Retrospective Audit of Prophylactic Use of Antibiotic-Containing Bone Cement for Primary Total Hip and Knee Arthroplasty in the Calgary Health Region

Deana M Sabuda, Charmaine Clark, and Andrew L Pattullo

ABSTRACT

Background: Total hip and knee replacements are among the most common orthopedic procedures performed. Although the rate of deep infection after primary arthroplasty is relatively low, infection can lead to significant morbidity and both direct and indirect costs. Antibiotic-containing bone cement has therefore been used to prevent infections after joint replacement procedures, although there are no established guidelines for this practice.

Objective: To determine the proportion of orthopedic surgeons in the Calgary Health Region who used antibiotic-containing bone cement as prophylactic therapy in conjunction with primary hip and knee arthroplasty, to identify which antibiotics were used and in what amounts, and to determine patient-related factors that might have influenced the use of such therapy.

Methods: A descriptive, retrospective chart audit was conducted for procedures performed between March and May 2006. Data were collected for up to 4 hip and 4 knee arthroplasty procedures for each of 14 orthopedic surgeons.

Results: Eleven (79%) of the 14 surgeons who performed the majority of primary arthroplasties used antibiotic-containing bone cement at premixed concentrations. Of the 109 patients whose charts were reviewed, 65 (60%) had received prophylactic therapy with an antibiotic-containing bone cement during the arthoplasty procedure. Patients with at least one immune-status risk factor were significantly more likely to receive this type of therapy than patients with no identified immune-status risk factors (p < 0.001).

Conclusion: Orthopedic surgeons in the Calgary Health Region did not follow a standardized practice for the selection of antibiotic-containing bone cement as primary prophylaxis for hip and knee arthroplasty. Rather, practice appeared to be based on individual preference. The reasons for selection of particular products could not be determined from this study.

RÉSUMÉ

Contexte : L'arthroplastie totale de la hanche et du genou sont parmi les chirurgies orthopédiques les plus pratiquées. Bien que le taux d'infection profonde après une arthroplastie primaire soit relativement faible dans la pratique d'aujourd'hui, l'infection peut entraîner une morbidité importante ainsi que des coûts directs et indirects. Le ciment orthopédique additionné d'antibiotiques est utilisé pour prévenir les infections secondaires à une arthroplastie, bien qu'il n'existe aucune ligne directrice définie sur son utilisation.

Objectif : Déterminer la proportion de chirurgiens orthopédistes du Calgary Health Region qui ont recours au ciment additionné d'antibiotiques à titre prophylactique dans le cadre d'une arthroplastie primaire de la hanche et du genou, dresser la liste des antibiotiques utilisés et de leur dose, et établir les facteurs liés aux patients qui pourraient influer sur le recours à ce traitement prophylactique.

Méthode : Un audit descriptif et rétrospectif des dossiers médicaux a été mené entre les mois de mars et mai 2006. Les données ont été collectées sur un total d'au plus quatre arthroplasties de la hanche et quatre du genou pour chacun des 15 chirurgiens orthopédistes.

Résultats : Onze (79 %) des 14 chirurgiens qui ont pratiqué la majorité des arthroplasties primaires ont eu recours à un ciment additionné d'antibiotiques à des concentrations prémélangées. Des 109 patients dont les dossiers médicaux ont été analysés, 65 (60 %) ont reçu un traitement prophylactique au moyen de ciment additionné d'antibiotiques durant l'arthroplastie. Les patients qui présentaient au moins un facteur de risque immunitaire étaient significativement plus susceptibles de recevoir cette prophylaxie que ceux qui n'en présentaient pas (p < 0,001).

