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How to Survive OOH!
Mini Series

Session 3: Some Common OOH Presentations

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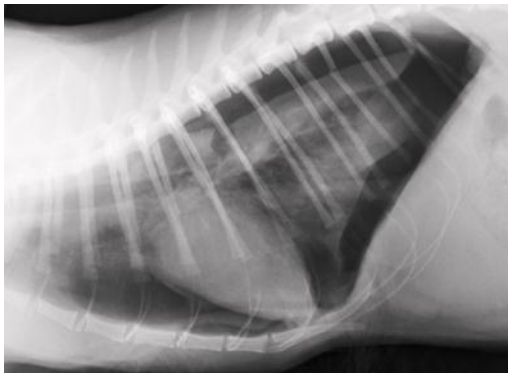


‘COLLAPSE’: Meaning and Causes

Collapse: “To break down suddenly in strength or health and thereby fall into a condition of extreme prostration”

All ‘collapse’ is not created equally! All collapsed animals are recumbent but not all recumbent animals are necessarily classified as ‘collapsed’.

Ultimately the semantics of the terminology are less important than understanding the need to establish which system(s) is affected and hence the sense of urgency.

[Comment on SYNCOPE: Syncope usually occurs due to a transient but significant decrease in cerebral perfusion that causes the animal to collapse; of course if it is not transient then the situation is of even greater concern. A variety of different factors can cause syncope in dogs most notably phenomena causing decreases in cardiac output e.g. significant dysrhythmias, outflow obstruction, vasovagal episodes. Dogs typically present with a history of intermittent short-lived syncopal episodes – indeed some may occur in the practice. Syncope will not be discussed in more detail in this course as the focus of this course is dogs that are suffering from more sustained collapse that will typically not resolve without intervention/assistance.]

Some Causes of Collapse

There are a large number of potential causes of collapse but as described below the initial priority is to focus on understanding the mechanism for collapse rather than jumping straight to specific differentials – no matter how tempting that can sometimes be! In particular identifying cardiovascular compromise as the main – or at any rate a contributing – mechanism is essential. Some of the causes of collapse in the dog are clearly much more common than others and to some extent this incidence is **signalment**-dependent, especially bigger versus smaller dogs but also with respect to specific breeds.

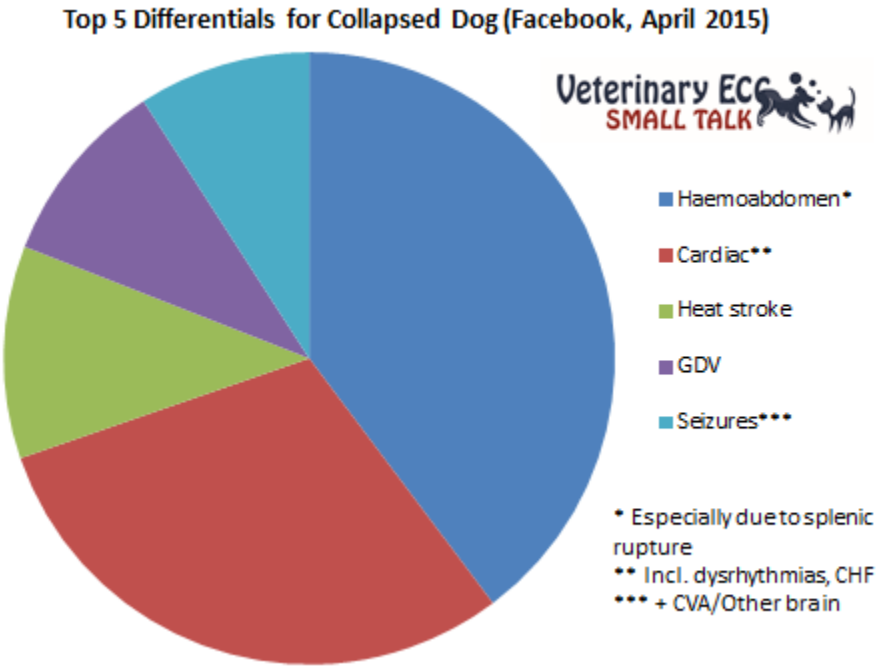
A long list will not be presented here. However out of interest:

The author recently conducted a **Facebook survey with fans of the Veterinary ECC Small Talk Facebook page** posing the following question: “When You Hear About A 'Collapsed Dog' What Are The Top Three Differentials That Come To Mind? Don't over-think this or worry about the vague question...just tell me the first 3 disorders that come to mind!”

There were 479 responses from approximately 150 responders (most people mentioned three differentials, some mentioned more and a few mentioned less) and the main results were:

Haemoabdomen – especially due to splenic rupture	117
Heart disease (including primary cardiac dysrhythmias; congestive heart failure)	88
Heat stroke (exhaustion)	33
Gastric dilation-volvulus syndrome (GDV)	29
Seizures (and cerebrovascular accident/brain)	27
Pericardial effusion	21
Spinal disorder – especially IVDD	21
Vestibular disease	19
Various musculoskeletal disorders – especially osteoarthritis/DJD of hips	19
Hypoglycaemia	18
Respiratory crisis (incl. BOAS, laryngeal paralysis, tracheal collapse)	17
Anaphylaxis	13
Intoxication/envenomation	12

Hypoadrenocorticism (Addisonian crisis)	11
Shock (cause unspecified) – especially hypovolaemic	10
Severe anaemia (incl. IMHA)	9
Other	8
Diabetic ketoacidosis (DKA)	7

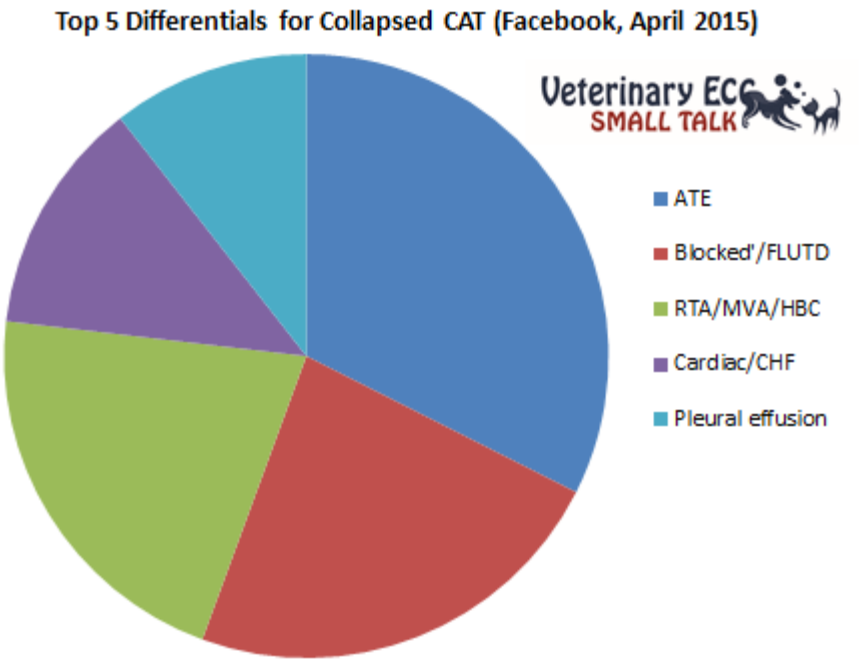


Please bear in mind that this is not case-derived clinical data, it is just what popped into the respondents' head at the time!

[A similar smaller (192 responses, 64 respondents) Facebook survey for collapsed CATS was also performed and showed:

Arterial thromboembolism	49
'Blocked' Tomcats/FLUTD	35
RTA/MVA/HBC (+Other blunt trauma)	32
Heart disease/failure (CHF)	19
Pleural effusion	16
Intoxication (esp. ethylene glycol)	10
Kidney disease-related	5
Diabetic ketoacidosis (DKA)	5

A variety of other disorders were mentioned 1-3 times: FIP, hypoglycaemia, unspecified respiratory disease, anaemia, feline asthma, sepsis, pharyngeal foreign body, seizure, snakebite, heartworm, tick paralysis, heatstroke]



A number of different mnemonics exist to help consider differential diagnoses for a problem such as collapse. One of the most common ones is VITAMIN D adapted to VITAMIN CDE and there are no doubt several versions of what this stands for. This is the author's:

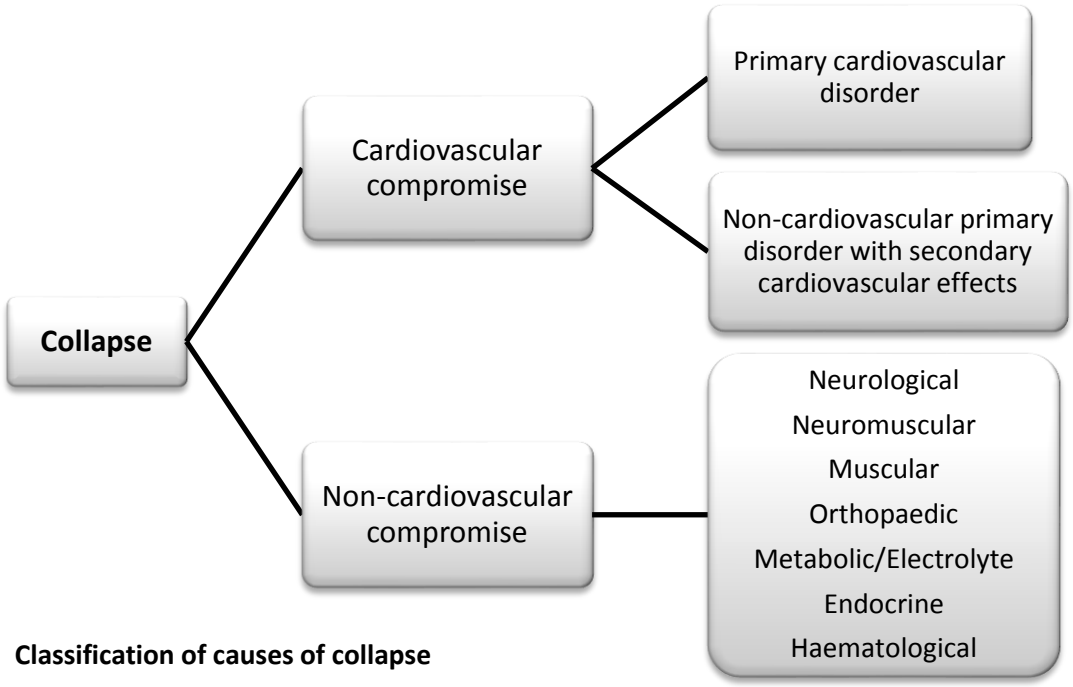
V = Vascular/Ischaemic
I = Infectious. Inflammatory. Immune-mediated. Iatrogenic. Idiopathic.
T = Traumatic. Toxic.
A = Anomalous
M = Metabolic
I = Inherited
N = Neoplastic

C = Congenital
D = Drugs. Developmental. Degenerative.
E = Endocrine. Electrolyte. Environmental/Exposure.

Another mnemonic is THE DUCT IN DAM:

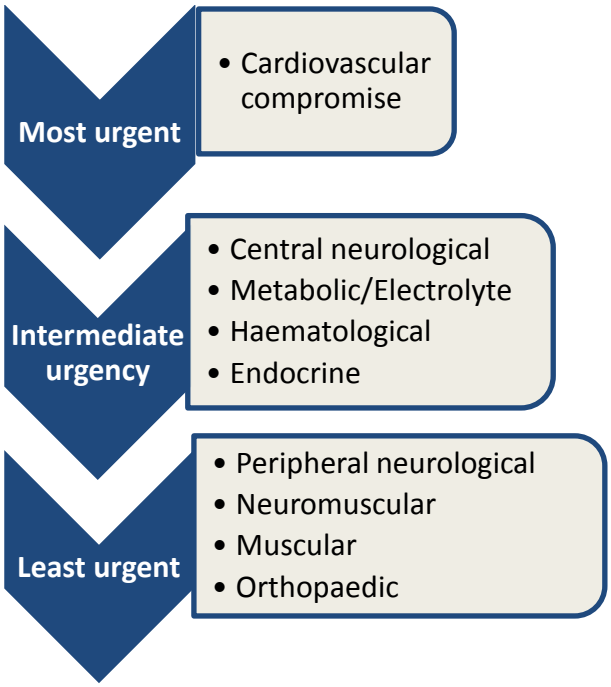
T = Traumatic
H = Hereditary. Haematological.
E = Endocrine. Electrolyte. Environmental/Exposure.
D = Degenerative. Developmental.
U = Unclassified
C = Cardiovascular. Congenital.
T = Toxic
I = Infectious. Inflammatory. Immune-mediated. Iatrogenic. Idiopathic.
N = Neoplastic
D = Drugs
A = Anomalous
M = Metabolic

The most important thing to establish in a collapsed/recumbent patient is whether the primary reason is cardiovascular compromise or not



Classification of causes of collapse

The suspected/confirmed cause of the collapse will to a large extent determine the sense of urgency and prioritisation. In general:



Urgency of intervention for different causes of collapse

Cardiovascular compromise causes collapse as a result of inadequate tissue perfusion – typically generalised hypoperfusion with potential to cause inadequate perfusion of neurological and muscular systems.

The author considers causes of collapse under the following categories:

- Primary cardiovascular disorders
- Non-cardiovascular primary disorders causing cardiovascular collapse
- Non-cardiovascular primary disorders causing non-cardiovascular collapse/recumbency

Clearly in any one collapsed patient, the cause may well overlap between these categories as the body works as a whole unit, e.g.

- Collapse from severe haemorrhage may be due marked hypovolaemia plus lack of oxygen-carrying capacity
- Cats with aortic thromboembolism typically have marked neurological abnormalities due to poor/absent perfusion, i.e. cardiovascular cause with neuromuscular manifestations.

Nevertheless considering the causes of collapse in the way described is important as cardiovascular abnormalities are frequently the most life-threatening and generally require most urgent treatment.

Primary cardiovascular disorders

The majority of **primary cardiovascular causes of collapse** relate to primary cardiac dysfunction, e.g.

- Congestive heart failure and cardiogenic shock
- Severe bradydysrhythmia, e.g. sick sinus syndrome
- Severe tachydysrhythmia, e.g. ventricular tachycardia in Boxer arrhythmogenic right ventricular cardiomyopathy

- Congenital aortic stenosis in the German Shepherd dog

Non-cardiovascular primary disorders causing cardiovascular collapse

Non-cardiovascular primary disorders causing collapse due to secondary cardiovascular effects:

E.g.

- Hypovolaemic, maldistributive or obstructive shock
- Severe dysrhythmias, e.g. vagally-mediated bradydysrhythmia due to an intrathoracic mass; severe ventricular tachycardia due to splenic neoplasia
- Hypoadrenocorticism (Addison's disease) – multifactorial causes of collapse

Non-cardiovascular primary disorders causing non-cardiovascular collapse/recumbency

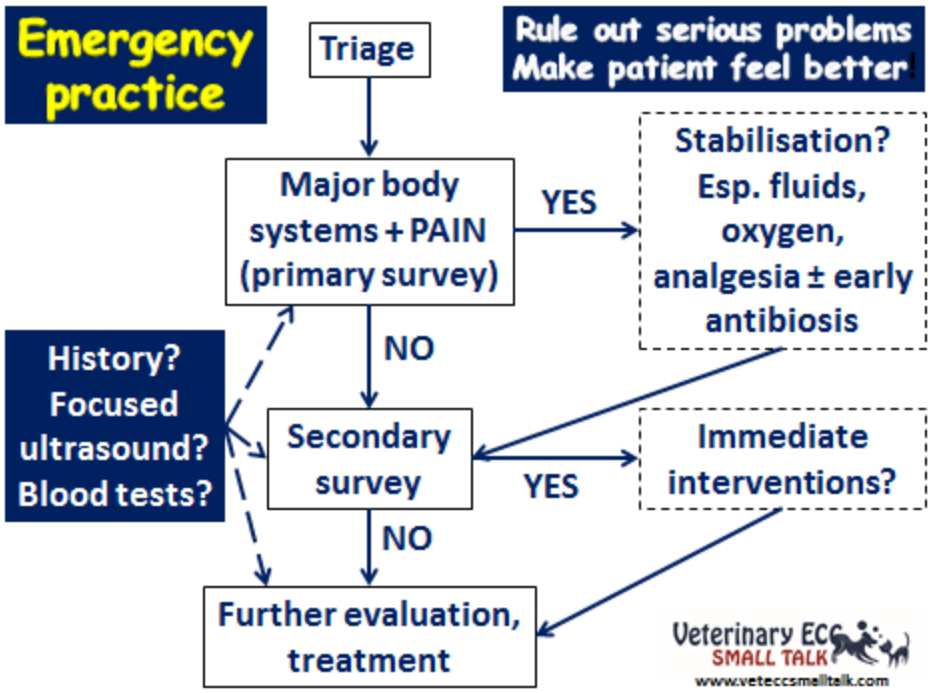
Non-cardiovascular primary disorders causing non-cardiovascular collapse or recumbency:

This category includes a wide variety of disorders that may be classified as neurological, neuromuscular, muscular, orthopaedic, metabolic/electrolyte-related, endocrine, and haematological.
Depending on the nature of the primary disorder, cardiovascular abnormalities of varying degrees may or may not be expected, e.g.

- A cervical spinal cord lesion may cause recumbency but is usually not associated with significant cardiovascular abnormalities (unless aetiology is traumatic or neurogenic shock occurs for example)
- Seizures, unless severe or prolonged, are not expected to cause significant cardiovascular abnormalities
- Significant cardiovascular abnormalities would not usually be expected with hypoglycaemic collapse (although severe hypoglycaemia can cause high vagal tone with consequent bradydysrhythmia)
- Animals with severe acute haemolytic anaemia may collapse due to a lack of tissue oxygen delivery. These animals would be expected to show signs of cardiovascular (and respiratory) compensation for the anaemia.
- Generalised myasthenia gravis is not typically associated with significant cardiovascular abnormalities

INITIAL APPROACH TO THE COLLAPSED DOG

The initial approach to the collapsed dog should follow standard principles of the initial approach to all emergency patients:



Comment on History:

The history should be taken at the appropriate time without compromising initial assessment and stabilisation of the patient. The author will often – but not always – get a very brief capsule history from the pet's carer(s) during initial admission of the patient to the emergency room with a more thorough history being taken once the patient has been assessed and urgent interventions undertaken. These circumstances will vary not just between patients but also between practices with respect to levels of staffing, policies about providing treatments without signed consent (where does 'first aid' end?) and so on; it is therefore not possible to be too prescriptive.
Clearly if the patient has a history of previous episodes of collapse this has significance with respect to ordering of possible differential diagnoses.

Triage and Primary Survey

Triage: classifying and prioritising patients based on how severely affected, critical or unstable they are assessed to be. Achieved by performing some or all of the **primary survey**, i.e. major body systems examination.

Major body systems: so-called because a significant abnormality in any of these systems may be rapidly life-threatening; cardiovascular, respiratory and central nervous systems.

A head-to-tail examination is usually not appropriate when assessing an emergency patient as it does not identify potentially life-threatening abnormalities most efficiently. A more focused approach is required.

In essence each major system is assessed to see if it is normal or abnormal; if abnormal, what is the abnormality, how do you interpret it, and what needs to be done? Remember that systems may be abnormal because of a primary problem within that system itself and/or secondary influence from a

problem outside that system. In the latter scenario, it is important to reassess the major system once the influencing factor has been addressed, e.g. after adequate analgesia where pain was causing tachypnoea; after adequate warming where hypothermia was causing depression.

More detailed description of assessment of the major body systems is beyond the scope of these notes. However as mentioned above identifying whether a collapsed dog does or does not have cardiovascular compromise is essential and this will be discussed in greater detail below.

Respiratory system: a variety of primary respiratory disorders – and non-respiratory disorders with secondary effects on the respiratory system – may be implicated in the collapsed patient. It is typically obvious that the patient has respiratory compromise which could be localised to the upper respiratory tract, trachea, lower airways, lung parenchyma, pleural space, thoracic cage or diaphragm. Upper respiratory tract compromise is often readily identified presenting with stridor or stertor but localising intrathoracic causes of dyspnoea can be more challenging especially in the collapsed patient – to some extent how challenging depends on the patient in question. As mentioned below focused ultrasonography can be very helpful in initial evaluation of these patients. A more comprehensive discussion of the approach to the dyspnoeic patient is beyond the scope of these notes.

Central nervous system:
A full description of evaluation of the central nervous system is beyond the scope of these notes but information that may be of particular importance in the collapsed patient is described in *Appendix 1*. Remember also that in a patient with suspected spinal cord injury it is essential to determine whether pain sensation remains intact differentiating conscious perception from a local withdrawal reflex.

Pain assessment is also part of the primary survey.

Pain assessment

If in doubt, treat for pain! As long as they are used rationally, analgesic agents, opioids in particular, carry little risk but offer potentially great benefit, i.e. the risk-benefit assessment lands heavily on the side of benefit. Give a low testing dose and assess the patient for a positive response confirming that pain has been alleviated.

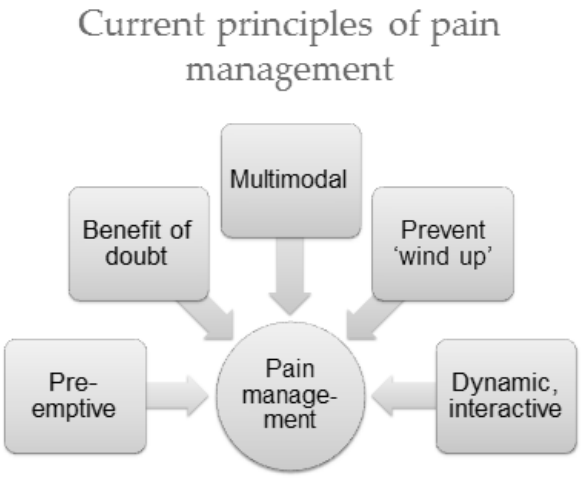
Untreated pain is clearly bad for patient welfare.
Pain may also affect physiological parameters thereby confusing clinical assessment; however it is essential to realise that physiological parameters such as heart rate and respiratory rate may be normal in a painful animal – normal parameters do not exclude the possibility of pain!
Detecting pain can be difficult, especially in cats. Sick animals may also be unable to exhibit behavioural signs of pain.

Sensitisation or 'wind up' pain:

'Wind up' refers to changes in nervous system processing that occur following noxious stimulation and result in greater conscious pain perception with continued pain that is harder to control. A proactive preventative approach to pain management is therefore essential.

Emergency patients are often already painful at presentation. To minimise wind up:

- Administer analgesia as soon as possible to reach a pain-free state
- Maintain the patient at this pain-free plateau
- Ensure adequate analgesia prior to any surgical or other potentially noxious procedures



Pain management was discussed in depth in the study notes for Session 2 of this mini-series.

Secondary Survey

A more comprehensive examination performed once initial stabilisation of the major body systems and analgesia are underway. Important aspects include abdominal evaluation, rectal temperature measurement and hydration assessment.

Abdominal evaluation

Many emergency patients present with intra-abdominal disorders, some of which can be life-threatening. Abdominal palpation is therefore important early on but in collapsed patients may be limited depending on the patient in question. Although abdominal palpation can be extremely useful, it is affected by many factors, both patient- and clinician-related. As such, apparently normal abdominal palpation does not exclude potentially severe intra-abdominal disease.

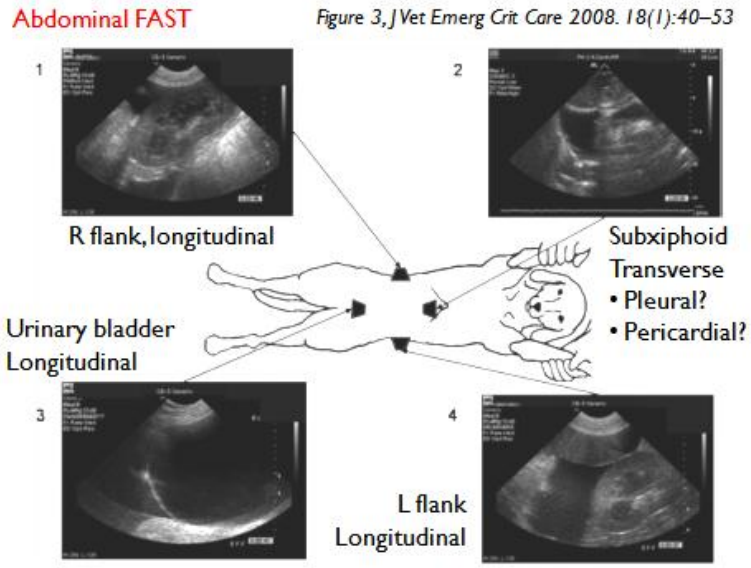
The abdomen should be gently palpated for pain, focal lesions and fluid thrill (fluid wave). If suspected, pain should be categorised as localised or diffuse. It is important when palpating the abdomen to avoid

pressing on the spine (e.g. with the thumbs in a standing animal) in order not to misdiagnose spinal pain for abdominal pain.

A significant volume (maybe up to 40 ml/kg) of free peritoneal fluid is necessary for a fluid thrill to be detected and palpation with the patient standing is most likely to be successful. Radiology offers some improvement – fluid causes loss of serosal detail – but if available, ultrasonography provides a much more sensitive and patient-friendly means of detecting peritoneal fluid as compared to both palpation and radiography. 'Abdominal focussed assessment with sonography for trauma, triage and tracking (AFAST)' has been evaluated in dogs and shown to be extremely useful for detecting peritoneal fluid in both dogs and cats. This technique involves having the patient in left (or right) lateral recumbency and then performing transverse and longitudinal scans at the following sites (see picture on next page):

- Just caudal to the xiphoid process
- On the midline over the urinary bladder
- At the left and right flank regions

Peritoneal fluid appears as anechoic-to-hypoechoic material bathing the intra-abdominal structures. Failure to identify fluid using the above protocol means that it is nearly 100% certain that there is none *at that point in time* (i.e. some may be identified on repeat scanning) – this is true even in inexperienced hands as long as the protocol is followed. Although abdominal scanning for free fluid in emergency patients may have first been introduced in trauma patients it is now used for a variety of scenarios and strictly speaking the FAST acronym should not be used for non-trauma patients; at this time another acronym has not been agreed upon to the author's knowledge.



Abdominal radiography is useful for identifying **free peritoneal gas** (often most readily seen between the liver and diaphragm) as well as diagnosing intestinal foreign body material and obstruction. Radiography will be less useful in this respect if a large volume of free peritoneal fluid is present due to increased loss of contrast.

In animals without a history of recent (last 3-4 weeks) laparotomy or open system abdominocentesis, free peritoneal gas suggests rupture of a hollow viscus and is an indication for emergency surgical exploration. This also applies to animals that have suffered penetrating injuries as free peritoneal gas implies full thickness penetration into the abdomen.

Rectal temperature

Although it is important to know rectal temperature early on, it may not be appropriate to check this in all animals (e.g. often best avoided in animals with pelvic fractures) so make a risk-benefit assessment: how likely is it that the temperature will be significantly abnormal prompting you to do something different/in addition to what you already plan to do? How is the patient likely to respond to temperature measurement? The use of other sites (e.g. aural, axillary, subcutaneous thermistor microchips) has not been validated in conscious dogs or cats (as yet anyway).

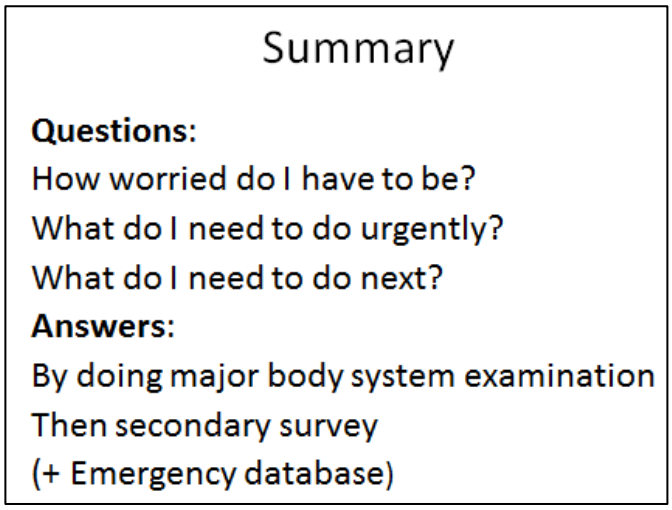
Not all increases in rectal temperature are the same! There is an important distinction between hyperthermia and pyrexia (fever) which impacts on patient assessment and management.

Hydration

Physical hydration parameters are different to cardiovascular parameters and include moistness of mucous membranes, skin elasticity (turgor) and whether or not there is globe retraction (sunken eyes). Hydration assessment using physical examination is insensitive at best and both historical information and blood/urine parameters help to improve hydration assessment. See Hypovolaemia, Shock and Dehydration for more.

Focused ultrasonography in emergency patients

The use of focused ultrasonography in emergency patients is gaining increasing traction both in human medicine and more recently in veterinary medicine. As suggested by the word 'focused' the purpose of this type of scan, ideally using portable devices that can be taken to the patient, is to answer specific and essential questions based on the patient's presentation. Fluid (peritoneal, pleural, pericardial) detection is often the purpose but other uses include evaluation of left atrial size and cardiac contractility in possible cardiogenic cases and indeed lung ultrasound for pulmonary oedema, as well for example as for the detection of pneumothorax, pyometra, foetal heart beats…! Some of these are more challenging and require more training and expertise than others but the overall message is that focused ultrasonography is very useful in emergency patients and many of its uses do not require specialist skill by any means.



Cardiovascular system

As mentioned previously identifying cardiovascular compromise in a collapsed patient is one of the earliest priorities.

Examination of the cardiovascular system was described in the study notes for Session 2 of this mini-series.

The most important questions to answer in a collapsed patient are:

- Is systemic perfusion normal? Perfusion is a key concept in emergency medicine.
- Is there a murmur or gallop sound suggesting possible primary cardiac disease?
- Is there suspicion of a potentially clinically significant dysrhythmia?

