



Encéphalites

Dr Marion Le Maréchal, Infectiologie, CHU Grenoble Alpes

DU de Thérapeutiques anti-infectieuses de Grenoble

14 février 2025

1. Référentiels

Référentiels conseillés – Recommandations françaises



Recommandation SPILF 2017 Encéphalites infectieuses aiguës de l'adulte

Jeu de diapositives réalisées par le comité
des référentiels de la SPILF
7 avril 2017

Synthèse réalisée par la SPILF



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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. Honnoratⁱ, M. Lecuit^{j,k}, A. Mailles^{l,1},
L. Martinez-Almoyna^m, P. Morandⁿ, L. Piroth^o, P. Tattevin^{p,1}, The reviewing group²

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. Whitley¹⁰**

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

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. Luring,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

2. Épidémiologie

Épidémiologie en France



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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. Gueitⁱ, 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 committee¹ the investigators²,



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
<i>Listeria monocytogenes</i>	23	7,1	4,7	21	2	0
<i>Mycobacterium tuberculosis</i>	11	3,4	2,2	8	2	1
Inconnu	170	-	34,4	-	-	-

Épidémiologie en France

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Épidémiologie en France

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Major Criterion (required):

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Documented fever $\geq 38^{\circ}$ 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.

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Épidémiologie en France

2009

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

2022

Cause of encephalitis	N =	% of cases identified	Total (494) %
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Épidémiologie en France

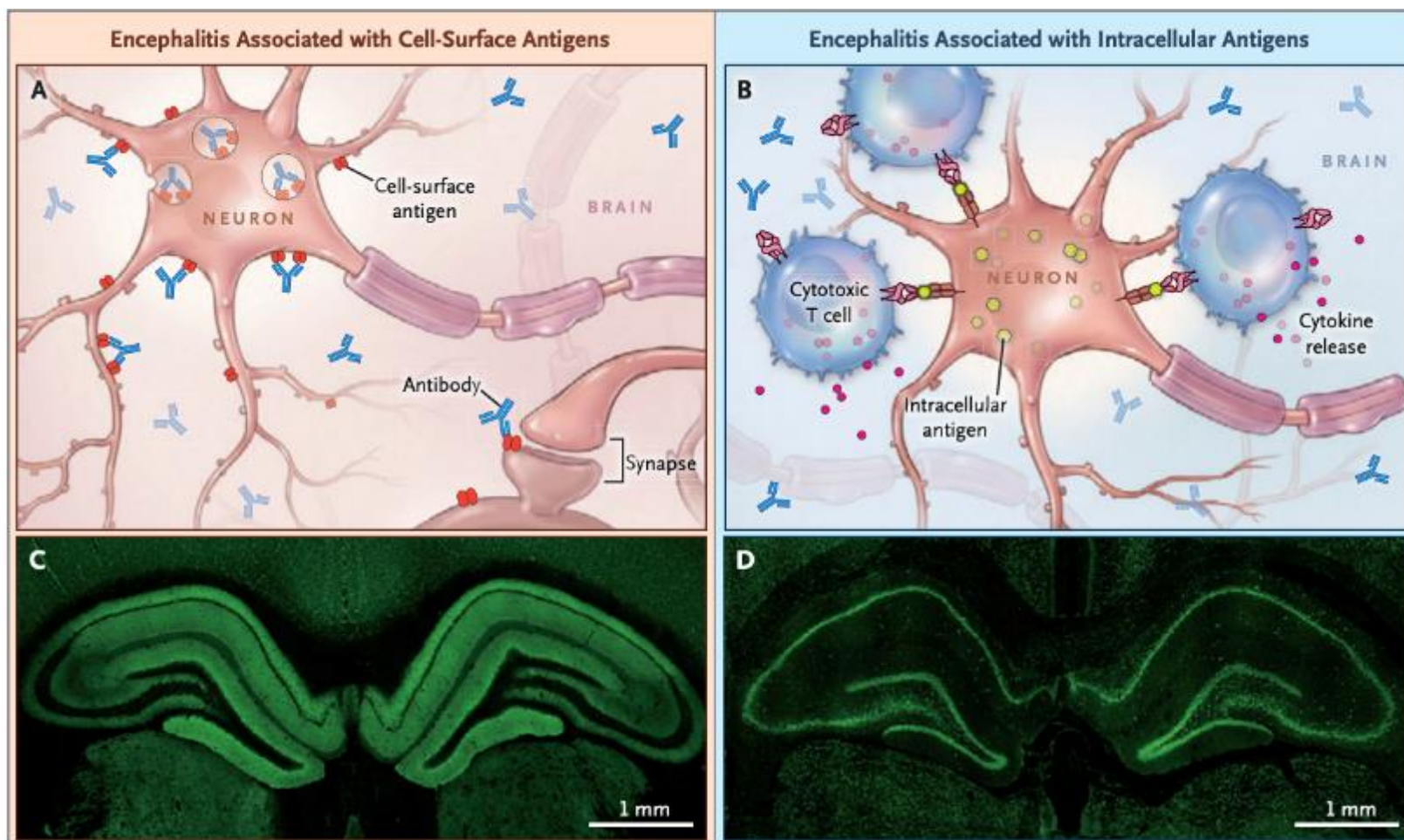
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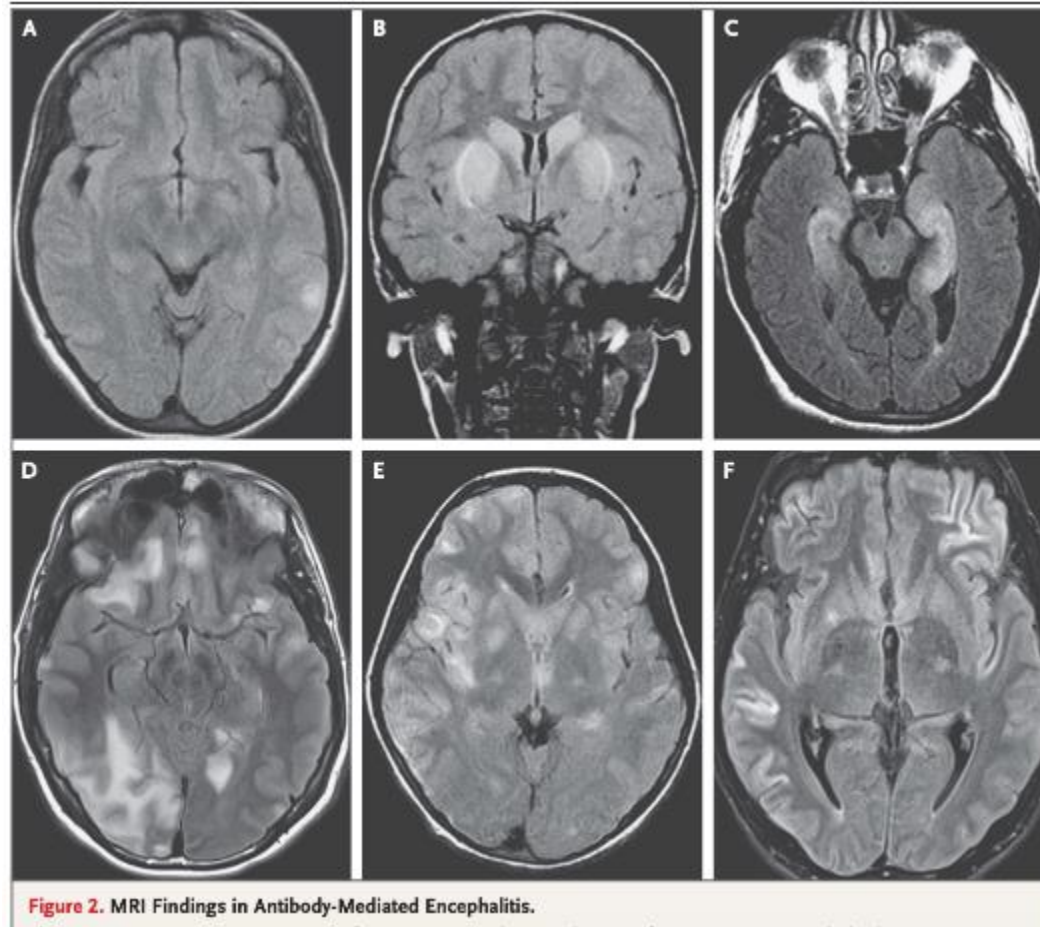
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Et les encéphalites auto-immunes ?



Et les encéphalites auto-immunes ?



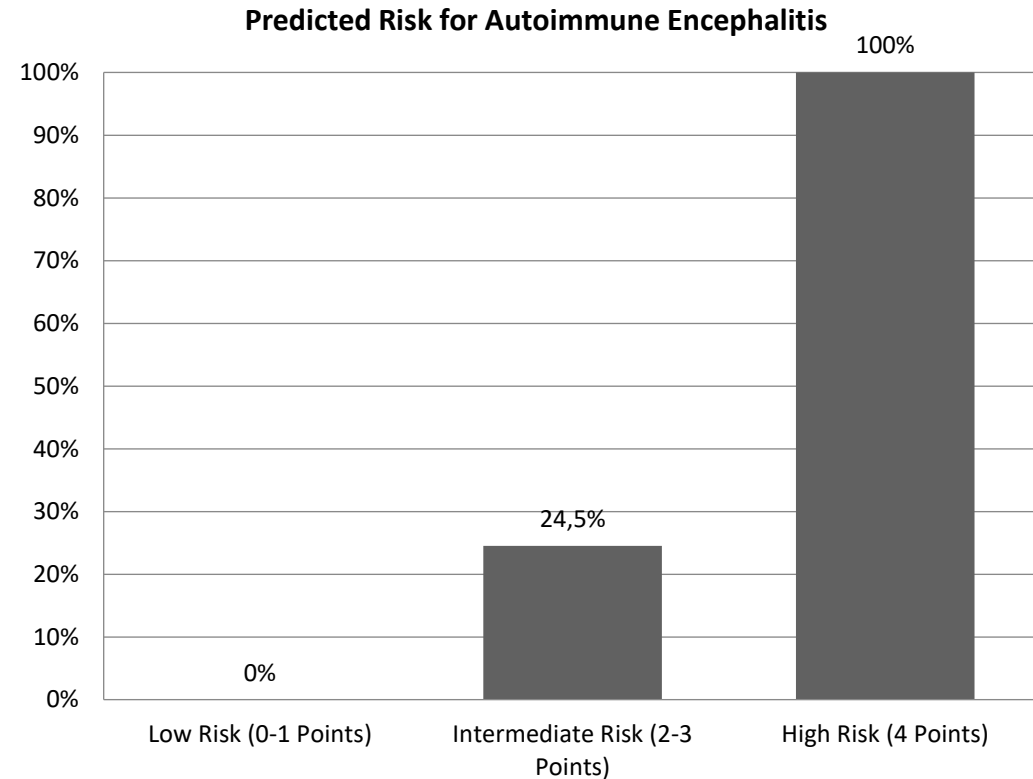
Et les encéphalites auto-immunes ?

