INFECTIOUS LESIONS OF THE SPINE: DRAFT NATIONAL CLINICAL GUIDELINES*

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A draft national clinical guidelines for spinal infectious lesions are submitted for discussion. Clinical guidelines are intended to optimize the diagnosis and treatment of infectious spondylitis and based on modern information about the pathology under consideration. The authors invite interested professionals to the discussion.

Key Words: spondylitis, infectious spondylitis, granulomatous osteomyelitis, nonspecific osteomyelitis of the spine, tuberculosis, diagnosis, differential diagnosis, treatment.

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Motivation

The purpose of these clinical guidelines is to improve the quality of diagnosis and treatment for infectious spondylitis and unify multidisciplinary approaches to this pathology.

The clinical guidelines have been developed based on previously published guidelines [1, 2], draft guidelines [3], and educational materials [4] with allowance for modern approaches to the problem of spinal infection.The guidelines have not included the issues of treatment of spinal and spinal cord infection, which were previously presented in detail [1], and data on the management of infectious spondylitis, which have been actively discussed but not been unambiguously resolved yet [5].

The guidelines comply with the requirements of the Association of Medical Societies for Quality in Medical Care and Medical Education (ASMOK, Appendix) [6].

Terms and definitions

Description of infectious processes in the spine is based on anatomical terminology (Table 1).

Infectious complications developed after surgery (manipulations) in the spine are described by the term "surgical site infection in spinal surgery (SSIs)".

1. Brief information

1.1. Definition

Spinal infection is an inflammatory destructive disease of the spine and its structural components (vertebral bodies, intervertebral discs, ligaments, intervertebral joints) caused by any bacterial agent.

1.2. Etiology and pathogenesis

Infectious and non-infectious (aseptic) spondylitis are distinguished (Fig.).

The infectious process in spondylitis can be associated with hematogenous (septic) or contact spread and be postmanipulative (iatrogenic), i.e. associated with previous surgical or anesthetic manipulations on the spine. A source of infection can be any infection process: carious teeth, ENT infection, phlegmon and endocarditis, including penetrating injuries, in particular iatrogenic ones [8–13].

The causative agent of nonspecific spondylitis is detected in blood cultures of 20–40 % of patients (recommendation strength: C; level of evidence: 2+) [14–19]:

– gram-positive (gram+) cocci occur in 2/3rd of cases, with predominance of *Staphylococcus* including more than 20 species; the most pathogenic are coagulase-positive strains of *S. aureus* and *S. intermedius* and a coagulase-negative strain of *S. epidermidis*;

– gram-negative (gram-) isolates occur in 1/3rd of cases, with predominance of *Escherichia coli* (10.5 %), *Proteus spp.* (6.7 %),and *Pseudomonas aeruginosa* (5.7 %).

The most common (90.0 %) cause of granulomatous spondylitis is *M. tuberculosis complex*. In third world countries, brucellosis is relatively common. Parasitic (more often echinococcal) and mycotic lesions are less common; rare pathogens include salmonella, campylobacter, non-tuberculous mycobacteria, bacteroids, etc. The role of mycotic (more often aspergillosis) infection increases significantly in the setting of immunodeficiencies, primarily HIV infection: mycoses are considered as their markers (2+, C) [20–24].

1.3. Epidemiology

The rate of infectious spondylitis is 1.0–2.5 cases per 100,000 population and accounts for 4–8 % of purulent-inflammatory diseases of the skeleton. Septic complications develop in 5.8 to 14.6 % of cases; the rate of death is 1.2–8.0 % [4, 8, 17, 20].

**The project was previously sent to leading spinal surgeons; the authors include those who have provided their recommendations. The publication is presented for wider discussion before approval by professional societies.*

Table 1
Clinical terminology used in inflammatory diseases of the spine [7, with additions]

Anatomical localization	Affected area (involved structures)	Terms
Anterior spinal column	Vertebral body	Osteomyelitis of vertebra Spondylodiscitis Spondylitis
	Intervertebral disc	Discitis
	Paravertebral space	Paravertebralabscess Retropharyngeal abscess Mediastinitis Mediastinal abscess Empyema, pericarditis Subphrenic abscess Peritonitis Psoas abscess
Posterior spinal column	Subcutaneous space	Superficial infection Infected seroma
	Subfascial space	Deep infection Paraspinal abscess
	Posterior structures	Osteomyelitis Facet joint arthritis Deep wound infection
Spinal canal	Epidural space	Epiduritis Epidural abscess
	Pia mater	Meningitis
	Arachnoid membrane	Arachnoiditis
	Subdural space	Subdural abscess
	Spinal cord	Intramedullaryabscess Myelitis

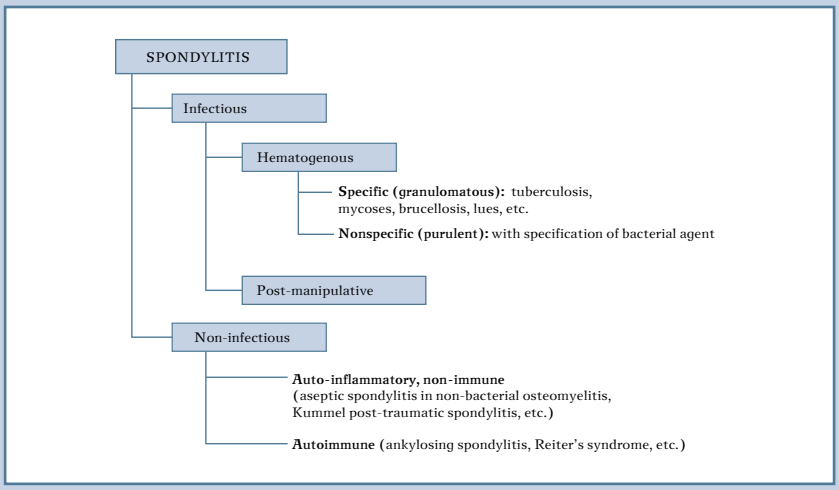

Fig.
Etiological classification of spondylitis

1.4. ICD-10 code

In accordance with ICD-10, infectious lesions of the spine are categorized based on the syndromic and/or etiological principle (Table 2). A combination of spondylitis with inflammatory diseases of the central nervous system (myelitis, meningitis, epidural abscesses) is classified in sections G00–G09. An additional codes B95–B98 are used for verification of the infectious agent.

