series. Large et al. reported four cases of deep infection. Two were positive for *Staphylococcus aureus*, one for *Staphylococcus epidermidis* (*S. epidermidis*) and one with no growing organism but a clinical diagnosis of infection [4]. Antuña et al. reported on the outcome of semiconstrained TEA after fracture of the distal humeral and observed 3 infections in 16 patients, 2 being positive for *S. epidermidis* and 1 having negative cultures [5].

Peden et al. reported on the outcome for TEA for an ankylosed or fused elbow, reporting 3 infections out of 13 cases. One occurred perioperatively and the other occurred at 2 and 15 years. Two cases were diagnosed with *Staphylococcus coagulase negative methicillin-resistant* and *S. aureus* [6]. Tachihara et al. reported on the outcome for TEA for rheumatoid arthritis and reported on three infections positive for *enterobacter*, *pseudomona* and *S. aureus*. In all of those cases, the infection was considered monobacterial [7].

Curiously, in a clinical series reporting on 20 elbows diagnosed with periprosthetic joint infection, Streubel et al. reported that 6 out of 21 infections were polymicrobial [8]. In that series, the most frequent pathogen was S. Coagulase-negative (13 patients) followed by *S. aureus* (9 patients) and *Corynebacterium* (3 patients). These patients were initially treated with vancomycin in 10 cases, cefazolin in 8, rifampin in 3 and ceftriaxone in 1 case [8]. This information is in accordance with other studies, although there is a risk of a partial duplicate patient population. In a group of 51 patients, Zarkadas et al. found 17 cases of *S. aureus*, 11 of *S. epidermidis*, 1 of *Serratia*, 1 of *Costiridium*, 1 of *Mycobacteria*, 1 of *C. acnes*, 10 multiorganism infections and 8 cases in which no bacteria was actually grown [9].

Although they are obviously universally used, only 4 of the 35 studies specified the use of prophylactic antibiotics. Of these, only 2 mentioned in their methods the type and dose of antibiotic (a first-generation and a second-generation cephalosporin prior to skin incision in both) [10,11]. Kodde et al. reported the use of 1 gm of intravenous cefazolin 30 minutes prior to skin incision and extended the use for 48 postoperative hour [10]. Lami et al. reported the use of systematic prophylactic antibiotic at induction using a second-generation cephalosporin with no further description. No other information regarding the duration of perioperative antibiotic therapy has been found.

Discussion

The available information is poor regarding infection as a complication after elbow replacement. Specific information on the pathogen, the type and dose of prophylactic antibiotic or the surgical prepping solutions used in cases complicated with an infection after elbow replacement are almost universally lacking in the analyzed studies. The reasons for this are unclear, but might be related to wording restrictions and focus on other aspects of research. Moreover, a definition of infection was not reported and different authors could have used different definitions.

Even though only four studies specified the use of prophylactic antibiotics, we assume these are universally used. Based on the scarce information found and our own clinical experience, first-generation cephalosporin seems to be the most widely used antibiotic. Other options could be used, based on allergies, intolerance or concomitant diseases. However, no sound conclusion can be extracted from literature on this regard.

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Authors: Pierre Mansat, Bernard Morrey

QUESTION 2: What is the evidence and recommendation for the use of antibiotic-laden bone cement (ALBC) in primary total elbow arthroplasty (TEA) or in revision TEA?

RECOMMENDATION: There is inadequate evidence to support the use of ALBC during primary or revision TEA.

LEVEL OF EVIDENCE: Consensus

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

The response to the question regarding the value of ALBC in a primary and revision setting of TEA requires an understanding of several issues:

1. The specific answer to these questions referable to the elbow cannot be directly answered from the available literature addressing the elbow. Very little information exists for the

elbow, regardless of the level of evidence [1].

2. The clinical features of elbow pathology by definition place all TEAs "at risk," including the underlying diagnosis (a systemic inflammatory disorder or failed intervention for a post-traumatic condition). Primary osteoarthritis is not an indication for TEA as it is effectively treated with debridement. TEA for primary arthrosis was only performed in 18 patients over a 20-year period at the Mayo Clinic, representing about a 2% incidence in our institution [2].
3. Even the less common inflammatory etiology is at particular risk due to the virtual universal management with the immunocompromising disease remitting agents.
4. The subcutaneous location of the joint with little or no muscle protection places it at risk for wound healing problems, which has been documented to increase the likelihood of infection [3,4].
5. The subcutaneous nature and the less robust osseous structure of the elbow increases the complication rate of revision for infection, especially compromising triceps function in more than 25% of patients. In other words, the management of infection by surgical means is poorly tolerated at the elbow (level 4 and 5 evidence) [4].
6. The above observations are supported by the documented infection rate of the primary TEA to be around 5% (3) compared to 1–2% associated with primary hip or knee replacement, but similar to the infection rate of the revision procedures on these joints [4,5].
7. Finally, all the higher-quality literature on the subject relates only to knee and hip replacement with the preponderance of data relating to the knee.

