**Organ Failure**

Friday 3\(^{rd}\) October 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.45-09.15</td>
<td>Registration and refreshments</td>
<td></td>
</tr>
<tr>
<td>09.20-09.50</td>
<td>Is the golden age of antibacterials about to end?</td>
<td>Ian Battersby</td>
</tr>
<tr>
<td>09.55-10.25</td>
<td>PROTECT: The responsible use of antibacterials</td>
<td>Ian Battersby</td>
</tr>
<tr>
<td>10.30-11.00</td>
<td>Perioperative antibiotics</td>
<td>Dr A. Freeman</td>
</tr>
<tr>
<td>11.00-11.30</td>
<td>Refreshments</td>
<td></td>
</tr>
<tr>
<td>11.30-12.00</td>
<td>Medical management of hepatic encephalopathy</td>
<td>Penny Watson</td>
</tr>
<tr>
<td>12.05-12.35</td>
<td>RESEARCH: A review of shunt anatomy</td>
<td>Prof. Rob White</td>
</tr>
<tr>
<td>12.40-13.10</td>
<td>Outcome measures for shunt cases</td>
<td></td>
</tr>
<tr>
<td></td>
<td>both surgical and medical- a review</td>
<td>Mickey Tivers</td>
</tr>
<tr>
<td>13.10-14.10</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>14.10-14.50</td>
<td>RESEARCH: Experiences of feline ureteral obstruction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>From stents to SUBS – where are we now?</td>
<td>Nicola Kulendra</td>
</tr>
<tr>
<td>14.55-15.35</td>
<td>Renal biopsies – they’re back!</td>
<td>Rosanne Jepson</td>
</tr>
<tr>
<td>15.40-16.10</td>
<td>Refreshments</td>
<td></td>
</tr>
<tr>
<td>16.10-17.00</td>
<td>Maxillofacial reconstruction</td>
<td>Timothy Martin</td>
</tr>
<tr>
<td>17.00-18.30</td>
<td>Free time</td>
<td></td>
</tr>
<tr>
<td>18.30 – 20.00</td>
<td>Ghost tour</td>
<td></td>
</tr>
<tr>
<td>20.30.......</td>
<td>Gala dinner</td>
<td></td>
</tr>
</tbody>
</table>
Antibiotics are regularly prescribed in practice and it is not uncommon for veterinary surgeons to prescribe them without having first documented an infection [1]. As such, antibiotics are not always prescribed appropriately. In contrast to many drugs prescribed, the more frequently antibiotics are used, the less effective they become, due to the selection of resistant bacteria. It is, therefore, important that clinicians understand the implications of the overuse of antibiotics and the principles of optimal prescribing.

The problem of emerging multi-resistant bacteria is well recognised in human medicine. The proportion of methicillin resistant Staphylococcus aureus (MRSA) among all S. aureus bacteraemias remained under 3% until 1992, but by 2002 this had risen to 43% (2). In the second volume of the Chief Medical Officer (CMO) report of 2011 Professor Sally Davies chose to focus on the rise of antibiotic resistance, calling for this ‘very real threat’ to be placed on the national risk register (3). The British Society for Antimicrobial Chemotherapy is currently highlighting the slow development of new antibacterial agents and is actively petitioning the government to increase research in this area (www.antibiotic-action.com ).

The impact of veterinary antibiotic prescribing on human health is an area attracting attention. An open meeting between the Royal College of Veterinary Surgeons, Royal College of Pathologists and Royal College of Physicians in October 2012 was held to debate the current opinions based on available evidence (The presentation slides can be found at www.rcvs.org.uk/news-and-events/past-events/joint-symposium-on-antimicrobial-resistance). The complex interaction between animals, humans and the environment e.g. sewage and soil, means that this is not a simple relationship to assess comprehensively, so work in this area continues.

Antibiotic usages (per ton) is significantly higher in farm animals than small animals, despite this our responsibilities to use antibiotics to minimise the development of resistance bacteria is not negated. Multiresistant nosocomial infections impacts on patient welfare but also to minimise the theoretical risks to human health. In addition by adopting a unified responsible approach to antibiotic prescribing across the veterinary profession we can justifiably argue that restrictions on veterinary prescribing of antibiotics is not required.

MRSA is a well-publicised multiresistant bacteria with relevance to human health. There are documented cases of MRSA infection in companion animal practice; the multi-drug resistant strains of Methicillin Resistant Staphylococcus pseudointermedius (MRSP) (previously S. intermedia) are, however, more of a concern (4,5). Hospitalisation and antibiotic treatment are risk factors for MRSP carriage in dogs (6). A UK laboratory reported that in 2008, MRSP accounted for 14% of coagulase positive Staphylococci isolated from dogs (7). Worryingly, in this study, the MRSP resistance profiles were more extensive than those for MRSA.

In small animal practice the close relationship between pets and owners has raised concerns regarding transmission of resistant bacteria(8). Dogs can acquire MRSA from humans, and, conversely, domestic animals can act as a vehicle for MRSA transmission to humans. The significance of this interspecies transmission of MRSA is not yet clear, but its incidence is believed to be low (9).

In the case of MRSP, although S. pseudointermedius rarely colonises humans, carrier rates are increased amongst individuals exposed to dogs.(10) There is, therefore, the possibility of a clinically significant MRSP infection developing in a human carrier (11). Furthermore MRSP could be considered a potential source of genetic material encoding resistance which could transfer to Staphylococcal strains that colonise or cause disease in humans and vice versa(12).

How does antibiotic usage influence the development of resistance?
Bacterial resistance can be categorised as follows:
1 - Inherent resistance – The absence of a cell wall in some bacterial species, for example Mycoplasmas, render agents which inhibit cell wall synthesis, such as β lactams, ineffective. Similarly anaerobic bacteria are inherently resistant to aminoglycosides as drug uptake mechanisms are oxygen dependent.
2- Spontaneous chromosomal mutation – It is estimated that once in approximately 10 million bacterial divisions, a mutation occurs. Each mutation may or may not result in a survival advantage. If the mutation is not detrimental to the bacteria then it is passed onto future generations. Such a mutation might confer resistance to antibiotics.

3- Transferred resistance – An example of a transmissible genetic elements are plasmids which can be transferred between individuals of the same or different bacterial species. If a plasmid encodes antibacterial resistance this can be transferred and disseminated amongst a bacterial population. Mutations which encode resistance do not require the presence of antibiotics for their generation. the introduction of selection pressure (an antibacterial) will preferentially select the strain that bears an advantageous genotype and the longer the exposure to the antibacterial the more rigorous the selection process. Therefore the presumption that long courses of antibiotics prevent resistance is incorrect; prolonged courses eliminate the sensitive bacteria and exert positive selection pressure favouring resistant strains. Furthermore since plasmids may encode resistance to several antibiotic classes, use of one antibiotic may result in selection for strains with resistance to multiple antibiotic classes. Observations have also shown that in the presence of an antibacterial, bacteria can become hypermutable through inactivation of the proofreading and DNA mismatch repair-systems that normally correct DNA copying errors. The transient induction of a hypermutable state adds a further twist to the selection pressure exerted by antibiotics and may explain why multiple mutations have emerged more rapidly than predicted.

Antibacterial resistance is a complex and dynamic process, and for further information on resistance development see (3,13,14)

References
PROTECT: The responsible use of antibiotics?

Ian Battersby BVSc DSAM DipECVIM-CA MRCVS
RCVS and European Specialists in Internal Medicine
Davies Veterinary Specialists Manor Farm Business Park Herts.

The PROTECT Antibiotics Campaign is a SAMSOC/BSAVA initiative that was conceived on the SAMSOC discussion forum. The forum post expanded on the lack of prescribing policies in veterinary practice and its potential impact. The P.R.O.T.E.C.T acronym was design to remind clinicians some of the key principles in responsible antibiotic prescribing. In addition to help design a practice policy with suggestions of antibiotics that may be/may not be appropriate in common clinician situations.

Developing a Practice Prescribing Policy.
Antibiotic stewardship is designed to ensure cost-effective therapy and improve patient outcome while minimising selection for bacterial resistance. Stewardship can be instigated at multiple levels; including awareness campaigns, hospital guidelines, or implementation of restricted antibiotic usage.

A practice policy should also include a list of conditions for which antibiotics are not indicated and guidelines on perioperative and post-operative antibiotic prescribing. Following implementation of a practice policy, monitoring of culture profiles within the practice allows adjustments to the policy if trends are identified.

The positive impact of empirical prescribing guidelines on resistant profiles in hospitals has been highlighted in human medicine. Protocols normally involve multiple strategies, making accurate assessment of the antibiotic stewardship programmes challenging due to their complexity. Stewardship in combination with other infection control protocols has assisted in the reduction of hospital acquired infections in England, which in 2011 had a prevalence of 6.4% compared to 8.2% in 2006 (1). Active involvement of staff in development of the policy has shown to improve compliance and policies that involve the restriction of certain antibacterials have also proven effective (2). Such studies are rare in veterinary practice, nevertheless those that have been performed, have demonstrated a positive effect on prescribing habits. In 2006, for example, a Canadian teaching hospital demonstrated a reduction in the frequency of antibacterial prescribing, particularly of fluoroquinolones over a 9 year period (3).

Principles of prescribing antibiotics
The is a large topic however the following text will expand on some of the key points.

1- Are antibiotics really indicated in this patient?? This may seem a basic question, but it is the first and most important question to consider when deciding whether to prescribe antibiotics. It could be an easy decision in cases with an obvious bacterial aetiology (e.g. pyothorax) but less clear cut in others. Consider the following points before starting treatment:

• Consider the specificity of your findings for bacterial infection - The presence of bacteria, seen on cytology or culture, in the presence of an appropriate inflammatory response (e.g. cytologically) is a specific indication of infection. Elevated temperature is not specific for bacterial infection.

• If a patient fails to respond to an initial course of antibiotics, should a second course be prescribed? If empirical therapy fails it is important to question if the initial diagnosis was correct, or if an inappropriate drug was chosen (spectrum/pharmacokinetics). Changing antibiotic should only be considered following a review of the diagnosis, confirmation of infection and exclusion of factors that may affect treatment efficacy.

• Owner expectations - Owners are increasingly aware of bacterial antibiotic resistance, and are now more open to discussion about the over usage of antibiotics. Changing our own habits - does my case really need 7 days of antibiotics or with 3 or 5 and then review be ok. Do I prescribe antibiotics just in case in some situations?

2- Selection of the most suitable antibiotic
The VMD recently produced a document summarising its position on antibiotic prescribing and minimising resistance. In the document it states “ The VMD considers that it is justified on a case by case basis to prescribed an antibiotic on the cascade in the interest of minimising resistance, particularly were culture and sensitivity indicates that a particular antibiotic is
against a bacterial pathogen i.e. prescription of a narrow spectrum antibiotic on the cascade over a broad spectrum antibiotic that has a specific indication for that condition.”

There are a number of factors that must be considered when selecting an antibiotic. These include the site of infection, the most likely pathogen (if culture results are not available), the spectrum of activity of the drugs available, and their pharmacokinetic properties, potential side effects, route of administration, drug interactions and the prescribing cascade. Not all can be covered in this lecture.

**Spectrum of activity and target organism**

An understanding of which pathogens are likely to be encountered in specific infections can aid the clinician when prescribing empirically. Particularly if a gram stain can be performed and, antibacterials can be selected which are likely to be efficacious.

When considering the available drugs, selection of one with the narrowest spectrum of activity possible will minimise the selection of resistant organisms. Generally antibiotics used in veterinary medicine are broad spectrum some. Combination therapy can increase spectrum of activity in polymicrobial infections and, in some situations, there is synergism which improves efficacy (e.g. trimethoprim sulphonamides). Combination therapy is not effective at preventing antibiotic resistance except in very few situations (4) and, with the potential for drug antagonism, monotherapy is preferred to combination therapy for the majority of infections. Combination therapy should not be instigated without the support of culture and sensitivity testing, given the potential impact on selection for resistance (4).

**Pharmacokinetics and optimising drug penetration and treatment.**

Although some perceive certain antibacterials to be 'stronger' than others, the efficacy of the drug is determined by multiple factors including lipid permeability, environment of the target tissue (e.g. tissue pH, necrosis or presence of a foreign body), the spectrum of activity of the drug, in addition to antibacterial resistance. The pharmacokinetics of specific antibiotics can be obtained from a reference pharmacology text. These factors mean that sensitivity of bacterium to drugs in-vitro, does not guarantee success in-vivo.

The status of the host's immune system should also not be forgotten. Antibiotics have a role in killing and curing an infection, however, they assist the immune system to control an overwhelming infection. Treatment failure can occur when using appropriate antibiotics in patients with immunodeficiency due to chronic debilitation or malnutrition. The application of an antibacterial topically or locally can result in higher drug levels at the target site compared to systemic administration. Cultures and in-vitro resistance testing can offer a guide to the sensitivity of bacteria to a given drug based on anticipated serum or tissue levels following standard dosing (5). Topical therapy can achieve much higher local concentrations of antibiotics and can overcome apparent in-vitro resistance.

**Duration of course. How long?? As short as possible……**

Unfortunately to date the data to determine the shortest effective period of therapy for veterinary species is very limited. In human medicine there has been a shift towards much shorter courses of antibiotics (typically shorter than those used in veterinary species). Although there will, no doubt, be species differences, the author encourages readers to consider the shift in human medicine towards shorter course and whether, as vets, we have a tendency to prescribe longer courses than might be necessary.

**Minimise the use of second line antibiotics and those reserved for life threatening human conditions**

In human medicine a first line (or empirical) treatment is usually chosen on the basis of its efficacy. In veterinary medicine we adopt the definition that first-line antibiotics typically are older and less expensive drugs e.g. amoxicillin or potentiated sulphonamides. As veterinary surgeons we should minimise the empirical use of second line antibiotics, which should be reserved for cases in which culture and sensitivities indicate first line choices are ineffective. There are strong arguments that antibiotics restricted for use in life-threatening infections in human medicine (e.g. imipenem, linezolid, teicoplanin, vancomycin) should not be used in animals under any circumstances.
References

Perioperative antibacterial administration
Alistair Freeman BVM&S PhD DSAS(Soft Tissue) MRCVS
RCVS Recognised Specialist in Small Animal Surgery (Soft Tissue)
Senior Lecturer in Small Animal Surgery, University of Liverpool

Introduction
All surgical wounds become contaminated with bacteria, but whether or not this progresses to surgical site infection (SSI) depends on various factors. Surgical wounds can be classified according to the likely degree of bacterial contamination\(^1\), with SSI rates increasing with higher risk of contamination\(^2-5\) (Table 1).

