Spondylitis is osteomyelitis of the spinal column. This is defined as infection accompanied by destruction of the vertebral bodies, starting at the endplates, but with secondary involvement of the intervertebral discs. The term "spondylodiscitis" means primary infection of the intervertebral disc by a pathogen, with secondary infection of neighboring vertebral bodies. At diagnosis, inflammatory changes in both the vertebral bodies and intervertebral discs are usually evident in the x-ray, so that the origin of the bacterial infection is no longer clear. For this reason, both terms are used (1–5).

The average period between the first symptoms and diagnosis has been reported to be two to six months (3–10). This delay is because the symptoms are often diffuse. During primary medical care, the patients are frequently thought to be suffering from degenerative diseases of the spinal column. They are then treated correspondingly, even though the prognosis is better with early diagnosis.

The prognosis of spondylodiscitis was unfavorable before antibiotics became available. Even today, it is potentially fatal. Current studies report that the mean time in hospital is from 30 to 57 days and that hospital mortality is from 2% to 17% (3, 7–9, 11, 12).

This review article is based on a selective review of the literature and on our own research.

Path of infection
A distinction is made between endogenous and exogenous paths of infection. Endogenous spondylodiscitis is mostly preceded by infection distant from the vertebral bodies. This infection is then spread by the blood, leading to colonization of one or several vertebral bodies by the pathogen. In principle, dissemination can be through either the arteries or the veins. Inflammation usually spreads in the ventral sections of the spinal column. The primary focus of infection is frequently no longer recognizable when spondylodiscitis is diagnosed in the clinic. Exogenous spondylodiscitis can be caused by operations or by injections near the spinal column. On the other hand, spinal column infections can also arise from the lymphatic system and be continuously spread by this (1, 3).
Spectrum of pathogens

Possible pathogens include bacteria, fungi, or (more rarely) parasites. Most infections are bacterial. Depending on the pathogen, a distinction is made between specific and non-specific spondylitis (1, 5, 6) (box).

The most frequent bacterial pathogen is Staphylococcus aureus, with an incidence of between 30% and 80% (1, 5–10, 12, 14).

Specific spondylitis always occurs by the endogenous path. Skeletal tuberculosis is found in 3% to 5% of HIV-negative tuberculosis patients and in up to 60% of HIV-positive tuberculosis patients (15). Half of all skeletal tuberculosis occurs in the spinal column (15, 16).

**Relative frequency of pathogens causing non-specific spondylodiscitis (Nolla et al. [9])**

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Staphylococci, 39%</strong></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>36%</td>
</tr>
<tr>
<td>Staphylococcus epidermis</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Gram-negative bacteria, 39%</strong></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>23%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>5%</td>
</tr>
<tr>
<td>Eikenella corrodens</td>
<td>3%</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Streptococci, 19%</strong></td>
<td></td>
</tr>
<tr>
<td>Streptococcus sanguis</td>
<td>8%</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>5%</td>
</tr>
</tbody>
</table>

**Epidemiology**

The incidence of non-specific spondylodiscitis is about 1 : 250,000 (1, 3, 5), corresponding to about 3% to 5% of all cases of osteomyelitis (1, 3, 5–7). Men are up to three times more often affected than women (3, 4, 6–9, 11, 12, 14).

Although patients may be in any age group, spondylodiscitis is most frequent in the fifth to seventh decades of life (4, 6, 8, 9, 11–14, 17).

Spondylodiscitis may occur after lumbar operations on intervertebral discs; the frequency depends on the invasiveness of the operation and is given as between 0.1% and 0.6% for microsurgical operations and from 1.4% to 3% for macrosurgical operations (5, 18–20). 10% to 15% of all vertebral infections can be ascribed to exogenous spondylodiscitis (3, 4, 8, 14, 17).

**Predisposition**

Predisposing factors include age, multimorbidity, diabetes mellitus, cardiovascular diseases, obesity, renal failure, chronic hepatitis, rheumatic diseases, chronic steroid intake, cancer, administration of immunosuppressives, preceding systemic diseases, old tuberculosis, prior visceral operations, sickle cell anemia, drug abuse, and HIV (3–9, 14, 17).

**Differential diagnoses**

Differential diagnoses include erosive osteochondrosis, osteoporotic and pathological fracture, cancer-related destruction, ankylosing spondylarthritis, and Scheuermann’s disease.

