UNIVERSITÉ DE NANTES

CENTRE HOSPITALIER UNIVERSITAIRE DE NANTES

SMIT CHU NANTES

Abcès cérébraux à pyogènes & relais per os des antibiotiques

Dr Antoine Asquier-Khati

GERICCO Mars 2024

Sommaire

- Introduction
- Que proposent les recommandations ?
- Peut-on faire un relais per os : Oui ? Non ?
- Quelle est la diffusion des molécules PO dans l'abcès?
- Quel relais per os proposer ?
- Conclusion et perspectives : essai européen ORAL

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- Introduction

Introduction

RELAIS PO ?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøl, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

ORIGINAL ARTICLE

Oral versus Intravenous Antibiotics for Bone and Joint Infection

H.-K. Li, I. Rombach, R. Zambellas, A.S. Walker, M.A. McNally, B.L. Atkins, B.A. Lipsky, H.C. Hughes, D. Bose, M. Kümin, C. Scarborough, P.C. Matthews, A.J. Brent, J. Lomas, R. Gundle, M. Rogers, A. Taylor, B. Angus, I. Byren, A.R. Berendt, S. Warren, F.E. Fitzgerald, D.J.F. Mack, S. Hopkins, J. Folb, H.E. Reynolds, E. Moore, J. Marshall, N. Jenkins, C.E. Moran, A.F. Woodhouse, S. Stafford, R.A. Seaton, C. Vallance, C.J. Hemsley, K. Bisnauthsing, J.A.T. Sandoe, I. Aggarwal, S.C. Ellis, D.J. Bunn, R.K. Sutherland, G. Barlow, C. Cooper, C. Geue, N. McMeekin, A.H. Briggs, P. Sendi, E. Khatamzas, T. Wangrangsimakul, T.H.N. Wong, L.K. Barrett, A. Alvand, C.F. Old, J. Bostock, J. Paul, G. Cooke, G.E. Thwaites, P. Bejon, and M. Scarborough, for the OVIVA Trial Collaborators*

Introduction

RELAIS PO ?

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Introduction

RELAIS PO ?

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- Moins de complications liées au cathéter
- Hospitalisations moins prolongées
- Moindre coût économique
- Meilleure qualité de vie

-

Introduction

RELAIS PO ?

+

- Moins de complications liées au cathéter
- Hospitalisations moins prolongées
- Moindre coût économique
- Meilleure qualité de vie

−

- Peu de données…
- Diffusion des AB via la BHE puis dans le capsule de l'abcès ?
- Pas de recommandations autorisant le relais

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- Que proposent les recommandations ?

Recommandations

2000

Recommandations de la BSAC
(British Society for Antimicrobial Chemotherapy)

The rational use of antibiotics in the treatment of brain abscess

administered by the intravenous route. After 1–2 weeks, depending on clinical response, an appropriate oral regimen can be considered.

De Louvois, E.M. Brown, R. Bayston, J. The rational use of antibiotics in the treatment of brain abscess. Br J Neurosurg. janv 2000;14(6):525-30.

Recommandations

2010

GISIG (Gruppo Italiano di Studio sulle Infezioni Gravi)

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

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

Consensus document on controversial issues for the treatment of infections of the central nervous system: bacterial brain abscesses

Massimo Arlotti [a,*], Paolo Grossi [b], Federico Pea [c], Giustino Tomei [d], Vincenzo Vullo [e], Francesco G. De Rosa [f], Giovanni Di Perri [f], Emanuele Nicastri [g,j], Francesco N. Lauria [g,j], Giampiero Carosi [h,j], Mauro Moroni [i,j], Giuseppe Ippolito [g,j], and the GISIG (Gruppo Italiano di Studio sulle Infezioni Gravi) Working Group on Brain Abscesses[1]

Recommendations

We do not believe there is sufficient information to give recommendations for orally administered antibiotics. However, the choice of completing treatment using this method should to reserved for those cases where the bacteria have been isolated and there is a sensitivity profile, using drugs with good penetration into the infection site [D].

Arlotti M, Grossi P, Pea F, *et al.* Consensus document on controversial issues for the treatment of infections of the central nervous system: bacterial brain abscesses. *International Journal of Infectious Diseases* 2010; **14**: S79–92.

Recommandations

2020

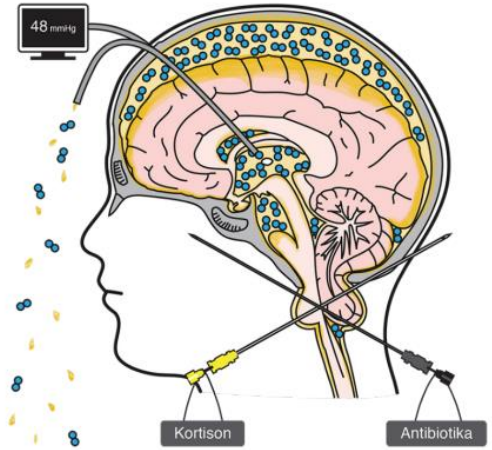
Recommandations suédoises

Vårdprogram

Bakteriella CNS-infektioner

Avser vuxna patienter med akut bakteriell meningit, neurokirurgisk infektion, tuberkulös meningit, hjärnabscess och neuroborrelios

Reviderat 2020
Svenska Infektionsläkarföreningen



Le relais PO de la Béta-lactamine et du Métronidazole fait partie des alternatives thérapeutiques si bonne évolution clinique, biologique et radiologique à 2-3S

Tabell 4 (Faktaruta 28).

Tänkbara antibiotika för peroral uppföljning vid behandling av hjärnabsces

amoxicillin	1 g x 3
klindamycin	450 mg x 3
ciprofloxacin	750 mg x 2
moxifloxacin	400 mg x 1
metronidazol	400–500 mg x 2–3
trimetoprim/sulfametoxazol	(160–320 mg/800–1600 mg) x 2
linezolid	600 mg x 2
fusidinsyra	500 mg x 3
rifampicin	600 mg x 1

Blackberg J, Brink M, Ericsson M, Glimåker M, Johansson B, Lindquist L, et al. Vårdprogram, Bakteriella CNS-infektioner. 2010. https://infektion.net/wpcontent/uploads/2017/05/vardpr_cns_100916.pdf. [Accessed 13 January 2020].

Recommandations

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Guidelines

European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults

#6 What is the appropriate duration of antimicrobial therapy for bacterial brain abscess?

We conditionally recommend a total duration of 6–8 wk of intravenous antimicrobials for aspirated or conservatively treated brain abscesses.
On the basis of expert opinion, a shorter duration (e.g. 4 wk) may be considered in patients treated with excision of brain abscess.

#7 Should early transition to oral antimicrobials be used in treatment of patients with bacterial brain abscess?

No recommendation. For early transition to oral antimicrobials in patients with brain abscess, there is insufficient evidence at the time of writing to provide a recommendation.

Bodilsen J, D'Alessandris QG, Humphreys H, *et al.* European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults. *Clinical Microbiology and Infection* 2023: S1198743X23003993.

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- **Peut-on faire un relais per os : Oui ? Non ?**

Relais PO : données de la littérature

Table 1
Overview of studies describing the use of early transition from intravenous (IV) to oral antimicrobials in the treatment of brain abscess

Author, year	Country	Study design	Overall case-fatality rate	Early orals		Standard IV treatment	
				Case-fatality rate	Recurrence	Case-fatality rate	Recurrence
Brown, 1993 [19]	England	Retrospective, single-centre	1/12	1/12	0/12	—	—
Jamjoom, 1996 [20]	England and Saudi Arabia	Bi-directional, multi-centre	0/26	0/26	0/26	—	—
Jamjoom, 1997 [22]	Saudi Arabia	Retrospective, single-centre	5/37	—	—	—	—
Srinivasan, 1999 [30]	India	Retrospective, single-centre	1/37	1/37	0/37	—	—
Skoutelis, 2000 [21]	Greece	Bi-directional, single-centre	0/8	0/8	0/8	—	—
Babu, 2002 [27]	India	Retrospective, single-centre	5/45	5/45	—	—	—
Jansson, 2004 [25]	Sweden	Prospective, single-centre	8/66	—	—	—	—
Sichizya, 2005 [26]	South Africa	Retrospective, single-centre	16/121	—	—	—	—
Carpenter, 2007 [34]	England	Retrospective, single-centre	5/49	0/21	—	5/28	—
Sharma, 2009 [36]	England	Retrospective, single-centre	9/47	—	—*	—	—
Qasim, 2010 [28]	Pakistan	Retrospective, single-centre	0/40	0/40	—	—	—
Madhugiri, 2011 [23]	India	Retrospective, single-centre	5/139	—	—	—	—
Felsenstein, 2012 [32]	England	Retrospecitive, multi-centre	7/118	—	—	—	—
Ndubuisi, 2017 [24]	Nigeria	Retrospective, multi-centre	8/79	—	—	—	—
Kafle, 2018 [29]	Nepal	Retrospective, single-centre	2/51	2/51	—	—	—
Udayakumaran, 2019 [31]	India	Retrospective, single-centre	1/48	—	—	—	0/29
Asquier-Khati, 2020 [33]	France	Retrospective, single-centre	13/108	7/48**	—	23/60**	—
Lauda-Maillen, 2021 [35]	France	Retrospective, multi-centre	13/101	1/24	1/24	12/77	4/77

* 5/8 recurrences had been switched to early oral antimicrobials of first or second generation cephalosporin.
** Unfavourable outcome assessed by Glasgow Outcome Scale Score <4 was used as proxy for case-fatality.

Bodilsen J, Nielsen H. Early switch to oral antimicrobials in brain abscess: a narrative review. *Clinical Microbiology and Infection* 2023; **29**: 1139–43.

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2 études inclues dans la méta-analyse

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Sharma, 2009 [36]	England	Retrospective, single-centre	9/47	—	—*	—	—
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Relais PO : données de la littérature

administered by the intravenous route. After 1–2 weeks, depending on clinical response, an appropriate oral regimen can be considered.

Brown EM, Stranjalis G, Jamjoom A, Griffith GB. Short-course antimicrobial therapy for brain abscess and subdural empyema. JNNP 1993;57:387e95.
Jamjoom AB. Short course antimicrobial therapy in intracranial abscess. Acta Neurochir (Wien). 1996;138(7):835-9. doi: 10.1007/BF01411262. PMID: 8869712.

Relais PO : données de la littérature

administered by the intravenous route. After 1–2 weeks, depending on clinical response, an appropriate oral regimen can be considered.

Basé sur 2 séries avec un TTT IV court sans relais PO
Arrêt quand récupération clinique / apyréxie / négativation CRP

Brown 1993 (présentation congrès)
20 patients traités par 14J IV en médiane
Un décès (embolie pulmonaire)
Pas de rechute

Jamjoom 1996
12 patients traités par 20J IV en médiane
Pas de rechute

Brown EM, Stranjalis G, Jamjoom A, Griffith GB. Short-course antimicrobial therapy for brain abscess and subdural empyema. JNNP 1993;57:387e95.
Jamjoom AB. Short course antimicrobial therapy in intracranial abscess. Acta Neurochir (Wien). 1996;138(7):835-9. doi: 10.1007/BF01411262. PMID: 8869712.

Relais PO : données de la littérature

Eur J Clin Microbiol Infect Dis (2000) 19:332–335

Article

Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy

A.T. Skoutelis, C.A. Gogos, T.E. Maraziotis, H.P. Bassaris

8 patients
Refus d'un traitement IV prolongé en hospitalisation
Relais PO Amoxicilline 1,5 g 3/j + Ciflox 750 mg 2/j + Flagyl 500 mg 4/j
Evolution favorable : 8/8

Skoutelis AT, Gogos CA, Maraziotis TE, Bassaris HP. Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy. *European Journal of Clinical Microbiology & Infectious Diseases* 2000.

Relais PO : données de la littérature

Eur J Clin Microbiol Infect Dis (2000) 19:332–335

Article

Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy

A.T. Skoutelis, C.A. Gogos, T.E. Maraziotis, H.P. Bassaris

hospital stay for personal or social reasons. The mean duration of intravenous antibiotic therapy was 7.6 (range 6–12) days, the mean total duration of antibiotic therapy was 17.5 (range 16–20) weeks, and the mean

8 patients
Refus d'un traitement IV prolongé en hospitalisation
Relais PO Amoxicilline 1,5 g 3/j + Ciflox 750 mg 2/j + Flagyl 500 mg 4/j
Evolution favorable : 8/8

Caractéristiques des patients
Pas de critère de gravité neurologique (GCS 14 au pire)
Taille de l'abcès : maximum 3 cm
Pas de comorbidité majeure
Pas de prise en charge chirurgicale

Skoutelis AT, Gogos CA, Maraziotis TE, Bassaris HP. Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy. *European Journal of Clinical Microbiology & Infectious Diseases* 2000.

