Papers

Current British veterinary attitudes to the use of perioperative antimicrobials in small animal surgery

C. B. Knights, A. Mateus, S. J. Baines

A questionnaire was sent to 2951 mixed and small animal veterinary practices to examine the use of perioperative antimicrobials in cats and dogs in the UK. The percentage of respondents who always used antimicrobials in two surgical procedures classified according to NRC criteria as 'clean' was 25.3 per cent for removal of a 1 cm cutaneous mass and 32.1 per cent for routine prescrotal castration. Factors considered important in decision-making about when to use antimicrobial agents included immunosuppression, presence of a drain, degree of wound contamination, potential for spillage of visceral contents and implantation of prosthesis. The most common antimicrobial agents mentioned were potentiated amoxicillin (98.0 per cent), amoxicillin (60.5 per cent), clindamycin (21.8 per cent), enrofloxacin (21.7 per cent), cephalexin (18.6 per cent) and metronidazole (12.7 per cent). Forty-three per cent of all responding veterinarians listed a long-acting preparation for perioperative use. The routes used were subcutaneous (76.1 per cent), intravenous (25.8 per cent), intramuscular (19.8 per cent), oral (13.5 per cent) and topical (7.7 per cent). Antimicrobials were given before surgery (66.6 per cent), during surgery (30.2 per cent), immediately after surgery (12.0 per cent) and after surgery (6.3 per cent). This survey has identified the suboptimal use of perioperative antimicrobials in small animal surgery with improvements needed with respect to timing, duration, choice of antimicrobial and a more prudent selection of surgical cases requiring prophylaxis.

WOUND infection following veterinary surgery is uncommon following most surgical procedures, with an overall estimated surgical infection rate of about 5.5 per cent (Brown and others 1997), provided that high standards of aseptic technique are maintained. When surgical wound infection occurs, it may adversely affect the outcome of the procedure and the health of the animal.

All surgical procedures result in some bacterial contamination either from the patient or from the environment. Development of infection depends on a number of factors including the number and virulence of contaminating bacteria, the local wound environment and competence of host defences. Patient-related factors include age, sex, endocrinopathy and American Association of Anaesthesiologists score which provides an indication of the physical status of the patient (Saklad and others 1941). Operative factors influencing infection rates include duration of surgery and anaesthesia, aseptic preparation, use of certain anaesthetic drugs, clipping before anaesthesia, number of personnel in the operating theatre and hypothermia (Cruse and others 1973, Vasseur and others 1988, Horan and others 1992, Brown and others 1997, Heldmann and others 1999, Beal and others 2000, Nicholson and others 2002, Eugster and others 2004). Classification according to the likelihood of bacterial contamination using a system developed by the National Research Council (NRC) in 1964 has shown to be predictive. Four wound classes were described: clean, clean-contaminated, contaminated and dirty with an increasing risk of bacterial contamination and therefore surgical site infection (Ad hoc Committee of the Committee on Trauma 1964).

Veterinary studies have shown that perioperative antimicrobials may reduce the incidence of wound infection in some, but not all, procedures (Brown and others 1997, Eugster and others 2004). However, the use of antimicrobials is not a substitute for appropriate preoperative planning, case selection, good surgical technique, proper postoperative care and appropriate infection control strategies. In addition, inappropriate and indiscriminate use of antimicrobials has a number of disadvantages including development of bacterial drug resistance, increased cost, suppression of the normal host flora, idiosyncratic drug reactions in the patient, development of super-infection and increased risk of hospital-acquired infection (Brown and others 1997, Martin and others 1998, Song and others 1998, Bailly 2001).

There are no official guidelines for the use of perioperative antimicrobials in small animal surgery, although most surgical texts list recommendations, supported in part by the veterinary literature and extrapolated from human medicine.

Veterinary Record doi: 10.1136/vr.100292

C. B. Knights, BVetMed MRCVS, Wolfson Centre for Age Related Disease, Room 1.24 Hodgkin Building, Guys Campus, Kings College London, St Thomas St, London, SE1 1UL, UK
A. Mateus, BVetMed, MVPH, PhD, MRCVS, Department of Veterinary Clinical Sciences, Royal Veterinary College, Hawkshead Lane, North Mymms, Hertfordshire AL9 7TA, UK
S. J. Baines, MA, VetMB, PhD, CertVR, CertSAS, DipECVS, DipClinOnc, MRCVS, Willows Referral Service, Highlands Road, Shirley, Solihull, West Midlands, B90 4NH, UK

E-mail for correspondence: chancie.knights@googlemail.com

Additional materials are published online only. To view the files please visit the journal online (http://veterinaryrecord.bvapublications.com)

Provenance: not commissioned; externally peer reviewed

Accepted February 8, 2012

Essentially, the basic principles of antimicrobial prophylaxis are to (1) limit use to procedures with a relatively high rate of septic complications or in which the consequences of infection are especially serious, (2) use of narrow spectrum antimicrobial agents effective against major anticipated contaminating bacterial species, (3) the administration of antimicrobials sufficiently in advance of the operation and by such a mode of administration that effective tissue concentrations are reached before and maintained during surgery (Flynn and others 1979).

There are very few data available on the extent to which these recommendations are routinely applied. In one study of dogs undergoing surgery for cranial cruciate ligament rupture, discrepancies were noted between standard recommendations and the antimicrobial prophylaxis used, with 16 per cent not receiving the drug within 60 minutes of surgery, 49 per cent receiving additional doses at an incorrect time and 19 per cent receiving unnecessary repeated doses. Similar discrepancies are found in human hospitals where surgical antimicrobial prophylaxis is often not concordant with local or national guidelines. One report from a tertiary teaching hospital in Brazil (Heineck and others 1999) showed that only 3 per cent of the procedures were given appropriate prophylaxis according to hospital guidelines, in terms of antimicrobial choice, duration, dose and timing. A study of public hospitals in Victoria, Australia (Bull and others 2006), showed that the choice of antimicrobial was in agreement with national guidelines for 53.3 per cent of procedures, timing was consistent with the national guidelines for 76.4 per cent of all procedures when documented; however, surgical antimicrobial prophylaxis was considered to be inadequate for 18.9 per cent of the procedures examined. A prospective, multicentre audit of elective procedures at 13 Dutch hospitals showed that overall concordance with local guidelines was 34 per cent (Van Kasteren and others 2003). While antimicrobial choice was appropriate in 92 per cent of cases, major discrepancies were noted on duration of antimicrobial administration and dosing interval with over 50 per cent of dosing intervals being discordant with the local guidelines.

