INFECTIONOUS COMPLICATIONS IN THE NEURO-ICU

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Infectious complications in the neuro-ICU patient population presenting as
-meningitis,
-ventriculitis,
-encephalitis/cerebritis,
-brain abscess, and
-subdural or epidural empyema
are frequently associated with invasive procedures such as craniotomy or placement of intracranial devices necessary, for example, for intracranial pressure (ICP) monitoring or diversion of the cerebrospinal fluid (CSF) from an obstructed ventricular system.
The majority of these infections must be considered **nosocomial**, that is, hospital-acquired.

Recently, the term nosocomial has been suggested to be replaced by **healthcare-associated** (Lujan et al 2009).

This concept may be highly useful for the categorization of infections in the **non**-ICU setting, but seems to be **less** applicable in the **neuro**-ICU patient population.
Due to the severity of the underlying neurological illness such as aneurysmal subarachnoid hemorrhage or severe traumatic brain injury, neurocritical care patients often require the full range of ICU measures including mechanical ventilation, intravascular catheters, and so on.
Therefore, these patients are also at high risk for infections arising at distant foci, e.g.,
-endocarditis,
-bloodstream infections,
-pneumonia,
-urinary tract infections
-colitis, etc
Noteworthy, a neuro-ICU patient suffering from sepsis originating from an extracranial focus is at risk for *sepsis-related neurological complications* like -septic encephalopathy or -critical illness neuromyopathy.
In addition, infectious complications may arise from more ‘exogenous’ sources such as transmission of pathogens from ICU personnel or the ICU environment.

**Poor hand hygiene** has been demonstrated to be one of the most important causes of healthcare-associated infections.
Definition of intracranial infectious complications

Recently, the National Healthcare Safety Network, Division of Healthcare Quality Promotion of the Centers for Disease Control and Prevention (CDC/NHSN) has updated the surveillance definition of healthcare-associated infection and published criteria for various types of infections in the acute care setting.

(Horan et al 2008)
There are three specific types of central nervous system (CNS) infections:

(1) Intracranial infection:
   a) brain abscess
   b) subdural or epidural infection, and
   c) encephalitis

(2) Meningitis or ventriculitis

(3) Spinal abscess without meningitis
As per the CDC/NHSN definition of **CNS infection**, **intracranial infection** must meet at least one of the following criteria:

1) Patient has organisms cultured from brain tissue or **dura**

2) Patient has an **abscess** or evidence of **intracranial infection** seen during a surgical operation or on histopathologic examination.
3) Patient has at least two of the following signs or symptoms with no other recognized cause:
- headache,
- dizziness,
- fever (>38°C),
- localizing neurologic signs,
- changing level of consciousness, or
- confusion,

and at least one of the following:
(a) organisms seen on microscopic examination of brain or abscess tissue obtained by needle aspiration or by biopsy during a surgical operation or autopsy,
(b) positive antigen test on blood or urine,
(c) radiographic evidence of infection, and
(d) diagnostic single antibody titer (IgM) or four-fold increase in paired sera (IgG) for pathogen;
(e) and if diagnosis is made ante-mortem, physician institutes appropriate antimicrobial therapy.
As per the CDC/NHSN definition of meningitis or ventriculitis, at least one of the following criteria must be met:
(1) Patient has organisms cultured from CSF
(2) Patient has at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), headache, stiff neck, meningeal signs, cranial nerve signs, or irritability

and at least one of the following:
(a) increased white cells, elevated protein, and/or decreased glucose in CSF,
(b) organisms seen on Gram’s stain of CSF,
(c) organisms cultured from blood,
(d) positive antigen test of CSF, blood, or urine, and
(e) diagnostic single antibody titer (IgM) or four-fold increase in paired sera (IgG) for pathogen; and if diagnosis is made antemortem, physician institutes appropriate antimicrobial therapy.
In addition to these major types, other intracranial infections may arise in the neuro-ICU patient population such as septic thrombosis of cerebral sinus and/or veins.
Infection versus contamination and catheter colonization

Infections that require immediate therapeutic attention must be differentiated from contamination and catheter colonization.

Contamination constitutes an isolated positive CSF culture in the absence of abnormal CSF findings

Catheter colonization is defined by at least two positive CSF cultures with expected CSF profiles and lack of clinical signs.

