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Lumbiganon P, Chaikitpinyo A

Lumbiganon P, Chaikitpinyo A.
Antibiotics for brain abscesses in people with cyanotic congenital heart disease.
Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD004469.
DOI: 10.1002/14651858.CD004469.pub3.

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TABLE OF CONTENTS

[Intervention Review]

Antibiotics for brain abscesses in people with cyanotic congenital heart disease

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Editorial group: Cochrane Heart Group.
Publication status and date: Stable (no update expected for reasons given in 'What's new'), published in Issue 4, 2021.

Citation: Lumbiganon P, Chaikitpinyo A. Antibiotics for brain abscesses in people with cyanotic congenital heart disease. *Cochrane Database of Systematic Reviews* 2013, Issue 3. Art. No.: CD004469. DOI: 10.1002/14651858.CD004469.pub3.

ABSTRACT

Background

Brain abscess is a focal, intracerebral infection that begins as a localized area of brain infection and develops into a collection of pus surrounded by a well-vascularized capsule. People with cyanotic congenital heart disease are at risk of developing brain abscess.

Objectives

To evaluate the effectiveness of antibiotic regimens for treating brain abscess in people with cyanotic congenital heart disease.

Search methods

We updated the searches of the Cochrane Central Register of Controlled Trials (CENTRAL) on *The Cochrane Library* Issue 12 of 12, December 2012, MEDLINE Ovid (1946 to December Week 4 2012), EMBASE Ovid (1980 to 2013 Week 01) and LILACS (1980 to 9 January 2013) on 9 January 2013. No language or publication restrictions were applied.

Selection criteria

Randomized controlled trials that reported clinically meaningful outcomes and presented results on an intention to treat basis, irrespective of blinding, publication status, or language.

Data collection and analysis

Data were to be extracted, unblinded, by the two reviewers independently.

Main results

No studies meeting the inclusion criteria were identified.

Authors' conclusions

There are no randomized controlled trials about the effectiveness of antibiotic regimens for treating people with cyanotic congenital heart disease who developed a brain abscess. Currently, the antibiotic regimens used are based on previous retrospective studies and clinical experience. There is a need for a well designed multicentre randomized controlled trial to evaluate the effects of different antibiotic regimens.

PLAIN LANGUAGE SUMMARY

Antibiotics for brain abscesses in people with cyanotic congenital heart disease

Serious congenital heart disease leads to abnormal blood flow through the heart and lungs. This results in an inability to carry enough oxygen around the body which makes patients blue (cyanotic) and severely limits their physical activity. People with cyanotic congenital heart disease are at risk of developing brain abscess. This condition is serious and can lead to death because the abscess causes abnormal brain function. Treatment includes antibiotic therapy to kill the bacteria that cause the infection. In people with a large abscess, an operation to drain the abscess may be carried out. Antibiotic therapy for brain abscess should include drugs that penetrate into the abscess cavity. The drugs chosen should also be matched to the sensitivity of the bacteria obtained from the abscess in laboratory culture. There is no evidence from randomized controlled trials to show the best antibiotic regimen for treating people with cyanotic congenital heart disease who develop brain abscess.

BACKGROUND

Brain abscess

Brain abscess is a focal, intracerebral infection that begins as a localized area of infection and develops into a collection of pus surrounded by a well-vascularized capsule (Mathisen 1997). It can originate from infection of contiguous structure (e.g. otitis media, dental infection, mastoiditis, sinusitis), as the result of hematogenous spread from a remote site (particularly in people with cyanotic congenital heart disease), after skull trauma or surgery and, rarely, following meningitis. In at least 15% of cases no source can be identified.

Cyanotic congenital heart disease

Cyanotic congenital heart disease is a congenital defect of the heart that leads to hemodynamic abnormality. Systemic venous return to the right-side of the heart is shunted across the defect into the systemic circulation, resulting in persistent arterial desaturation and cyanosis. People with cyanotic congenital heart disease are at risk of developing brain abscess. Intracardiac right-to-left shunt bypass, by which blood is not filtered through pulmonary circulation where bacteria are intercepted by phagocytosis, may allow direct entry to cerebral circulation. In addition, decreased arterial oxygenation can result in compensatory polycythemia. Increased blood viscosity can cause a focal area of ischemia that serves as a nidus for infection. Shunted blood containing micro-organisms may be seeded in such lesions, forming a cerebral abscess (Matson 1961; Fischbein 1974).

