

Pocket Guide to Diagnosis & Treatment of Cranial Neurosurgical Infections



Version 1: 1 October 2018

CLASSIFICATION according to involved tissue/device

Group	Infection type
Extradural infections	• Bone flap infection (with infected fixation devices ¹)
	• Cranioplasty infection (PMMA, PEEK, titan, ceramics)
	• Postoperative epidural empyema (with/without duraplasty)
Intradural infections	• Postoperative Meningitis
	• Postoperative brain abscess
	• Postoperative subdural empyema (with/without duraplasty)
Other device-associated infections	• Ventriculoperitoneal (VPS) and ventriculoatrial shunt (VAS) infection
	• External ventricular (EVD) and lumbar drainage (ELD) infection
	• Neurostimulator infection

¹ Sutures are not considered fixation devices

CLASSIFICATION according to time of occurrence²

	Early infection (acute)	Delayed and late infection (chronic)
When	≤ 6 weeks after implantation	> 6 weeks after implantation
Biofilm	“Immature”	“Mature”
Surgical principle	Debridement and implant retention possible	Removal or exchange of the implant necessary (in one or two stages)

² Only relevant for implant-associated infections with biofilms

Abbreviations:

CNS: Central nervous system

CSF: Cerebrospinal fluid

EVD/ELD: External ventricular/lumbar drainage

VPS/VAS: Ventriculoperitoneal/ventriculoatrial shunt

PMMA: Poly Methyl Methacrylate

PEEK: Polyether Ether Ketone

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For individual recommendations contact our Consultation Portal at: cp.pro-implant-foundation.org

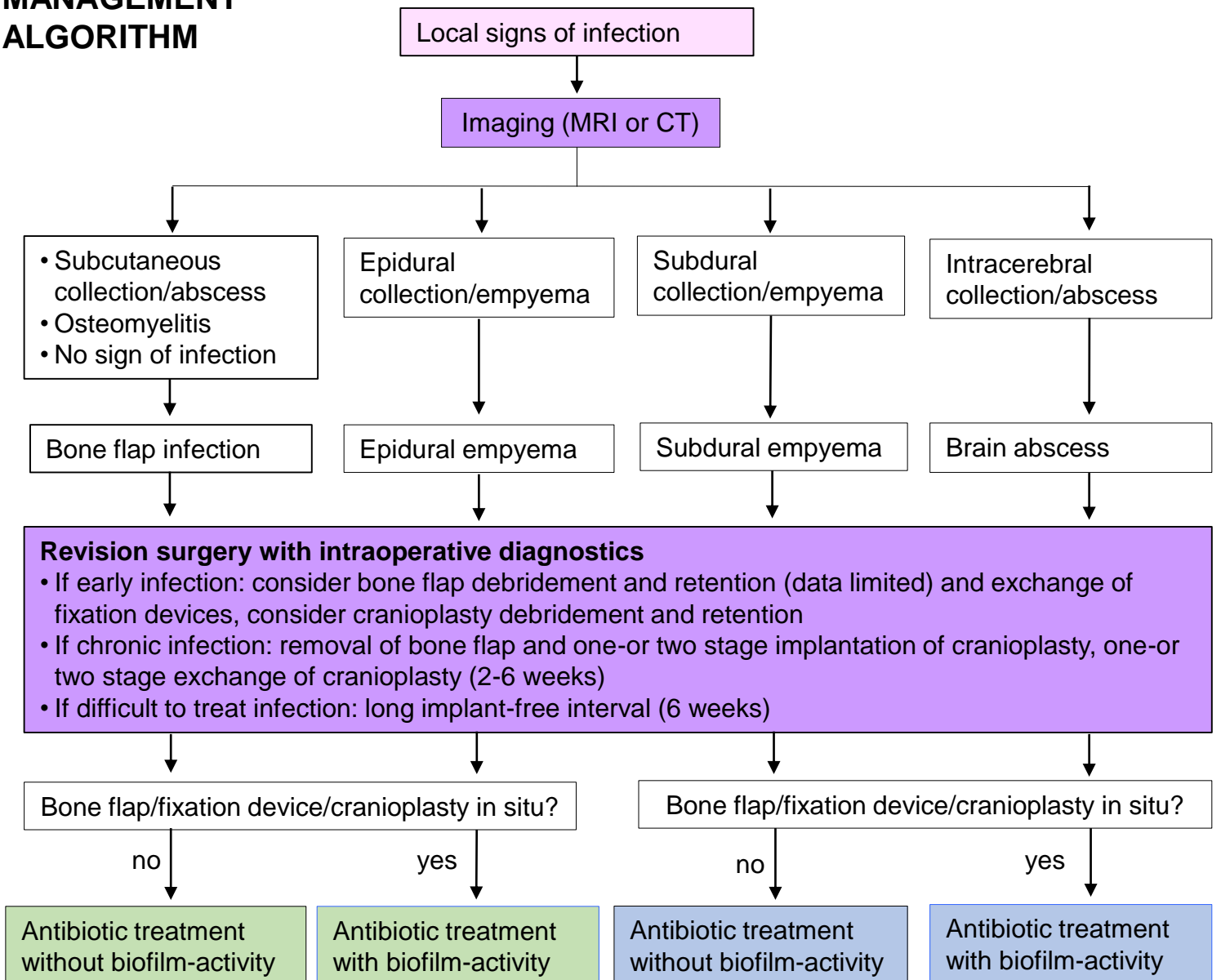
Infection after craniotomy or cranioplasty (bone flap infection, cranioplasty infection, epidural empyema, subdural empyema, brain abscess, meningitis)