Pathological CSF findings in the absence of positive cultures characterizes a suspected device-related infection, whereas definite nosocomial meningitis or ventriculitis is defined by:
- positive CSF culture accompanied by
- abnormal CSF findings or
- appropriate clinical signs and symptoms.
In addition, ‘aseptic’ inflammation resulting from tissue response to tissue injury or stimulation by noninfectious agents such as blood breakdown products or chemicals should be distinguished from infection.
Epidemiology, pathogenesis, and microbiology

The true prevalence of healthcare-associated intracranial infectious complications is difficult to estimate because epidemiological data are limited.

Most reports refer to postneurosurgical (e.g., craniotomy and ventriculostomy) infectious complications.

In contrast, only few studies on the epidemiology of infections secondary to traumatic brain injury are available.
Important risk factors for nosocomial intracranial infections are
- a history of neurosurgery,
- CSF leakage or
- recent head trauma,
- presence of cranial or extracranial infectious foci such as otitis, sinusitis or pneumonia and,
- potentially, an immunocompromised state.
Incidence of ventriculostomy-related infections: 2 to 27%.

A recent meta-analysis of 23 retrospective studies reported a cumulative rate of positive CSF cultures of 8.8% per patient and 8.1% per external ventricular drainage (EVD). (Lozier, 2002)

It has been claimed that the majority of EVD-related infections occurs within the first week after insertion, but recent studies identified a later peak of infection even after 2 weeks, particularly in patients with prolonged EVD placement due to severe intracranial disease. (van Zanten, 2005, Lackner, 2008)
As infection may be acquired by introduction of bacteria following insertion of a new catheter, routine exchange of catheters might be actually harmful by possibly increasing the rates of infection (Lo, 2002).

Other relevant risk factors for EVD-related intracranial infection are
- frequency of CSF sampling,
- intraventricular hemorrhage,
- surgical technique, and
- presence of other distant infections.

(Korinek, 2005)
The incidence of bacterial meningitis after moderate or severe **traumatic brain injury** has been estimated to range between 1 and 2% with **CSF leakage** as the major risk factor and **fracture of the basal** skull increasing the risk up to **25%**.

Approximately, 1.5% of patients suffer from postcraniotomy nosocomial meningitis as a serious complication. (Weisfelt, 2007)
Underlying conditions such as a history of neurosurgery or CSF leakage are seen in 94% of the episodes,

28% of the patients have more than one risk factor.

Any kind of neurosurgical intervention accounts for 64% of the infections, whereas an immuno-compromised state is present in 28% of the cohort, and distant focus of infection is identified in 18%.

(Weisfelt, 2007)
Staphylococci have been incriminated to be the most important and most frequent causative agents (up to 80%), whereas Gram-negative bacilli account for 10-15%.

Anaerobes and fungi, primarily Candida species are rarely identified.

(Beer 2010)
Clinical features and diagnosis
Any suspected intracranial infection must prompt an immediate diagnostic workup and the initiation of empirical antimicrobial chemotherapy.

-Fever and
deterioration in the level of consciousness or
-an increase in ICP in the comatose or sedated patient
are important early indicators for the potential presence of intracranial infections.
Neuroimaging and CSF analysis are the cornerstones in the diagnosis of CNS infections. It should be emphasized that performance of such examinations must not delay initiation of anti-infective therapy.

In many cases, lumbar puncture may be contraindicated due to increased intracranial pressure. CSF recovery may be possible through ventricular catheters.
Analysis of **ventricular CSF** does not always allow the diagnosis of bacterial meningitis, as **CSF circulation** and thereby spread of the infection might be blocked with blood or expanding masses.

The presence of a **focal collection of pus** (e.g., abscess, empyema) warrants immediate **neurosurgical evacuation** both to reduce ICP and to allow for microbiological analysis of the purulent collection.
In addition, cultures from blood and other body fluids such as secretions from paranasal sinus must be obtained.

However, cultures may require prolonged incubation times and the result may be negative in patients with prior antibiotic therapy.

Comparing the results from Gramstains and CSF cultures: Gram staining has a very high specificity but an un-acceptably low sensitivity (18%) in screening for device-related bacterial meningitis.

Schade 2006
In every patient with a history of neurosurgery or head trauma, there must be a high level of suspicion for intracranial infectious complications in case of the development of **systemic inflammatory response syndrome**.