1.5. Classification

Principles of the spondylitis classification

The main classification features that determine the approach for treating the spondylitis patient include etiopathogenesis (I), the type of organ and tissue inflammatory response (II), the anatomical localization of the lesion (III), the area of destruction (IV), activity of the disease (V), and the presence of complications (VI) [25, 26]:

I. Etiopathogenesis. Infectious and non-infectious (aseptic) spondylitis are distinguished (Fig.). The infectious process can be associated with hematogenous (septic) or contact spread and be post-manipulative (iatrogenic), i.e. associated with previous surgical or anesthetic manipulations in the spine.

II. Type of inflammatory response. Inflammatory lesions can occur in the form of edema and focal or diffuse destruction, and the tissue response pattern can be alternative necrotic, exudative, or proliferative (productive). Different inflammation types can occur in any infectious spondylitis; however, nonspecific bacterial spondylitis is characterized by infiltrative and diffuse destruction, while specific spondylitis is associated with focal and extensive destruction with exudative-necrotic lesions.

III. Localization of the lesion. Spondylitis is localized in the lumbar spine in about 50% of cases, in thoracolumbar spine in 25 % of cases, in thoracic spine in 20 % of cases, and in cervical spine in 5 % of cases [8]. The vertebrae of different spine departments are simultaneously affected in 10 % of cases.

General terminology is used to designate infectious complications developing after surgery/manipulations (SSI) (Table 1).

IV. The spread of spondylitis determines the number of affected vertebrae or spinal motion segments (SMS; Table 3).

V. Activity of the disease is assessed based on the disease duration according to clinical and laboratory criteria. Traditionally, the process is considered acute if the disease duration is less than 2 months (60 days) and subacute if the disease duration is 2 to 6 months; nonspecific disease is considered chronic if its duration is more than 6 months, and specific disease is considered chronic if its duration is more than 1 year. However, given the modern interpretation of the term "chronic osteomyelitis" (including spondylitis), this diagnosis can be established not only on the basis of the disease duration but also upon detection of any of two criteria that do not directly correlate with the disease duration: morphological – mainly necrotic inflammation or clinical – the development of sequesters or fistulas.

To estimate the time of SSI development, the following terms and criteria are used (Table 4) [26].

VI. Complications of infectious spondylitis are presented in Table 5.

1.6. Examples of diagnosis

• Spondylodiscitis of T4–T5, chronic. Complications: chronic pain.

• Nonspecific osteomyelitis of T8–T9, active. Complications: paravertebral and epidural abscesses. Lower paraplegia (Frankel grade A), dysfunction of the pelvic organs.

• Tuberculous spondylitis of L4–S1. Complications: paravertebral, presacral, epidural, and bilateral psoas abscesses. Spinal instability. Bilateral L5 radiculopathy. Dysfunction of the pelvic organs (hyperreflexic bladder).

• B20 grade 4B on antiretroviral therapy (ART). Generalized tuberculosis: disseminated pulmonary tuberculosis (Mycobacterium tuberculosis: MTB). Extensive drug resistance (EDR). Tuberculous spondylitis of T3–T5, T7–T12, and L2–L5. Complications: intrathoracic and bilateral psoas abscesses. Lower paraparesis (Frankel grade C). Spinal instability with pain.

• Nonspecific osteomyelitis of T4–T5. Complications: epidural abscess. Surgery: laminectomy, abscess drainage. Postoperative complications: postlaminectomy kyphosis, superficial SSIs.

• Echinococcal spondylitis of T12–L2, chronic. Complications: epidural echinococcal cysts, lower paraparesis (Frankel grade D).

Table 2
ICD-10 chaptersappropriate for classification of infectious spondylitis

ICD section	Disease code
M45 Spondylopathies	–
M46 Other inflammatory spondylopathies	M46.0 Spinal enthesopathy M46.1 Sacroilitisnot elsewhere classified M46.2 Osteomyelitis of vertebra M46.3 Infection of intervertebral disc (pyogenic) M46.4 Discitis, unspecified M46.5 Other infective spondylopathies M46.8 Other specified inflammatory spondylopathies M46.9 Unspecified inflammatory spondylopathy
M48 Spinal osteomyelitis	–
M49 Spondylopathies in diseases classified elsewhere	M49.0 Spine tuberculosis A18.0 M49.1* Brucellosis spondylitis A23 M49.2* Enterobacterial spondylitis A01—A04 M49.3* Spondylopathies in other infectious and parasitic diseases classified elsewhere
M86	M86 Osteomyelitis

Table 3
Classification of spinal infectiondepending on its spread

Vertebral lesion	Characterization of lesion
Monovertebral	Single affected vertebra
Monosegmental	Single affected spinal motion segment
Polysegmental	Two or more affected adjacent spinal motion segments
Multilevel	Affected vertebrae separated by intact segments

2. Diagnosis of infectious spondylitis

2.1. Complaints and medical history

When collecting medical history and complaints, attention is paid to the following facts:

– body temperature rise;

– back pain poorly controlled by analgesics;

– previous infectious diseases, surgery, manipulations, contacts with infectious patients, etc. in medical history;

– concomitant diseases including those with primary or secondary immunodeficiency conditions (diabetes mellitus, viral hepatitis, HIV infection, etc.);

– neurological (motor and/or sensory) disorders and/or dysfunctions of the pelvic organs.

2.2. Examination

Clinical examination includes height, body weight, and body temperature measurements, assessment of the osteoarticular system condition, and detection of spinal deformity and instability. Pain is assessed using VAS; the neurological status is evaluated using

ASIA scales; dysfunction of the pelvic organs is identified.

2.3. Laboratory diagnostics (recommendation strength: 1; level of evidence: B, C)

Chemistry panel and complete blood count. Assessment of the C-reactive protein (CRP) and a procalcitonin test (PCT).

Commentary. The hemogram and chemistry panel parameters are not specific, but reflect activity of the inflammatory process. In acute nonspecific spondylitis, an increased number of leukocytes is detected in 50 % of cases (C), but it may remain within normal limits in the case of subclinical or chronic infection. ESR and CRP increase in more than 90 % of patients with acute spondylitis (recommendation strength: C) [2, 7, 9].

PCT is one of the most sensitive markers for septic complications of bacterial infection (recommendations). An elevated PCT level (>2 ng/mL), in particular in spondylitis, is considered as sepsis (recommendations, B) [27]. Pathogen verification based on bacteriological tests is recommended.

