

# Pocket Guide to Diagnosis & Treatment of Spinal Infections



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For individual consultations and workshops contact our Consultation Portal at: [cp.pro-implant.org](http://cp.pro-implant.org)

## DEFINITION

**Vertebral osteomyelitis** is confirmed, if the following 3 criteria are fulfilled:

Investigation	Criteria
Clinical features	Acute or chronic back pain
Imaging	Computed tomography (CT) or magnetic resonance imaging (MRI) consistent with vertebral osteomyelitis
Microbiology or Histology	Microbial growth in blood culture or vertebral tissue <sup>1</sup>  Acute or chronic inflammation in vertebral tissue

**Implant-associated spinal infection** is confirmed, if  $\geq 1$  criterion is fulfilled:

Investigation	Criteria
Clinical features	<ul style="list-style-type: none"><li>• Wound healing disturbance or sinus tract (fistula)</li><li>• Visible purulence around the implant</li><li>• Positive „probe to implant“ test</li></ul>
Histology	Inflammation in peri-implant tissue
Microbiology	Significant microbial <sup>2</sup> growth in: <ul style="list-style-type: none"><li>• <math>\geq 2</math> peri-implant tissue samples</li><li>• Sonication fluid (<math>\geq 50</math> CFU/ml)</li></ul>

<sup>1</sup> Low virulent skin pathogens must be interpreted in the clinical context (prior infiltrations? Intravascular device present?)

<sup>2</sup> For highly virulent organisms (e.g. *S. aureus*, *E. coli*, streptococci) or patients under antibiotics already one positive sample confirms infection and  $< 50$  CFU/ml in sonication can be significant

## Supportive criteria for infection:

- Prolonged discharge from wound
- Secondary wound dehiscence
- Loosening of the implant/screws
- Non-union (pseudarthrosis)