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



3. Démarche diagnostique

Clinique

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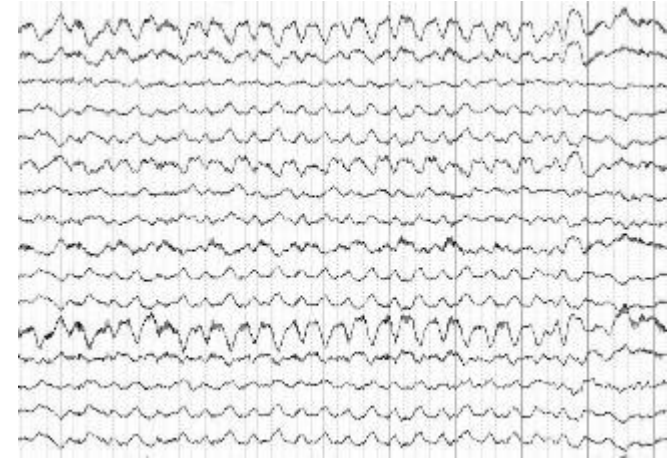
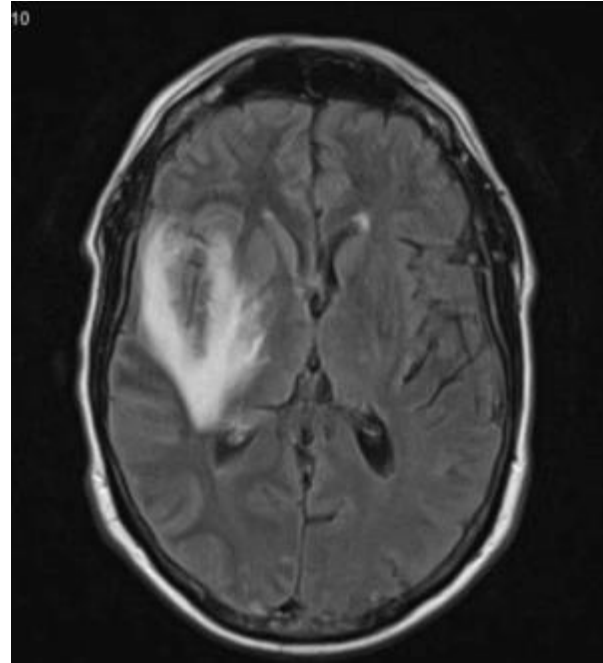
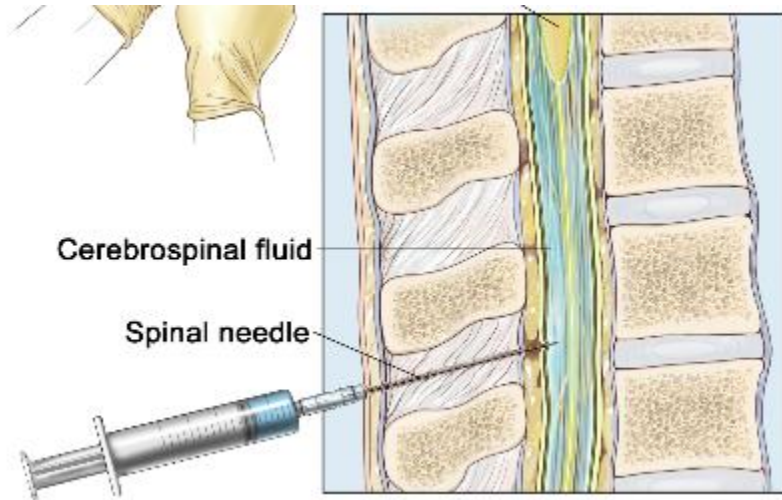
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Paraclinique



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 – BioFire

Virus	Bactéries	Levure
<ul style="list-style-type: none">● Cytomégalovirus (CMV)● Entérovirus● Virus herpès simplex 1 (HSV-1)● Virus herpès simplex 2 (HSV-2)● Herpèsvirus humain 6 (HHV-6)● Paréchovirus humain● Virus varicelle-zona (VZV)	<ul style="list-style-type: none">● <i>Escherichia coli</i> K1● <i>Haemophilus influenzae</i>● <i>Listeria monocytogenes</i>● <i>Neisseria meningitidis</i>● <i>Streptococcus agalactiae</i>● <i>Streptococcus pneumoniae</i>	<ul style="list-style-type: none">● <i>Cryptococcus neoformans / gattii</i>

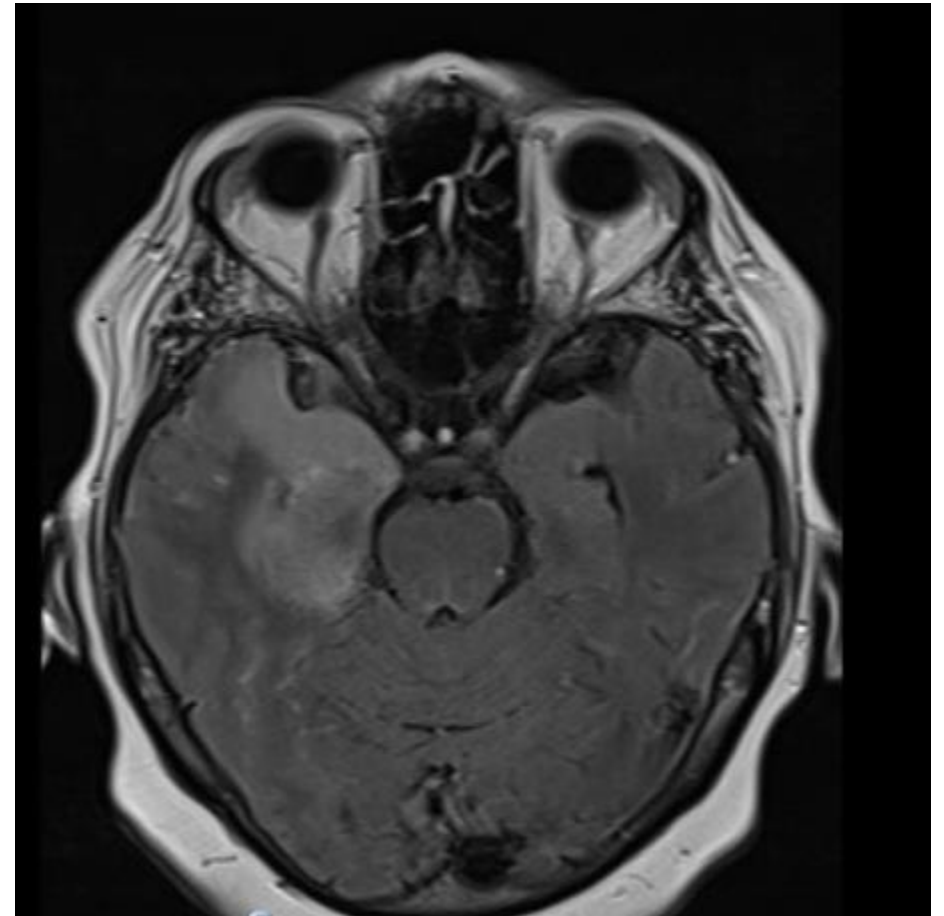
Paraclinique – Ponction lombaire – BioFire

- Les avantages :
 - 14 pathogènes screenés
 - Disponible en 90 min
 - Peut être fait sans validation biologiste / horaires de garde
 - Petit volume (200µL/4 gouttes)
- Les inconvénients :
 - Résultat négatif peut être « faussement » rassurant
 - Mauvaise sensibilité sur Listeria
 - Panel peu intéressant en terme de cibles (panel ID ?)