DEFINITION (≥1 fulfilled criterion required)

Criteria	
Local signs of infection	<ul style="list-style-type: none"> Local signs of inflammation¹, purulent wound secretion, sinus tract, abscess or wound dehiscence or implant on view (plates, screws, cranioplasty) Abscess or pus seen intraoperatively
Imaging (CT/MRI)	<ul style="list-style-type: none"> Osteomyelitis (bone flap infection), epidural empyema, subdural empyema, intracerebral abscess
Microbiology	<ul style="list-style-type: none"> Positive cultures from CSF, intraoperative tissue or explanted foreign material

¹ Erythema, swelling, warmth, pain, tenderness (indicating infection)

MANAGEMENT ALGORITHM



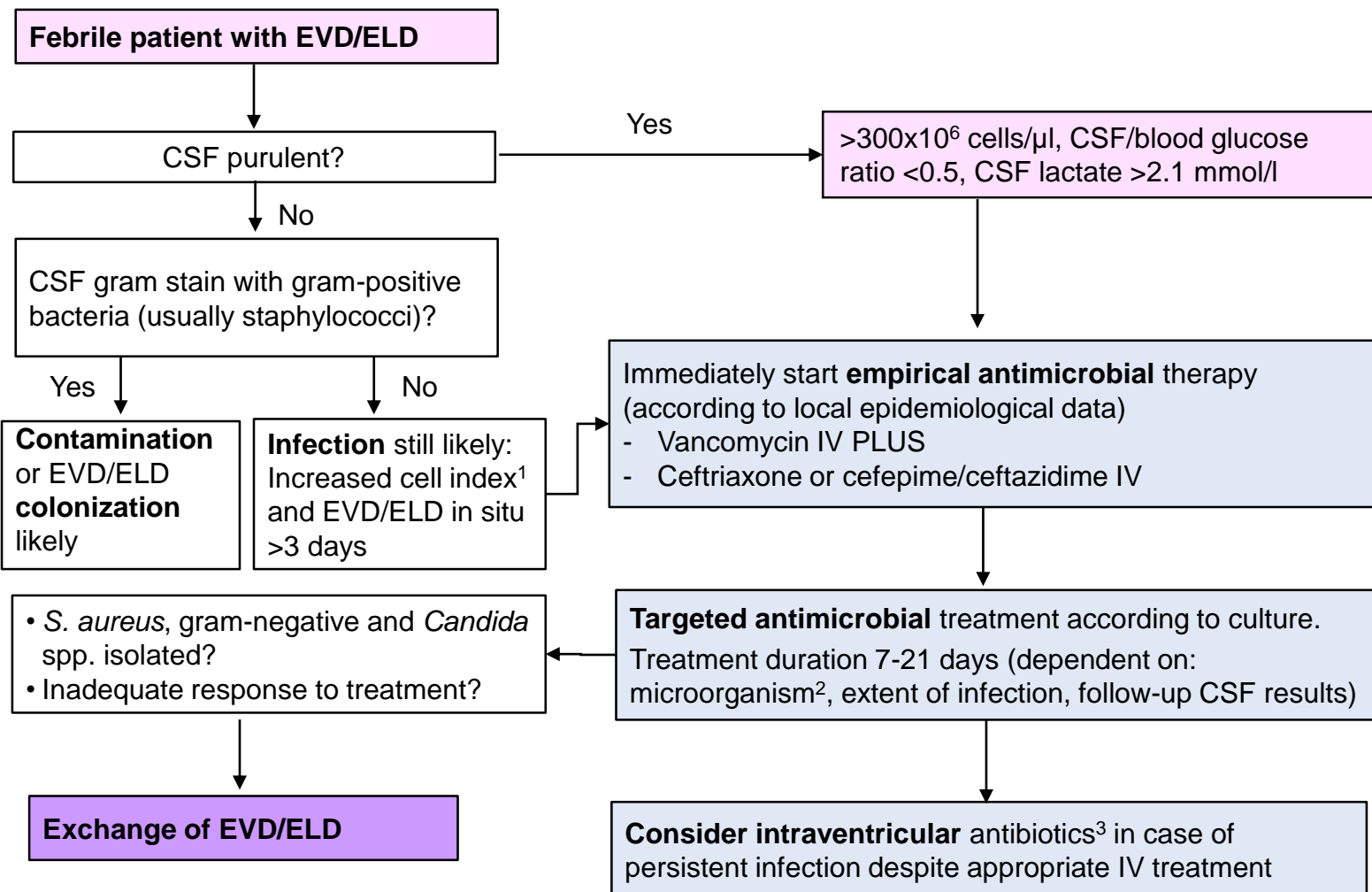
External ventricular drainage (EVD) / external lumbar drainage (ELD) infection

