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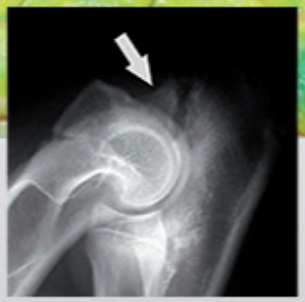
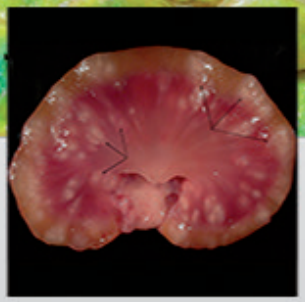
A practical approach to anaesthesia in reptile

Dysplastic elbow disease

Looking at kidneys and beyond





Heart patients and anaesthesia, Uroliths in dogs, Treating dogs with IMHA, "They're not the henemy" and liver tumours in pets

EJCAP ONLINE
Volume 23(1), April 2013

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Dogs


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Dogs and Cats/Small animals


Rabbits


Less common pets


Anaesthesia


Cardiovascular


Dermatology


Diagnostic imaging


Digestive System


Ear Nose Throat


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Neurology


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Anaesthesia in dogs and cats with cardiac disease – An impossible endeavour or a challenge with manageable risk?

*R. Steinbacher**[1], R. Dörfelt[1]*

SUMMARY

Anaesthesia in patients with cardiac disease often poses a challenge for the veterinarian. Due to cardiovascular dysfunction, these patients have an increased anaesthetic risk. This review article summarizes the most important pathological alterations with cardiac disorders in dogs and cats and their relevance for the anaesthetist. Pre-anaesthetic evaluation, premedication, induction and maintenance of anaesthesia as well as monitoring of anaesthetised patients and possible complications are also discussed.

Keywords: anaesthesia, cardiac disease, dog, cat, monitoring, blood pressure

This paper originally appeared in:
Wiener Tierärztliche Monatsschrift – Veterinary Medicine Austria 99 (2012)*

Abbreviations used:

ACE = angiotensin converting enzyme;
AVA = Association of Veterinary Anaesthetists;
DCM = Dilated Cardiomyopathy;
CRI = constant rate infusion;
ETCO2 = end-tidal carbon dioxide;
HCM = Hypertrophic Cardiomyopathy;
HDO = High-Definition Oscillometry;
SACHC = International Small Animal Cardiac Health Council; LiDCO = Lithium Dilution Cardiac Output

Introduction

For many veterinary practitioners, anaesthesia in cardiac patients represents both a challenge and a psychological barrier. This is why the majority of such patients are referred to specialist clinics. However, a sound knowledge of the pathophysiology of heart disease, good perioperative monitoring and management as well as appropriate medication will enable every small animal practitioner to carry out anaesthesia in patients with cardiac disease.

Technically speaking, the left ventricle of the heart can be considered as a “pressure pump”, as it pumps the blood into a high pressure system, while the right ventricle works as a “volume pump” pumping the blood into a low pressure system. This explains why the left ventricle tolerates high pressures without major problems (e.g. in subaortic stenosis or systemic hypertension), while the right ventricle is well able to compensate for volume increases (e.g. in tricuspid regurgitation).

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There are some basic terms, which are important in order to understand the pathophysiology of heart disease, e.g. preload and afterload. Preload is the end diastolic volume of the heart and is basically determined by the venous return to which the hearts' pumping capacity automatically adapts, although within physiological limits. In the healthy heart, increased venous return also increases the ejection volume of the heart. In the pathologically altered heart, an increased preload may initially contribute to maintenance of cardiac output, but in the long run, eccentric hypertrophy, myocardial remodelling, apoptosis of the myocardial cells and general worsening of the cardiac disease occur [BORGARELLI, 2005]. Cardiac afterload is the impedance to ventricular emptying presented by aortic pressure, against which the cardiac muscle has to pump blood into the arteries (aorta and pulmonary artery). Elevated systemic vascular resistance leads to increased afterload and, as a consequence, to an increase in myocardial strain and oxygen consumption. Chronically increased afterload (e.g. due to systemic hypertension or stenosis of arteries near to the heart) causes concentric hypertrophy [BORGARELLI, 2005]. Contractility of the heart is defined as the intrinsic ability of the myocardium to contract. It can be increased and decreased, respectively, by adapting to the actual preload and afterload as well as by positive or negative inotropic drugs (see Table 1).

Maintenance of blood pressure is necessary to ensure peripheral perfusion. The arterial blood pressure is closely related to the stroke volume, the heart rate and the vascular resistance.

Perianaesthetic considerations for animals with cardiac disease

To perform anaesthesia in cardiac patients, some basic preconditions are required, i.e. establishing an intravenous access, use of an oxygen supply, equipment for intubation and ventilation, appropriate drugs for emergencies and devices for monitoring cardiovascular function (electrocardiography [ECG] machine, blood pressure unit, pulse oximeter, capnograph) [SKARDA et al., 1995a; HARVEY and ETTINGER, 2007].
Any excitement of the patient must be avoided. In some cases, the intramuscular administration of a sedative drug before establishing the venous access may reduce the stress for the patient (PASCOE, 2005). Preoxygenation before inducing anaesthesia reduces myocardial hypoxia and avoids apnoea during induction. During maintenance of anaesthesia, oxygen supply (via oxygen tubing, oxygen mask or laryngeal mask) prevents hypoxia due to hypoventilation (ERHARDT, 2004). In order to keep the duration of anaesthesia as

Table 1: Cardiovascular effects of some important drugs used for anaesthesia

Drug	Heart rate	Inotropy	Cardiac output	Vascular resistance	Arterial blood pressure
Acepromazine	↔	↔	↔	↓	↓
Midazolam	↔	↔	↔	↔	↔
Diazepam	↔	↔	↔	↔	↔
Butorphanol	↔	↔	↔	↔	↔
Buprenorphine	↔	↔	↔	↔	↔
Methadone	↓	↔	↔	↔	↔
Fentanyl	↓	↔	↔	↔	↔
Xylazine Medetomidine Dexmedetomidine	↓↓	↔	↓	↑	↑↓
Ketamine	↑	↑	↑	↑	↑
Propofol	↔	↓	↓	↓	↓
Thiopental	↑	↓	↓	↓	↓
Alphaxalone	↑	↓	↓	↓	↓
Etomidate	↔	↔	↔	↔	↔
Isoflurane	↑	↔	↔	↓	↓
Sevoflurane	↔	↔	↔	↓	↓

↓: Decrease ↑: Increase ↓↓: pronounced decrease ↔: no influence ↑-↓: initially increase, then decrease

short as possible, all preparations for surgery should be concluded by the time of induction of anaesthesia. In the cardiac patient, anaesthesia must aim at maintaining a stable cardiovascular system. Both heart rate and blood pressure should show only minimum variations. Due to cardiovascular depression induced by many anaesthetic drugs, deviations of heart rate and blood pressure values from those of unanaesthetized animals are unavoidable, but should be as minimal as possible (HARVEY and ETTINGER, 2007). It is therefore important to assess the individual baseline values during preanaesthetic examination.

Preanaesthetic examination - Risk assessment

A thorough preanaesthetic examination is of utmost importance, when it comes to the safety of the patient. Special attention should be paid to the parameters of the cardiovascular system: pulse rate and quality, colour of mucous membranes and capillary refill time; in addition, auscultation of heart and lungs, control of absence of pulse deficits and blood pressure measurement have to be performed. Relevant predisposing diseases should always be kept in mind, particularly in older animals as well as in certain breeds (e.g. Great Dane, Boxer; Maine Coon). The absence of clinical signs is no guarantee for the absence of cardiovascular disease. In a study performed in cats with a cardiac murmur but without any clinical symptoms, ultrasound examination of the animals revealed that 53 % of these cats suffered from heart disease [NAKAMURA et al., 2011].

The anaesthetic risk is increased for patients with cardiac disease, even if they are able to compensate for the heart failure; the risk is increased even more in animals with decompensated heart failure [SKARDA et al., 1995b; POSNER, 2007]. In cases of suspected cardiac disease, diagnostic ultrasonography should be performed to identify the type of disease and the degree of compensation [CLUTTON, 2007; HARVEY and ETTINGER, 2007]. Particularly for elective surgery, patients should be duly stabilized before the anaesthesia by administering appropriate drugs. Although patients have to be fasted before all kinds of surgical interventions under general anaesthesia, it is necessary and important to continue administering the prescribed drugs at the usual times in order to maintain effective blood levels of the agent [PASCOE, 2005].

Drugs and their effects on the cardiovascular system

Nearly all drugs used for anaesthesia have an effect on the cardiovascular system. While the healthy heart is able to tolerate these effects, pre-existing cardiac conditions may lead to acute decompensation and heart failure in these patients. Depending on the disease, an adequate anaesthetic protocol has to be chosen in order to keep the stress for the cardiovascular system as low as possible and, ideally, to provide additional support to the heart [HARVEY and ETTINGER, 2007. The most important cardiovascular effects of currently used anaesthetic drugs are summarized in Table 1.

Premedication

Phenothiazines

Acepromazine, a phenothiazine derivative psychotropic drug, is a frequently used sedative drug. It causes a dose dependent reduction of the stroke volume and the cardiac output. Due to alpha1-adrenergic blocking effects on the vascular walls, vasodilation occurs and arterial blood pressure sinks [FARVER et al., 1986]. Possible effects on the heart rate are discussed controversially in literature. LEMKE and TRANQUILLI (1994) as well as EBERSPÄCHER et al. (2005) reported a more or less constant heart rate when acepromazine was administered at moderate doses. According to ERHARDT et al. (2004) and PADDLEFORD and ERHARDT (1992a), a reflex increase in the heart rate was also observed. At very high doses (1 mg/kg), bradycardia and sinoatrial blocks may occur [LEMKE and TRANQUILLI, 1994]. Acepromazine desensitizes the myocardium to the potentially arrhythmogenic effect of catecholamines. Due to its effect on the myocardial alpha1-receptors, it prevents the development of ventricular arrhythmias [LEMKE u. TRANQUILLI, 1994].

Benzodiazepines like midazolam and diazepam hardly have any effect on the cardiovascular system, if administered at usual doses. Diazepam does not produce any clinically relevant alterations of heart rate, myocardial contractility, cardiac output and arterial blood pressure [JONES et al., 1979]. In the dog, midazolam may increase heart rate and cardiac output by 10-20 %, if administered at higher doses (0.25 – 1 mg/kg) [JONES et al., 1979].

Ketamine is a dissociative anaesthetic drug and stimulates the cardiovascular system by activating the

sympathetic nerve system [LIN, 2007]. This exerts a positive inotropic effect on the myocardium, causing an increase of heart rate, blood pressure and cardiac output [PADDLEFORD and ERHARDT, 1992b]. It also increases myocardial oxygen consumption and vascular tone [ZSIGMOND et al., 1974].

Opioids

μ-agonists (e.g. methadone, morphine, fentanyl) increase the vagal tone, thereby causing a dose dependent decrease in heart rate. However, myocardial contractility seems to remain unchanged under therapeutic doses of these drugs [PADDLEFORD and ERHARD, 1992b]. At moderate doses, cardiac output and arterial blood pressure are only minimally influenced [LAMONT and MATHEWS, 2007]. Intravenous administration of morphine may cause vomiting and release of histamine, followed by vasodilation; for this reason, it is preferable to administer it via the intramuscular route. Butorphanol, the synthetic opioid with both agonist and antagonist activities, has only minimum influence on the cardiovascular system. It causes a clinically irrelevant decrease in heart rate and blood pressure, while stroke volume and peripheral vascular resistance remain unchanged [LAMONT and MATHEWS, 2007]. The partial agonist buprenorphine decreases both heart rate and blood pressure, but increases the peripheral resistance, although – like with butorphanol – the cardiovascular alterations are of no clinical relevance [MARTINEZ et al., 1997].

α2-agonists reduce cardiac output [VICKERY et al., 1988; FLACKE et al., 1993; PYPENDOP and VERSTEGEN, 1998]. Initially, a pronounced vasoconstriction with reflex bradycardia is observed [LEMKE, 2007]. In the further course, vasoconstriction gradually decreases, while bradycardia remains unchanged due to a direct effect on the central nervous system (by reducing the sympathetic tone) [LÖSCHER, 2003b]. When using xylazine, considerable cardiovascular alterations can be observed; these effects are more pronounced after intravenous administration than after intramuscular application. The drop in heart rate is comparable to that occurring after administration of medetomidine, while the increase in blood pressure is less with xylazine than with medetomidine [REDONDO et al., 1999; DIFILIPPO et al., 2004]. Xylazine reduces the cardiac output by 30–50 % and the blood pressure by 20–30 %, respectively [KERR et al., 1972; KLIDE et al., 1975; MUIR et al., 1979; HASKINS et al., 1986]. The cardiovascular alterations produced by dexmedetomidine and medetomidine are similar, although peripheral vasoconstriction lasts longer after the administration of dexmedetomidine [KUUSELA et al., 2003]. The administration of alpha2-agonists may produce first and second degree atrioventricular (AV) blocks even in healthy animals [VAINIO and PALMU, 1989; PADDLEFORD and ERHARDT, 1992a]. Most alpha2-agonists, particularly xylazine, sensitize the myocardium for adrenaline induced arrhythmias [MUIR et al., 1975; TRANQUILLI et al., 1988; LEMKE and TRANQUILLI., 1994]. In contrast, dexmedetomidine is even considered to have a certain cardioprotective effect, as it has been shown in a trial that even a threefold increase of arrhythmia producing doses of adrenaline did not induce any arrhythmias in animals treated with dexmedetomidine [SAVOLA, 1989; HAYASHI et al., 1991].

Induction of anaesthesia

Propofol induces a dose dependent decrease in both arterial blood pressure and cardiac contractility. At clinically relevant doses, the decrease in blood pressure is caused by arterial and venous vasodilation and only to a lesser extent by reduced myocardial contractility [ILKIW et al., 1992; GELISSEN et al., 1996]. Venous and arterial vasodilation also decreases both preload and afterload [MUZI et al., 1992; LOWE et al., 1996]. In addition, propofol inhibits the activity of the sympathetic nerve system and reduces the response to the baroreceptor reflex [EBERT et al., 1992; EBERT and MUZI, 1994; SELLGREN et al., 1994].

The barbiturate thiopental sensitizes the myocardium to catecholamines, which may cause arrhythmias, even in patients with no heart disease. Thiopental reduces both cardiac output and blood pressure. Pronounced vasodilation may occur, particularly if administered fast [PLUMB, 2005]. The decrease in blood pressure leads to a reflex increase in heart rate, which in turn increases the oxygen consumption of the myocardium.

Etomidate does not induce any changes in heart rate or blood pressure, nor does it have any effect on the myocardium [NAGEL et al., 1979]. It is well suited for anaesthesia in patients with severe myocardial disease and cardiovascular instability [ROBERTSON, 1992]. Etomidate is available as a lipid emulsion preparation and in a formulation with propylene glycol as a solvent. At high doses, the etomidate preparation with propylene glycol may cause haemolysis. For that reason, it is preferable to use the lipid emulsion [KULKA et al., 1993; DOENICKE et al., 1997].

Alphaxalone is one of a group of steroid anaesthetics. When used at clinically relevant doses, alphaxalone has similar effects on the cardiovascular system as propofol [AMBROS et al., 2008]. In dogs, it induces a dose dependent decrease of arterial blood pressure and simultaneously an increase in heart rate so that the cardiac output is maintained [MUIR et al., 2008]. In the cat, it causes a dose-dependent decrease in heart rate, blood pressure and consequently in cardiac output [MUIR et al., 2009].

Maintenance of anaesthesia

All inhalation anaesthetics reduce the stroke volume by decreasing myocardial contractility [EGER, 1985; PAGEL et al., 1991; BOBAN et al., 1992; WARLTIER and PAGEL, 1992]. The strongest depression is caused by halothane [KLIDE, 1976; STEFFEY and HOWLAND, 1978, 1980; EGER, 1985]. At usual concentrations, isoflurane, sevoflurane and desflurane may maintain cardiac output at almost normal levels [WARLTIER and PAGEL, 1992; EGER, 1994; MALAN et al., 1995; STEFFEY et al., 2005]. Both vagal and preganglionic sympathetic activity is inhibited by inhalation anaesthetics, but vagal inhibition is more pronounced producing a slight increase in heart rate [PADDLEFORD and ERHARDT, 1992b]. While this increase is very small to non-existing in halothane anaesthesia, it is clearly present with isoflurane, sevoflurane und desflurane, as they possess stronger vasolytic activity [PICKER et al., 2001]. Inhalation anaesthetics produce a dose dependent decrease in blood pressure, which is based on the reduction of the stroke volume and on the vasodilatory effect of these drugs [STEFFEY and HOWLAND, 1977, 1978; MERIN et al., 1991; FRINK et al., 1992]. While the decrease in blood pressure caused by isoflurane, sevoflurane and desflurane is primarily based on the vasodilatory activity of the anaesthetic, halothane decreases blood pressure almost exclusively by reducing myocardial contractility and cardiac output [RIVENES et al., 2001].

Apart from inhalation anaesthetics, injectable anaesthetics (e.g. propofol or alphaxalone constant rate infusion) can be used for maintenance of anaesthesia. In terms of a balanced anaesthesia, fentanyl, ketamine or lidocaine can be administered by constant rate infusion to reduce the amount of the inhalation anaesthetic [MARTIN et al., 2001; PYPENDOP and ILKIW, 2005; VILLALBA et al., 2011].

In most cases, spontaneous breathing during anaesthesia means less stress for the cardiovascular system than forced mechanical ventilation. Forced ventilation may produce an increase in intrathoracic pressure followed by compression of venous vessels and reduction of venous return. Therefore, ventilation at low pressures (approx. 12 cmH2O) is recommended, which should only be initiated when there is a dramatic increase (>60 mmHg) of the end-tidal CO^2 ($ETCO^2$). However, patients with hypoxia or acidosis represent an exception: They should receive forced ventilation already at an end-tidal CO^2 of 45 mmHg or an oxygen saturation of less than 90 % [ERHARDT, 2004; CLUTTON, 2007].

Perianaesthetic monitoring

Perianaesthetic monitoring is of great importance, not only, but above all in patients with cardiovascular disease. The objective of close monitoring of the anaesthetized patient is to ensure optimum anaesthetic depth with a minimum of physiological alterations [HASKINS, 2007]. Evaluation of the anaesthetic depth can be done by clinical monitoring (e.g. palpebral reflex, position of the bulbus, muscle tone of the jaws), supported by additional instrument based monitoring. In the cardiac patient, instrument based monitoring is required in addition to the assessment of clinical parameters to evaluate cardiovascular function (pulse frequency, colour of mucous membranes, capillary refill time). Performing an ECG provides information on both heart rate and cardiac rhythm. As the induction phase of general anaesthesia is particularly challenging for the cardiovascular system, close monitoring of cardiac patients from the very beginning of this stage by performing an ECG is extremely important. Many anaesthetics cause a decrease in blood pressure. If this adds to existing disease related cardiovascular dysfunction, severe consequences may result. In some cases, a perianaesthetic increase in blood pressure may occur, which must immediately be diagnosed and treated. To monitor blood pressure, several invasive and non-invasive methods are available. The most precise results are obtained using the invasive technique (catheterization of a peripheral artery). Apart from exact blood pressure measuring, this technique offers the advantage of allowing sampling for arterial blood gas analysis. However, as with all invasive methods, the risk of potential infections should always be born in mind. It is therefore mandatory to perform catheterization of peripheral arteries under strictly aseptic conditions and

only in critically ill patients. For non-invasive blood pressure measuring, the oscillometric method and the Doppler ultrasound can be used. The so-called "High-Definition Oscillometry" HDO) provides results, which show a very high degree of concordance with results obtained by invasive methods. In contrast to the oscillometric method and the Doppler technique, HDO provides exact measurements even at low blood pressures (systolic blood pressure <60 mmHg). The Doppler technique is primarily used to evaluate blood flow, but can also measure blood pressure; it should be kept in mind, however, that in the anaesthetized patient it does not measure the systolic but the mean blood pressure [CAULKETT et al., 1998]. Capnography is a technique that measures the carbon dioxide concentrations in the exhaled air (ETCO2) and the respiratory frequency. Combined monitoring of respiratory frequency and heart rate together with the control of reflexes allows a good evaluation of the anaesthetic depth and helps identify apnoeic episodes. Measuring ETCO2 provides information on the ventilation (normocapnia or hypocapnia with hyperventilation and hypercapnia with hypoventilation, respectively). A decrease in ETCO2 is not only observed during hyperventilation, it also indicates that the transport of CO2 from the periphery to the alveoli is impaired due to a drop in blood pressure or a cardiac arrest. For that reason, it is of utmost importance to relate all results from instrument based monitoring to other diagnostic data obtained and to interpret them in connection with the clinical picture of the patient.
Pulse oximetry provides information on pulse frequency and oxygenation of the arterial blood. This technique helps identify pulse deficits (difference between the simultaneously counted heart rate [ECG] and the pulse rate) and hypoxaemia. Therefore, pulse oximetry does not only allow an evaluation of the cardiovascular system, but also of the respiratory system.
Another technique to monitor the cardiovascular system is measuring the central venous pressure (e.g. by means of a catheter introduced in the jugular vein). It provides information about the blood volume returning to the heart and the hearts' capacity to pump it into the arterial system. However, this method is only rarely used in veterinary medicine. There are several other methods to measure cardiac output (e.g. the thermodilution method using a cold thermal indicator; LiDCO technique), but these are rarely used in the routine clinical setting due to their invasiveness and high costs.

Emergency cardiac drugs

Anticholinergic drugs (e.g. atropine, glycopyrrolate) have a parasympatholytic effect, with parasympathetic inhibition of the cardiovascular and gastrointestinal system [LEMKE, 2007]. In perioperative medication, anticholinergics are primarily used for prevention or therapy of bradycardia. In many cases, administration of these drugs produces sinus tachycardia. As this results in increased myocardial work and decreased myocardial perfusion, parasympatholytics should be used with caution in cardiac patients. At clinically relevant doses (0.02–0.04 mg/kg IV/IM), atropine increases both heart rate by 30-40 % for about 30 minutes and atrial contractility [HENDRIX and ROBINSON, 1997]. At

Table 2: Receptor binding, mode of action and dosage guide for antihypotensive drugs

Drug	Receptor	Mode of action	Dose	Indication
Ephedrine	Alpha-1 Beta-1	Release of norepinephrine Vasoconstriction Positive chronotropy	0.03–0.1 mg/kg	Severe hypotension
Noradrenaline	Alpha-1	Vasoconstriction	0.01–0.05 µg/kg/min	Aortic or pulmonic stenosis Hypertrophic cardiomyo-pathy
Phenylephrine	Alpha-1	Vasoconstriction	1-3 µg/kg/min	Aortic or pulmonic stenosis Hypertrophic cardiomyo-pathy
Dopamine	Beta-1	ositive inotropy and chronotropy, Dose-dependent vasodilation	1-20 µg/kg/min	Valvular insufficiency PDilated cardiomyopathy
Dobutamine	Beta-1 Minor Alpha-1 and Beta-2	Positive inotropy and chronotropy	1-20 µg/kg/min	Valvular insufficiency Dilated cardiomyopathy

lower doses, a drop in heart rate and AV blocks might occur [KANTELIP et al., 1985; RICHARDS et al., 1989]. Glycopyrrolate has similar cardiovascular effects, which last about one hour. While in human patients, tachycardia caused by glycopyrrolate was less pronounced than that induced by atropine, this could not be confirmed by studies in animals [SHORT et al., 1974; RICHARDS et al., 1989]. At therapeutic doses (0.005–0.01 mg/kg IM/IV), an increase in heart rate and atrial contractility occur, while lower doses may also induce a drop in heart rate.
Sympathomimetics (see Table 2) have a stimulant effect on the sympathetic nervous system, leading to an increase in heart rate and blood pressure. Dopamine is a positive inotropic drug inducing an increase in heart rate. The effect on the vascular system is dose-dependent. While low doses (0.5–2 µg (micrograms) /kg) lead to vasodilation, intermediate dose levels (2–10 µg/kg) do not produce any vasomotor changes, but organ perfusion improves due to the positive inotropic effect [KELLY and SMITH, 1996; PLUMP, 2008]. High doses of dopamine (10–12 µg /kg) cause peripheral vasoconstriction leading to an increase in blood pressure [KELLY and SMITH, 1996; MARKS and ABBOTT, 1998]. Dobutamine has a positive inotropic and chronotropic effect. Increased myocardial contractility leads to an increase in cardiac output, which indirectly raises the blood pressure. Ephedrine indirectly stimulates the sympathetic nervous system due to the release of noradrenaline. Additional sympathomimetic properties are based upon the effect on α (alpha)- and β (beta)-receptors, which leads to positive inotropy and vasoconstriction. Due to the increase in blood pressure, reflex bradycardia occurs [WAGNER et al., 1993].
Adrenaline acts on both α- and β-adrenergic receptors. By stimulating the β1-receptors of the heart, it induces an increase in heart rate and contractility [LÖSCHER, 2003]. The effect on the vascular system is dose dependent. While low doses (< 1 µg/kg) cause a predominantly β-adrenergic stimulation leading to dilation, higher doses stimulate the α-receptors and induce vasoconstriction [LÖSCHER, 2003].
The local anaesthetic lidocaine is one of the Class IB antiarrhythmics (sodium channel blockers). Due to the lidocaine induced conduction slowing, it is often used to treat ventricular arrhythmias (e.g. premature ventricular contractions). As all antiarrhythmics of Class I, lidocaine has a negative inotropic and vasodilatatory effect [SCHÜTZ, 1998].
Beta-blockers (e.g. esmolol, atenolol, propranolol) are used for the treatment of tachycardia and hypertension, as they inhibit the effect of the endogenous catecholamines adrenaline and noradrenaline [SCHÜTZ, 1998].

Recovery phase

Duration of general anaesthesia and the stress it causes to the cardiovascular system should be as short as possible. The use of antagonisable or short-acting agents is recommended. If long-acting drugs are administered, lower doses should be used [CLUTTON, 2007]. Patients should be allowed to awake in a quiet room. Additional oxygen supply using e.g. an oxygen mask improves myocardial oxygenation during the recovery phase. However, some animals do not tolerate the mask and come under stress. In those cases, the produced stress for the patients' heart must be balanced against the advantages of additional oxygen supply. Depending on the size of the animal, an oxygen box can be used, if a mask is really unacceptable. Monitoring of cardiovascular parameters (pulse quality, capillary refill time; if necessary, blood pressure and ECG) and regular auscultation of heart and lungs should be continued during the recovery phase, as decompensation might occur and lead to fatal outcome. This has been proved by a study, which found out that 45–60 % of perioperative deaths occurred during the recovery phase after general anaesthesia [BRODBELT et al., 2008].

Cardiac disease in the dog

Mitral valve insufficiency

Mitral valve insufficiency is the most common cardiac disease in the dog accounting for 75–80 % of all cardiac disorders. Although it is typically found in older dogs, there is a certain breed predisposition in Papillons, Poodles, Chihuahuas, Dachshunds and Cavalier King Charles Spaniels [DAS and TASHJIAN, 1965; DETWEILER and PATTERSON, 1965; BUCHANAN, 1977; THRUSFIELD et al., 1985; THRUSFIELD, 1986; DARKE, 1987; HÄGGSTRÖM et al. 1992; BEARDOW and BUCHANAN, 1993; BUCHANAN, 1999; SISSON and KVART, 1999]. In the course of the disease, the left atrioventricular valve progressively thickens and degenerates in a way that correct closure of the valve becomes impossible. The functional consequence of this degenerative process is mitral valve regurgitation, where blood leaks back from the

ventricle into the left atrium. Depending on the degree of pathological alterations of valvular structures, the condition is classified as mild, moderate or severe mitral valve insufficiency. Clinical consequences depend on the extent of regurgitation and its sequelae. Mild mitral valve regurgitation does not cause any changes in heart function and size. Even with progressive regurgitation, the forward stroke volume is compensated by increasing the preload and occasionally by increasing the heart rate [HÄGGSTRÖM et al., 1996; LORD et al., 2003]. In fact, even patients with severe mitral valve insufficiency can survive several years [BRAUNWALD, 1997; SISSON and KVART, 1999]. However, pathological alterations like increase in cardiac size and hypercontractility develop and, in the later course of the disease, a slowly progressing decrease in myocardial contractility [URABE et al., 1992; SISSON and KVART, 1999; LORD et al. 2003]. Due to increased venous return and the related volume increase in the left atrium, the pulmonary veins get congested and pulmonary oedema develops. In larger dog breeds, the disease usually progresses faster and takes a more dramatic course [HÄGGSTRÖM et al., 2005]. The most common clinical signs, which do not become manifest until the valve insufficiency has reached its severe form, include coughing (compression of the mainstem bronchus due to volume increase in the left atrium), particularly in the second half of the night until early morning, as well as dyspnoea (pulmonary oedema due to increased pressure in the pulmonary veins). Weakness and reduced stamina may also be present as a consequence of the reduced left-ventricular ejection. In rare cases, secondary right heart failure may develop due to mitral valve insufficiency. Permanent pulmonary hypertension causes dilation and dysfunction of the right ventricle, leading to dilation of the tricuspid valve annulus and, as a consequence, to valvular insufficiency [SHIRAN and SAGIE, 2009]. Typical clinical signs of right heart failure are fluid accumulation in the thorax and ascites. The mild and moderate forms of mitral valve insufficiency hardly cause any clinical symptoms [ISACHC 1(-2)], see Table 3), and in most cases, coughing is the only sign [HÄGGSTRÖM et al., 2005].

Table 3: ISACHC classification (International Small Animal Cardiac Health Council): Classification of the degrees of severity of cardiac disease in small animals (FOX et al., 1999)

Class I Asymptomatic animals	
I A	No radiographical evidence of cardiomegaly
I B	Radiographical evidence of cardiac enlargement
Class II Mild to moderate cardiac insufficiency	
	Reduced exercise tolerance, mildly increased respiratory rate at rest, dyspneoa and coughing on physical exertion
Class III Severe cardiac insufficiency	
	dyspnoea and coughing at rest; frequent oedema

Anaesthesia in patients with mitral valve insufficiency

The exact degree of valve insufficiency should be assessed prior to anaesthesia. First signs of early decompensation are, apart from clinical symptoms like cough, radiological or sonographic evidence of congestion [HARVEY and ETTINGER, 2007; ENGELMANN, 2009]. In case of decompensated valvular disease, the afterload should be reduced administering ACE inhibitors and furosemide [PASCOE, 2005]. In addition, a calcium sensitizer (e.g. pimobendan) may be used to support inotropy [KANNO et al., 2007]. However, pimobendan should only be used in patients with marked clinical symptoms. While it reduces clinical signs in these patients, it may have negative morphological and functional effects in asymptomatic patients [LOMBARD et al., 2006; CHETBOUL et al., 2007]. Heart rate and blood pressure should be assessed already during preanaesthetic examination, in order to obtain reference values for intraoperative monitoring of these parameters [HARVEY and ETTINGER, 2007].
During anaesthesia, an increase of regurgitation must be avoided. Therefore, no centrally effective α2-agonists or massive infusion therapy should be given to avoid any increase in afterload [PASCOE, 2005; HARVEY and ETTINGER, 2007]. In these patients, a significant decrease in heart rate also leads to increased regurgitation as the increased ventricular filling enhances contractility [EVANS, 1992]. Any drugs, which induce an increase in vascular tone and, consequently, in afterload, like dopamine (in vasoconstrictive doses) and ephedrine, should also be avoided [PASCOE, 2005]. Reducing the systemic vascular resistance by administering very small doses of acepromazine as a premedication in order to reduce the afterload is beneficial, as it reduces regurgitation and increases cardiac output despite reduced contractility [PASCOE, 2005; HARVEY and ETTINGER, 2007]. Excessive vasodilation, however, causes a drop in blood pressure, which in most cases can hardly be compensated for by the patient. Opioids like methadone or butorphanol, in combination with

acepromazine, produce adequate sedation and, in addition, analgesia [CLUTTON, 2007]. As opioids, above all μ-agonists (e.g. methadone), can reduce the heart rate if administered at higher doses, an anticholinergic drug (like atropine or glycopyrrolate) should always be at hand when μ-agonists are used, in order to be prepared in case a drop in heart rate should occur [HARVEY and ETTINGER, 2007]. Whenever possible, induction of anaesthesia should be performed under complete monitoring and good preoxygenation. In severe cases, etomidate is a good choice as it has minimum cardiovascular side effects. In stable patients, low doses of ketamine can be used as an alternative, together with benzodiazepines or low doses of propofol [HARVEY and ETTINGER, 2007; FAYYAZ et al., 2009]. Negative inotropic drugs like propofol at high doses and thiopental can increase the regurgitation fraction in patients with severe valvular disease due to reduced forward propulsion of the blood and should therefore be used with caution [PASCOE, 2005].

To maintain anaesthesia, inhalation anaesthetics can be used at concentrations that should be as low as possible. Another possibility is a partial or total intravenous anaesthesia using propofol, fentanyl or ketamine combinations (subanaesthetic doses) [PASCOE, 2005]. Table 4 summarises dose suggestions for the mentioned drugs for premedication, induction and maintenance of general anaesthesia. In case hypotension and bradycardia should occur, these can be treated by administration of anticholinergics. In doing so, the target heart rate should lie within the preanaesthetic range or slightly above [DAY, 2002]. Should hypotension not be accompanied by bradycardia and not return to normal levels after reducing the concentration of the inhalant, positive inotropic drugs like dobutamine should preferably be administered [PASCOE, 2005]. The most important properties and dosages of antihypotensive drugs are listed in Table 2.

Table 4: Anaesthesia protocols for dogs with cardiac disease

Drugs	Indication	Dosage	Comments
Premedication*			
Acepromazine	Valvular insufficiency, DCM	5–20 μg/kg	
Butorphanol	All cardiac conditions	0.1-0.4 mg/kg	Visceral analgesia
Methadone	All cardiac conditions	0.1-0.4 mg/kg	Good somatic analgesia
Midazolam	All cardiac conditions	0.1-0.5 mg/kg	Warning: paradoxical reactions in generally healthy patients
Induction			
Propofol	Mild valvular insufficiency, mild DCM	2-6 mg/kg	Respiratory depression, hypotension Long maintenance of pharyngeal reflex
Etomidate	All cardiac conditions	1-2 mg/kg	Not to be used with adrenal disease Good somatic analgesia
Alphaxalone	Mild valvular insufficiency, DCM	1-2 mg/kg	Possibly hypotension and respiratory depression
Ketamine	Valvular insufficiency	1-5 mg/kg	Combination with benzodiazepines or low-dosed propofol possible
Maintenance**			
Isoflurane/ Sevoflurane	All cardiac conditions		Concentration depending on chosen anaesthetic/ analgesic; vasodilation, hypotension; keep doses low Not to be used with adrenal disease Good somatic analgesia
Propofol (CRI)	All cardiac conditions	6–12 mg/kg/h	Possibly respiratory depression
Fentanyl (CRI)	All cardiac conditions	10-20 μg/kg/h	Possibly respiratory depression and bradycardia, somatic analgesia
Ketamine (CRI)	All cardiac conditions	0.3-0.6 mg/kg/h	Analgetic dose

*Combinations with premedication in same doses possible (except methadone with butorphanol), **Combinations can be freely chosen

Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is the most frequently diagnosed myocardial condition in dogs (SISSON et al., 1999). Dilated cardiomyopathy is characterized by cardiomegaly and reduced systolic function of one or both ventricles [RICHARDSON et al., 1996]. Particularly medium-sized to large canine breeds are affected by DCM. With certain regional differences, the condition is most frequently diagnosed in Doberman Pinschers, Irish Wolfhounds, Great Danes, Cocker Spaniels, Airedale Terriers, Newfoundlands, Boxers, English Cocker Spaniels, Portuguese Water Dogs and Dalmatians [HARPSTER, 1983; MONNET et al., 1995; FREEMAN et al., 1996; TIDHOLM and JÖNSSON, 1997; SISSON et al., 2000]. With the exception of the Portuguese Water Dog, cardiac symptoms do not become manifest until the dogs have reached adulthood [SLEEPER et al., 2002]. DCM takes a progressive course with gradually increasing exercise intolerance and reduction of body mass [DAMBACH et al., 1999]. Due to myocardial insufficiency and the resulting systolic dysfunction, emptying of the chamber is incomplete. Filling of the ventricle during diastole produces an increased end-diastolic pressure, which leads to dilatation of the ventricle. In the further course of the disease, ventricular dilation causes geometric distortion of the atrioventricular valve apparatus, leading to insufficiency and atrial dilation [MEURS, 2005]. Clinical signs of DCM-related congestive heart failure are primarily due to the left heart failure and include coughing, dyspnoea and tachypnoea [CALVERT et al., 1982; CALVERT, 1986]. Only occasionally, ascites is observed as a symptom of right heart failure.