Relais PO : données de la littérature

Eur J Clin Microbiol Infect Dis (2007) 26:1–11
DOI 10.1007/s10096-006-0236-6

ARTICLE

Retrospective analysis of 49 cases of brain abscess and review of the literature

J. Carpenter · S. Stapleton · R. Holliman

Etude rétrospective sur 49 patients
21 relais PO précoce (≤ 2S)
Vs relais PO plus tardif (2,5-7S) pour les 28 autres

Carpenter J, Stapleton S, Holliman R. Retrospective analysis of 49 cases of brain abscess and review of the literature. *Eur J Clin Microbiol Infect Dis* 2007; **26**: 1–11.

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Vs relais PO plus tardif (2,5-7S) pour les 28 autres

Groupe relais PO précoce
Mortalité 0% (0/21)
Groupe relais PO tardif
Mortalité 18% (5/28)

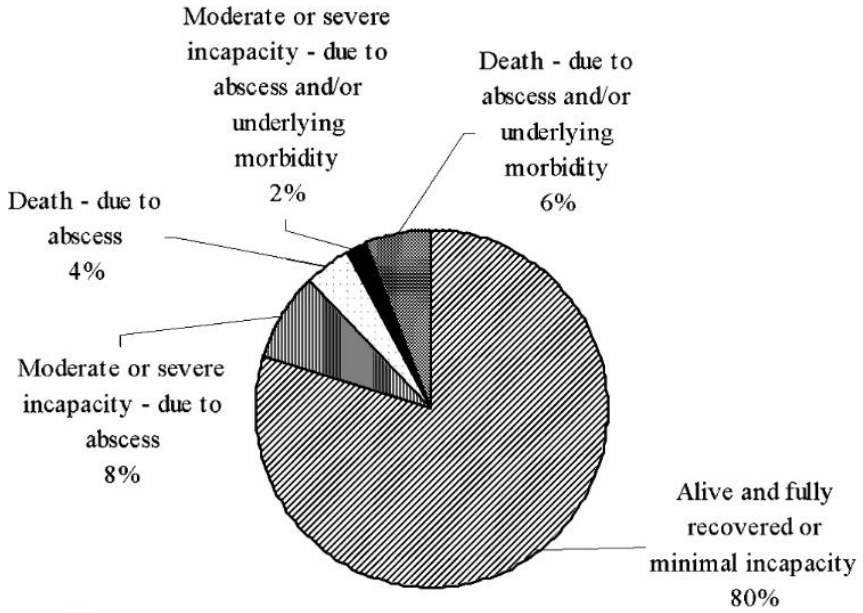

Fig. 2 Outcomes after brain abscess

Carpenter J, Stapleton S, Holliman R. Retrospective analysis of 49 cases of brain abscess and review of the literature. *Eur J Clin Microbiol Infect Dis* 2007; **26**: 1–11.

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Groupe relais PO précoce
Mortalité 0% (0/21)
Groupe relais PO tardif
Mortalité 18% (5/28)

Pose la question de la sélection des patients bénéficiant d'un relais PO

Carpenter J, Stapleton S, Holliman R. Retrospective analysis of 49 cases of brain abscess and review of the literature. *Eur J Clin Microbiol Infect Dis* 2007; **26**: 1–11.

Relais PO : données de la littérature

J Antimicrob Chemother
doi:10.1093/jac/dkaa285

Journal of Antimicrobial Chemotherapy

Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients

Antoine Asquier-Khati[1]*, Colin Deschanvres[1], David Boutoille[1], Maeva Lefebvre[1], Paul Le Turnier[1], Benjamin Gaborit[1], Karim Lakhal[2], Kevin Buffenoir[3], Lydie Khatchatourian[4] and Nathalie Asseray[1] on behalf of the Nantes Brain Abscesses study group†

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020;

Relais PO : données de la littérature

Etude monocentrique rétrospective
108 patients Nantais

Relais PO complet
48/108 (44%)
Pas de relais PO complet
60/108 (56%)

J Antimicrob Chemother
doi:10.1093/jac/dkaa285

Journal of Antimicrobial Chemotherapy

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Table 1. Patient characteristics and therapeutic management

	All patients ($n = 108$)	3 month GOS $\geq 4^a$ ($n = 78$)	3 month GOS $\leq 3^b$ ($n = 30$)
Therapeutic management			
medical treatment alone	23 (21.3)	14 (17.9)	9 (30.0)
initial IV therapy	106 (98.1)	77 (98.7)	29 (96.7)
total duration of antibiotic therapy (days)	65 (45–95)	73 (47–101)	62 (32–85)
oral switch	48 (44.4)	41 (52.6)	7 (23.3)
time to antibiotic introduction (days)	3 (2–6)	3 (2–5)	3.5 (2–9)
time to oral switch (days)	19 (12–28)	19 (12–28)	14 (5.5–39)
time before surgery (days)	4 (2–12)	4 (2–8)	11 (3.3–20)
antiepileptic drugs	64 (59.3)	46 (59.0)	18 (60.0)
corticosteroid	44 (40.7)	35 (44.9)	9 (30.0)
ICU stay >3 days	49 (45.4)	30 (38.5)	19 (63.3)
LOS (days)	37 (24–56)	33 (21–47)	59 (28–84)

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020;

Relais PO : données de la littérature

Etude monocentrique rétrospective
108 patients Nantais

Facteurs influant le GOS à M3

Relais PO
GOS ≤ 3 : 7/48 (15%)
Pas de relais PO
GOS ≤ 3 : 23/60 (38%)

J Antimicrob Chemother
doi:10.1093/jac/dkaa285

Journal of Antimicrobial Chemotherapy

Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients

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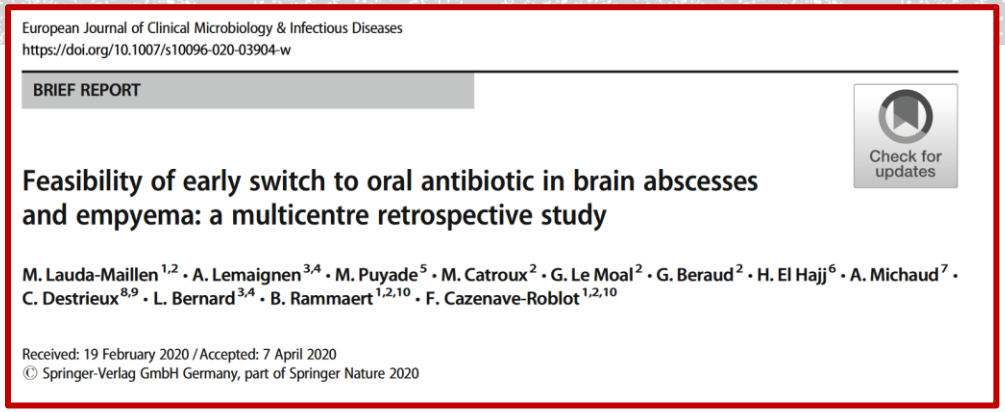
Table 2. Factors associated with unfavourable 3 month GOS

Total population ($n = 108$ patients)			Univariate analysis		Multivariate analysis	
	Favourable GOS ($n = 78$)	Unfavourable GOS ($n = 30$)	OR (95% CI)	*P* value	ORa (95% CI)	*P* value
Male sex	58 (74.4)	22 (73.3)	1.1 (0.4–2.7)	0.913	1.6 (0.5–5.0)	0.430
Charlson scale ≥2	49 (62.8)	25 (83.3)	3 (1.1–9.5)	0.046	4.8 (1.4–19.4)	0.020
GCS ≤14	32 (41)	22 (73.3)	4 (1.6–10.5)	0.004	4.4 (1.6–14.0)	0.010
Number of abscesses ≥2	29 (37.2)	11 (36.7)	1 (0.4–2.3)	0.961	0.9 (0.3–2.9)	0.850
Total duration of antibiotics >8 weeks	48 (61.5)	16 (53.3)	0.7 (0.3–1.7)	0.438	1 (0.3–2.9)	0.940
Duration of IV antibiotics >3 weeks	51 (65.4)	21 (70.0)	1.2 (0.5–3.2)	0.649	0.4 (0.1–1.7)	0.210
Antibiotic oral switch	41 (52.6)	7 (23.3)	0.3 (0.1–0.7)	0.008	0.2 (0.0–0.6)	0.010
time before oral switch >2 weeks	24/41 (58.5)	3/7 (42.9)	0.5 (0.1–2.7)	0.444	—	—
Surgery	64 (82.1)	21 (70)	0.5 (0.2–1.4)	0.175	0.3 (0.1–1.2)	0.100
number of surgical procedures ≥2	17/64 (26.6)	11/21 (52.4)	2.8 (1–7.7)	0.047	—	—
time before surgery >3 days	35/64 (54.7)	16/21 (76.2)	2.2 (0.8–6.8)	0.142	—	—
ICU stay	56 (71.8)	23 (76.7)	1.3 (0.5–3.6)	0.609	2.3 (0.6–10.6)	0.240

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020;

Relais PO : données de la littérature



European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03904-w

BRIEF REPORT

Check for updates

Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study

M. Lauda-Maillen[1,2] · A. Lemaignen[3,4] · M. Puyade[5] · M. Catroux[2] · G. Le Moal[2] · G. Beraud[2] · H. El Hajj[6] · A. Michaud[7] · C. Destrieux[8,9] · L. Bernard[3,4] · B. Rammaert[1,2,10] · F. Cazenave-Roblot[1,2,10]

Received: 19 February 2020 / Accepted: 7 April 2020

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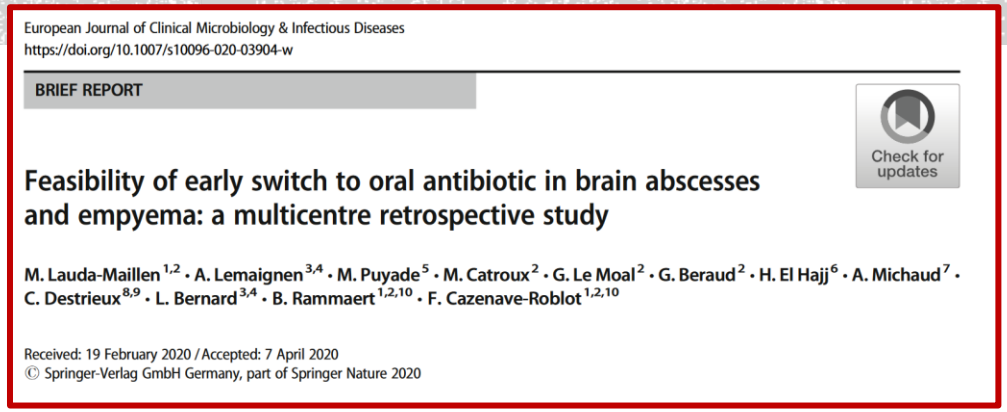
Relais PO : données de la littérature

Etude multicentrique (Poitiers & Tours)
101 patients

Relais PO ≤ 14 jours
24/101 (23,8%)

Pas de relais PO ou > 14 jours
77/101 (76,2%)



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Relais PO : données de la littérature

Etude multicentrique (Poitiers & Tours)
101 patients

Evolution à M3

Relais PO ≤ 14 jours
Récurrence 1/24 (4%)
Mortalité 1/24 (4%)

Pas de relais PO ou > 14 jours
Récurrence 4/77 (5%)
Mortalité 12/77 (16%)

Table 1 Baseline characteristics, management and 3-month outcome of 101 patients with brain abscesses or empyema

	TOTAL ($n = 101$) (unless specified)	PO group ($n = 24$)	IV group ($n = 77$)	p value
3-month outcome				
Recurrence	5 (5)	1 (4)	4 (5)	0.84
Median time to recurrence, days	44 (43–49)	44	46 (39–56)	1
All-cause mortality	13 (13)	1 (4)	12 (16)	0.18
Attributable mortality	11 (11)	0	11 (14)	0.15
Median time between diagnosis and death, days	24 (17–50)	71	24 (14–35)	0.14
Neurologic sequelae	39 (39) ($n = 99$)	7 (29)	32 (43) ($n = 75$)	0.39
Primary endpoint criteria fulfilled (no death, no recurrence, no sequelae)	46 (46) ($n = 99$)	16 (67)	30 (40) ($n = 75$)	0.02

Lauda-Maillen M, Lemaignen A, Puyade M, *et al.* Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 209–13.

