

Méningo-Encéphalites

B. Mourvillier

Médecine Intensive Réanimation Polyvalente

Hôpital R. Debré – CHU Reims

Aucun lien d'intérêt



S'agit il d'une encéphalite?

A. Venkatesan et al. 2013

Critère majeur (requis)

Patient présentant une altération des fonctions cérébrales définie par des troubles de la vigilance, une somnolence ou des troubles de la personnalité depuis plus de 24h, sans cause clairement identifiée.

Critères mineurs (2 = encéphalite possible; ≥3 encéphalite probable ou confirmée):

Fièvre $\geq 38^{\circ}$ C, 72h avant ou après le début des signes cliniques

Convulsions partielles ou généralisées chez un patient non épileptique

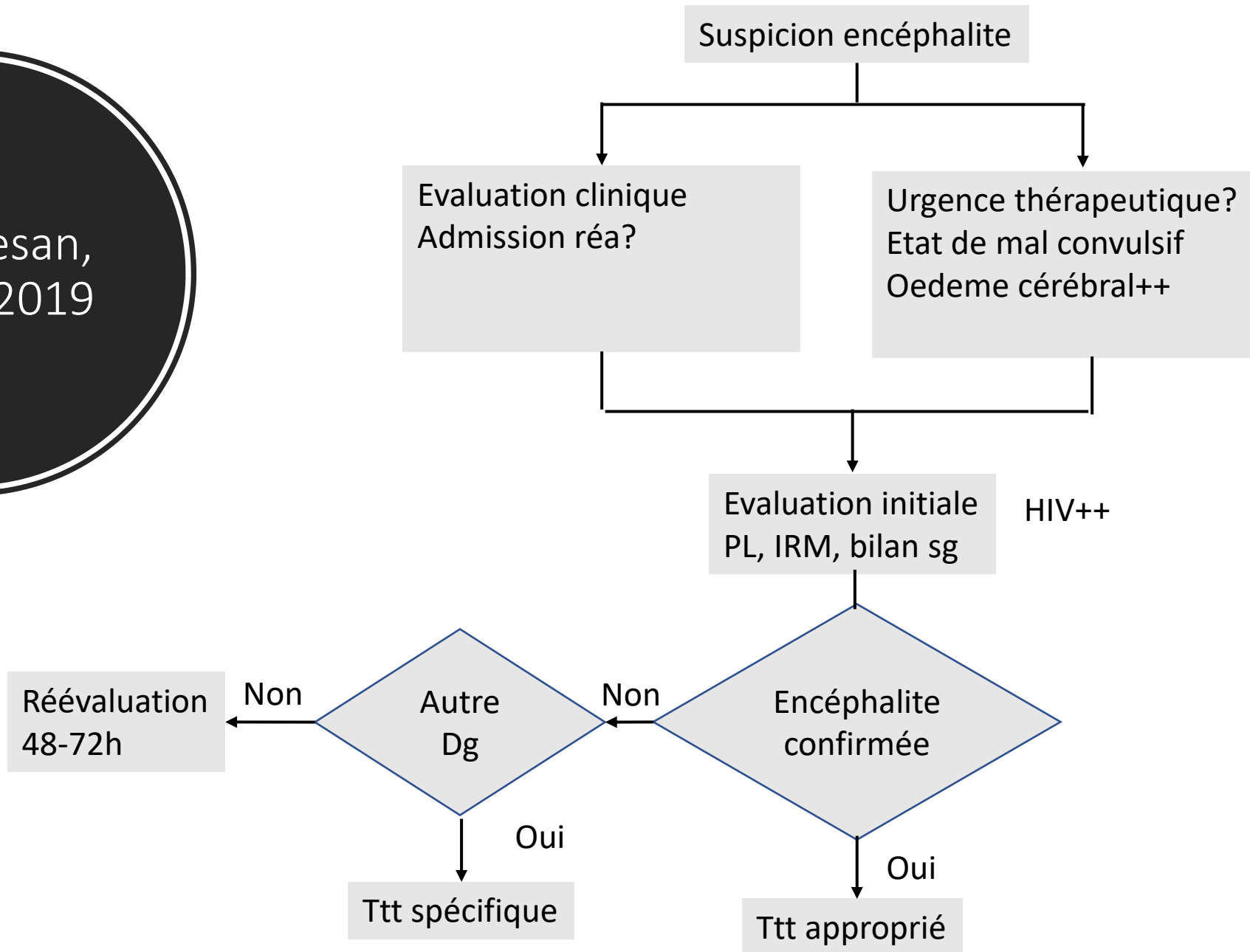
Anomalies focales à l'examen neurologique