<table>
<thead>
<tr>
<th>National Research Council (NRC) wound classification</th>
<th>Description of wound</th>
<th>Reported infection rates in dogs and cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>Non-traumatic, non-inflamed surgical wounds not entering the respiratory, gastrointestinal or urogenital tracts or oropharynx.</td>
<td>2.0-4.8%</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>Surgical wounds entering the respiratory, gastrointestinal or urogenital tracts or oropharynx with no unusual contamination. Clean surgeries where a drain is placed.</td>
<td>3.5-5.0%</td>
</tr>
<tr>
<td>Contaminated</td>
<td>Traumatic wounds with no purulent discharge. Surgical wounds entering the respiratory, gastrointestinal or urogenital tracts or oropharynx. Surgical wounds where spillage of contents occurs. Surgical wounds where a major break in aseptic technique occurs.</td>
<td>4.6-12%</td>
</tr>
<tr>
<td>Dirty</td>
<td>Traumatic wounds with purulent discharge, devitalized tissue or foreign material contamination. Surgery in the presence of abscessation or perforated viscer.a.</td>
<td>6.7-18.1%</td>
</tr>
</tbody>
</table>

Table 1: National Research council classification of wounds and reported wound infection rates in dogs and cats.

Patient factors including presence of an endocrinopathy and being male increase SSI rates\(^6\), as do duration of surgery and anaesthesia, anaesthetic protocol, time of clipping, type of skin preparation, number of personnel in the operating theatre and perioperative hypothermia\(^2-9\). Perioperative antibacterials may be prophylactic (used to protect the patient from future bacterial invasion and thus from future infection) or therapeutic (used to treat an infection that already exists). Here we will concentrate on prophylactic antibacterials.

Current recommendations
In principle, prophylactic antibacterials should be reserved for procedures with a high risk or serious consequences of SSI, should be narrow-spectrum and effective against the expected contaminants and should be given at a dose and by a route that ensures effective tissue concentrations at the time of surgery\(^10\). In humans, guidelines for prophylaxis in various types of surgery are based on large systematic reviews e.g. those published by the Cochrane Collaboration on penetrating abdominal trauma\(^11\), colorectal surgery\(^12\) and breast cancer surgery\(^13\). No similar guidelines for veterinary patients exist, but recommendations are
published in surgical texts and journal articles based partly on evidence from veterinary studies and partly on extrapolation from human medicine.

**Which patients should receive prophylactic antibacterials?**

As noted above, the risk of SSI in veterinary surgical patients varies with NRC wound classification. Because of this, recommendations for antibacterial prophylaxis are based around these categories (Table 2). Since contaminated and dirty wounds have a higher SSI rate than clean and clean-contaminated wounds, perioperative antibacterials are recommended for surgeries involving these classes of wound\(^2\,\text{\textsuperscript{5}}, 6\). As many dirty wounds are likely to be infected already, it may be advisable to continue this as a postoperative therapeutic antibacterial course based on culture and sensitivity results. For clean and clean-contaminated wounds, however, evidence is conflicting. Several studies show no effect of perioperative antibacterials on SSI rates in clean wounds\(^3, 5, 14-16\) and one study of cruciate surgeries reported a lower rate of infection-inflammation with use of postoperative oral antibacterials\(^17\), despite the fact that this is not recommended for prophylaxis. However, studies of orthopaedic procedures\(^18\) and some experimental studies e.g. on experimentally-induced bacteraemia following endovascular grafting in dogs\(^19\) demonstrate a beneficial effect of prophylactic antibacterials in clean wounds. Other studies report no effect of perioperative antibacterial administration in clean-contaminated wounds\(^6, 16\).

<table>
<thead>
<tr>
<th>Actual / anticipated NRC wound classification</th>
<th>Prophylactic antibacterial recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>Only in patients where another significant risk factor exists (e.g. anticipated long surgical / anaesthetic time, endocrinopathy etc.) or where consequences of infection would be catastrophic for the patient.</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>Use prophylactic antibacterials</td>
</tr>
<tr>
<td>Contaminated</td>
<td>Use prophylactic antibacterials</td>
</tr>
<tr>
<td>Dirty</td>
<td>Use therapeutic antibacterials</td>
</tr>
</tbody>
</table>

Table 2: prophylactic antibacterial recommendations for small animal patients based on NRC wound classification.

These disparate results may be due to study design (e.g. lack of power) or to the same NRC category including wounds that are at quite different risk of contamination, e.g. both gastrotomy and subtotal colectomy could be considered clean-contaminated even though the bacterial flora of the gut at these sites are very different. Despite the conflicting evidence, current recommendations\(^20\) are that prophylactic antibacterial use is justified in clean wounds where there is a high risk of infection due to the presence of one or more of the other risk factors detailed above or where the consequences of infection would be catastrophic (e.g. when implants are placed). As many wounds anticipated to be clean-contaminated may become contaminated and antibacterials may be beneficial in some clean-contaminated procedures, prophylactic antibacterial use is generally recommended for these too\(^20\).

**Which drug should we use?**

The expected bacterial contaminants in a wound vary by surgical site (Table 3). The antibacterial used should be effective against these organisms.

<table>
<thead>
<tr>
<th>Type of surgical procedure</th>
<th>Common pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophageal / gastroduodenal</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Gram +ve cocci</td>
</tr>
<tr>
<td>Biliary</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
</tr>
<tr>
<td></td>
<td>Clostridia</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Anaerobes</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
</tr>
<tr>
<td>Neurological</td>
<td>Staphylococci</td>
</tr>
<tr>
<td>Ophthamalic</td>
<td>Staphylococci</td>
</tr>
<tr>
<td></td>
<td>Streptococci</td>
</tr>
<tr>
<td></td>
<td>Enteric Gram –ve bacilli Pseudomonas</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Staphylococci</td>
</tr>
<tr>
<td>Orthopaedic</td>
<td>Staphylococci</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Staphylococci</td>
</tr>
</tbody>
</table>
Table 3: common pathogens encountered during surgical procedures:

<table>
<thead>
<tr>
<th></th>
<th>Streptococci</th>
<th>Enteric Gram –ve bacilli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>Staphylococci</td>
<td>Enteric Gram –ve bacilli</td>
</tr>
<tr>
<td></td>
<td>Clostridia</td>
<td></td>
</tr>
</tbody>
</table>

Cefalosporins or clavulanate-potentiated amoxicillin are a good choice for most antibacterial prophylaxis as they are relatively safe and effective. The Gram positive activity of cefalosporins decreases and the Gram negative increases as the generation of the drug increases from first to third: for most clean or clean-contaminated small animal surgeries where the expected pathogens are from the skin (Gram positive Staphylococci) and upper gastrointestinal (GI) tract (Gram negative bacilli) a first-generation cephalosporin is a suitable choice. For surgeries where anaerobic bacteria may be contaminants (e.g., lower GI tract or biliary system) either using a second-generation cephalosporin with antianaerobic activity or adding an antianaerobic agent such as metronidazole would be suitable.

**When should the drug be given, and for how long?**
The drug should be at an effective concentration in tissues when surgery begins and throughout the procedure. For cefalosporins, a common recommendation based on pharmacokinetic studies is to give the drug intravenously within 1 hour prior to surgery (for most procedures this will be either at or just after induction) and to repeat dosing every 2 hours until the end of surgery, then to discontinue use. Interestingly, administration of antibacterials preoperatively does not affect intraoperative bladder or urine culture results, so withholding antibacterials until bacteriology samples have been obtained during exploratory celiotomy may be unnecessary. Some authors recommend continuing prophylactic antibacterial use up to 24 hours postoperatively if there is a significant risk of contamination during that time before the wound is sealed: however, they should not be used for longer than this as this may actually increase SSI rates.

**Consequences of inappropriate prophylactic antibacterial use**
Inappropriate prophylactic antibacterial use may increase SSI rates, drive bacterial resistance, increase cost, cause alterations in normal bacterial flora and cause drug reactions.

**Are we following the guidelines?**
Unfortunately it appears not. A study of clean cruciate surgeries in Canada revealed that 15% of patients did not receive the first dose of antibacterial within 1 hour of the start of surgery, 49% did not receive an additional dose intraoperatively when it was required, 19% received an unnecessary second dose intraoperatively and 29% received postoperative antibacterials. A recent survey of mixed and small animal practices in the UK revealed the use of inappropriate drugs for prophylaxis such as third-generation cefalosporins and fluoroquinolones. Up to 32.1% of respondents said they would use antibacterials for a clean surgical procedure, only 25.8% of respondents said they gave perioperative antibacterials intravenously and only 66.6% gave them before surgery. This failure to follow published guidelines may be due to a lack of (or conflicting) evidence from veterinary studies as noted above, anaesthetists being reluctant to administer antibacterials around induction due to the risk of antibacterial-induced hypotension, higher perceived risk of SSI due to bacterial infection elsewhere in the patient, lack of knowledge, reliance on habit or inappropriate sources of information about antibacterial use, practice policy or to compensate for poor aseptic technique. In my opinion, another possible reason is fear of additional morbidity/mortality for the patient, the requirement for additional procedures, additional cost for the client and the potential for client complaints.

**Strategies for improving compliance**
There is a need for more evidence regarding the efficacy of perioperative antibacterials in veterinary patients, although conducting appropriate studies may be challenging. Many of the possible reasons for incorrect perioperative antibacterial use can be addressed by continuing to educate the wider profession about this topic and encouraging a high standard of surgical asepsis and surgical technique. While we are always going to be concerned about the impact of SSI on our patients, our concerns about their effect on client relationships can be...
addressed by thorough preoperative discussion of complications and provision of realistic estimates of cost.


**Medical Management of Portosystemic Shunts**

Penny Watson, Queen’s Veterinary School Hospital, University of Cambridge  
[Email](mailto:pjw36@cam.ac.uk)

**Which cases should be managed medically?**

It is clear that ACQUIRED PSS and micovascular dysplasia (MVD)/portal vein hypoplasia cases should be managed medically long term as there is no surgical option for these cases. These dogs can do very well – particularly dogs with congenital MVD where the clinical signs tend to be mild and the reported outcome with medical management is generally very good.

What about congenital PSS? Surely the best treatment is surgical ligation returning the liver to normal? Of course, this is not always possible – what happens if the dog has a concurrent MVD and portal hypertension develops as soon as ligation is attempted? What about partially ligated PSS which cannot be fully ligated at future surgeries? Do all these require long term medical management? How long should dogs which are fully ligated be managed medically post-operatively? And how long should all surgical cases be managed medically pre-operatively? And should all dogs be managed surgically, or can some be managed medically long term? What happens if the owner can’t afford surgery – is medical management even worth while? And what evidence do we have to base our decisions on? The truth is we have very little other than anecdote and dogma – although our recent prospective study of medical vs surgical management was an attempt to begin to start to answer some of these questions. There is also very little evidence to support the ‘traditional’ methods of medical management and it is time we updated the way we do this, as detailed in the next section.

There are some common ‘myths’ which appear repeatedly in the literature which don’t currently have an evidence base. It has been suggested that if you cannot ligate a congenital PSS (either for technical reasons or because the owner declines or can’t afford surgery) these animals should be euthanased and not managed medically long term as they have a poor prognosis; that without ligation, the liver progressively atrophies and fails in a short time and that dogs managed medically live short, unhappy lives. This can of course become a self-fulfilling prophesy. If we advise owners that their dog will live a short, unhappy life without surgery they are very likely to consider euthanasia very quickly, or to give up as soon as the dog or cat shows any clinical signs. In fact, many dogs and even some cats can be successfully medically managed for a very long time. We can often also reverse a neurological crisis (which usually has a defined trigger) and the animal can continue to live a long life. In both our original retrospective study (Watson and Herrtage 1998) and the recently published prospective study (Greenhalgh et al. 2014), some dogs were medically managed for more than 8 years after diagnosis.

The myth of short, unhappy lives is likely based on logical extension from the pathophysiology of the disease: the portal blood usually supplies about 50% of the liver’s oxygen requirement, but this is obviously reduced in PSS. Animals
with PSS typically have arteriolar hyperplasia in an attempt to make up for the reduced portal flow but they often still have some degree of hepatic underperfusion. In addition, PSS results in reduced delivery of ‘hepatotrophic factors’ such as insulin to the liver which contributes to hepatic atrophy. However, it should be noted that, although animals with PSS have small livers, hepatic atrophy does not appear to be progressive throughout life: rather, the liver reaches a ‘stable’ small size and remains at that size. It is even possible for the liver to regenerate after removal of a lobe surgically in a dog with a PSS.

Until very recently, there is been very little information available directly comparing the success of medical vs surgical management of congenital PSS. A recent multi-centre study co-ordinated from Cambridge suggests that dogs live longer after surgical management (Greenhalgh et al. 2014). In this study of 124 dogs recruited prospectively from three different referral centres, 78% were surgically managed by a variety of means while 22% had medical management.

The majority of cases were extrahepatic PSS (110) but there was no significant difference in the proportion of extrahepatic and intrahepatic shunts or age at diagnosis between the medically and surgically managed dogs. The survival rate of surgically managed dogs was significantly greater than the medically managed dogs.

Does this mean we don’t manage any dogs medically long term any more? No! We still manage a number of cases medically both in the short and long term for both clinical and financial reasons. Dogs in both the medical and surgical arms of the study did have surprisingly long survival times – in fact, this recent study was an add-on to a previously published study which had only followed up the dogs for three years, by which time most were still alive (Greenhalgh et al 2010). The study also doesn’t address the outcome in dogs with PSS which don’t have clinical signs because all the dogs in the study presented with clinical signs of their PSS. Do these do better when managed medically than dogs with clinical signs?

**What is the ideal medical management of dogs and cats with PSS?**

It is important to do this properly, understanding the new concepts about concurrent inflammatory disease and protein requirements. There is a risk of inappropriate medical management either pre or post surgery resulting in protein-calorie malnutrition and a worse outcome and of course this must be avoided as much as possible.

Both acquired and congenital shunts result in a significant amount of portal blood bypassing the hepatic sinusoids and directly entering the systemic circulation. The most obvious clinical consequence of this is the development of hepatic encephalopathy (HE) as a result of toxins of gut origin reaching the brain. Many compounds are implicated in causing HE in dogs and cats but ammonia remains the most important encephalopathic toxin and treatments for acute and chronic HE are usually aimed at lowering blood ammonia levels. Additional effects of portal blood bypassing the liver are reduced clearance of bacteria and potential bacteraemia; hepatic atrophy and a reduction in the metabolic activity
of the liver contributing to inefficient use of dietary components, poor growth and loss of lean body mass. This is important! It is known that dogs with experimentally induced PSS have an increase in dietary protein requirements. A recent study of dietary management of dogs with PSS showed serum albumin in one dog dropping from 16 g/l to 9 g/l after feeding a low protein diet, which is likely to have significant clinical consequences (Proot et al. 2009).

Traditionally, treatment of HE relied on feeding a low protein diet little and often combined with antibiotics and lactulose. However, the emphasis in human medicine has moved away from dietary protein restriction in HE for the reasons outlined below and the author no longer uses protein restriction in dogs with congenital or acquired PSS but relies on feeding a digestible diet little and often and managing concurrent inflammatory disease (Frederick 2011; Shawcross & Jalan 2005).

