 février 2024

Diplôme Universitaire de Thérapeutiques Anti-Infectieuses
Université Grenoble Alpes
2ème session – février 2024

1. Référentiels

Référentiels conseillés – Recommandations françaises

ELSEVIER
CrossMark
Disponible en ligne sur ScienceDirect www.sciencedirect.com
Elsevier Masson France EM|consulte www.em-consulte.com
Médecine et maladies infectieuses
Médecine et maladies infectieuses 47 (2017) 179–194

Recommendations/Recommandations

Guidelines on the management of infectious encephalitis in adults

Recommandations de prise en charge des encéphalites infectieuses de l'adulte

J.P. Stahl[a,*,1], P. Azouvi[b], F. Bruneel[c], T. De Broucker[d], X. Duval[e], B. Fantin[f], N. Girard[g], J.L. Herrmann[h], J. Honnorat[i], M. Lecuit[j,k], A. Mailles[l,1], L. Martinez-Almoyna[m], P. Morand[n], L. Piroth[o], P. Tattevin[p,l], The reviewing group[2]

Stahl, Med Mal Inf, 2017

Référentiels conseillés – Recommandations américaines

IDSA GUIDELINES

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

Allan R. Tunkel,[1] Carol A. Glaser,[2] Karen C. Bloch,[3] James J. Sejvar,[4] Christina M. Marra,[5] Karen L. Roos,[6] Barry J. Hartman,[7] Sheldon L. Kaplan,[8] W. Michael Scheld,[9] and Richard J. Whitley[10]

[1]Monmouth Medical Center, Long Branch, New Jersey; [2]California Department of Health Services, Richmond; [3]Vanderbilt University School of Medicine, Nashville, Tennessee; [4]Centers for Disease Control and Prevention, Atlanta, Georgia; [5]University of Washington School of Medicine, Seattle; [6]Indiana University School of Medicine, Indianapolis; [7]Weill Cornell Medical Center, New York, New York; [8]Baylor College of Medicine, Houston, Texas; [9]University of Virginia School of Medicine, Charlottesville; and [10]University of Alabama at Birmingham

Tunkel, CID, 2008

Référentiels conseillés – Définitions de l'IEC

MAJOR ARTICLE

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

A. Venkatesan,[1] A. R. Tunkel,[2] K. C. Bloch,[3,4] A. S. Lauring,[5] J. Sejvar,[6] A. Bitnun,[7] J-P. Stahl,[8] A. Mailles,[9] M. Drebot,[10] C. E. Rupprecht,[11] J. Yoder,[12] J. R. Cope,[12] M. R. Wilson,[13,14] R. J. Whitley,[15,16,17,18] J. Sullivan,[19] J. Granerod,[20] C. Jones,[21,22] K. Eastwood,[23] K. N. Ward,[20,24] D. N. Durrheim,[25,26] M. V. Solbrig,[27] L. Guo-Dong,[28] and C. A. Glaser;[29] on behalf of the International Encephalitis Consortium

Venkatesan, CID, 2013

2. Épidémiologie

Épidémiologie en France

ELSEVIER

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Original article

Changing profile of encephalitis: Results of a 4-year study in France

A. Mailles[a,b,*], X. Argemi[c], C. Biron[d], P. Fillatre[b,e], T. De Broucker[f], R. Buzelé[g], A. Gagneux-Brunon[h], I. Gueit[i], C. Henry[f], S. Patrat-Delon[j], A. Makinson[k], E. Piet[l], H. Wille[m], M.O. Vareil[m], O. Epaulard[b,n], M. Martinot[o], P. Tattevin[b,j], J.P. Stahl[b,n], the scientific committee[1] the investigators[2],

Mailles, ID Now, 2022

Épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %	Confirmed	Probable	Possible
HSV	132	40,7	26,7	131	0	0
VZV	65	20,1	13,2	64	0	1
TBEV	26	8,0	5,3	12	12	2
Listeria monocytogenes	23	7,1	4,7	21	2	0
Mycobacterium tuberculosis	11	3,4	2,2	8	2	1
Inconnu	170	-	34,4	-	-	-

Mailles, ID Now, 2022

Épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %	Confirmed	Probable	Possible
HSV	132	40,7	26,7	131	0	0
VZV	65	20,1	13,2	64	0	1
TBEV	26	8,0	5,3	12	12	2
Listeria monocytogenes	23	7,1	4,7	21	2	0
Mycobacterium tuberculosis	11	3,4	2,2	8	2	1
Inconnu	170	-	34,4	-	-	-

Mailles, ID Now, 2022

Épidémiologie en France

Table 1. Diagnostic Criteria for Encephalitis and Encephalopathy of Presumed Infectious or Autoimmune Etiology

Major Criterion (required):
Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting ≥24 h with no alternative cause identified.
Minor Criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed[a] encephalitis):
Documented fever ≥38° C (100.4°F) within the 72 h before or after presentation[b]
Generalized or partial seizures not fully attributable to a preexisting seizure disorder[c]
New onset of focal neurologic findings
CSF WBC count ≥5/cubic mm[d]
Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset[e]
Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.[f]

Abbreviations: CNS, central nervous system; CSF, cerebral spinal fluid; EEG, electroencephalogram; RBC, red blood cell; WBC, white blood cell.

[a] Confirmed encephalitis requires one of the following: (1) Pathologic confirmation of brain inflammation consistent with encephalitis; (2) Defined pathologic, microbiologic, or serologic evidence of acute infection with a microorganism strongly associated with encephalitis from an appropriate clinical specimen (for examples, see references [1, 2]); or (3) Laboratory evidence of an autoimmune condition strongly associated with encephalitis.

Venkatesan, CID, 2013

Épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %	Confirmed	Probable	Possible
HSV	132	40,7	26,7	131	0	0
VZV	65	20,1	13,2	64	0	1
TBEV	26	8,0	5,3	12	12	2
Listeria monocytogenes	23	7,1	4,7	21	2	0
Mycobacterium tuberculosis	11	3,4	2,2	8	2	1
Inconnu	170	-	34,4	-	-	-

Mailles, ID Now, 2022

Épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %	Confirmed	Probable	Possible
HSV	132	40,7	26,7	131	0	0
VZV	65	20,1	13,2	64	0	1
TBEV	26	8,0	5,3	12	12	2
Listeria monocytogenes	23	7,1	4,7	21	2	0
Mycobacterium tuberculosis	11	3,4	2,2	8	2	1
Inconnu	170	-	34,4	-	-	-

Mailles, ID Now, 2022

Épidémiologie en France

2009

Cause of encephalitis	N =	% of cases identified	Total (253) %
HSV	55	42	21,7
VZV	20	15,2	7,9
Mycobacterium tuberculosis	20	15,2	7,9
Listeria monocytogenes	13	10	5,1
CMV	3	2,3	1,2
Inconnu	122		48,2

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7
Mycobacterium tuberculosis	11	3,4	2,2
Inconnu	170	-	34,4

Mailles, CID, 2009
Mailles, ID Now, 2022

Épidémiologie en France

2009

Cause of encephalitis	N =	% of cases identified	Total (253) %
HSV	55	42	21,7
VZV	20	15,2	7,9
Mycobacterium tuberculosis	20	15,2	7,9
Listeria monocytogenes	13	10	5,1
CMV	3	2,3	1,2
Inconnu	122		48,2

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7
Mycobacterium tuberculosis	11	3,4	2,2
Inconnu	170	-	34,4

Mailles, CID, 2009
Mailles, ID Now, 2022

Épidémiologie en France

2009

Cause of encephalitis	N =	% of cases identified	Total (253) %
HSV	55	42	21,7
VZV	20	15,2	7,9
Mycobacterium tuberculosis	20	15,2	7,9
Listeria monocytogenes	13	10	5,1
CMV	3	2,3	1,2
Inconnu	122		48,2

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7
Mycobacterium tuberculosis	11	3,4	2,2
Inconnu	170	-	34,4

Mailles, CID, 2009
Mailles, ID Now, 2022

Épidémiologie en France

2009

Cause of encephalitis	N =	% of cases identified	Total (253) %
HSV	55	42	21,7
VZV	20	15,2	7,9
Mycobacterium tuberculosis	20	15,2	7,9
Listeria monocytogenes	13	10	5,1
CMV	3	2,3	1,2
Inconnu	122		48,2

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7
Mycobacterium tuberculosis	11	3,4	2,2
Inconnu	170	-	34,4

Mailles, CID, 2009
Mailles, ID Now, 2022

Épidémiologie en France

2009

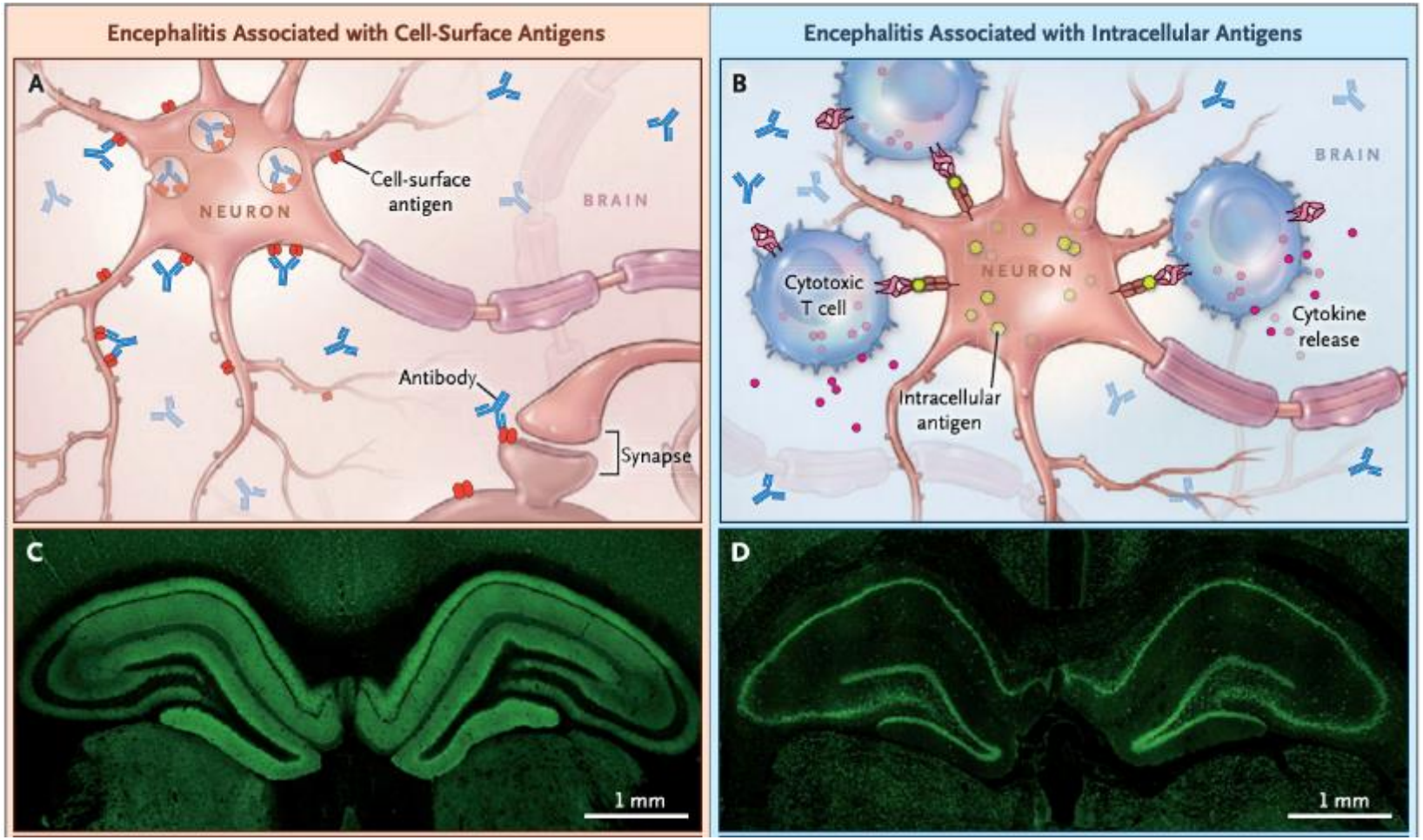
Cause of encephalitis	N =	% of cases identified	Total (253) %
HSV	55	42	21,7
VZV	20	15,2	7,9
Mycobacterium tuberculosis	20	15,2	7,9
Listeria monocytogenes	13	10	5,1
CMV	3	2,3	1,2
Inconnu	122		48,2

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7
Mycobacterium tuberculosis	11	3,4	2,2
Inconnu	170	-	34,4

Mailles, CID, 2009
Mailles, ID Now, 2022

Et les encéphalites auto-immunes ?



Dalmau, NEJM, 2018

Et les encéphalites auto-immunes ?