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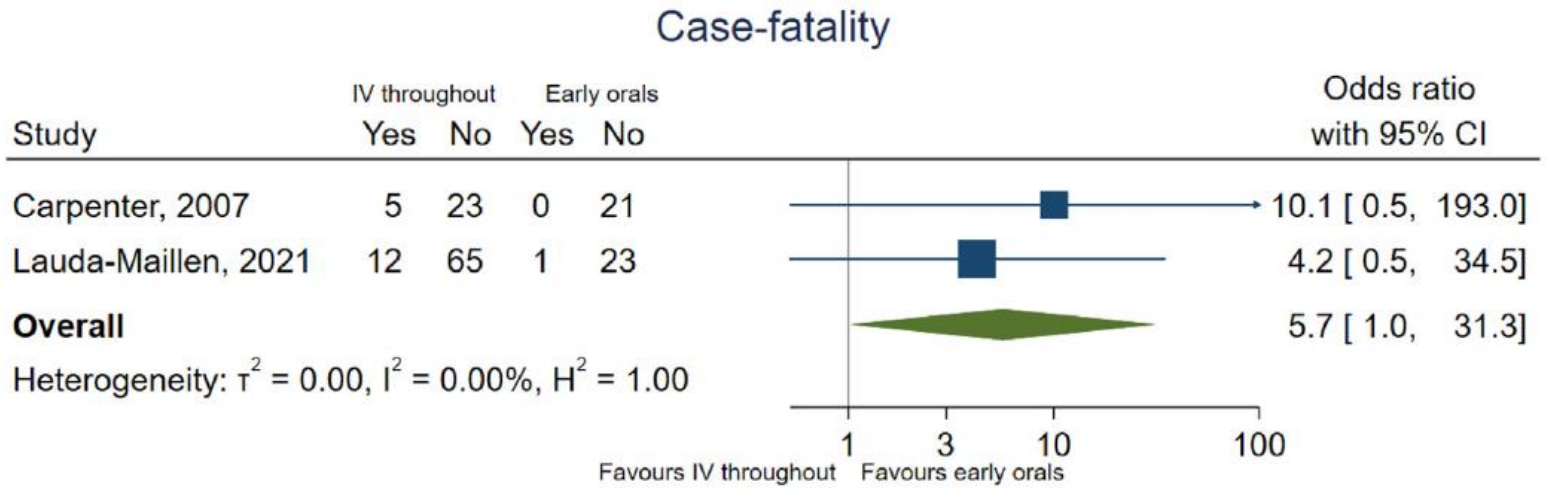

Fig. 15. Risk of death according to early switch to oral antimicrobials or not.

Bodilsen J, D'Alessandris QG, Humphreys H, *et al.* European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults. *Clinical Microbiology and Infection* 2023: S1198743X23003993.

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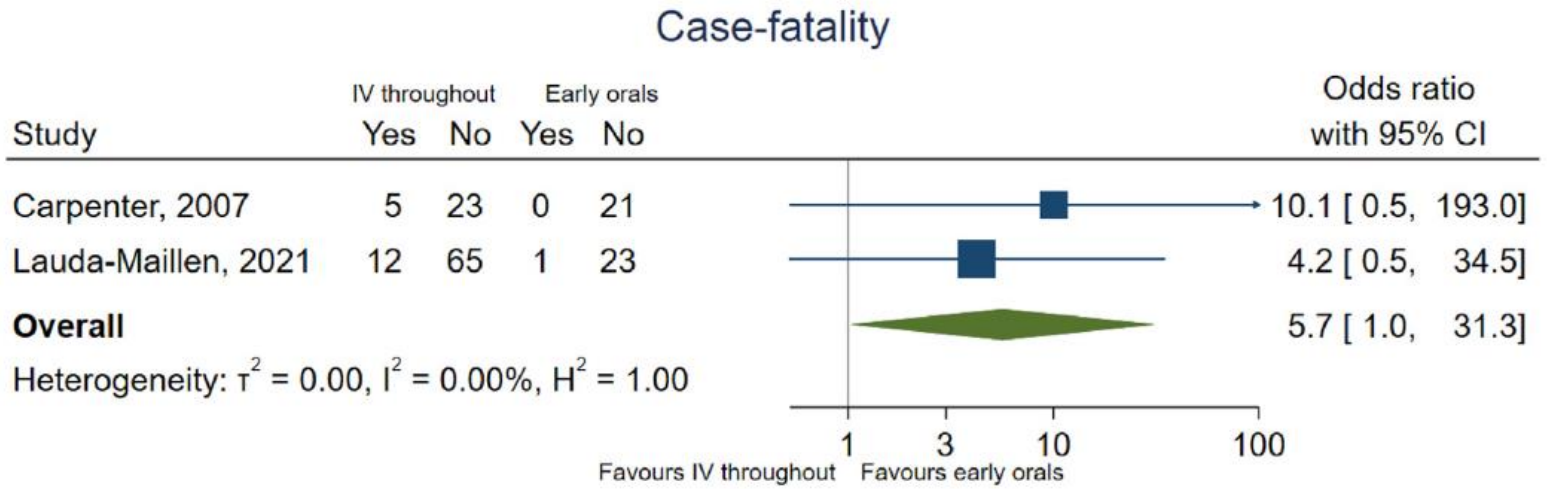


Fig. 15. Risk of death according to early switch to oral antimicrobials or not.

Avis du panel d'expert des recommandations Européennes :

Données pas suffisamment solides pour autoriser le relais PO

Bodilsen J, D'Alessandris QG, Humphreys H, *et al.* European society of Clinical Microbiology and Infectious Diseases guidelines on diagnosis and treatment of brain abscess in children and adults. *Clinical Microbiology and Infection* 2023: S1198743X23003993.

Sommaire

- Introduction
- Que proposent les recommandations ?
- Peut-on faire un relais per os : Oui ? Non ?
- Quelle est la diffusion des molécules PO dans l'abcès ?
- Quel relais per os proposer ?
- Conclusion et perspectives : essai européen ORAL

Sommaire

- **Quelle est la diffusion des molécules PO dans l'abcès ?**

Diffusion des antibiotiques au sein de l'abcès

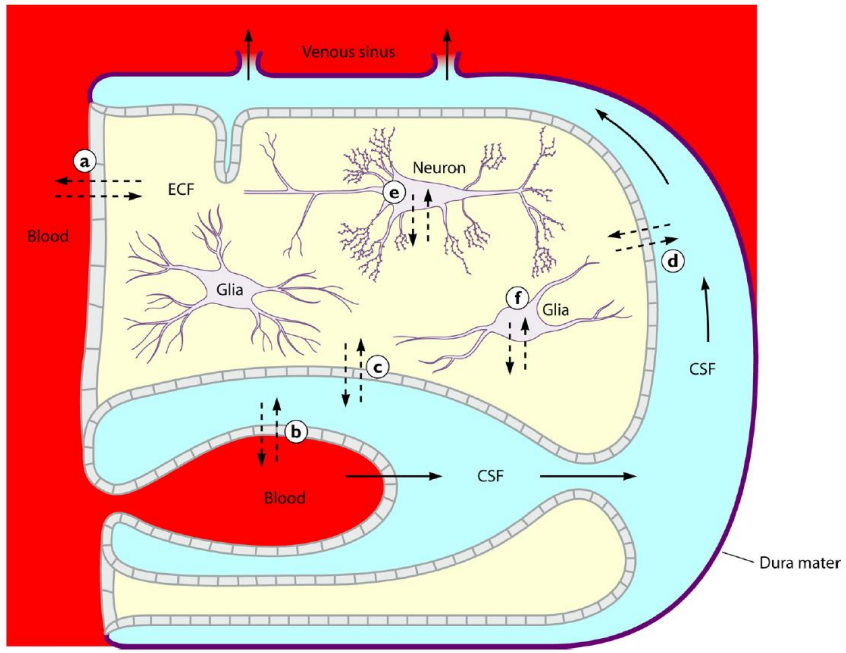
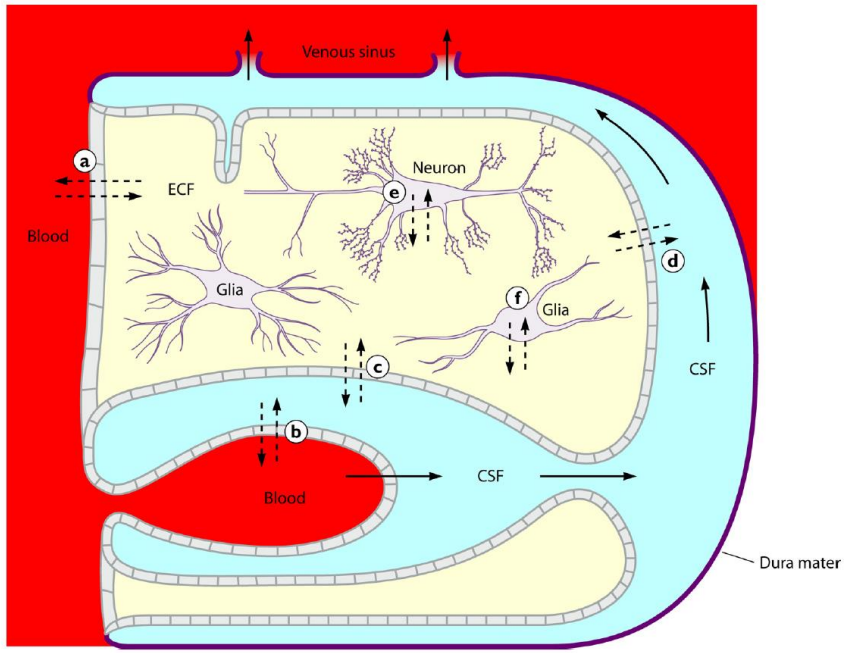


FIG. 1. Intracranial fluid compartments. Continuous arrows represent the direction of the CSF flow. Interrupted arrows indicate where a diffusion of water or solutes can occur between brain capillaries, CSF, and nervous tissue: (a) across the blood-brain barrier; (b) across the epithelium of the choroid plexus; (c) across the ependyma; (d) across the pia-glial membranes at the surface of the brain and spinal cord; (e and f) across the cell membranes of neurons and glial cells. The thick line represents the dura mater and arachnoidea surrounding the system. (Reproduced from reference 42 with permission of Churchill Livingstone.)

Question complexe !
Problème de la compartimentation du SNC :
Caractéristiques différentes du LCR vs parenchyme cérébral vs abcès

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès



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Question complexe !
Problème de la compartimentation du SNC :
Caractéristiques différentes du LCR vs parenchyme cérébral vs abcès

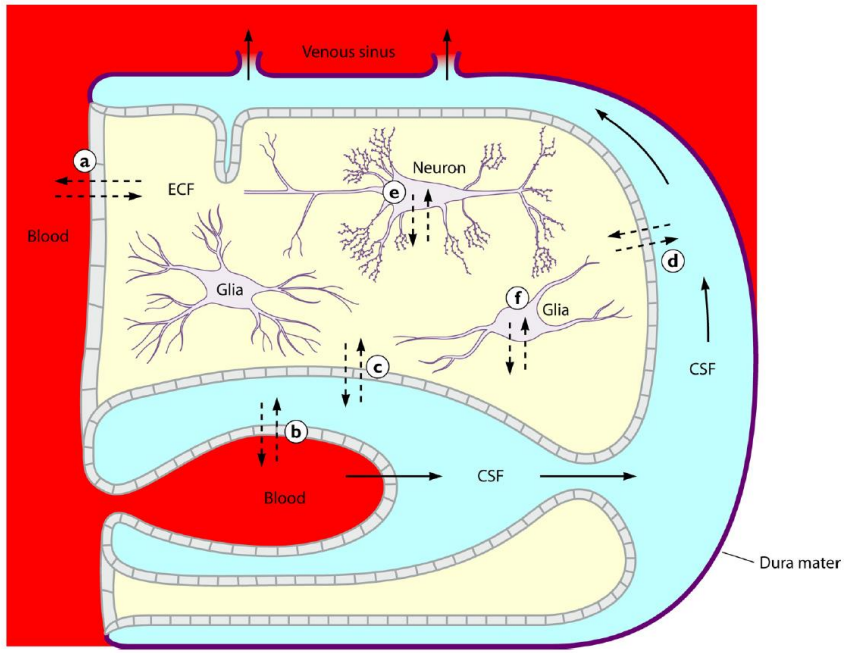
Peu de données
Etudes très anciennes
Données sur l'animal (rat) et l'homme (en IV+++)

Ponction de l'abcès effectuée avant la mise sous antibiotiques !

