Osteomieliti

- Osteomyelitis is the inflammation of bone caused by pyogenic organisms.

- Major sources of infection:
  - haematogenous spread
  - tracking from adjacent foci of infection
  - direct inoculation from trauma or surgery

- **Haematogenous spread** is the most common source of infection in children, typically affecting the long bones

ACUTE: less then 2 weeks

SUBACUTE: 2 weeks-3 months

CRONIC: > 3 months

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EPIDEMIOLOGY

- Incidence: 1-13: 100.000
- Boys : girls = 2 : 1
- 50% under 5 years old
- In most cases **solitary lesion**
  (multifocal in neonates)

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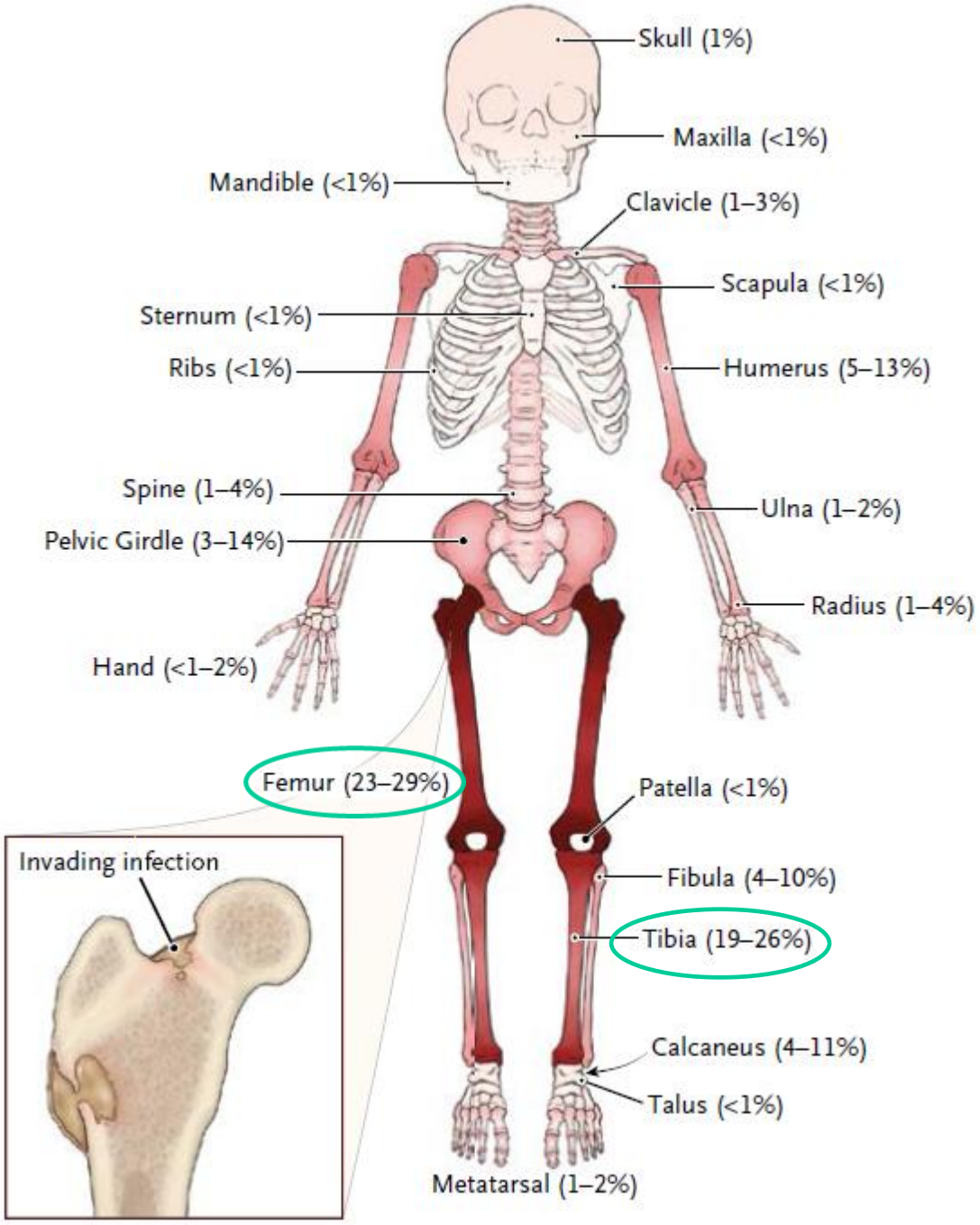
RISK FACTORS