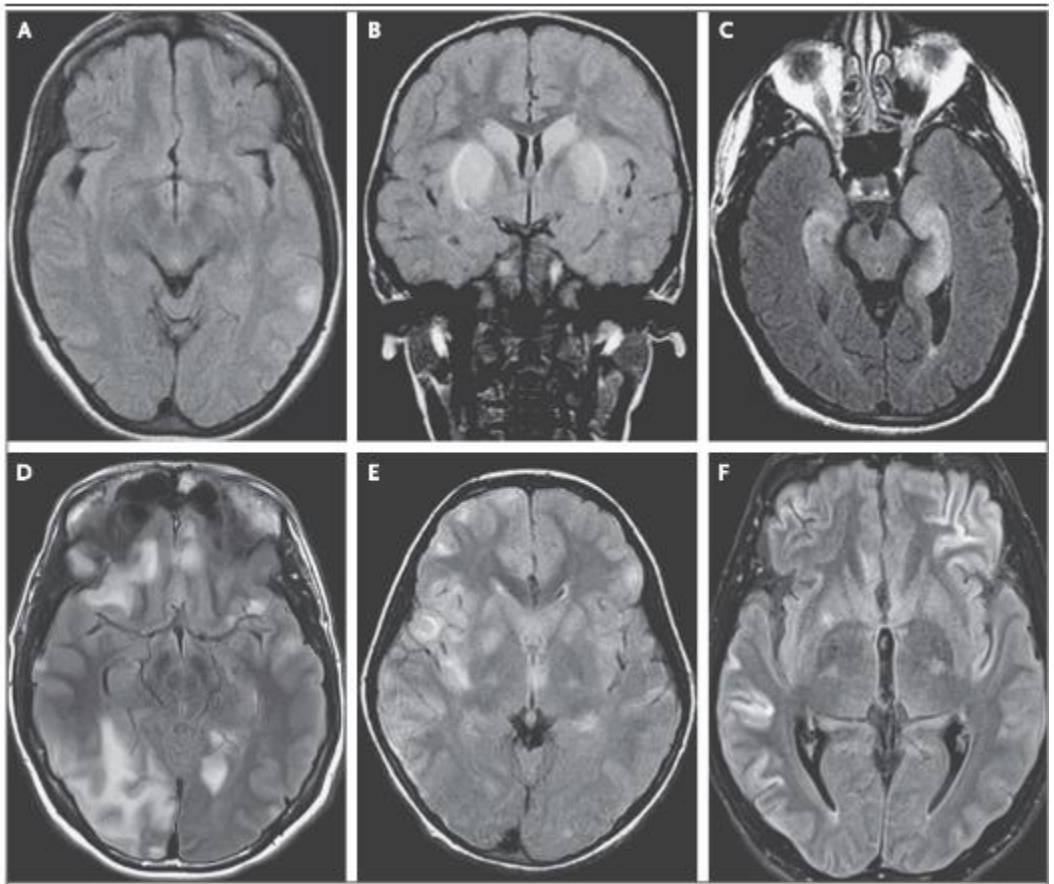


Figure 2. MRI Findings in Antibody-Mediated Encephalitis.

Dalmau, NEJM, 2018

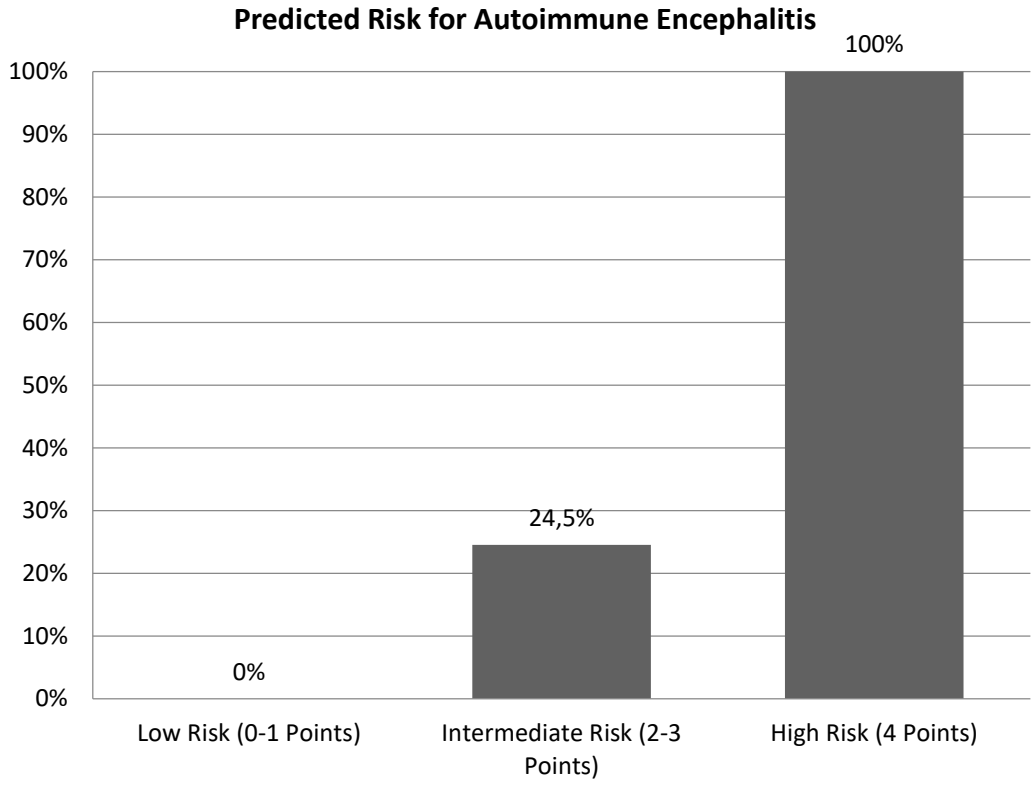
Et les encéphalites auto-immunes ?

Incidence encéphalite auto-immune : 5-8/100,000

Incidence encéphalite infectieuse : 8/100,000

Et les encéphalites auto-immunes ?

- Début subaigue
- Charlson < 2
- Signes mémoire/psy
- Peu d'inflammation à la PL



Granillo, CID, 2022

3. Démarche diagnostique

Clinique

Table 1. Diagnostic Criteria for Encephalitis and Encephalopathy of Presumed Infectious or Autoimmune Etiology

Major Criterion (required):
Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting ≥24 h with no alternative cause identified.
Minor Criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed[a] encephalitis):
Documented fever ≥38° C (100.4°F) within the 72 h before or after presentation[b]
Generalized or partial seizures not fully attributable to a preexisting seizure disorder[c]
New onset of focal neurologic findings
CSF WBC count ≥5/cubic mm[d]
Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset[e]
Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.[f]

Abbreviations: CNS, central nervous system; CSF, cerebral spinal fluid; EEG, electroencephalogram; RBC, red blood cell; WBC, white blood cell.

[a] Confirmed encephalitis requires one of the following: (1) Pathologic confirmation of brain inflammation consistent with encephalitis; (2) Defined pathologic, microbiologic, or serologic evidence of acute infection with a microorganism strongly associated with encephalitis from an appropriate clinical specimen (for examples, see references [1, 2]); or (3) Laboratory evidence of an autoimmune condition strongly associated with encephalitis.

Venkatesan, CID, 2013

Clinique

Table 1. Diagnostic Criteria for Encephalitis and Encephalopathy of Presumed Infectious or Autoimmune Etiology

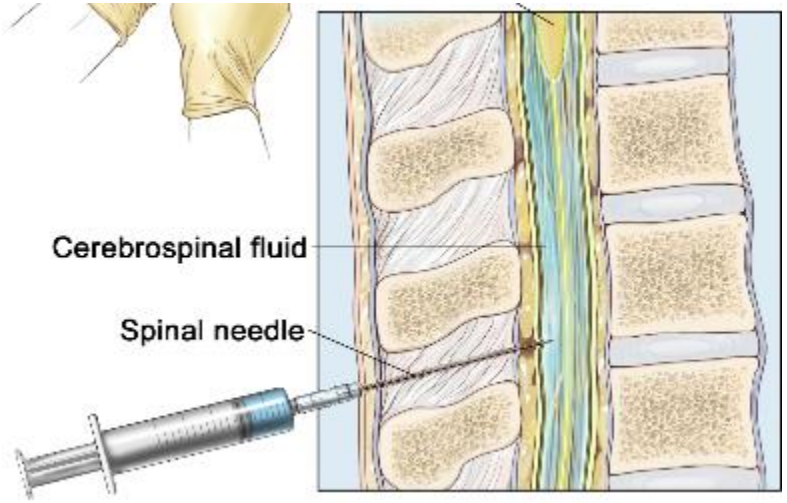
Major Criterion (required):
Patients presenting to medical attention with altered mental status (defined as decreased or altered level of consciousness, lethargy or personality change) lasting ≥24 h with no alternative cause identified.
Minor Criteria (2 required for possible encephalitis; ≥3 required for probable or confirmed[a] encephalitis):
Documented fever ≥38° C (100.4°F) within the 72 h before or after presentation[b]
Generalized or partial seizures not fully attributable to a preexisting seizure disorder[c]
New onset of focal neurologic findings
CSF WBC count ≥5/cubic mm[d]
Abnormality of brain parenchyma on neuroimaging suggestive of encephalitis that is either new from prior studies or appears acute in onset[e]
Abnormality on electroencephalography that is consistent with encephalitis and not attributable to another cause.[f]

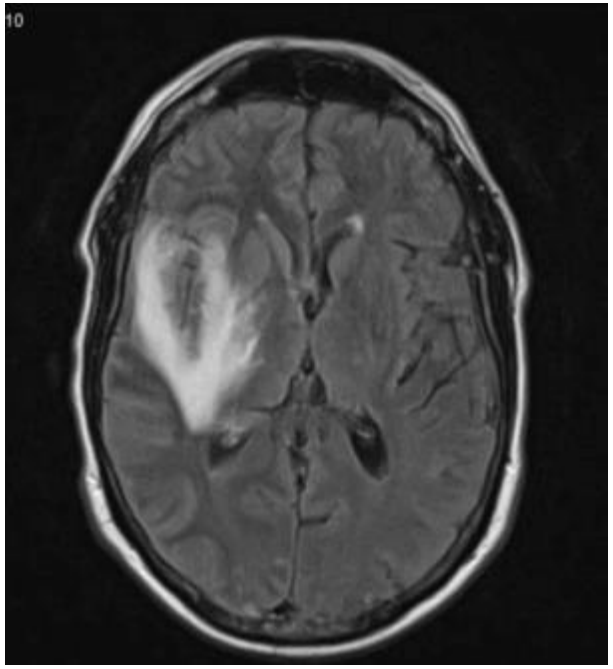
Abbreviations: CNS, central nervous system; CSF, cerebral spinal fluid; EEG, electroencephalogram; RBC, red blood cell; WBC, white blood cell.

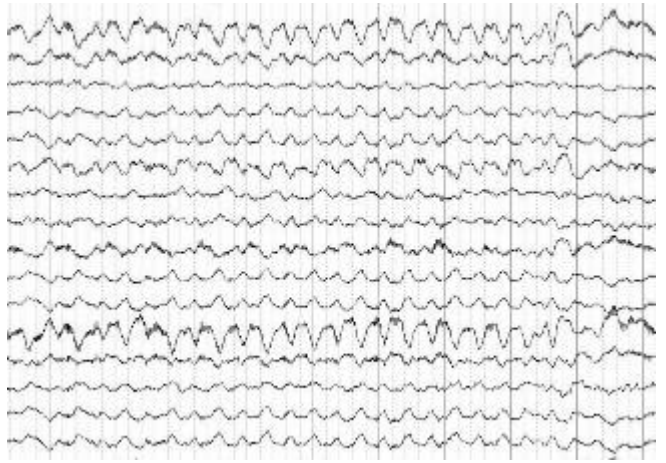
[a] Confirmed encephalitis requires one of the following: (1) Pathologic confirmation of brain inflammation consistent with encephalitis; (2) Defined pathologic, microbiologic, or serologic evidence of acute infection with a microorganism strongly associated with encephalitis from an appropriate clinical specimen (for examples, see references [1, 2]); or (3) Laboratory evidence of an autoimmune condition strongly associated with encephalitis.

Venkatesan, CID, 2013

Paraclinique







Paraclinique – Ponction lombaire

0,5mL par tube = 10 gouttes par tube

1) Biochimie
2) Bactériologie
3) Cytologie
4) Analyses moléculaires (PCR)
5) +/- Ac onco-neuronaux

Paraclinique – Ponction lombaire

	Bacterial meningitis *n* = 35	Viral meningitis *n* = 218	*P*
Glucose level (mmol/L) (min - max)	2.5 ± 1.5 (0.1-5)	3.4 ± 1 (2.1-14)	0.0001
CSF/serum glucose ratio (min - max)	0.24 ± 0.3 (0.1-0.5)	0.51 ± 0.15 (0.3-1.8)	0.01
Lactate (mmol/L) (min - max)	9 ± 5 (3.2-25)	2.6 ± 1.6 (0.5-3.7)	0.0001
CSF/serum lactate ratio (min - max)	3.7 ± 2.7 (1.5-8.4)	1.5 ± 1.4 (1-1.9)	0.0001
Protein level (g/L) (min - max)	4.9 ± 4.6 0.5-24	1 ± 0.6 0.3-4	0.0001

Viallon, Crit Care, 2011

Paraclinique – Ponction lombaire

	Bacterial meningitis *n* = 35	Viral meningitis *n* = 218	*P*
Glucose level (mmol/L) (min - max)	2.5 ± 1.5 (0.1-5)	3.4 ± 1 (2.1-14)	0.0001
CSF/serum glucose ratio (min - max)	0.24 ± 0.3 (0.1-0.5)	0.51 ± 0.15 (0.3-1.8)	0.01
Lactate (mmol/L) (min - max)	9 ± 5 (3.2-25)	2.6 ± 1.6 (0.5-3.7)	0.0001
CSF/serum lactate ratio (min - max)	3.7 ± 2.7 (1.5-8.4)	1.5 ± 1.4 (1-1.9)	0.0001
Protein level (g/L) (min - max)	4.9 ± 4.6 0.5-24	1 ± 0.6 0.3-4	0.0001

Viallon, Crit Care, 2011

Paraclinique – Ponction lombaire

	Plasma	LCR
Na+	150 mmol/l	147 mmol/l
K+	4.6 mmol/l	2.8 mmol/l
Ca++	2.4 mmol/l	1.1 mmol/l
CL-	108 mmol/l	130 mmol/l
HCO3-	26 mmol/l	22 mmol/l
pH	7.4	7.3
Lactate	15 mg/dl	22 mg/dl
Glucose	100 mg/dl	60 mg/dl
Protéines	80 g/l	0.4 g/l