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès

Barrières lipidiques avec jonctions serrées ++



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Diffusion selon les caractéristiques des antibiotiques

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Diffusion des antibiotiques au sein de l'abcès

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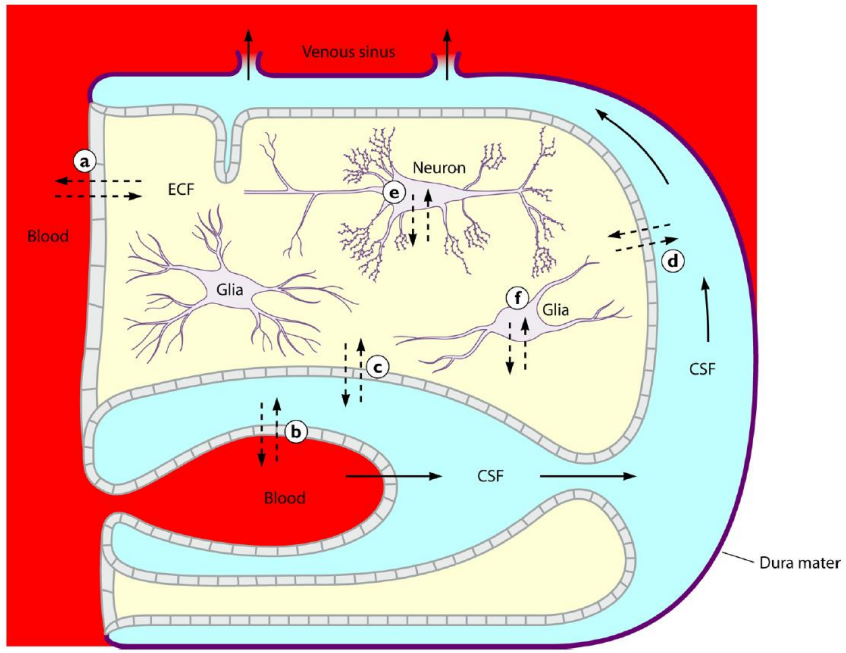

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Diffusion selon les caractéristiques des antibiotiques

↓

Biodisponibilité
Faible liaison aux protéines plasmatiques

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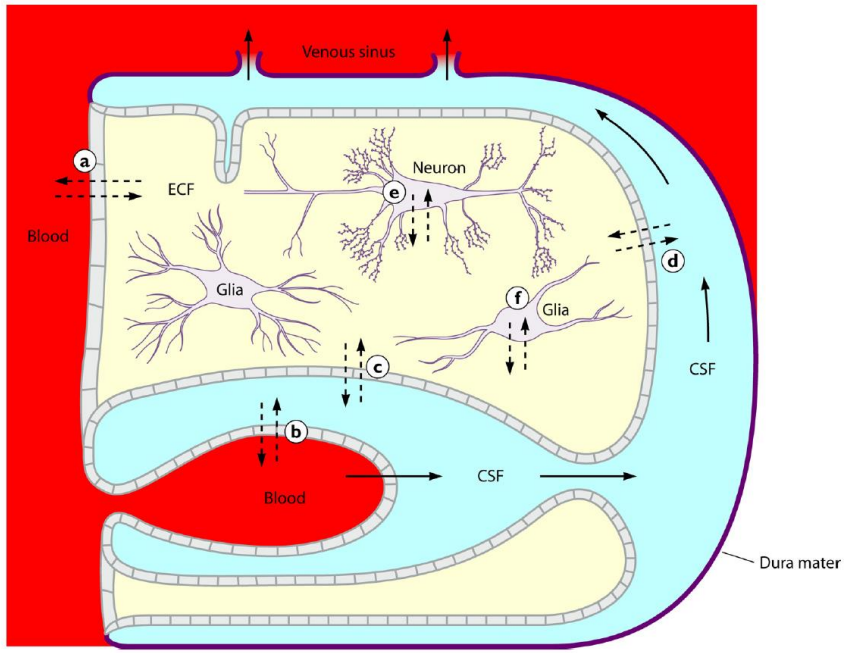

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Diffusion selon les caractéristiques des antibiotiques

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Caractère lipophile
Faible poids moléculaire

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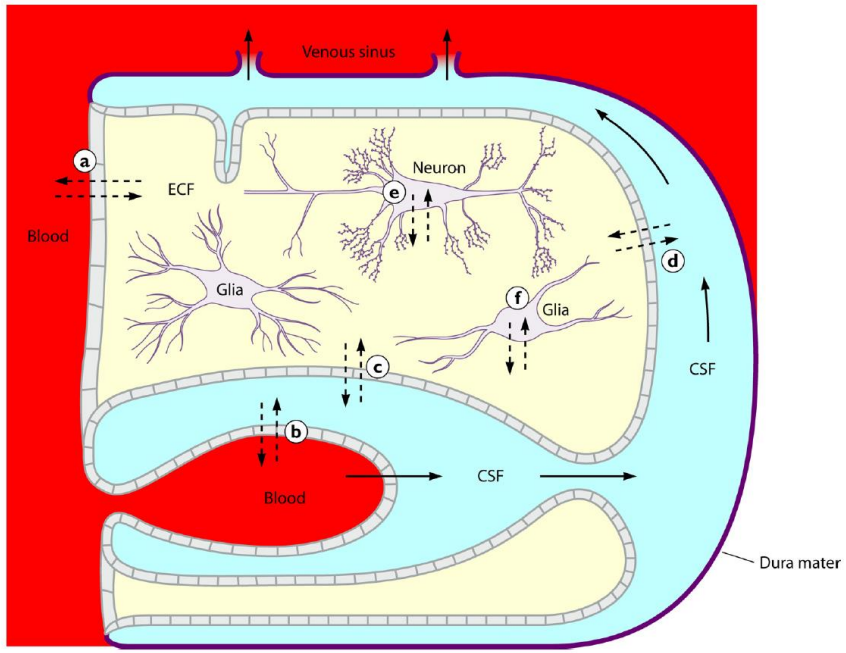

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Faible liaison aux protéines plasmatiques

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Caractère lipophile
Faible poids moléculaire

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Métabolisme intracérébral ?
Affinité avec les pompes à efflux ?

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès

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DRUG METABOLISM AND DISPOSITION
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Vol. 37, No. 4
24125/3446185
Printed in U.S.A.

Unbound Drug Concentration in Brain Homogenate and Cerebral Spinal Fluid at Steady State as a Surrogate for Unbound Concentration in Brain Interstitial Fluid

Xingrong Liu, Kristine Van Natta, Helen Yeo, Olga Vilenski, Paul E. Weller, Philip D. Worboys, and Mario Monshouwer

greater than 3-fold of C_m for hydrophilic or P-gp substrates. The present study indicates that the brain homogenate and cerebral spinal fluid methods may be used as surrogate methods to predict brain interstitial fluid concentrations within 3-fold of error in drug discovery and development settings.

Comparaison concentration dans le LCR et concentration cérébrale par microdialyse

In vitro microdialysis probe recovery, unbound plasma and brain fraction, plasma, brain, and CSF concentration, and C_m of the nine compounds in rats (mean ± S.D., n = 3–6)

All of the concentrations were from the samples collected at 6 h after start of infusion.

Compound	C_{CSF}	C_m
	ng/ml	*ng/ml*
Carbamazepine	124 ± 72	172 ± 76
Citalopram	197 ± 19	219 ± 41
Ganciclovir	101 ± 35	111 ± 52
Metoclopramide	42.4 ± 17	59 ± 9
N-Desmethylclozapine	4.92 ± 0	3.55 ± 2
Quinidine	249 ± 47	118 ± 73
Risperidone	33.7 ± 8	15.6 ± 2
9-OH-Risperidone	25.7 ± 12	5.37 ± 1
Thiopental	3.22 ± 1	5.48 ± 2

TABLE 4

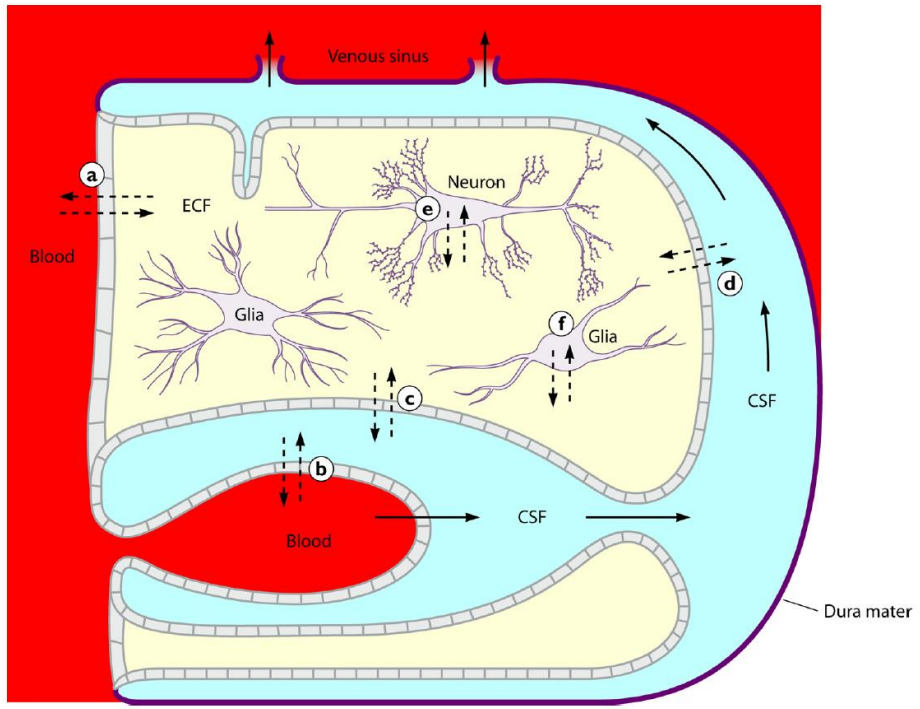
The -fold difference of use of the unbound brain concentration measured by brain homogenate method (C_{ub}), CSF concentration (C_{CSF}), and unbound plasma concentration (C_{up}) to predict the unbound brain interstitial concentration measured by brain microdialysis (C_m) of the nine compounds

Compound	C_{ub} vs. C_m [a]	C_{CSF} vs. C_m [a]	C_{up} vs. C_m [a]
Carbamazepine	(2)	1	1
Citalopram	1	1	1
Ganciclovir	2	1	14
Metoclopramide	1	1	3
N-Desmethylclozapine	1	1	6
Quinidine	(3)	2	6
Risperidone	(2)	2	2
9-OH-Risperidone	(2)	5	9
Thiopental	(4)	1	1

[a] Concentrations used in the calculations were the values at 6 h after starting intravenous infusion. The reported number represents the -fold difference determined by the ratios of mean values rounded to the nearest whole number. Numbers in parentheses represent -fold underpredictions.

Liu X, Van Natta K, Yeo H, Vilenski O, Weller PE, Worboys PD, Monshouwer M. Unbound drug concentration in brain homogenate and cerebral spinal fluid at steady state as a surrogate for unbound concentration in brain interstitial fluid. Drug Metab Dispos. 2009 Apr;37(4):787-93.

Diffusion des antibiotiques au sein de l'abcès



Compound (reference[s] for CSF penetration)	AUC_{CSF}/AUC_S [b]	
	Uninflamed or mildly inflamed meninges	Strong meningeal inflammation
Penicillins	**0.02**	**0.2**
Cephalosporins	**0.007–0.1**	**0.15**
Carbapenems	**0.2**	**0.3**
Fluoroquinolones	**0.3–0.7**	**0.7–0.9**
Ciprofloxacin (173, 261)	0.24, 0.43	0.92
Ofloxacin (169)	0.62	
Levofloxacin (189, 223)	0.71	
Moxifloxacin (4, 5, 105)	0.46	0.79 (0.71–0.94)
Macrolides (98)		
Clarithromycin (137)	Not available	0.18
Tetracyclines	Ratios of individual CSF and serum samples suggest AUC ratio ~0.2	Ratios of individual CSF and serum samples suggest AUC ratio ~0.2
Doxycycline (56, 107, 108, 269)		
Linezolid (20, 252)	0.9 (0.8–1)	Not available
Metronidazole (93, 101, 258)	Not available	0.87
Rifamycins		
Rifampin (52, 62, 89, 106, 150, 163, 174)	0.22	Not available
Trimethoprim and sulfamethoxazole (57, 125, 257)		
Trimethoprim	0.18	0.42–0.51
Sulfamethoxazole	0.12	0.24–0.30

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès

FLUOROQUINOLONES

Très bonne diffusion neurologique même sans inflammation méningée
Faible PM
Caractère lipophile
Faible liaison plasmatique

Diffusion LCR

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FLUOROQUINOLONES

Très bonne diffusion neurologique même sans inflammation méningée
Faible PM
Caractère lipophile
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Concentrations dans LCR seulement 2 fois supérieures aux concentration cérébrales (Brain Interstitial Fluid)

Research Article | Article

Quantitative Brain Microdialysis Study on the Mechanism of Quinolones Distribution in the Central Nervous System

Tsuyoshi Ooie, Tetsuya Terasaki, Hiroshi Suzuki, and Yuichi Sugiyama

Drug Metabolism and Disposition July 1997, 25 (7) 784-0789;

Steady-state concentration of quinolones in the serum, brain, brain ISF, and CSF of rats

	Abbreviation	Unit	NFLX	OFLX	FLRX	PFLX
Brain ISF concentration	C_{ISF}	μg/ml	0.233 ± 0.065	0.603 ± 0.206	0.539 ± 0.071	0.716 ± 0.034
CSF concentration	C_{CSF}	μg/ml	0.229 ± 0.028	1.21 ± 0.30	1.55 ± 0.21	1.82 ± 0.26

serum concentrations due to restricted distribution in the brain. Cerebrospinal fluid concentrations of the quinolones were approximately twice as high as the brain ISF concentrations, except for

Ooie T, Terasaki T, Suzuki H et al. Quantitative brainmicrodialysis study on the mechanism of quinolones distribution in the central nervous system. DrugMetab Dispos 1997; 25: 784–9.