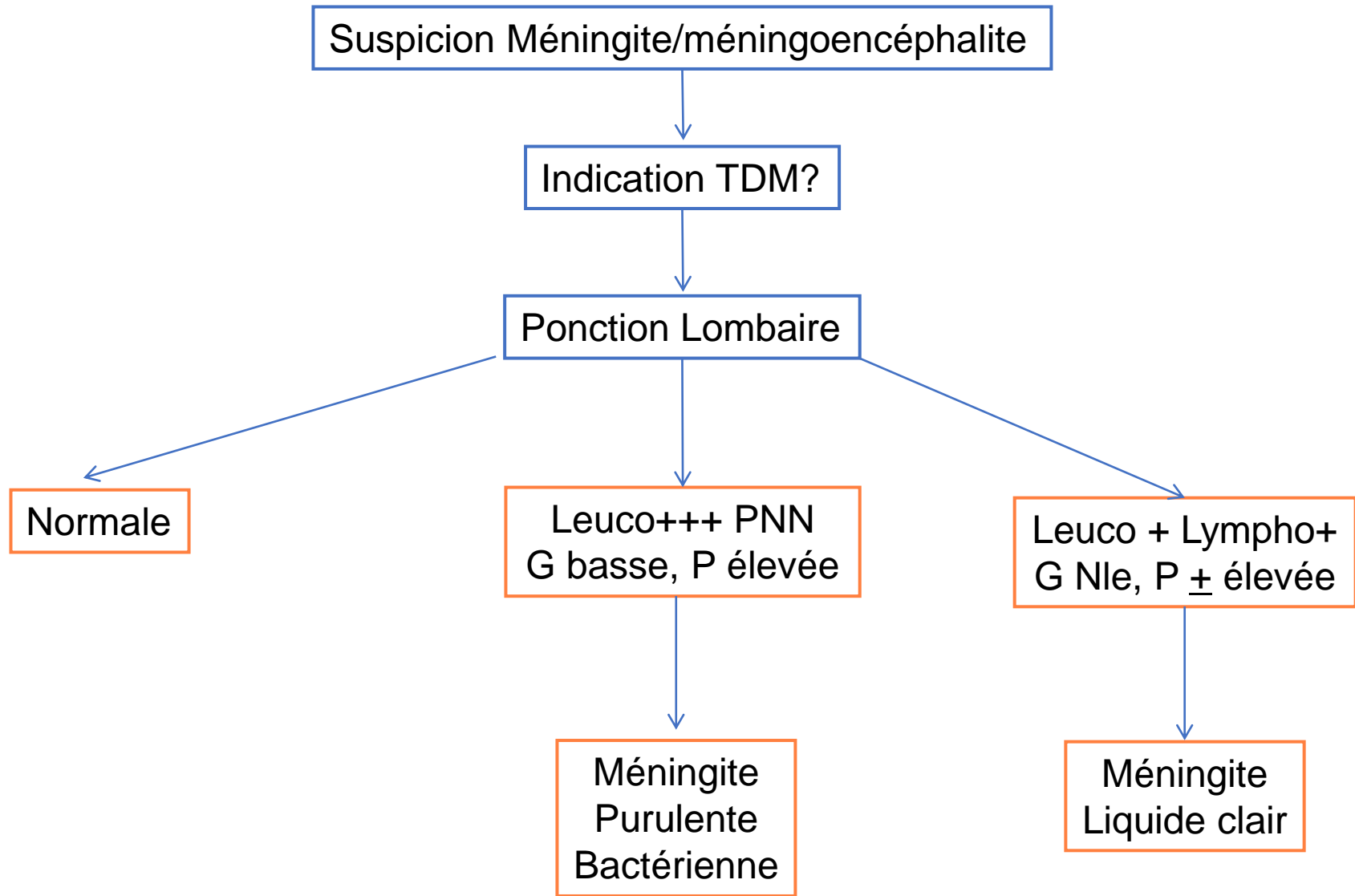
GB dans le LCS $\geq 5/$ mm³

Anomalies du parenchyme cérébral (lésions nouvelles ou évolutives) évocatrices d'encéphalite à l'imagerie

Anomalies à l'EEG évocatrices d'encéphalite et non attribuables à une autre cause

Venkatesan,
Lancet 2019





Encéphalite confirmée si:

- Identification pathogène (PCR le plus souvent) connu pour être associé à encéphalite
- Identification d'une pathologie auto-immune associée à encéphalite
- Biopsie cérébrale retrouvant une inflammation

Algorithme initial de diagnostic chez adulte

LCR (20 cc + congel+ PO)

- Gram/cultures
- PCR: HSV/VZV, enterovirus
- Crypto Ag ou encre de Chine - VDRL
- Bandes oligoclonales et IgG index

Serum

- Hémocultures
- HIV, syphilis
- Serum au congelateur

Imagerie

- IRM > CT, RP et TDM thorax
- EEG

Autres prélèvements en fonction du contexte
(Biopsie cutanée, LBA, prélèvement gorge...)

Algorithme initial de diagnostic chez adulte

IDP?

CMV, HHV6
HIV, JC Virus
Toxo
M. Tuberculosis
Champignons

Facteurs géographiques

Arbovirus+++
Trypanosomiase
.....

Saison et exposition

- Infection Tick-borne, *Bartonella*, Rabies,
arbovirus, *Naegleria fowleri*....