50% → NO RISK FACTORS

- Immunocompromised
- Premature infants
- Chronic illness

(es. Sickle cell disease, pulmonary or heart disease)


Skull (1%)
Maxilla (<1%)
Mandible (<1%)
Clavicle (1–3%)
Scapula (<1%)
Sternum (<1%)
Ribs (<1%)
Humerus (5–13%)
Spine (1–4%)
Ulna (1–2%)
Pelvic Girdle (3–14%)
Radius (1–4%)
Hand (<1–2%)
Femur (23–29%)
Patella (<1%)
Invading infection
Fibula (4–10%)
Tibia (19–26%)
Calcaneus (4–11%)
Talus (<1%)
Metatarsal (1–2%)

DIFFERENTIAL DIAGNOSES FOR ACUTE OSTEOMYELITIS

Vascular

- Vaso-occlusive disease—for example, bone infarct secondary to sickle cell disease

Infection

- Septic emboli
- Chronic recurrent multiple osteomyelitis
- Septic arthritis

Trauma

- Stress fracture

Tumour

- Osteoid osteoma
- Acute lymphoblastic leukaemia
- Eosinophilic granuloma
- Metastatic neuroblastoma
- Ewing's sarcoma
- Osteosarcoma

DIAGNOSE

- Insidious onset
- Variable clinical presentation
- Non specific clinical findings

No single test to confirm Osteomyelitis!

Careful hystory and clinical examination
High index of suspicion
Laboratory
Imaging

CLINICAL EXAMINATION

- Pain (81%)
- Swelling and erythema (70%)
- Fever (62%)
- Reduce jonts movements or pseudoparalysis (50%)
- Reduced weight bearing or Limp (49%)

Young child:

- Irritability
- Refuse to use a limb

Dartnell J, Haematogenous acute and subacute paediatric osteomyelitis: a sistematic review of literature. J Bone Joint Surg Br 2012

CLINICAL FEATURES TO LOOK FOR IN A CHILD WITH SUSPECTED OSTEOMYELITIS

History

- Listen to the child and observe his or her interaction with the parents (there could be other causes for pain or a limp[25])
- Ask about the site of pain (beware referred pain—children with hip disease often complain of knee pain instead)
- Ask about the duration of symptoms (fever for >7 days or localised symptoms for >10 days are suggestive of a complicated course)
- Ask about prodromal symptoms (for example, recent fever, cough, cold, diarrhoea)
- Ask about changes in behaviour (in a young child, subtle features such as irritability and being quieter than usual may be the only presenting sign)
- Ask about recent trauma (30% of patients have this as a feature)
- Ask about chronic illnesses (especially sickle cell disease or diabetes)

Examination

- Take the child's temperature (in 40% of cases, children may be afebrile)
- Observe the movement of all four limbs (pseudoparalysis may be the only feature in an infant)
- Observe the resting position of the child's limb—children may hold their hip in a flexed and externally rotated position, or the knee in a flexed position (fig 2⇓)
- If the child is of walking age, look for a limp or reluctance to weight bear
- Look for swelling and erythema, which can be subtle (the femur and tibia are the most commonly affected sites)
- Look for open wounds
- Look for localised tenderness and restricted range of joint motion
- Examine the rest of the child, as osteomyelitis can be multifocal or present in unusual sites (see fig 1)
- Most importantly, have a high index of suspicion, and, if in doubt, refer acutely to paediatrics, paediatric infectious disease, or paediatric orthopaedics

LABORATORY

- PCR and PCT sensitive as diagnostic test

- PCT > 0.4 ng/ml sensitive and specific marker for septic arthritis and osteomyelitis
  (Karthikeyan et al., J Orthop Surg and Research 2013; 8:19)

- Sensitivity highest when VES and PCR increased (98%)

- PCR useful for monitoring response to treatment
  (BMJ 2014; 348: 1-8)

- Microbiology → BLOOD CULTURE positive only in 50%
  → Bone or joint aspirates in 70%