Conclusion : Les chirurgiens orthopédistes du Calgary Health Region ne suivent pas de lignes directrices communes dans le choix du ciment additionné d'antibiotiques utilisé comme traitement prophylactique primaire de l'arthroplastie de la



Key words: antibiotic-containing bone cement, surgical prophylaxis

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INTRODUCTION

Judicious use of perioperative antibiotics and advances in the design of operating theatres have helped to reduce the incidence of infection after primary total hip and knee replacement to 1.5% and 2.5%, respectively.¹ However, deep infection involving a prosthetic joint can be a serious complication. What begins as clean, elective surgery can be associated with a devastating outcome such as loss of joint function, bacteremia, osteomyelitis, or amputation. Patients with chronic infections of the joint space may experience significant morbidity because of subsequent surgical procedures that may be required, immobilization, and long-term IV administration of antibiotics, all of which are associated with high direct and indirect costs.

The incorporation of antibiotic into bone cement for joint replacement surgery is a strategy that began in Europe in the 1960s as an attempt to reduce the rate of infection at surgical sites.² The use of antibiotic-containing bone cement (ABC) has been controversial, because of limited evidence of efficacy, concerns about safety, and potential effects on antibiotic resistance.3,4 Prospective randomized controlled trials using ABC have been small or were conducted decades ago. The most widely quoted data are observational results from large Swedish and Norwegian arthroplasty registries, which showed a beneficial effect on revision rates,⁴ although some have argued that the impact on the already-low absolute rate of infection has been minimal. Nevertheless, premixed, commercially available ABCs are now marketed in North America and are classified as class 3 medical devices (not drugs) in Canada.

The Calgary Health Region is a major referral centre for hip and knee arthroplasty, serving a population base of 1.2 million people in the southern and southeastern regions of Alberta. About 1680 primary hip and knee arthroplasty procedures were performed in 2004 at the region's 3 urban acute care hospitals (D. Hawkins, Senior Analyst, Health Systems Analysis, Calgary Health Region; personal communication by telephone, December 14, 2005). On occasion, staff pharmacists are asked to provide antibiotic powder for incorporation into bone cement during orthopedic procedures, and hanche et du genou. Le choix semble plutôt reposer sur les préférences individuelles. Il a été impossible de cerner les raisons sous-tendant le choix d'un produit particulier.

Mots clés : ciment orthopédique additionné d'antibiotiques, prophylaxie chirurgicale

this practice raised the question of how these antibiotics were being used. Dialogue among pharmacists across Canada through an infectious diseases electronic discussion group indicated that the use of ABCs in orthopedic surgery is a topic of high interest and that practice patterns are poorly known.

It was hypothesized that given the lack of guidelines in the literature for the use of ABC with hip and knee arthroplasty, there would be no common practice among orthopedic surgeons in the Calgary Health Region. The objectives of this audit were therefore to quantify the prophylactic use of ABC for primary total hip and knee arthroplasty and to determine if orthopedic surgeons differed with respect to choice of antibiotic and amount incorporated into bone cement for these procedures. Finally, for orthopedic surgeons who used ABC inconsistently for these procedures, a further objective was to identify any patient factors that might be influencing their choices.

METHODS

Given the time and budgetary constraints of a pharmacy residency project, it was feasible to retrospectively audit a total of about 120 medical records from any of the 3 hospitals in the region, as a convenience sample. Approval was granted by the Conjoint Health Research Ethics Board of the University of Calgary on February 9, 2006, and data were collected and summarized by mid-June 2006.

Of the 44 orthopedic surgeons on staff in the region, 15 focused on knee and hip arthoplasty and had a primary affiliation with the Subdivision of Joint Reconstruction. The practice of these subspecialists was of most interest, and each was assigned a unique identifier letter to allow stratification by surgeon. The hospital site where each procedure was performed was deemed to be of lesser importance, so there was no stratification by site; instead, the practice of each of the surgeons was simply followed sequentially, regardless of where the operations were performed.