Size of the problem

Brain abscess is not common and is a rare complication of cyanotic congenital heart disease. In one study the frequency of brain abscess in people with cyanotic congenital heart disease was 2% among 1,270 patients during a 13-year period (Fischbein 1974). The peak incidence occurs when the patient is between 4 years and 7 years of age, although cases of brain abscess may occur in adults with cyanotic congenital heart disease (Kagawa 1983). Among the 149 patients with brain abscess in one report, 103 (69.1%) had cyanotic congenital heart disease. In this study, the most common form of cyanotic congenital heart disease was tetralogy of Fallot (51 patients), followed by complete transposition of the great arteries (12 patients) and double outlet of right ventricle (10 patients) (Takeshita 1997). The reported case fatality rates for cyanotic brain abscess in the pre-computerized tomography (CT) era were 38% (Fischbein 1974), 40% (Brewer 1975) and 37% (Kagawa 1983). In the CT era, the in-hospital case fatality in one report was 13.3% (Prusty 1993).

Interventions used

Treatments include intravenous antibiotics alone, or concomitantly combined with surgical interventions such as aspiration of the abscess (Takeshita 1997) and /or abscess excision (Mathisen 1997). The most common organisms isolated in cyanotic brain abscess include *Streptococcus viridans*, microaerophilic streptococci, anaerobic streptococci, and occasionally, *Haemophilus* species (De Louvois 1978; Saez-Llorens 1989). On theoretical grounds, antibiotic therapy for bacterial brain abscess should include agents that penetrate into the abscess cavity and have in vitro activity against the pathogens isolated. Drugs should be given intravenously in order to yield high serum levels and therefore high levels in the abscess cavity. Other adjunctive therapy includes the use of corticosteroid to control cerebral edema in patients with potentially life-threatening complications such as impending cerebral herniation. Severe brain edema may also necessitate the administration of intravenous mannitol and intubation with forced hyperventilation. Rarely, placement of a ventriculostomy catheter for cerebrospinal fluid drainage, to relieve intracranial pressure, may prove lifesaving. Seizures are a frequent complication of brain abscess and anticonvulsants may be needed (Mathisen 1997).

Specific antibiotic treatment

For the past 20 years high dose intravenous penicillin G and chloramphenicol have been used to treat brain abscess in this setting with satisfactory outcomes (Jadavji 1985). The most important drawback of chloramphenicol is its toxic hematologic effect including a common and predictable, but reversible, erythroid suppression of the bone marrow. However, serious irreversible aplastic anemia, leading in many cases to fatal pancytopenia, has been described in patients who received chloramphenicol (Jimenez 1987). Third generation cephalosporins, either cefotaxime or ceftriaxone have good central nervous system penetration (Sjolin 1991; Yamamoto 1993), and excellent in vitro activity against many pathogens isolated from bacterial brain abscess. Metronidazole is highly active against anaerobic bacteria, including *Bacteroides fragilis*, the most resistant anaerobe. Therefore, metronidazole is usually combined with third generation cephalosporins or penicillin G for the treatment of cyanotic brain abscess (Sjolin 1993). As third generation cephalosporins are much more expensive than penicillin G there is a need to evaluate the effects of different antibiotic regimens for the treatment of brain abscess in children with cyanotic congenital heart disease.

OBJECTIVES

To determine, from the best available evidence, the effects (both harms and benefits) of antibiotic regimens for treating people with cyanotic congenital heart disease who develop a brain abscess.

METHODS

Criteria for considering studies for this review

Types of studies

All randomized controlled trials, irrespective of blinding, publication status, or language were to have been included because it was expected that only a small number of trials would be found. This included unpublished trials if the methodology and the data of the trial could be accessed in written form. Only data from the first period of crossover trials would have been included. Trials in which patients were allocated by a quasi-random method, e.g. day of birth or date of admission, were excluded.

Types of participants

People who have cyanotic congenital heart disease and have developed brain abscess. No restrictions on age were made in the search.

Types of interventions

Trials were considered if they compared at least two different antibiotic regimens. In addition to the comparison of different

antimicrobial agents, studies were also included if there was a comparison between the route of administration, the timing of administration and the number of doses of drugs given.

Types of outcome measures

All outcomes were considered at the end of treatment and at maximum follow-up according to the individual trial.

