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A to Z of Rabbits Mini Series

Session Three: The Ageing Rabbit

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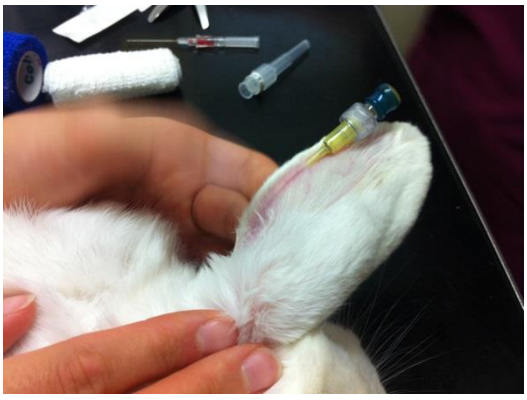

The A-Z of Rabbits: Part Three The Aging Rabbit

- **Cardiac disease: potential differential diagnoses for heart disease, diagnostic modalities and treatment options**

  Heart disease is not well recognised in rabbits, perhaps because of the challenges faced in trying to hear a murmur or arrhythmia in an animal with a heart rate that is potentially greater than 300bpm. Equally exercise intolerance is not often reported by owners, perhaps because rabbits are very good at managing their activity levels and hiding distress. The commonest symptom reported in rabbits that are eventually diagnosed with cardiac disease is unexplained weight loss. The weight loss maybe a combination of dyspnoea (mouth breathing and therefore not eating) or exercise intolerance (unable or unwilling to move to obtain food). A clinical suspicion of heart disease may be suggested in a rabbit that has recently lost weight but still appears to be eating, with an elevated heart rate, possibly pulse deficits or a murmur/thrill apparent and even perhaps an enlarged liver or ascites noted. Often a rabbit with severe heart disease will rapidly develop cyanosis during examination. Another useful sign is rapid but deep breathing (different form the common, paradoxical breathing which tends to be very shallow and rapid, almost bouncy).

- Rabbits can suffer from both congenital and acquired heart disease, this is increasingly recognized as the population ages

- Clinical signs can include dyspnea, exercise intolerance, weight loss and anorexia. There may however be NO noticeable clinical signs.

- Diagnostic evaluation should include a full physical examination, auscultation, ECG, chest radiography and echocardiography.

- Treatment recommendations follow those for other species. Once a diagnosis is made, use of the 'Cascade' allows suitable medical treatment.

- In an emergency decompensation situation, oxygenation, and application of 5mm of nitroglycerine gel to the inside of the pinna can be life-saving.

Disease Conditions

Most recorded information about cardiac diseases relates to infectious, toxin-induced or diet-related diseases of laboratory rabbits. Heart disease also occurs in pet rabbits and more information has become available as rabbits live longer and more diagnostic and therapeutic procedures are adopted for the individual animal. Congenital abnormalities such as ventricular septal defects occur as do age related cardiac problems such as valvular disease. Commonly noted clinical signs include exercise intolerance and dyspnea, however they may be very non-specific such as anorexia or weight-loss. On examination it may be possible to detect cyanosis of the mucus membranes, or appreciate a heart murmur or arrhythmia. Diagnosis and treatment follow the same lines as for dogs and cats. Clinical examination, auscultation, electrocardiography, chest radiography should form part of the minimum database. Many cases can be positively diagnosed by echocardiography. Most cardiac disease is diagnosed in pet rabbits over the age of four years, and the larger breeds such as New Zealand Whites and French Lops are over-represented.
Cardiomyopathy occurs in pet rabbits. Giant breeds appear most susceptible, but the aetiology is unknown at the present time. Hypertrophic, restrictive and dilated forms have all been reported. Histopathological findings indicate the presence of myocardial fibrosis.

The rabbit myocardium can be affected by several diseases. Vitamin E deficiency, coronavirus infection and some bacterial infections such as salmonellosis and pasteurellosis have been recorded as causes of cardiomyopathy in laboratory rabbits. Tyzzer's disease not only causes intestinal and hepatic lesions but can also cause a myocarditis resulting in myocardial fibrosis in those animals that survive. *Encephalitozoon cuniculi* has been reported as a cause of myocarditis in rabbits. Stress and catecholamines are proven causes of cardiomyopathy. Myocardial necrosis and fibrosis have been recorded in rabbits anaesthetized with ketamine/xylazine combinations by continuous infusion.

