

# Abcès cérébraux

## Prise en charge médicale

**Romain Sonnevile**

Réanimation médicale et infectieuse

Hôpital Bichat-Claude Bernard, APHP, Paris

INSERM U1148

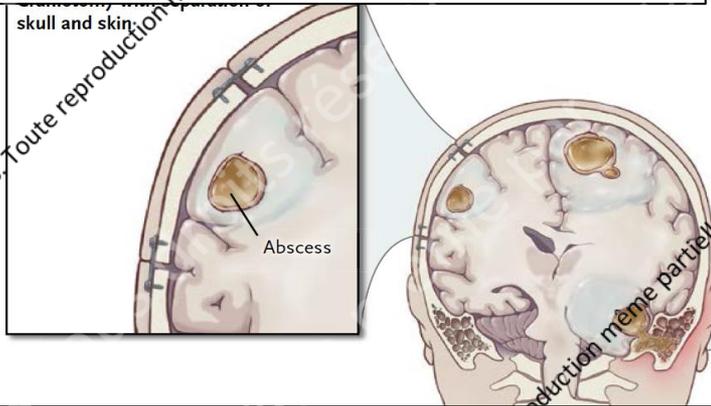
# Introduction

- **Infection focale** du SNC, de **symptomatologie** et de **gravité très variables**
- **Etiologies variées** : pyogènes, mycobactéries, champignons, parasites
- **Pathologie rare** :
  - Incidence 0.3-0.9 cas / 100 000 personnes / an
  - Plus importante chez immunodéprimés
- **Diagnostic et pronostic améliorés** par :
  - Neuroimagerie
  - Diagnostic moléculaire
  - Neurochirurgie

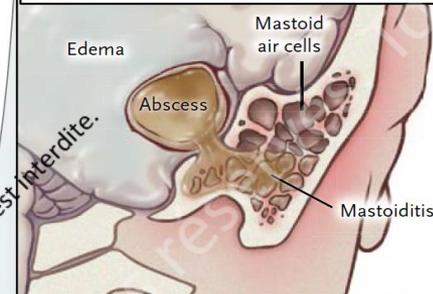
# Physiopathologie

Infection par contiguïté: 50%

Traumatisme SNC, neurochirurgie



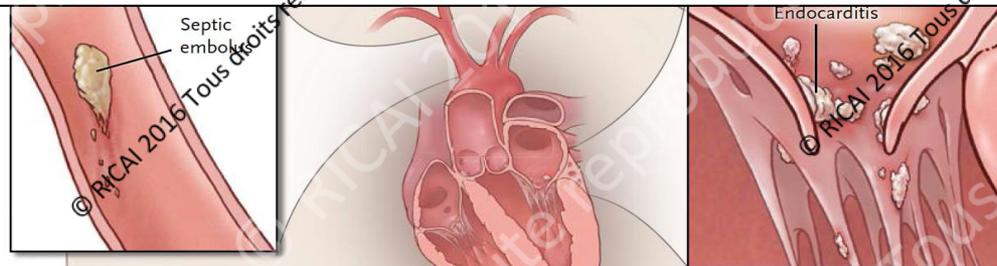
Infection ORL



Inconnue  
????  
15-20%

**Dissémination hémato-gène: 30-35%**

(endocardite, cardiopathie congénitales, foyers dentaires ou pulmonaires chroniques, shunts D-G, infections cutanées ....)



# Bacterial Brain Abscesses: A Retrospective Study of 94 Patients Admitted to an Intensive Care Unit (1980 to 1999)

Pierre Tattevin, MD, Fabrice Bruneel, MD,  
Bernard Clair, MD, François Lellouche, MD,  
Thomas de Broucker, MD, Sylvie Chevret, MD,  
Jean-Pierre Bédos, MD, Michel Wolff, MD,  
Bernard Régnier, MD

Category	Number of Patients (%)	Comments
<b>Streptococcus</b>	53 (56)	<i>Streptococcus milleri</i> (n = 15) <i>Streptococcus anginosus</i> (n = 4) <i>Streptococcus constellatus</i> (n = 3) <i>Streptococcus intermedius</i> (n = 3) Anaerobic streptococci (n = 10) <i>Streptococcus pneumoniae</i> (n = 5) Other <i>Streptococcus</i> organisms (n = 23)
<b>Non-<i>Streptococcus</i> anaerobes</b>	15 (16)	<i>Bacteroides</i> (n = 5) <i>Actinomyces</i> (n = 4) <i>Fusobacterium</i> (n = 4)
<b>Staphylococcus</b>	12 (13)	<i>Staphylococcus aureus</i> (n = 10) Methicillin resistant (n = 2) Methicillin sensitive (n = 8) <i>Staphylococcus epidermidis</i> (n = 2)
Enterobacteriaceae	8 (9)	<i>Klebsiella</i> (n = 4), <i>Proteus</i> (n = 2) <i>Escherichia coli</i> (n = 1) <i>Enterobacter cloacae</i> (n = 1)
<i>Listeria monocytogenes</i>	8 (9)	
Others	4 (4)	<i>Acinetobacter</i> (n = 3) <i>Nocardia asteroides</i> (n = 1)
<b>No documentation*</b>	16 (17)	
<b>Polymicrobial brain abscess</b>	22 (23)	Documented by abscess aspiration in 17 patients

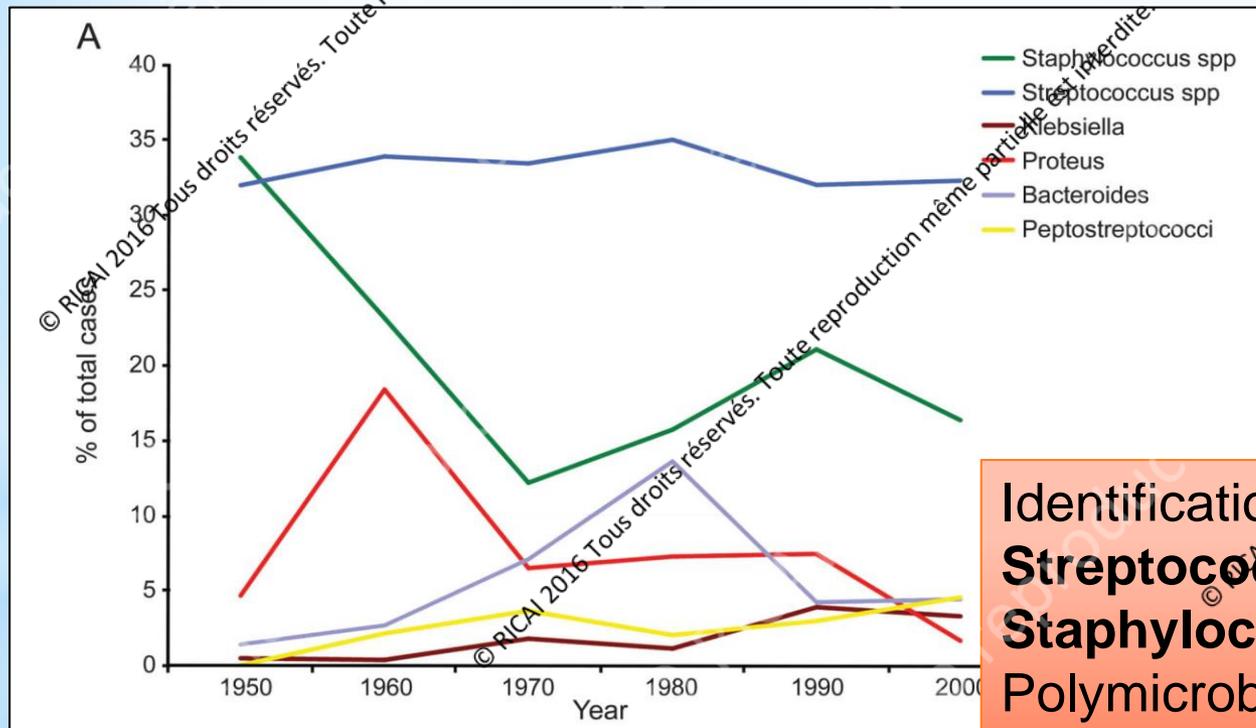
\* Diagnosis of brain abscess based on the favorable evolution of focal brain lesions on computed tomographic scan during antibacterial treatment.

