THE ROLE OF INFECTION AND INFLAMMATION IN INTERVERTEBRAL DISC DEGENERATION

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Objective. To analyze the frequency and types of microbial infection of the intervertebral disc in degenerative diseases of the spine and to compare the obtained data with the results of pathohistological, X-ray and MRI studies to determine tactical approaches to surgical interventions on the spine.

Material and Methods. The study was performed in 97 patients who underwent surgical treatment for degenerative spine disease. Discectomy was performed in 48 patients, and single- or multilevel decompression and stabilization in 49. Microbiological (117 samples) and pathohistological (73 samples) studies of disc material, clinical and neurological examinations of patients, and evaluation of X-ray and MRI findings were carried out.

Results. Bacterial culture of the disc material was positive in 27.0 % of cases of discectomy and in 30.6 % of decompression and stabilization cases. The most frequent pathogens were obligate-anaerobic gram-positive bacteria (*P. acnes*) and epidermal staphylococci (*S. epidermidis*), in 42.8 % and 31.4 % of cases, respectively. The mixed microflora was detected in 20.0 % of observations. Pathohistological study revealed the signs of chronic inflammation in 42.8 % of patients with disc infection and in 5.7 % of patients without infection. There was no significant correlation between infection of the disc and chronic diseases, clinical manifestations, sequester, Modic type 1 changes in MRI, segment instability, and changes in CT.

Conclusion. The probability of disc infection is higher in repeated operations and in degenerative lesion of discs with pain and radicular syndrome. The most reliable mechanism of intervertebral disc infection is the theory of microbial biofilms.

Key Words: degenerative diseases of the spine, intervertebral disc infection, *P. acnes, S. epidermidis*.

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At present, there is no single concept of etiopathogenesis of degenerative intervertebral disc disease (DDD). Several triggers have been identified: biomechanical ones [24], cytokines [37], nutrition factors of DDD [33], genetic triggers [29, 39]. In 2001, Stirling et al. [36] suggested the role of low-virulent *P. acnes* bacteria in DDD. Later researchers repeatedly addressed the issue of infectious etiology of intervertebral disc degeneration, but the results were largely contradictory [28]. The main issue is the mechanism of the spread of the infection: bacteremia, intraoperative contamination, infection during paravertebral or epidural administration of drugs into a intervertebral disc, or surgical interventions on the spine. The role of DDD as a nutrient medium for microorganisms has been elucidated. Comparison of the results of clinical and neurological status of patients with MRI and CT data has been performed.

Therefore, the role of bacteria in etiopathogenesis, clinical manifestations and the course of the postoperative period after surgical interventions on the spine in patients with DDD requires further study, which was the impetus for our work.

The aim of the study was to analyze the frequency and types of microbial infection in DDD, to compare the data obtained with the clinical and neurological status of patients, the results of pathohistological, radiologic studies and MRI to determine tactics for surgical interventions on the spine.

Study design: prospective cohort randomized study.

Material and Methods

The inclusion criteria were: age over 18 years, presence of degenerative disease of lumbar intervertebral discs with clinical manifestations.

The exclusion criteria were: age up to 18 years, spine trauma, cancer, infectious process.

The study was conducted in the Department of Traumatology and Orthopedics No 10 of the Russian Ilizarov Scientific Center for Restorative Traumatology and Orthopaedics in the period from October 2016 to June 2017.

Surgical intervention for hernias of the lumbar spine was performed in the volume of the discectomy by minimally invasive tubular removal of the hernial sequestrum. In case of herniated discs of the cervical spine, anterior cervical discectomy and fusion (ACDF) were per-

formed. In case of stenosis of the spinal canal, the following decompression and stabilization interventions were performed: variants of reconstruction of the spinal canal (facetectomy, resection of the yellow ligament, removal of the compressing substrate) with the use of instrumental fixation of the segment and posterior lumbar interbody fusion (PLIF).

All surgeries were performed with strict adherence to aseptic and antiseptic rules, after preventive antibacterial therapy (cefazolin 2.0 g intramuscularly 2 hours prior to the start of surgical intervention). After microdiscectomy, the material was divided into two parts: for microbiological study and for pathohistological study.

General characteristics of the patients. All patients were examined by a neurologist and a neurosurgeon prior to the surgery. Clinical examination included identification of signs of the infectious process, evaluation of the neurological status, assessment of presence of concomitant diseases (arterial hypertension, diabetes mellitus and other chronic diseases in remission).

The study included 97 patients (56 men, 41 women, mean age 54.1 ± 8.4 years) who underwent surgery for DDD. Microdiscectomy was performed in 48 patients (29 men, 19 women, mean age 52.8 ± 7.9 years), single- and multi-level decompression and stabilization operations with reconstruction of the spinal canal and fixation of spinal motion segments were performed in 49 (18 men, 31 women, mean age 55.4 ± 8.5 years).