Diffusion des antibiotiques au sein de l'abcès

MLS

MACROLIDES

Diffusion moyenne
Caractère lipophile
Mais fort PM et affinité P-gp

Diffusion LCR

Compound (reference[s] for CSF penetration)	AUC_{CSF}/AUC_S[b]	
	Uninflamed or mildly inflamed meninges	Strong meningeal inflammation
Macrolides (98)		
Clarithromycin (137)	Not available	0.18

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Diffusion des antibiotiques au sein de l'abcès

MLS

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Diffusion moyenne
Caractère lipophile
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LINCOSAMIDES

Peu de données de diffusion cérébrale
Forte liaison plasmatique
Expérience du VIH et de la Toxo

Diffusion des antibiotiques au sein de l'abcès

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Mais fort PM et affinité P-gp

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Expérience du VIH et de la Toxo

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 1998, p. 3014–3017 Vol. 42, No. 11
0066-4804/98/$04.00+0

Penetration of Clindamycin and Its Metabolite *N*-Demethylclindamycin into Cerebrospinal Fluid following Intravenous Infusion of Clindamycin Phosphate in Patients with AIDS

GIORGIO GATTI,[1]* MARINA MALENA,[2] ROSETTA CASAZZA,[1] MARIE BORIN,[3] MATTEO BASSETTI,[1] AND MARIO CRUCIANI[2]

Infectious Diseases Institute, University of Genoa, Genoa,[1] and Infectious Diseases Institute, University of Verona, Verona,[2] Italy, and Pharmacia and Upjohn, Kalamazoo, Michigan[3]

and from 0.120 to 0.283 mg/liter at 2.5 h following the beginning of the infusion. The concentrations of clindamycin in CSF were well above the 50% inhibitory concentration of 0.001 mg/liter and the parasiticidal

Patient no.[a]	Age (yr)	Concn of clindamycin in:		
		Plasma (mg/liter)	CSF (mg/liter)	CSF/plasma ratio[c]
1	39	8.3	0.091	0.011
2	29	10.5	0.231	0.022
3	54	14.7	0.158	0.011
4	36	14.0	0.429	0.031
5	40	26.5	0.234	0.009
Mean	40	14.8	0.229	0.017
SD (%CV[d])	11 (27)	6.3 (43)	0.113 (50)	0.008 (51)
6	35	17.7	0.143	0.008
7	42	10.6	0.120	0.011
8	33	19.6	0.259	0.013
9	62	15.8	0.283	0.018
10	30	14.6	0.221	0.015
Mean	40	15.7	0.205	0.013
SD (%CV)	13 (32)	3.1 (19)	0.064 (31)	0.003 (25)

Clindamycine
1 dose 1200 mg IV

Gatti, G., M. Malena, R. Casazza, M. Borin, M. Bassetti, and M. Cruciani. 1998. Penetration of clindamycin and its metabolite N-demethylclindamycin into cerebrospinal fluid following intravenous infusion of clindamycin phosphate in patients with AIDS. Antimicrob. Agents Chemother. 42:30143017.

Recommandations

MLS

MACROLIDES

Diffusion moyenne
Caractère lipophile
Mais fort PM et affinité P-gp

LINCOSAMIDES

Peu de données de diffusion cérébrale
Forte liaison plasmatique
Expérience du VIH et de la Toxo

Pyrimethamine-Clindamycin vs. Pyrimethamine-Sulfadiazine as Acute and Long-Term Therapy for Toxoplasmic Encephalitis in Patients with AIDS

Christine Katlama, Stephane De Wit, Elizabeth O'Doherty, Martine Van Glabeke, Nathan Clumeck, and the European Network for Treatment of AIDS (ENTA) Toxoplasmosis Study Group*

From the Department of Infectious Diseases and Tropical Medicine, Pitié-Salpêtrière Hospital, Paris, France; and EORTC Data Centre; the Division of Infectious Diseases, Saint-Pierre Hospital; and ENTA Data and Coordinating Centre, Brussels, Belgium

Table 3. Results of an intent-to-treat analysis of the appearance of brain mass lesions during maintenance treatment of patients with AIDS and TE.

Variable	No. (%) of patients	
	Pyr-Cm (n = 93)	Pyr-Sdz (n = 82)
Recurrent brain lesions	32 (34)	20 (24)
Relapse of toxoplasmosis	20 (22)	9 (11)
Biopsy-proven TE	1	0
Favorable response to therapy	19	9
Biopsy-proven lymphoma	2 (2)	2 (2)
No definitive diagnosis	10 (11)	9 (11)
Brain lesions unresponsive to therapy	4	7
Efficacy unknown	5	1
No treatment	1	1

NOTE. Cm = clindamycin; Pyr = pyrimethamine; Sdz = sulfadiazine; TE = toxoplasmic encephalitis.

p = 0,02

Pas de différence entre Pyr/Sdz vs Pyr/Cm lors des 6S de la phase d'attaque (Clinda 2400 mg/j)

Plus de rechute dans le groupe Pyr/Cm lors de la phase de maintenance (Clinda 1200 mg/j)

Katlama C, De Wit S, O'Doherty E, Van Glabeke M, Clumeck N. Pyrimethamine-clindamycin vs. pyrimethamine-sulfadiazine as acute and long-term therapy for toxoplasmic encephalitis in patients with AIDS. Clin Infect Dis. 1996 Feb;22(2):268-75. doi: 10.1093/clinids/22.2.268. PMID: 8838183.

Diffusion des antibiotiques au sein de l'abcès

IMIDAZOLES

Diffusion bonne
Caractère lipophile
Faible poids moléculaire

Diffusion LCR

Compound (reference[s] for CSF penetration)	AUC_{CSF}/AUC_S [b]	
	Uninflamed or mildly inflamed meninges	Strong meningeal inflammation
Metronidazole (93, 101, 258)	Not available	0.87

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès

IMIDAZOLES

Diffusion bonne
Caractère lipophile
Faible poids moléculaire

Dosages intra-abcès

chloramphenicol. The pus was centrifuged and the supernatant diluted twofold in Ringers solution prior to assay. Standards were also prepared in Ringers. A level of 42 µg/ml was obtained. We feel this level was not influenced by other antibiotics as the fluid produced a zone of inhibition less than 1 mm around wells cut in an agar plate lawned by *Bacillus subtilis*.

Our study has shown that either oral or intravenous administration of metronidazole results in high concentrations of active agent in the pus of cerebral abscesses. This, coupled with the extremely rapid bactericidal activity that has been shown in

TABLE III—*Medronidazole levels in cerebrospinal fluid and pus from cerebral abscesses. Values in parentheses are concurrent serum levels*

Case No	Dose of metronidazole	Route of administration	Material	Concentration of metronidazole (µg/ml)	
				Biological assay	Polarographic assay
4	400 mg 8 hourly	Oral	Pus		35·0 (11·5)
5	600 mg 8 hourly	Intravenous	Pus		45·0 (12·5)
8	400 mg 8 hourly	Oral	Pus	21·0 (14)	34·4 (35·1)
9	400 mg 8 hourly	Intravenous	Ventricular fluid	16·8	20·7

CMI Flagyl Bacteroides < 6

Ingham HR, Slekon JB, Roxby CM. Bacteriological study of otogenic cerebral abscesses: chemotherapeutic role of metronidazole. Br Med J. 2(6093), 991–993 (1977).
George RH, Bint AJ. Letter: Treatment of a brain abscess due to Bacteroides fragilis with metronidazole. J. Antimicrob. Chemother. 2(1), 101–102 (1976).

Diffusion des antibiotiques au sein de l'abcès

RIFAMPICINE

Caractère lipophile
Fort poids moléculaire
Forte liaison plasmatique

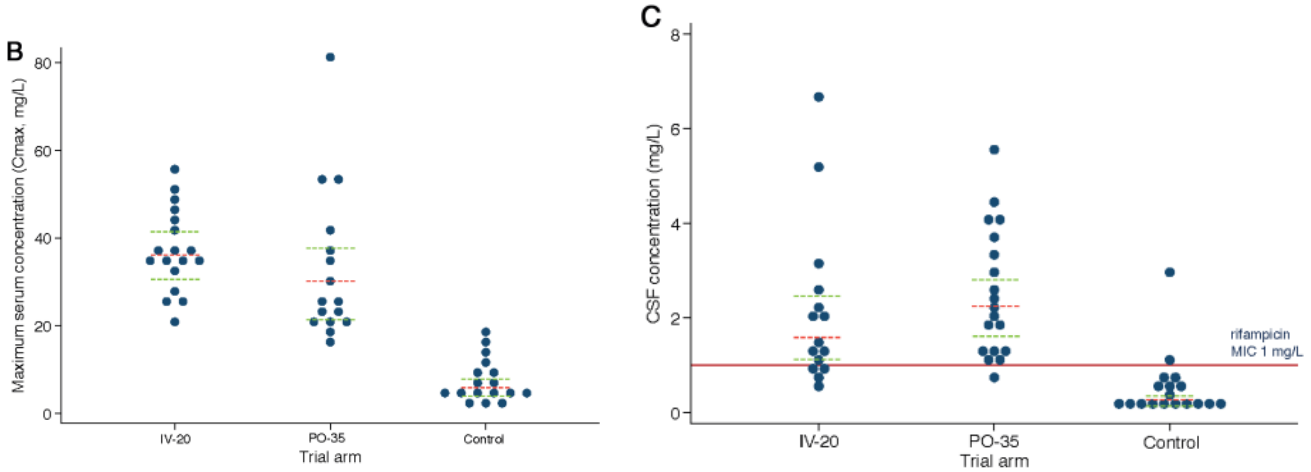
Rifamycins		
Rifampin (52, 62, 89, 106, 150, 163, 174)	0.22	Not available

Clinical Infectious Diseases
MAJOR ARTICLE

High-Dose Oral and Intravenous Rifampicin for the Treatment of Tuberculous Meningitis in Predominantly Human Immunodeficiency Virus (HIV)-Positive Ugandan Adults: A Phase II Open-Label Randomized Controlled Trial

Fiona V. Cresswell, David B. Meya, Enock Kagimu, Daniel Grint, Lindsey te Brake, John Kasibante, Emily Martyn, Morris Rutakingirwa, Carson M. Quinn, Micheal Okirwoth, Lillian Tugume, Kenneth Ssembambulidde, Abdu K. Musubire, Ananta S. Bangdiwala, Allan Buzibye, Conrad Muzoora, Elin M. Svensson, Rob Aarnoutse, David R. Boulware, and Alison M. Elliott

Serum concentration **LCR concentration**



IV 20 mg/kg/j vs PO 35 mg/kg/j vs control (PO 10 mg/kg/j)

Cresswell FV, Meya DB. High-Dose Oral and Intravenous Rifampicin for the Treatment of Tuberculous Meningitis in Predominantly Human Immunodeficiency Virus (HIV)-Positive Ugandan Adults: A Phase II Open-Label Randomized Controlled Trial. Clin Infect Dis. 2021 Sep 7;73(5):876-884. doi: 10.1093/cid/ciab162. PMID: 33693537; PMCID: PMC8423465.