Shock and Systemic perfusion assessment

Shock and Systemic Perfusion Assessment was described in the study notes for Session 2 of this mini-series.

Hypovolaemia

Hypovolaemia was described in the study notes for Session 2 of this mini-series.

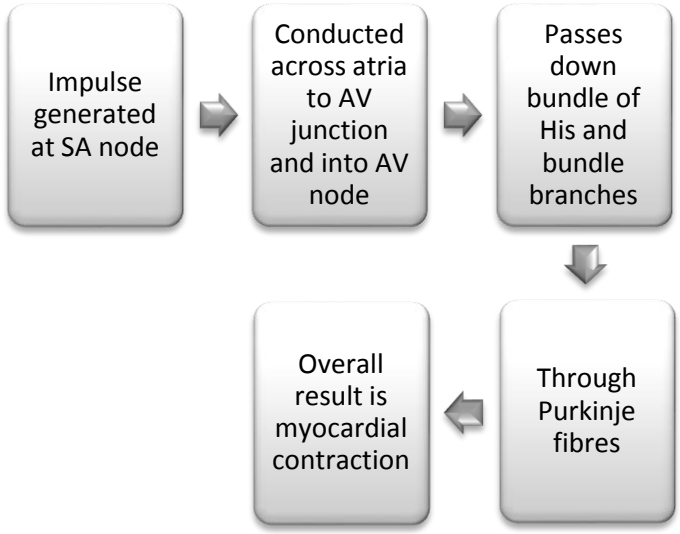
Cardiac Dysrhythmias

Relatively common; probably under-diagnosed

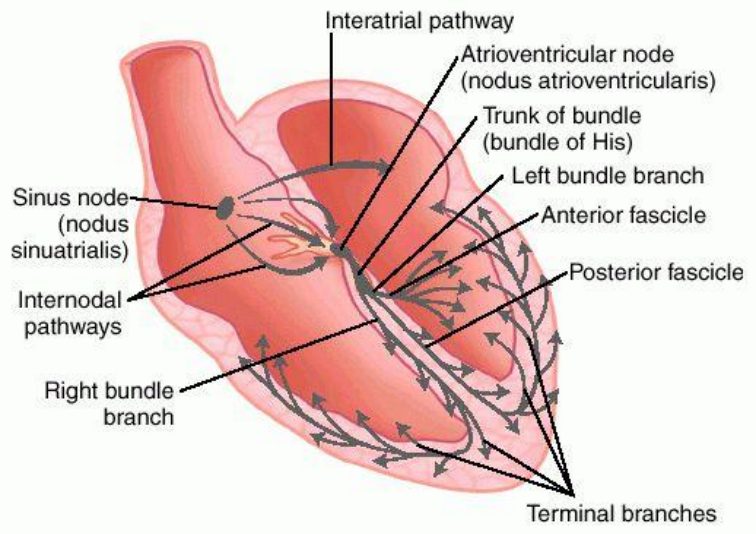
Can be suspected, sometimes with a very high index of suspicion (e.g. atrial fibrillation), on physical examination (e.g. pathologically fast or slow heart rate; pulse deficits) but electrocardiography needed to confirm and diagnose

Causes may be of primary cardiac origin or non-cardiac systemic origin
Anti-dysrhythmic therapy generally not used unless dysrhythmia associated with clinically significant haemodynamic compromise – emphasise treatment of underlying disorder (if known)
Haemodynamically significant dysrhythmias may need to be treated prior to diagnosis of underlying cause
Anti-dysrhythmic agents are not benign and may have pro-dysrhythmic adverse effects

Normal conduction

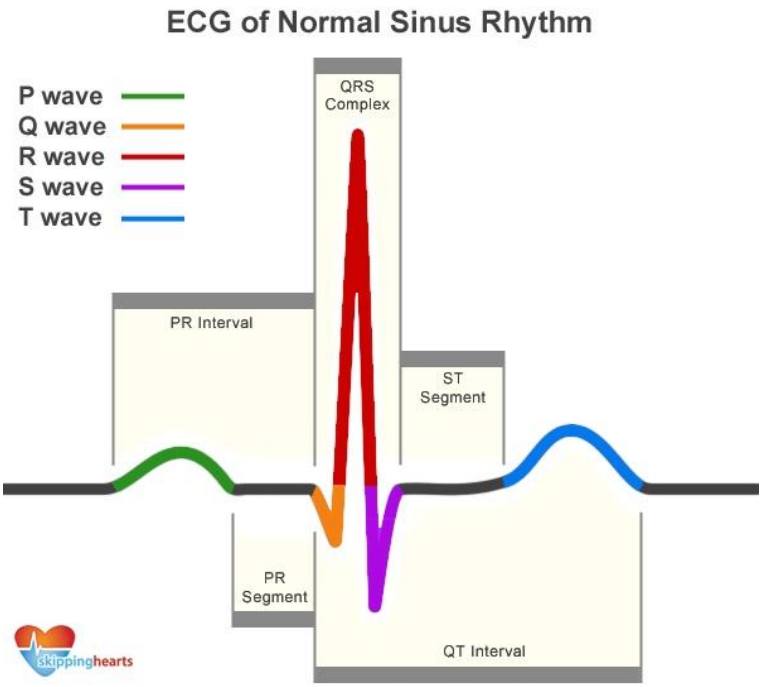


Normal sinus impulse conduction
(SA node = sinoatrial node (dominant pacemaker);
AV = atrioventricular)



Impulse conduction is reflected as the normal sinus beat (P-QRS-T)

Normal sinus rhythm results from impulses being generated at the SA node at a normal rate



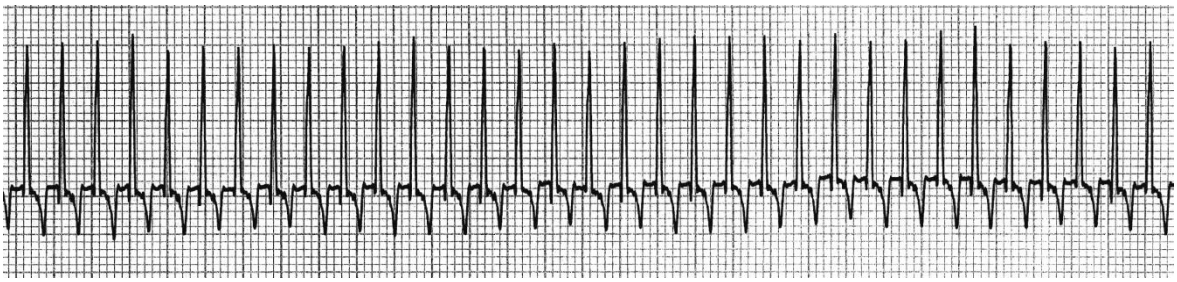
Tachydysrhythmias

Physiological or appropriate sinus tachycardia, including in response to severe hypovolaemia, rarely exceeds a rate of 220-240 beats per min in dogs at rest (300 beats per min in cats); heart rate may exceed this in dogs such as Greyhounds during intense exercise. Finding a heart rate above this level on physical examination should prompt electrocardiography.

Supraventricular tachycardia

Supraventricular tachycardia (SVT) may originate from the atria or the AV junction
Can be difficult to distinguish from ventricular tachycardia (VT) in some cases:

- On physical examination both may manifest rapid weak pulses with pulse deficits
- Potential distinguishing features for SVT on electrocardiography include:
    - Tall and narrow QRS complexes in lead II (usually wide and bizarre with VT)
    - Complexes typically uniform (may be multiform with VT)



Supraventricular tachycardia in a dog (lead II)

SVT most commonly due to **primary heart diseases** that result in atrial dilation (e.g. dilated cardiomyopathy, mitral or tricuspid regurgitation); some animals present in congestive heart failure
May also be due to non-cardiac disorders, especially intoxications

Anti-dysrhythmic therapy is typically reserved for cases in which:

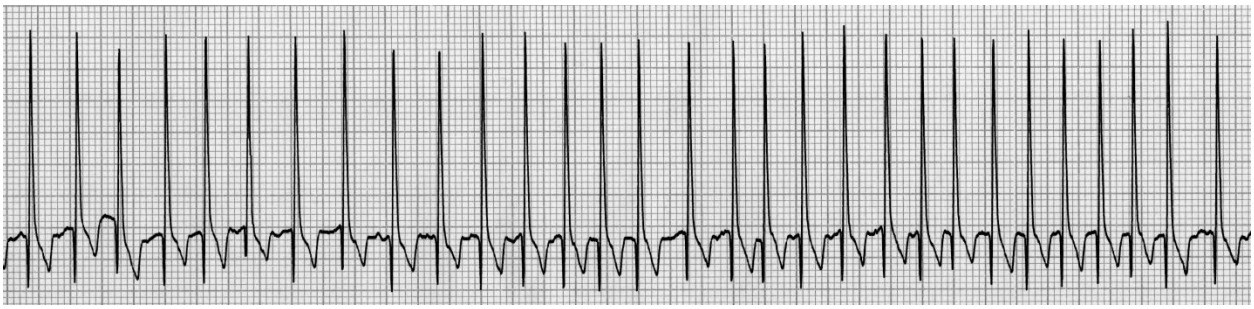
- Heart disease: SVT is clinically significant and does not improve with medical therapy for congestive heart failure; oral digoxin is usual first choice
- SVT is perceived to be clinically very significant, potentially life-threatening – this is relatively rare

Vagal manoeuvres (carotid sinus massage; applying pressure to the closed eyes) may be effective
Medical therapy:

- Diltiazem (calcium channel blocker) used most commonly, intravenously if available, otherwise orally
    - Use cautiously in animals with heart failure as has negative inotropic effects that may cause clinical deterioration – the same is true for beta-blockers (β-adrenergic antagonists, e.g. esmolol) that have also been used for SVT
- Lidocaine: typically used, and most effective, for ventricular tachycardia but *may* have some efficacy in SVT (very limited evidence base)
    - If no other injectable agents are available and the situation is urgent, use of lidocaine is likely to have little risk even if the beneficial effect is negative or limited

Main aim is to slow the ventricular response rate such that the SVT no longer causes haemodynamic compromise; conversion to sinus rhythm not always possible

Atrial fibrillation



Atrial fibrillation in a dog (lead II)

Most common SVT
Characterised by a chaotic irregularly irregular heart rhythm on auscultation (sounds like an active washing machine) with marked pulse deficits
Typically highly suspected based on auscultation but need electrocardiography to confirm:

- Absent P waves and irregular undulations of the baseline
- Normal-looking (tall and narrow) QRS complexes but an *irregular RR interval* (this is an important diagnostic feature)

In emergency practice, typically (although not always) seen in animals with severe **primary structural heart disease**, usually involving atrial dilation (e.g. dilated cardiomyopathy)

- Ventricular rate typically fast (potentially > 200 beats per minute)
- Usually evidence of congestive heart failure

Lone AF = AF in dogs without evidence of structural heart disease (e.g. some Irish Wolfhounds)

Does occur in cats but less frequently than in dogs

Approach to management depends on rate, underlying cause, and whether congestive heart failure is present Stabilisation of congestive heart failure is the priority; treatment to control the ventricular response rate may then be included in subsequent therapy if still required

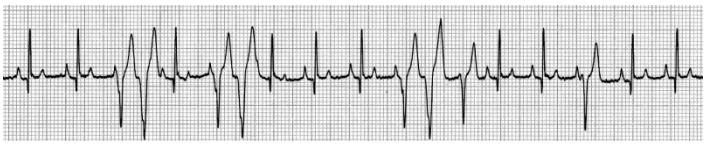
Treatment designed to slow the heart rate (typically to less than 160 beats per min in dogs) in order to improve cardiac output

- Animals with severe heart failure may require some degree of compensatory tachycardia to maintain cardiac output so excessive reduction of ventricular response rate may not be desirable
- Conversion to sinus rhythm is difficult and in fact not shown to be associated with any additional benefit

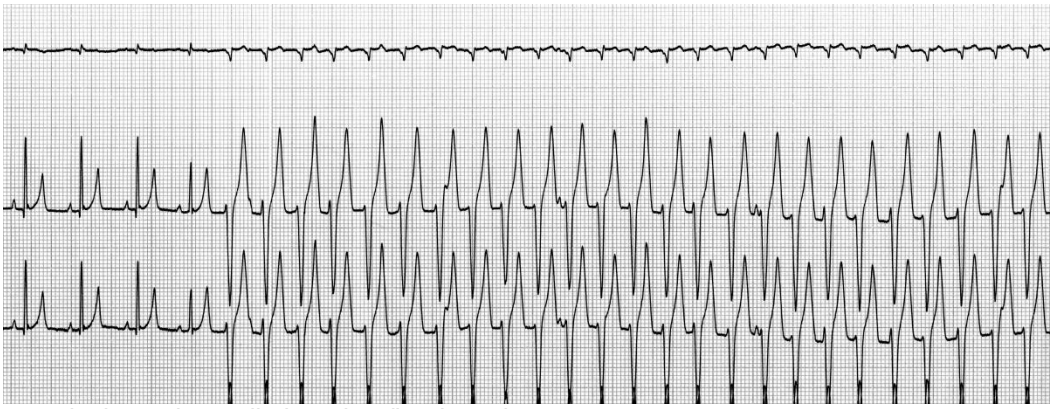
Oral digoxin is usual agent of choice for dogs with heart disease
Congestion should also be treated as required
Occasionally additional anti-dysrhythmic therapy (e.g. oral diltiazem) is indicated if treatment of congestion plus oral digoxin do not provide adequate ventricular rate control

- Dose calcium channel blockers or beta-blockers cautiously as they have negative inotropic effects that may cause clinical deterioration

Ventricular tachycardia



VPCs in a dog (lead II) – couplets and triplets



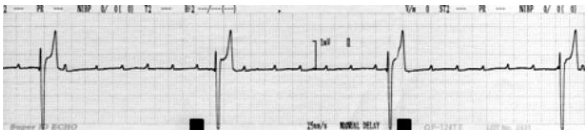
Ventricular tachycardia in a dog (leads I-III)

Ventricular premature complexes (VPCs) and ventricular tachycardia (VT) are commonly identified in emergency patients, especially dogs

- Ventricular tachycardia = 7 or more consecutive VPCs

Complexes are usually wide and bizarre, and not associated with P waves

Comment on ventricular escape complexes



3rd degree AV block in a dog (lead II) – ventricular escape complexes are evident

Ventricular escape complexes essentially keep bradydysrhythmic animals alive and must not be treated with anti-dysrhythmic therapy

Ventricular (or junctional) escape complexes typically occur in animals with severe bradydysrhythmia; the escape rhythm is responsible for maintaining cardiac output
A ventricular intrinsic escape rate (idioventricular rhythm) of less than 50 beats per min is typical in dogs, less than 100 beats per min in cats.

The ventricular complexes in these cases must not be treated.

Causes of ventricular tachycardia

Non-cardiac (systemic)	Primary cardiac
Intraabdominal disorders, e.g. • Splenic disease • Gastric dilation-volvulus (GDV) • Canine haemorrhagic gastroenteritis (HGE) Hypoxaemia and tissue hypoxia Systemic inflammation (e.g. SIRS/sepsis) CNS disease, e.g. • Brain disorders • Inflammatory CNS disease Variety of drug therapies (Electrolyte abnormalities) (Acid-base abnormalities)	Variety of congenital and acquired heart diseases Boxer arrhythmogenic right ventricular cardiomyopathy Dilated cardiomyopathy in Doberman Pinscher Heart failure Myocardial trauma, inflammation, ischaemia, hypoxia, neoplasia Pericardial effusion

Treatment

Indications for treatment

VPCs typically do not require specific intervention – treatment aimed at underlying disorder

Ventricular tachycardia is only treated when one of the following criteria is met:

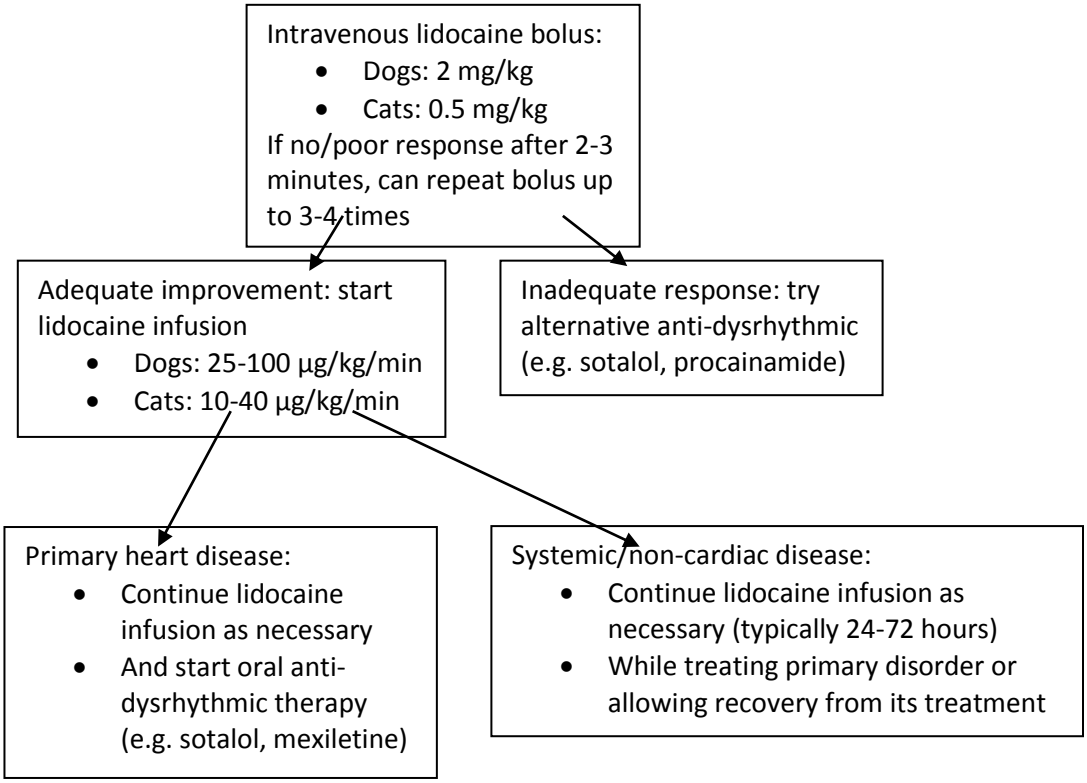
- Causing significant clinical signs e.g. lethargy, exercise intolerance, collapse
- Associated with evidence of sustained systemic hypoperfusion (pallor, poor peripheral pulses, slow capillary refill time)
- Sustained (more than 30 seconds) at a rate above 180 beats per minute
- R-on-T present (ectopic R wave superimposed on T wave of preceding complex) – indicates risk of ventricular fibrillation
- (Significant number of) multiform complexes
- Structural heart disease, Boxer arrhythmogenic right ventricular cardiomyopathy or Doberman dilated cardiomyopathy suspected and rate exceeds 180 beats per minute (sustained or not)

Accelerated idioventricular rhythm:

- Ventricular rhythm occurring at a slower rate than VT, typically less than 100 to 140 beats per minute (definitions vary)
- QRS complexes typically regular and uniform
- Causes include major surgical procedures or other trauma, and systemic disease
- Not typically associated with haemodynamic compromise therefore typically not treated

Anti-dysrhythmic therapy

Sustained conversion to sinus rhythm is unlikely, at least in the short-tem; many animals remain in a predominantly ventricular rhythm or sinus rhythm with frequent VPCs. Treatment is considered successful if there is sufficient improvement in terms of either haemodynamic compromise or rhythm malignancy.



Lidocaine: class IB (membrane-stabilising) anti-dysrhythmic agent (blocks fast sodium channels)
Sotalol: non-selective beta-blocker; class III anti-dysrhythmic agent (selectively inhibits potassium channels)

Bradydysrhythmias

Some forms of bradydysrhythmia (e.g. sinus bradycardia, first degree AV block) may occur in animals that have a physiological elevation in vagal tone either through high levels of fitness or for example when asleep. Clinical signs are typically not associated with the slow heart rate in such cases and treatment is not required.

Sinus bradydysrhythmias

Due to:

- Decreased impulse generation by sinoatrial node, or
- Decreased impulse conduction through atria
- Examples include sinus bradycardia, sinus arrest and sinoatrial block

Causes:

Primary cardiac causes – typically relate to sinoatrial node pathology (e.g. idiopathic fibrosis, myocardial disease)

Systemic/non-cardiac causes:

- Increased vagal tone
  - Relatively common
  - Many examples .g. central neurological, gastrointestinal, other intra-abdominal, respiratory
- Raised intracranial pressure
- Hyperkalaemia (e.g. urethral obstruction, hypoadrenocorticism (Addison's disease))
- Hypothermia
- Hypoglycaemia (probably only if moderate-to-severe)
- Drug therapy (e.g. opioids, some sedatives)

Treatment depends on cause and whether clinically significant – address underlying cause where possible; vagolytic therapy (e.g. atropine) should work in patients with high vagal tone and may variably work in other cases too.

Sick sinus syndrome

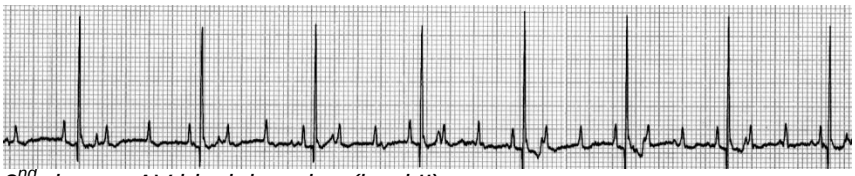
Combination of dysrhythmias that typically include abnormalities in both impulse generation by sinoatrial node and subsequent conduction
Sinus bradycardia, sinus arrest and supraventricular tachycardia occur in variable combinations
Usually idiopathic
Occurs most commonly in West Highland White terriers and Miniature Schnauzers amongst others; (reported but very rare in cats)

Treatment:

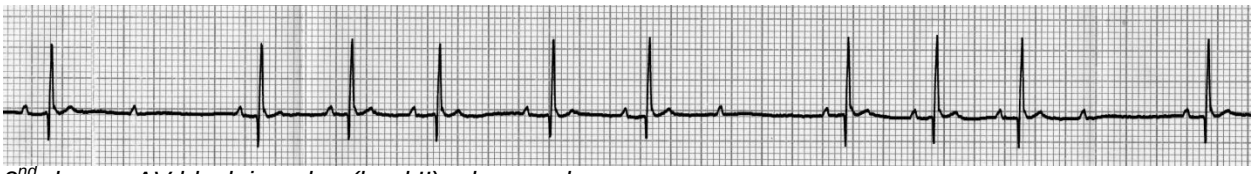
Indicated in all symptomatic dogs – common signs of low cardiac output include cardiac syncope, exercise intolerance, variable weakness
Can try medical therapy (e.g. terbutaline, theophylline) in less severe cases – some clinical improvement may be observed, at least for a short while
More severe cases need pacemaker implantation, potentially urgently

Atrioventricular (AV) block

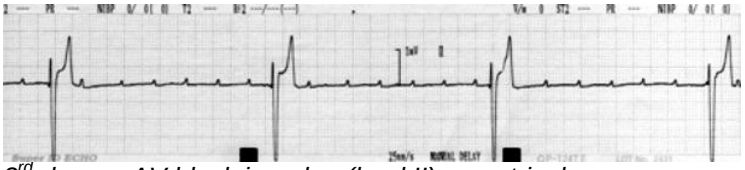
Delayed or failed impulse conduction through AV node
Three types – first degree, second degree, and third degree – with some further sub-classification



2nd degree AV block in a dog (lead II)



2nd degree AV block in a dog (lead II) – low grade



3rd degree AV block in a dog (lead II) – ventricular escape complexes are evident

Causes:

Primary AV node disease (e.g. idiopathic fibrosis, myocardial disease) – third degree AV block is almost always due to heart disease.
Systemic/non-cardiac causes – especially first and second degree; similar to sinus bradydysrhythmias

Treatment:

Treatment depends on cause and whether clinically significant – address underlying cause where possible
Symptomatic patients may require medical therapy:

- E.g. terbutaline, theophylline
- Vagolytic therapy (e.g. atropine) should work in patients with high vagal tone and may variably work in other cases too

First degree AV block unlikely to cause clinical signs
Second degree AV block may be clinically significant
Third degree AV block almost always associated with haemodynamic compromise (e.g. exercise intolerance, variable weakness, cardiac syncope)
Animals with irreversible cardiac damage and clinical signs of low cardiac output may require a permanent pacemaker to be implanted

Parenteral Fluid Therapy

Parenteral Fluid Therapy was described in the study notes for Session 2 of this mini-series.

Emergency Diagnostics

What are 'emergency diagnostics'?

Key features:

- Designed to answer specific questions to aid in the initial stabilisation and evaluation of the emergency patient
- Provide the information that we need in a rapid time frame – hence generally taking about in-house or point-of-care testing

Emergency Database

Traditional **Minimum Emergency Database (MDB)**:

- Manual packed cell volume (PCV)
- Refractometric plasma total solids
- Blood urea nitrogen – traditionally obtained by dipstick methodology
- Blood glucose

A lot of information can be derived from this minimum emergency database. As in-house testing becomes more available and sophisticated the traditional MDB may not be being performed as often; nevertheless it is essential to recognise the information these parameters provide.

If available blood venous lactate measurement may also be included as part of the MDB in many emergency patients.

Extended Emergency Database:

Minimum Emergency Database plus e.g.

- Peripheral blood smear evaluation
- Plasma electrolytes
- Creatinine in order to augment information obtained from urea
- Urinalysis

No strict criteria as such.

Other potential emergency diagnostic tests:

Focused ultrasonography as mentioned earlier to answer specific questions in emergency patients.
Electrocardiography
Clotting times

A comprehensive discussion of all of these diagnostic tests is beyond the scope of these notes. However more information is provided about the components of the traditional MDB.

Minimum Emergency Database

Manual PCV and plasma total solids

Manual PCV and plasma TS should always be interpreted together

Manual **packed cell volume (PCV)** = fraction of whole blood volume that consists of red blood cells
Refractometric plasma **total solids (TS)** = solutes dissolved in the plasma as measured using a hand-held refractometer

- TS is usually roughly equivalent to plasma total protein (TP) concentration although an increase in the concentration of other solutes may potentially affect the TS reading; however this is a poorly defined subject with little evidence base.

For further discussion on PCV vs. haematocrit and on the relationship between TS and TP see this blog post: http://bit.ly/pcvhcttstp.

PCV	TS	Possible causes
Normal	↑	Hyperglobulinaemia[1] Artefactual increase[2]
Normal	↓	Acute blood loss Hypoproteinaemia[3] Severe vasculitis (protein exudation)
↓	Normal	Acute haemolytic anaemia Chronic anaemia (e.g. chronic disease, aplastic anaemia)
↓	↓	Blood loss Chronic anaemia + additional cause of hypoproteinaemia[3] Dilutional effect of significant fluid therapy
↑	Normal	Dehydration with concurrent protein loss Breed-related normal variation (e.g. Greyhound) Absolute polycythaemia
↑	↑	Dehydration (i.e. relative polycythaemia)

Possible causes of changes in manual PCV and plasma TS

Superscript notes:

1. Causes of hyperglobulinaemia:
   - Dehydration
   - Inflammation (typically chronic)
   - Polyclonal gammopathy (e.g. feline infectious peritonitis, inflammatory bowel disease, chronic inflammatory disease)
   - Monoclonal gammopathy (e.g. plasma cell myeloma)

2. The 'normal' reference range for plasma TS is generally considered to be the same as the reference range for total protein. However in certain circumstances, TS measured using a refractometer may be increased above total protein (e.g. hyperglycaemia, hyperlipidaemia) as the refractometer may detect these additional solutes; however this is a poorly defined subject with little evidence base.