Microbiological study. The material for microbiological examination was collected intraoperatively, in accordance with aseptic rules, into sterile containers, which were immediately delivered to the laboratory. When necessary, homogenization of biomaterials was carried out in sterile boxes. To isolate aerobic and facultative anaerobic bacteria, they were plated on the nutrient agar containing 5 % of blood, yolk-salt agar, Levin's medium, and Saburo's medium. The cultures were incubated at 37 °C for 24–48 hours. Cumulative cultures of anaerobic bacteria were obtained on a thioglycolic medium, isolated colonies of anaerobic cultures, on Colombian agar with commercial additives. Anaerobic conditions were created with the help of GENbox incubation systems and associated gas-generating packages; the plates were incubated at 37 °C until 5 days with a daily visual control. To determine the microbial burden, the cultures were seeded on the sectors of nutrient medium plates in a Petri dish; after the incubation the number of colonies of each type in the sectors was counted, the result was expressed in terms of the decimal logarithm of the grown colonies (CFU/ml). Identification and assessment of the antibiotic susceptibility of pure bacterial cultures was carried out using a bacteriological analyzer and appropriate test systems.

Pathohistological study. The material for pathohistological examination consisted of fragments of the nucleus pulposus and annulus fibrosis. Following a fixation in a solution of 10% formalin, the material was subjected to short decalcification, standard histological processing and then embedded in paraffin; microtom was used to prepare sections 4–5 microns thick, which were stained with hematoxylin-eosin.

X-ray and MRI studies. The analysis of MRI data was used to assess pathological changes in the bone marrow and end plates of adjacent vertebral bodies using classification scheme by Modic et al. [32]. X-ray parameters included the mobility of the segment according to the functional study and changes in the end plates of the vertebral bodies of aseptic spondylodiscitis type according to CT.

Ethical expertise. Studies were conducted in accordance with the requirements of the Helsinki Declaration of 1964 [42]. All patients included in the study gave written informed consent for conducting diagnostic tests and medical intervention.

Statistical processing of data. «Microsoft Excel 2016» was used for data processing. The calculation of the arithmetic mean (M) and the deviation of the mean (± m), Pearson correlation coefficient with the Chaddock score were used. To assess the significance of the difference in means, the Student's t-test was used to determine the indicator of statistical significance. The level of significance was $p < 0.05$

Results

Based on the results of bacteriological study, the patients were divided into two groups: Group 1 with negative cultures of degenerated intervertebral disc material (69 patients) and Group 2 with identified bacterial growth (29 patients). In 19 patients, the disc material was collected at two levels, therefore, a total of 117 samples have been studied. Disc material samples were also divided into two groups: Group 1 (87 samples) with negative and Group 2 (30 samples) with positive cultures.

In six patients, who were operated at two levels, the material from one disc did not give rise to microorganisms, but the bacterial growth was observed in the material from the other disc. These patients were classified into Group 2, and the data of the disc studies were distributed into two groups according to the result. In two patients, positive growth of cultures was observed on both levels of intervention.

Demographic and clinical laboratory characteristics of patients are presented in Table 1.

Most often, surgical interventions were carried out at the levels L4–L5 and L5–S1 (Fig. 1).

Positive cultures of the disc material was observed in 27% of discectomy cases, and in 30.6% of decompression and stabilization cases.

There was only very weak correlation between positive staining of the disc material and concomitant diseases ($r < 0.1$). The correlation between repeated interventions and infection of the disc material ($r = 0.08$) was also weak; in Group 2, the specific weight of re-operations was 17.8 %.

No patient had any manifestations of an infectious disease, and clinical analysis of blood revealed no typical inflammatory changes. Patients were admitted for routine surgical treatment after examination by a therapist and a dentist and in the absence of exacerbation of chronic diseases.

Table 1
General characteristics of the patients in the study

Parameter	Group 1: negative cultures of the disc material (n = 69)	Group 2: positive cultures of the disc material (n = 28)
Age, years	55.8 ± 7.8* (от 26 до 71)	51.1 ± 9.9* (от 28 до 68)
Men: Women, n	33 : 36	11 : 17
Discectomy/decompression and stabilization intervention, n (%)	35 / 34 (50.7 / 49.3)	13 / 15 (46.4 / 53.6)
Level of intervention: cervical / thoracic / lumbar, n (%)	9 / 1/ 59 (13.0 / 1.4 / 85.5)	3 / 1/ 24 (10.7 / 3.5 / 85.7)
Mobility in functional X-ray study, n (%)	30 (43.7)	13 (46.4)
Modic type 1 changes according to MRI, n (%)	19 (27.5)	7 (25)
Aseptic spondylodiscitis-type changes according to CT, n (%)	8 (11.5)	4 (14.3)
Repeated spine surgeries, %	7.2	17.8
Arterial hypertension, %	47.8	53.5
Diabetes, %	14.5	10.7
Other chronic diseases in remission, %	58.0	46.4
Undiagnosed chronic diseases, %	14.5	25.0

*significant difference between groups based on t-criterion (Student), $p < 0.05$.

The assessment of the clinical and neurological status revealed radiculopathy of the involved spinal cord roots with a clinical presentation of radicular syndrome, radiculomyelopathy with clinical manifestations of neurogenic intermittent claudication or paresis of extremities of varying severity depending on the level of lesion, and vertebrogenic pain syndrome resistant to conservative treatment as prevailing in the clinical presentation without the topical involvement of the spinal cord structures (Fig. 2).