It has been postulated that hypoxaemia and coronary vasoconstriction result in cell death and necrosis. The rabbit has limited collateral coronary circulation and is therefore predisposed to ischaemia induced by coronary vasoconstriction. The authors draw an analogy with rabbits used as models of catecholamine-induced cardiomyopathy in which alpha-adrenergic mediated coronary vasoconstriction occurs. Hypotension and hypoxaemia are further contributory factors.

Arteriosclerosis is a thickening and hardening of the arteriolar walls resulting from proliferative or degenerative changes. Aortic arteriosclerosis occurs in rabbits and can cause seizures or vague symptoms such as inactivity and weight loss. Mineralization of the aorta occurs in hypercalcaemic rabbits, usually in association with renal disease that impairs calcium excretion. Mineralization of the aorta is seen radiologically and may be asignificant but incidental finding. Calcification of the aorta is often associated with calcification of the kidney. Calcification of soft tissues can be caused by excessive intestinal absorption of calcium, such as in cases of vitamin D toxicity.
Coronavirus infection in rabbits can result in cardiomyopathy and pleural effusion. Experimentally, coronavirus infected rabbits are used as laboratory models to study virus induced cardiomyopathy. An analogy has been made between rabbit coronavirus and feline infectious peritonitis. Clinical signs vary, but infected rabbits are generally pyrexic and many die within 5 days of infection. Pulmonary oedema, pleural effusion and dilation of the right ventricle are found at *post-mortem*. As in feline infectious peritonitis, hypergammaglobulinaemia is a feature of chronic infection that can be manifested by myocardial degeneration, ascites and uveitis. An enteric form has also been described. At the present time, coronavirus induced pleural effusion and cardiomyopathy\have only been reported in experimentally inoculated rabbits. It has not been described in pet rabbits.

Cardiac Diagnostics

1. A thorough history is essential and should include information regarding the diet, animals in contact, neutering and exposure to potentially toxic substances. Remember that cardiac disease may be subtle, and rabbits as a prey animal may conceal relevant clinical signs. Unexplained weight loss, exercise intolerance and anorexia are all potentially significant.
2. Physical examination: this should include a thorough general examination, paying attention to the respiratory rate, heart rate, presence or absence of murmur and pulse deficits. Remember that at heart rates above 300bpm murmurs, arrhythmias and deficits can be difficult to detect. It is also important to evaluate the lung fields thoroughly to determine the likely origin of any adventitious sounds. Any concurrent diseases found during the physical examination should be fully evaluated.
3. ECG: this diagnostic method is easy to adapt for use in rabbits. The leads are applied as for other species, and a reading can usually be made without the need for sedation. Normal measurements are available.
4. Blood pressure monitoring: with the correct cuff this can be easy to achieve in general practice. Normal values are available.
5. Radiography: most thoracic radiography will require sedation. In my experience both Hypnorm (the licensed sedative) and alpha-2 agonists (commonly used as part of the ‘triple combination’ for sedation) can have negative effects on cardiac function. It is also not ethical to consider use of inhalant gases alone because rabbits will commonly breath-hold particularly if isofluorane is used. Possible alternatives include the use of midazolam alone or in combination with ketamine or an opiate. NB the advantages of sedation may be outweighed by the risks of not having an intubated patient, and considerations of the risks and benefits of both options should be discussed with the owner.
   Chest xrays should ideally be taken at the point of maximal inspiration, and two perpendicular views are required. Normal measurements for cardiac size are available.
6. Echocardiography: this can often be performed without sedation, depending on the temperament of the patient. Echocardiography will give the best determination of the structural and haemodynamic issues occurring within the heart. Normal measurements for rabbits are available.

Treating cardiac arrhythmias

Cardiac arrhythmias should be characterized using electrocardiography and heart structure and function assessed echocardiographically.

- Tachyarrhythmias: Prolonged rapid heartbeat over a period of weeks to months can lead to congestive heart failure. Short episodes may contribute to syncope.

    1. Supraventricular tachycardias: these can be treated using digoxin (0.005 mg/kg SID-BID); however, there is a significant risk of toxicity with this drug. Ideally blood digoxin levels should be monitored after the first few days of treatment. The levels are usually checked 6–7 h post-dosing. Alternatively the rabbit can be watched carefully and the drug dose reduced/stopped if signs of anorexia or gastrointestinal stasis occur. Diltiazem, a calcium channel-blocker, can also be used to treat tachycardia by slowing atrioventricular conduction (0.5–1 mg/kg SID-TID). The downside to this medication is that it reduces myocardial contractility and may cause a drop in blood pressure.