Signes et symptômes spécifiques

Ex: signes respiratoires *M. pneumoniae*

Les incontournables


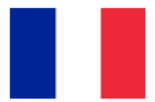



- IRM

- Plus sensible et spécifique que TDM
- Séquences particulières peuvent détecter anomalies précoces
- Caractère très évocateurs de certaines images (HSV)
- Permet d'évaluer diagnostics différentiels

- EEG

- Rarement utile au diagnostic
- Principal bénéfice: éliminer pathologie épileptique partielle
- A réaliser dans la quasi-totalité des encéphalites

Principaux pathogènes

Auteur, pays	n	%réas	Predominants	Cause x
Glaser CA et al. 2006 	1570	58	HSV1, enterovirus, <i>M. pneumoniae</i>	63
Stahl JP et al 2009 	253	29	HSV1, VZV, TB	48
Granerod J et al. 2010 	203	??	HSV1, autoimmune	37
Parpia et al. 2016 	6463	??	Viral	51
Thakur KT et al. 2013 	103	Tous	HSV1, VZV, autoimmune	47

Cohorte rétrospective à Bichat Claude Bernard

CAUSES	N = 279
INFECTIONS	149(53%)
BK	65 (23%)
HSV1	40 (14%)
VZV	14 (5%)
<i>Listeria</i>	19 (7%)
Autres	11 (4%)
AUTO-IMMUNE	41 (15%)
ADEM	24 (9%)
Anti-NMDAR	6 (2%)
Autres	11 (4%)
INCONNU	89 (32%)



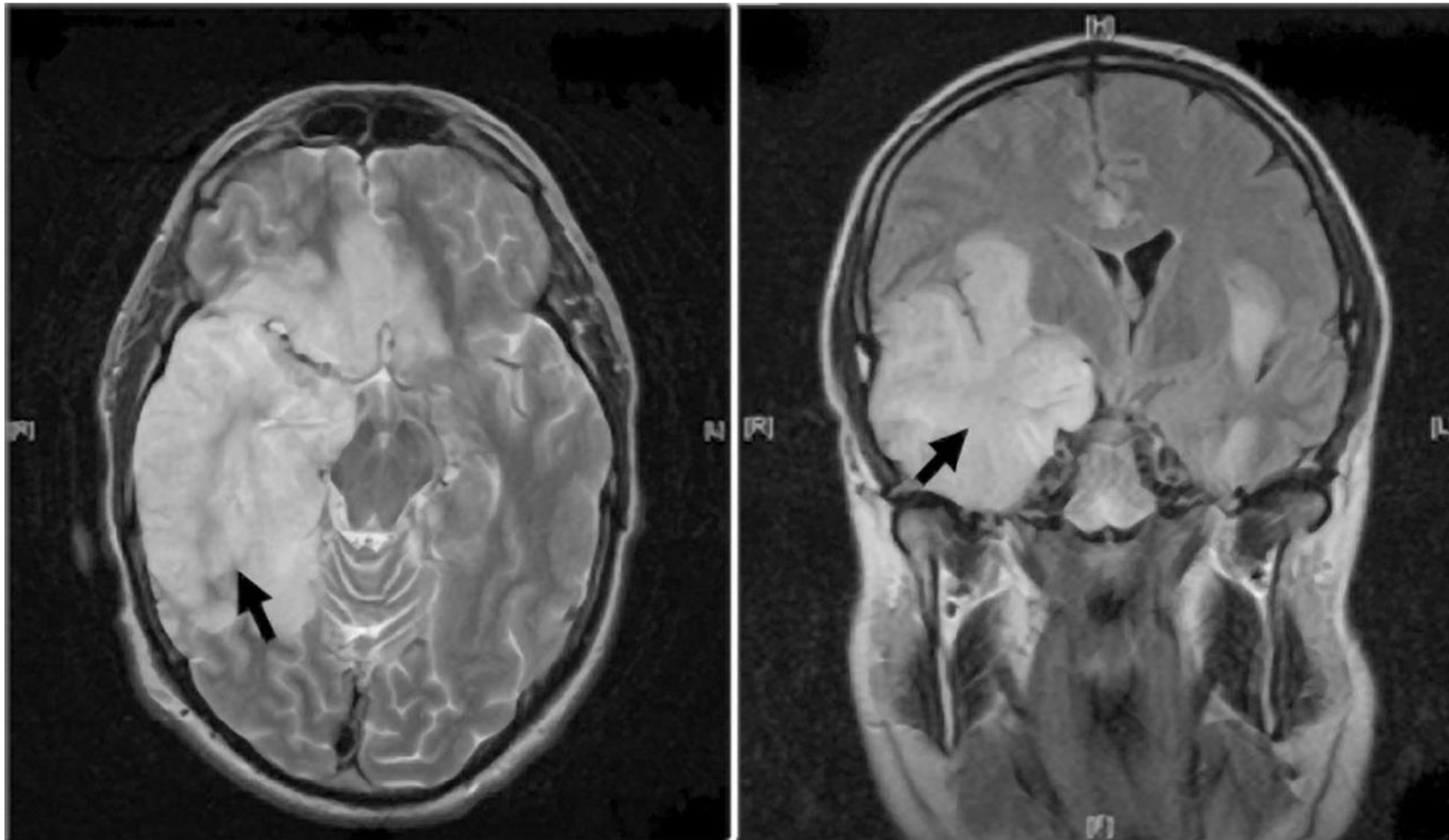
Evolution étiologies encéphalites en France