When comparing clinical manifestations and the infected material of the disc, a very weak correlation was established with Chaddock coefficient of 0.03.

Pathohistological examination was performed in 73 cases: in 51 patients in Group 1 and 22 patients in Group 2. The surgical material consisted of fragments of the annulus fibrosus and nucleus pulposus, sometimes with bone inclusions. The results of the study were divided into three variants:

1) micro-slides contained fragments of intervertebral structures with different severity of dystrophic changes and no signs of inflammatory reaction;

2) with a weak inflammatory reaction, micro-slides contained fragments of intervertebral structures with insignificant number of cellular elements of inflammatory nature;

3) with a distinct inflammatory response predominantly with clusters of lymphohistiocyte cells with a negligible representation of neutrophilic leukocytes.

Morphological signs of inflammatory changes were most common in the group of patients with disc infection (Fig. 3).

Based on the results of a microbiological study, 35 strains of microorganisms were obtained from 28 patients out of 97 examined (30 samples out of 117). The most commonly detected growth was that of obligate-anaerobic gram-positive bacteria and epidermal staphylococci (Table 2).

In six cases, mixed infection was diagnosed: *P. n sp.* + *P. asaccharolyticus* (2 samples), *S. t epidermidis* + *P. acnes* (3 samples), *S. haemolyticus* + *S. warneri* (1 sample). Methicillin-resistant strains of *S. epidermidis* (MRSE) have been identified in three observations.

When comparing the data of pathohistological and microbiological studies, it has been established that morphological signs of inflammation were most often encountered in sample from which the cultures of staphylococcus, obligate-anaerobic gram-positive bacteria and mixed microflora were isolated (Fig. 4).

X-ray examination was used to study the parameters that may indicate inflammatory changes in the spine: mobility in functional X-ray study and CT data. MRI study was used to identify pathological changes in the bone marrow and end plates of adjacent vertebrae of the Modic type 1. Based on the results of X-ray examination and MRI, a uniform distribution of the assessed parameters in the patient groups was established.

The correlation between the instability of the spinal motion segment of interest, changes in CT, and Modic type 1 changes was very weak ($r < 0.1$).

Intraoperatively, hernial sequestration was visualized and removed in 24 (37 %) patients of the Group 1 and in 10 (50 %) of Group 2. There was no significant correlation between hernial sequestrum and infection of the disc material ($r = 0.1$).

In the postoperative period, the patients received a course of antibacterial therapy with 1st generation cephalosporins (cefazolin 2.0 im 2 times a day for 5–7 days).