# Clinical characteristics and outcome of brain abscess

Systematic review and meta-analysis

n= 9699 patients

123 études (monocentriques 90%, rétrospectives 94%)



Identification pathogène : 68%  
**Streptocoque : 34%**  
**Staphylocoque : 18%**  
Polymicrobien : 23%

# Facteurs prédisposants

**Table 1. Predisposing Conditions and Microbial Isolates in Patients with Brain Abscess.\***

Predisposing Condition	Common Microbial Isolates
<b>Contiguous spread of bacteria</b>	
Penetrating trauma or neurosurgery	<i>Staphylococcus aureus</i> , <i>S. epidermidis</i> , streptococcus species (anaerobic and aerobic), Enterobacteriaceae, clostridium species†
Otitis media or mastoiditis	Streptococcus species (anaerobic and aerobic), bacteroides and prevotella species, Enterobacteriaceae†
Paranasal sinusitis	Streptococcus species (anaerobic and aerobic), bacteroides species, Enterobacteriaceae, <i>S. aureus</i> , haemophilus species†
<b>Hemogenous spread of bacteria</b>	
Lung abscess, empyema, bronchiectasis	Fusobacterium, actinomyces, bacteroides, prevotella, nocardia, streptococcus species
Bacterial endocarditis	<i>S. aureus</i> , streptococcus species
Congenital heart disease	Streptococcus and haemophilus species
Dental infection	Mixed infection with fusobacterium, prevotella, actinomyces, bacteroides, and streptococcus species (anaerobic and aerobic)

\* HIV denotes human immunodeficiency virus.

† The Enterobacteriaceae include *Escherichia coli* and enterobacter, klebsiella, proteus, and salmonella species.

# Facteurs prédisposants

Etiologie non bactérienne = 90% des cas !

**Table 1. Predisposing Conditions and Microbial Isolates in Patients with Brain Abscess.\***

Predisposing Condition	Common Microbial Isolates
Immunocompromise	
HIV infection	<i>Toxoplasma gondii</i> , nocardia and mycobacterium species, <i>Listeria monocytogenes</i> , <i>Cryptococcus neoformans</i>
Neutropenia	Aerobic gram-negative bacilli, aspergillus species, Mucorales, candida and scedosporium species
Transplantation	Aspergillus and Candida species, Mucorales, scedosporium species, Enterobacteriaceae, nocardia species, <i>T. gondii</i> , <i>Mycobacterium tuberculosis</i>

# Clinical characteristics and outcome of brain abscess

Systematic review and meta-analysis

Manifestations cliniques non spécifiques

Installation subaiguë, fonction taillé / localisation de l'abcès

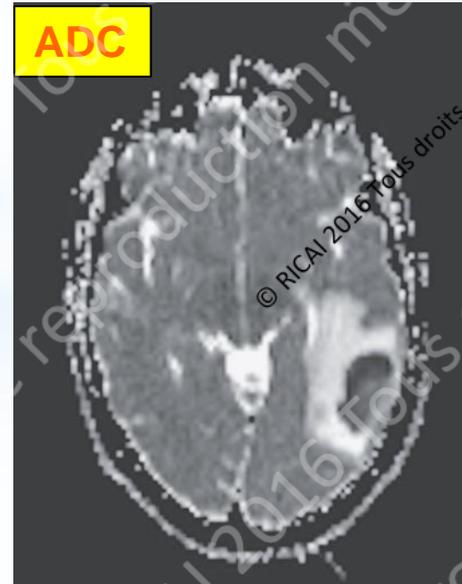
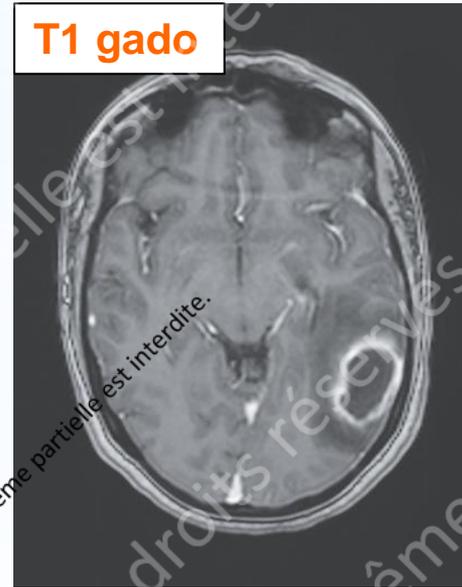
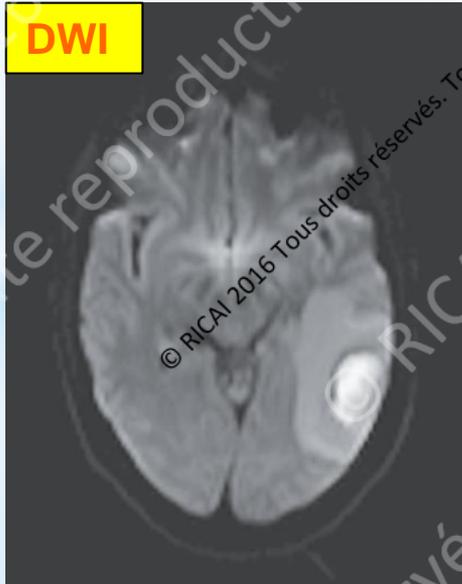
Symptoms and signs	
Headache	4,526/6,575 (69)
Nausea/vomiting	1,993/4,286 (47)
Fever	3,718/6,970 (53)
Altered consciousness	3,207/7,479 (43)
Neurologic deficits	2,996/6,241 (48)
Seizures	1,647/6,581 (25)
Nuchal rigidity	1,465/4,629 (32)
Papilloedema	845/2,428 (35)
Mean duration of symptoms <sup>f</sup>	8.3 d
Triad of fever, headache, focal neurologic deficits	131/668 (20)



Homme 57 ans, troubles du comportement « isolés »  
Abscess frontal droit unique  
Œdème périlésionnel  
Effet de masse  
Déviation des structures médianes

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# Diagnostic : imagerie cérébrale



# Can diffusion-weighted imaging be used to differentiate brain abscess from other ring-enhancing brain lesions? A meta-analysis