EVD / ELD infection is confirmed, if ≥ 1 criterion is fulfilled:

Investigation/sign	Criteria
Clinical signs of meningitis	<ul style="list-style-type: none"> Fever, headache, neck stiffness, vomiting
Local signs of infection	<ul style="list-style-type: none"> Local signs of inflammation at insertion site¹ Purulent wound secretion or abscess
CSF analysis	<ul style="list-style-type: none"> Increased cell count, lactate and protein Decreased CSF/blood glucose ratio Positive culture
Microbiology	<ul style="list-style-type: none"> Positive cultures from tissue or explanted drainage

¹ Erythema, swelling, warmth, pain, or tenderness

MANAGEMENT ALGORITHM



¹ Cell index: Ratio of leukocyte/erythrocyte ratio in CSF and leukocyte/erythrocyte ratio in blood

² Coagulase-negative staphylococci and *Cutibacterium* spp. 5-7 days; *S. aureus*, *Streptococcus* spp., *Enterococcus* spp. and culture-negative infections 14 days; Enterobacteriaceae and *Pseudomonas aeruginosa* 21 days

³ Daily intraventricular antibiotic doses → vancomycin (10-20 mg), daptomycin (2-5 mg), gentamicin (1-8 mg), tobramycin (5-20 mg), colistin (formulated as colistimethate: 10 mg), amphotericin B deoxycholate (0.01-0.5 mg in 2 ml 5% dextrose in water); dosing intervals based on EVD output: <50 ml/d: every 3. day, 50-100 ml/d: every 2. day, 100-150 ml/d: once daily, 150-200 ml/d: ↑ dose by 25%, 200-250 ml/d: ↑ dose by 50% (Tunkel AR et al. CID 2017, 64: e34)

Ventriculoperitoneal shunt (VPS) / ventriculoatrial shunt (VAS) infection

Criterion (≥1 fulfilled confirmative criterion required for diagnosis)		
Confirmative criteria	Clinical signs	<ul style="list-style-type: none"> • <u>Meningitis</u>: Fever, headache, neck stiffness, vomiting • Purulent discharge, sinus tract or abscess, wound dehiscence or shunt on view
	CSF analysis ²	<ul style="list-style-type: none"> • Decreased CSF/blood glucose ratio
	Microbiology	<ul style="list-style-type: none"> • Positive cultures from tissue or explanted foreign material • Positive CSF culture
	Imaging	<ul style="list-style-type: none"> • Abdominal sonography or CT scan (VPS): Pseudocysts, intestinal perforation through shunt migration • Brain MRI or CT: Cerebral abscess in direct contact with shunt
Suggestive criteria	Clinical signs	<ul style="list-style-type: none"> • <u>Peritonitis</u> (in VPS): Abdominal pain, rebound tenderness • <u>Endocarditis</u> (in VAS): positive blood cultures, TTE/TEE (shunt/valve vegetation) • <u>Nephritis</u> (in VAS): Glomerulonephritis (urine sediment)
	CSF analysis ²	<ul style="list-style-type: none"> • Increased cell count, lactate and protein
	Microbiology	<ul style="list-style-type: none"> • Positive blood cultures (VAS)