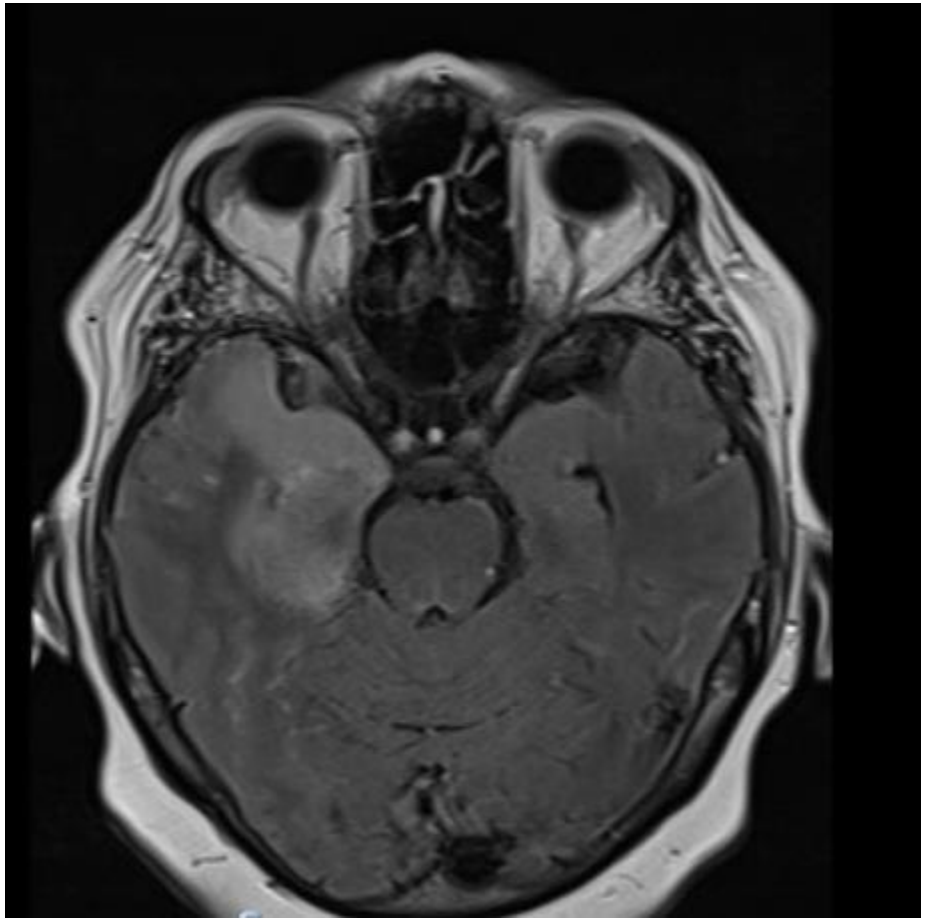
Paraclinique – Ponction lombaire

	Bacterial meningitis *n* = 35	**Viral meningitis *n* = 218**	***P***
Leucocyte count/mm^3 (min - max)	1,515 ± 2,000 (25-10,320)	257 ± 520 (23-6,500)	0.0001
Neutrophil count/mm^3 (min - max)	1,003 ± 2,000 (22-10,000)	75 ± 160 (15-1,188)	0.0001

Viallon, Crit Care, 2011

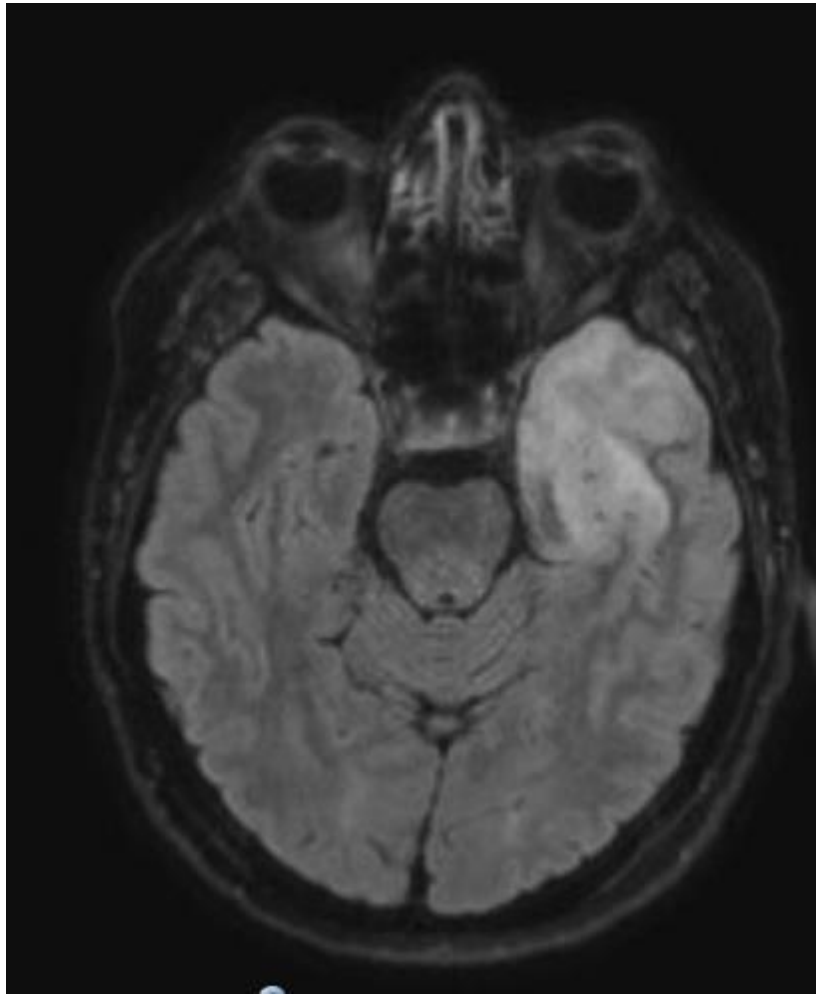
Paraclinique – IRM

Paraclinique – IRM



Paraclinique – IRM

Paraclinique – IRM

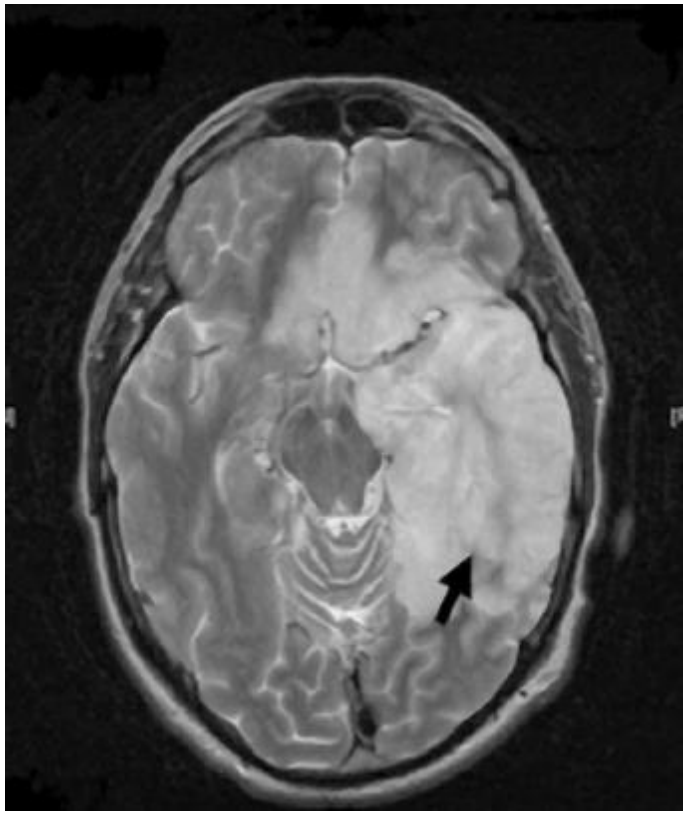


Paraclinique – EEG

- A faire systématiquement en aigu
- Témoin de la souffrance aigue
- Aide au diagnostic si anomalie
- Anomalies secondaires peuvent se mettre en place

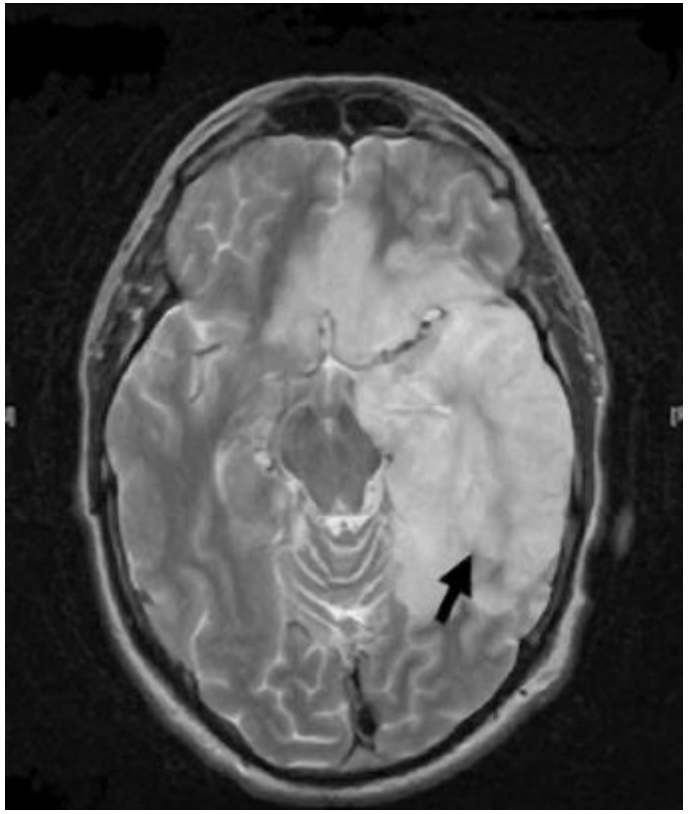
4. Prise en charge thérapeutique

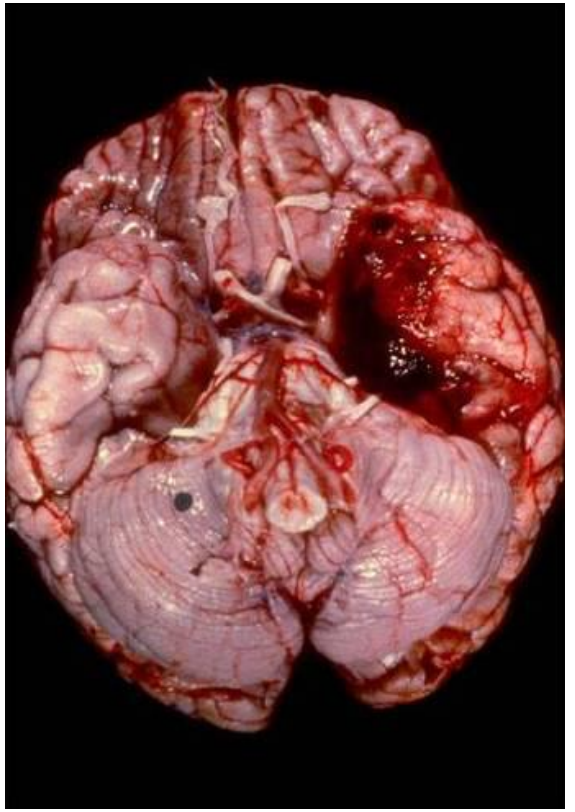
Quelle gravité des encéphalites ?



Kuker, Neroradiol, 2004

Quelle gravité des encéphalites ?





Kuker, Neroradiol, 2004

Quelle gravité des encéphalites ?

Status at start of treatment	Treatment and outcome (no of patients)									
	No or minor sequelae		Moderate sequelae		Severe sequelae		Died		All patients	
	Acyclovir	Vidar	Acyclovir	Vidar	Acyclovir	Vidar	Acyclovir	Vidar	Acyclovir	Vidar
Lethargy	11*	3*	3	1	1	5	2	2	17	11
Semicoma/coma	4	0	0	1	3	2	3†	10†	10	13
Total	15‡	3‡	3	2	4	7	5§	12§	27	24

Skoldenberg, Scand J ID, 1985

Quelle gravité des encéphalites ?

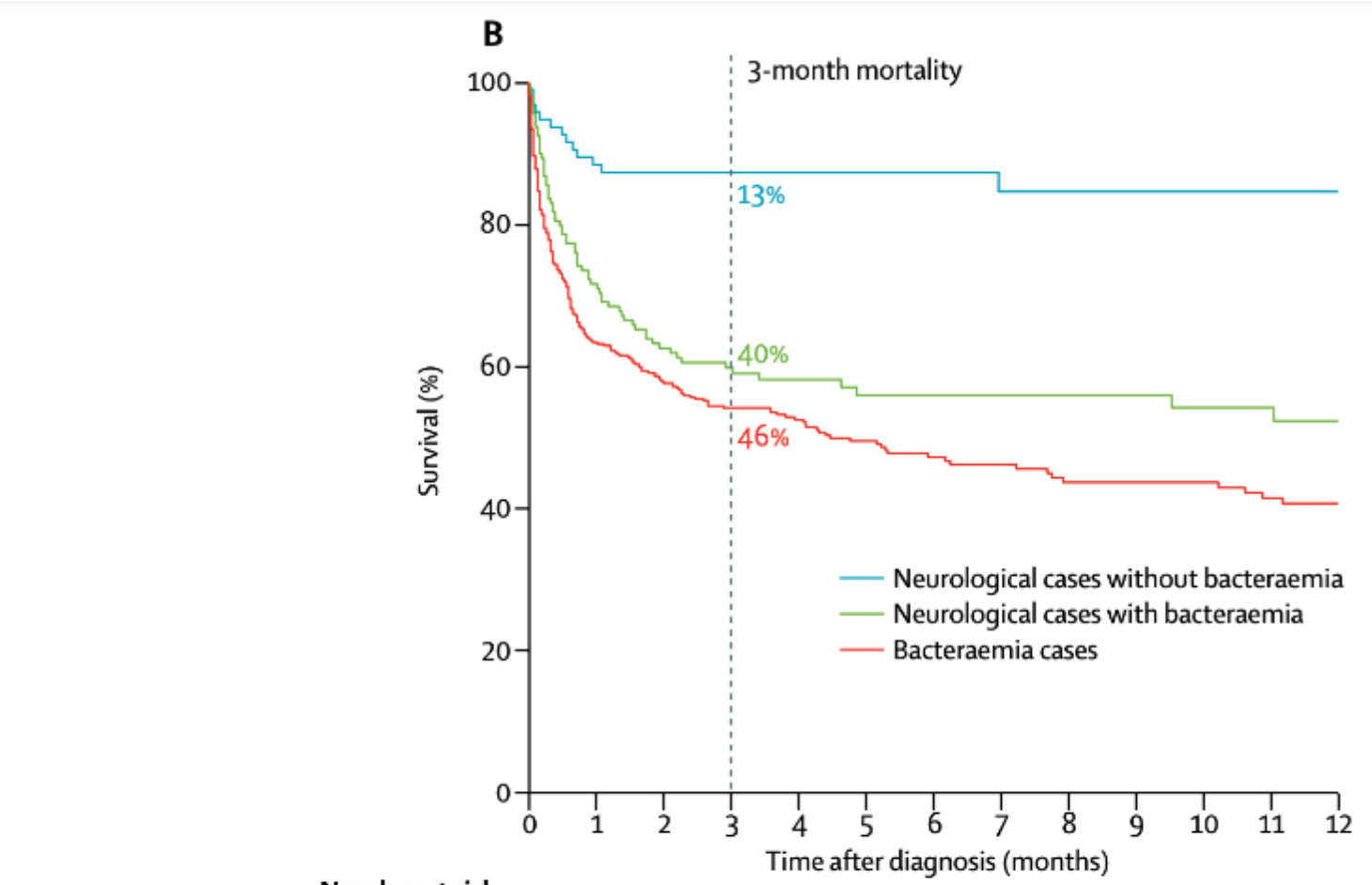
Table 3. Univariate analysis of factors associated with outcomes at 6 months for 85 patients with herpes simplex encephalitis.