3. Causes of hypoproteinaemia:
   - Panyhypoproteinaemia (hypoalbuminaemia + hypoglobulinaemia):
     - Blood loss
     - Protein-losing enteropathy (PLE)
   - Hypoalbuminaemia:
     - Protein-losing nephropathy (PLN)
     - Malnutrition/malabsorption
     - Hepatic failure
     - Chronic effusions
     - Burns (and other severely exudative skin lesions)

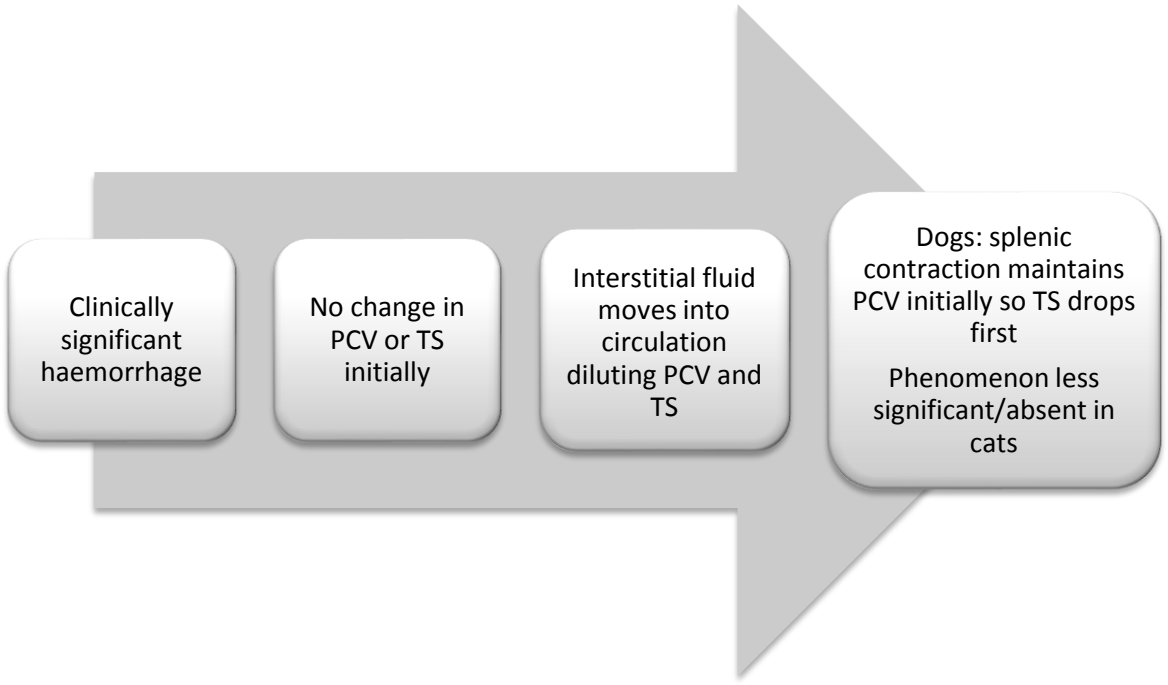
PCV/TS in blood loss

Both red blood cells and protein are lost from the circulation in haemorrhage and therefore PCV and TS do not change initially:

- Remember that PCV is a percentage and TS a concentration, i.e. neither is a measure of absolute quantity
- In the first few minutes following haemorrhage, the absolute number of red blood cells and plasma protein molecules will be reduced but PCV and TS are unchanged

Fluid then moves from the interstitial compartment into the bloodstream diluting the remaining red cells and protein and causing a decrease in the measured PCV and TS:

- It takes a while for fluid shift and therefore dilution to occur although it is not possible to be too precise about the exact length of time in clinical patients
    - In dogs the spleen contracts in response to haemorrhage and expels a large amount of stored red blood cells into the circulation; therefore PCV may remain in the normal range for a while despite low TS, i.e. with blood loss, TS is usually expected to fall first followed by PCV in dogs.
    - The response of the spleen in cats is either much less substantial or in fact non-existent depending on which reference one consults
- As yet more time passes PCV will also fall depending on whether haemorrhage is on-going and its severity, and any treatment instituted



Changes in PCV and TS following clinically significant haemorrhage

Gross plasma appearance

Centrifugation of whole blood for measurement of PCV/TS also allows gross plasma appearance to be evaluated for:

- Lipaemia: may occur post-prandially but also for example in hyperadrenocorticism ("Cushing's") or pancreatitis
- Haemolysis: due to intravascular haemolysis or poor sampling
- Jaundice (icterus):
    - Pre-hepatic (haemolysis)
    - Hepatic (intrahepatic cholestasis)
    - Post-hepatic (typically biliary tract obstruction)

Centrifuged samples can also be evaluated for the size of the **buffy coat** – this is the fraction that contains most of the white blood cells (and platelets). Although this is a crude estimation of white cell count it may draw one's attention to severe abnormalities.

Blood glucose concentration

Hypoglycaemia

Causes

- *Neonates, juveniles or toy breed dogs: typically at times of illness (especially gastrointestinal)
- *Excess circulating insulin levels (hyperinsulinism):
    - Neoplasia: especially canine insulinoma (produces insulin); also some liver tumours (paraneoplastic syndrome)
    - Excessive exogenous insulin administration, typically accidental overdose
- *Exercise-induced/working dog hypoglycaemia
- *Xylitol intoxication (dogs)
- Hypoadrenocorticism (Addison's disease) – including in cats
- Liver failure
- Sepsis
- Severe seizures/status epilepticus
- Heatstroke

* Hypoglycaemia that is severe enough to causes clinically significant effects is seen most often with these causes. However this may occur with any of the other listed causes too.

Note that adult animals should not become hypoglycaemic from malnutrition or starvation alone

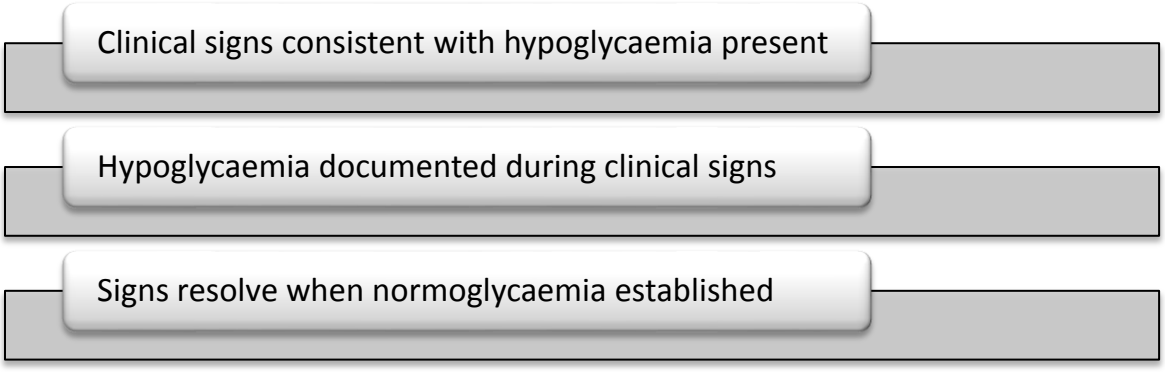
Clinical signs

Hypoglycaemia should be considered as a possible cause in any animal presenting for seizures or depressed mentation

Clinical signs of hypoglycaemia usually relate to brain dysfunction due to neuroglycopaenia (i.e. reduced cerebral glucose availability) and to sympathetic nervous system stimulation. Depending on the severity of the hypoglycaemia, clinical signs range from mild (e.g. lethargy, weakness) to moderate (e.g. depression, ataxia, muscle tremors) to very severe (e.g. collapse, seizures, coma). Hypoglycaemia (probably only moderate-to-severe) can also cause sinus bradycardia/bradydysrhythmia.

The blood glucose levels at which signs develop can vary between individuals, but in general:

- Clinical signs usually do not occur until blood glucose is < 3 mmol/l
- Secondary neurological signs are unusual while blood glucose > 1.5-2 mmol/l



Whipple's triad criteria for clinically significant hypoglycaemia

Treatment

The appropriate treatment for hypoglycaemia depends on the blood glucose concentration, the clinical signs, and in some cases the cause and suspected chronicity.

Topical mucosal therapy:

- Either a proprietary topical 'fast acting' glucose solution (e.g. Glucogel®, BBI Healthcare) or sugary water or honey for example can be applied to the gums or other mucosal surfaces
- This route of treatment is unlikely to resolve the hypoglycaemia but may alleviate clinical signs sufficiently while other routes of intervention are instigated
- Dosing is usually empirical

Enteral therapy:

- Enteral therapy may be adequate in less severe cases and is the most physiological route of supplementation
- Patients are fed small amounts of palatable food regularly (e.g. every 1-2 hours) and in some cases sugar solutions, honey or similar are included
- Contraindications for enteral therapy include inability or refusal of the patient to eat voluntarily, absent gag reflex, obtundation or vomiting

Parenteral therapy:

- More severe cases of hypoglycaemia require more aggressive intervention in the form of parenteral therapy; this is usually intravenous but intraosseous administration may be required in some cases.
- Glucose is administered until clinical signs are controlled but a starting dose of 0.25-0.5 g/kg is usually recommended – this is equivalent to 0.5-1.0 ml/kg of a 50% glucose (dextrose) solution.
- 50% glucose solution should be diluted (e.g. with an equal volume of crystalloid solution) prior to administration as it can cause venous irritation and inflammation (phlebitis).
- Clinical signs usually resolve quickly with treatment:
    - Occasionally animals that are showing signs of brain dysfunction, including seizures, continue to do so despite establishing normoglycaemia – signs may or may not eventually abate. This phenomenon may be due to continued neuroglycopaenia despite normoglycaemia or due to residual injury suffered during the hypoglycaemic period.

Following bolus administration of glucose (which can be repeated), a glucose infusion is usually required to prevent recurrence of clinical signs. Some glucose solutions for infusion are available commercially (e.g. 0.9% sodium chloride + 5% glucose) but they can also be readily constituted:

Glucose solution required	Size of isotonic crystalloid fluid bag	
	500 ml	1000 ml
	Volume to be removed and added	
1.25 % (12.5 mg/ml)	12.5 ml	25 ml
2.5 % (25 mg/ml)	25 ml	50 ml
5 % (50 mg/ml)	50 ml	100 ml
7.5 % (75 mg/ml)	75 ml	150 ml
10 % (100 mg/ml)	100 ml	200 ml

This table presumes the use of a 50% (500 mg/ml) glucose (dextrose) solution and either 0.9% sodium chloride (normal saline) or buffered lactated Ringer's solution (Hartmann's solution, compound sodium lactate).

[The volumes listed are the amount of fluid that should be removed from the isotonic crystalloid bag, and then replaced by an equal volume of 50% glucose solution in order to make a glucose solution of the desired concentration.
For example, to make a 5% glucose saline solution, remove 50 mL from a 500 mL bag of 0.9% sodium chloride and then add 50 mL of 50% glucose solution to the bag.]
Glucose solutions for long-term infusion are usually of 2.5% or 5% concentration. Occasionally it is necessary to administer a 10% glucose solution. The tonicity/osmolarity of this solution may pose a risk of phlebitis when administered via a peripheral vein and if possible it is recommended to infuse through a central vein (larger blood flow and more rapid dilution reduce the risk of localised adverse effects on the vessel).

Note that except for patients with type I diabetes mellitus (i.e. absolute insulin deficiency due to pancreatic islet cell destruction, unable to significantly increase insulin output), it may be better to try and manage patients in need of glucose supplementation with an infusion rather than intermittent bolus therapy. This is because boluses may stimulate repeated surges in insulin production which is less physiological and may make it harder to establish good control of the patient.

Treatment of hypoglycaemia should be guided by clinical signs and if available, regular monitoring of blood glucose concentration.

In middle to older-aged dogs with clinically significant hypoglycaemia, a blood sample should be collected for measurement of serum insulin concentration prior to glucose supplementation if possible.

- Insulinomas seen most commonly in medium-to-large breed dogs
- Have been identified in dogs as young as 3 years old

If blood glucose cannot be checked, it may be appropriate to administer conservative empirical glucose therapy where there is a high index of suspicion for clinically significant hypoglycaemia, e.g.
Puppies and kittens, especially with diarrhoea
Adult dogs with a possible insulinoma (e.g. intermittent self-resolving collapse, generalised weakness or neuromuscular signs, especially during exercise)

Hyperglycaemia

Diabetes mellitus is the only cause of hyperglycaemia that requires specific treatment with exogenous insulin. Hyperglycaemia may be detected in other cases but treatment is not indicated; examples include other endocrine disorders (hyperadrenocorticism ("Cushing's") and acromegaly), secondary to stress (especially cats) and following seizures or traumatic brain injury.

Hyperglycaemia in critical illness:

Hyperglycaemia may be detected in critical patients with a variety of disorders. In human medicine there is an established evidence base supporting 'tight control' of blood glucose in critically ill patients with a number of both surgical and medical problems. However at this time there is insufficient evidence to suggest that normalising hyperglycaemia in critically ill dogs and cats has a beneficial effect on morbidity or outcome. This treatment is practically intensive and expensive and as such it is not recommended at this time in dogs and cats.

Comment on glucometers

Glucometers are an inexpensive means of checking blood glucose concentration, require minimal blood to be taken, and produces rapid 'point-of-care' results. However it is important to bear a couple of things in mind.

Firstly try and ensure that the same device is used throughout if repeatedly monitoring a patient's blood glucose level as different devices and models can generate different results. Likewise, avoid directly comparing glucometer results with those from a chemistry analyser.

Secondly, many of the glucometers used in veterinary medicine are actually manufactured for use in people; some – but not all – have been validated for use in dogs and cats. These devices are generally accurate in the mid-to-high glucose range but often programmed to generate blood glucose readings that are lower than the true concentration in the low range – this is a safety mechanism to allow treatment to be implemented before hypoglycaemia worsens.

Thirdly an abnormal haematocrit can affect blood glucose concentration if it is measured using whole blood with a single-channel point-of-care glucometer. This is because these devices calculate the glucose concentration on the assumption that the whole blood sample has a normal plasma fraction. There are some conflicting reports as the effect may depend on the specific glucometer used. However, in most cases the consensus seems to be that anaemia can result in an artificially high blood glucose concentration (i.e. the patient's real blood glucose concentration is lower than the glucometer reports). This makes sense because anaemic patients have relatively more plasma but the glucometer cannot account for this, i.e. it underestimates the plasma volume. A high haematocrit may have the opposite effect.

Some people have suggested using mathematical formulae and correction factors to work out what the correct glucose concentration is in an anaemic patient; however there is controversy over these formulae which are yet to be validated both in humans and in dogs and cats.

The problem can be avoided by using analysers that use plasma rather than whole blood, but most POC glucometers use whole blood.

More recently, multichannel POC glucometers have become available that are able to actually measure the haematocrit and correct the glucose concentration based on the plasma volume. It is unclear if or when these devices will be adopted in veterinary medicine.

Blood urea nitrogen

An increase in BUN via dipstick does not necessarily mean that the patient is azotaemic. Azotaemia refers to an increase in the concentration of urea and creatinine (and other nitrogenous substances) in the blood. An increase in BUN alone may occur due to extra-renal factors such as increased dietary protein intake, gastrointestinal haemorrhage and increased protein breakdown. An increase in BUN via dipstick serves as a useful flag of possible renal insufficiency but should prompt measurement of serum creatinine concentration which is considered a more reliable indicator of renal function.

Azotaemia

Type of azotaemia	Causes	Severity	Reversibility	Other comments
Pre-renal	Reduced renal perfusion causes a functional decrease in GFR; e.g. dehydration, hypovolaemia, heart failure	Typically mild	Typically reversible unless prolonged hypoperfusion causes renal injury and renal azotaemia	Characterised by increased PCV, TS and USG
Renal	Reduced GFR occurs secondary to structural renal changes, e.g. due to nephrotoxicity, neoplasia, infection, ischaemia etc.	Mild, moderate or severe	Reversible or irreversible	Isosthenuria (USG 1.007-1.015) as kidneys no longer able to dilute or concentrate the urine Anaemia may be present with chronic renal insufficiency
Post-renal	Failure to clear BUN and creatinine from the body due to urinary tract obstruction or rupture	Often very severe at diagnosis	Frequently fully reversible	Prolonged urinary outflow obstruction can result in damage to the renal parenchyma and consequent intrinsic acute renal failure

[GFR: glomerular filtration rate; USG: urine specific gravity]
Features of the different types of azotaemia

COMMON CAUSES OF COLLAPSE IN THE DOG

Haemoabdomen

Causes

Non-traumatic:

- Rupture of intra-abdominal neoplasm (especially splenic; also hepatic, adrenal and others)
- Coagulopathy, e.g. anticoagulant rodenticide intoxication; *Angiostrongylus vasorum* infection
- Post-operative following abdominal surgery: primary surgical complication versus secondary to existing coagulopathy (e.g. congenital (especially von Willebrand's disease) versus canine angiostrongylosis)
- Gastric dilatation/volvulus syndrome (GDV)
- Splenic torsion
- Splenic infarction
- Splenic haematoma rupture
- Liver disease (including neoplasia, necrosis, amyloidosis, rupture), especially in cats
- Liver lobe torsion

Trauma usually causes rupture of intra-abdominal viscera (especially liver, spleen):

- Blunt trauma, especially motor vehicle accident
- Penetrating trauma

In the author's experience rupture of intra-abdominal haemangiosarcoma lesions is by far the most common cause of clinically significant haemoabdomen.

Occasionally umbilical and peri-testicular skin discolouration is observed in dogs with significant intra-abdominal haemorrhage. This is the result of blood dissecting through the abdominal muscle planes and subcutis.

Diagnosis

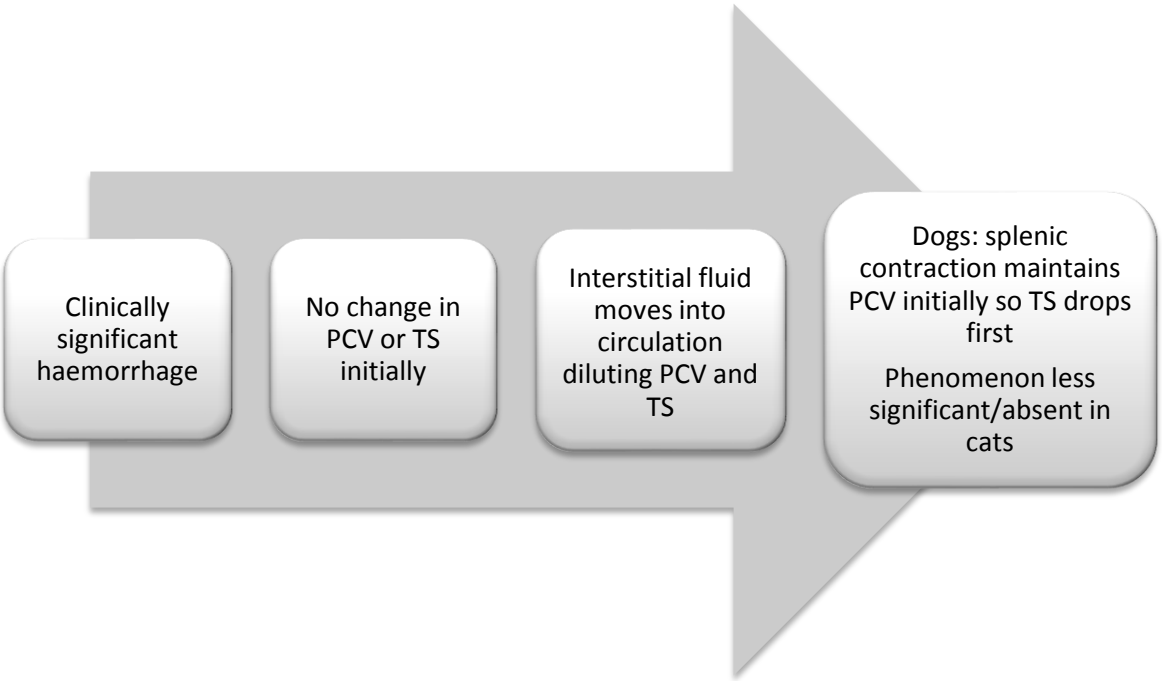
Manual packed cell volume (PCV) and plasma total solids/protein (TS/TP) measurement may be suggestive of significant haemorrhage within the patient although changes are clearly not specific to intra-abdominal haemorrhage.

Both red blood cells and protein are lost from the circulation in haemorrhage and therefore PCV and TS do not change initially.

- Remember that PCV is a percentage and TS a concentration, i.e. neither is a measure of absolute quantity.
- In the first few minutes following haemorrhage, the absolute number of red blood cells and plasma protein molecules will be reduced but PCV and TS are unchanged.

Fluid then moves from the interstitial compartment into the bloodstream diluting the remaining red cells and protein and causing a decrease in the measured PCV and TS.

- It takes a while for fluid shift and therefore dilution to occur although it is not possible to be too precise about the exact length of time in clinical patients.
- In dogs the spleen contracts in response to haemorrhage and expels a large amount of stored red blood cells into the circulation; therefore PCV may remain in the normal range for a while despite low TS, i.e. with blood loss, TS is usually expected to fall first followed by PCV in dogs.
    - The response of the spleen in cats is either much less substantial or in fact non-existent depending on which reference one consults.
- As yet more time passes PCV will also fall depending on whether haemorrhage is on-going, the severity of any on-going haemorrhage, and any treatment instituted.



A definitive diagnosis of haemoabdomen requires identification, aspiration and consistent analysis of peritoneal fluid:

See earlier notes on abdominal free fluid scanning.

Blood lost into the abdomen (and other cavities) often has an echogenic appearance.
When analysed the fluid will:

- Be grossly sanguineous but non-clotting
- Have a PCV that is similar to (could be lower, same or higher than) the patient's circulating PCV
- Have red blood cells, possible occasional erythrophagocytosis, and typically no platelets on cytology
    - Note: although cytology is not required to diagnosis haemoabdomen, it should always be performed to exclude the presence of a concurrent septic process which would then make surgery an emergency following stabilisation.

Beware of over-interpreting fluid aspirated from any body cavity as being consistent with haemorrhage purely based on gross appearance. It is not unusual for fluid to grossly appear consistent with bleeding only for PCV measurement to then be inconsistent – grossly sanguineous fluid can for example have a PCV of less than 5-10%.

Comment on blood loss into a body cavity:

Following haemorrhage into the peritoneal (or pleural) cavity, platelets quickly aggregate, degranulate and disappear (within a few hours) – the presence of platelets in the effusion suggests peracute haemorrhage (or iatrogenic).
Within 24 hours, macrophages become activated and begin to phagocytose red blood cells (erythrophagocytosis) – therefore if there is erythrophagocytosis on microscopy of the effusion, this would suggest a degree of chronicity (> 1 day) and would exclude iatrogenic haemorrhage.

It is intuitive therefore that following a single episode of haemorrhage, the PCV of the free fluid is initially at its peak and then decreases. If the PCV of a fluid sample obtained via aspiration is very similar to that of peripheral blood, this is consistent with severe (per)acute haemorrhage or splenic/blood vessel aspiration - the latter as we know can be ruled out if the fluid does not clot.

In the author's experience, free peritoneal fluid is readily detected and sampled in most animals presenting with clinically significant haemoabdomen and DPL is typically not required; this is especially the case when ultrasonography is used to assist fluid detection/aspiration. However if DPL is used, the subsequent dilution must be kept in mind when interpreting the results of fluid analysis. A packed cell volume of DPL fluid of 2-5% or more is reportedly suggestive of significant haemorrhage.

In patients not suspected of having suffered trauma, further diagnostic tests that may be required to identify the cause of the haemoabdomen include for example:

- More comprehensive diagnostic imaging to evaluate intra-abdominal organs for structural lesions (e.g. due to haemangiosarcoma) that may have ruptured
- Clotting times for anticoagulant rodenticide intoxication: clotting times may be prolonged following bleeding but will be significantly prolonged or 'off the scale' in patients bleeding from this poisoning
- In-house testing (plasma antigen test, faecal smear examination,) +/- Baermann's faecal analysis for canine angiostrongylosis

Case management

Following diagnosis of a haemoabdomen, aspects of management include:

- Intravascular volume resuscitation for haemorrhagic hypovolaemia
- Analgesia as required
- Identifying the underlying cause and initiating treatment if possible
- Deciding whether surgical intervention is required and if so, in what timeframe

See earlier notes on resuscitation of hypovolaemia and hypotensive/haemostatic resuscitation.

If available, a cell-saver device can be used to harvest blood from the peritoneal cavity and autotransfuse the patient. There is some debate about the use of autologous transfusion in patients with suspected neoplasia in terms of disseminating the disease systemically if systemic metastasis has not already occurred; however it may be rational as a life-saving measure?

Comment on abdominal pressure bandages:

The intended purpose of an abdominal pressure bandage is to apply external pressure that will increase intra-abdominal pressure and thereby tamponade bleeding. Realistically intra-abdominal pressure is only likely to be increased sufficiently to exceed venous pressure and reduce venous haemorrhage. Therefore excessively tight bandages do not offer any greater advantage and are likely to be associated with greater complications.

There remains much debate about the use of abdominal pressure bandages and in cases in which specific contraindications do not exist, the decision at this time seems to be opinion-based rather than based on a clinical evidence base. The author does not routinely employ these bandages.

Abdominal bandages are contraindicated with:

- Pelvic or femoral fractures
- Respiratory distress due to pneumothorax or pleural effusion
- Diaphragmatic rupture
- Head trauma

Repeated abdominal free fluid scanning is increasingly used a means of monitoring patients with free abdominal fluid for disease progression, including on-going blood loss, and this cannot be done if an abdominal pressure bandage is in place. Their use in post-operative patients may also be far from ideal as they may significantly increase patient discomfort.

Traditionally a soft material has been used as the primary layer of an abdominal pressure bandage with an elastic material applied on top. In the author's experience however these bandages are more likely to slip and the author prefers to use an elastic adhesive primary layer despite the inherent difficulties in subsequent removal. The bandage should be placed starting caudally approximately at the level of the pubis and moving in a cranial direction up to the xiphoid, stopping before the caudal rib margin.

The bandage should be removed once the patient has remained stable for a reasonable period. Removal should commence at the cranial end (i.e. in the opposite direction to how the bandage was placed) and ideally should be staggered by cutting a small section every 30-60 minutes over a period of several hours. The patient should be monitored closely for signs of deterioration during bandage removal.

An abdominal pressure bandage technique has been described that incorporates the pelvic limbs to try and improve venous return to the heart (something similar has been used in people). However this technique is not recommended – although it may offer a theoretical benefit, this is outweighed by the potential disadvantages, e.g.:

- Painful and distressing to apply
- Difficult to apply safely
- Compartmentalisation of blood in the pelvic limb vasculature
- May occlude the caudal abdominal vena cava

Analgesia

As always the level of analgesia a patient with haemoabdomen requires should be determined based on the individual patient's assessment and proposed management plan (e.g. surgical versus non-surgical). Opioids are generally used in the first instance, often pure (full μ-agonist) opioids initially and especially if surgery is planned. Non-steroidal anti-inflammatory drugs (NSAIDs) are contraindicated in the presence of hypovolaemia. Moreover these drugs can potentially interfere with platelet function and contribute to a coagulopathic state.

Surgical intervention for haemoabdomen

The key considerations in deciding whether emergency surgery is indicated are **patient stability**, **the likely cause/source of bleeding**, and whether **on-going active bleeding** is suspected.

Emergency surgical intervention may be required for patients with persistent haemodynamic instability but clearly only if a localised source of haemorrhage amenable to surgical intervention (e.g. ruptured splenic lesion, isolated ruptured hepatic lesion, slipped surgical ligature) is suspected. Surgery would not for example be considered appropriate in haemorrhage due to primary coagulopathic conditions.

The author's experience is that emergency surgery for haemoabdomen is infrequently indicated:

The majority of, but certainly not all, dogs with **neoplastic** haemoabdomen can be stabilised with elective surgery being performed subsequently if desired.
Traumatic haemoabdomen is most commonly mild and self-limiting; occasionally it can be catastrophic with patients presenting dead on arrival or undergoing cardiopulmonary arrest despite immediate aggressive intervention. Patients with traumatic haemoabdomen can be monitored for on-going blood loss by repeated ultrasonography and fluid analysis comparing PCV values of abdominal fluid and peripheral venous blood samples regularly (e.g. every 1-4 hours):

- These parameters will theoretically trend in opposite directions if bleeding has stopped:
    - Venous blood is diluted by fluid therapy so PCV will decrease
    - Abdominal PCV will initially remain stable and then start to increase as the abdominal fluid is resorbed
- If haemorrhage is on-going, venous PCV will decrease; abdominal PCV will also decrease slowly as there is continued loss of blood with an ever-lower PCV from the circulation.

Clearly the above guidelines are invalidated by the use of red cell products or if there is another source of abdominal contamination (e.g. concurrent uroabdomen).

Canine Haemangiosarcoma

Relevant theory

Haemangiosarcoma (HAS) is a malignant cancer of the vascular endothelium and any site in the body that contains vascular endothelium can theoretically be affected. Canine HSA is most commonly diagnosed in German Shepherd dogs followed very closely by Golden Retrievers. Other large breed dogs, especially Labrador Retrievers, are also overrepresented. It is most prevalent in males and in middle-to-older aged dogs.

The spleen is the most common site of origin but right atrial, pericardial and hepatic canine HSA is also reported relatively frequently. With respect to splenic HSA, many clinicians use the '**double two thirds rule**':

- Approximately two thirds of dogs with splenic masses will have malignant tumours
- Approximately two thirds of these malignant tumours will be diagnosed as HSA
- Hence approximately 43% of canine splenic masses are ultimately diagnosed as HSA; the remainder are benign or low grade malignancies

The author has not explored the literature to substantiate this rule-of-thumb.

Rupture of a HSA lesion in the spleen or less commonly the liver is the most common cause of haemoabdomen in dogs. Occasionally one is presented with a dog with peritoneal effusion that instead of being secondary to bleeding is a modified transudate. It is important to check for pericardial effusion in these patients as they may in fact have a primary cardiac HSA lesion that has given rise to pericardial effusion with secondary right-sided heart failure, cardiac tamponade and obstructive shock.

In terms of biological behaviour HSA is highly metastatic and splenic or hepatic HSA is presumed to have metastasised at the time of diagnosis in virtually all cases regardless of whether metastases are detected by currently available imaging modalities or not. Metastases essentially may occur anywhere and the brain is reportedly the most common site. Approximately 25% of patients with splenic HSA will also have right atrial lesions.

Diagnosis

Dogs with HSA may present with a variety of findings including:

- Weakness/collapse and variable degrees of hypoperfusion
- Bleeding
- Abdominal distension
- Pericardial disease
- Dysrhythmias
- Palpable mass

The diagnosis is suspected in a dog with haemoabdomen and consistent splenic and/or hepatic lesions; cytology of peritoneal fluid is not a reliable means of diagnosis. Clearly the patient's signalment acts to raise the index of suspicion and some owners will also report intermittent self-limiting episodes of lethargy or exercise intolerance in the preceding weeks that retrospectively are presumed to be due to recurrent bleeding. It should be remembered that the nature (benign or malignant) of structural lesions that may be identified in such cases cannot be definitively determined based on ultrasonographic appearance and that histopathology is required for a definitive diagnosis.

It is important to perform thoracic imaging for lung metastases in a patient with suspected intra-abdominal HSA before surgical intervention. Although more recently there is some suggestion that even patients with detectable metastases at diagnosis can respond favourably to chemotherapy, the presence of detectable lung metastases clearly makes the patient's position more precarious in terms of developing dyspnoea and owners may not wish to pursue surgical intervention in such cases.

Case management

Stabilisation of dogs with ruptured splenic and/or hepatic HSA is as described for haemabdomen in general.

In dogs presenting with haemoabdomen presumed to be secondary to rupture of a splenic lesion, splenectomy will be palliative and remove the risk of recurrent haemorrhage in the short term. Palliative

surgery may not be an option in primary hepatic haemangiosarcoma but may be possible if gross lesions are confined to a single lobe.