CAUSATIVE AGENTS

All ages

S. Aureus (70-90%)

Neonates and young infants

Group B Streptococcus
Bacilli gram- (E.coli)

→ Salmonella species in developing countries and among patients with sickle cell disease

→ Community acquired MRSA
-increasing incidence
-incidence up to 30%
-more aggressive disease

Kingella kingae

- Gram- coccobacillus
- common pathogen respiratory tract
- increasing incidence (2° most common cause of osteomyelitis < 5 y)

95% K. Kingae osteomyelitis in children 6 months-3 years

- PPV 90% of PCR detection in pharynx
- more benign features BUT

difficult to culture!

↓

Polymerase change reaction

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CAUSATIVE PATHOGEN

Not identified

55% of cases

IMAGING

Radiographs:
-acute skeletal changes not visible before 5-10 days
BUT
-exclude fractures or malignancy

Scintigrafy:
-sensitive and useful (symptoms not localized!)
BUT
-extensive radiation exposure

Computed tomography (CT):
-excellent multiplanar images reconstructions
-useful in chronic osteomyelitis (scleotic changes, abnormal thickening bone..)
BUT
-poor soft tissue contrast
-high exposure radiation

MAGNETIC RESONANCE

- The best imaging method
- High sensitivity (82-100%)
- High specificity (75-99%)
- Identifying location and extent of disease
- More detailed evaluation adiacent structures (pyomyositis, joint effusion, subperiostal abscesses)
- SAFE!

BMJ 2014

TREATMENT

NEJM 2014

•S. aureus methicillin-susceptible

Cefazolin (100 mg/kg/24 h every 8h) or **Nafcillin** (150-200 mg/kg/24 h every 6h)

Clindamycin (30-40 mg/kg/24 h every 8h) when rate Clindamycin Resistance S.aureus ≤ 10%

•MRSA infections

Vancomycin (45 mg/kg/24 h every 8h OR 60 mg/kg/24 h every 6h)

•S. pneumoniae, A group Streptococcus, K. Kingae:

Penicillin (Beta lactams)

•S. pneumoniae penicillin-resistant and Salmonella

Cezotaxime or **Ceftriaxone**

•Patients with Sickle cell Disease

Cefotaxime (150-225 mg/kg/24 h every 8h) AND **Vancomycin** (45 mg/kg/24 h every 8h) OR **Clindamycin** (40 mg/kg/24 h every 6h)

Table 1. Antibiotic Treatment for Acute Osteomyelitis in Children.*

Antibiotic	Dose	Maximal Daily Dose†	Bone Penetration‡	Reference
	mg/kg/day		%	
Empirical treatment				
First-generation cephalosporin, if prevalence of MSSA in community >90%§	≥150 administered in 4 equal doses¶	2–4 g	6–7	Dose: Peltola et al.,[9] Peltola et al.[20]; extent of bone penetration: Tetzlaff et al.[21]
Antistaphylococcal penicillin (cloxacillin, flucloxacillin, dicloxacillin, nafcillin, or oxacillin), if prevalence of MSSA in community >90%	≤200 administered in 4 equal doses	8–12 g	15–17	Dose: Jagodzinski et al.[8]; extent of bone penetration: Tetzlaff et al.[21]
Clindamycin, if prevalence of MRSA in community ≥10% and prevalence of clindamycin-resistant *S. aureus* <10%	≥40 administered in 4 equal doses	Approximately 3 g	65–78	Prevalence of microorganisms: Liu et al.[14]; dose: Peltola et al.,[9] Liu et al.,[14] Peltola et al.[20]; extent of bone penetration: Feigin et al.[22]
Vancomycin, if prevalence of MRSA in community ≥10% and prevalence of clindamycin-resistant *S. aureus* ≥10%	≤40 administered in 4 equal doses	Dosing adjusted according to trough level, with a target of 15 to 20 μg per milliliter	5–67	Prevalence of microorganisms: Liu et al.[14]; dose: Liu et al.[14]; extent of bone penetration: Landersdorfer et al.[23]
Linezolid, if no response to vancomycin	30 administered in 3 equal doses	1.2 g for no more than 28 days	40–51	Dose: Kaplan et al.,[24] Chen et al.[25]; extent of bone penetration: Landersdorfer et al.[23]
Alternatives for specific agents				
Ampicillin or amoxicillin for group A beta-hemolytic streptococcus, *Haemophilus influenzae* type b (beta-lactamase–negative strains), and *S. pneumoniae*	150–200 administered in 4 equal doses	Approximately 8–12 g	3–31	Dose: Peltola et al.[9]; extent of bone penetration: Landersdorfer et al.[23]
Chloramphenicol, if safer agents not available or affordable	75 administered in 3 equal doses‖	2–4 g	39	Dose: Krogstad[1]; extent of bone penetration: Summersgill et al.[26]