Working with a proposed maximum of 120 charts for review, 4 knee and 4 hip procedures were sought for each of the 15 surgeons. The Department of Quality,



	No. (%) of Patients*					
Characteristic	All Pat	ients (<i>n</i> = 109)	Patients Who Received Antibiotic Bone Cement (<i>n</i> = 65)			
Age (mean and range)	70	(32–91)	69	(48–85)		
Sex (female)	71	(65)	36	(55)		
Comorbidity						
Osteoarthritis	96	(88)	34	(52)		
Rheumatoid arthritis	9	(8)	1	(2)		
Diabetes mellitus	17	(16)	6	(9)		
Chronic renal insufficiency	4	(4)	2	(3)		
Inflammatory bowel disease	1	(1)	0	(0)		

Table 1. Demographic Characteristics of Patients in an Audit of Prophylactic Use
of Antibiotic-Containing Bone Cement for Arthroplastic Surgery

*Except where indicated otherwise.

Safety and Health Information (QSHI) was asked to provide a list of all adult patients who had undergone a primary, cemented total hip (dual component, using bone cement alone or combined with bone graft) or knee (tri-component, using bone cement alone or combined with bone graft) arthroplasty procedure at any of the 3 tertiary care hospitals, and a list of patients' medical record numbers was generated. Given the high probability of seasonal coverage, the summer months were avoided, and a 3-month block of time (March to May 2006) was chosen; this period was recent, and there was also a high probability that medical records would be complete and accessible. Consecutive operative reports from the list were screened and selected according to the surgeon who had performed the arthoplasty (not the admitting or discharging surgeon) and the procedure that had been performed (as recorded in operating room data, rather than QSHI data) until data on 8 procedures per surgeon had been found. Each of the medical records was reviewed by a single investigator (C.C.) to determine the patient's age, sex, weight, height, allergy status, and baseline creatinine level; the use of bone cement (type, quantity, and concentration of antibiotic if an ABC was used); the hospital site of the procedure; the patient's history of smoking tobacco and comorbid conditions (diabetes mellitus, rheumatoid arthritis, inflammatory bowel disease, chronic renal insufficiency); and the patient's use of concurrent immunosuppressive medications.

The data were entered into a Microsoft Excel spreadsheet, which was used to generate descriptions of aggregate data and to allow comparison of the various patient characteristics. A 2-tailed Fisher's exact test for significance was applied to compare unpaired groups, as appropriate. No external funding was secured for this descriptive, exploratory audit.

RESULTS

Because of coding inaccuracies, a total of 380 consecutive operative reports were hand-screened to generate the desired sample size. In particular, the orthopedic surgeon who performed the procedure was often different from the attending physician listed by QSHI, and the procedure performed was often different from the procedure code listed by QSHI. Limits of time and physical space (in the medical records department) precluded random sampling of patients treated by each subspecialist. In the 3-month study period, data for equal numbers of total hip and knee replacements were sought for each of the 15 orthopedic surgeons who performed the majority of primary hip and knee procedures in the Calgary Health Region; however, data for 1 surgeon could not be found. Further, for one of the surgeons (identified by letter E), only 5 operative reports for the predefined period could be found. Therefore, a total of 109 charts were reviewed in detail and were included in the analysis.

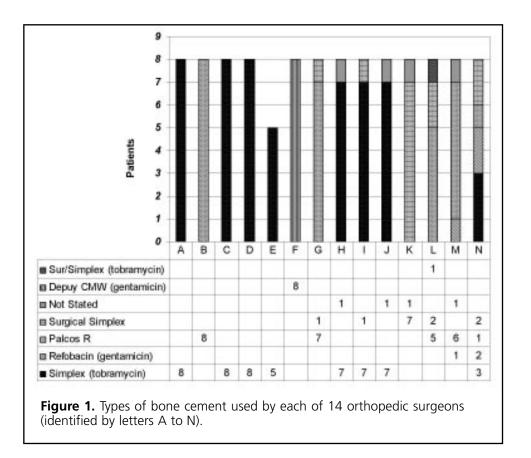
Sixty-five (60%) of the 109 patients received bone cement that contained antibiotic. Osteoarthritis was common in both the overall sample and the subset of those who received ABC (Table 1). Aggregate QSHI data were used to calculate the mean and median American Society of Anesthesiologists (ASA) score for all patients who underwent primary total hip or knee arthroplasty at all 3 hospital sites during the study period. The ASA score, a preoperative rating of the patient's general health status and coexisting conditions, ranges from 1 (healthy) to 5 (not expected to survive longer than 24 h)⁵; both the mean and median scores for all patients were 2 (M. Brandt, Consultant, Health Outcomes, Calgary Health Region; personal communication by telephone, December 21, 2007).