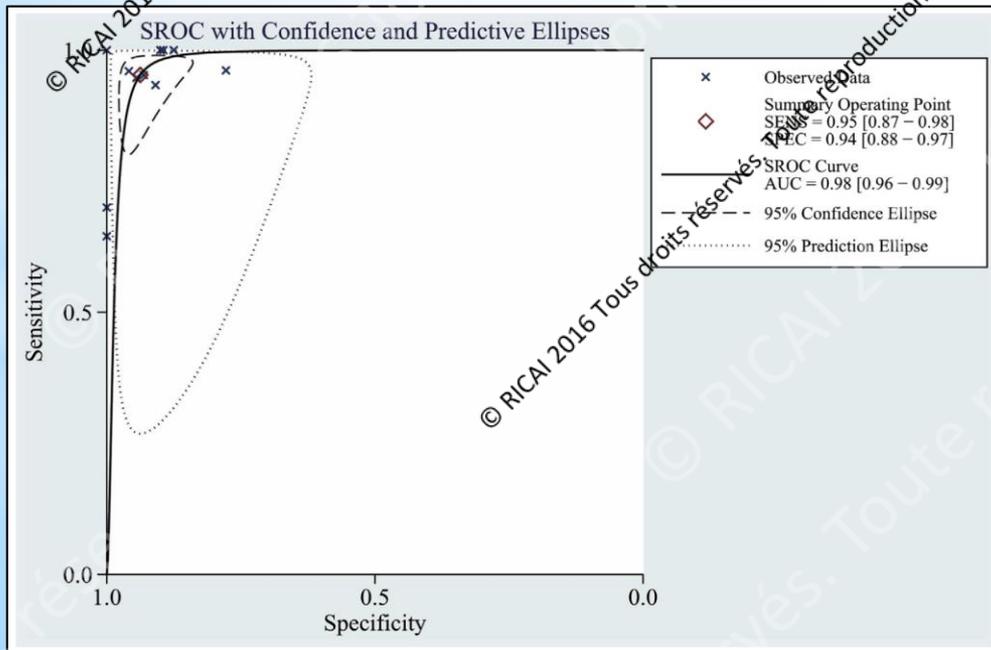
Méta-analyse 2014

N=504 patients, 11 études

**IRM de diffusion (DWI) pour le dg d'abcès cérébral**

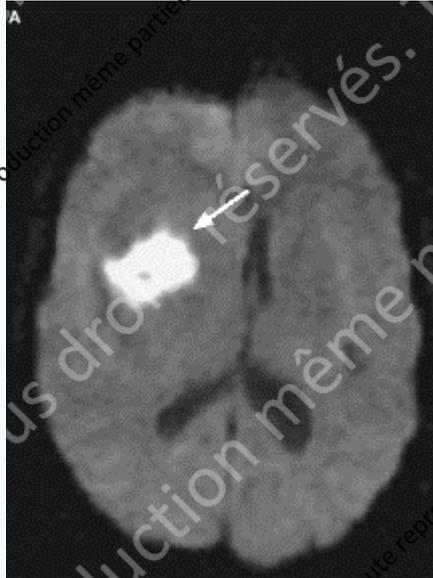
Sensibilité 0.95 (95% CI 0.87-0.98)

Spécificité 0.94 (95% CI 0.88-0.97)

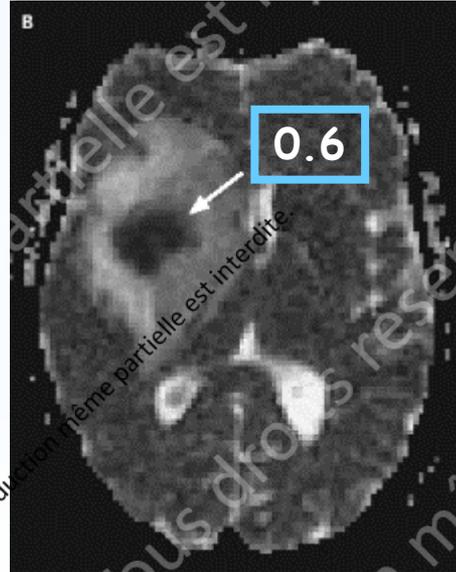


Abcès pyogènes

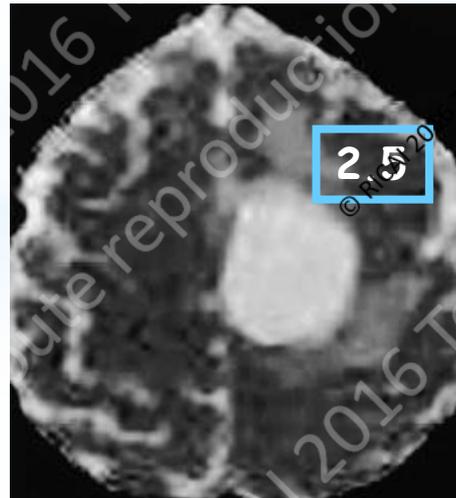
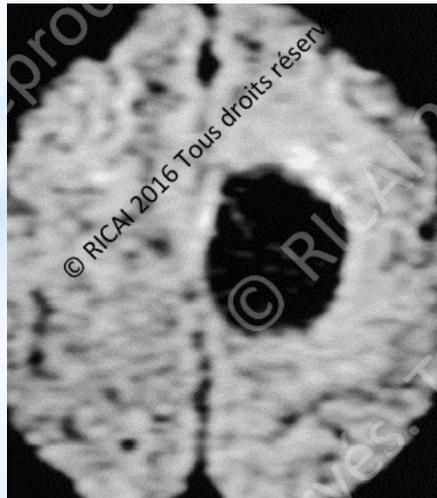
DWI



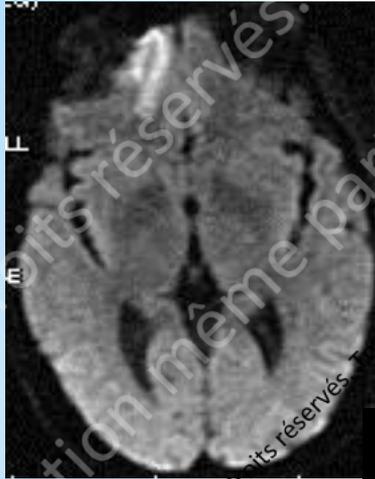
ADC



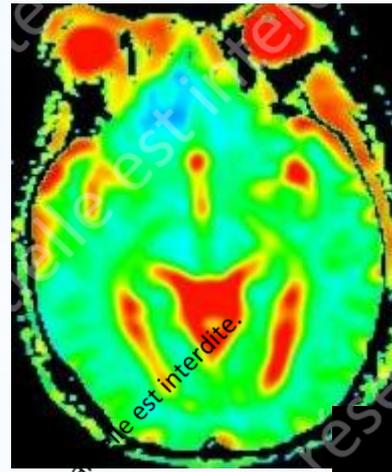
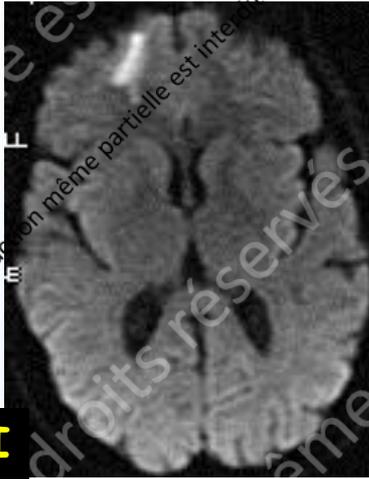
Tumeur cérébrale



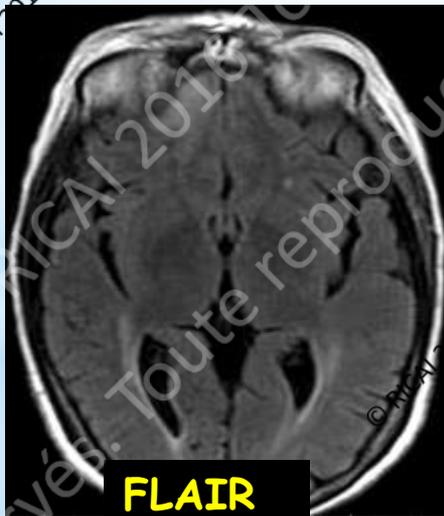
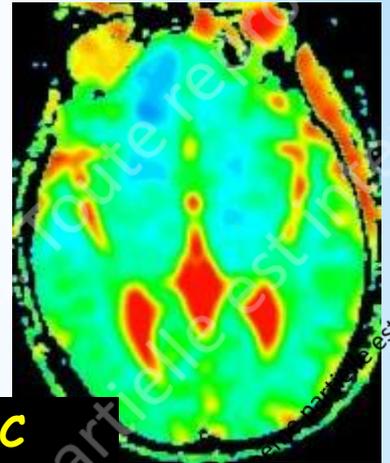
# Anomalies précoces, phase « pré-suppurative »