Ammonia originates from a number of sources, varying between patients. In most dogs, the primary source is the gut, but a significant amount can also be derived from breakdown of body protein if the dog or cat is in negative nitrogen balance. Gut-derived ammonia was traditionally assumed to be a by-product of intestinal bacterial metabolism in the colon. This remains an important source in some conditions such as uraemia and malaena. However, recent studies in other species suggest that small intestinal enterocyte metabolism of glutamine as their main energy source is the most important source of post-prandial ammonia absorption in the portal vein. This is something which can’t be stopped or the gut dies! However, it can be reduced by feeding little and often and it may be that some foods require less energy to digest than others. Indeed, some dietary protein sources appear to be better than others in dogs with HE. Dogs on soya protein diets show a lower plasma ammonia concentration than those fed meat protein (Proot et al. 2009)

An additional important trigger for HE in humans and rodents is inflammation: recent studies have confirmed that inflammatory cytokines are synergistic with ammonia in precipitating HE and that controlling inflammation in other organs is an important part of managing the patient with HE. There is increasing evidence that this is also true in dogs (Gow et al. 2012).

The management of HE can be summarised as follows:

1) Manage precipitating factors – most cases are actually precipitated by inflammatory disease elsewhere and management of this will often resolve the HE. Anecdotally, this is often an occult urinary tract infection so perform a urine culture and consider the possibility of pyelonephritis.

2) Give appropriate fluid and electrolyte therapy. Dehydration, hypokalaemia and alkalosis will precipitate HE. Hypoglycaemia will worsen the outcome. It is therefore very important to measure electrolytes and blood glucose in these cases and supplement as necessary. IV fluids are necessary in acute cases, appropriately supplemented.

3) Treat and prevent constipation. Lactulose is still often used in humans and animals. It has many theoretical benefits in maintaining soft faeces
and reducing ammonia absorption, although experimental evidence for its efficacy is lacking. In acute cases, lactulose enemas followed by per rectal administration or neomycin can be very helpful.

4) Consider antibiotic therapy: ampicillin is often used in small animals and is proposed to reduce ammonia production in the intestine, but perhaps in many cases it is also efficacious as it reduces any other bacterial infections which precipitated the HE in the first place. Neomycin is a good short term choice. There is some limited evidence in support of probiotics in humans but no work in dogs. Rifaximin is the current antibiotic of choice in humans with HE but is not licensed for use in dogs and there are no studies on its use in this species.

5) Do not starve your patient: institute little and often feeding of a moderate protein, highly digestible diet as soon as possible - remember that ammonia production as a result of negative nitrogen balance (ie protein-calorie malnutrition) will precipitate HE just as easily (perhaps more easily!) than intestinal feeding.

6) Animals which seizure (uncommon) can be treated initially with iv or per rectal diazepam, although this is often ineffective because of the effect of HE on the benzodiazepine receptor. If this is not effective, propofol infusions are usually efficacious. The dose of propofol is calculated by giving an initial bolus to effect (usually about 1mg/kg), timing how long it takes for the animal to show mild signs of seizures, such as mild limb paddling again, and then dividing the dose by the time to calculate an infusion rate. In practice, the dose of propofol to give by constant rate infusion is usually about 0.1 to 0.2 mg/kg/min Dogs sometimes need to remain on the infusion for hours or days, but the rate can be gradually reduced to control seizures while still allowing the dog to regain consciousness—in some cases, even enough to start eating. Propofol infusions can result in Heinz body hemolytic anemia in both dogs and cats. Pre treatment with Levetiracetam administered at 20 mg/kg p.o. q8h for a minimum of 24 hours before surgery has been shown to reduce post operative seizures and death in dogs undergoing surgical attenuation of extrahepatic PSS with ameroid constrictors (Fryer et al 2011) but there are no studies showing the efficacy if given once the animal starts seizing. It would be rational to try it given its efficacy in other seizure disorders.

Acute HE is a true medical emergency. Fortunately, it is much less common than chronic, waxing and waning HE. Animals may present in status epilepticus or comatose, and although HE initially causes no permanent brain damage, prolonged seizures, status epilepticus, or coma will; prolonged severe HE by itself may lead to serious cerebral edema as a result of accumulation of the osmolyte glutamine (from ammonia detoxification) in astrocytes. In addition, the systemic effects of acute HE, particularly hypoglycemia, can be fatal if not recognized and treated. Intensive management is required. However, treatment is worthwhile because some animals can go on to complete recovery and successful long-term medical management, particularly if the acute crisis was triggered by a definable event (e.g., acute gastrointestinal bleeding in a dog with chronic liver disease and portal hypertension).
Selected references/further reading


Gow, A.G. et al., 2012. Dogs with congenital porto-systemic shunting (cPSS) and hepatic encephalopathy have higher serum concentrations of C-reactive protein than asymptomatic dogs with cPSS. *Metabolic Brain Disease*, 27(2), pp.227–229.


Greenhalgh, S.N., Reeve, J.A. & Johnstone, T., 2014. Long-term survival and quality of life in dogs with clinical signs associated with a congenital portosystemic shunt after surgical or medical treatment. ... *Veterinary Medical* ....


The role of portal blood flow in the morphology of congenital extrahepatic portosystemic shunts

Robert N White, Chris Shales and Andrew Parry
Willows Referral Service

Although the embryological development of the venous system is well described, there remains little information available regarding the embryological basis of portosystemic shunt development.

Knowledge of the normal development of the abdominal venous system is required to understand the abnormal development of congenital portosystemic shunts. Three pairs of venous channels drain into a single venous sinus of the developing heart in the early embryo. The vitelline veins return blood from the yolk sac, the umbilical veins bring oxygenated blood from the chorion (part of the early placenta) and the common cardinal veins return blood from the body of the embryo. All three systems are initially bilaterally symmetrical, but as a result of unequal patterns of vascular degeneration this symmetry is lost during embryonic development (Nodend and DeLahunta 1985).

The caudal vena cava (CVC), azygos vein, ductus venosus and portal vein develop by selective anastomosis, persistence and degeneration of components of four embryologic vessels; the supracardinal, subcardinal, umbilical and vitelline veins. The abdominal CVC, although ultimately a single continuous vessel, develops in five segments (pre-renal, renal, pre-hepatic, hepatic and post hepatic) from initially discontinuous portions of the supracardinal, subcardinal and vitelline veins. The portal vein develops from the vitelline veins (Figure 1).

![Figure 1. Schematic diagram of the contribution of different embryologic veins (supracardinal, subcardinal, umbilical and vitelline) to the caudal vena cava (CVC), portal vein and ductus venosus. (Hunt and others 1998)](image)

In the embryo there is continuity between the developing portal vein and the hepatic veins. Normally, this continuity should cease for two reasons; the development of the hepatic sinusoids and, following birth, the closure of the ductus venosus (Hunt and others 1998). Failure of one or both of these mechanisms will result in the formation of an intrahepatic portosystemic shunt (IHPSS).

Inappropriate anastomosis between the vitelline veins and the developing CVC will result in the formation of an extrahepatic portosystemic anastomosis. This anastomosis usually
involves the pre-hepatic segment of the CVC derived from the right subcardinal vein, which is not surprising considering that this vein is programmed within the embryo to anastomose with both the supracardinal vein and the cranial portion of the vitelline veins. This results in an extrahepatic portosystemic (caval) shunt (EHPSS) at the level of the epiploic foramen. Alternatively, the anastomosis might involve the embryonic precursor of the left phrenic vein leading to the development of an EHPSS (phrenic) shunt.

Recently, two studies have described the computed tomography angiographic (CTA) anatomy of EHPSSs (Nelson and Nelson 2011, White and Parry 2013). These studies have confirmed the consistent anatomy of some of the more common EHPSS observed in dogs and cats; for example, the splenocaval shunt, left gastro-phrenic shunt and the right gastro-caval shunt.

Over the last five years, the morphology of EHPSS emanating from the left and right gastric veins discerned by CTA, intra-operative mesenteric portography (IOMP) and gross findings during surgery have been reviewed and compared. The findings were also compared to abdominal vein CTA studies from both normal dogs and cats. Although there was some variation in shunt morphology, in the majority of cases the findings demonstrated remarkable consistency with the majority of the venous structures identifiable as ‘normal’ vessels associated with venous drainage of the spleen, stomach, pancreas, small intestine, diaphragm, et cetera. In the majority of cases, it proved possible to create the same ‘normal venous map’ of the portal system for each animal. Then, by imposing preferential flow through one of the draining vessels, it proved possible to create the various shunt types that were recorded by CTA, IOMP and gross findings during surgery. The lack of valves within the veins of the portal system allows for both hepatopetal (normal) and hepatofugal blood flow (Ref ?). As such, the presence of a portosystemic anastomosis will invariably produce hepatofugal venous flow in one or more of the veins of the portal system. This unusual attribute of the portal venous system allows venous blood flow to be controlled entirely by venous pressure gradients alone. The presence of an abnormal communication between the portal venous system and the systemic venous system will alter venous pressure gradients resulting in abnormal hepatofugal flow in one or more of the veins of the portal system and, hence, the angiographic findings on CTA and IOMP.

Although not proven, we suggest that many of the commonly recognised congenital EHPSS seen in both the dog and cat actually have very similar venous anatomy but the presence of preferential flow leads to the development of the commonly recognized EHPSS seen on both CTA, IOMP and at open surgery.

References

Outcome measures for shunt cases (surgical and medical) – a review
Mickey Tivers BVSc PhD CertSAS DipECVS MRCVS

Introduction
Having reliable and repeatable outcome measures for medical and surgical interventions is extremely important in veterinary practice in general. In dogs with congenital portosystemic shunts (CPSS) such measures are vital for assessing an individual’s response to treatment and the requirement for additional interventions. In addition outcome measures are critical for allowing valid comparisons between different treatment modalities in the hope of identifying optimal management regimes. A wide variety of different outcome measures have been proposed for and are used commonly in dogs with CPSS and the ‘best’ measure of outcome
is unclear. Indeed, many studies use a variety of different outcome measures and at a variety of different time points.

The overall aim of treatment of CPSS would be:

- To resolve clinical signs and provide the dog with a normal quality and quantity of life.

A more specific aim of surgical treatment would be:

- To attenuate the shunt to improve or restore normal portal blood flow in order to improve or restore normal liver function.

Intuitively the second aim should fulfil the first aim. However, the situation may be more complex and it remains unclear how important the degree of attenuation is in achieving the first aim. Therefore the precise end point of treatment is potentially unknown and it is possible that we are under or over treating some dogs with CPSS.

**Challenges**

There are a number of factors that present challenges to assessing the treatment outcome of CPSS.

- Wide variation in CPSS in terms of morphology and clinical signs, which may affect response to treatment.
- Wide variation in treatment strategies with variable end points of success.
- The significance of persistent shunting is unclear in dogs with an apparently good response to treatment.
- Dogs may be sub-clinically affected and this could lead to under-treatment of individuals.
- Quality of life assessments somewhat dependent on owners assessing whether their dog had returned to ‘normal’ when it may never have been ‘normal’ in the first place.
- How do we assess response to treatment in dogs with incidental CPSS and should we be treating these individuals anyway?
- Some outcome measures, such as objective assessment of persistent shunting, not relevant to medically managed dogs.

**Persistent or recurrent shunting**

Many objective outcome measures rely on the assessment of persistent or recurrent shunting. Persistent shunting can be due to on going blood flow through the CPSS due to a partial or incomplete attenuation. It can also be due to the development of multiple acquired shunts (MAS) presumably due to excessive or too rapid attenuation and a failure of the liver to cope with the increased blood flow.

Techniques employed to assess persistent or recurrent shunting include ultrasonography, scintigraphy, portovenography and computed tomography angiography (CTA). All of these techniques have their own advantages and disadvantages. However, one challenge is in deciding the importance of the persistent or recurrent shunting. Clearly if the dog has clinical signs attributable to shunting then action should be taken. However, how should we manage dogs with persistent or recurrent shunting but no clinical signs?

Several studies have shown that partial shunt attenuation or the development of persistent or recurrent shunting can be associated with clinical signs, sometimes resulting in euthanasia and therefore should be avoided (Hottinger and others 1995, Hunt and Hughes 1999, Komtebedde and others 1995, White and others 1998). Conversely, individual dogs treated with partial attenuation can have a good outcome without recurrence of clinical signs and studies have documented progressive closure of the shunt with time (Burton and White 2001, Komtebedde and others 1995, Lawrence and others 1992, Mehl and others 2007, Meyer and others 1999, Van Vechten and others 1994, White and others 1998).

Gradual attenuation devices such as ameroid constrictors and cellophane bands are commonly used to obtain gradual shunt attenuation. However, it has been shown that both techniques can result in persistent or recurrent shunting due to failure to achieve complete attenuation or the development of MAS. One study found that 28/116 dogs (24.1%) had persistent shunting on scintigraphy at 4-14 weeks post-op (Falls and others 2013). Dogs with
negative scintigraphy were 10.7 times more likely to experience a successful long-term outcome than those with persistent shunting. This finding suggests that incomplete shunt attenuation or the development of MAS is not desirable. In another study 6/16 dogs (37%) had increased shunt fractions on scintigraphy at 10 weeks following cellophane banding due to incomplete shunt closure in three dogs and the development of MAS in three dogs.

A recent study used CTA to assess for persistent shunting following ameroid constrictor placement (Hunt and others 2014). Although there was residual flow through the shunt in four dogs (18%) shunt fraction was only increased in one dog. This suggests that a small amount of persistent flow may be clinically irrelevant. It is likely that CTA provides the most reliable evidence of the presence and nature of persistent shunting.

A study reported the use of endovascular treatment of intrahepatic CPSS in dogs in which 92/95 dogs were treated with partial attenuation (Weisse and others 2014). The authors stated, “A complete attenuation of the shunt is not always the goal, as such, continued shunting may be anticipated in many cases…” Overall outcome was considered excellent in 66% of dogs, fair in 15% and poor in 19%. 33% of dogs that were re-evaluated had recurrence or persistence of clinical signs and 5 had an additional procedure that resolved the signs.

The importance of persistent flow through a CPSS or the development of MAS is therefore unclear and whilst this is certainly important as an outcome measure it must be interpreted in light of clinical and biochemical findings. The potential concern in an asymptomatic dog is whether they may subsequently develop clinical signs as a result of the shunting. Identifying this group of dogs represents a considerable challenge.

**Outcome measures based on liver function tests**

Liver function tests and in particular dynamic bile acid testing are commonly used to assess outcome in dogs with CPSS (Hunt and Hughes 1999, Hunt and others 2004, Lee and others 2006, Weisse and others 2014). However, studies have found that dogs with apparently good outcomes often have persistently increased serum bile acid concentrations although significantly reduced from pre-surgery (Hunt and Hughes 1999, Hunt and others 2004, Weisse and others 2014). As bile acids can be persistently increased, despite a good response to treatment, this questions their usefulness as an absolute indicator of outcome. Persistently increased bile acids might suggest that there is persistent shunting that we are unable to quantify using other methods or that there is underlying hepatic pathology that fails to resolve following treatment.

Ammonia tolerance testing may be more useful than bile acids for evaluating outcome but is not commonly used due to technical limitations.