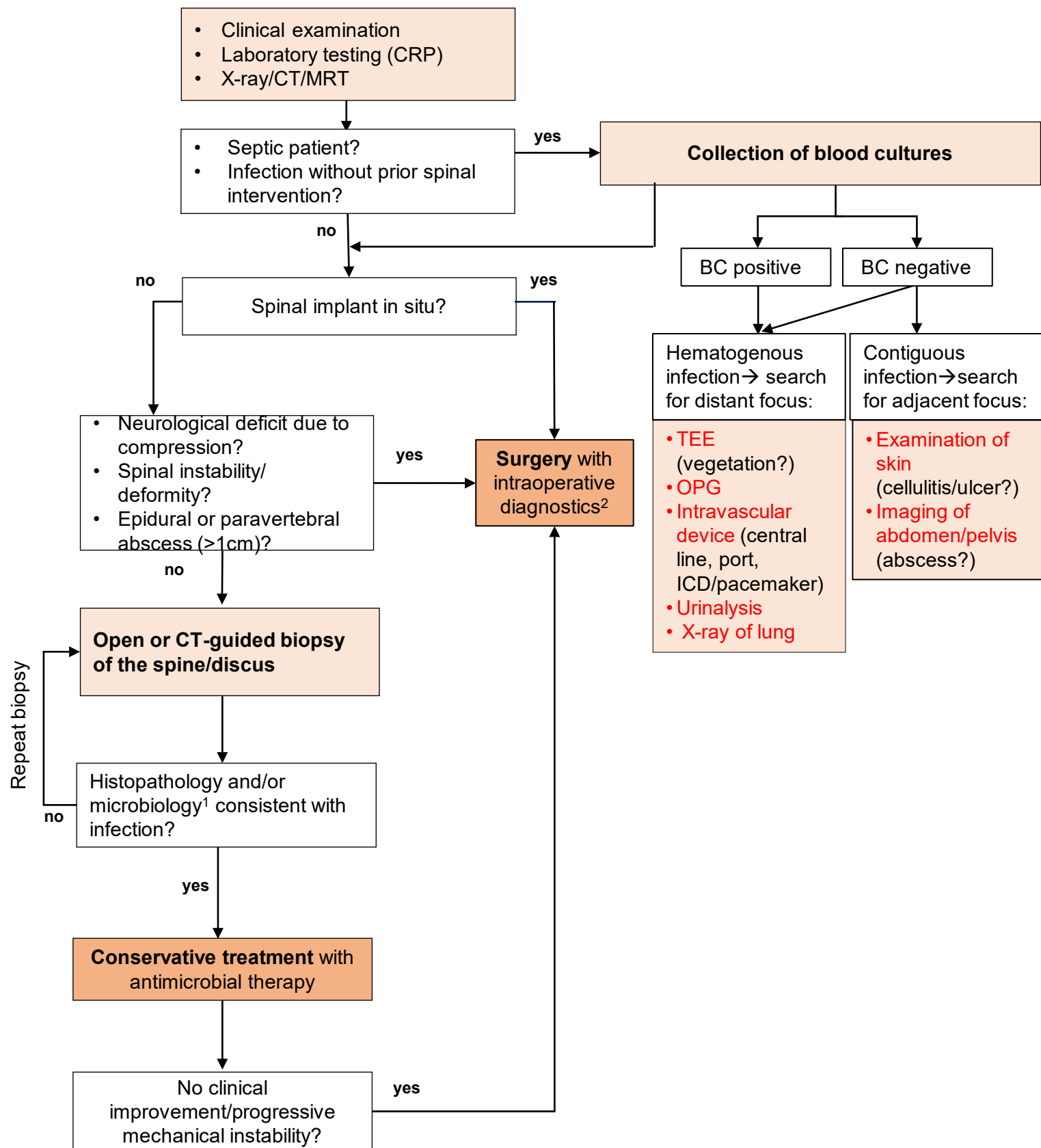
## PATHOGENESIS

Post-interventional	Hematogenous	Contiguous
<p>After</p> <ul style="list-style-type: none"> <li>• Surgery/instrumentation</li> <li>• Spinal infiltration/injections</li> <li>• Open/CT-guided biopsy</li> </ul>	<ul style="list-style-type: none"> <li>• Primary bacteremia/sepsis</li> <li>• Urosepsis</li> <li>• Endocarditis/infected intravascular device</li> <li>• Dental focus (abscess/after interventions)</li> <li>• Pulmonary infection</li> <li>• Abdominal infection/tumor</li> </ul>	<ul style="list-style-type: none"> <li>• Skin infection</li> <li>• Pressure ulcer</li> <li>• Gastrointestinal sinus tract (oesophagus, intestine)</li> <li>• Aortic infection</li> </ul>

## CLASSIFICATION

	Acute spinal infection	Chronic spinal infection
<p>Pathogenesis</p> <ul style="list-style-type: none"> <li>▪ Post-interventional</li> <li>▪ Hematogenous <u>or</u> contiguous</li> </ul>	<p>&lt;6 weeks after intervention (early)</p> <p>&lt;6 weeks of symptom duration</p>	<p>≥6 weeks after intervention (delayed/low-grade)</p> <p>≥6 weeks of symptom duration</p>
<p>Clinical features</p>	<p>Acute pain, fever, prolonged wound discharge (&gt;7-10 days), acute neurologic impairment</p>	<p>Chronic pain, loosening/dislocation of the implant, sinus tract (fistula), neurologic impairment</p>
<p>Causative microorganism</p>	<p>High-virulent: <i>Staphylococcus aureus</i>, <i>Streptococcus</i> spp., gram-negative bacteria</p>	<p>Low-virulent: Coagulase-negative staphylococci, <i>Cutibacterium</i> (formerly <i>Propionibacterium</i>) <i>acnes</i></p>