The aim of this study was to examine the attitudes to the use of perioperative antimicrobials in cats and dogs in first opinion veterinary practice in the UK.

Materials and methods

A questionnaire (see supplementary online material) was designed to determine the attitudes to the use of perioperative antimicrobials by veterinary surgeons in general practice. The questionnaire was designed to be completed by an individual veterinary surgeon in 10 minutes or less. The questionnaire was pretested and validated before being sent to veterinary practices.

Five veterinary surgeons assessed the question content (range and appropriateness of questions) and question construction (mistakes or ambiguity). Eight veterinary surgeons involved in first opinion practice then completed the questionnaire to detect difficulties in completion of the questionnaire. A test-retest procedure, where five individuals completed the questionnaire on two separate occasions, three weeks apart, was performed. Ten RCVS-recognised or European specialists in small animal surgery then completed the questionnaire and their answers were recorded separately as a reference group.

The survey was divided into three basic parts. Section A consisted of questions relating to the demographics of the respondents, such as the year of graduation, veterinary school attended, sex of the applicant, further education qualifications, type of practice (per cent small animal), number of veterinary surgeons in the practice, location of the practice and Royal College of Veterinary Surgeons (RCVS) Practice Standard. Section B was divided into seven questions relating to the veterinarian's attitudes to the use of prophylactic antimicrobials in small animal surgery and the factors that governed decision-making. In Section C, respondents were asked whether they agreed or disagreed with seven different statements regarding the use of perioperative antimicrobials.

The questionnaire was sent to 2951 small and mixed animal practices in the UK in July 2005 identified using a Royal Veterinary College database derived from the list of all practices published by the RCVS. A covering letter explained the aims of the study and stated that the results were anonymous and could not be traced; a reply-paid envelope addressed to the authors was sent with each questionnaire, and letters were placed in the veterinary press to encourage a high return rate. Replies were accepted up to six months after the initial mailing and logged onto a spreadsheet (Excel 2003; Microsoft Corporation). If any of the questions were not answered or answered ambiguously, then the data from that specific question were excluded from analysis.

The responses given in the test-retest procedure were analysed with the intraclass correlation coefficient. Simple descriptive statistics were generated for the entire dataset and comparisons were made between groups using Fisher's exact and chi-squared tests for categorical variables and Mann-Whitney and Kruskal-Wallis tests for continuous variables (Prism: Graphpad Software).

Results

The questionnaires answered by the eight veterinary surgeons engaged in first opinion practice were fully completed and no questions were marked as ambiguous, misleading or inappropriate. In the test-retest procedure, questions with an ordinal scale response had good reliability (intraclass correlation coefficient of 0.83 to 0.87) and questions with a binomial response, tick box or free text had identical responses, apart from the question examining source of information. Questionnaires were returned by 1121 respondents, an apparent response rate of 38 per cent.

Replies were received from veterinary surgeons throughout the UK; 60.7 per cent were male and 39.3 per cent were female. Respondents included veterinary surgeons who had graduated between the 1940s and the present day although 30.5 per cent had graduated within the past 10 years. The demographics of respondents are summarised in Table 1; 83.4 per cent of the respondents graduated from veterinary schools in the UK, 6.0 per cent from veterinary schools within the rest of the European Union and 10.7 per cent from elsewhere; 3.3 per cent held a certificate or diploma in small animal surgery; 63.7 per cent of respondents were employed in 100 per cent small animal practice and 36.3 per cent were employed in mixed practices with a median percentage of small animal work of 70 per cent (range 5 per cent to 99 per cent). The median number of veterinary surgeons in the practice was four with a range of one to 34.

TABLE 1: Numbers of veterinary surgeons responding to the survey who graduated in different decades

	Decade during which respondents graduated						
	1940s	1950s	1960s	1970s	1980s	1990s	2000s
Male	0	0	31	176	225	176	48
Female	1	0	3	31	106	163	120
Total replies	1083						

Use of antimicrobials in various surgical procedures

The results for the use of antimicrobials in eight different surgical procedures are displayed in Table 2. The procedures were selected to

TABLE 2: Frequencies and percentages of veterinarians who use perioperative antimicrobials for particular surgical procedures

		Never (%)	Rarely (%)	Sometimes (%)	Frequently (%)	Always (%)	Variable (%)
Clean	Local excision of 1 cm non-ulcerated cutaneous mass	239 (21.4)	268 (24)	178 (15.9)	150 (13.4)	283 (25.3)	596 (53.3)
	Routine prescrotal castration	347 (31.1)	172 (15.4)	110 (9.9)	129 (11.6)	358 (32.1)	411 (36.9)
Clean-contaminated	Full thickness wedge resection of a lip mass	48 (4.3)	115 (0.4)	193 (17.4)	203 (18.3)	551 (49.6)	511 (46.1)
	Laparotomy and full thickness gastrointestinal biopsy	9 (0.8)	17 (1.5)	46 (4.1)	86.7 (7.8)	953 (85.7)	138 (12.4)
Contaminated	Cystotomy in a dog with urinary tract infection	5 (0.4)	13 (1.2)	31 (2.8)	78 (7.0)	987 (88.6)	122 (11.0)
	Surgery of a fresh traumatic wound	22 (2.0)	79 (7.1)	209 (18.7)	241 (21.6)	567 (50.7)	530 (47.4)
Dirty	Ovariohysterectomy for ruptured pyometra	3 (0.3)	2 (0.2)	7 (0.6)	12 (1.1)	1090 (97.8)	21 (1.9)
	Lateral wall resection for otitis externa	6 (0.5)	6 (0.5)	22 (2.5)	106 (9.5)	964 (86.9)	134 (12.5)

TABLE 3: Number of respondents, percentage and median score of veterinarians who ranked various factors in the decision whether to use perioperative antimicrobials (1=unimportant and 5=very important)