**Diagnosis**

**Clinical examination**

The clinical examination includes inspection concentrating on local changes and taking a detailed neurological status. There is typically pain on heel strike, impaction, and percussion, but little local pain on pressure. The patient takes a relieving posture and avoids stressing the ventral sections of the spinal column. In particular, inclination and re-erection are described as being painful.

**Laboratory**

The laboratory parameters to be determined are leukocytes, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). In patients with acute disease, there is a massive increase in the inflammation parameters and in the ESR. In patients with chronic disease, these may be normal or exhibit threshold increases. There may be no leukocytosis, but a marked increase in CRP is typical (1, 5).

**Radiology**

**Conventional x-rays** – If a patient suffers from diffuse pain in the spinal column, the first investigation is to take a conventional x-ray, although this procedure is unreliable in the early phase of spondylodiscitis, as there are usually no skeletal changes (1, 6, 14). Even in the

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**Figure 1:** MRI: sagittal and axial cross-sections T1 and contrast medium in a patient with specific spondylitis (atypical mycobacteria: Mycobacterium xenopi) at the level of thoracic vertebral body 10.
later stages, the radiological changes may only be slight and may be impossible or difficult to distinguish from degenerative diseases of the spinal column.

**Magnetic resonance imaging (MRI)** – MRI is the diagnostic procedure of choice if spondylodiscitis is suspected. This provides an image of the whole length of the spinal column, so that infection of other sections can also be detected. This procedure also reliably detects any spread of the inflammation to the paravertebral or spinal space (13, 14, 21, 22) (figure 1).

**Computed tomography (CT)** – Computed tomography is inferior to magnetic resonance imaging with respect to the specificity and sensitivity in the diagnosis of spondylitis (13, 14, 21, 22). On the other hand, computed tomography provides a much more detailed image of bone destruction (14). Moreover, computed tomography can provide good images of paravertebral abscesses after administration of contrast medium (14). Computed tomography is indicated when magnetic resonance imaging is not possible, perhaps because the patient wears a cardiac pacemaker.

**Multiple phase scintigraphy** – With skeletal scintigraphy, it is not possible to distinguish between infections of the bone and activated osteochondroses. This is therefore not the diagnostic method of first choice (23). On the other hand, a normal skeletal scintigram provides very reliable evidence for the absence of osseous inflammation.

**Inflammation scintigraphy with labeled leukocytes or Tc-99m-labeled antibodies** – Leukocyte scintigraphy is a supplement to multiphase scintigraphy, in which radioactively labeled native blood cells or (now preferably) Tc-99m-labeled anti-granulocyte antibodies are used to detect inflammatory changes in bone tissue. However, anti-granulocyte antibodies also label hematopoiesis in the bone marrow, so that the spinal column is subject to physiological enrichment. Inflammation scintigraphy is therefore more suitable for the extremities.

**Positron emission tomography with fluorine-18 fluorodeoxyglucose (F-18 FDG PET)** – F-18 FDG PET is of increasing importance in the diagnosis of spondylodiscitis. There is hardly any physiological enrichment of F-18 FDG in the bone marrow or the spinal column, so that inflammatory processes are imaged as "hot spots." The degree of uptake of F-18 FDG is linked to the enhancement of glucose metabolism in the inflammatory cells. The advantages of F-18 FDG PET include the rapid imaging and the relatively low exposure to radiation (3.7 to 7.4 mSv) (23). In contrast to MRI, it is perfectly possible to distinguish between initial spondylodiscitis and degenerative changes in the vertebral body endplates. On the other hand, specific differentiation from malignant processes may present a problem (23, 24) (figure 2, table).

**Pathogen detection**

Specific antibiotic therapy is one of the keystones of spondylodiscitis treatment and this necessitates specific identification of the decisive pathogen and determination of its sensitivity to antibiotics. Overall, the pathogen can be detected in 49% to 83% of cases – more often in acute than in chronic cases. One of the main reasons for failure to identify the pathogen is prior systemic antibiotic therapy (3, 4, 7, 8, 10). For this reason, it is particularly important only to start antibiotic therapy after the material for the microbiological diagnosis has already been isolated. If antibiotic treatment had already started, the authors have considered its discontinuation for some days up to the puncture of the focus of infection, coupled to close monitoring of the course of the disease.

**Blood culture** – Blood culture is the easiest procedure to detect the pathogen. A positive culture can be expected in as many as 70% of patients not previously treated with antibiotics. The authors recommend that at least two to three pairs of blood cultures should be taken. The pathogen is often successfully detected, not only in the acute phase of fever or with septic disease, but also in clinically bland cases and afebrile patients (9).