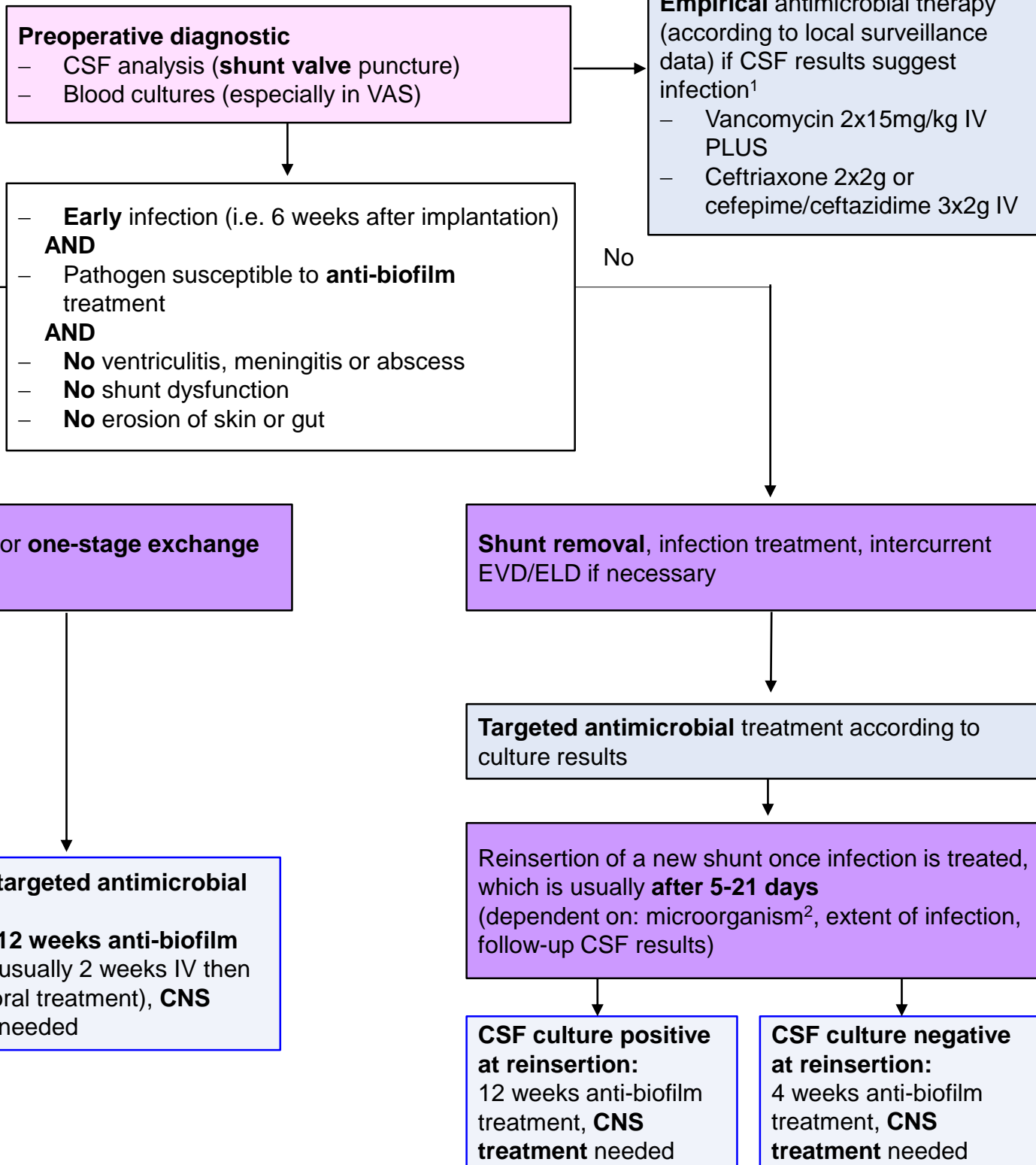
Neurostimulator infection

Investigation/sign	Criteria (≥1 fulfilled criterion required)
Generator pocket or wire (=cable) infection <u>without</u> CNS infection	
Local signs of infection	<ul style="list-style-type: none"> • Local signs of inflammation¹, purulent discharge, sinus tract, abscess, wound dehiscence or generator/electrodes on view
Microbiology	<ul style="list-style-type: none"> • Positive cultures from tissue or device
Lead (=electrode) infection or CNS infection	
Clinical signs of meningitis	<ul style="list-style-type: none"> • Fever, headache, neck stiffness, vomiting
Eventually local signs of infection	<ul style="list-style-type: none"> • Local signs of inflammation¹, purulent discharge, sinus tract, abscess, wound dehiscence or generator/electrodes on view
CSF analysis	<ul style="list-style-type: none"> • Increased cell count, lactate and protein • Decreased CSF/blood glucose ratio
Microbiology	<ul style="list-style-type: none"> • Positive cultures from tissue, device or CSF
Imaging (MRI or CT)	<ul style="list-style-type: none"> • Brain or epidural abscess