Anaesthesia in patients with dilated cardiomyopathy

In all dogs with DCM, just as in dogs with valvular insufficiency, the degree of severity of the condition should be assessed prior to anaesthesia. As sinus tachycardia, atrial fibrillation or ventricular tachyarrhythmias are to be expected in the late form of dilated cardiomyopathy, it is recommended to perform not only a radiographic and sonographic examination, but also an electrocardiographic examination and blood pressure measurement in order to identify and evaluate the haemodynamic effects of the cardiac disease [MEURS, 2005]. In patients with retrograde congestion in the pulmonary and systemic circulation, vasodilatory support with loop diuretics and ACE inhibitors is also indicated. As inotropy is particularly compromised in patients with DCM, inotropic therapy using pimobendan represents a cornerstone of preanaesthetic stabilization [FUENTES et al., 2002]. If supraventricular tachycardia occurs, therapy can be complemented by administration of digoxin or beta-blockers [ABBAH et al., 1994; GILBERT et al., 1999; ATKINS, 2007]. For premature ventricular contractions, Class IB antiarrhythmics (e.g. mexiletine) are recommended [OPIE et al., 2009]. For the anaesthesia protocol, the same principles apply as for valvular insufficiency. However, with DCM, it is even more important to avoid negative inotropy. Mild vasodilation reduces the afterload and increases contraction effectivity [PASCOE, 2005]. Eligible drugs for induction of anaesthesia are etomidate and alphaxalone [HARVEY and ETTINGER, 2007]. Perioperative monitoring using ECG and blood pressure measurement is indispensable for patients suffering from dilated cardiomyopathy. In patients with advanced disease, invasive blood pressure measurement is recommended [SKARDA et al., 1995b]. Should this not be possible, non-invasive methods like oscillometry or Doppler technique should be used. For emergencies in DCM patients, lidocaine and esmolol for treatment of ventricular and supraventricular tachyarrhythmias should be kept at hand apart from glycopyrrolate for treating bradycardia.

Aortic stenosis

Depending on the site of stenosis, there are three types of aortic stenosis: subvalvular, valvular and supravalvular. In the vast majority of dogs, the aortic stenosis is located in the subvalvular region [ETTINGER and SUTER, 1970]. Breeds like Newfoundland, Golden Retriever, German Shepherd, Boxer, Bouvier, Rottweiler and Bull Terrier are predisposed to aortic stenosis [PATTERSON, 1968; ETTINGER and SUTER, 1970; O´GRADY et al., 1989; TIDHOLM and JÖNSSON, 1997]. As a consequence of the increased myocardial strain caused by the outflow obstruction during systole, symmetrical left ventricular hypertrophy develops [ETTINGER and SUTER, 1970; PYLE et al., 1976; BRAUNWALD, 1988; FRIEDMAN, 1988]. Due to the concentric hypertrophy, myocardial ischaemia occurs leading to ventricular arrhythmias [SCHWARTZ et al., 1969; PYLE et al., 1976; BORKON et al., 1982; BRAUNWALD, 1988; FRIEDMAN, 1988]. In the healthy heart, physical strain reduces the arterial tone and increases the stroke volume. However, with aortic stenosis, this physiological reaction is possible to only a limited extent, as the increase in stroke volume is limited by the obstruction of the left ventricular

outflow tract [HOSSACK, 1987; FRIEDMAN, 1988]. Cardiac output, which depends on both stroke volume and heart rate, becomes increasingly dependent on the heart rate only, as volume capacity and ventricular elasticity are reduced. As the diseased heart is not able to increase the stroke volume, weakness (reduced oxygen supply to the muscles), syncope (reduced oxygen supply to the brain) and/or ventricular arrhythmias (myocardial hypoxia) develop [SCHWARTZ et al., 1969; PYLE, 1983; BRAUNWALD, 1988; FRIEDMAN, 1988]. In rare cases only there are signs of a gradual development of congestive heart failure. Pulmonary oedema only develops if simultaneous mitral valve insufficiency or an extremely severe form of aortic stenosis is present [BRAUNWALD, 1988; O´GRADY et al., 1989].

Anaesthesia in patients with aortic stenosis

Taking into account that patients with aortic stenosis are not able to compensate for cardiovascular alterations, it is important to keep any influences on the cardiovascular parameters to a minimum. Bradycardia reduces cardiac output, because it is impossible to increase the stroke volume. Tachycardia increases the myocardial oxygen consumption reducing at the same time coronary perfusion. Vasodilatory drugs (e.g. acepromazine) should be avoided as the organ tries to counteract hypotension by tachycardia [PASCOE, 2005]. Positive inotropic drugs should not be used either, because the increased contractility would only worsen the outflow obstruction [BUBENHEIMER, 2007].

Premedication with a benzodiazepine and an opioid seems to be a promising option for patients affected by aortic stenosis, as they only have little effect on inotropy and vascular tone. Induction and maintenance of general anaesthesia should, whenever possible, only have a minimum negative inotropic effect. For this reason, it is recommended to use etomidate to induce anaesthesia. For maintenance of anaesthesia, an opioid (e.g. fentanyl) administered as a constant rate infusion may be used in combination with an inhalant (at the lowest possible concentration) or with a constant rate infusion of propofol. In hypotensive patients, α_1-agonists (with vasoconstrictive effect) like phenylephrine should be preferred to positive inotropic or chronotropic drugs (dopamine, dobutamine) [CLUTTON, 2007].

Pulmonic stenosis

Also this form of vascular stenosis can be located either in the subvalvular, valvular or supravalvular region. The most common form in the dog is valvular stenosis [TRAUTVETTER et al., 2007]. The condition is frequently diagnosed in Beagles, Samoyeds, Chihuahuas, English Bulldogs, Miniature Schnauzers, Labrador Retrievers, Mastiffs, Chow Chows, Newfoundlands, Boxers, Basset Hounds, Fox Terriers, West Highland White Terrier and other Terrier and Cocker breeds [STAFFORD JOHNSON and MARTIN, 2004; WARE, 2006; TRAUTVETTER et al., 2007]. As a consequence of the pulmonic stenosis, concentric right ventricular hypertrophy develops. Hypertrophy of the myocardium leads to hypoperfusion with hypoxia and ventricular arrhythmias. Due to the outflow obstruction, the filling pressure in the right ventricle increases, leading to tricuspid valve regurgitation and, as a consequence, to right heart failure [KITTLESON and KIENLE, 1998; STAFFORD JOHNSON and MARTIN, 2004]. Most dogs suffering from pulmonic stenosis do not show any clinical signs of disease (WARE, 2006). In about 35 % of dogs with severe pulmonic stenosis, exercise intolerance, syncopes or ascites may be observed [GORDON et al., 2002].

Anaesthesia in patients with pulmonic stenosis

Perianaesthetic management of patients with pulmonic stenosis is the same is with aortic stenosis. Also in these patients, tachycardia may increase myocardial oxygen consumption without increasing the pulmonary arterial pressure. Appropriate premedication should therefore provide good sedation without inducing an increase in heart rate. In most cases, this is only possible using opioids [PASCOE, 2005]. For induction of general anaesthesia, etomidate is particularly suitable, perhaps together with simultaneous administration of a benzodiazepine. For maintenance of general anaesthesia, the dose of the inhalation anaesthetic should be reduced as much as possible by providing a partial intravenous anaesthesia using a constant rate infusion of an opioid [PASCOE, 2005].

Cardiac disease in the cat

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most frequently diagnosed cardiac disease in cats. A breed predisposition for the primary form has been reported for Maine Coons, Persians, British Shorthairs, Norwegian Forest Cats, Ragdolls, Turkish Vans and Scottish Folds [KITTLESON, 2005]. With the secondary form of the

condition, concentric hypertrophy develops due to increased myocardial strain caused by aortic stenosis, systemic hypertension or hyperthyroidism [KITTLESON, 2005]. The disease causes mild to severe thickening of the ventricular myocardium, above all in the region of the free wall of the left ventricle, reducing diastolic filling capacity. Hypertrophy of the chamber musculature leads to insufficient blood supply of the myocardium and, as a consequence, to ischaemia, hypoxia, myocardial necrosis and fibrosis. The circulatory system tries to maintain cardiac output, leading to a compensatory increase in heart rate. In the more advanced stages of hypertrophic cardiomyopathy, the left atrium becomes increasingly dilated. Due to the resultant blood stasis in the atrium, thrombi may form and be flushed into the blood stream. Increased intraventricular pressure and reduced filling volume of the ventricle lead to chronic heart failure with pulmonary oedema and/or fluid accumulation in the thorax. Many cats with hypertrophic cardiomyopathy also suffer from compensatory tachycardia. Due to that increase in heart rate, diastolic dysfunction is further aggravated due to diastolic shortening.

Anaesthesia in patients with hypertrophic cardiomyopathy

When performing a preanaesthetic examination of cats with HCM, a Hyperthyroidism or chronic kidney disease should be ruled out and, if present, be treated prior to surgery. Therefore, blood pressure measurement is mandatory, because in the primary form of the condition hypotension is predominantly present, while the secondary form of hypertrophic cardiomyopathy is characterized by hypertension. In addition, sonographic and radiographic examinations should be performed to identify possible pulmonary congestion. As diastolic dysfunction typically occurs with the condition, tachycardia should be identified as soon as possible and, if present, be treated with beta-blockers, as any increase in heart rate inevitably leads to elevated myocardial oxygen consumption and reduced perfusion of the coronary arteries during diastole [BEDNARSKI, 1992]. Drugs, which reduce the preload by inducing vasodilation (e.g. acepromazine), should be avoided. In contrast, centrally effective α2-agonists administered at low doses may increase the preload by inducing vasoconstriction, thus enhancing diastolic filling of the heart [PASCOE,

Table 5: Anaesthesia protocols for cats with hypertrophic cardiomyopathy

Drugs	Dosage	Comments
Premedication*		
Butorphanol	0.1-0.4 mg/kg	Visceral analgesia
Methadone	0.1-0.4 mg/kg	Good somatic analgesia
Midazolam	0.1-0.5 mg/kg	Warning: paradoxical reactions in generally healthy patients
Medetomidine	1-20 µg/kg	Increases vascular tone, decreases heart rate
Dexmedetomidine	0.5-10 µg/kg	Increases vascular tone, decreases heart rate
Induction		
Propofol	2-6 mg/kg	Respiratory depression, hypotension
Etomidate	1-2 mg/kg	Pharyngeal reflex is maintained, first-choice drug
Alphaxalone	1-4 mg/kg	Possibly hypotension, dose-dependent respiratory depression
Maintenance**		
Isoflurane/ Sevoflurane		Concentration depending on chosen anaesthetic/analgesic; vasodilation, hypotension
Fentanyl (CRI)	10-20 mg/kg/h	Possibly respiratory depression and bradycardia, good somatic analgesia
Propofol (CRI)	6-12 mg/kg/h	Respiratory depression

*Combinations with premedication in same doses possible (except methadone with butorphanol), **Combinations can be freely chosen

2005]. Positive inotropic drugs should be avoided due to the risk of outflow obstruction caused by increased contractility of the hypertrophic myocardium. This might also occur when reducing the afterload. For that reason, all should be done to maintain the afterload at physiological levels or to slightly increase it. Table 5 contains a list of drugs suitable for premedication, together with recommended dosages.
The ideal drug for induction of general anaesthesia in cats with hypertrophic cardiomyopathy is etomidate. Propofol at low doses may be used as an alternative. Thiopental and ketamine should, if possible, not be used due to their arrhythmogenic and positive inotropic effect; in addition, they would induce an increase in heart rate. Inhalation anaesthetics are well suited for maintenance of anaesthesia in patients with HCM as they provide myocardial depression [POLIAC et al., 2006].
In case hypotension should occur, an α1-agonist like phenylephrine or noradrenaline can be given to produce vasoconstriction[(PASCOE, 2005].

Conclusion

Before performing surgery under general anaesthesia in cardiac patients, the type of disease must be identified and the degree of compensation assessed. In decompensated cardiac disease, the anaesthetic risk can be reduced by providing specific medical therapy prior to anaesthesia.
The entire perianaesthetic period should be as stress free as possible for the patient. Establishing a venous line, intubating the patient and supplying oxygen are indispensable measures to be taken before performing anaesthesia in cardiac patients. For most animals with cardiac disease, premedication with an opioid and, where indicated, with a benzodiazepine, and induction of anaesthesia with etomidate are a good option. Monitoring of anaesthesia should include clinical monitoring, ECG, blood pressure measurement, capnography and pulse oxymetry. Emergency drugs should be at hand at all times in case any complications should present.

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COMMISSIONED PAPER (CZ)

A practical approach to Anaesthesia in Reptiles

Zdenek Knotek[1 2]

SUMMARY

Various combinations of anaesthetics have been recommended for surgical procedures in reptiles. The challenging categories of reptilian patients include – reptiles suffering from dehydration, anaemia or hypoglycaemia, reptiles with ascites, patients suffering from gastrointestinal tympany and metabolic bone disease. The minimum diagnostic testing includes packed cell volume, complete blood count, total protein, phosphorus and uric acid concentrations. Preoperative fasting is recommended in all cases of reptile anaesthesia if the surgery is performed as emergency procedure. The combination of ketamine with benzodiazepines results in smooth induction and recovery with muscle relaxation and analgesia. The effects of propofol and alphaxalone in reptiles can be seen within one minute, producing short-term anaesthesia for about 20 minutes. Intravenous administration of alphaxalone in small reptiles is easier than with propofol. Inhalant anaesthesia with isoflurane or sevoflurane is preferred to injections because of easy control of anaesthetic depth and rapid recovery. During the recovery period it is essential to keep reptiles in their preferred optimum temperature zone. All fluids have to be warmed prior to administration – to have the similar temperature like the body of the patient 30 – 35°C.

Key Words: Reptiles, monitoring, propofol, alphaxalone, inhalant anaesthesia

This paper was commissioned by FECAVA for EJCAP.

Introduction

In modern reptilian medicine, the need for an improved quality of anaesthesia and analgesia is evident. Safe anaesthesia of long duration is still important, despite the dynamic development of minimally invasive surgical techniques. Some of the hidden problems (metabolic diseases) have a strong influence on the quality and safety of the anaesthesia. Therefore all reptiles before anaesthesia induction should be examined physically (Fig. 1) and blood profile examination and radiographs must be performed. The challenging (critical)

Fig. 1 Pale mucosa in lizard suspected to have chronic renal failure (CRF).

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categories of reptilian patients include – reptiles suffering from dehydration, patients with anaemia, hypoglycaemia, females with a high number of eggs or foetuses, reptiles with ascites, patients suffering from gastrointestinal tympany and metabolic bone disease.

Preanaesthetic assessment

The minimum diagnostic testing required includes packed cell volume, complete blood count, total protein, phosphorus and uric acid concentrations. It is also recommended to stimulate the urination reflex of the reptile patient by gently massaging the cloacal mucosa (the urinary bladder of some reptiles has a very high capacity and would be extremely distended by urine).Some authors have suggested that pre-anaesthetic fasting is not necessary for most reptiles[1-2], but I strongly recommend fasting for reptilian patients. Preoperative fasting is recommended in all cases of reptile anaesthesia if the surgery is not performed as an emergency procedure. The minimal fasting period for big carnivorous reptiles (crocodiles, aquatic turtles, monitor lizards, boid snakes and pythons) is two to four days. I recommend the minimal fasting period for herbivorous reptiles to be four days. Please do not forget to ask the reptilian owner about the time of the last feeding (force feeding)! The gastrointestinal tract (especially the stomach) of small lizards (chameleons, geckoes, anoles, basilisks) would be very full with invertebrates! In herbivorous tortoises when the colon is full with faeces it would be a large heavy organ that could be responsible for lung depression during prolonged surgery.

Anaesthetics

Various combinations of anaesthetics with analgesics have been recommended for surgical procedures in reptiles[1-11]. Intramuscular or subcutaneous injections are preferentially administered into the cranial part of the reptilian body (front legs of chelonians and lizards, the first third (cranial) of the snake body). There should theoretically be some differences in the pharmacokinetic processes when comparing intramuscular with subcutaneous administration of anaesthetics, but it is without any significant effect in clinical practice with reptiles. Compared with birds and small mammals vascular access is more difficult to perform in reptiles. The palatine vein should be very gently catheterized in large snakes, but any trauma of the mouth cavity mucosa in snakes would be followed by inflammation and infection (stomatitis caused with Aeromonas sp., Pseudomonas sp.). Intracardiac injection has been described for administration of parenteral anaesthetics in snakes, but it is associated with the risk of the trauma to the heart[2]. The ventral coccygeal vein is the site of choice for intravenous drug administration in snakes, lizards and small crocodiles[1,3-5,7,12]. The subcarapacial plexus is the optimal site for intravenous injections in chelonians (jugular or dorsal coccygeal veins are easy to be catheterized in large tortoises, but it is not easy to use them for intravenous administration in medium to small turtles and terrapins)[10]. Intraosseous catheterization of long bones (humerus, tibia, femur) has been described in turtles and lizards[2,13,14]. It is recommended to use the local anaesthesia (lidocaine infiltration of the cannulation site).[4,13] The correct and easy placement of the catheter depends on the needle quality and the bone structure. In large lizards the cannulation of the bone is not easy, and general anaesthesia with radiography to ensure the correct placement of the catheter is therefore recommended. Intraosseous catheterization of the bony bridge between the carapace and plastron of tortoises has also been described[2], but another author has been unsuccessful with this method[6,7]. The limited intramedullary space of the bridge was responsible for the problem and fluid infusion ran directly into the coelom. It is possible that another part of the chelonian shell bone would be more suitable for catheterization. Recently, different vascular access points for fluid therapy in tortoises have been investigated. The feasibility of the use of catheter placement into the bony bridge between the carapace and plastron or gular scute was controlled with a gamma camera after administration of a radioisotope. None of the bone sites (bony bridge between the carapace and plastron, gular scute, femur or humerus) distributed the fluid as efficiently as the jugular site[15].

Ketamine, tiletamine

Dissociative anaesthetics ketamine and tiletamine are characterized by the reduction of impulse transmissions and with a limited capacity of inducing visceral analgesia in reptiles.[16] Ketamine produces hypertension and can cause tachycardia, bradypnoea and hypoventilation. [1,2,4,7,9,17,18] Repeated administration is not recommended, because it results in accumulation and a risk of overdosing. Ketamine and tiletamine are not appropriate for use as stand-alone analgetics in painful surgeries. These agents used alone at high dosages, are associated with cardiopulmonary depression, prolonged recovery time and

poor muscle relaxation. Ketamine or tiletamine-zolazepam would not be used in reptiles suffering from severe renal or liver failure.[11,19] The combination of ketamine with benzodiazepines and propofol results in a smooth induction and recovery with good muscle relaxation and analgesia. Semi-aquatic terrapins are very resistant to the ketamine or tiletamine-zolazepam activity.[20] High doses of tiletamine-zolazepam will produce variable sedation in red-eared terrapins and it is therefore the author´s recommendation to only use tiletamine-zolazepam in this species for the induction of anaesthesia (with low doses).[8,19] Xylazine or medetomidine alone produces minimal sedation. However in combination with dissociative anaesthetics (ketamine), they produce very good chemical immobilization.[1,2,20,21] By combining it with xylazine, the dosage of ketamine is reduced. The important advantage of using α-2 adrenergic agonists for anaesthesia is the possibility to reverse their effect with the antagonist (atipamezole). This reduces the recovery time. The combination of medetomidine with ketamine (and atipamezole for rapid reversal) is a feasible method for anaesthesia in large lizards.

Propofol

When administered properly (intravenously), the effect of propofol in reptiles can be seen within one minute, producing a short duration anaesthesia of about 20 minutes.[4,7,13,14, 22] Propofol is rapidly metabolized, but it is a poor analgesic. Reptiles show a marked change in the respiratory frequency that is not accompanied by any significant change in Sp02. The duration and severity of respiratory depression (apnoea) depends on the dose. Although dosages in reptiles of 10 to 15 mg/kg have been reported, it is the author´s opinion (which is in accordance with other colleagues) that dosage 5 mg/kg may be enough to allow for intubation in many reptilian species.[7,22,23] Low doses (1-5 mg/kg) are safe, without any negative influence on the respiration. Nevertheless it is recommended to use propofol very carefully in reptiles suffering from chronic heart diseases and/or respiratory diseases. Propofol induces central nervous system depression.

Alphaxanole

The combination of steroids alphaxalone (3α-hydroxy-5α pregnane-11, 20-dione) with alphadolone (21-acetoxy-3α-hydroxy-5α pregnane-11, 20-dione) has been used for anaesthesia in many reptiles, with good results in snakes, chelonians and lizards.[24] This combination is not available on the European veterinary market, but alphaxalone alone is available for use in reptiles as Alfaxan (Vétoquinol, France).[2,25] The main advantage of the steroid anaesthetic alphaxalone in reptiles is its short duration of effect. If administered intravenously, the effect of alphaxalone begins within one minute. Short-term anaesthesia is maintained for about 20 minutes. Propofol and alphaxalone are not painful for reptiles and perivascular injections are not associated with tissue necrosis. The manipulation with alphaxalone is very easy (it would be stored within the room temperature). The fact that alphaxalone is a clear fluid makes the intravenous administration of this drug easier than propofol, especially in very small reptiles. No adverse reaction or side effects have been documented in reptiles after alphaxalone anaesthesia. Alphaxalone has become the author´s most popular choice for induction of all reptilian species, when intravenous access can be obtained.

Inhalation anaesthesia

Inhalation anaesthesia is preferred to injections because of easy control of anaesthetic depth and rapid recovery.[4,7,8,9,10,23,26] However inhalant anaesthesia is not the method of choice for induction of anaesthesia. The existence of air sacs in snakes and some groups of lizards accounts for the observation that reptiles remain anaesthetised even during a prolonged period of apnoea. Tidal volume, oxygen requirement, CO2 elimination, respiratory rate and body temperature must all be maintained under anaesthesia. Inhalation anaesthesia in reptiles is performed by the use of simple machines (Fig. 2 - 4). The breathing system for a majority of reptile patients is non-rebreathing. The optimal 02 rates for reptiles lie from 200 to 1.000 ml/min, depending on the size and species of reptile. Masks for inhalant anaesthesia of medium to large reptiles are constructed from syringes and plastic bottles. Masks for very small reptiles can be constructed from a piece (finger part) of gloves. Good quality endotracheal tubes and a system free from leaks are essential. Small endotracheal tubes are constructed from over-the needle catheters. Many anaesthetic agents depress respiration in reptiles and this can lead to the production of hypercapnia, hypoxia and acidosis. To maintain blood carbon dioxide and oxygen concentrations within normal levels, it is often necessary to assist ventilation. Inspiration and expiration have to be regulated by the veterinarian (manually) or with

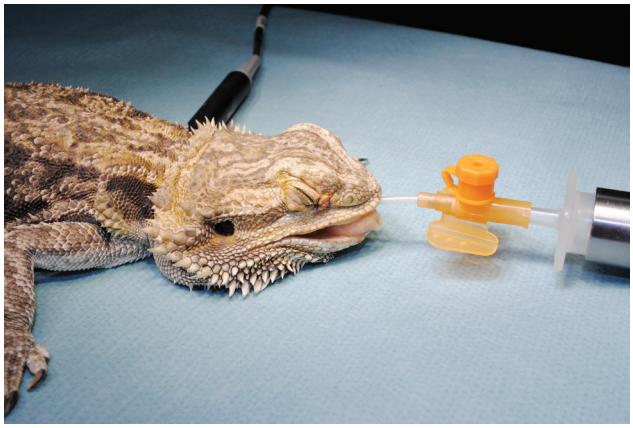

Fig. 2 Bearded dragon. Recovery period.

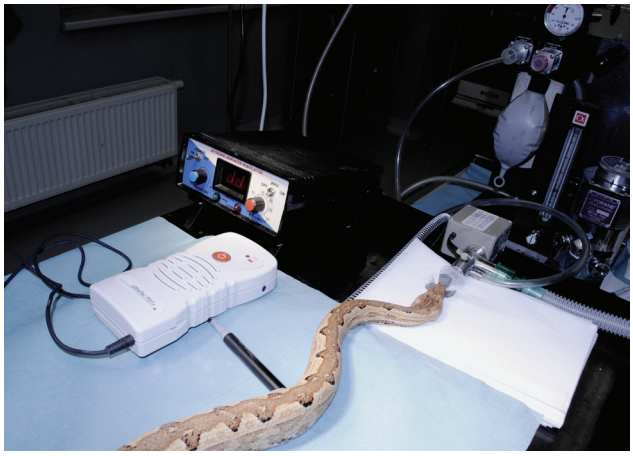

Fig. 4 Boa constrictor – snake connected to small animal ventilator. Heart frequency controlled with Doppler pencil probe.

Fig. 3 Green iguana – monitoring the vital functions by BAS Vital Scan monitor (Vetronic, UK).

special ventilators. Using a ventilator will often be more convenient than manually assisting ventilation. There are basically two ways in which gas can be delivered during inspiration. The ventilator may deliver gas at a set pressure pattern, but another type of ventilator may be set to produce a fixed flow pattern. In selecting a ventilator for use in reptiles, the most important factor to be considered is the ability to ventilate a wide range of patients. Volume cycled ventilators should generally be avoided for small reptiles because the margin of error in volume delivery is very small. Pressure cycling ventilators are therefore better suited to these patients. Most patients require a ventilation pressure of between 5 and 12 cm water pressure. The minute volume is calculated on a very basic principle (minute volume = 10 ml/kg tidal volume x breaths per minute). Fresh gas flow is recommended to be 3 x minute volume (inspiration to expiratory ratio is assumed to be 1:2). An excellent piece of equipment for inhalant anaesthesia in reptiles is the Small Animal Ventilator (SAV 03, Vetronics, UK, (Fig. 5 - 8). This ventilator has been used for exotic anaesthesia since 1994. It has been designed to perform the repetitive task of intermittent positive pressure ventilation (IPPV). It enables careful control and monitoring of intra-airway pressure and ventilation rate. [23] The SAV machine is used as a classical T-piece system, with the IPPV switch off until IPPV is required.

Anaesthetic induction of reptiles with mask has been published by number of authors and therefore seems to be a very easy procedure. Large reptiles like green iguanas could stop breathing for more than 20 minutes after a mask with isoflurane is attached to the head. [27] The most difficult and dangerous procedure for the staff is the mask induction in large and aggressive aquatic chelonians or crocodiles. Similar problems appear with the induction-chamber method. The best and safest method of anaesthesia induction is the use of parenteral administration of drugs like propofol, alphaxalone or tiletamine-zolazepam (in a very low dose).[7,8,11,17,19,23]

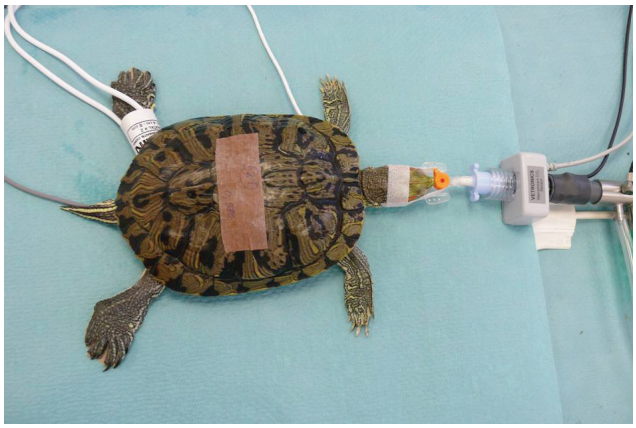

Fig. 5 Red-eared terrapin – monitoring the vital functions by BAS monitor (Vetronic, UK).

Fig. 6 Soft shell turtle – monitoring heart frequency during the recovery period.

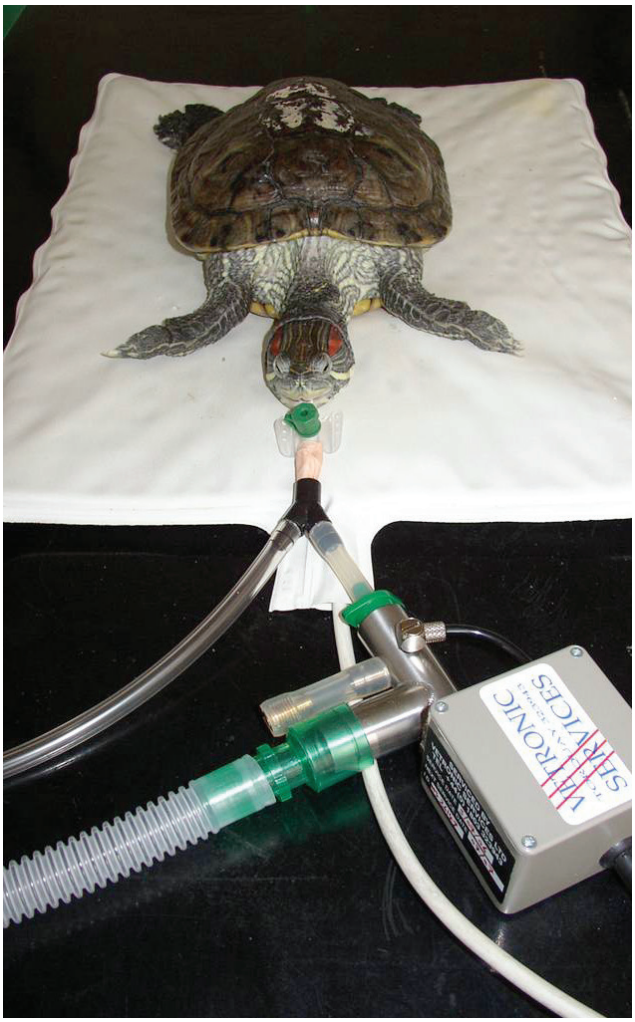

Fig. 7 Red-eared terrapin connected to small animal ventilator (SAV).

Intubation is very easy in snakes, but it is a difficult step of the inhalant anaesthesia in some species of lizards and chelonians. Special approach has to be used for intubation of crocodiles (Fig. 9) and small chameleons. It is not only the presence of a large tongue in the mouth cavity, but the shape of the cranial part of the trachea that makes the intubation of small chameleons rather difficult.

Isoflurane, sevoflurane

The inhalant anaesthetics of choice for reptiles are isoflurane and sevoflurane.[1,3,4,6,28] Both of these inhalant agents produce a dose dependent cardiopulmonary depression (decrease of the blood pressure).[4,29] Isoflurane delivered at 2.5 – 3% results in sustained depression of blood pressure in lizards and it is reported that only some of the adrenergic agonists used in veterinary anaesthesia (norepinephrine at 0.3-0.5 µg/kg/min) can significantly increase blood pressure

Fig. 8 Young crocodile – inhalant anaesthesia with isoflurane.

in hypotensive reptiles.[30] Minimum anaesthetic concentration (MAC) in reptiles is defined as the anaesthetic concentration that produces immobility in 50 % of anaesthetized animals. Maintenance of surgical anaesthesia requires vaporizer settings that are approximately 25 % higher than MAC. Premedication

Fig. 9 Tracheal tube insertion in a crocodile under alphaxalone anaesthesia.

with opioids and the use of parenteral anaesthetics for induction decrease MAC in reptiles. The cardiopulmonary effects of butorphanol-isoflurane and butorphanol-sevoflurane anaesthesia is similar, however the quality and speed of induction and recovery was significantly shorter with sevoflurane when compared to isoflurane in green iguanas.[31]

Monitoring

Assessing anaesthetic depth in reptiles is challenging. The assessment of the depth of chemical drug desensitisation in reptiles is based on evaluation of the righting reflex, and the control of head, neck, and frontal body lifting reflexes.[1-3,7,8] In terrapins, the disappearance of the reflex of hiding the head, neck, and legs in the carapace upon touch is an evidence of good immobilization, but it is the absence of a corneal reflex that indicates deep anaesthesia.[10] The neck and legs can be easily pulled out even under light anaesthesia. Heart rates and blood SpO2 parameters, in particular, are commonly used for monitoring anaesthesia and analgesia in reptiles in clinical practice.[32] Monitoring SpO2 in small reptiles is challenging due to the low pulse volume and difficulty in probe placement. A tape would be used for marking the position of the heart in snake and for monitoring its activity.[2] A Doppler flow monitor can be used to assist control of the heart function – the pencil probe is ideal for the majority of small reptiles[2].

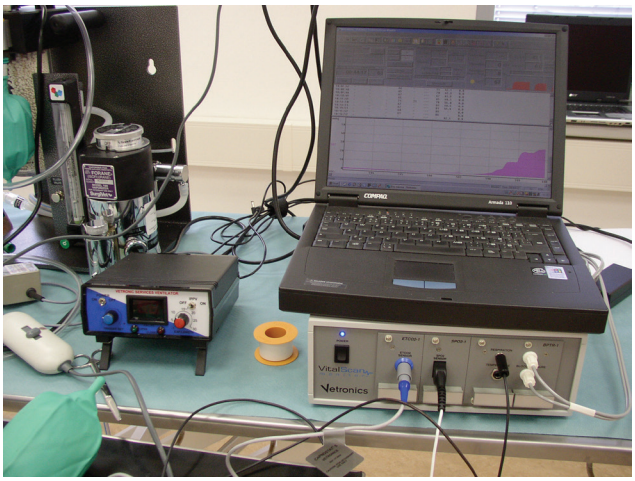

Fig. 10 BAS Vital Scan monitor connected with laptop.

In comparison with mammals the anatomy of reptiles makes continuous monitoring of respiratory and heart rates, ECG parameters, tissue oxygen saturation and the CO2 concentration in the expired gasses (ETCO2), blood pressure and body temperature rather difficult. Continuous monitoring of these functions is possible in medium to large reptiles with the use of BAS monitor (Vetronic, UK, Fig. 3, 10).[2] Recently, an implanted direct blood pressure transducer and a non-invasive oscillometric unit were compared in a group of adult green iguanas.[29] Blood pressure was measured non-invasively with a cuff over the left femoral region of iguana while the catheter tip of the blood pressure transducer was placed in the aortic arch of lizards. The oscillometric device failed to provide a reading in over 80 % of the attempts and it provided measurements that did not consistently correlate with the direct measurements[29]. However it is not clear if the oscillometric device was unreliable or the problem resulted from the wrong system used.

Low metabolic activity and relatively very low oxygen rate

Fig. 11 Young crocodile – recovery period. Ventilation support with the use of Ambu-Vac.

consumption in reptiles lead to very specific challenges during the introduction of anaesthesia as well as during the recovery period (Fig. 11). The patient is allowed only oxygen during the period when the pleuroperitoneum is closed with suture. (the reptile is ventilated with air when the skin is to be sutured). Spontaneous breathing is stimulated with gently touching the most sensitive parts of the body (tongue, tail, base of the tail). The heart is monitored with the Doppler flow monitor and the pencil probe. During recovery heat pads, infrared lamps, hair-dryers or another source of heat may be used to warm reptiles. Care should be taken not to exceed the species´ optimum temperature range, otherwise the poor post-operative care would exacerbate and prolong the metabolic disturbances caused by the surgery. It is essential to keep reptiles in their preferred optimum temperature zone (POTZ), without any stress and pain.

Basic equipment of the post-operative box (terrarium) is a clean paper as a substrate and a shelter. Analgesics with long activity, like meloxicam or carprofen, are used at 24 hour intervals. Following a similar surgical procedure, different reptiles can have markedly different analgesic requirements. Dehydration is common in reptile patients. It is true that subcutaneous administration of fluids is not used regularly in reptiles (due to slow absorption and a small subcutaneous space). Intravenous (or intraosseous) fluid administration is advisable, but it is not an easy method in reptiles. Intracoelomic fluid administration is a feasible method of rehydration, but with the risk of organ puncture. All fluids have to be warmed prior to administration – to have the similar temperature like the body of the patient (preferred body temperature, PBT), 30 – 35 °C.

