How to...

Use antibiotics in surgical patients

For this special edition of **companion** Jonathan Bray, Senior Lecturer in Small Animal Surgery at Massey University, New Zealand, describes the rational use of antibiotics in surgical patients

The skin and mucosal surfaces provide an important barrier to bacterial colonisation of the underlying tissues. When these barriers are penetrated as part of a surgical intervention, there is a risk of developing an infection.

Although surgical site infections are rarely a cause of death, they can contribute to a delayed surgical recovery, increased morbidity or debilitation, or cause catastrophic failure of a repaired wound or fracture. Surgical site infections are inevitably associated with increased costs – both financial and emotive – and surgeons obviously strive to do all they can to prevent an infection from developing.

The role of antibiotics in preventing infection following surgery has been recognised from the 1950s. Since that time, there has been an enormous amount of research, comment and opinion published that has advanced our understanding surrounding the perioperative use of antibiotics.

When considering the role of antibiotics in the perioperative period, it is important to recognise the distinction between prophylactic and empirical antibiotic therapy. The goal of **prophylaxis** is to reduce the incidence of postoperative wound infection, and assumes use where contamination *might* occur, but has not yet happened. **Empirical** therapy is the continued use of antibiotics after the operative procedure based upon the intraoperative findings (e.g. leakage of a viscus). **Inappropriate prophylaxis** is characterised by the unnecessary use of broad-spectrum agents and continuation of therapy beyond the recommended time period. These practices increase the risk of adverse effects and promote the emergence of resistant organisms.

Why all the fuss about antibiotics?

There is no question that antibiotics are effective in preventing development of an infection following surgery. A meta-analysis of 26 *other* meta-analysis studies strongly supported the hypothesis that antibiotic prophylaxis was an effective intervention for preventing surgical site infection over a broad range of surgical procedures.

However, administration of antibiotics increases the prevalence of antibiotic-resistant bacteria causing infection. It is well accepted that increased antibiotic

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use leads to the development of more resistance. In human surgery over the last 10 years, an increasing number of resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Candida* species, and infection with organisms such as *Clostridium difficile* (a cause of antibiotic-associated colitis), have been commonly implicated in surgical wound infections. Such developments have forced a tougher evaluation of antibiotic usage, and a strict adherence to national guidelines.

Good data on the incidence of surgical site infection is not available for the veterinary profession. However, there is no reason to believe that we should be immune to similar trends. Reported cases of MRSA infection in domestic animals have been increasing, particularly in orthopaedic procedures where surgical implants are used. This suggests that veterinary patients are not immune to the changes in antibacterial resistance of bacterial flora that are occurring in the population.

Although an individual veterinarian may believe their own hospital policies are unlikely to make a significant impact on the global trend of antibiotic resistance, there is good evidence to suggest that inappropriate use of perioperative antibiotics may increase the risk of surgical site infection with more difficult opportunistic organisms. This is because surgical site infections typically develop due to colonisation of the wound with bacteria arising from either the patient's own endemic flora or from the human staff involved in its care.

In one recent study, 2 out of 10 staff in a veterinary orthopaedic referral hospital were found to be positive for nasal colonisation with MRSA, and a higher rate of MRSA-associated wound complications was identified in cases managed by one surgeon who was consistently positive for nasal MRSA during the study period. It must now be assumed that animals coming into a veterinary hospital for surgery will also be carriers of opportunistic bacteria they have acquired from their own environment.

The prevalence of antibiotic-resistant bacteria in any population is related to the proportion of the population that receives antibiotics, and the total antibiotic exposure. Therefore, as the trend for increasing rates of antibiotic resistance in all human hospitals rises, so too does the likelihood that staff and animals will be carriers of antibiotic-resistant organisms.

This trend is important as it has been shown that if antibiotic usage following routine surgery is prolonged, selection for these resistant organisms may lead to infection. In a small study comparing short term (24 hour) with longer term (five day) prophylaxis following excision of head and neck lesions, significantly fewer patients in the short term group

developed wounds infected with MRSA (4/33 compared with those treated long term (13/31, $p=0.01$).

Historical perspectives

The principles of antibiotic prophylaxis were founded from several key experiments performed in the 1950s and '60s. Although these experiments may seem unsophisticated by today's standards, they continue to give a valuable insight into the interaction between the host tissues and bacteria, and the role of antibiotics.

In 1957, Miles *et al.* defined what they termed a 'decisive period', which represented an intense period of activity between the host defense mechanisms and the bacteria. These defense systems – which we now know to represent opsonin proteins and other non-specific neutralisers of bacterial activity – act immediately when bacteria are introduced into normal tissue. These tissue defenses are capable of decreasing the infectivity of contaminating bacteria, thus lowering or eliminating the potential for visibly evident inflammation or for infection to develop.