Commentary. The following is optimal:

– a bacteriological blood test to detect bacteremia, which is performed before antibiotic therapy at the temperature elevation maximum (standard); however, if the virulence of bacteria is low, the result may be negative in 75 % of patients. The hemoculture test is especially important for patients in septic or critical condition (C) [28];

– in patients with negative blood culture tests and suspicion for spinal infection in the presence of visual and available substrate of the disease (abscess, infiltration zone, altered vertebral region, fistula, etc.), a biopsy is recommended for the bacteriological and morphological tests of substrate [29]. Due to a low detection level of pathogenic isolates on antibiotic therapy during exacerbation or a chronic process, a biopsy is carried out 1 to 2 weeks after stopping antibiotics.

Verification of Mycobacterium tuberculosis [30]. Standard tests for M. tuberculosis include Ziehl-Neelsen stain microscopy, liquid culture (Bactec MGIT), molecular genetic typing methods (PCR, Geen-expert, tests for drug resistance genes; standard, recommendation strength: A), as well as luminescent microscopy with Auramine O staining. Cultural studies of diagnostic (surgical, biopsy) material are mainly performed on liquid nutrient media with automatic growth detection [17, 20, 28] because of a prolonged duration of culture on solid media (Lowenstein–Jensen, Finn) (recommendation). The level of MTB culture verification is 30–44 %, and DNA isolation and nucleotide sequence amplification increase it to 89.7 %.

A morphological (cytological and histological) examination of the biopsy specimen is recommended.

Commentary. Collection of contents from the destruction site or purulent cavities, destroyed vertebral bodies, and abscesses. The informative value of closed puncture (aspiration of liquid pus if presents) or trepanation biopsy reaches 41–90 % (B) [28, 29, 31]. An open biopsy, usually during debridement surgery, is indicated in the case of non-informative puncture biopsy, a lesion inaccessible for puncture, destruction with compression of nerve structures, and a clinical picture of myelopathy. The material is examined by cultural and molecular genetic methods (standard), in particular for aerobic and anaerobic bacteria.

NB! Even one course of antibacterial (so-called "empirical") therapy reduces the likelihood of bacteriological confirmation by more than half.

Table 4
Onset of surgical site infection (SSI) in spinal surgery

SSI grade	Period after surgery
Early	Up to 3 weeks
Delayed	3 weeks to 3 months
Late	Over 90 Days

Table 5
Complications of spinal infection [5, 23, 25]

Nature of complications	Type of complication	Characterization, valid assessment methods
Infectious	Systemic	Sepsis: clinical and laboratory manifestations
	Local: abscesses, fistulas, bedsores	Clinical, radiographic imaging
Neurological	Motor: paresis, paralysis, dysfunction of pelvic organs	Frankel scale, motor component of the ASIA standard, electroneuromyography
	Pain, sensory disorders	Pain syndrome: visual analogue or integral scale, sensory component of the ASIA scale
Orthopedic	Deformities, instability, contractures	Angulometry, roentgenometry
Social exclusion	Depression, functional dependence on others	Assessment of quality of life on Oswestry, FIM, Barthel, Tsung, and SF-36 scales

NB!! The morphological conclusion, which corresponds to an inflammatory process, does not confirm infection, except some specific signs: granuloma with epithelioid and multinuclear giant Pirogov-Langhans cells and central necrosis is considered specific for tuberculosis (level of evidence: 2+; recommendation strength: C).

The informative value of immunohistochemical methods for the diagnosis of tuberculosis has not been proven. In immunodeficiencies, typical specific granulomas may be absent due to impaired phagocytosis.

Immunological blood serum tests are not specific and used only to assess activity of the inflammatory process and infectious disease (option), but not to verify the etiology of spondylitis. Tuberculin skin tests (TSTs) and ESAT6/CFP10-induced tests (quantiferon test, T-SPOT-TB, recombinant tuberculosis allergen (RTA) test) are not valid for verification of the etiology of vertebral lesions (standard) [30].

2.4. Instrumental diagnostics (recommendation strength: 1; level of evidence: C)

Radiographic imaging. There is a clear hierarchy of methods for imaging of spondylitis:

– X-ray (plain, in two projections) is used for approximate assessment of vertebral destruction, spinal deformities, and body balance. X-ray tomography, contrast-enhanced tomography, and fistulography are used only if CT and MRI can not be conducted (claustrophobia, metal implants, pacemakers, etc.);

– CT is the main method for imaging of the spinal bone structures. CT myelography is used for visualization of the spinal canal if MRI can not be conducted;

– MRI is the method of choice for imaging the spinal canal, spinal cord, paravertebral tissues, as well as inflammatory processes in the spine at an early pre-radiographic stage [32, 33];

– ultrasonography is a method for investigatory imaging of paravertebral abscesses; bone scintigraphy and positron emission tomography (PET CT) are methods for identifying inflammatory foci (primary and metastatic) andactivity of their metabolism.

Commentary. At the early stage (2nd–3rd day) of nonspecific spondylitis, the disease can be detected only by MRI. Changes in MRI scans are detected in 55 % of cases at disease duration of less than two weeks and in 76 % of cases at a longer duration. In the case of acute spondylitis, a T1-weighted MRI image reveals a decreased intensity of the signal from the affected vertebral bodies and intervertebral disc; in the T2 mode, the signal is enhanced. After administration of gadolinium-containing agents, the T1 signal intensity around fluid accumulation areas increases; an enhanced signal around low-density areas indicates abscess formation. Gadolinium is used to differentiate the inflammatory process from degenerative changes in the endplate and intervertebral disc. Signs of epidural and paraspinal abscesses are detected in the form of isodense (in T1 mode) and hyperdense (in T2 and STIR modes) spindle-shaped areas. At the later stages, changes in MRI scans may not coincide with clinical data [33].

The first radiographic and CT signs of spondylitis are detected as destruction foci with uneven and fuzzy contours no earlier than at the 2nd week of the disease (C). Progression of the disease can lead to the formation of irregular-shaped sequesters, detachment of the periosteum and anterior longitudinal ligament, and the development of periosteal and spondylous growths. Later, an osteosclerosis area develops around the lesion.

NB! A CT-based increase in the bone destruction area 4–6 weeks after disease onset upon relief of subjective complaints and normalization of laboratory parameters during treatment should not be considered as disease progression because of a time lag between imaging findings and morphological recovery processes.

Upon bone scintigraphy in nonspecific spondylitis, reliable uptake of a radioactive tracer (RAT), more than 30 %, is detected in 2/3rd of cases (C); an increase in the uptake ratio over time may indicate progression of the disease.

The diagnostic significance of different methods for diagnosis of nonspecific spondylitis is presented in Table 6.