**General response to treatment**

In general successful treatment should be associated with resolution of clinical signs and haematological and biochemical abnormalities. These are particularly useful for evaluating an individual’s response to treatment but are not commonly reported as an outcome measure. Clearly recurrence of clinical signs would be considered a poor outcome. However, some clinical signs or laboratory parameters are non-specific and future problems may not be attributed to the CPSS. In addition the requirement for ongoing medication can be considered unsatisfactory for surgically treated animals.

Increased body weight and, possibly more importantly, body condition score may be reasonably good indications of response to treatment. However, it is difficult to know whether dogs have achieved their full potential or have just improved.

Serum albumin concentration has been associated with successful CPSS treatment and this could be used as a marker of outcome (Kummeling and others 2012).

**Morbidity and mortality**

Blunt but very definite measures of outcome are peri-operative complications and mortality. Clearly dogs that die peri-operatively or that are euthanized or die as a result of their condition can be considered to have had a bad outcome. Many studies have focused on short
or long-term mortality as an outcome measure and this has been used to compare treatments (Tivers and others 2012). However, the situation is complicated by different definitions of short and long-term between studies. For long-term follow-up, in particular, it can be challenging to definitively ascribe mortality to CPSS rather than other possible causes.

**Quality of life assessment**
Quality of life is potentially the most useful outcome measure and may be more important than presumed objective end points. Whilst aiming for complete shunt attenuation may be ideal, if the dog goes on to have a poor quality of life or a rapid mortality then this should be considered a treatment failure. Quality of life is potentially very subjective and we are typically reliant on retrospective owner assessment, with all the inherent bias and variability associated with this. Studies have used a variety of different approaches including telephone interviews with owners and basic quality of life assessments. These typically take the form of a grade such as ‘Excellent’, ‘Good’ and ‘Poor’, based on persistent or recurrent clinical signs and the use of on going medication (Falls and others 2013, Komtebedde and others 1995, Smith and others 1995, Weisse and others 2014).

A recent study used a combination of survival and a quality of life assessment to evaluate the long term outcome of medically and surgically treated dogs (Greenhalgh and others 2014). This was a more robust assessment that incorporated the frequency of differing clinical signs into a composite score. Importantly, both quality of life and overall survival were looked at together.

However, there is a significant problem with quality of life assessments that is often overlooked. In general these assessments are asking the owner to assess whether their dog has returned to ‘normal’ following treatment. However, it is important to recognise that affected dogs may never have been ‘normal’. This may make assessing the response to treatment less accurate. Indeed, it is possible that there is significant ‘under-treatment’ of individuals that we assume to have made a complete recovery but may still have subtle clinical signs. This is also complicated by the fact that affected dogs can suffer from a wide variety of clinical signs. Whilst resolution of urinary tract calculi may be easy to quantify, normal weight gain and complete resolution of hepatic encephalopathy may be less clear-cut. In people with liver disease a syndrome of minimal hepatic encephalopathy is recognised. People appear normal but demonstrate significant abnormalities on psychometric testing and in neurophysiological performance (Groeneweg and others 1998, Shawcross and others 2007). It is unknown whether this occurs in dogs and may be impossible to test for in any event. A health related quality of life assessment scheme, which uses responses from unaffected dogs as a base line may provide more accurate assessment of outcome in dogs with CPSS.

**Other outcome measures**
Several studies have shown that liver volume, as assessed by CT or MRI increases following successful surgical management of CPSS (Kummeling and others 2010, Stieger and others 2007, Zwingenberger and others 2014). The most recent study showed that increased liver volume on CT was also associated with decreased hepatic arterial flow and that the increase in volume was greater in dogs with smaller livers (Zwingenberger and others 2014). This suggests that CTA could be used to assess response to treatment although further information is needed.

Some studies have focused on the presence of hepatic encephalopathy and associated inflammation in dogs with CPSS (Gow and others 2012, Kilpatrick and others 2014, Tivers and others 2014). It is possible that monitoring resolution of this inflammation may also provide additional information on outcome.

**Conclusions**
There are many different outcome measures for dogs with CPSS and it is clear that no single measure provides a definitive answer. A variety of factors pose specific challenges for determining outcome in CPSS. In most instances a combination of assessments will provide the best measure for an individual or group of animals. Further work should concentrate on establishing definite treatment goals, although these are likely to vary based on the characteristics of an individual dog. Overall, a reliable and repeatable measure of quality of
life, taken in light of survival data, is very important in determining outcome. Further work to refine such assessments as well as the validation of other measurements is recommended.

References


Gow, A. G., Marques, A. I., Yool, D. A., Crawford, K., Warman, S. M., Eckersall, P. D., Jalan, R. & Mellanby, R. J. (2012) Dogs with congenital porto-systemic shunting (cPSS) and hepatic encephalopathy have higher serum concentrations of C-reactive protein than asymptomatic dogs with cPSS. Metab Brain Dis 27, 227-229


Hunt, G. B., Culp, W. T., Mayhew, K. N., Mayhew, P., St...


Experiences of feline ureteral obstruction. From stents to SUBS – where are we now?

Ureteric obstruction is an increasingly diagnosed condition in cats. Medical management was successful in only a small proportion of cats and traditional surgical techniques such as ureterotomy was associated with a high rate of uroabdomen post-operatively or stricture formation in these cats who are recurrent stone formers.

Previous experience of placing ureteric stents was associated with a relatively high rate of complications in particular dysuria post-operatively which affected 40% of cats. Some of these cats could be managed with anti-inflammatory doses of prednisolone, however in others the dysuria was refractory; these cats either had their stents removed or were euthanised.

The subcutaneous ureteric bypass (SUB) device is an extra-anatomic device, which consists of a pigtail nephrostomy catheter connected to a cystostomy tube via a subcutaneous port.

Pre-operatively, haematology, biochemistry, urinalysis and stabilisation of the cat is performed as routine. Abdominal ultrasound is used to document the obstruction and to measure the size of the renal pelvis; the diameter of the pelvis ideally needs to be more than 5mm to allow the locking loop of the nephrostomy tube to sit in the pelvis. Also, cats who have chronic renal failure and no evidence of an obstruction or renal pelvis dilatation are not candidates and so ultrasound is important for case selection. If there is any doubt in the diagnosis, an antegrade pyelogram can be performed, although it is not performed routinely prior to SUB placement.

A midline laparotomy is performed and the obstructed kidney is identified and the caudal pole of the kidney is cleared of fat. An 18 gauge intravenous catheter is used to puncture the renal pelvis from the caudal pole and a urine sample is obtained for urinalysis and culture. Iodinated contrast is injected to perform antegrade pyelography (iohexol diluted 50:50 with sterile saline). On these initial images, the tip of the catheter should be inside the renal pelvis, it can be confirmed that the ureter is obstructed.

A 0.035” angle tipped hydrophilic guidewire (Weasel Wire) is advanced through the catheter and coiled inside the renal pelvis being careful to avoid perforation. Once 1-2 loops are made inside the renal pelvis another fluoroscopic image is obtained and if the wire is in the renal pelvis then the catheter is removed while the wire is carefully secured with some haemostats to avoid losing access.
The 6 French locking-loop nephrostomy catheter is prepared by removing the central sharp stylette and leaving the hollow trochar inside the tube. The nephrostomy tube (with the hollow trocar) is advanced over the guidewire into the renal parenchyma. Once it enters the renal pelvis the hollow trocar is removed as the catheter is carefully advanced into the renal pelvis over the guidewire. The locking string is pulled to prevent catheter dislodgement and clamped with a hemostat to maintain tension. There is a black marker on the nephrostomy tube; this should be placed within the renal parenchyma to prevent leakage. The Dacron cuff is then gently advanced down the nephrostomy catheter so it is snug with the renal capsule. Sterile cyanoacrylate glue is applied between the Dacron and the renal capsule to provide security and prevent leakage.

The urinary bladder catheter is placed. A purse string suture of 1.5 Metric PDS is placed at the apex of the bladder. In the centre of this purse string a Number11 blade is used to puncture a small hole into the bladder lumen. The catheter is advanced into the bladder lumen until the Dacron cuff is against the serosal surface of the bladder, and the purse-string suture is tied. Using 2 Metric PDS, the Dacron and silicone cuff is sutured to the bladder wall (full thickness) in 4 quadrants. Sterile cyanoacrylate glue is used to further secure the Dacron to the serosal surface of the urinary bladder. Once secure, the hollow trocar is removed. Sterile cyanoacrylate glue is used to further secure the Dacron to the serosal surface of the urinary bladder. Once secure, the hollow trocar is removed.

The skin and subcutaneous tissues immediately lateral to the ventral abdominal incision on the ipsilateral side of the nephrostomy tube is dissected down to the abdominal musculature. Both catheters are passed gently through body wall. Using blunt dissection with a hemostat, a puncture is made from the body wall through the abdominal musculature and into the abdomen. The ends of the hemostat carefully clamp the locking string of the nephrostomy tube at the junction of the catheter and string being careful not to clamp the catheter itself, only the string to maintain the lock. Then, the string and catheter are pulled through the body wall in unison. The same is done on the bladder catheter side. The very end of the bladder catheter is cut with a scissors so the end that was grasped with hemostat is discarded. The holes in the body wall are located such that when connected to the port, the metal prongs on the port and blue boots pass through the body wall, rather than the white tubing to avoid kinks.

A blue boot is advanced over each catheter and the shunting port is attached to the nephrostomy catheter. Once the nephrostomy tube is attached to the shunting port, the string of the pigtail is cut flush with the tube to prevent leakage. The blue boot is advanced over the junction of the catheter and the
metallic port. Pending the size of the patient, the bladder catheter may need to have some of the tubing cut. The catheter is then secured to the shunt port and the blue boot is advanced over the junction of the metallic pin and silicone catheter. Finally, sterile tissue glue is used to further secure the blue boot to the metal and each catheter (bladder and kidney side).

Prolene sutures are placed around the blue boots to help reduce leakage. The port is sutured relatively loosely to the body wall using 2 Metric Prolene sutures. Another fluoroscopic study is performed to check for leaks using the subcutaneous access port. A non-coring huber needle is used to prevent damage to the port. Any areas of leakage should be addressed prior to closure. Bilateral ports are also available and are placed in a similar manner to the single port.

Post-operative care is as for any animal with ureteric obstruction whereby fluid ins and outs are monitored. It is not necessary to place urethral catheters unless urine output measurement is essential.

So far we have placed 35 SUBs in cats at the RVC. Although surgery times are generally less than that associated with the stents, there are numerous technical challenges associated with their placement, in particular in placing the nephrostomy tube and in ensuring there are no leaks in the system. So far only one cat died peri-operatively and all but 5 have been discharged from the hospital. Short-term complications noted so far have included perforation of the dorsal capsule of the kidney leading to sub capsular urine leakage which requires a revision surgery, perforation of the renal artery leading to blood clots obstructing the system and leakage of urine from the port. Long-term complications included obstruction or kinking of the tubes.
**Renal biopsies – they're back!**

Rosanne E. Jepson

**Indications for performing a renal biopsy**

The primary reason for obtaining a renal biopsy is the investigation of persistent proteinuria associated with primary glomerular disease. There are a number of different aetiologies for proteinuria and it is therefore important that both pre- and post-renal causes of proteinuria have been excluded and that persistence of proteinuria of a magnitude considered likely to represent glomerular disease is ascertained before a renal biopsy is considered (Lees et al., 2005).

In patients with acute kidney injury (AKI) renal biopsy may be considered in order to try and gain a greater understanding of the underlying pathology. However, an underlying aetiology is not always identified in this scenario and even if a renal biopsy does indicate the likely aetiology of AKI, e.g. crystal-associated forms of tubular injury (Brown et al., 2007), there may be no additional therapeutic interventions possible even with this knowledge. Nevertheless renal biopsy in patients with AKI may give an information about signs of a regenerative response and hence prognosis which can be useful in for clients trying to decide how long to continue expensive modalities of therapy such as haemodialysis.

Renal biopsy is not indicated in patients with chronic tubulointerstitial disease. Patients that have reached International Renal Interest Society stage 3 or 4 with primary tubulointerstitial disease may show evidence of proteinuria. However, biopsy in such patients is unlikely to provide information that modifies treatment or management and should therefore be avoided where possible. Occasionally renal biopsy may be considered in patients with an unclassified juvenile nephropathy where further information regarding the underlying pathogenesis is sought although again results may not support change in therapeutic approach in many such patients. A final scenario when renal biopsy may be considered, is in patients with suspected renal neoplasia, e.g. renal carcinoma, although the diagnosis of certain neoplastic conditions, e.g. renal lymphoma, can often be made on the basis of fine-needle aspiration alone.

In patients with glomerular disease, performing a renal biopsy and the risks associated with this procedure must be balanced against the potential benefits of better understanding the underlying aetiology. Renal biopsy should therefore always be performed with the goal that clinical treatment and/or management strategies can be modified or improved on the basis of results. A renal biopsy sample may give important information regarding the severity of a disease process, the chronicity of changes present and evidence for ongoing active damage as well as possibly indicating the degree of reversibility of any injury. If results of the renal biopsy are considered unlikely to change management or prognosis then renal biopsy should not be performed. Other factors that may preclude renal biopsy include financial restrictions and lack of appropriately trained and experienced personnel to perform the biopsy or review the histopathology (Subgroup et al., 2013).
**Considerations before obtaining a renal biopsy**

The presentation of patients with primary glomerular disease can be variable, ranging from the patient that is clinically asymptomatic, apart from demonstrating persistent proteinuria, through to patients that present with clinical and biochemical evidence of nephrotic syndrome (proteinuria, hypoalbuminaemia, hypercholesterolaemia and oedema/ascites). The International Renal Interest Society have formulated a number of consensus recommendations for the investigation of patients with suspected glomerular disease dependent on their clinical presentation (e.g. presence of proteinuria, hypoalbuminaemia, azotaemia and systemic hypertension) or tier (see Table 1 in ‘Update on the IRIS consensus recommendations for glomerular disease in dogs’). It is important that initial investigations including a thorough history, physical examination, routine biochemistry and urinalysis and where appropriate infectious disease testing and diagnostic imaging have been performed prior to considering renal biopsy in order to investigate and rule out concurrent disease that may be contributing to proteinuria. Persistence of proteinuria should be documented particularly for those patients with a lower magnitude of glomerular proteinuria e.g. UP/C <2.0.

Renal biopsy is currently recommended for patients where UP/C is persistently ≥3.5, where proteinuria is unresponsive to standard management and/or progressive despite this therapy. Renal biopsy would also be advocated if immunosuppressive therapy for immune complex mediated glomerulonephritis is being considered as a treatment option. The IRIS consensus recommendations report that renal biopsy may be ‘potentially helpful’ in Tier 1 patients with uncomplicated renal proteinuria but are ‘recommended’ for those patients in Tier 2 and 3 where proteinuria is associated with hypoalbuminaemia and azotaemia respectively. However, ideally renal biopsy should be performed prior to glomerular disease reaching an advanced stage (i.e. IRIS stage IV azotaemia) given that the prognosis for such patients is guarded and there is an increased risk of biopsy-associated complications such as bleeding in these patients. In patients with primary glomerular disease where the kidneys are small and irregular, this suggests that the disease process is likely to be chronic, and renal biopsy may not be of benefit particularly if chronic and advancing azotaemia has been documented. However, if the duration of azotaemia is unknown or has been rapid in progression, then there may be indication for renal biopsy given that alteration in therapeutic options may improve prognosis particularly if an underlying immune mediated glomerulonephritis is identified.