Miles *et al.* (1957) also demonstrated that the ultimate size of a lesion was determined by the effectiveness of the antibacterial reactions mustered by the tissues during this period. Crucially, they were able to demonstrate that the duration of this 'decisive period' was brief – lasting for just 2–3 hours after bacterial inoculation. Changes to the host defenses after this period had no impact on outcome; in essence, the battle between bacteria and host had been decided within these first few hours of bacterial contamination.

Miles *et al.* concluded that because this 'decisive period' was predictively short, the point at which preventive antibiotic supplementation may be stopped after surgery could also be accurately determined – assuming there was no ongoing contamination.

In 1961, Dr John Burke published the results of an important study that addressed many fundamental issues of wound infection and antibiotic usage. In this

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study, he created similar sized incisional wounds on animals, and inoculated each wound with the same quantity of bacteria known to induce an infection. The wound was then closed. Dogs were grouped according to the timing of administration of the antibiotic.

In Group 1, dogs were given an intravenous antibiotic 1 hour before the wound was created and bacterial inoculation performed. In Group 2, dogs were given the antibiotic at the same time as the wound was created and bacteria inoculation occurred. In Group 3, dogs were given the antibiotic after wound creation, bacterial inoculation and wound closure had occurred. In the final Control Group, no antibiotics were given at all.

Crucially, none of the dogs in Group 1 developed a wound infection, whereas dogs in both Groups 2 and 3 developed an infected lesion that was roughly of similar size and extent as the Control Group. This simple experiment reaffirmed the observations of Miles *et al.*, and demonstrated the importance of antibiotic being in the circulation when contamination of the wound occurred.

In a second phase of Burke's experiment, the treatment of Group 1 dogs was expanded to include two new groups. In Group A, just a single preoperative intravenous antibiotic was given. In Group B, antibiotics were continued for 5 days after surgery. In this study, there was no difference in infection rates between the two groups, indicating that continued courses of antibiotic were unnecessary if no further contamination of the wound occurred. This experiment, again, reaffirmed Miles *et al.* observation of a time-dependant decisive period.

Based on his experiments and understanding, Burke was able to make the following pertinent observations, which remain relevant today:

1. "The effectiveness of defense against bacteria depends largely on host resistance.
2. Host resistance is reduced by the abnormal physiology induced by anesthesia and surgery.
3. The risk of infection can be reduced, or prevented, by supplementing the host's antibacterial resistance, but only if the supplement is delivered before bacterial contamination of the tissue has occurred.
4. Supplements to host resistance serve no purpose if they are delivered for periods longer than four hours after the end of the period of active bacterial contamination of tissue.
5. Preventive antibiotic supplement is reasonable only if the risk of infection or infectious morbidity or mortality is clearly greater than the risk of side effects to the preventative antibiotic."

Reducing the need for antibiotics

It is often quoted that infection will develop if more than 10^6 bacteria per gram of tissue are present. However, the number of bacteria required to produce infection in guinea pig muscle will be reduced 1,000-fold if the muscle has been crushed. Even fewer bacteria are required if foreign material is also introduced. Thus, the surgeon's technical skill is also a key factor in whether contaminating bacteria are able to gain the upper hand against tissue defenses, and allow an infection to develop.

When considering the causes of infection, Louis Pasteur recognized the importance of factors other than the mere presence of bacteria when he observed that *"the germ is nothing: it is the terrain in which it grows which is everything."* In human medicine, it is known that infection rates can vary from surgeon to surgeon, from hospital to hospital, from one surgical procedure to another and – most importantly – from one patient to another. Clearly, development of a wound infection involves an interplay between host factors, the wound environment and the virulence (and quantity) of bacteria contaminating the wound.

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Bacterial contamination of a surgical wound is more likely to arise from the patient's own flora; however, the surgeon and the surgical environment (including instruments) are also possible sources. Many of the rituals of surgical preparation are directed at reducing the potential for bacterial contamination of the open wound. Such rituals include:

1. Preparation of the patient by clipping fur around the surgical site and using antiseptic washes to remove oil, organic debris and to reduce the numbers of transient and resident bacteria.
2. The use of dedicated surgical attire for the surgeon (including scrubs, hats, mask), and similar decontamination of the surgeon's hands using antiseptic washes and surgical gloves.
3. Sterilisation of instruments.
4. Utilising drapes and other barriers to isolate the surgical wound from the unprepared areas of the animal and surgical table.

In human surgery, such routines are universally accepted as a minimum standard of care in the operating theatre. However, there is good evidence that the veterinary profession in the UK has a low level of implementation of such accepted practices. In a recent survey of first-opinion practices, sterile surgical gloves were utilised in just 37.5% of practices, with gowns, masks and facemasks being worn in just 14.3%, 12.5% and 10.7% of practices, respectively.