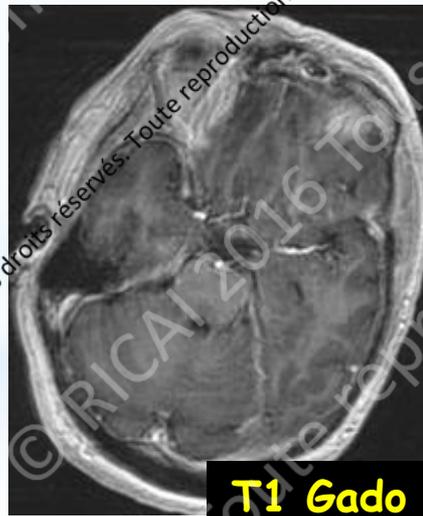
**DWI**



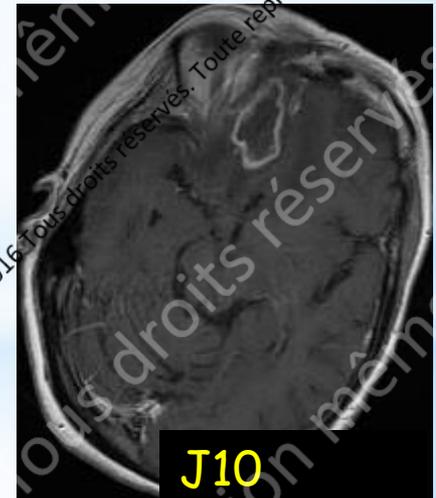
**ADC**



**FLAIR**



**T1 Gado**



**J10  
Abcès**

# Objectifs de prise en charge

## « Un exemple de prise en charge pluridisciplinaire »

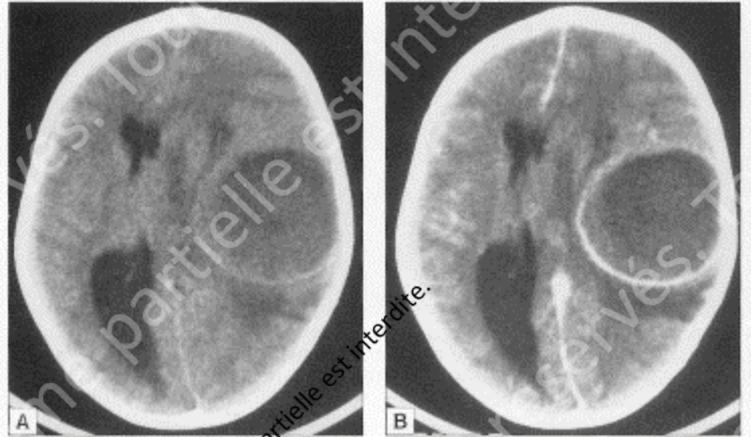
1. Traitement symptomatique, réanimation
2. Traitement de l'œdème cérébral et de l'effet de masse
3. Identification microbiologique
4. Contrôle de l'infection
5. Limiter les séquelles neurologiques



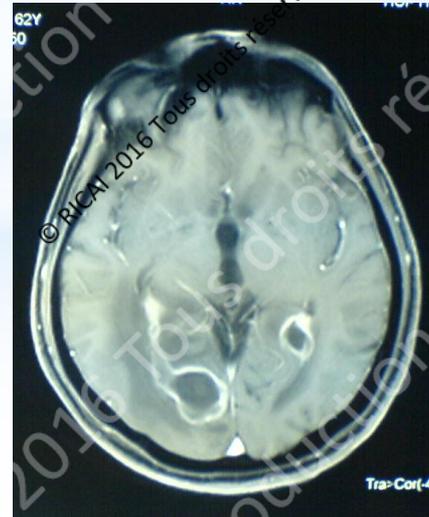
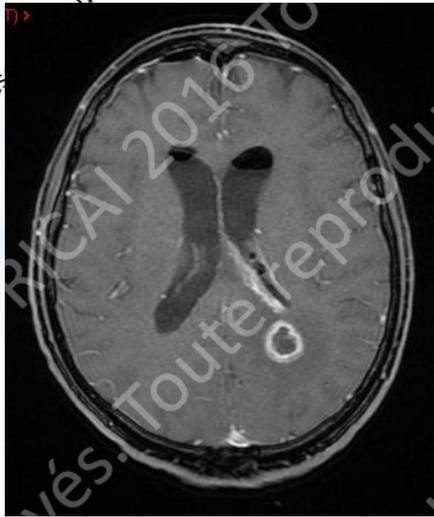
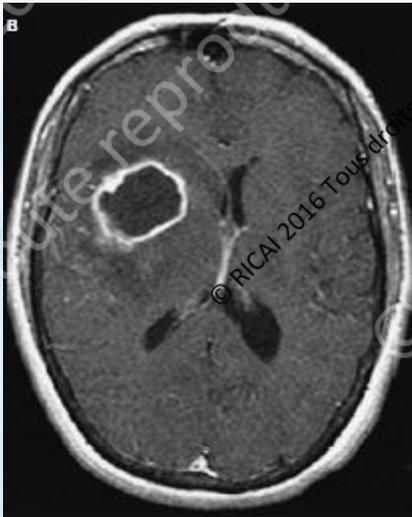
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Effet de masse ?



Risque de rupture intraventriculaire ?





# En pratique ...



## Ponction lombaire uniquement si

- suspicion clinique de méningite
- ou rupture ventriculaire
- **En l'absence de CI classiques +++**
  - déplacement structures médianes
  - Troubles de l'hémostase



Foyer  
ORL ?  
Dentaire ?



TDM  
TAP

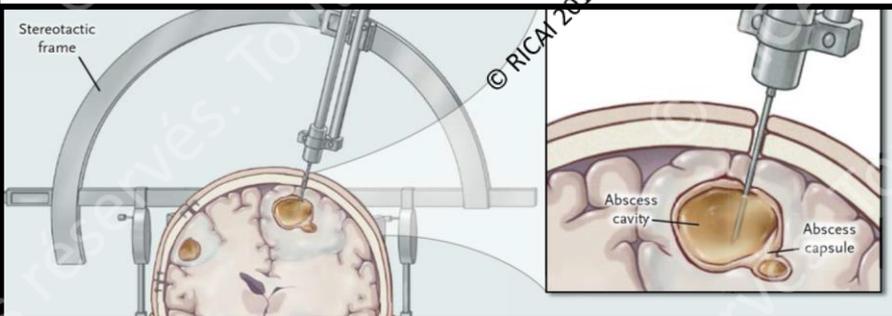


ETT/ETO  
....



Hémocultures

## Ponction-aspiration neurochirurgicale



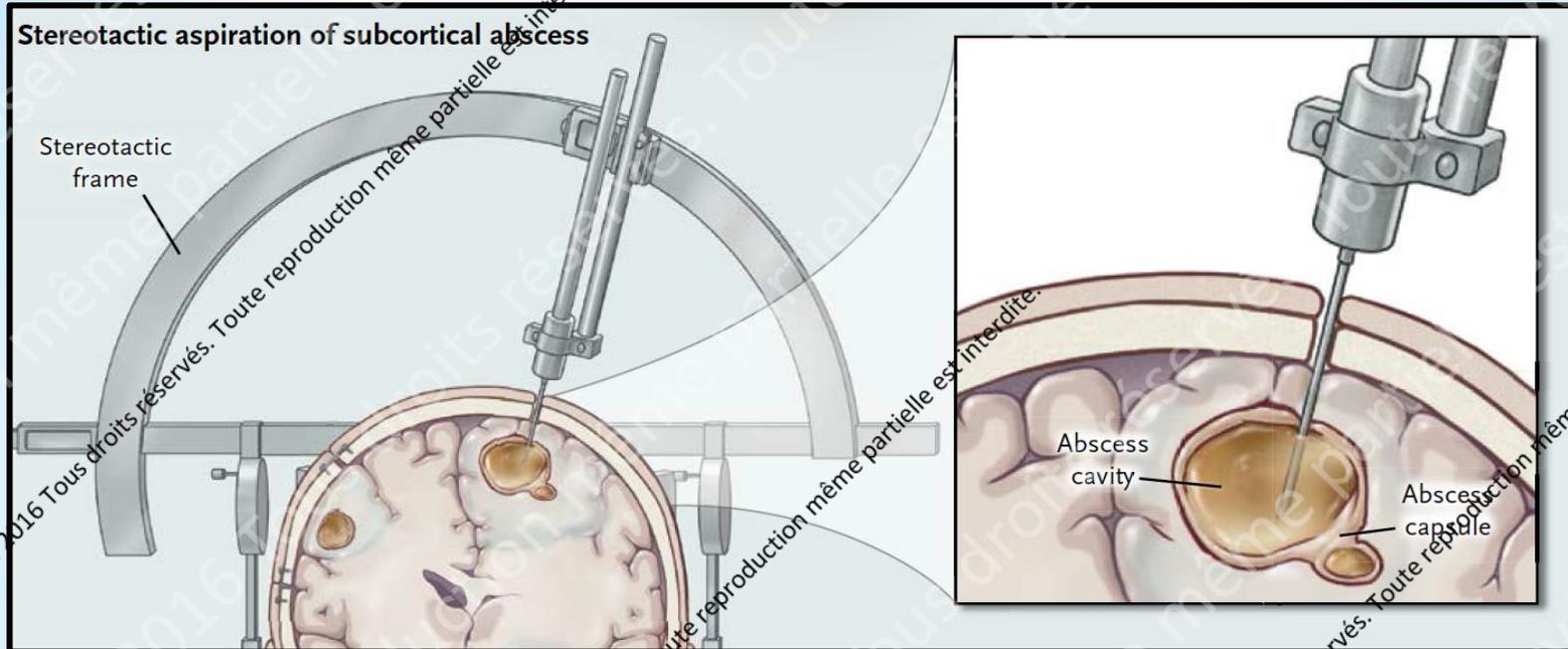
Gram  
Cultures aéro anaérobies  
Mycobactéries ? Nocardia ?  
Cultures fongiques ?  
PCR *Toxoplasma* ?  
16s ribosomal DNA sequencing ?