Having decided that renal biopsy may provide important information for an individual patient some additional factors should be considered prior to performing renal biopsy.

- It is important that systemic hypertension, where present is adequately controlled as the presence of systemic hypertension may increase risk of bleeding.
- Furthermore assessment of coagulation including platelet numbers, buccal mucosal bleeding time, prothrombin and activated partial thromboplastin times should be assessed and adequate prior to proceeding with a renal biopsy.
- Should the patient be receiving anti-thrombotic therapy, e.g. aspirin, this should be discontinued for at least 3 days prior to the procedure.

**How to obtain a renal biopsy**

The preferred methodology for obtaining a renal biopsy is via ultrasound guided tru-cut performed typically under general anaesthesia. It is extremely important that experienced personnel perform this procedure and that the sample obtained is handled carefully and appropriately prepared prior to submission. General anaesthesia is advised to ensure minimal movement during the procedure and control of respiration where necessary. Ultrasound guided tru-cut allows the collection of a core of cortical tissue. It is not advisable to perform biopsy samples, which include medullary tissue due to the lack of significant pathology that will alter medical therapy in this region and also the inherent risk of haemorrhage if the biopsy needle tract crosses the corticomedullary junction and damages arcuate arteries.

Other methods that have been described include the use of tru-cut biopsy or wedge biopsy as a surgical or laparoscopic procedure. However, a common problem encountered when tru-cut biopsy specimens are obtained during surgical exploration is that the sample is not cortical in origin and that subsequent handling of tissue can be detrimental to assessment. An ultrasound guided tru-cut biopsy is the preferred method for renal sampling by the WSAVA renal standardization panel.

In order to ensure that an adequate sample has been obtained it is usually recommended to obtain at least two long (>10mm) core samples. In the situation that shorter or fragmented samples are obtained it may be necessary to obtain ≥3 samples. Biopsy specimens should be kept moist using physiological saline and should be inspected under light microscopy (×10-40) to confirm cortical tissue and the presence of glomeruli before submission. They should be handled extremely carefully without the use of forceps to ensure preservation of the architecture and quality of the sample. Core samples must be appropriately divided to ensure that glomeruli are present in each sample submitted for light microscopy (LM: 10% buffered formalin), immunofluorescence (IF: Michel’s medium) and transmission electron microscopy (TEM: 3% gluteraldehyde respectively) and appropriate transport mediums must be available. Pre-packaged kits for renal biopsy preparation can be obtained from the nephropathology service either at The Ohio State University or Utrecht.

If wedge biopsy samples are obtained during exploratory surgery then these must be processed to ensure they are no greater than 1-2mm in diameter to allow appropriate fixation. Renal biopsy samples submitted for histopathology also require careful handling by the laboratory and protocols for embedding and
sectioning have been produced in order to optimize histopathological assessment (Cianciolo et al., 2013).

**Submission of a renal biopsy for histopathology**

Light microscopy alone is no longer considered adequate to fully assess a renal biopsy. It is strongly recommended that renal biopsy samples are submitted to the WSAVA nephropathology service (see WSAVA consensus recommendation notes for details) and that tissue is examined by a nephropathologist. Standard examination of renal biopsy material should include light microscopy (Haematoxylin and eosin, Masson's trichrome, Periodic acid-Schiff, Jones’ methenamine silver and congo red if there is suspicion for amyloidosis). In addition samples should be examined by immunofluorescence (IF; IgG, IgM, IgA, C1q, C3, anti-lambda and anti-kappa light chains) and by transmission electron microscopy (TEM).

A study by Schneider and colleagues supported that 27% of immune complex glomerulonephritis cases could only be definitively diagnosed on the basis of TEM and that 6% of cases there had been no suspicion of immune complex disease on light microscopy alone (Schneider et al., 2013). Conversely in this study 23% of cases required TEM to exclude immune complex disease and of these 7% had been presumptively misclassified as immune complex disease on the basis of light microscopy alone (Schneider et al., 2013).

**Risks and benefits of renal biopsy**

The IRIS consensus recommendations state that:

‘Renal biopsy should not be performed in dogs:
(1) with IRIS stage 4 CKD
(2) when other medical contraindications are present that cannot be mitigated (including coagulopathy, renal cystic disease, moderate to severe hydrenephrosis, pyelonephritis, perirenal abscessation, uncontrolled hypertension (SBP >160mmHg), anaemia and pregnancy)
(3) when results of renal biopsy are deemed unlikely to alter treatment, outcome or prognosis’ (Subgroup et al., 2013).

This was accepted with a 95% consensus and 75% of voting members being in strong agreement.

The main risks associated with renal biopsy include (Vaden et al., 2005):

- Severe peri-renal hemorrhage
- Microscopic and macroscopic hematuria
- Hydronephrosis secondary to obstruction of the renal pelvis or ureter by blood clots
- Renal infarction
- Alterations of renal vasculature and intrarenal arteriovenous fistula formation
Studies have evaluated the effect of renal biopsy on renal function and have identified that ultrasound guided renal biopsy in patients with normal renal function has little effect. However, such studies have not been performed to evaluate patients with pre-existing renal disease (Groman et al., 2004, Drost et al., 2000). A retrospective study performed by Vaden and colleagues reported complications associated with renal biopsy in 13% of dogs and 18.5% of cats (Vaden et al., 2005) with the most common complication being severe haemorrhage in 10% of dogs and 17% of cats. Less frequent complications included gross haematuria (4% dogs, 3% cats), hydronephrosis (0.4% dogs, 3% cats) and death (2.5% dogs, 3% cats). In that study, of dogs that had abnormal coagulation profiles (n=67) 14% developed severe haemorrhage in comparison to dogs with normal coagulation profiles (n=97) where 10% still developed severe haemorrhage. In cats, 28.6 % (4/14) with abnormal coagulation profiles developed severe haemorrhage compared to 15.3% (2/13) with normal coagulation profiles. In dogs complications were more likely to occur in the following scenarios:

- If they were between 4-7 years and > 9 years of age
- If they weighed less than 5kg
- If serum creatinine concentrations were >440umol/l (5mg/dL)

Similarly cats with high serum urea nitrogen concentrations were more likely to both have complications associated with renal biopsy or to have haemorrhage associated with the procedure. The cost of performing a renal biopsy should also be considered and discussed carefully with clients as submission of a renal biopsy to the WSAVA scheme is no longer free of charge and requires shipment either to Europe or USA for evaluation.

Despite the potential risks and the expense of performing a renal biopsy important information can be gleaned from histopathological examination of kidney tissue and specifically the structure of glomeruli and identifying the presence of immune complex deposition in patients with primary glomerular disease. It is only through the study and careful characterisation of histopathological findings in patients with glomerular disease and by analyzing their response to therapy and clinical progression of disease that we may, in the future, be able to make stronger recommendations with regards to the optimal therapy for such patients.

References:


Ileus is currently defined as **the functional inhibition of propulsive bowel activity, irrespective of pathogenetic mechanism** and excludes mechanical obstruction.\(^1\) Whilst the term *ileus* refers to the failure of the aboral passage of intestinal contents it originally included intestinal obstruction amongst its causes (Gk. *eileós*, "intestinal obstruction" from *Corpus Hippocraticum*). Its original definition was further confused by the use of terms such as "atony" for gastric dysmotility and "paralytic ileus" and "adynamic ileus" to distinguish induced ileus from "mechanical ileus". Mechanical obstruction is now excluded and will not be discussed here, as its management is almost inevitably surgical.

In the context of an AVSTS meeting, post-operative ileus (and how to treat it) is probably of most concern to delegates, but there are many other causes of ileus that are unrelated to surgery, with a range of inflammatory, ischaemic, metabolic, neurogenic and pharmacological/toxic causes. Rare cases of primary dysmotility can mimic surgical disease (so-called pseudo-obstruction), and may require surgical biopsy for a definitive diagnosis, but very few cases of ileus can be fixed by surgery.

There are many ways of assessing gastrointestinal (GI) motility that aim to evaluate gastric emptying and/or intestinal transit time of solid food. For solid phase gastric emptying, radionuclide scintigraphy is still considered the gold standard. Radiographic contrast studies (barium "meal", BIPS) are unreliable and \(^{13}C\) breath tests are not readily available.\(^2\) However, ultrasonographic quantification of gastric emptying by measurement of the frequency and amplitude of antral contractions is achievable in practice.\(^3\) Intestinal peristalsis may be observed during ultrasonographic examination, but is insensitive, as the procedure itself (through 'stress' and even cutaneous stimulation) may temporarily inhibit peristalsis. Breath tests have fallen from favour as the marker substances (e.g. lactulose) in themselves can alter GI motility. Swallowed wireless motility capsules (SmartPill\textsuperscript{TM}) can assess intestinal transit times whilst recording temperature, pressure and pH, but their use is limited by expense and patient size.\(^6,7\)

The clinical signs of ileus are decreased appetite or anorexia, signs of nausea, vomiting (often delayed after ingestion), pica and/or polydipsia, and decreased frequency of defecation. On physical examination there may be bloating and abdominal discomfort on palpation, and absence of borborygmi on auscultation. As methods for assessing intestinal motility are either unreliable, or not available in practice, ileus is suspected on clinical signs, and diagnosed presumptively on crude radiographic evidence of intestinal dilatation and absence of a foreign body or other obstructive lesion.

Causes of ileus are listed:

**Common**
- Hypokalaemia etc.
- Uraemia
- Drugs
  - Opioids
  - Anticholinergics
  - Phenothiazines
- Viral enteritis
- Shock and septicaemia
- IBD
- Peritonitis
  - Septic
  - Pancreatitis
  - Uroabdomen
  - Bile peritonitis
- Postoperative

**Uncommon**
- Hypothyroidism
- Diabetes mellitus
- Lead poisoning
- Dysautonomia
- Visceral neuropathy/myopathy
- Spinal cord injury

**Rare (or never)**
- Mesenteric arteritis or phlebitis
- Mesenteric avulsion
- Muscular dystrophy
- Idiopathic sclerosing peritonitis
- Brain (medullary) disease/trauma
- Radiation enteritis (rare in pets)

Ileus can be caused by smooth muscle weakness due to metabolic disturbances (e.g. hypokalaemia) but is more often a consequence of neural inhibition of intestinal motility,
mediated either locally (e.g. by opioids, intra-abdominal inflammation etc.) or centrally, mainly through sympathetic inhibition of motility and decreased vagal activity.

**Metabolic causes**

Hypokalaemia is a common consequence of GI disease (lack of intake, loss through diarrhoea) and, in itself, can induce ileus. It should be readily diagnosed and treated with potassium supplementation before other causes of ileus are pursued. Abnormalities of serum calcium and magnesium concentrations, and uraemia can also cause ileus. Shock and sepsicaemia will result in ileus, but their other consequences are of greater importance.

**Endocrine disease**

Hypothyroidism in dogs has been shown to reduce the frequency of electrical activity in the stomach and duodenum, and reduced mechanical response to feeding. However, ileus is not a major feature of the condition. Gastroparesis is a feature of human diabetes mellitus but has not yet been characterised in dogs or cats.

**Parvoviral enteritis**

Ileus is a frequent finding in young dogs with parvoviral enteritis. Ultrasonographic examination in one study of 92.5% of 40 affected puppies showed a fluid-filled small intestine, and fluid in the stomach and colon in 80% and 62.5% respectively. Complete lack of peristaltic activity was noted in 75% of cases, and the remainder had weak contractions. These findings are not surprising considering the severe mucosal damage that occurs with parvoviral infection, and are probably caused by a combination of inflammation with disruption of the enteric nervous system, hypokalaemia, and sympathetic-mediated ‘stress’. The marked, generalised ileus seen on radiographs, can trap the unwary into undertaking an exploratory laparotomy to look for an obstruction. A metoclopramide CRI appears to be the most effective treatment for management of vomiting in these patients and has some prokinetic activity in the stomach; it can be combined with daily maropitant. An early return to enteral feeding is also recommended as it reduces morbidity perhaps by restoring epithelial integrity and stimulating motility.

**Opioid-induced bowel dysfunction**

The beneficial analgesic and anti diarrhoeal effects of opioids have to be balanced against their tendency to reduce peristalsis and induce ileus and constipation. They are thought to act on µ receptors both on the intestinal smooth muscle, and the interstitial cells of Cajal, the intestinal pacemaker cells. Their frequent use post-operatively contributes to post-operative ileus, but they are not the sole reason for this common problem.

**Peritonitis**

Intra-abdominal inflammation will result in ileus whatever the underlying cause, but is most commonly seen in pancreatitis and septic peritonitis. There may be a suspicion that post-operative ileus following intestinal surgery is related to wound leakage and peritonitis, but hopefully that is not the case, and post-operative ileus is also seen after non-intestinal abdominal surgery.

**Post-operative ileus**

This is a significant problem after abdominal surgery in humans, and has massive economic implications for the health industry in terms of extended hospitalisation. Multiple mechanisms are involved in causing the ileus, but are mostly related to the effect of the mechanical manipulation of the intestine. This induces both neurogenic, endogenous opioid and inflammatory inhibition of intestinal motility. This problem can be compounded by the effect of anaesthetic agents and opioids.

Post-operative ileus has been investigated in dogs using wireless motility capsules and breath testing. Gastric emptying in healthy dogs anaesthetised for laparoscopic spay was delayed and did not return to normal for up to 40 hours. Laparotomy was found by breath testing to delay gastric emptying: after open abdominal surgery it was delayed for up to 48 hours, but surprisingly the effect was more pronounced for non-GI surgery than GDV surgery.

**Treatment of post-operative ileus.**

In uncomplicated cases, probably all that is needed is to limit (but not stop) oral intake, maintain the intravascular volume and correct any electrolyte abnormalities. Dietary manipulation (liquid, low caloric density, low fat, high digestibility) can hasten gastric emptying.

If ileus is prolonged, then withdrawal of any medications that may be responsible, and investigation of possible pancreatitis or septic complications is indicated. Nasogastric intubation and aspiration is no longer practised in human medicine as it may contribute to
respiratory complications, but has never been a recommended treatment in dogs and cats anyway. Pharmacological intervention may be necessary in more severe cases. In humans NSAIDs improve GI transit post-operatively, although some of this effect is probably related to a simultaneous reduction in the dose of opioids. Epidural analgesia also reduces ileus by blocking the sympathetic inhibition of GI motility. Epidurals with bupivacaine alone seem more effective than with opioids alone or combined bupivacaine and opioids.