2.5. Other diagnostics

Patients with infectious spondylitis are advised, if indicated, to consult the following specialists (recommendation strength: 1; level of evidence: C):

– neurologist (commentary: all patients for identifying disease type and complications);

– urologist (commentary: in the case of dysfunction of the pelvic organs, renal failure, and acute and chronic urinary tract infection);

– clinical pharmacologist (commentary: in the presence of antibiotic-resistant microflora, prescription of more than five drugs, and signs of sepsis).

2.6. Differential diagnosis

The diagnosis of infectious spondylitis is established on the basis of a body of clinical data and their changes during therapy as well as findings of laboratory, biochemical, and molecular genetic tests and radiography. However, the diagnosis of spondylitis is considered reliably established if the case of morphological confirmation and reliably proven only in the case of bacteriological confirmation.

The list of major diseases requiring differentiation from infectious spondylitis is presented in Table 7.

3. Treatment

Treatment of infectious spinal lesions includes conservative therapy, surgery, and symptomatic treatment [1, 2, 4, 5, 7–10, 28, 34].

3.1. Conservative treatment

Comprehensive conservative treatment includes antibacterial treatment, anti-inflammatory and immunocorrective therapy, infusion therapy (if indicated), administration of general strengthening agents, and orthosis (recommendations). Timely (early) conservative treatment stops the disease in 56–75 % of patients with acute spondylitis [5, 28, 35].

Commentary. Conservative treatment options as the main and only ones can be used in the following situations:

– in partial destruction of the vertebrae in the absence of clinical signs of the disease (accidental radiographic finding) or the risk of disease complications;

– in acute processes in the absence of clinical signs of spinal cord compression and abscesses;

– in progressive and chronic spondylitis in the case of severe concomitant somatic diseases when the risk of life-threatening complications of surgery exceeds the expected efficacy (option).

3.1.1. Principles of rational antibiotic therapy of spondylitis and monitoring of its efficacy

1. Antimicrobial agents should be used since the time of infectious spondylitis diagnosis (1C).

2. The basis for antibacterial drugs is the identification of pathogen and its drug sensitivity/resistance. Rational antibacterial therapy is based on the examination of puncture and surgical biopsy specimens and/or blood culture (standard: see Section 1.3).

3. Upon assessing the staphylococcus population, the rate of detection of resistant strains (including MRSA, PRSA, VRSA, MRSE) accounts for 10.0–25.0 % of the total amount of gram-positive flora. Initial therapy of resistant *Staph. spp* strains can include vancomycin, cubicin, levofloxacin (tavanic), etc., for up to 6–8 weeks [28, 35–37] (recommendations). In severe sepsis with development of hospital infection or in critical condition of the patient, a case conference, with participation of a clinical pharmacologist, is held. Given the side effects of antibiotic therapy, protected penicillins (sulbactam, piperacillin-tazobactam), carbapenems (imipenem, meropenem, ertapenem, doripenem), or fluoroquinolones (levofloxacin, moxifloxacin) are used [38–40].

4. Indications for empirical antibiotic therapy should be limited to the impossibility to conduct the above measures, their negative effects, or severity of the patient's condition requiring initiation of antibiotic therapy before receiving the results of bacteriological tests.

5. Correction of antimicrobial therapy should be performed with allowance for its efficacy and potential changes in the sensitivity of microflora (1B).

Table 6

Specificity and sensitivity of various methods to diagnose infectious spondylitis [8]

Method	Specificity, %	Sensitivity, %
Spine X-ray	64.0	62.0
Bone scintigraphy with Te99	62.5	86.0
MRI	81.0	95.0
CT	68.0	73.0
Densitometry	23.0	31.0
Histological examination (bone biopsy)	99.0	95.0
Microbiological examination (surgical material)	90.0	83.6

6. The total duration of antibiotic therapy for acute nonspecific osteomyelitis is 6–8 weeks [37].

7. Antibacterial therapy of tuberculous spondylitis is regulated by standard chemotherapy regimens based on the WHO standards and approved by national clinical guidelines (standard) [30].

8. Switch of antibiotics is performed with allowance for the efficacy of treatment and the risk of adverse events due to prolonged use of drugs.

Monitoring of chemotherapy efficacy. The criteria of effective antibiotic therapy for nonspecific spondylitis include a decrease in the body temperature, a reduction in the severity of pain (usually, on the 2nd–3rd day), and a decrease in CRP and ESR (standard). A rapid decrease in CRP (more than 50 % of the baseline value) indicates the adequacy of antibiotic therapy (C) and allows switching from intravenous to oral antibiotics after 3–4 weeks.

Commentary. For a septic condition, it is considered effective to decrease the procalcitonin level by more than 80 % of the peak value or achieve a level of <0.5 ng/mL [38]. A decrease in the level of procalcitonin or similar biomarkers to the normal value is a criterion for termination of empirical antimicrobial therapy in the case of unconfirmed bacterial infection (2, C).

Monitoring of tuberculosis chemotherapy (TCT). Chemotherapy for tuberculous spondylitis is conducted in accordance with the National Clinical Guidelines based on the WHO guidelines and standards [Order of the Ministry of Health of the Russian Federation No. 951 of 2014; Clinical Guidelines for Tuberculosis Chemotherapy] (recommendations, B) [30].

Commentary. TCT begins with diagnosis of tuberculosis. The duration of TCT in the preoperative period depends on the period necessary to organize transfer of the patient to a specialized department for patients with osteoarticular tuberculosis. In the postoperative period, TCT is continued in the TB dispensary. The duration of the main TCT course in tuberculous spondylitis depends on drug sensitivity of the pathogen and is at least 12 months for sensitive and mono-resistant mycobacteria and at least 18 months for multi-resistant forms.

3.1.2. Features of therapy for HIV-infected patients

The combination of infectious spondylitis and HIV infection is considered as confounding co-infection [41, 42]. Tuberculous spondylitis in HIV-positive patients is characterized by rapid progression, prevalence of extensive and multilevel lesions, and a high rate of generalized forms of tuberculosis. The detection rate of drug-resistant mycobacterium strains in HIV patients is 1.5-fold higher than in immune non-compromised patients. Antiretroviral therapy (ART) is conducted

in accordance with national protocols that usually allow for the CD4 count of lymphocytes (recommendation, B). The WHO guidelines (2010) indicate the need for ART in all HIV-infected patients with a CD4 count of less than 350 cells/μL [42].

Supportive therapy for spondylitis includes infusion-transfusion therapy, correction of hemocoagulation disorders, extracorporeal detoxification, and immunosubstitution (recommendation).

3.2. Orthotics (recommendation strength: 1; level of evidence: C)

External immobilization with a removable orthosis is mandatory in the treatment of infectious spondylitis accompanied by spinal instability and pain. In the absence of spinal deformity, removable modular orthoses can be used; in the presence of deformity, orthoses are prepared individually for the patient.