Paraclinique – IRM



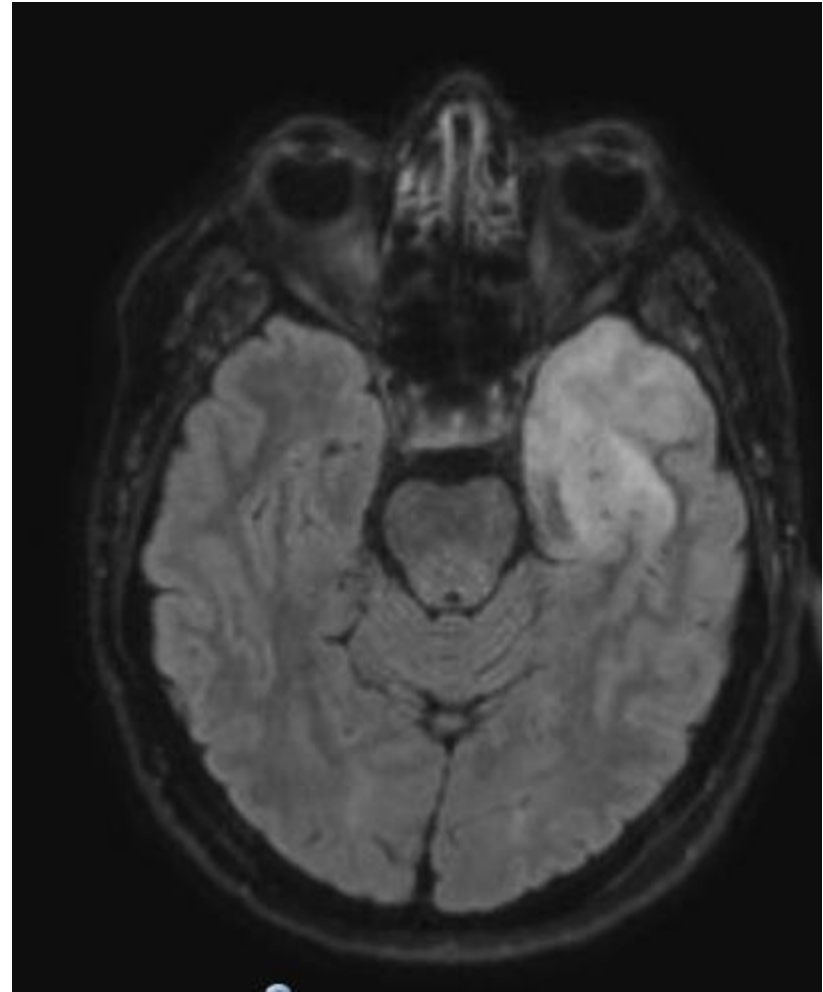
Paraclinique – IRM



Paraclinique – IRM



Paraclinique – IRM

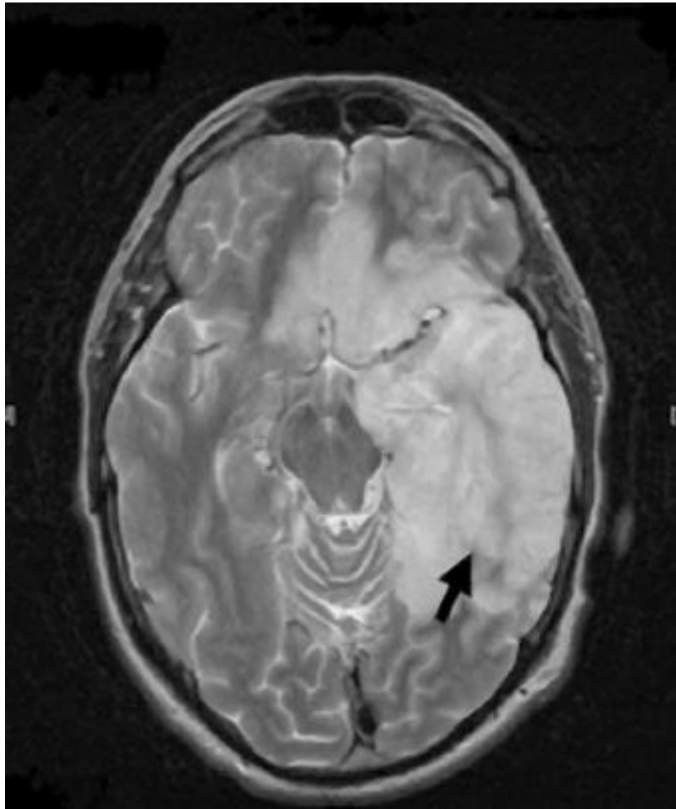


Paraclinique – EEG

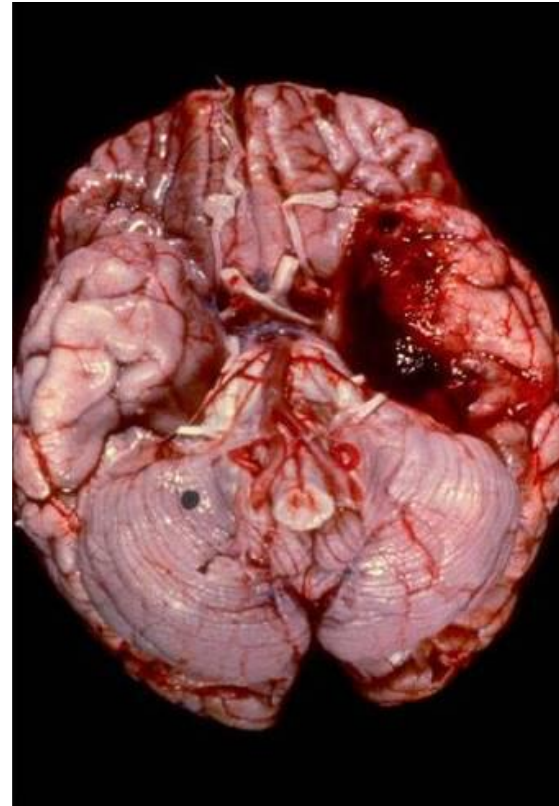
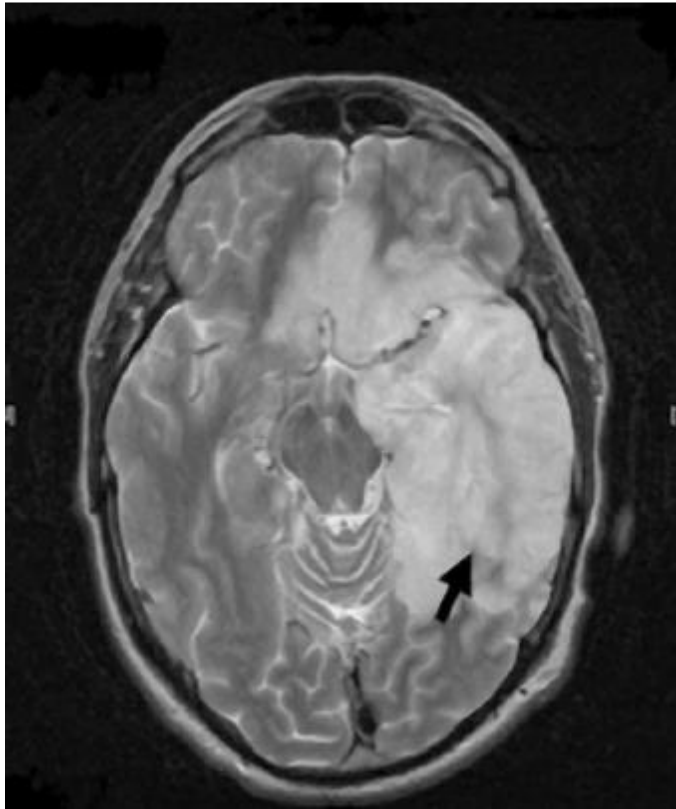
- A faire systématiquement en aigu
- Témoin de la souffrance aiguë
- Aide au diagnostic si anomalie
- Anomalies secondaires peuvent se mettre en place

4. Prise en charge thérapeutique

Quelle gravité des encéphalites ?



Quelle gravité des encéphalites ?



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

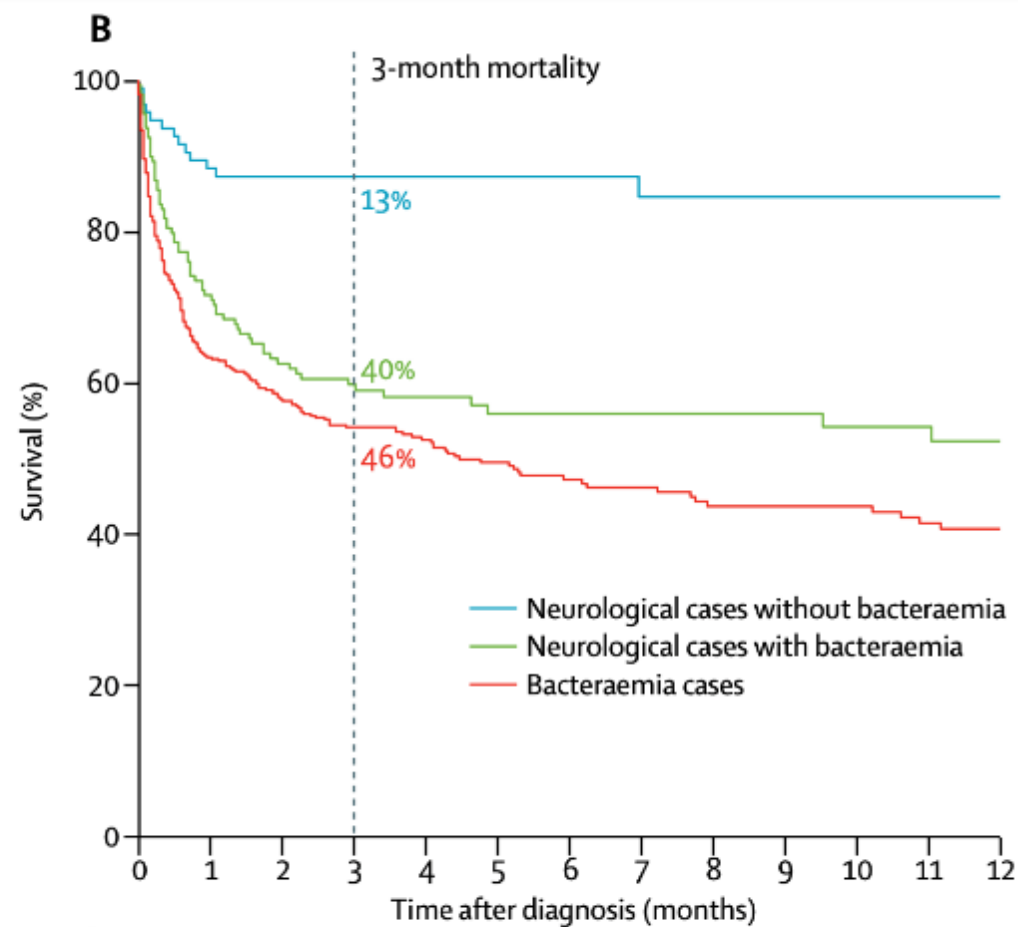
Quelle gravité des encéphalites ?