Factor	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	Total	Median score	Weighted mean
Degree of wound contamination	21 (1.9)	5 (0.5)	25 (2.3)	166 (15.0)	892 (80.4)	1109	5	4.7
Potential for spillage of visceral contents	20 (1.8)	11 (1.0)	57 (5.1)	197 (17.7)	825 (74.3)	1110	5	4.6
Immunosuppression	21 (1.9)	9 (0.8)	39 (3.5)	203 (18.2)	843 (75.6)	1115	5	4.6
Presence of a drain	23 (2.1)	17 (1.5)	100 (9.0)	322 (29.1)	643 (58.2)	1105	5	4.4
Surgery involving prosthesis implantation	19 (1.8)	27 (2.5)	106 (9.8)	286 (26.4)	645 (60.0)	1083	5	4.4
Standard of aseptic preparation or technique	54 (4.9)	75 (6.8)	188 (17.1)	252 (23.0)	529 (48.2)	1098	4	4.0
Pre-existing prosthesis or surgical implant	40 (3.6)	111 (10.1)	247 (22.4)	322 (29.2)	382 (34.7)	1102	4	3.8
Physical condition of the patient	35 (3.2)	81 (7.3)	270 (24.4)	395 (35.7)	325 (29.4)	1106	4	3.8
Duration of surgery	52 (4.7)	94 (8.5)	267 (24.1)	389 (35.2)	304 (27.5)	1106	4	3.7
Incision into a hollow viscus	58 (5.3)	113 (10.3)	267 (24.3)	356 (32.4)	306 (27.8)	1100	4	3.7
Emergency versus elective surgery	123 (11.1)	163 (14.7)	336 (30.4)	279 (25.2)	205 (18.5)	1106	3	3.3
Level of clinical experience	191 (17.5)	187 (17.1)	357 (32.7)	209 (19.1)	149 (13.6)	1093	3	2.9
Period of hospitalisation	243 (21.9)	320 (28.9)	342 (30.8)	136 (12.3)	68 (6.1)	1109	2	2.5
Presence of IV catheter	375 (34.0)	324 (29.3)	268 (24.3)	82 (7.4)	55 (5.0)	1104	2	2.2

include an equal number of clean, clean-contaminated, contaminated and dirty operations as classified by the NRC (Ad hoc Committee of the Committee on Trauma 1964).

Antimicrobials were always used in 25.3 per cent and 32.1 per cent of clean surgeries depending on which of the two scenarios were being considered, 49.6 per cent and 85.7 per cent of clean-contaminated surgeries, 50.7 per cent and 88.6 per cent of contaminated surgeries and 86.9 per cent and 97.8 per cent of dirty surgeries. Antimicrobials were never used in 21.4 per cent and 31.1 per cent of clean surgeries, 4.3 per cent and 0.8 per cent of clean-contaminated surgeries, 0 per cent and 2 per cent of contaminated surgeries and 0.3 per cent and 0.5 per cent of dirty surgeries. The use of antimicrobials in some cases (ie, respondents selecting options other than never and always) ranged from 1.9 per cent to 53.3 per cent (median 24.7 per cent), with two clean, one clean-contaminated and one contaminated procedure having the greatest number of respondents giving these scores.

Importance of factors in determining the use of antimicrobials

The importance of various factors in the decision to use antimicrobials is given in Table 3. Respondents were asked to score the factors on a scale where one represented unimportant and five was very important. The factors considered important in the decision to use antimicrobials perioperatively by respondents included immunosuppression, presence of a drain, degree of wound contamination, potential for spillage of visceral contents and surgery involving implantation of a prosthesis (median score 5) and physical condition of the patient, duration of surgery, pre-existing prosthesis or implant, standard of aseptic preparation or technique and incision into a hollow viscus (median score 4). Level of clinical experience and emergency rather than elective surgery received a median score of 3 and period of hospitalisation received a median score of 2.

Antimicrobial agents and drug classes used

The classes of drugs chosen are given in Table 4. Beta-lactamase-resistant and beta-lactamase-susceptible beta-lactam antibiotics were listed most commonly (99.4 per cent and 98.2, respectively). Other classes of drugs mentioned by more than 10 per cent of respondents included fluoroquinolones (30.2 per cent), lincosamides (30.0 per cent) and nitroimidazoles (29.0 per cent). The majority of veterinarians listed two or three antimicrobials and choices included a variety of antimicrobial classes. One hundred and twenty-three respondents listed a single agent, 332 respondents listed two agents, 426 respondents listed three agents, 153 respondents listed four agents, 50 respondents listed five agents, 19 respondents listed six agents and four respondents listed seven different antimicrobial agents.

The most common choice of antimicrobial was potentiated amoxicillin with 99.2 per cent of all respondents listing it as being used for surgery (Table 5). Other drugs mentioned by more than 10 per cent of respondents included amoxicillin (61.2 per cent), clindamycin (22.0 per cent), enrofloxacin (22.0 per cent), cephalexin (18.9 per cent) and metronidazole (12.8 per cent); 43.7 per cent of all responding veterinarians listed a long-acting preparation.

TABLE 4: Number of veterinarians listing a particular antimicrobial class for perioperative use in small animal surgery

Frequency of antimicrobial listings by antimicrobial class (%)	
Beta-lactamase-resistant beta-lactam	1100 (99.4)
Beta-lactamase-susceptible beta-lactam	1087 (98.2)
Fluoroquinolones	334 (30.2)
Lincosamides	321 (30.0)
Nitroimadazole	142 (29.0)
Sulfonamides	39 (3.5)
Tetracyclines	20 (1.8)
Macrolide/nitroimadazole	15 (1.4)
Aminoglycoside/penicillin	9 (0.8)
Aminoglycosides	4 (0.4)
Phenicol	1 (0.1)

Importance of factors determining selection of an antimicrobial

The opinion of the importance of various factors when selecting an antimicrobial for prophylactic use is given in Table 6. The factors considered important in the selection of a particular antimicrobial were spectrum of activity and activity against likely infecting organisms (median score 5) and duration of activity, potential for side effects, bactericidal versus bacteriostatic, and presence of a veterinary product licence (median score 4). Available routes of administration, wound location, practice policy, availability of information on the drug's mode of action and potential for the development of resistance in environmental bacteria received a median score of 3 and cost and shelf-life received a median score of 2.

Route of administration

Multiple answers were often given to the route of antimicrobial administration; 64.6 per cent of respondents listed a single route of administration, 23.5 per cent listed two routes, 9.1 per cent listed three routes, 1.9 per cent listed four routes and 0.9 per cent of responding veterinarians listed five different routes of administration. The most common route was subcutaneous injection with 76.1 per cent of responding veterinarians listing it as a route of administrating prophylactic antimicrobials for surgery; 25.8 per cent of respondents listed the intravenous route, but only 7.7 per cent listed this as the only route used. Other routes included intramuscular (19.8 per cent), oral (13.5 per cent) and topical (7.7 per cent).