3.3. Principles of surgical treatment (recommendation strength: 2; level of evidence: C)

The basic principle of surgical treatment for infectious spondylitis is syndromic-nosological [1, 2, 4, 5, 8–10, 43–56], and its purposes are to stop the inflammatory process and to restore stability and supportability of the spine (standard).

3.3.1. Indications and contraindications for surgical treatment

Indications for surgical treatment of infectious spondylitis are as follows (standard):

– disease progression during antibiotic therapy;

– development/progression or persistence of neurological disorders with verified spinal cord compression by an epidural abscess, sequesters, etc.;

– chronic spondylitis accompanied by clinical complaints (back pain, fistula, fever, laboratory activity and/or development of spinal instability, and deformity). Contraindications for surgery:

– absolute: extremely severe patient's somatic condition that threatens his/her life;

– relative: sub-compensated indicators of somatic status – septic condition, except purulent leakages and abscesses requiring urgent surgery; severe concomitant diseases and somatic conditions when surgery is associated with a high risk of death (ASA grade IV, APACHE >16 points).

3.3.2. Surgical stages in infectious spondylitis

Debridement of the lesion is performed as an independent procedure or as a stage of reconstructive surgery. It can be performed openly, minimally invasively, endoscopically [47, 48].

Restoration of spinal stability is achieved by following methods (2+, C) [44, 45, 49, 53–55]:

a) reconstruction of the anterior spinal column using autografts (iliac wing crest, ribs, tibia), allografts, or non-biological implants. In the case of radical debridement of the lesion(s), the optimal results are ensured by a combination of supporting non-biological implants (titanium meshes, carbon grafts) and bone grafts;

b) posterior instrumented fixation;

c) combination of methods.

In most cases, correction of spinal deformity [24, 56] is provided by stable posterior spinal instrumentation. The variants of posterior metal implant arrangement (hook, transpedicular, hybrid) are optional.Transpedicular screws are not used at the level of destroyed vertebrae (recommendation).

Commentary. Laminectomy as an independent operation is performed only as the urgent treatment for acute (less than 48 h) neurological disorders and spinal cord compression confirmed by radiographic methods. If spondylitis with spinal instability is suspected, laminectomy should be followed by stabilization (instrumented fixation), otherwise this may lead to deformity progression (postlaminectomy kyphosis).

Principles of surgical treatment for SSIs associated with application of metal implants [26, 57]. The development of early SSIs requires active debridement/drainage of the surgical site; in this case, stable implants can be spared. In the case of unstable fixation, implants must be removed, and re-stabilization can be performed after stopping inflammation.

In the case of late SSIs, debridement/drainage of the surgical site should be accompanied by removal of implants. Repeated instrumentation can be performed after stopping the inflammatory process.

During debridement in delayed SSIs, the decision to remove stable implants is made individually, depending on the severity of inflammation and the response to complex conservative treatment – antibacterial therapy and active drainage, including VAC-therapy.

NB! The loss of stable instrumented fixation of the spine (peri-instrumental resorption), not accompanied by clinical signs of an infectious process or accompanied by it's minor manifestations, requires examination of the removed implants for low-grade pathogenic isolates, including their ultrasound treatment (sonication) to destroy the biofilms (recommendation).

Table 7

Diseases to be differentiated from infectious spondylitis

Disease	ICD code
Rheumatoid and seronegative spondyloarthritis	M05–M14, M45–M49
Systemic lesions of connective tissue	M30–M36
Degenerative and dystrophic diseases of the spine	M42, M46
Congenital malformations of the skeleton	M41, M43, Q46
Benign neoplasms of vertebral column	D16.6
Malignant neoplasms	C40–C41
Tumor metastases	C76, C80
Osteitis deformans (Paget's disease)	M88

4. Rehabilitation

Rehabilitation treatment is started in a surgical hospital and continued in specialized rehabilitation centers (outpatient and inpatient).

5. Prevention and follow-up care

The main methods for monitoring disease dynamics are clinical examination and control radiographic examinations, such as radiographs, CT of the spine, and MRI in the case of neurological disorders. The criterion of effective treatment of nonspecific infectious spondylitis is stopping of clinical and laboratory manifestations of the disease. Radiographic manifestations of bone repair upon conservative treatment (bone restoration, staple formation, osteosclerosis, blocking of vertebrae) are detected within 4–6 months from the start of treatment.

Patients after nonspecific spondylitis are examined by the orthopedic traumatologist and neuropathologist once every 2 months during the first 6 months. In the absence of clinical, radiographic, and laboratory signs of exacerbation or complications, recovery is concluded. In the presence of complications, the patient continues follow-up/treatment by particular specialists:

– by the surgeon, orthopedic traumatologist, and neurosurgeon in the case of fistulas, instability and deformity of the spine; if these complications can be eliminated, surgical treatment is performed in specialized departments/centers for spinal surgery after informing the patient about the appropriate surgical risks and receiving his consent;

– by the neuropathologist, urologist, and rehabilitation therapist in the case of manifestations of post-spondylotic myelopathy/radiculopathy;

– by the surgeon, plastic surgeon, neuropathologist, and social workers in the case of irreversible neurological and neurotrophic disorders.

Spinal tuberculosis patients are followed-up at the TB dispensary (active process – dispensary group 1; chronic course – dispensary group 2; consequences and residual effects – dispensary group 3) and examined by the orthopedist once every 3 months within the first year after surgery.

6. Additional information affecting the course and outcome of the disease Outcomes and prognosis

The prognosis for nonspecific spondylitis depends on the severity of clinical manifestations and severity of neurological complications. Prescription of etiopathogenic therapy in the early stages determines a favorable prognosis and improves the quality of life, preventing disability. In the case of neurological complications caused by direct contact injury to the spinal cord and/or myelosemia, the prognosis is extremely unfavorable both in terms of restoration of functions and quality of life. In septic conditions, there is a high risk of death within 1–2 years due to the risk of exacerbation of local and generalized processes [27, 38].

The prognosis for tuberculous spondylitis in the setting of HIV infection depends on the severity of immune deficiency, severity of neurological disorders, and resistance of MTB to TCT. Disability in this category of patients reaches 85–87 % of cases [23].

The criteria for assessing the quality of care are presented in Tables 8 and 9.