Characteristic	Patients with favorable outcome (n = 55)	Patients with poor outcome (n = 30)	P
Age, mean years ± SD	50 ± 16.2	56.6 ± 16.8	.1
MacCabe score, mean ± SD	0.11 ± 0.4	0.1 ± 0.3	.92
Knaus score, mean ± SD	1.16 ± 0.4	1.43 ± 0.7	.04
GCS score, mean ± SD	13.7 ± 2.5	12.5 ± 3.4	.03
SAPS II, mean ± SD	27.6 ± 16.1	29.6 ± 12.1	.45
SAPS II >27, no. (%) of patients	9 (16)	17 (57)	.0001
Seizures, no. (%) of patients	18 (33)	9 (30)	.79
Focal neurological deficit, no. (%) of patients	11 (20)	9 (30)	.3
Serum sodium level, mean mM ± SD	132.4 ± 5.5	131.3 ± 5	.32
CSF parameters, mean ± SD			
Leukocyte count, cells/mL × 10^3	250 ± 546	170 ± 197	.39
Protein level, g/L	0.83 ± 0.6	0.78 ± 0.4	.39
Less than 2 days between hospital admission and initiation of acyclovir therapy, no. (%) of patients	41 (75)	9 (30)	.00008
Mechanical ventilation, no. (%) of patients	23 (42)	18 (60)	.97
Hospital-acquired infection, no. (%) of patients	17 (31)	20 (67)	.001

NOTE. GCS, Glasgow Coma Scale; SAPS, Simplified Acute Physiology Score.

Raschilas, CID, 2002

Quelle gravité des encéphalites ?



Number at risk

Neurolisteriosis cases without bacteraemia	94	76	49	35	30	26	25
Neurolisteriosis cases with bacteraemia	158	93	59	41	35	29	23
Bacteraemia cases	423	235	149	94	68	59	53

Charlier, Lancet ID, 2017

Rappel de l’épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %
HSV	132	40,7	26,7
VZV	65	20,1	13,2
TBEV	26	8,0	5,3
Listeria monocytogenes	23	7,1	4,7

Cause traitable par ACICLOVIR

Cause traitable par AMOXICILLINE

Mailles, ID Now, 2022

Conduite initiale (premières 48 h)

- **Traitements anti-infectieux (1)**

✓ A débuter en urgence

✓ Absence d'orientation étiologique (clinique ou biologique),

- Acyclovir : 10 mg/kg IV toutes les 8 heures **et**
- Amoxicilline : 200 mg/kg/jour en au moins 4 perfusions, ou en administration continue
- Réévaluation systématique à 48h.

✓ Si vésicules cutanées ou signes de vasculopathie à l'imagerie

- Acyclovir : 15 mg/kg IV toutes les 8 heures.

Néphrotoxicité de l'acyclovir

Table 2
Intervention-related risk factors for AKI in patients treated with aciclovir.

Factor (Y/N)	AKI n = 35 (%)	No AKI n = 234 (%)	P value	Odds ratio (95% CI)/ 95% CI of difference
Any nephrotoxic	26/9 (74)	173/61 (74)	1	1.0 (0.4–2.2)
Aminoglycoside	0/35 (0)	10/224 (4)	0.370	N/A
Beta-lactam	14/21 (40)	85/1549 (36)	0.708	1.2 (0.6–2.4)
Glycopeptide	0/35 (0)	2/232 (1)	1	N/A
Antiviral	0/35 (0)	13/221 (6)	0.387	N/A
Antifungal	1/34 (3)	9/225 (4)	1	0.7 (0.1–6.0)
Immunosuppressive	1/34 (3)	16/218 (7)	0.488	0.4 (0.1–3.1)
ACE inhibitors	4/31 (11)	21/213 (9)	0.753	1.3 (0.4–4.1)
Diuretics	4/31 (11)	28/206 (12)	1	1.0 (0.3–2.9)
Chemotherapy	0/35 (0)	0/234 (0)	1	N/A
Other nephrotoxics	4/31 (11)	28/206 (12)	1	1.0 (0.3–2.9)
Contrast	16/19 (46)	81/153 (35)	0.258	1.6 (0.8–3.3)
Aciclovir dose				
Mean daily dose (mg)	2173.7 (1952.7–2394.7)	1819.9 (1738.4–1901.3)	**0.004**	111.8–595.9
Mean cumulative dose (mg)	7848.2 (4665.6–11030.8)	9664.7 (8386.0–10943.3)	0.417	1487.4–2145.5

Ryan, Int J ID, 2018

Journal of Clinical Virology 61 (2014) 608–610

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Case report

Aciclovir-induced neurotoxicity: Utility of CSF and serum CMMG levels in diagnosis

L. Berry*, P. Venkatesan

Department of Infectious Diseases, Nottingham City Hospital, Hucknall Road, Nottingham NG5 1PB, United Kingdom

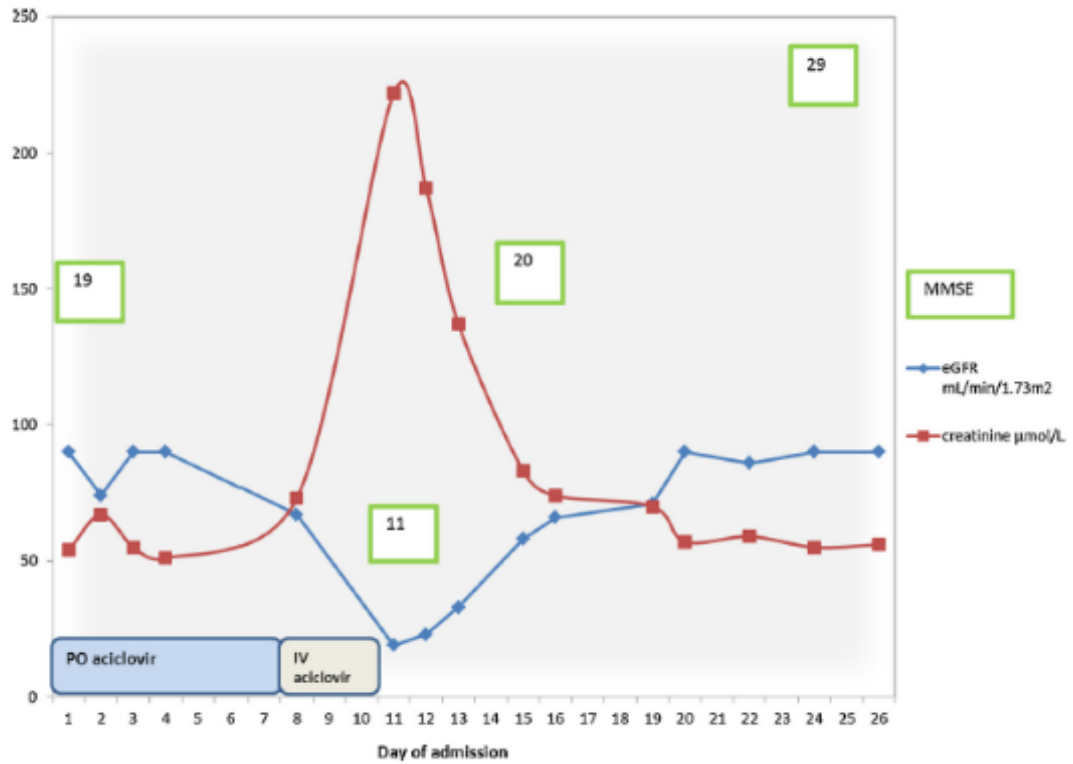


Fig. 1. Results of patient's creatinine, eGFR and MMSE level during admission.

CMMG : 9-carboxymethoxymethylguanine
(métabolite de l'aciclovir)

Table 1
Patient's CSF and serum CMMG and aciclovir levels.

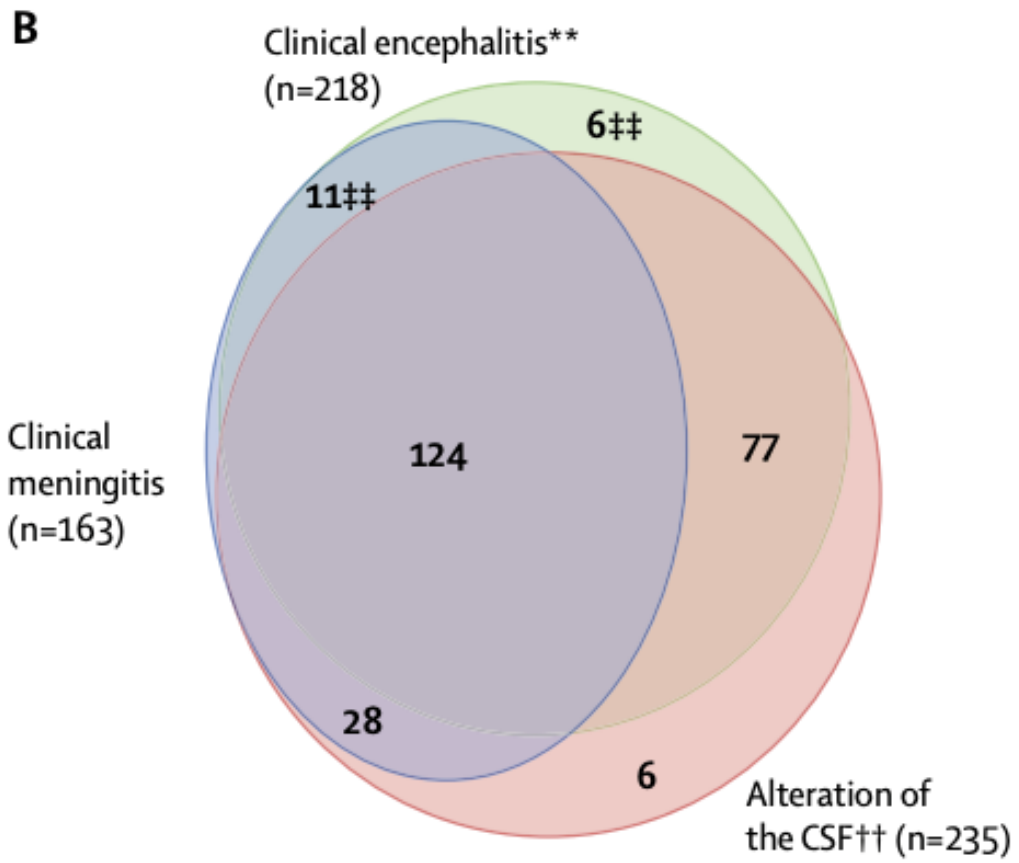
	CSF (day 5 of admission) (µmol/L)	Serum (day 8 of admission) (µmol/L)
CMMG	1.6	57.3
Aciclovir	0.88	182.2

Paraclinique – Orientation étiologique ?

CSF Profile	CSF pleocytosis group (WBC > 5cells/mm^3)	Normocellular CSF group (WBC ≤ 5cells/mm^3)
Days of CSF examination after neurological onset	Day 0—1: 5 (29.4 %) Day 2—10: 12 (70.6 %)	Day 0—1: 1 (16.7 %) Day 2—10: 5 (83.3 %)
CSF protein	0–60 mg/dl: 1 (6.3 %) 61–100 mg/dl: 7 (43.8 %) >100 mg/dl: 8 (50 %) Not available: 1	0–60 mg/dl: 2 (33.3 %) 61–100 mg/dl: 4 (66.7 %) >100 mg/dl: 0
CSF glucose	<30 mg/dl: 1 (6.3 %) 31–60 mg/dl: 7 (43.8 %) >60 mg/dl: 8 (50 %) Not available: 1	<30 mg/dl: 0 31–60 mg/dl 1 (16.7 %) >60 mg/dl: 5 (83.3 %)
Average CSF viral load	12,200 copies/ml (39–11,755,813 copies/ml) (11 cases available: 6 had qualitative test)	3027 copies/ml (59–5970 copies/ml) (4 cases available: 3 had qualitative test)

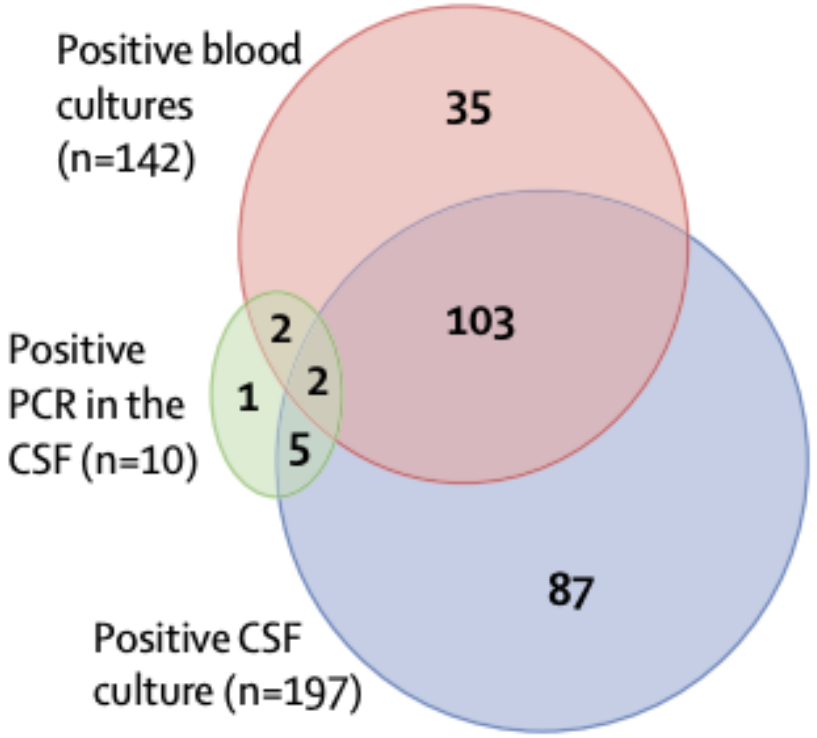
Sareya, BMC Res Notes, 2016

Paraclinique – Orientation étiologique ?