Timing of administration

Multiple answers were often given to the timing of antimicrobial administration; 66.6 per cent of respondents gave antimicrobials before surgery, although only 55.6 per cent of respondents only used this time point; 48.5 per cent of respondents reported that they used time points other than before surgery to administer prophylactic antimicrobials. These comprised during surgery (30.2 per cent), immediately after surgery (12.0 per cent) and postsurgery (6.3 per cent).

Source of knowledge about antimicrobial use

Multiple answers were often given as to the source of information on the use of perioperative antimicrobials; 20.6 per cent of respondents

TABLE 5: Number of veterinarians listing a particular antimicrobial by generic drug for perioperative use in small animal surgery

Total number of respondents listing a particular antimicrobial (%)	
Potentiated amoxicillin	1098 (99.2)
Amoxicillin	678 (61.2)
Clindamycin	244 (22.0)
Enrofloxacin	243 (22.0
Cephalexin	209 (18.9)
Metronidazole	142 (12.8)
Ampicillin	92 (8.3)
Marbofloxacin	90 (8.1)
Lincomycin	77 (7.0)
Cefuroxime	46 (4.2)
Procaine benzylpenicillin	46 (4.2)
Trimethoprim sulfonamide	39 (3.5)
Oxytetracycline	19 (1.7)
Spiramycin/metronidazole	15 (1.4)
Dihydrostreptomycin sulphate + procaine penicillin	9 (0.8)
Cefazolin	8 (0.7)
Cephadrine	4 (0.4)
Gentamicin	4 (0.4)
Ceftazidime	3 (0.3)
Potentiated ticarcillin	2 (0.2)
Ceftiofur	1 (0.1)
Chlortetracycline hydrochloride	1 (0.1)
Florfenicol	1 (0.1)
Ibafloxacin	1 (0.1)
Total number of replies	1107

listed a single source, 24.8 per cent listed two sources, 30.1 per cent listed three sources, 14.4 per cent listed four sources, 6.0 per cent listed five sources, 2.5 per cent listed six sources and 1.6 per cent listed seven sources of information. The sources of knowledge listed by respondents and the frequency with which this source was listed were clinical experience (67.8 per cent), undergraduate teaching (44.6 per cent), continuing education (39.8 per cent), colleagues (38.1 per cent), journal articles (27.7 per cent), commercial literature and data sheets (22.4 per cent) and textbooks (19.1 per cent).

The statements regarding the use of perioperative antimicrobials and the proportion of respondents that agreed or disagreed with these are given in Table 7. There was complete agreement between the specialist surgeons. For all but one statement, the majority of respondents agreed with the specialist surgeons' unanimous opinion although this ranged from 69 per cent to 93.2 per cent.

Discussion

According to data published by the RCVS (2010), UK veterinary practices are composed of 53.3 per cent small animal clinics and 28.7 per cent mixed practices which is a similar proportion to respondents of this survey with 63.7 per cent and 36.3 per cent, respectively. Respondents had also graduated from a similar distribution of veterinary schools (predominantly the UK) with a small number from the EU and elsewhere. Our demographic data showed that a wide range of age groups were represented and the changes observed in the population of male to female veterinary surgeons followed current trends in the profession. Thus, the results are representative of the UK profession involved in small animal surgery.

In this study, the use of perioperative antimicrobials in specific circumstances was investigated along with factors affecting their decision-making; 25.3 per cent and 32.1 per cent of veterinarians would always use antimicrobials for the clean surgical procedures listed. Perioperative antimicrobials have no effect on the incidence of wound infection in routine clean veterinary surgical procedures performed by experienced surgeons (Vasseur and others 1985, Brown and others 1997, Vasseur and others 1998). In clean orthopaedic surgeries where an implant may be placed, the evidence is conflicting with some studies showing no effect (Holmberg 1985, Weese and Halling 2006) and other studies showing a beneficial effect (Whittem and others 1999, Casale and McCarthy 2009).

The proportion of respondents that always used perioperative antimicrobials for clean-contaminated surgery (49.6 per cent and 85.7 per cent) was similar to the proportions for contaminated surgery (50.7 per cent and 89.0 per cent). The use of perioperative antimicrobials for clean-contaminated procedures is controversial, since this category encompasses a wide range of procedures (eg, ovariohysterectomy to cholecystoenterostomy) with a range of potential for wound contamination. One study with an overall infection rate of 8.9 per cent concluded that prophylaxis was not required for clean and clean-contaminated procedures (Daude-Lagrave 2001) and another study with an overall infection rate of 5.9 per cent showed no benefit of perioperative antimicrobials in clean-contaminated surgery (Nicholson and others 2002).

The clean procedures as well as one clean-contaminated (full-thickness wedge resection of a lip mass) and one contaminated procedure (surgery of a fresh traumatic wound) had the highest proportion of respondents whose use of perioperative antimicrobials was variable (ie, not 'never' and not 'always') suggesting that additional factors dictated whether antimicrobials would be used in these circumstances. Some potential factors are presumably listed in Table 3, but further work should be designed to investigate which factors are associated with which clinical situations. This response may also indicate that some veterinary surgeons do not consider fresh traumatic wounds to be contaminated or at risk of infection, or that perioperative antimicrobial use is not warranted.

Perioperative antimicrobials are chiefly indicated for contaminated surgical procedures and it is interesting to note that the proportion of respondents always using perioperative antimicrobials for these procedures was 50.7 per cent and 88.6 per cent, although most of the remainder would use these at some point, with only 0 per cent to 2 per cent of respondents never using perioperative antimicrobials in this situation. This suggests that the decision to use an antimicrobial in some cases is based on other factors associated with the patient or procedure rather than the NRC classification of the likelihood of wound contamination (Ad hoc Committee of the Committee on Trauma 1964).

Perioperative antimicrobials may well be used for patients with dirty surgical wounds, although in this case antimicrobial use is therapeutic rather than prophylactic and may well have begun preoperatively.