SWITCH INTRAVENOUS → ORAL THERAPY

- Improvement
- Normalization PCR (ridotta del 50%) and VES (ridotta del 20%)
- No fever for > 48-72 h

ORAL ANTIBIOTIC

- Excellent bone penetration
- Same degree of antibacterial coverage as parenteral drug
- Ability to take oral drug

Cephalexin (80-100 mg/kg/24 h every 8h)
OR
Clindamycin (30-40 mg/kg/24 h every 8h)

Increasing incidence CA-MRSA and Clindamycin-resistant SA
Lack of studies in children

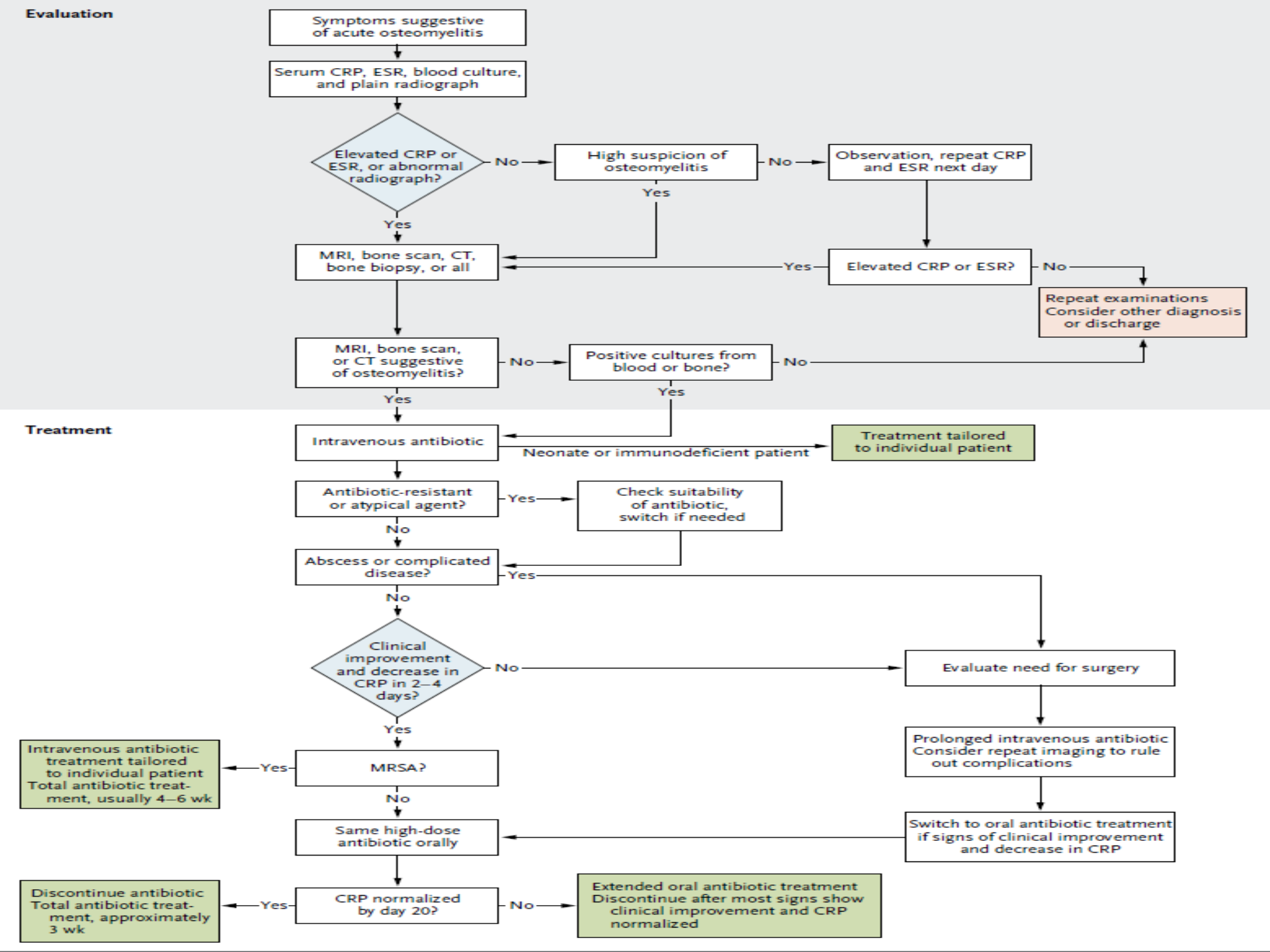
Expert Rev Anti Infect Ther 2010

DURATION OF THERAPY

Depending on

- Organism isolated
- Age
- Clinical course
- Locus of infection

At least **4-6 Weeks** (NEJM 2014)


Evaluation
Symptoms suggestive of acute osteomyelitis
Serum CRP, ESR, blood culture, and plain radiograph
Elevated CRP or ESR, or abnormal radiograph?
No
High suspicion of osteomyelitis
No
Observation, repeat CRP and ESR next day
Yes
Yes
MRI, bone scan, CT, bone biopsy, or all
Yes
Elevated CRP or ESR?
No
Repeat examinations Consider other diagnosis or discharge
MRI, bone scan, or CT suggestive of osteomyelitis?
No
Positive cultures from blood or bone?
No
Yes
Yes
Treatment
Intravenous antibiotic
Neonate or immunodeficient patient
Treatment tailored to individual patient
Antibiotic-resistant or atypical agent?
Yes
Check suitability of antibiotic, switch if needed
No
Abscess or complicated disease?
Yes
No
Clinical improvement and decrease in CRP in 2–4 days?
No
Evaluate need for surgery
Yes
Prolonged intravenous antibiotic Consider repeat imaging to rule out complications
Intravenous antibiotic treatment tailored to individual patient Total antibiotic treatment, usually 4–6 wk
Yes
MRSA?
No
Switch to oral antibiotic treatment if signs of clinical improvement and decrease in CRP
Same high-dose antibiotic orally