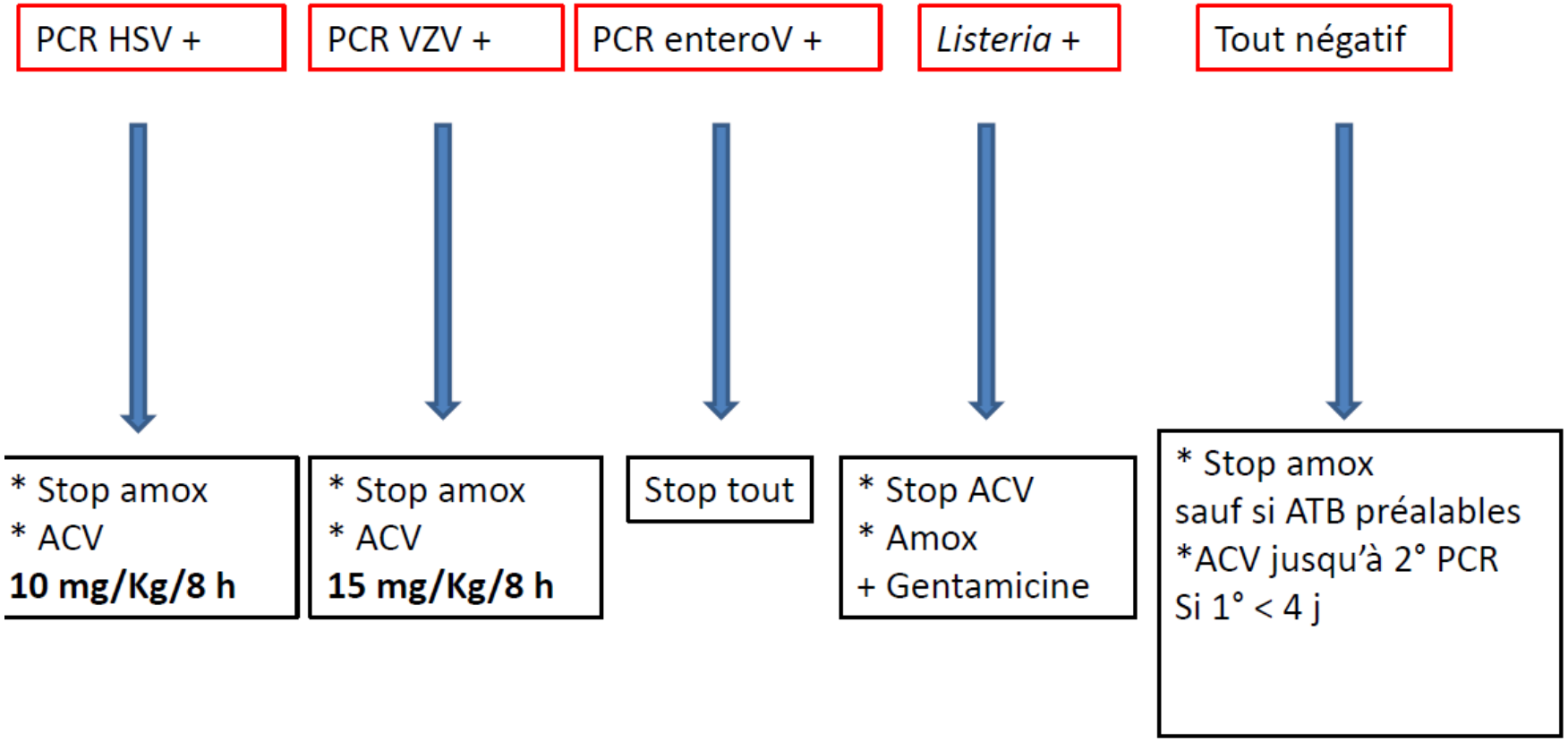
Charlier, Lancet ID, 2017

Paraclinique – Orientation étiologique ?



Charlier, Lancet ID, 2017

Réévaluation à 48h



Q3 : Diagnostic **déjà** fait **à** 48h, quelle CAT ?

- HSV

Grade A	**La dose d'aciclovir dans le traitement de l'encéphalite à HSV de l'adulte est de 10 mg/kg pendant 1 heure toutes les 8 heures.**
Grade B	**En cas d'encéphalite herpétique prouvée par la positivité de la PCR initiale, le contrôle systématique de la PCR HSV dans le LCS à la fin du traitement n'est pas recommandé si l'évolution est favorable**
Grade C	**La durée recommandée de traitement est de 14 jours chez l'adulte immunocompétent.**
Grade C	**Pour les patients immunodéprimés, une durée de 21 jours est recommandée.**
Grade C	**En cas d'évolution clinique non favorable à la fin du traitement, une ponction lombaire avec PCR HSV et recherche d'auto-anticorps sur le LCS doit être réalisée. La positivité de la PCR HSV peut conduire à prolonger le traitement par aciclovir à 21 jours.**

encephalite.spilf@infectiologie.com

Q3 : Diagnostic **déjà** fait **à** 48h, quelle CAT ?

- *Listeria*

Recommandations

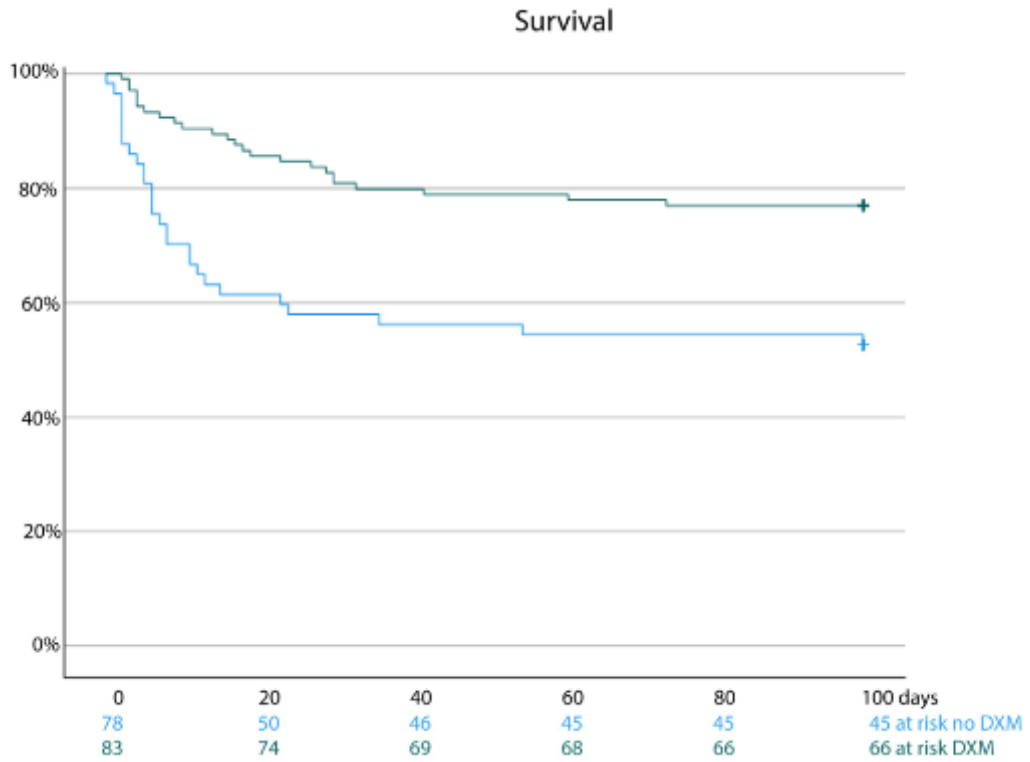
Grade A	**Le traitement recommandé de l'encéphalite listérienne documentée est l'amoxicilline à la dose de 200 mg/kg/jour en 4 perfusions au moins ou en administration continue par 24 heures pendant 21 jours + gentamicine 5 mg/kg/j en dose unique quotidienne pendant au maximum 5 jours (grade C, recos AFSSAPS aminosides)**
Grade A	**En cas de contre-indication à l'amoxicilline (allergie grave prouvée), l'association triméthoprime-sulfaméthoxazole à forte dose (6 à 9 ampoules par jour en 3 injections iv) doit être administrée pendant 21 jours.**

Quid de la corticothérapie ?

3-month mortality for neurolisteriosis (n=252)		
Female sex	2·68 (1·24–5·83)	0·013
Age (years)	1·35 (0·99–1·85)	0·058
Ongoing organ neoplasia	4·58 (1·53–13·73)	0·007
Recent major weight loss	2·65 (1·08–6·55)	0·034
Multi-organ failure	3·08 (1·25–7·58)	0·014
Aggravation of any pre-existing organ dysfunction	2·75 (1·23–6·16)	0·014
Influenza-like symptoms	0·47 (0·20–1·12)	0·087
Mechanical ventilation	2·89 (1·31–6·37)	0·009
Monocytopenia <200 cells per µL	3·57 (1·24–10·23)	0·018
Positive blood cultures	3·67 (1·60–8·40)	0·002
Protein concentration in the CSF	1·18 (0·99–1·41)	0·062
Adjunctive dexamethasone for meningitis	4·58 (1·50–13·98)	0·008

Charlier, Lancet ID, 2017

Quid de la corticothérapie ?



Brouwer, EclinMed, 2023

Quid de la corticothérapie ?

La dexamethasone en traitement complémentaire des encéphalites à Herpes Simplex Virus

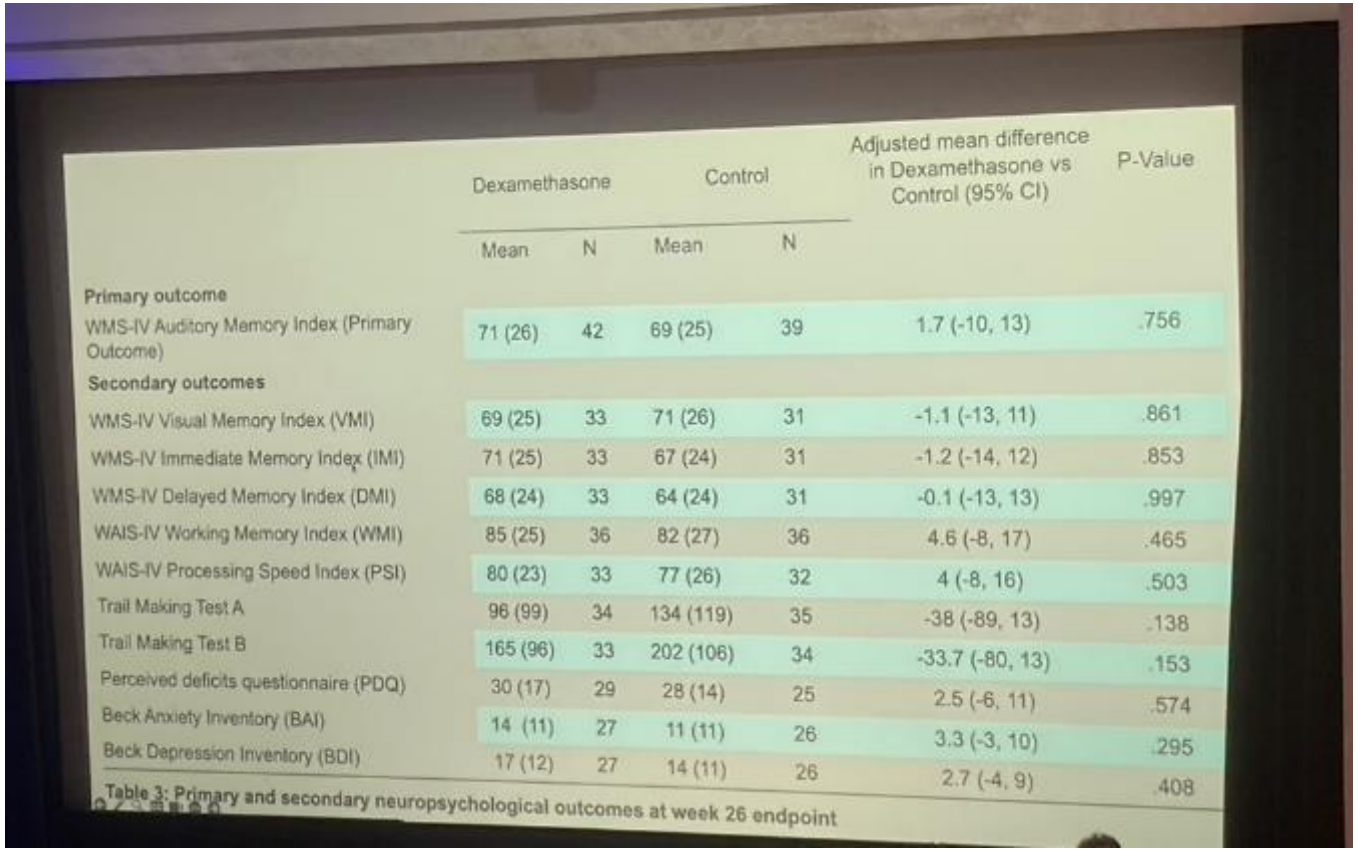
DexENCEPH

PHRC:

Investigateur principal: J.P. Stahl (Grenoble)

Co-investigateurs: X. Argemi (Strasbourg), D. Boutoille(Nantes), T. De Broucker (Saint Denis), I. Gueit (Rouen), V. le Moing (Montpellier), C. Pulcini (Nancy), R. Sonneville (Paris), P. Tattevin (Rennes).