The factors that were rated most highly in the decision to use antimicrobials in this study were immunosuppression, presence of a drain, degree of wound contamination, potential for spillage of visceral contents and prosthesis implantation. All of these factors may have an effect on the risk of wound infection through interactions with the host's immune system, local tissue defences or bacterial load and are therefore important considerations. Degree of wound contamination and potential for spillage of visceral contents are important factors in the development of wound contamination and therefore infection and indeed form part of the NRC classification of surgical wounds (Ad hoc Committee of the Committee on Trauma 1964). Immunosuppression is a risk factor for surgical wound infection in human surgery (Gil-Egea and others 1987, Slaughter and others 1993) although this was not found to be the case in one veterinary study (Brown and others 1997).

The implantation of a prosthesis is often given as a reason why antimicrobial prophylaxis is indicated in clean surgeries in the veterinary and human literature. The incidence of wound infection after such surgery is reported to be 1.0 per cent for total hip replacement hip prosthesis surgery and 0.7 per cent for knee replacement in human surgery (Wilson and Elgohari 2009). In any case, infection of the prosthesis is likely to be disastrous and measures such as antimicrobial prophylaxis and antimicrobial-impregnated cement are used. The use of antimicrobials in patients with pre-existing implants that undergo subsequent surgical procedures is controversial, although the swift use of therapeutic antimicrobials in these patients is recommended if they develop an intercurrent infection (Averns and Kerry 1995).

In one veterinary study, use of a drain was found to be associated with the development of postoperative infection/inflammation (more than two of inflammation, serous discharge or dehiscence) but not the development of infection (purulent drainage, abscess or fistula) (Eugster and others 2004).

Of the factors that were rated next most highly (median score 4), physical condition of the patient (eg, age), duration of surgery and incision into a hollow viscus have been shown to have an effect on wound infection rates in human and small animal patients (Brown

TABLE 6: Number of respondents, percentage and median score of veterinarians who ranked various factors in the decision to use a particular antimicrobial perioperatively (1=unimportant and 5=very important)

Factor	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	Total	Median score	Weighted mean
Activity against likely infecting organisms	6 (0.5)	15 (1.3)	44 (3.9)	205 (18.3)	785 (70.0)	1055 (94.1)	5	4.7
Spectrum of activity	8 (0.7)	5 (0.4)	52 (4.6)	359 (32.0)	634 (56.6)	1058 (94.4)	5	4.5
Duration of activity	28 (2.5)	117 (10.4)	336 (30.0)	359 (32.0)	197 (17.6)	1037 (92.5)	4	3.6
Potential for side effects	47 (4.2)	166 (14.8)	294 (26.2)	333 (29.7)	209 (18.6)	1049 (93.6)	4	3.5
Bactericidal versus bacteriostatic	50 (4.5)	119 (10.6)	327 (29.2)	360 (32.1)	200 (17.8)	1056 (94.2)	4	3.5
Veterinary product license	92 (8.2)	134 (12.0)	285 (25.4)	277 (24.7)	260 (23.2)	1048 (93.5)	4	3.5
Potential for development of resistance in environmental bacteria	46 (4.1)	132 (11.8)	359 (32.0)	319 (28.5)	198 (17.7)	1054 (94.0)	3	3.5
Available routes of administration	43 (3.8)	176 (15.7)	383 (34.2)	298 (26.6)	145 (12.9)	1045 (93.2)	3	3.3
Wound location	85 (7.6)	178 (15.9)	317 (28.3)	307 (27.4)	163 (14.5)	1050 (93.7)	3	3.3
Availability of information on drugs' action	68 (6.1)	196 (17.5)	380 (33.9)	260 (23.2)	144 (12.8)	1048 (93.5)	3	3.2
Practice policy	297 (26.5)	225 (20.1)	265 (23.6)	155 (13.8)	108 (9.6)	1050 (93.7)	3	2.6
Cost	230 (21.9)	302 (28.8)	344 (32.8)	130 (12.4)	43 (4.0)	1049 (93.6)	2	2.5
Shelf-life	422 (37.6)	339 (30.2)	201 (17.9)	63 (5.6)	33 (2.9)	1058 (94.4)	2	2.0

and others 1997, Heldmann and others 1999, Nicholson and others 2002, Eugster and others 2004) through compromised immune defences and increased contamination of the surgical field and should indeed be important considerations in the decision to use perioperative antimicrobials.

Standards of asepsis (median score 4) should always be excellent and cannot be compensated for by the use of antimicrobials. It should therefore not be a consideration for the use of perioperative antimicrobials. Attention must be given to preoperative management of comorbidities, control of the operative environment and use of aseptic technique with antimicrobial prophylaxis playing a minor role among other preventive measures in reducing postoperative infection. No study has evaluated the effect of the overall standard of aseptic technique on the development of wound infection, as this is a prerequisite for elective surgery, although one human study showed how improvement in the general standard of asepsis in a hospital managed to control a sudden increase in surgical site infections (Roesler and others 2010). In addition, there are many studies examining the efficacy of individual elements of aseptic technique, for example, wound infection rates are higher for emergency procedures than for elective procedures of a given class and one reason for this may be abbreviated aseptic preparation. However, the classification of a procedure as an emergency procedure rather than an elective procedure was not ranked highly by respondents in this survey.

A large number of different antimicrobials were listed as being used for prophylaxis in surgical procedures and respondents often listed drugs with a broad spectrum and long duration of activity. The most appropriate choice of antimicrobial for surgical prophylaxis is one that has a proven efficacy against the likely organisms, has a narrow spectrum of activity against these organisms, is bactericidal and can be given by the intravenous route in order to reach high plasma and tissue levels soon after administration (Mangram and others 1999). These factors all had a median score of 4 or 5, apart from route of administration. Other factors given a median score of 4 or 5 were duration of activity, and presence of a veterinary product licence. Duration of activity is relatively un-important; since agents with a short duration of activity may be administered more frequently and indeed, appropriate agents are given by the intravenous route generally have a shorter duration of activity than preparations given by other routes. Presence of a veterinary product licence is an important consideration for the selection of drugs for use in animals, but none of the currently available bactericidal antimicrobials of an appropriate class available as an intravenous preparation has a veterinary product licence. Selection of a drug with a veterinary product licence but an unsuitable route of administration should not take precedence over one without a licence but with a suitable route of administration.