Table 8
Organizational and technical conditions for provision of medical care

Type of medical care	Specialized medical care
Conditions for provision of medical care	Inpatient/day hospital
Form of medical care	Elective; urgent in the case of acute septic and neurological complications

Table 9
Criteria of medical care quality

Criterion	Confidence level of parameter	Grades of recommendation
Assessing severity of systemic inflammatory response syndrome (CRP, PCT)	C	1
Complete blood count	C	1
Bacteriological, PCR, and histological examination of material from the lesion site	C	1
Rational antibiotic therapy	C	1
CT scan of the spine	C	1
MRI in patients with neurological manifestations	C	2

References

1. **Gushcha AO, Semenov MS, Poltorako EA, Kashcheev AA, Vershinin AV.** Clinical Recommendations for Diagnosis and Treatment of Inflammatory Diseases of the Spine and Spinal Cord. Krasnoyarsk, 2015. In Russian.
2. **Berbari EF, Kanj SS, Kowalski TJ, et al.** 2015 Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. Clin Infect Dis. 2015;61:e26–e46. DOI: 10.1093/cid/civ482.
3. **Mushkin AYu, Vishnevsky AA.** Clinical recommendations for the diagnosis of infectious spondylitis. Project for discussion. Medictsinskij Aljans. 2018;(3):65–74. In Russian.
4. Nonspecific Purulent Diseases of the Spine: Diagnosis, Tactics and Treatment. Clinical Recommendations, ed. by MYu Goncharov. Yekaterinburg, 2017. In Russian.
5. **Pola E, Autore G, Formica VM, Pambianco V, Colangelo D, Cauda R, Fantoni M.** New classification for the treatment of pyogenic spondylodiscitis: validation study on a population of 250 patients with a follow-up of 2 years. Eur Spine J. 2017;26(Suppl 4):479–488. DOI: 10.1007/s00586-017-5043-5.
6. **Polubentseva EI, Ulumbekova GE, Sajtkulov KI.** Clinical recommendations and quality indicators in the quality management system in health care: Methodological recommendations. Moscow, 2006. In Russian.
7. **Calderone RR, Larsen JM.** Overview and classification of spinal infection. Ortop Clin North Am. 1996;27:1–8.
8. **Tikhodeev SA, Vishnevsky AA.** Nonspecific Osteomyelitis of the Spine. St.Petersburg, 2004. In Russian.
9. **Vetryle ST, Morozov AK, Kuleshov AA, Kolbovsky DA.** Diagnosis and Surgical Treatment of Nonspecific Hematogenous Osteomyelitis of the Spine. Moscow, 2012. In Russian.
10. **Carragee EJ.** Pyogenic vertebral osteomyelitis. J Bone Joint Surg Am. 1997;79:874–880. DOI: 10.2106/00004623-199706000-00011.
11. **Berdyugin KA, Karenin MS.** Complications of transpedicular fixation and its prophylactic. Fundamental'nye issledovaniya. 2010;(9):61–71. In Russian.
12. **Petrova NV.** Evidence-based diagnosis of implant-associated infection in orthopedic surgery. Hir. Pozvonoc. 2012;(1):74–83. In Russian. DOI: 10.14531/ss2012.1.74-83.
13. **Choi KB, Lee CD, Lee SH.** Pyogenic spondylodiscitis after percutaneous endoscopic lumbar discectomy. J Korean Neurosurg Soc. 2010;48:455–460. DOI: 10.3340/jkns.2010.48.5.455.
14. **Lora-Tamayo J, Euba G, Narvaez JA, Murillo O, Verdaguer R, Sobrino B, Narvaez J, Nolla JM, Ariza J.** Changing trends in the epidemiology of pyogenic vertebral osteomyelitis: the impact of cases with no microbiologic diagnosis. Semin Arthritis Rheum. 2011;41:247–255. DOI: 10.1016/j.semarthrit.2011.04.002.
15. **Menon KV, Sorour TM.** Epidemiologic and demographic attributes of primary spondylodiscitis in a middle eastern population sample. World Neurosurg. 2016;95:31–39. DOI: 10.1016/j.wneu.2016.07.088.
16. **Gaydash IS, Flegontova VV, Biryukova SV, Suglobov EV, Kuchma IYu, Volancky AYu.** Microbiological spectrum of opportunistic pathogenic bacteria-causative agents of posttraumatic osteomyelitis. Ortopediya, travmatologiya i protezirovanie. 2000;(2):89–92. In Russian.
17. **Vishnevsky AA, Babak SV.** Nonspecific osteomyelitis of the spine caused by methicillin-resistant staphylococcus: rational antibiotic treatment. Trudnyj Patsient. 2014;12(3):39–43. In Russian.
18. **Gelalis ID, Arnaoutoglou CM, Politis AN, Batzaleksis NA, Katonis PG, Xenakis TA.** Bacterial wound contamination during simple and complex spinal procedures. A prospective clinical study. Spine J. 2011;11:1042–1048. DOI: 10.1016/j.spinee.2011.10.015.
19. **Yoon SH, Chung SK, Kim KJ, Kim HJ, Jin YJ, Kim HB.** Pyogenic vertebral osteomyelitis: identification of microorganism and laboratory markers used to predict clinical outcome. Eur Spine J. 2010;19:575–582. DOI: 10.1007/s00586-009-1216-1.
20. **Turunc T, Demiroglu YZ, Uncu H, Colakoglu S, Arslan H.** A comparative analysis of tuberculous, brucellar and pyogenic spontaneous spondylodiscitis patients. J Infect. 2007;55:158–163. DOI: 10.1016/j.jinf.2007.04.002.
21. **Kim CW, Perry A, Currier B, Yaszemski M, Garfin SR.** Fungal infections of the spine. Clin Orthop Relat Res. 2006;444:92–99. DOI: 10.1097/01.blo.0000203451.36522.4c.
22. **Lu YA, Hsu HH, Kao HK, Lee CH, Lee SY, Chen GH, Hung CC, Tian YC.** Infective spondylodiscitis in patients on maintenance hemodialysis: a case series. Ren Fail. 2017;39:179–186. DOI: 10.1080/0886022X.2016.1256313.
23. **Reshetneva EV, Mushkin AY, Zimina VN.** Risk analysis for post-surgical complications in tuberculosis spondylitis patients with concurrent HIV infection. Tuberculosis and Lung Diseases. 2015;(4):36–41. In Russian. DOI: 10.21292/2075-1230-2015-0-4-36-41.
24. Guidelines for Pulmonary and Extrapulmonary Tuberculosis, ed. by Levashev YuN, Repin YuM. St. Petersburg, 2008. In Russian.
25. **Mushkin AYu, Vishnevsky AA.** Methodology of classification of infection spondylitis. In: Prospects of Spine Surgery: Materials of the 4th Congress of Interregional Public Organization "Association of Spine Surgeons" with international participation. Novosibirsk, 2013:123–127. Electronic resource. In Russian.
26. **Dowdell J, Brochin R, Kim J, Overley S, Oren J, Freedman B, Cho S.** Postoperative spine infection: diagnosis and management. Global Spine J. 2018;8(4 Suppl);37S–43S. DOI: 10.1177/2192568217745512.
27. Clinical Guidelines for the Diagnosis and Treatment of Severe Sepsis and Septic Shock in Medicoprophylactic Institutions of St. Petersburg. St. Petersburg, 2016. In Russian.
28. **Duarte RM, Vaccaro AR.** Spinal infection: state of the art and management algorithm. Eur Spine J. 2013;22:2787–2799. DOI: 10.1007/s00586-013-2850-1.
29. **McNamara AL, Dickerson EC,** Gomez-Hassan DM, Cinti SK, Srinivasan A. Yield of image-guided needle biopsy for infectious discitis: A systematic review and meta-analysis. AJNR Am J Neuroradiol. 2017;38:2021–2027. DOI: 10.3174/ajnr.A5337.
30. International standards in tuberculosis care. 3rd ed. WHO, 2014.
31. **Global Tu**berculosis Report 2015. WHO/HTM, 2015.
32. **Sovetova NA, Vasilyeva GYu, Solovyeva NS, Zhuravlev VY, Baulin IA.** Tuberculous spondylitis in adults: clinical and radiographic manifestations. Tuberculosis and Lung Diseases. 2014;(10):33–37. In Russian. DOI: 10.21292/2075-1230-2014-0-10-33-37
33. **Modic MT, Feiglin DH, Piraino DW, Boumphrey F, Weinstein MA, Duchesneau PM, Rehm S.** Vertebral osteomyelitis: assessment using MR. Radiology. 1985;157:157–166. DOI: 10.1148/radiology.157.1.3875878.
34. **Turgut M.** Spinal tuberculosis (Pott's disease): Its clinical presentation, surgical management, and outcome. A survey study on 694 patients. Neurosurg Rev. 2001;24:8–13. DOI: 10.1007/PL00011973.
35. **Bettini N, Girardo M, Dema E, Cervellati S.** Evaluation of conservative treatment of non specific spondylodiscitis. Eur Spine J. 2009.18(Suppl 1):143–150. DOI: 10.1007/s00586-009-0979-8.
36. **Kang SJ, Jang HC, Jung SI, Choe PG, Park WB, Kim CJ, Song KH, Kim ES, Kim HB, Oh MD, Kim NJ, Park KH.** Clinical characteristics and risk factors of pyogenic spondylitis caused by Gram-negative bacteria. PloS One. 2015;10:e0127126. DOI: 10.1371/journal.pone.0127126.
37. **Bernard L, Dinh A, Ghout I, Simo D, Zeller V, Issartel B, Le Moing V, Belmatoug N, Lesprit P, Bru JP, Therby A, Bouhour D, Denes E, Debard A, Chir-**