# Clinical characteristics and outcome of brain abscess

Systematic review and meta-analysis

<b>Blood investigation</b>	
Leukocytosis	1,366/2,273 (60)
Elevated CRP	196/316 (60)
Elevated ESR	311/434 (72)
Positive blood culture	135/484 (28)
<b>CSF investigation</b>	
LP	1,286/1,298 (99)
Normal CSF	96/588 (16)
Pleocytosis	758/1,063 (71)
Elevated CSF protein	222/381 (58)
Culture positive	263/1,108 (24)
Clinical deterioration attributed to LP	76/1,030 (7)

# Ponction-aspiration neurochirurgicale



Diagnostic de certitude  
Identification microbiologique

Drainage, réduction inoculum

Diminution effet de masse

=> Indication très large, dès que lésion > 25 mm ?

(Sauf qq cas particulier(s) ....)

# Clinical characteristics and outcome of brain abscess

Systematic review and meta-analysis

Treatment	
Operation	6,728/7,697 (87)
Aspiration <sup>a</sup>	3,902/5,894 (66)
Excision <sup>a</sup>	1,343/5,167 (26)
Aspiration and excision <sup>a</sup>	342/2,497 (14)
Stereotactic operation	390/1,809 (22)
Reoperation	882/2,830 (31)
Medical treatment	637/5,471 (12)

# Antibiothérapie

## Quand ?

Rapidement, mais **si possible après ponction neurochirurgicale +++**

Ne pas attendre si altération conscience, HC+, sepsis .....

## Molécules ?

Aucun RCT, études monocentriques, rétrospectives....

## Désescalade ?

Oui, une fois le(s) germe(s) identifié(s)

## Durée ?

IV 6-8 semaines si drainage

Parfois + long..... (*Nocardia*, *Actinomyces*, champignons.....)

## Relai per os ?

Oui, selon molécules

Rifampicine, FQ, TMP-SMX, métronidazole, linézolide



# Antibiothérapie initiale

## PATIENT IMMUNOCOMPÉTENT

### Infection « communautaire » (contiguïté / orig. indéterminée)

Céfotaxime : 2g x 6 / jour IVL

(ou ceftriaxone 2g x 2 / j IVL)

+

Métronidazole : 500 mg x 3 (ou x 4) / j IVL

### Infection « post-opératoire ou post-traumatique »

Méropénème : 2g x3 / jour IVL

(ou céfépime ou ceftazidime)

+

Vancomycine : 15 mg/kg/8heures IVL

# Antibiothérapie initiale

## PATIENT IMMUNODEPRIME

Céfotaxime : 2g x 6 / jour IVL  
(ou ceftriaxone 2g x 2 / j IVL)

+

Métronidazole : 500 mg x 3 (ou x 4) / j IVL

**+ si transplanté d'organe solide / hémato :**

- TMP-SMX (*Nocardia*)

- Voriconazole (*Aspergillus*)

**+ si patient VIH +**

- Pyriméthamine-sulfadiazine (Si IgG anti-toxoplasme +)

- Antituberculeux (zone d'endémie, FDR ...) ??

# Autres mesures symptomatiques

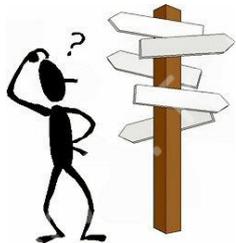
## Anticonvulsivants

Prophylaxie primaire systématique recommandée par certains ...

## Corticoides (dexaméthasone)

Effet anti-oedémateux

A discuter uniquement si lésion(s) avec effet de masse et risque d'engagement, courte durée



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# Traitement médical seul ?

## Si et seulement si ...

- GCS > 12
- Absence de signe d'engagement
- Absence de risque de rupture intraventriculaire
- Abscès (multiples) de petite taille < 2.5 cm
- Microorganisme documenté
- Etiologie « non-fongique »
- Amélioration clinique / Rx sous ATB (15 jours)

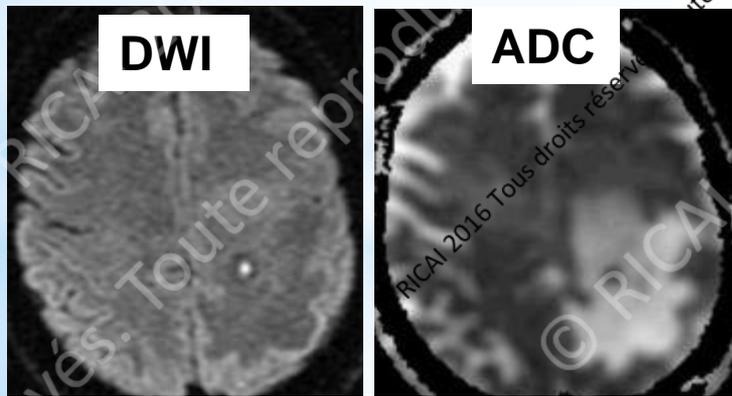
# Réponse thérapeutique et ADC

Persistance d'un ADC bas: mauvaise réponse ttt

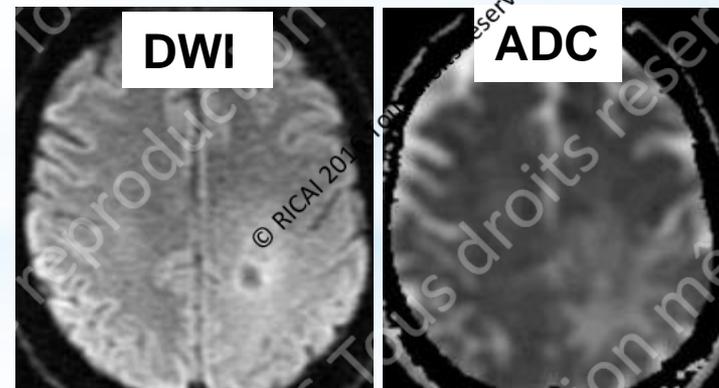
Elévation de l'ADC: régression clinique et morphologique  
(œdème et volume lésionnel)