    2. In emergency situations rapid ventricular tachycardias may respond to boluses of intravenous lidocaine (1–2 mg/kg IV PRN).

    3. Solatol and mexiletine have also been used anecdotally in rabbits at dog doses.

- Bradyarrhythmias: Severe bradycardia may lead to episodic weakness or syncope.

    1. Bradycardia during anaesthesia (not in the case of α_2-agonists) should be treated with glycopyrrolate (0.01 mg/kg).

    2. Severe atrioventricular block may respond to oral theophylline (10–20 mg/kg); however, mechanical pacing may be required.

Emergency treatment of congestive heart failure.

- Oxygen
- Percutaneous nitroglycerine 1cm on the internal pinna
- Furoseamide 1–2 mg/kg intravenously
- ACE-inhibitors: enalopril 0.25–0.5 mg/kg once daily
- Pimobendan: 0.1–0.3 mg/kg SID-BID

Treating Chronic Cardiac Disease

Diuretics

- Furosemide

Furosemide is a loop diuretic that exerts its effect on the ascending limb of the Loop of Henle. It increases excretion of calcium, magnesium and hydrogen as well as renal blood flow and glomerular filtration rate. This drug is commonly used in the management of congestive heart failure, often in combination with ACE inhibitors or pimobendan. There have been many studies on the cellular effects of furosemide on the rabbit kidney, demonstrating that despite the rabbits relative inability to excrete H^+ ions through the kidney, furosemide is still effective in this species.

ACE inhibitors

- Enalapril

Enalapril inhibits the conversion of angiotensin I to angiotensin II, resulting in decreased pre- and after-load from venous and arteriodilation. It also decreases salt and water retention by reducing aldosterone production. It is often used in combination with loop diuretics in the treatment of congestive heart failure. ACE inhibitors may exacerbate pre-renal azotaemia in animals that are hypotensive or that have poor renal blood flow. They are of benefit in cases of hypertension and some cases of chronic renal failure.

- Benazepril

Benazepril exerts its effects in a similar manner to enalapril. It is commonly used in association with loop diuretics in the treatment of congestive heart failure. Benazepril is also useful in the treatment of hypertension and chronic renal insufficiency. Benazepril has significant hepatic metabolism to the active form benazeprilat. In rabbits regular monitoring of blood pressure, serum creatinine, urea and electrolytes is recommended, and hypotension, hyperkalaemia and azotaemia would be indications to re-evaluate the therapeutic plan.

- Pimobendan

Pimobendan is both a positive inotrope and a vasodilator (inodilator). The advantage associated with pimobendan is that it exerts positive inotropic effects without causing an increase in myocardial oxygen demand. This is achieved by sensitization of the myocardial contractile apparatus to intracellular calcium and by phosphodiesterase III inhibition. It is used in the management of congestive heart failure in dogs due to dilated cardiomyopathy (DCM) or valvular insufficiency. It is contraindicated where augmentation of the cardiac output through the mechanism of increased contractility is impossible, for example in cases of hypertrophic cardiomyopathy. The bioavailability of this drug is significantly reduced in the presence of food, meaning that its efficacy may be limited in rabbits compared with that in dogs, however this may be mitigated by use of the new injectable formulation, particularly in emergency situations.

- **Renal disease: diagnosis and treatment of renal disease**
  Renal disease is a common finding particularly in older rabbits. Although often linked to infection with *Encephalitozoon cuniculi*, this is by no means the only cause of renal disease in rabbits. Clinical signs of renal disease in rabbits can include: polydipsia, polyuria, loss of litter training, urine scalding, weight loss, poor appetite, or there may be no obvious symptoms. The main diagnostic modality in blood sampling: looking for elevations in urea and creatinine, and possibly either an increase or decrease in serum phosphorus. However: remember that both urea and creatinine are more labile in the normal rabbit than they are in other species, so elevations must be interpreted with caution: ie in conjunction with other parameters marking dehydration (eg total protein or PCV) as well as urine specific gravity (although this is also very variable). In order to determine the cause of disease, more information is required: ie an encephalitozoon titre, potentially an ultrasonographic scan of the kidneys, and for the gold standard answer, biopsy and histology. A word of caution however: renal biopsy is an invasive procedure, and whilst this is being performed more often in dogs and cats (particularly younger animals with unexpected renal disease) this can have lasting consequences in the rabbit, in terms of leading to chronic adhesions that can affect gut motility and lead to lifelong problems. Also renal biopsy is not without potential risk so the pros and cons and potential for a different treatment regime must be considered very carefully.