Methodology

The question was addressed in the context of the above and the current literature relating to hip and knee surgery, primarily over the last 10 years. A PubMed literature review was conducted exploring level 1 and 2 randomized control trials, meta-analyses and national registry data. As noted above, all such studies relate only to hip and knee replacement. This review prompted a need for more detail in some instances, followed by level 3 and 4 case series and reports being included.

RESULTS

Use of ALBC in the Primary Total Knee Arthroplasty

- Currently, no conclusive evidence exists regarding the efficacy of antibiotic-loaded cement at the knee in uncomplicated, non-risk patients [6–11].
- Currently, based on the highest-level studies, no recommendation can be made regarding the routine use of antibiotic-loaded cement in primary knee arthroplasty.
- The justification is further weakened by poor cost-effectiveness data for primary knee [12,13], yet primary hip replacement may be cost-effective [14].
- As noted above, this recommendation has no bearing on the question at hand, as by definition all primary TEAs occur in an at-risk population.
- Consensus does exist that ALBC should be used in patients with a high risk of infection (Obesity, body mass index > 35, diabetes mellitus, revision total joint arthroplasty, operative time > 150 minutes, rheumatoid arthritis, a prior history of periprosthetic joint infection, organ transplantation and hemophilia) [5,6,15].

Use of ALBC in Hip Replacement Surgery

- Evidence [16–18], and consensus [19,20] is strong indicating that ALBC does statistically lessen the likelihood of infection after a primary hip replacement, independent of the at-risk patient [21–23].
- Evidence also indicates that ALBC decreases the incidence of deep infections at the hip and at the knee [24] and in hemi-replacement of the hip after fracture [25].
- Therefore, should antibiotic-impregnated cement be used:
  - **A. For primary TEA? Yes, based on:**
    1. Strong evidence supporting its use in primary hip replacement
    2. Strong consensus for ALBC in the at-risk patient and the features of the elbow defining it as an at-risk joint

    Confidence: Extrapolated: moderate; subjective: strong. 100%.
  - **B. For revision TEA? Yes, based on:**
    1. Moderate evidence for effectiveness in revision knee and hip surgery [5,26]
    2. Infection rate of revision TEA exceeds hip and knee revision, as well as increased difficulty and complication rates when treating an infected TEA [27]

    Confidence: Strong. 100%.

Additional Questions to Consider

1. **Which antibiotics(s) should be used?**
   - For primary and revision, combination therapy is recommended (total of 2 gm/40 gm monomer).
   - An aminoglycide, either 1 gm/40 gm cement gentamycin or tobramycin (tobramycin is much more expensive) and 1 gm/40 gm vancomycin.
   - Target likely-offending organisms [6]. Over the last 15 years in 231 infected elbows treated at Mayo Clinic: Coag – Staph – 22%; Staph A. 14% (data generated for this review – JSS).
   - A single low-dose gentamycin cement (1 gm/40 gm cement) may actually select an increase in coag – infections [6].
2. **Which cement should be used?**
   Palacos has better elution properties, but this does not seem to matter clinically.
3. **Will bacterial resistance develop?**
   No evidence of this to date [28].
4. **Will the altered mechanical properties of the cement affect loosening rate**?
   No evidence of this to date.

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Authors: Raul Barco Laakso, Samuel Antuña

QUESTION 3: Does previous surgery (arthroscopic, fracture fixation, other non-arthroplasty) increase the risk of subsequent elbow periprosthetic joint infection (PJI) after total elbow arthroplasty (TEA)?

RECOMMENDATION: There is an apparent increase in the percentage of infections among patients with a previous operation in the affected elbow joint, though the association is not robust and needs to be further analyzed.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A comprehensive literature search of three online databases (PubMed/Medline, the Cochrane database for clinical trials, and Embase) was performed using the following MeSH search terms: "elbow," "elbow joint," "joint prosthesis," "arthroplasty," "replacement," "elbow replacement," "elbow arthroplasty" and "elbow prosthesis."

Because of the evolution of TEA techniques, only articles published from January 2000 until September 2018 were reviewed. By the titles and abstracts, two reviewers independently identified potentially relevant articles for review of the full text. The reference lists of the included articles were manually checked to avoid missing relevant articles. When the entire text was obtained, the authors independently selected articles. Studies were not blinded for author, affiliation or source.

Inclusion and Exclusion Criteria

The included articles presented original data on patients who had undergone TEA. The diagnoses included the following indications: osteoarthritis, trauma/fracture, post-traumatic osteoarthritis, rheumatoid arthritis, hemophilia and other inflammatory diseases. Studies with a minimum duration of follow-up of two years and a minimum of five patients were included. Studies on revision operations were not included. Articles presenting the results of both revision and primary TEA were excluded unless the information for primary TEA could be extracted. Articles presenting the results for interposition arthroplasties, fully-hinged prostheses, hemiarthroplasty or partial resurfacing of the elbow were reviewed if they included information regarding the outcome of further treatment