Diffusion des antibiotiques au sein de l'abcès

RIFAMPICINE

Caractère lipophile
Fort poids moléculaire
Forte liaison plasmatique

Clinical Infectious Diseases
MAJOR ARTICLE

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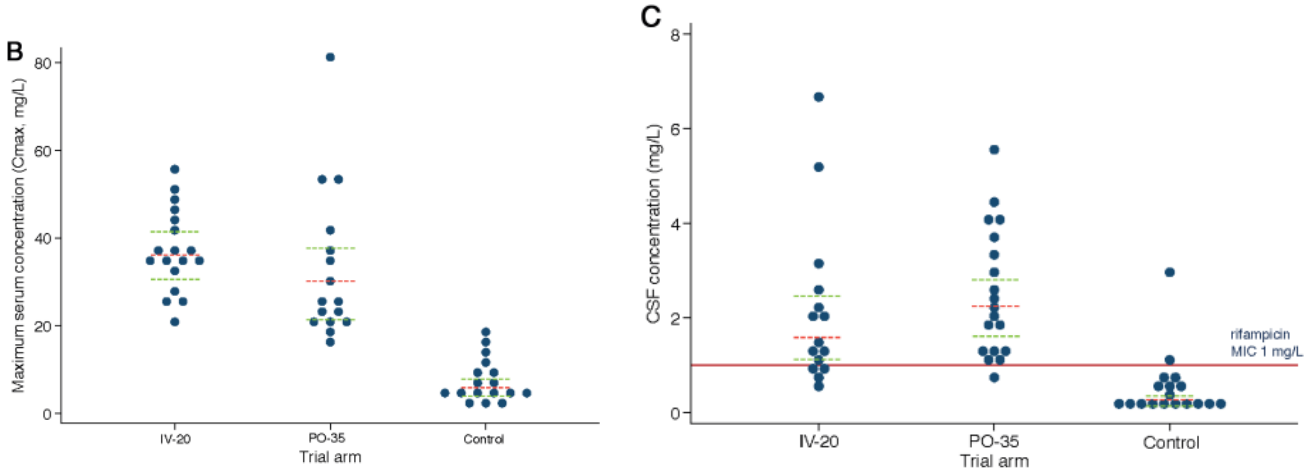
Wellcome Open Research
Wellcome Open Research 2020, 4:190 Last updated: 07 OCT 2020

Check for updates

STUDY PROTOCOL

REVISED **High dose oral rifampicin to improve survival from adult tuberculous meningitis: A randomised placebo-controlled double-blinded phase III trial (the HARVEST study)**

Serum concentration **LCR concentration**



IV 20 mg/kg/j vs PO 35 mg/kg/j vs control (PO 10 mg/kg/j)

Diffusion des antibiotiques au sein de l'abcès

BACTRIM

Diffusion bonne
Caractère lipophile
Faible poids moléculaire

Diffusion LCR

Compound (reference[s] for CSF penetration)	AUC_{CSF}/AUC_S[b]	
	Uninflamed or mildly inflamed meninges	Strong meningeal inflammation
Trimethoprim and sulfamethoxazole (57, 125, 257)		
Trimethoprim	0.18	0.42–0.51
Sulfamethoxazole	0.12	0.24–0.30

Nau R, Sorgel F, Eiffert H. Penetration of Drugs through the Blood-Cerebrospinal Fluid/Blood-Brain Barrier for Treatment of Central Nervous System Infections. ClinMicrobiol Rev. 1 oct 2010;23(4):85883.

Diffusion des antibiotiques au sein de l'abcès

BACTRIM

Diffusion bonne
Caractère lipophile
Faible poids moléculaire

Utilisation ++
Toxoplasmose 15 mg/kg/j TMP
Nocardiose 10-20 mg/kg/j TMP
Listeria 15 mg/kg/j TMP

Intravenous therapy is generally preferred, at least initially, in most patients with nocardiosis. However, some patients with a non-severe presentation (e.g. primary skin nocardiosis or mild isolated pulmonary nocardiosis) may start with oral antimicrobial therapy if the selected agent has good oral bioavailability (e.g. trimethoprim-sulfamethoxazole) and if the patient is able to take and absorb oral drugs.

Clinical Microbiology and Infection 27 (2021) 550–558

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journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

How do I manage nocardiosis?

Ili Margalit [1,2,*], David Lebeaux [3,4], Ori Tishler [5], Elad Goldberg [2,5], Jihad Bishara [1,2], Dafna Yahav [1,2], Julien Coussement [6,7]

Nocardiosis extent	Primary skin	Isolated pulmonary	Dissemination* without CNS involvement	CNS involvement
Initial treatment (i.e., before species identification and AST results)	Trimethoprim-sulfamethoxazole ** Possible alternative: LZD**	Trimethoprim-sulfamethoxazole ± IMI or AMK or CRO or CTX** Possible alternatives: LZD ± IMI or CRO or CTX** Monotherapy (e.g., with trimethoprim-sulfamethoxazole) is probably appropriate in selected patients with non-severe pulmonary nocardiosis	Trimethoprim-sulfamethoxazole ± IMI or AMK or CRO or CTX** Possible alternatives: LZD ± IMI or CRO or CTX**	Trimethoprim-sulfamethoxazole with IMI ± AMK**† Possible alternative: LZD with IMI**

**Treatment regimens: trimethoprim-sulfamethoxazole: 10–20 mg trimethoprim/kg/day (possibly lower dose in patients with primary skin nocardiosis), secondary prophylaxis: daily oral at least 800/160 mg (unclear effectiveness, and breakthrough nocardiosis described while on 800/160 mg once daily[17]); linezolid: IV, oral: 600 mg twice daily; minocycline: oral: 100–300 mg twice daily; AMK: IV: 20–30 mg/kg/day; CRO: IV: 2000 mg once daily or twice daily if CNS involvement; CTX: IV: 2000 mg three times daily or 4000 mg three times daily if CNS involvement; IMI: IV: 500 mg four times daily. Dose adjustment for renal function is required for the following drugs: trimethoprim-sulfamethoxazole, AMK, CTX, IMI.

Margalit I, Lebeaux D, Tishler O, Goldberg E, Bishara J, Yahav D, Coussement J. How do I manage nocardiosis? Clin Microbiol Infect. 2021 Apr;27(4):550-558.

Sommaire

- Introduction
- Que proposent les recommandations ?
- Peut-on faire un relais per os : Oui ? Non ?
- Quelle est la diffusion des molécules PO dans l'abcès ?
- Quel relais per os proposer ?
- Conclusion et perspectives : essai européen ORAL

Sommaire

- Quel relais per os proposer ?

Microbiologie des abcès à pyogènes

Table 1 Culture results and major groups of causative microorganisms[a]

Characteristic	All patients	Children
Positive culture	4,543/6,663 (68)	631/1,093 (63)
Monomicrobial	3,067 (77)	325 (73)
Polymicrobial	902 (23)	117 (27)
Cultured microorganisms	5,894	724
Streptococcus spp	2,000 (34)	260 (36)
Viridans streptococci	755 (13)	58 (6)
S pneumoniae	139 (2)	27 (4)
Enterococcus	49 (0.8)	2 (0.3)
Other/not specified	1,057 (18)	173 (24)
Staphylococcus spp	1,076 (18)	128 (18)
S aureus	782 (13)	80 (11)
S epidermidis	148 (3)	31 (4)
Not specified	146 (2)	16 (2)
Gram-negative enteric	861 (15)	114 (16)
Proteus spp	417 (7)	60 (8)
Klebsiella pneumoniae	135 (2)	11 (2)
Escherichia coli	126 (2)	18 (2)
Enterobacteriae	101 (2)	9 (1)
Pseudomonas spp	122 (2)	13 (2)
Actinomycetales	148 (3)	16 (2)
Nocardia	57 (1)	0
Corynebacterium	49 (0.8)	7 (1)
Actinomyces	48 (0.8)	8 (1)
Mycobacterium tuberculosis	41 (0.7)	1 (0.2)
Haemophilus spp	124 (2)	41 (6)
Peptostreptococcus spp	165 (3)	45 (6)
Bacteroides spp	370 (6)	33 (5)
Fusobacterium spp	119 (2)	17 (2)
Parasites	5 (0.1)	0
Fungi	83 (1)	8 (1)

Brouwer MC, Coutinho JM, Van De Beek D. Clinical characteristics and outcome of brain abscess: Systematic review and meta-analysis. *Neurology* 2014; **82**: 806–13.

Microbiologie des abcès à pyogènes

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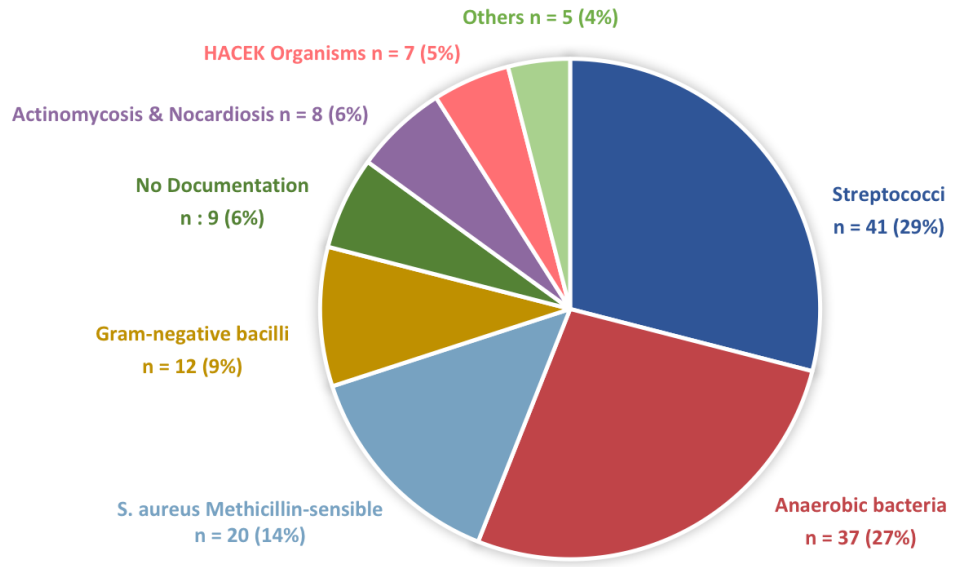
Streptocoques viridans ++ (alpha-hémolytique)

Dont SAG = *Streptoccosus anginosus* Group (*S. anginosus/milleri*, *S. constellatus*, *S. intermedius*), Streptocoques oraux *(S. mitis, S. oralis, S. sanguinis), S. mutans*, *S. salivarius*.

Brouwer MC, Coutinho JM, Van De Beek D. Clinical characteristics and outcome of brain abscess: Systematic review and meta-analysis. *Neurology* 2014; **82**: 806–13.

Microbiologie des abcès à pyogènes

Figure 2 : Microbiology Results (Percentage of Identified Bacteria n = 139)



microbial infections occurred in 30 patients. The most common species were streptococci (29.5%; 41/139), particularly from the *Streptococcus anginosus* group, anaerobic bacteria (26.6%; 37/139), MSSA (14.4%; 20/139) and Gram-negative bacilli (8.6%; 12/139). There were three cases of nocardiosis and five cases of actinomycosis.

Streptocoques chez 42/109 patients (38,5%)

Dont Streptocoques viridans +++
Chez 35/42 patients (83,3%)
Caractère polymicrobien 11/35 (31,4%)
Groupe Anginosus chez 31/35 patients (88,6%)
Streptocoques oraux chez 4/35 patients (11,4%)

Polymicrobien
69/109 (63%)
Monomicrobien
30/109 (27%)

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020; **75**: 3062–6.

Microbiologie des abcès à pyogènes

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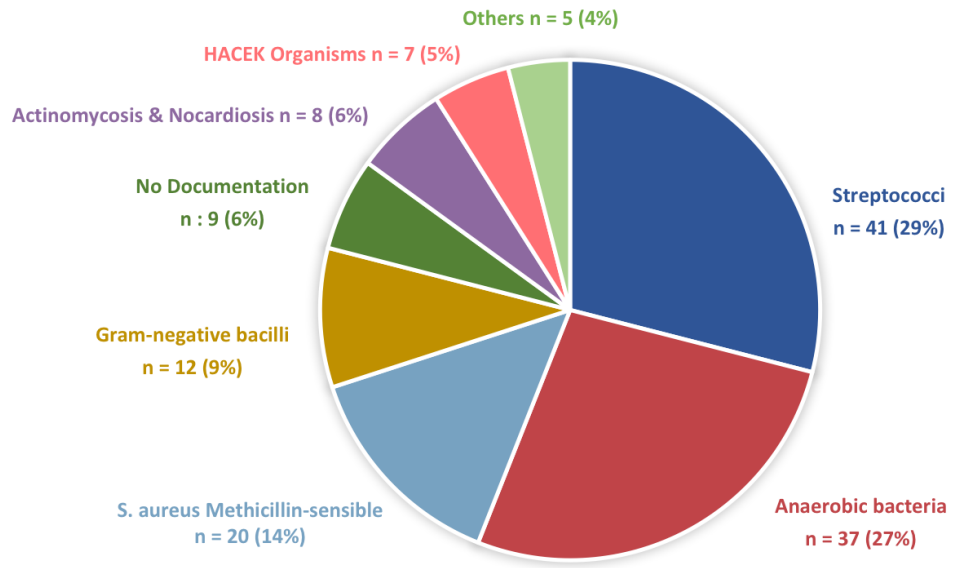

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Bactéries anaérobies

Retrouvées chez 30/109 patients (27,5%)

Caractère polymicrobien 20/30 (66,7%)

Anaérobies BGN (56,6%)

Fusobacterium (40%)

Peptostreptococcus (26,7%)

Aucun *Bacteroides*

Anaérobies CGP (26,7%)

Prevotella (23,3%)

Anérobies BGP (16,7%)

Proprionibacterim acnes (16,7%)

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020; **75**: 3062–6.