The timing of surgery varies from case to case in so far as some patients are either relatively stable at presentation or can be stabilised relatively easily and surgery may then be less urgent (e.g. can wait until the next day in a dog presenting at night). In other cases based on the severity of the patient's presentation and other clinical findings, surgery is performed on more of an emergency basis.

Prognosis

Clearly the prognosis in patients in which surgical intervention is not performed is grave due to the inevitable recurrence of haemorrhage most likely in the short-term. The prognosis in patients having successful palliative surgery is very poor with survival times in the region of 1-4 months. In more recent times there has been increasing experience with post-operative chemotherapy in dogs with splenic and/or hepatic HSA. It is apparent that HSA is a tumour that can be responsive to chemotherapy and survival may in some cases be improved potentially by several or more months. Moreover adverse effects of the most common protocols used (e.g. VAC = vincristine + doxorubicin + cyclophosphamide; doxorubicin + cyclophosphamide) appear to be relatively mild in most cases and as such it is worth discussing chemotherapy with owners. Metronomic chemotherapy is also often employed.

Based on current evidence adjuvant chemotherapy, i.e. after surgery, should always be recommended and this includes for patients in which metastases are detectable at the time of surgery. Other ways in which chemotherapy has been employed include neoadjuvant treatment to shrink lesions prior to surgery and as sole treatment if surgery (and radiotherapy) are not options.

Canine Pericardial Effusion

Relevant theory

Pericardial effusion is seen most commonly in older large-breed dogs and especially in Golden Retrievers. It represents an abnormal accumulation of fluid in the pericardial sac. The haemodynamic consequences of this fluid accumulation depend on the rate of accumulation, the volume of fluid, and the compliance of the pericardium. Fluid accumulation results in an increase in intrapericardial pressure that compromises ventricular filling (diastolic dysfunction). The right side of the heart is typically affected more than the left initially as the myocardium is thinner and intraventricular pressure is lower on the right side.

The most severe clinical manifestation of this cardiac tamponade is obstructive shock characterised by low cardiac output failure and systemic hypotension; this is essentially cardiac compartment syndrome. With more chronic effusion, signs of right-sided congestive heart failure usually predominate.

Causes

The two most common causes of canine pericardial effusion are **neoplasia** and **idiopathic pericarditis**. Intrapericardial tumours include haemangiosarcoma and heart base tumours. Echocardiographic findings may be highly suggestive of tumour type but histopathology is needed for definitive diagnosis; this is not realistic ante-mortem.

Haemangiosarcoma is the most commonly diagnosed canine cardiac tumour and arises most often from the wall of the right atrium or auricle. It is the most common cause of canine pericardial effusion and is assumed to have metastasised in virtually all cases at the time of diagnosis. Surgical resection and adjuvant chemotherapy is offered by some referral centres. The most common heart base tumours in dogs are aortic body tumours (chemodectomas). Mesothelioma is a diffuse neoplasm affecting serosal surfaces including the serous pericardium and does not cause obvious pericardial thickening on

echocardiography. Pericardial fluid cytology is unable to differentiate effusion secondary to idiopathic pericarditis from effusion secondary to mesothelioma, and pericardial histopathology may also not be able to differentiate the two causes. Mesothelioma should therefore always be considered a differential diagnosis for presumed idiopathic pericardial effusion.

Although pericardial fluid analysis is of limited benefit in most cases, cardiac lymphoma may be diagnosed in this way and is potentially responsive to chemotherapy.

Other causes of pericardial effusion include coagulation disorders, congestive heart failure, trauma, infectious causes and uraemia although clinically significant effects with respect to tamponade are unlikely in these cases. Pericardial effusion and cardiac tamponade secondary to anticoagulant rodenticide toxicity has been reported in a dog and if facilities allow, evaluation of coagulation is recommended prior to pericardiocentesis.

Constrictive and effusive-constrictive pericarditis:

In some dogs historical and clinical findings are consistent with tamponade secondary to pericardial effusion but little or no effusion is subsequently identified. A diagnosis of constrictive or effusive-constrictive pericarditis due to fibrosis should be considered in such cases.

Left atrial rupture:

Left atrial rupture and consequent haemopericardium is uncommon but may occur in dogs with chronic mitral valve disease. Associated clinical signs include collapse as well as coughing and dyspnoea, and physical examination findings include a heart murmur, poor peripheral pulses and muffled heart sounds. Dogs that suffer left atrial rupture are typically much smaller than those that present with pericardial effusion of other aetiologies and the presence of an audible heart murmur is another distinguishing feature.

Only partial drainage of the pericardial effusion is recommended as thorough drainage may exacerbate bleeding. Regardless of intervention, the prognosis is very poor with this condition.

Clinical findings

Clinical signs:

More common clinical signs include lethargy, exercise intolerance, variable appetite and progressive abdominal distension. Weakness, episodic collapse, polydipsia, gastrointestinal signs, coughing and dyspnoea are also reported.

Physical examination:

Cardiovascular:

- Tachycardia is common
- Heart sounds may be (relatively) muffled
- Evidence of systemic hypoperfusion may be present
- Pulse deficits may be present but are not especially common
- Jugular venous distension may be identified
- Pulsus paradoxus* may be present

(*Pulsus paradoxus is a decrease in pulse strength during inspiration reflecting a decrease in systemic arterial blood pressure. Pulse quality varies during respiration in normal dogs, becoming weaker on inspiration (poorly defined causes but likely multifactorial) and stronger on expiration. However this normal variation is exaggerated in cardiac tamponade and may be clinically detectable.)

Respiratory: panting is a common finding; lung field auscultation is often unremarkable in non-panting dogs

Central nervous system: may be relatively normal but some dogs are anxious while others may be depressed and recumbent

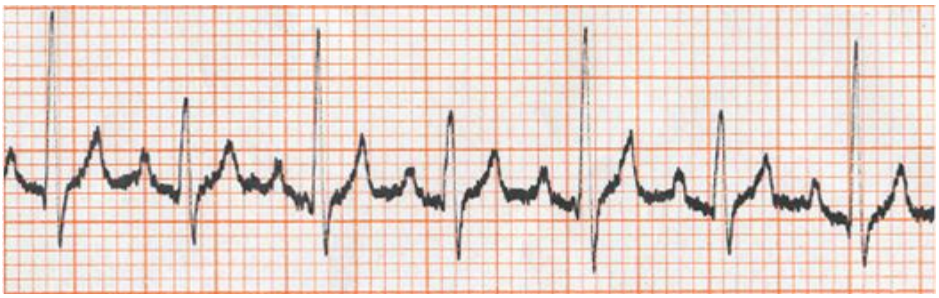
Marked abdominal distension with a palpable fluid thrill may be detected

Diagnosis

If available, echocardiography is the imaging modality of choice for confirming pericardial effusion. It is relatively easy to detect pericardial effusion as an anechoic space around the heart – PICTURE – and ultrasonography is both more sensitive and specific and less stressful to the patient when compared to thoracic radiography. An enlarged globoid cardiac silhouette and an enlarged caudal vena cava may be identified radiographically but changes may be more subtle especially in more acute cases. Thoracic radiography is usually indicated at some point during management of a dog with pericardial effusion in particular to evaluate the lung field for neoplastic metastases.

Electrocardiography:

Should be performed in any patient in whom pericardial effusion is suspected including throughout pericardiocentesis. Many dogs with pericardial effusion are found to be in sinus tachycardia. Low voltage QRS complexes are relatively common and electrical alternans may also be seen. Electrical alternans is alternate-beat variation in the direction, amplitude or duration of any component of the ECG waveform, most obviously the QRS complexes:



(Courtesy of Adrian Boswood)

Swinging of the heart in the fluid-filled pericardial sac is one of the causes of this phenomenon. In addition to sinus tachycardia, ventricular dysrhythmias are relatively common in dogs with pericardial effusion and may require specific therapy. Supraventricular dysrhythmias are identified less frequently.

Treatment

Pericardiocentesis is the treatment of choice for pericardial effusion; medical therapies *may* be/become indicated as well depending on the underlying cause but will not resolve a tamponade crisis. Not all dogs suffering from pericardial effusion require immediate pericardiocentesis. Fluid in the pericardial sac increases the sensitivity for detecting intrapericardial masses; in dogs that are relatively stable with only mild cardiovascular compromise it may be possible to delay drainage until comprehensive echocardiography can be performed.

There is some debate about the administration of aggressive fluid therapy to dogs presenting with cardiac tamponade and clinically significant hypoperfusion. An intravenous fluid bolus administered while diagnosis is achieved and preparations are made for pericardiocentesis may help by enhancing diastolic

filling if there is the capacity for this to occur; on the other hand intravenous fluid therapy will also further increase the venous blood volume in a patient that is already potentially volume overloaded. The effect of a fluid bolus can be unpredictable in these patients and ultimately relief of tamponade by aspiration is the priority intervention. Nevertheless there is some evidence from experimental animal and clinical human studies that a *conservative* fluid bolus can improve haemodynamics as a temporising measure prior to drainage; this may especially be the case in hypotensive patients.

Pericardiocentesis is usually performed under some degree of judicious chemical restraint, e.g. butorphanol (0.2 mg/kg IM) and midazolam (0.2 mg/kg IM). A notable improvement in cardiovascular status is typical once tamponade is successfully relieved.

Pericardiocentesis

Equipment list:

- Clippers
- Surgical scrub materials
- Materials for peripheral intravenous catheter placement
- 2% lidocaine (without adrenaline), 2 ml syringe, 23 gauge needle – for local anaesthesia
- 2% lidocaine (without adrenaline), 10 ml syringe (dog) or 1 ml syringe (cat), needle – in case needed for ventricular dysrhythmia
- Sterile gloves
- Sterile scalpel blade (No. 11)
- Over-the-needle BD Angiocath™ 14, 16 or 18 (cat) gauge, 3¼ or 5 inch; or similar over-the needle intravenous catheter
    - Pericardiocentesis catheters (or suitable central venous catheters or chest tubes) are increasingly available and can be left in situ short-term for repeated drainage if indicated
- Sterile 3-way tap or 'centesis valve'
- Extension tubing and 60 ml syringe (dog) or 20 ml syringe (cat)
- Sterile sample pots: EDTA and additive-free
- Kidney dish, jug or similar
- Continuous electrocardiogram (ECG) monitor if available

Procedure:

1. Place and secure a peripheral intravenous catheter
2. Restrain the patient in left lateral recumbency so that aspiration is performed from the right side
    - Sternal recumbency may also be used according to patient preference
3. Connect the patient to ECG monitoring if available
4. Clip a large area ventrally on the right thoracic wall from the 3rd-8th intercostal space:
    - Area should extend from sternum to mid-thoracic level
5. Infiltrate lidocaine (1 ml of 2% solution) subcutaneously and down to the parietal pleura at the site of needle insertion
    - The catheter is typically inserted at the level of the costochondral junction in the 4th-6th intercostal space and cranial to the rib (to avoid lacerating the intercostal neurovascular bundle that lies caudal to the rib).
6. Scrub the clipped area and then wearing sterile gloves make a stab incision in the skin at the site of needle insertion
7. Insert the catheter through the chest wall pointing slightly cranially and dorsally towards the opposite shoulder (or at the most appropriate angle determined by ultrasonography).

8. Advance the catheter until it enters the pericardial space – it may be possible to feel a 'pop' as the catheter goes through the pericardium:
    - Pericardial effusion is usually sanguineous or port-wine coloured
    - As the effusion is under pressure, it is expelled forcefully through the catheter when the pericardium is punctured and flows out of the hub
    - Pleural effusion can have a similar appearance to pericardial effusion although it is usually less sanguineous; however pleural effusion is not under high pressure in the pleural cavity and is not therefore expelled forcefully through the hub.
9. Advance the catheter off the stylet slightly further and then remove the stylet
10. Swiftly attach one end of the extension tubing to the catheter and give the other end to an assistant; the assistance should connect the 3-way tap or centesis valve and the 60 ml or 20 ml syringe to the extension tubing.
11. The assistant should then gently drain the effusion until no further fluid is obtained or the patient is no longer tolerant – the first sample of fluid obtained should be transferred aseptically into the sterile pots.
12. Remove the catheter; it is not usually necessary to cover the insertion site
    - If a pericardial catheter is being left in-situ then clearly it needs to be secured and lightly dressed

Complications:

Ventricular dysrhythmias:

Not uncommon during pericardiocentesis; significant rhythm disturbances may be the result of contact between the catheter and the myocardium (i.e. if the catheter has been advanced too far) and typically improve if the catheter is withdrawn slightly. If the dysrhythmia is very severe or if it does not improve when the catheter is withdrawn slightly, the catheter should be removed completely.

Lidocaine should be administered intravenously (start with 2 mg/kg bolus in dogs, 0.25-0.5 mg/kg bolus in cats) if a ventricular dysrhythmia is haemodynamically significant but only if there is no improvement once the catheter has been removed – i.e. do not administer lidocaine as a way of trying to continue with the procedure! Ventricular dysrhythmias are relatively common following pericardiocentesis and occasionally require treatment with lidocaine.

Iatrogenic injury:

Iatrogenic puncture of a cardiac chamber (typically right ventricle) or laceration of a sizeable blood vessel will result in blood being aspirated instead of pericardial effusion:

- A sample of fluid collected into an additive-free pot at the start of the procedure should be checked frequently for clotting as the procedure progresses. Blood will clot whereas being devoid of platelets and clotting factors, pericardial effusion should not (unless it is the result of active or very recent bleeding).
- In addition, drainage of pericardial fluid is typically associated with a fairly rapid improvement in patient status (e.g. heart rate decreases, pulse quality improves, and patient mentation improves).

Iatrogenic pneumothorax secondary to lung injury is a potential but rarely clinically significant complication.

Notes:

Restraint:

More than with many other procedures, pericardiocentesis must only be performed in adequately restrained patients given the proximity of the needle to the myocardium.

Depending on the patient in question and his/her clinical condition, variable degrees of manual restraint are required for pericardiocentesis. However, as always, excessive manual restraint is to be avoided in any potentially unstable or critically ill animal. Most animals in which this procedure is performed are large dogs and typically suffering variable degrees of cardiovascular compromise. As such many are compliant without the need for any chemical restraint.

Where necessary butorphanol (0.1-0.3 mg/kg IV) may be administered prior to the procedure especially if an in-dwelling drain is being placed. A benzodiazepine (e.g. midazolam 0.2 mg/kg IV) may be added if required but more potent chemical restraint is rarely indicated. Any drugs used must have minimal adverse cardiovascular effects.

Laterality:

Although the left ventricle is thicker and there would therefore be less risk of penetrating the ventricular chamber during the procedure, aspiration is typically performed from the right side. This is to minimise the risk of injury to major coronary arteries (mainly left-sided) and to the lung.

Ultrasonography can be used to confirm that the pericardial sac lies in close proximity to the thoracic wall at the site chosen for needle insertion; some clinicians prefer to perform the entire procedure under ultrasound guidance.

Drainage into pleural space:

In some cases, despite a significant volume of pericardial effusion being identified on ultrasonography, only a small volume is actually aspirated and yet the patient's clinical status improves markedly. This is because puncture of the pericardial cavity leads to drainage of the pericardial effusion into the pleural cavity where it is of much less clinical consequence and from where it is likely to be gradually cleared. This is a perfectly acceptable clinical outcome.

Canine Hypoadrenocorticism (Addison's Disease)

Theory refresher

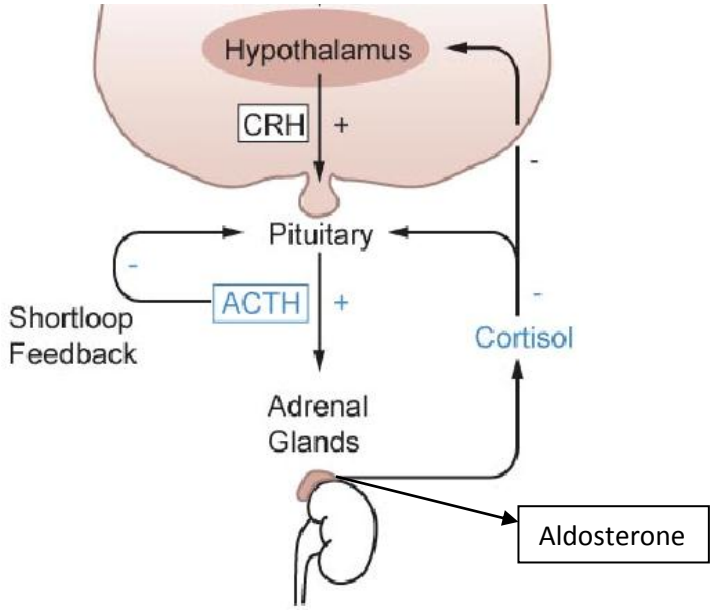
The adrenal cortex produces corticosteroid hormones, including mineralocorticoids (the most important one being aldosterone) and glucocorticoids (the most important one being cortisol). Aldosterone promotes sodium (and chloride) and water absorption in the distal renal tubule and expansion of the extracellular fluid volume occurs secondary to sodium retention. Aldosterone also promotes potassium and hydrogen ion excretion in the distal renal tubule. Its main target organ is the kidney.

Naturally-occurring ***primary*** hypoadrenocorticism in dogs and cats is thought to be the result of immune-mediated destruction of both adrenal cortices and is the focus of this discussion. The clinical syndrome occurs when at least 85% to 90% of the adrenocortical tissue is destroyed, resulting in deficiencies of mineralocorticoids and glucocorticoids. Other than immune-mediated disease, other rare causes of primary adrenal cortex destruction include infiltration by fungus (*Histoplasma*, *Blastomyces*, *Coccidioides*, *and Cryptococcus*), neoplasia, amyloidosis, trauma, or coagulopathy. Iatrogenic primary hypoadrenocorticism can result from drugs that cause destruction of the adrenal cortices.

Secondary adrenocortical failure may also occur, either naturally due to diseases of the brain or as a result of chronic exogenous corticosteroid administration (i.e. iatrogenic causes). Secondary cases have reduced ACTH production by the pituitary gland; ACTH only minimally stimulates mineralocorticoid production and therefore electrolyte abnormalities are uncommon. Lack of ACTH leads to severe atrophy of the adrenal zona fasciculata (secretes glucocorticoid) and the zona reticularis (secrete sex hormones) with an intact mineralocorticoid-secreting zona glomerulosa. Plasma electrolytes therefore remain normal because aldosterone secretion is preserved.

Causes of secondary hypoadrenocorticism include destruction of the pituitary gland by neoplasia, inflammation, or head trauma. This form of Addison's disease is much less common than primary hypoadrenocorticism, although its true incidence is not known. Secondary hypoadrenocorticism can prove an insidious disease, as the blood work and other diagnostics may be relatively normal. Consequently, clinicians must maintain a high index of suspicion for these patients.

Iatrogenic secondary hypoadrenocorticism usually results from exogenous glucocorticoid administration and is more common than the naturally occurring form. Typically, it results from chronic use and can occur with injectable, oral, ophthalmic, otic, and topical preparations. Feedback inhibition from exogenous glucocorticoids suppresses anterior pituitary secretion of ACTH, which in turn leads to atrophy of the zona fasciculata and the zona reticularis. If the exogenous glucocorticoid is withdrawn too quickly, hypocortisolism results. Individuals show variable susceptibility to this problem, and it is not possible to predict which animals may develop clinical illness. In general, exogenous glucocorticoids should be tapered carefully, particularly if chronic administration has occurred. Iatrogenic hypoadrenocorticism may also occur with misuse of trilostane and especially mitotane.



Primary hypoadrenocorticism classically manifests with signs of both mineralocorticoid and glucocorticoid deficiency. Aldosterone secretion by the zona glomerulosa is stimulated by the renin-angiotensin-aldosterone system (RAAS) (aldosterone secretion is stimulated by angiotensin II) and by high potassium concentration. Lack of aldosterone results in hyponatraemia (and hypochloraemia) with concurrent extracellular fluid volume depletion. Reduced cardiac output, systemic hypoperfusion and hypotension may ensue as a result of chronic renal fluid loss, acute gastrointestinal fluid loss and inadequate dietary intake. Reduced glomerular filtration rate (GFR) results in pre-renal azotaemia. The aetiology of hyperkalaemia in primary hypoadrenocorticism is multifactorial and the most deleterious effects occur on cardiac function.

Cortisol affects almost every tissue in the body, and is significantly involved in haemodynamics and the cardiovascular system, metabolism, inflammation and immunological function, and gastrointestinal integrity. Its production increases during times of physiological stress. Lack of secretion may result in gastrointestinal signs, reduced mentation and activity levels, reduced energy metabolism and fasting hypoglycaemia and especially impaired tolerance to stress.

Atypical primary hypoadrenocorticism:

Some dogs have so-called *atypical* primary hypoadrenocorticism such that electrolyte abnormalities are not present. Traditionally it has been suggested that these dogs only have significant glucocorticoid insufficiency at the time of presentation; this may occur secondary to gradual loss of adrenocortical tissue in which loss of glucocorticoid-secreting portions (middle layer, zona fasciculata) precedes loss of the mineralocorticoid- secreting layer (outer layer, zona glomerulosa) of the adrenal cortex.. These dogs do not have electrolyte abnormalities but must be monitored closely as mineralocorticoid deficiency and consequent electrolyte abnormalities are likely to develop over days to months. However more recently it has been shown in one study that significant basal and ACTH-stimulated aldosterone (mineralocorticoid) deficiency may exist even in dogs with normal electrolyte concentrations. As such the pathogenesis in these cases is the same as in typical cases and the term 'atypical' is perhaps being reconsidered. To the author's knowledge, why plasma electrolytes are normal despite aldosterone deficiency remains to be elucidated but clearly other mechanisms despite aldosterone are at play.

Autoimmune polyglandular syndrome:

Autoimmune polyglandular syndrome has rarely been described in the dog, but reportedly occurs in about 50% of humans with primary hypoadrenocorticism. Although uncommon among dogs with primary hypoadrenocorticism, it is important not to overlook the possibility of other concurrent endocrine disorders.

Clinical signs

In dogs primary hypoadrenocorticism is suspected to have a genetic basis, similar to humans, but the mode of inheritance is still being investigated. The disease is diagnosed most commonly in young to middle age female dogs although a wide age range can be affected. Breeds at increased risk include Poodle breeds, the Portuguese water dog, the Great Dane, the West Highland White terrier (and other terrier breeds), the Bearded Collie, the Rottweiler and especially the Nova Scotia duck tolling retriever. On a numerical basis however, mixed breed dogs are most commonly affected.

Clinical signs are non-specific and variable both in nature and severity and can often be attributed to multiple body systems. Most dogs are chronically affected. However owners may not have noticed more subtle abnormalities or may not have considered them significant. Thus some dogs are only presented for veterinary attention when they suffer an acute Addisonian crisis; literature reports suggest 30% of dogs may present in a crisis. Acute exacerbation of chronic hypoadrenocorticism may result from stress such as boarding, grooming, lifestyle changes, moving, or even a trip to the vets!

Clinical signs reported in primary hypoadrenocorticism include:

- Depression
- Inappetence/anorexia
- Lethargy
- Vomiting (regurgitation)
- Weight loss
- Weakness, usually episodic

- Diarrhoea (including possible haematochezia or melaena)
- Waxing and waning illness
- Polyuria, polydipsia
- Shaking, shivering or restlessness
- Episodic collapse or syncope
- Abdominal discomfort
- (Episodic muscle cramps – especially exercise-induced)
- (Seizures: e.g. exercise-induced and/or due to severe hypoglycaemia)

Prior response to non-specific fluid and/or corticosteroid therapy may also be reported.

These signs are vague and non-specific and may also occur in a large number of other disorders. It is therefore **essential to keep primary hypoadrenocorticism on the differential diagnosis list** for all dogs presenting with any of these signs until a definitive diagnosis is made. Addison's disease is frequently referred to as the 'great pretender' due to the variety of signs and clinical findings that mimic other disorders.

Clinical Evaluation

Physical examination findings may include:

- Reduced mentation
- Weakness/lethargy
- Hypoperfusion
- Bradycardia*, inappropriately normal heart rate (relative bradycardia) or tachycardia
- Hypothermia
- Dehydration
- Abdominal pain
- Shaking/shivering
- Melaena/haematochezia

(* There are several causes of bradycardia in hypoadrenocorticism and it can be found in patients that are not significantly hyperkalaemic. Causes include:

- Hyperkalaemia
- Impaired response to endogenous catecholamines due to glucocorticoid deficiency preventing tachycardia which would be more appropriate in a hypoperfused patient
- Hypoxia secondary to hypoperfusion/hypovolaemia
- Hypoglycaemia (typically only if moderate-to-severe)
- Hypothermia
- Increased vagal tone e.g. due to gastrointestinal abnormalities)

Hypotension may be documented and ECG changes include those consistent with hyperkalaemia as well as other possible dysrhythmias that do not typically require specific treatment.

There are a large number of potential **clinicopathological** abnormalities reported; some of the more common include:

- Evidence of haemoconcentration
- Hyponatraemia is very often present: usually moderate-to-severe (but sodium can only be mildly reduced or indeed within normal limits)*
- Hyperkalaemia is very often present (but varies in severity and potassium may be within normal limits)*

- Reduced plasma sodium:potassium ratio*:
    - Normal range 27:1-40:1
    - Dogs with primary hypoadrenocorticism frequently show ratios < 27:1, and sometimes < 20:1
    - Ratios < 15:1 strongly suggest hypoadrenocorticism rather than other disorders that can cause the ratio to decrease, although the diagnosis still must be confirmed with an ACTH stimulation test
- Hypochloraemia
- Hypoglycaemia (cortisol is involved in maintaining normal blood glucose via several mechanisms): can be severe enough to cause clinical signs, including severe signs such as seizures.
- Azotaemia (pre-renal): mild-to-moderate
    - Urea may also be elevated due to gastrointestinal bleeding giving a disproportionate rise relative to creatinine
- Hyperphosphataemia (likely due to reduced renal excretion)
- Metabolic acidosis (mild-severe) due to lack of hydrogen ion excretion +/- hypoperfusion-induced lactic acidosis
- Hypoalbuminaemia and possible panhypoproteinaemia due to e.g. gastrointestinal haemorrhage, protein-losing enteropathy, decreased albumin synthesis.
- Total hypercalcaemia – ionised calcium may or may not be increased: typically mild and resolves with the fluid therapy used for the Addisonian crisis; aetiology likely multifactorial but remains unclear.
- Elevation in liver transaminases (ALT/AST): typically mild-to-moderate; likely multifactorial aetiology
- Absence of stress leukogram** (i.e. increased neutrophils/monocytes, decreased lymphocytes/eosinophils) on blood smear; possible eosinophilia; lymphocytosis in a sick dog should especially raise suspicion.
- Anaemia: bone marrow suppression due to hypocortisolism can result in anaemia that may be mild to moderate in severity. A normocytic normochromic non- or minimally regenerative anaemia is identified. Anaemia of chronic disease may also be involved. However manual packed cell volume (PCV) at presentation may also be affected by both haemoconcentration (increases PCV) and potentially also gastrointestinal blood loss (decreases PCV).
- Isosthenuria: many dogs with primary hypoadrenocorticism have isosthenuric urine (specific gravity 1.007-1.015) or at least inappropriately low USG. Increased urine specific gravity is usually expected in the face of pre-renal azotaemia; however chronic urinary sodium loss disturbs the normal medullary concentration gradient (renal medullary washout) and therefore impairs water reabsorption. Azotaemia, together with dilute urine specific gravity, normally suggests intrinsic renal failure, which is an important differential for hypoadrenocorticism and carries a very different prognosis. In Addisonian dogs, BUN and creatinine will often improve readily, rapidly, and completely with appropriate intravenous fluid support and hormone replacement. If this does not occur, it raises concerns about insufficient fluid support, a concurrent and primary intrinsic renal problem, or renal damage secondary to hypovolaemia and renal hypoperfusion.

* The majority of dogs presenting in an acute crisis will have electrolyte abnormalities but electrolytes are normal in a small percentage (*atypical* primary hypoadrenocorticism) as well as in secondary hypoadrenocorticism. Other causes of hyperkalaemia and/or hyponatraemia should also be considered as appropriate.

** Stress leukogram mnemonic: SMILED – segmented (neutrophils), monocytes increased; lymphocytes, eosinophils decreased.

Thoracic radiography: changes secondary to severe hypovolaemia (especially microcardia and narrowed caudal vena cava) are relatively common in dogs presenting in an acute Addisonian crisis. However these findings are not specific to this disorder and may also result from other causes of hypovolaemia.

Megaoesophagus is occasionally identified and resolves quickly with stabilisation. The exact pathogenesis remains unclear but may be related to muscle weakness.

Confirming the diagnosis:

At least two studies have been published suggesting that there may be a role for single resting plasma cortisol measurement as a screening test for Addison's disease. These studies suggest that if a sick dog has plasma cortisol greater than 2 µg/dl (55 mmol/l) hypoadrenocorticism is very unlikely. On the flipside this diagnosis is very likely in a sick dog with plasma cortisol less than 1 µg/dl (28 mmol/l). A sick dog with plasma cortisol greater than 2 µg/dl (55 mmol/l) would be considered not to have the disease, a sick dog with plasma cortisol less than 2 µg/dl (55 mmol/l) would need an ACTH stimulation test performed due to the poor predictive value of this test below this cut-off. Bear in mind that each reference laboratory and indeed in-house analyser will likely have its own cut-offs for resting cortisol.

However given that a single plasma cortisol measurement cannot definitively achieve the diagnosis, and bearing in mind the importance of making this diagnosis definitively, the role of single plasma cortisol measurement is perhaps unclear at least in patients with moderate-to-severe illness. The ACTH stimulation test is easy to perform and only takes one hour and dexamethasone can be administered to patients in whom glucocorticoid administration is considered too urgent to wait. In a practice with access to in-house cortisol measurement both a one-off measurement and an ACTH stimulation test could be performed. As such it may be that other issues such as financial costs or availability of synthetic ACTH are more likely to prompt the use of single plasma cortisol measurement in the diagnosis of Addison's disease than clinical reasoning in the sick patient.