Selected anaesthetic protocols

Excellent results have been reported with the following anaesthetic protocols:

Chelonians (terrestrial tortoises, semiaquatic terrapins)	
a.	Induction (butorphanol+meloxicam) + 20-30 minutes propofol + intubation and isoflurane anaesthesia.
b.	Induction (butorphanol+meloxicam) + 20-30 minutes alphaxalone + intubation and isoflurane anaesthesia.
c.	Induction (butorphanol+meloxicam) + 20-30 minutes tiletamine/zolazepam + intubation and isoflurane anaesthesia
Lizards, snakes (very small species)	
a.	Induction (butorphanol+meloxicam) + 20-30 minutes – mask isoflurane + intubation/mask and isoflurane anaesthesia
b.	Induction (butorphanol+meloxicam) + 20-30 minutes tiletamine/zolazepam + intubation and isoflurane anaesthesia.
Lizards, snakes (medium to large species)	
a.	Induction (butorphanol+meloxicam) + 20-30 minutes propofol + intubation and isoflurane anaesthesia.
b.	Induction (butorphanol+meloxicam) + 20-30 minutes alphaxalone + intubation and isoflurane anaesthesia.
c.	Induction (butorphanol+meloxicam) + 20– 30 minutes tiletamine/zolazepam + intubation and isoflurane anaesthesia.

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REPRINT PAPER (F)

Results of infrared spectrophotometry analysis of 1131 canine urinary stones, collected in France from 2007 to 2010.

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SUMMARY

This is the first study conducted in France to offer a precise description and analysis of 1131 canine urinary stones. Samples are classified according to their mineral type, and also to the breed, sex and age of the animals. Calcium oxalate and struvite are the main stones encountered and are far more common than urate and cystine stones. Small breed dogs are over-represented for oxalate and struvite and the Yorkshire Terrier, Shih Tzu, Bichon and Poodle seem particularly predisposed. The Dalmatian is the most common breed producing urate stones. This study also differentiates monohydrated from dihydrated calcium oxalate stones, demonstrating that some canine breeds are predisposed to one or the other of these crystal forms.

Key Words: Urinary stones, Dog, Struvite, Oxalate, Spectrophotometry, Urolithiasis, Stone

This paper originally appeared in:
Pratique médicale et chirurgicale de l'animal de compagnie (2012) 47, 7—16*

Introduction

In dogs, struvite (magnesium ammonium phosphate hexahydrate) and calcium oxalate are the most common stones. Beyond this initial statement, French veterinarians have no alternative but to refer to studies that present typically North American statistics and to extrapolate these results to our canine population. However, one study shows that there may be significant differences within U.S. territory regarding the animal (breed, age, sex) or the chemical composition of the stones[1]. We therefore considered it of interest to present statistical data obtained from a sampling of dogs living in France. Royal Canin and Laboratoire d'Analyses Médicales Billiemaz in Toulon have collaborated together since 2007 and offer an analysis service for urinary stones to veterinarians. This collaboration now provides the basis for this work and deeper understanding of the issues involved.

Abbreviations used:

C1 = Whewellite
C2 = Weddellite
CYS = Cystine P
AM = Struvite
URAM = Ammonium Urate

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Compared to similar existing work, this study has several unique features. At present, it is the only French study concerning the identification and quantification of stones by infrared spectrometry. It is also one of the rare veterinary publications where the oxalates of calcium are differentiated into whewellite (monohydrate) and weddellite (dihydrate) and where certain morphology concepts are introduced (size, number, presence of a stone...)[2]. We must therefore remember that to be pure, a stone must contain at least 85% of a single component. Otherwise, it is considered a mixed stone. An element with a presence between 5 and 15% will be referred to as trace.

Furthermore, the nucleus is an element of the stone that differs in terms both of its morphology and its composition. It is at the origin of the crystallisation process and its analysis is imperative for management of the aetiology (Figure 1).

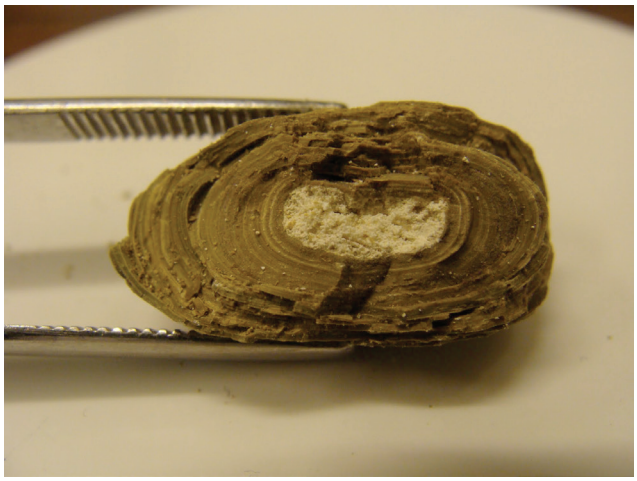

Figure 1: Cross section of a stone showing the presence of a nucleus and a matrix of distinct crystalline shapes.

Materials and Methods

Selection and Case Studies

This article is a retrospective study from the files of canine urinary stones analysed between 2007 and 2010 by the Laboratoire d'Analyses Médicales Billiemaz in partnership with Royal Canin France.

Information about the animal was obtained from the requested file for analysis that accompanies each stone. The breed, age, sex of the animal are recorded, as well as the morphology and location of the stones. The distribution of breeds in the sampling is compared to the overall French canine population[3], in order to identify possible breed predispositions, limiting the risk of bias.

Mineral Analysis

Whenever its size exceeds 5 mm, the stone is sectioned (Figure 2-a). The section is then observed under a binocular microscope to determine the presence of different layers (Figure 2-b). If need be, each layer is removed and analysed separately. An analysis of the surface, section and nucleus is thus systematically performed. This applies even when, for the same animal, stones of different morphology are revealed. For stones less than 5 mm in size, a single analysis is performed after crushing the entire stone.
The stones are analysed by infrared spectrometry (IR) using a FT-IR spectrometer (Fourier Transform InfraRed).

The method involves obtaining an IR spectrum by collecting the interferogram from a sample signal using an interferometer. It is currently the reference method for the identification and quantification of lithiasis. This technique is semi-quantitative and accurate to within 5% for identifying the composition of the stones[2,4].
The infrared analysis is based on a technique known as micropelletising, which involves several steps. In practice, the area of interest for the stone (surface, section or nucleus of the stone) is crushed with a buffer (crystalline powder of potassium bromide (KBr)) (Figure 2-c) before being placed in a press. Once the pellet has been produced (Figure 2-d), it is introduced to the spectrophotometer to obtain the specific spectrum (Figure 2-e).

The number of stones, their size and their macroscopic structure are listed for each record.

Statistical Analysis

Statistical analysis of the data and their graphical representation were performed using the R software (R Development Core Team (2010)[5]). Parametric tests (chi ² test of independence, adjusted chi ² test, Welch test extension) and non-parametric (Wilcoxon test) were used.

Results

Population Studied

1131 stones were analysed over a period of 3 years. They came from 1131 dogs.

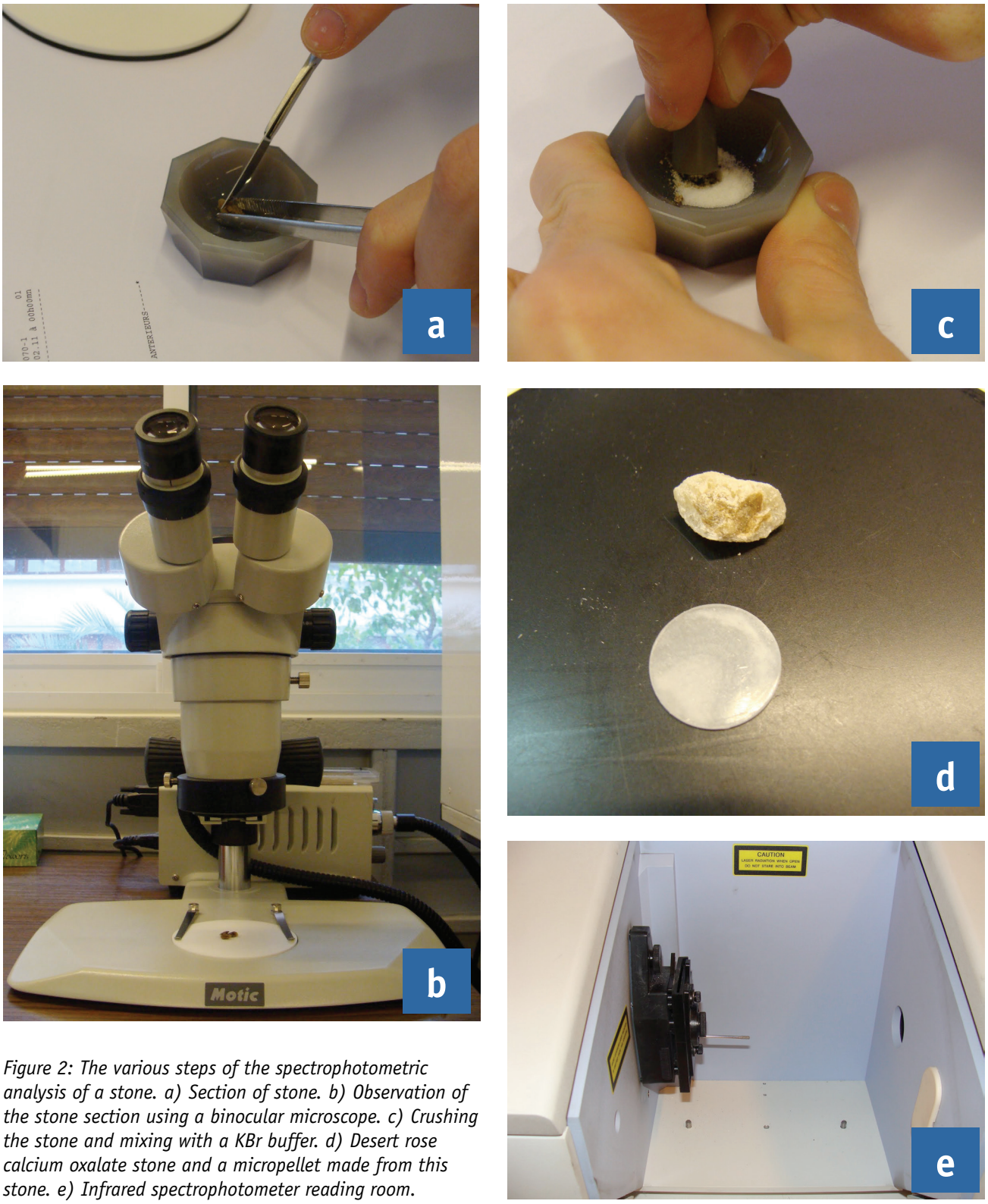

Figure 2: The various steps of the spectrophotometric analysis of a stone. a) Section of stone. b) Observation of the stone section using a binocular microscope. c) Crushing the stone and mixing with a KBr buffer. d) Desert rose calcium oxalate stone and a micropellet made from this stone. e) Infrared spectrophotometer reading room.

Population Observed

Of the 1131 original dogs analysed for stones, we recorded: 291 Yorkshire Terriers (25.7%), 160 Shih Tzu (14.2%), 67 Bichons (6%), 55 Poodles (4.8%), 35 cross breeds (3%), 33 Labrador Retrievers, 32 Brittany Spaniels and other Spaniels, 30 Dalmatians, 28 English Cocker Spaniels, 25 Jack Russell Terriers, 22 Fox Terriers, 19 Griffons, 19 Pinschers, 18 Pekingese Spaniels, 17 Cavalier King Charles Spaniels (CKCS), 16 Dachshunds, 15 Cairn Terriers, 15 Pyrenean Shepherds, 15 French Bulldogs, 14 Chihuahuas, 14 West Highland White Terriers (WHWT), 13 Pugs, 12 Golden Retrievers, 11 Schnauzers, 10 German Shepherds, 9 Basset Hounds, 8 Beauce Sheepdogs, 8 Dobermans, 7 English Bulldogs, 7 Beagles, 7 Rottweilers, 6 Boxers and 93 others where each breed was represented by fewer than 5 individuals per breed (Table 1).

Table 1. Composition of stones for the most represented breeds in the study based on gender. Only breeds represented over 30 times are listed in this table. NS= Gender not specified.

			Composition of stones			
Breed	**Sex**	**Number (n) and Frequency (%) of Stones**	**Calcium Oxalate**	**Struvite**	**Ammonium Urate**	**Others**
Yorkshire Terrier	M=225 F=63 NS=3	291 (25.7%)	184 21	28 39	8 0	5 3
Shih Tzu	M=86 F=73 NS=1	160 (14.1%)	50 11	26 59	7 1	3 2
Bichon	M=28 F=39	67 (5.9%)	23 9	0 26	1 1	4 3
Poodle	M=31 F=24	55 (4.8%)	19 1	8 23	1 0	3 0
Cross-breeds	M=19 F=16	35 (3%)	11 4	5 11	1 1	2 0
Labrador Retriever	M=19 F=14	33 (2.9%)	2 0	14 13	1 0	2 1
Brittany Spaniel and other Spaniels	M=16 F=16	32 (2.8%)	9 1	7 14	0 0	0 1
Dalmatian	M=29 F=1	30 (2.6%)	0 0	0 0	26 1	3 0
Others		428 (37.8%)				

In purebred dogs, Yorkshire Terriers (5.6% of the French canine population[3]) and Shih Tzus (2% of the French canine population[3]) showed a strong predisposition to urolithiasis. Bichons (2.4% of the French canine population[3]) were also over-represented ($p < 0.001$).

The Labrador Retriever represented only 2.9% of our sample, although it is the most popular breed in France (9.1%[3]).

Finally, the Dalmatian was also highly susceptible since although it represents only about 0.1% of the French population, it is the source of 2.6% of analysed stones.

Age

Animals whose stones were submitted to the laboratory had an average age of 7.8 years (median: 8.0 years) with a minimum of 3 months and a maximum of 19 years (Figure 3).

Cystine and ammonium urate stones were significantly found in younger animals ($p < 0.001$). Indeed, animals with cystine stones had an average age of 5.3 years and

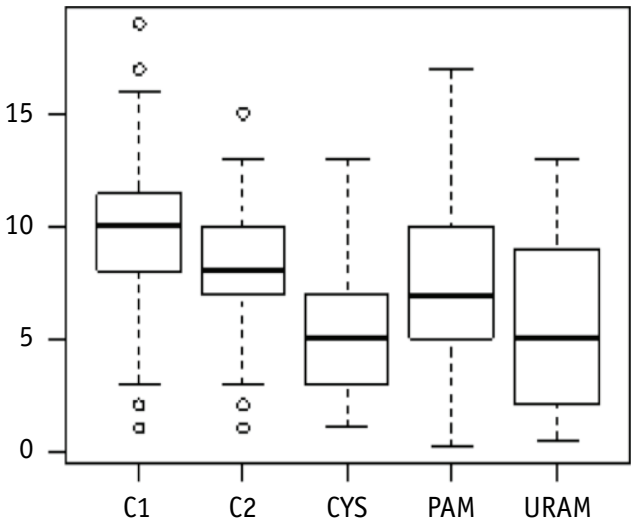

Figure 3: Distibution of ages based on the crystalline type and influence of age on the composition of stones.

5.6 years for dogs with urate stones (median: 5 years for both populations).

Struvite urolithiasis may occur very early (under 3 months) or very late (17 years for the oldest animal) with an

average age of 7.2 years (median: 7 years).

Oxalate urolithiasis also had a very broad occurrence over time with the youngest animals being one year old and the oldest being 19 years (C1). A quarter of the animals with calcium oxalate monohydrate stones were older than 13 years. On average, oxalate monohydrate stones occurred at 9.5 years (median: 10 years) and dihydrate stones at 8.3 years (median: 8 years).

Gender and Sterilisation

Taking into account all types of stones, there was a clear predisposition among males as against females with 716 males (64.6%) and 391 females (35.3%) (Figure 4). However, the overall gender distribution in the French population was 47.2% male and 52.8% female[3] ($p < 0.001$). The gender was not specified in 24 cases.

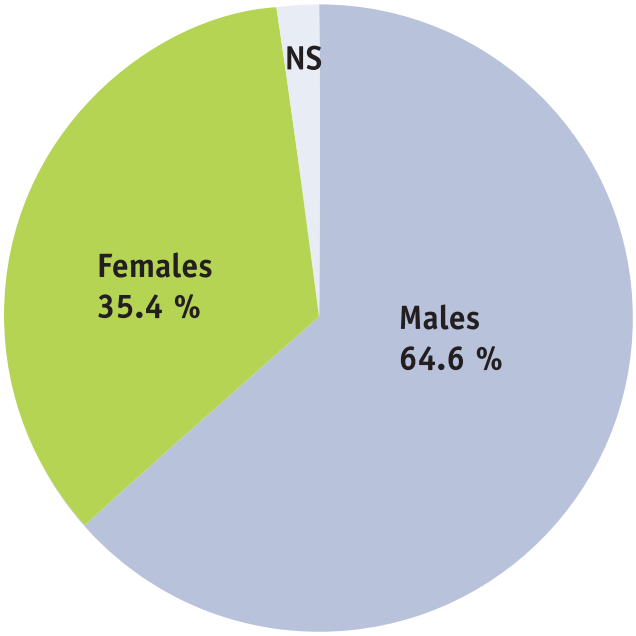

Figure 4: Gender distribution within the source population of analysed stones.

Gender and sterilisation were the criteria least often entered on the analysis request forms. Only 284 (25.3%) files were correctly filled out. It is therefore difficult to establish a possible link between sterilisation and the occurrence of urinary stones in dogs.

Morphological Analysis

Origin

Most stones submitted for analysis were extracted from the bladder (754 or 66.6%). 118 (10.4%) came from the urethra. In some cases, the stones were of mixed localisation and were present in both the bladder and urethra (81 or 7.1%). Finally, only two kidney stones were identified in this study. The localisation of stones was not entered in 176 cases (15.6%).

Frequency and Composition of Urolithiasis in the Sample

Struvite and calcium oxalate stones were the most common and together accounted for 86.9% of the stones analysed in this study (Tables 2 and 3). Their respective frequencies were almost identical: 42.6% for struvite stones and 44.3% for calcium oxalate. As regards oxalate stones, the monohydrate form was more often encountered (56.3% of calcium oxalates) than the dihydrate form (43.7%).

Ammonium urate and cystine stones were 5.3% and 3.7% respectively for the uroliths analysed.

Finally, stones of carbapatite, brushite, xanthine and opal, urates of sodium or potassium, uric acid and amorphous calcium phosphate were rarely identified and, for this reason, are grouped here under "Others". The overall total of these stones represents only 4.1% of the samples submitted to the laboratory.

Table 2: Distribution of different mineral types in the sample of stones submitted to the laboratory.

Composition	Number	Frequency (%)
Struvite	*482*	*42.6*
Calcium Oxalate:	*501*	*44.3*
For C1	282	24.9
For C2	219	19.4
Ammonium Urate	*60*	*5.3*
Cystine	*42*	*3.7*
Others:	*46*	*4.1*
Carbapatite	19	1.6
Brushite	9	0.8
Xanthine	8	0.7
Opal	5	0.5
Sodium Urate	2	0.2
Potassium Urate	1	0.1
Uric Acid	1	0.1
Amorphous Calcium Phosphate	1	0.1
	1131	***100***

Table 3: Frequency of elements present in trace amounts in the analysed stones

Composition	Number	Frequency (%)
Carbapatite	*392*	*55.6*
Proteins	*122*	*17.3*
Calcium Oxalate:	*80*	*11.3*
For C1	43	6
For C2	37	5.3
Struvites	*33*	*4.7*
Amorphous Calcium Phosphate	*33*	*4.7*
Ammonium Urate	*26*	*3.7*
Others	*19*	*2.7*
Newberyite	8	1.2
Whitlockite	3	0.4
Oxypurinol	3	0.4
Brushite	3	0.4
Sodium Urate	2	0.3

When an element makes up less than 15% of the composition of the stone, it is called "trace". The traces most commonly found were carbapatite (55.6% of cases) and protein (17.3% of cases) (Table 3).

Carbapatite is a carbonated calcium phosphate hexahydrate; brushite is a phosphate acid of calcium dihydrate crystallised in a monoclinic system. Newberyite is a trihydrate of magnesium phosphate acid in crystal form. Finally, whitlockite is a mixed phosphate of calcium and magnesium hydrate. Oxypurinol is of medicinal origin (especially treatment with Allopurinol).

Breed Predispositions

We highlighted a predisposition among Yorkshire Terriers and Bichons to oxalate stones; and Shih Tzus, Poodles and Labrador Retrievers to struvite stones; and, of course, Dalmatians to ammonium urate stones ($p < 0.001$) (Table 1). In other breeds, significant differences were also observed with the predispositions arranged in Table 4 ($p < 0.001$).

Relationship between the Nature of Stones and Sex of Animal

There was a significant difference between males and females. We noted a clear male predisposition to stones of calcium oxalate, cystine and ammonium urate (Table 1),

Table 4: Relationship between breeds and stone composition.

Composition	Breeds
Struvite	Beauce Sheepdog, Pug, English Cocker Spaniel, Griffon, Labrador Retriever, Golden Retriever, Rottweiler, Dachshund
Calcium Oxalate	Pinscher, Schnauzer, Terrier (Cairn, WHWT, Jack Russell)
Ammonium Urate	Dalmatian
Cystine	English Bulldog, American Staffordshire Terrier

while females seemed prone to struvite urolithiasis ($p < 0.001$).

Despite the limited number of cases, this study also suggested that males were prone to brushite stones (8 males to 1 female) and opal stones (5 males out of 5 cases). These data remain to be confirmed through a greater recruitment for this urolithiasis, which is very rare.

Size of Stones

Among the stones analysed, 714 are bigger than 5 mm. These uroliths were all subjected to at least a double spectral analysis (surface and section). The other 417 stones were below the threshold of 5 mm and thus underwent a comprehensive spectral analysis.

The stones submitted for analysis were on average 9.5 mm with a minimum of 0.1 mm for urinary sand and up to a maximum of 70 mm. The smallest stones were found primarily in males ($p < 0.001$) (Figure 5).
We also note that the larger stones were often composed of magnesium ammonium phosphate ($p < 0.001$) (Figure 6). In our study, a diagnostic threshold of 3 cm in diameter could be considered specific enough for a struvite urolithiasis with a positive predictive value of 0.96.

Presence of a Nucleus, Pure Stones and Mixed Stones: Basic Morphology

Of all the samples analysed, only 20 stones (1.76%) had a nucleus. In veterinary medicine, the presence of a crystallisation nucleus seems to be a fairly rare and marginal phenomenon. However, it remains a very important factor to take into account. Thus, three stones had a foreign body as a starting point for the lithogenic process (2 spikelets and a plastic tube).

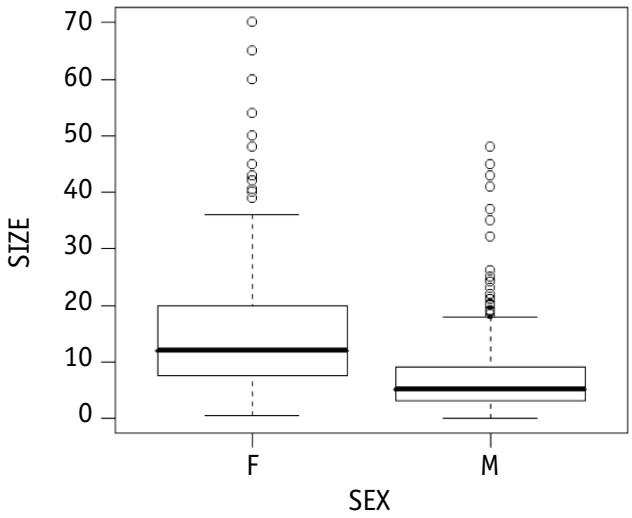

Figure 5: Relationship between the stone size and animal gender.

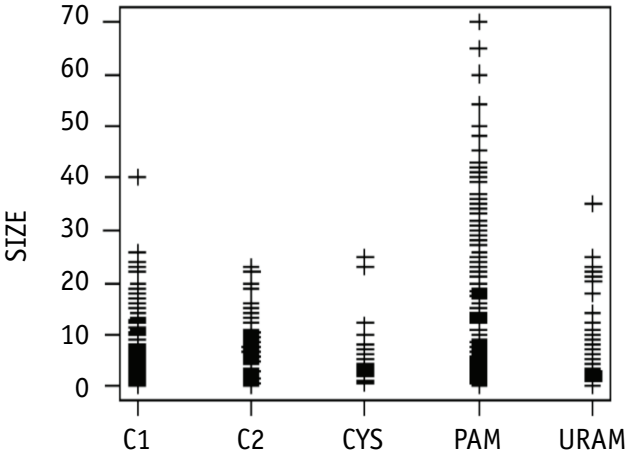

Figure 6: Relationship between the size and crystal type of the stones.

Of the 17 remaining stones, 15 nuclei were mainly composed of whewellite with the surface presence of struvite (Figure 7), carbapatite or weddellite. Thus, the presence of whewellite at the core of the nucleus gave evidence of a crystal conversion and the presence of struvite and carbapatite in the peripheral layers of a secondary urinary infection.

The phenomenon of crystal conversion corresponds with the passage of the dihydrate to the monohydrate form (passage of weddellite to the whewellite) by dehydrating the nucleus of the crystallisation. This phenomenon is common. The nucleus is no longer in contact with the urine and thus it dehydrates.

In the course of this study, we encountered almost as many pure as compound stones: 57% pure stones compared with 42% compound stones. While the struvite, cystine and ammonium urate stones were often more

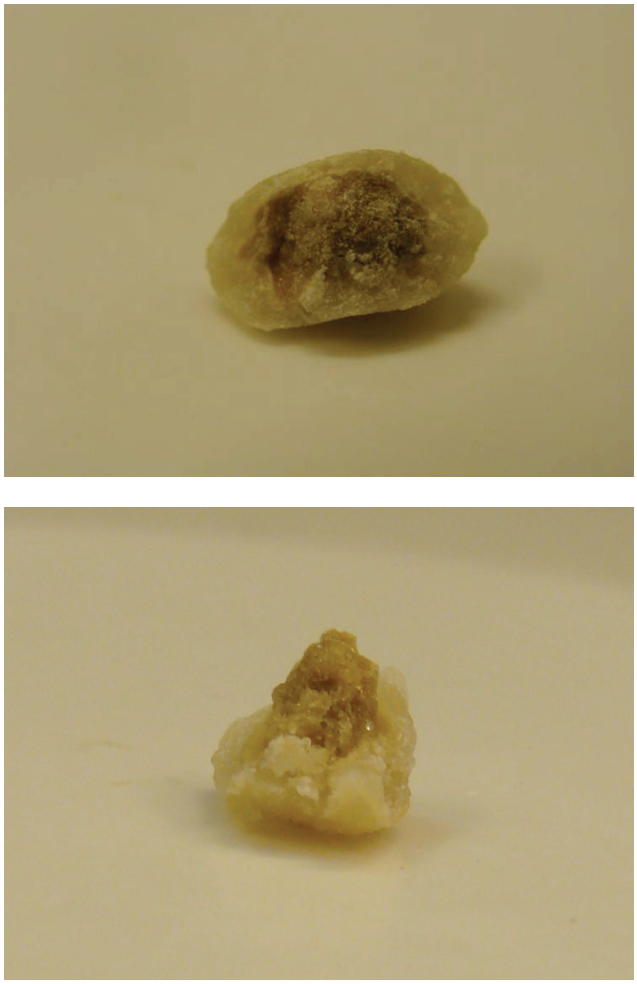

Figure 7: Compound stones having a nucleus of calcium oxalate and a surface of struvite.

pure, the oxalate stones were very often mixed with monohydrates and dihydrates ($p < 0.001$).

Discussion

Our results highlight the significant prevalence of urinary stones in the population of small dog breeds. In fact, by combining the four most represented breeds and considering that the Poodle in France is generally toy or miniature, our study confirms the susceptibility of small breeds of dogs (adult weight less than 10 kg) to the formation of urinary stones. These four breeds (Yorkshire Terrier, Shih Tzu, Bichon and Poodle) account for only 16.2% of the French canine population[3], yet were the source of more than 50% of the stones analysed. This trend was only confirmed when we added other small breeds to the grouping shown here: Jack Russell Terriers, Fox Terriers, Pinschers, Pekingese Spaniels, CKCS, Dachshunds, Cairn Terriers, Chihuahuas, WHWT, Pugs; and indeed French Bulldogs, Pyrenean Shepherds or even Schnauzers, with some weighing less

than 10 kg. As a minimum, we can therefore consider that 746 stones (65.9%) came from small breeds. This predisposition is echoed in the studies of Picavet et al[7], Houston and Moore[8], Wisener et al[9], and Low et al[10]. A study comparing urinary variables between a group of Miniature Schnauzers (8 dogs) and a group of Labrador Retrievers (also 8 dogs) showed that Schnauzers urinate less frequently and in smaller volume (relative to body weight) and that the concentration of calcium in the urine was greater in these smaller dogs[11]. These differences could explain this predisposition of small breeds to the formation of urinary stones. In fact, the smaller the animal, the more calories ingested and thus the higher the mineral content[11]. Such a predisposition highlights the importance of a preventive approach, especially through nutrition, that should be outlined to the small dog owner by the practitioner. This presents a strong argument for the prescription of a physiological diet based on a veterinary range that factors in the size of the dog and whose formula provides a urinary environment hostile to the formation of struvite and oxalate crystals and stones.

Our work also highlights a strong correlation between certain breeds of dogs and certain types of crystals. Thus, we emphasise the major susceptibility of the Yorkshire Terrier, and Bichons to a lesser extent, to oxalate stones; and that of the Shih Tzu and Poodle to struvite stones. The same trends were echoed in the studies cited above [7,10,12]. Finally, Dalmatians seemed highly prone to ammonium urate stones.

The recent analysis of Low et al[10] identified four breeds predisposed to magnesium ammonium phosphate stones: Bichon Frise, Miniature Schnauzer, Shih Tzu, and Pekingese Spaniel; and nine breeds predisposed to oxalates: Bichon Frise, Miniature Schnauzer, Shih Tzu, Lhasa Apso, Pomeranian, Dwarf Spitz, Cairn Terrier, Yorkshire Terrier, Maltese Bichon. Note that only small breeds are concerned. Some authors suggest the possibility of genetic factors[12], for example, as is the case for urate or cystine stones in other breeds[13] or for oxalates in humans[14].

Furthermore, we noted that Dobermanns, Spaniels and all Terriers as a whole, during calcium oxalate urolithiasis, seemed inclined to form monohydrates, which might suggest a particular crystallisation and thus a pathogenesis specific to these breeds. In fact, in humans, whewellite (monohydrate) stones are usually caused by hyperoxaluria, whereas weddellite (dihydrate) stones are caused by hypercalciuria[15] (Figure 8).

We noted a predisposition in males to calcium oxalate, cystine and ammonium urate stones and in females to struvite stones. Other authors have also reported

Figure 8: Depending on the mode of crystallisation, oxalate stones take on a very different macroscopic appearance: Type Ia stone, whewellite, evokes a hyperoxaluria of flow or concentration in terms of human medicine. b: Type IIb stone called "desert rose," weddellite, evokes in humans an intermittent hypercalciuria or a stasis.

a predisposition in males to oxalate stones[10,12]. The susceptibility of females to struvite stones has been verified in the majority of other findings[10,12].

Unfortunately, our analysis request form did not inquire into body condition and the gender status (neutered or not) was rarely indicated (25% of cases). However, the relationship between the oxalate stones and other criteria (breed, age and sex) is echoed here.

In a study by Lekcharoensuk et al[16], an increased risk of oxalate stones was reported in purebred dogs in contrast

to cross breeds, dogs over 8 years old, neutered males and overweight dogs. In contrast, in Wisener et al[9], the criterion of purebred was not a risk factor, except in the case of small breeds. The relationship between oxalate and purebred criterion for the male gender of advanced age (8-12 years) is echoed in Ling et al[17].

Our results can be compared with those of other international studies (North American for the most part). In most recent studies, oxalates were the most common stones: 46% in Picavet et al in 2007 (compared to 40% for struvite stones)[7], 52% in Houston and Moore in 2009 (compared to only 30% for struvite stones[8]. However, for Low et al, struvite stones remained in the majority, representing 53% of the stones analysed compared to only 42% for oxalate urolithiasis[10]. The authors commonly observe an increase in oxalate stones and a stagnation/ decrease in the proportion of struvite stones[9,10,12,17]. A better understanding of the pathogenesis of magnesium ammonium phosphate would allow for prevention and more effective dissolution, which would decrease the number of samples submitted for analysis. However, other types of minerals (calcium phosphate, cystine, silica) did not record an increase comparable to that of oxalates, which would have been the case if it were merely a mathematical phenomenon[17]. In addition, the formation of struvite stones in dogs is usually secondary to the presence of a urinary tract infection[19]. Improving additional examinations (imaging, more routine bacteriological tests) and anti-infective therapies may also reduce the incidence of these stones[6,12].

Another theory holds that due to the increasing longevity of dogs and the greater prevalence of calcium oxalate stones in older animals, it is logical to note an increase in these stones[11].

Finally, Low et al[10] highlight the change in canine populations towards miniaturisation and increasing obesity, which is identified as a predisposing factor for oxalate stones.

In the canine species, magnesium ammonium phosphate stones developed mainly as a result of urinary tract infections by urease-positive bacteria[19]. It has been shown that two weeks may suffice for a urinary tract infection to cause formation of stones. In our study, we observe a female predisposition to kidney stones, which has also been reported by other authors[10]. Of course, this is linked to increased risk of urinary tract infection in female dogs, which has already been highlighted by several authors[20]. The results of urine culture were requested on our stone submission form in the laboratory, but again, this criterion was too infrequently completed for us to be able to take it into account.

The dissolution of struvite stones proves more difficult in dogs than in cats. The prevalence of secondary stones due to a urinary tract infection, the presence of fine concentric layers of low porosity and the regular presence of carbapatite or calcium phosphate within the matrix of struvite are some factors that explain this particularity[6,20]. In fact, calcium compounds have very low solubility. Carbapatite may be present in stones where the original crystallisation process was infectious (particularly in struvite stones), but also secondary to oxaluria and calciuria.

In the case of a lithogenic urinary tract infection, bacteria may be incorporated into the matrix of the stone during lithogenesis. They can then be released during the dissolution phase and induced by a calculolytic diet. Therefore, it is important to note that antibiotic treatment should be maintained throughout the dissolution phase and continued 2 to 4 weeks beyond the complete disappearance of the stone(s). In the absence of such compliance a failure to dissolve, or a rapid recurrence of lithiasis, are to be feared.

The ammonium urate stones came third – and far behind the first two crystal types – in our ranking, echoing other studies[7,9,10,12]. The breeds predisposed to these stones obviously include the Dalmatian, but also (again!) the Miniature Schnauzer, English Bulldog, Bichon Frise, Pekingese Spaniel (again!) and Scottish Terrier[8,10]. We are aware of the predisposition of the Dalmatian due to its heightened excretion of uric acid, its inability to reabsorb urate at the proximal renal tubular level (SLC2A9 mutation) and its failure to transport plasma uric acid to the liver, where uricase should convert into a more hydrosoluble allantoin. Finally, note that the lithiasic risk is much higher in male Dalmatians than in females (26 times in our study).

The English Bulldog (and the Black Russian Terrier) are both susceptible to the same SLC2A9 gene mutation that leads to hyperuricosuria and predisposes to urate stones. Besides breeds with a genetic abnormality, dogs

may form ammonium urate stones secondarily to liver disease, including a portosystemic shunt. One study cited Havanese, Yorkshire Terriers, Maltese and the Dandie Dinmont Terriers as prone to congenital shunts. Once again, smaller dog breeds are concerned.