ouze C, Fevre K, Dupon M, Aegerter P, Mulleman D. Antibiotic treatment for 6 weeks versus 12 weeks in patients with pyogenic vertebral osteomyelitis: an open-label, non-inferiority, andomized, controlled trial. Lancet. 2015;385:875–882. DOI: 10.1016/S0140-6736(14)61233-2.

38. Sepsis: Classification, Clinicodiagnostic Concept, and Treatment: Practical Guideline, ed. by VC Saveliev, BR Gelfand. Moscow, 2011. In Russian.
39. **Kumar A.** Optimizing antimicrobial therapy in sepsis and septic shock. Crit Care Clin. 2009;25:733–751. DOI: 10.1016/j.ccc.2009.08.004.
40. **Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R.** Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013;41:580–637. DOI: 10.1097/CCM.0b013e31827e83af.
41. **Siewe J, Oppermann J, Eysel P, Zarghooni K, Sobottke R.** Diagnosis and treatment of spondylodiscitis in HIV-positive patients. Acta Orthop Belg. 2013;79:475–482.
42. **Panteleev AM, Savina TA, Suprun TYu.** Extrapulmonary tuberculosis in HIV-infected people. In: Socially Significant Infections. St. Petersburg, 2007:35–36. In Russian.
43. **Chung TC,Yang SC, Chen HS, Kao YH, Tu YK, Chen WJ**. Single-stage anterior debridement and fibular allograft implantation followed by posterior instrumentation for complicated infectious spondylitis: report of 20 cases and review of the literature. Medicine (Baltimore). 2014;93:e190. DOI: 10.1097/MD.0000000000000190.
44. **Kuklin DV, Belyakov MV, Serdobintsev MS, Dorofeev LA.** Tactics for using titan implants for tuberculous spondylitis depending on the stagittal spine profile. Tuberculosis and Lung Diseases. 2015;7:81. In Russian.
45. **Assaghir YM, Refae HH, Alam-Eddin M.** Anterior versus posterior debridement fusion for single-level dorsal tuberculosis: the role of graft-type and level of fixation on determining the outcome. Eur Spine J. 2016;25:3884–3893. DOI: 10.1007/s00586-016-4516-2.
46. **Lee JS, Moon KP, Kim SJ, Suh KT.** Posterior lumbar interbody fusion and posterior instrumentation in the surgical management of lumbar tuberculous spondylitis. J Bone Joint Surg Br. 2007;89:210–214. DOI: 10.1302/0301-620X.89B2.17849.
47. **Chang JJ, Ma X, Feng HY, Huo JZ, Chen C, Zhang YN, Wang YF, Zhang YN, Liu J.** Clinical efficacy of single-stage posterior radical debridement, bone grafting and internal fixation in lumbar spinal tuberculosis with kyphotic deformity. Int J Clin Exp Med. 2016;9:14383–14389.
48. **Yin XH, Liu SH, Li JS, Chen Y, Hu XK, Zeng KF, Yu HG, Zhou ZH, Zhang HQ.** The role of costotransverse radical debridement, fusion and postural drainage in the surgical treatment of multisegmental thoracic spinal tuberculosis: a minimum 5-year follow-up. Eur Spine J. 2016;25:1047–1055. DOI: 10.1007/s00586-015-4283-5.
49. **Zhang PH, Peng W, Wang XY, Luo CK, Xu ZQ, Zeng H, Liu Z, Zhang YP, Ge L.** Minimum 5-year follow-up outcomes for single-stage transpedicular debridement, posterior instrumentation and fusion in the management of thoracic and thoracolumbar spinal tuberculosis in adults. Br J Neurosurg. 2016;30:666–671. DOI: 10.1080/02688697.2016.1206182.
50. **Buyukbebeci O, Seckiner I, Karsli B, Karakurum G, Baskonus I, Bilge O, Kacira BK.** Retroperitoneoscopic drainage of complicated psoas abscesses in patients with tuberculous lumbar spondylitis. Eur Spine J. 2012;21:470–473. DOI: 10.1007/s00586-011-2049-2.
51. **Li J, Li XL, Zhou XG, Zhou J, Dong J.** Surgical treatment for spinal tuberculosis with bilateral paraspinal abscess or bilateral psoas abscess: one-stage surgery. J Spinal Disord Tech. 2014;27:E309–E314. DOI: 10.1097/BSD.0000000000000120.
52. **Yang H, Hou KD, Zhang L, Zhang XF, Wang Y, Huang P, Xiao S.** Minimally invasive surgery through the interlaminar approach in the treatment of spinal tuberculosis: A retrospective study of 31 patients. J Clin Neurosci. 2016;32:9–13. DOI: 10.1016/j.jocn.2015.11.036.
53. **Yang H, Song F, Zhang L, Li N, Zhang X, Wang Y.** Management of spine tuberculosis with chemotherapy and percutaneous pedicle screws in adjacent vertebrae: a retrospective study of 34 cases. Spine. 2016;41:E1415–E1420. DOI: 10.1097/BRS.0000000000001858.
54. **Fukuta S, Miyamoto K, Masuda T, Hosoe H, Kodama H, Nishimoto H, Sakaeda H, Shimizu K.** Two-stage (posterior and anterior) surgical treatment using posterior spinal instrumentation for pyogenic and tuberculotic spondylitis. Spine. 2003;28:E302–E308. DOI: 10.1097/01.BRS.0000083318.40123.5E.
55. **Jain AK, Dhammi IK, Prashad B, Sinha S, Mishra P.** Simultaneous anterior decompression and posterior instrumentation of the tuberculous spine using an anterolateral extrapleural approach. J Bone Joint Surg Br. 2008;90:1477–1481. DOI: 10.1302/0301-620X.90B11.20972.
56. **Rajasekaran S, Rajoli SR, Aiyer SN, Kanna R, Shetty AP.** A classification for kyphosis based on column de ciency, curve magnitude, and osteotomy requirement. J Bone Joint Surg Am. 2018;100:1147–1156. DOI: 10.2106/JBJS.17.01127.
57. **Jimenez-Mejias ME, de Dios Colmenero J, Sanchez-Lora FJ, Palomino-Nicas J, Reguera JM, Garc a de la Heras J, Garc a-Ordonez MA, Pachon J.** Postoperative spondylodiskitis: etiology, clinical findings, prognosis, and comparison with nonoperative pyogenic spondylodiskitis. Clin Infect Dis. 1999;29:339–345. DOI: 10.1086/520212.