# MANAGEMENT ALGORITHM

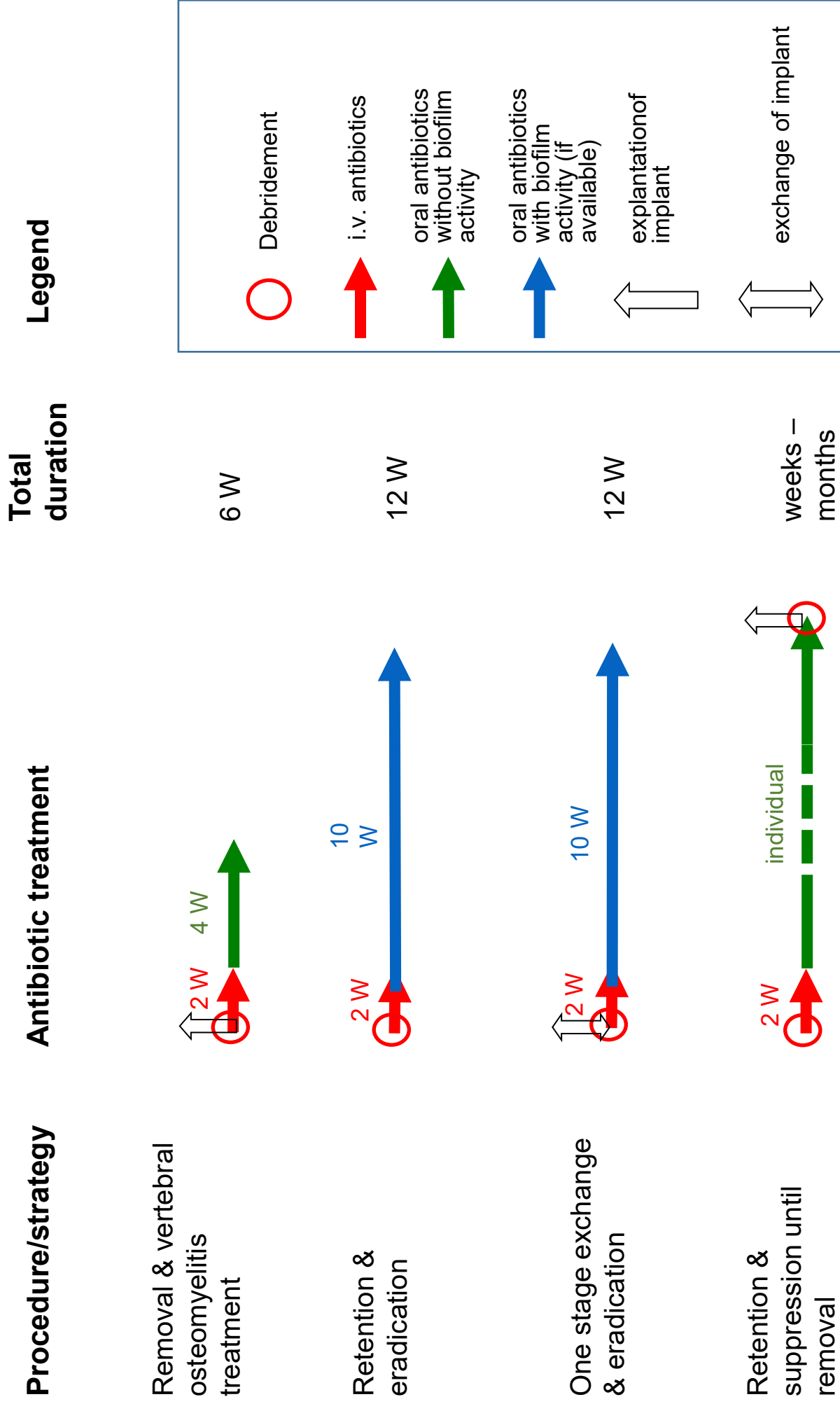


<sup>1</sup> For highly virulent organisms (e.g. *S. aureus*, *E. coli*, *streptococcus spp.*) or for patients on antibiotic therapy one positive sample confirms infection, for low-virulent organisms (e.g. *S. epidermidis*, *C. acnes*)  $\geq 2$  positive samples are required to confirm infection.