On the contrary, clinical and biochemical parameters such as **fever** or increase in **acute-phase proteins** may also be a manifestation of the underlying neurological disease.
NEUROCRITICAL CARE COMPLICATIONS IN THE ICU

However, monitoring of inflammatory parameters does not allow discrimination between systemic or intracranial infection in the neuro-ICU patient population.

Studies investigating the value of CSF biochemical parameters such as
- CSF leukocyte count,
- CSF protein,
- increased CSF lactate, and
- decreased CSF/serum glucose ratio
conclude that no single parameter can reliably predict or exclude nosocomial intracranial infection.
Further, CSF analysis might be of limited value in identifying intracranial infections due to aseptic inflammation in case of hemorrhagic CSF.

In this setting, calculation of the so-called cell index (ratio of leukocytes and erythrocytes in CSF divided by the ratio of leukocytes and erythrocytes in peripheral blood) may confirm intracranial infection.

(Pfausler, 2004)
A significant increase in the **cell index** preceded the diagnostic capacity by conventional means on average by 3 days.
Therapeutical considerations

Delayed or inappropriate antimicrobial therapy is associated with
-increased morbidity and
-mortality
for many infectious diseases.

(Rasmussen 2008, Proulx 2006, Lala, 2005)
Therapeutical considerations

Risk factors for the administration of inadequate anti-infective therapy are
- preceding antibiotic therapy during the same hospitalization,
- longer duration of indwelling catheterization, and
- infections caused by multidrug resistant bacteria and infections by *Candida* species.  (Iregui, 2002)
Empirical antimicrobial therapy of nosocomial intracranial infections must consider the most likely pathogens involved, local resistance pattern, underlying disease, and patient factors such as age, comorbidities, and immune status.
The antibiotics selected must adequately **penetrate** the **blood–brain** and **blood–CSF barriers**.
# NEUROCRITICAL CARE COMPLICATIONS IN THE ICU

Table 1: Recommendations for empiric antimicrobial therapy for bacterial intracranial infections in adults according to risk factor

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Common pathogens</th>
<th>Preferred antimicrobial therapy(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post craniotomy</td>
<td>Staphylococci (e.g., <em>S. aureus</em>, <em>S. epidermidis</em>), Gram-negative bacilli</td>
<td>Vancomycin or linezolid plus third(^b) (or fourth(^c)) generation cephalosporin</td>
</tr>
<tr>
<td>Penetrating head injury</td>
<td>Staphylococci (e.g., <em>S. aureus</em>, <em>S. epidermidis</em>), Gram-negative bacilli</td>
<td>Vancomycin or linezolid plus third(^b) (or fourth(^c)) generation cephalosporin</td>
</tr>
<tr>
<td>Basal skull fracture (early)</td>
<td><em>Streptococcus pneumoniae</em>, hemolytic streptococci, anaerobes (i.e., microbial oral flora)</td>
<td>Third(^b) generation cephalosporin plus vancomycin or linezolid (plus metronidazol)</td>
</tr>
</tbody>
</table>

\(^a\) Suggested daily dosing in adult patients with normal renal and/or hepatic function: vancomycin 15 mg/kg every 8 h to maintain a serum trough concentration of 15–20 g/l; linezolid 600 mg every 12 h; meropenem 2 g every 8 h.

\(^b\) Suggested daily dosing in adult patients with normal renal and/or hepatic function: cefotaxime 2 g every 4–6 h (antimicrobial coverage should be based on local antimicrobial susceptibility).

\(^c\) Suggested daily dosing in adult patients with normal renal and/or hepatic function: cefepime 2 g every 4–6 h (antimicrobial coverage should be based on local antimicrobial susceptibility).
Klebsiella pneumonieae - Resistance to 3\textsuperscript{rd} cephalosporines 2005 vs 2011
Antibacterial antibiotics in nosocomial central nervous system infections

Klebsiella pneumoniae - Resistance to carbapenem 2005 vs 2011

EARS-net 02/2012
Antibacterial antibiotics in nososcomial central nervous system infections