Microbiologie des abcès à pyogènes

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03904-w

BRIEF REPORT

Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study

M. Lauda-Maillen[1,2] · A. Lemaignen[3,4] · M. Puyade[5] · M. Catroux[2] · G. Le Moal[2] · G. Beraud[2] · H. El Hajj[6] · A. Michaud[7] · C. Destrieux[8,9] · L. Bernard[3,4] · B. Rammaert[1,2,10] · F. Cazenave-Roblot[1,2,10]

Received: 19 February 2020 / Accepted: 7 April 2020

Abscesses were predominantly caused by *Streptococcus* species ($n = 46$; 46%) and anaerobes ($n = 39$; 39%) (Table 1). There were more *Staphylococcus* species ($n = 9$; 38% vs $n = 14$; 18%; $p = 0.05$) and fewer *Streptococcus* species ($n = 6$; 25% vs $n = 40$; 52%; $p = 0.02$) in PO group. There was no difference between groups regarding anaerobes ($p = 0.54$). No *Bacteroides* species were isolated.

63% monomicrobien

Table 1 Baseline characteristics, management and 3-month outcome of 101 patients with brain abscesses or empyema

	TOTAL ($n = 101$) (unless specified)	PO group ($n = 24$)	IV group ($n = 77$)	p value
Microbiological features				
Monomicrobial	63 (63)	15 (63)	48 (62)	0.9
Anaerobic bacteria	11 (11)	3 (13)	8 (10)	
- *Cutibacterium acnes*	5 (5)	2 (8)	3 (4)	
Actinomyces spp.	1 (1)		1 (1)	
Gram-negative bacilli	8 (8)	2 (8)	6 (8)	
Staphylococcus aureus	17 (17)	7 (29)	10 (13)	
Streptococcus spp.	26 (26)	3 (13)	23 (30)	
Listeria	1 (1)		1 (1)	

Lauda-Maillen M, Lemaignen A, Puyade M, *et al.* Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 209–13.

Microbiologie des abcès à pyogènes

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39% polymicrobien

Table 1 Baseline characteristics, management and 3-month outcome of 101 patients with brain abscesses or empyema

	TOTAL ($n = 101$) (unless	PO group ($n = 24$)	IV group ($n = 77$)	p value
Polymicrobial	39 (39)	9 (38)	30 (39)	0.9
Anaerobic bacteria	28 (28)	5 (21)	23 (30)	
- *Cutibacterium acnes*	2 (2)		2 (3)	
Actinomyces spp.	10 (10)	3 (13)	7 (9)	
Gram-negative bacilli	16 (16)	3 (13)	13 (17)	
Staphylococcus epidermidis	2 (2)	1 (4)	1 (1)	
Staphylococcus aureus	4 (4)	1 (4)	3 (4)	
Enterococcus faecalis	2 (2)		2 (3)	
Streptococcus spp.	20 (20)	3 (13)	17 (22)	

Lauda-Maillen M, Lemaignen A, Puyade M, *et al.* Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 209–13.

Quel relais PO proposer ?

De Louvois, E.M. Brown, R. Bayston, J. The rational use of antibiotics in the treatment of brain abscess. Br J Neurosurg. janv 2000;14(6):525-30.

Quel relais PO proposer ?

Eur J Clin Microbiol Infect Dis (2000) 19:332–335

Article

Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy

A.T. Skoutelis, C.A. Gogos, T.E. Maraziotis, H.P. Bassaris

8 patients
Refus d'un traitement IV prolongé en hospitalisation
Evolution favorable : 8/8

was done prospectively and all patients received the same oral regimen (ciprofloxacin 750 mg every 12 h, amoxicillin 1.5 g every 8 h, metronidazole 500 mg every 6 h). All patients were followed up at monthly intervals, CT and MRI being performed monthly.

Skoutelis AT, Gogos CA, Maraziotis TE, Bassaris HP. Management of Brain Abscesses with Sequential Intravenous/Oral Antibiotic Therapy. *European Journal of Clinical Microbiology & Infectious Diseases* 2000.

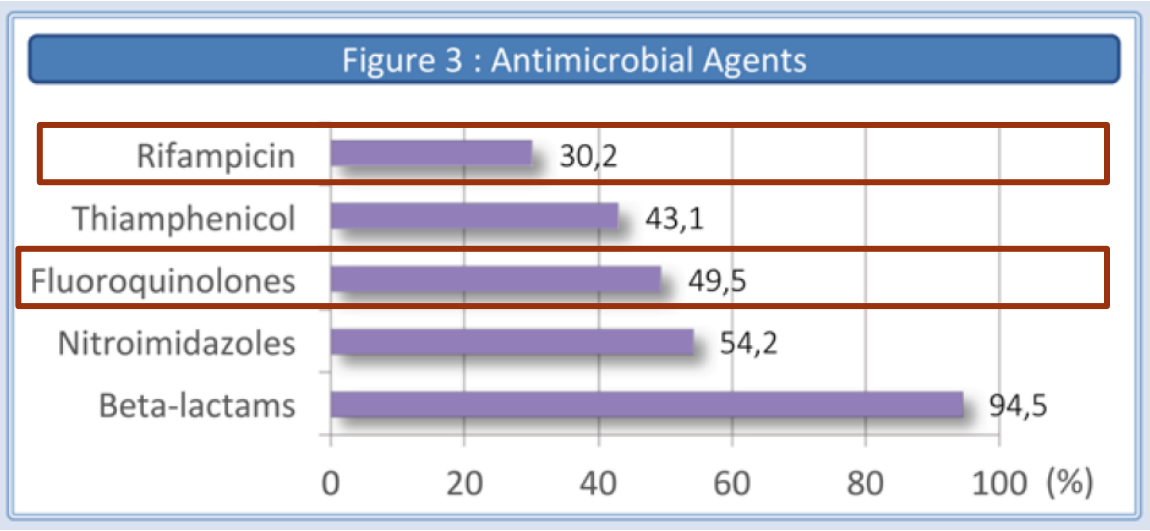
Quel relais PO proposer ?

J Antimicrob Chemother
doi:10.1093/jac/dkaa285

Journal of Antimicrobial Chemotherapy

Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients

Antoine Asquier-Khati[1]*, Colin Deschanvres[1], David Boutoille[1], Maeva Lefebvre[1], Paul Le Turnier[1], Benjamin Gaborit[1], Karim Lakhal[2], Kevin Buffenoir[3], Lydie Khatchatourian[4] and Nathalie Asseray[1] on behalf of the Nantes Brain Abscesses study group†



20 cases of thiophenicol-induced reversible cytopenia. Forty-eight patients (44.4%) were switched to an oral regimen after a median length of 19 days (IQR: 12–28), with associations of fluoroquinolones (49%), rifampicin (29.4%), clindamycin (25.5%), nitroimidazoles (21.6%) and co-trimoxazole (19.6%). Among the patients switched to oral therapy, 38 (79.2%) received a combined therapy. The most common combination was a fluoroquinolone with rifampicin (20.4%).

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020; **75**: 3062–6.

Quel relais PO proposer ?

J Antimicrob Chemother
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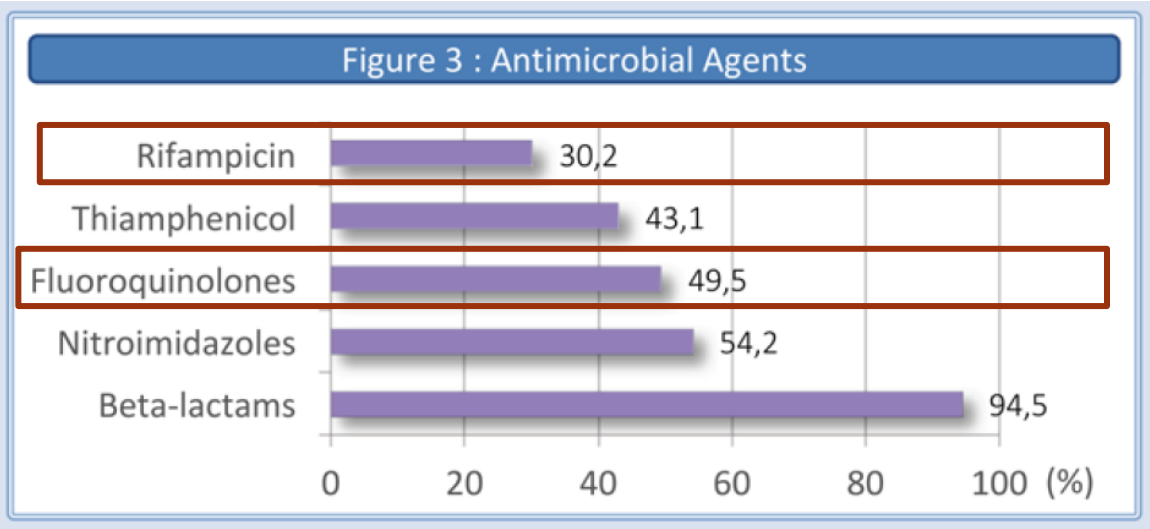
Journal of Antimicrobial Chemotherapy

Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients

Antoine Asquier-Khati[1]*, Colin Deschanvres[1], David Boutoille[1], Maeva Lefebvre[1], Paul Le Turnier[1], Benjamin Gaborit[1], Karim Lakhal[2], Kevin Buffenoir[3], Lydie Khatchatourian[4] and Nathalie Asseray[1] on behalf of the Nantes Brain Abscesses study group†



20 cases of thiophenicol-induced reversible cytopenia. Forty-eight patients (44.4%) were switched to an oral regimen after a median length of 19 days (IQR: 12–28), with associations of fluoroquinolones (49%), rifampicin (29.4%), clindamycin (25.5%), nitroimidazoles (21.6%) and co-trimoxazole (19.6%). Among the patients switched to oral therapy, 38 (79.2%) received a combined therapy. The most common combination was a fluoroquinolone with rifampicin (20.4%).

Patients inclus : 2003-2016
48/109 (44%) relais PO
Depuis bithérapie majoritaire :
Moxifloxacine + Clindamycine

Asquier-Khati A, Deschanvres C, Boutoille D, *et al.* Switch from parenteral to oral antibiotics for brain abscesses: a retrospective cohort study of 109 patients. *Journal of Antimicrobial Chemotherapy* 2020; **75**: 3062–6.

Quel relais PO proposer ?

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03904-w

BRIEF REPORT

Check for updates

Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study

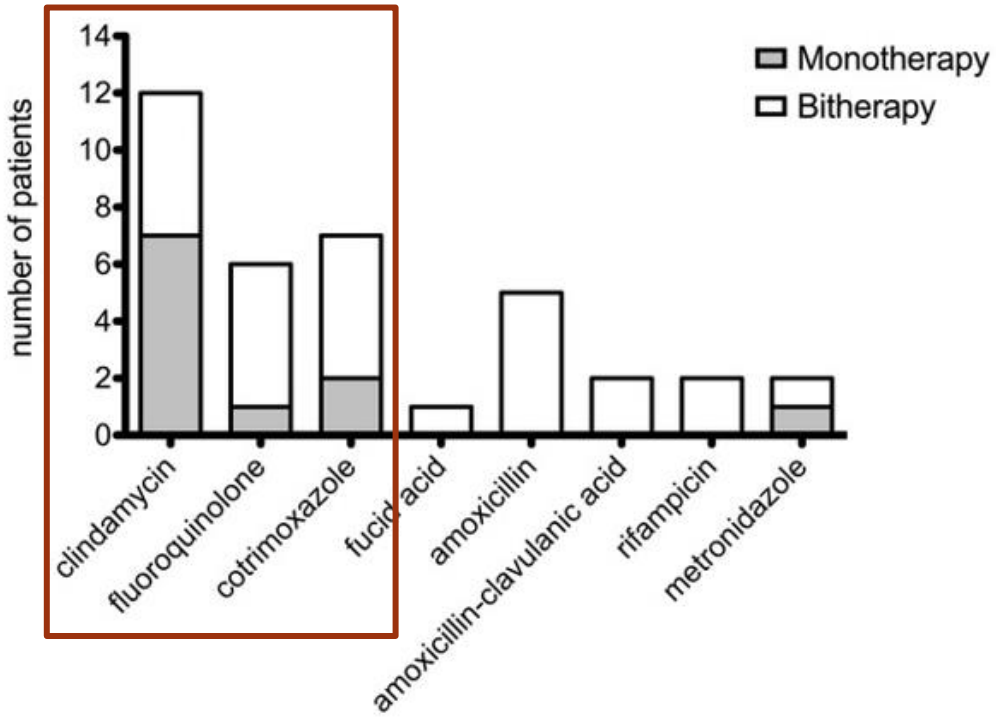
M. Lauda-Maillen[1,2] · A. Lemaignen[3,4] · M. Puyade[5] · M. Catroux[2] · G. Le Moal[2] · G. Beraud[2] · H. El Hajj[6] · A. Michaud[7] · C. Destrieux[8,9] · L. Bernard[3,4] · B. Rammaert[1,2,10] · F. Cazenave-Roblot[1,2,10]

Received: 19 February 2020 / Accepted: 7 April 2020

Période d'inclusion : 2007-2018
24/101 (23,7%) relais PO

of 21 days (IQR 14–26). Clindamycin was the most widely used drug for oral switch in PO group (12 cases; 50%), alone ($n = 7$) or in combination with another antibiotic drug ($n = 5$) (Supplemental data; Sd4 and Sd5).