The author is not aware of the reliability and accuracy of in-house cortisol analysers. A SNAP® Cortisol Test is also available from Idexx that (I believe) reports results within certain bands of cortisol concentrations. To the author's knowledge no clinical validation studies have been published beyond those of the manufacturer.

However as measuring a single resting plasma cortisol level is undoubtedly cheaper than an ACTH stimulation test, cortisol measurement may well have a role as an affordable screening test in dogs in whom there is some suspicion of Addision's on the basis of history or clinical findings; the suspicion is not considered sufficient to warrant the expense of an ACTH stimulation test but a cheaper screening test is considered entirely reasonable. If the test result is not supportive of the disease but the patient continues to prompt suspicion then an ACTH stimulation test can be performed going forward. Nevertheless given that 30% of dogs according to literature present in an acute crisis which could prove fatal without timely intervention, the author would encourage a low threshold for performing an ACTH stimulation test reserving single cortisol screening for a minority of cases!

The ACTH stimulation test results will not be available in-house for most practices at this time. This test assesses the reserve capacity of the adrenal glands to secrete cortisol when stimulated by ACTH. Most Addisonian dogs will have minimal basal cortisol and a flat-line response to exogenous ACTH administration. More details of how to perform this test can be found in other resources/formularies. It is noteworthy that in the past it was standard to administer 250 µg of ACTH to all dogs however more recent data suggests that a dose of 5 µg/kg (up to a maximum dose of 250 µg even in dogs > 50 kg bodyweight) is equally effective at stimulating the adrenal glands. This lower dose protocol should be cheaper for clients and saves unnecessary consumption of synthetic ACTH which often has an unpredictable and unreliable availability.

The ratio of cortisol to endogenous ACTH concentration has also been investigated in the diagnosis of hypoadrenocorticism. It is important to remember that if this test is being used the sample for ACTH measurement should be collected before glucocorticoid, including dexamethasone, administration which may affect endogenous ACTH levels.

Case management

Initial priorities: fluid therapy to correct perfusion abnormalities; treat clinically significant hypoglycaemia if present; treat clinically significant hyperkalaemia if present.

An acute Addisonian crisis is one of the true canine emergencies with a very real risk of rapid deterioration and death. Death as a result of an acute Addisonian crisis is more likely to be due to hypovolaemia and cardiovascular collapse than the effects of hyperkalaemia. While hyperkalaemia may be common in dogs with Addison's disease, in the author's experience specific intervention beyond fluid therapy (causes dilution and promotes kaliuresis) is rarely indicated. A standard approach using calcium gluconate and possibly insulin/glucose and/or sodium bicarbonate is used when hyperkalaemia is considered to be clinically significant.

Isotonic crystalloid fluid therapy for hypovolaemia is therefore the most important intervention. There is on-going debate regarding the relative merits of 0.9% sodium chloride (physiological, 'normal' saline) versus buffered lactated ringer's solution (Hartmann's solution, compound sodium lactate). Ultimately which of these is chosen is likely to be inconsequential in the vast majority of cases and starting fluid therapy is the priority. Conservative boluses are given to correct perfusion abnormalities and then low rate infusion used; the latter is typically administered at 4-6 ml/kg/hour but should be tailored to the individual patient according to replacement, maintenance and on-going loss requirements. Rapid correction of hyponatraemia should be avoided as far as possible due to risks of rare but potentially serious central pontine myelinolysis.

Clinically significant hypoglycaemia should also be addressed.

Administer exogenous glucocorticoid:

Patients with hypoadrenocorticism are deficient in cortisol and mineralocorticoid. While fluid therapy is essential for initial stabilisation, ultimately exogenous steroid preparations are needed for continued stabilisation.

A variety of exogenous glucocorticoid preparations may be used to treat an acute Addisonian crisis. Some authors prefer the use of hydrocortisone or prednisolone as these agents have some mineralocorticoid activity but their clinical superiority over dexamethasone remains controversial. Intravenous therapy is essential in these cases and injectable dexamethasone is the most widely available agent in general veterinary practice. There is usually time to perform an ACTH stimulation test prior to glucocorticoid administration, i.e. while the patient is being resuscitated with fluid therapy, but it is noteworthy that dexamethasone is the only routinely used agent that does not react with the cortisol assay thereby increasing the measured concentration. Dexamethasone can therefore be administered before completion of the test.

The recommended dose of dexamethasone is 0.5 mg/kg IV q 2-6 hours initially and then 0.05-0.1 mg/kg IV q 8-12 hours once the patient is stable and until oral medication is possible.

Hydrocortisone: 0.5-0.625 mg/kg/h CRI; 2-4 mg/kg IV q 3-6 hours

- Perform ACTH stimulation test prior to commencing treatment
- Mainly glucocorticoid but has some mineralocorticoid activity

Prednisolone: 2-5 mg/kg IV q 3-6 hours initially; then 0.1-0.2 mg/kg per os q 12-24 hours

- Perform ACTH stimulation test prior to starting treatment
- Mainly glucocorticoid but has some mineralocorticoid activity

Methylprednisolone: 1-2 mg/kg IV q 2-6 hours

- Negligible mineralocorticoid activity
- Perform ACTH stimulation test prior to starting treatment

Additional **symptomatic and supportive care** is provided as required.

Progression/Prognosis

In dogs that respond well to treatment, significant improvement is often noted within 24 hours, often in just several hours, in terms of demeanour, appetite and improvement of other signs. Clinicopathological abnormalities may take a little longer to improve, e.g. 24-48 hours.

Oral mineralocorticoid (fludrocortisone 0.01 mg/kg per os q 12 hours) and glucocorticoid (prednisolone 0.2-0.25 mg/kg per os q 24 hours) supplementation is started as appetite improves and parenteral therapy can be discontinued. In some countries an injectable mineralocorticoid preparation, desoxycorticosterone pivalate (DOCP, Percorten-V; Novartis Animal Health, Basel, Switzerland) is available. This is a long-acting pure mineralocorticoid given by intramuscular injection every 25 days approximately.

The results of an ACTH stimulation test consistent with hypoadrenocorticism are (very) low basal blood cortisol concentration that fails to increase with administration of synthetic adrenocorticotrophin. Since the ACTH stimulation assay measures cortisol levels, it only evaluates the ability of the adrenal cortex to produce glucocorticoids. It does not assess the ability of the adrenal cortex to produce mineralocorticoids, and so cannot differentiate primary from secondary adrenal insufficiency. In many situations, mineralocorticoid deficiency is inferred from abnormal sodium and potassium levels at initial diagnosis. If sodium and potassium levels remain normal; however, it is not clear whether mineralocorticoid supplementation will be required along with glucocorticoid supplementation. An endogenous ACTH level can help determine this, as dogs with primary hypoadrenocorticism have elevated endogenous ACTH levels while dogs with secondary hypoadrenocorticism have very low endogenous ACTH concentration.

At patient discharge, a good deal of time should be spent educating the owner on the disease, including provision of a client education leaflet, and a comprehensive plan for on-going management agreed. Prednisolone is usually tapered off and thereafter used as short-term bolus therapy at times of stress (e.g. surgery, trauma, illness, environmental stressors) while mineralocorticoid therapy is continued lifelong. Owners should be advised that prednisolone would ideally be started prior to stressful episodes, continued during and then tapered off subsequently. A good prognosis with normal life expectancy and death due to non-related conditions is reported as long as lifelong appropriate management can be provided. Spontaneous recovery has not been reported. A more in-depth discussion of chronic management is beyond the scope of these notes.

Also see this podcast episode on Canine hypoadrenocorticism (Addison's Disease):
http://www.veteccsmalltalk.com/episode/10

Canine Heart Diseases

Acute decompensated heart failure

Relevant theory

Progressive heart disease results in **failure of the heart to pump adequately** and this may manifest as:

- Low-output (forward) heart failure, where enough blood is not pumped into the aorta or pulmonary artery, or
- Congestive (backward) heart failure (CHF)

In congestive heart failure, there is inadequate emptying of blood from the venous system:

- **Left-sided** CHF results in congestion of the pulmonary circulation with pulmonary oedema
- **Right-sided** CHF causes congestion of the systemic circulation with jugular distension, ascites and pleural effusion
- **Bilateral** heart failure presents with a combination of both types of signs

Failure of the heart to pump adequately may result from systolic dysfunction, i.e. the heart is unable to physically eject blood adequately, or from diastolic dysfunction, i.e. the ventricles are unable to fill properly. Both mechanisms are often involved and the end result is reduced cardiac output and a lowering of arterial blood pressure (circulatory failure).

***Systolic* dysfunction** may result from:

- Failure of the myocardium itself (e.g. dilated cardiomyopathy)
- An increase in ventricular pressure (pressure overload; e.g. pulmonic stenosis, sub-aortic stenosis)
- Volume overload (e.g. atrioventricular valve disease)

***Diastolic* dysfunction** (impaired ventricular filling) may result for example from:

- Ventricular hypertrophy
- Dilated cardiomyopathy
- Atrioventricular valve stenosis
- Pericardial effusion (cardiac tamponade)

Compensatory mechanisms during heart disease include:

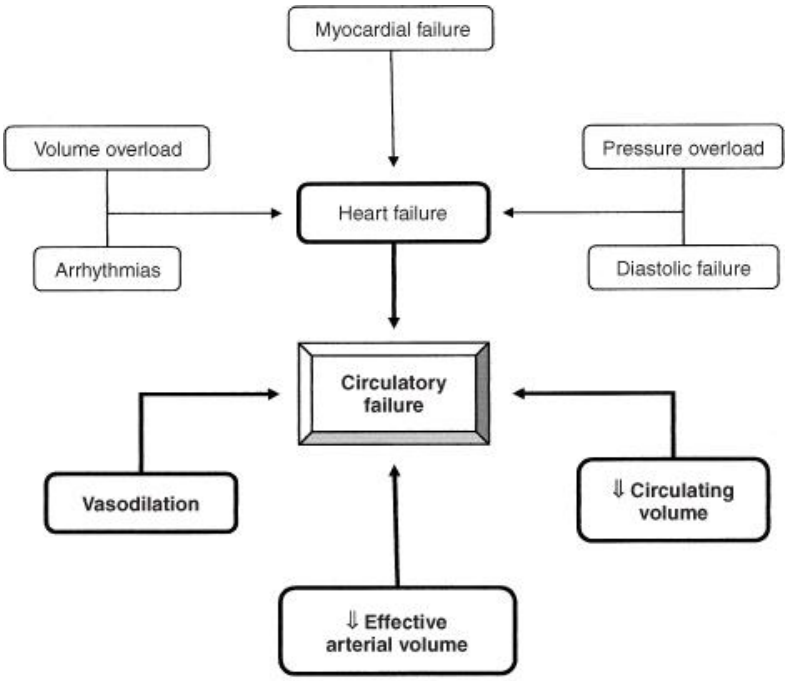
- Mechanisms relating to the heart itself, such as:
    - Tachycardia
    - Increased inotropy (force of contraction)
    - Myocardial hypertrophy
- Peripheral compensation:
    - Vasoconstriction
    - Sodium and water retention

Neuroendocrine activation and the renin-angiotensin-aldosterone system (RAAS) are involved.

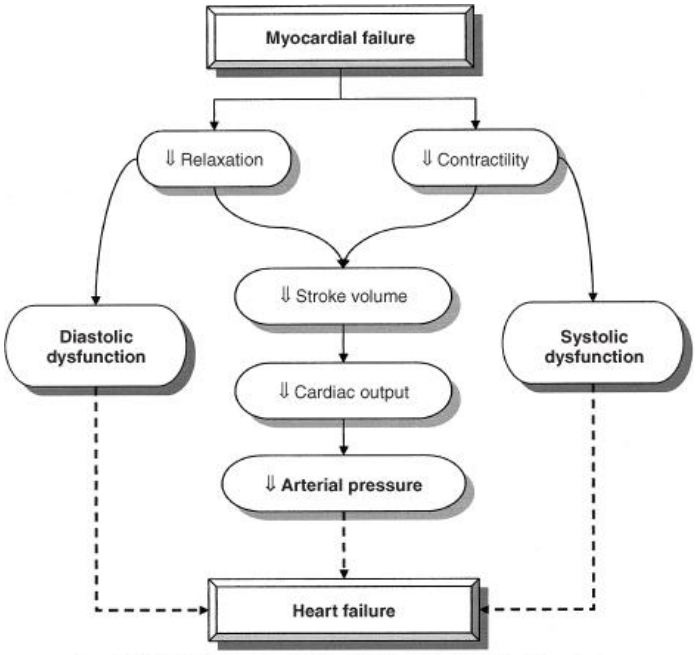
In time these compensatory mechanisms become detrimental and are responsible for clinical signs.

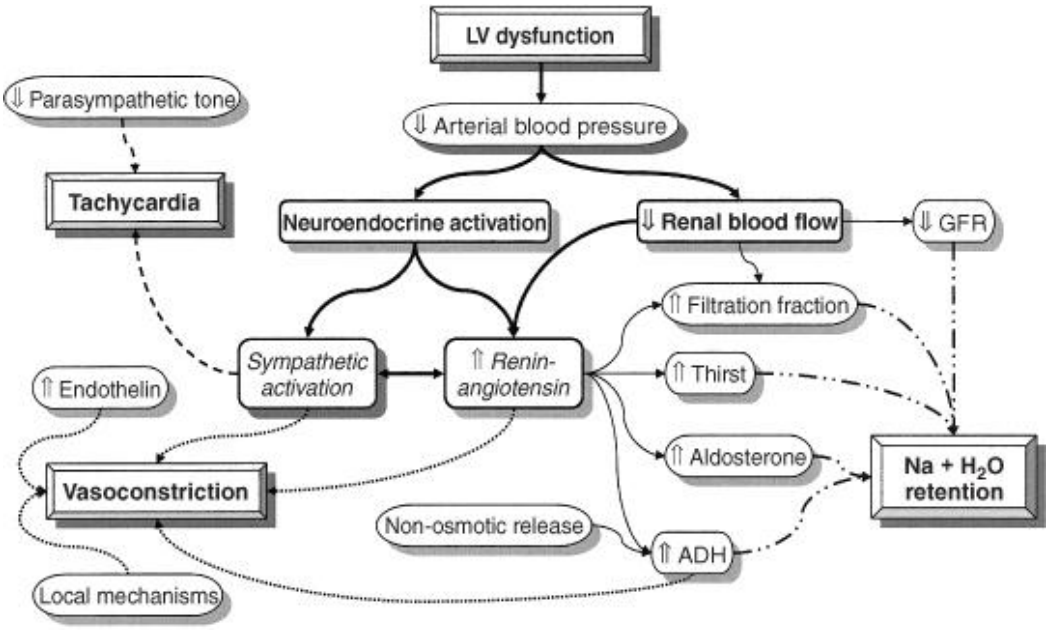
Interlocked vicious cycles lead to progression of congestive heart failure: these include increased afterload, increased left atrial pressure and ventricular and vascular remodeling.

Images from Ettinger – Textbook of Veterinary Internal Medicine, 6th edition…

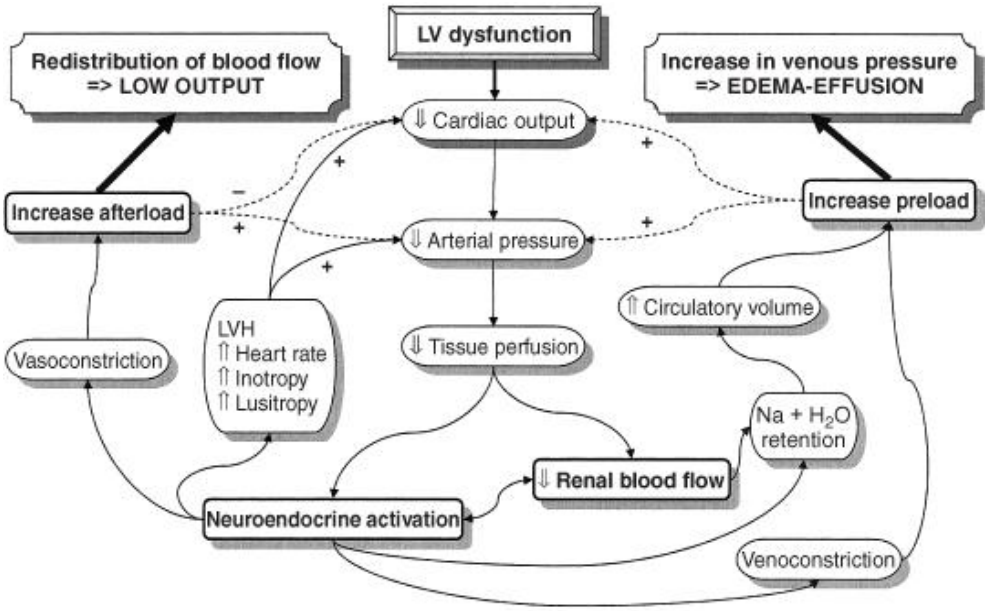


Causes of circulatory and heart failure



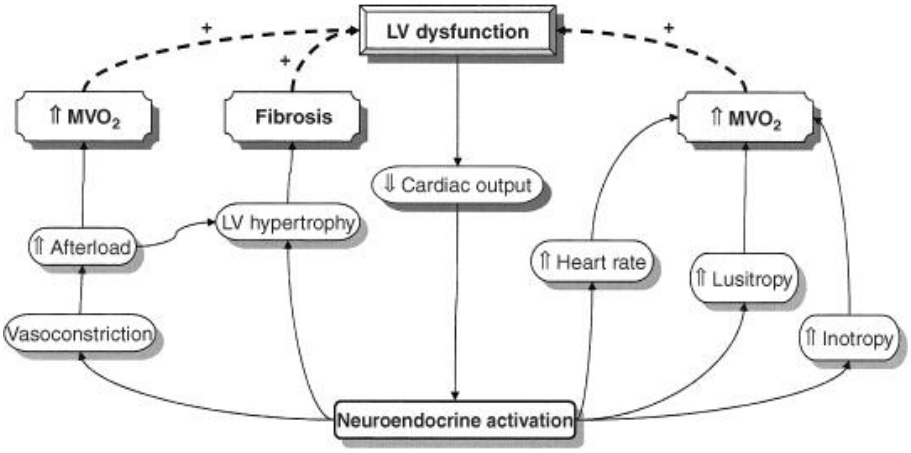


Compensation in congestive heart failure. Left ventricular (LV) dysfunction decreases cardiac output and arterial blood pressure. The decrease in renal blood flow and concomitant neuroendocrine activation set in motion compensatory mechanisms designed to restore blood pressure: sodium and water retention (dash-and-dot line); vasoconstriction (dotted line); and tachycardia (dashed line). ADH, Vasopressin; GFR, glomerular filtration rate.

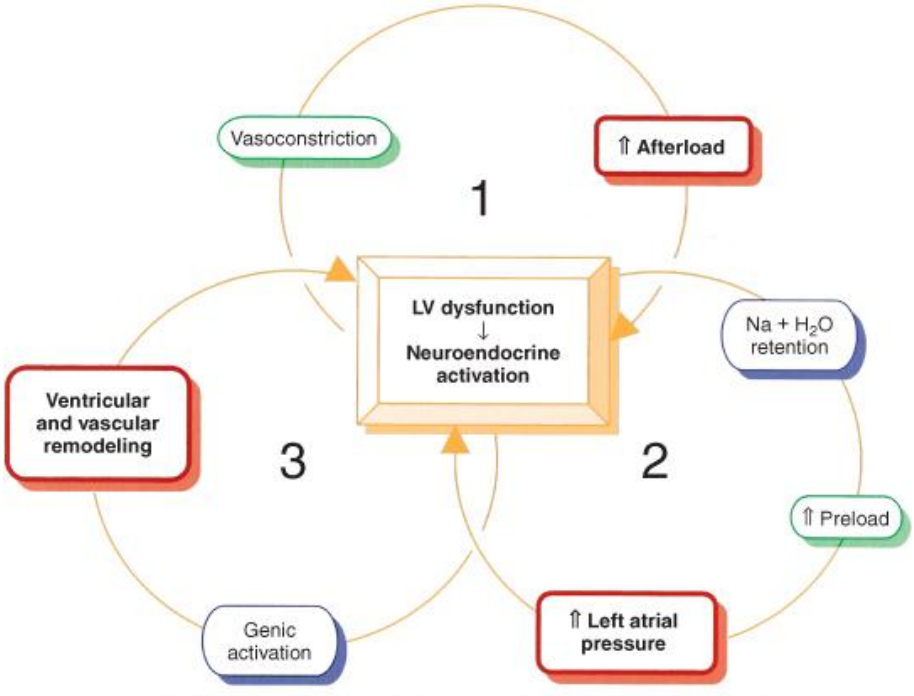


Compensation and clinical signs of congestive heart failure. The compensatory mechanisms activated to restore arterial blood pressure during heart failure are ultimately responsible for the clinical signs of the disorder. Retention of sodium and water leads to the formation of edema and effusions, and an increased

afterload decreases cardiac output. (+), Increases arterial pressure or cardiac output; (-), decreases cardiac output; ADH, vasopressin; LV, left ventricle; LVH, left ventricular hypertrophy.



Compensation process and progression of left ventricular dysfunction. The compensatory mechanisms activated to restore arterial blood pressure during heart failure are ultimately responsible for progression of the disease. Increased afterload and increased cardiac activity increase myocardial oxygen consumption (MVO2); left ventricular (LV) hypertrophy is associated with fibrosis. (+), Causes further left ventricular dysfunction.



Interlocked vicious cycles that lead to progression of congestive heart failure: increased afterload (cycle 1), increased left atrial pressure (cycle 2), and ventricular and vascular remodeling (cycle 3). LV, Left ventricle.

Clinical findings

Clinical signs:

Many – but not all – dogs presenting with acute decompensated heart failure will have some suggestive chronic history that may include progressive lethargy and exercise intolerance, reduced appetite, change in breathing effort/pattern, coughing, and potential episodes of weakness/collapse. As is often the case, signs often more vague and subtle in cats with a problem not being identified until a crisis develops.

Physical examination:

Usually performed while flow-by oxygen supplementation is being provided.

Cardiovascular findings may include:

- Tachycardia (or potentially bradycardia depending on severity and nature of heart disease)
- Heart murmur and/or gallop sound
- Evidence of systemic hypoperfusion
- Suggestion of dysrhythmia: pulse deficits, possible abnormal rhythm on auscultation
- Evidence of volume overload/right-sided failure, e.g. jugular venous distension, ascites

Respiratory:

- Rate is usually increased
- Pattern/effort: tachypnoea (rapid, shallow) or dyspnoea (more increased effort) may be present
- Lungfield auscultation may be unremarkable or suggestive of pulmonary oedema – can vary from diffuse increase in noise to more diffuse harshness/crackles; crackles can also be focal

Central nervous system:

- May be unremarkable or altered mentation – depression or anxiety
- May also be recumbent depending on severity

Abdomen may be distended with possible fluid thrill
Rectal temperature may be normal, mildly elevated, or potentially reduced depending on degree of hypoperfusion if present

Emergency database:

A baseline minimum emergency database (manual packed cell volume, plasma total solids, blood urea nitrogen, blood glucose) plus plasma creatinine and electrolytes is sensible in these patients both as their primary disease can affect hydration status and renal function, and because subsequent treatment is likely to cause fluid and electrolyte changes.

Diagnosis

Acute decompensated heart failure is suspected in a patient with compatible clinical findings and especially if a previous diagnosis of heart disease exists or has been suspected. There is increasing access to ultrasonography in small animal practice and growing experience amongst non-cardiologists in evaluating the heart for left atrial size, subjective contractility and the presence of pericardial effusion. This rapid and non-invasive test can be very useful in providing further evidence of probable heart failure.

Depending on the severity and temperament of the individual patient, it is often sensible to start presumptive treatment for heart failure with oxygen supplementation and furosemide administration before performing either more comprehensive echocardiography (if available) and thoracic radiography.

Response to empirical furosemide administration can also be very helpful in establishing the diagnosis as pulmonary oedema will show some positive response in many cases whereas other differentials are unlikely to.

Thoracic radiography:

Thoracic radiography is useful both for evaluating the lungs for oedema and for evaluating the dimensions of the cardiac silhouette; however it should not be prioritised over initial empirical stabilisation and should only be performed in patients that are compliant paying close attention to the risk-benefit profile. Judicious chemical restraint (e.g. morphine 0.1 mg/kg, butorphanol 0.1-0.2 mg/kg) should also be considered and is safer than aggressive manual restraint. Flow-by oxygen supplementation should be provided throughout if tolerated.

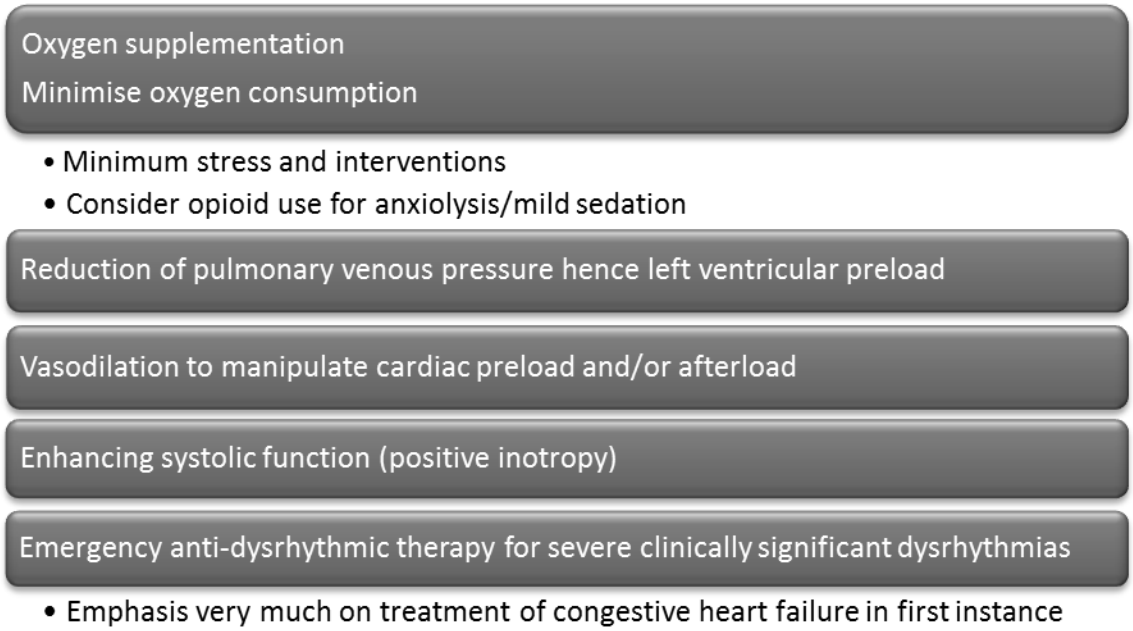
Pulmonary oedema:

- In radiographs of dogs with acute left-sided cardiac failure, pulmonary oedema typically appears as a symmetrical alveolar pattern that is most marked in the caudodorsal lung field, although it can become generalised.
- In cats: a range of patterns and variable distribution

Treatment

Although signalment and history may help to some small degree, emergency treatment of animals with acute decompensated heart failure often needs to be performed without a definitive diagnosis of the nature of the underlying heart disease.

Management may involve:



The things we need to think about can be summarised in the mnemonic OH CRAP:

O Oxygenation
H Haemodynamics

C Contractility
R Rate/Rhythm
A Afterload
P Preload

Drugs that may be indicated in the management of heart failure patients include:

Furosemide
Glyceryl trinitrate
Pimobendan
ACE inhibitors
Sodium nitroprusside
Dobutamine

Furosemide:

Doses:

- Dogs: 2-6 mg/kg IV or IM q 1-2 hours until clinical improvement; then q 6-12 hours
- Cats: 1-4 mg/kg IV or IM q 1-2 hours until clinical improvement; then q 12 hours

Diuresis and natriuresis using furosemide is typically the first line in trying to clear pulmonary interstitial/alveolar oedema and reduce pulmonary venous pressure to reduce left ventricular preload.

Has a variety of effects* including:

- Works in the renal tubule (thick ascending limb of the loop of Henle, 'loop diuretic') to decrease sodium, potassium and chloride reabsorption; inhibiting sodium reabsorption also prevents otherwise obligatory water reabsorption
- Also has other renal effects

Overall increases renal excretion of water, sodium, potassium, chloride, calcium, magnesium, hydrogen, and bicarbonate (and possibly phosphate)!

(* Not all are in the kidney (e.g. mild systemic venodilator, lung effects, possible bronchodilation), some still unknown)

Diuretic effect after intravenous administration: onset within 5 minutes, peak within 30 minutes, duration 2-3 hours; expect urination in most cases within an hour of administration

Metabolism: small amount of non-hepatic metabolism; mostly excreted unchanged in urine or bile

Plasma half-life: elimination half-life in dogs after IV administration 1-1.5 hours but may be prolonged in patients with renal failure or congestive heart failure

May cause fluid and electrolyte abnormalities:

- Dehydration including producing pre-renal azotaemia
- Hyponatraemia; hypokalaemia, hypocalcaemia, hypomagnesaemia

- Hypochloraemic metabolic alkalosis

These effects are most likely to be of concern with intensive treatment of acute cases and especially in cats – dogs will often start to drink and eat as pulmonary oedema improves and they feel better whereas cats are notoriously good at not eating! Cats may therefore need very judicious rehydration and correction of electrolyte abnormalities after life-threatening pulmonary oedema has been addressed.

Reportedly physically compatible with all commonly used intravenous solutions including replacement isotonic crystalloids.

Glyceryl trinitrate:

(2% topical preparation): primarily a systemic venodilator reducing preload and potentially therefore alleviating pulmonary oedema

- No real clinical evidence of efficacy but also unlikely to do any harm
- However Percutol® may no longer be available and there are significant practical constraints with using GTN spray

Glyceryl trinitrate paste can be absorbed through human skin and it is therefore important to take certain precautions. These include wearing gloves to apply the paste, and making sure that there are signs on the kennel and kennel sheet alerting personnel that paste has been applied to the patient. The site used must also be clearly identified; the paste is typically applied to clipped or hairless skin, such as the inner aspect of the pinna, and the site used is rotated between applications.