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.

Quelle gravité des encéphalites ?



	0	1	2	3	4	5	6	7	8	9	10	11	12
Neurological cases without bacteraemia	94	76	49	35	30	26	25						
Neurological cases with bacteraemia	158	93	59	41	35	29	23						
Bacteraemia cases	423	235	149	94	68	59	53						

Rappel de l'épidémiologie en France

Cause of encephalitis	N =	% of cases identified	Total %	
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VZV	65	20,1	13,2	
TBEV	26	8,0	5,3	
<i>Listeria monocytogenes</i>	23	7,1	4,7	Cause traitable par AMOXICILLINE

Conduite initiale (premières 48 h)



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

- ✓ A débiter 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



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*

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

L. Berry, P. Venkatesan / Journal of Clinical Virology 61 (2014) 608–610

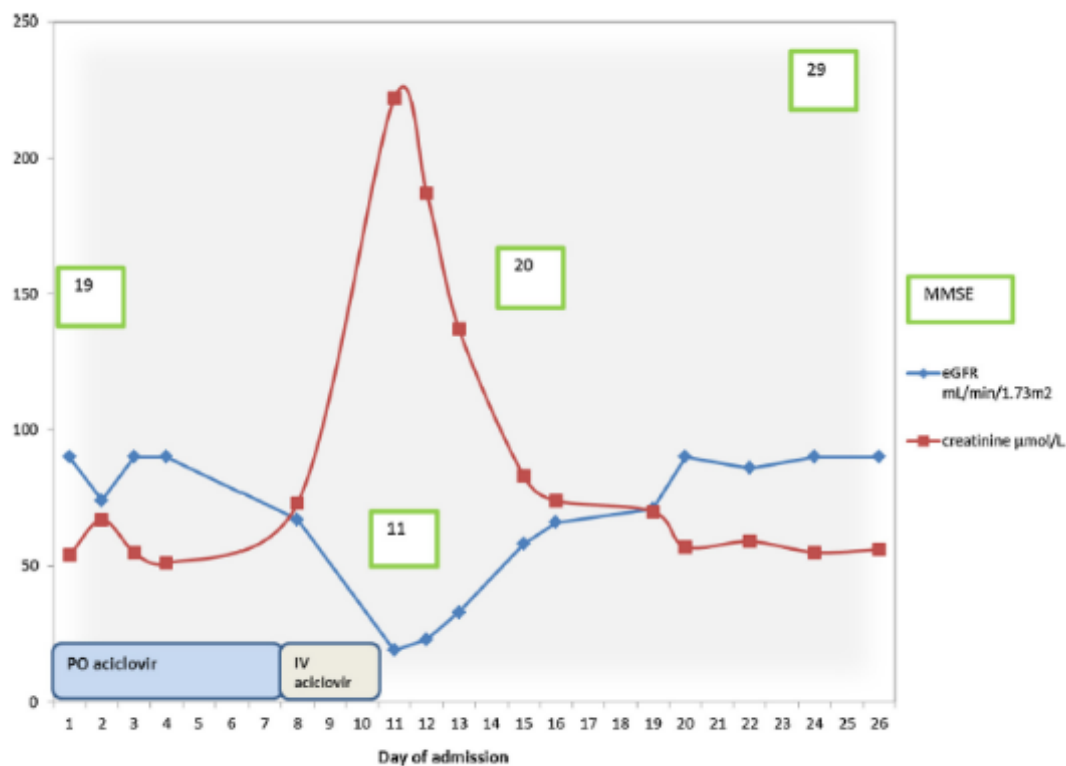


Fig. 1. Results of patient's creatinine, eGFR and MMSE level during admission.

Table 1

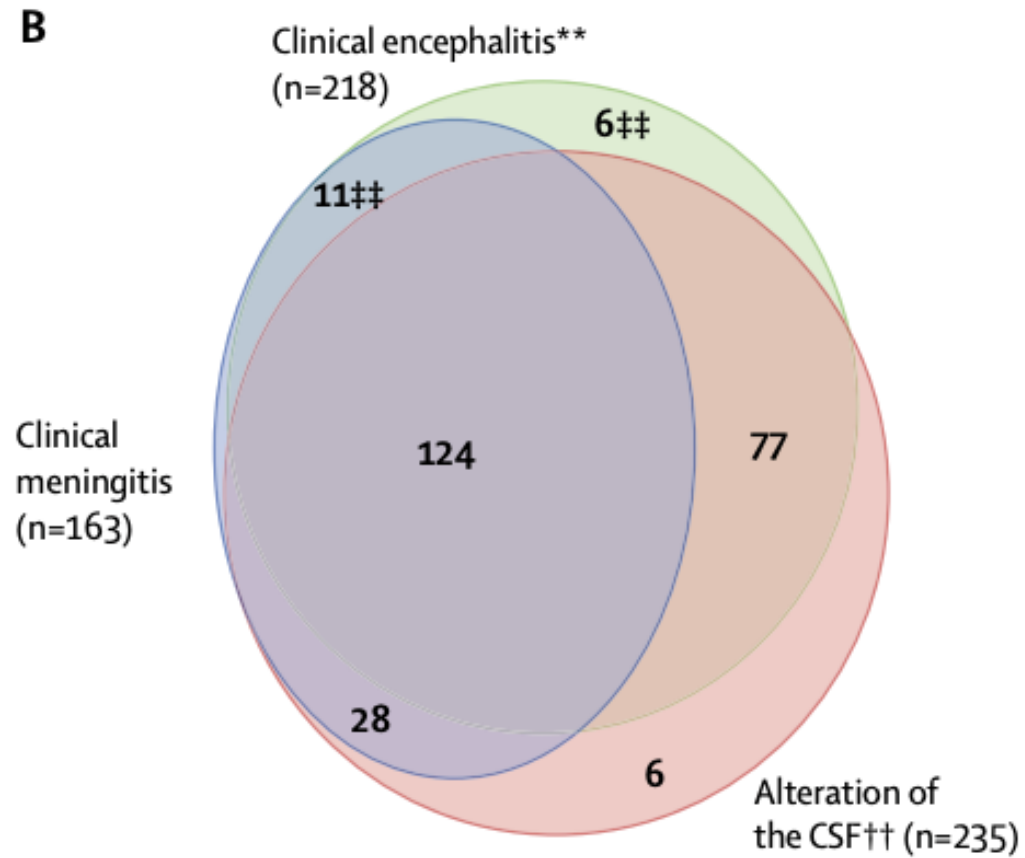
Patient's CSF and serum CMMG and aciclovir levels.

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

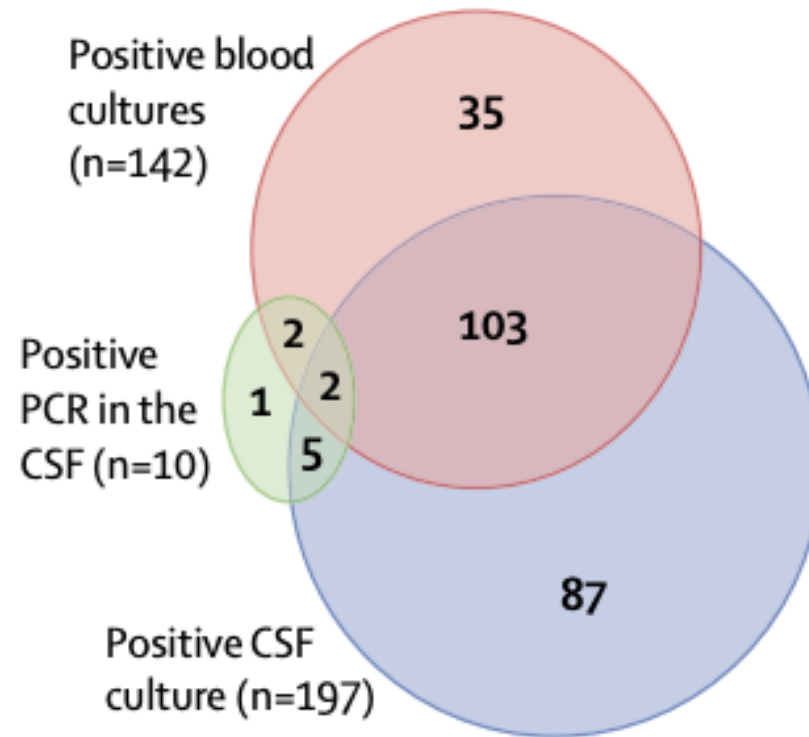
Paraclinique – Orientation étiologique ?