The classical prokinetic drugs, metoclopramide and cisapride (if available), act on pre-synaptic serotonin (5-HT) receptors. The anti-emetic effect of metoclopramide is mediated by antagonism of dopamine and 5-HT3 receptors, and the prokinetic effect of both drugs is related to agonist activity on 5-HT4 receptors. Using implanted instrumentation, the prokinetic effect of metoclopramide has been demonstrated in dogs. However, metoclopramide is a weak prokinetic and only stimulates the stomach and perhaps the duodenum. Cisapride (and tegaserod) was (were) withdrawn because of their adverse effects on myocardial calcium channels and their potential to cause sudden death. Related drugs have a similar prokinetic activity but not the cardiac effect: mosapride is available in Japan but like metoclopramide its activity is limited to the stomach and duodenum; prucalopride (Resolor) is available in Europe. A number of alternative/novel prokinetic drugs have been suggested/used.

- Erythromycin at low doses (1 mg/kg) stimulates the motilin receptor in the GI tract and in dogs triggers migrating motor complexes (MMCs type III) that sweep a wave of peristalsis along the length of the gut, and normally occur in the interdigestive phase. In the USA it is the preferred treatment for post-op ileus of some surgeons, but cisapride is unavailable.
- The H2 antagonists ranitidine and nizatidine also have weak prokinetic effects: they inhibit acetylcholinesterase and increase the concentration of acetylcholine at the post-ganglionic myenteric nerve-smooth muscle synapse. They have been recommended not only for post-operative ileus, but also feline idiopathic megacolon following in vitro evidence of a prokinetic effect on feline colonic muscle. Their efficacy in recurrent constipation and megacolon is questionable, and they are clearly not as effective as cisapride.
- High doses of mirtazapine have been shown to accelerate gastric emptying and colonic transit, in addition to the better known appetite stimulant and anti-nausea effects.
- Acotiamide facilitates muscarinic acetylcholine activity and has been shown to stimulate post-prandial gastroduodenal and colonic activity in dogs at a dose of 30 mg/kg. It has been approved (Acofide) for use in humans in Asia.
- Capsaicin, the ingredient of chillies, stimulates GI motility when in the stomach through stimulation of the TrpV1 channel causing the release of calcitonin gene-related peptide, but it inhibits motility once in the small intestine. Finally intra-colonic installation of capsaicin stimulates colonic motility and defecation.

**Dysautonomia**

This is a generalised autonomic neuropathy originally seen as an epidemic in UK cats in the 1970’s. It is now much less common, but sporadic cases are still seen in both cats and dogs worldwide. The clinical signs encompass a range of autonomic dysfunctions causing one or more of the following: mydriasis, dry eye, xerostomia, fixed heart rate, megaoesophagus or oesophageal hypomotility, gastric atony, SI ileus, constipation and urinary retention. The cause is unknown but toxic, dietary and infectious causes have all been proposed. The prognosis is guarded and treatment only symptomatic. Prokinetics are used to treat for the gastric atony and intestinal ileus symptomatically.

**Chronic intestinal pseudo-obstruction (CIP)**

There are a number of causes of CIP in humans and these are usually divided into: primary neuropathic causes (visceral neuropathies); primary myopathic causes (visceral myopathies); secondary to an underlying disease, e.g. autoimmune progressive systemic sclerosis (PSS), amyloidosis, muscular dystrophy, endocrinopathies, paraneoplastic syndrome, electrolyte disorders, drugs or intoxications, generalised neurologic diseases.
Visceral neuropathy. Selective loss of myenteric neurones can lead to ileus and chronic intestinal pseudo-obstruction (CIP). Mesenteric ganglionitis is poorly described in dogs, whereas the classic example is grass sickness in horses is well recognised. It is currently believed to be due to Clostridial toxins, with a vaccine being trialled.

Visceral myopathy. Primary human visceral myopathies can be divided into familial forms or idiopathic non-familial forms also known as sporadic hollow visceral myopathy. One of the familial forms and the sporadic (non-familial forms) show degeneration and fibrosis of GI smooth muscle and simultaneous changes to the urinary smooth muscle cells. Visceral myopathy, presenting with CIP is rarely reported in veterinary patients: the largest case series is three dogs, but there are at least twelve single case reports in dogs and two in cats. Fibrosis and infiltration of the tunica muscularis by mononuclear cells are typically reported and the lesion appears to be a leiomyositis. One of the two feline cases documented histopathological changes consistent with true visceral myopathy, the other had an actin deficiency. We have seen one case with CIP and partial gastric torsion (gastric instability). The prognosis is generally grave, but there is one case report of successful management with steroids, and one of the feline cases was managed symptomatically.

References


Medical management of tracheal collapse – post Lomotil

Simon Tappin MA VetMB CertSAM DipECVIM-CA MRCVS
European and RCVS recognised Specialist in Veterinary Internal Medicine
Hon. Assoc. Professor of Small Animal Medicine, University of Nottingham

Dick White Referrals, The Six Mile Bottom Veterinary Specialist Centre,
Station Farm, London Road, Six Mile Bottom, Suffolk, CB8 0UH

Tracheal collapse is progressive disease seen in mainly middle aged, small and toy breed dogs. It occurs due to degeneration of the cartilage rings as a result of reduced glycosaminoglycan and cellularity. Clinical signs depend on the severity of the collapse, from mild airway irritation and coughing, through to respiration distress as a result of dynamic airway collapse. Many dogs improve with medical management (weight control, harnesses, cough suppressants, anti-inflammatory steroids and bronchodilators), however in severe cases, where airway collapse and respiratory distress is documented, surgery or intraluminal stent placement may need to be considered.

In the United Kingdom the use of Lomotil (co-phenotrope which contains diphenoxylate hydrochloride and atropine) has been the mainstay of medical management for dogs with tracheal collapse. Diphenoxylate acts as a narcotic anti-tussive with the atropine acting to reduce the volume of mucus secreted into the lower respiratory tract and acts as a muscarinic bronchodilator. Although no clinical studies are available to support its use anecdotally there has been widespread acceptance of its benefit in clinical cases (Herrtage 2009). Doses of 0.2-0.5mg/kg have been suggested; with constipation an occasional side effect seen (these effects are usually managed easily with dietary manipulation or the addition of faecal softeners). Due to recent supply and manufacturing issues Lomotil has not been consistently available to the veterinary market. Although generic co-phenotrope is intermittently available, we need to consider other options for the management of dogs with tracheal collapse.

Management measures
A good proportion of dogs with tracheal collapse are overweight and the accumulation of intra-thoracic adipose tissue may reduce respiratory function by limiting thoracic movement and reducing chest wall compliance. Strict weight loss regimes with dietary and controlled exercise programs, will lead to an improvement in clinical signs in a good proportion of cases. Avoidance and removal of environmental inhaled irritants (namely tobacco smoke) will help in many dogs, although compliance may be difficult to achieve. A harness rather than a collar should be used to reduce tracheal compression and associated irritation. Diligent management of comorbidities such as congestive heart failure and respiratory tract infection will also improve clinical signs. Additionally, any upper airway narrowing secondary for example secondary to brachycephalic upper airway syndrome or laryngeal paralysis will increase intra-thoracic pressure and worsen tracheal collapse; carefully consideration to surgical management of the upper airway should be given to these cases.

Anti-tussives
In the absence of Lomotil alternative narcotic anti-tussives have been suggested for the management of tracheal collapse. In the United States hydrocodone is used commonly (0.22mg/kg q6-12 hours), with codeine (0.5mg-2mg/kg q12 hours) and butorphanol (0.5-1mg/kg q6-12 hours) being more commonly used in Europe. All of these anti-tussives appear less effective than Lomotil, with butorphanol in particular being a good deal more expensive. Dosing can also be an issue as there are no licensed veterinary products and the human tablets are often very large for the small breed dogs affected. Re-compounding pharmacies such as Nova Laboratories (novalabs.co.uk) or Summit Veterinary Pharmaceuticals limited (svprx.co.uk) may be able to help with drug formation into liquids or smaller tablets for smaller sized patients.
Steroid therapy
The use of carefully judged steroid therapy is likely to be beneficial to many dogs with tracheal collapse, by reducing airway inflammation. However they should be used tactically, for short courses and at the lowest doses possible to control clinical signs, as adverse effects may worsen clinical signs in the longer term. In particular there use may increase the risk of bacterial infection, increase respiratory rate and may make weight gain very difficult to achieve. Initial doses of prednisolone (0.5mg/kg q12 hours) have been suggested with the dose being tapered quickly to the lowest level that controls signs. Inhaled steroids such as fluticasone may be of benefit to some patients that are dependent on steroid to reduce airway irritation, but that side effects are adversely affecting their quality of life (Bexfield et al, 2006).

Bronchodilators
Bronchodilators are suggested in the management of tracheal collapse to induce bronchial dilation, which at least in theory, should reduce intra-thoracic pressure during expiration and reduce expiratory tracheal collapse. Methylxanthine based bronchodilators (such as theophylline 15-20mg/kg q12-24 hours) may be beneficial by improving mucociliary clearance and reducing diaphragm fatigue, as well as increasing airway diameter. β₂-adrenergic bronchodilators such as terbutaline, have also been suggested, with injectable or inhaled administration being most useful in the emergency setting. The benefit of bronchodilators in dogs with tracheal collapse has not yet been fully evaluated, so their introduction should be regarded as a therapeutic trial, with them being withdrawn if no improvement is seen. Some dogs (especially older animals) appear very susceptible to the effects of methylxanthines, the restlessness and anxiety commonly seen, if these effects occur medication should be swiftly withdrawn.

References

Experiences with intralumenal tracheal stenting

Simon Tappin MA VetMB CertSAM DipECVIM-CA MRCVS
European and RCVS recognised Specialist in Veterinary Internal Medicine
Hon. Assoc. Professor of Small Animal Medicine, University of Nottingham
Dick White Referrals, The Six Mile Bottom Veterinary Specialist Centre,
Station Farm, London Road, Six Mile Bottom, Suffolk, CB8 0UH

Classically extra luminal support of the trachea with the placement of synthetic rings has been the treatment of choice. Although successful in many cases the technique is technically challenging, can only treat the extra-thoracic portion of the trachea and is associated with complications such as laryngeal paralysis. As a result intraluminal tracheal self-expanding metallic stent (SEMS) placement has been investigated as an alternative. This is a minimally invasive procedure with rapid improvements seen in patients post placement. Studies have documented improvement in 75-90% of dogs treated with intraluminal stainless steel self-expanding stents (Moritz et al, 2004) and long term improvement in 10 out of 12 dogs treated with nitinol self-expanding metallic stents, with 9 dogs alive after 1 year and 7 dogs alive after 2 years (Sura and Krahwinkel 2008). An owner based survey of the owners of 18 dogs with nitinol self-expanding metallic stents (Vet stent-Trachea) reported good to fair improvement in all dogs after stent placement (Durrant et al 2012).

Stent placement is not a curative procedure and owners should be carefully counselled that continued long term medical management and careful monitor is essential to achieve a good long term outcome. Tracheal stenting only be considered if options for medical management have been exhausted, however stent placement can significantly improve patient quality of life. Complications do occur and are associated with problems during placement or late complications such as inflammatory tissue formation, stent fracture or progressive tracheal collapse.

Potential Complications
Stent sizing is critical to the successful outcome of stent placement, as if too small the stent will migrate and too large pressure necrosis of the wall can occur. Measurements of tracheal width are carefully taken in lateral recumbency with radiographs, or were possible under fluoroscopic evaluation. Measurements of maximal tracheal diameter are taken during positive pressure ventilation (to +20cm of water). This is then compared to a marker catheter which has metal rings the start of which are 10mm apart, this is placed within the oesophagus so that it is at the same level as the trachea and limits the effects of magnification. The stent diameter is usually oversized by approximately 10-20% to minimise the risk of stent migration and to counter the effect that the trachea is oval in cross section, usually having a slightly larger diameter across its width, compared to its height. Evaluation of the collapsing portion is done under negative pressure (to -20cm water) and it is possible to only stent the extra thoracic or intra thoracic portion of the trachea, however most clinicians stent the whole length of the trachea as the disease progression will usually mean a second stent is needed if only a portion of the trachea is stented.

Placement should be at least 5mm caudal to the larynx and the cricoid cartilage is usually used as this landmark; stenting within the larynx may lead to laryngospasm, cough and laryngeal dysfunction. The caudal edge of the stent should be placed at least 5mm cranial to the tracheal bifurcation and placement too caudally can lead to the caging of a main stem bronchus leading to mucus entrapment and complications such as infection. To avoid these potential problems, the suggested guidelines for stent measurement is that the stent is placed 1cm caudal to the cricoid cartilage to 1cm cranial to the tracheal bifurcation.

Stent Fracture
Tracheal stents are made from durable materials; however excessive compression or movement, such as that caused by coughing, can lead to metal fatigue and subsequent fracture. Initial case series reported relatively high rates of stent fracture, for example Sura
and colleagues reported fractures in 5 of 12 dogs which had had self-expanding nitinol stents placed. Recent advancement in stent design has led to the development of more flexible stents, which has reduced complication rates. Care not to oversize the stent by more than 20% and control of coughing will limit this risk. The introduction of tapered stents has helped to reduce the need to over size stents in the trachea, where there is a marked difference in the proximal and distal tracheal diameter. Stent fractures with the newer stents occur rarely, however if a fracture does occur the stent may lose all of its structural integrity and clinical signs will recur, thus stent fracture should be a differential for any animal with a stent presenting with a new cough or worsening of its clinical signs. If stent fracture occurs stability is usually obtained by the placement of a second stent within the lumen of the fractured stent. This can be more technically challenging and the placement of a guidewire through the fractured stent lumen is suggested to confirm that stent placement will be intraluminal before deployment.

Inflamatory Tissue Formation
A common consequence of stent placement is the formation of excessive inflammatory tissue within the trachea. This is most commonly seen at the ends of the stent and is likely to be associated with excessive movement of the stent, most often as a result of coughing. The development of woven nitinol stents such as the Vet Stent-Trachea (Infiniti medical), with rounded edges and a high quality finish to the nitinol, anecdotally seem to have reduced the formation inflammatory tissue compared with mesh steel stents such as the Boston Wallstent, however this has not been rigorously proven and it may be that other factors such as better stent sizing and more aggressive cough suppression have reduced this complication. Rigorous attention to the control of coughing and a tapering course of prednisolone after stent placement are key to limiting the potential formation of inflammatory tissue.

Inflammatory tissue within the trachea reduces tracheal diameter and leads to reduced airflow, with signs of exercise intolerance and respiratory distress. Radiographs may document the presence of inflammatory tissue, but this is best observed endoscopically. Most excessive inflammatory tissue will respond rapidly to medical therapy with steroids and a 6-8 week course (starting dose prednisolone 2mg/kg/day) tapering to the lowest dose that controls clinical signs is suggested (Scansen & Weisse 2014). Oral colchicine use has also been reported and may be useful in the management of refractory cases (Brown et al, 2008). In some instances excess granulation tissue can be removed endoscopically with loop electrocautery or laser resection.