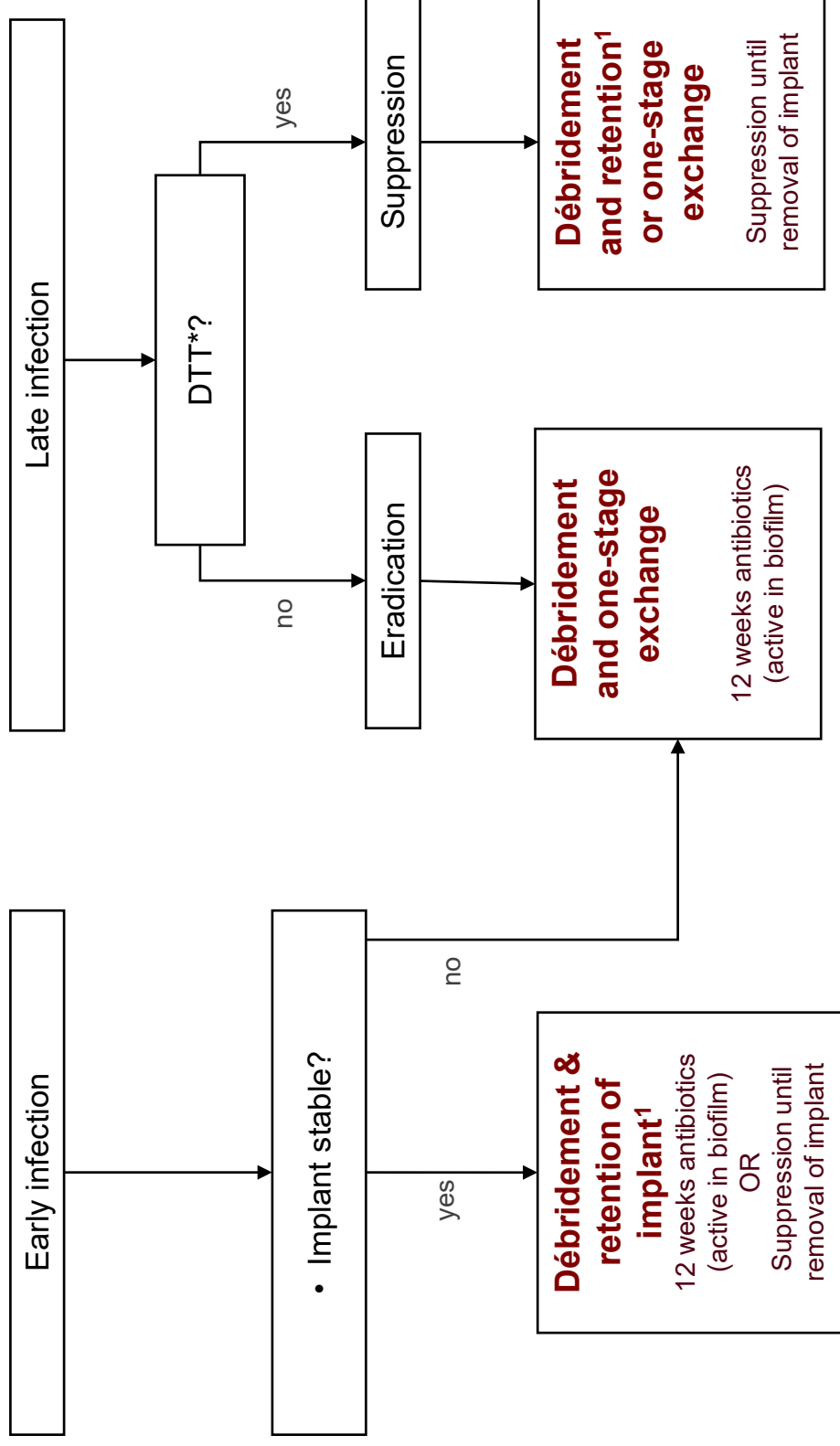
<sup>2</sup> See procedures on the following page. Histopathology, microbiology (+/- sonication), additional microbiological investigations (Mycobacteria, Brucella), if exposure/risk factors present.

TEE: transesophageal echocardiography, OPG: orthopantomogram, BC: blood cultures

# SURGICAL PROCEDURES FOR IMPLANT ASSOCIATED SPINAL INFECTIONS



# TREATMENT ALGORITHM FOR IMPLANT-ASSOCIATED SPINAL INFECTIONS



\* DTT = difficult-to-treat, caused by pathogens resistant to biofilm-active antimicrobials:  
 - Rifampin-resistant staphylococci  
 - Ciprofloxacin-resistant gram-negative bacteria  
 - Fungi (Candida)