Quid de la corticothérapie ?



	Dexamethasone		Control		Adjusted mean difference in Dexamethasone vs Control (95% CI)	P-Value
	Mean	N	Mean	N		
Primary outcome						
WMS-IV Auditory Memory Index (Primary Outcome)	71 (26)	42	69 (25)	39	1.7 (-10, 13)	.756
Secondary outcomes						
WMS-IV Visual Memory Index (VMI)	69 (25)	33	71 (26)	31	-1.1 (-13, 11)	.861
WMS-IV Immediate Memory Index (IMI)	71 (25)	33	67 (24)	31	-1.2 (-14, 12)	.853
WMS-IV Delayed Memory Index (DMI)	68 (24)	33	64 (24)	31	-0.1 (-13, 13)	.997
WAIS-IV Working Memory Index (WMI)	85 (25)	36	82 (27)	36	4.6 (-8, 17)	.465
WAIS-IV Processing Speed Index (PSI)	80 (23)	33	77 (26)	32	4 (-8, 16)	.503
Trail Making Test A	96 (99)	34	134 (119)	35	-38 (-89, 13)	.138
Trail Making Test B	165 (96)	33	202 (106)	34	-33.7 (-80, 13)	.153
Perceived deficits questionnaire (PDQ)	30 (17)	29	28 (14)	25	2.5 (-6, 11)	.574
Beck Anxiety Inventory (BAI)	14 (11)	27	11 (11)	26	3.3 (-3, 10)	.295
Beck Depression Inventory (BDI)	17 (12)	27	14 (11)	26	2.7 (-4, 9)	.408

Table 3: Primary and secondary neuropsychological outcomes at week 26 endpoint

Dexenceiph, Encephalitis conference, Décembre 2023

Table 1 Clinical and neuropsychological profiles of cases of herpes simplex encephalitis

Case	Age and sex	Duration of memory disorder (y)	Amnesia severity* score (/24)	NART estimated IQ score	Verbal IQ subtest scores	Performance IQ subtest scores	Picture naming	Card sorting
1	53 Male	7	0	106	Infor = 8 Arith = 12 Simil = 6†	Pict ar = 8 B des = 15 D sy = 11	Impaired 2/30	Normal
2	39 Female	15	1	117	Infor = 6† Arith = 8 Simil = 7	Pict ar = 8 B des = 8 D sy = 8	Normal 11/30	Pronounced impairment
3	42 Female	10	2	113	Infor = 7 Arith = 12 Simil = 11	Pict ar = 8 B des = 10 D sy = 14	Normal 15/30	Normal
4	45 Female	3	3	110	Infor = 5† Arith = 10 Simil = 7	Pict ar = 8 B des = 9 D sy = 10	Impaired 2/30	Mild impairment
5	59 Male	7	4	122	Infor = 10 Arith = 12 Simil = 13	Pict ar = 14 B des = 12 D sy = 14	Normal 21/30	Normal
6	39 Male	4	7	(Long-standing dyslexia)	Infor = 5† Arith = 6† Simil = 8	Pict ar = 13 B des = 12 D sy = 6†	Impaired 5/30	Normal
7	70 Male	3	9	98	Infor = 12 Arith = 12 Simil = 11	Pict ar = 7 B des = 11 D sy = 8	Normal 13/30	Mild impairment
8	57 Female	2	12	(Dysphasia affected test score)	Infor = 5† Arith = 7 Simil = 7	Pict ar = 12 B des = 12 D sy = 11	Impaired 0/30	Normal
9	65 Male	7	13	89	Infor = 7 Arith = 9 Simil = 7	Pict ar = 7 B des = 8 D sy = 9	Normal 11/30	Pronounced impairment
10	24 Female	1	23	107	Infor = 9 Arith = 11 Simil = 10	Pict ar = 9 B des = 10 D sy = 7	Normal 22/30	Normal

* Severity of amnesia was based on a composite score reflecting performance on the Wechsler memory scale-revised, the recognition memory test, and the current awareness test. † Impairment. Infor = Information; Arith = Arithmetic; Simil = Similarities; Pict ar = Picture arrangement; B des = Block design; D sy = Digit symbol.

Kapur, J Neurol, Neurosurg, Psy, 1994

Table 1 Participant characteristics and interview details of participants with HSV encephalitis

Person with HSV encephalitis	Age at interview	Gender M/F	Timing of interview post-discharge	Interview details	Duration of stay in hospital (days)	Destination on discharge	Employment status at time of interview
Retrospective Cohort							
1	45	M	6 years	Interviewed with partner	22	Home	No longer working: receiving Disability Living Allowance
2	47	F	7 Years	Interviewed with mother	211	Home	No longer working: receives income from previous employer's insurance
3	43	M	6 years	Interviewed with partner	20	Home	No longer working: receiving Disability Living Allowance
4	58	M	5 years 10 months	Interviewed with wife	30	Home	Employed: took a role with fewer responsibilities after being made redundant.
5	15	M	1 year 11 months	Interview conducted with the parents	63	Home	N/A – in school
6	62	F	5 years 9 months	Interviewed alone	48	Home	No longer working: sold her business
7	68	F	7 years 1 month	Interviewed alone	16	Home	Took early retirement
8	55	F	5 years	Interviewed with friend	15	Home	Took early retirement
9	36	M	1 year	Interviewed with wife	10 (continued acyclovir at home)	Home	Employed: took a role with fewer responsibilities post-encephalitis
10	5	M	5 years 7 months	Interview conducted with the child's mother	37	Home	N/A – in school
11	56	F	3 years 6 months	Interview conducted with husband	126	Neuro-rehabilitation	No longer able to work
12	20	F	5 years 10 months	Interviewed alone	39	Home	Student (university)
13	34	F	4 years 4 months	Interviewed with partner	21	Home	No longer working: receiving Disability Living Allowance
14	55	F	7 years 7 months	Interviewed alone	12	Home	Took early retirement
15	6	M	3 years	Interview conducted with the child's father	42	Home	N/A – in school
16	33	M	1 year 2 months	Interviewed with Mother	25	Home	Employed: returned to work
17	61	F	6 years 5 months	Interviewed alone	58	Home (offered rehabilitation but declined)	Took early retirement

Cooper, BMC Health Ser Res, 2017

5. Particularités de l’immunodéprimé

Les différents types d'immunodépression

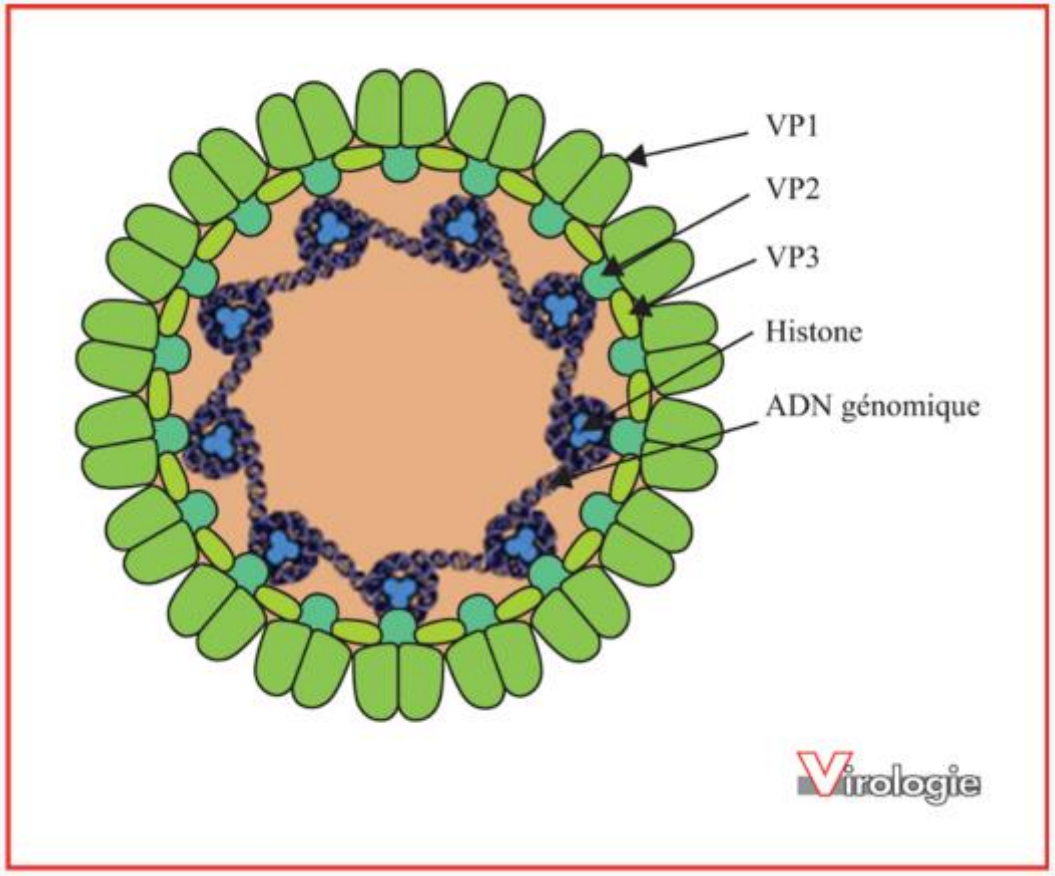
VIH

- Toxoplasmose cérébrale
- Cryptococcose neuroméningée
- LEMP
- Tuberculose neuroméningée
- Neurosyphilis
- Encéphalite à CMV
- Encéphalite à VIH
- Lymphome cérébral

Hors VIH

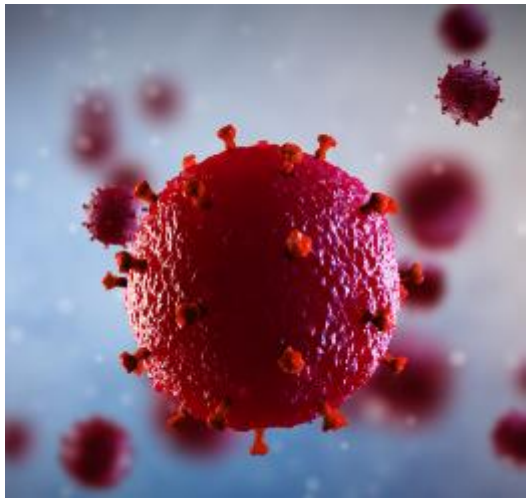
- Encéphalite infectieuse
- Encéphalite auto-immune
- Encéphalite paranéoplasique
- Localisation neurologique de la maladie
- Lymphome
- Toxicité du traitement

La leucoencéphalopathie multifocale progressive (LEMP)



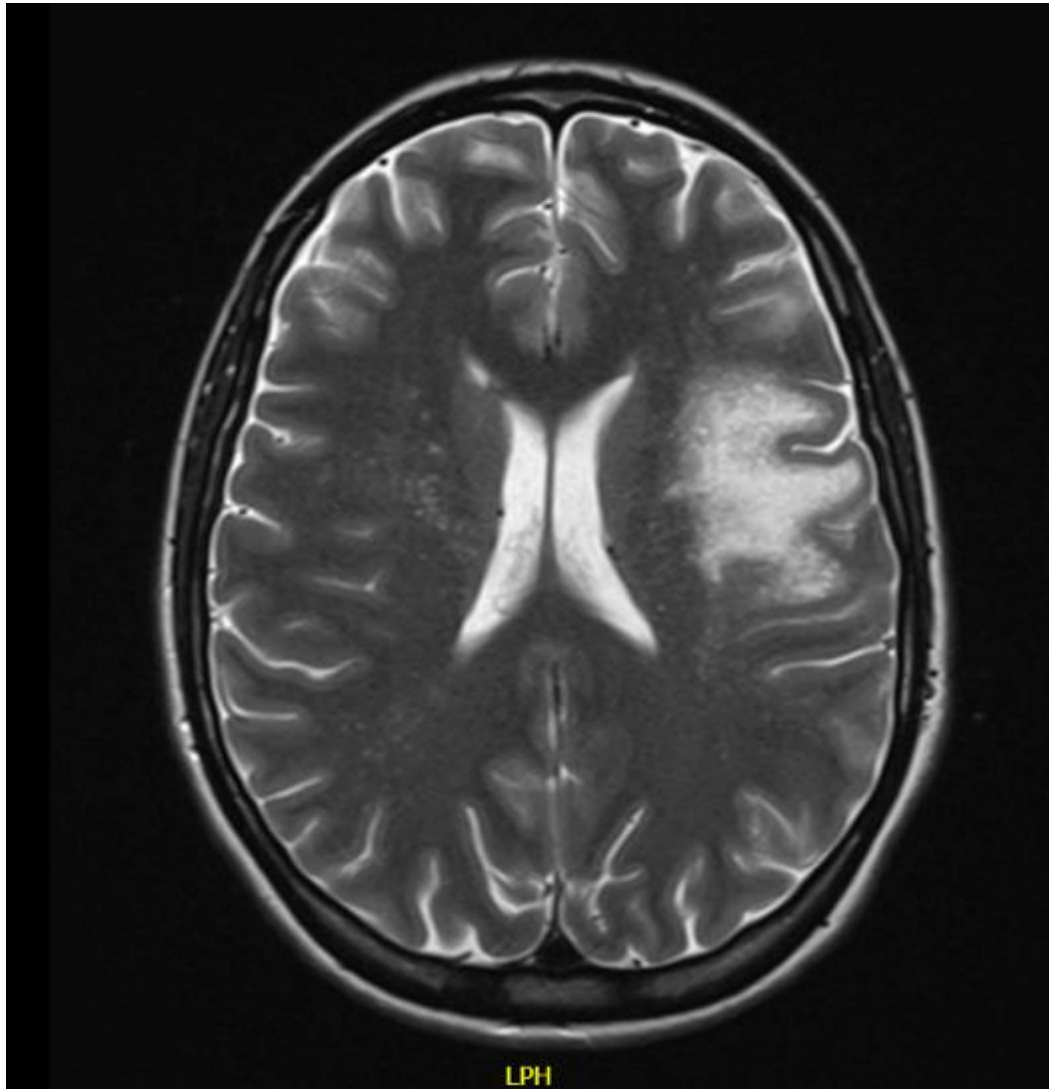
- JC virus = polyomavirus
- Petit virus à ADN non enveloppé
- 3 protéines virales
- Décrite initialement dans le SIDA
- De plus en plus chez les ID hors VIH