<table>
<thead>
<tr>
<th>Gram-negative Erreger</th>
<th>Pseudomonas aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Material</strong></td>
<td><strong>BK</strong> *</td>
</tr>
<tr>
<td><strong>Antibiotikum</strong></td>
<td><strong>Imipenem</strong></td>
</tr>
<tr>
<td>2005</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>(7/23)</td>
</tr>
<tr>
<td>2006</td>
<td>47%</td>
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<td>(8/17)</td>
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<td>2007</td>
<td>50%</td>
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<tr>
<td></td>
<td>(9/18)</td>
</tr>
<tr>
<td>2008</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>(6/14)</td>
</tr>
<tr>
<td>2009</td>
<td>35%</td>
</tr>
<tr>
<td></td>
<td>(7/20)</td>
</tr>
<tr>
<td>2010</td>
<td>57%</td>
</tr>
<tr>
<td></td>
<td>(17/30)</td>
</tr>
</tbody>
</table>

**P. aeruginosa**
(Trachealsekret, bronchoalveolare Lavagen)

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Getestet</th>
<th>Sensibel</th>
<th>Resistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem</td>
<td>178</td>
<td>137</td>
<td>41</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>178</td>
<td>137</td>
<td>41</td>
</tr>
<tr>
<td>Ceftazidim</td>
<td>178</td>
<td>146</td>
<td>32</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>178</td>
<td>151</td>
<td>27</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>178</td>
<td>163</td>
<td>15</td>
</tr>
<tr>
<td>4.Gen.Cephalosporin</td>
<td>178</td>
<td>159</td>
<td>19</td>
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</table>

Resistance Report Medical University Innsbruck 2011
C. Lass-Floerl, M. Fille 04/2012
Antibacterial antibiotics in nososcomial central nervous system infections

Teilbefund vom 19.05.2011

Untersuchungsauftrag: aerobe Kultur, Pilze, Langzeitbebrütung
Pilze: Befund folgt
Liquor-Antibiotikaspiegel: Antibiotikaspiegel nachgewiesen

Kultur:
1. E. coli
   Beta-Laktamasebildner mit breitem Wirkungsspektrum (ESBL)

<table>
<thead>
<tr>
<th>Antibiotikum</th>
<th>Nr.</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>1</td>
<td>R</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>43</td>
<td>R</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>44</td>
<td>R</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>9</td>
<td>R</td>
</tr>
<tr>
<td>Cefazolin (c)</td>
<td>5</td>
<td>R</td>
</tr>
<tr>
<td>Tetracyclin</td>
<td>10</td>
<td>S</td>
</tr>
<tr>
<td>Trimethoprim + Sulfonamid</td>
<td>11</td>
<td>R</td>
</tr>
<tr>
<td>Aminopenicillin (d)</td>
<td>3</td>
<td>R</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>17</td>
<td>R</td>
</tr>
<tr>
<td>Aminopen. + Clav. (e)</td>
<td>4</td>
<td>R</td>
</tr>
<tr>
<td>Cefuroxim - Axetil (f)</td>
<td>6</td>
<td>R</td>
</tr>
<tr>
<td>Cefuroxim (f)</td>
<td>22</td>
<td>R</td>
</tr>
<tr>
<td>Cefixim (g)</td>
<td>7</td>
<td>R</td>
</tr>
<tr>
<td>Cefoxitin (h)</td>
<td>23</td>
<td>S</td>
</tr>
<tr>
<td>Ciprofloxacin (i)</td>
<td>14</td>
<td>R</td>
</tr>
<tr>
<td>Piperac.-Tazobactam</td>
<td>39</td>
<td>S</td>
</tr>
<tr>
<td>Ceftiraxon (j)</td>
<td>25</td>
<td>R</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>28</td>
<td>R</td>
</tr>
<tr>
<td>Cefotaxim</td>
<td>24</td>
<td>R</td>
</tr>
<tr>
<td>Imipenem</td>
<td>27</td>
<td>S</td>
</tr>
<tr>
<td>Ceftazidim (k)</td>
<td>26</td>
<td>R</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>31</td>
<td>S</td>
</tr>
<tr>
<td>Amikacin</td>
<td>19</td>
<td>S</td>
</tr>
<tr>
<td>Cefepim</td>
<td>37</td>
<td>R</td>
</tr>
</tbody>
</table>

S = sensibel, I = intermediär, R = resistent
Significance of the newer/alternative antibiotics in the therapy of nosocomial meningitis

- successfully treated single/small case series

  • Daptomycin: Gram-positive and negative, incl MRSA, MRSE, VRE. Single case reports in MRSA meningitis (+fälle)