The follow-up period was 3–6 months. Superficial inflammation of the

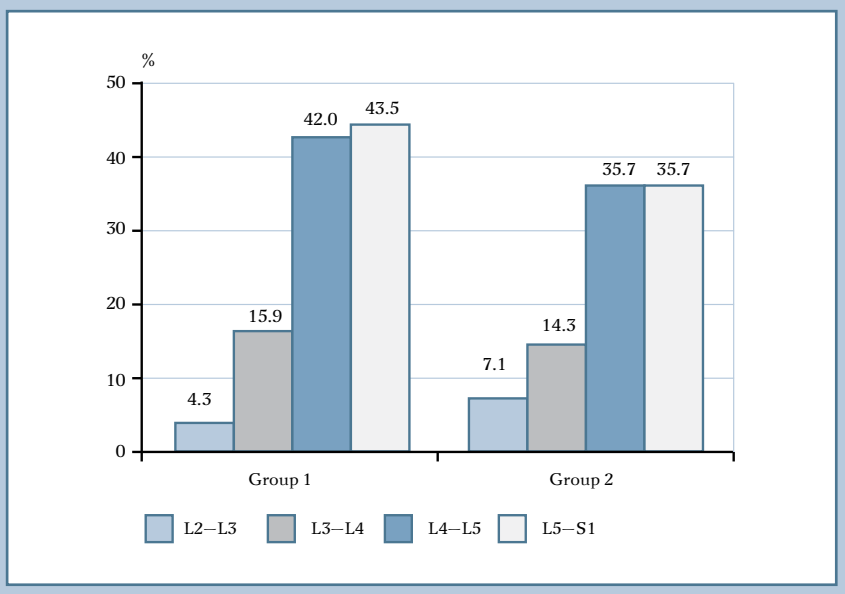

Fig. 1
Distribution of patients by levels of lumbar intervertebral discs

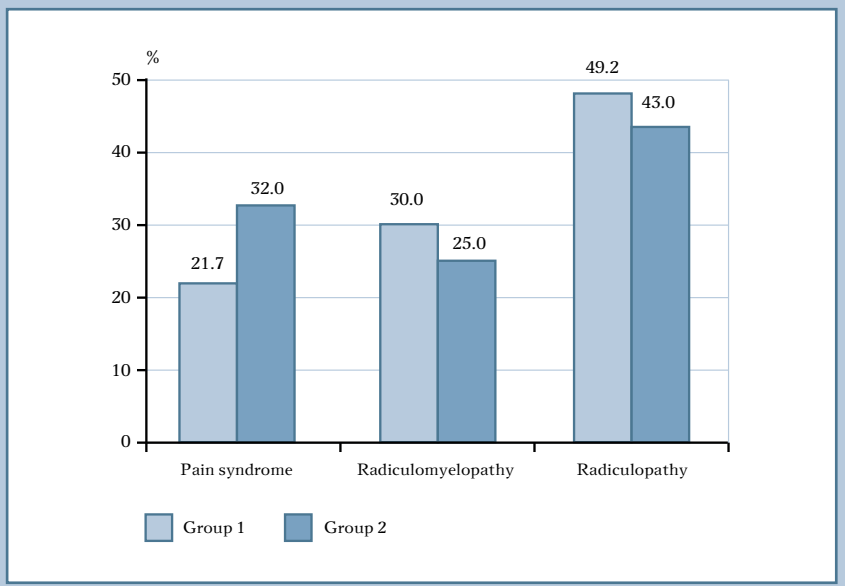

Fig. 2
Patient distribution by clinical manifestations of the disease

postoperative wound, which was managed by conservative treatment, was diagnosed in 1 patient from Group 1.

Discussion

The hypothesis of the infectious etiology of intervertebral disc degeneration was proposed by Stirling et al. [36] based on the results of microbiological analysis of the materials from 36 patients who underwent discectomy which produced 53 % of positive cultures. Bacteria *P. acnes* (84 % of seeds) and vancomycin-resistant *Staphylococcus* (11 %) were detected most often [11, 36].

Carricajo et al. [16] investigated not only the intervertebral disc, but also paravertebral muscles and yellow ligament of 54 patients with herniated discs. The incidence of positive samples was 7.4 % for disc materials and 22.2 % for muscles and ligaments.

Wedderkopp et al. [41] reported on bacterial growth in biopsy of 8.3% of patients out of 24 examined.

According to Agarwal et al. [7], positive cultures were detected after discectomy in 10 (19.2 %) patients. *P. acnes* were isolated from 7 (13.5 %) patients, in the remaining cases mixed microflora (*Peptostreptococcus* and *Staphylococcus species*) was identified.

A study by Arndt et al. [11] found the growth of bacteria in 40 discs out of 83: *Propionibacterium acnes* (18 people), vancomycin-resistant *Staphylococcus* (16 cases), Gram-negative bacilli (3 samples), *Micrococcus* (3 cultures), *Corynebacterium* (3 discs) and others (5 cases).

Having examined 61 patients, Albert et al. [10] found the growth of bacteria in 44 % of cases.

A prospective study by Coscia et al. [17] of 169 discs of 87 patients from different groups (cervical hernias, lumbar hernias, lumbar stenosis, two comparison groups with idiopathic scoliosis and spine injuries) showed positive cultures in 76 (45 %) discs. *P. acnes* was identified in 34 cultures, vancomycin-resistant *Staphylococcus*, in 30.

Ben-Galim et al. [13] deny the importance of infectious factor in DDD process. Only 4 positive samples were obtained for 120 cultures (30 samples). According to the researchers, the identified bacteria are normal skin microflora, the result of the study depends on the protocol for collection and delivery of the material.

A systematic review by Ganko et al. [24], based on 9 publications and 602 patients, shows the average bacterial growth rate from the disc material in 36.2 % of cases. The most frequent pathogens are *P. acnes* (59 % of cultures) and

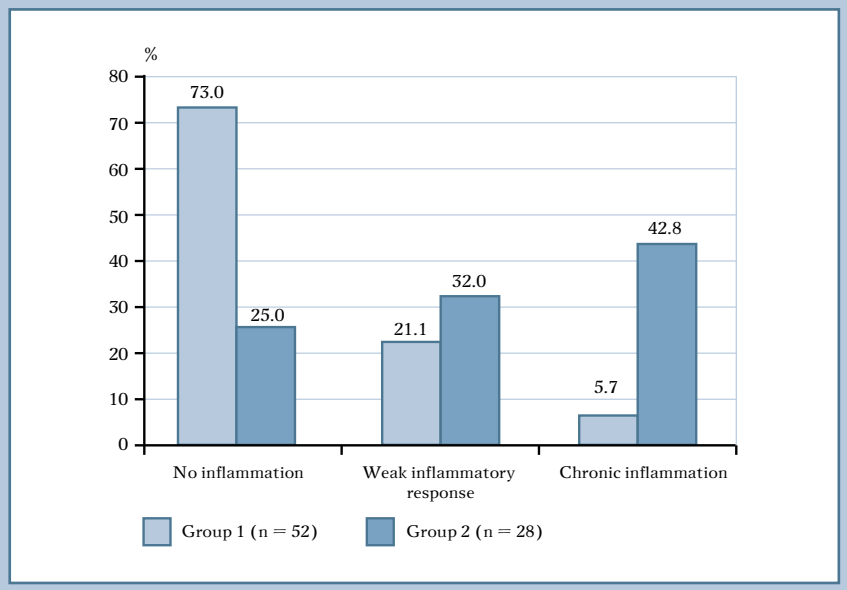

Fig. 3
Distribution of pathological findings in patient groups (specific weight)

Staphylococcus aureus (4 to 60 % of samples) [7, 11, 15, 17, 18].