- **Liver lobe torsion: diagnosis and surgical correction of this newly described and incredibly painful condition**
  This condition causes severe and potentially acute, escalating abdominal pain in rabbits, and has very likely been underdiagnosed in the past. Although it is the right liver lobe that is most commonly involved, it is thought than any liver lobe could be potentially involved. The condition occurs without any warning in rabbits that are apparently otherwise healthy. Because of the acute and rapidly progressive nature of this condition, many rabbits are severely ill or moribund at the time of presentation, although some workers report rabbits exhibiting a brief period of anorexia from which they recover. The degree of torsion and the ability for this to self correct will determine the outcome to a large degree.
  Treatment is rapid diagnosis, stabilisation and surgical removal of the affected liver lobe. Clinical signs include a palpable painful mass in the right cranial abdomen. Ultrasonography can be used to confirm the diagnosis, and in this condition is more useful than radiography. There may be free serosanguinous fluid noted in the peritoneal cavity.
  Early surgical intervention is associated with the best chance of good clinical outcome because the condition is rapidly progressive and endotoxaemia is a significant possibility.

- **Osteoarthritis and hock sores: A common disease of older rabbits OA has far reaching consequences for the welfare of the older pet. Urine sludging, hock sores, failure to eat caecotrophs, flystrike and other conditions are all interlinked with a reduction in mobility.**
  Osteoarthritis can occur in rabbits of any age secondary to previous injury, alterations in mobility or simply aging changes. Very typically in rabbits an alteration in mobility can be manifested as hock sores, a mite infestation, inability to eat caecotrophs or perineal scalding and urine sludging. So apparently unrelated clinical signs can play a significant role in leading to a clinical suspicion of osteoarthritis. The key diagnostic intervention is radiography, however as in other species the degree of arthritic change is poorly related to the degree of dysfunction apparent.
  Treatment again follows that of more familiar species, and includes analgesia, anti-inflammatories, physiotherapy and potentially nutraceuticals.

- **Neoplasia: increasingly well recognised in rabbits, many types of neoplasia have been reported. Less common are reports of successful treatment. Diagnostic and treatment modalities will be discussed.**
  Although rabbits reportedly are not commonly affected by neoplasia, in a survey of necropsies performed in rabbits, neoplastic lesions were found in 1 in 3 individuals. As rabbit medicine is advancing and particularly with the increased availability of advanced imaging modalities, neoplastic lesions are increasingly being recognised.

Neoplasia is defined as the abnormal proliferation of cells, which is is uncontrolled and not synchronised with surrounding tissues. This leads either to a solid mass of abnormal cells within a tissue (tumour or neoplasm), or a population of abnormal cells in the circulation. Neoplastic disease can be further categorised according to the expected behaviour of the disease. Benign neoplasia (e.g. squamous papilloma) refers to an abnormal proliferation of cells that is localised, well circumscribed and does not spread around the body. Benign tumours do not transform into malignancies (cancer). Pre-cancerous neoplasia (e.g. carcinoma in situ) does not invade local tissue, however given time will transform into malignant disease. Malignant neoplasia often invades and destroys local tissues and has the potential to form secondary metastases at distant locations (e.g. uterine adenocarcinoma). Obviously for mass lesions neoplasia is a significant differential, however any rabbits with unexplained weight loss, or one where cachexia is evident should be robustly assessed for neoplasia. Although less is known directly about the specific behaviour of certain tumours in rabbits, the ability to diagnose and infer from behaviour of similar disease in other species is available. The difficulty is then planning for ongoing treatment.

Treatments

The goal of treatment is to promote the patient's welfare while treating the neoplasia. The risks, side-effects and recovery period associated with the treatment must be balanced against the potential benefits. These decisions should be made with the owner's input and a frank discussion of euthanasia in severe cases should take place early in this process. For some cases euthanasia is the best option.

Surgery: Surgery is the commonest treatment for neoplasia in both humans and animals and results in more cures than all other treatments combined. Surgery is not immunosuppressive, is non-carcinogenic and is more effective for large lesions than either chemotherapy or radiotherapy. Surgery is the most commonly reported treatment for neoplasia in pet rabbits. Several strategies can be used:

- Excision: this technique is indicated where removal of the lesion will be associated with minimal morbidity, will preserve the functional integrity of the underlying tissue where possible and where knowledge of the underlying tumour type would not alter the clinical decision (i.e. where the tumour is felt likely to be benign). Surgery should be planned such that a margin of visually normal tissue can be removed, and the overlying skin can be suitably closed. The use of reconstructive techniques including skin advancement flaps may be indicated. The whole tumour should be submitted for histology and revision surgery planned to remove a wider margin of normal tissue if necessary. Figure 18.6 Surgical removal of a tumour.