We observed that the larger stones corresponded to struvite stones. Houston and Moore established that a urolith whose size exceeds 10 mm has a 92% probability of being composed of struvite and it is rare that a stone of another crystal type exceeds 15 mm[8]. Our results showed, however, that oxalate stones and urate stones may often be larger than 15 mm. Regarding struvite stones, it seemed more appropriate to propose a "virtual certainty size" of 30 mm. The positive predictive value for the threshold of 30 mm was 96% in our sample. However, it should be remembered that the nucleus even of a large struvite stone may have a different mineral composition or even be constituted by a foreign body. For this reason, we recommend the systematic analysis of the stone.

As in all other studies, the source of the stones was mainly the bladder. However, we were surprised to note only two uroliths of renal origin – less than 0.2%. The diagnosis of renal stones was certainly more difficult and their surgical removal was performed less often. According to other publications, the proportion of kidney stones in dogs was generally between 1% and 4%[21].

Conclusion

Multiple interconnected factors influence the mineral content of stones (breed, age, sex, obesity) in dogs. Nevertheless, it is important to emphasise that smaller size breeds are much more prone to urolithiasis. In the population studied, the incidence of calcium oxalate stones was comparable to that of struvite stones, far more than other crystal types. Struvite stones were often the largest stones found in certain predisposed breeds (primarily Shih Tzu, Poodle and Labrador Retriever) and particularly in females. Oxalate stones were more commonly found in males with a significant predisposition among Yorkshire Terriers and Bichons. In some breeds, oxalates seemed to crystallise preferentially in monohydrate form. In human medicine, some oxalate morphologies are specific to very different pathological processes. Future studies may better highlight the significance of this difference in dogs, by comprehensively researching the urolithiasis aetiology of whewellite and weddellite. A morpho-etiological description might also result from this process.

Declaration of interest

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REPRINT PAPER (UK)

Evaluation of immunosuppressive regimens for immune-mediated haemolytic anaemia: a retrospective study of 42 dogs

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SUMMARY

OBJECTIVES: Immune-mediated haemolytic anaemia (IMHA) is a severe disease for which evidence is lacking to make informed choices regarding immunosuppressive regimen. The aims of the current study were to determine the effect of different treatment regimens on outcome in affected animals and to identify parameters that may be used as prognostic factors for the disease.

METHODS: The records of dogs presenting to a veterinary hospital in the period 2002 to 2010 for treatment of IMHA were examined and follow-up data were obtained. Statistical tests were performed to establish whether treatment regimen affected outcome and to identify prognostic factors for outcome.

RESULTS: Treatment regimen had a significant effect on the outcome (measured as survival of hospitalisation) but there were insufficient subjects to determine the cause of the difference. Serum bilirubin and urea concentrations were found to be significant negative prognostic factors for the outcome of IMHA cases and the concentrations of these parameters were significantly different between animals that survived or died while hospitalised.

CLINICAL SIGNIFICANCE: This study presents the first report of a significant difference in outcome comparing animals treated with immunosuppressive drugs which are in widespread clinical usage. Although possible confounding factors should be considered, these findings could have major consequences for the treatment of IMHA.

This paper originally appeared in:
Journal of Small Animal Practice (2011)* **52**, 353–358

Introduction

Immune-mediated haemolytic anaemia (IMHA) is the result of a type II (antibody-mediated) autoimmune response directed at antigens expressed on the surface of erythrocytes. The majority of cases of IMHA are considered to have no apparent cause, although certain

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subtypes of the disease may be associated with particular dog leucocyte antigen (DLA) haplotypes[1].

Secondary IMHA may be incited by parasite infection, neoplasia (particularly lymphoproliferative and histiocytic disease and haemangiosarcoma) and by reactions to drugs, toxins and live vaccines[2-4].

Cases of IMHA present a considerable diagnostic and therapeutic challenge with reported mortality rates of between 50 and 70%[5-10]. A variety of immunosuppressive agents are used in the treatment of the disease, including corticosteroids, cyclosporine, cyclophosphamide, human gamma globulin, danazol, mycophenolate mofetil, leflunomide and azathioprine but there is currently little evidence to indicate which regimen produces the most favourable outcome[11-15].

Studies have indicated that the use of cyclophosphamide with prednisolone produces no beneficial effect when compared with prednisolone alone and it may even increase mortality[6,16,17]. Further work suggests that azathioprine may exert a beneficial effect but with results that did not always achieve significance[5, 16].

Several studies have also attempted to identify factors capable of predicting the outcome of cases with IMHA and elevated serum bilirubin, alkaline phosphatase (ALP) and urea concentrations, hypoproteinaemia, thrombocytopenia, autoagglutination and prolonged clotting times have all been variously associated with a poorer prognosis[5,7-9].

The aim of the current study was to determine whether treatment regimen affected outcome in a retrospective analysis of cases diagnosed with IMHA at a veterinary referral hospital in the UK. Follow-up data were also obtained to try to identify possible prognostic factors for the disease.

Materials and Methods

Inclusion criteria

Clinical records were searched to identify dogs treated for IMHA between 2002 and 2010. Cases were included if they were anaemic on admission [packed cell volume (PCV) ≤35%], if no underlying cause was identified by clinical examination, examination of a blood smear, assay for exotic parasites (Ehrlichia canis, Babesia canis if the dog had travelled to an endemic area), or diagnostic imaging, and if they fulfilled at least one of the following defining criteria for haemolytic anaemia: positive in-saline agglutination test, clinical evidence of haemolysis (haemoglobinuria or haemolysed plasma), presence of significant numbers of spherocytes on a blood film (>1 per high power field), or a significant positive titre (>1:16) from a Coombs' test. Animals with concurrent thrombocytopenia (platelet count ≤50 x 109/L), whether considered to be of immune-mediated or inflammatory origin, were included in the study.

Data collection

Data were obtained from the clinical records of selected animals and by contacting the practices of referring veterinary surgeons by telephone. The following data were collected for each animal: age, breed, sex, vaccination status, season of presentation, duration from initial presentation to referral, results of haematological and biochemical analyses performed on admission (PCV, neutrophil, platelet and reticulocyte counts, clotting times [activated partial thromboplastin time (APTT) and one-stage prothrombin time (OSPT)], D-dimer concentration and concentrations of serum protein, albumin, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), ALP, creatine kinase (CK) and bilirubin), results of in-saline agglutination and Coombs' tests, blood transfusions administered, treatment regimen instituted before referral and during hospitalisation, and survival time after discharge, if known. Analysis of blood samples was conducted by the same laboratory for all cases and the PCV at presentation was measured using the manual technique. Transfusions of whole blood or packed red blood cells were administered whenever the PCV dropped below 12% and on the basis of clinical examination findings and an assessment of the rate at which the PCV had decreased over time. Cross-matching was not performed for animals that had not previously received a transfusion but this was carried out for all subsequent transfusions.

A population of 84 control animals was assembled by selecting those animals with the case numbers on either side of the IMHA cases. The age, breed and sex of these animals were recorded.

Analysis

All statistical analyses were performed using SPSS (version 16, SPSS Inc, IBM Company) with significance designated as P≤0.05, unless otherwise stated.

Binary logistic regression was used to determine whether dogs with IMHA were more likely to be of a particular age, breed or sex. Variables (containing data from the control and test populations) were stratified into suitable groups and entered into separate models as categorical variables.

For the purpose of the analysis, animals were grouped according to the treatment they received: group A received prednisolone (Prednidale; Dechra Veterinary Products) and cyclosporine (Atopica; Novartis Animal Health), group B received prednisolone and azathioprine (Azathioprine; Generics [UK] Ltd) and group C received only prednisolone. Survival data were analysed using a Kaplan-Meier procedure stratified according to treatment group. Survival time was measured from the date of admission to the hospital to the date of known death or euthanasia or, for censored data points, to the date on which follow-up data were obtained. The percentage mortality figures for the different treatment groups during hospitalisation, at 1 month after discharge from the referral institute and at 1 year after discharge were compared using a chi-squared test. Where significant differences were detected, z tests were performed to compare proportions between treatment groups.

Differences between treatment groups in terms of other variables were further assessed using Student's t tests and Mann-Whitney U tests for parametric and non-parametric numerical data, respectively. Chi-squared tests were used for categorical variables and Shapiro-Wilks tests were used to classify variables as parametric or non-parametric. Comparisons of animals that survived or died at different time points and associations between corticosteroid dosage and prevalence of adverse effects were assessed using the same tests.

To identify putative prognostic factors for the outcome of cases, data from variables collected on admission were evaluated using a Cox proportional hazard model. Individual variables (for which data from >90% cases were available) were first entered into a univariate model and retained if they were significant to the level $P<0.15$. These variables were then entered together into a multivariate analysis using a forward conditional method with the input criterion $P<0.05$ in a likelihood ratio test.

Results

Signalment

Forty-two dogs fulfilled the inclusion criteria with a median age of 6.0 years (range: 0.5 to 12, n=42). Ten dogs (23.8%) were first presented in the period from 1st January to 31st March, nine (21.4%) from 1st April to 30th June, eight (19%) from 1st July to 30th September and fifteen (35.7%) from 1st October to 31st December. There was no significant difference in the proportion of cases that presented during each period (chi-squared: 2.762, P=0.430).

Data were recorded from 23 different breeds, with the most prevalent being the cocker spaniel (19.0%) and Labrador (14.3%). Animals of these breeds constituted 2.5 and 12.7% of the control population, respectively. Logistic regression models were produced to compare the breed (divided into cocker spaniels and all others), age (stratified into four equal groups: 1 to 2 years, 3 to 5 years, 6 to 7 years and more than 7 years) and sex (female and male entire and neutered) prevalence of IMHA with a control population. The results of these models are shown in Table 1.

Table 1. Results of binomial logistic regression performed to determine whether animals with IMHA were more likely to be of a particular age group, breed or sex

	Odds ratio	P
Breed		
Other breed	1.0	
Cocker spaniel	9.1	0.007
Age		
1 to 2 years	1.0	
3 to 5 years	0.5	0.245
6 to 7 years	0.4	0.081
>7 years	0.2	0.011
Sex		
Female entire	1.0	
Male entire	0.7	0.485
Female neutered	0.5	0.227
Male neutered	0.4	0.170
IMHA Immune-mediated haemolytic anaemia		

Clinical signs

The median time to referral from the onset of clinical signs was 4 days (range: 1 to 38, n=41). Fifteen cases (38.5%, n=39) were tachycardic on presentation (heart rate >140 beats per minute) and 23 (79.3%, n=29) were tachypnoeic (respiratory rate >20 breaths per minute). The median heart and respiratory rates were 125 and 36 per minute, respectively. Five dogs (17.9%, n=28) were hyperthermic (rectal temperature >39.4°C), with a median value of 39.1°C.

Laboratory parameters

The median PCV and platelet count on admission were 17.0% (range: 3 to 35, n=41) and 147 x 109/L (range: 5 to 839, n=42), respectively. Eight animals (19.0%) therefore had concurrent thrombocytopenia (defined as platelet count ≤50 x 109/L). Twenty-six (61.9%) animals were positive to an in-saline agglutination test, 29 (69%) showed evidence of significant spherocytosis when a blood smear was examined and 2 (4.8%) showed evidence of haemoglobinuria on presentation. A Coombs' test was performed in 23 (54.8%) cases and a significant positive titre was detected in 7 (30.4%) of these dogs.

Diagnostic imaging

Radiographic or ultrasonographic imaging was performed in all cases to rule out underlying causes of IMHA. No such abnormalities were detected in any of the subjects examined.

Adjunctive therapy

In addition to immunosuppressive therapy, transfusions of whole blood or packed red blood cells were administered to 23 animals (54.8%), of which 17 (73.9%) received one transfusion, 5 (21.7%) received two transfusions and 1 animal (4.3%) received three transfusions.

Twenty-four (58.5%) dogs received gastroprotectant or gastrointestinal promotility drugs, of which the products most commonly prescribed were 1 to 2 mg/kg ranitidine (Zantac syrup or injection; GlaxoSmithKline) orally or intravenously twice a day (43.0% cases), 500 mg to 2 g sucralfate (Antepsin suspension; Chugai Pharma UK Ltd) orally three times a day (46.3%), 0.5 to 1.5 mg/kg omeprazole (Losec tablets or injection; AstraZeneca) orally or intravenously once a day (12.2%) and 0.2 to 0.5 mg/kg metoclopramide (Maloxon injection ; Amdipharm) subcutaneously three times a day (9.8%). Administration of these products was begun at varying points after admission to the referral institute according to the onset of vomiting, diarrhoea or anorexia.

Seven (16.7%) dogs also received a median dose of 107 iu/kg (range: 17 to 222) heparin injections (Heparin Sodium; Wockhardt UK Ltd) while hospitalised, subcutaneously three times a day. A dose of 1 to 2 mg/kg aspirin (Aspirin; M and A Pharmaceuticals Ltd) was administered orally to two (4.8%) dogs once a day while they were hospitalised.

Treatment outcomes

Animals were assigned to groups according to the immunosuppressive treatment regimen they underwent, with group A receiving prednisolone and cyclosporine (n=17, 40.4%), group B receiving prednisolone and azathioprine (n=9, 21.4%) and group C receiving only prednisolone (n=11, 26.2%). The remainder of cases (n=5, 11.9%) received all three or different combinations of drugs but were not included because of their small group sizes. Two dogs in group A also received single injections of 1.1 to 2.8 mg/kg cyclophosphamide (Cyclophosphamide injection; Pharmacia) intravenously and four dogs received 0.5 to 1.0 g/kg single intravenous infusions of human gamma globulin (Flebogamma; Grifols UK Ltd). Of the animals that received human gamma globulin, three belonged to group A and one to group B. No animals received both cyclophosphamide and human gamma globulin.

The median dose rates of azathioprine and cyclosporine used were 1.8 mg/kg (orally, once a day, range: 1.3 to 2.7) and 5.0 mg/kg (orally, once a day, range: 3.0 to 8.0), respectively. The respective median dose rates for prednisolone used in dogs in groups A, B and C were 2.0 mg/kg (mean: 2.35, range: 1.40 to 4.00), 2.50 mg/kg (mean: 2.57, range: 2.00 to 3.75) and 2.0 mg/kg (mean: 1.65, range: 1.00 to 2.50), all given orally as single or divided daily doses. In all cases, the immunosuppressive regimen was begun within 24 hours of admission to the hospital.

Comparisons performed between groups determined that animals in group C received a significantly lower dose of prednisolone than those in group B (Mann-Whitney U: 18.0, P=0.014), that these animals had significantly lower serum urea concentrations at presentation than those in group B (Mann-Whitney U: 10.0, P=0.004) and that a significantly lower proportion of these animals

received a blood transfusion compared with both groups A and B [chi-squared (A versus C): 7.337, P=0.007; (B versus C): 4.848, P=0.028]. No other significant differences were found between any treatment groups for any other variable (data not shown) but 68.2 and 36.4% of those animals treated with cyclosporine suffered from vomiting and diarrhoea, respectively, compared with 40.0 and 15.0% of pooled cases from groups B and C.

Adverse effects

Twelve (28.6%) of the animals receiving corticosteroids developed polyuria or polydipsia after treatment was initiated but the prednisolone dose used was not significantly associated with the development of either form of morbidity (data not shown). In total, 23 dogs (54.8%) had at least one bout of vomiting while hospitalised and a significantly higher proportion of these animals received one or more gastroprotectant drugs (chi-squared: 10.087, P=0.001).

Comparison of mortality between treatment groups

The mean and median survival times for each treatment group were group A: 158 and 9 days; group B: 360 and 194 days and group C: 620 and 452 days. The Kaplan-Meier survival curve stratified by treatment group is shown in Fig 1.

Thirty-two animals (76.2%) were discharged after a median hospitalisation period of 5.0 days (range: 1 to 14). Of these dogs, 28 (66.7%) were found to survive for at least 1 month after discharge. Follow-up data at 1 year after discharge were not available for nine animals, either because they could not be traced (n=4) or because 1 year had not elapsed since they were admitted to the hospital (n=5). Of the 19 cases for which data were available, 14 were still alive giving an overall mortality rate of 57.6% at 1 year after discharge. Four (40.0%) of the animals that died while hospitalised (n=10) showed signs of dyspnoea.

Percentage mortality figures stratified by treatment group during hospitalisation, at 1 month after discharge and at 1 year after discharge are shown in Fig 2. Mortality during the period of hospitalisation was significantly different between treatment groups (chi-squared: 7.338, P=0.026) but the number of cases was insufficient to determine the cause of the difference. There was no significant difference in the percentage mortality at 1 month or 1 year after discharge (data not shown).

Prognostic factors

Nine putative prognostic variables were retained after univariate Cox proportional hazard analysis (Table 2) and, where data were available for more than 90% cases, these were included as covariates in a multi-variate analysis. This procedure showed that serum urea and bilirubin concentrations significantly predicted the likelihood of survival of IMHA (Table 3).

The median serum urea concentrations in the animals that did and did not survive hospitalisation were 6.05

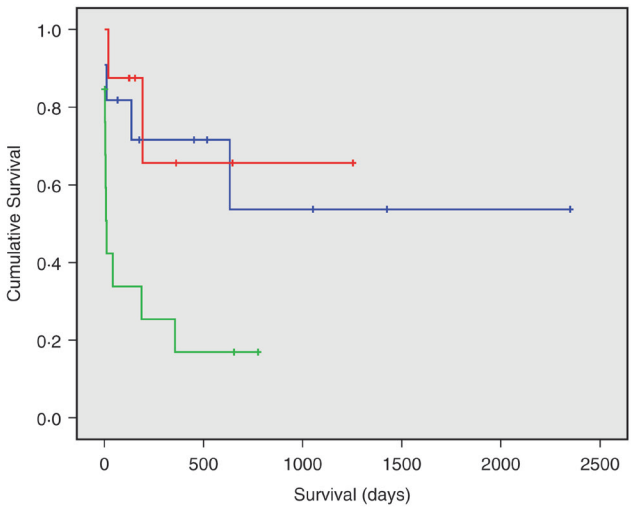

Fig 1. Kaplan-Meier curve showing difference in survival between groups A (treated with cyclosporine and prednisolone; green line), B (azathioprine and prednisolone; red line) and C (prednisolone only; blue line). Vertical lines indicate censored data

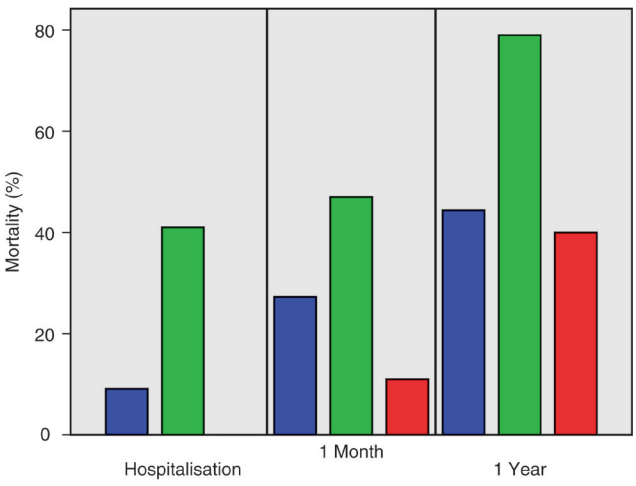

Fig 2. Bar graph to show percentage mortality in groups A (treated with cyclosporine and prednisolone; green bars), B (azathioprine and prednisolone; red bars) and C (prednisolone only, blue bars) during hospitalisation (n=37), at 1 month after discharge (n=37) and at 1 year after discharge (n=28)

Table 2. Variables retained after univariate Cox proportional hazard analysis with significance at P≤0·15

	HR	n	P
Bilirubin	1.011	34	0.001
Urea	1.146	35	0.003
APTT	1.302	20	0.007
ALT	1.001	33	0.022
OSPT	1.243	20	0.033
Creatinine	1.005	36	0.033
Albumin	0.934	36	0.083
Haemoglobin	0.841	37	0.085
HR Hazard ratio			

Table 3. Variables included in the model of survival produced by multi-variate Cox proportional hazard analysis with forward conditional entry

	HR	95% CI	P
Urea	1.211	1.073 to 1.367	0.002
Bilirubin	1.014	1.003 to 1.024	0.010
Hazard ratio, CI Confidence interval			

mmol/L (sd=4.31, range: 2.00 to 19.30) and 10.15 mmol/L (sd=6.39, range: 6.40 to 22.80), respectively. The median serum bilirubin concentrations for those that did and did not survive were 12.2 µmol/L (sd=47.9, range: 4.7 to 191.5) and 36.5 µmol/L (sd=51.80, range: 10.0 to 140.8), respectively. Comparisons of the distribution of serum urea and bilirubin concentrations between these animals showed that both parameters differed significantly between groups (urea: Mann-Whitney U: 56.0, P=0.007; bilirubin: Mann-Whitney U: 52.5, P=0.006).

Discussion

The results of this study indicate that treatment regimen had a significant effect on the outcome of cases with IMHA during hospitalisation at a veterinary referral hospital. This is the first reported study to directly compare the use of these three commonly used immunosuppressive agents.

The apparent difference in mortality between the groups treated with prednisolone alone and prednisolone with cyclosporine, although not significant, should be viewed with suspicion as further tests showed that a smaller proportion of animals in the former group received blood transfusions and because these animals received lower doses of prednisolone and had lower serum urea concentrations at presentation. It is therefore possible that the difference in survival is underlain less by the choice of drug and more by the severity of disease with which the animal presented, although values for all other clinical and diagnostic parameters did not differ significantly between treatment groups.

There are several possible explanations for the observed difference in survival between treatment groups A and B. Cyclosporine is known to have an availability of approximately 35% after oral dosing in healthy animals and it is to be expected that this absorption would be reduced in hypovolaemic animals with constricted splanchnic vessels[18,19]. One possibility therefore is that, although cyclosporine may be an effective immunosuppressive agent, it may not be absorbed in sufficient concentrations to control the immune response in collapsed animals, including those with IMHA.

Given that azathioprine is known to control autoimmune responses only after some delay[20], it is possible that the difference in survival between treatment groups also relates to the adverse effects produced by cyclosporine. It is well documented that cyclosporine may cause gastrointestinal adverse effects such as vomiting and diarrhoea, in addition to the nephrotoxicity, hepatotoxicity and gingival hyperplasia observed at the higher doses used after transplantation[21]. A recent meta-analysis examining the adverse effects associated with the use of cyclosporine in the management of atopic dermatitis found that 25% of animals experienced vomiting and 18% diarrhoea in the month following the initiation of treatment at a standard dose of 5 mg/kg/day[22]. The prevalence of adverse effects was much higher in animals receiving cyclosporine in the current study and this may reflect the large variety of dose rates employed.

Although vomiting and diarrhoea are common adverse effects associated with cyclosporine, they could also be related to several other factors, such as the use of very high doses of corticosteroids, the effect of hypoxia on gastrointestinal tissues and possible diagnostic confusion with regurgitation due to muscle weakness. Whatever the cause of the gastrointestinal disease described, it is reasonable to suggest that further perturbations

of electrolyte concentrations, acid-base balance and hydration status could make a significant contribution to mortality in the period immediately following a haemolytic crisis.

The observed difference in survival between groups B and C has been described in another study of 70 dogs with IMHA but this analysis also contained insufficient subjects to compare directly between treatment groups[5].

Although the use of all of the follow-up data would have been preferable when drawing conclusions about survival, comparisons of the Kaplan-Meier curves produced for each treatment group may have given misleading results in the current study as the marked difference in short-term survival is not observed at later stages. The conclusions of the study are therefore limited to the survival of the acute haemolytic crisis and it remains to be determined whether any of the treatment regimens would have a significant effect on long-term survival.

Adverse effects frequently reported with corticosteroid therapy include polydipsia, polyuria, polyphagia, panting and lethargy, all of which may affect the quality of life of the animal. Although the prevalence of adverse effects was not associated with the dose of corticosteroid used in this study, it is worth noting that a considerable proportion of animals developed polyuria and polydipsia after treatment was initiated. As corticosteroid dose was also not found to have a significant effect on survival in this study, there appears to be little rationale in using doses of prednisolone beyond 2 mg/kg/day when polypharmaceutical options are available.

The mortality rate at 1 year reported in this study is similar to those of several recent retrospective analyses[5,7,9,23]. Using Cox proportional hazard analysis, serum urea and bilirubin concentrations at presentation were each found to be significantly negatively associated with survival. Serum bilirubin concentration has previously been identified as a major negative prognostic factor in a number of other studies[5,7,24,25] and previous authors have speculated that this may be related to hepatic injury (hypoxia, thromboembolism or haemoglobinaemic endothelial damage) reducing the ability of the liver to take up, conjugate, transport and excrete bilirubin and to the release of unconjugated bilirubin from lysed erythrocytes[26,27]. In either case, increasing bilirubin concentration is likely to reflect the severity of the injury inflicted on hepatocytes or erythrocytes and to explain its continued recognition as a prognostic marker.

Serum urea concentration greater than 20 mmol/L has also been described previously as a negative prognostic indicator in IMHA[9] and this elevation is likely to be of pre-renal, renal or gastrointestinal origin in patients with IMHA. Pre-renal failure may occur with reduced plasma oxygen-carrying capacity whereas thromboemboli may cause direct renal damage. Further elevations may be associated with gastrointestinal haemorrhage.

The major limitations of the current study are its small sample size and the lack of consistency in the treatment regimens used in different animals within the same treatment groups. The subjects examined were treated by a large number of different clinicians over a period of 8 years, meaning that animals were treated according to a range of professional guidelines that were developed and enforced over this time. In particular, the range of dose rates used for each drug and the inconsistent use of additional immunosuppressive and adjunctive products may affect the reliability of the results shown above. The small number of subjects in the study is also likely to explain the failure to identify other prognostic factors that have been described previously[9].

Further work should be directed at examining the effect of treatment regimen on outcome, preferably through a prospective double-blinded study, and at determining whether treatment failure is caused by a failure to control the immune response in IMHA or by the prevalence of adverse effects with the use of particular drugs.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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REPRINT PAPER (IE)

They're Not The Henemy

Pete Wedderburn[1**]

INTRODUCTION

Hens are increasingly being kept as domestic animals in back gardens by people who have no previous poultry experience, and whose past experience of veterinary care has involved pets like dogs and cats. If a hen falls ill, there's a conflict between the high expectations of owners for quality veterinary care and the low economic and emotional value that is often placed on hens. Companion animal vets may have a limited knowledge base about poultry, creating an additional challenge. This article aims to provide basic background information on hen keeping and common poultry diseases, together with a suggested method for in-practice handling of "sick pet hens".

This paper is based on a lecture given at the VICAS Congress , Dublin Jan 212 and published in the Veterinary Ireland Journal* **Volume 2** Number 4 April 2012 **p 192-194**

Background to backyard hen keeping

A typical modern poultry owner may have anywhere between two and ten hens, often in a small enclosed space such as a suburban back garden. (Fig 1) The hens may be entirely enclosed in a henhouse or run, or they may be allowed to free range around the garden in the daytime, being shut up in the hen house at night to protect them against nocturnal predators. The henhouse may be a converted garden shed, or may be specifically designed for the purpose. Hens require perches to sleep on at night, and a nesting box to lay eggs in. Bedding is usually wood shavings, although shredded newspaper, straw or even dried leaves may be used.

There are two aspects of a henhouse that are often deficient, and these can contribute to disease

1) Ventilation. Often the air in a henhouse is stagnant, and this may be exacerbated by the fact that the bedding may not be changed often enough, leading to the accumulation of ammonia-like fumes.

2) Hygiene. Many henhouses have nooks, crannies, cracks and corners that may be difficult to clean thoroughly. This can make it challenging to treat diseases that that have an environmental stage (e.g. red mites)

Fig 1 A typical suburban hen set up

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Hens may be bought at poultry shows, local agricultural markets, or directly from breeders online. They are most commonly bought as point-of-lay pullets. There is an increasing trend for suburban owners to buy hens that have been discarded by commercial set-ups after their first season. These birds are usually inexpensive and still have plenty of laying potential ahead of them.
The most common type of hen is a hybrid brown laying hen, but a range of breeds may be kept. Hybrid laying hens have been bred to produce the maximal number of eggs, and they often fall ill with reproductive tract disease by two or three years of age.
Pure breed birds may not lay as regularly, but they are likely to live longer lives and are less likely to fall ill.
Roosters are not normally kept in suburbia because of the noise created by early morning crowing.

Hens are generally fed on a staple diet that is bought commercially, such as "layers' pellets": this should make up at least 80% of the hens' diet. This is often supplemented with household scraps such as crusts of bred, porridge etc, as well as free range scavenging around the garden.
Grit should also be provided, with a typical hen consuming around 30g (1 ounce) per month.
Food and water are usually provided in custom designed feeders and drinkers that need to be regularly cleaned.
Food is usually stored in dustbins. Careful attention needs to be given to ensuring that rodents cannot access food (either waste or stored) or they will become a problem.
If owners get the basic husbandry right, most hens are healthy for most of the time. However, when a hen does fall sick, the local vet clinic may be the first place to be called.

How to handle "sick hen" phone calls

It's best to set up a practice policy for dealing with hens, so that initial calls can be dealt with confidently.
The problem for vet clinics is that hens are not pets: but suburban hen owners may have high expectations. They are familiar with dealing with the other animals (typically dogs and cats) in their house as pets. So if a hen falls ill, the owner wants to do everything possible to help. Unfortunately, they often don't want to invest the funds to carry out the full scale investigations needed to make an accurate diagnosis, and hence to provide the optimal treatment.

For staff taking the initial phone call about a sick hen, it's important that the cost implications are spelt out at the start, so that the owner has a clear idea of the financial implications of what is involved.
I have kept hens myself for the past decade, and in that time, I have dealt with a number of common problems. To use one of my own hens as an example of what sort of costs can be involved in a detailed investigation of illness:

Signs: Off food, not laying, fluffed up, swollen abdomen (Fig 2)

Consult:	€50
Bloods:	€60
Xrays:	€80
Ultrasound:	€170
Diagnosis:	Egg peritonitis
Result: euthanasia and disposal of body:	€50
Total cost as per normal pricing:	€410

Fig 2 Egg peritonitis

Pet vet clinics have an added discomfort in the situation because they are not familiar with dealing with sick hens, so they may lack confidence, and they may then feel that it is in some way unfair to charge appropriate fees for their work.

It may help to have a separate pricing structure designed for the backyard hen. Few owners will pay €50 for a hen that costs €15. Perhaps a way forwards would be to start with a consult fee that is affordable, and design a cost structure that includes the most likely scenarios. This can then be outlined to the owner before the hen is examined. An example cost structure could be:

1) Consult, advice only €25
2) Consult, mite investigation and treatment €60 (hen with feather loss)
3) Consult, blood samples, treatment €120 (sick hen)
4) Consult, blood samples, xrays, treatment €150 (very sick hen)
5) Consult, full post mortem examination, treatment €150 (sick hen in a flock)
6) Consultation, euthanasia, disposal of body €60 (very sick then ex-hen)

If you write down your basic estimated fees so that phone queries can be given this information before the hen is even brought to the clinic, this will avoid people being disappointed when they are presented with the reality further down the track.
Also, explain in advance the routine that will follow when they arrive at the clinic:

1) Ask client to bring hen in a large airy box or a cat carrier.
2) Stress that no sawdust or hay should be in box/carrier – just newspaper on floor. (avoids making a mess of consult room)
3) Leave the hen in the car when arrive at clinic.
4) Check in at reception.
5) Fill in a questionnaire before they see the vet (See Appendix).
6) Nurse will then hand questionnaire to vet while client in waiting room.
7) Vet can then read this before seeing the hen.
8) Hen can then be brought in.
9) Vet will carry out necessary examinations and investigations before reaching a diagnosis
10) Finally, treatment will be given.
    Warn that the whole process might take up to an hour for the owner.

This approach minimises the vet's time spent dealing with the sick hen, and hence keeps costs down to an affordable level.

Physical examination of a hen

To pick up a bird, have it facing towards you. Place both hands over its wings, then lift it, placing the bird under your left arm so that its head is under your armpit, facing backwards and its body is resting on your left forearm. Keep hold of both legs with your left hand, and keep the wings closed between your elbow and your body. You can then inspect the bird's body carefully, using your right hand. (If left-handed, do this the other way round). Examine the bird thoroughly all over, looking for dry nostrils, a red comb, bright eyes, shiny feathers with no bald areas, good muscle cover over the sternum, clean vent area, smooth skin on the legs, and healthy feet. Check for parasites: northern fowl mite and lice are easily seen, crawling through the feathers especially in the vent area. Remember that red mites do not live on the bird; the henhouse has to be checked to find these. Check the skin on the legs for the thickening and irregularity caused by scaly mites. Palpate the abdomen, feeling for unusual swellings. Check the rectal temperature (should be 40 – 42^{0}C). Open the mouth to check the back of the throat (for trichomonosis) and also to view the mucous membrane colour.

Diagnostic tests

The full range of diagnostic tests are available for hens just as for other species, but the cost is often prohibitive to hen owners.
Blood samples – The right jugular vein is often used, or in large birds, the medial metatarsal vein can be useful. (Fig3a and 3b) These same locations are also useful for euthanasia by intravenous injection. The ulnar vein on

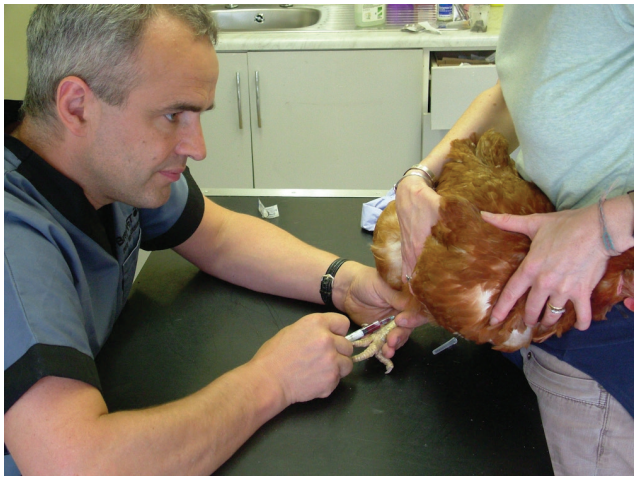

Fig 3a Collecting blood sample from medial metatarsal vein

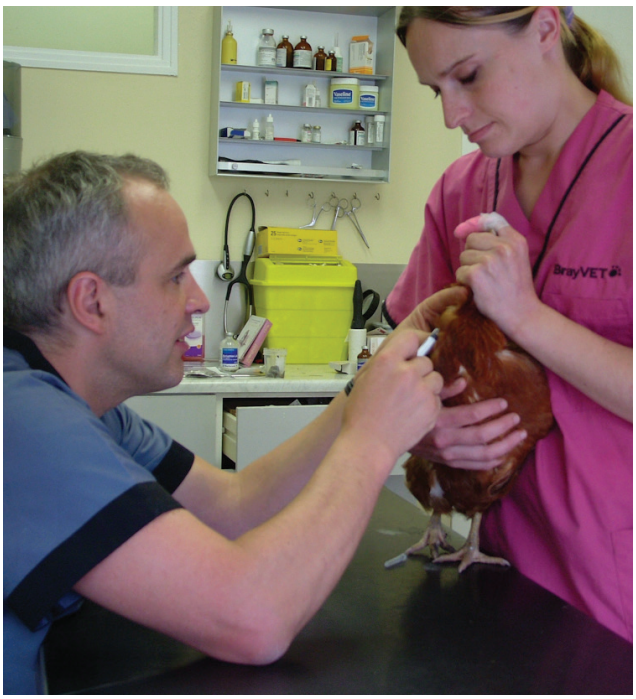

Fig 3b Collecting blood sample from right jugular vein

the wing can be used too but it's prone to developing haematomata.
Diagnostic imaging – Xrays and ultrasound can give useful information about conditions such as ascites, egg peritonitis or hepatomegaly. (Fig 4)
Endoscopy – This can be useful but is probably beyond the average general practitioner

Treatments

Treatment of back yard hens is complicated by several factors:

- Small numbers of birds. Many poultry medicines are designed for flocks of thousands of birds, so it can be difficult to organise treatment for half a dozen hens.
- Small number of licensed products. Those available in Ireland are listed in table one; each country in Europe will have a different range available. The use of unlicensed products should be avoided if possible, and needs to be done with care, following the cascade as usual.
- Egg withdrawal time. Many hen keepers depend on their birds for a regular egg supply, so it is important to be clear about withdrawal times following treatments

Further education in poultry medicine

A large veterinary team, based in Devon UK that supplies many commercial poultry producers

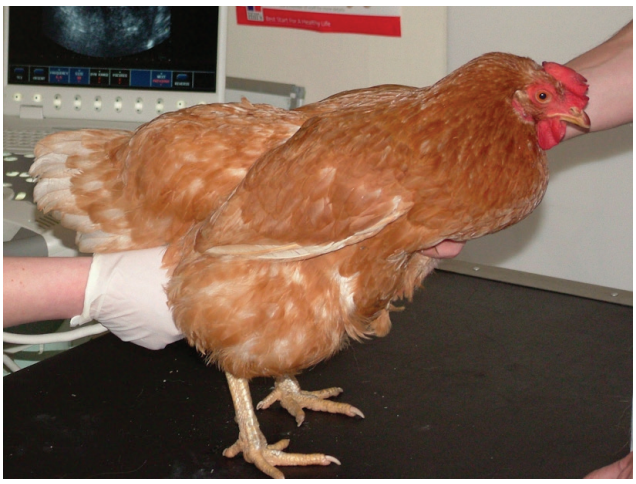

Fig 4 Ultrasound of hen

with veterinary care has recently branched out into assisting vets with the treatment of back yard hens. "Chicken Vet" was set up to handle the increasing numbers of queries from small animal vets and owners about sick chickens. Monthly CPD courses are organised for vets on chicken medicine for the backyarder. The website www.chickenvet.co.uk has useful disease information and an online shop which sells vitamins and red mite treatments. The Chicken Vet team writes monthly articles in a number of poultry magazines including Fancy Fowl.