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)

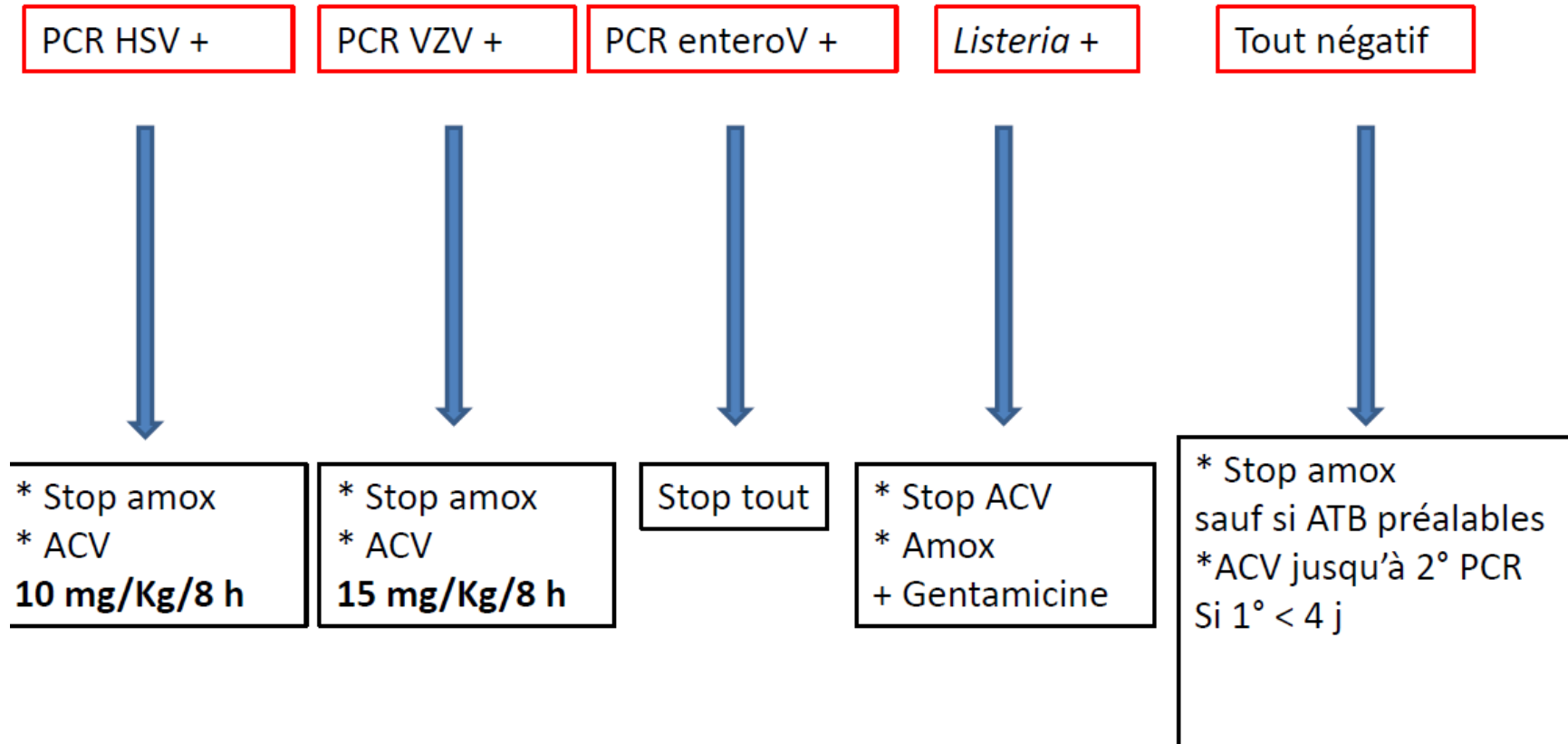
Paraclinique – Orientation étiologique ?



Paraclinique – Orientation étiologique ?



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.

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

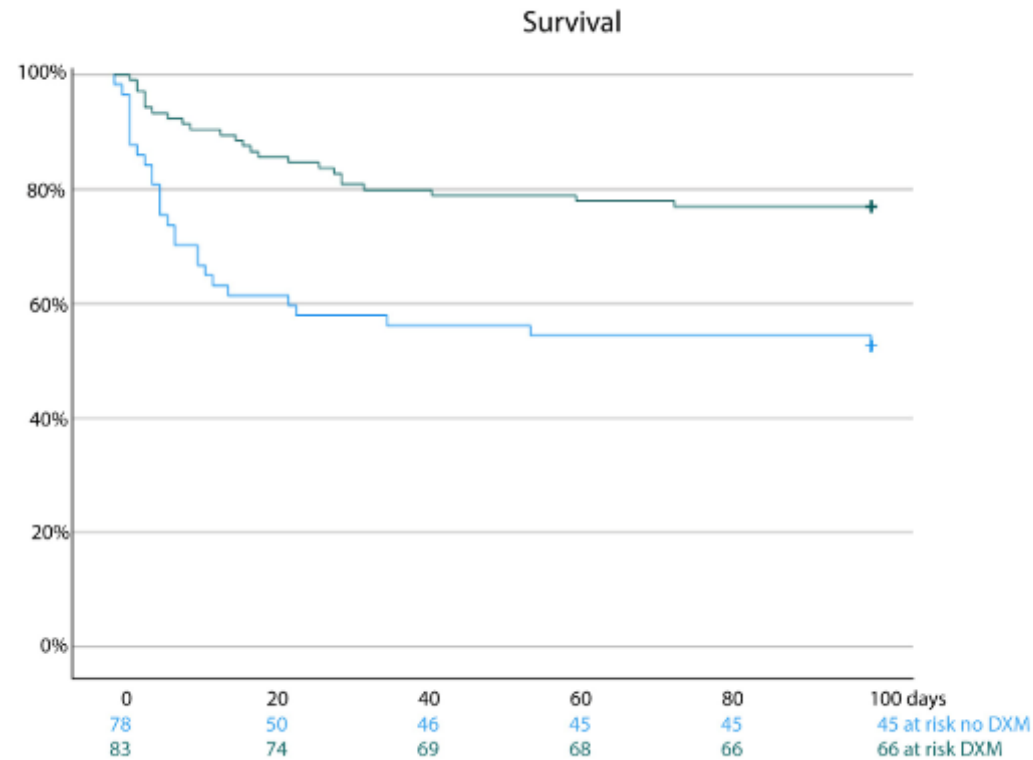
En cas de contre-indication à l'amoxicilline (allergie grave **prouvée**), l'association triméthoprime-sulfaméthoxazole à forte dose (6 à 9 ampoules par jour en 3 injections iv) doit être administrée pendant 21 jours.

Quid de la corticothérapie ?

3-month mortality for neurolisterosis (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

Quid de la corticothérapie ?



Quid de la corticothérapie ?



*La dexaméthasone en traitement
complémentaire des encéphalites à Herpes
Simplex Virus*
DexENCEPH

PHRC:

Investigateur principal: J.P. Stahl (Grenoble)

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

Quid de la corticothérapie ?

****Primary Outcome: Auditory Memory Index for dexamethasone patients versus controls at 6 months**

	Dexamethasone (n=42)	Control (n=39)	Adjusted Mean Difference (95% CI)	P-Value
Primary outcome				
WMS-IV Auditory Memory Index Mean (SD)	71 (26)	69 (25)	1.7 (-10, 13)	.756

(Normal WMS-IV is 100; possible scores range 40 – 160)

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) 98	Infor = 5† Arith = 6† Simil = 8	Pict ar = 13 B des = 12 D sy = 6†	Impaired 5/30	Normal
7	70 Male	3	9		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) 89	Infor = 5† Arith = 7 Simil = 7	Pict ar = 12 B des = 12 D sy = 11	Impaired 0/30	Normal
9	65 Male	7	13		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.

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

5. Particularités de l'immunodéprimé

Les différents types d'immunodépression

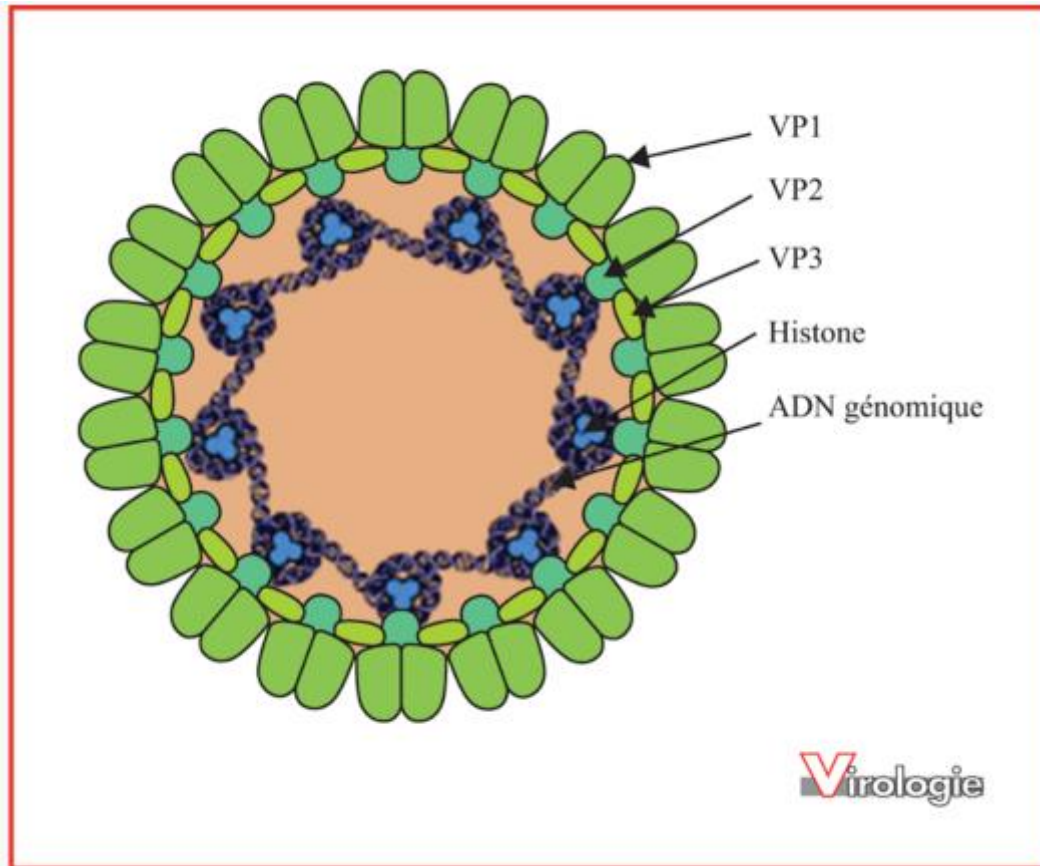
VIH

- 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

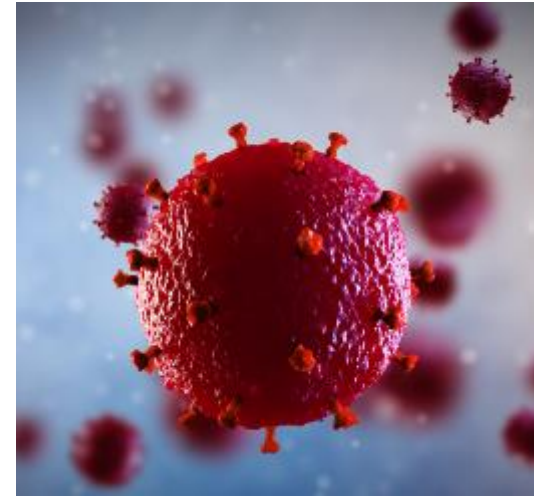
La leucoencéphalopathie multifocale progressive (LEMP)