*Cartes-Zumelzu AJNR 2004*

*Duprez et al. AJNR 2005*



**En début de ttt**

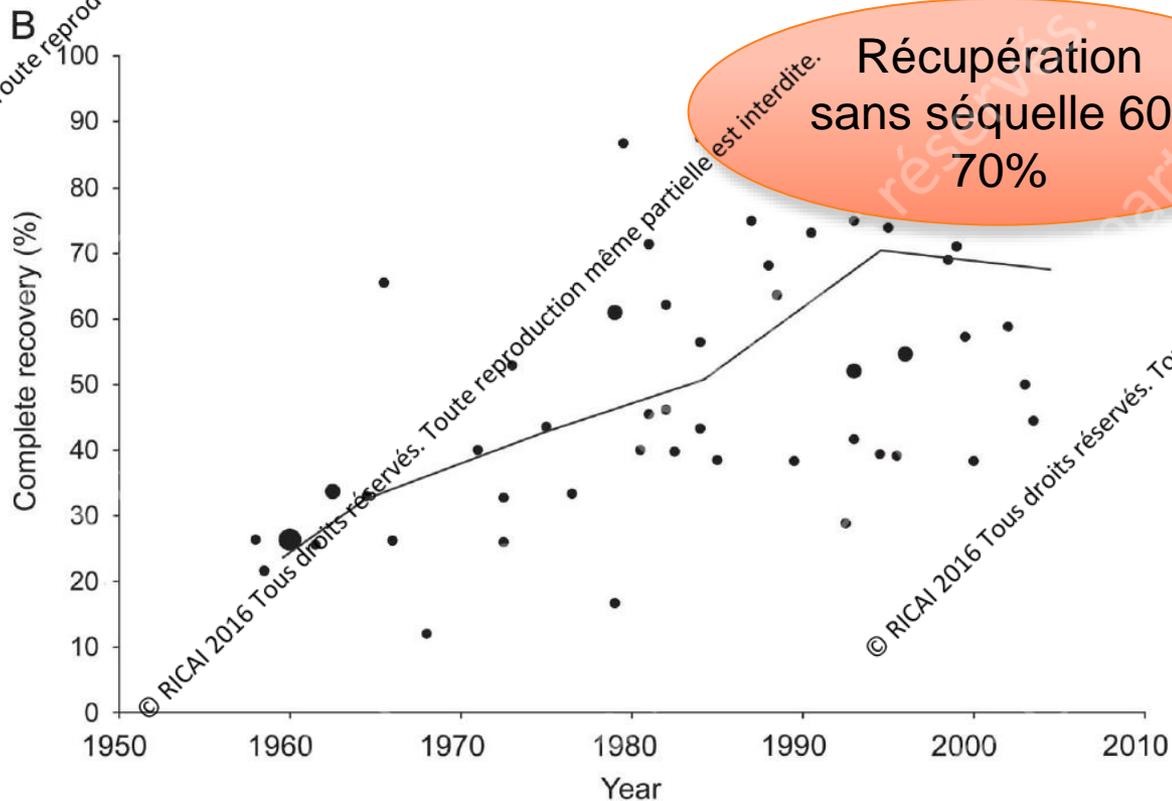


**M1**



# Clinical characteristics and outcome of brain abscess

Systematic review and meta-analysis



# Pyogenic brain abscess, a 15 year survey

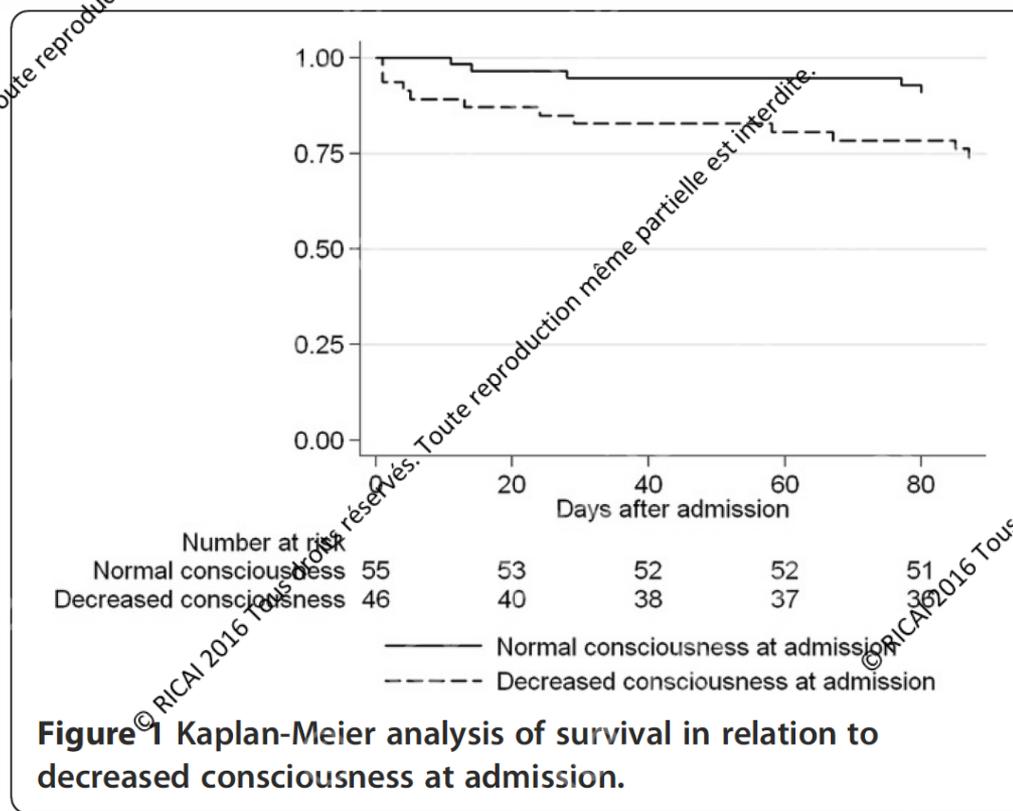
Jannik Helweg-Larsen<sup>1\*</sup>, Arnar Asradsson<sup>2</sup>, Humeira Richhall<sup>2</sup>, Jesper Erdal<sup>3</sup>, Alex Laursen<sup>4</sup> and Jannick Brennum<sup>2</sup>

**Table 6 Predictors of adverse outcome, logistic regression analysis**

Characteristic	Good outcome GOS > 3, alive	Adverse outcome GOS ≤ 3/death	Univariate OR, 95% CI	Multivariate, OR, 95% CI, p-value
Age, mean (SD)	45 (15.9)	42 (15.6)	1.03, 1.0-1.06	1.02, 0.98-1.07, p=0.28
No predisposing factors	48	7 (13%)	3.5, 1.3-9.4	9.3, 1.6-54.7, p=0.014
Comorbidity	31	16 (34%)		
GCS at presentation				
12-15	68	11 (14%)	1.0	1.0
8-11		3 (30%)	1.7, 0.6-12	3.5, 0.7-17.5, p=0.113
<8	1	8 (89%)	26.5, 3.6-81	80.6, 2.5-2574, p=0.013
Burr hole aspiration	54 (79%)	14 (21%)	1.0	
Craniotomy	17 (81%)	4 (19%)	0.9, 0.3-3.1	
Medical	8 (62%)	5 (38%)	2.4, 0.7-8.5	
Duration of symptoms before admission, days median (IQR)	4.0 (0-10)	3.0 (0-7)	0.99, 0.97-1.03	
Time from admission to surgery, days median (IQR)	5.0 (1-13)	7.0 (1-14)	1.02, 0.97-1.07	
Intraventricular rupture of brain abscess	4 (40%)	6 (60%)	6.6, 1.7-26.2	11.5, 2.5-53.2, p=0.002
Meningitis*	20 (25%)	11 (48%)	2.7, 1.03-7.1	1.5, 0.3-6.3, p=0.597

# Pyogenic brain abscess, a 15 year survey

Jannik Helweg-Larsen<sup>1\*</sup>, Arnar Asradsson<sup>2</sup>, Humeira Richhall<sup>2</sup>, Jesper Erdal<sup>3</sup>, Alex Laursen<sup>4</sup> and Jannick Brennum<sup>2</sup>



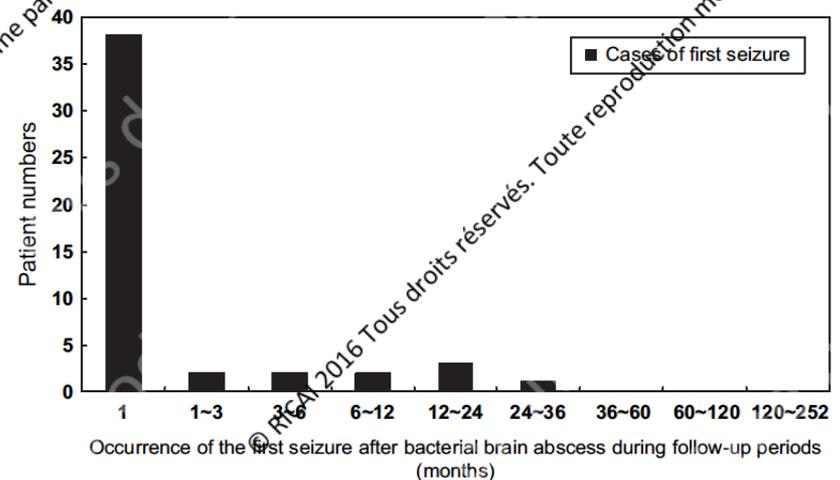
**Figure 1** Kaplan-Meier analysis of survival in relation to decreased consciousness at admission.