Vets in general practice are offered training in poultry medicine on day courses, and they are then registered as "associated practices". For an annual subscription fee, ongoing support and domestic poultry veterinary advice is available. The company also provides poultry medication and vaccines to vets in the UKand this is currently under discussion for the Republic of Ireland.

Licensed drugs for poultry in Ireland

Hydrodoxx (Doxycycline)
Amoxinsol (Amoxicillin)
Denagard (Tiamulin)
Tylan (Tylosin)
Baycox (Toltrazuril)
Baytril (Enrofloxacin)
Apralan (Apramycin)

Common disease problems

1. Feather pecking. Missing feathers are a common problem in hens, and they may be caused by trauma from other hens or by external parasites. If hens are bored or overcrowded, or if there is social disruption (e.g. introduction of new hens to a flock), then they commonly peck each other, causing red, sore skin and bald areas. Once this starts, it can be difficult to stop. The provision of more living space, more greenery to peck and to entertain the birds, and areas for dust baths will all help.
   External parasites. There are a number of these, each requiring a specific approach
2. Northern Fowl Mite (*ornithonyssus sylviarum*). These small mites can be seen with the naked eye: they tend to cluster around the tail base. They cause irritation, baldness, and can cause anaemia if not controlled. Treat with insecticides.
3. Lice These cause skin irritation and baldness. They can be easily seen by visually inspecting the plumage, especially around the vent area. Treat with insecticides.
4. Scaly leg is characterized by the appearance of extensive, rough and hard crusts on the featherless part of the legs. Adult birds are generally affected: it is caused by *Cnemidocoptes mutans*. The lesions are secondary to an inflammatory reaction, with thickening of the skin and the production of an exudate, forming crusts and scabs on the legs. The mite spreads by contact between birds. Control by isolating affected birds, and bathing legs with warm acaricidal solution and warm vegetable oil. Ivermectin (off licence) is also sometimes recommended.(Fig5)

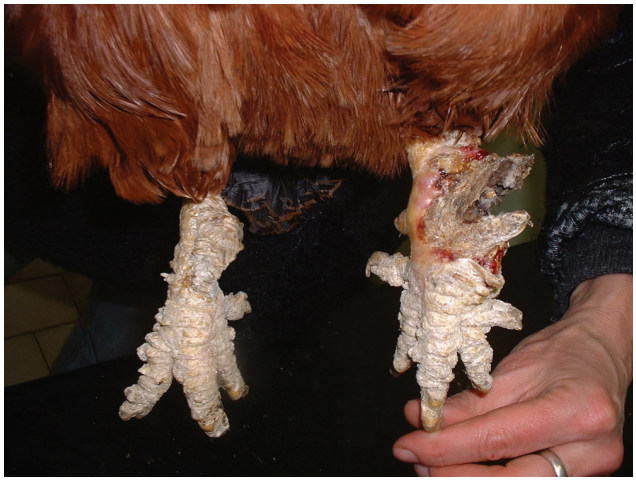

Fig 5 Severe case of scaly leg mite with secondary bacterial infection

5. Red mite An external parasite of chickens and turkeys which lives in the environment, but feeds by sucking blood from its host, causing both skin irritation and general ill thrift through anaemia (a pale comb and wattle may be noticed). Birds can become either restless or lethargic when heavily infested. Owners often notice a drop in egg production, with loss of condition from depressed feed intake. Can even cause death of young birds. Red mite is diagnosed by inspecting the perches in the hen house: if you look beneath the perches, you'll see clusters of the pinpoint sized red coloured mites.(Fig6) If you inspect the birds themselves at night, with a torch, you will often see the mites on their undersides. Treatment involves treating both the hens and the environment with insecticidal products. Thorough cleaning, fumigation and insecticide treatment between batches are essential to keep mites under control. Where there is a heavy infestation, regular repeat treatments may be necessary. Good henhouse design to eliminate cracks and crevices helps by reducing the places that mites can hide.

Fig 6 Red mite on the underside of a perch (turned on its side for the photo)

6. Internal parasites. Tapeworm, roundworms, capillaria, fluke and gapeworm may all be found, causing ill thrift, diarrhoea and other signs. Routine treatment twice a year with flubendazole (Solubenol) is recommended.
7. Impacted crop. Ingestion of tough, fibrous grass, foreign bodies or even feathers can cause the crop to become impacted. This can progress to "sour crop" due to yeast infection. Sometimes this can be resolved by manual manipulation and flushing with warm water, but often surgery is needed to remove the contents.

Fig 7a Egg peritonitis showing indentation of swollen abdomen

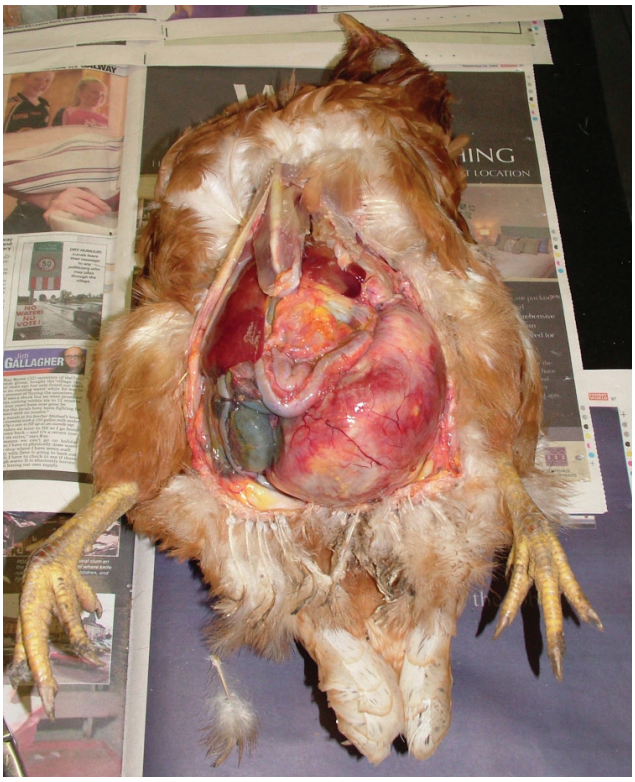

Fig 7b Gross autopsy of hen showing enlarged uterus full of purulent material

8. Oral canker or Trichomonas. This protozoa can be easily identified by examining the back of the throat: a white/pale yellow cheesy coating is seen here. Treated with metronidazole (unlicensed).
9. Egg peritonitis. At ovulation, the new egg yolk is released by the ovary, but instead of entering the infundibulum (oviduct) it passes into the abdominal cavity (like an ectopic pregnancy). Peritonitis follows, with abdominal distension and infection. Treatment using antibiotics and non steroidal anti-inflammatory medication can be given, but the prognosis is poor.(Fig 7a and7b)
10. Cloacal prolapse. Similar to vaginal prolapse, the vent can turn "inside out" due to poor muscle tone in this area. An egg is often inside the prolapsed vent: the hen has been straining to try to release this. The egg should be broken and removed, and the prolapse should be cleaned, coated with lubricant and returned. A purse string suture may be placed, but due to the likelihood of recurrence, such birds are often culled.
11. Respiratory disease. Hens often develop a syndrome known as a "cold", with coughing, sneezing, and runny eyes/nose. There's often an underlying environmental stress (poor ventilation, crowding etc). There may be a primary viral cause (see below) with secondary bacterial infection, so antibiotics are often helpful.
12. Infectious coryza or "cold". Caused by *Haemophilus paragallinarum*. Signs include dyspnoea and swollen eyelids. Responds to treatment with antibiotics e.g. enrofloxacin. (In UK chickens are specifically excluded from being treated with enrofloxacin – see relevant data sheets.)
13. Infectious bronchitis. Caused by a coronavirus that starts in the respiratory tract, moving to the reproductive tract. May start with respiratory signs which resolve, then followed with reproductive disease such as mis-shapen eggs or shell-less eggs. There is no treatment but a vaccine may be given.
14. *Mycoplasma Gallisepticum* is a common, highly infectious cause of nasal discharge and swollen sinuses. There is usually a foul, sickly sweet odour around the head. Treatment involves Tylosin (Tylan Soluble: Elanco). Carriers are common, and prevention includes a thorough disinfection routine, as well as good husbandry to minimise stress.
15. Mareks Disease. A herpesvirus, signs include lameness in young hens, followed by the development of tumours. This is common in certain breeds, and the history is especially important. Infection is transmitted via feather dander, so keeping adults and young birds separate is important. A vaccine is available but if this is initiated, it needs to be continued with each new batch, indefinitely.

16. Zoonoses include Campylobacter, Salmonella, and Chlamydophilia. It's important to stress the need for good human hygiene, including handwashing after handling hens.
17. Coccidiosis. A common disease causing poor performance and mortality. Characteristic signs include ruffled feathers and a hunched posture. It is spread by litter/droppings from affected birds, equipment, humans, wild birds/animals and poor hygiene. Diagnosis can be made from faeces samples or by post mortem examination.
18. Avian Influenza and Newcastle Disease. These notifiable diseases tend to cause large numbers of depressed, sick and dying birds with respiratory signs including discharge from eyes and nostrils, open mouth breathing and high fever.
19. Poor egg quality. Small, misshapen, cracked or soft or shell-less eggs may be seen from time to time.

Useful websites

Discussions of poultry diseases and husbandry, both for poultry owners and for vets:

http://www.chickenvet.co.uk
http://www.backyardchickens.com
http://www.thepoultrysite.com
http://www.bhwt.co.uk
http://www.poultryclub.org
http://www.vetark.co.uk

Further reading

Victoria Roberts (Editor), Freda Scott-Park (Editor), BSAVA Manual of Farm Pets (Paperback) published by The British Small Animal Veterinary Association (15 Feb 2008)
Jeremy Hobson and Celia Lewis, Keeping Chickens" - published by David and Charles, 2007

Appendix

Hen questionaire

a) Flock

Number of birds?
Breed?
Age?
When and where they were acquired?
Any new birds recently?
Type of housing?
Type of run?
Type of bedding?
How often cleaned out?
Access to free range?
Type of food?
How is water offered?
Any abnormal behaviours recently?
Any changes to hens' set up recently?
How many eggs are laid by group?
Have external parasites been treated?
Have internal parasites been treated?
Any other treatments given?

b) Sick hen

When was illness first noticed?
What are the main signs of illness?
Is she eating normally?
Describe the following for the sick bird:
Nostrils – dry or discharge? If so, describe
Comb – red or pale?
Eyes – open/bright or dull/closed?
Weight – normal or thin?
Feathers – clean and shiny or dull and dirty?
Any bald areas?
Appearance of area around vent?
Appearance of lower legs ("shanks")?
Appearance of feet/ toes?

Will you be prepared to sacrifice this bird for an autopsy in order to make an accurate diagnosis for the rest of the flock?

REPRINT PAPER (RU)

Diagnosis and treatment of canine and feline liver tumours: a study of 40 cases.

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SUMMARY

Objective - To determine the clinical & pathological findings, outcome, and prognostic factors in dogs and cats treated surgically and with local ablative therapies for primary and metastatic liver tumours.

Methods - Medical records were examined for diagnostic and surgical findings, and postoperative outcomes. The patients were treated surgically. In the case of multiple liver lesions a combination of lobe resection and other local techniques were undertaken, including sclerotherapy and cryotherapy. Data was analysed to identify prognostic factors and determine and compare rates of tumour control and survival time.

Results – 40 dogs and cats were treated surgically or with combination of surgery and ethanol injections and/or cryosurgery. The most important prognostic factors were tumour sizes larger than 5 cm and the number of the affected liver lobes. Of the 24 patients which received ethanol injections and/or cryosurgery, local tumour recurrence was not observed in any case, confirmed by histological evaluation of liver tissue samples one month after treatment

Clinical Significance - A combination of surgery and ablative treatment procedures is recommended for animals with multiple liver tumours to minimize the operation extent and avoid local recurrence.

Key words Liver, tumours, cats, dogs, cryosurgery, ethanol injection

This paper originally appeared in:
The Proceedings of the 65th SCIVAC Rimini International Congress, Rimini, 28th-30th May 2010

Introduction

Tumours affecting the liver can be either primary or metastatic. Primary liver tumours are uncommon and account for 0.6% to 1.3% of all canine liver tumours and 1.0% to 2.9% of all feline liver tumours[12,14,16,18]. According to the data of various authors, metastatic lesions of the liver are 2,5 – 30 times more common than primary liver tumours[5,7,10,18]. The liver is a common metastatic site for mammary carcinoma, primary cancers of the spleen, ovary and gastrointestinal tract[5]. The liver is also often involved in other malignant processes, such as lymphoma[7].

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Hepatobiliary tumours are asymptomatic until the tumour affects 70% of cells[15,16]. Physical examination findings can be equally unrewarding. To make the diagnosis of a liver tumour as well as to clarify the tumour stage and define treatment tactics, the use of ancillary diagnostic tests is essential[1,17].

Surgery is considered to be the optimal treatment modality for liver tumours in small animal practice[2,6,9]. Not many tumours however can be surgically treated because of multifocal diseases. In human medicine most of surgically-ineligible patients have to receive a combination of surgery and interventional treatments (e.g. cryotherapy, percutaneous ethanol injection, local ablation, chemoembolization)[11,19]. This combination can improve the survival rate of patients with multifocal hepatobiliary tumours[1,3,15].

The aim of this study was to document the clinical and pathological findings in 40 consecutive cases of spontaneous canine and feline liver tumours which underwent surgical resections and local ablative therapies. Specifically, we sought to examine the usefulness of the diagnostic tools available at the time of the case study which were used to establish the diagnosis. The objective was also to determine the outcome in dogs and cats treated with combination of surgery and other interventional managements for liver tumours and compare survival times of either unilateral or multifocal liver tumours.

Materials and Methods

A study was undertaken which included all dogs and cats with primary and metastatic liver tumours which were presented to the veterinary clinic «Biocontrol» during the period from January 2002 till June 2009.

Criteria for inclusion in the study were:

1) Primary or metastatic liver tumours confirmed by use of open surgery and histopathological confirmation.
2) Sufficient data available from medical records.
3) Surgical resection and/or local treatment modalities (sclerotherapy, cryotherapy)
4) At least 6 month follow-up of surviving cases.

From the records, 40 cases were suitable for inclusion in the study.

For all animals in the study, breed, gender, age, and clinical signs at initial evaluation were reviewed. A thorough clinical examination was performed for each case, including inappetence, weight loss, lethargy, vomiting, polydipsia/polyuria, hair condition, eyes (colour of the sclera and mucous membranes). The presence of palpable liver tumour was also noted. Preoperative diagnostic tests included a complete blood cell count, serum biochemical profile, coagulation profile, thoracic and abdominal radiography and abdominal ultrasound.

Radiography and ultrasonography imaging techniques were used for the diagnosis, staging, and surgical planning of cats and dogs with liver tumours. Thoracic radiography in the right lateral projection was performed for assessing lung metastasis. Abdominal radiographs (right lateral and dorsoventral projection) were also performed.

Abdominal ultrasonography was used to differentiate between liver tumours in solid tumour masses and cysts, haemangiomas and malignant tumours in the abdominal cavity. Pre- and intraoperative ultrasound (DC6 – Mindrey; a 6.5-8 MHz convex transducer) was performed by an interventional radiologist, who noted the exact size (maximum diameter), number, and location of all tumour nodules. An ultrasound-guided biopsy was undertaken using spinal needles (Spinocan 25 Gx and 16G Tru-cut). The surgery reports were reviewed for liver lobe involvement, size of the tumour, evidence of local extension and metastatic disease, resection technique, and intraoperative complications such as blood loss and death. The liver lobe affected by the tumour was recorded as either, left, central, or right. Tumour size was determined from the surgery report.

In cases with one or two affected liver lobes, we performed lobectomy or marginal excision of liver. We performed an original surgical approach to the liver, described elsewhere[16]. The liver was approached by midline laparotomy. We performed a lateral laparotomy incision from the xiphoid process, along the caudal rib. Resection of the falciform ligament of the liver was undertaken. We exposed the affected part and placed two ligatures.

In cases with multiple liver lesions, a combination of lobe resection and other local ablative techniques was undertaken, including sclerotherapy and cryotherapy. Sclerotherapy was made with 95% ethanol via a 21-gauge needle under ultrasonographic guidance in summary dosage of 0.5 ml/kg body weight (fig. 1). Cryotherapy protocol included two freeze-thaw cycles for 15 minutes each procedure (fig. 2).

Fig.1. Ethanol injection into a hepatocellular carcinoma of a dog showing the needle penetrating liver parenchyma

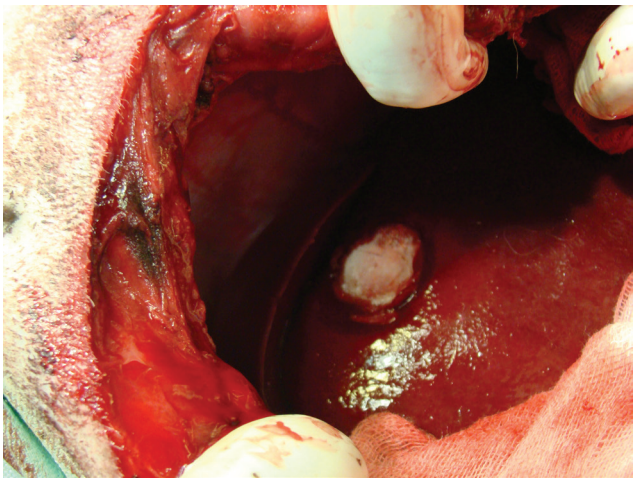

Fig.2. Liver tumour after the cryotherapy procedure. Complete resection of this tumour was not possible due to multiple liver lobe involvement.

Liver tissue samples were submitted for microscopic examination. The tumour sections were stained with haematoxylin/eosin. All cases were reviewed by a single pathologist.

Data were analyzed to determine and compare rates of tumour control and survival time. Median survival time was calculated from the time of surgery to death or termination of the study period. Survival time was explored using the Kaplan–Meier product-limit method followed by log-rank test to compare survival after surgical resection of a primary liver tumour or metastatic liver tumour, and also survival in animal with 1-2 affected lobes or multiple lobe diseases.

Results

Epidemiology

During the period, liver tumours were histologically confirmed in 40 dogs and cats after laparotomy. Of the 40 cases, 5 (12.5%) were cats and 35 (87.5%) were dogs. The mean age at presentation for dogs was 8.6 years (range, 7 to 14 years), and for cats 14.3 years (range, 8 to 16 years).

A wide variety of dog breeds was presented. 22 purebred dogs representing 10 different breeds were affected; mixed breeds accounted for 37% of cases. Of the 5 cats, all were domestic shorthaired. Most dogs with liver tumours were medium-sized dogs with a mean bodyweight of 19.4 kg (range, 6 to 54 kg). Cats presented with liver tumours had a mean bodyweight of 3.4 kg (range, 3 to 4 kg).

A sex predisposition has not been confirmed in dogs and cats with primary liver tumors in our study. The ratio between males and females with primary tumours is approximately 1:1, whereas male:female ratio for metastatic liver tumors was 1:6.

Diagnostic results

Palpation of the liver revealed a mass in 20/40 cases (50%). Abdominal radiographs, abdominal ultrasound and 1-view thoracic radiographs were obtained in all patients. A cranial abdominal mass was identified in 23% of dogs that were radiographed. A hepatic mass was detected in 40/40 cases during abdominal ultrasonography. 21/40 cases (52.5%) had one or two affected liver lobes and 19/40 cases (47.5%) had three or more affected lobes.

Surgery

35 dogs and 5 cats underwent surgery (table 1). A mass was visible in 38/40 cases (95%) of neoplasia. In 2/40 cases, the tumours were detected using intraoperative ultrasound(IOUS). In 9 patients IOUS findings differed from preoperative data: in 6 patients IOUS identified more metastatic lesions, whereas in 3 cases we did not confirm the presence of the tumour identified during the preoperative ultrasound. Additional information on the localization of the hepatic lesions was gathered by IOUS and changed the surgical treatment in 9 cases.

The side of liver involvement was recorded in all cases; the left liver lobe was affected in 32/40 (80%) cases, the central and right liver lobes were affected in 3/40 (7.5%) and 5/40 (12.5%) cases, respectively.

Histology

Histopathological features of the liver tumours were consistent in all 40 dogs and cats. Surgical margins were assessed in all animals and incomplete resection was not

Table 1: Treatment regimes performed in dogs and cats with benign and malignant liver tumours depending on the number of affected liver lobes.

Treatment	Malignant				Benign	
	Primary		Metastatic			
	1-2 lobes affected	>2 lobes affected	1-2 lobes affected	>2 lobes affected	1-2 lobes affected	>2 lobes affected
Lobectomy	3(7.5%)	0	10(25%)	0	3(7.5%)	0
Combination of lobectomy and local ablative therapies	0	10(25%)	0	5(12.5%)	0	4(10%)
Local ablative therapies	1(2.5%)	1(2.5%)	2(5%)	1(2.5%)	0	0

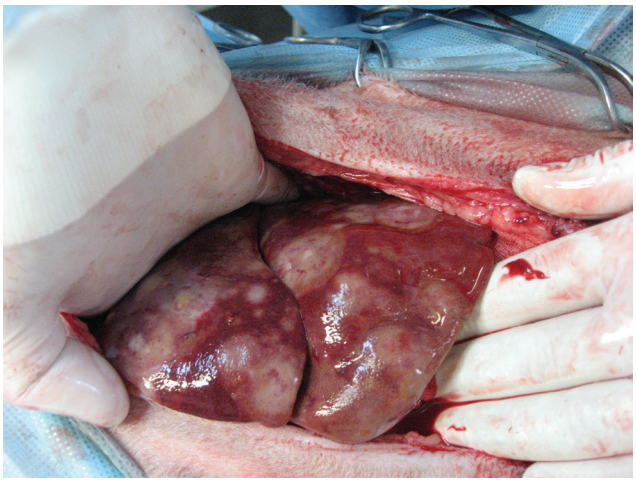

Fig.3. Hepatocellular carcinoma

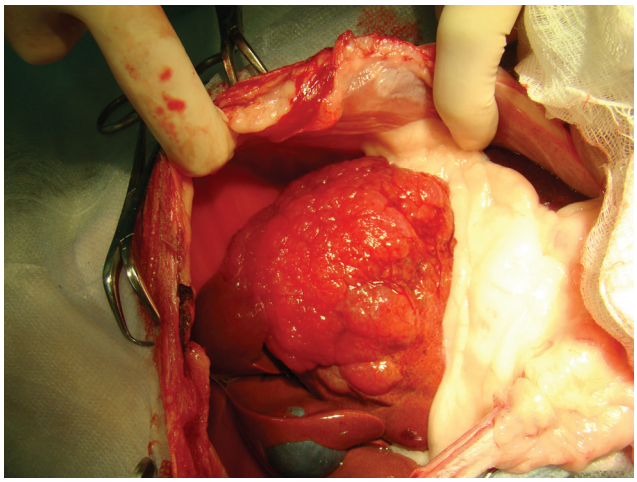

Fig.4. Liver haemangioma

detected in any case.

Primary liver tumours were diagnosed in 22/40 cases (55.0%), and ofthese 7 (17.5%) were benign and 15 (37.5%) were malignant. Amongst the primary malignant liver tumours hepatocellular carcinoma was the prevalent histological type (fig.3), which accounted for 11 of 40 (27.5%) tumours. Four haemangiomas (fig.4), two cholangiocarcinomas and one fibrosarcoma (fig.5) accounted for 5.0% and 2.5% of tumours, respectively. One (2.5%) liver tumour showed mixed morphological features. From the 22 primary tumours 9/22 (40.9%) were localized in 1 or 2 liver lobes, and 13/22 (59.1%) affected 3 or more liver lobes.

From the 18 metastatic lesions (45.0%), metastatic mammary adenocarcinoma was the most prevalent histological type (fig.6), accounting for 7/40 cases (17.5%) (table 2). In our study metastatic lesions more frequently affected 1 or 2 liver lobes (12/18). 6/18 (33.3%) metastatic tumours affected more than 2 liver lobes.

Complications

Major haemorrhage was the most severe complication occurring in 5/40 (12.5%) operations. In 4/40 (10%)

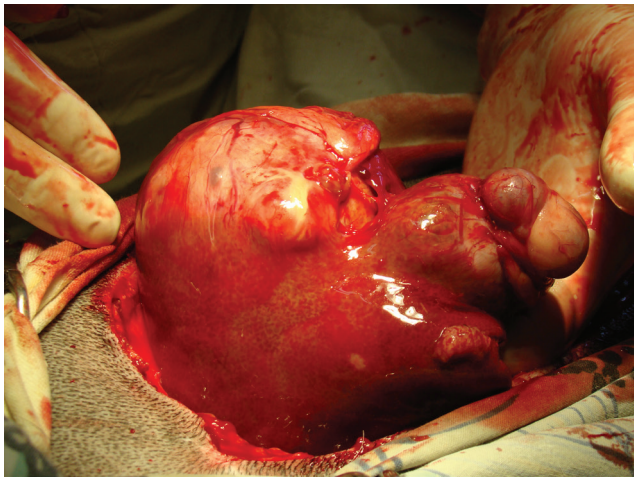

Fig.5. Primary liver fibrosarcoma

cases the bleeding was stopped intraoperatively. In one case (2.5%) we had to make a second laparotomy within several hours. Two animals (5%) died on day one after the operation as a result of the extensive bleeding. The operative mortality rate was 5%.

Follow-up examination revealed anorexia, vomiting, and diarrhoea in 21/40 cases (52.5%) caused by hepatic insufficiency. In 3 cases these symptoms were revealed during preoperative examination. In three cases (7.5%) chronic kidney insufficiency was diagnosed preoperatively

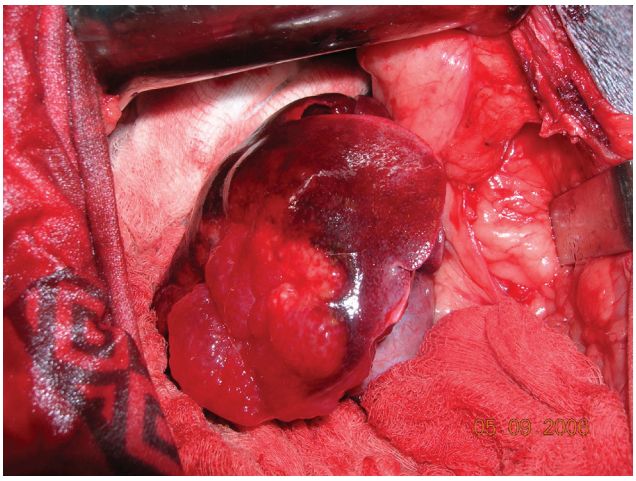

Fig.6. Liver metastases of a mammary carcinoma

Table 2: Histopathology findings in dogs and cats with liver tumours (n=40)

Histological type	Number of dogs (%)	Number of cats (%)
Primary		
Benign		
Haemangioma	4(10%)	3(7.5%)
Malignant		
Hepatocellular carcinoma	11(27.5%)	
Bile duct carcinoma	2(5.0%)	
Fibrosarcoma	1(2.5%)	
Mixed tumour	1(2.5%)	
Metastatic		
Mammary carcinoma	7(17.5%)	2(5.0%)
Ovarian carcinoma	4(10%)	
Endometrial carcinoma	1(2.5%)	
Renal cell carcinoma	1(2.5%)	
Soft tissue sarcoma	2(5%)	
Spleen fibrosarcoma	1(2.5%)	

which progressed after operative treatment in one case leading to fatal outcome 8 days after surgery.

Postoperative follow-up

The patients were monitored on days 1, 7 & 30 after operation. Follow-up examination included physical examination, complete blood cell count and serum biochemical profile.

In 6/40 cases we performed a second operation after 30 days for exploration and repetition of local treatment. Tissue samples were taken by laparoscopy or percutaneous biopsy from those tumours treated with ethanol and nitrous oxide. Samples were submitted for microscopic examination to estimate the histological response to the treatment.

Prognosis

At the conclusion of the study period, 7 dogs and 3 cats were still alive, whereas the remaining 30 had died.

21 (70%) deaths were tumour related, including two intraoperative deaths (5%). The most common metastatic site was the lungs, observed in 18/21 patients. From the ten survivors 8 have no evidence of local recurrence or distant metastases at 72, 90, 111, 120, 240, 540, 720, and 870 days. At the conclusion of the study period two survivors had lung metastases.

To evaluate risk factors, associated with poorer prognosis in animal with liver tumours, we compared information from the medical records.

We found no significant association between MST (mean survival time) in animals with primary (n=22) and metastatic (n=18) liver tumours The MST for primary tumours was 255 days (range, 35 to 870 days) in comparison to 420 days (range, 105 to 740 days) for metastatic liver tumours.

To evaluate the association between the tumour size and survival, we divided all animals in two groups: Group 1 (n=22) with tumour size <5cm, and Group 2 (n=18) with liver tumour size more than 5 cm. With Kaplan – Meier analysis, in Group 1 the MST was 717 days (range, 27 to 212 days). In comparison, the MST for dogs in Group 2 was 262 days (range, 34 to 200 days)(Table 3). Dogs in Group 1 had significantly (p= 0.002) longer MST than dogs in Group 2.

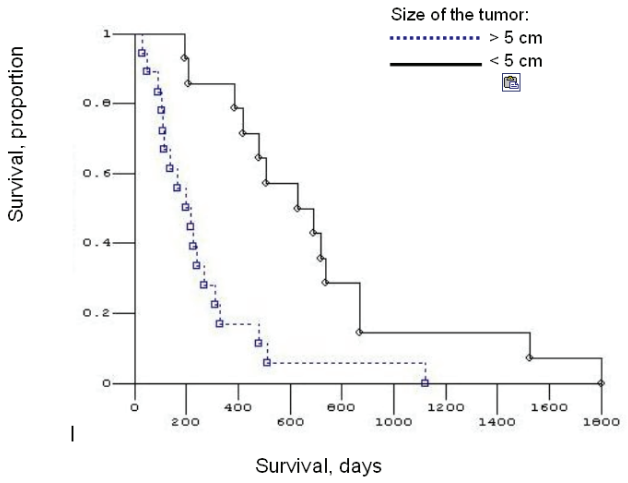

Table 3: Kaplan-Meier diagram for overall survival of dogs and cats with liver tumours depending on the size of the tumour: group (n=22) with tumour less than 5 cm versus group (n=18) with tumour size more than 5 cm.

We also found a significant association between MST and number of affected liver lobes ($p<0.001$). In the group (n=21) with one or two affected lobes the calculated MST was 722 days (range, 105 to 1800 days). In comparison, animals with multifocal tumours involving more than 2 liver lobes (n=19) had a MST for 200 days (range, 30 to 480 days).

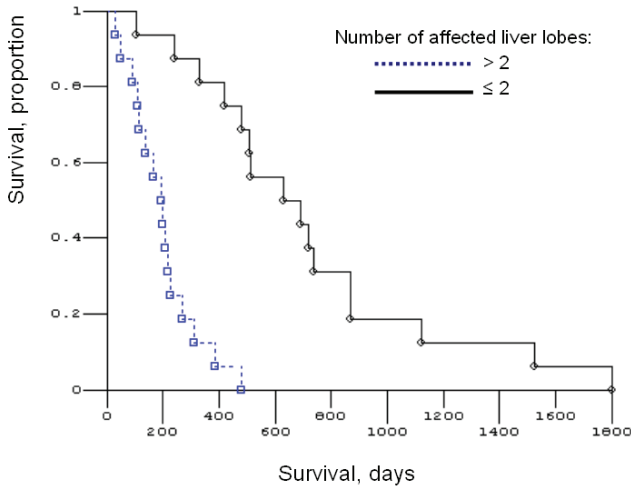

Table 4: Kaplan-Meier survival curves illustrating the prognostic differences in patients (n=21) with 1 to 2 liver lobes affected and more than two affected lobes (n=18).

Discussion

In order to characterize canine and feline primary and metastatic liver tumours, we studied 40 cases, in which surgery alone or in combination with local techniques was performed.

Left-sided liver lobes were involved in 80% of dogs and cats, with central and right-sided liver lobes less frequently affected. The predilection of hepatocellular carcinoma for left liver lobes has been reported earlier by Martin[10]. We found a male predilection for metastatic liver tumours, reported earlier[7]. In our study a tumour mass was palpable in 50% of cats and dogs. Palpation can be misleading since hepatic enlargement may be absent in nodular and diffuse forms of liver tumour and confusing in case of adipose animals.

Despite improvement in preoperative imaging technology, the intraoperative use of ultrasonography remains of crucial importance in human oncology liver surgery. The detection of preoperatively unknown lesions remains high with great consequence on surgical therapy[13]. In our study intraoperative ultrasound was carried out both for lesion characterization and new nodule detection. It has been shown that intraoperative ultrasound (IOUS) is the most accurate diagnostic technique for detecting focal liver lesions and has a great impact on the surgical approach to liver tumours.

Surgery is considered to be an optimal treatment modality for liver tumours in small animal practice[2,6,9]. However, surgery has limited application in cases of multifocal diseases. In human medicine patients with surgically-ineligible tumours have to receive a combination of surgery and interventional treatments, including cryosurgery and ethanol injections[19]. Cryosurgical ablation has been in use in human medicine since the 1960s and liquid nitrogen is primarily used for hepatic tumour ablation[11]. In small animal practice cryosurgery has been used successfully to treat various cancers, including skin and prostate cancer[4,8]. Individual sources used cryosurgery for treatment of liver tumours[20]. The application of the local methods of intervention on a liver tumour alone or in combination with part resection of the liver can be used to eradicate tumours while minimizing the loss of functioning hepatic tissue that is inevitable with surgical resection. In our study, of the 24 patients receiving local ablation of liver tumours, local recurrence of the tumour was not observed in any case during the follow-up operation or laparoscopy one month after treatment. This was confirmed by histological examination. We suggest that a combination of surgery and interventional treatments (cryotherapy, ethanol injections) can be indicated for dogs and cats with multifocal liver disease to achieve tumour tissue necrosis and avoid local recurrence

We found no association between prognosis and metastatic or primary origin of the hepatobiliary tumours. In our study there was a significant association between median survival time and the tumour nodule size ($p= 0.002$). We also found a significant association between MST and cases with more than two affected liver lobes ($p<0.001$).

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REPRINT PAPER# (B)

Dysplastic elbow diseases in dogs

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SUMMARY

Elbow dysplasia (ED) is a term used to describe the most common causes of elbow lameness. It consists out of ununited anconeal process (UAP), fragmented coronoid process (FCP), osteochondritis dissecans (OCD) and elbow incongruity, according to the International Elbow Working Group (IEWG). All conditions are polygenic and multi-factorial diseases that often occur in young popular breeds. Elbow incongruity has been suggested as a causative factor in most of these pathologies.