In the presented study, among 117 discs from cervical, thoracic and lumbar spine of 97 patients with degenerative lesions, the incidence of positive samples was 25.6 %. The most frequent pathogens were obligate-anaerobic gram-positive bacteria (*P. acnes*) and epidermal staphylococci (*S. epidermidis*), in 42.8 % and 31.4 % of cases, respectively. The mixed microflora was detected in 20.0 % of observations.

Table 2
Types of pathogens at microbiological study (n = 35)

Type of pathogen	Isolated strains, n	Specific weight, %
Epidermal staphylococci		
S. epidermidis	9	25.7
S. capitis	1	2.8
S. warneri	1	2.8
Hemolytic Staphylococci		
S. haemolyticus	3	8.6
S. hominis subsp. hominis	2	5.7
S. simulans	1	2.8
Obligatory anaerobic gram-positive bacteria	15	42.8
P. acnes		
Non-fermenting gram-negative bacteria	1	2.8
A. lwoffii		
Peptostreptococcus *P. asaccharolyticus*	2	5.7
Paragemolytic vibrio	1	2.8
V. parahaemolyticus		

It should be noted that in six patients the results of seedings from discs at different levels were different: one disc was infected and the other one was not. In two patients, growth of cultures was observed on both levels of intervention.

Features of the blood supply of the disc and degenerative processes in it are favorable factors of infectious processes. Intervertebral disc is an isolated avascular structure consisting of nucleus pulposus and annulus fibrosus. Angiogenesis in the disc is activated due to ruptures and cracks in the fibrous ring. Avascular disc tissues provide an ideal environment for anaerobic low-virulent bacteria, which cause a slowly developing inflammatory process [10, 38, 43]. The degenerative process leads to changes in the nucleus pulposus and is characterized by a local inflammatory reaction with the presence of macrophages. The same reaction occurs in case of acute formation of a hernial sequestrum [9, 30]. Immunohistological studies have shown that the formation of the disc extrusion causes the proliferation of mononuclear cells and inflammatory mediators, forms autoimmune response that can lead to development of chronic inflammatory reaction [20, 34].

In our study, pathohistological examination of 73 samples revealed signs of inflammatory reaction of different degree of severity both in patients with bacterial infection of the disc and without it, which is explained by nonspecific inflammatory reaction in the presence of degenerative processes. In patients with disc infection, morphological signs of inflammation were diagnosed in 60.0 % of cases, in those without infection, in 5.7 %. Most often, these changes were detected during isolation of obligatory anaerobic gram-positive bacteria and epidermal staphylococcus.

Discussions about the ways of spreading the infection in the disc are of great interest. Primary infection can occur during initial surgery on the spine, joints and other bone structures, as well as during the discography, punctures, epidural or

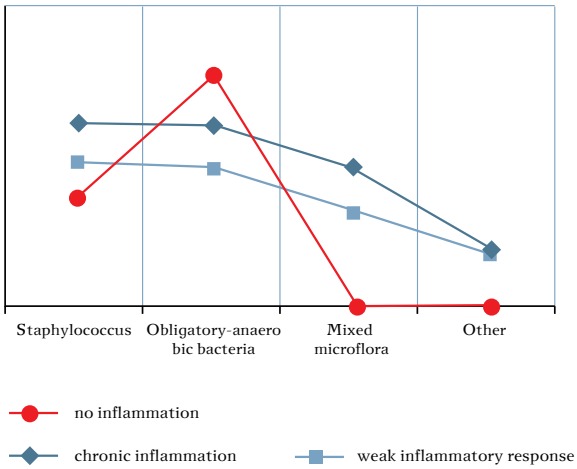

Fig. 4
Distribution of species of pathogen and pathohistological data

paravertebral administration of drugs [36].

According to the supporters of hematogenous theory, the spread of infection occurs from foci of chronic diseases, from the oral cavity during tooth cleaning, odontogenically [14, 19, 22, 27, 35, 36].

In the presented study, there was no correlation between chronic diseases and infection of the disc.

Li et al. [28] conducted a clinical and experimental study, during which a culture of infected human intervertebral disc was administered to rabbits into the discs and intravenously through the ear vein. After 6 weeks, there was no evidence for the degeneration of infected lumbar discs and infection of the discs by bacteremia.

A study by Lee et al. [27] showed that some pathogens (*Propionibacterium acnes*) persist in the skin after standard surgical treatment. The causative agent that inhabits the sebaceous glands and hair bulbs is out of reach of antiseptic solutions, while operative interventions causes the infection of surrounding tissues. The development of chronic slow infection and the seeding of the material subjected to microbiological analysis are both possible [8, 13, 27].

Zhou et al. [43] performed an immunohistological study of the disc material and paravertebral muscles after lumbar spine discectomy by PCR to detect 16S rDNA of *P. acnes*. Bacterial DNA were diagnosed in 11 (23.9 %) patients, 2 of them in muscle cultures. This allowed us to draw a conclusion that the infection of the surgical wound occurs from the skin or laminar air flow [43]. This theory is also supported by other authors [16, 31].