Primary outcomes

1. Complete recovery rate
2. Mortality rate

Secondary outcomes

1. Adverse events, defined as any untoward medical occurrence in a patient which did not necessarily have a causal relationship with the treatment, but resulted in a dose reduction or discontinuation of treatment
2. Severe adverse events, defined according to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use guidelines (ICH-GCP 1997) as any event that would increase mortality; was life-threatening; required in-patient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability; or any important medical event, which might have jeopardized the patient or required further intervention.
3. Length of hospital stay
4. Cost-effectiveness analysis

Search methods for identification of studies

The original search from 2006 (Appendix 1) was updated in 2009 (Appendix 2) and in 2013 (Appendix 3). On 9 January 2013 we searched the Cochrane Central Register of Controlled Trials (CENTRAL) on *The Cochrane Library* Issue 12 of 12, December 2012, MEDLINE Ovid (1946 to December Week 4 2012), EMBASE Ovid (1980 to 2013 Week 01) and LILACS (1980 to 9 January 2013).

The originally used randomized controlled trial filters for MEDLINE (Dickersin 1994) and EMBASE (Lefebvre 1996) were updated (Lefebvre 2011).

The reference lists of relevant articles were checked for any unidentified trials and the authors of included studies, and pharmaceutical companies, contacted where necessary. No language restriction was applied.

Data collection and analysis

Selection of trials for inclusion

Decisions on which trials to be included were taken independently by both reviewers who were unblinded with regard to the names of the authors, investigators, institution, source, and results. Disagreements were resolved by discussion. Excluded trials are listed with the reason for exclusion in the characteristics of excluded studies table.

Methodological quality

Methodological quality was defined as the level of confidence that the design and report restricted bias in the intervention comparison (Moher 1998). According to empirical evidence (Jadad 1996; Juni 2001; Kjaergard 2001; Moher 1998; Schulz 1995), we planned to assess methodological quality in relation to the allocation sequence, allocation concealment, and double blinding. Further, we planned to extract the number of dropouts and withdrawals (Jadad 1996) and how these were included in the analyses (if and how intention-to-treat analyses had been performed) (Hollis 1999).

Data extraction

We planned to extract the following data (by the two reviewers, independently, using standardised extraction sheets). The authors of the trials would be approached to specify the following data, if they had not been reported sufficiently in the article.

Trial characteristics

Methodological quality
Parallel or crossover design
Number of intervention arms
Length of follow-up
Estimation of sample size
Use of intention-to-treat analyses

Patient characteristics

Number of patients randomised to each intervention arm
Mean (or median) age
Number of male and female
Type of cyanotic congenital heart disease
Method for detection of brain abscess
Site and size of brain abscess
Inclusion and exclusion criteria

Intervention characteristics

Type of antibiotics
Dose of antibiotics
Duration of antibiotics
Route of administration
Type and dose of additional intervention(s) and type of surgical interventions, e.g. aspiration or excision of the abscess

Outcome measures

All outcome measures will be extracted from each randomized controlled trial.

Statistical methods

We planned to perform all analyses according to the intention-to-treat method using the last reported observed response (carry forward) and including all patients irrespective of compliance or follow-up. Binary outcomes would be expressed as relative risks and 95% confidence intervals. Continuous data would be analysed using weighted mean difference. Depending on the presence or absence of trial variability (significant heterogeneity defined as $P < 0.1$) a random-effects model (DerSimonian 1986) or a fixed-effect model (Demets 1987) would be used. Rare events would be estimated by Peto odds ratio (Deeks 1998). In case of significant heterogeneity, the potential causes for the heterogeneity would be explored by performing sensitivity analyses. All studies would be combined. Subgroup analyses would be performed analysing all-cause mortality, type of cyanotic congenital heart disease, according to methodological quality, class of antibiotics and duration of treatment. If sufficient trials were found the presence of publication bias would be assessed by funnel plots (Egger 1997).

RESULTS

Description of studies

In the original search in 2006 we found 498 articles (including 8 non-English articles), of which 152 were articles on brain abscess. Most of these 152 articles were case series and case reports. We found eight potentially eligible reports. There were case series of patients, some with cyanotic congenital heart disease, with brain abscess and most articles mentioned the type of antibiotic used for treatment (Abdullah 2001; Gonzalez-Garcia 1999; Hirsch 1983; Jansson 2004; Lu 2002; Mampalum 1988; Seneviratne Rde 2003; Yang 1981). A review on the rational use of antibiotics in the treatment of brain abscess was published in the *British Journal of Neurosurgery* (British Society 2000). These reports are described below in the Discussion.

We found no studies that met the criteria for inclusion in this review. There are no ongoing studies on antibiotic regimens for brain abscess in cyanotic congenital heart disease.

The updated search in June 2009 found an additional 63 references none of which met the inclusion criteria.

