Adverse Events Related to Use of Antibiotic-Impregnated Materials in Treatment of Prosthetic Joint Infections

as Reported by a National Network of Infectious Diseases Consultants

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ABSTRACT

BACKGROUND: Use of antibiotic-impregnated materials, including antibiotic beads, cement or impregnated spacers, in the treatment of prosthetic joint infections (PJIs) is almost universal. These materials require hand mixing of cement and antibiotics at the time of implantation, so drug(s) and dosages vary greatly. Although these materials are generally considered to be safe, there are no studies that specifically address safety and these devices have not been evaluated or approved by the FDA. Despite a few anecdotal reports of toxicity, the actual frequency of adverse events resulting from these materials is unknown.

OBJECTIVE: To determine the frequency of adverse events associated with use of antibiotic-impregnated materials in the treatment of PJIs as reported by a national network of infectious diseases consultants (IDCs).

METHODS: 994 IDCs who are members of the Emerging Infections Network (EIN) were surveyed regarding their practices in the diagnosis and therapy of PJIs. Members were also queried about any observations of adverse effects associated with the use of antibiotic-impregnated material to treat PJIs.

RESULTS: 360 of the 545 respondents (55% overall response rate) stated they were never or rarely asked for input regarding use of antibiotic-impregnated materials. The antibiotics used most commonly are aminoglycosides (25%) or vancomycin (14%) alone, but more commonly these are used in combination (60%). Adverse reactions due to use of these impregnated materials were reported by 49 IDCs (11%), most commonly nephrotoxicity (by 15) related to aminoglycoside use, followed by skin reactions (by 9) related to vancomycin or cephalosporin use. Skin reactions included: toxic epidermal necrolysis (by 2 IDCs; 1 related to vancomycin in cement and 1 related to tobramycin in cement), rash (by 2) and rash related to vancomycin allergy (by 5). Measurable antibiotic levels for sustained periods of time (i.e., weeks) were mentioned by 3 IDCs.

CONCLUSIONS: Advice from infectious diseases consultants is rarely sought for selection or dose of antibiotics used in antibiotic-impregnated materials. The respondents' reports of toxicity related to antibiotic-impregnated material were significant, and the safety of these materials needs to be further studied. Development of a registry tracking the safety of these materials should be investigated

INTRODUCTION

- **The number of primary joint replacements (hips and knees) has increased steadily in recent years and is projected to increase further by the year 2030 (hips 174, knees 673%).**
- **Although the infection rate after primary joint replacement is low (around 1% for both hips and knees), the demand for revision procedures is projected to double for hips and knees by the year 2026 and 2015, respectively.**
- **The burden of prosthetic joint infections will likely increase as both the number of primary joint replacements and revisions increase.**
- **Although the medical and surgical approach to prosthetic joint infections vary greatly, the use of local antibiotics in the form of antibiotic impregnated materials (cement, joint spacer or beads) is almost universal.**
- **Hand mixing of antibiotic and cement (or other materials used) is required at the time of surgery as no commercial products are available. The drug(s) and dosages chosen may vary be institution and surgeon.**
- **Although generally considered a safe practice, there are anecdotal reports of toxicity from the use of these materials.**
- **With increasing numbers of prosthetic joint revisions, complications from use of antibiotic-impregnated materials may also increase.**
- **The objective of the survey was to determine the frequency of adverse events associated with the use of antibiotic-impregnated materials in the treatment of prosthetic joint infections as reported by a national network of infectious disease consultants.**

METHODS

- **In July 2008 a survey (see below) was distributed to 994 infectious disease consultants who primarily see adult patients in the United States.**
- **The survey contained two focus areas; (1) the management of prosthetic joint infections and (2) potential toxicities related to the use of antibiotic-impregnated materials.**

FIGURE 1
Sample of the survey.

EMERGING INFECTIONS NETWORK QUERY

Treatment of Prosthetic Joint Infections
Name: _____

1. Have you treated any patients with prosthetic joint infections in the past year?
☐ No, *proceed to question 10.*
☐ Yes, *circle number*: 1-5 6-25 26-50 51-100 >100

2. How common are the following approaches to prosthetic joint infections in your institution(s)?

☐ *Do not know*	Never	Rarely	Occasionally	Often	Always
Retention of prosthesis	☐	☐	☐	☐	☐
Single stage procedure	☐	☐	☐	☐	☐
Two stage procedure	☐	☐	☐	☐	☐

3. Please indicate when you are consulted during treatment of prosthetic joint infections:

	Never	Rarely	Occasionally	Usually
At diagnosis	☐	☐	☐	☐
Perioperatively	☐	☐	☐	☐
Following surgery	☐	☐	☐	☐
Following discharge (outpatient basis)	☐	☐	☐	☐