Bronchial collapse
Dogs will tracheal collapse often have concurrent bronchial collapse, due progressing cartilage weakness. At present bronchial stent placement is not generally recommended as stent placement will cage of lower bronchi and will prevent mucus drainage from other lobes. In addition disease progression, will usually lead to lower airway collapse limiting the efficacy of the stent placed. In patients with both tracheal and bronchial collapse, tracheal stent placement may help to improve airflow, especially if the dog’s main sign is inspiratory dyspnea. If coughing is the dogs main sign then tracheal stent placement is unlikely to completely alleviate clinical signs due to continued bronchial and lower airway collapse. A recent case report (Dengate et al, 2014) documented a successful outcome after stent bronchial stent placement in a dog with focal left main stem bronchial collapse and left atrial enlargement. Although the case report documents severe respiratory distress after stent placement the dogs quality of life was improved in the longer term.

Feline tracheal stenting
Although the most stents are placed in dogs with tracheal collapse stent placement has been described in cats for the management of tracheal stenosis secondary to trauma and airway occlusion due to neoplasia. Outcome for all reported feline cases is favourable, with good tolerance of the stent and no long term complications reported (Culp et al, 2007).
References and further reading


How I perform..... Extralumenal tracheal stenting

Professor John Williams MA VetMB LLB CertVR DipECVS FRCVS
Northwest Surgeons, Cheshire, UK.

Tracheal collapse is severely debilitating disease which can lead to absolute airway obstruction and death if not controlled. Over the years a number of management techniques have been described ranging from medication alone, to surgery on the trachea, the use of extraluminal supports and lately intraluminal stenting. The diversity of described techniques suggests that we have not yet managed to develop an ideal strategy for treating this difficult condition.

Classification of collapsing trachea:

- **Grade I** - tracheal membrane is slightly pendulous, cartilage maintains normal shape, lumen reduced approximately 25%
- **Grade II** - tracheal membrane widened and pendulous, cartilage is partially flattened, lumen reduced approximately 50%
- **Grade III** - tracheal membrane is almost in contact with dorsal trachea, cartilage is nearly flat, lumen is reduced approximately 75%
- **Grade IV** - tracheal membrane is lying on dorsal cartilage, cartilage is flattened and may invert, lumen is essentially closed

Treatment of tracheal collapse is focused on palliation of clinical signs; initially using medical therapy (White & Williams 1994; Maggiore 2014), but this may not in all cases resolve clinical signs in the long term. If conservative therapy fails, reported treatment options include use of tracheal ligament plication, extraluminal prosthetic rings or endoluminal tracheal stents.

It is the author’s current management to use medical therapy such as weight loss, co-phenotrope (generic version of Lomotil®) orally, and the use of bronchodilators and anti-inflammatory agents as required. In those cases where medical therapy does not work or in grade IV cases, the use either extra or intraluminal prostheses is discussed with the client. Intraluminal stenting is reserved for older patients as the risk of complication is high in the author’s experience.

Extraluminal Prostheses

This is a procedure (Tangner & Hobson 1982) that had fallen out of favour in the recent past following the advent of intraluminal stenting procedures. Recent work suggest that this is still a viable option for severe cases of tracheal collapse. The concern has always centred on the fact that it is only possible to successfully place prostheses on the cervical trachea; with the concern being that the intrathoracic trachea would continue to collapse.

The trachea is ‘reinforced’ by suturing a number of polypropylene rings around it. The rings (approx. 5 mm wide) are made from polypropylene syringe holder with four to six
holes drilled for suture placement. A ventral midline skin incision is made from the larynx to the thoracic inlet. The subcutaneous tissue and sternohyoideus muscles are separated to expose the trachea. The thyroid arteries and recurrent laryngeal nerves are identified and gently bluntly dissected from the trachea but only in the area of ring placement and a polypropylene ring is placed between the tracheal wall and the recurrent laryngeal nerves, this is sutured to the tracheal cartilages and the trachealis muscle with three to four sutures of 4-0 (1.5m) or 3-0 (2m) polypropylene. It is essential to place the rings along the length of the cervical trachea and the cranial aspect of the portion within the thoracic inlet. In order to achieve this the trachea is gently drawn as far cranially as possible in order to expose the portion within the thoracic inlet. Once all the rings are placed at regular intervals the muscles are apposed and the skin closed routinely.

Laryngeal paralysis is a recognized complication of extraluminal prostheses being placed and is reported in up to 17% of cases. Patients may present acutely with laryngeal paralysis (within 48 hours) or it may be seen as a late complication months to years following surgery. There is merit in advocating contemporaneous arytenoid lateralization where extraluminal ring placement is performed (WHITE 1995).

Recent work indicates that survival times post surgery is excellent (Chisnell & Pardo 2014) and that the presence of intrathoracic tracheal collapse does not prevent this procedure being carried out. (Becker et al. 2012) reported that median survival in cases with both cervical and intrathoracic collapse was 1500 days. Up to 35% dogs may require continued medical support.

The Future

We do not have an ideal solution for this challenging condition as yet. If medical management fails to control then consider surgery or stent placement. Does the future lie in using three-dimensionally printed tracheal supports or grafts?

Further reading


White, R.N., 1995. Unilateral arytenoid lateralisation and extra luminal polypropylene ring prostheses for correction of tracheal collapse in the dog. The Journal of small
**Pancreatitis – the role of pancreatic biopsy**

Penny Watson, Queen’s Veterinary School Hospital, University of Cambridge  
 pjw36@cam.ac.uk

**Why Biopsy the pancreas?**

Pancreatitis in dogs and cats, either acute or chronic, is usually diagnosed non-invasively with blood tests and diagnostic imaging. Is there role for pancreatic biopsy?

Biopsies are inherently invasive – some more than others – and pancreatic biopsies are on the more invasive end of the spectrum. For any biopsy to be justified clinically, the benefits should outweigh the risks. Ultimately, the results should alter outcome in the case and this usually means they should alter treatment decisions. In small animals, there are situations where a biopsy might give prognostic rather than treatment information and also alter outcome (for example, the owner may decide on euthanasia as a result). If the biopsy doesn’t do either of these things, then it is difficult to justify ethically. It is difficult to biopsy a pancreas non-invasively and the procedure usually requires laparotomy or laparoscopy. Fine needle aspiration cytology of the pancreas has been described and shows some promise in helping differentiate pancreatitis from neoplasia in dogs (Bjorneby and Kari, 2002) although our own experience suggests this is as challenging as prostatic cytology and requires a cytologist experiences at looking at pancreatic aspirates to differentiate hyperplasia from neoplasia (and how many veterinary cytologists look at a lot of pancreatic aspirates?)

The gold standard for diagnosis of pancreatitis is biopsy and histopathological examination but even histology of a pancreatic biopsy is not 100% sensitive because the lesions of pancreatitis are patchy particularly early in the disease process, so a small surgical biopsy may miss the disease. To diagnose the disease definitively needs multiple large sections taken throughout the organ (Newman et al. 2004), and this is clearly only possible PM. No single clinicopathological test currently available has 100% sensitivity and specificity for the diagnosis of pancreatitis in dogs, cats or humans, and non-invasive diagnosis often remains presumptive, based on supportive results from clinical and diagnostic imaging findings as well as the results of blood tests. The pancreas may also become inflamed secondary to other diseases such as septic peritonitis (Haworth et al. 2014). It is therefore very important for the clinician to remember to work-up suspected pancreatitis cases in the same way as any other medical case and not jump immediately to a diagnosis on the basis of a positive enzyme test. Other investigations such as diagnostic imaging and analysis of free abdominal fluid will often be necessary to rule out other concurrent serious disease such as intestinal perforation.

There are no clearly defined veterinary guidelines about when to biopsy the pancreas. However, we reflect the human situation quite closely: the single
biggest reason to biopsy a pancreas is to rule in or out neoplasia. In this case, there is often a justification to undertake a laparotomy or laparoscopy and obtain a biopsy. Nodules in the pancreas are as likely to be inflammatory as neoplastic, particularly in cocker spaniels with IgG4+ chronic pancreatitis (see below) so a biopsy is required to definitively diagnose neoplasia and dogs and cats with pancreatic masses should NOT be euthanased on the table without histology.

What about the indications in pancreatitis? Generally, the cause of pancreatitis in dogs and cats is unknown so the treatment is supportive and non-specific and a biopsy will not change that. There is one exception which is the multi-systemic immune-mediated disease in English Cocker spaniels, described below: but even in this disease, diagnosis can be made presumptively on the basis of immune-mediated disease in other organs and a pancreatic biopsy is not necessary. Undertaking a GA and laparotomy or laparoscopy in a dog or cat with acute disease is dangerous: these dogs or cats have systemic inflammatory response and multi-organ dysfunction and need stabilizing before surgery. What kills dogs and cats with pancreatitis is this multi-organ failure, not the localized pancreatitis itself, and undertaking a GA and laparotomy in a dog which is already unstable is likely to make things worse. We don’t have published evidence for this in dogs and cats, but in human medicine they have evidence that performing a necrosectomy early in the course of acute pancreatitis actually increases mortality compared with delaying surgery for a month (Wittau et al 2010). Surgical intervention within 2 weeks of symptom onset is associated with a prohibitive mortality rate (McKay et al 2004) and even with infected pancreatic necrosis, surgery may not reduce mortality over medical management.

However, bearing all these factors in mind, it is still well worthwhile taking a careful pancreatic biopsy in any animal which is having a exploratory laparotomy or surgery for another reason and pancreatitis is a possibility. In the past, these were discouraged because of a fear of post operative pancreatitis. However, this appears to be a theoretical rather than real concern as long as the surgeon only takes a small biopsy and preserves pancreatic blood supply. Pancreatic biopsy appears to be safe and does not carry a high risk of postoperative pancreatitis, provided that the pancreas is handled gently and the blood supply is not disrupted. A study of pancreatic biopsy in 27 normal dogs showed elevations in some pancreatic enzyme levels postbiopsy, but not in cPLI, and there were no clinical signs of pancreatitis after surgery (Cordner et al, 2010).

**Autoimmune pancreatitis in English Cocker Spaniels**

English cocker spaniels suffer from a distinctive form of chronic pancreatitis (CP) which shows similarities to human autoimmune CP, which is part of a multisystemic autoimmune disease now called ‘IgG4+ related disease’.

Human autoimmune CP is associated with infiltration of T lymphocytes focused on pancreatic ducts and veins (Dite et al. 2008). The most recent classifications split autoimmune CP in to two types (Deshpande et al. 2012). Type 1, the most commonly recognized, is a multisystemic disease affecting kidney, liver, tear
ducts and other organs as well as the pancreas. This form is associated with elevation in serum IgG4 levels and increased IgG4-expressing plasma cells within the lesions and is now termed ‘IgG4 related disease’ (Bateman & Deheragoda 2009; Deshpande et al. 2012; Stone et al. 2012). Type 2 autoimmune pancreatitis is more controversial, is confined to the pancreas with or without gut involvement and shows no association with IgG4. IgG4 is one of 4 subtypes of IgG (types 1, 2, 3 and 4) which are recognized in humans and also in dogs (Day et al. 1996; Day & Mazza 1995). The serum and tissue concentrations in healthy individuals of both species usually decrease in numerical order, with IgG1 being the most abundant and IgG4 the least abundant.

English Cocker spaniels show a disease which is remarkably similar to human IgG4 related disease. They demonstrate duct-centred infiltrates of T-lymphocytes in the pancreas and affected dogs also often have other immune-mediated diseases such as keratoconjunctivitis sicca and also glomerulonephritis (Watson et al. 2011). A predominance of IgG4+ plasma cells has been demonstrated in pancreatic and renal histology in a small number of affected cocker spaniels a and it has also been shown to be associated with the same DLA haplotype as autoimmune haemolytic anaemia in the breed b, suggesting a remarkable similarity to the human disease, but more studies on greater numbers of dogs will be required to confirm this. Clinically, these dogs often present with mass-like inflammatory lesions on diagnostic imaging and surgery which must not be mistaken for neoplasia.

Footnotes:


References


‘How I perform…’ Pancreatic surgery

Robert N White, Willows Referral Service

Surgical anatomy

The pancreas of dogs and cats is composed of a right and a left limb and a small central body. The right limb of the pancreas lies within the mesoduodenum and is closely associated with the duodenum, particularly at its cranial aspect. The dorsal aspect of the right pancreatic lobe is visualized by retracting the duodenum ventrally and toward the midline; the ventral aspect of the right pancreatic lobe is examined by retracting the duodenum laterally. The pancreatic body (angle) lies in the bend formed by the pylorus and the duodenum. The left pancreatic lobe is viewed within the deep leaf of the greater omentum by retracting the stomach cranially and the transverse colon caudally.

The main blood supply to the left pancreatic lobe is provided via branches of the splenic artery; however, branches from the common hepatic and gastroduodenal arteries also supply portions of it. The main vessels of the right lobe of the pancreas are the pancreatic branches of the cranial and caudal pancreaticoduodenal arteries that anastomose in the gland. The cranial pancreaticoduodenal artery is a terminal branch of the hepatic artery; the caudal pancreaticoduodenal arises from the cranial mesenteric vessel. These vessels also provide branches that supply the duodenum. Because they are closely associated with the proximal portion of the right lobe of the pancreas, care must be taken not to damage these vessels during pancreatic surgery, or devitalization of the duodenum may occur.

The pancreas has both endocrine (insulin) and exocrine (digestive secretions) functions. Digestive secretions enter the duodenum via one of two ducts. These ducts may communicate within the gland or may cross each other. When the two ducts do not communicate, the pancreatic duct drains the right lobe and the accessory pancreatic duct drains the left lobe. The accessory pancreatic duct is the largest excretory pancreatic duct in dogs. It opens into the duodenum at the minor duodenal papilla. The smaller pancreatic duct is occasionally absent. The latter usually enters the duodenum on the major duodenal papilla, adjacent to the common bile duct. Cats have different embryological development and anatomy of the pancreas from other species, including dogs. The pancreatic duct is derived from the ventral anlage and is the main functional pancreatic duct in cats, but it is of minor importance, and may be absent in dogs. In cats the accessory pancreatic duct generally does not persist, with 80% of cats having only one pancreatic duct. The accessory pancreatic duct enters the duodenum through the minor duodenal papilla. The pancreatic duct enters through the major duodenal papilla. In cats this is the main, and frequently the only, pancreatic duct opening into the duodenum, contiguous with the bile duct. It is implied that this single opening of the pancreatic duct (that is contiguous with the opening of the common bile duct) is the reason for an association between pancreatitis and extrabiliary tract obstruction in the species (Warman and Harvey 2007, Son and others 2010).