Type of Bone Cement (Manufacturer)	Antibiotic	Concentration of Antibiotic (w/w)	No. (%) of Procedures	
Containing antibiotic				
Simplex P (Stryker, Rutherford, NJ)	Tobramycin	1 g/40 g	53	(49)
DePuy CMW 1 (Johnson & Johnson, New Brunswick, NJ)	Gentamicin	1 g/40 g	8	(7)
Refobacin Palacos R (Biomet, Warsaw, IN)	Gentamicin	0.5 g/40 g	3	(3)
Not containing antibiotic				
Palacos R (Zimmer, Inc, Warsaw, IN)	NA	NA	27	(25)
Simplex P (Stryker, Rutherford, NJ)	NA	NA	13	(12)
Multiple products*	NA	NA	1	(1)
Not stated	NA	NA	4	(4)

Table 2. Types of Antibiotic Bone Cement Used for Hip and Joint Arthroplasty

*For one procedure, the surgeon used 2 products: Simplex P containing tobramycin and Simplex P without antibiotic.



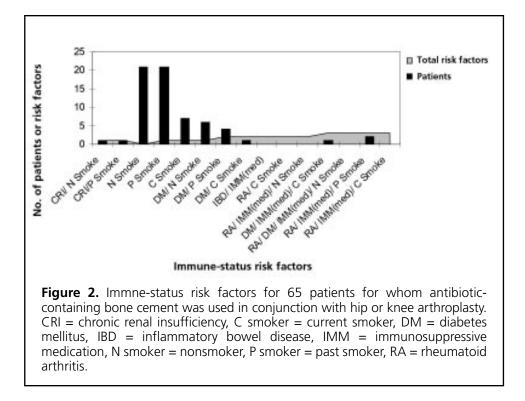
The most frequently selected ABC was a product containing 1 g of tobramycin per 40 g of bone cement (Table 2). Of the 14 surgeons for whom data were available, 11 (79%) used a commercially available ABC. Half of the surgeons (A, C, D, E, H, I, J) consistently used ABC and chose the product containing tobramycin 1 g/40 g (Figure 1). Most (57 or 88%) of the patients who received ABC had either none (23/65) or one (34/65) of the predefined immune-status factors (Figure 2). However, patients with at least one immune-status

factor were significantly more likely to receive ABC than patients with no immune-status factors (Fisher's exact test, 2-tailed p < 0.001). Finally, of the 4 patients who had chronic renal insufficiency, 2 received bone cement containing either gentamicin or tobramycin.

DISCUSSION

Eleven (79%) of the 14 orthopedic surgeons who performed the majority of arthroplasties in the Calgary





Health Region during the study period used ABC for at least one patient in the cohort studied, a rate considerably higher than that reported by Heck and others6 in 1995 for a sample from the United States. In that survey of 1015 orthopedists, 56% of respondents stated that they used ABC in their work, but only 11% and 13%, respectively, always used ABC for primary hip and knee arthroplasty; conversely, 69% reported never using ABC for primary arthroplasty. The sample for that study was much larger than that of the study presented here, but it was also limited by the fact that only 14% of the physicians surveyed identified themselves as having an adult reconstructive practice, whereas 49% characterized themselves as general orthopedists. In a major teaching centre such as the Calgary Health Region, each orthopedic surgeon declares a primary subspecialty. In the current study, this simplistically allowed for a focused analysis of the practice of the surgeons who performed most of the hip and knee arthroplasties. Unfortunately, no other similar North American data could be found for comparison.