¹ Erythema, swelling, warmth, pain, or tenderness

² Preferably from shunt valve puncture

MANAGEMENT ALGORITHM: Shunt infection

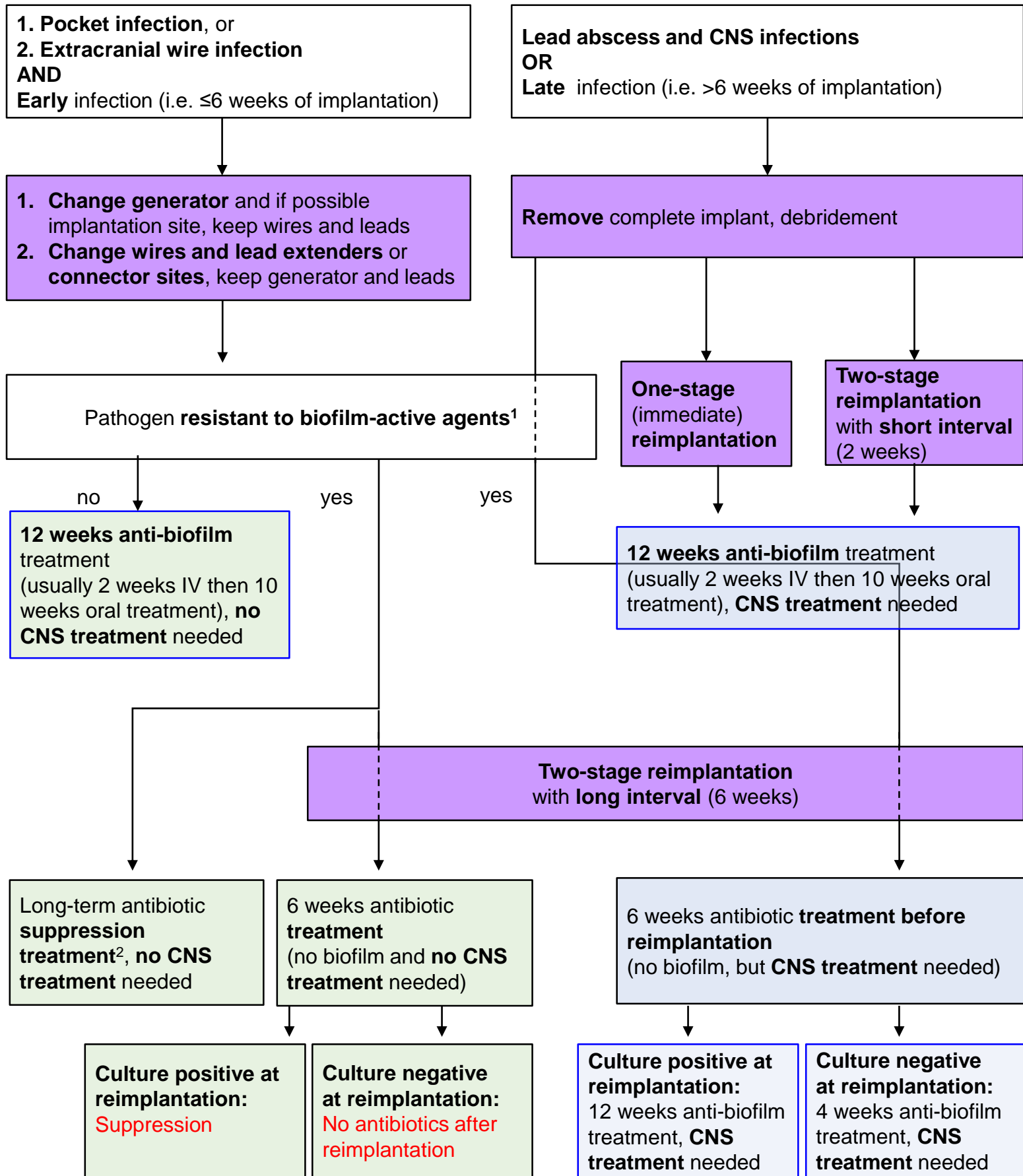


Abbreviations: CSF: Cerebrospinal fluid; EVD/ELD: external ventricular/lumbar drainage; IV: intravenous; CNS: central nervous system, **blue frame = biofilm active**