Pimobendan:

Doses: Dogs: 0.1-0.3 mg/kg per os or IV q 12 hours

Used in the management of heart failure in dogs, most commonly caused by myxomatous mitral valve disease (also known as endocardiosis), or dilated cardiomyopathy.

Although not authorised for use in cats, pimobendan (1.25 mg per cat q 12 hours) may be helpful for cats with systolic dysfunction, and can be tried as long as there is no murmur present (this may be due to hypertrophic cardiomyopathy in which pimobendan is contraindicated).

Inodilator:

- Positive inotropy mainly by increasing intracellular calcium sensitivity in the cardiac contractility apparatus (increases efficiency of contraction so enhancing systolic function)
- Vasodilation via vascular phosphodiesterase-III inhibition causing smooth muscle relaxation – both arterial and venous (i.e. ‘balanced’) so reduces both cardiac afterload and preload

Onset of haemodynamic effects can be within 24 hours (reportedly even much less)

Bioavailability of oral preparations is considerably reduced when administered with or shortly after food – it is therefore recommended that animals are treated approximately 1 hour before feeding. This may only be necessary for a few days until a steady state is reached after which administration with food is considered acceptable.

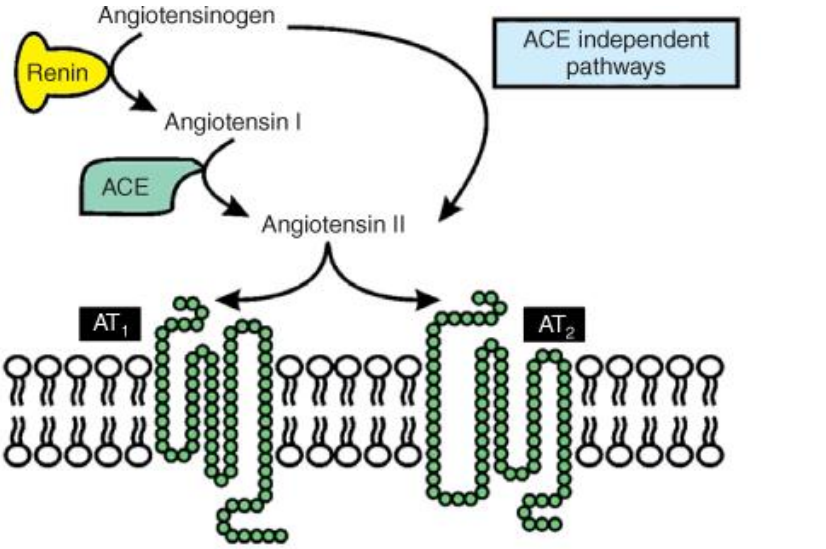
Capsules, flavoured tablets. Intravenous preparation now available; relatively expensive but can be very useful in critical cases.

There are very few published or anecdotal reports of a variety of predominantly gastrointestinal or cardiovascular clinically significant side-effects and overall appears so far to be safe and relatively well tolerated.

Should not be used in cases of hypertrophic cardiomyopathies or clinical conditions where an augmentation of cardiac output is not possible for functional or anatomical (e.g. aortic stenosis) reasons.

ACE inhibitors:

Angiotensin-converting enzyme (ACE) inhibitors:



Inhibition of ACE leads to a reduced conversion of inactive angiotensin I into angiotensin II and therefore reduction in the effects mediated by angiotensin II, including:

- Vasoconstriction of both arteries and veins
- Retention of sodium and water by the kidney
- Remodelling effects (including pathological cardiac hypertrophy and degenerative renal changes)

In heart failure, ACEi lower the blood pressure and volume loading effect on the heart by vasodilation. They should not be used in any patient that has evidence of cardiac output failure, for example, due to aortic stenosis.

Main risks relate to the role angiotensin-II normally plays in preserving systemic blood pressure and preserving glomerular filtration rate when renal blood flow decreases. Renal impairment is a significant adverse effect of all ACE inhibitors. Renal blood flow may be affected by angiotensin II because it

vasoconstricts the efferent arterioles of the glomeruli of the kidney, thereby increasing glomerular filtration rate (GFR). Hence, by reducing angiotensin II levels, ACE inhibitors may reduce GFR, a marker of renal function; azotaemia may develop and occasionally may become severe. Systemic hypotension is possible and may induce pre-renal azotaemia – though rarely clinically significant in dogs reportedly.

ACE inhibitors may also cause hyperkalaemia. Suppression of angiotensin II leads to a decrease in aldosterone levels. Since aldosterone is responsible for increasing the excretion of potassium, ACE inhibitors ultimately cause retention of potassium.

Sodium nitroprusside (sodium nitroferricyanide):

Dose – dogs and cats:

- Start at 0.5-1 µg/kg/min
- Increase by 0.5-1 µg/kg/min every 5 minutes until target blood pressure reached

In the context of congestive heart failure, this agent is generally used as a short-term life-saving/stabilisation measure in severe/fulminant cases to improve haemodynamics while other longer-acting but potentially slower onset and/or less potent agents become effective. These cases are often ones that will also be treated with intravenous dobutamine to avoid significant hypotension.

NB. Typically only used if reliable and constant blood pressure monitoring can be performed.

Works very quickly and amenable to titration as used as an intravenous infusion and effects begin almost immediately

- Blood pressure returns to pre-treatment levels quickly when treatment is stopped (e.g. within 1-10 minutes)

Causes peripheral arterial and venous vasodilation (by producing nitric oxide in vascular smooth muscle)
Overall effects are likely to be lowering of blood pressure and significant reduction in total peripheral resistance (afterload) with increase in cardiac output
Tolerance does not develop at recommended doses (unlike with the organic nitrates) but effects may be attenuated with on-going use (due to reflex mechanisms)

Metabolism: rapid (half-life few minutes) non-enzymatically in blood and tissues to cyanogen (cyanide radical); this is converted in the liver to thiocyanate and then eliminated in faeces and urine or exhaled air.

Most adverse effects relate to lowering of blood pressure, especially if done too quickly
Continued use may lead to thiocyanate and cyanide toxicity

Monitoring: blood pressure throughout; acid-base balance; sodium

Overdose/Acute toxicity:

Profound hypotension – reduce or stop infusion; give intravenous fluids; monitor blood pressure
Profound hypotension and/or cyanogen or thiocyanate toxicity most likely in:

- Excessive doses
- Prolonged therapy
- Depleted hepatic thiosulphate (sulphur) supply
- Severe hepatic or renal insufficiency

Metabolic acidosis is an early sign of cyanogen toxicity; hydroxocobalamin (vitamin B12a) may prevent cyanogen toxicity
Tolerance to therapy is also an early sign of nitroprusside toxicity

Administration information:

Typically reconstituted in D5W (5% dextrose in water); other solutions not recommended
Promptly protect solution from light – don't need to protect administration set though; aluminium foil often recommended but other opaque material can be used
(Light exposure causes reduction of ferric ion to ferrous ion with loss of potency and change to bluish colour)
Solution may have a slightly brownish tint but discard if blue/dark red/green
Stable for 24 hours after reconstitution
Do not add any other medications to intravenous line/catheter running nitroprusside
Must use flow control device (e.g. infusion pump, syringe driver)

Dobutamine:

Doses:

- Dogs: 2-20 µg/kg/min
- Cats: 1-5 µg/kg/min

β_1-selective adrenergic agonist causing increased myocardial contractility; used as a rapidly-acting positive inotrope in heart failure or cardiogenic shock
(Racemic mixture actually has various beta- and alpha-adrenergic agonist and antagonist effects but β_1-selectivitiy is thought to be the predominant pharmacodynamics profile)

(Dobutamine may also potentially have a role in other types of shock in which myocardial dysfunction and poor contractility is considered a significant component (e.g. possible in septic shock) but an agent with mixed effects of positive inotropy and vasoconstriction (e.g. noradrenaline) is likely more rational; noradrenaline (norepinephrine) is currently most widely recommended but adrenaline (epinephrine) may also have a role. Hypovolaemia must be addressed first/concurrently in these patients.)

Generally start at low dose, titrate upwards until desired clinical effect achieved. Onset of action within a few minutes (e.g. 2 minutes with peak by 10 minutes) – hence amenable to titration.
Plasma half-life: short (approximately 2 minutes in dogs/humans; longer in cats) so effect diminishes rapidly when treatment stopped and must be used as infusion

Adverse effects

Tachycardia including tachydysrhythmias, especially ventricular, may occur; may be able to continue therapy at lower dose; usually resolves with discontinuing exposure due to short duration of action.

Other possible effects are hypertension; also nausea, vomiting, dyspnoea

Monitor ECG, heart rate and blood pressure during use.

Canine Chronic Mitral Valve Insufficiency

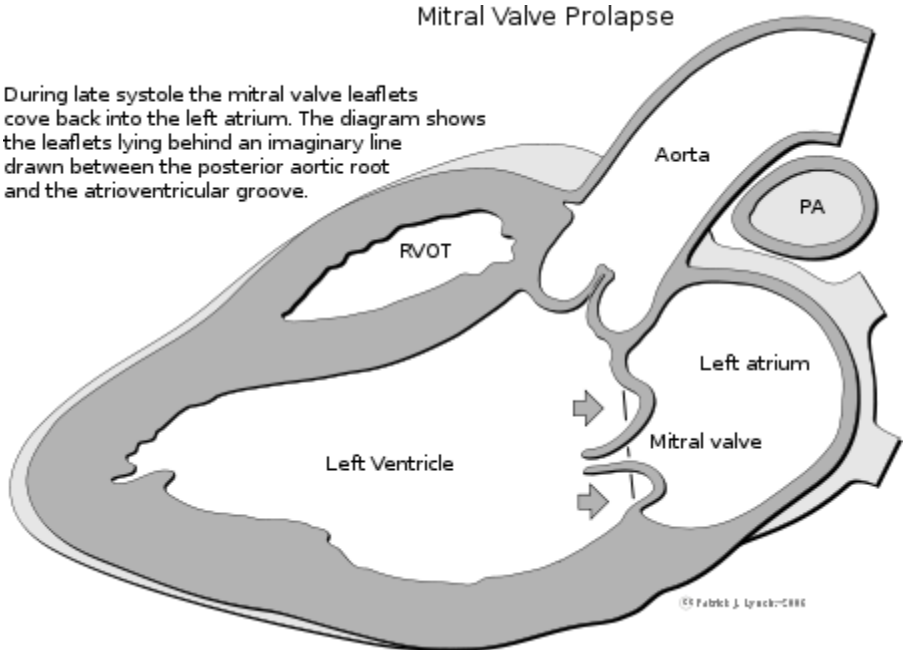
The mitral valve complex comprises leaflets, chordae tendinae, mitral annulus, and papillary muscles.

Chronic mitral valve insufficiency is usually the result of progressive valvular myxomatous degeneration (degeneration occurs in conjunction with an accumulation of dermatan sulphate, a glycosaminoglycan, within the connective tissue matrix of the valve; the exact mechanism is unknown) and has a high prevalence in older dogs, especially of small to medium size. The most commonly affected breeds include

the Cavalier King Charles spaniel, terrier breeds and poodles. The disease usually progresses over a period of years and is the most common cause of CHF in dogs.

Leakage (regurgitation) through the mitral valve results in an increasing percentage of the left ventricle's stroke volume being ejected into the low pressure left atrium; this leads to increased left atrial size. Chronic mitral insufficiency allows time for the left atrium to dilate and the chamber becomes more compliant buffering the pressure rise.

Echocardiography shows mitral valve prolapse (dorsal displacement of the valve leaflets relative to the mitral annulus into the left atrium). Mitral valve prolapse can precede but is often found with varying degrees of mitral insufficiency. There is change in size and shape of the cardiac chambers as the disease progresses.



(Patrick J. Lynch, medical illustrator; C. Carl Jaffe, MD, cardiologist)

In the long-term, mitral regurgitation results in tachycardia, myocardial hypertrophy, and reduced myocardial contractility; left atrial size and pressure increases, and pulmonary venous congestion and oedema may occur. Coughing may be the result of left main stem bronchus compression by the enlarged left atrium and/or pulmonary oedema.

Acute severe decompensated heart failure may occur in dogs with mitral valve insufficiency due to:

- Chordae tendinae rupture
- Onset of atrial fibrillation – possible consequence of atrial enlargement
- Inadequate therapy of existing heart failure
- Overexertion

Right-sided heart failure is relatively common in dogs with chronic mitral valve insufficiency. This is presumed to be due to concurrent tricuspid valve insufficiency as a result of myxomatous degeneration and/or pulmonary hypertension due to persistently elevated left atrial and pulmonary venous pressures.

Canine Tricuspid Valve Insufficiency

Tricuspid valve insufficiency is often an incidental finding in dogs and cats. Clinically significant tricuspid valve insufficiency may be seen with:

- Chronic mitral valve insufficiency
- Biventricular or right-sided dilated cardiomyopathy
- Bacterial endocarditis
- Chordae tendinae rupture
- Right ventricular dilation due to increased right ventricular pressure – e.g. secondary to pulmonary hypertension or pulmonary thromboembolism (PTE)

Right atrial enlargement may result in supraventricular tachydysrhythmias, and increased right atrial pressure may result in jugular distension, ascites, pleural effusion, pericardial effusion, hepatomegaly, and splenomegaly. From an emergency perspective, animals with tricuspid valve insufficiency are more likely to require treatment for a concurrent disorder than for primary right-sided heart failure.

Idiopathic Canine Dilated Cardiomyopathy

Dilated cardiomyopathy (DCM) is a progressive primary myocardial disease characterised by enlargement and remodelling of the heart (first the ventricle(s) then the atrium(a)), reduced systolic function and possible impaired diastolic function. The disease is seen most commonly in adult large and medium size dogs with some breeds being overrepresented (e.g. the Great Dane, the Doberman Pinscher, the Irish Wolfhound, the Cocker Spaniel). There is significant variation between breeds with respect to both historical and clinical findings, and rate of disease progression.

In some breeds (e.g. Doberman, Boxer) ventricular dysrhythmias are an early indicator of DCM. Dilated cardiomyopathy is definitively diagnosed by echocardiography and requires:

- LV dilation (especially in systole but also in diastole)
- Depressed systolic function
- Altered geometry of the LV
    - DCM induces cardiac remodelling such that the LV dilates and becomes more spherical in shape and the walls appear thinner.
- Reduced myocardial contractility

A significant and important echo-finding in DCM is increased LV internal dimensions.

Left (and perhaps bilateral) atrial enlargement may also be seen, as may RV enlargement
Mitral regurgitation may be identified in association with the dilated left ventricle

Idiopathic DCM is a diagnosis of exclusion based on the combination of history, physical examination, ECG, and diagnostic imaging. Secondary causes of myocardial systolic failure must be ruled out before a diagnosis of idiopathic or primary DCM is made.
Causes of secondary systolic dysfunction include:

- Sepsis
- Congenital heart disease e.g. mitral valve dysplasia
- Infectious disease e.g. parvovirus
- Cardiomyopathy of dysrhythmia
- Myocardial failure secondary to severe volume loading e.g. PDA, mitral valve endocardiosis (especially in large breed dogs), aortic insufficiency resulting from endocarditis
- Cardiomyopathy secondary to systemic disease e.g. hypothyroidism
- Drugs e.g. doxorubicin
- Nutritional e.g. carnitine deficiency; taurine deficiency in cats

Treatment:

Major initial considerations are:

- Is there a clinically significant tachydysrhythmia?
- Is congestive heart failure present?

Tachydysrhythmias, especially atrial fibrillation, are relatively common in dogs with DCM and sometimes are the reason for presentation, i.e. the owner detects that the dog has a very fast heart rate by palpation.

Atrial fibrillation is suspected on examination by the presence of an irregularly irregular (chaotic, jungle drum, washing machine!) heart rhythm on auscultation with pulse deficits that are often marked. It is definitively diagnosed however by electrocardiography – irregularly irregular R-R intervals are typical. Most dogs with atrial fibrillation have severe heart disease involving left atrial enlargement, and are in congestive heart failure of variable severity. Unless the dysrhythmia is very severe, the emphasis in these cases is very much on treating the congestive heart failure with furosemide and oral digoxin. Additional anti-dysrhythmic therapy is only indicated if treatment of congestion fails to reduce the ventricular response rate satisfactorily (conversion to sinus rhythm is very difficult and not necessarily of benefit).

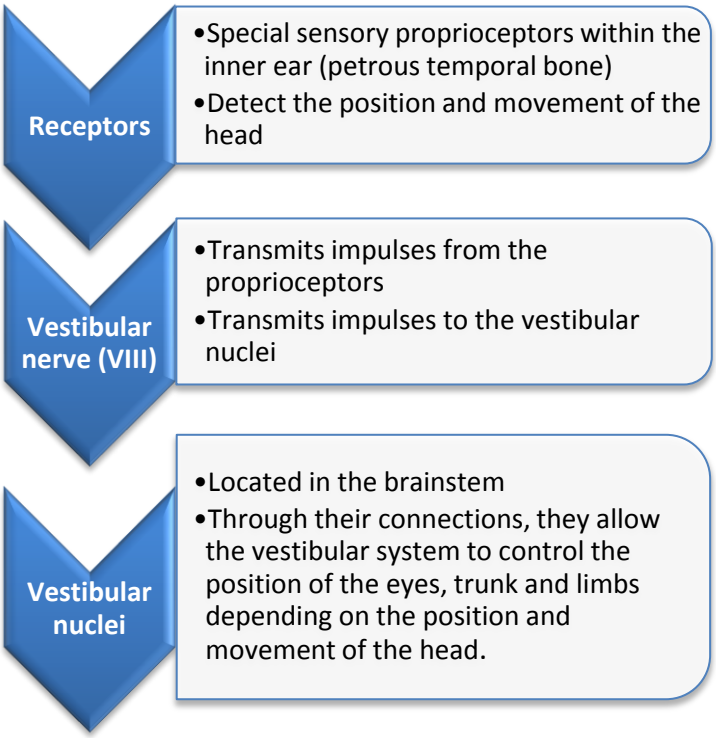
Pimobendan is typically used in the treatment of DCM and an ACE inhibitor may also be included.

Canine Vestibular Disease

The vestibular system

Responsible for balance and coordinating movements of the eyes, trunk, and limbs with changes in head position

The vestibular system consists of:



Vestibular disease may be the result of a lesion affecting either the central or the peripheral component of the vestibular system.

PERIPHERAL vestibular dysfunction: lesions affecting the inner ear proprioceptors or the vestibular portion of vestibulocochlear nerve nerve (VIII).

CENTRAL vestibular dysfunction:

Most commonly due to lesions affecting the brainstem vestibular nuclei
There is also a cerebellar component of the vestibular system and less frequently, central vestibular dysfunction is due to a lesion affecting this area; these animals have a paradoxical head tilt and circle away from the side of the lesion.

Paradoxical vestibular disease:

Refers to a syndrome of nystagmus, head tilt and circling due to cerebellar disease. Head tilt and circling occur contralateral to the side of the lesion and there are usually other more typical signs of cerebellar disease (e.g. head tremor, ipsilateral dysmetria).

Clinical evaluation and Signs of dysfunction

Observation of the animal's body and head posture at rest, and evaluation of its gait, can provide a lot of information about vestibular function. The vestibular system is more specifically assessed by testing *the vestibulo-ocular reflex* (physiological nystagmus).

Nystagmus:

In the absence of head movement, nystagmus should never be present in a normal animal. Spontaneous or positional jerk nystagmus indicates vestibular dysfunction but does not further localise to peripheral or central. Notable exceptions: • Positional, spontaneous and physiological nystagmus are usually absent with bilateral lesions • Vertical nystagmus and nystagmus that changes direction with different head positions are most commonly seen with central lesions

'Jerk' nystagmus is an involuntary rhythmic movement of the eyes. Typically presents with:

- Slow phase in one direction
- Fast phase in the other direction
    - The direction of the nystagmus is classically described by that of the fast-phase movement

Jerk nystagmus can occur in normal animals (*physiological* or *vestibular nystagmus*). Physiological nystagmus can be induced by lateral rotation of the head, i.e. testing the vestibule-ocular reflex:

- Slow phase in the direction opposite to that of the head rotation
- Fast phase in the same direction as the head rotation
    - The eye movements are thus slower than the head movement but the eyes eventually return to the centre of the palpebral fissure

Nystagmus may also be associated with an underlying abnormality (*pathological nystagmus*); typically:

- Slow (pathological) phase towards the side of the lesion
- Fast (corrective) phase away from the side of the lesion

Clinical signs of vestibular dysfunction:

Any or all of the following:

- Head tilt
- Falling
- Leaning
- Rolling
- Circling
- Abnormal and/or positional nystagmus
- Positional strabismus
- Asymmetrical ataxia
- (Vomiting/nausea)

Placing an animal in dorsal recumbency can help in detecting a positional nystagmus or strabismus by 'challenging' the vestibular system

Nystagmus in *central* vestibular disease can be horizontal, rotatory, vertical or positional, with the fast phase towards or away from the lesion:

- Affected animals may well have additional clinical signs that reflect brain involvement (e.g. reduced mentation from depression through to coma) or ipsilateral paresis and proprioceptive deficits.

Nystagmus in *peripheral* vestibular disease can be horizontal or rotatory, with the fast phase away from the side of the lesion:

- Affected animals may have normal mentation or they may be markedly disorientated
- Signs of brainstem abnormality are not expected unless there has been extension of inner ear disease
- Paresis and proprioceptive deficits should not occur

Patients with peripheral disease may also show:

- Horner's syndrome: third eyelid protrusion, pupillary constriction, drooping of upper eyelid, enophthalmos
- Facial nerve deficits, e.g. ipsilateral drooping of and inability to move ear and lip; widened palpebral fissure; absent blinking
- Typically not recognised in the idiopathic form though

Bilateral vestibular disease is characterised by:

- Head sway from side to side
- Loss of balance on both sides
- Symmetrical ataxia with a wide-based stance
- Physiological nystagmus cannot be elicited

Vestibular disease – unilateral

Head tilt and nystagmus typically associated with unilateral disorders of the vestibular system

Causes:

Central, e.g.

- Especially:
  - Neoplasia
  - Inflammation – infectious or non-infectious
- Also:
  - Trauma
  - Metronidazole intoxication

Peripheral, e.g.

- Especially:
  - Idiopathic
  - Otitis media or interna
- Also:
  - Ototoxicity (e.g. due to topical medications)
  - Middle or inner ear neoplasia
  - Middle or inner ear trauma
  - Hypothyroidism
  - Nasopharyngeal polyps (cats)

Signalment and History:

Signalment may help to raise or lower the index of suspicion for certain differential diagnoses, e.g.

- Idiopathic peripheral vestibular disease seen most often in older dogs
- Congenital vestibular disease most likely in very young animals

As always, a thorough history should be taken in all cases. Important information includes:

- Onset and progression – clinical signs are usually progressive with central disease
- History of ear disease
- Clinical signs consistent with ear disease
- Non-vestibular potentially multifocal neurological signs suggestive of brain involvement
- History of trauma
- Medical therapy, e.g. potentially ototoxic topical therapy, metronidazole
- Clinical signs consistent with other diseases, e.g. hypothyroidism

Physical examination:

Major system examination:

- Neurological system is often the only system to be significantly affected
- Animals with central vestibular disease due to a primary brain lesion may have potentially significant cardiovascular abnormalities
- Hyperthermia may be identified in some very disorientated dogs
- Range of abnormalities may be identified following trauma

Bilateral otoscopic examination should be performed in animals with peripheral vestibular signs:

- Tympanic membrane is often ruptured but if it remains intact it may not be possible to detect fluid in the middle ear
- Myringotomy may need to be performed both for diagnostic purposes and to collect a fluid sample for cytology and microbiology
- Most animals require heavy sedation or preferably general anaesthesia for a reliable otoscopic examination to be performed

Emergency database:

Likely to be unremarkable in many cases
Dehydration possible
Peripheral blood smear examination may reveal leucocytosis in some cases (e.g. otitis media or interna, inflammatory brain disease)

Diagnostic imaging:

Animals with signs of *central* vestibular disease require referral for advanced diagnostic imaging (computed tomography or magnetic resonance imaging) and cerebrospinal fluid analysis.

Peripheral vestibular disease:

- Well-positioned plain skull radiographs designed to highlight the tympanic bullae may provide evidence of infection or neoplasia of the middle or inner ear
- However general anaesthesia is required and this should therefore only be undertaken in cases with signs suggestive of peripheral disease
- Advanced diagnostic imaging modalities are considerably more sensitive so referral may be appropriate

Treatment:

Centres on addressing the underlying disorder if this is possible, e.g.

- Discontinue administration of toxic drugs
- Treat bacterial otitis with several weeks of systemic antibiosis (preferably based on culture and sensitivity testing)

Supportive care also required, e.g.

- Intravenous fluid therapy if unable or unwilling to drink
- Provide assistance for toileting
- Other nursing measures including well-padded bedding

Treat vomiting patients with anti-emetic therapy (e.g. maropitant, metoclopramide, ondansetron)

- Even if not vomiting, nausea is thought likely so empirical use in most cases may be rational

Animals presenting with head trauma must be stabilised as required

Idiopathic peripheral disease

Form of vestibular disease seen most commonly in routine emergency practice
Especially in older dogs; may also affect cats of any age
Diagnosis: compatible history and examination findings + exclusion of other causes

- Do not usually have Horner's syndrome or facial nerve deficits

Clinical signs can be per-acute and often quite severe; however improvement, sometimes, marked, possible over several days (typically within 48-72 hours) with adequate supportive care
Prognosis: good with complete recovery common (may take up to 4 weeks and mild residual signs may persist); recurrence may occur
No evidence for a beneficial effect from corticosteroid administration
Propentofylline (Vivitonin®) is sometimes used – again, no evidence base for beneficial effect especially in acute phase

As idiopathic peripheral disease often occurs in older dogs, the major differential diagnosis is central vestibular disease secondary to a brain tumour which clearly carries a worse prognosis. Thorough neurological examination to differentiate peripheral versus central signs is essential for reasonable prognostication. Owners can then be counselled appropriately and reassured about the rationale of giving their dog some time to improve.

Appendix 1 Central Nervous System

Important aspects of the Central Nervous System in the collapsed patient

Observation

Mental status and behaviour

Awareness (consciousness) is maintained by the brainstem (ascending reticular activating system) and the cerebral cortex

Behaviour is typically associated with the forebrain limbic system (made up of portions of the cerebrum and the thalamus/hypothalamus)

Normal	Alert, with normal response to environmental stimuli
Depressed/obtunded:	Decreased functional activity; mentally dulled; drowsy; less responsive to environmental stimuli
Stuporous:	Unresponsive to normal environmental stimuli but responsive to painful stimuli
Comatose:	Unresponsive to environmental or painful stimuli
Hyperaesthetic:	Increased sensitivity to a normal level of stimulation
Confused/disorientated (delirious):	Responding to environmental stimuli in an inappropriate manner

Posture and body position at rest

Head tilt:

Seen most commonly due to an abnormality in the non-cerebellar portion of the vestibular apparatus – the head is usually tilted towards the same side as the lesion in peripheral or central vestibular disorders.

May also be caused by lesions affecting the cerebellar portion of the vestibular apparatus; this is therefore a central vestibular disorder but with a paradoxical head tilt, i.e. the head is tilted to the contralateral side of the lesion.

Wide-based stance:

A wide-based stance is characteristic of a balance disorder and is especially associated with cerebellar diseases.

Decerebrate rigidity:

Caused by a rostral brainstem lesion and characterised by:

- Extension of all limbs
- Opisthotonos (head and neck extension)
- Stuporous or comatose mental status
- Grave prognosis

Decerebellate rigidity:

Typically due to acute lesions affecting the rostral part of the cerebellum – this area inhibits the stretch reflex mechanism of anti-gravity muscles (extensor muscle tone). Characterised by:

- Extended thoracic limbs
- Opisthotonos (head and neck extension)
- Hips may be flexed by the increased tone in the iliopsoas muscles
- Posture may be episodic
- Normal mentation
- Significantly better prognosis that decerebrate rigidity

Schiff-Sherrington posture:

The Schiff-Sherrington posture is only present in acute lesions but it is important to realise that it has not been shown to have any prognostic significance.

Caused by an acute severe thoracic or cranial lumbar spinal cord lesion. Such a lesion may interfere with inhibitory ascending neurons that project cranially from the lateral grey matter of the cranial lumbar spinal cord segments to inhibit the thoracic limb extensor motor neurons.

Posture consists of:

- Extensor hypertonia of the thoracic limbs with retention of voluntary movements and normal conscious proprioception in these limbs
- Paralysis of the pelvic limbs with intact reflexes
    - Classically hypotonic paralysis – despite the fact that it is caused by direct interference with the upper motor neuron pathway
    - In practice hypotonia is transient and tone is usually normal at presentation

Abnormal involuntary movements

Tremors:

Tremors are synchronous involuntary oscillating contractions of antagonistic muscle groups that can affect all or part of the body – generalised tremors are more commonly encountered.

Classified as:

- Resting tremors
- Intention tremors:
    - Occur as the animal intends to move, i.e. exaggerated by goal-oriented movements (e.g. eating)
    - Most often constitute a dysmetria of the head movements associated with cerebellar disease
- Action tremors:
    - Occur as parts of the body are maintained in certain positions

Epileptic seizures:

Epileptic seizures are the clinical manifestation of excessive or hypersynchronous electrical activity in the cerebral cortex, i.e. they imply a forebrain disorder. They may be focal or generalised and especially for generalised seizures, the cause may originate intra- or extracranially.

Other abnormal involuntary movements include myotonic movements, myoclonus, cataplexy and head-bobbing.

