[11] Bettini N, Girardo M, Dema E, Cervellati S. Evaluation of conservative treatment of non specific spondylodiscitis. Eur Spine J. 2009;18. doi:10.1007/s00586-009-0979-8.

[12] Valancius K, Hansen ES, Hoy K, Helmig P, Niedermann B, Bünger C. Failure modes in conservative and surgical management of infectious spondylodiscitis. Eur Spine J. 2013;22:1837–1844. doi:10.1007/s00586-012-2614-3.

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QUESTION 4: How do early and late infectious complications differ following spine surgery?

RECOMMENDATION: Early infections, defined as occurring within 30 days of surgery, often present with local signs of infection such as increased surgical site pain, erythema, warmth and wound drainage. Conversely, late infections (> 90 days after surgery) commonly present with an insidious onset of chronic pain and implant failure/ pseudarthrosis if following a fusion.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 87%, Disagree: 0%, Abstain: 13% (Super Majority, Strong Consensus)

RATIONALE

Postoperative spine infection occurs at a rate of 0.7–16% depending on the procedure; the lumbar spine is the site of 51% of infections [1].

A postoperative infection is classified as early when it occurs within 30 days of the initial surgery. Early infections typically present with increasing back pain (83–100%) as the primary symptom [2,3]. Fever, weight loss, erythema, swelling, warmth, tenderness and elevated white blood cell (WBC) count may also be present, with fever having an incidence of 16–65% [2–4]. One of the most reliable and specific signs of early infection is increased wound drainage (67%) as it can occur in both deep and superficial infections [4].

A postoperative infection occurring three to nine months following surgery can be classified as a late infection. As opposed to early infections, late infections typically present with delayed symptoms such as lack of adequate fusion, chronic pain or implant failure months after surgery [5]. Local symptoms may also occur, including increased pain and tenderness at the incision site. Wound drainage may occur but is less common than in early infections [5].

Complications of postoperative spine infection include impairment of function, significant morbidity and increased health care costs approximating up to $200,000 per patient [1,3]. Increase in hospital stay and increased rates of repeat surgery have also been observed.

Gram-positive bacteria, specifically *Staphylococcus aureus,* are responsible for approximately 45% of spine infections [6]. Other gram-positives such as *Staphylococcus epidermis* and *Enterococcus* as well as gram-negatives *Pseudomonas aeruginosa* and *Escheria coli* have been observed at lower incidences [1,2,6]. There is no clear association between type of surgical procedure and bacteria strain. However, gram-negatives tend to present more commonly in sacral and lumbar regions [6]. Fungal infections may occur in immunocompromised patients. *C. acnes* has recently been identified as another potential causative organism [2]. No significant difference has been observed in the type of organism present in early and late infections.

REFERENCES

[1] Pawar A, Biswas S. Postoperative spine infections. Asian Spine J. 2016;10:176–183.

[2] Chahoud J, Kanafani Z, Kanj S. Surgical site infections following spine surgery: eliminating the controversies in the diagnosis. Front Med (Lausanne). 2014;1:17.

[3] Parchi P, Evangelisti G, Andreani L. Postoperative spine infections. Orthop Rev. 2015;7(3):5900.

[4] Kasliwal MK, Tan LA, Traynelis VC. Infection with spinal instrumentation: review of pathogenesis, diagnosis, prevention, and management. Surg Neurol Int. 2013;4(Suppl 5):S392.

[5] Radcliff K, et al. What is new in the diagnosis and prevention of spine surgical site infections? Spine J. 2015;15:336–347.

[6] Abdul-Jabbar A, et al. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 239 cases. Spine. 2013;38:E1425–E1431.

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QUESTION 5: Are there patients with degenerative pathology, such as disc herniations, who are actually infected with a low-grade infection (e.g., *Propionibacterium acnes*)?