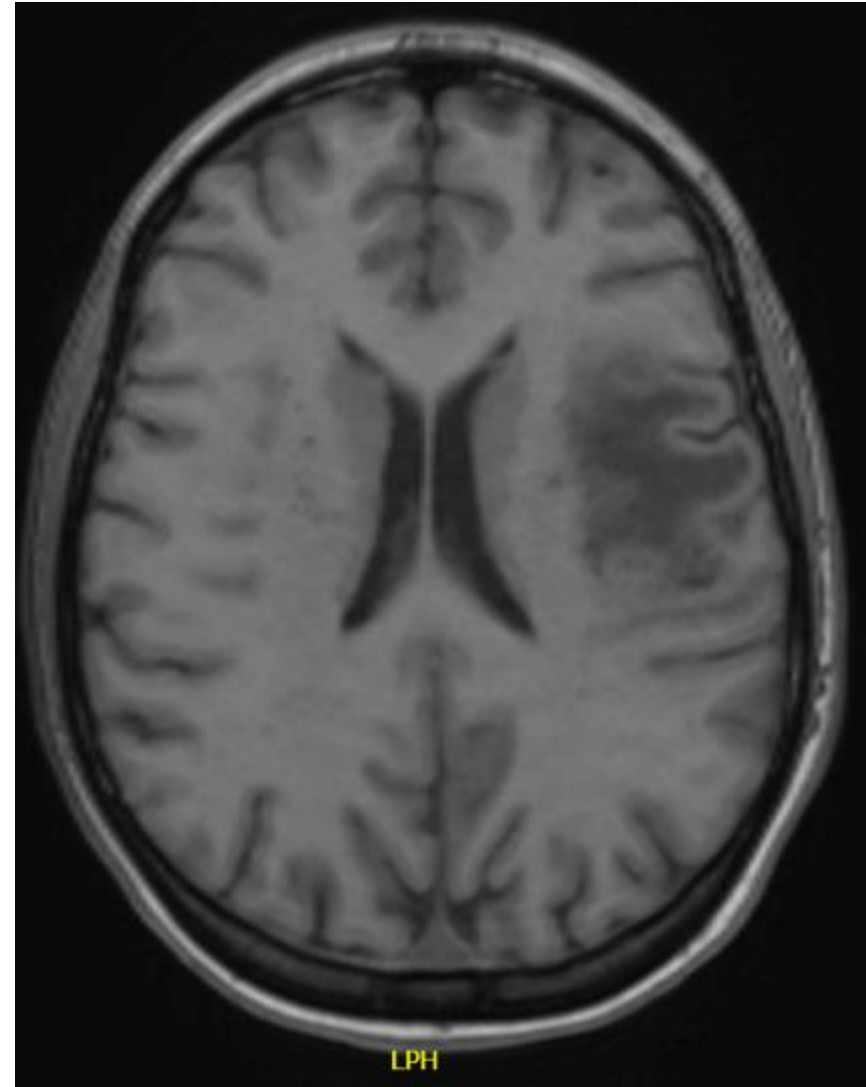
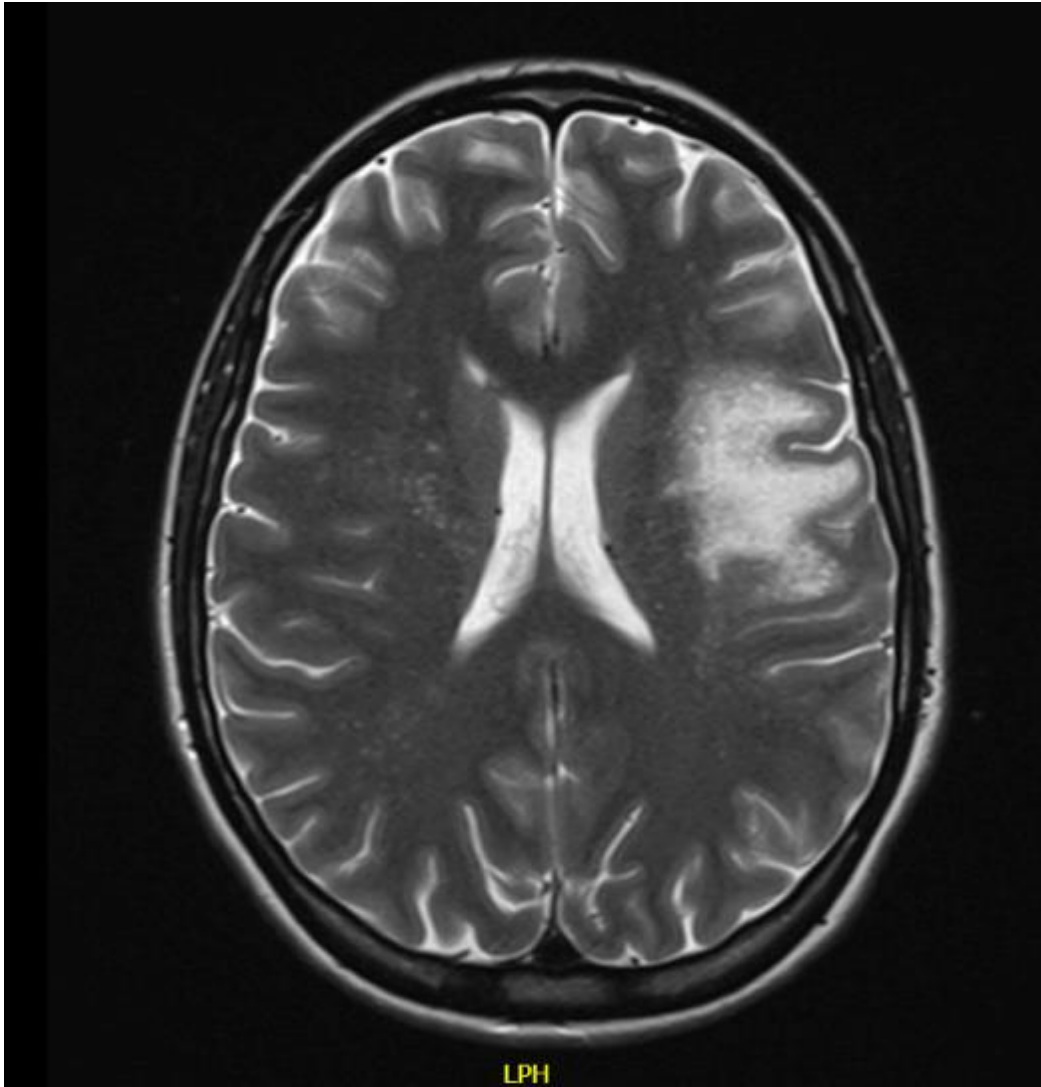
- JC virus = polyomavirus
- Petit virus à ADN non enveloppé
- 3 protéines virales
- Décrite initialement dans le SIDA
- De plus en plus chez les ID hors VIH

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)



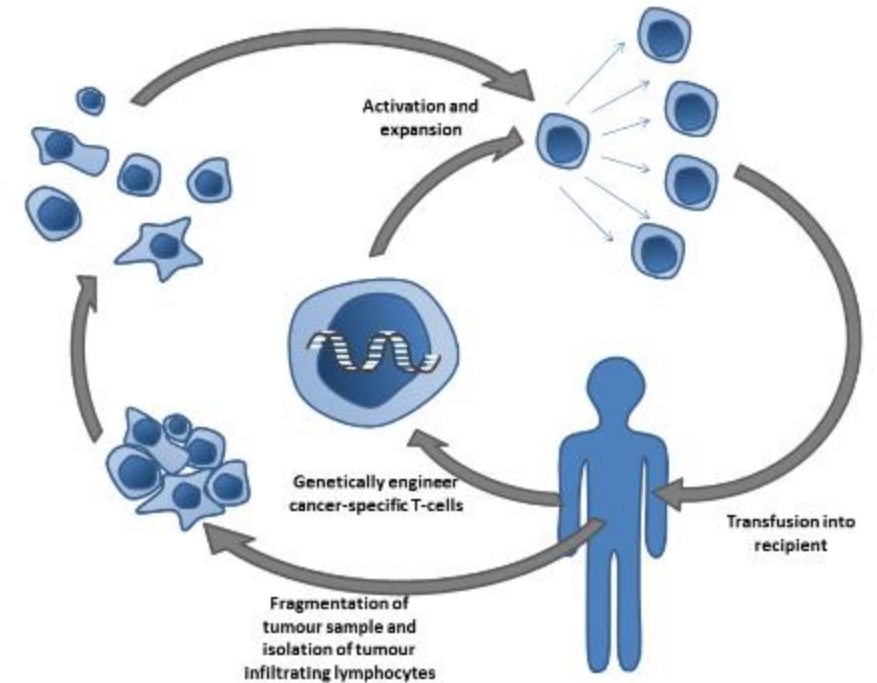
La leucoencéphalopathie multifocale progressive (LEMP)