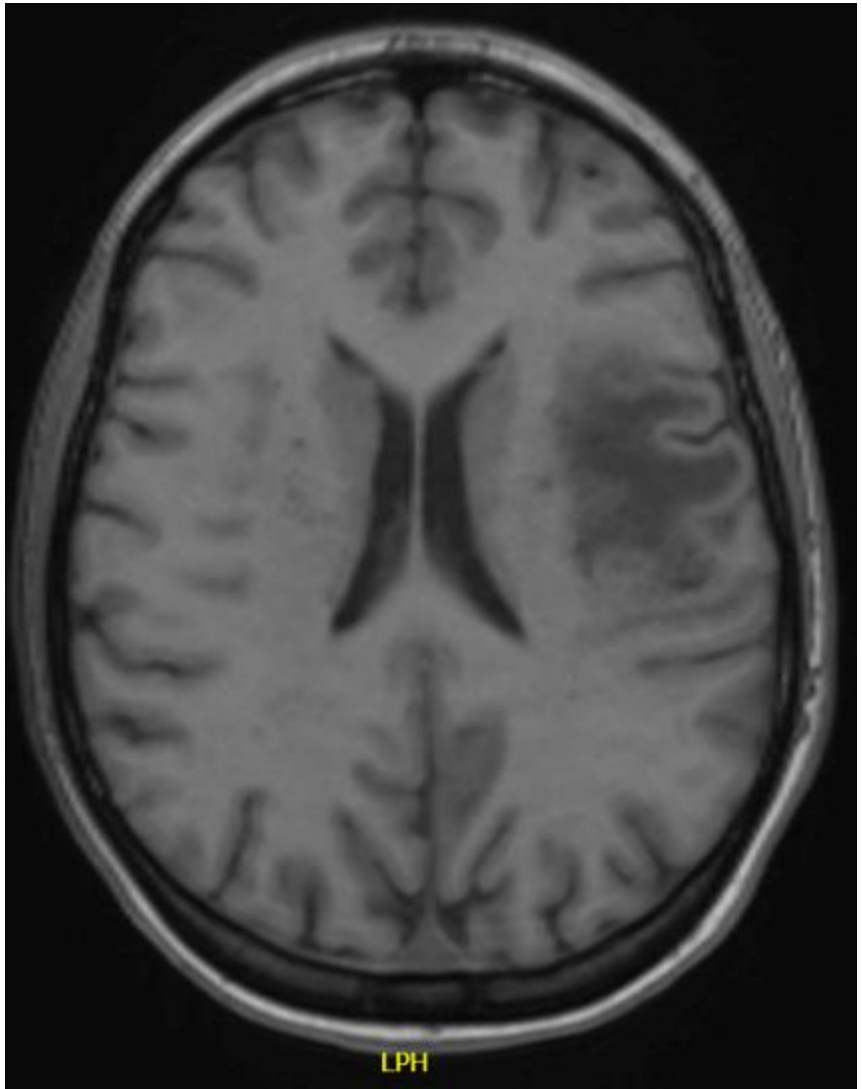
La leucoencéphalopathie multifocale progressive (LEMP)



- Déficit de l'immunité cellulaire et humorale
- Réactivation du JC virus
- Présentation subaigue
- Symptômes : aphasie, déficit sensitif ou moteur, troubles de la mémoire
- Pronostic très sombre

La leucoencéphalopathie multifocale progressive (LEMP)



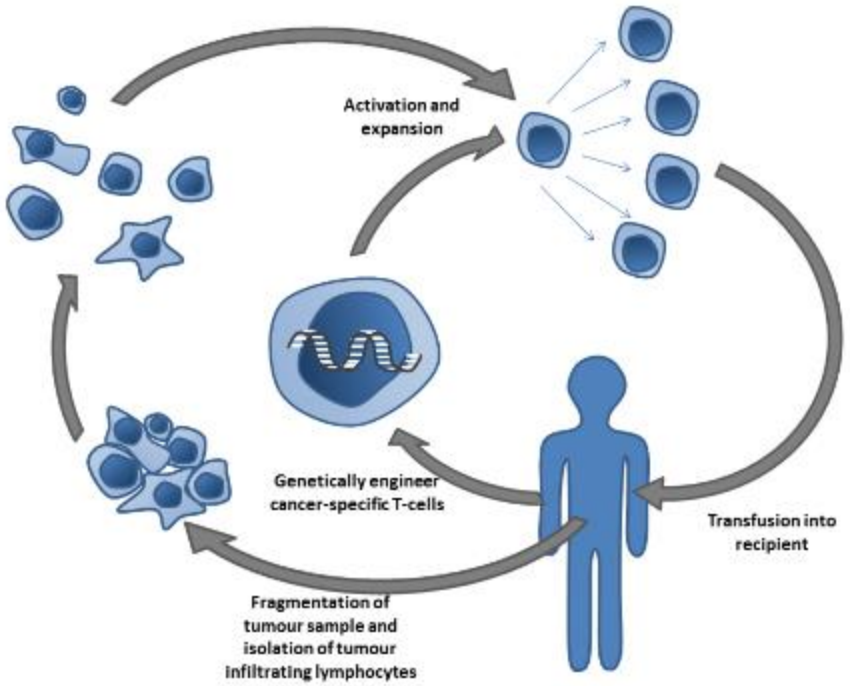


La leucoencéphalopathie multifocale progressive (LEMP)

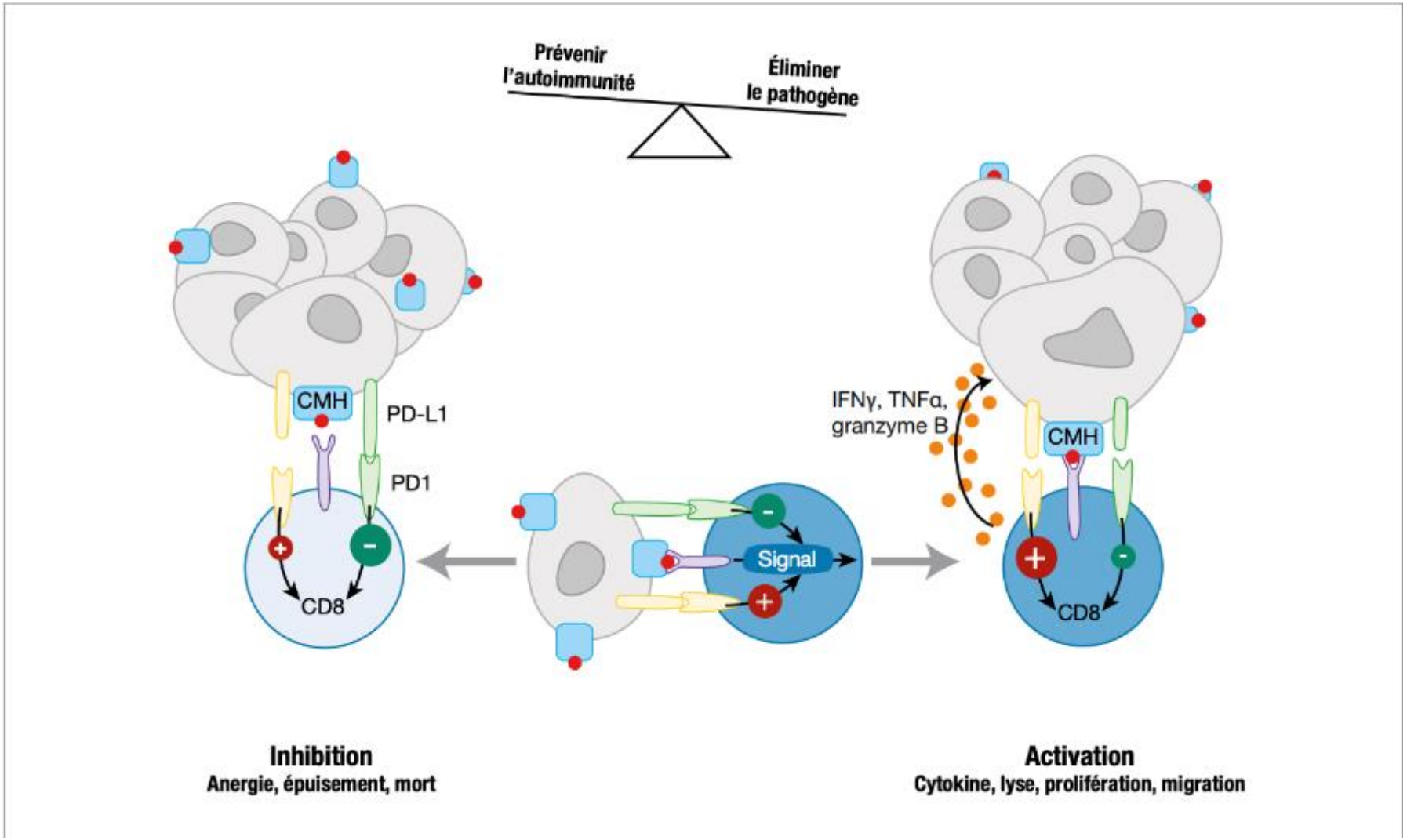
- PCR JCv positive dans le LCS
- Peut aussi être positive dans le sang et les urines

La leucoencéphalopathie multifocale progressive (LEMP)

Traitement = RESTAURATION DE L'IMMUNITÉ

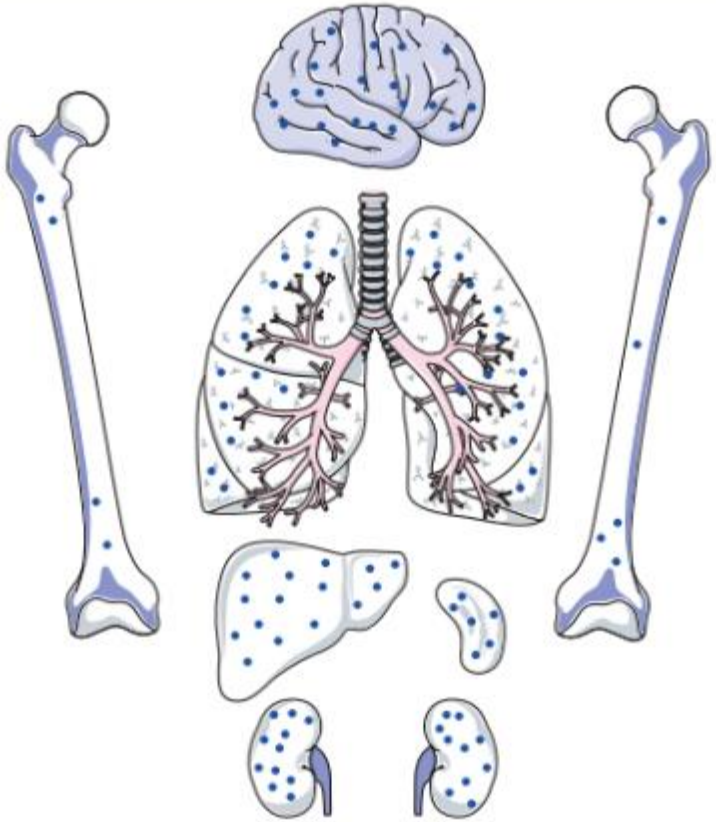


La leucoencéphalopathie multifocale progressive (LEMP)



La tuberculose neuroméningée

F-159-4 : **Principales localisations de la miliaire tuberculeuse**



- *Mycobacterium tuberculosis*
- Localisation secondairement à une miliaire
- Surtout chez les immunodéprimés type SIDA (immunité cellulaire)
- 1% des cas de tuberculose, 5% des tuberculose extra-pulmonaires
- Morbi-mortalité de 50%
- 100 cas/an en France

La tuberculose neuroméningée

Panel: The Vietnam diagnostic rule[39]

Entry criteria

- Adult (age >15 years) with meningitis and ratio of CSF to plasma glucose <0·5

Clinical features and scores

- Age ≥36 years (score +2)
- Age <36 years (score 0)
- Blood white cell count ≥15×10⁹/L (score +4)
- Blood white cell count <15×10⁹/L(score 0)
- History of illness ≥6 days (score –5)
- History of illness <6 days (score 0)
- CSF white cell count ≥0·75×10⁹/L (score +3)
- CSF white cell count <0·75×10⁹/L (score 0)
- CSF neutrophils ≥90% of total white cells (score +4)
- CSF neutrophils <90% of total white cells (score 0)

Interpretation

- Total score ≤4 = tuberculous meningitis
- Total score >4 = alternative diagnosis

- Phase prodromique : plusieurs semaines/mois avec installation chronique (somnolence, AEG, céphalées, fébricule)
- Pas forcément de syndrome méningé complet
- Altération de la vigilance
- Paralysie des nerfs crâniens (oculomotrice++)
- Convulsions