- Debulking: debulking should be considered where the mass is large but not amenable to complete removal due to size or location. It means removal of a proportion of the mass to allow improved comfort, diagnostics, improved success of chemo- or radiotherapy or intra-lesional therapy. Surgery should be planned to allow improved mobility, minimal morbidity and reasonable potential for healing to occur.

Chemotherapy

- Systemic: this is the administration of anti-neoplastic drugs either orally or intravenously. The dose given is the maximum dose with the minimum risk of side effects. Most drugs have a therapeutic dose very close to the toxic dose, so careful dose calculation is needed. The therapeutic ratio of a drug is the toxic dose divided by the effective dose, and this value is usually small for chemotherapeutic agents, indicating how close the toxic dose is to the therapeutic dose. Chemotherapeutic doses are usually based on body surface area rather than weight, although some authors feel that dose calculations based on metabolic rate may be more appropriate in exotic species. This sort of dosage calculation is not yet validated.
- Intra-lesional: this involves injecting antineoplastic drugs into and around a tumour. It allows a higher therapeutic index and reduces the likelihood of side-effects. It is a simple and direct approach for treating solid tumours. Aqueous drugs used in this manner may be rapidly cleared from the tumour site meaning the length of time the tissue is exposed to the drug is short and allowing systemic exposure that may result in toxicity. Currently the drug of choice for this method is cisplatin suspended in a water/sesame oil emulsion or a collagen matrix to allow slow release of the drug locally. Cisplatin has good activity against all histologic types of solid tumours and it does not cause tissue necrosis.

Side-effects: Chemotherapeutic drugs affect cells that are dividing. This is why side-effects are often noted as gut signs or immunosuppression (the gut lining and bone marrow divide actively at all times). In rabbits, side-effects may manifest as inappetence and gut stasis, or immunosuppression allowing the expression of pre-existing subclinical infections such as pasturellosis or encephalitozoonosis. Patients may exhibit side-effects at the time of treatment or up to a few days afterwards. Those rabbits showing inappetance may require parenteral fluids and supportive care (e.g. assisted feeding, prokinetic drugs and anti-ulcer treatments). Subsequent chemotherapy doses may need to be reduced by up to 20% in order to avoid repeated problems. The degree of immunosuppression can be evaluated by monitoring white blood cells counts. Those rabbits with very depressed heterophil/lymphocyte counts should have their immunotherapy delayed until the white cell levels return to normal. Concurrent infections should be treated and the animal stabilised prior to continuing chemotherapeutic treatments. Reducing chemotherapy doses or frequency will result in fewer side-effects but also less efficient tumour cell destruction.

Monitoring: Routine monitoring should include pre-treatment haematology to allow decision making regarding the suitability of the patient for treatment at a particular time. Organ function tests should also be carried out regularly (the timing will depend on the baseline parameters, the treatment being given and the site of the tumour) animals with depressed renal or liver function may have prolonged drug clearance and an increased risk of toxicity occurring. Consideration should also be given to repeat imaging (radiography, CT, MRI) in order to repeat the tumour staging and assess for metastasis. The specifics of timing will depend on the individual patient.

Radiotherapy: This refers to the use of ionising radiation to treat localised solid tumours. Ionising radiation works by damaging DNA causing cell death. The radiation will also kill surrounding normal cells, so the radiation is applied using several focussed beams set up to intersect at the tumour. This allows the abnormal tissue to absorb a much higher radiation dose than the surrounding tissue. If the tumour appears to have already spread to the local lymph nodes then these may also be included in the treatment field, and in most cases a margin of normal tissue around the mass is irradiated in an attempt to remove areas of micro-metastases. The amount of radiation delivered is measured in ‘Greys’ (Gy). The total radiation dose is divided into multiple small doses (fractions) to reduce the possibility of side effects in surrounding healthy tissues. The times between the fractions allows normal cells to recover, while in general tumour cells are less able to do this. Radiotherapy can be used in order to cure a tumour, or as part of a multimodal approach that might include surgery and chemotherapy as well. It can be applied either pre- or post-operatively. In cases where the disease is terminal, radiation can be used palliative in order to prolong good quality life.