RECOMMENDATION: The association between the *Cutibacterium acnes (C. acnes)* (formerly *P. acnes*) and degenerative spinal disease is inconclusive.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 86%, Disagree: 14%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

The initial connection between potential low-level infection and degenerative spinal pathology was drawn when a group identified over half of discectomies performed for disc herniation as culture positive for *C. acnes* or coagulase-negative *Staphylococcus spp* [1]. A large number of predominantly small studies have since come to opposite conclusions on the connection between these bacteria and degenerative spinal disease, most commonly evaluated radiographically by the presence of Modic changes (examples of those finding no relationship [2–7] versus those finding a correlation [8–12]). One controversial placebo-controlled, double-blinded trial administered extended-duration antibiotic therapy to those patients with Modic type 1 changes and demonstrated better pain resolution in those receiving antibiotics [8].

Recent systematic reviews, each published in 2015, independently concluded that while there was strong evidence from multiple studies that patients undergoing spinal surgery have increased rates of bacteria at the site of degenerative disease of spine, causation between that finding and the pathologic changes resulting in back pain were unclear [1,13,14].

One important cause for heterogeneity in the data is the possibility that microbiologic sampling could be more readily contaminated with bacteria based on differences in surgical and collection technique [3,15]. However, this does not fully explain the fact that in clinical studies, *C. acnes* is consistently the most common, if not only, organism isolated. Recent studies, including control groups of patients not anticipated to have infectious etiologies for their spinal condition, have also noted increased rates of bacterial presence in degenerative disease compared to patients without degenerative disease [2,16]. Methods attempting to disrupt biofilm-encapsulated bacteria have attempted to explain negative culture results from earlier studies [10,17]. Similarly, molecular subtyping of *C. acnes* allows for better characterization of these isolates into those more likely to be routine skin contamination from those more likely to be pathogenic [2,17–19]. These studies have demonstrated a mixture of these subtypes present, with those generally not representing skin flora predominating. Recent studies have additionally investigated histologic methods [20], inflammatory cytokine responses [16,21] and proteomic analysis [22] in addition to bacterial presence as a marker for true infection. Finally, some groups have recently used animal models to attempt to support a connection between bacterial inoculation and symptomatic spinal pathology [23,24].

Though still unverified, there is an enlarging body of evidence using modern techniques and accounting for technical limitations in earlier studies for the role of infection in at least some types of degenerative spinal pathology. A well-designed, multicenter trial effort, which successfully confirms this connection would allow for reasonable consideration of further studies utilizing antibiotic therapy as a non-invasive therapy option for degenerative disc disease.

REFERENCES

[1] Stirling A, Worthington T, Rafiq M, Lambert PA, Elliott TS. Association between sciatica and Propionibacterium acnes. Lancet. 2001;357(9273):2024–2025.

[2] Coscia MF, Denys GA, Wack MF. Propionibacterium acnes, coagulase-negative Staphylococcus, and the "biofilm-like" intervertebral disc. Spine (Phila Pa 1976). 2016;41(24):1860-1865.

[3] Rigal J, Thelen T, Byrne F, Cogniet A, Boissière L, Aunoble S, Le Huec JC. Prospective study using anterior approach did not show association between Modic 1 changes and low grade infection in lumbar spine. Eur Spine J. 2016;25(4):1000–1005.

[4] Arndt J, Charles YP, Koebel C, Bogorin I, Steib JP. Bacteriology of degenerated lumbar intervertebral disks. J Spinal Disord Tech. 2012;25(7):E211–E216.

[5] Wedderkopp N, Thomsen K, Manniche C, Kolmos HJ, Secher Jensen T, Leboeuf Yde C. No evidence for presence of bacteria in modic type I changes. Acta Radiol. 2009;50(1):65–70.

[6] 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 (Phila Pa 1976). 2006;31(21):2507–2509.

[7] Alamin TF, Munoz M, Zagel A, Ith A, Carragee E, Cheng I, Scuderi G, Budvytiene I, Banei N. Ribosomal PCR assay of excised intervertebral discs from patients undergoing single-level primary lumbar microdiscectomy. Eur Spine J. 2017;26(8):2038–2044.

[8] 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(4):697–707.

[9] Albert HB, Lambert P, Rollason J, Sorensen JS, Worthington T, Pedersen MB, Nørgaard 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(4):690–696.