Criteria	2007 Study <i>n</i> = 222	ENCEIF cohort <i>n</i> = 494	<i>P</i> -value
Age (median, IQR)	59 (39–72)	65 (47–75)	0.006
Sex ratio	1.6	1.6	ns
Comorbidities (<i>n</i> , %)	72 (32.7%)	112 (23.3%)	0.005
Immunodeficiency (<i>n</i> , %)	24 (10.8%)	59 (11.9%)	ns
Duration of hospital stay (in days, median, IQR)	21 (14–34)	23 (17–34)	ns
ICU admission (<i>n</i> , %)	111 (50%)	205 (42%)	0.04
Case fatality rate	12%	8%	0.06
Cases with an identified cause	117 (52.7%)	324 (65.7%)	0.001
Cause of encephalitis (<i>n</i> , %)			
HSV	54 (24.3%)	132 (26.8%)	ns
VZV	17 (8%)	65 (13.2%)	0.03
<i>Listeria monocytogenes</i>	13 (6%)	23 (5%)	ns
<i>Mycobacterium tuberculosis</i>	19 (8.6%)	11 (2.2%)	0.0001
TBEV	3 (1.4%)	26 (5.3%)	0.01
Arboviral infections (<i>n</i> , %)	6 (2.7%)	35 (7.1%)	0.02
Vector-borne infections (<i>n</i> , %)	8 (3.6%)	40 (8.1%)	0.03
Zoonotic infections (<i>n</i> , %)	19 (9%)	67 (14%)	0.06
Vaccine-preventable infections (<i>n</i> , %)	39 (18%)	118 (24%)	0.06
Duration of ACV treatment in HSV patients (in days, mean, range)	20.1 (4–42)	17.7 (1–30)	0.004

Encéphalite Herpétique HSV1

- 1ere cause d'encéphalite infectieuse
- Le plus souvent pas de terrain favorisant
- 2 pics de fréquence: < 20 ans et 50-70 ans
- Tableau d'encéphalite aiguë fébrile le plus souvent
- Atteinte temporale le plus souvent à l'imagerie
- Traitement par Aciclovir IV pendant 14 jours

Méningo-encéphalite herpétique





Etude rétrospective, 47 Réanimations, 259 patients

Table 3 Multivariate analysis of factors associated with poor functional outcome (mRS > 2)

Variables	Odds ratio	95% CI	P value
Age, years			
< 50	1	–	0.03
≥ 50 and < 65	2.00	[0.92; 4.36]	–
≥ 65 and < 75	2.06	[0.89; 4.78]	–
≥ 75	4.81	[1.72; 13.5]	–
Body temperature ≥ 38.3 °C	2.21	[1.18; 4.16]	0.01
Invasive mechanical ventilation	2.21	[1.21; 4.03]	0.01
MRI brain lesions > 3 lobes	3.04	[1.35; 6.81]	<0.01
Direct ICU admission (versus initial admission to the hospital wards)	0.52	[0.28; 0.95]	0.03

ORIGINAL

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



Romain Sonnevile
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
Female 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)
Spinal cord symptoms, n (%)	11 (55)

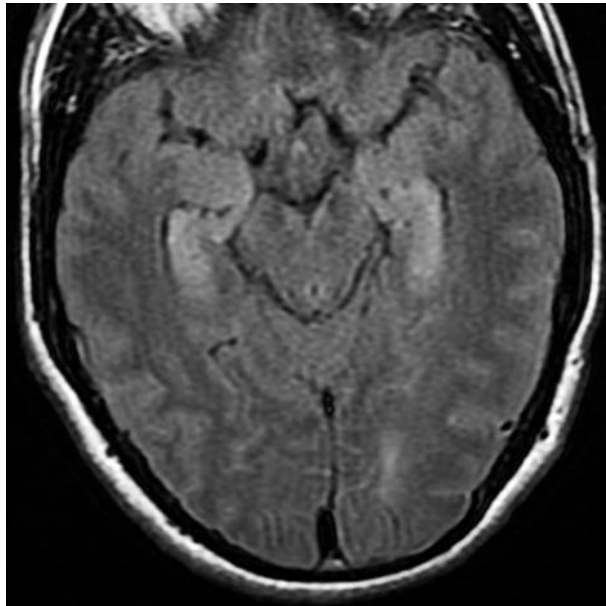
Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies



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

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



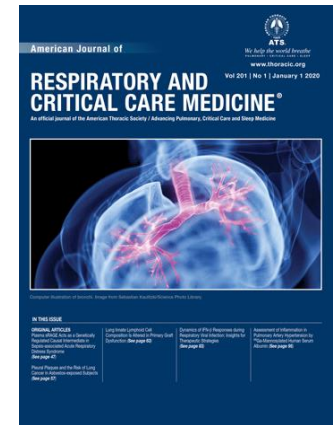
Brain MRI

Total with abnormal findings	55
Medial temporal lobes	22
Cerebral cortex	17
Cerebellum	6
Brainstem	6
Basal ganglia	5
Contrast enhancement in cortex, meninges, basal ganglia	14
Other†	8

IRM Normale chez 45% des patients

Anti-N-Methyl-D-Aspartate Receptor Encephalitis in Adult Patients Requiring Intensive Care

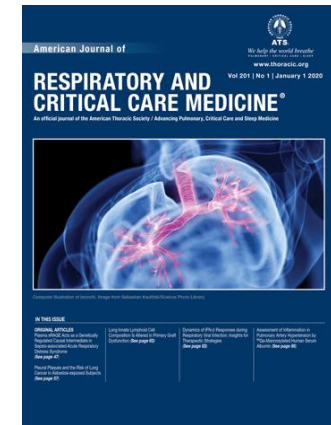
Etienne de Montmollin¹, Sophie Demeret², Noëlle Brulé³, Marie Conrad⁴, Frédéric Dailler⁵, Nicolas Lerolle⁶, Jean-Christophe Navellou⁷, Carole Schwebel⁸, Mikaël Alves⁹, Martin Cour¹⁰, Nicolas Engrand¹¹, Jean-Marie Tonnelier¹², Eric Maury¹³, Stéphane Ruckly¹⁴, Géraldine Picard¹⁵, Véronique Rogemond¹⁵, Éric Magalhaes¹⁶, Tarek Sharshar¹⁷, Jean-François Timsit^{14,16}, Jérôme Honnorat^{15,18*}, and Romain Sonnevile^{16,19*} on behalf of the ENCEPHALITICA Study Group[‡]



Variable	N= 77 patients
Age, years	24 (20-31)
Female sex	68/76 (89%)
GCS, median (IQR)	11 (7-13)
Seizures / status epilepticus	30 (76%)
CSF WBC, n / mm ³	36 (9-112)
CSF protein levels, g/l	0.4 (0.3-0.6)
Normal CT scan	49/62 (95%)
Normal brain MRI	56 / 75 (75%)
Presence of tumor	36/76 (47)
Delay between ICU admission and tumor resection, median (IQR) days	24 (14-51)

Anti-N-Methyl-D-Aspartate Receptor Encephalitis in Adult Patients Requiring Intensive Care

Etienne de Montmollin¹, Sophie Demeret², Noëlle Brulé³, Marie Conrad⁴, Frédéric Daillet⁵, Nicolas Lerolle⁶, Jean-Christophe Navellou⁷, Carole Schwebel⁸, Mikaël Alves⁹, Martin Cour¹⁰, Nicolas Engrand¹¹, Jean-Marie Tonnelier¹², Eric Maury¹³, Stéphane Ruckly¹⁴, Géraldine Picard¹⁵, Véronique Rogemond¹⁵, Éric Magalhaes¹⁶, Tarek Sharshar¹⁷, Jean-François Timsit^{14,16}, Jérôme Honnorat^{15,18*}, and Romain Sonnevile^{16,19*} on behalf of the ENCEPHALITICA Study Group[‡]



Variable	Odds Ratio (95% CI)	p
First-line immunotherapy		0.008
Late immunotherapy	Reference	
Early* IgIV only	3.33 (0.66–16.79)	0.14
Early* steroid administration only	4.96 (0.76–32.23)	0.09
Early* combined immunotherap administration	16.16 (3.32–78.64)	<0.001
Second-line immunotherapy		0.01
White blood cells in first CSF		
>50 cells/mm ³	Reference	0.04
5–50 cells/mm ³ ,	3.97 (1.16–13.65)	0.03
<5 cells/mm ³	9.83 (1.07–90.65)	0.04

Early is defined as administration of treatment before ICU admission or after 8 days of ICU admission

Traitement à discuter en cas d'encéphalite anti-NMDA

TABLE 5. Acute Immunotherapies for Anti-N-Methyl-D-Aspartate Receptor Encephalitis in the ICU (2, 38, 39)