However, in case of such mechanism of bacterial infection spread, the incidence of infection of the surgical wound from the skin surface should also be identical in patients without degenerative changes (scoliosis, trauma), which researchers have not found [36], or it should be significantly lower [17]. In addition, positive samples were obtained after disc biopsy, when the probability of percutaneous infection is negligible [41]. Therefore, this theory is questionable [6, 17, 36]. The most likely etiologic factor of low-virulent infections is described by a theory of microbial films. The bacteria in bacterial biofilms in the body and/or in the environment, as well as those located directly in the disc can be activated under the influence of triggering factors [2, 4, 17, 21]. In this case, the disc with its anatomical and physiological features is a biofilm capable of preserving a low-grade infection for a long time [1, 3, 5]. This mechanism explains the infection of discs not only by obligate anaerobic bacteria, but also by other pathogens or microbial microorganisms, and the presence of infection at one level and the absence of the other, which we diagnosed in 6 patients. According to the data obtained, the disc samples contained not only *P. acnes,* but also epidermal staphylococcus; in 6 patients the microflora was mixed. The concept of microbial films also explains long asymptomatic existence of infection after primary surgery. In the presented study, the proportion of repeated interventions was 17.8 % in the group of patients with disc infection, whereas in the group of patients with negative cultures, the spinal surgery was previously performed in 7.2 % of cases. Researchers also analyze clinical manifestations in case of background of infection of the disc. Expressed acute pain syndrome and radiculopathy are signs of sequestration of disc herniation with compression of the spinal cord roots. This stage is the one when surgical interventions are most often performed and positive samples of the disc material are collected [13, 23, 43].

According to the results of our study, the infection of the disc was almost uniformly detected with decompression and stabilization surgeries (30.6 %) and discectomies (27.0 %). In patients with disc infection, the clinical manifestations are dominated by pain syndrome and radiculopathy. In patients without infection, by radiculopathy and radiculomyelopathy. However, in determining the strength of the correlation, these parameters showed a very weak correlation with Chaddock coefficient of 0.1. There was no significant correlation between the presence of a hernial sequestrum and the positive cultures either ($r = 0.1$).

Pathological changes in the bone marrow and end plates of adjacent vertebrae (Modic I), interpreted as aseptic

spondylodiscitis, are believed to be one of the etiological factors of the pain syndrome. These changes are observed in 6% of the population and in 35–40% of people with back pain [9, 26, 32]. Modic type 1 changes are more commonly associated with back pain than Modic II [8, 25, 40]. One of the causes of this condition is the infectious factor: low-virulent anaerobic microorganisms were detected in these patients in 7–53% of cases. These findings support the theory of formation of the bone marrow edema in case of disc infection during its sequestration [9, 12, 33]. Treatment of patients with back pain and Modic I changes with antibiotics is much more effective than placebo, which indirectly confirms the infectious nature of the changes [10]. However, according to the data of other authors [11], there was no correlation between disc infection and Modic I changes.

X-ray signs of inflammatory changes in the disc are the mobility of the segment in functional X-ray examination and the results of CT with changes in the contour of the end plate of the vertebrae. During the X-ray measurement of the height of the disc, Zhou et al. [43] identified decrease in the height and instability in case of *P. acnes* infection due to rupture of annulus fibrosus and sequestration of the disc into the lumen of the spinal canal.

The analysis of the data showed very weak correlation between the instability of the involved spinal motion segment, manifestations of nonspecific spondylodiscitis and Modic I changes in the patients under study ($r < 0.1$).

The use of antibacterial therapy did not affect the results of study, because the drug used (cefazolin) does not penetrate the disc [13, 37].

Conclusion

Examination of 117 intervertebral disc samples from 97 (25.6 %) patients revealed the presence of microorganisms, confirmed by morphological changes. The most frequent pathogens are obligate-virulent gram-positive bacteria (*P. acnes*) and epidermal staphylococcus (*S. epidermidis*).

There was no significant correlation between disc infection and chronic diseases, clinical manifestations, presence of a sequester, Modic I changes in MRI, segment instability, and changes in CT study.

The probability of disc infection is higher in repeated operations and in degenerative lesions of discs with pain and radicular syndrome.

The most reliable mechanism of intervertebral disc infection is the theory of microbial biofilms.

Studies of not only the disc, but also of the yellow ligament, paravertebral muscles, bone tissue of the vertebrae and skin are rather promising. It requires microbiological, pathohistological and molecular genetic (PCR) studies to detect bacterial DNA.