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Appendix

Methodology for development of clinical guidelines

Target audience of these clinical guidelines:

1) general practitioners (family doctors);
2) orthopedic traumatologists;
3) neurosurgeons;
4) medical students;
5) residents and graduate students.

Methods used for collecting/selecting evidence: search in electronic databases. Description of the methods used to assess the quality and strength of evidence: the evidence base for guidelines includes publications from the Cochrane library and EMBASE, MEDLINE and PubMed databases. The search depth is 5 years.

Methods used to assess the quality and strength of evidence:

– consensus of experts;
– significance assessment in accordance with the rating scheme.

Methods used to review evidence:

– reviews of published meta-analyses;
– systematic reviews with tables of evidence.

Description of methods used to review evidence. When selecting publications as potential sources of evidence, the methodology used in each study is investigated to ensure its validity. The result of this investigation affects the level of evidence assigned to the publication, which, in turn, affects the strength of recommendations. To minimize potential errors, each study was evaluated independently. Differences in estimates were discussed by the entire team of authors. If the consensus was not reached, independent experts were invited.

Tables of evidence were filled in by the authors of the clinical guidelines.

Methods used to formulate the guidelines: expert consensus.

Good Practice Points (GPPs). Most of the guidelines for the diagnosis and treatment of infectious spondylitis belongs to the level of evidence 2+; the strength of recommendation C.

The recommended good practice is based on clinical experience of the authors of the developed guidelines.

Economic analysis. The cost analysis was not conducted, and publications on pharmacoeconomics were not analyzed.

Methods for validation of guidelines:

– external expert assessment;
– internal expert assessment.

Description of the guidelines validation method. A preliminary version of these guidelines was peer-reviewed by independent experts who, first of all, were asked to comment on how understandable was the interpretation of evidence underlying the guidelines.

Primary care physicians provided their comments on comprehensibility and reproducibility of guidelines presentation as well as importance of the proposed guidelines as a tool for everyday practice.

All comments received from experts were systematized and discussed by members of the working group (authors of the guidelines).

The draft clinical guidelines for the diagnosis of infectious spondylitis have been presented on the website of the National Association of Phthisiologists (NAP) and discussed at the 5th NAP Congress.

Consultation and expert assessment. The draft guidelines were peer-reviewed by independent experts who were first of all asked to comment on the intelligibility and accuracy of interpretation of the evidence base underlying the guidelines.

Working group. For the final revision and quality control, the guidelines were re-analyzed by members of the working group, who came to the conclusion that all expert comments and suggestions were taken into account, and the risk of systematic errors in the development of guidelines was minimized.

Key recommendations. The strength of recommendations (1 or 2) based on the appropriate levels of evidence (A–D; Table 10) and good practice points (GPPs) are provided in the text of the guidelines.

The clinical guidelines will be updated at least once every three years. The decision to update will be made on the basis of proposals submitted by medical professional non-profit organizations, with allowance for the results of comprehensive assessment of drugs and medical devices, as well as the results of clinical testing.

Table 10
Scheme for grading the level of recommendation

Strength	Description
A	At least one meta-analysis, systematic review, or RCT rated as 1++ directly applicable to the target population and demonstrating robust results, or a body of evidence including research results rated as 1+ directly applicable to the target population and demonstrating overall consistency of results.
B	A body of evidence including research results rated as 2++ directly applicable to the target population and demonstrating overall consistency of results, or extrapolated evidence from studies rated as 1++ or 1+
C	A body of evidence including research results rated as 2+ directly applicable to the target population and demonstrating overall consistency of results, or extrapolated evidence from studies rated as 2++
D	Level 3 or 4 evidence or extrapolated evidence from studies rated 2+

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