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

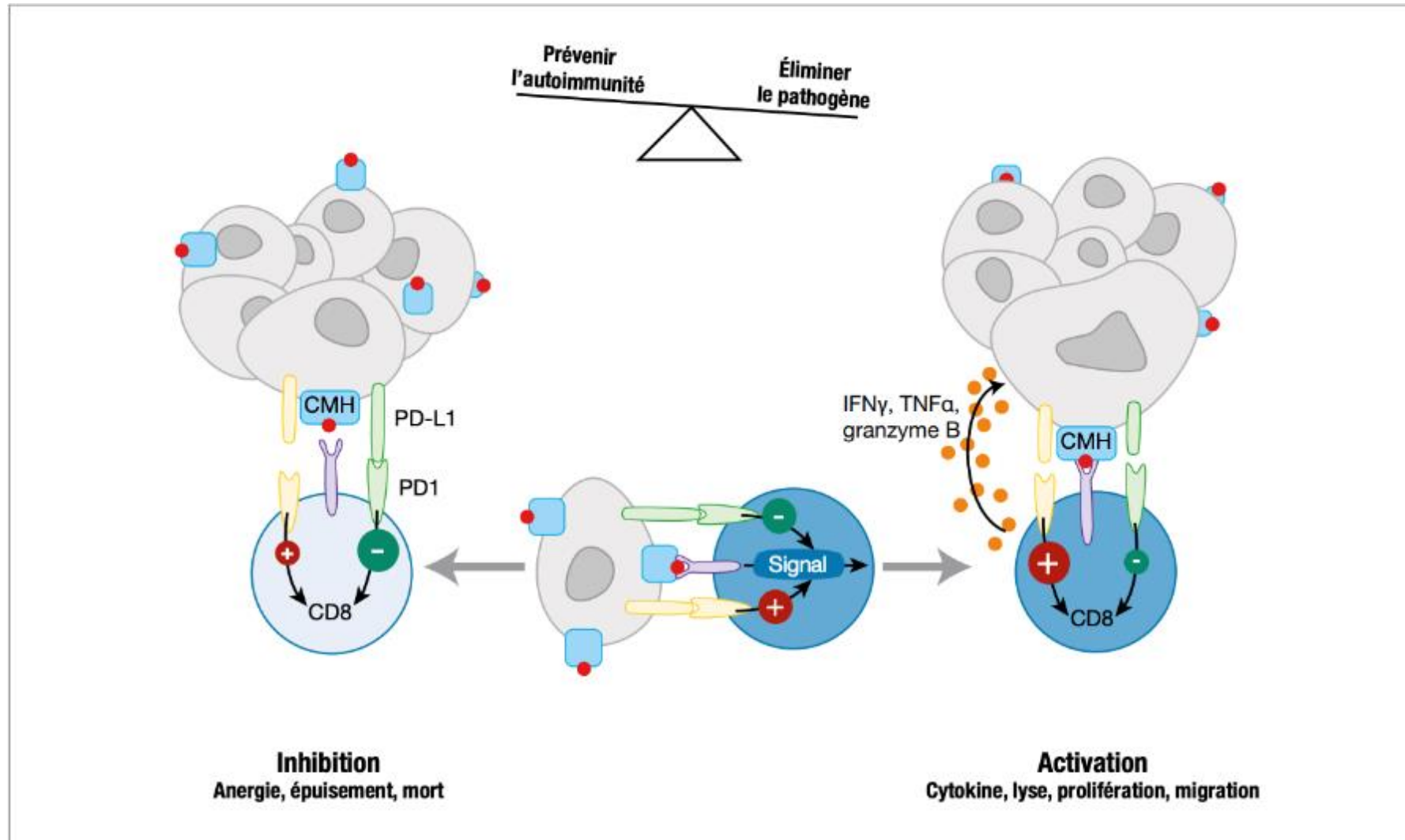


La leucoencéphalopathie multifocale progressive (LEMP)

Traitement = RESTAURATION DE L'IMMUNITÉ

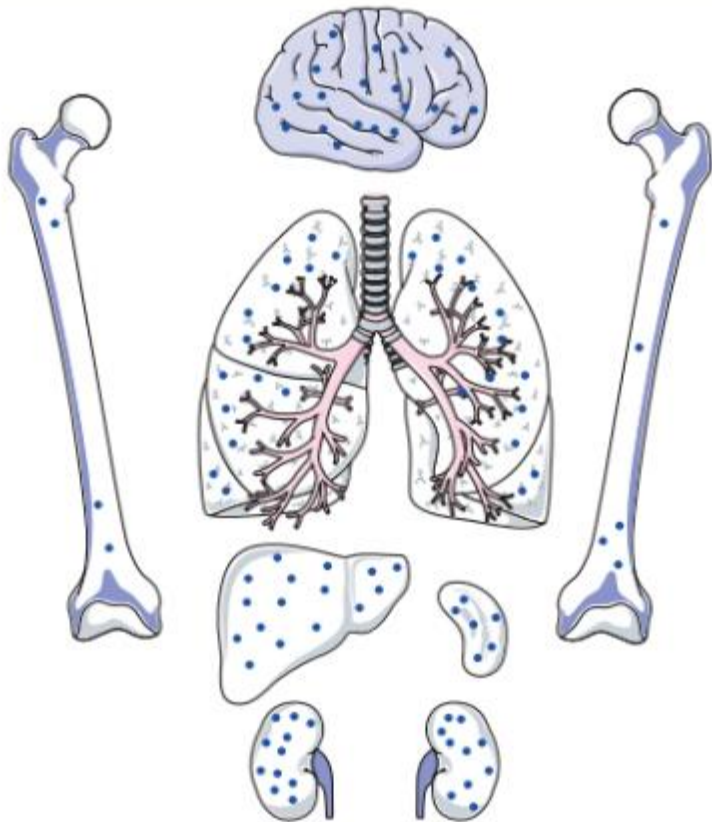


La leucoencéphalopathie multifocale progressive (LEMP)



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 rule³⁹

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 $\geq 15 \times 10^9/L$ (score +4)
- Blood white cell count < $15 \times 10^9/L$ (score 0)
- History of illness ≥ 6 days (score -5)
- History of illness <6 days (score 0)
- CSF white cell count $\geq 0.75 \times 10^9/L$ (score +3)
- CSF white cell count < $0.75 \times 10^9/L$ (score 0)
- CSF neutrophils $\geq 90\%$ 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

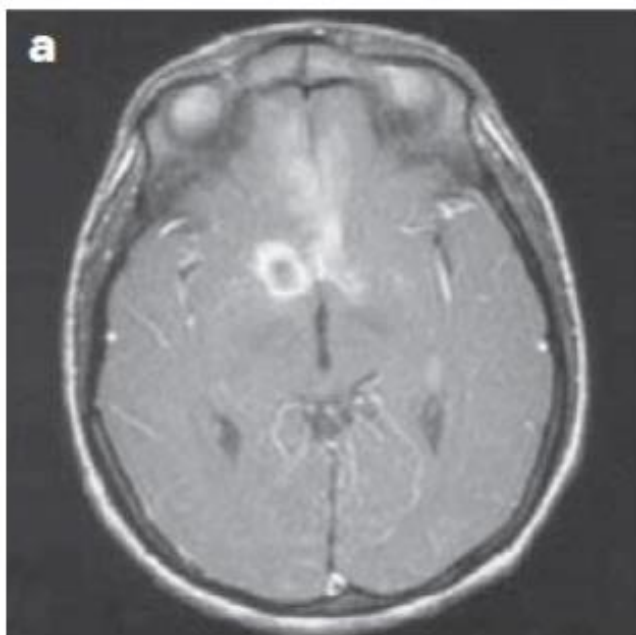
- Phase prodromique : plusieurs semaines/mois avec installation chronique (somnolence, AEG, céphalées, fébricule)
- Pas forcément de syndrome méningé complet
- Altération de la vigilance
- Paralysie des nerfs crâniens (oculomotrice++)
- Convulsions

La tuberculose neuroméningée

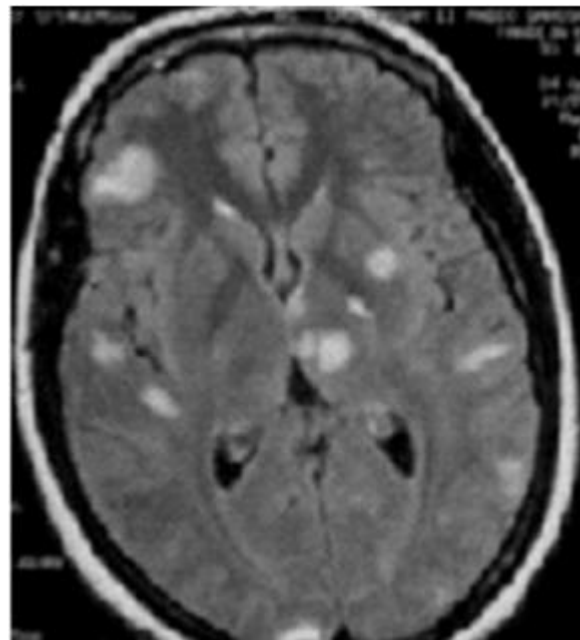
- Coloration de ZN dans le LCS : 10-20% de Se
- Culture sensible (>60-70%) mais longue (>2 semaines)
- PCR : sensibilité de 60%