The updated search in January 2013 identified 158 new references, none of which met the inclusion criteria.

Risk of bias in included studies

No studies were identified that met the inclusion criteria.

Effects of interventions

No studies were identified that met the inclusion criteria. We did not find any quasi-randomized studies.

DISCUSSION

The treatment of brain abscess requires a multidisciplinary approach. Imaging studies allow early diagnosis and permit rapid and precise localization of brain lesions that may require surgical intervention. Stereotactic needle aspiration permits therapeutic drainage and provides diagnostic specimens for identification of the causative organisms. Empirical antibiotic therapy should be started on the basis of the likely associated pathogens which depend on the presumptive precipitating source of infection and the Gram stain results. The antibiotic regimen can be modified, if necessary, once culture results on aspirated pus are available. Serial imaging studies are done to monitor the therapeutic response and identify recurrent or secondary lesions that may require repeated drainage.

Not surprising, as brain abscess is a rare condition, randomized controlled trials of different therapies do not appear to have been conducted. All of the published studies were retrospective, and most of the reports focused on neurosurgical and radioimaging, and as a result did not contain comprehensive information on microbiological data or details of the antibiotic regimens used.

Yang 1981 reviewed 400 cases of brain abscess treated in China over 20 years (April 1952 to December 1972). Sixteen cases had congenital heart disease as a predisoposing factor. The antibiotic regimens were penicillin and streptomycin in the earlier cases, when they routinely used penicillin and chloramphenicol. Mampalum 1988 described 102 cases over 17 years. They grouped their patients according to the treatment received: excision, aspiration and nonsurgical therapy. Hirsch 1983 reported 34 children treated for brain abscess during 15 years. Thirteen cases had cyanotic heart disease. Their treatment included puncture of the abscess, antibiotic administration and redraining if indicated. Gonzalez-Garcia 1999 retrospectively analysed 100 cases of brain abscess diagnosed between 1979 and 1998. Abdullah 2001 reported 60 cases of brain abscesss during the 7-year period from 1990 to 1996. Twenty patients had cyanotic heart disease. The combination of a beta-lactam agent with chloramphenicol and/or metronidazole was used as standard treatment. Lu 2002 reported 123 cases of brain abscess over a period of 15 years (January 1986 to December 2000). Of these 123 patients, 103 had community-acquired infections, while the other 20 were diagnosed with nosocomial infection. The portal of entry in 94 culture-positive cases included hematogenous spread (n = 32), postneurosurgical states (n = 17), contiguous infection from parameningeal foci (n = 22) and unknown (n = 24). No information regarding congenital heart disease as a predisposing factor was described. Seneviratne Rde 2003 reported 41 patients with cerebral abscess, 30% of cases had congenital heart disease as the predisposing factor. The antibiotic regime used in this neurosurgical unit consisted of cefotaxime and metronidazole and the result of treatment was satisfactory. Jansson 2004 described 66 cases of brain abscess treated initially with cefotaxime over a period of 10 years (January 1990 to December 1999). The predisposing factor was cardiopathy (type not specified) in nine cases. Sixty-two of these patients were treated additionally with metronidazole and surgery was also performed in 53 patients. Side effects which included nonpruritic rash, leukopenia, drug fever etc., were reported in 42 patients, of whom cefotaxime was terminated prematurely in 38 patients. The overall mortality was 12%.The Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy reviewed the rational use of antibiotics in the treatment of brain abscess by reviewing all English language publications between 1975 and 1999. They found no randomized controlled trials (British Society 2000). Their recommendations are inevitably based on pathological and surgical principles of choosing the most appropriate antibiotic combination based on likely pathogens and in vitro antibiotic sensitivity, abscess drainage and supportive treatment.

AUTHORS' CONCLUSIONS

Implications for practice

The clinical management of people with cyanotic congenital heart disease who developed a brain abscess has to rely on the results of retrospective studies and previous clinical experience other than that obtained through randomized controlled or controlled clinical trials.

Implications for research

As it is unlikely that a trial of treatment of brain abscess will be conducted owing to the rarity of the condition and concensus about the approach to choice of antibiotic regimens and indications for surgical drainage, future research may be best directed towards diagnosis and early detection of brain abscess, molecular methods to detect the infecting organism as an alternative to culture, and exploring more effective and practical drainage methods to improve quality of care.

ACKNOWLEDGEMENTS

Faculty of Medicine, Khon Kaen University, Thai Cochrane Network.