The most common bacteria involved in surgical site infections in cats and dogs are skin commensals (Owen and others 2009), Gram-positive cocci, along with the normal flora from the gastrointestinal and other tracts, predominantly Gram-negative rods, depending on the surgical procedure. Since many staphylococci produce beta-lactamase, broad-spectrum agents like ampicillin are not suitable for prophylaxis, but clavulanate-potentiated amoxicillin and first-generation cephalosporins, such as cefazolin, are good choices where skin commensals are the likely contaminating organisms (Rosin and others 2003). Where Gram-negative bacteria are more important, a second-generation cephalosporin, such as cefuroxime, is more appropriate. Third-generation cephalosporins and fluoroquinolones should not be prescribed for surgical prophylaxis as the use of these broad-spectrum agents may increase the likelihood of emergence of resistant bacteria and superinfection (Martin and Pourriat 1998). In this respect, there are relatively few choices of suitable drugs, although many respondents listed more than three drugs that were routinely used. Of the choices given, only potentiated amoxicillin (99.2 per cent of respondents), cephalexin (18.9 per cent), cefuroxime (4.2 per cent), cefazolin (0.7 per cent) and cephradine (0.4 per cent) represent potentially suitable choices.

Nearly half the respondents indicated that they used a long-acting preparation, administered via the subcutaneous or intramuscular route, for prophylaxis. This may be for reasons of ease, practicality and cost but are not an appropriate choice as they reach lower plasma and tissue concentrations compared with intravenous preparations, take longer to reach the peak concentration and result in antimicrobial in the tissues beyond the operative period, which is not indicated and may contribute to antimicrobial-associated morbidity (Brown and others 1997).

Most veterinary surgeons administered antimicrobials before surgery, but 48.5 per cent of veterinarians stated that they administer antimicrobials after the initiation of surgery (ie, during or immediately after surgery, or postoperatively). It is essential, however, that the route and timing of administration of antibacterial therapy reliably achieves serum and tissue concentrations that exceed, from the point of the first incision and for the duration of the operation, the Minimum Inhibitory Concentrations for the likely contaminating organisms (Song and others 1998). This is most consistently achieved by intravenous injection of the antimicrobial within 60 minutes of the first incision.

Most respondents listed multiple sources of knowledge for the use of antimicrobials. The sources likely to have been derived from a good evidence base, teaching from undergraduate and continuing education sources, journal articles and textbooks, were listed by 19.7 per cent to 44.6 per cent of respondents. Clinical experience (67.8 per cent) and colleagues (38.1 per cent) were commonly cited as sources of information, although these sources of information may not have a good evidence base. A review of studies of the information-seeking behaviour of human physicians indicated that, in most studies, textbooks were the preferred source of information, followed by professional colleagues (Davies 2007).

Reliance on habit rather than more objective evidence may lead to poor decision-making. Reliance on professional colleagues is potentially problematic if the validity of the information is not assessed. By applying evidence-based medicine, the use of perioperative antimicrobials can be optimised and unnecessary usage avoided. Commercial literature and data sheets were listed by 22.4 per cent of respondents, and yet no veterinary products are licensed for this use.

The answers to the final section of the questionnaire highlighted some misconceptions held by veterinary surgeons in the role antimi-

TABLE 7: The proportion of respondents who agreed with or disagreed with seven statements regarding the use of perioperative antimicrobials. The unanimous opinion of 10 specialist surgeons is indicated in bold

Statement	% Agreed	% Disagreed
Antibiotics decrease wound infections in clean surgical procedures	31.0	**69**
All animals undergoing surgery benefit from perioperative antibiotic administration	22.7	**77.3**
Owners are happy to pay for the costs involved in administering antibiotics	**93.2**	6.8
If I am not sure if antibiotic prophylaxis is needed, I tend to give it	79.9	**20.1**
Antibiotic cover is needed for all surgical procedures	11.4	**88.6**
Inappropriate antibiotic use in small animal surgery contributes to antibiotic resistance in bacteria	**83.3**	16.7
There is no difference in efficacy in the prevention of surgical wound infection between giving antibiotics preoperatively and postoperatively	11.7	**88.3**

crobials play in small animal surgery; 22.7 per cent of respondents agreed that 'All animals undergoing surgery benefit from perioperative antimicrobial administration' although only 11.4 per cent agreed that 'Antibiotic cover is needed for all surgical procedures'. More interestingly, 31 per cent agreed that 'Antibiotics decrease wound infections in clean procedures'. As previously discussed, antimicrobials are rarely indicated in clean surgical procedures and may even increase the risk of infection in some circumstances (Brown and others 1997). Since the majority of surgical procedures for which antimicrobial use does not influence the development of infection are clean procedures, a figure lower than the percentage figure given for the previous two answers would be expected. It would be useful to examine a wider range of procedures to identify which procedures are felt by veterinary surgeons not to benefit from perioperative antimicrobial use if these are not the clean surgical procedures.

Veterinary surgeons (79.9 per cent) agreed with the statement 'If I am not sure if antibiotic prophylaxis is needed, I tend to give it'. Veterinary surgeons may over-use antimicrobials because they perceive that they will have a positive effect in all cases, to make up for deficiencies in aseptic technique and surgical proficiency, and to adhere to a practice policy of antimicrobial use. The costs associated with postoperative complications due to surgical site infections are also higher than the cost of using antimicrobials perioperatively in an appropriate manner for a single individual, but not for the population as a whole. The excessive or inappropriate use of antimicrobials will not reduce the incidence of surgical site infections (Burke and others 1961, Vasseur and others 1988). It would be useful to identify what reasons would be given to justify the use of perioperative antimicrobials in these circumstances. The most appropriate course of action would be to limit the degree of uncertainty and seek further information to identify whether there is any evidence in support of using prophylaxis in these circumstances.