¹ CSF leukocyte count $>5 \times 10^6$ cells/ μ l, with predominance of granulocytes, CSF lactate >1.9 mmol/l, CSF total protein >0.45 g/l, glucose CSF/blood ratio <0.5

² For low-virulent microorganisms, including coagulase-negative staphylococci and *Cutibacterium* spp., re-implantation after 5-7 days; for *S. aureus*, *Streptococcus* spp., *Enterococcus* spp. and culture-negative infections 14 days; for Enterobacteriaceae and *P. aeruginosa* 21 days

MANAGEMENT ALGORITHM: Neurostimulator infection

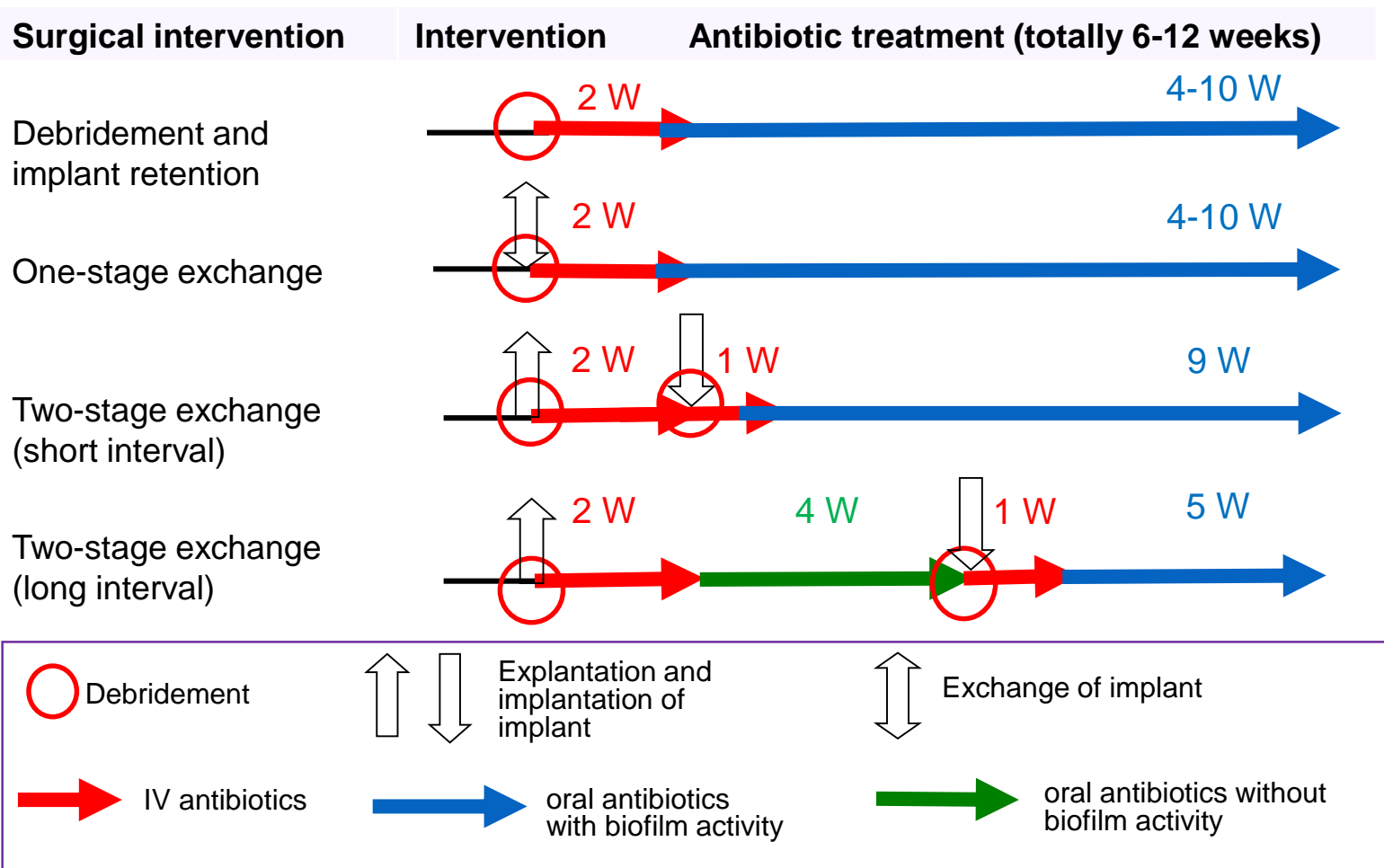


Abbreviation: blue frame = biofilm active

¹ Rifampin-resistant staphylococci, quinolone-resistant gram-negative bacilli, *Enterococcus* spp., *Candida* spp.