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References

1. **Gostev VV, Sidorenko SV.** Bacterial biofilms and infections. Journal Infectology. 2010;2(3):4–15. In Russian. DOI:10.22625/2072-6732-2010-2-3-4-15.
2. **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.
3. **Kolchanova NE, Okulich VK, Shilin VE.** Determination of the biofilm formation by periodontal pocket bacteria and the resistance of microbial communities to chemical and biological objects. Immunopathology, allergology, infectology. 2015;(3):56–61. In Russian. DOI: 10.14427/jipai.2015.3.56.
4. **Isaykin AI, Chernenko OA, Ivanova MA, Stitsenko AN.** Back pain caused by disorders of the intervertebral discs. Consilium medicum. 2015;17(2):52–60. In Russian.
5. **Tets VV, Tets GV.** Microbial biofilms and antibiotic therapies. Pulmonologia i allergologia. 2013;(4):60–64. In Russian.
7. **Agarwal V, Golish SR, Alamin TF.** Bacteriologic culture of excised intervertebral discfrom immunocompetent patients undergoing single level primary lumbar microdiscectomy. J Spinal Disord Tech. 2011;24:397–400. DOI: 10.1097/BSD.0b013e3182019f3a.
8. **Albert HB, Lambert P, Rollason J, Sorensen JS, Worthington T, Pedersen MB, Norgaard HS, Vernallis A, Busch F, Manniche C, Elliott T.** Does nuclear tissue infected with bacteria following disc herniations lead to Modic changes in the adjacent vertebrae? Eur Spine J. 2013;22:690–696. DOI: 10.1007/s00586-013-2674-z.
9. **Albert HB, Manniche C.** Modic changes following lumbar disc herniation. Eur Spine J. 2007;16:977–982. DOI: 10.1007/s00586-007-0336-8.
10. **Albert HB, Sorensen JS, Christensen BS, Manniche C.** Antibiotic treatment in patients with chronic low back pain and vertebral bone edema (Modic type 1 changes): a double-blind randomized clinical controlled trial of efficacy. Eur Spine J. 2013;22:697–707. DOI: 10.1007/s00586-013-2675-y.
11. **Arndt J, Charles YP, Koebel C, Bogorin I, Steib JP.** Bacteriology of degenerated lumbar intervertebral disks. J Spinal Disord Tech. 2012;25:E211–E216. DOI: 10.1097/BSD.0b013e318269851a.
12. **Bailly F, Maigne J, Genevay S, Marty M, Gandjbakhch F, Rozenberg S, Foltz V.** Inflammatory pain pattern and pain with lumbar extension associated with Modic 1 changes on MRI: a prospective case–control study of 120 patients. Eur Spine J. 2013;23:493–497. DOI:10.1007/s00586-013-3036-6.
13. **Ben-Galim P, Rand N, Giladi M, Schwartz D, Ashkenazi E, Millgram M, Dekel S, Floman Y.** Association between sciatica and microbial infection: true infection or culture contamination? Spine. 2006;31:2507–2509. DOI:10.1097/01.brs.0000238657.13263.b2.
14. **Bhanji S, Williams B, Sheller B, Elwood T, Mancl L.** Transient bacteremia induced by tooth brushing: a comparison of the Sonicare toothbrush with a conventional toothbrush. Pediatr Dent. 2002;24:295–299.
15. **Butler JS, Shelly MJ, Timlin M, Powderly WG, O'Byrne JM.** Nontuberculous pyogenic spinal infection in adults: a 12-year experience from a tertiary referral center. Spine. 2006;31:2695–2700. DOI: 10.1097/01.brs.0000244662.78725.37.
16. **Carricajo A, Nuti C, Aubert E, Hatem O, Fonsale N, Mallaval FO, Vautrin AC, Brunon J, Aubert G.** Propionibacterium acnes contamination in lumbar disc surgery. J Hosp Infect. 2007;66:275–277. DOI: 10.1016/j.jhin.2007.04.007.
17. **Coscia MF, Denys GA, Wack MF.** Propionibacterium acnes, Coagulase-Negative Staphylococcus, and the "Biofilm-like"Intervertebral Disc. Spine. 2016;41:1860–1865. DOI: 10.1097/BRS.0000000000001909.
18. **D'Agostino C, Scorzolini L, Massetti AP, Carnevalini M, d'Ettorre G, Venditti M, Vullo V, Orsi GB.** A seven-year prospective study on spondylodiscitis: epidemiological and microbiological features. Infection. 2010;38:102–107. DOI: 10.1007/s15010-009-9340-8.
19. **Debelian GJ, Olsen I, Tronstad L.** Electrophoresis of whole-cell soluble proteins of microorganisms isolated from bacteremias in endodontic therapy. Eur J Oral Sci. 1996;104:540–546. DOI: 10.1111/j.1600-0722.1996.tb00139.x.
20. **Doita M, Kanatani T, Harada T, Mizuno K.** Immunohistologic study of the ruptured intervertebral disc of the lumbar spine. Spine. 1996;21:235–241.
21. **Itoh H, Asou Y, Hara Y, Haro H, Shinomiya K, Tagawa M.** Enhanced type X collagen expression in the extruded nucleus pulposus of the chondrodystrophoid dog. J Vet Med Sci. 2008;70:37–42.
22. **Farrar MD, Ingham E.** Acne: inflammation. Clin Dermatol. 2004;22:380–384. DOI: 10.1016/j.clindermatol.2004.03.006.
23. **Fritzell P, Bergstrom T, Welinder-Olsson C.** Detection of bacterial DNA in painful degenerated spinal discs in patients without signs of clinical infection. Eur Spine J. 2004;13:702–706. DOI: 10. 1007/s00586-004-0719-z.
24. **Ganko R, Rao PJ, Phan K, Mobbs RJ.** Can bacterial infection by low virulent organisms be a plausible cause for symptomatic disc degeneration? A systematic review. Spine. 2015;40:E587–E592. DOI: 10.1097/BRS.0000000000000832.
25. **Jarvinen J, Karppinen J, Niinimaki J, Haapea M, Gronblad M, Luoma K, Rinne E.** Association between changes in lumbar Modic changes and low back symptoms over a two-year period. BMC Musculoskeletal Disorders. 2015;16:98. DOI:10.1186/s12891-015-0540-3.
26. **Jensen TS, Karppinen J, Sorensen JS, Niinimaki J, Leboeuf-Yde C.** Vertebral endplate signal changes (Modic change): a systematic literature review of prevalence and association with non-specific low back pain. Eur Spine J. 2008;17:1407–1422. DOI: 10.1007/s00586-008-0770-2.
27. **Lee MJ, Pottinger PS, Butler-Wu S, Bumgarner RE, Russ SM, Matsen FA** 3rd. Propionibacterium persists in the skin despite standard surgical preparation. J Bone Joint Surg Am. 2014;96:1447–1450. DOI: 10.2106/JBJS.M.01474.
28. **Li B, Dong Z, Wu Y, Zeng J, Zheng Q, Xiao B, Cai X, Xiao Z.** Association between lumbar disc degeneration and propionibacterium acnes infection: clinical research and preliminary exploration of animal experiment. Spine. 2016;41:E764–E769. DOI: 10.1097/BRS.0000000000001383.
29. **Matsui H, Kanamori M, Ishihara H, Yudoh K, Naruse Y, Tsuji H.** Familial predisposition for lumbar degenerative disc disease. A case-control study. Spine. 1998;23:1029–1034. DOI: 10.1097/00007632-199805010-00013.
30. **Martin MD, Boxell CM, Malone DG.** Pathophysiology of lumbar disc degeneration: a review of the literature. Neurosurg Focus. 2002;13:E1. DOI: 10.3171/foc.2002.13.2.2.
31. **McLorinan GC, Glenn JV, McMullan MG, Patrick S.** Propionibacterium acnes wound contamination at the time of spinal surgery. Clin Orthop Relat Res. 2005;(437):67–73.
32. **Modic MT, Masaryk TJ, Ross JS, Carter JR.** Imaging of degenerative disk disease. Radiology. 1988;168:177–186. DOI: 10.1148/radiology.168.1.3289089.
33. **Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N.** Magnetic resonance classification of lumbar intervertebral disc degeneration. Spine. 2001;26:1873–1878. DOI: 10.1097/00007632-200109010-00011.
34. **Risbud MV, Fertala J, Vresilovic EJ, Albert TJ, Shapiro IM.** Nucleus pulposus cellsupregulate PI3K/Akt and MEK/ERK signaling pathways underhypoxic conditions and resist apoptosis induced by serum withdrawal. Spine. 2005;30:882–889.
35. **Roberts GJ, Holzel HS, Sury MR, Simmons NA, Gardner P, Longhurst P.** Dental bacteremia in children. Pediatr Cardiol. 1997;18:24–27. DOI: 10.1007/s002469900103.
36. **Stirling A, Worthington T, Rafiq M, Lambert PA, Elliott TSJ**. Association between sciatica and Propionibacterium acnes. Lancet. 2001;357:2024–2025. DOI: 10.1016/S0140-6736(00)05109-6.