Supplemental data 4 (Sd4): Oral antibiotics used in the PO group (n=24)



Lauda-Maillen M, Lemaignen A, Puyade M, *et al.* Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 209–13.

Quel relais PO proposer ?

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Supplemental data 5 (Sd5): Oral antibiotics in PO group (n=24) and abscess microbiology

Antibiotics	Isolated bacteria
clindamycin (n=7)	*Propionibacterium avidum* (n=1)
	Streptococcus intermedius (n=2)
	MSSA (n=4)
clindamycin+ cotrimoxazole (n=2)	*Cutibacterium acnes* (n=1)
	Actinomyces, Aggregatibacter (n=1)
clindamycin + amoxicillin (n=1)	*Streptococcus salivarius, Prevotella denticola, Fusobacterium nucleatum, Parvimonas micra*
clindamycin + fluoroquinolone (n=2)	*Staphylococcus epidermidis, Fusobacterium nucleatum* (n=1)
	Actinomyces, Aggregatibacter (n=1)
fluoroquinolone (n=1)	*Salmonella houtenae*
cotrimoxazole (n=2)	*Streptococcus pneumoniae, Haemophilus influenzae* (n=1)
	Klebsiella pneumoniae, MSSA (n=1)
cotrimoxazole+ fluoroquinolone (n=2)	*MSSA* (n=1)
	Enterobacter cloacae (n=1)
cotrimoxazole + fusidic acid (n=1)	*MRSA*
rifampicin + fluoroquinolone (n=1)	*MSSA*
metronidazole (n=1)	*Parvimonas micra+ Fusobacterium nucleatum*
amoxicillin + amoxicillin-clavulanic acid (n=2)	*Streptococcus constellatus* (n=1)
	Actinomyces, Parvimonas micra, Peptoniphilus assacharolyticus, Campylobacter ureolyticus
amoxicillin + rifampicin (n=1)	*Cutibacterium acnes*

Lauda-Maillen M, Lemaignen A, Puyade M, *et al.* Feasibility of early switch to oral antibiotic in brain abscesses and empyema: a multicentre retrospective study. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 209–13.

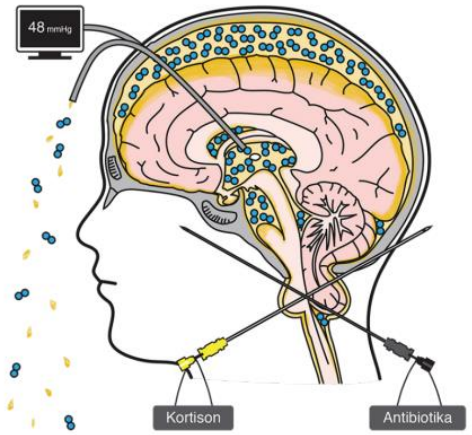
Quel relais PO proposer ?

Vårdprogram

Bakteriella CNS-infektioner

Avser vuxna patienter med akut bakteriell meningit, neurokirurgisk infektion, tuberkulös meningit, hjärnabscess och neuroborrelios

Reviderat 2020
Svenska Infektionsläkarföreningen



Antibiothérapie PO en cas d'abcès non documenté

ciprofloxacin 750 mg x 2 + amoxicillin 1 g x 3 + metronidazol 400 mg x 3.

Antibiothérapie PO adaptée à la documentation : Garder une couverture anaérobie

Tabell 4 (Faktaruta 28).

Tänkbara antibiotika för peroral uppföljning vid behandling av hjärnabsces

amoxicillin	1 g x 3
klindamycin	450 mg x 3
ciprofloxacin	750 mg x 2
moxifloxacin	400 mg x 1
metronidazol	400–500 mg x 2–3
trimetoprim/sulfametoxazol	(160–320 mg/800–1600 mg) x 2
linezolid	600 mg x 2
fusidinsyra	500 mg x 3
rifampicin	600 mg x 1

Blackberg J, Brink M, Ericsson M, Glimåker M, Johansson B, Lindquist L, et al. Vårdprogram, Bakteriella CNS-infektioner. 2010. https://infektion.net/wpcontent/uploads/2017/05/vardpr_cns_100916.pdf. [Accessed 13 January 2020].

Introduction

European Journal of Clinical Microbiology & Infectious Diseases
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ORIGINAL ARTICLE

Check for updates

Treatment of community-acquired bacterial brain abscess: a survey among infectious diseases specialists in France, Sweden, Australia, and Denmark

Jacob Bodilsen[1,2] · Pierre Tattevin[2,3,4] · Steven Tong[5,6] · Pontus Naucler[7] · Henrik Nielsen[1,2,8]

Sondage d'infectiologues (310)
Novembre 2019
Pays concernés :
Suède (29%), Danemark (11%),
France (35%), Australie (25%)

Bodilsen J, Tattevin P, Tong S, Naucler P, Nielsen H. Treatment of community-acquired bacterial brain abscess: a survey among infectious diseases specialists in France, Sweden, Australia, and Denmark. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 255–60.

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Empiric intravenous antimicrobials		
Cefotaxime + metronidazole	154/273	56
Ceftriaxone + metronidazole	68/273	25
Ceftriaxone + metronidazole + vancomycin	11/273	4
Cefotaxime + metronidazole + vancomycin	6/273	2
Benzylpenicillin + metronidazole	6/273	2
Meropenem + vancomycin	5/273	2
Other	23/273	8
Oral antimicrobials		
Early transition to oral antimicrobials*	134/269	50
Consolidation therapy with oral antimicrobials after a full course of IV antimicrobials**	123/264	47
Preferred oral antimicrobials for brain abscess treatment***		
Trimethoprim/Sulfamethoxazole	59/133	44
Amoxicillin + metronidazole	52/133	39
Clindamycin	41/133	31
Moxifloxacin	30/133	23
Amoxicillin + metronidazole + ciprofloxacin	27/133	20
Linezolid	20/133	15
Other	75/133	56

* Denotes transition to oral antimicrobials before a full 4 weeks of intravenous antimicrobials for brain abscess

** Denotes oral antimicrobials after a full course of intravenous antimicrobials for brain abscess for 4–8 weeks

Bodilsen J, Tattevin P, Tong S, Naucler P, Nielsen H. Treatment of community-acquired bacterial brain abscess: a survey among infectious diseases specialists in France, Sweden, Australia, and Denmark. *Eur J Clin Microbiol Infect Dis* 2021; **40**: 255–60.

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Other	75/133	56

La bithérapie ne semble pas indispensable si la molécule utilisée couvre les streptocoques et les anaérobies

* Denotes transition to oral antimicrobials before a full 4 weeks of intravenous antimicrobials for brain abscess

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Sommaire

- Introduction
- Que proposent les recommandations ?
- Peut-on faire un relais per os : Oui ? Non ?
- Quelle est la diffusion des molécules PO dans l'abcès ?
- Quel relais per os proposer ?
- Conclusion et perspectives : essai européen ORAL

Sommaire

- **Conclusion et perspectives : essai européen ORAL**

Essai Européen ORAL

Partial oral antibiotic treatment for bacterial brain abscess: an open-label randomized non-inferiority trial (ORAL)

Jacob Bodilsen[1,2*], Matthijs C. Brouwer[2,3], Diederik van de Beek[2,3], Pierre Tattevin[2,4,5], Steven Tong[6,7], Pontus Naucler[8] and Henrik Nielsen[2,9]

Essai International de phase 3

Suède : 4 centres

Danemark : 4 centres

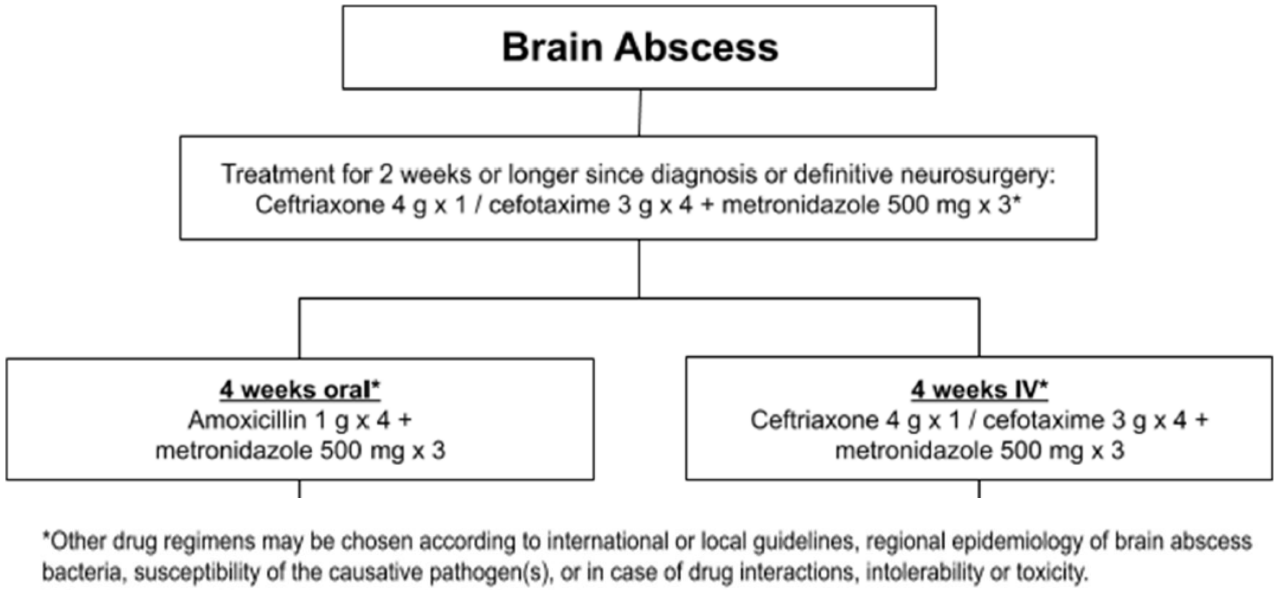
Pays-Bas : 1 centre

France : 17 centres

Australie : 4 centres

33 inclusions en mars 2024

ClinicalTrials.gov



Randomisation à S2 de traitement IV
Pas d'aggravation neurologique ou de reprise chirurgicale envisagée

Bodilsen J, Brouwer MC, Van De Beek D, *et al.* Partial oral antibiotic treatment for bacterial brain abscess: an open-label randomized non-inferiority trial (ORAL). *Trials* 2021; **22**: 796.

Essai Européen ORAL

Traitement de relais proposé

Table 1 Antibiotic treatment recommendations for the ORAL trial[a]

	Intervention group (2 weeks IV + 4 weeks oral)	Standard group (6 weeks IV)
First 2 weeks	Ceftriaxone 4 g × 1 / cefotaxime 3 g × 4 + metronidazole 500 mg × 3	Ceftriaxone 4 g × 1 / cefotaxime 3 g × 4 + metronidazole 500 mg × 3
Next 4 weeks	Oral amoxicillin 1 g × 4 + metronidazole 500 mg × 3	Ceftriaxone 4 g × 1 / cefotaxime 3 g × 4 + metronidazole[b] 500 mg × 3
In case of *Streptococcal spp.* with a minimal inhibitory concentration for penicillin ≥1 mg/L, beta-lactam allergy, non-susceptibility, interaction with other drugs, or development of drug fever.	a) Oral moxifloxacin 400 mg × 1 + metronidazole 500 mg × 3 b) Oral linezolid 600 mg × 2 + metronidazole 500 mg × 3 c) Oral clindamycin 600 mg × 4	a) Meropenem 2 g × 3 b) Moxifloxacin 400 mg × 1 + metronidazole 500 mg × 3 c) Clindamycin 600 mx 4

[a]Other drug regimens may be chosen by the local study investigator at each site according to international or local guidelines, regional epidemiology of brain abscess bacteria, susceptibility of the causative pathogen(s), renal or liver impairment, or in case of drug interactions, intolerability or toxicity. Such changes should be consulted with infectious disease specialists and/or clinical microbiologist taking into consideration the pharmacokinetic/pharmacodynamic properties of the chosen antibiotics

Antibiothérapie laissée à la libre appréciation du prescripteur

Bodilsen J, Brouwer MC, Van De Beek D, *et al.* Partial oral antibiotic treatment for bacterial brain abscess: an open-label randomized non-inferiority trial (ORAL). *Trials* 2021; **22**: 796.

Je vous remercie de votre attention

Bodilsen J, Nielsen H. Early switch to oral antimicrobials in brain abscess: a narrative review. *Clinical Microbiology and Infection* 2023; **29**: 1139–43.