Chemotherapeutic drugs (for example cisplatin) may be used to enhance the sensitivity of tissues to radiation. One of the draw-backs of radiation therapy is that it requires repeated anaesthetics, often within a short period of time. Different tumours types respond differently to radiation. Leukaemias and lymphomas are thought to be very sensitive, epithelial tumours are only moderately sensitive, while renal tumours and melanomas are insensitive.

Side effects: Radiotherapy is painless; however pain may occur a few days after treatment, associated with tissue swelling in treated areas compressing nerves. Skin irritation, similar to sunburn might also be recognised, and lead to self-trauma. Areas affected by radiation will heal rapidly, however these are often less elastic than normal tissue due to the formation of fibrous scarring. Hair loss may also be seen, and regrowth may well be white. Heart damage is reported in human patients with breast cancer because of the proximity of the heart to the irradiated area, and is a possibility in rabbits treated with radiotherapy for thymomas, for example.

Photodynamic therapy: Photodynamic therapy (PDT) involves using non-toxic light sensitive compounds that become toxic on exposure to light, thereby killing malignant cells. Light sensitive agents accumulate preferentially in neoplastic tissues and light is applied selectively to affected areas to reduce the effect on normal tissue. PDT is a technique that is recognised as being minimally invasive and minimally toxic. PDT has most often been used to treat squamous cell carcinoma in animals; however the success rate has been variable. The disadvantages of PDT are the expense of the equipment required, the limited ability of this modality to treat deep tumours and the fact that the skin of many animals remains sensitive to light for a few weeks after treatment. While rabbits have been used extensively in PDT research no published examples of its use clinically in rabbits were found.

Cryotherapy: This is the use of cryogens (nitrous oxide or liquid nitrogen) to freeze tissues causing cell rupture and death. Tumours found on the skin, lips, eyelids and the perianal region are particularly amenable to this type of treatment. The advantage of this type of treatment is that it does not always require repeated anaesthetics (this depends on the area that is to be frozen). The disadvantage is that there can be post-freezing swelling, pain and self-trauma.

Immunotherapy: Immunotherapy is the treatment of disease by inducing, enhancing or suppressing the immune response. This treatment modality has been used with some success in certain types of cancer. Acemannan (a polysaccharide found in aloe vera) has been used to treat neoplasia in a variety of species. Acemannan causes macrophage activation, leading to release of tumour necrosis factor, interkeukin-1 and interferon. Its use has been reported intertumorally and systemically, in combination with surgical debulking. Whilst acemannan has been extensively tested in rabbits and found to be safe, there are few reports of its use in clinical cases. Other immunomodulatory agents such as interferon and retinoids have been used with apparent clinical success in rabbits.

NSAID Therapy: Many non-steroidal agents have shown anti-tumour activity in vivo. Piroxicam in particular has documented activity against several types of tumour in dogs. The mode of action is thought to be related to the prevention of platelet aggregation or the inhibition of angiogenesis (thus restricting the potential for tumour growth). Currently meloxicam, a drug very commonly used in rabbit medicine, is undergoing evaluation for its use in neoplastic conditions.

Other therapeutic considerations

Nutrition: In all species the alteration of carbohydrate, lipid and fat metabolism is a common paraneoplastic syndrome. Cachexia, the loss of muscle and fat despite adequate nutritional intake can be the first clinical sign noted before primary signs of neoplasia are evident. Anorexia, lethargy and impaired immune function are possible consequences. Nutritional therapy is therefore very important and should be instituted early in the treatment regime. Rabbits are reliant on long stem fibre to maintain gut motility and support the bacterial population in the caecum. Provision of ad lib hay, fresh vegetables and a small amount of good quality pellets is a good basic strategy, however some rabbits will still lose weight despite eating well. Supportive feeding can be instituted (there are several commercial formulas available) however the provision of high levels of simple carbohydrates can support tumour growth even though weight is maintained. Therefore, selection of assisted feeding products that are higher in fibre and lower in simple carbohydrates should be advocated. In cases where anorexia is a significant problem the placement of nasogastric or pharyngostomy tubes can be considered for supportive feeding during treatment.

Nasogastric tubes are not large enough in most cases to allow the provision of a fibrous diet, and in the author's experience can be poorly tolerated by many rabbits. Pharyngostomy tubes, being wider, do allow feeding of a more suitable diet, however there are many reported cases of complications at the insertion site (abscessation in particular) so the benefits must outweigh the potential risks.