**Biopsy** – Other possible ways of detecting the pathogen are to use a percutaneous punch under anesthesia and CT-guided fine needle puncture. The latter can be performed during the same session, to lay a drain to reduce stress on the abscess. A disadvantage of CT-guided puncture is that it gives relatively low quantities of tissue, so that pathogens are only successfully detected in about half of the patients (2, 3, 9).
Intraoperative sampling – Intraoperative removal of tissue samples is the most reliable method of detecting the pathogen, as it gives relatively large quantities of tissue (3–6, e1). The pathogen detection rate is then about 75% (9) (figure 3).

**Treatment**

**Basic principle**

Because of the very inhomogenous group of patients and the differences in treatment, the establishment of standard therapeutic guidelines is only possible to a limited extent (e7). There have not yet been any prospective randomized trials and the level of evidence for treatment recommendations does not exceed level C (e7).

The essential elements for successful treatment leading to cure of spondylodiscitis are the fixation of the affected section of the spinal column, antibiotic therapy, and (depending on the severity of the condition) debridement and decompression of the spinal canal. If at all possible, specific intravenous antibiotic therapy should only be started after the pathogen has been detected and the resistogram prepared. If the patient is extremely ill and treatment is urgently required, blood cultures are taken and therapy is started with the antibiotics appropriate for the commonest pathogens for spondylodiscitis – Staphylococcus aureus and Escherichia coli. There are no published standard guidelines for the duration of the antibiotic therapy. It is generally recommended to administer the antibiotics for at least two to four weeks and parenterally as the bioavailability is usually better then.

The individual patient can be switched earlier to oral administration, if his or her general condition has improved and the clinical chemical inflammation parameters have normalized or greatly improved. Oral antibiotic therapy is possible if the active substance has high oral bioavailability, as is the case with the fluoroquinolones, clindamycin, and linezolid. Linezolid is particularly indicated for the treatment of MRSA infections, although treatment over several weeks may cause problems, because of the risk of hematological side effects (9, e2).

Oral antibiotic therapy for a period of six weeks to three months is recommended for non-specific spondylodiscitis (1, 5, 6, 8, 11, e2, e3).

The duration of treatment should be extended for patients at risk. The authors perform antibiotic therapy for up to six weeks after normalization of the inflammation parameters.

If there is a strong suspicion of tubercular spondylodiscitis, tuberculostatic therapy can be initiated. However, the course of the disease in these cases is mostly not particularly fulminant, so that one can wait for the result of the pathogen diagnosis. To assure care and prevent recurrences, the antitubercular chemotherapy should last for 18 to 24 months, although there are no unambiguous prospective scientific data on the matter.

If there is a fungal infection, appropriate antymycotic treatment must be started (e4). In general, it is difficult to detect fungi as pathogens of spondylodiscitis and antymycotic therapy presents problems. Ooij et al. therefore recommend early surgery (e5).

Treatment must also obviously include effective analgesia, as some patients suffer severe pain.

**Conservative treatment**

Conservative treatment can be considered if the clinical symptoms and destruction are relatively mild or the risk of operation appears to be too great (4, 7). As the patients with this disease are mostly older and in poorer general condition, the option of a conservative procedure is often worth considering. The main problem in conservative treatment is to achieve adequate fixation of the affected section of the spinal column. Reclining orthoses distribute the stress over the unaffected spinal column joints, thus decreasing stress in the infected ventral area (5). The patient can be fully

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**TABLE**

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Native x-Ray</th>
<th>Scintigraphy</th>
<th>Inflammation Scintigraphy</th>
<th>F-18 FDG PET</th>
<th>Magnetic Resonance Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>82</td>
<td>90</td>
<td>–</td>
<td>100</td>
<td>96–100</td>
</tr>
<tr>
<td>Specificity</td>
<td>57</td>
<td>78</td>
<td>31–76</td>
<td>–</td>
<td>92</td>
</tr>
</tbody>
</table>

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**Algorithm for the intraoperative removal of tissue samples**

[Diagram showing the steps: Blood cultures, CT-guided puncture, Intraoperative removal of tissue samples, Wide punch under anesthesia, Culture, PCR, No pathogen detected after 2–3 days, No Op, Op planned.]
mobilized in the orthosis. If however there are major defects in the ventral column or the lower lumbar column or the lumbosacral border is affected, the necessary fixation can only be achieved by at least six weeks' bed rest (1, 5). The mobilization of the patient is only recommended once osseous infiltration becomes visible. Aside from the risk of immobilization, there is a high rate of pseudoarthroses (16% to 50%), which may eventually lead to kyphotic malposition and chronic pain syndrome (1–5). If there is no fusion reaction, continuing destruction, or no clinical improvement, it is not promising to continue conservative treatment beyond four to six weeks (4, 5, 7). Although protracted bed rest used to be prescribed, this practice is now being abandoned.