<sup>1</sup> exchange all loose parts (screws) if possible

# RECOMMENDED ANTIMICROBIAL TREATMENT

## Empiric therapy (intravenous):

Clinical situation	Primary focus	1 <sup>st</sup> choice	Alternative
<b>Hematogenous vertebral osteomyelitis (without implant)</b>	Without known primary focus	Ampicillin/Sulbactam <sup>a</sup> 3 x 3 g	+ Fosfomycin 3 x 5 g (severe infection)
	Infectious endocarditis suspected	Ampicillin/Sulbactam <sup>a</sup> 4 x 3 g + Gentamicin <sup>e</sup> 1 x 240 mg	Ampicillin/Sulbactam <sup>a</sup> 4 x 3 g + Fosfomycin 3 x 5 g
	Primary focus in urogenital tract or abdomen suspected	Piperacillin/Tazobactam 3 x 4.5 g	Meropenem 3 x 1 g
	Allergy to penicillins: - non-Type 1	Cefuroxim 3 x 1.5 g	Meropenem 3 x 1 g
	- Type 1 (anaphylaxis)	Vancomycin <sup>d</sup> 2 x 1g + Fosfomycin 3 x 5g	Daptomycin 1 x 8 mg/kg+ + Fosfomycin 3 x 5g
<b>Post-interventional spinal infection (+/- implant)</b>	First revision	Ampicillin/Sulbactam <sup>a</sup> 3 x 3g + Fosfomycin 3 x 5g	Cefuroxim 3 x 1.5 g + Vancomycin <sup>d</sup> 2x1g
	Multiple previous revisions	Piperacillin/Tazobactam 3 x 4.5g + Fosfomycin 3 x 5g	Vancomycin <sup>d</sup> 2 x 1g + Fosfomycin 3 x 5 g

## Targeted eradication therapy (deescalate as soon as the pathogen is known):

Microorganism (red: difficult-to-treat)	Antibiotic (check pathogen susceptibility before)	Dose <sup>b</sup> (blue: renal adjustment needed)	Route
<b>Staphylococcus spp.</b>			
- Oxacillin-/methicillin-susceptible	Flucloxacillin <sup>a</sup> (+/- Fosfomycin) for 2 weeks, followed by (according to susceptibility)	4 x 2 g (3 x 5 g)	i.v. i.v.
	Rifampin <sup>c</sup> +	2 x 450 mg	p.o.
	- Levofloxacin or	2 x 500 mg	p.o.
	- Cotrimoxazole or	3 x 960 mg	p.o.
	- Doxycycline or	2 x 100 mg	p.o.
	- Fusidic acid	3 x 500 mg	p.o.
- Oxacillin-/methicillin-resistant	Daptomycin or Vancomycin <sup>d</sup> (+/- Fosfomycin) for 2 weeks, followed by an oral <b>rifampin</b> combination as above	1 x 8 mg/kg 2 x 1 g (3 x 5 g)	i.v. i.v. i.v.
- <b>Rifampin-resistant</b>	Intravenous treatment according susceptibility for 2 weeks (as above), followed by long-term suppression for ≥1 year (e.g. Doxycycline)		
<b>Streptococcus spp.</b>			
	Penicillin G <sup>a</sup> or Ceftriaxone for 2-3 weeks, followed by:	4 x 5 million U 1 x 2 g	i.v. i.v.
	Amoxicillin or Doxycycline (suppression ≥1 y.)	3 x 1000 mg 2 x 100 mg	p.o. p.o.
<b>Enterococcus spp.</b>			
- Penicillin-susceptible	Ampicillin + Gentamicin <sup>e</sup> (+/- Fosfomycin) for 2-3 weeks, followed by:	4 x 2 g 1 x 120 mg (3 x 5 g)	i.v. i.v. i.v.
	Amoxicillin	3 x 1000 mg	p.o.
- <b>Penicillin-resistant or allergy to penicillin</b>	Vancomycin <sup>d</sup> or Daptomycin + Gentamicin <sup>e</sup>	2 x 1 g 1 x 10 mg/kg 1 x 120 mg	i.v. i.v. i.v.