In contrast, the prophylactic use of ABC for primary arthroplasty is widespread in the European Union, where commercial products have been available for some time. For example, in Norway, the prophylactic use of ABC has doubled in the past 10 years and now occurs in more than 90% of primary arthroplasty cases.⁷ Although data on use of ABCs is lacking for North America, the results of this audit show that such products are being used prophylactically and relatively commonly for joint reconstruction in the Calgary Health Region. It was beyond the scope of this audit to determine whether the use of ABC by surgeons in the Calgary Health Region has been influenced by European data published in orthopedic journals (and disseminated through conferences), by the marketing strategies of medical device manufacturers (e.g., complimentary samples), by peer behaviour (at the current hospital site or health region relative to a previous workplace), by health-system influences at the hospital site and at a private facility where some of the surgeons also work (e.g., through products stocked or not stocked on shelves in the operating area, wait times), or by the known or perceived infection rate and a desire to reduce it (taking into account the design and age of the operating room theatre, postoperative care, and other factors).

The European literature may be influencing the use of ABC in current practice. In a cohort study based on data from the Norwegian arthroplasty register for 1987 and 2001, Engesaeter and others⁸ found that for primary total hip arthroplasty performed for osteoarthritis, prophylactic antibiotics administered both systemically and in bone cement reduced the risk of revision due to infection and also reduced the risk of aseptic loosening. In that study, patients who received systemic prophy-



laxis alone had a risk of revision due to infection 1.8 times higher than the risk for patients who received ABC as well as systemic agents (95% confidence interval 1.1–3.0; p = 0.01). Although the time frame extended back to 1987, the study specified only certain types of prostheses and ABCs, and the product that consisted of gentamicin 0.5 g per 40 g of Palacos cement was the type of ABC most commonly used. This large-scale observational study, along with earlier studies of hip arthroplasty from Sweden and Germany, provides important evidence and may be guiding clinical practice in the Calgary Health Region. There are insufficient studies of ABC prophylaxis for primary arthoplasty of the knee, despite the fact that the rate of surgical site infections is higher for this procedure than for hip arthroplasty.

The study reported here represents the first audit of the use of ABCs in a Canadian health region, providing insight on the use of this form of primary prophylaxis. There are barriers to evaluating the use of ABC. For example, very few hospital regions in Canada have pharmacists with advanced knowledge of surgical services who would be positioned to evaluate the use of ABC. Of note, it is the department of Distribution Services (rather than the pharmacy) that is responsible for the inventory of this drug product for use in the operating theatres in the Calgary Health Region, which makes utilization studies more difficult. In fact, ABCs may have eluded review for the region's formulary, given that the cost of these products puts them outside the scrutiny of the pharmacy's budgetary review processes.

Although the Safer Healthcare Now! initiative in Canada supports surveillance of systemic antibiotics used for prophylaxis in conjunction with surgical procedures, the use of ABC is not included in the initiative's systematic approach. Fifty-nine percent of the patients (65/109) whose charts were reviewed in the present audit received a premixed antibiotic in bone cement as prophylactic therapy. The variant practice for different patients cannot be ascribed to buying contracts, since all patients were treated in one health care region. As such, differences in the use of ABCs constitute yet another variable, in addition to differences in the design or ventilation of operating theatres, workflow, organizational culture, and human resources, that may affect rates of surgical site infection. Overall, the rates of infection in the Calgary Health Region are in keeping with current practice and are closely monitored by the region's infection control practitioners. The quarterly rates of deep infection and organ space

infection for primary total hip surgery ranged from 0.40% to 2.15% for the first 3 quarters of 2004/2005, whereas for primary total knee arthroplasty they ranged from 0.48% to 2.01% (W. Runge, Infection Control Practitioner, Calgary Health Region; personal communication by telephone, December 14, 2005).