Analgesia: Many cancers are associated with significant pain, and analgesia is a vital part of the treatment plan. Pain can be mild to severe, acute, chronic or intermittent and either associated with the disease itself or the treatment given. Mild to moderate pain can be adequately controlled using non-steroidal agents, while more severe pain may require opiates. Consideration can also be given to other modalities such as acupuncture. Many rabbits tolerate acupuncture well and subjectively appear to benefit from this. The use of acupuncture to relieve pain in humans with cancer is well documented, and its use in animals is becoming more widespread. The author has used acupuncture, delivered by a veterinary surgeon experienced with rabbits, with apparent good success in many cases
Radical surgical excision is always going to be the best treatment option for most masses, however this is not always physically possible, and chemotherapy and radiotherapy need to be considered as does palliative care. Having used chemotherapy on several rabbits, my experience is that they appear to tolerate it relatively well (as long as other potential confounding factors such as pre-existing renal, hepatic and cardiac disease are addressed). However post-therapy effects such as severe bone marrow depression leading to thrombocytopenia and bleeding have been noted. There are also confounding issues surrounding the use of radiotherapy in terms of the fact that it requires several fractions and therefore repeated general anaesthetics and there is also the issue of collateral damage particularly to the heart.

- **Nutritional strategies and supplements for the aging rabbit: many foods have additives that are anecdotally beneficial for many of the conditions recognised in older rabbits. A critical look at the evidence base for these supplements/compounds and their use in rabbits will be taken.**
  There are a variety of feed supplements used to assist in treatment of many medical conditions, and the usage of these is generally based on evidence gathered from other animal species of humans.
  Common ones include: cranberry, glusoamine/chondroitin, pre/pro-biotics, ginseng, Co-enzyme Q10, milk thistle and green tea extract.
  Other nutritional strategies employed by animal feed companies include calorie restriction, increasing fibre content, restricting calcium content and supplementing with additional vitamins.
  Currently the evidence base for the use of many of these ingredients is scarce, although these ingredients are not thought to be harmful. In the case of ingredients such as CoQ10 we know that there are measurable physiological effects associated with its use, and the primary issue is proving the benefits. The same is true of pro-biotics and cranberry extract. The evidence base is growing; however it is a work in progress.
  In regards to some of the nutraceuticals marketed for cats and dogs, many of these are flavoured with meat extracts, so
- **Palliative care and euthanasia: the final decision that probably should be made for the older rabbit: considerations of long term use of medications, the use of contraversial medications such as steroids to improve welfare and euthanasia will be discussed.**

Euthanasia is always an emotive subject, and the decision to euthanase a pet rabbit is as difficult as it is in other species. Rabbits are perhaps unusual in that while they are often treasured family pets they are also often thought of as disposable children's pets. In some instances euthanasia is a simple business decision. This can mean that the reasons for requesting euthanasia are different from those we are comfortable with in other pet species. While euthanasia itself is not a welfare issue (failure to euthanase in a timely fashion can be) it is an ethical one. It is not uncommon for euthanasia to be requested for young rabbits with treatable conditions.

The RCVS code of Professional Conduct states: 'No veterinary surgeon is obliged to kill a healthy animal unless required to do so under statutory powers as part of their conditions of employment. Veterinary surgeons do, however, have the privilege of being able to relieve an animal's suffering in this way in appropriate cases'.Variations in how owners think of their pets dictate how and when euthanasia takes place. Some owners may not be aware of appropriate treatment options, while others have discounted them for whatever reason. In some circumstances rehoming the rabbit may be a welcome option. In all circumstances the welfare of the rabbit must be protected and undue fear, pain and distress avoided.

The most common method of euthanasia of pet animals in the UK is an intravenous injection of a lethal dose of pentobarbital. This is certainly an appropriate method in the pet rabbit. Rabbits are not tolerant of intravenous injections unless moribund or sedated. They often respond by struggling or screaming (albeit nearly silently in many cases). Either situation can be very distressing to the rabbit and also to the owners so it is preferable to consider placing an intravenous catheter prior to euthanasia to avoid the rabbit reacting to injection of irritant euthanasia solution. I use the marginal ear vein for catheter placement. Applying EMLA (Astra Zeneca) local anaesthetic cream to the area first can make catheterisation less painful and less stressful. Once the catheter is secured in place then it should be flushed with heparin saline to prevent blood clots blocking the end.

In some circumstances sedation of the rabbit prior to euthanasia may be viewed as a good option particularly in cases where the owners wish to remain present but the rabbit is not moribund. It depends on the situation and the temperament of the rabbit as well as the degree of discomfort the rabbit is suffering.