Surgery
Indications for emergency surgery in spondylodiscitis include losses in neurological function and sepsis, instability, threatened or current deformities, intraspinal space-occupying lesions, unclear etiology with possible malignant processes, and failure of conservative therapy. Relative OP indications are uncontrollable pain and the patient’s lack of compliance with conservative treatment (1, 3, 5, 6, 11).

The objectives of the operation are to remove the septic focus, simultaneously to detect the pathogen and to stabilize the infected section of the spinal column, followed by formation of fused vertebrae. This provides a more reliable and more rapid treatment of the consequences of the infection. Rapid postoperative mobilization is also possible (2, 4, e1).

The established standard procedure involves debridement and span interposition, followed by instrumented stabilization. This has the advantages of more rapid postoperative mobilization and lower rates of pseudoarthroses and kyphotic malposition (3–5).

The implantation of osteosynthesis material in an infected wound area can lead to microbial colonization of the metal surface and persistent infection. This risk is reduced by thorough debridement, with simultaneous application of an antibiotic carrier (1). Titanium implants are now mostly used and these are apparently not associated with an increased rate of recurrence (10, e6).

The recommendations for the operative strategy are still a highly controversial issue (1, 3–8, 10, 11). The operation for spondylodiscitis can be monolateral or bilateral. The monolateral operation has the advantage that the patient can recover from the first operation. The second operation then takes place one or two weeks later, depending on how well the patient has recovered.

There is also a variety of recommendations for osteosynthetic stabilization. There are recommendations for purely ventral, purely dorsal, or combined dorsoventral (or ventrodorsal) stabilization (1–7, 10, 11) (figures 4, 5).

Prognosis
There are frequently residual symptoms after either conservative or operative treatment of spondylodiscitis.

Figure 4: Cervical non-specific spondylodiscitis in cervical vertebral bodies 3/4 and postoperative native radiological follow-up with properly positioned bone span and plate.

Figure 5: Three month postoperative native radiological follow-up after bilateral dorsoventral spondylodesis of thoracic vertebral bodies 2 and 3.

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185
These are due to destruction and secondary degeneration of the neighboring segments after the inflammation has subsided. Using the questionnaire Short Form 36 (SF-36), Woertgen et al. performed a non-randomized, retrospective study of the neurological results and the health-related quality of life on 62 patients with spondylitis 16.4 months after either conservative treatment (45%) or surgery (55%). The authors showed that motor deficits persisted in 30% of patients with preoperative neurological deficits, and hypesthesia in 90%. They also reported that the quality of life was much lower than for the normal population. The patients who had been operated exhibited a somewhat better quality of life and significantly better patient satisfaction (12). Lerner et al. found that the neurological situation was improved in 76% of 25 spondylodiscitis patients with neurological deficits after 2.6 years, although there was no change in 20%. Ability to walk could be restored in 75% of patients with acute cross-section (10). Similar results have been reported in other publications (3, 17).

The rate of recurrence has been reported as lying between 0% and 7% (2–4, 10, 11, 17). At a follow-up after a mean of 5.4 years, Frangen et al. found five patients in a group of 69 who were suffering from recurrent spondylodiscitis (3) (figure 6).

Figure 6: CT in recurrent spondylodiscitis one year after dorsoventral fusion

Conflict of interest statement
Professor Seifert has received lecture honoraria and travel funds from Pfizer. The other authors declare that there is no conflict of interest in the sense of the guidelines of the International Committee of Medical Journal Editors.

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   GK: 1.FDG Positron Emission Tomography for differentiation of
degenerative and infectious endplate abnormalities in the lumbar

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REVIEW ARTICLE

Current Diagnosis and Treatment of Spondylodiscitis

Rolf Sobottke, Harald Seifert, Gerd Fätkenheuer, Matthias Schmidt, Axel Goßmann, Peer Eysel

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