The aim of this review is to describe the aetiology and clinical appearance on radiography, computed tomography (CT) and arthroscopy, together with their treatment options and prognosis.

This paper originally appeared in:
*Vlaams Diergen Tijds. 2011 Sept-Oct;80(**5**)*:327-38.*

Introduction

Elbow pathology is a frequent cause of lameness and osteoarthritis in young, rapidly growing, large and giant breed dogs [1-3]. The most common causes of elbow lameness are incorporated under the term elbow dysplasia [4].

Up till 1974 no distinction was made between the different types of osteoarthritis in the elbow joint. It was believed that every degenerative joint disease (DJD) in the elbow was caused by an ununited anconeal process. This theory was abandoned when severe cartilage damage on the medial part of the humeral condyle was reported caused by a loosely attached fragment of the medial coronoid process of the ulna [5, 6].

More reports on other causes of DJD were made and in 1975 fragmented coronoid process and osteochondritis dissecans were attributed to osteochondrosis, a group of disorders caused by a disturbed endochondral ossification of the growth cartilage [6].

The term elbow dysplasia was introduced in the mid 80's. Several studies tried to find the underlying cause of the three conditions mentioned above and suggested an underlying mechanical stress or malarticulation of the elbow joint that was causing the fragmentation [6-8]. One histomorphometric study has reported on microfracture (fatigue microdamage) in the medial coronoid process as the initiating event for fragmentation [9]. Elbow incongruity is often mentioned as a causal factor for elbow fragmentation although vast evidence that incongruity is always present upon fragmentation can not be found [3, 10-13].

Nowadays elbow dysplasia is known as a polygenic and multifactorial condition often diagnosed in Labrador retrievers, Golden retrievers, Rottweilers, German shepherds and Bernese mountain dogs and refers to UAP, FCP, OCD, or elbow incongruity [14-16]. Some authors also include incomplete ossification of the humeral condyle [17, 18] and medial compartment disease [19], but this review is confined to the conditions described by the IEWG. The clinical signs usually start at the age of four to eight months [16] although adult dogs and atypical breeds can also be affected [20, 21].

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* Presented by SAVAB (B)
# Part of this work was presented as an abstract

The diagnosis of elbow dysplasia results from several investigations. Clinical examination is of great value since muscle atrophy, joint pain, joint effusion and decreased range of motion can indicate the localization of the problem [16]. Based on the initial clinical examination, additional imaging techniques, such as radiography, CT or arthroscopy can be performed.

Radiography is the most commonly used screening technique to diagnose elbow dysplasia. The standard projections are a mediolateral extended and flexed projection combined with a 15° oblique craniomedial-caudolateral projection [4]. Unfortunately, radiography is not always sufficient to detect the lesions, especially in cases of FCP [12, 22-24]. CT and arthroscopy can help in the diagnosis of elbow dysplasia since both techniques allow a better visualization of the joint structures. CT provides detailed information on the bony structures of the elbow without superimposition [25]. Arthroscopy allows direct inspection of the joint cartilage and can simultaneously be used to treat the dysplastic elbow [1, 26, 27]. An early diagnosis is not only required to solve the lameness but also to improve the long term outcome [28, 29]. The aim of this paper is to give an overview of the pathophysiology, diagnosis, treatment and prognosis of every condition classified under elbow dysplasia.

Anatomy of the Elbow Joint

The elbow joint is a complex, accurately matching joint formed by the distal part of the humerus and the proximal part of the radius and ulna (Figure 1) [30]. The elbow is designed for flexion and extension, although limited pronation and supination are permitted. The lateral part of the humeral condyle is in contact with the radial head, while the medial part is supported by the medial coronoid process. Previously, the radial head was considered the major weight bearing structure in the joint [31] but more recent studies have shown that the weight is almost equally divided between the radial head and the medial coronoid process of the ulna [32].
The incisura trochlearis of the ulna bends around the humeral condyle, and restricts the caudal movement of the humerus. When extending the elbow, the processus anconeus is locked into the foramen supratrochlear of the humerus, and contributes to the lateromedial stability.
The radial head is enclosed by both the medial and the lateral coronoid processes and the connecting annular ligament. Because of its size and position, the medial coronoid process is more vulnerable to damage than the lateral coronoid process (Figure 2).
The medial and lateral collateral ligaments are, together with the annular ligament, the most important soft tissue structures for elbow stability.

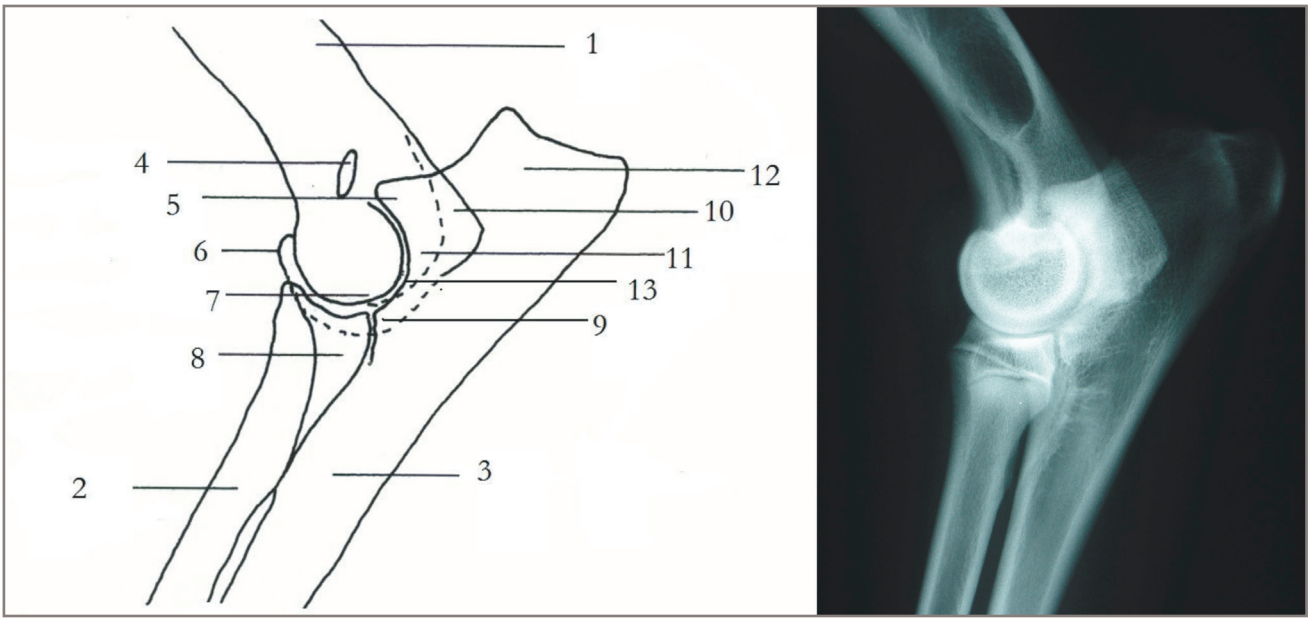

Figure 1. Schematic drawing and radiographic anatomy of the elbow (lateral position). 1. Humerus, 2. Radius, 3. Ulna, 4. Supratrochlear foramen, 5. Anconeal process, 6. Medial part of the humeral condyle (trochlea), 7. Lateral part of the humeral condyle (capitulum), 8. Medial coronoid process, 9. Lateral coronoid process, 10. Medial epicondyle, 11. Lateral epicondyle, 12. Olecranon, 13. Incisura trochlearis or trochlear notch of the ulna [30].

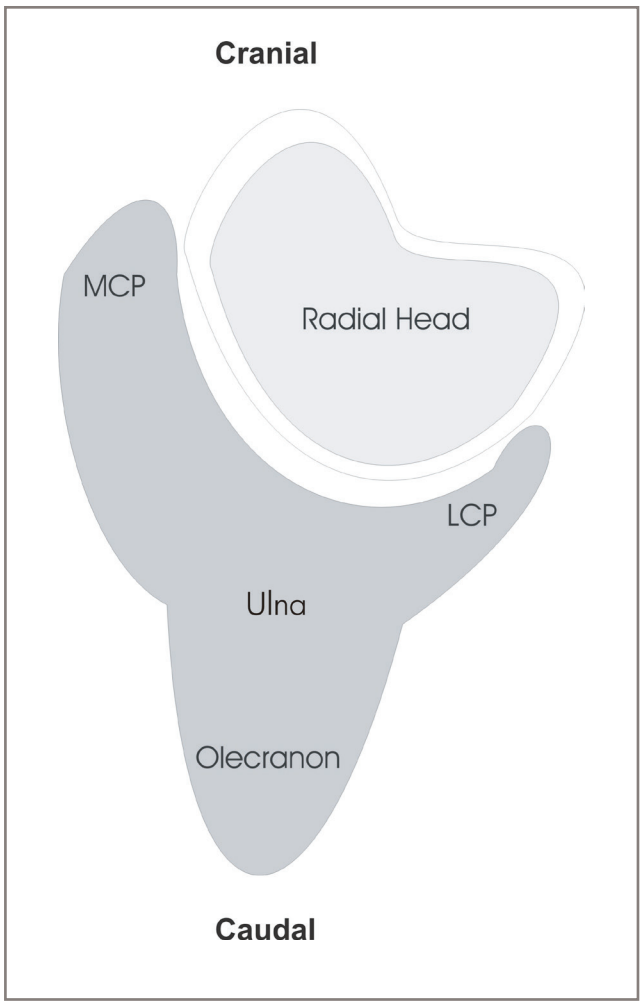

Figure 2. Schematic cross section of radius and ulna. MCP and LCP respectively stand for medial and lateral coronoid process.

Ununited anconeal process

Aetiology

In large dogs the anconeal process is either formed as a direct extension of the proximal ulnar growth centre or originates from a separate ossification centre formed between eleven and twelve weeks of age [33, 34]. In breeds that have a separate ossification centre, such as the German shepherd and chondrodystrophic breeds, fusion with the ulna occurs at approximately five months, therefore a UAP should never be diagnosed before that age [31, 33]. Greyhounds should have full fusion at fifteen weeks. When there is no radiographic fusion at twenty weeks (or fifteen weeks in Greyhounds), the finding is pathologic and is called an ununited anconeal process [35, 36]. A more recent study demonstrated that a separate ossification centre also occurs in some medium to large breed dogs without being correlated to the development of UAP. This might allow an earlier diagnosis of UAP [37]. Ununited anconeal process was the first elbow pathology which was generally believed to induce elbow osteoarthritis [6]. Although the exact aetiology of the disease is still unknown, a multifactorial cause is proposed. Trauma, metabolic and genetic disorders are believed to have influence on the occurrence of UAP [7, 8, 36]. The main cause, however, is a short ulna which causes stress on the anconeal process. German shepherd dogs are known to have the highest incidence of UAP [36, 38]. A recent breed susceptibility study however, has shown that the Labrador and Golden retrievers run an equal risk or even higher risk of developing UAP [39].

Clinical signs

Affected dogs are often presented between two and nine months of age with uni- or bilateral fore limb lameness [31, 33]. Since bilateral lesions occur in up to 47% of cases both elbows should be clinically and radiographically examined [40, 41]. Clinical examination reveals a painful, distended elbow. Crepitation is frequently present with flexion or extension of the involved joints. Due to pain and/or osteoarthritis, a decreased range of motion (ROM) can be detected [31, 36].
Although UAP is a developmental problem, adult dogs can also be affected without any history of lameness at an early age. Signs are most frequently seen around the age of seven years and are often associated with trauma or heavy exercise. This suggests that young dogs may suffer from a subclinical form of UAP [33].

Radiographic findings

In most cases a latero-medial radiograph of the flexed elbow is diagnostic [40]. In cases of a non-displaced detached or ununited anconeal process, a fracture line is visible. The fragment may also be displaced proximally. Secondary osteoarthritis is present in most cases (Figure 3).

CT findings

CT adds information about the displacement of the fragment, lesions of the medial coronoid process and the severity of incongruity [25]. The best location to diagnose an ununited anconeal process on CT is the proximal part of the incissura trochlearis (trochlear notch) on transverse slices and on sagittal reconstructions through the centre of the notch (Figure 4).

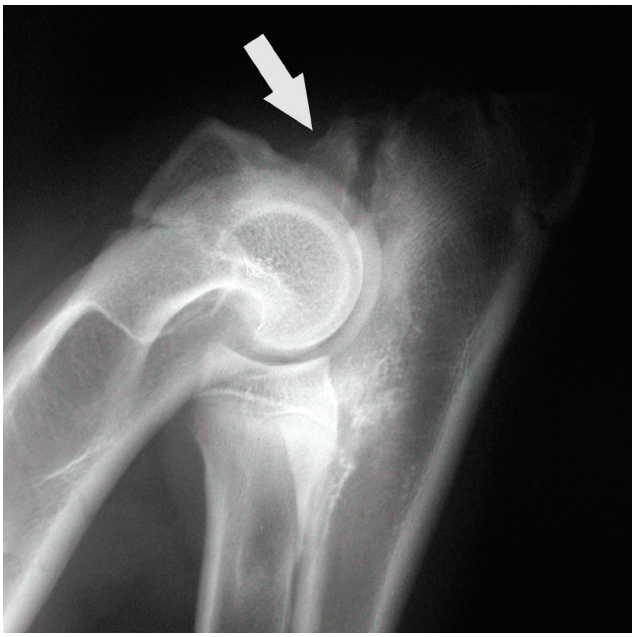

Figure 3. Radiographic features of a UAP in a young dog. The fragment is indicated by the arrow. In this early case there is slight osteoarthritis.

Arthroscopic findings

Arthroscopy can be performed using a medial approach [1]. Arthroscopic examination of an affected joint reveals a detached fragment in the proximal part of the trochlear notch. Additionally, erosions on the condyle of the humerus can be seen and concomitant lesions of the medial coronoid process can be diagnosed (Figure 5).

Treatment

Treatment is either conservative or surgical. When the clinical signs are minimal, a conservative treatment with rest and NSAID's can be proposed [33]. In all other cases surgical treatment is advised. Several techniques have been described, such as fixation with a lag screw, removal of the anconeal process and a proximal ulnotomy [28, 31, 33]. In young dogs, a dynamic proximal ulnar osteotomy combined with fragment fixation yields the best results.

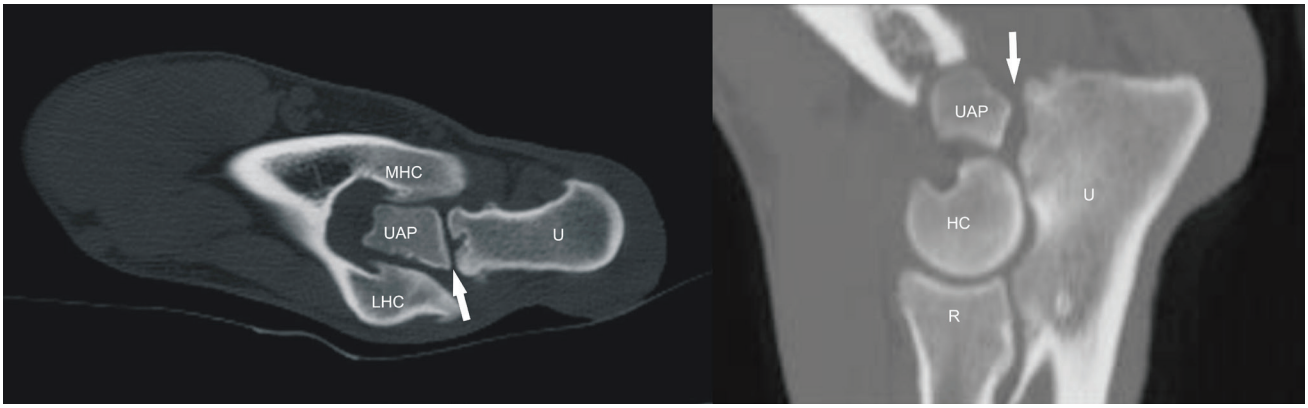

Figure 4. Transverse (left) and sagittal reconstruction CT images of an elbow affected with ununited anconeal process (UAP). The white arrow indicates the fragmentation line.
HC= Humeral condyle, MHC= Medial part of the humeral condyle, LHC= Lateral part of the humeral condyle, UAP= Ununited anconeal process (fragment), U= Ulna, R= Radius.

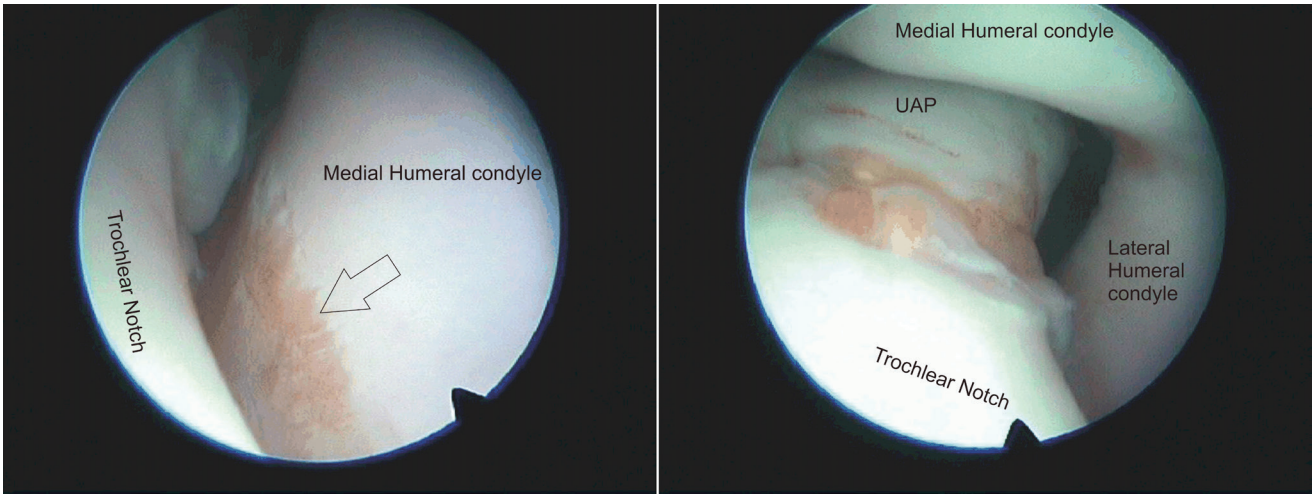

Figure 5. Arthroscopic images of an elbow with UAP. The left image shows erosion on the medial part of the humeral condyle (transparent arrow). The right image shows the fragmentation line (red region) of the anconeal process. The detached fragment is located proximally (UAP).

In adult dogs, the fragment is removed via arthrotomy or arthroscopy [42]. Prognosis is good to guarded because of subsequent joint instability and secondary osteoarthritis [31, 33].

Fragmented medial coronoid process

Aetiology

FCP is the most common disorder of the elbow dysplasia complex [1, 6, 31]. Unlike the anconeal process the medial coronoid process never has a separate ossification centre. The exact aetiology is not yet fully understood but genetics, trauma, metabolic factors, exercise and nutrition play an important role in the development of a fragmented coronoid process [9, 10, 36]. Before the age of five months, the coronoid process consists of cartilage which slowly ossifies from base to tip [6]. It is believed that, as a part of the osteochondrosis complex, the lesion starts in the cartilage and later extends to the bone. Due to a defect in the cartilage ossification, chondromalacia occurs, which leads to fissures and fragmentation in the cartilage and underlying bone [6, 16, 31].
The current belief is that (temporary) radio-ulnar incongruity causes an increased pressure on the immature medial coronoid process resulting in microfractures and fragmentation [7, 9, 13, 28, 36]. In smaller breed dogs, the ossification process is completed earlier than in large dogs. This may explain why FCP more often occurs in large rather than small breed dogs [36]. Often affected breeds are Basset hounds, Bernese mountain dogs, Bouvier des Flandres, bullmastiffs, Chow chows, German shepherd dogs, Golden retrievers, Gordon setters, Irish wolfhounds, Labrador retrievers, mastiffs, Newfoundlands, Rottweilers and Saint Bernards [39].

Clinical signs

Dogs affected with FCP are most frequently presented with lameness between the ages of seven and nine months. Some dogs (between four and five months old) suffer from "morning stiffness". This early lameness is often temporary and may be falsely considered as "growing pains" [16]. In a recent study however, 12% of the presented dogs were 6 years or older [20]. These dogs may have been chronically lame, but most of them had a history of recent lameness. The review demonstrated that the lesions were similar to those of young dogs except for the high prevalence of extensive cartilage erosions (medial compartment disease). A typical feature on clinical examination is the mild abduction of the affected front limb(s). Lameness varies from subtle to very severe [6] and palpation shows a variety of joint distension, pain and a decreased range of motion [43].

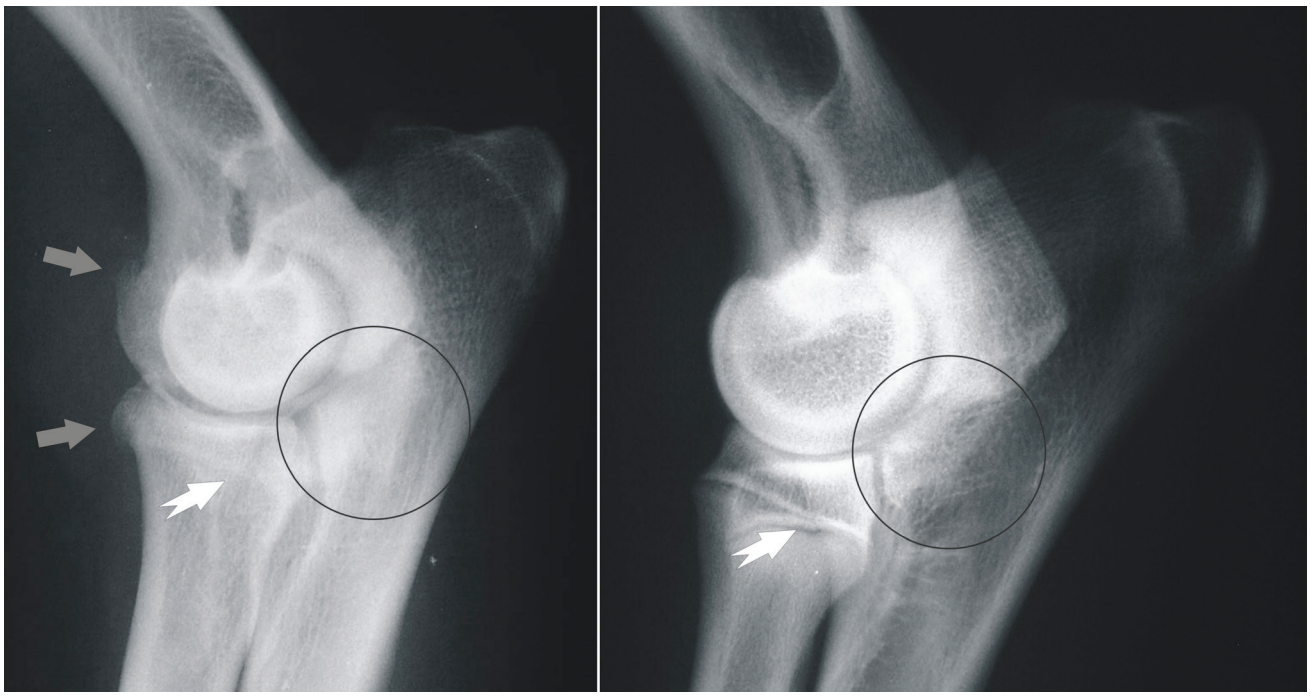

Figure 6. Radiographic features of FCP in the affected and normal elbow. Left image shows an elbow affected with FCP. The white arrow indicates an irregular, blurred shape. A fracture line and fragment are visible above the arrow. The grey arrows show osteoarthritic changes on the cranial border of the radial head and distal humerus. On the right image the white arrow indicates a sharply delineated coronoid process. No osteoarthritis is present .The circles demonstrate obvious sclerosis in the affected elbow (left), while no sclerosis is visible in the normal joint (right).

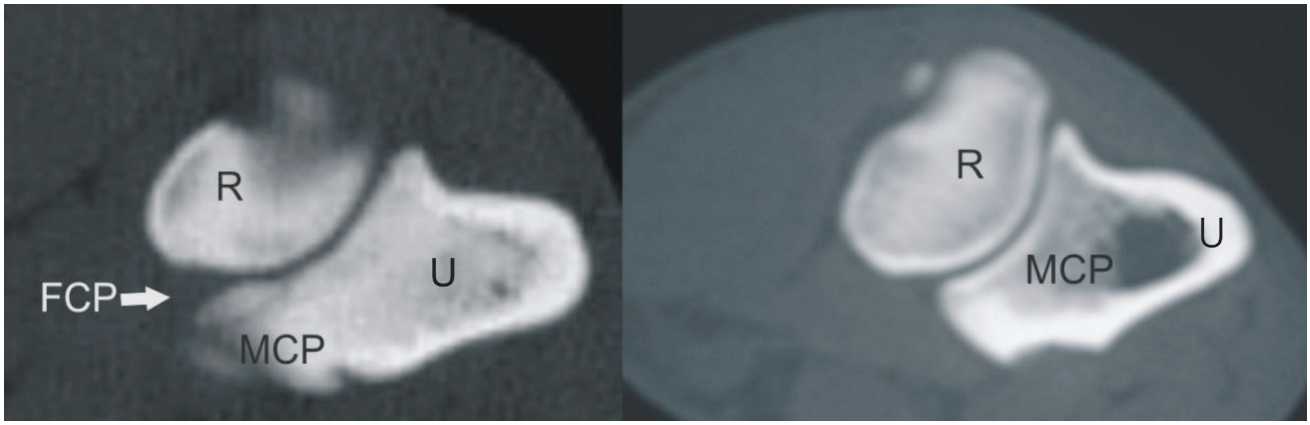

Figure 7. Fragmentation of the medial coronoid process seen on CT. The left image shows an elbow with FCP. The white arrow indicates the detached fragment. The right image shows a normal elbow. R= Radius, U= Ulna, MCP= medial coronoid process, FCP= fragmented coronoid process

Radiographic findings

Radiographic evaluation of the medial coronoid process is often challenging and should be based on high quality mediolateral extended, mediolateral flexed and 15° oblique craniomedial-caudolateral views [24]. The primary lesion is often not visible because of the superimposition of the medial coronoid on the radial head [16, 43, 44]. Primary and secondary changes can be subtle and thus diagnosis can be missed on plain radiographs [21].

Typical radiographic abnormalities are subtrochlear sclerosis of the trochlear notch of the ulna [45], unsharp delineation of the proximal aspect of the medial coronoid process and secondary osteoarthritis [44] (Figure 6). A recent study has demonstrated that subtrochlear sclerosis is a good indication for the medial coronoid process pathology in the Labrador retriever but is believed to be too unreliable for routine use [45, 46].

Radiography is often insufficient to reach a conclusive diagnosis requiring further examination with CT or arthroscopy [1, 44].

CT findings

CT scan is considered superior for diagnosing FCP [47, 48]. With the dog positioned in lateral recumbency, both elbows can be easily assessed simultaneously. In this way, the medial coronoid process can be evaluated without superimposition of the bony structures [25] (Figure 7).

Arthroscopic findings

Arthroscopy allows a direct and detailed inspection of the medial coronoid process. Different types of fragmentation and cartilage lesions of the medial coronoid process can be identified and kissing lesions or concomitant OCD of the medial part of the humeral condyle can be demonstrated [1] (Figure 8).

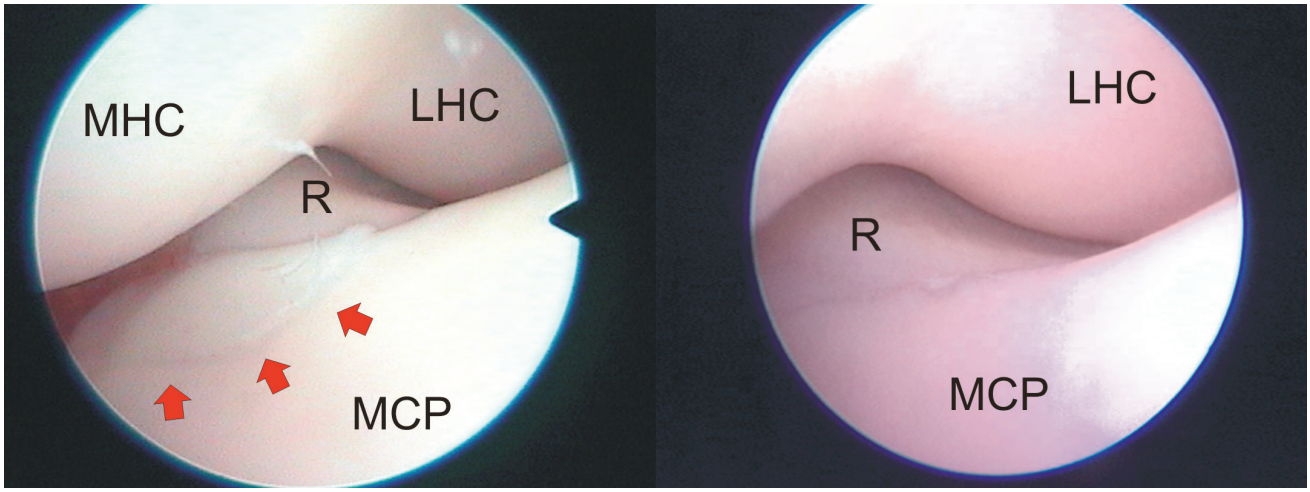

Figure 8. Arthroscopic image of an elbow joint affected with FCP (left) and a normal elbow (right). The red arrows indicate the fragmentation. MHC= medial part of the humeral condyle; LHC= lateral part of the humeral condyle; R= radial head; MCP= medial coronoid process of the ulna

Treatment

In mild cases, conservative treatment with rest and NSAID's and nutroceuticals can be considered [49]. In all other cases, surgical treatment is advised. Treatment consists of the removal of the loose fragment(s). A clinical improvement in 90% of the patients is to be expected when using arthroscopy. When using arthrotomy, only 72 % of the cases show clinical improvement [50, 51]. Fragment removal can be performed via arthrotomy, but arthroscopy is the preferred technique [1, 16, 49, 52]. Surgery performed at a young age yields better results than conservative treatment [53].

Osteochondritis dissecans

Aetiology

The exact aetiology of OCD remains unclear but a combination of genetics, age, increased birth weight, sex, breed, rate of growth and nutritional factors could influence the expression of the condition [41, 54]. OCD of the elbow is a common orthopaedic condition consisting of localized cartilage detachment of the medial part of the humeral condyle in juvenile dogs [55]. In at least 12% of cases it appears simultaneously with FCP [41, 48].
Most likely OCD is caused by a disturbed endochondral ossification [54, 56] (Figure 9), leading to cartilage retention and the formation of a flap. In some cases the flap tends to ossify [6, 16, 31]. Because of its location, it's not always easy to differentiate an OCD lesion from a kissing lesion [6]. Breeds with a high susceptibility are Chow chows, German shepherd dogs, Golden retrievers, Great Danes, Labrador retrievers, Newfoundlands and Rottweilers [39].

Clinical signs

Clinical signs are very similar to those of FCP [6, 16].
Radiographic findings
OCD lesions are diagnosed on a 15° craniomedial-caudolateral oblique (pronated) view. The lesion appears from the age of five to six months as a small, flattened, or concave radiolucent lesion on the medial part of the humeral condyle [57] (Figure 10). Osteoarthritis or a sclerotic rim surrounding the lesion can be visible [6, 16]. A mediolateral projection can show a flattening of the caudal part of the humeral trochlea [16]. When OCD is accompanied by FCP, radiographic changes of the medial coronoid process can also be present.

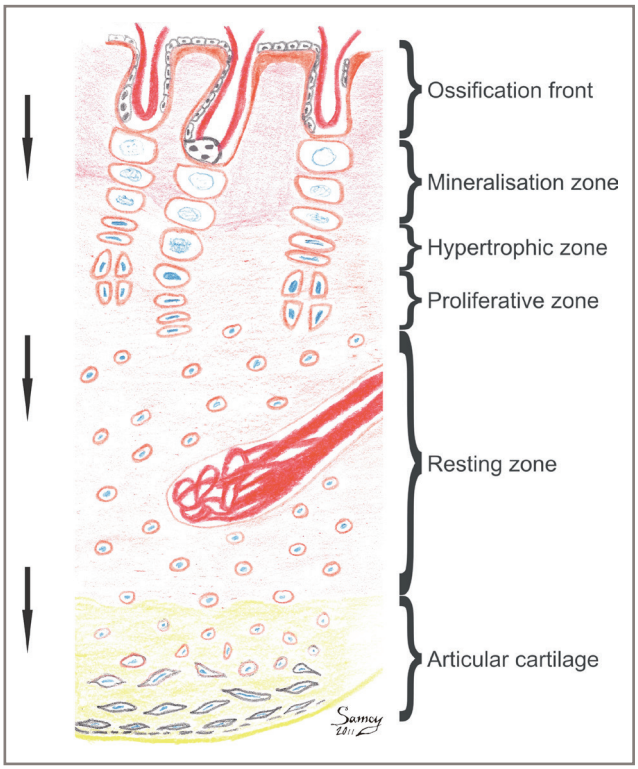

Figure 9. Schematic drawing of endochondral ossification. Cartilage formation occurs in the direction of the arrows. In the immature animal, the invasion of cartilage by blood vessels is necessary to provide a normal endochondral ossification. A disruption of this blood flow leads to a disturbed ossification and eventually to an OCD lesion.

CT findings

The OCD lesion is characterized by a sclerotic area surrounding a region with diminished opacity on the (medial) humeral condyle. [58] (Figure 11).

Arthroscopic findings

Arthroscopy allows the detection of the flap and simultaneous treatment [1, 51, 52, 59] .The localized pathologic cartilage of the medial part of the humeral condyle can still be attached, or partially or fully detached [1] (Figure 12).

Treatment

In cases where only small lesions are visible a conservative treatment might be considered. In all other cases, surgical removal of the flap is advised, preferably via arthroscopy [1, 16, 31, 49]. Since OCD and FCP tend to occur together, a thorough inspection of the joint is advised when treating one of both lesions [41]. Although only limited information is available on long-term

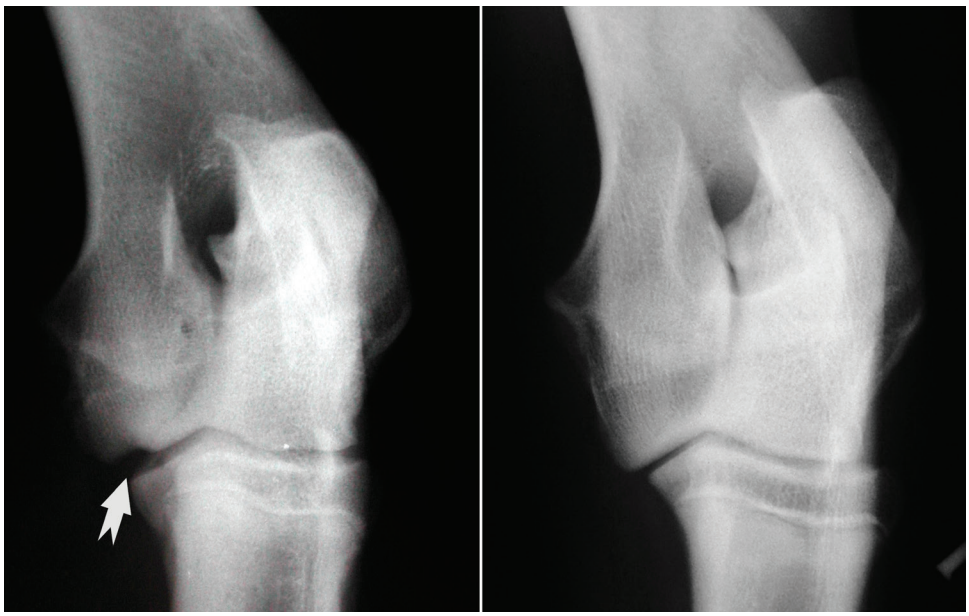

Figure 10. Radiographic features of elbow OCD. The left radiograph shows an elbow affected with OCD. The arrow indicates the defect caused by an OCD lesion. The right radiograph is a normal elbow.