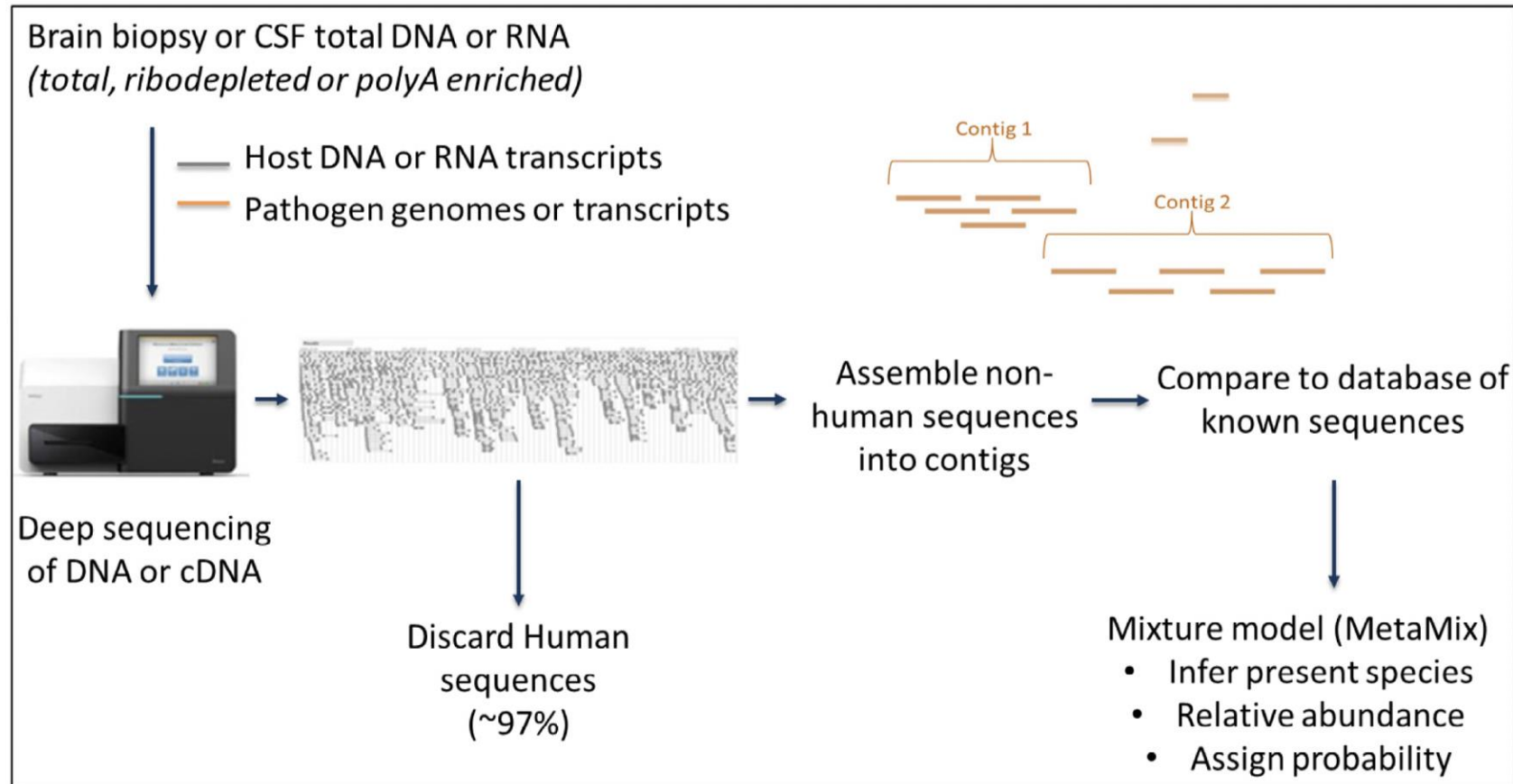
Agent	Dosage	Adverse Effects	Pearls
Glucocorticoids	Acute: methylprednisolone 1 g daily × 3–5 d Maintenance: prednisone 60–80 mg (≈ 1 mg/kg) daily, followed by prolonged taper	Infection, weight gain, hyperglycemia, hypertension, osteoporosis, cataracts, insomnia, psychosis, myopathy, peptic ulcers	Maintenance indication and duration not defined
Plasmapheresis (PLEX)	30–40 mL/kg (1–1.5 plasma volumes)/cycle Typically five cycles per treatment (may be repeated)	Hypotension, coagulopathy (replace factors with fresh frozen plasma)	Avoid angiotensin-converting inhibitors during PLEX Schedule concomitant drugs to minimize removal
IVIg	0.4 g/kg daily × five doses (may be repeated)	Infusion reactions, aseptic meningitis, deep vein thrombosis, kidney injury	Premedicate to minimize infusion reactions May cause positive anti-HBV antibodies (product specific)
Rituximab	375 mg/m ² weekly × 4 wk	Infusion reactions, cytopenias, infection	Premedicate to minimize infusion reactions Obtain baseline HBV status (preferably before IVIg); if positive, consider antiviral prophylaxis to minimize risk of reactivation
Cyclophosphamide	750 mg/m ² every 4 wk (may delay based on blood counts) × 4–6 mo	Nausea, vomiting, myelosuppression, infection, malignancy, infertility	Infertility less likely in this treatment scenario (higher risk if cumulative dose > 50 g) Low risk of cystitis with low doses Monitor for leukopenia
Bortezomib	1.3 mg/m ² on 21-d cycle (given on days 1, 4, 8, and 11) × 1–6 cycles	Infusion reactions, cytopenias, neuropathies, heart failure exacerbation, infection, herpes reactivation	Premedicate to minimize infusion reactions Monitor for cytopenias If history of herpes simplex virus, consider antiviral prophylaxis to minimize risk of reactivation Consider subcutaneous injection to minimize risk of adverse events

HBV = hepatitis B virus, IVIG = IV immunoglobulin, PLEX = plasma exchange.