Good communication with the owner is vital at all stages of the euthanasia process. It is worth letting owners know what to expect at each point, from how the rabbit needs to be restrained to how rapidly loss of consciousness occurs. At times where emotions are heightened keeping up a non-intrusive narrative about everything that is going on can be helpful and often gives the owner something to focus on. Many owners are surprised how rapidly death occurs once the intravenous agents are given, so preparing them for this is very helpful for them.

Where the euthanasia takes place should also be carefully thought through. Some practices are lucky enough to have a separate room (ie not a consulting room) that can be used for this purpose. This allows the owner enough time to experience the process without the added stress of being rushed. Ideally the euthanasia should be scheduled at a quiet time of the day, and plenty of time allowed so that the consultation room is not needed for other routine work. Making certain a chair is available and having blankets or towels placed over the examination table or on the floor to reduce slipping and struggling is helpful. The idea is to make the room more comfortable for both the rabbit and the owner.

Increasingly owners are requesting euthanasia in their own homes. This is often less distressing for both the rabbit and the owner. The visit can be planned at the owner's convenience and can take place in surroundings that are familiar for the rabbit. The downside is that veterinary facilities are not available other than those brought in the visit bag.

Other methods of euthanasia have been published. Several are acceptable in practice (although perhaps not with owners present). These include:

- An overdose of inhalant anaesthetic: this method can be rapid however many rabbits breath-hold in response to the smell of anaesthetic gases and may struggle or scream. Injectable anaesthetics used as a premedication can make the process smoother however it is difficult to understand why this method would be chosen over injection of pentobarbitone.
- Injection of potassium chloride to an anesthetised rabbit: this method can be acceptable even with owners present. The rabbit is anaesthetised and potassium chloride is injected intravenously in order to stop the heart. Again it is difficult to think of a circumstance where this would be chosen over pentobarbitone injection.

- Intraperitoneal injection of barbiturates: this method has been commonly used for the euthanasia of pet rabbits over the years. An overdose of pentobarbitone is injected into the peritoneal cavity and the drug diffuses into the circulation, eventually causing death. The injectable pentobarbitone solution is fairly irritant so the action of putting it into the peritoneum causes discomfort. Because the drug must diffuse into the circulation in order to work, the process is fairly slow and some rabbits exhibit an excitation phase that can be distressing both for the rabbit and the owner. This method is not one I would advocate unless all other options have been explored and discounted.
- Alternative methods that may be suitable in a moribund or sedated/anaesthetised rabbit where intravenous access is not possible are intra renal, intrahepatic or intracardiac injection of pentobarbitone, which are quicker than using the intraperitoneal route but again the potential for discomfort must be considered.

Afterwards.

Many rabbits are kept in bonded pairs, so it is important to consider the surviving individual's welfare within the euthanasia decision. In some circumstances, particularly where the surviving animal has been very reliant on the euthanased one, it may be decided to euthanase both individuals at the same time. Should the surviving rabbit be healthy then consideration should be given to allowing the rabbit to see its companion after it has died. This allows the remaining rabbit to understand somehow what has happened. Most rabbits will approach their companion, sniff and nudge them and some will lie down and groom the dead animal. Eventually, and usually sooner rather than later, the surviving rabbit appears to understand, lose interest and move away. At that point the rabbit can be taken away from the body.

Grieving

The circumstance of a rabbit's death can have a strong impact on grief. An unexpected or traumatic death is shocking and can bring feelings of anger and guilt to the surface. There are several stages of grieving: denial, weeping, bodily distress, anger, guilt and eventual acceptance. This process can take a significant amount of time. It is also important to remember that adult owners grieve differently than children. Information on grief counselling and resources for helping children cope with the loss of a pet can be obtained from the internet. Books for both adults and children on pet loss and grieving can be obtained and kept in the practice. Many practices send a sympathy card or flowers after the loss of a pet, and this, as much as the treatment owners receive at this difficult time, can help owners cope with the loss of their pet.

The options for disposal of the body after death are the same as for other species. Many local authorities do not condone the burial of animals in their jurisdictions even on private land. Animals that are buried should be wrapped in plastic and buried fairly deeply to avoid being dug up by local wildlife. Animals euthanased using barbiturates pose a significant risk to any animal excavating and consuming that body. Owners should be advised that cremation is often the better option; ashes can be returned and buried or scattered. Many owners still prefer burial and ignore local bylaws.