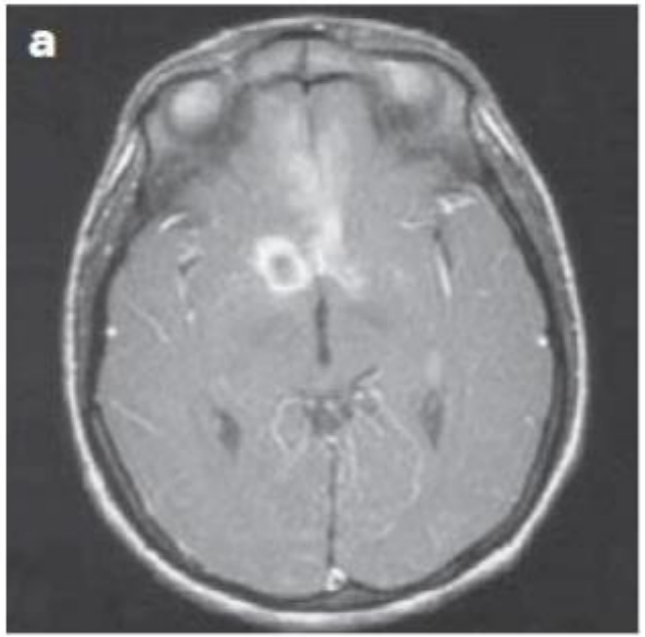
Thwaites, Lancet, 2002

La tuberculose neuroméningée

- Coloration de ZN dans le LCS : 10-20% de Se
- Culture sensible (>60-70%) mais longue (>2 semaines)
- PCR : sensibilité de 60%

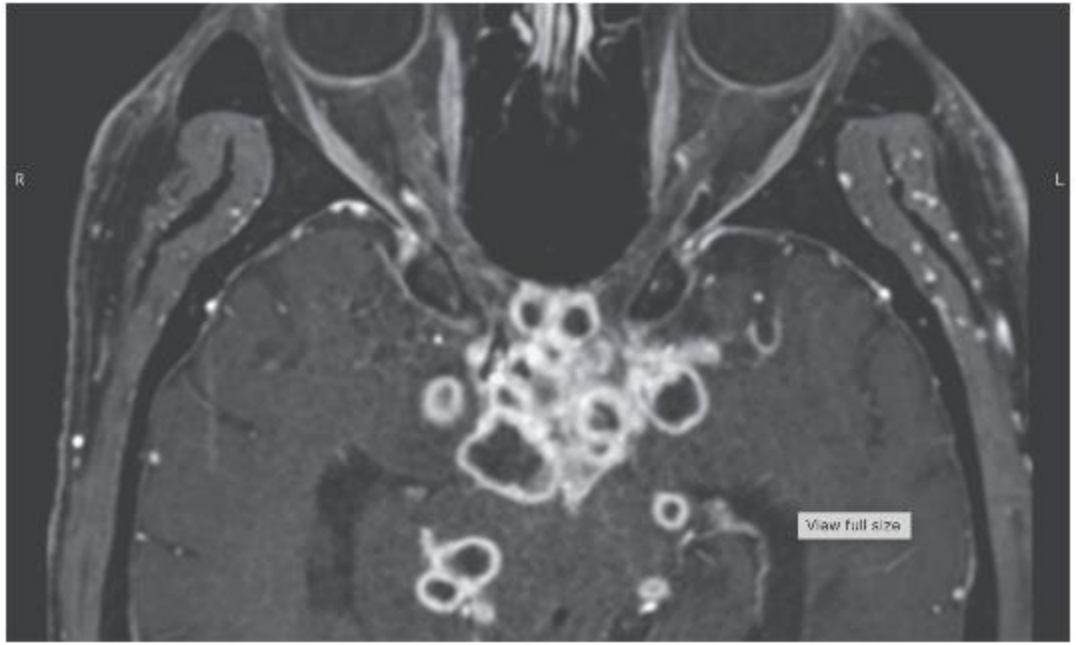
Thwaites, Lancet, 2002

La tuberculose neuroméningée



Granulome

Tuberculome



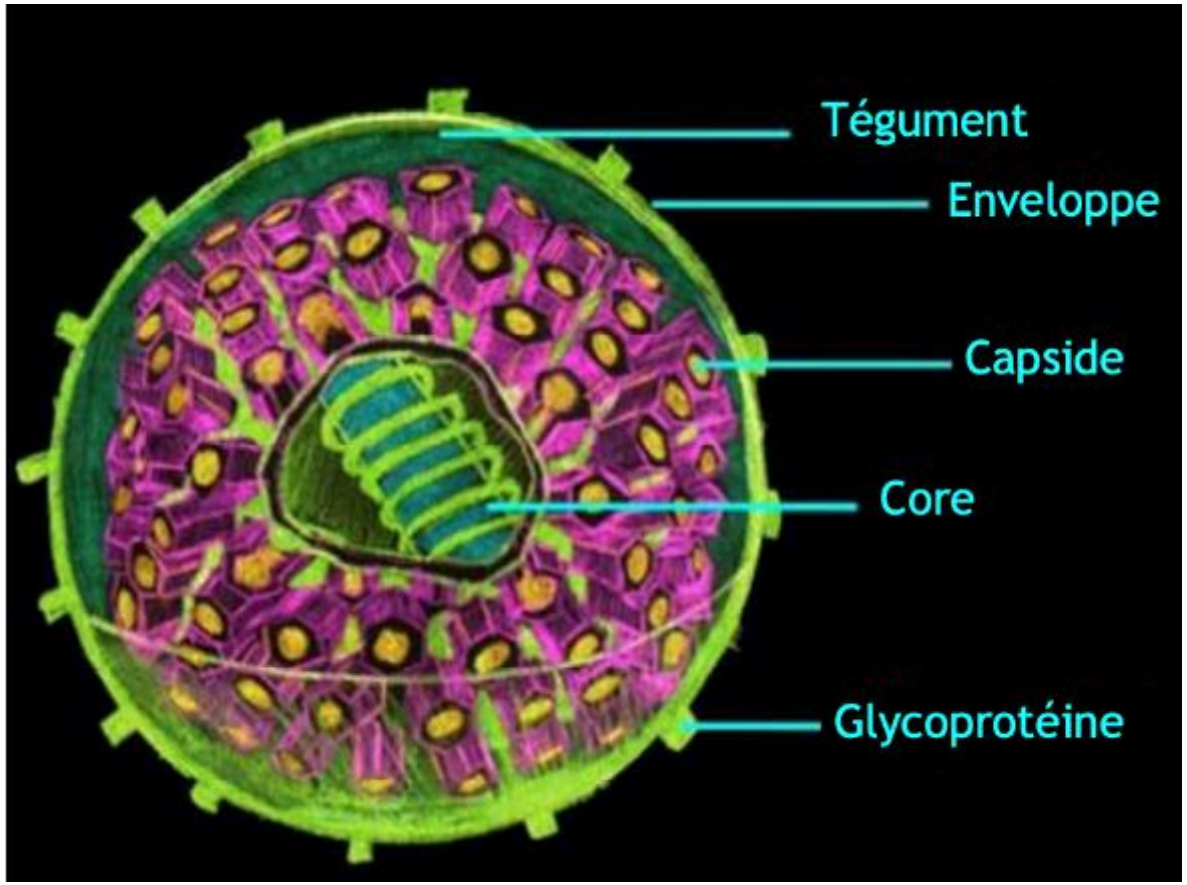
Arachnoïdite du chiasma optique

Wilkinson, Nat Rev Neurol, 2017
Amado, NEJM, 2023

La tuberculose neuroméningée

- Quadrithérapie anti-tuberculeuse
- Corticothérapie
- Durée prolongée++
- Bien doser ISONIAZIDE et RIFAMPICINE en début de traitement

L’encéphalite à HHV-6



- Herpès humain 6
- Virus à ADN double brin avec une capside
- Peut s’intégrer au génome de l’hôte
- Responsable de la roséole infantile/ exanthème subit

L’encéphalite à HHV-6

- Tableau polymorphe
- Troubles neurologiques aigus dans un contexte d’infection
- PCR positive dans le LCS (disponible dans la BioFire®)

L'encéphalite à HHV-6

ATTENTION A L'INTÉGRATION

TABLE 1. Identification of chromosomal HHV-6 integration together with numbers of viral DNA copies/cell or lysed cell in various samples from patients 1 to 6

Patient no.	Whole blood		LCL derived from patient's lymphocytes		HHV-6 DNA variant and no. of copies/ lysed cell[b] for serum	HHV-6 DNA variant and no. of copies/ cell[a] for hair follicle
	HHV-6 chromosomal integration identified in leukocytes	HHV-6 DNA variant and no. of copies/ leukocyte[a]	HHV-6 chromosomal integration identified	HHV-6 DNA variant and no. of copies/ cell[a]		
1	Yes	B, ≥1	NT	NT	B, ≥1[c]	B, ≥1
2	NT[d]	NT	Yes	B, ≥1	NT	B, ≥1
3	Yes	B, ≥1	NT	NT	B, ≥1	B, ≥1
4	NT	NT	Yes	B, ≥1	B, ≥1	B, ≥1
5	NT	NT	Yes	A, ≥1	A, ≥1	A, ≥1
6	NT	NT	Yes	B, ≥1	NT	B, ≥1

[a] HHV-6 DNA copies/cell is twice the number of HHV-6 DNA copies/the number of β-globin DNA copies.
[b] HHV-6 DNA copies/lysed cell is twice the number of HHV-6 DNA copies/the number of β-globin DNA copies.
[c] Plasma also was tested, with the same result.
[d] NT, not tested.

Ward, J Clin Microb, 2006

L'encéphalite à HHV-6

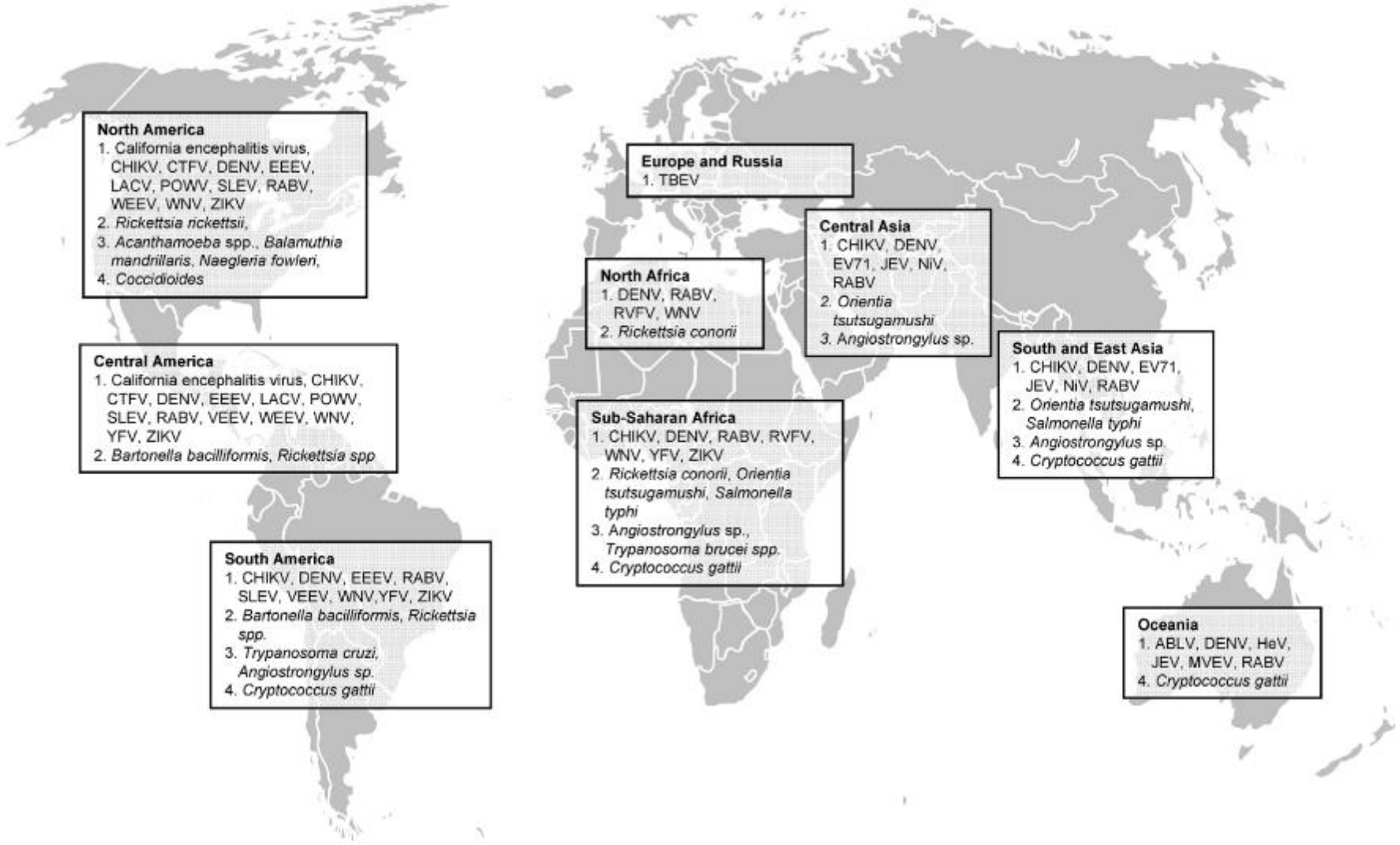
Antiviral	Type d'antiviral	Efficacité *in vitro*	EC 50 (µM)*	Efficacité *in vivo* rapportée	Auteurs
Ganciclovir	Analogue nucléosidique	Bonne	69	Bonne	[Mookerjee and Vogelsang et al., 1997]; [Yoshida et al., 2002]
Aciclovir	Analogue nucléosidique	Faible	185	Inefficace	[Yoshida et al., 1998]
Foscarnet	Analogue pyrophosphate	Excellente	25	Efficace	[Deray et al., 1989]
Cidofovir	Analogue nucléotidique	Excellente	9,8	Efficace	[Denes et al., 2004]
Maribavir	Analogue nucléosidique	Inefficace	>100	Inefficace	[Williams et al., 2003]
Cyclopropavir	Analogue méthylenecyclopropane	Bonne	7,8	En cours d'étude	[Kern et al., 2005]

*EC50: 50% concentration efficace. Toutes les EC50 ont été déterminées sur des cellules MOLT-3-T infectées par de l'HHV-6B de la souche Z-29, sauf pour le cyclopropavir où ce sont des lymphocytes de sang de cordon qui ont été utilisés

Guéry, thèse UL, 2010

6. Particularités du voyageur

Les encéphalites du voyageur



Kenfak, CMI, 2019

CHU GRENOBLE ALPES

UGA Université Grenoble Alpes

GIN Grenoble Institut Neurosciences

Merci de votre attention