Aspects of Neurological Examination/Localisation

Testing the cranial nerves:

Cranial nerve test	Afferent cranial nerve	Intermediate brain region	Efferent cranial nerve	Principal effect noted
Palpebral reflex	Trigeminal (V) – ophthalmic or maxillary branch	Brainstem	Facial (VII)	Blink elicited by touching of medial or lateral canthus
Corneal sensation	Trigeminal (V) – ophthalmic	Brainstem	Facial (VII) Abducens (VI)	Blink and globe retraction elicited by touching cornea
Vestibulo-	Vestibulocochlear (VIII)	Brainstem	Oculomotor (III)	Nystagmus induced

ocular reflex			Trochlear (IV) Abducens (VI)	by moving the head
Menace response	Optic (II)	Forebrain Cerebellum Brainstem	Facial (VII)	Blink elicited by a menacing gesture
Nasal mucosa stimulation response	Trigeminal (V) – ophthalmic	Forebrain Brainstem	None	Withdrawal of head elicited by touching nasal mucosa
Pupillary light reflex	Optic (II)	Brainstem	Oculomotor (III)	Pupillary constriction elicited by shining a light in the eye
Gag reflex	Glossopharyngeal (IX) Vagus (X)	Brainstem	Glossopharyngeal (IX) Vagus (X)	Contraction of the pharynx elicited by its palpation

The **vestibular system** is discussed earlier in these notes.

Spinal reflexes, Muscle tone and size:

Upper versus lower motor neuron

Lower motor neuron (LMN):

The cell bodies of the lower motor neurons lie within the ventral horn of the spinal cord grey matter or within the cranial nerve nucleus of the brainstem. The axons leave the central nervous system as the ventral nerve roots becoming spinal nerves and then peripheral nerves which synapse with an effector organ, e.g. muscle.

The central nervous system is arranged in a segmental manner. Each spinal cord segment innervates a specific muscle or group of muscles. Identification of segmental LMN signs allows accurate clinical neurolocalisation to a peripheral nerve, a nerve root or a motor neuron within the spinal cord or the brainstem.

Upper motor neuron (UMN):

Upper motor neurons are efferent neurons originating in the brain and synapsing indirectly (via an interneuron) with lower motor neurons; the UMN modulates the activity of the LMN. Upper motor neuron cell bodies lie within the cerebral cortex, basal nuclei or brainstem.
Lesions of the UMN system typically result in loss of motor function and the release of the inhibitory effect (disinhibition) that the UMN system has on LMNs located caudal to the level of the injury.

Unlike LMN signs, identification of UMN signs does not allow accurate clinical neurolocalisation to a specific spinal cord segment or brainstem nucleus.

Criterion	LMN paresis	UMN paresis
Posture	Difficulty in supporting weight Crouched stance as a result of overflexion of the joints	Often normal (unless the animal is paralysed) Abnormal limb position (knuckling, abducted, adducted or crossed over)
Gait	Short strides Tendency to collapse	Stiff and ataxic strides Delayed protraction
Motor function	Flaccid paresis/paralysis	Spastic paresis/paralysis
Segmental reflexes	Decreased (hyporeflexia) to absent (areflexia)	Normal to increased (hyperreflexia)

Resting muscle tone	Decreased (hypotonia) to absent (atonia)	Normal to increased (hypertonia)
Passive limb flexion and extension	Decreased resistance	Slight resistance due to extensor hypertonia
Muscle atrophy	Early, rapid and severe neurogenic atrophy	Late, slow and mild-moderate disuse atrophy

Thoracic versus pelvic limbs

Spinal lesion localisation refers to the segment rather than the vertebral bodies. Functionally the spinal cord can be divided into 4 regions:

- Cranial cervical (C1-C5)
- Cervicothoracic (C6-T2) – thoracic limbs
- Thoracolumbar (T3-L3)
- Lumbosacral (L4-S3) – pelvic limbs

A spinal cord segment = a portion of the spinal cord that gives rise to one pair of spinal nerves

The spinal cord can functionally be divided into 4 regions:

- Cranial cervical (C1-C5)
- Cervicothoracic (C6-T2)
- Thoracolumbar (T3-L3)
- Lumbosacral (L4-S3)

LMN cell bodies are located within the grey matter of the:

- Cervicothoracic intumescence (segments C6-T2) for the thoracic limbs
- Lumbosacral intumescence (segments L4-S3) for the pelvic limbs

Lesions at these levels result in LMN signs in the corresponding limb(s)

Site of the lesion	Thoracic limbs	Pelvic limbs
Brain	UMN	UMN
C1-C5	UMN	UMN
C6-T2	LMN	UMN
T3-L3	Normal	UMN
L4-S3	Normal	LMN
Polyradiculopathy Polyneuropathy	LMN	LMN

Impact of neurological lesions at different sites on the thoracic versus pelvic limbs

Thoracic limb evaluation

Reflex	Response	Tested
Withdrawal (flexor) reflex*	Reflex contraction of flexor muscles causes limb withdrawal	Spinal cord segments C6-T2 (and associated nerve roots) Brachial plexus Peripheral nerves (ulnar, median, musculocutaneous, axillary)
	Extension of the contralateral limb (crossed-extensor reflex)	Indicates UMN lesion cranial to C6 spinal cord segment
Extensor carpi radialis reflex	Slight extension of the carpus	Spinal cord segments C7-T2 and associated nerve roots

		Radial nerve

(* If withdrawal is absent, individual toes should be tested to determine if specific nerve defects are present, i.e. because the sensory nerve in question varies between toes)

Remember that the withdrawal reflex is a segmental spinal cord reflex that only depends on the function of the local spinal cord segments and not on conscious pain perception

Pelvic limb evaluation

Reflex	Response	Tested
Withdrawal (flexor) reflex*	Flexion of: • Hip (femoral nerve) • Stifle and hock (sciatic nerve) Extension of the contralateral limb (crossed-extensor reflex)	Spinal cord segments L4-S2 (and associated nerve roots) Femoral nerve Sciatic nerve Indicates UMN lesion cranial to L4 spinal cord segment
Patellar reflex	Extension of the limb due to reflex contraction of quadriceps femoris muscle	Spinal cord segments L4-L6 and associated nerve roots Femoral nerve In the absence of other neurological deficits, an exaggerated patellar reflex means little and can be observed in an excited or nervous animal.
Cranial tibial and Gastrocnemius reflexes	Flexion of tarsus Extension of hock	Spinal cord segments L6-S1 (cranial tibial) and L7-S1 (gastrocnemius) and associated nerve roots Peroneal (cranial tibial) and tibial (gastrocnemius) peripheral nerves Less reliable than patellar reflex

(* If withdrawal is absent, individual toes should be tested to determine if specific nerve defects are present, i.e. because the sensory nerve in question varies between toes)

Perineal reflex

Stimulation of the perineum with a haemostat results in anal sphincter contraction and flexion of tail. This tests the integrity of:

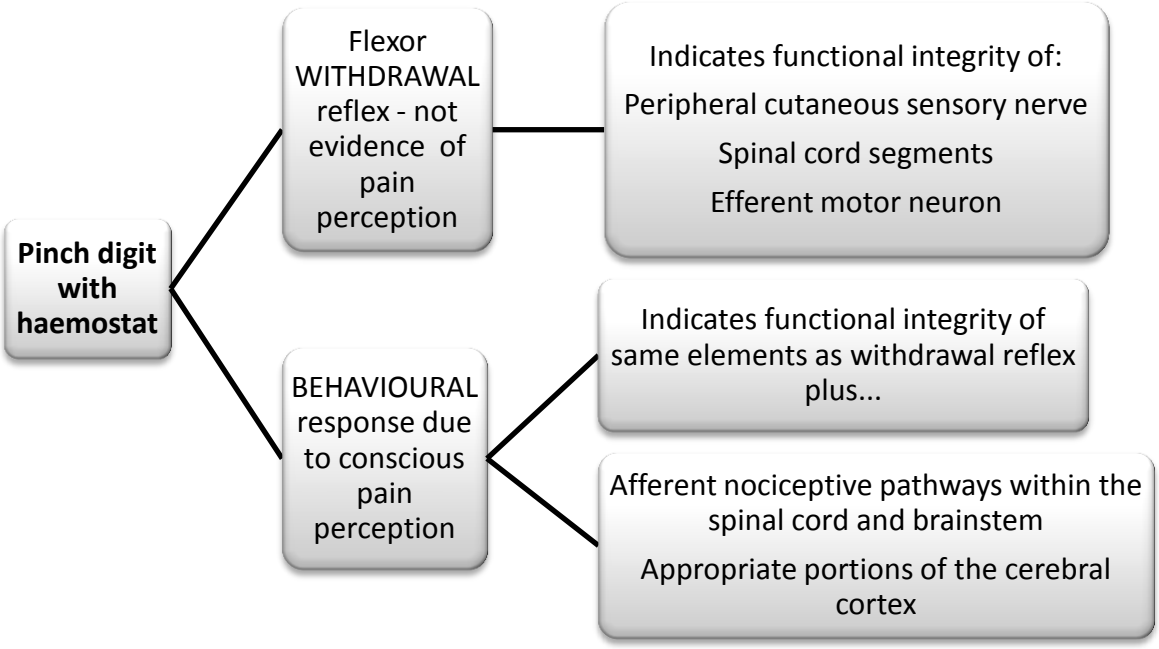
- Caudal nerves of the tail
- Pudendal nerve
- Spinal cord segments S1-Cd5 (caudal, coccygeal) and associated nerve roots

Sensory evaluation

Apart from conscious proprioception, evaluation of the sensory system in animals largely depends on testing pain perception (nociception):

Limb deep pain perception

The pathways that carry deep pain sensation are located deep in the spinal cord white matter and project to both sides of the spinal cord forming a multisynaptic bilateral network. Therefore only a severe bilateral spinal cord lesion impairs deep pain sensation. Deep pain perception is usually tested in all four limbs, the tail and the perineal region as appropriate.



The different nervous system elements involved in a limb withdrawal reflex versus a behavioural response to conscious pain perception

What does the 'deep' refer to? This is pain that can still be elicited by heavy pressure to the bones of the digits with a haemostat even when superficial cutaneous pain sensation is diminished or lost.

Cutaneous sensory testing

Nerve	Spinal cord segment	Cutaneous sensory distribution
Musculocutaneous	C6, C7, C8	Medial antebrachium
Radial	C7, C8, T1, T2	Cranial aspect of the antebrachium and foot except 5th digit
Median and ulnar	C8, T1, T2	Caudal aspect of the antebrachium and foot including 5th digit
Femoral	L3, L4, L5, L6	Medial aspect of the limb and 1st digit (saphenous branch)
Sciatic • Peroneal branch • Tibial branch	L6, L7, S1, S2	 Craniolateral aspect of limb distal to stifle Caudal aspect of limb distal to stifle

Dermatome mapping of clinical use in dogs

Cutaneous trunci (panniculus) reflex

In the absence of other neurological deficits, little significance can be given to an apparently absent cutaneous trunci reflex

This reflex is tested by pinching the skin of the dorsal trunk between vertebral level T2 and L4-L5 (reflex is absent in the neck and sacral regions); this should induce contraction of the cutaneous trunci muscles bilaterally causing twitching of the overlying skin.

Testing is usually started at the level of the ilial wings:

- If the reflex is present at this level, the entire reflex pathway is intact
- With spinal cord lesions the reflex is lost caudal to the affected spinal cord segment indicating the presence of a transverse myelopathy – the site of the maximal spinal cord lesion is usually 0-4 vertebrae, often 2-3 vertebrae, cranial to the cutaneous trunci reflex cut-off point.

The cutaneous trunci reflex can be lost ipsilaterally (with a normal contralateral reflex) with diseases affecting the brachial plexus (and hence the motor lateral thoracic nerve) regardless of the level at which the skin is stimulated.

More detail about the reflex:

The sensory nerve for the dermatome being tested enters the spinal cord at the level of the segments corresponding to that dermatome; these segments are approximately 2 vertebrae cranial to where the skin is pinched. The afferent sensory information then ascends the spinal cord and synapses bilaterally at the C8-T1 segments with the motor neurons of the lateral thoracic nerve – this nerve courses through the brachial plexus and innervates the cutaneous trunci muscle.

Localisation of common neurological signs

In localising a lesion, it is not necessary that all of the clinical signs referable to one location are present If a single lesion cannot explain all the abnormal findings, the anatomical diagnosis is considered as multifocal or diffuse

Clinical signs	Neurolocalisation
Seizures	Forebrain
Narcolepsy-cataplexy	Diencephalon
Abnormal behaviour	Forebrain
Visual dysfunction	Eye, optic nerve, optic chiasm, forebrain
Head pressing	Forebrain
Circling • With loss of balance • Without loss of balance	 Vestibular apparatus Forebrain
Head tilt, nystagmus, rolling, falling	Vestibular apparatus
Strabismus	Vestibular apparatus CN III, IV, VI
Depression, stupor, coma	Brainstem or forebrain
Abnormal prehension	CN V, XII, caudal brainstem
Dysphagia	CN IX, X, caudal brainstem
Dropped jaw	Bilateral CN V
Paralysis of eyelid, lip, nostril and/or ear	CN VII
Megaoesophagus	CN X
Laryngeal paralysis	CN X
Tongue paralysis	CN XII

Deafness	Auditory apparatus

[CN: cranial nerve]

APPROACH TO THE BLUNT TRAUMA PATIENT

General Initial Approach

The general initial approach to the trauma patient is similar to that for any emergency patient and was discussed above under Initial Approach to the Collapsed Dog.

General Approach to the Trauma Patient

Trauma is relatively common in companion animals; cats hit by vehicles are probably the most common examples but other types of blunt trauma as well as for example injuries following fights are also seen relatively commonly.

Most common causes:

- Motor vehicle accidents
- Animal (especially dog) bite injuries
- Tail pull injuries
- Falls from a height (esp. feline high-rise syndrome)
- Puppies and kittens trodden on
- Dogs kicked by horses

Cranial, thoracic and pelvic injuries especially common in cats

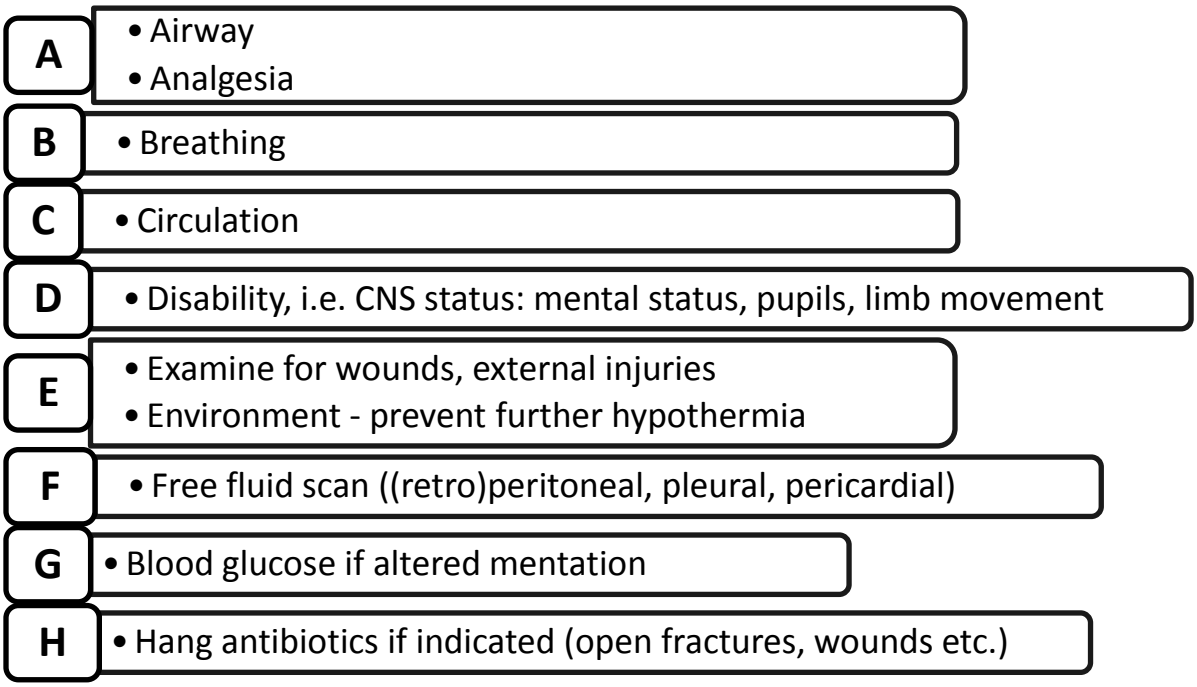
Some injuries following motor vehicle accidents:

- Head
  - Traumatic brain injury
  - Ocular injury
  - Skull fracture
  - Dental injury
- Thorax
  - Pulmonary contusions
  - Pneumothorax
  - Diaphragmatic rupture
  - Haemothorax
  - Rib fractures
  - (Flail chest)
- Abdomen
  - Abdominal wall rupture
  - Haemoabdomen
  - Uroabdomen – non-abdominal urinary tract rupture possible
  - Bile peritonitis
  - Septic peritonitis from gastrointestinal rupture
- Spine (vertebral column)/spinal cord
  - Vertebral fracture
  - Vertebral luxation/subluxation
  - Intervertebral disc extrusion/herniation/prolapse
- Pelvic fractures
- Limbs
  - Long bone fracture
  - Joint luxation/subluxation

- Tendon/ligament injury
- Degloving injury
- Wounds

A **general approach to the emergency patient** involves the application of certain core principles or treatments before providing specific therapies or interventions for the particular problems present, and this approach applies equally to trauma cases.

Mnemonic for basic approach – performed sequentially or concurrently depending on your circumstances:



Alternative (better?) version:

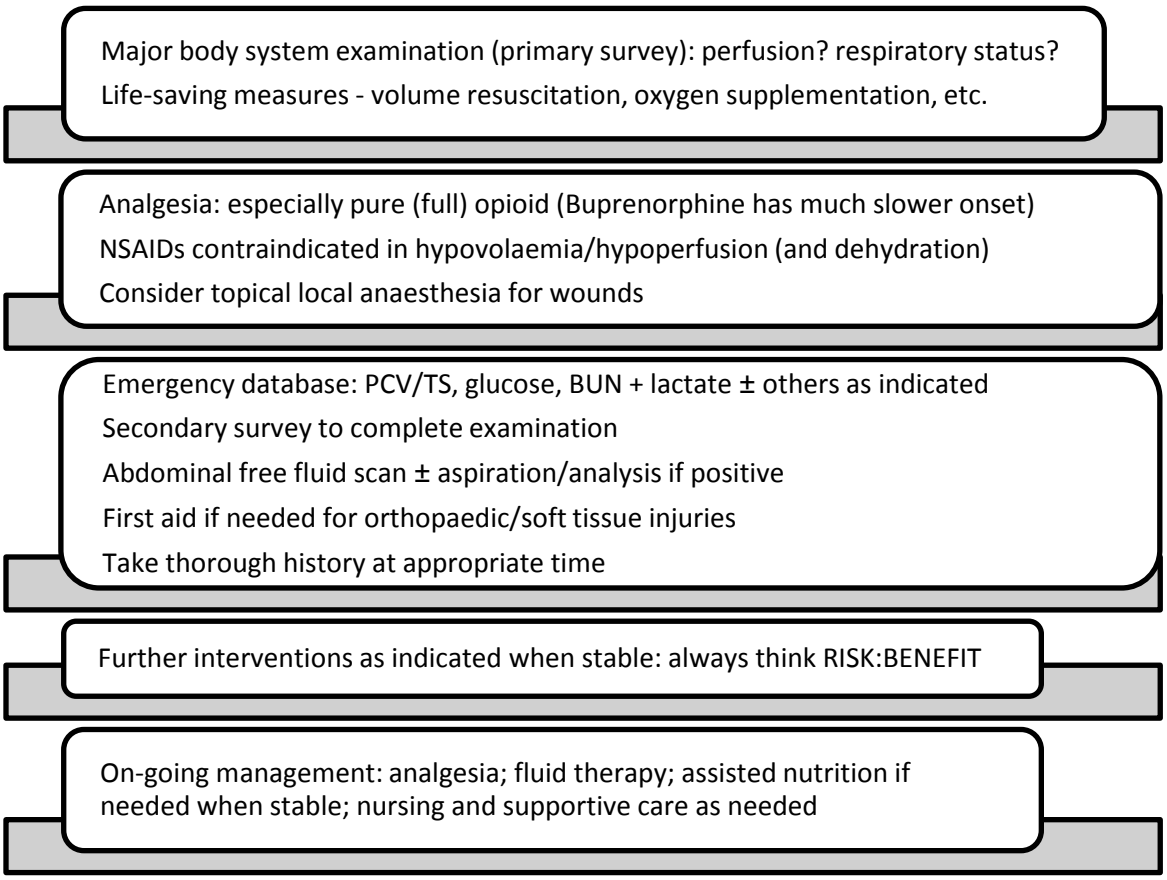
A Airway, Analgesia +/- Antibiotics
B Breathing
C Circulation
D Disability
E Examine for wounds, injuries. Environment. Emergency database.
F Free fluid scan

It is essential to realise that the early management of the trauma patient can have significant consequences on subsequent morbidity and mortality. A rational approach to the trauma patient starts with a major body system examination – cardiovascular system, respiratory system, and the central nervous system (mentation, gait). The two most important problems to look for are:

- Poor systemic *perfusion* due to *hypovolaemia*: does the patient need immediate intravenous fluid therapy to correct hypovolaemia?
- *Respiratory compromise*: does the patient need oxygen supplementation and perhaps thoracocentesis for dyspnoea?

Next consider what level of *analgesia* the patient requires. Then go on to perform a **more thorough assessment**, ideally including an abdominal free fluid scan and some sort of emergency database bloodwork, and provide specific interventions for injuries sustained as indicated. A complete physical examination should be undertaken to search for any soft tissue, skeletal or neurological injuries; first aid should be applied to soft tissue and orthopaedic injuries identified in the initial stabilisation period. A thorough history should be obtained from the owner, including previous medical/surgical diseases and concurrent medications.

Bear in mind that any interventions should only be performed at the appropriate time based on patient stability always thinking about the risk-benefit assessment: how beneficial is the proposed intervention to the patient? Is it informative? Essential? Will it impact on-going management or prognosis? Does it need to be performed at all? At that moment in time? What are the associated risks? Etc. A lot of emergency medicine – in fact medicine in general – revolves around making risk-benefit assessments.



The abdomen in trauma

In the author's experience, clinically significant intra-abdominal injuries are relatively rare in companion animals that sustain blunt trauma (clearly some animals suffer bite or other wounds to the abdomen that may or may not penetrate full-thickness). However they do occur and most will manifest with free peritoneal fluid that can be detected by ultrasonography as described above; as such the author would strongly encourage free fluid scans to be performed in all patients that have suffered abdominal trauma. Where fluid is detected aspiration should be performed, preferably with ultrasound guidance, to allow analysis – chemistry analysis, cytology etc. – to be performed and a diagnosis to be achieved.

It is noteworthy that in humans the concept of 'occult' injuries is described. These are injuries that do not manifest initially with free fluid on ultrasonography but are detected on CT scanning. Detecting injuries at this time allows patients to be monitored with a greater index of concern and/or interventions to be performed as deemed necessary. In veterinary medicine the most realistic approach may be to recognise that free fluid should develop in patients with initially occult injuries. For patients that have a negative initial free fluid scan, on an individual patient basis based on progression, it may therefore be sensible to repeat the scan at least once subsequently (e.g. after 2-4 hours). It is important to note that at this time, to the author's knowledge, there is little or no information published on the prevalence and progression of so-called occult injuries in veterinary patients.

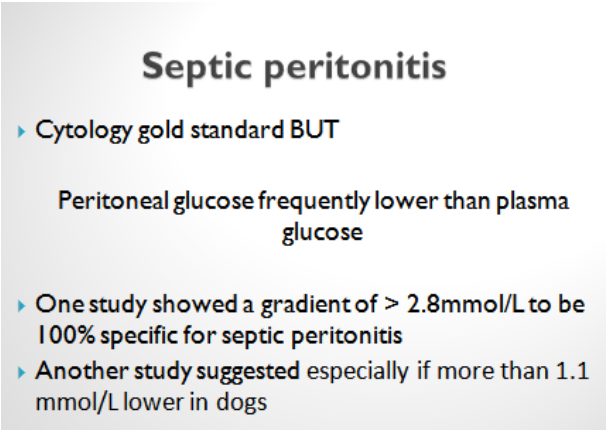
The incidence of peritoneal haemorrhage following blunt trauma is thought to be low; however this may be because for many years we did not look for evidence of haemorrhage until and unless a patient became clinically compromised – it may be more accurate to say that at this time the incidence of *clinically significant* peritoneal haemorrhage is low. Thankfully surgical intervention is rarely required for intra-abdominal haemorrhage following trauma in companion animals.

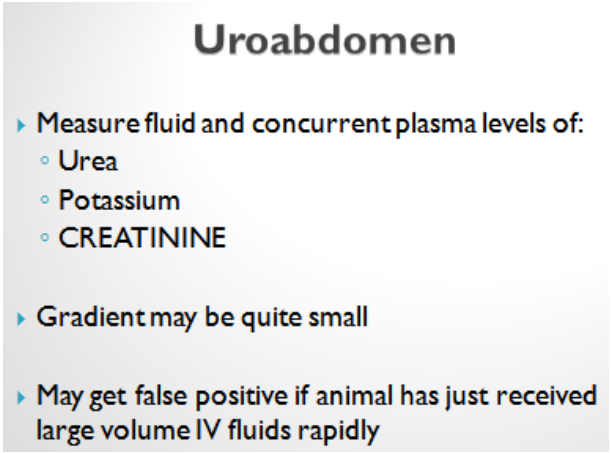
If a free fluid scan is not performed routinely in these patients, then it certainly should be considered in a patient in which hypovolaemia on presentation and assessment of venous packed cell volume/total protein as part of the emergency database suggest haemorrhage has occurred – is the source in the abdomen? Similarly elevations of urea, creatinine or potassium should prompt evaluation for urinary tract rupture (be this peritoneal, retroperitoneal or outside of the abdomen). Likewise for elevated plasma bilirubin and bile peritonitis and it should always be remembered that gastrointestinal tract rupture resulting in septic peritonitis does occur….

Abdominal fluid parameter	Finding	Suggestive of…
Packed cell volume (PCV)	Similar to peripheral blood PCV	Haemoabdomen
Potassium	Significantly greater than peripheral blood potassium (typically more than 1.4:1)	Uroabdomen
Creatinine	Significantly greater than peripheral blood creatinine (typically more than 2:1)	Uroabdomen
Glucose	Lower than peripheral blood glucose	Septic peritonitis

Accidental aspiration of blood vessels, liver and spleen can be differentiated in non-coagulopathic animals as blood will normally clot with time, while haemorrhagic fluid will not.

Lactate	(Significantly) higher than peripheral blood lactate	Septic peritonitis
Bilirubin	Significantly greater than peripheral blood bilirubin	Bile peritonitis – abdominal fluid may also be dark green or black in appearance
Microscopy	Degenerate neutrophils with intracellular bacteria Intestinal/plant/food material Golden refractile pigment	Diagnostic of septic (bacterial) peritonitis Diagnostic of septic peritonitis due to GI leakage Bile peritonitis





Trauma is the most common cause of urinary tract rupture:

- Especially blunt abdominal/pelvic trauma – urine leakage usually from the bladder
- Also iatrogenic – especially urethral rupture during urethral catheter placement

Neoplasia and prolonged urinary tract obstruction are less common causes.

While the loss of large amounts of urine into the abdomen will quickly become apparent, small leaks may take several days to produce clinical signs such as ascites or azotaemia. Note that the presence of a palpable bladder does not rule out bladder rupture, nor does the ability to pass apparently normal streams of urine.

It is important to consider not only the bladder but also the urethra and ureters as potential sites of rupture. Positive contrast radiography is helpful in determining the site of urinary tract rupture:

- Antegrade pyelography or intravenous urography for ureters
- Retrograde urethrocystography for urethra and bladder

Aside from the bladder, surgical repair or management of urinary tract rupture in other sites is often best done in the hands of a specialist surgeon. As such it may be appropriate to refer animals with uroabdomen following initial stabilisation without performing general anaesthesia for contrast radiography.

Urethral rupture is easily missed, as it rarely leads to uroperitoneum due to the retroperitoneal location of the urethra. Instead, such cases often present after a few days with soiling and possible sloughing of the skin in the perineal region caused by leakage of large volumes of urine into the tissues. Retrograde urethrography is a simple technique and should be performed whenever urethral injury is suspected. If a

urethral tear is documented, passage of a urinary catheter should be attempted; if this is not possible, a cystotomy tube should be placed surgically (or potentially percutaneously if facilities allow) to provide urinary diversion while the urethra heals. Traumatic avulsion of the ureter is also an uncommon occurrence, but can result in uroabdomen or uroretroperitoneum 12-24 hours after injury. This is most easily identified by performing intravenous urography. Leakage of urine from the kidneys or proximal ureters will result in uroretroperitoneum potentially without uroabdomen.

In most cases of uroperitoneum, the peritoneal fluid will be serosanguineous, which may be misleading. Animals with uroabdomen typically have severe azotaemia, and variable hyperkalaemia may be present. Diagnosis is aided by comparing fluid and blood creatinine and potassium concentrations. Increased abdominal concentrations of creatinine and potassium compared with blood concentrations are suggestive of urinary tract rupture. Creatinine and potassium in peritoneal effusion equilibrate more slowly with the intravascular space and are therefore considered more reliable than blood urea nitrogen for detecting uroabdomen. Note that blood urea, creatinine and potassium may not be increased at presentation, even in the presence of a ruptured bladder and may take up to 24 hours or longer to develop depending on the extent of the leak. Urine is hyperosmotic and therefore will tend to draw fluid from the tissues into the peritoneal cavity, resulting in dehydration and hypovolaemia. As creatinine is a large molecule, it remains trapped within the peritoneum causing on-going fluid shifts.

Management of urinary tract injuries should be delayed until the animal is otherwise stable.

Treatment of urinary tract rupture involves initial stabilisation of the patient's major body systems followed by re-establishment of urine drainage.