[10] Capoor MN, Ruzicka F, Machackova T, Jancalek R, Smrcka M, Schmitz JE, Hermanova M, Sana J, Michu E, Baird JC, Ahmed FS, Maca K, Lipina R, Alamin TF, Coscia MF, Stonemetz JL, Witham T, Ehrlich GD, Gokaslan ZL, Mavrommatis K, Birkenmaier C, Fischetti VA, Slaby O. Prevalence of Propionibacterium acnes in intervertebral discs of patients undergoing lumbar microdiscectomy: a prospective cross-sectional study. PLoS One. 2016;11(8):e0161676.

[11] 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(11):2496–2502.

[12] Aghazadeh J, Salehpour F, Ziaeii E, Javanshir N, Samadi A, Sadeghi J, Mirzaei F, Naseri Alavi SA. Modic changes in the adjacent vertebrae due to disc material infection with Propionibacterium acnes in patients with lumbar disc herniation. Eur Spine J. 2017;26(12):3129–3134.

[13] 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 (Phila Pa 1976). 2015;40(10):E587–E592.

[14] Urquhart DM, Zheng Y, Cheng AC, Rosenfeld JV, Chan P, Liew S, Hussain SM, Cicuttini FM. Could low grade bacterial infection contribute to low back pain? A systematic review. BMC Med. 2015;13:13.

[15] Javanshir N, Salehpour F, Aghazadeh J, Mirzaei F, Naseri Alavi SA. The distribution of infection with Propionibacterium acnes is equal in patients with cervical and lumbar disc herniation. Eur Spine J. 2017;26(12):3135–3140.

[16] Yuan Y, Chen Y, Zhou Z, Jiao Y, Li C, Zheng Y, Lin Y, Xiao J, Chen Z, Cao P. Association between chronic inflammation and latent infection of Propionibacterium acnes in non-pyogenic degenerated intervertebral discs: a pilot study. Eur Spine J. 2017 Oct 31. [Epub ahead of print].

[17] Capoor MN, Ruzicka F, Schmitz JE, James GA, Machackova T, Jancalek R, Smrcka M, et al. Propionibacterium acnes biofilm is present in intervertebral discs of patients undergoing microdiscectomy. PLoS One. 2017;12(4):e0174518.

[18] Rollason J, McDowell A, Albert HB, Barnard E, Worthington T, Hilton AC, Vernallis A, et al. Genotypic and antimicrobial characterisation of Propionibacterium acnes isolates from surgically excised lumbar disc herniations. Biomed Res Int. 2013;2013:530382.

[19] Achermann Y, Goldstein EJ, Coenye T, Shirtliff ME. Propionibacterium acnes: from commensal to opportunistic biofilm-associated implant pathogen. Clin Microbiol Rev. 2014 Jul;27(3):419–440.

[20] Yuan Y, Zhou Z, Jiao Y, Li C, Zheng Y, Lin Y, Xiao J, Chen Z, Cao P. Histological identification of Propionibacterium acnes in nonpyogenic degenerated intervertebral discs. Biomed Res Int. 2017;2017:6192935.

[21] Dudli S, Miller S, Demir-Deviren S, Lotz JC. Inflammatory response of disc cells against Propionibacterium acnes depends on the presence of lumbar Modic changes. Eur Spine J. 2017 Sep 7. [Epub ahead of print].

[22] Rajasekaran S, Tangavel C, Aiyer SN, Nayagam SM, Raveendran M, Demonte NL, Subbaiah P, et al. ISSLS Prize in Clinical Science 2017: Is infection the possible initiator of disc disease? An insight from proteomic analysis. Eur Spine J. 2017;26(5):1384–1400.

[23] Dudli S, Liebenberg E, Magnitsky S, Miller S, Demir-Deviren S, Lotz JC. Propionibacterium acnes infected intervertebral discs cause vertebral bone marrow lesions consistent with Modic changes. J Orthop Res. 2016 Aug;34(8):1447–1455.

[24] Chen Z, Zheng Y, Yuan Y, Jiao Y, Xiao J, Zhou Z, Cao P. Modic changes and disc degeneration caused by inoculation of Propionibacterium acnes inside intervertebral discs of rabbits: a pilot study. Biomed Res Int. 2016;2016:9612437.