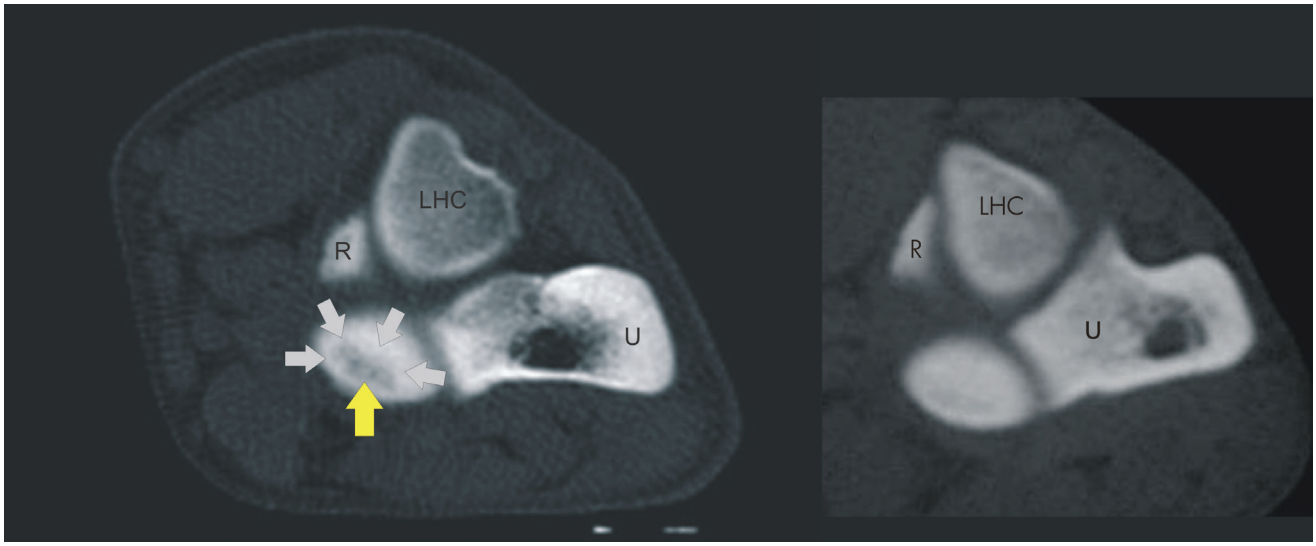

Figure 11. CT image of an elbow affected with OCD on the medial part of the humeral condyle. The white arrows indicate the sclerotic region around the OCD lesion. The yellow arrow shows the OCD lesion. The right image is a normal elbow joint. LHC= lateral part of the humeral condyle, R= radial head, U= ulna.

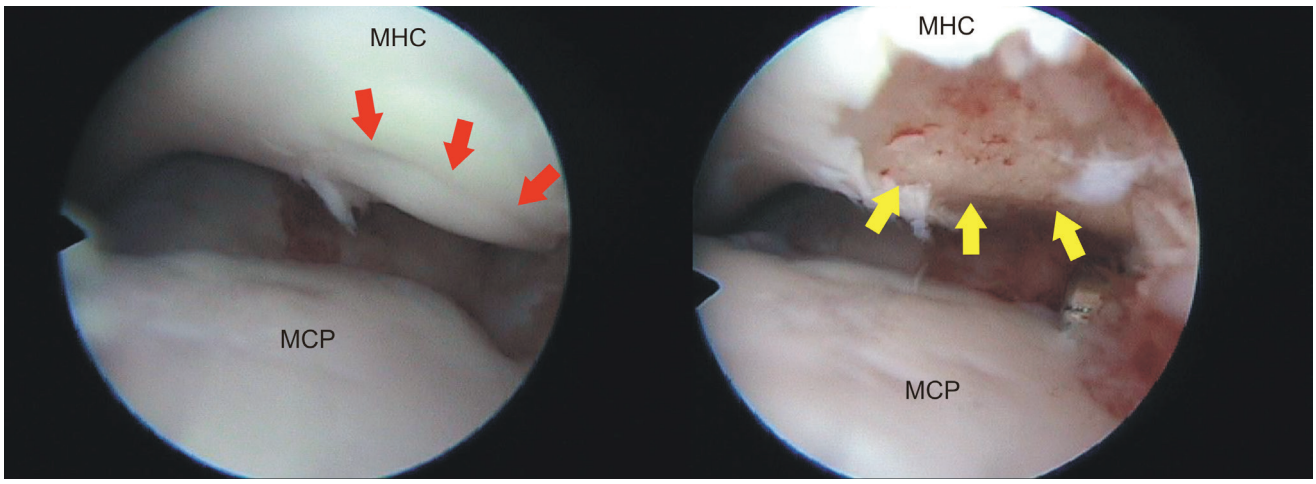

Figure 12. Arthoscopic images of an elbow affected with OCD. The red arrows on the left image indicate the location of the cartilage flap. The yellow arrows on the right image show the region after arthroscopic cartilage flap removal. Notice the petechial bleedings in the subchondral bone on the right image after curretage.
MCP= medial coronoid process, MHC= medial part of the humeral condyle.

treatment results of elbow OCD, the prognosis can be considered good if early diagnosis and treatment are performed [60, 61].

Elbow Incongruity

Aetiology

The exact impact of elbow incongruity is not yet fully understood. In both human and canine cases, reports have been made on physiological incongruity to optimise stress distribution in the fully loaded joint [10, 62, 63]. Two pathological types of incongruity have been described. The first is called short radius or short ulna incongruity and is caused by a disturbed growth of the distal ulnar or radial growth plate due to trauma or metabolic disorders. This leads to a short radius or short ulna. In some cases, severe limb deformity develops together with valgus or varus and severe elbow and carpal deformation [30, 64] The second type of incongruity is the malformed elliptic shape of the trochlear notch of the ulna, which is caused by a difference in growth rate between the proximal part of the ulna and the humeral condyle. The slower growth of the proximal ulna results in a smaller trochlear notch that impinges on the humeral trochlea. This last condition is often seen in the Bernese mountain dogs [7, 8]. Incongruity is visible from the age of four to six months [65].

Clinical signs

Because of the frequent concurrent finding of other forms of elbow dysplasia (FCP, UAP, OCD), it is impossible to link lameness uniquely to elbow incongruity. The clinical signs are similar to the ones in other types of dysplastic elbows: lameness, joint distension, pain and muscle atrophy. The degree of incongruity also plays a role in the nature of this lameness. Severe incongruity is more likely to cause radiographic changes than milder forms [30, 65].

Radiographic signs

Although incongruity is not always easy to detect radiographically[22, 32], four typical features have been described on the standard mediolateral extended and craniocaudal projections: a radioulnar step, an elliptic shape of the trochlear notch, an increased humeroulnar and humeroradial space and a cranial displacement of the humeral condyle [7] (Figure 13).
The correlation between the severity of the incongruity and the degree of secondary osteoarthritis is good [66].

CT findings

Several signs for incongruity have been described on CT [10, 67, 68]. The most frequently seen features are shown in Figure 14.

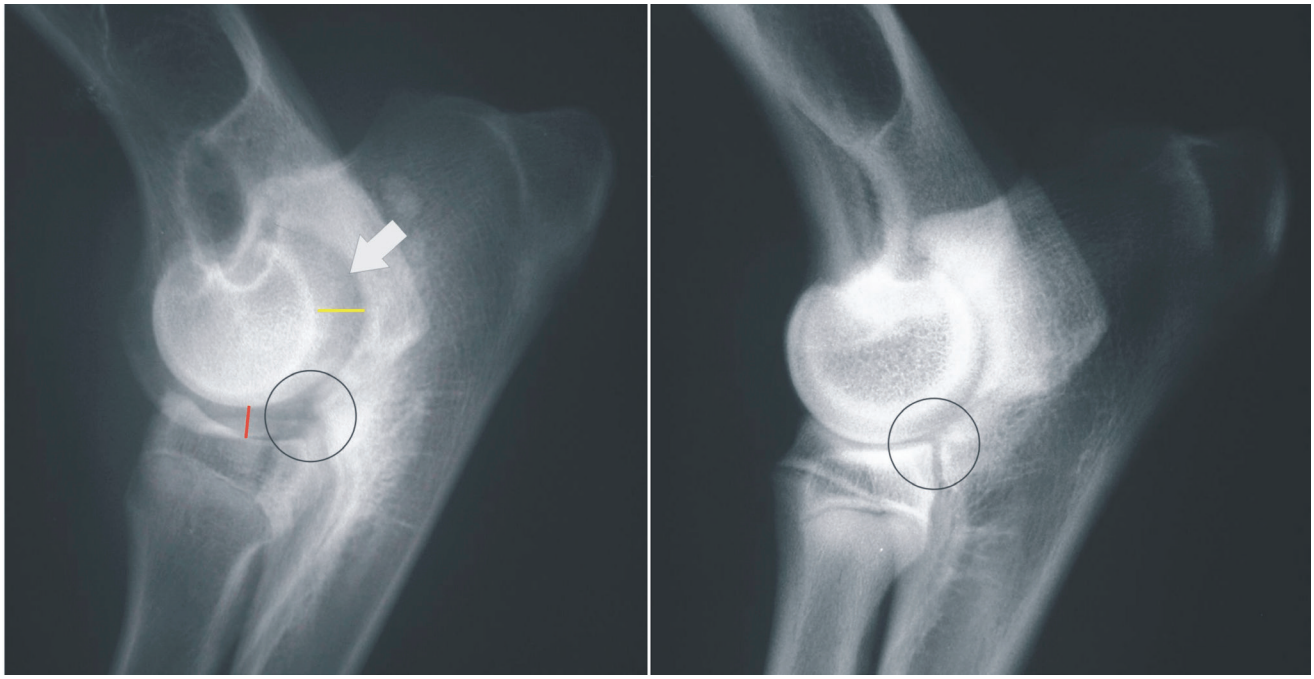

Figure 13. Radiographic features of elbow incongruity. The left image shows a severely incongruent elbow joint. The white arrow indicates the increased humero-ulnar joint space and the elliptic shape of the trochlear notch. The circle indicates a clear step between the distal border of the ulna and the radial head. Cranial displacement of the humeral condyle is seen as the relative position of the condyle to the radius and ulna. The yellow line indicates widening of the humero-ulnar joint space. The red line demonstrates the widening of the humeroradial joint space. The right image shows a normal elbow joint.

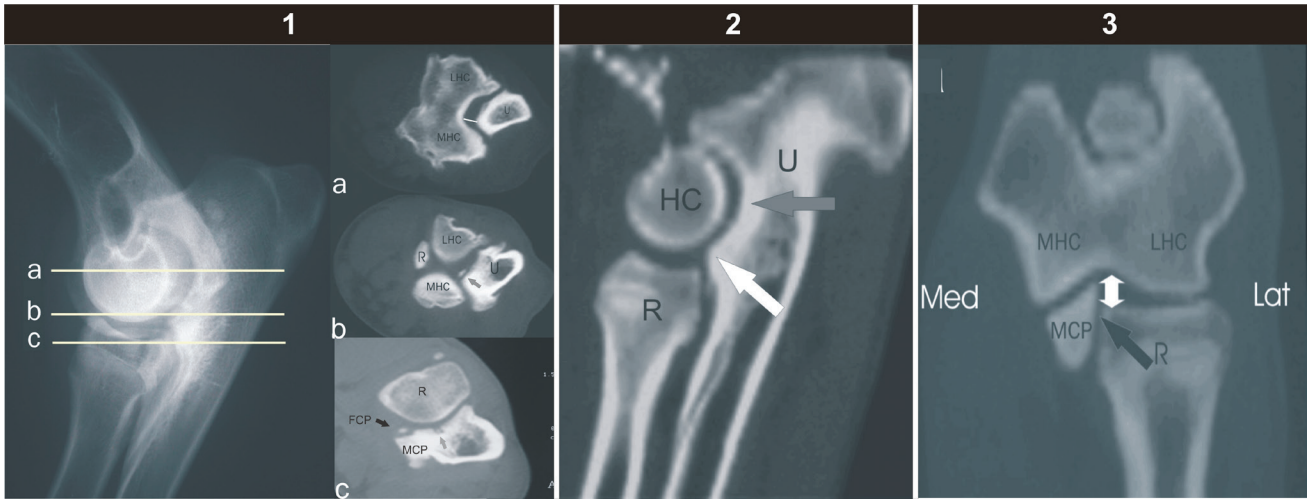

Figure 14. Location and comparison of the transverse (left), sagittal reconstruction (middle) and dorsal reconstruction (right) CT images in an incongruent elbow. The X-ray on the far left shows the level of the corresponding CT images [68].

Transverse slices
Level a. Slice through the humeral condyle(s) (lateral = LHC, medial = MHC) and the trochlear notch of the ulna (U). The white line indicates the widened joint space between the humerus and the ulna where the measurement was made.
Level b. Transverse slice through the distal part of the trochlear notch. At this level, the proximal part of the radial head (R) is visualised. Fragmentation is indicated by the arrow.
Level c. Slice through the medial coronoid process (MCP) and the radial head (R). This view shows the radio-ulnar transition and visualises the fragmented coronoid process (FCP) (black and white arrows) and the pseudocystic lesion (grey arrow).

Sagittal reconstruction
The white arrow shows the step between radius and ulna. The black arrow indicates the widened joint space between the humerus and the trochlear notch. Also note the widening of the humero-radial joint space.

Dorsal reconstruction
The black arrow indicates the step between the radius and the medial coronoid process. The double white arrow shows the abnormal medial humeroradial joint space.

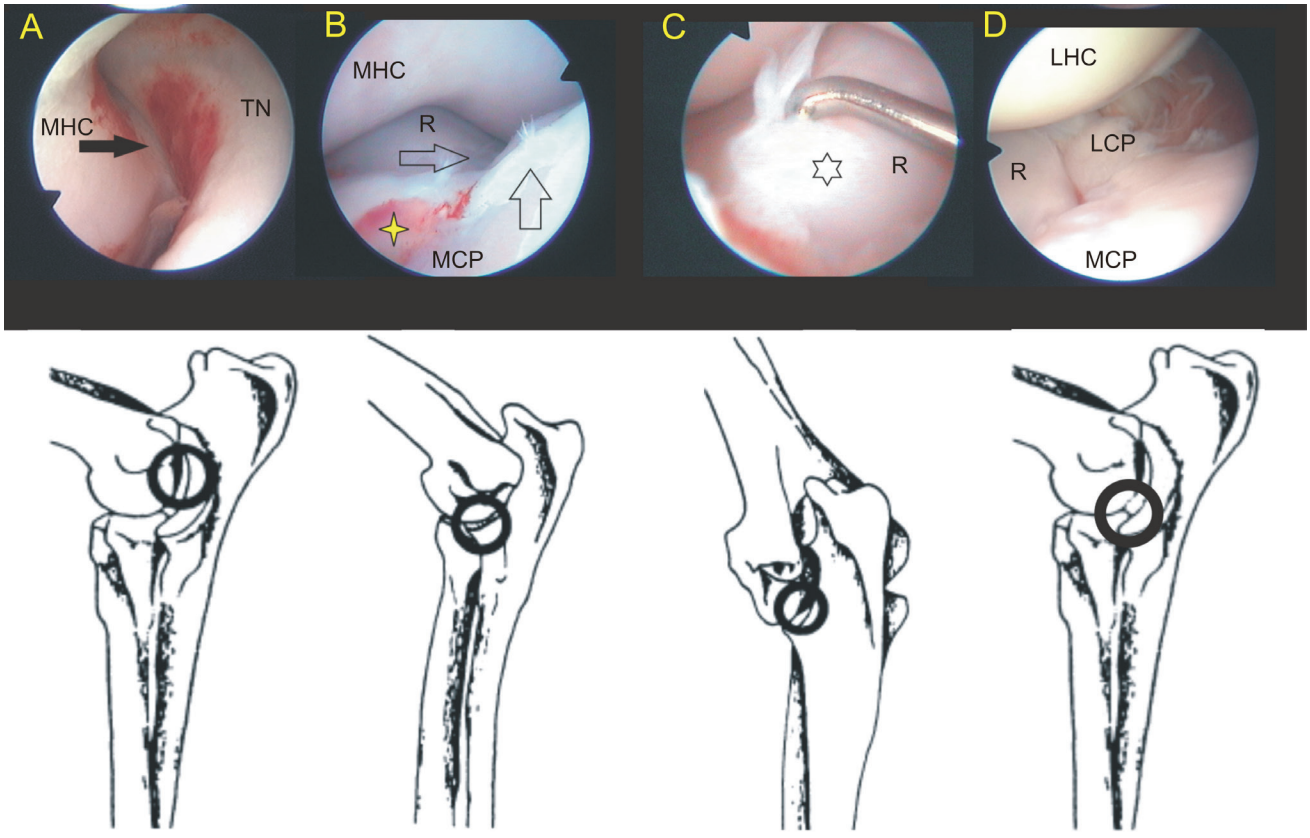

Figure 15. Arthroscopic features in an incongruent elbow. The drawings below the arthroscopic images show their locations [69].

Arthroscopic findings

Arthroscopy allows the direct visualization of the level differences between radius and ulna. Additionally, typical changes are present in more severely incongruent joints [69] (Figure 15).

Treatment

Since incongruity is often accompanied by other elbow pathologies, treatment should also involve these lesions. There are several types of treatment of elbow incongruity [30]. A proximal ulnotomy is the most commonly used technique to solve IC. The goal of this treatment is to relieve the pressure in the joint by tilting of the ulna. Radial lengthening has similar results as a proximal ulnotomy. Although this was suggested as a good alternative to an ulnotomy this technique is currently rarely used [70]. Coronoidectomy was described by one author [71].
A recent study described the results of arthroscopic removal of the coronoid process without correction of the incongruity [72].

Conclusion

Until now elbow dysplasia remains one of the most commonly diagnosed causes of fore limb lameness [16]. Elbow dysplasia is a polygenic, hereditary, developmental disease which can be controlled by selective breeding. The susceptible breeds are well-known and the screening of these dogs is highly recommended, especially as not all of the affected dogs show lameness [39, 65]. Although treatment is often successful, the owner should be aware that the affected joint(s) remain(s) vulnerable and that this might interfere with later athletic activity [16, 65]. Because of the similar clinical signs it is not always easy to differentiate the types of elbow dysplasia from each other. Other pathologies such as panosteitis and shoulder OCD should also be considered in the differential diagnosis of fore limb lameness [11, 31]. Thorough clinical and radiographic examination is needed to reach a proper diagnosis. In some cases, radiographic examination is not sufficient and other techniques such as computer tomography or arthroscopy are needed to come to a definitive diagnosis.

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COMMISSIONED PAPER (LV)

Gross pathology of the most common lesions in the urinary tract of companion animals

Ilze Matise[1]

SUMMARY

The aim of this paper is to systematically review the most commonly encountered gross lesions in the urinary tract of companion animals, addressing their gross appearance and giving a brief pathogenesis. Veterinary practitioners may encounter these lesions during exploratory laparotomy, tumour excision or post-mortem necropsy. It has to be emphasized that severe clinical disease will not always manifest itself with severe gross or even microscopic lesions. This is especially true in case of severe acute renal failure which leads to rapid death.

To tailor this review for veterinary practitioners, the most commonly encountered lesions in kidneys are divided based on their macroscopic appearance – those that cause significant enlargement of the organ or part of it, those that alter parenchyma (colour, shape, and various infiltrative diseases), and those that cause significant reduction in size. The review of lesions in lower urinary tract focuses on the most common lesions in the bladder. The list of lesions is not all inclusive.

This paper was commissioned by FECAVA for EJCAP

Kidney

Post-mortem examination tips, normal anatomical features and sample collection

The kidneys should be examined for changes in size, shape (symmetry), colour and consistency. The renal capsule should be removed to enable visualisation of changes in the colour and shape on the surface of the kidney. Lesions that are visible from the surface should be cut into to see if they extend into sub capsular parenchyma. The kidney should be cut sagitally in order to examine the cut surface of the cortex (thickness, capsular surface) and medulla and to allow examination of the renal pelvis (shape, width, and presence of calculi).

Canine kidneys have a dark red brown, radially striated cortex and slightly paler, brown medulla (Fig. 1).

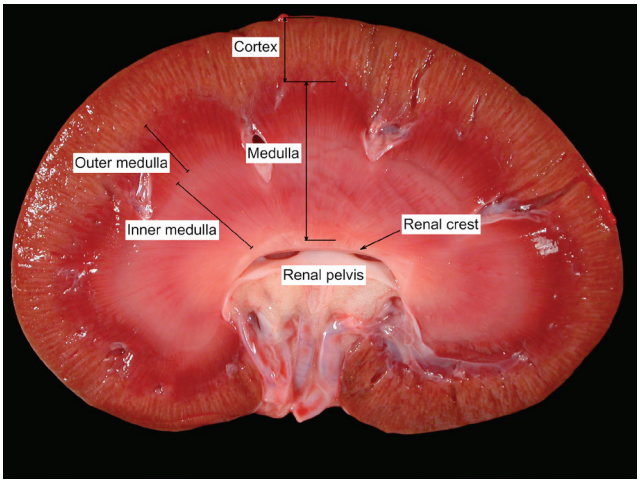

Figure 1. Kidney of a dog. Canine kidneys are red brown with a striated cortex. The medulla is two times thicker than the cortex and divided into outer and inner parts.
This is a kidney from a dog with acute raisin toxicity. The renal cortex is lightly oedematous.

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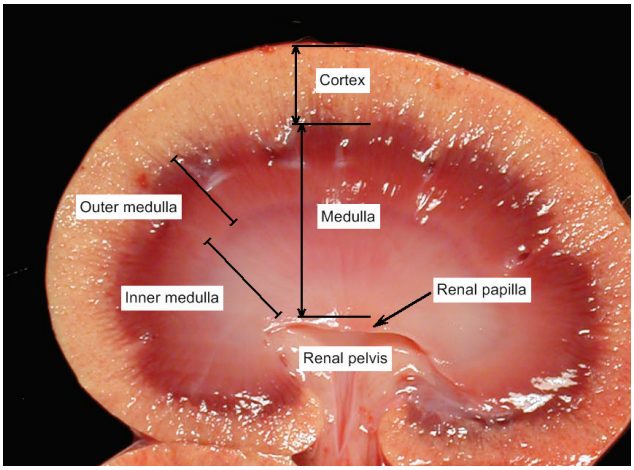

Figure 2. Kidney of a cat. The renal cortex of feline kidneys often is pale yellow due to the abundance of the fat in renal epithelial cells.

Kidneys of adult cats normally are pale yellow because of the large lipid content in the tubular epithelial cells (Fig. 2). The amount of fat (and paleness) is apparently hormonally determined: pregnant females and sexually inactive males have the most fat whereas females in anoestrus have the least. It is much easier to remove capsule from a cat kidney than from that of a dog.

Biopsy samples of the kidney are most commonly obtained from material collected during diagnostic laparatomy, unilateral nephrectomy (in the case of renal tumours) or percutaneous needle biopsy of the kidney.

General guidelines for tissue collection are provided in Table 1. Samples from a kidney should include all parts of the organ: cortex with capsular surface, medulla and pelvis. If the entire kidney is affected by a tumour, representative samples should be taken.

Enlarged kidney

Renal cysts - fluid filled cysts in the cortex and medulla

Hydronephrosis - dilated renal pelvis

Tumours

- ***Metastatic*** - more common than primary
  - *Lymphoma* (cats and dogs)
    yellow to tan variably sized nodules, limited to the cortex.
  - *Haemangiosarcoma* (dogs)
    well delineated dark red foci that replace renal parenchyma and are markedly haemorrhagic.
  - *Adenocarcinoma*, variable origin (dogs)
    variable appearance, may be tan, firm, multiple nodules.
- ***Primary***
  - *Renal cell adenoma*
    discrete, <2cm, tan nodule in the cortex.
  - *Renal cell carcinoma*
    yellow to tan-brown, +/- cystic masses in one or both kidneys; metastases in 50-60% of cases.
  - *Nephroblastoma*
    congenital, lobulated and cystic tumour; contains embryonic epithelial and mesenchymal tissues.

Granulomatous nephritis - multifocal yellow nodules in the cortex and medulla.

Renal cysts are fluid filled cavities that can be single or multiple and arise from any part of the nephron. A single or few cysts in an otherwise normal renal parenchyma can be considered an incidental finding (Fig. 3). Multiple, usually small cysts that occur in a fibrotic and shrunken kidney are likely to be due to chronic interstitial nephritis (see below). Multiple, large cysts in both kidneys indicate the polycystic kidney disease that is inherited in Persian cats, Persian-related cat breeds and several dog breeds,

Table 1 General guidelines for collection of samples for histo-pathological evaluation

Collection of tissues from grossly changed parts of the organs for histo-pathologcial examination is necessary if it is important to determine precise type, location and cellular changes within lesion. Samples should be sent to veterinary pathologist for professional evaluation. Histopathology alone may not be enough to enable the determination of the exact cause and additional tests such as microbiological and toxicological evaluation may needed. Additionally, in some chronic cases the specific cause may no longer be detectable.

Tissue collection	Collect tissues as soon as possible after death. Handle tissue gently. Take sample from the interface between the lesion and normal tissues. Collect samples that represents all layers of the organ. For solid tissues, sample thickness should be less than 7-10mm.
Fixation	Immerse tissues into 10% neutral buffered formalin solution. Formalin should be 10x more than tissues. Use wide mouth jars.
Dont's	Do not freeze tissues. Do not use other fixatives.

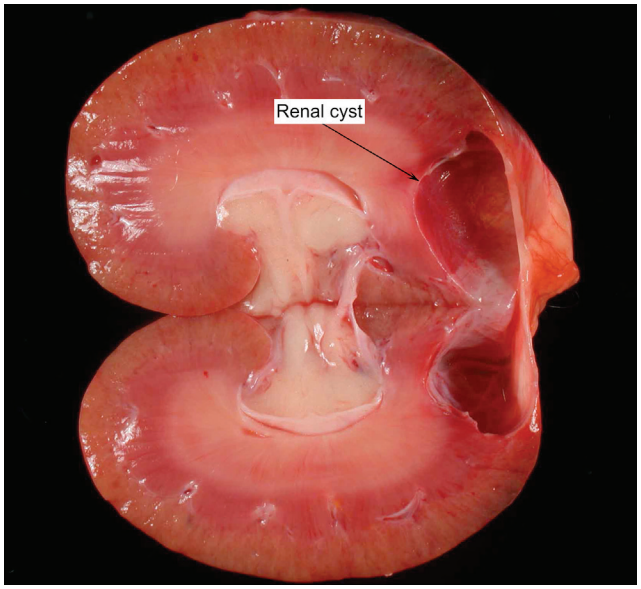

Fig 3. Kidney of a dog – renal cyst. A large renal cyst occupies the cortex and part of medulla.

such as Bull terriers, Beagles, Cairn terriers and West Highland White terriers. In the latter two breeds cysts also occur in the liver and as part of the same syndrome. Renal cysts in Persian cats grow progressively over time, and lead to chronic tubulointerstitial nephritis and renal failure in adult life. Multiple cysts need to be differentiated from cystic tumours such as nephroblastoma,and renal adenocarcinoma.

Hydronephrosis is dilation of renal pelvis with subsequent progressive atrophy and cystic enlargement of the kidney (Fig. 4). The cause is some form of urinary obstruction at any level from renal pelvis to urethra (partial or complete). Most severe hydronephrosis is unilateral with an obstruction localized in the ureter (due to calculus, inflammation, fibrosis or neoplasia). The pathogenesis of hydronephrosis is based on the persistence of glomerular filtration in the presence of urinary obstruction. The end result is renal tubular and glomerular atrophy and progressive decrease in glomerular filtration. Typical gross changes in hydronephrosis are a variably dilated renal pelvis with blunting of renal calices. In most severe cases the kidney is transformed into a thin-walled, fluid-filled sac containing multilocular cysts supported by fibrous tissue. The ureter should be examined for dilation (hydroureter) and to ascertain the cause of obstruction (within the lumen and from the surrounding tissues).

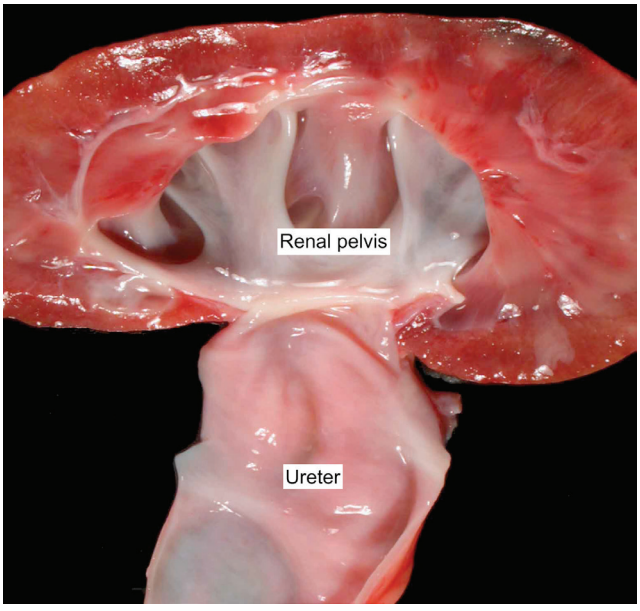

Figure 4. Kidney of a dog – hydronephrosis and hydroureter. The renal pelvis and ureter are markedly dilated. The renal medulla and cortex are thinner than usual because of atrophy caused by gradually increasing pressure.

Tumours: The size and location of suspected tumours, histology, regional lymph node involvement, and the low prevalence of primary renal cell tumours are deciding factors when considering the differential diagnoses for tumour-like lesions in the kidneys.

Metastatic tumours in the kidney are far more common than those that arise from renal parenchyma. Of these the most common in both cats and dogs is the lymphoma. Usually the kidney is not the only organ involved and one or both kidneys may be affected containing soft, white-tan nodules to confluent masses (Fig. 5). Concurrent enlargement of lymph nodes and other lymphoid tissues would be expected in the case of *lymphoma*. Lymphoma in the kidney needs to be differentiated from tumours of myeloid or histiocytic origin, metastatic carcinomas and granulomatous inflammation. Generally, lymphoma is confined to the renal cortex whereas granulomatous

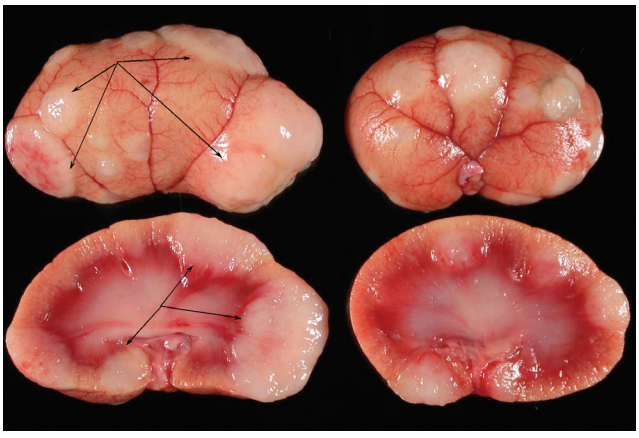

Figure 5. Kidney of a cat – renal lymphoma. The renal cortex contains multifocal, large gray-white nodules with a raised surface (arrows). Note that lymphoma in cats typically is limited to the cortex.

inflammation also affects medulla. The *metastatic carcinomas* most commonly encountered in the kidneys are of mammary, prostatic and pulmonary origin. Finding a primary tumour in these locations is essential. *Haemangiosarcomas* in dogs present as multifocal haemorrhagic infiltrative masses that can occur anywhere, including kidneys, but most commonly involving the spleen and right auricle of the heart.

Primary renal tumours in cats and dogs are rare and in the order of decreasing incidence include: renal carcinoma, nephroblastoma and renal adenoma.

Renal carcinoma is a malignant primary tumour of kidney and is usually unilateral, consisting of a well demarcated, yellow to tan-brown sometimes cystic mass, often located at one pole and varying in size from 2cm to occupying more than 80% of the kidney. Metastases are detected in 50-60% of canine cases.

It is difficult to differentiate between low grade renal carcinoma and renal adenoma.. Features that point to renal carcinoma include multiplicity of nodules, presence of necrosis, infiltration of adjacent parenchyma with atypical cellular histology and cytology. In German shepherd dogs a unique syndrome encompasses multiple subcutaneous fibrous nodules, uterine leiomyomas and multiple renal adenomas and cystic adenocarcinomas

Renal nephroblastoma is a malignant, congenital primary renal tumour that develops during the foetal period but is not detected until later in life. It can be unilateral or bilateral occupying a large portion of the kidney and forming metastases in >50% cases. The cut surface is lobulated, meaty to firm, white to tan, with cystic areas. Rarely, fat, muscle, cartilage and bone may be present. Histologically, tumours consist of a disorganized mixture of embryonic epithelial and myxomatous mesenchymal tissues.

Renal adenoma is a benign primary tumour that arises from the renal tubular epithelial cells. It is a discrete, non-encapsulated, solitary, tan to white, small (<2cm) tumour located in the renal cortex. It may be found incidentally.

Granulomatous nephritis – see the section in the next column

Kidney with slightly to moderately altered in size

- **Acute and subacute glomerulonephritis** – pinpoint red dots on the cut surface of the cortex (acute); finely granular capsular surface with stippled cortical cut surface (subacute and mild chronic glomerulonephritis).
- **Amyloidosis (glomerular)** – enlarged, pale brown kidney with waxy appearance.
- **Acute tubular necrosis (nephrosis)** – diffusely swollen, slightly enlarged kidney; cut surface produces slight bulge.
- **Granulomatous / lymphoplasmacytic / suppurative tubulointerstitial nephritis** – multifocal tan to yellow nodules or infiltrates in the cortex and medulla.
- **Pyelonephritis** – renal papillary crest irregular; red to yellow streaks in medulla and cortex.
- **Renal infarcts (acute)** – well delineated wedge-shaped lesions with apex in the medulla; colour varies from red to pale gray.
- **Renal papillary necrosis** – tan yellow to green tissue along the medullary crest; irregular medullary crest outline.
- **Nephroliths** – calculi in the renal pelvis.

Most canine and feline glomerulonephritides are of immune-complex origin and of a membrano-proliferative type implying that within glomeruli there is membrane thickening and mesangial cell proliferation as a response to immune-complex deposition or formation. The term glomerulonephritis is interchangeable with the term glomerulonephropathy. Secondary tubulointerstitial and vascular changes accompany primary glomerular disease. Basically any infection that is able to produce persistent antigenemia has the potential to cause immune-complex disease (for example, pyometra, bacterial endocarditis, feline infectious peritonitis) Individual factors, however, such as genetic susceptibility or immune mechanisms determine whether glomerulonephritis will develop or not. Besides infectious diseases, also hereditary disease, autoimmune diseases (systemic lupus erythematosus, autoimmune haemolytic anemia, immune-mediated polyarthritis) and endocrine diseases (hyperadrenocorticism, diabetes mellitus) have been associated with glomerulonephritis.

Gross lesions of acute glomerulonephritis are usually subtle. The kidneys are slightly swollen, have smooth capsular surface, are of normal or pale colour, and have

glomeruli that are visible as pinpoint red dots on the cut surface of the cortex. Pinpoint red dots may also be petechial haemorrhages which can be observed in acute glomerulonephritis cases as well as due to disseminated intravascular coagulopathy and thrombocytopenia. Glomerulonephritis commonly precedes end-stage kidney disease and renal failure in cats and dogs in which case kidneys are of decreased size (see below).

Renal amyloidosis is caused by deposits of insoluble fibrillar protein either in the glomeruli or the medulla. It is most commonly derived from serum amyloid-associated protein produced in increased amounts during chronic inflammatory diseases (reactive amyloidosis). Amyloidosis however can be also idiopathic, and not associated with an inflammatory disease process. In dogs, with exception of Shar-Peis, amyloidosis most commonly affects the glomeruli and if severe enough can cause proteinuria. Kidneys affected with glomerular amyloidosis are enlarged and pale, with increased firmness, and a waxy appearance. On the cut surface the cortex appears widened. Long standing amyloidosis impairs vascular perfusion and can lead to ischaemic renal papillary necrosis (see below). Amyloid deposits in the medulla are observed in Shar-Pei dogs and Abyssinian cats. Medullary amyloidosis usually does not result in changes that can be appreciated grossly and, more importantly, it does not result in proteinuria. However, it may be associated with renal papillary necrosis (see below).