About 2000 patients undergo primary total hip or total knee replacement each year in the Calgary Health Region. Extrapolating from this audit, we estimate that about 1000 of these patients may receive ABC each year. The association between prophylactic use of ABC and the prevalence of antibiotic-resistant organisms has not been well studied, but the possibility of such an association exists. For example, emergence of antibiotic resistance after primary arthroplasty in which gentamicin was included in bone cement has been reported.9 Bone cement is an optimal surface for bacterial colonization, and prolonged exposure to an antibiotic at subinhibitory levels allows mutational resistance to occur.¹⁰ If the use of ABC in the operating room were to be captured electronically and entered into a provincial surveillance registry database, the effect of ABC on resistance could be better analyzed through prospective population-based studies.

Three commercial types of ABC were used in the Calgary Health Region during the audit period (Table 2). Tobramycin was more commonly used (54/65 [83%]) than gentamicin (11/65 [17%]), and tobramycin was always used at one of the hospitals. It was unclear from this audit if surgeons selected particular ABCs on the basis of perceptions of local microbial epidemiology, susceptibility patterns, or other subjective factors such as the texture or workability of the cement. The preference for tobramycin is consistent with practice in the United States, but is inconsistent with practice in Europe.¹¹ For infectious diseases in general, tobramycin is typically reserved for Pseudomonas and for situations in which gentamicin resistance is too strong a possibility to risk failure by administering the latter. Local community patterns for the Calgary Health Region indicate that the organisms of concern are adequately susceptible to gentamicin (92% susceptibility for coagulase-negative staphylococci and 98% susceptibility for Staphylococcus aureus, for the period July 2004 to June 2005); therefore, it remains unclear why tobramycin-containing bone cement was most frequently chosen for elective procedures. A qualitative survey of the orthopedic surgeons would be helpful to elicit their opinions and beliefs. An initial survey of orthopedic surgeons to determine their practice preferences regarding ABCs was aborted because of anticipated low participation



rates. It seems doubtful that 3 different aminoglycosidecontaining products are needed for prophylaxis in this setting, and efforts are therefore under way to limit the number of products, although consensus and simplification of ABC selection may be difficult to achieve.

In the 1995 survey of US orthopedic surgeons,⁶ 11% of respondents reported incorporating liquid antibiotics as an admixture into the bone cement. Surgeons must be mindful that the addition of large amounts of antibiotic can significantly damage the mechanical properties of the bone cement and can lead to systemic toxic effects.¹² To provide perspective, use of up to 8 g of antibiotic per 40 g of bone cement has been reported for cases of active infection.¹³ From the charts reviewed. it was reassuring to find that the surgeons did not add extra antibiotics (e.g., vancomycin) to the commercial products. Instead, premixed commercial products were used. The actual amount of bone cement (and therefore the "dose" of antibiotic) deposited in the patient's joint was not known with precision because, although the batches of cement prepared for the procedure were counted, excess cement was discarded without measurement. The audit showed that surgeons used a relatively low dose of ABC, which never exceeded 1 g of antibiotic per 40 g of cement. Although there have been no cases of toxicity reported with the low-dose ABC used for primary prophylaxis, the safety of higherdose ABC for arthroplasty revisions warrants more caution and greater study.14-16

It was theorized that specific patient factors might have influenced a surgeon to use ABC in a particular orthopedic case, if it was perceived that the patient was at increased risk of infection or if there was potential for healing to be prolonged. Whether a patient had refrained from smoking tobacco was considered because the literature suggests that smoking inhibits bone healing after fracture, and smokers have a greater risk of infection than nonsmokers.17 Diabetes mellitus was included, as patients with diabetes have a higher risk of infection after total knee arthroplasty than patients who do not have this condition.^{18,19} Overall, patients with at least one immune-status factor were significantly more likely to receive ABC than those with no identified immune-status factors (p < 0.001). The orthopedic surgeons in the Calgary Health Region may be relatively conservative in making decisions about the use of ABC when only one risk factor is present, although these data should be confirmed by a larger and more robust study. Of note, patients with several immune-status risk factors did not appear to consistently receive ABC, although the sample size of this study prevented detailed analysis.

