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QUESTION 4: Is there a role for combination antibiotics (i.e., dual or triple) in treating patients with surgical site infection (SSI) following spinal surgery?**RECOMMENDATION:** There is insufficient evidence to recommend the routine use of combination antibiotics in the setting of postoperative spine infections. However, there may be a role for combination antibiotics in certain circumstances related to specific pathogens.**LEVEL OF EVIDENCE:** Consensus**DELEGATE VOTE:** Agree: 87%, Disagree: 13%, Abstain: 0% (Super Majority, Strong Consensus)**RATIONALE**

The incidence of postoperative spine infection has been reported as between 0.7 and 16%, with higher rates noted in procedures with hardware implantation [1,2]. The most common organisms isolated are *Staphylococcus aureus*, *Staphylococcus epidermidis*, methicillin-resistant *S. aureus* and *Enterococcus*. Up to 20 to 30% of infections are noted to be poly-microbial [3,4].

Antibiotic treatment is directed at the isolated micro-organism/s and usually only a single anti-microbial agent is used. There are a few reports of dual antibiotic therapy with rifampin, the most common additive agent [3,5]. Rifampin is chosen due to its ability to penetrate biofilms associated with implant-related infections [6]. Evidence from a mouse model has shown that the addition of rifampin to vancomycin led to an increase in bacterial death, but no change in the final outcome from the SSI [7]. There are no clinical studies comparing the use of single to multi-agent antibiotic therapy for postoperative spine infections.

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QUESTION 5: How long should antibiotics be administered after surgical debridement for an acute postsurgical spinal infection?**RECOMMENDATION:** For vertebral osteomyelitis: Initial intravenous treatment for one to two weeks, followed by an oral treatment of four to five weeks to reach a total treatment duration of six weeks.

For deep surgical site infections: There is limited knowledge about the ideal duration of antibiotic treatment and which intravenous and/or oral agents should be given. As extrapolated from studies in periprosthetic joint infections (PJIs) and retrospective studies in spine infections, 12 weeks of antibiotic treatment can be recommended in cases with early infection and implant retention, six weeks if the implant is removed and prolonged suppressive treatment in delayed infections without removal of the implant.

LEVEL OF EVIDENCE: Moderate for vertebral osteomyelitis. Limited for surgical site infections after spine surgery**DELEGATE VOTE:** Agree: 80%, Disagree: 13%, Abstain: 7% (Super Majority, Strong Consensus)**RATIONALE****Vertebral Osteomyelitis**

In vertebral osteomyelitis (spondylodiscitis) without an implant, experts recommend a treatment duration of 6 to 12 weeks [1]. However, a retrospective study over 10 years by Roblot et al. [2] found no difference in relapse rate between 6 and 12 weeks of treatment [2]. An open label, non-inferiority, randomized, controlled trial by Bernard et al. first showed that 6 weeks was not inferior to

12 weeks. In both groups, intravenous treatment was only given for a median time of 14 to 15 days followed by an oral fluoroquinolone and rifampin combination or aminopenicillin (both regimens with high oral bioavailability) [3]. The authors could not see a difference in the proportion of treatment failure between patients given intravenous treatment for more than one week and those for less than one week.

Postsurgical infection with an implant

There are many studies in this field regarding optimal treatment duration and agents in spinal implant-associated infections, but they are all retrospective with low levels of evidence. There are no up-to-date prospective and/or randomized studies published investigating the optimal duration of antibiotic treatment and the role of oral antibiotics in implant-associated spinal infections.

Most studies demonstrated successful treatment of spinal implant-associated infections with a total duration of six weeks [4–6]. If implants are not removed, reported durations of treatment are up to 12 weeks with intravenous treatment for six weeks, followed by oral antibiotic treatment for another six weeks [7,8].

Yet, regarding duration of intravenous treatment, there are no clear recommendations. Some studies treat intravenously for a prolonged time for up to four [8–10] or six weeks [4,11–13]. But there are also retrospective studies in which intravenous treatment was given for two weeks or less followed by oral antibiotics with good oral bioavailability [14]. Billieres et al. did a multivariate analysis on risk factors for relapse of infection and did not find an association with duration of total or intravenous antibiotic treatment [14]. Another study by Kowalsky et al. also concluded that duration of intravenous treatment is not a risk factor for acute chronic infections [15].

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QUESTION 6: How long should antibiotics be continued when spinal wounds are left to heal by secondary intention?

RECOMMENDATION: Only standard perioperative antibiotic prophylaxis is recommended.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 93%, Disagree: 0%, Abstain: 7% (Super Majority, Strong Consensus)

RATIONALE

Following spine surgery, surgical wounds are normally closed via primary intention where all tissue is fastened closed with sutures, staples, glue or some other form of closure material. In rare cases, however, wounds are left to close naturally via secondary intention. Normally, this is done in cases where the risk of persistence of infection is high or when a large gap in soft tissue exists as a result of tissue loss.

Antibiotic prophylaxis has been shown to be useful in preventing infection following spine surgery. However, no specific agent or schedule has been identified as superior over any other [1].

In a randomized, blinded, controlled study, Gupta et al. found that topical antibiotics, specifically sucralfate, increased wound healing in patients at four weeks following hemorrhoidectomy left to heal via secondary intention when compared to placebo (78% compared to 52%) [2]. In contrast, Doung et al. found that the use of trimethoprim-sulfamethoxazole in pediatric skin abscess treatment

compared to placebo did not significantly affect the recurrence of new lesions in the long term [3].

A systematic review by Norman et al. found that no robust evidence exists on the relative effectiveness of any antibiotic preparation in cases where surgical wounds have been left to heal by secondary intention [4]. There is no high-level evidence directly related to spine surgery for this topic. In general, if there is hardware present, patients often should receive at least six weeks of intravenous antibiotics and continued suppressive antibiotics until the wound heals.

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