Acute tubular necrosis, often called "nephrosis", is usually caused by nephrotoxic or ischaemic damage to the kidney and is characterized microscopically by degeneration and necrosis that affects renal tubular epithelium. It is the most important cause of acute renal failure. Decreased renal perfusion from any cause (e. g., hypotension due to shock), results in renal cortical necrosis affecting all cortical structures. Because of the high metabolic activity proximal convoluted tubules are most severely affected and damage extends into basement membranes. In contrast, nephrotoxins damage cells but leave basement membranes intact. In theory, microscopically the difference between ischaemic and toxic tubular damage can be discerned but in practice it is often difficult to do so, especially since there is component of ischaemic damage secondary to nephrotoxic damage. Some nephrotoxins that need to be mentioned are endogenous pigments (haemoglobin and myoglobin – when released), antibiotics (oxytetracycline, sulfonamides, aminoglycosides), plant toxins (lilies in cats, raisins in dogs), antifreeze (ethylene glycol), bacterial and fungal toxins. It may be difficult to recognize acute tubular necrosis grossly – the cortex is slightly swollen, pale brown to beige with a shiny, smooth cortical surface. The cut surface of renal cortex bulges and is excessively moist; striations are muted or accentuated by radially oriented white streaks (Fig. 1).

Tubulointerstitial nephritis is one of the most common lesions in the kidney, mainly as a secondary disease that accompanies a primary process that started elsewhere. It is characterized by inflammatory cell infiltrate within the interstitium and tubules and tubular changes (degeneration, necrosis, regeneration, atrophy). There are many ways for tubulointerstitial inflammation to start – it can follow ascending infection from lower urinary tracts as in case of pyelonephritis, it can be caused by systemic infection (e. g. leptospirosis, feline infectious peritonitis) or it can be a sequelae of glomerulonephritis. Based on the predominant inflammatory cell population, it can be divided into suppurative (usually acute), lymphoplasmacytic and granulomatous or pyogranulomatous. Suppurative tubulointerstitial nephritis is a characteristic change following embolic nephritis caused by the haematogenous spread of bacteria.

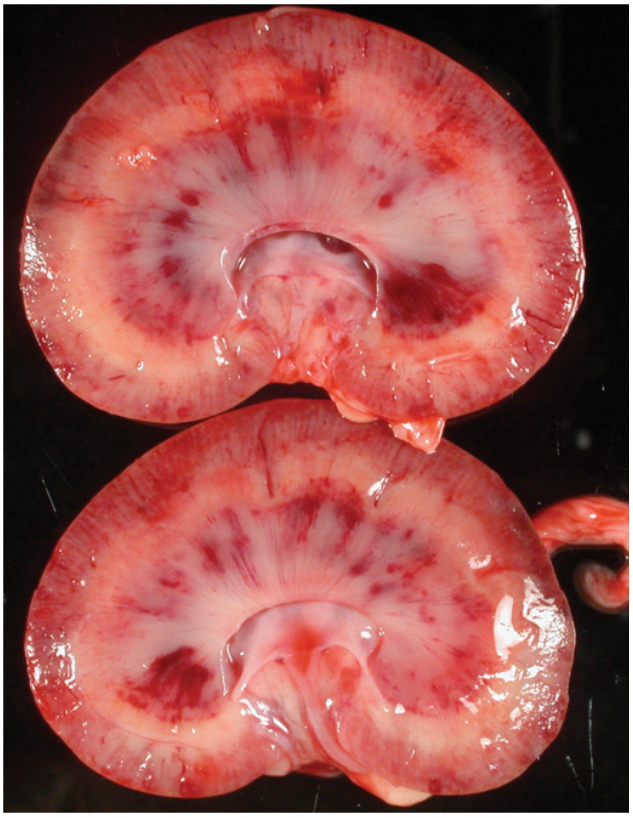

Figure 6. Kidney of a dog – suppurative tubulointerstitial nephritis,due to leptospirosis. The cortex and medulla contain multifocal haemorrhages and indistinct gray infiltrates.

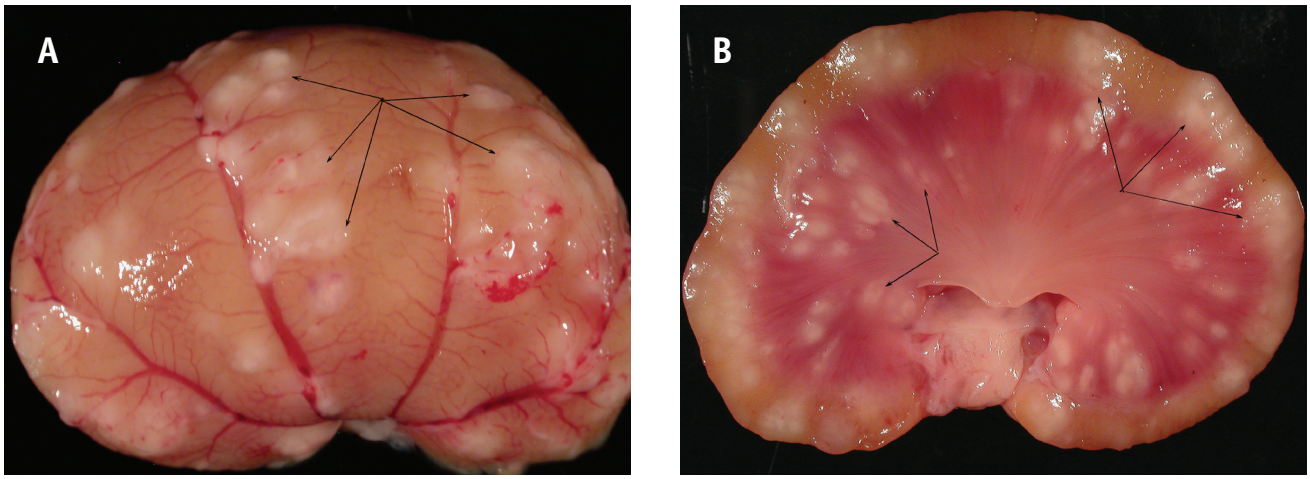

Figure 7A and B. Kidney of a cat – granulomatous nephritis due to feline infectious peritonitis infection. The renal cortex and medulla contain multifocal small white-gray nodules (arrows) that follow blood vessels. The renal cortex is slightly irregular.

Leptospira infection usually results in subacute to chronic, lymphoplasmacytic interstitial nephritis but this lesion by itself is very non-specific, and commonly encountered (Fig. 6). Granulomatous nephritis is a characteristic presentation of the dry form of feline infectious peritonitis (FIP) and generally focused in the perivascular regions due to immune-mediated vasculitis (Fig. 7A and B). In the effusive form of FIP, lymhocytic plasmacytic infiltrates predominate. Other causes of granulomatous nephritis are fungal organisms and parasites.

The gross appearance of tubulointerstitial nephritis depends on its severity, the duration of the process and type of inflammatory infiltrate. Acute embolic suppurative tubulointerstitial nephritis is characterized by widely disseminated red or yellow foci scattered mainly within cortex. Large accumulations of lymphocytes and plasma cells along with fibrosis in the subacute to chronic tubulointerstitial nephritis cases present grossly as variably sized white to gray slightly firm foci multifocally within cortex and medulla. Granulomatous nephritis is characterized by variably sized yellow to tan infiltrates present in cortex and medulla. Their presence in medulla helps to distinguish granulomatuos nephritis from lymphoma.

Pyelonephritis is an inflammation of renal pelvis and renal parenchyma usually resulting from ascending infection from the lower urinary tract caused most commonly by uropathogenic strains of *Escherichia coli*. Other common bacteria that cause pyelonephritis are *Klebsiella sp., Proteus sp., Streptococcus sp. Staphylococcus sp.* and *Pseudomonas aeruginosa*. Acute pyelonephritis is characterized by suppurative inflammation and necrosis that first affects renal medullary crest and tubulointerstitial tissues of renal medulla but later on ascends higher, affecting cortex as well (Fig. 8A and B). It is important to examine ureters for presence of suppurative exudate.

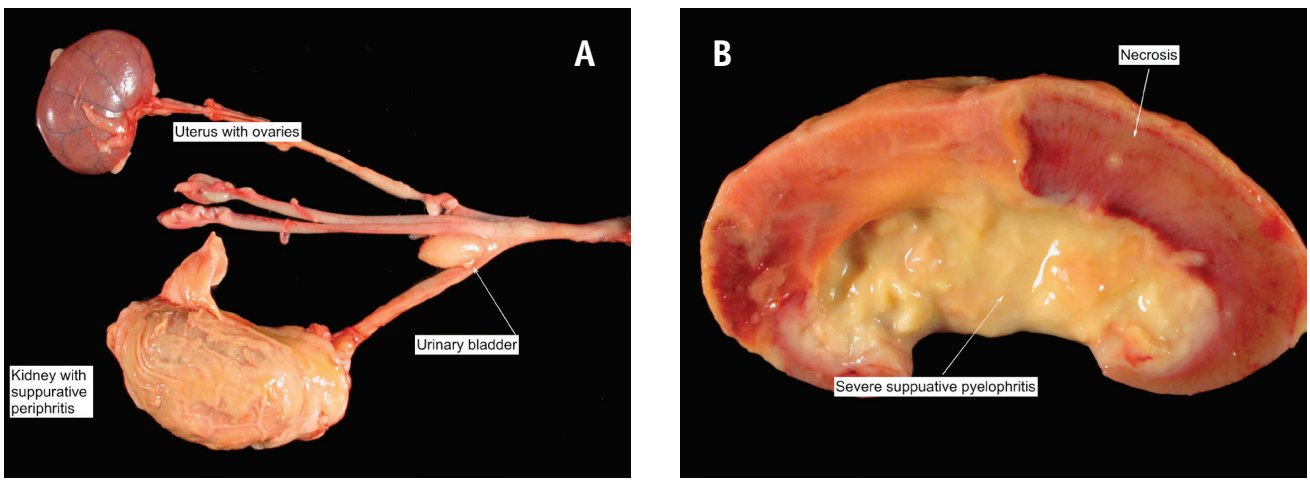

Figure 8A and B. Urinary tract of a cat – unilateral, marked suppurative nephritis, perinephritis and pyoureter (A) due to ascending Escherichia coli infection from the urinary bladder. The cat had severe suppurative pyelonephritis and renal necrosis (B).

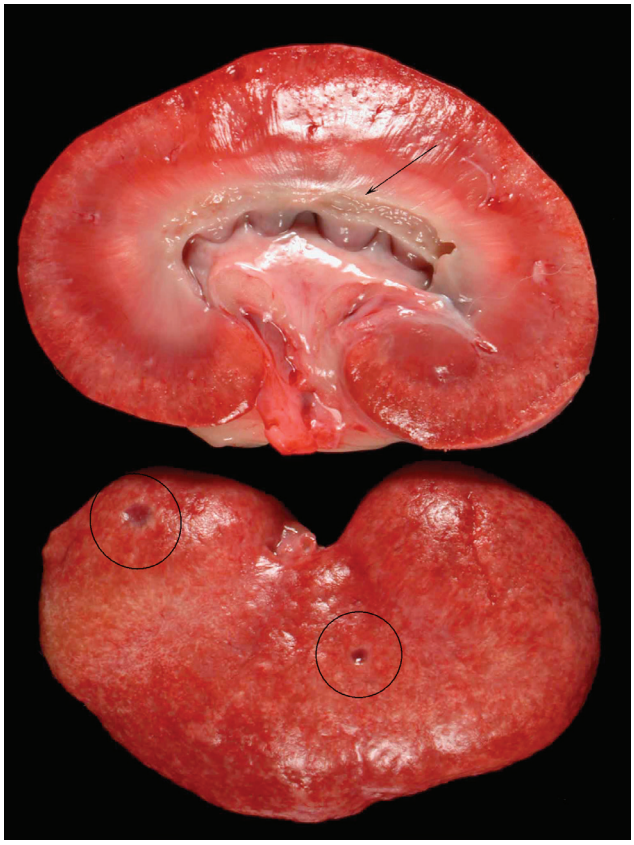

Figure 9. Kidney of a dog with chronic pyelonephritis. The renal pelvis is slightly dilated. The renal medullary crest is irregular and gray (arrow). The cortical surface is slightly granular and contains small cysts (circles).

Grossly pyelonephritis appears as an ulceration and hyperemia of the renal medullary crest and dark red or yellow radial streaks in the medulla and extending into the cortex. Chronic lesions of pyelonephritis involve scarring along with persisting tubulointerestitial inflammation that is both suppurative and lymphoplasmacytic (Fig.9). The scars in chronic pyelonephritis extend from the capsule to the pelvis and frequently may be located in the poles of the kidney. Although these scars are difficult to distinguish from those produced by renal infarcts or glomerulonephritis, in case of chronic pyelonephritis there is also concurrent fibrosis and deformities in renal pelvis and medullary crest. Nevertheless, total involvement of kidney due to pyelonephritis may produce a firm, pale shrunken kidney with an irregular surface that may be difficult to differentiate from other causes of end-stage kidney.

Renal infarcts are areas of coagulative necrosis that result from the vascular occlusion of the renal artery or one its branches. Causes of infarcts include, but are not limited to, thromboembolism (secondary to hypertrophic cardiomyopathy or valvular endocarditis), thrombosis secondary to sepsis, loss of antithrombin III or neoplastic emboli.

Acute infarcts are easy to recognize grossly because they are wedge-shaped, well delineated, slightly swollen (raised capsular surface), red or pale gray depending on the location of thrombus, size of the vessel and time interval after vascular occlusion. If the arcuate artery is occluded, there will be wedge shaped necrosis in cortex and medulla; if interlobular artery is occluded, infarct will affect only cortex (Fig. 10A and B). Infarcts at the onset are red due to haemorrhage within necrotic zone. After 2-3 days erythrocytes in the centre of infarct are broken down and tissue become dehaemoglobinized and pale gray. Inflammation and healing via fibrosis start from the periphery of the necrotic tissue. Healed infarcts persist as pale gray-white scars, wedge-shaped depressions in cortex. These scars may be difficult or impossible to distinguish grossly from focal healed pyelonephritis. The sequelae of septic thrombi may be abscesses.

Renal papillary necrosis is the response of the inner medulla to ischaemia which can be primary or secondary. Primary renal papillary necrosis occurs in animals treated

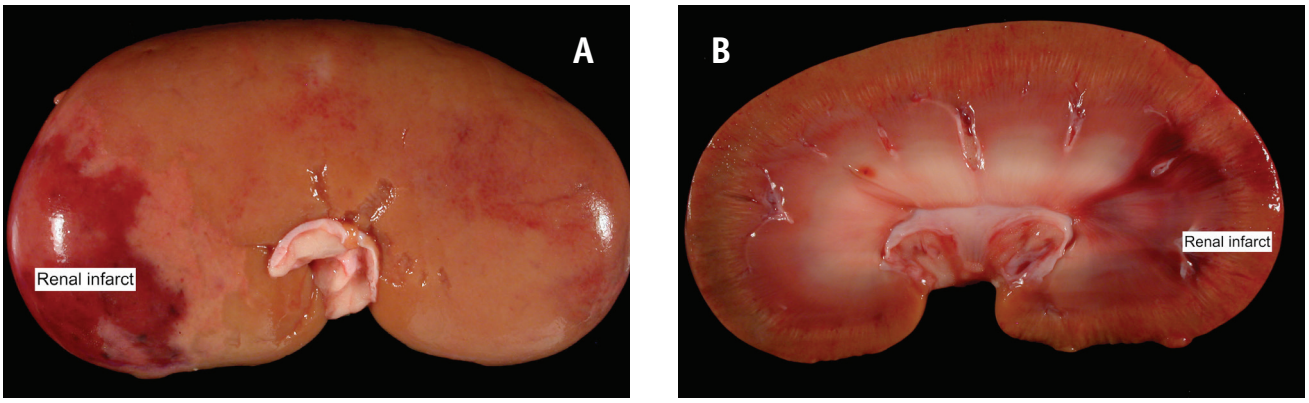

Figure 10A and B. Kidney of a dog with an acute, haemorrhagic infarct. The cortical surface contains haemorrhagic and necrotic tissue (A). The infarcted area is dark red, wedge shaped, and located at the pole of a kidney (B).The infarct extends into medulla indicating obstruction of the arcuate artery.

with non-steroidal anti inflammatory drugs which result in the inhibition of prostaglandins (such as PgE2) needed to ensure vasodilation within the inner renal medulla. Common causes of secondary renal papillary necrosis are urinary obstruction, pelvic calculi (nephrolyths), pyelonephritis, interstitial medullary amyloidosis and fibrosis. The mechanism is either direct compression of the renal medulla (eg by calculi) or compression of blood vessels that supply renal medulla (eg by medullary amyloidosis).

Grossly acute renal papillary necrosis appears as irregular yellow-gray, green or pink, well delineated tissue within the inner medulla, adjacent to pelvis (Fig. 11). With time, the necrotic tissue may slough off with the remaining inner medulla becoming narrowed, irregular and scarred. The overlaying cortex may be shrunken because of atrophy of some nephrons caused by blockage of the tubules.

Nephroliths are occasionally found in the renal pelvis of cats and dogs. Similarly to urinary calculi elsewhere (see below), nephroliths are variable in size, shape and structure. If they are large, they can obstruct renal pelvis or ureter, predispose to pyelonephritis, and result in compressive injury of the renal parenchyma leading to renal medullary crest necrosis.

Severely irregular and small kidney

- **End-stage kidney / renal fibrosis** – shrunken, firm kidney with irregularly pitted surface
  - o Chronic glomerulonephritis
  - o Chronic interstitial nephritis (tubulointerstitial nephropathy)
  - o Chronic renal infarcts
  - o Chronic pyelonephritis
- **Renal atrophy**– small but normally shaped kidney

The so called "**end-stage kidney**" is frequent finding in cats and dogs with chronic renal failure. In such kidneys there is extensive fibrosis that replaces the renal parenchyma – glomeruli and tubules. Concurrently, there is tubular atrophy, cystic dilation, glomerulosclerosis and chronic lymphoplasmacytic inflammation of variable severity. It is nearly impossible to determine the cause since glomerulonephritis, infarcts, tubular necrosis, tubulointerstitial nephritis and pyelonephritis as in the chronic stages they can all look the same.

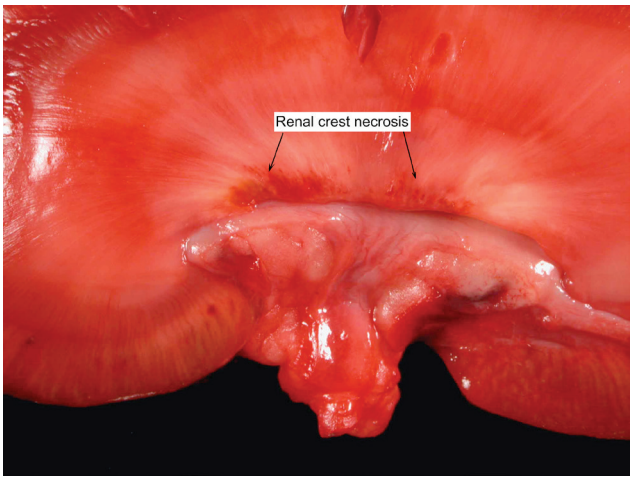

Figure 11. Kidney of a wolf with renal crest necrosis. The renal crest contains dark red to slightly brown tissue (arrows) indicative of acute renal crest necrosis.

Grossly, the kidneys are shrunken and firm, with an irregular, pitted capsular outline, irregular thinning of cortex, radial white to tan streaks in cortex and medulla, multifocal variably sized cysts and variable distortion of renal pelvis (Fig. 12, 13A and B) . There may be excessive adhesions of renal capsule to parenchyma. Fibrosis may

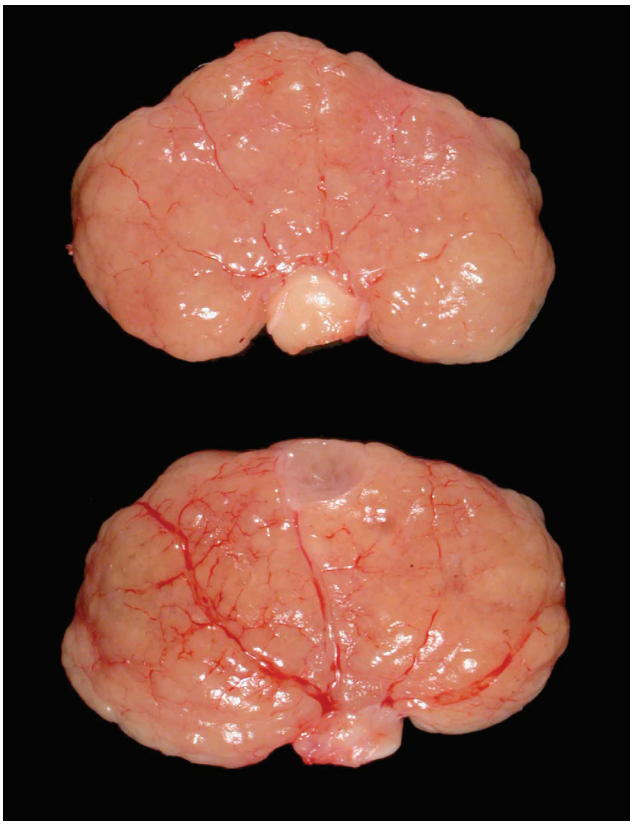

Figure 12. Kidney of a cat with chronic interstitial nephritis (end-stage kidney). The tidney is shrunken and firm, with an irregular capsular surface that is pitted and contains cysts. This cat had developed secondary renal hyperparathyroidism.

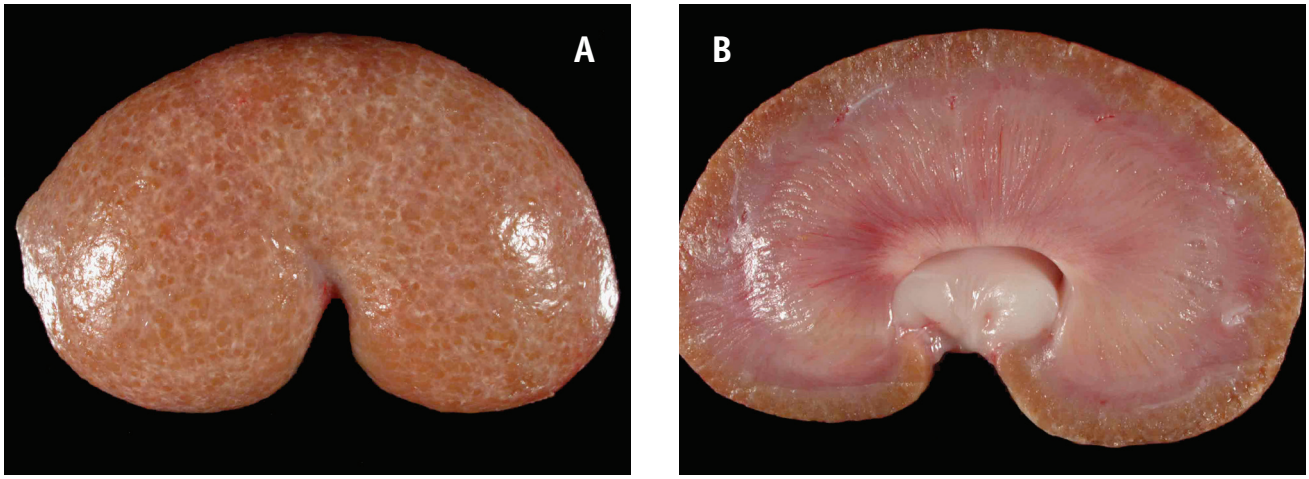

Figure 13A and B. Kidney of a dog with chronic tubulointerstitial nephritis (end-stage kidney). The kidney is smaller and firm with a finely granular and pitted surface (A). The renal cortex is reduced in thickness (atrophy). The medulla is fibrotic tissue and contains small cysts (B).

be diffuse and finely stippled with pinpoint dimpling and granularity on the capsular surface (as in case of chronic glomerulonephritis), or it can be coarser as seen by deep and irregularly shaped depressions of the capsular surface.

In some animals, more frequently in cats than in dogs, unilateral, marked, and proportional decrease in kidney size is observed consistent with **renal atrophy** (Fig. 14). The presumed but not proven pathogenesis is neurogenic shutdown.

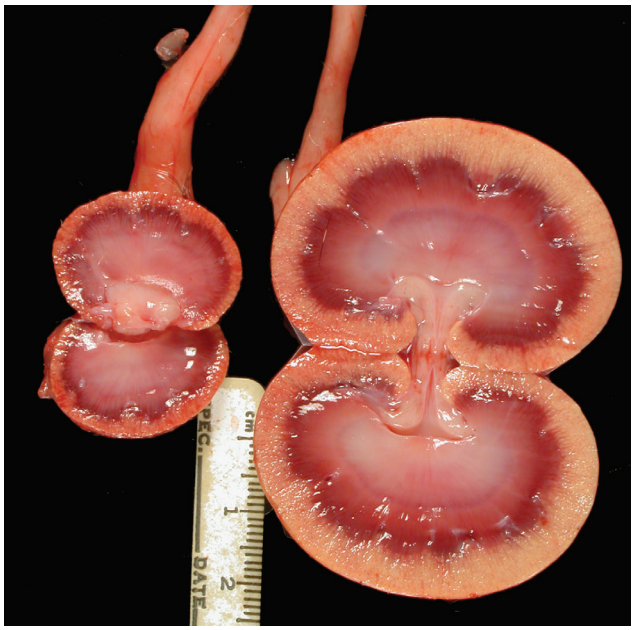

Figure 14. Kidney of a cat with unilateral renal atrophy. One kidney is 2.5 times smaller than the other kidney (atrophy) and the ureter is dilated (hydroureter).

Lower Urinary Tract

Post-mortem examination

When examining the urinary system post-mortem, it is best to remove kidneys together with ureters, urinary bladder and urethra as one unit. This allows better examination of lower urinary tract. The diameter of ureters should be assessed and opened if necessary. The urinary bladder and urethra should be opened and their mucosa examined. If the urinary bladder is empty, it is to be expected that its wall will appear quite thick because of the contracted smooth muscle.

Urolithiasis

- ***Calculi***
  - Struvite (magnesium ammonium phosphate hexahydrate) – white to gray, chalky, usually smooth and easily broken.
  - Oxalate (calcium oxalate monohydrate or dihydrate) – hard, heavy, white or yellow, typically covered with jagged spines although some are smooth.
- ***Urethral plugs*** (in castrated male cats)
  - Struvite "sand".
  - Rubber-like protein matrix.
  - Mixture of struvite sand and protein matrix.

Urolithiasis is the presence of calculi in the urinary passages frequently observed in companion animal post-mortem necropsies. Calculi are grossly visible hard spheres or ovoids with a small amounts of organic matrix impregnated with inorganic salts. The most common types of calculi in dogs and cats are struvite and oxalate calculi.

Small calculi may be voided in the urine, but impaction in the urethra is common in males. The common site of impaction is the proximal end of the os penis in dogs and anywhere along the urethra of male cats. At the point of impaction in the urethra there is usually local pressure necrosis with ulceration of the mucosa which may lead to haemorrhage and bacterial infection that can ascend to the bladder and even to the kidney.

In cats more important than urinary calculi, are urethral plugs – masses of sandy sludge with a much higher organic component than in calculi. In male cats obstructed with urethral plugs, the urethral mucosa is markedly oedematous, congested and haemorrhagic.

Cystitis and bladder tumours

- ***Cystitis***
  - Haemorrhagic – diffusely dark red, oedematous mucosa; may also have fibrin and ulceration (commonly due to acute bacterial infection).
  - Emphysematous –mucosa irregularly raised, contains gas bubbles within lamina propria.
  - Eosinophilic – irregularly thickened mucosa with small multifocal ulcers; may contain large, firm, fibrous nodules.
  - Lymphoplasmacytic – irregularly reddened and thickened mucosa.
  - Follicular – disseminated, small, raised gray to red nodules within submucos consisting of lymphoid follicles.
  - Polypoid. – single or multiple nodular, firm mucosal masses.
- ***Tumours***
  - Papilloma – benign, pedunculated or sessile.
  - Transitional cell carcinoma – malignant – papillary, polypoid or sessile. thickens mucosa diffusely or in the trigone area.
  - Rhabdomyosarcoma – malignant striated muscle tumour (rare; affects young large breed dogs).) – large, grape-like masses that protrude into the bladder lumen.

Variable types of cystitis and tumours are the most commonly encountered lesions in the urinary bladder. Cystitis most often, but not always, is caused by bacterial infection. Normally the bladder is resistant to infections; however predisposition to urinary tract infection occurs when there is stagnation of urine due to obstruction, incomplete voiding or urothelial trauma. The bacteria that cause cystitis are the same ones that were mentioned in discussion regarding pyelonephritis. Haemorrhagic cystitis is always acute and characterized by haemorrhage, necrosis, oedema, ulceration, and fibrinopurulent exudate. It can be a result of bacterial infection or, especially in cats, this type of inflammation may be observed following urethral obstruction by urethral plugs.
Emphysematous cystitis is most commonly observed in dogs with diabetes mellitus. It is characterized by mucosal thickening with gas bubbles because of action of sugar fermenting bacteria (Fig 15).

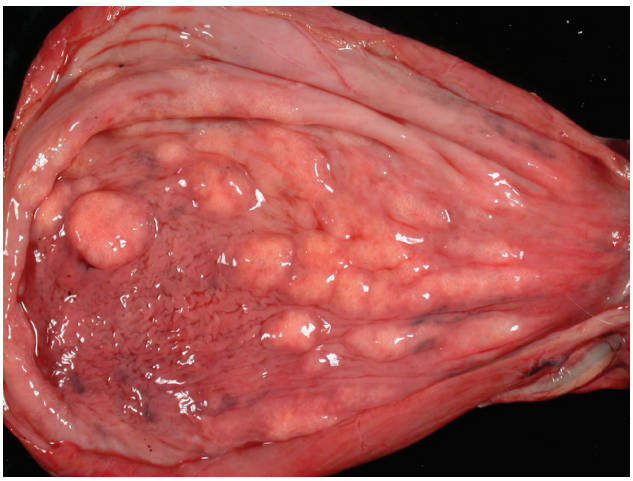

Figure 15. Urinary bladder of a dog with emphysematous cystitis. The bladder mucosa is multifocally elevated with variably sized bubbles because of gas accumulation in the submucosa.

Chronic cystitis frequently is present in animals with urolithiasis or chronic bacterial infection. Chronic cystitis can be quite variable -- characterized by lymphoplasmacytic or eosinophilic infiltrates concurrently with thickening of the submucosa and variable hyperplasia of the urothelium. If lymphocytes form multiple, distinct round aggregates that are visible grossly as gray nodules in the mucosa of urinary bladder, this is designated as follicular cystitis (Fig 16). In some cases polypoid cystitis can be observed characterized by mucosal folds and villus-like sessile projections. Biopsy may be needed to differentiate this from renal polyps and transitional cell carcinoma.

Epithelial tumours of the urinary bladder are more common than mesenchymal tumours and most are malignant. In contrast with renal tumours, most tumours in urinary bladder are primary. Papilloma is a benign tumour of urothelium with either a narrow or broad based attachment to the mucosa; however these tumours are difficult to differentiate from polyps which are a common feature of

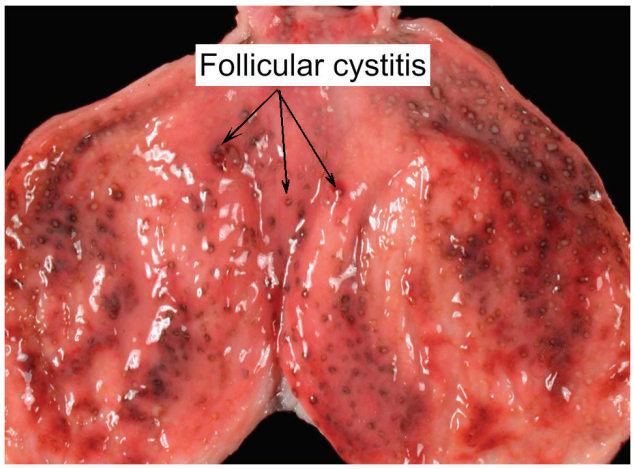

Figure 16. Urinary bladder of a dog with follicular cystitis. The bladder mucosa contains small gray nodules surrounded by thin rim of hyperemia (arrows). Gray nodules correspond to dense lymphoid aggregates in the submucosa of bladder.

chronic cystitis. Transitional cell carcinoma is a malignant tumour and is by far the most commonly diagnosed tumour in urinary bladder The most common location of this tumour is trigone area of the urinary bladder (Fig 17). Prostatic and lower urinary tract urethra are other common sites in dogs. In cats these carcinomas are usually located in the fundus or ventral wall rather than the neck of the bladder. Transitional cell carcinoma may be papillary or sessile (or flat) and infiltrating or non infiltrating. Infiltrating tumours represent some of the most aggressive tumours in dogs as evidenced by high rate of metastases that target the lungs, bone and even skin.

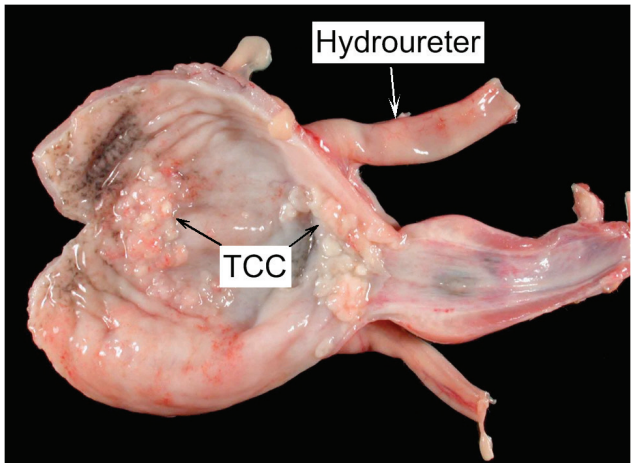

Figure 17. Urinary bladder of a dog with transitional cell carcinoma (arrows). The bladder mucosa is irregularly thickened by a nodular mass part of which occupies the trigone area. One ureter is dilated (hydroureter). The mass is sessile and, infiltrating.

Rhabdomyosarcoma is an uncommon but interesting tumour in young (less than 2 years old), large breed dogs. Tumours originate from skeletal muscle or undifferentiated mesenchyme in the bladder wall. They arise in the trigone as botryoid or polypoid masses and protrude into the lumen of the bladder (Fig18). Surgical excision is difficult and prognosis is poor.

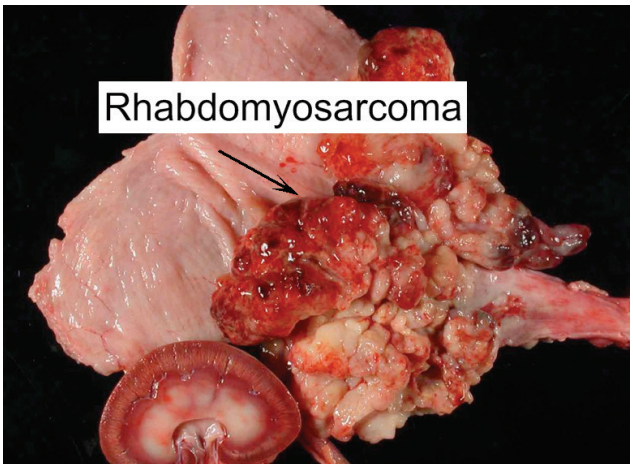

Figure 18. Urinary bladder of a dog with rhabdomyosarcoma. The Trigone area of the bladder contains large botryoid, papillary mass (arrow).

Suggested Literature

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Acknowledgements

The gross images used in this article were taken by veterinary pathologists of Minnesota Veterinary Diagnostic Laboratory.