² Agents for long-term antimicrobial suppression therapy are cotrimoxazole and doxycycline in case central nervous system is involved, and additionally clindamycin, if central nervous system is not involved

SURGICAL TREATMENT



Treatment duration

Infection type	Duration (blue color = biofilm treatment)
Cranioplasty infection	If synthetic coverage (PMMA, PEEK, titan, ceramics): 12 weeks If autologous bone flap with fixation devices: 6 weeks If no foreign material in situ, i.e. implants removed: 6 weeks
Epidural empyema	6 weeks (biofilm-active if duraplasty in situ)
Postoperative meningitis	1-3 weeks ¹
Postoperative brain abscess	If surgically evacuated: 6 weeks If conservative treatment: until no residual infection in brain imaging (biofilm-active if duraplasty in situ)
Subdural empyema	
CSF shunt infection	12 weeks (if shunt retained or 1-stage exchange)
EVD/ ELD infection	1-3 weeks ¹
Neurostimulator infection	12 weeks

¹ For low-virulent microorganisms, including coagulase-negative staphylococci and *Cutibacterium* spp., re-implantation after 5-7 days; for *S. aureus*, *Streptococcus* spp., *Enterococcus* spp. and culture-negative infections 14 days; for Enterobacteriaceae and *P. aeruginosa* 21 days

ANTIMICROBIAL TREATMENT

Empiric intravenous treatment

Constellation	1. choice	Alternative
Extradural (bone flap or cranioplasty infection, epidural empyema)	Ampicillin/sulbactam 3x3g OR Amoxicillin/clavulanate 3x2.2g	Cefuroxime 3x1.5g
<i>with foreign material</i>	<i>plus Vancomycin¹ 2x15mg/kg</i>	<i>plus Daptomycin 1x8mg/kg</i>
Intradural (subdural empyema, meningitis, brain abscess)	Cefepime 3x2g	Meropenem 3x2g
<i>with foreign material</i>	<i>plus Vancomycin¹ 2x15mg/kg</i>	<i>plus Vancomycin¹ 2x15mg/kg</i>

¹ Vancomycin trough level in serum: 15-20 mg/l, measure at least twice weekly

Targeted intravenous treatment

Pathogen	Extradural	Intradural
<i>Staphylococcus spp.</i> Methicillin susceptible	Flucloxacillin 4x2g	Flucloxacillin 6x2 g
Penicillin allergy (non-type 1)	Cefazolin 3x2g	Cefepime 3x2g OR Meropenem 3x2g
Methicillin-resistant or penicillin allergy (type 1)	Vancomycin ¹ 2x15mg/kg OR Daptomycin 1x8mg/kg	Cotrimoxazole 3x1920mg OR Vancomycin ¹ 2x15mg/kg
<i>with foreign material</i>	<i>All plus Rifampin² 2x450 PO</i>	<i>All plus Rifampin² 2x600 PO</i>
<i>Streptococcus spp.</i>	Penicillin G 4x5 Mio IE OR Ceftriaxone 1x2g	Penicillin G 4x5 Mio IE OR Ceftriaxone 2x2g
<i>Cutibacterium acnes</i>	Penicillin G 4x5 Mio IE OR Ceftriaxone 1x2g	Penicillin G 4x5 Mio IE OR Ceftriaxone 2x2g
<i>with foreign material</i>	<i>All plus Rifampin² 2x450 PO</i>	<i>All plus Rifampin² 2x600 PO</i>

¹ Vancomycin trough level 15-20 mg/l, measure at least twice weekly

² Start rifampin as soon as all drainages are removed and wounds are dry; start with caution in vancomycin therapy and only if vancomycin trough levels are in the therapeutic range (15-20 mg/l), earlier switch to the oral treatment combination with better CSF penetration recommended