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British Society 2000 *{published data only}*

Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy. The rational use of antibiotics in the treatment of brain abscess. *British Journal of Neurosurgery* 2000;**14**(6):525-30.

Gonzalez-Garcia 1999 *{published data only}*

Gonzalez-Garcia J, Gelabert M, Pravos AG, Villa JMF. Intracranial collections of pus: A review of 100 cases. *Revista de neurologia* 1999;**29**:416-24.

Hirsch 1983 *{published data only}*

Hirsch JF, Roux FX, Sainte-Rose C, Renier D, Pierre-Kahn A. Brain abscess in childhood. A study of 34 cases treated by puncture and antibiotics. *Childs Brain* 1983;**10**(4):251-65.

Jansson 2004 *{published data only}*

Jansson AK, Enblad P, Sjolin J. Efficacy and safety of cefotaxime in combination with metronidazole for empirical treatment of brain abscess in clinical practice: a retrospective study of 66 consecutive cases. *European Journal of Clinical Microbiology & Infectious Diseases* 2004;**23**:7-14.

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Mampalum 1988 *{published data only}*

Mampalum TJ, Resenblum ML. Trends in the management of bacterial brain abscesses: a review of 102 cases over 17 years. *Neurosurgery* 1988;**23**(4):451-8.

Seneviratne Rde 2003 *{published data only}*

Senevirantne Rde S, Navvasivayam P, Perera S, Wickremasinghe RS. Microbiology of cerebral abscess at the neurosurgical unit of the National Hospital of Sri Lanka. *Ceylon Medical Journal* 2003;**48**(1):14-6.

Yang 1981 *{published data only}*

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Jadavji 1985

Jadavji T, Humphreys RP, Prober CG. Brain abscesses in infants and children. *Pediatric Infectious Diseases* 1985;**4**:394-8.

Jimenez 1987

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role of bacterial metabolites of chloramphenicol. *Blood* 1987;**70**:1180-5.

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Juni P, Altman D, Egger M. Systematic reviews in health care: Assessing the quality of controlled clinical trials. *British Medical Journal* 2001;**323**(7303):42-6.

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Sjolin 1991

Sjolin J, Eriksson N, Arneborn P. Penetration of cefotaxime and desacetylcefotaxime into brain abscesses in humans. *Antimicrobial Agents Chemotherapy* 1991;**35**:2606-10.

Sjolin 1993

Sjolin J, Lilja A, Eriksson N, Arneborn P, Cars O. Treatment of brain abscess with cefotaxime and metronidazole: prospective study on 15 consecutive patients. *Clinical Infectious Diseases* 1993;**17**:857-63.

Takeshita 1997

Takeshita M, Kagawa M, Yato S, Izawa M, Onda h, Takakura K, et al. Current treatment of brain abscess in patients with congenital cyanotic heart disease. *Neurosurgery* 1997;**41**(6):1270-8.

Yamamoto 1993

Yamamoto M, Jimbo M, Ide M. Penetration of intravenous antibiotics into brain abscess. *Neurosurgery* 1993;**33**:44-9.

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdullah 2001	Not a randomized controlled trial: reported on a case series of brain abscess (60 cases).
British Society 2000	Literature review on the antimicrobial treatment of brain abscess.
Gonzalez-Garcia 1999	Not a randomized controlled trial: reported on a case series of brain abscess (100 cases).
Hirsch 1983	Not a randomized controlled trial: reported on a case series of brain abscess in children (34 cases).
Jansson 2004	Not a randomized controlled trial: reported on a case series of brain abscess (66 cases).

Study	Reason for exclusion
Lu 2002	Not a randomized controlled trial: reported on a case series of brain abscess (125 cases).
Mampalum 1988	Not a randomized controlled trial: reported on a case series of brain abscess (102 cases).
Seneviratne Rde 2003	Not a randomized controlled trial: reported on a case series of brain abscess (41 cases).
Yang 1981	Not a randomized controlled trial: reported on a case series of brain abscess (400 cases).