# Predictors and long-term outcome of seizures after bacterial brain abscess

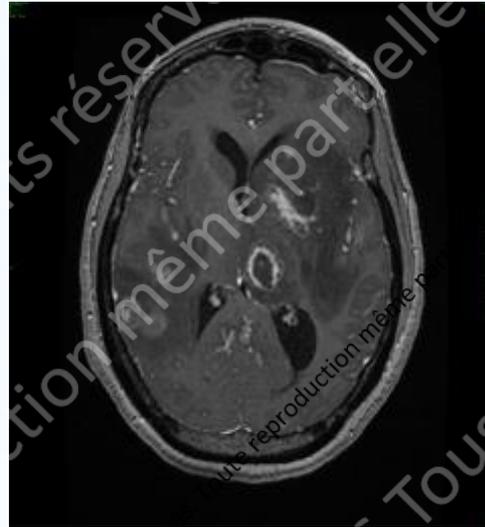
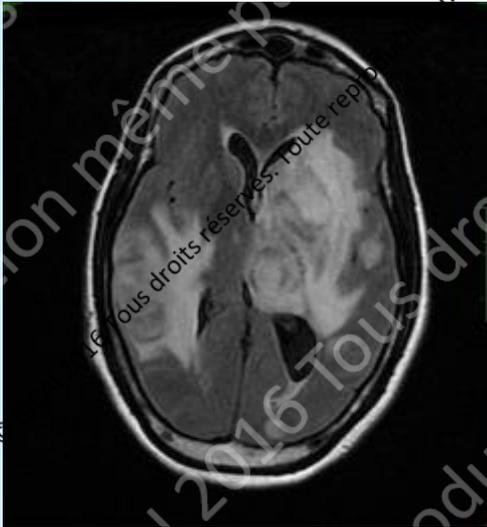
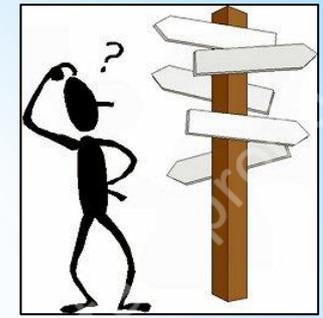
Ming-Jung Chuang,<sup>1</sup> Wen-Neng Chang,<sup>2</sup> Hsueh-Wen Chang,<sup>3</sup> Wei-Che Lin,<sup>4</sup>  
 Nai-Wen Tsai,<sup>2</sup> Mei-Jen Hsieh,<sup>2</sup> Hung-Chen Wang,<sup>1</sup> Cheng-Hsien Lu<sup>2</sup>

Acute seizures 48/205 : 23%

Epilepsy : 7/48 (15%)



H 48 ans, pas d'ATCD connu  
Vit en région Parisienne  
AEG depuis plusieurs semaines, céphalées,  
Admis en réa. pour troubles de conscience, 1/2 parésie D  
t° 37.8 °C



## Toxoplasmose cérébrale inaugurale

Bio : lymphopénie 900 / mm<sup>3</sup>

Test rapide VIH +, CD4 48/mm<sup>3</sup>, CV > 5 log  
Sérologie toxo + en IgG

Evolution (lentement) favorable sous pyriméthamine – adiazine – acide folinique (et qq jours de corticoïdes...)

H 42 ans

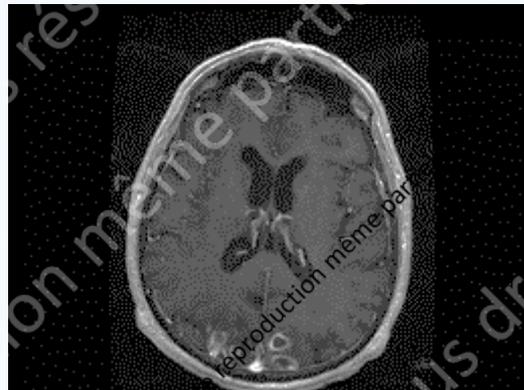
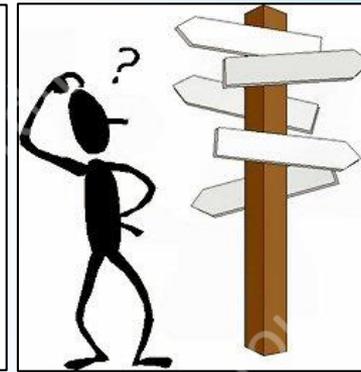
« Confusion fébrile », GCS 13, PA 85/40 mmHg.....

2 hémoc. puis C3G

PL : 250 él. / mm<sup>3</sup>, prot. 1.2 g/l, glyco 2.6 mmol/l

direct –

TDM cérébral sans particularité...



HC + CGP amas en 10 heures.....

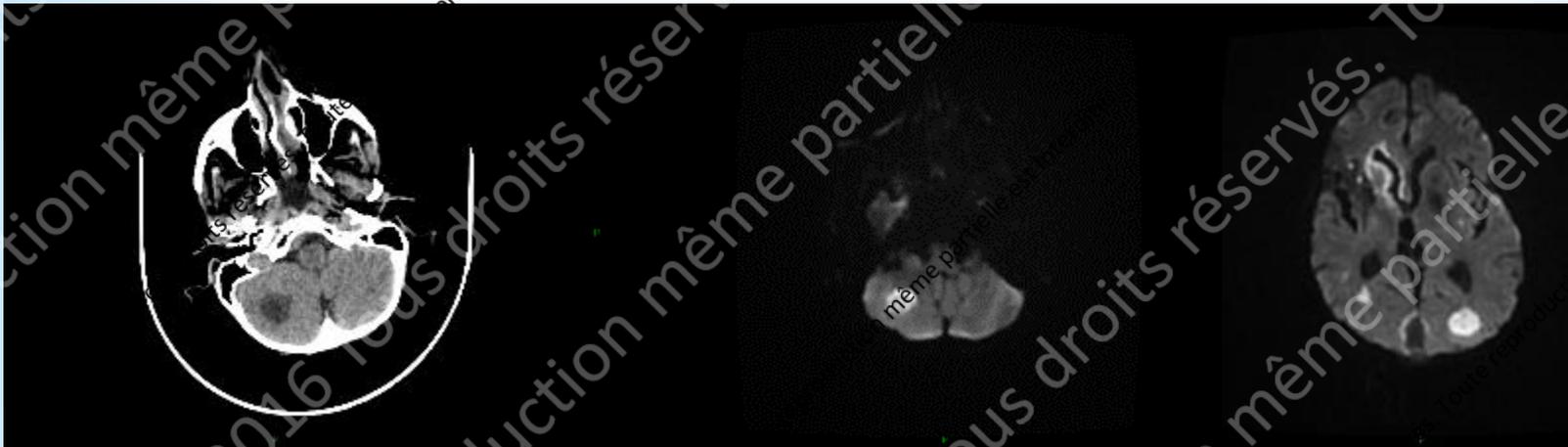
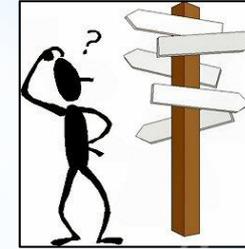
Oxacilline 12g/j, gentamicine 3mg/kg ....

Chirurgie de RVM

puis oxacilline - rifampicine

**Endocardite mitrale à *S.aureus***

H 45 ans 6 mois post transplantation cardiaque  
cellcept, prograf, cortancyl, bactrim  
confusion, GCS 12, 38.6°C hémiparésie gauche  
PL : 790 él. / mm<sup>3</sup>, 89 % PNN, prot. 2.1 g/l, glyco. 5.2  
mmol/l, D- .....