In a separate study, practices were evaluated on their use of different skin preparation techniques. This study found that 79% of practices were unaware of the concentration of scrub preparation being used, or the contact time necessary between the antiseptic and skin during surgical preparation. In some cases, the concentration of antiseptic being used may actually have been too low to be effective at killing bacteria. Twelve percent of practices used chlorhexidine gluconate and povidone-iodine together to prepare the skin; however, these two agents are incompatible and the combination effectively provides limited or no skin asepsis.

Veterinarians may be unwilling to 'buy into' the entire gamut of surgical rituals for a variety of reasons: financial costs are likely to be uppermost, but others may cite the lack of evidence for an individual item to lower infection rates. However, the *collective* value of dedicated surgical attire and sterile barriers such as gloves, gowns and drapes in lowering wound contamination rates is well accepted, and will continue to represent 'best practice' in human and veterinary hospitals. The concern is that anecdotal evidence suggests that veterinarians tend to rely on *ad hoc* administration of antibiotics to mask poor practice.

Guidelines for antibiotic use

Surgical site infection is by no means an inevitability of surgery. Therefore, the routine administration of antibiotics for every surgical intervention in the hope of eliminating infection is shortsighted. The surgeon must weigh up the likelihood of encountering contamination during the surgery, or whether the surgical wound is likely to favour the perpetuation of bacteria (e.g. because of the use of implants). In those instances, the use of prophylactic antibiotics may be justified.

From these experiments, and the results of further clinical studies, guidelines for the use of antibiotic prophylaxis have been established. These include:

■ **Prophylactic antibiotics should be administered within 1 hour prior to incision**

Based on the work of Miles *et al.* and Burke, we know that for antibiotics to be effective, therapeutic tissue levels must be present within the first hour or two of wounding – to supplement the tissue defenses during the 'decisive period'. This is best

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achieved by the use of an intravenous preparation; the diffusion gradient created by the higher peak plasma concentration allows antibiotic levels in the tissue to be more predictable. If subcutaneous preparations are used, it becomes more difficult to determine when tissue levels are likely to be adequate, as a range of factors can influence antibiotic absorption from the injection site.

However, it may be assumed that injection of a subcutaneous antibiotic at the time of surgery will fail to meet the objectives of prophylaxis as illustrated by Miles et al. and Burke.

■ **A single preoperative dose of antibiotic is as effective as a 5-day course of postoperative therapy assuming an uncomplicated procedure**

Burke's work (and others) has clearly shown that a single course of antibiotic provides adequate protection from the contamination that occurs during routine surgery – provided that any contamination was not excessive (e.g. spilled viscus). When contamination does occur, continuation of a *therapeutic* course of antibiotics is then appropriate. In all other instances, once surgery has finished and no further contamination of the wound is expected, antibiotics can safely be stopped.

■ **During prolonged procedures, antibiotic prophylaxis should be re-administered every 2–3 hours**

The duration of surgery directly affects the number of bacteria that can gain access to the wound. For every hour of surgical time, the infection rate can double. To maintain tissue levels of antibiotic during the operative period, repeated intravenous administration is recommended every 2–3 hours.

■ **Prophylactic antibiotics should target the anticipated organisms**

In human surgery, there has been little change in the incidence and distribution of pathogens isolated from surgical site infections during the last decade. The predominant skin bacteria are staphylococci, streptococci and corynebacteria, with Gram-negative enteric bacteria present around the caudal aspect of the body. In most instances, therefore, coverage with a cephalosporin or clavulanate-potentiated amoxicillin is appropriate for this bacterial spectrum. When entering the GI tract, the potential for exposure to other organisms will increase, and supplements to this standard protocol may be required. The colon and distal small intestine will

contain an enormous reservoir of facultative and anaerobic bacteria, so antibiotics targeted at these organisms would be appropriate for surgical procedures including these organs.

Changing practice policies

It is likely that many surgeons and veterinary practices will have a practice of antibiotic administration that is founded on custom, unsupported beliefs or adherence to dogma. However, many surgical procedures performed in general practice do not meet the guidelines whereby prophylactic antibiotics would be considered necessary. In brief, this includes surgeries that are of short-duration, elective procedures performed on systemically healthy individuals; and those procedures where no contaminated viscus is going to be penetrated. Such procedures include elective neutering, simple lumpectomies and other minor surgical interventions. In most other instances, a single-dose of intravenous antibiotic (a cephalosporin or clavulanate-potentiated amoxicillin) given in the immediate preoperative period is safe, and in accordance with international practice.

Changing hospital practices can be difficult to achieve as the anxiety regarding infection often subjugates any desire to reduce a reliance on antibiotics. However, if this article has made you question your existing procedures, then it has fulfilled its brief. The next step requires a commitment to change. You may choose to do this as a clinical trial – to randomise the administration of a new antibiotic protocol to patients, and monitor wounds closely for signs of infection. If you have confidence in your perioperative routines, surgical site infection should be evident in no higher than 2.5–4.8% of patients. The ideal would be to achieve this standard of care without 'masking' poor clinical practice with antibiotics. ■

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