APPENDICES

Appendix 1. Search strategies 2006

CENTRAL

#1(HEART-DEFECT-CONGENITAL)
#2 (BRAIN* near ABSCESS*)
#3 (CEREBRAL near ABSCESS*)
#4 (CEREBELLA* near ABSCESS*)
#5 (TETRALOGY* near FALLOT*)
#6 (CYANOTIC near HEART)
#7 (CONGENITAL near HEART)
#8 (#1 or #2) or #3) or #4) or #5) or #6) or #7)
#9 ANTIBIOTICS*:ME
#10 ANTIBIOTIC*
#11 CHLORAMPHENICOL*
#12 PENICILLIN*
#13 METRONIDAZOLE*
#14 CEPHALOSPORINS*
#15 CEFOTAXIME*
#16 CEFTRIAXONE*
#17 AMPICILLIN*
#18 CLINDAMYCIN*
#19 CEFTAZIDIME*
#20 ANTI-INFECTIVE*
#21 (#9 or #10) or #11) or #12) or #13) or #14) or #15) or #16) or #17) or #18) or #19) or #20)
#22 (#8 and #21)

MEDLINE on Ovid

1 exp Heart Defects, Congenital/
2 Brain Abscess/
3 brain abscess$.tw.
4 cerebral abscess$.tw.
5 cerebella$ abscess$.tw.
6 (tetralogy adj3 fallot$).tw.
7 (cyanotic adj3 heart).tw.
8 (congenital adj3 heart).tw.
9 (congenital adj3 cardiac).tw.
10 or/1-9
11 exp Antibiotics/
12 chloramphenicol$.tw.
13 penicillin$.tw.
14 cephalosporin$.tw.
15 metronidazole$.tw.
16 cephotaxime$.tw.
17 ceftriaxone$.tw.
18 ampicillin$.tw.

19 clindamycin$.tw.
20 ceftazidine$.tw.
21 Anti-Infective Agents/
22 anti-infective.tw.
23 antiinfective.tw.
24 antibiotic$.tw.
25 or/11-24
26 10 and 25
and RCT filter terms

EMBASE on Ovid

1 exp Congenital Heart Malformation/
2 Brain Abscess/
3 brain abscess$.tw.
4 cerebral abscess$.tw.
5 cerebella$ abscess$.tw.
6 (tetralogy adj3 fallot$).tw.
7 (cyanotic adj3 heart).tw.
8 (congenital adj3 heart).tw.
9 (congenital adj3 cardiac).tw.
10 or/1-9
11 exp Antibiotic Agent/
12 chloramphenicol$.tw.
13 penicillin$.tw.
14 cephalosporin$.tw.
15 metronidazole$.tw.
16 cephotaxime$.tw.
17 ceftriaxone$.tw.
18 ampicillin$.tw.
19 clindamycin$.tw.
20 ceftazidine$.tw.
21 Antiinfective Agent/
22 anti-infective.tw.
23 antiinfective.tw.
24 antibiotic$.tw.
25 or/11-24
26 10 and 25
27 clinical trial/
28 random$.tw.
29 randomized controlled trial/
30 trial$.tw.
31 follow-up.tw.
32 double blind procedure/
33 placebo$.tw.
34 placebo/
35 factorial$.ti,ab.
36 (crossover$ or cross-over$).ti,ab.
37 (double$ adj blind$).ti,ab.
38 (singl$ adj blind$).ti,ab.
39 assign$.ti,ab.
40 allocat$.ti,ab.
41 volunteer$.ti,ab.
42 Crossover Procedure/
43 Single Blind Procedure/
44 or/27-43
45 exp animal/
46 nonhuman/
47 exp animal experiment/
48 or/45-47
49 exp human/
50 48 not 49

51 44 not 50
52 51 and 26

Appendix 2. Search strategies 2009

CENTRAL on The Cochrane Library

#1 MeSH descriptor BRAIN ABSCESS this term only
#2 (brain* in All Text near/6 abscess* in All Text)
#3 (cerebral in All Text near/6 abscess* in All Text)
#4 (cerebella* in All Text near/6 abscess* in All Text)
#5 cerebritis* in All Text
#6 (#1 or #2 or #3 or #4 or #5)
#7 MeSH descriptor Anti-Bacterial Agents explode all trees
#8 antibiotic* in All Text
#9 chloramphenicol* in All Text
#10 penicillin* in All Text
#11 metronidazole* in All Text
#12 cephalosporin* in All Text
#13 cefotaxime* in All Text
#14 ceftriaxone* in All Text
#15 ampicillin* in All Text
#16 clindamycin* in All Text
#17 ceftazidime* in All Text
#18 anti-infective* in All Text
#19 MeSH descriptor ANTI-INFECTIVE AGENTS explode all trees
#20 (#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19)
#21 (#6 and #20)

MEDLINE (On Ovid)