Respondents (11.7 per cent) agreed with the statement that 'There is no difference in efficacy in the prevention of surgical wound infection between giving antibiotics preoperatively and postoperatively'. Burke and others (1961) were the first to show the critical dependence of perioperative efficacy on the timing of administration of antimicrobials. Burke demonstrated that, when antimicrobials were administered before surgery, experimental incisions contaminated with *Staphylococcus aureus* could not be distinguished from incisions that had not been contaminated. The incidence of infection increased significantly for each hour delay in the administration of an antimicrobial relative to the time of inoculations;

Yet, 16.7 per cent disagreed with the statement 'Inappropriate antibiotic use in small animal surgery contributes to antibiotic resistance in bacteria'. However, drug toxicity, allergic reactions and the evolution of bacterial resistance are all potential hazards associated with antimicrobial administration (Song and Glenny 1998, Bailly 2001). The judicious and prudent use of antimicrobials is essential to reduce the potential for side effects and the development and spread of resistant bacteria or of their resistance genes;

Veterinary surgeons (93.2 per cent) agreed that 'Owners are happy to pay for the costs involved in administering antibiotics', so cost alone should not prevent the correct use of perioperative antimicrobials by choosing an appropriate product and route and timing of administration. Use of an intravenous preparation is likely to be more expensive than a preparation suitable for subcutaneous injection, although use of perioperative antimicrobials alone is less expensive than prescribing postoperative antimicrobials, for which there is little justification for many procedures.

Overall comments

This survey has demonstrated a suboptimal use of antimicrobials for perioperative use in cats and dogs in the UK. Improvements can and should be made with respect to timing, duration, choice of antimicrobial and a more prudent selection of surgical cases requiring prophylaxis. This study shares many similarities with those performed in the medical profession which have also revealed the suboptimal administration of perioperative antimicrobials (Silver 1996, Bailly 2001, Gul and others 2005).

The reason for inappropriate perioperative antimicrobial administration may be multi-factorial. Failure to keep up to date and reliance on habit rather on evidence-based practice are two possible explanations. This is supported by analysis of Section C of the questionnaire which revealed some misunderstanding of the role antimicrobials play in preventing surgical wound infections and the way in which they must be used for optimum effect.

Although free text comments were not solicited as part of this study, a number of respondents made additional comments. Many veterinarians commented that the use of perioperative antimicrobials is enforced in all surgical procedures by practice policy. More worrying were comments made by veterinarians that stated that they felt the need to use antimicrobials to compensate for suboptimal levels of asepsis, for example, not wearing sterile surgical gloves. Some veterinarians felt justified in their use of antimicrobials to prevent postoperative contamination leading to surgical site infections. However, within 24 hours of a surgical procedure, the surgical site is considered to be sealed and resistant to microorganism entry. Good-quality suturing technique, appropriate dressing, the use of Elizabethan collars and client education will minimise licking and self-mutilation that might compromise wound integrity.

The use of antimicrobial drugs in people and animals is under close scrutiny at present owing to their direct and indirect effects on microbial ecology, and because of the importance of preserving the efficacy of antimicrobial therapy. This study has highlighted the inappropriate and often excessive use of perioperative antimicrobials in small animal surgery in the UK and highlighted the need for greater understanding and guidance on the principles of antimicrobial prophylaxis.

Limitations

There may be some bias in the study as return of questionnaires was voluntary and no reminders were sent, which meant that the surveyed population could not be predetermined and a representative sample could not be guaranteed. The direction and significance of the bias is difficult to assess because questionnaires may not have been returned for many reasons. However, the demographic data of respondents correlated well with the UK profession as a whole and are probably representative of those involved in small animal surgery.

Despite pretesting of the questionnaire, it is possible some of the questions should have been re-worded to provide greater clarity. Also, the design of the questionnaire meant that multiple answers were received to many of the questions limiting our ability to interpret the data.

Further work

Further work will focus on the relationship between theoretical knowledge of perioperative antimicrobial use and its practical use in order to identify what factors are likely to affect whether perioperative antimicrobials are used appropriately or not. It would also be useful to compare the attitudes and practical use of antimicrobial prophylaxis at veterinary hospitals, as previous studies have provided some data

to show that the antimicrobial prophylaxis is not always used in an appropriate manner in veterinary (Brown and others 1997, Eugster and others 2004) and human hospitals (Heineck and others 1999, Van Kasteren and others 2003, Bull and others 2006).

In conclusion, this survey has demonstrated inappropriate and excessive use of perioperative antimicrobials in cats and dogs in the UK. Some of the reasons for this have been identified. Further education needs to be provided to ensure that use of perioperative antimicrobials conforms to recommendations and/or accepted practices to avoid the potential detriments of inappropriate antimicrobial use.

Acknowledgements

The author thanks the veterinary surgeons who took the time to complete the questionnaire. Without their generous time and cooperation, this study would not have been possible.

References

Ad hoc Committee of the Committee on Trauma, Division of Medical Sciences. National Research Council: postoperative wound infections: the influence of ultraviolet irradiation of the operating room and other factors. (1964) *Annals of Surgery* **160,** 23

AVERNS, H. L. & KERRY, R. (1995) Role of prophylactic antibiotics in the prevention of late infection of prosthetic joints: results of a questionnaire and review of the literature. *Rheumatology* **34,** 380-338

BAILLY, P., LALLEMAND, S., THOUVEREZ, M. & TALON, D. (2001) Multicentre study on the appropriateness of surgical antibiotic prophylaxis. *Journal of Hospital Infection* **49,** 135-138

BEAL, M. W., BROWN, D. C. & SHOFER, F. S. (2000) The effects of peri-operative hypothermia and the duration of anesthesia on postoperative wound infection rate in clean wounds: a retrospective study. *Veterinary Surgery* **29,** 123-127

BROWN, D. C., CONZEMIUS, M. G., SHOFER, F. & SWANN, H. (1997) Epidemiologic evaluation of postoperative wound infections in dogs and cats. *Journal of the American Veterinary Medical Association* **210,** 1302-1306

BULL, A. L., RUSSO, P. L., FRIEDMAN, N. D., BENNETT, N. J., BOARDMAN, C. J. & RICHARDS, M. J. (2006) Compliance with surgical antibiotic prophylaxis-reporting from a statewide surveillance programme in Victoria, Australia. *Journal of Hospital Infection* **63,** 140-147

BURKE, J. F. (1961) The effective period of preventive antibiotic action in experimental incisions and dermal lesions. *Surgery* **50,** 161-168

CASALE, S. A. & MCCARTHY, R. J. (2009) Complications associated with lateral fabellotibial suture surgery for cranial cruciate ligament injury in dogs: 363 cases (1997-2005). *Journal of the American Veterinary Medical Association* **234,** 229-235

CRUSE, P. J. E. & FOORD, R. (1973) A five-year prospective study of 23,649 wounds. *Archives of Surgery* **107,** 206-210