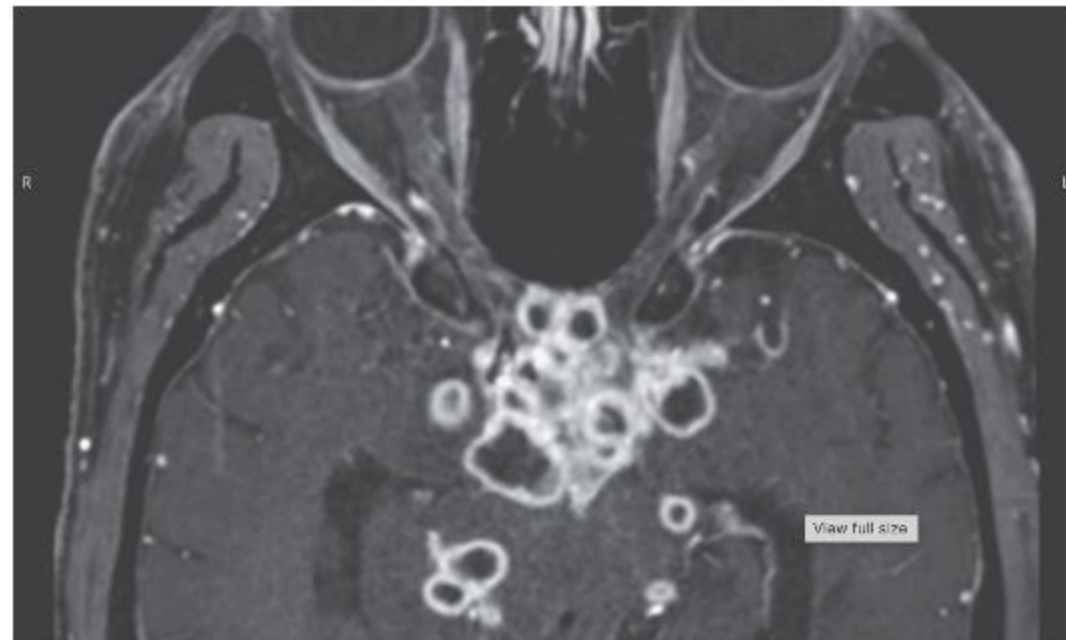
La tuberculose neuroméningée



Granulome



Tuberculome

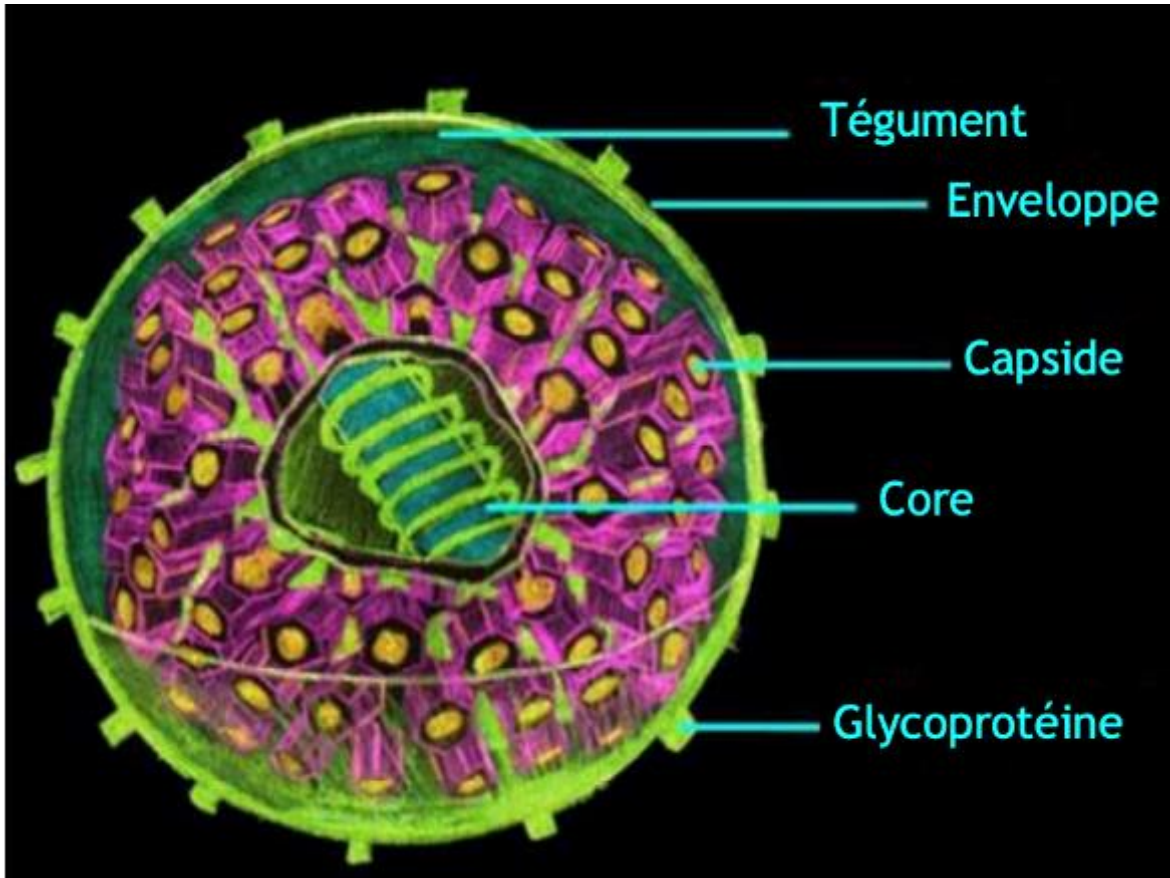


Arachnoïdite du chiasma optique

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 capsid
- 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.

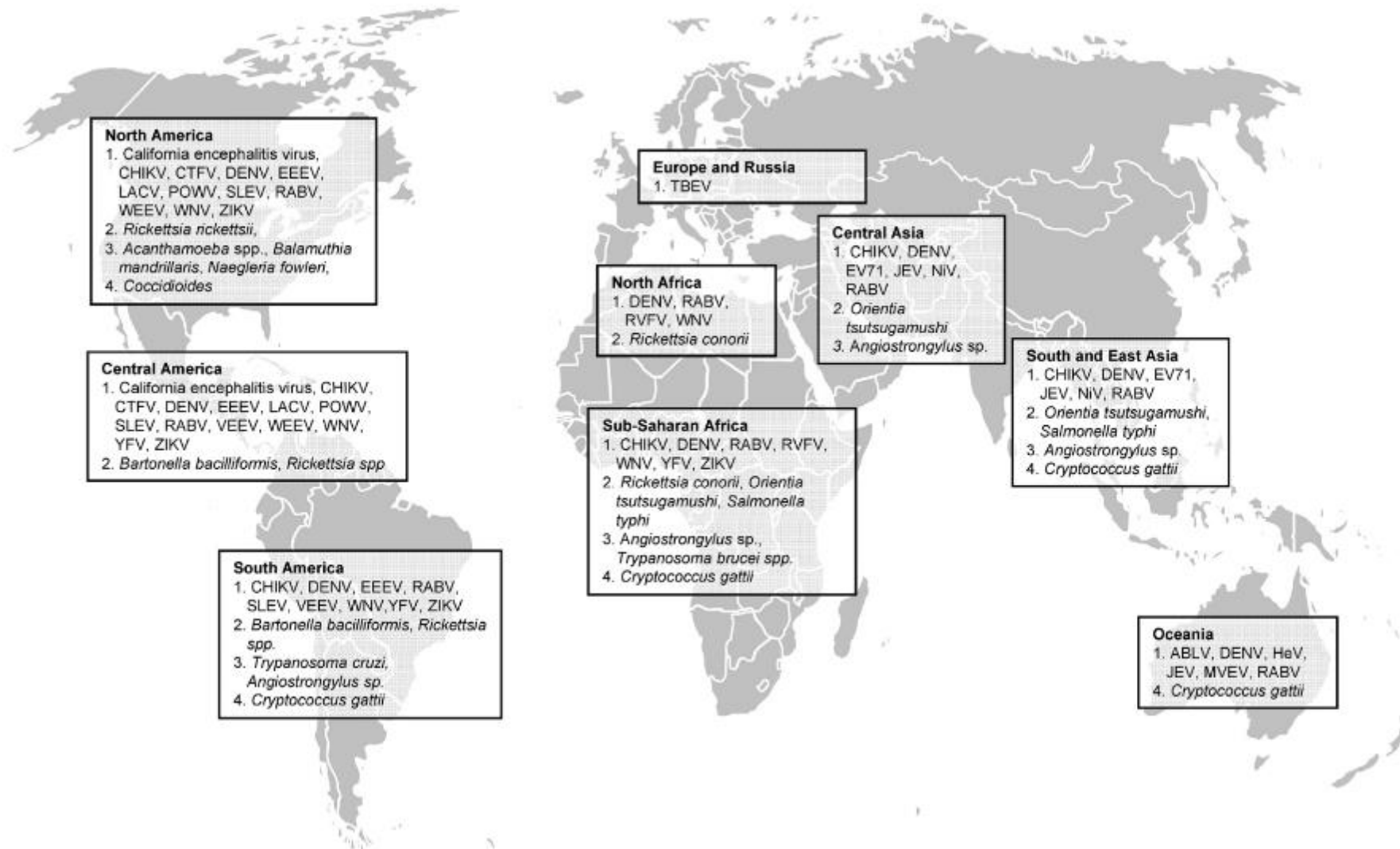
L'encéphalite à HHV-6

Antiviral	Type d'antiviral	Efficacité <i>in vitro</i>	EC 50 (µM)*	Efficacité <i>in vivo</i> 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 méthylencyclopropane	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

6. Particularités du voyageur

Les encéphalites du voyageur





Merci de votre
attention