Encephalitis diagnosis using metagenomics: application of next generation sequencing for undiagnosed cases



Julianne R. Brown ^{a,*}, Tehmina Bharucha ^{b,c}, Judith Breuer ^{a,c}



Pronostic encéphalites à 3 ans

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)
<i>M. tuberculosis</i>	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).

Encéphalite en réanimation: facteurs associés au décès

Variables	Adj OR	95%CI	p
Statut fonctionnel mauvais	6.34	1.98-21.75	0.002
Température°C	0.72	0.53-0.97	0.03
Glasgow Coma score < 8	7.09	3.06-17.03	< 0.001
Délai admission hopital-réa, j	1.04	1.01-1.07	0.008
Pneumonie inhalation	4.02	1.47-11.03	< 0.001
Proteinorachie, g/L	1.57	1.17-2.11	< 0.001

Virus émergents

Virus	Zones géographiques
West Nile	Monde
Toscana	Italie, Espagne, Portugal, France
Encéphalite Japonaise	Asie
Entérovirus 71	Asie, Australie
Rage	Asie, Afrique, US
Chikungunya	Réunion, Inde, Indonésie
Nipah et Hendra	Australie, Asie
Lyssavirus	Australie, Europe

Flavivirus Encephalitis

Tom Solomon, M.D., Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

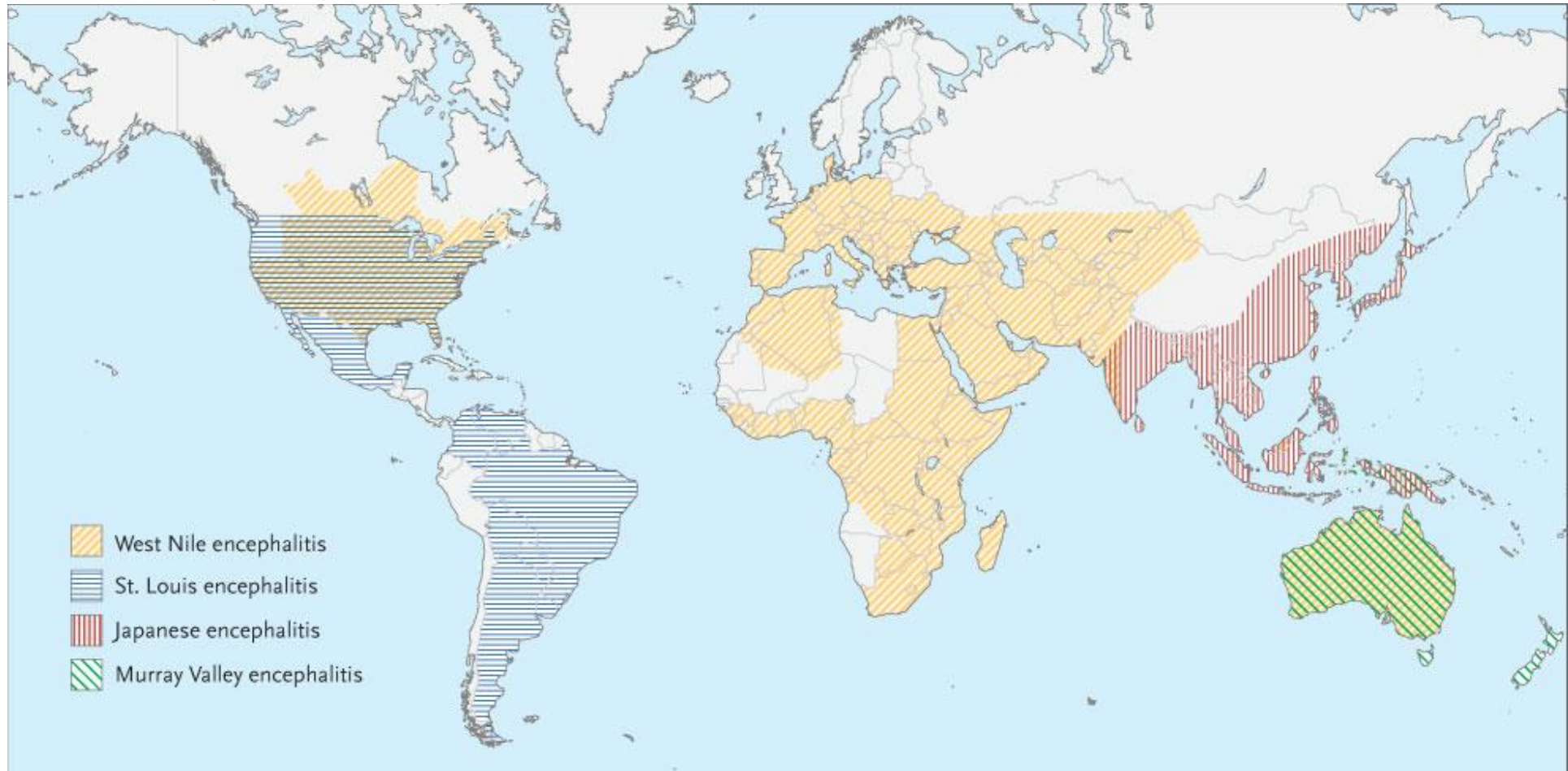
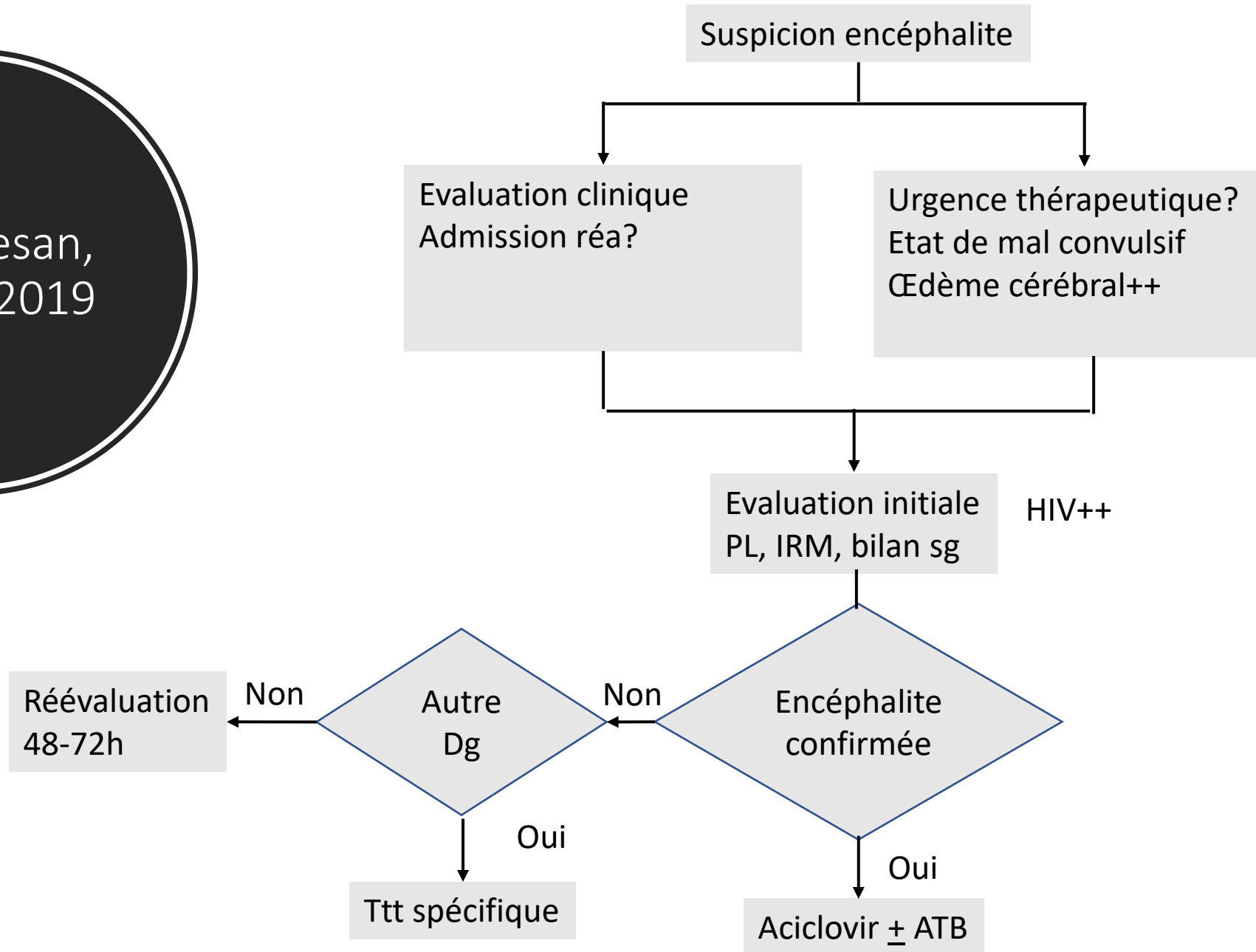


Figure 1. Approximate Global Distribution of Medically Important Members of the Japanese Encephalitis Serogroup of Flaviviruses. This group consists of St. Louis encephalitis, Japanese encephalitis, Murray Valley encephalitis, and West Nile viruses (including Kunjin virus, which is a subtype of West Nile virus found in Australia).



Conclusions

1. En France, HSV, VZV, Listeria et BK sont les 4 pathogènes les plus fréquents
2. Les recommandations et algorithmes récents aident à la prise en charge
3. L'IRM est un élément central du diagnostic
4. Encéphalites auto-immunes mieux connues
5. NGS technique d'avenir?