Targeted intravenous treatment

Pathogen	Extradural	Intradural
Enterobacteriaceae	Ceftriaxone 1x2g OR Ampicillin/sulbactam 3x3g OR Amoxicillin/clavulanate 3x2.2g	Ceftriaxone 2x2g
Non-fermenters (e.g. <i>P. aeruginosa</i> , <i>Acinetobacter spp.</i>)	Ceftazidim ⁴ 3x2g OR Cefepime ⁴ 3x2g OR Meropenem ⁴ 3x2g OR Piperacillin/tazobactam ⁴ 3x4.5g	Ceftazidime 3x2g OR Cefepime 3x2g OR Meropenem 3x2g All plus tobramycin ³ 1x3-5 mg/kg
<i>Enterococcus spp.</i> Penicillin-susceptible	Ampicillin 6x2g plus Gentamicin ³ 1x3mg/kg OR Ceftriaxone 2x2g OR Fosfomycin 3x5-8g	Ampicillin 6x2g plus Gentamicin ³ 1x3mg/kg OR Fosfomycin 3x5-8g
Penicillin-resistant	Vancomycin ¹ 2x15mg/kg plus Gentamicin ³ 1x3mg/kg OR Fosfomycin 3x5-8g	Vancomycin ¹ 2x15 mg/kg plus Gentamicin ³ 1x3mg/kg OR Fosfomycin 3x5-8g
Culture-negative infection	Ampicillin/sulbactam 3x3g OR Amoxicillin/clavulanate 3x2.2g plus Vancomycin ¹ 2x15mg/kg	Ceftriaxone 2x2g plus Vancomycin ¹ 2x15mg/kg
with foreign material	plus Rifampin ² 2x450 mg PO	plus Rifampin ² 2x600 PO

¹ Vancomycin trough level 15-20 mg/l, measure at least twice weekly

² Start rifampin as soon as all drainages are removed and wounds are dry; start with caution in vancomycin therapy and only if vancomycin trough levels are in the therapeutic range (15-20 mg/l), earlier switch to the oral treatment combination with better CSF penetration recommended

³ Monitor aminoglycoside trough levels and creatinine at least twice weekly

⁴ Consider combination therapy with aminoglycoside, particularly in case of multidrug resistance (e.g. tobramycin 3-5 mg/kg body weight or gentamicin 3 mg/kg body weight once daily)

Targeted oral treatment

Pathogen	Extradural	Intradural
<i>Staphylococcus</i> spp.	Levofloxacin 2x500mg OR Cotrimoxazole 3x960mg OR Doxycycline 2x100mg OR Fusidic acid 3x500mg	Cotrimoxazole 2x1920mg OR Levofloxacin 2x500mg OR Doxycycline 2x100mg
with foreign material	All plus Rifampin ¹ 2x450 mg	All plus Rifampin ¹ 2x600mg
<i>Streptococcus</i> spp.	Amoxicillin 3x1g	Prolonged IV treatment recommended (outpatient therapy with ceftriaxone 1x2g IV possible), then Moxifloxacin 1x400mg
<i>Cutibacterium acnes</i>	Amoxicillin 3x1g OR Levofloxacin 2x500mg	Levofloxacin 2x500mg OR Moxifloxacin 1x400mg OR Amoxicillin 3x1g
with foreign material	All plus Rifampin ¹ 2x450 mg	All plus Rifampin ¹ 2x600 mg
Enterobacteriaceae	Ciprofloxacin 2x750mg	Prolonged IV treatment recommended, then Cotrimoxazol 3x1920mg OR Ciprofloxacin 2x750 mg
with foreign material	Ciprofloxacin 2x750 mg	Ciprofloxacin 2x750 mg
Non-fermenters (e.g. <i>P. aeruginosa</i> , <i>Acinetobacter</i> spp.)	Ciprofloxacin 2x750mg	Prolonged IV treatment recommended, then Ciprofloxacin 2x750mg
with foreign material	Ciprofloxacin 2x750 mg	Ciprofloxacin 2x750 mg
<i>Enterococcus</i> spp. Penicillin-susceptible	Amoxicillin 3x1g	Prolonged IV treatment recommended, then consider in selected patients
Penicillin-resistant	Linezolid 2x600mg	Linezolid 2x600mg OR Doxycycline 2x100mg
Culture-negative infection	Levofloxacin 2x500mg PLUS (Clindamycin 3x600mg OR Cotrimoxazole 3x960mg)	Prolonged IV treatment, then Cotrimoxazole 2x1920mg PLUS (Levofloxacin 2x500mg OR Moxifloxacin 1x400mg)
with foreign material	Levofloxacin 2x500mg PLUS Rifampin ¹ 2x450mg	Levofloxacin 2x500mg OR Moxifloxacin 1x400mg All plus Rifampin ¹ 2x600mg

¹ Start rifampin as soon as all drainages are removed and wounds are dry