	(+/- Fosfomycin) for 2-4 weeks, followed by	(3 x 5 g)	i.v.
	Linezolid (max. 4 weeks)	2 x 600 mg	p.o.
- <b>Vancomycin-resistant (VRE)</b>	Individual; removal of the implant <u>or</u> life-long suppression necessary (e.g. with Doxycycline)		
<b>Gram-negative</b>			
- Enterobacteriaceae ( <i>E. coli</i> , <i>Klebsiella</i> , <i>Enterobacter</i> etc.)	Ciprofloxacin <sup>f</sup>	2 x 750 mg	p.o.
- Nonfermenters ( <i>Pseudomonas aeruginosa</i> , <i>Acinetobacter</i> spp.)	Piperacillin/tazobactam or Meropenem or Ceftazidim/Cefepime +Tobramycin (or gentamicin) for 2-3 weeks, followed by:	3 x 4.5 g 3 x 1 g 3 x 2 g 1 x 300 mg 1 x 240 mg	i.v. i.v. i.v. i.v. i.v.
- multiresistant	Depending on susceptibility: a combination of meropenem 3 x 1 g i.v., colistin 3 x 3 million U i.v. and/or fosfomycin 3 x 5 g i.v., consider oral suppression (if <b>Cipro-R</b> )	2 x 750 mg	p.o.
<b>Anaerobes</b>			
- Gram-positive ( <i>Cutibacterium</i> , <i>Peptostreptococcus</i> , <i>Finegoldia magna</i> )	Penicillin G <sup>a</sup> or Ceftriaxon for 2 weeks, followed by:	4 x 5 million U 1 x 2 g	i.v. i.v.
	Rifampin <sup>c</sup> + Levofloxacin or Amoxicillin	2 x 450 mg 2 x 500 mg 3 x 1000 mg	p.o. p.o. p.o.
- Gram-negative ( <i>Bacteroides</i> )	Ampicillin/sulbactam <sup>a</sup> for 2 weeks, followed by Metronidazol	3 x 3 g 3 x 400 mg or 500 mg	i.v. p.o.
<b>Candida spp.</b>			
- <b>Fluconazole-susceptible</b>	Caspofungin <sup>g</sup> or Anidulafungin for 2 weeks, followed by: Fluconazole (suppression for ≥1 year)	1 x 70 mg 1 x 100mg (1. Day 200mg) 1 x 400 mg	i.v. i.v. p.o.
- <b>Fluconazole-resistant</b>	Individual (e.g. with voriconazole 2 x 200 mg p.o.); removal of the implant or long-term suppression		
<b>Culture-negative</b>			
	Ampicillin/sulbactam <sup>a</sup> for 2 weeks, followed by:	3 x 3 g	i.v.
	Rifampin <sup>c</sup> + Levofloxacin	2 x 450 mg 2 x 500 mg	p.o. p.o.

<sup>a</sup> **Penicillin allergy** NON-type 1 (e.g. skin rash): cefazolin (3 x 2 g i.v.). In case of anaphylaxis (= type 1-allergy such as Quincke's edema, anaphylactic shock) or cephalosporin allergy: vancomycin (2 x 1 g i.v.) or daptomycin (1 x 8 mg/kg i.v.) Ampicillin/sulbactam is equivalent to amoxicillin/clavulanic acid (3 x 1.2 g or 3 x 2.2 g i.v.)

<sup>b</sup> **Laboratory testing** 2x weekly: leukocytes, CRP, creatinine/eGFR, liver enzymes (AST and ALT). Dose-adjustment according to renal function and body weight (<40 or >100kg)

<sup>c</sup> **Rifampin** is administered only when a newimplant is in situ. Add it orally to i.v.-treatment as soon as wounds are dry; in patients aged >75 years, rifampin is reduced (2 x 300 mg).

<sup>d</sup> Check **Vancomycin** concentration at least 1x/week(take blood before next dose); therapeutic range: 15-20 µg/ml

<sup>e</sup> Give gentamicin only, if **gentamicin high-level (HL)** is tested susceptible (consult your microbiology laboratory). In gentamicin HL-resistant *E. faecalis* or patients with impaired renal function: gentamicin is exchanged with ceftriaxone 1 x 2 g i.v. or Fosfomycin 3 x 5 g i.v.