  • Linezolid: only in Gram-positive spectrum effective. Excellent CSF penetration (unsere daten)

  • Fosfomycin: Gram-positive and negative (partially MRSA). Only in combination with β-lactams or carbapenems. Excellent CSF penetration
Significance of the newer/alternative antibiotics in the therapy of nosocomial meningitis (2)

- Aminoglycosides
  limited penetration into CSF
  „medicate high dosage, once a day and short“
  measure of trough levels necessary (side-effects)
  rescue therapy for gram-negative meningitis (especially enterococci and pseudomonas)

- Colistin
  efficacious against Enterobacteriaceae (especially P. aeruginosa, Acinetobacter baumannii)
  application only, if all other antibiotics are not susceptible to identified isolates
Infectious intracranial complications in the neuro-ICU patient population
Ronny Beer, Bettina Pfausler and Erich Schmutzhard

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Current Opinion in Critical Care 2010, 16:117–122

Figure 1 Flow diagram for the management of suspected nosocomial cerebrospinal fluid infection

- Febrile patient with EVD
  - Necessary examinations:
    - Obtain CSF sample and blood culture
    - Perform CSF Gram’s stain
    - CSF culture
    - Calculate ‘cell index’

- CSF purulent?
  - No (i.e., CSF primarily hemorrhagic)
    - CSF Gram stain yields Gram-positive bacteria (most likely staphylococci)
      - Yes
        - Rule out contamination or colonization
      - No
        - Increase in ‘cell index’ >5 and EVD in situ >3 days

- Systemic antimicrobial therapy according to surveillance data:
  - Flucloxacillin plus rifampicin or fosfomycin
  - In areas with high prevalence of MRSE or MRSA:
    - Intrathecal vancomycin (if blood culture negative) or
    - Intrathecal vancomycin (if blood culture positive) plus intrathecal vancomycin
  - As alternative
    - Intravenous linezolid as alternative (especially in patients with impaired renal function)
  - If polymicrobial infection is suspected or immunosuppressed patient
    - Coverage with 3rd or 4th generation cephalosporin or meropenem

- EVD replacement in patients with inadequate response to antimicrobial therapy
  - In case of positive CSF culture adapt antimicrobial therapy according to resistance testing

- Treat immediately with broad-spectrum antimicrobial therapy covering Gram-positive and Gram-negative bacteria:
  - 3rd generation cephalosporin plus rifampicin or fosfomycin
  - In areas with high prevalence of MRSE, MRSA and multiresistant Gram-negative rods
    - Vancomycin intravenously plus 4th generation cephalosporin or meropenem (according to local prevalence of ESBL-producing or ganisms)

- Consider EVD replacement

- In case of positive CSF culture adapt antimicrobial therapy according to resistance testing

- Consider intraventricular aminoglycosides in case repeated CSF culture yield Gram-negative bacteria despite appropriate intravenous antimicrobial therapy

- Caveats:
  - Always look further for other sources of nosocomial infections, in particular in patients with long-term ICU stay (e.g. VAP, CRBSI, UTI, Clostridium difficile-induced [antibiotic-associated] colitis)
  - Prolonged therapy with broad-spectrum antibiotics may be complicated by fungal superinfection, primarily with Candida spp.

CRBSI, catheter-related blood stream infection; ESBL, extended-spectrum beta-lactamase; MRSA, methicillin resistant Staphylococcus aureus; MRSE, methicillin-resistant Staphylococcus epidermidis; UTI, urinary tract infection; VAP, ventilator associated pneumonia. Adapted from Beer et al. [1].
Febrile patient with EVD

Necessary examinations:
- Obtain CSF sample and blood culture
- Perform CSF Gram’s stain
- CSF culture
- Calculate ‘cell index’

CSF purulent?