DAUDE LAGRAVE, A. (2001) Infection rates in surgical procedures: a comparison of cefalexin vs a placebo. *Veterinary and Comparative Orthopaedics and Traumatology* **14,** 146-50

DAVIES. (2007) The information-seeking behaviour of doctors: a review of the evidence. *Health Information Library Journal* **24,** 78-94

EUGSTER, S., SCHAWALDER, P., GASCHEN, F. & BOERLIN, P. (2004) A prospective study of postoperative surgical site infections in dogs and cats. *Veterinary Surgery* **33,** 542-550

FLYNN, N. M. & LAWRENCE, R. M. (1979) Antimicrobial prophylaxis. *Medical Clinics of North America* **63,** 1225-1244

FORSE, R. A., KARAM, B., MACLEAN, L. D. & CHRISTOU, N. V. (1989) Antibiotic prophylaxis for surgery in morbidly obese patients. *Surgery* **106,** 750-6; discussion 756

GIL-EGEA, M. J., PI-SUNVER, M. T., VERDAGUER, A., SANZ, F., SITGES-SERR, A. & ELEIZEGUI, L. T. (1993) Surgical wound infections: prospective study of 4,486 clean wounds. *Infection Control* **8,** 277-80

GUL, Y. A., HONG, L. C. & PRASANNAN, S. (2005) Appropriate antibiotic administration in elective surgical procedures: still missing the message. *Asian Journal of Surgery* **28,** 104-108

HEINECK, I., FERREIRA, M. B. & SCHENKEL, E. P. (1999) Prescribing practice for antibiotic prophylaxis for 3 commonly performed surgeries in a teaching hospital in Brazil. *American Journal of Infection Control* **27,** 296-300

HELDMANN, E., BROWN, D. C. & SHOFER, F. (1999) The association of propofol usage with postoperative wound infection rate in clean wounds: a retrospective study. *Veterinary Surgery* **28,** 256-259

HOLMBERG, D. L. (1985) The use of prophylactic penicillin in orthopaedic surgery: a clinical trial. *Veterinary Surgery* **14,** 160-165

HORAN, T. C., GAYNES, R. P., MARTONE, W. J., JARVIS, W. R. & EMORI, T. G. (1992) CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infection Control and Hospital Epidemiology* **13,** 606-608

HOSGOOD, G. (1992) Wound complications following thoracolumbar laminectomy in the dog: a retrospective study of 264 procedures. *Journal of the American Animal Hospital Association* **28,** 47-52

MANGRAM, A. J., HORAN, T. C., PEARSON, M. L., SILVER, L. C. & JARVIS, W. R. (1999) Guidelines for prevention of surgical site infection, Infection Control Hospital *Epidemiology* **20,** 247-278. Health Protection Agency. www.cdc.gov/ncidod/dhqp/pdf/guidelines/SSI.pdf. Date accessed March 20, 2011

MARTIN, C. & POURRIAT, J. L. (1998) Quality of postoperative antibiotic administration by French anaesthetists. *Journal of Hospital Infection* **40,** 47-53

NICHOLSON, M., BEAL, M., SHOFER, F. & BROWN, D. C. (2002) Epidemiologic evaluation of postoperative wound infection in clean-contaminated wounds: A retrospective study of 239 dogs and cats. *Veterinary Surgery* **31,** 577-581

OWEN, L. J., GINES, J. A., KNOWLES, T. G. & HOLT, P. E. (2009) Efficacy of adhesive incise drapes in preventing bacterial contamination of clean canine surgical wounds. *Veterinary Surgery* **38,** 732-737

ROSIN, E., UPHOFF, T. S., SCHULTZ-DARKEN, N. J. & COLLINS, M. T. (1993) Cefazolin antibacterial activity and concentrations in serum and the surgical wound in dogs. *American Journal of Veterinary Research* **54,** 1317-1321

ROYAL COLLEGE OF VETERINARY SURGEONS (2010). RCVS Facts, The Annual Report of the Royal College of Veterinary Surgeons: Part 2. Online. www.rcvs.org.uk

SAKLAD, M. (1941) Grading of patients for surgical procedures. *Anesthesiology* **2,** 281-4

SILVER, A. (1996) Timeliness and use of antibiotic prophylaxis in selected inpatient surgical procedures. *American Journal of Surgery* **171,** 548-552

SLAUGHTER, M. S., OLSON, M. M., LEE, J. T. & WARD, H. B. (1993) A fifteen-year wound surveillance study after coronary artery bypass. *Annals of Thoracic Surgery* **56,** 1063-8

SONG, F. & GLENNY, A. M. (1998) Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. *British Journal of Surgery* **85,** 1232-1241

VAN KASTEREN, M. E., KULLBERG, B. J., DE BOER, A. S., MINTJES-DE GROOT, J. & GYSSENS, I. C. (2003) Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *Journal of Antimicrobial Chemotherapy* **51,** 1389-1396

VASSEUR, P. B., LEVY, J., DOWD, E. & ELLIOT, J. (1988) Surgical wound infection rates in dogs and cats. *Veterinary Surgery* **17,** 60-64

VASSEUR, P. B., PAUL, H. A., ENOS, L. R. & HIRSH, D. C. (1985) Infection rates in clean surgical procedures: a comparison of ampicillin prophylaxis vs a placebo. *Journal of the American Veterinary Medical Association* **187,** 825-827

WEESE, J. S. & HALLING, K. B. (2006) Perioperative administration of antimicrobials associated with elective surgery for cranial cruciate ligament rupture in dogs: 83 cases (2003-2005). *Journal of the American Veterinary Medical Association* **229,** 92-95

WHITTEM, T. L., JOHNSON, A. L., SMITH, C. W., SCHAEFFER, D. J., COOLMAN, B. R., AVERILL, S. M., COOPER, T. K. & MERKIN, G. R. (1999) Effect of perioperative prophylactic antimicrobial treatment in dogs undergoing elective orthopedic surgery. *Journal of the American Veterinary Medical Association* **215,** 212-216

WILSON, J. & ELGOHARI, S. (2009) Fifth report of the mandatory surveillance of surgical site infection in orthopaedic surgery. www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1259151994683. Date accessed March 20, 2011

Current British veterinary attitudes to the use of perioperative antimicrobials in small animal surgery

C. B. Knights, A. Mateus and S. J. Baines

Veterinary Record 2012 170: 646 originally published online May 4, 2012
doi: 10.1136/vr.100292