1 Brain Abscess/
2 brain abscess$.tw.
3 cerebral abscess$.tw.
4 cerebella$ abscess$.tw.
5 or/1-4
6 exp Antibiotics/
7 chloramphenicol$.tw.
8 penicillin$.tw.
9 cephalosporin$.tw.
10 metronidazole$.tw.
11 cephotaxime$.tw.
12 ceftriaxone$.tw.
13 ampicillin$.tw.
14 clindamycin$.tw.
15 ceftazidine$.tw.
16 Anti-Infective Agents/
17 anti-infective.tw.
18 antiinfective.tw.
19 antibiotic$.tw.
20 or/6-19
21 5 and 20
22 randomized controlled trial.pt.
23 controlled clinical trial.pt.
24 Randomized controlled trials/
25 random allocation/
26 double blind method/
27 single-blind method/
28 or/22-27
29 exp animal/ not humans/
30 28 not 29
31 clinical trial.pt.
32 exp Clinical Trials as Topic/

33 (clin$ adj25 trial$).ti,ab.
34 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab.
35 placebos/
36 placebo$.ti,ab.
37 random$.ti,ab.
38 research design/
39 or/31-38
40 39 not 29
41 30 or 40
42 21 and 41

EMBASE on Ovid

1 Brain Abscess/
2 brain abscess$.tw.
3 cerebral abscess$.tw.
4 cerebella$ abscess$.tw.
5 or/1-4
6 exp Antibiotic Agent/
7 chloramphenicol$.tw.
8 penicillin$.tw.
9 cephalosporin$.tw.
10 metronidazole$.tw.
11 cephotaxime$.tw.
12 ceftriaxone$.tw.
13 ampicillin$.tw.
14 clindamycin$.tw.
15 ceftazidine$.tw.
16 Antiinfective Agent/
17 anti-infective.tw.
18 antiinfective.tw.
19 antibiotic$.tw.
20 or/6-19
21 5 and 20
22 controlled clinical trial/
23 random$.tw.
24 randomized controlled trial/
25 follow-up.tw.
26 double blind procedure/
27 placebo$.tw.
28 placebo/
29 factorial$.ti,ab.
30 (crossover$ or cross-over$).ti,ab.
31 (double$ adj blind$).ti,ab.
32 (singl$ adj blind$).ti,ab.
33 assign$.ti,ab.
34 allocat$.ti,ab.
35 volunteer$.ti,ab.
36 Crossover Procedure/
37 Single Blind Procedure/
38 or/22-37
39 (exp animals/ or nonhuman/) not human/
40 38 not 39
41 21 and 40

LILACs on BIREME

brain abscess$ or cerebral$ abscess$ or cerebella$ abscess$ [Palavras] and 2006 or 2007 or 2008 or 2009 [País, ano de publicação]

Appendix 3. Search strategies 2013

CENTRAL

#1MeSH descriptor: [Brain Abscess] this term only

#2brain* near/6 abscess*
#3cerebral near/6 abscess*
#4cerebella* near/6 abscess*
#5cerebritis*
#6cerebrum near/6 abscess*
#7encephalopyosis
#8intracranial near/6 abscess*
#9#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#11antibiotic*
#12chloramphenicol*
#13penicillin*
#14metronidazole*
#15cephalosporin*
#16cefotaxime*
#17ceftriaxone*
#18ampicillin*
#19clindamycin*
#20ceftazidime*
#21anti-infective*
#22MeSH descriptor: [Anti-Infective Agents] explode all trees
#23antiinfective
#24antibacterial
#25anti-bacterial
#26anti next bacterial
#27antimycobacterial
#28bacteriocid*
#29anti-mycobacterial
#30anti next mycobacterial
#31antimicrobial
#32anti-microbial
#33anti next microbial
#34microbicid*
#35#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22
#36#23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34
#37#35 or #36
#38#9 and #37

MEDLINE

1. Brain Abscess/
2. brain abscess$.tw.
3. cerebral abscess$.tw.
4. cerebella$ abscess$.tw.
5. cerebrum abscess*.tw.
6. encephalopyosis.tw.
7. intracranial abscess*.tw.
8. or/1-4
9. or/1-7
10. exp Anti-Bacterial Agents/
11. chloramphenicol$.tw.
12. penicillin$.tw.
13. cephalosporin$.tw.
14. metronidazole$.tw.
15. cephotaxime$.tw.
16. ceftriaxone$.tw.
17. ampicillin$.tw.
18. clindamycin$.tw.
19. ceftazidine$.tw.
20. Anti-Infective Agents/
21. anti-infective.tw.
22. antiinfective.tw.