No (i.e., CSF primarily hemorrhagic)  Yes
Neuro-ICU Innsbruck

No (i.e., CSF primarily hemorrhagic)

CSF Gram stain yields Gram-positive bacteria (most likely staphylococci)

Yes

Rule out contamination or colonization

Systemic antimicrobial therapy according to surveillance data:

Screen for CVAE if suspicion of infection

No

Increase in ‘cell index’ >5 and EVD in situ > 3 days

Yes

Treat immediately with broad-spectrum antimicrobial therapy covering Gram-positive and Gram-negative bacteria:

- 3rd generation cephalosporin plus rifampicin or fosfomycin

In areas with high prevalence of MRSE, MRSA and multiresistant Gram-negative rods

- Vancomycin intravenously plus 4th generation cephalosporin or meropenem (according to local prevalence of ESBL-producing or ganisms)

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**EVD replacement in patients with inadequate response to antimicrobial therapy**

In case of positive CSF culture adapt antimicrobial therapy according to resistance testing

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**Consider intraventricular aminoglycosides in case repeated CSF culture yield Gram-negative bacteria despite appropriate intravenous antimicrobial therapy**

**Caveats:**
Always look further for other sources of nosocomial infections, in particular in patients with long-term ICU stay (e.g., VAP, CRBSI, UTI, Clostridium difficile-induced [antibiotic-associated] colitis)

Prolonged therapy with broad-spectrum antibiotics may be complicated by fungal superinfection, primarily with Candida spp.
As in the neuro-ICU-patient population nosocomial intracranial infections can be caused by multidrug resistant Gram-positive and Gram-negative pathogens, initial empiric treatment with the glycopeptide antibiotic Vancomycin in combination with a Cephalosporin with antipseudomonal activity or a Carbapenem is recommended until culture results provide information to adapt antimicrobial therapy according to resistance testing.
In patients with a contraindication for systemic vancomycin administration in whom a ventricular catheter is placed, vancomycin can be safely administered intrathecally. (Pfausler, 2003)

For patients with severe allergy to betalactam antibiotics, moxifloxacin might prove as an alternative. (Beer 2012)
The efficacy of linezolide for the treatment of nosocomial Gram-positive ventriculo-meningitis has been demonstrated recently (Beer 2007).

Nosocomial intracranial infections due to antibiotic resistant Acinetobacter species is becoming an increasingly clinical entity.

In these cases, combination therapy of systemic and intrathecally administered polymyxins plus removal of infected devices is recommended.
Recommendations on the duration of antimicrobial therapy of infectious intracranial complications in the neuro-ICU population have not been studied rigorously. Mostly, treatment is continued for 10–14 days. If repeated CSF cultures are negative, some experts have suggested shorter durations.

However, it needs to be stressed that therapy of nosocomial intracranial infectious complications therapy must be individualized because some patients with preceding or concurrent anti-infective therapy may need appropriate empiric antimicrobial treatment despite negative microbiological testing.
Although the routine prophylactic exchange of non infected indwelling devices is still discussed controversially, consensus exists on the **timely removal of neurosurgical hardware** infected with pathogens capable of biofilm formation.

Importantly, catheter removal requires **concomitant antimicrobial** therapy. Recurrence of nosocomial infections is reported in 25% of cases. Therefore, a high level of suspicion needs to be maintained after termination of antimicrobial therapy.
Prevention
Because of difficulties in early diagnosis and subsequent delayed initiation of appropriate antimicrobial therapy, prevention of nosocomial intracranial infection is of paramount importance.

Preventive measures include adequate surgical techniques and hygiene as well as the preventive administration of antibiotics in patients undergoing neurosurgery.
However, the possible induction of antimicrobial resistance, leading to major healthcare problems, is a significant concern.

A relatively new option that may overcome this disadvantage is the introduction of ventriculostomy catheters impregnated with silver nano-particles. (Lackner, 2008)

A prospective pilot study and a retrospective analysis found reduced infection rates with the use of silver nano-particles bearing EVD catheters.
NEUROCRITICAL CARE COMPLICATIONS IN THE ICU

Prevention

strict surgical protocols (e.g. hair clipping not shaving)
minimizing blood loss and tissue trauma
avoidance of CSF leakage
use of double layer of gloves when handling implantable devices

Extra-ventricular drains

- percutaneous tunneling of the catheters for at least 5 cm (Sanders 2002)
- strict hand hygiene for catheter handling
- routine exchange of EVDs does not reduce the risk of infection (Holloway 1996, Korinek 2006)
CONCLUSION: Per-operative antibiotic prophylaxis, though clearly effective for the prevention of incision infections, does not prevent meningitis and tends to select prophylaxis resistant microorganisms.

A.M. Korinek, 2006
## Analysis 1.2. Comparison 1 Antibiotic-impregnated versus standard catheters, Outcome 2 Shunt infection.