Retention of Infected Prosthesis

4. Under what circumstances would you support antibiotic treatment with prosthesis retention?
☐ None; *skip to question 6.* *[Check any that apply]*
☐ Availability of a safe oral antibiotic
☐ Highly susceptible organism
☐ Poor surgical risk
☐ Early presentation postoperatively
☐ Other, *specify*: _____

5. Under what circumstances would you consider stopping oral suppressive therapy in a patient who has resolution of joint symptoms? *[Check any that apply]*
☐ Never (lifelong suppression)
☐ After a minimum period of time, *specify:* ___
☐ Normalization of inflammatory parameters
☐ Other, *specify*: _____

Two Stage Procedure for Replacing Infected Prosthetic Joints

6. How long do you recommend treating after infected prosthesis removal and before implanting a new prosthesis? *[Circle]* <2 weeks 2-4 weeks >4-6 weeks >6 weeks

7. Have you found it useful to follow CRP or ESR to evaluate progress in treating an infected prosthetic joint?
☐ No ☐ Yes

8. What minimum length of time off of antibiotics do you recommend prior to joint reimplantation? *[Circle]* None <7 days 7-14 days 15-28 days >28 days

9. Do you recommend any of the following at your institution? *[Check all that apply]*

	Yes	No	Not routinely available
Sonication of removed prosthesis	☐	☐	☐
Grind up cement from removed prosthesis	☐	☐	☐
Tissue biopsy (frozen section) before reimplantation	☐	☐	☐
Joint aspirate for culture before reimplantation	☐	☐	☐

Use of Antibiotic Impregnated Beads/Cement for Spacers/Joint Reimplantation
Check here ☐ if your institution never uses antibiotic-impregnated materials during surgical treatment of prosthetic joint infections.
Check here ☐ if you do not know.

10. Is ID input requested on antibiotic selection/dosage before use of these materials?
☐ Never ☐ Rarely ☐ Occasionally ☐ Often ☐ Always

11. Most commonly, which antibiotics are used in joint/spacer cement?
☐ Aminoglycoside ☐ Vancomycin ☐ Other, *specify*: _____

12. Have you personally seen toxicity attributable to antibiotics from impregnated materials?
☐ No
☐ Yes, *specify toxicity, antibiotic & type of impregnated material (e.g., PMMA beads, cement):*

13. Do you have comments about prosthetic joint infections or this survey?

Thank you for completing this survey.

RESULTS

- **Overall response rate: 545 of 994 (54.8%) of infectious disease consultants responded. Not all respondents answered all questions, so totals for individual questions vary.**
- **The most common time points Infectious disease consultant were usually asked to be involved early in the care with prosthetic joint infections were at the time of diagnosis (259, 59%) or around the time of surgery (114, 27%).**
- **Majority of respondents (360, 79%) stated they were never or rarely asked for input regarding use of antibiotic-impregnated materials.**

FIGURE 2
Treatment experience of infectious disease consultants noted as patient treated within the previous year

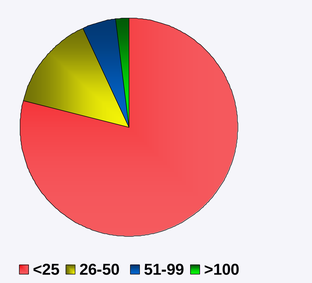

FIGURE 3
Antibiotics most commonly used to impregnate orthopedic material (cement, beads, joint spacers)

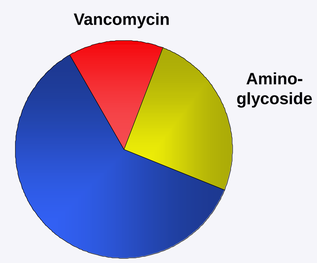

TABLE 2
Breakdown of adverse events noted by infectious disease consultants (49, 11%).

ADVERSE EVENT	FREQUENCY (%)	IMPLICATED ANTIBIOTIC
Nephrotoxicity	15 (31%)	Aminoglycoside
Skin reaction	9 (18%)	Vancomycin, cephalosporin
Ototoxicity	1 (2%)	Aminoglycoside
Thrombocytopenia	1 (2%)	Vancomycin
Mechanical complication (erosion of skin by beads)	1 (2%)	Vancomycin
Measureable blood level for extended period of time (weeks)	3 (6%)	Aminoglycoside
Did not specify adverse event	19 (39%)	

CONCLUSIONS

- **Advice from infectious diseases consultants is rarely sought for selection or dose of antibiotics used in antibiotic-impregnated materials.**
- **The respondents' reports of toxicity related to antibiotic-impregnated material were significant. Nephrotoxicity related to aminoglycoside use and skin reactions related to vancomycin or cephalosporin use were the most common adverse events.**
- **The safety of these materials needs to be further studied. Development of a registry tracking the safety of these materials should be investigated**