Galactomannane sang + (3.5)  
LBA: culture et Ag (6.7) + *Aspergillus fumigatus*  
LCR : Ag+ (7)

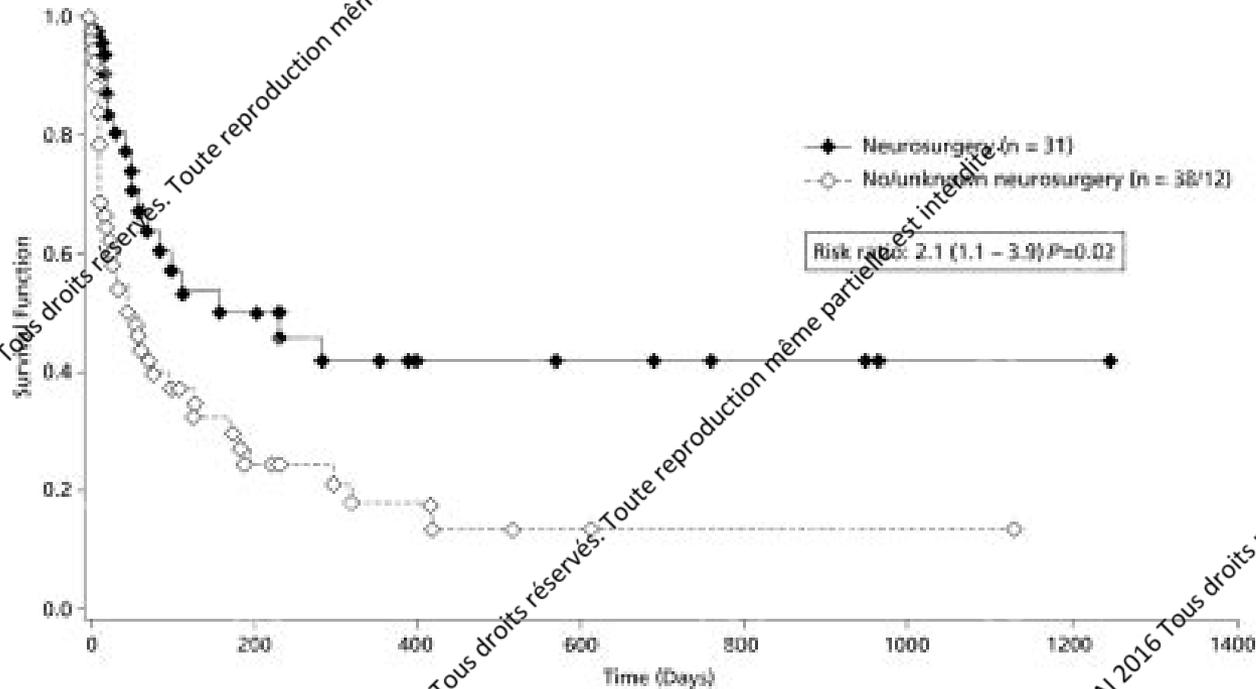


**Aspergillose  
cérébrale**

Voriconazole, neurochirurgie...

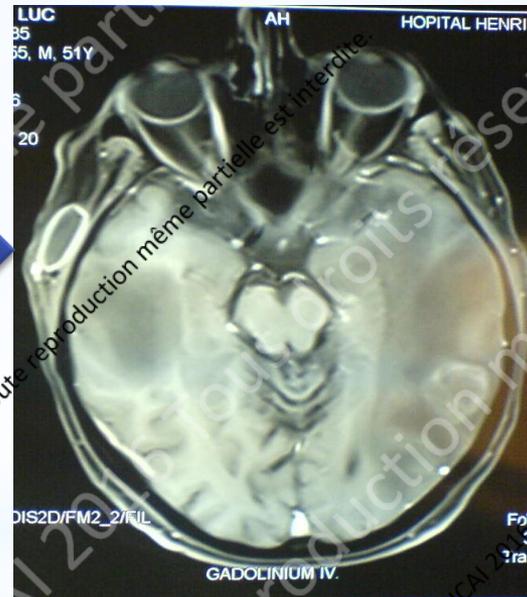
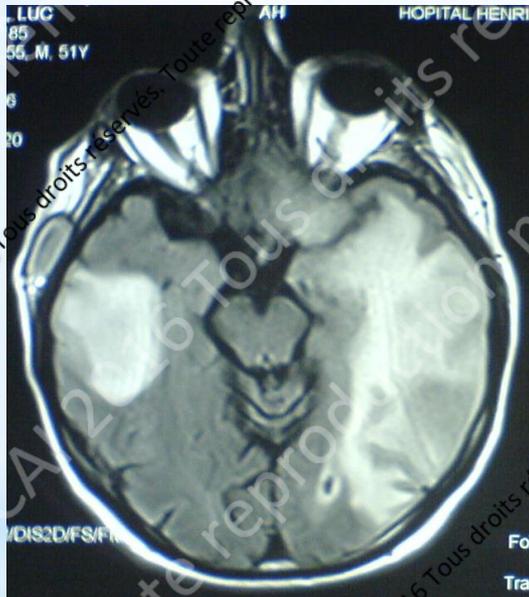
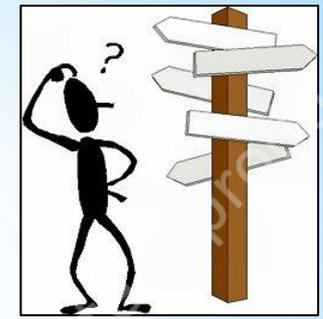
# Improved outcome in central nervous system aspergillosis, using voriconazole treatment

Stefan Schwartz, Markus Ruhnke, Patricia Ribaud, Lawrence Corey, Timothy Driscoll, Oliver A. Cornely, Ulrich Schuler, Irja Lutsar, Peter Troke, and Eckhard Thiel



**Figure 3. Kaplan-Meier survival curves of patients with CNS aspergillosis according to application of neurosurgical interventions.** Survival curves comparing voriconazole-treated patients who had neurosurgery (n = 31) versus those with no or unknown neurosurgery (n = 50).

H 50 ans, transplanté cardiaque il y a 1 an  
Corticoïdes, cellcept, tacrolimus  
Prophylaxie par cotrimoxazole  
céphalées, fièvre, vomissements depuis 1 semaine  
Admis en réa. pour troubles de conscience  
t° 38.4°C



**Nocardiose**

# *Nocardia* Infection in Solid Organ Transplant Recipients: A Multicenter European Case-control Study

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**Table 3. Risk Factors for Nocardiosis in 117 Cases Compared With 234 Controls After Multivariable Analysis by Conditional Logistic Regression**

Characteristic	OR (95% CI)	P Value
High calcineurin inhibitor level in the month before nocardiosis	6.11 (2.58–14.51)	<.001
Use of tacrolimus at diagnosis	2.65 (1.17–6.00)	.015
Corticosteroid dose at diagnosis (per mg <sup>a</sup> )	1.12 (1.03–1.22)	.002
Age at diagnosis (per year)	1.04 (1.02–1.07)	.001
Length of first ICU stay after transplant (per day)	1.04 (1.00–1.09)	.049

High calcineurin inhibitor level was defined as a trough blood level >10 ng/mL for tacrolimus and >300 ng/mL for cyclosporine.

Because of the large number of missing data, biological variables were not included in the multivariable analysis.

Abbreviations: CI, confidence interval; diagnosis, date of the diagnosis of nocardiosis; ICU, intensive care unit; OR, odds ratio.

<sup>a</sup> Expressed in milligrams (mg) of methylprednisolone equivalent per day.

# En conclusion

- Pathologie rare justifiant une **prise en charge multidisciplinaire rapide**
- Traitement initial guidé par **identification précoce des facteurs favorisants**
- **Pronostic** neurologique lié au **terrain**, à la **présentation neurologique initiale** et à la **rupture intra-ventriculaire**
- Des recommandations très anciennes ....
- **Aucune étude randomisée** sur antibiothérapie ou mesures adjuvantes (corticoïdes, antiépileptiques....)