Chronic renal insufficiency also impairs a patient's ability to recover from infection, but this condition might also make a surgeon hesitant to use an aminogly-coside for fear of systemic toxicity. Although ABC is suggested to have less potential for systemic toxicity because it is applied locally, there have been case reports of acute renal toxicity when large amounts of aminoglycosides were used in cement for joint revision; the condition improved when the ABC was removed.^{15,16} In this audit 4 patients were identified as having chronic renal insufficiency, of whom 2 received an aminoglycoside-containing bone cement; however, these numbers are too small to allow any conclusions.

A limitation of this audit is that only a small, convenience sample of medical records was reviewed and the results may not represent the true usage of ABC for primary prophylaxis in the Calgary Health Region. The study is also prone to bias, since the charts were not randomly selected. In addition, arthroplasties performed at the Health Resource Centre in Calgary, Alberta, were not included in the review. The Health Resource Centre is a private surgical facility, where primary total hip arthroplasty and uncomplicated total knee arthoplasty are performed as insured services (medically necessary procedures paid for by the Alberta Health Care Insurance Plan) under contract to the Calgary Health Region. Medical records from this centre were inaccessible for the purposes of this audit, yet the number of insured procedures performed there is substantial. Based on the renewal agreement with the centre,²⁰ it is estimated that about 700 insured hip and knee arthroplasty procedures are performed there each year.

The 2004 advisory statement from the National Surgical Infection Prevention Project²¹ states that "Despite the potential benefits of antibiotic impregnated bone cement for arthroplasty, controversies remain regarding its use . . . [and] there are no established guidelines for use of these agents as prophylaxis." Indeed, this audit of current Canadian practice has revealed that orthopedic surgeons do not seem to have a standard practice when using ABC for primary total hip and knee arthroplasty. Both benefits and risks are associated with the practice of adding antibiotics to bone cement, and continuous review of practice variation would be beneficial.

A summary of this study was presented and discussed at a meeting of the Calgary Health Region's Surgical Site Infection Committee, which was attended by orthopedic nurses, an orthopedic surgeon from the Division of Joint Reconstruction, an infectious diseases



pharmacist, and an infection control and prevention practitioner, among others. In this way, awareness of the cryptic use of antibiotics was raised, and education about this practice was provided. Although the literature suggests that ABC offers modest improvements in rates of surgical site infection with primary arthroplasty, the general impression of at least 2 committee members was that lowering the already-low infection rate would be desirable, regardless of the lack of pharmacoeconomic data. The results of the study were also presented to the Division of Infectious Diseases. Although some practitioners in that department recognized (through medical record notations) that use of ABC was occurring, most did not realize the extent of its use. Discussion with the Subdivision of Reconstructive Surgery is under way to try to standardize the selection and criteria for the use of ABCs in orthopedic surgery.

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Deana M Sabuda, BSc (Microbiology), BSP, ACPR, is an Infectious Diseases Pharmacist with the Calgary Health Region, Calgary, Alberta.

Charmaine Clark, BScPharm, ACPR, is with Pharmacy Services, Royal Alexandra Hospital, Capital Health Region, Edmonton, Alberta. At the time of the study, she was a hospital pharmacy resident with the Calgary Health Region.

Andrew L Pattullo, BSc, MD, FRCPC, is with the Department of Medicine, Division of Infectious Diseases, Calgary Health Region, Calgary, Alberta.

Address correspondence to:

Deana M Sabuda Pharmacy Services Foothills Medical Centre South Tower, Room 308 1403 29 Street NW Calgary AB T2N 2T9

e-mail: deana.sabuda@calgaryhealthregion.ca