37. **Tai CC, Want S, Quraishi NA, Batten J, Kalra M, Hughes SP.** Antibiotic prophylaxis in surgery of the intervertebral disc. A comparison between gentamicin and cefuroxime. J Bone Joint Surg Br. 2002;84:1036–1039. DOI: 10.1302/0301-620X.84B7.12862.
38. **Tolonen J, Gronblad M, Vanharanta H, Virri J, Guyer RD, Rytomaa T, Karaharju EO.** Growth factor expression in degenerated intervertebral disc tissue. An immunohistochemical analysis of transforming growth factor beta, fibroblast growth factor and platelet-derived growth factor. Eur Spine J. 2006;15:588–596. DOI: 10.1007/s00586-005-0930-6.
39. **Videman T, Battie MC, Ripatti S, Gill K, Manninen H, Kaprio J.** Determinants of the progression in lumbar degeneration: a 5-year follow-up study of adult male monozygotic twins. Spine. 2006;31:671–678. DOI: 10.1097/01.brs.0000202558.86309.ea.
40. **Wang Y, Videman T, Niemelainen R, Battie MC.** Quantitative measures of Modic changes in lumbar spine magnetic resonance imaging: intra- and inter-rater reliability. Spine. 2011;36:1236–1243. DOI: 10.1097/BRS.0b013e3181ecf283.
41. **Wedderkopp N, Thomsen K, Manniche C, Kolmos HJ, Secher Je**nsen T, Leboeuf Yde C. No evidence for presence of bacteria in Modic type I changes. Acta Radiol. 2009;50:65–70. DOI: 10.1080/02841850802524485.
42. **Williams JR.** The Declaration of Helsinki and public health. Bull World Health Organ. 2008;86:650–652. DOI:10.2471/BLT.08.050955.
43. **Zhou Z, Chen Z, Zheng Y, Cao P, Liang Y, Zhang X, Wu W, Xiao J, Qiu S.** Relationship between annular tear and presence of Propionibacterium acnes in lumbar intervertebral disc. Eur Spine J. 2015;24:2496–2502. DOI: 10.1007/s00586-015-4180-y.

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