Discontinue antibiotic Total antibiotic treatment, approximately 3 wk
Yes
CRP normalized by day 20?
No
Extended oral antibiotic treatment Discontinue after most signs show clinical improvement and CRP normalized

Physical Therapy

Affected extremity kept in extension with **temporary casts**

Follow up

- dynamic state of growth
- range of movements of joints
- bone lenght

Long term follow up!

Spondylodiscitis

1° Hp: Infection of a disc and two adjacent vertebrae
2° Hp: Self-limiting inflammatory condition

•Haematogenous isolated infection intervertebral disc (vascular in child) then involvement adiacent end-plates (60-80%)

•Classically refuse to walk, to sit down or to bend, gait disturbances, back/abdominal pain

•**S. Aureus** (but only 60% positive cultures) J Bone Joint Surg Br 2012
Streptococcus species

•Complication → extension paravertebral soft tissue
epidural space
meninges
spinal cord
→ bone distruction

Classification

- **Neonatal age (<6 months)**

most serious
Multiple infectious foci → septicemia
Vertebrae severely damaged
Neurologic findings
80% S. aureus

- **Infants (6 months - 4 years)**

60% of all spondylodiscitis
Biopsies: sterile or K. Kingae

- **Older child (> 4 years)**

Vertebral osteomyelitis
Febrile, ill-appearing

Swiss Med Wkly 2014

MRN

Gold standard for pyogenic spondylodiscitis
T1 weighted images with contrast → enhancement end-plat/disc interface
T2 weighted fat signal-suppressed → increased signal intensity within involved marrow

Management and outcome

- Spinal imobilization for 10-12 w
- Careful monitoring laboratory/clinic/radiology
- Accurate microbiological diagnosis (blood cultures, aspirates) and appropriate antibiotics
- 6-8 w therapy

J Infection and Public Health 2010