Specific surgical procedures

Pancreatic biopsy

- Blunt dissection and ligation technique (blunt separation technique)
- Suture fracture technique (guillotine technique)
- Use of surgical staples
- Use of vessel sealing device (advanced bipolar electrocautery or ultrasonic energy)
- Laparoscopic

Partial pancreatectomy

- Blunt dissection and ligation technique (blunt separation technique
• Suture fracture technique (guillotine technique)
• Use of surgical staples
• Use of vessel sealing device (advanced bipolar electrocautery or ultrasonic energy)
• Laparoscopic

The suture fracture technique is straightforward and is best for lesions at a tip of a pancreatic limb, at the edge of the parenchyma, or that involve lobules that are pedunculated. The blunt separation technique can be used for any region of the pancreas. The stapling technique and the use of vessel sealing devices are best used for larger resection of the distal end of a limb.

Enucleation is a form of blunt separation technique that is used for tumours of the pancreatic body. The body of the pancreas is thick, contains large ducts, and tumours in that location are often in close proximity to blood vessels. The meticulous dissection required to remove these tumours and preserve the important anatomical structures is referred to as enucleation. To achieve enucleation, use of sterile cotton-tip applicators and gentle separation of tissues with the fingers are performed.

Total pancreatectomy

Therapeutic total pancreatectomy is rarely performed in dogs and cats. Clinical indications for total pancreatectomy are few but might include acute trauma, intractable pancreatitis and severe chronic fibrosis. Total pancreatectomy is not indicated for the treatment of patients with pancreatic carcinoma because of early metastasis and the invasive nature of this tumour. The greatest difficulty in performing a total pancreatectomy is removal of the right limb of the pancreas while sparing the shared blood supply to the duodenum.

Pancreaticoduodenectomy

When total pancreatectomy is required and preservation of duodenal blood supply is not possible, pancreaticoduodenectomy may be considered. This procedure is rarely performed in animals because of the associated high rate of morbidity and mortality. Pancreaticoduodenectomy combines the techniques for total pancreatectomy with excision of the pylorus and duodenum. The duodenum is resected at the level of the distal end of the right lobe of the pancreas. The bile duct is ligated and transected as it enters the duodenum. Cholecystoenterostomy is required to establish biliary drainage. The patency of the gastrointestinal tract is re-established through a gastroenterostomy procedure. In addition to the resulting exocrine pancreatic insufficiency and diabetes mellitus that must be treated in these animals, marginal ulceration may occur at the site of jejunal anastomosis to the stomach.

Necrosectomy (pancreatic debridement) and pancreatic drainage

All techniques of pancreatic debridement are based on two principles; 1) wide removal of devitalized and necrotic tissue with thorough exploration and unroofing of all collections of solid and liquid debris, and, 2) the assurance of postoperative removal of the products of ongoing local inflammation and infection that persist after debridement. In man, for the treatment of acute necrotizing pancreatitis, techniques include debridement with closure over drains, debridement with open packing, and debridement with closure over irrigation drains and postoperative lavage.

The previous perception that surgical management is unwarranted in acute pancreatitis has been questioned recently (Thompson and others 2009). There are no established specific guidelines for surgical intervention in dogs and cats, but in dogs accepted criteria include evidence of infection, local complications (abscessation or biliary obstruction), diagnostic confirmation (of neoplastic versus non-neoplastic disease), persistent distant organ complications, and failure to respond to aggressive medical management (Thompson and others 2009).

There is similar confusion with regards to the management of chronic pancreatitis and its associated conditions including pancreatic pseudocysts and pancreatic abscessation. Pancreatic pseudocysts, and their treatment, have only rarely reported in dogs and cats.
(Bellenger and others 1989, Smith and Biller 1998, VanEnkevort and others 1999, Marchevsky and others 2000, Jerram and others 2004). Reported surgical managements include cystogastrostomy (Bellenger and others 1989), cystoduodenostomy and omentalization (Marchevsky and others 2000), omentalization (Jerram and others 2004), ultrasonographic-guided drainage (Smith and Biller 1998), and open external drainage (VanEnkevort and others 1999). The surgical management of pancreatic abscession involves pancreatic necrosectomy and omentalization in conjunction with either closed or open peritoneal drainage for suspected septic peritonitis (Salisbury and others 1988, Johnson and Mann 2006, Anderson and others 2008). In a recent retrospective review of 36 dogs diagnosed with pancreatic abscession despite surgical intervention 71% of the dogs died or were euthanized prior to discharge from the hospital (Anderson and others 2006).

References
Surgery of the pancreas in the dog may be required for a variety of reasons, including procurement of a biopsy during an exploratory laparotomy, or partial pancreatectomy for removal of a mass lesion (for example, insulinoma, pseudocyst, abscess etc). Total pancreatectomy has been performed in research animals to create models of diabetes mellitus or exocrine pancreatic insufficiency\(^1\), but is rarely indicated in clinical cases because of high postoperative morbidity and mortality, and because pancreatic carcinoma (probably the only theoretical clinical indication for canine total pancreatectomy) is highly invasive and metastasises early\(^2\).

The clinical impact and postoperative complications following partial pancreatectomy have been evaluated in normal research animals, but not in clinical patients\(^3\)-\(^5\). In humans, partial pancreatectomy resulted in a postoperative complication rate of 20% and a mortality rate of 3% in a prospective study of 61 patients\(^6\), but other retrospective studies have identified a morbidity of up to 47%\(^7\).

To assess postoperative complications following partial pancreatectomy in dogs, databases at the five UK referral centres were searched for dogs undergoing partial pancreatectomy between 2004 and 2013. The primary endpoint was the number of patients with one or more postoperative complications within 14 days postoperatively. Secondary endpoints included the severity of the postoperative complications as assessed by the mortality rate and the duration of hospitalisation.

Sixty seven dogs fulfilled the criteria for inclusion. Mean age at the time of surgery was 8.6 (+/- 2.3) years and the reason for undergoing partial pancreatectomy was for removal of mass lesions which were histopathologically confirmed as insulinoma (n=56), abcessation (n=4), adenocarcinoma (n=1), fibromyxosarcoma (n=1), fibrosing interstitial pancreatitis (n=1), nodular hyperplasia with chronic pancreatitis (n=1), metastatic neuroendocrine tumour (n=1) and normal pancreatic tissue (n=1, the partial pancreatectomy was performed for a pancreatic mass lesion which was presumed to be neoplastic preoperatively). One animal underwent pancreatectomy for treatment of pancreatic avulsion following trauma. Additional procedures performed included removal of enlarged local lymph nodes (n=17), liver biopsy (n=11), omentisation (for pancreatic abscessation, n=4), abdominal drain placement (n=4), removal of gastrointestinal foreign bodies (n=3), splenectomy (n=3), ovariectomy (n=1), jejunectomy (for excision of an abscess, n=1), right adrenalectomy (for concurrent cortical adenoma, n=1), resection of urinary bladder transitional cell carcinoma (n=1), omentectomy (following trauma, n=1), biopsy of a renal mass (n=1), and metastatectomy of the omentum (n=1) or liver (n=1).

Only one intraoperative complication was reported, being brisk haemorrhage from the cranial pancreaticoduodenal artery; a blood transfusion was not required.

A total of 60 post-operative complications were recorded. Thirty two dogs suffered one or more complication, resulting in an overall complication rate of 47.8%. Complications were not statistically significantly associated with patient age (p=0.6741, 95% CI -1.03 to 1.42), patient weight in kg (p=0.1648, 95% CI = -
10.083 to 1.763) or kg/m² (p=0.1529, 95% CI -0.65 to 4.04), pre-anaesthetic blood glucose (p=0.4774, 95% CI -1.49 to 0.707), insulin levels at diagnosis (p=0.3085, 95% CI -72.62 to 23.42), the presence or absence of metastasis (p=0.5655), anaesthetic induction agent used (being thiopentone (n=3), propofol (n=42) or alfaxalone (n=19); p=0.7380), inhalation agent used (being isoflurane (n=52) or sevoflurane (n=10); p=0.9551), surgery involving pancreatectomy alone or in combination with additional procedures (p=0.7006), pancreatectomy of the right lobe (n=22), left lobe (n=32) or body (n=13)(p=0.8925), pancreatectomy for treatment of malignancy or other reason (p=0.9482), size of the mass lesion excised (p=0.7602, 95% CI = -8.6 to 11.7) or whether excisional margins were histologically clean (n=43) or dirty (n=17)(p=0.7510).

The duration of postoperative hospitalisation was significantly greater when there was a postoperative complication (6 days vs 3 days, p=0.0007, 95% CI = -4 to -1).

Thirteen animals (13/67, 19.4%) did not survive until discharge from hospital. Animals which died were significantly more likely to have one or more complications compared with those which survived to discharge (p= 0.0129, 95% CI = -0.665 to -0.187).

Within this cohort of 67 dogs undergoing partial pancreatectomy for clinical reasons in one of five UK specialist referral institutions, 47.8% of patients developed one or more postoperative complications. Mortality was 19.4%. No risk factors for the development of postoperative complications were identified. Further prospective studies are required to confirm these findings.

Importantly, does anyone undertake complete pancreatectomy and what are your experiences?

References
BILIARY TRACT ANATOMY
The gallbladder is a pear-shaped sac that lies in a fossa between the right medial and quadrate lobes of the liver and is connected to the common bile duct by the cystic duct. It is divided anatomically into the fundus, body and neck and receives its blood supply from the cystic artery, a branch of the hepatic artery. The wall consists of a mucosal lining, smooth muscle fibers, submucosa, and an outer serosal covering. It has a capacity of approximately 1ml per kg body weight.

The extrahepatic portion of the biliary system consists of a variable number of hepatic ducts which enter the common bile duct at several locations. The free portion of the bile duct runs through the lesser omentum within the hepatoduodenal ligament and is. The distal portion of the bile duct in the dog (intramural portion) enters the dorsal mesenteric wall of the duodenum and courses obliquely through the duodenal wall for 1.5 to 2 cm and terminates along side, but separate from the pancreatic duct at the major duodenal papilla.

Gallbladder mucocoele
Gallbladder mucocoeles are being recognized with increasing frequency in dogs but have not been reported in cats. Older small-breed dogs tend to be affected, with Border Terriers, Cocker Spaniels, Shetland Sheepdogs and Miniature Schnauzers being over-represented. Hyperplasia of the mucus-secreting glands within the mucosa of the gallbladder leads to an abnormal accumulation of mucus within the gallbladder lumen. Accumulation of bile-laden mucus within the hepatic, cystic and common bile ducts results in extrahepatic biliary obstruction and can ultimately lead to rupture of the gallbladder. The aetiology is uncertain but biliary stasis, cholecystitis and liver disease have all been suggested to predispose to mucocoele formation. Genetic predisposition may also play a role. Shetland Sheepdogs are predisposed to gallbladder disorders, with mucocoeles and concurrent dyslipidemia or dysmotility in many affected dogs (Aguirre et al, 2007). Recently it has been suggested that dogs with hyperadrenocorticism are a 29 times greater risk for development of biliary mucocoeles compared to dogs without hyperadrenocorticism (Mesich et al, 2009).

Dogs usually present with non-specific signs such as vomiting, lethargy and anorexia, but some dogs have no clinical signs. Diagnosis relies on a combination of clinical signs, bloodwork abnormalities and the results of diagnostic imaging studies. Common examination findings include abdominal pain, fever and jaundice. Total bilirubin, ALT, ALP and total white blood cell count are usually elevated, however bilirubin can be normal in early cases. Abdominal radiographs are usually non-
specific. Ultrasonographically, biliary mucocoeles are characterized by the appearance of stellate or finely striated bile patterns (‘kiwi fruit-like’ pattern) and differ from biliary sludge by the absence of gravity-dependent bile movement. The wall of the gallbladder is variably thickened (Besso et al., 2000). Gallbladder wall discontinuity is suggestive of gallbladder rupture, as is the presence of pericholecystic hyperechoic fat or the accumulation of fluid within the abdomen. Gallbladder rupture secondary to ischaemic necrosis of the gallbladder wall is present in up to 60% of dogs with gallbladder mucocoele. Emergency cholecystectomy should be performed.

Cholecystectomy (is the treatment of choice as the gallbladder wall is the source of the abnormal mucous production. The gallbladder should always be submitted for histopathology and a sample of bile and gallbladder wall submitted for culture. Enterococcus spp and E.Coli are the most frequently reported organisms however, in the authors experience bacterial cultures are most frequently negative. Liver biopsy should be performed routinely at the time of cholecystectomy. The most common histopathologic findings are cholangiohepatitis, biliary hyperplasia and cholestasis.

Potential complications include leakage of bile, pancreatitis and re-obstruction of the common bile duct with gelatinous bile. Reported perioperative mortality rates range from 21.7% to 40% and in a recent study (Malek et al, 2013), elevations in serum lactate concentrations and immediate postoperative hypotension in dogs were associated with poor clinical outcomes. Despite this, If treated early before the gallbladder has ruptured, the prognosis is generally good if the dog survives the immediate postoperative period (Amsellem 2006, Besso et al, 2000, Mehler 2004, Pike et al, 2004).

**Cholecystectomy**

**Surgical approach**
A ventral midline abdominal approach is the most useful, starting at the xiphoid cartilage and extending well beyond the umbilicus caudally.

**Surgery**
The author places a 2 or 3 metric polypropylene suture in the apex of the gall bladder to aid with manipulation. Gently dissect the gallbladder away from the parenchyma of the hepatic fossa by blunt and if necessary sharp dissection. A selection of curved mosquito or Mixter forceps and cotton-tipped applicators are helpful. Alternatively cutting diathermy or an ultrasonic scalpel may be helpful if
available. Inevitably there will be some haemorrhage from the hepatic tissue and this can be controlled by packing the hepatic fossa with a moistened abdominal swab.

Once the gall bladder is dissected free, identify the cystic artery and ligate or seal near the gallbladder. Dissect the cystic duct from surrounding tissues down to its junction with the common bile duct; cross-clamp and sever. Remove the remaining clamp on the cystic duct stump, it is helpful to place a stay suture in the wall of the duct or to grip it with Debakey forceps and pass a suitably sized urinary catheter via the stump and down the common bile duct to ensure its patency. Gently lavage the duct with sterile saline to remove inspissated bile. In some dogs it may be necessary to perform a duodenotomy and catheterise the common bile duct via the duodenal papilla to aid flushing mucoid bile from the biliary tree. Once patency of the common bile duct has been determined, transfix and double ligate the stump of the cystic duct. Absorbable suture or haemostatic clips can be used for this.

It is essential prior to ligating that the common bile duct is identified and avoid damaging it during the procedure. In addition, sufficient cystic duct stump length should be left to prevent the ligatures encroaching on the hepatic ducts from the central division of the liver.

Once the duct is ligated and the duodenotomy repaired, carry out a liver biopsy, then check the hepatic fossa for haemorrhage. It can be packed with a topical haemostatic agent or omentum if required. Submit a portion of the liver, gallbladder wall and some bile for culture; submit the remainder of the gallbladder and liver for histopathology.

**Postoperative management**

It is important to monitor PCV post surgically as well as electrolyte status. In patients that have been inappetant preoperatively, the placement of an oesophagostomy tube immediately post coeliotomy is advantageous.

It is our experience that many of these patients are very painful post operatively and careful consideration must be given to developing an adequate pain plan for these cases.

**Further Reading**