23. antibiotic$.tw.
24. antibacterial.tw.
25. anti-bacterial.tw.
26. anti bacterial.tw.
27. antimycobacterial.tw.
28. bacteriocid*.tw.
29. anti-mycobacterial.tw.
30. anti mycobacterial.tw.
31. antimicrobial.tw.
32. anti-microbial.tw.
33. anti microbial.tw.
34. microbicid*.tw.
35. or/10-23
36. or/10-34
37. 8 and 35
38. 9 and 36
39. randomized controlled trial.pt.
40. controlled clinical trial.pt.
41. randomized.ab.
42. placebo.ab.
43. drug therapy.fs.
44. randomly.ab.
45. trial.ab.
46. groups.ab.
47. 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48. exp animals/ not humans.sh.
49. 47 not 48
50. 37 and 49
51. 38 and 49
52. 51 not 50
53. (200906* or 200907* or 200908* or 200909* or 200910* or 200911* or 200912* or 2010* or 2012* or 2013*).ed.
54. 50 and 53
55. 52 or 54

EMBASE

1. brain abscess/
2. brain abscess$.tw.
3. cerebral abscess$.tw.
4. cerebella$ abscess$.tw.
5. cerebrum abscess*.tw.
6. encephalopyosis.tw.
7. intracranial abscess*.tw.
8. or/1-4
9. or/1-7
10. exp antibiotic agent/
11. chloramphenicol$.tw.
12. penicillin$.tw.
13. cephalosporin$.tw.
14. metronidazole$.tw.
15. cephotaxime$.tw.
16. ceftriaxone$.tw.
17. ampicillin$.tw.
18. clindamycin$.tw.
19. ceftazidine$.tw.
20. antiinfective agent/
21. anti-infective.tw.
22. antiinfective.tw.
23. antibiotic$.tw.
24. antibacterial.tw.
25. anti-bacterial.tw.
26. anti bacterial.tw.

27. antimycobacterial.tw.
28. bacteriocid*.tw.
29. anti-mycobacterial.tw.
30. anti mycobacterial.tw.
31. antimicrobial.tw.
32. anti-microbial.tw.
33. anti microbial.tw.
34. microbicid*.tw.
35. or/10-23
36. or/10-34
37. 8 and 35
38. 9 and 36
39. random$.tw.
40. factorial$.tw.
41. crossover$.tw.
42. cross over$.tw.
43. cross-over$.tw.
44. placebo$.tw.
45. (doubl$ adj blind$).tw.
46. (singl$ adj blind$).tw.
47. assign$.tw.
48. allocat$.tw.
49. volunteer$.tw.
50. crossover procedure/
51. double blind procedure/
52. randomized controlled trial/
53. single blind procedure/
54. 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53
55. exp animals/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
56. human/ or normal human/ or human cell/
57. 55 and 56
58. 55 not 57
59. 54 not 58
60. 37 and 59
61. 38 and 59
62. 61 not 60
63. ("200925" or "200926" or "200927" or "200928" or "200929" or 20093* or 20094* or 20095* or 2010* or 2012* or 2013*).em.
64. 60 and 63
65. 62 or 64

LILACS

"BRAIN ABSCESS" [Subject descriptor] or brain abscess$ or cerebral$ abscess$ or cerebella$ abscess$ [Words] and 2009 or 2010 or 2011 or 2012 or 2013 [Country, year publication]

WHAT'S NEW

Date	Event	Description
26 March 2021	Review declared as stable	This Cochrane Review has had low usage and authors are not aware of new evidence. This review is therefore not a priority for updating.

HISTORY

Protocol first published: Issue 4, 2003
Review first published: Issue 3, 2007

Date	Event	Description
28 January 2013	New search has been performed	Updated
28 January 2013	New citation required but conclusions have not changed	The updated search on 9 January 2013 identified no new studies. The conclusion remains unchanged.
8 July 2009	New search has been performed	The search was updated on 25th June 2009, no new studies were identified. The conclusions remain unchanged.
8 September 2008	Amended	Converted to new review format.
14 May 2007	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

PL searched for studies, reviewed the abstracts to assess for inclusion and drafted the review.
AC assessed the studies independently, co-wrote the review and helped to revise the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Khon Kaen University, Thailand

External sources

- Thailand Research Fund, Senior Research Scholar, Thailand
- Thai Cochrane Network, Thailand

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Bacterial Agents [*therapeutic use]; Brain Abscess [*drug therapy]; Cyanosis [complications]; Heart Defects, Congenital [*complications]

MeSH check words

Humans