**Review:** Antibiotic prophylaxis for surgical introduction of intracranial ventricular shunts

**Comparison:** 1 Antibiotic-impregnated versus standard catheters

**Outcome:** 2 Shunt infection

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>Odds Ratio M-H,Fixed,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Internal shunts</td>
<td>Govender 2003: 3/50</td>
<td>10/60</td>
<td>39.2 %</td>
<td>0.32 [0.08, 1.23]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>50</td>
<td>60</td>
<td>39.2 %</td>
<td>0.32 [0.08, 1.23]</td>
<td></td>
</tr>
<tr>
<td>2 External shunts</td>
<td>Zabramski 2003: 2/149</td>
<td>13/139</td>
<td>60.8 %</td>
<td>0.13 [0.03, 0.60]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>149</td>
<td>139</td>
<td>60.8 %</td>
<td>0.13 [0.03, 0.60]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>199</td>
<td>199</td>
<td>100.0 %</td>
<td>0.21 [0.08, 0.55]</td>
<td></td>
</tr>
</tbody>
</table>

- Total events: 3 (Treatment), 10 (Control)
- Heterogeneity: not applicable
- Test for overall effect: Z = 1.66 (P = 0.097)

- Total events: 2 (Treatment), 13 (Control)
- Heterogeneity: not applicable
- Test for overall effect: Z = 2.63 (P = 0.0084)

- Total events: 5 (Treatment), 23 (Control)
- Heterogeneity: Chi² = 0.74, df = 1 (P = 0.39); I² = 0.0%
- Test for overall effect: Z = 3.13 (P = 0.0018)
Conclusion

- Nosocomial central nervous system infections are rather rare
- Clinical signs and symptoms as well as CSF findings are often hampered by concomitant neurological disease and altered CSF findings post neurosurgical procedures
- Guidelines conforming antibiotic therapy is efficacious in most cases
- Increasing numbers of multi-drug resistant microbes require an increasing alertness to adequate and alternative therapy(-ies)
- Intrathecal application of antibiotics could be an efficacious therapy in selected cases, especially, of ventriculitis
- Prophylactic procedures are able to reduce infection rate
THANK YOU FOR YOUR ATTENTION

AND MANY THANKS TO ALL MY

COWORKERS OF THE

NICU INNSBRUCK, AUSTRIA

BETTINA PFAUSLER,
RONNY BEER,
RAIMUND HELBOK,
GREGOR BROESSNER,
PETER LACKNER,
STEPHANIE KLIEN,
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A 6020 Innsbruck
Fax: 50424288 ( )

Endbefund vom 24.02.2007
Untersuchungsauftrag: A-aerobe Kultur

Kultur:
1. Pseudomonas aeruginosa
2. Enterococcus sp.
3. Morganella morganii

Antibiotikum  | Nr.  | 1 | 2 | 3 |
--- | --- | --- | --- | --- |
Penicillin G  | 1   | R | R | R |
Linsenoxacillin (a) | 2   | R | R | R |
Amoxycillin | 8   | R | R | R |
Cefazolin (e) | 5   | R | R | R |
Tetacyclin | 10  | R | R | R |
Trimethoprim + Sulfamid | 11  | R | R | R |
Aminopenicillin (d) | 3   | R | S | R |
Gentamycin | 17  | S | R | R |
Aminoglykoside, + Clav. (a) | 4   | R | S | R |
Cefuroxim - Axilin (f) | 5   | R | R | R |
Cefuroxim (f) | 22  | R | R | R |
Cefotaxim | 7   | R | R | R |
Cefotaxim (f) | 23  | R | S | S |
Ciprofloxacin (f) | 14  | S | S | R |
Piperacillin-Tazobactam | 39  | S | S | S |
Ceftriaxon (f) | 25  | R | R | R |
Aztreonam | 26  | S | S | S |
Cefotaxim | 24  | R | R | R |
Imipenem | 27  | S | S | S |
Cefazolin (f) | 26  | S | R | R |
Fosfomycin | 31  | S | R | R |
Amikacin | 19  | S | R | S |
Vancomycin | 32  | S | S | S |
Rifampicin | 33  | S | S | S |
Fusidinsäure | 34  | S | S | S |
Ceftazidim | 35  | S | R | S |