<sup>f</sup> Add **i.v. treatment** (piperacillin/tazobactam 3 x 4.5 g or ceftriaxon 1x 2 g or meropenem 3 x 1 g i.) in the first postoperative days (until wound is dry)

<sup>g</sup> In patients weighing <80 kg: a loading dose of 70 mg on day 1, then **reduce to 50 mg** from day 2.

## Oral therapy in vertebral osteomyelitis WITHOUT implant

Microorganism	Antibiotic (according to susceptibility, for dose see table above)
<i>S. aureus</i>	Rifampin combination (see above)
Coagulase-negative staphylococci	Cotrimoxazole or doxycycline or clindamycin
<i>Streptococcus</i> spp. <sup>1</sup>	Amoxicillin or clindamycin or doxycycline
<i>Enterococcus</i> spp. <sup>1</sup>	Amoxicillin (or linezolid, if resistant to amoxicillin)
Anaerobes (gram-positive)	Clindamycin or amoxicillin
Anaerobes (gram-negative)	Metronidazole or clindamycin
Gram-negative bacilli	Ciprofloxacin or cotrimoxazole
Fungi ( <i>Candida</i> spp.)	Fluconazole (voriconazole if fluconazole resistant)

<sup>1</sup> Consider longer intravenous treatment (4 weeks) in *S. agalactiae*, *S. dysgalactiae* and enterococci.

### Treatment duration:

- Native spinal infection (WITHOUT Implant): 6 weeks (in most cases but longer, if non-drained abscess)
- Implant associated spinal infection: 12 weeks (in most cases)

### Follow-up:

- clinical and laboratory (CRP) course
- NO scheduled CT or MRT imaging, only if new symptoms occur or clinical course is unfavorable

## INVESTIGATION OF PRIMARY FOCUS

Pathogen	Primary focus	Investigation	
<b>Staphylococcus</b> spp.	<i>S. aureus</i>	<ul style="list-style-type: none"> <li>• Skin lesions/furunculosis</li> <li>• Endocarditis</li> <li>• Primary bacteremia</li> </ul>	<ul style="list-style-type: none"> <li>• Skin examination</li> <li>• Blood cultures</li> <li>• Transesophageal echocardiography (TEE)</li> </ul>
	Coagulase-negative staphylococci	<ul style="list-style-type: none"> <li>• Intravascular implant</li> <li>• Endocarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Blood cultures, TEE</li> <li>• Intravascular implant in situ?</li> </ul>
<b>Streptococcus</b> spp.	Viridans group ( <i>S. mitis/oralis</i> )	<ul style="list-style-type: none"> <li>• Oral cavity</li> <li>• Endocarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Orthopantomogram</li> <li>• Blood cultures, TEE</li> <li>• Recent dental procedure?</li> </ul>
	<i>S. agalactiae</i> , <i>S. dysgalactiae</i>	<ul style="list-style-type: none"> <li>• Abdomen</li> <li>• Urogenital tract</li> <li>• Skin</li> <li>• Oral cavity</li> </ul>	<ul style="list-style-type: none"> <li>• Imaging of abdomen/pelvis</li> <li>• Urinalysis</li> <li>• Skin examination</li> <li>• Orthopantomogram</li> </ul>
	<i>S. gallolyticus</i> (formerly <i>bovis</i> )	<ul style="list-style-type: none"> <li>• Colon carcinoma /adenoma</li> </ul>	<ul style="list-style-type: none"> <li>• Colonoscopy</li> </ul>
<b>Enterococcus</b> spp.	<i>E. faecalis</i> , <i>E. faecium</i>	<ul style="list-style-type: none"> <li>• Abdomen</li> <li>• Urogenital tract</li> <li>• Endocarditis</li> </ul>	<ul style="list-style-type: none"> <li>• Imaging of abdomen/pelvis</li> <li>• Urinalysis</li> <li>• Blood cultures, TEE</li> </ul>
<b>Gram-negative rods</b>	<i>E. coli</i> , <i>Klebsiella</i> , <i>Enterobacter</i> spp.	<ul style="list-style-type: none"> <li>• Abdomen</li> <li>• Urogenital tract</li> </ul>	<ul style="list-style-type: none"> <li>• Imaging of abdomen/pelvis</li> <li>• Urinalysis</li> <li>• (Colonoscopy)</li> </ul>