Fluid therapy:

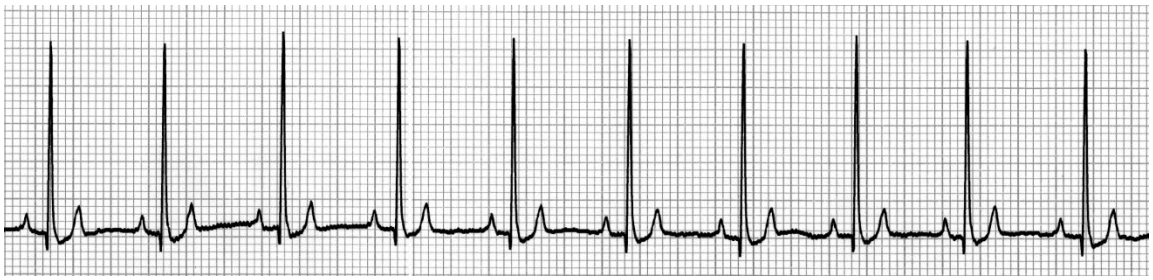
All patients will benefit from intravenous fluid therapy. An *isotonic replacement crystalloid* is the fluid of choice and should be administered as appropriate to restore perfusion. Normal saline (0.9% sodium chloride) has traditionally been recommended due to its lack of potassium. However this fluid may contribute to existing metabolic acidosis and there is no clinically significant difference between the use of 0.9% sodium chloride solution and Hartmann's (buffered lactated ringer's solution) which contains a small amount of potassium.

The priority is very much to start the patient on one or other of these solutions at a rate that is appropriate for the degree of hypovolaemia (if present).

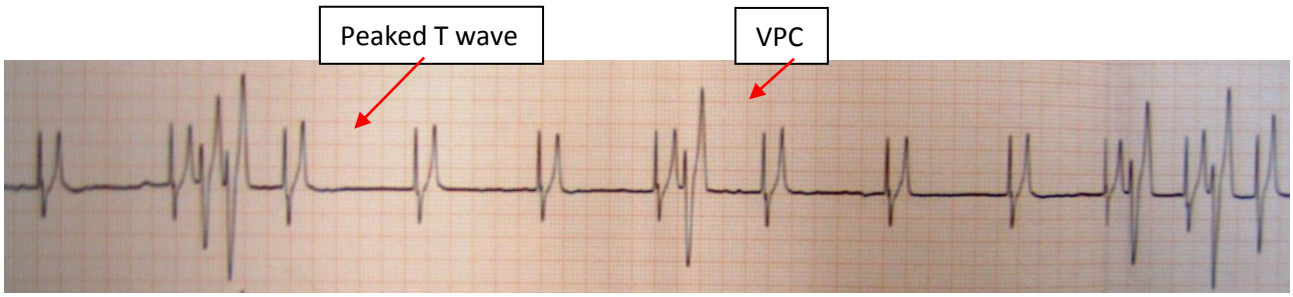
Hyperkalaemia:

Hyperkalaemia occurs mainly due to impaired urinary excretion of potassium. The clinical manifestations of hyperkalaemia reflect alterations in cell membrane excitability and of greatest concern are the potentially life-threatening effects on cardiac conduction:

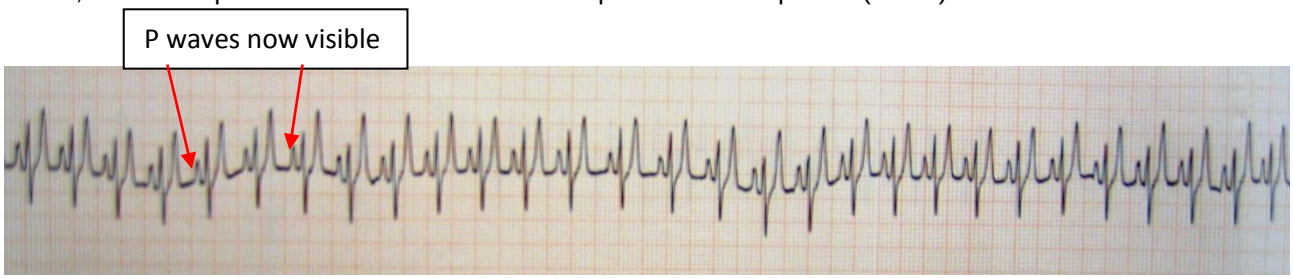
- Sinus bradycardia
- Prolongation of the PR interval
- Widening and bizarre appearance of the QRS complex, including sinoventricular rhythm
- Decreased amplitude, widening or complete absence (atrial standstill) of the P wave
- Peaked/tall T waves



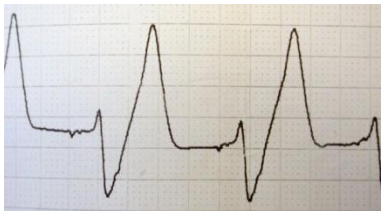
Normal sinus rhythm



Electrocardiogram from a cat with severe hyperkalaemia showing atrial standstill with absence of P waves, as well as peaked T waves and ventricular premature complexes (VPCs).



Electrocardiogram from the same cat following administration of calcium gluconate. P waves are visible and there are no VPCs in the post-treatment strip.



Atrial standstill and wide-complex sinoventricular rhythm in a cat due to severe hyperkalaemia showing merging of the QRS complex.

The severity of clinical signs resulting from hyperkalaemia does not necessarily correlate with the absolute increase in serum potassium concentration. The treatment required is therefore dependent not just on the serum potassium level but also very importantly on whether the hyperkalaemia is assessed to be clinically significant.

Treatment is directed at improving the patient's clinical status and not at the serum potassium concentration per se.

In some cases, intravenous fluid therapy and restoring urine drainage is all that is necessary for hyperkalaemia to resolve. Further treatment options for hyperkalaemia are summarised in the table below:

Agent	Dose / route	Comments
10% calcium gluconate	0.5-1.0 mL/kg i.v. bolus over 30-60 secs*	Rapid onset of action (can be a few secs) and first line choice in a crisis Short duration of action (often 10-15 min) Monitor ECG during administration Does not lower serum potassium concentration but restores normal cell membrane excitability Will also address possible ionised hypocalcaemia Bolus can be repeated while other measures are used to directly reduce hyperkalaemia
Neutral (Regular, Soluble) insulin **Glucose solution**	0.25-0.5 IU/kg i.v. 0.25-0.5 g/kg i.v.	Slower onset of action (can be more than 15 min) Lowers serum potassium concentration by moving potassium into cells Intravenous glucose supplementation typically required for several hours (monitor and adjust accordingly)
Sodium bicarbonate	1-2 mmol/kg slow i.v. (repeat if necessary)	Also lowers serum potassium concentration by moving potassium into cells Effect can persist for several hours Access to on-site acid-base analyser much preferred

(* Note: when calcium gluconate is given intravenously for the treatment of hypocalcaemia, it should be given slowly (e.g. over 20-30 min) as a constant rate infusion. However this is clearly not a rational approach in a patient with life-threatening hyperkalaemia and calcium gluconate is administered much more quickly in these cases.)

If serum electrolytes cannot be measured but clinically significant hyperkalaemia is suspected on the basis of electrocardiography or perhaps physical examination alone, the author firmly believes that empirical use of calcium gluconate, and potentially insulin with glucose, is appropriate. This treatment can be life-saving and is unlikely to cause any significant harm if not required.

Analgesia:

All of the causes of urinary tract rupture are likely to be associated with some degree of pain and as always, analgesia should be administered as part of the initial stabilisation. Pure opioids are the usual first choice and non-steroid anti-inflammatory drugs (NSAIDs) are contraindicated in animals that are hypovolaemic or azotaemic.

Re-establishing urine drainage:

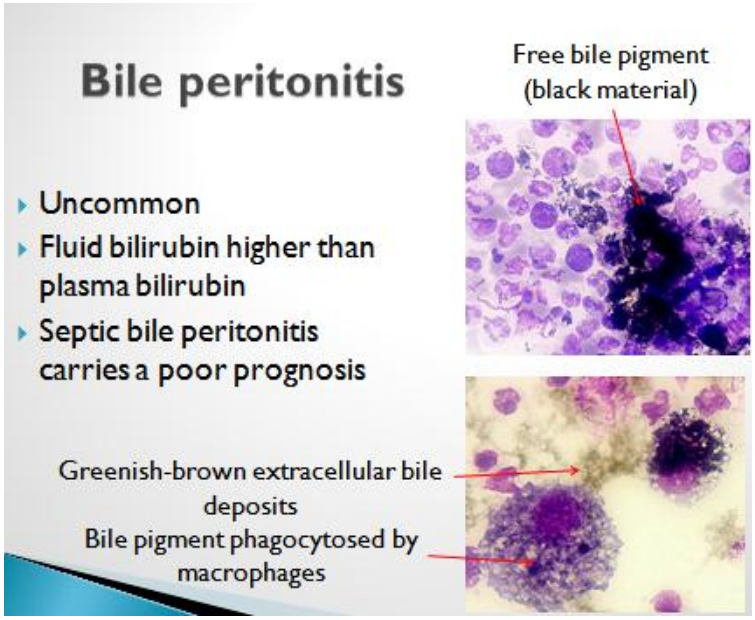
The approach to re-establishing urine drainage depends on the site of urine leakage as well as the severity of the animal's condition including other injuries and the extent of initial stabilisation required. The decision to be made essentially is between:

- Initial stabilisation followed by immediate diagnostic imaging to identify the site of leakage and surgical intervention, or
- Initial stabilisation that includes some form of temporary urinary drainage, and delayed surgical intervention

Bladder rupture often requires surgical intervention, although small leaks may heal with continuous decompression provided by a urinary catheter and drainage collection system. Urethral rupture is often managed by placing a urethral catheter and leaving it in situ for several days to act as a stent for urethral healing. Aside from the bladder, surgical repair or management of urinary tract rupture in other sites is often best done in the hands of a specialist surgeon. As such it may be appropriate to refer animals with urinary tract rupture following initial stabilisation without performing general anaesthesia for contrast radiography to identify the site of leakage.

In animals with uroabdomen that are more severely affected or if surgical intervention is to be delayed – for example due to referral – consider abdominal drainage. This will prevent reabsorption of electrolytes and waste products and help stabilise the patient for anaesthesia. A variety of drains have been used ranging from closed systems (e.g. proprietary peritoneal dialysis catheters) to over-the-needle catheters (e.g. central venous catheters, chest tubes) to Penrose drains. Omental occlusion of drain holes is a potential problem that can render drains dysfunctional.

If a suitable drain cannot be placed, needle abdominocentesis may be performed although repeated needle abdominocentesis is not ideal as a short-term management strategy.



Bile peritonitis occurs due to leakage from or rupture of the gallbladder and/or biliary tract. This may result from:

- Blunt or penetrating abdominal trauma; also iatrogenic
- Inflammation with or without infection, e.g. necrotising cholecystitis
- Obstruction, e.g. cholelithiasis, neoplasia

Clinical jaundice and hyperbilirubinaemia may be identified in animals with bile peritonitis, depending on the cause, along with varying degrees of cardiovascular compromise. Marked elevations in liver enzymes may also be seen.

Peritoneal fluid may be greenish in appearance and clusters of golden refractile pigment are identified. Septic bile peritonitis carries a worse prognosis. The bilirubin concentration of the peritoneal fluid is considerably higher than the plasma bilirubin concentration.

Bile peritonitis is a surgical emergency but the author cannot stress strongly enough the importance of referral of these cases to a specialist surgeon. Biliary tract surgery is highly challenging with the potential for disastrous consequences in inexperience hands.

Blunt trauma may result in body wall rupture with or without herniation of body organs. Blunt trauma involving ventral, femoral, paralumbar and prepubic sites may be detectable by careful palpation or may be apparent on radiographs. Can also be detected by ultrasonography – scanning a superficial structure like the body wall can be significantly enhanced by using a standoff; if a standoff pad is not available, a glove filled with ultrasound gel can work very well for this purpose. Strangulation of organs is uncommon, enabling the timing of these repairs to be semi-elective.

Emergency database

A minimum database consisting of manual packed cell volume (PCV), plasma total solids/protein (TS), blood glucose and blood urea nitrogen should be performed in the trauma patient. If available, blood lactate concentration is also extremely useful as a marker of hypoperfusion and successful resuscitation.

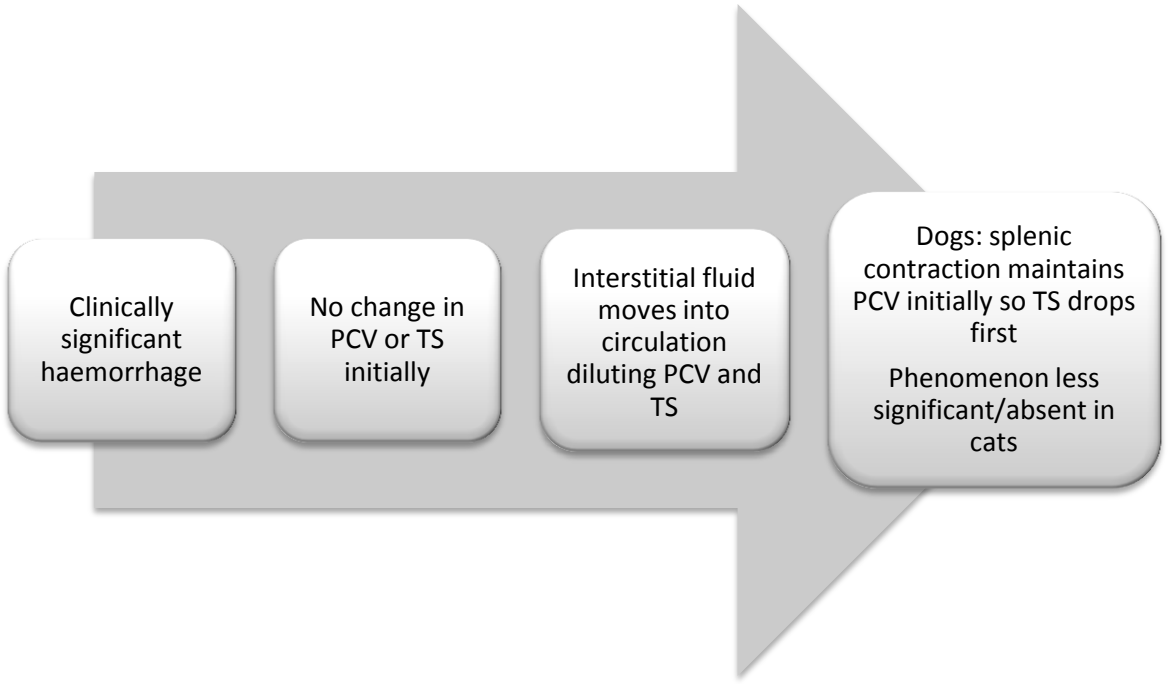
Manual packed cell volume (PCV) and plasma total solids/protein (TS/TP) measurement may be suggestive of significant haemorrhage within the patient although changes are clearly not specific to intra-abdominal haemorrhage.

Both red blood cells and protein are lost from the circulation in haemorrhage and therefore PCV and TS do not change initially.

- Remember that PCV is a percentage and TS a concentration, i.e. neither is a measure of absolute quantity.
- In the first few minutes following haemorrhage, the absolute number of red blood cells and plasma protein molecules will be reduced but PCV and TS are unchanged.

Fluid then moves from the interstitial compartment into the bloodstream diluting the remaining red cells and protein and causing a decrease in the measured PCV and TS.

- It takes a while for fluid shift and therefore dilution to occur although it is not possible to be too precise about the exact length of time in clinical patients.
- In dogs the spleen contracts in response to haemorrhage and expels a large amount of stored red blood cells into the circulation; therefore PCV may remain in the normal range for a while despite low TS, i.e. with blood loss, TS is usually expected to fall first followed by PCV in dogs.
    - The response of the spleen in cats is either much less substantial or in fact non-existent depending on which reference one consults.
- As yet more time passes PCV will also fall depending on whether haemorrhage is on-going, the severity of any on-going haemorrhage, and any treatment instituted.



Hypoglycaemia is a relatively rare finding in the trauma patient but may for example occur in very young or small animals. Mild(-to-moderate) hyperglycaemia on the other hand is relatively common but does not require any specific intervention. The significance of hyperglycaemia in traumatic brain injury is discussed below.

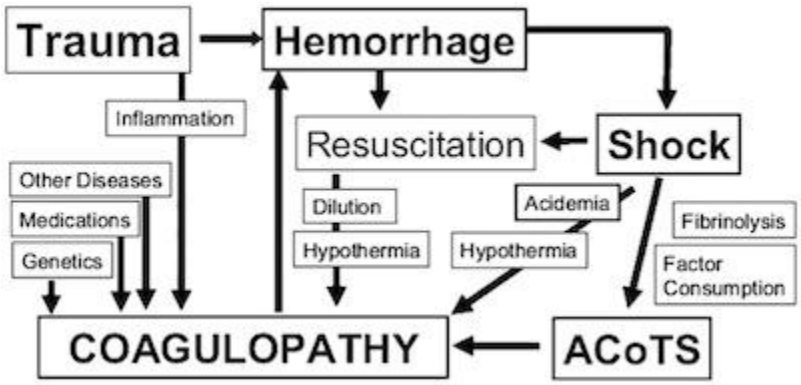
Blood urea may be elevated, either mildly-to-moderately due to pre-renal azotaemia and/or gastrointestinal haemorrhage, or more severely due to post-renal azotaemia secondary to urinary tract rupture.

Other plasma parameters such as potassium, creatinine or bilirubin may need to be measured for comparative purposes if abdominal free fluid is detected and uroabdomen or biliary peritonitis is suspected.

Transfusion in trauma

As mentioned later, haemostatic resuscitation is increasingly preferred in human traumatology essentially replacing loss of whole blood with equivalent constituents in the form of packed red blood cells, plasma and platelets. However this strategy is highly unrealistic given the limitations in financial and practical resources in veterinary medicine. Nevertheless following the initial resuscitative phase, some trauma patients will benefit from transfusion. Anaemia and coagulopathy may occur due to blood loss and be exacerbated by dilution from crystalloid and colloid fluid therapy; synthetic colloids can also cause a dose-dependent multifactorial coagulopathy.

As shown below there are various mechanisms of coagulopathy in trauma:



(ACoTS = Acute Coagulopathy of Trauma Shock)

An in-depth discussion is beyond the scope of these notes. Anaemic patients should be transfused not just on the basis of a specific PCV level but also with consideration to whether the anaemia appears to be clinically significant and whether blood loss is considered to be on-going. A relatively liberal approach to the use of plasma is suggested in patients with measured coagulopathy.

Nutrition in trauma

The benefits of ensuring adequate nutrition at the appropriate time are undisputed and several studies have documented a correlation between nutritional status and outcome during critical illness including trauma. Starvation of ill or injured animals may be associated with **hypermetabolism** (i.e. increased resting metabolic rate) and **stress starvation**, characterised by:

- Increase in protein catabolism proportional to the extent of disease leading to breakdown of stored protein
- Up-regulated production of catecholamines and other stress hormones leading to
    - Increased cardiac output and systemic vascular resistance
    - Insulin resistance and glucose intolerance
    - Proliferation of inflammatory mediators
    - Rapid onset of malnutrition
- An inability to store, mobilise, and interconvert nutrient substrates

Malnutrition results in:

- Persistent catabolic state and depletion of body protein stores
- Impaired wound healing
- Increase in infectious complications

Trauma patients frequently have decreased voluntary food intake for many reasons, including nausea, pain, and anxiety. Patients should be **cardiovascularly stable** and also have hydration, acid-base, blood glucose, and electrolyte abnormalities resolved before assisted nutrition is considered. Enteral nutrition is preferred if the gastrointestinal tract is completely or partially functional (i.e. functional enough to allow digestion and absorption), it is tolerated by the patient, and it is not contraindicated. Enteral nutrition is more physiological, safer and less expensive. Ideally avoid syringe feeding as this provides inadequate calorific intake, poses the potential risk of aspiration and is not especially patient friendly*. A naso-oesophageal or naso-gastric tube is an option although may not be ideal with facial injuries. An oesophagostomy tube is preferred once the patient is stable for anaesthesia. Parenteral nutrition may be employed in the interim if available.

(* See this blog post for further discussion on syringe feeding:
http://www.veteccsmalltalk.com/vetemccsmalltalk/2014/08/syringe-feeding-yes-no-or-it-depends.html)

The calorific requirements should be calculated using the following equation, which approximates the animal's resting energy requirements (RER):

Resting energy requirements (RER) (kcal) = (30 x Bodyweight) + 70

Patients suffering from trauma do not require an illness factor to be added in when calculating daily requirements. RER are more than adequate in most patients. Feeding more than the RER may lead to complications associated with overfeeding.

Summary approach to the trauma patient

Perform major system examination (primary survey) and consider especially:

Is the patient hypoperfused due to hypovolaemia; if so the patient needs immediate intravenous fluid resuscitation.
A replacement isotonic crystalloid is the first choice in most cases.

Is the patient dyspnoeic? Provide oxygen supplementation.
Is dyspnoea due to thoracic injury?
Pulmonary contusions (lung sounds louder/harsher than normal +/- crackles) and pneumothorax (lung sounds dull dorsally) are the two most common causes; if pneumothorax is suspected or you are not sure, consider thoracocentesis.

Provide analgesia.
Ideally use a pure opioid (e.g. morphine, methadone) as buprenorphine has a slower onset of action
NB. NSAIDs are contraindicated in hypovolaemic or dehydrated patients – if in doubt, do not give them early on! They are likely to be helpful though in trauma patients due to their anti-inflammatory effects so keep them in mind for later.
Can you employ topical local anaesthesia for wounds etc?

What about scanning the abdomen for free fluid (FAST)?
Remember with traumatic brain injury, the priority is to ensure the brain receives a good supply of well-oxygenated blood: correct perfusion, ensure oxygenation.

What about an emergency blood database of some sort – e.g. PCV/total protein, urea, glucose…
Any indication for more extensive chemistry testing – e.g. creatinine, electrolytes, bilirubin?

Perform a more thorough examination (secondary survey):

Does the patient need any specific interventions for injuries you have identified? If so, remember, think *risk-benefit assessment at all times*.

Going forward….

Maintain a liberal approach to opioid analgesia and consider NSAIDs at the appropriate time.
Continue fluid therapy including to correct any pre-existing dehydration (unlikely in peracute/acute trauma patients).
And, remember that nutrition is very important in the trauma patient:
Don't start feeding until and unless the patient is cardiovascularly stable, and withhold if there are neurological or other contraindications.
Consider a feeding tube (syringe feeding is very unlikely to meet calorific requirements, is stressful, may cause aspiration etc.)

Shock, Hypovolaemia and Dehydration

Parenteral Fluid Therapy

Analgesia for the Trauma Patient

These core concepts were discussed in detail in the study notes for Session 2 of this mini-series.

Thoracic Trauma

Respiratory system

It is very important not to stress animals in respiratory distress; these animals – especially cats – can be very unstable and may decompensate easily. In some cases even a brief major body system examination will not be tolerated. Observation from a distance, gentle handling, oxygen supplementation and empirical interventions are potentially important components of their management.

Evaluation involves examination of the following:

- Respiratory rate
- Respiratory effort
- Respiratory pattern/noise

Respiratory rate

Normal adult range in **dogs** and **cats**: 15-30 breaths per minute

- Higher rates are relatively common, often associated with shallow breathing (tachypnoea) and the key question to consider is whether this is the result of a primary respiratory abnormality or secondary for example to pain, anxiety, excitement amongst other causes.

Beware of (excessive) panting: don't automatically dismiss panting as being of minimal concern as occasionally it is the result of early compensation for respiratory embarrassment.

Respiratory effort

Abnormal respiratory rate and effort may be seen due to primary abnormalities in both the respiratory system and in other systems (neurological, metabolic). In general respiratory abnormalities secondary to non-respiratory factors are less severe.

Postural adaptations to alleviate air hunger in dyspnoeic patients include:

- Open-mouth breathing
- Neck extension
- Repeated changing of position
- Abduction of elbows (dogs)
- Sternal recumbency (cats)
- Anxious expression

Increased abdominal effort:

- Increased contraction of abdominal muscles
- Assists with expiration only

Paradoxical abdominal breathing:

- During normal inspiration both the thoracic (actively) and abdominal (passively) walls move outwards;
- In paradoxical abdominal breathing, they move in opposite directions
- Generally associated with severe respiratory distress; may also be more common with diaphragmatic dysfunction and pleural space diseases

Respiratory pattern/noise

Ideally the aim is to try to localise the cause of the patient's respiratory abnormality to one or more of the following:

<table>
<tr><th>Respiratory findings</th><th colspan="2">Localisation</th></tr>
<tr><td>Prolonged inspiration

Inspiratory stridor: harsh high pitched noise; especially from partial laryngeal obstruction (e.g. laryngeal paralysis)

Stertor: 'snoring'; usually due to partial obstruction of airflow through the nasal passages or nasopharynx (e.g. brachycephalic airway obstruction syndrome)</td><td>Dynamic obstruction</td><td rowspan="2">Upper respiratory tract</td></tr>
<tr><td>Inspiratory and expiratory stridor</td><td>Fixed obstruction (e.g. mass lesion)</td></tr>
<tr><td>Prolonged expiration with increased abdominal effort</td><td colspan="2">Lower airway disease</td></tr>
<tr><td>Lung sounds louder than normal: harshness, crackles*, wheezes</td><td colspan="2">Small airway or lung parenchymal disease
E.g. <u>pulmonary contusions</u>**</td></tr>
<tr><td>Lung sounds muffled ventrally</td><td colspan="2">Pleural space: effusion e.g. <u>haemothorax</u>**</td></tr>
<tr><td>Lung sounds quiet dorsally</td><td colspan="2">Pleural space: <u>pneumothorax</u>**</td></tr>
<tr><td></td><td colspan="2">Thoracic wall and diaphragm</td></tr>
<tr><td>Often rapid shallow breathing (tachypnoea)</td><td colspan="2">Primary neurological, metabolic or cardiovascular influences e.g. <u>pain</u>**</td></tr>
</table>

* It can be difficult to hear crackles in animals with a low tidal volume, e.g. during panting or tachypnoea.

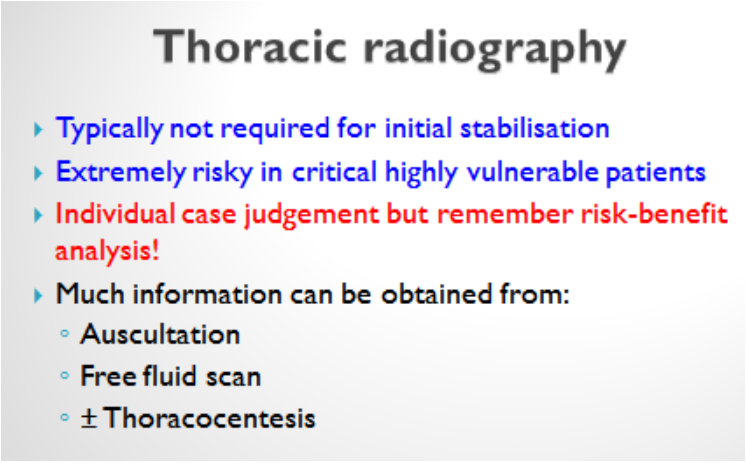
** Some of the potential findings following chest trauma.

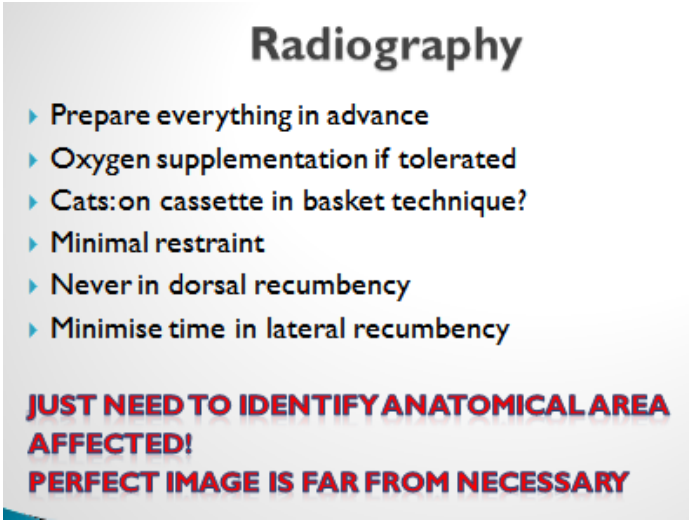
Causes of decreased lung sounds:

- Pleural fluid (ventrally)
- Pneumothorax (dorsally)
- Intra-thoracic masses (heart sounds displaced? reduced rib cage compliance?)
- Diaphragmatic hernia (bowel sounds in thorax?)
- Rarely decreased ventilation

Lung sounds must be related to the degree of respiratory effort the patient is showing – apparently normal lung sounds may be inappropriately quiet in a patient with a marked increase in effort.

The use of ultrasound to help localise causes of respiratory distress is increasing in human emergency departments and has also started to be engaged with in veterinary medicine; assessing for pleural effusion is easy to do and the technique can also be used for pneumothorax and lung parenchymal disease especially oedema; the latter require more expertise of course but can be done!





Thoracic Injury

Thoracic injuries following blunt trauma include:

- Pneumothorax
- Pulmonary contusions
- Haemothorax
- Rib fractures and flail segment
- Diaphragmatic rupture
- (Airway rupture)

In the author's experience, pulmonary contusions and pneumothorax are the most common.

It is often possible on the basis of observation and auscultation to make reliable judgements as to the most likely cause of dyspnoea in trauma patients and thoracic radiography is not recommended in distressed, painful or unstable patients. This is especially applicable to dyspnoeic cats as they may decompensate more easily than dogs.

Where significant pleural space disease (pneumothorax, haemothorax) is suspected, thoracocentesis (see below) may be both diagnostic and therapeutic. This procedure is relatively simple and clinically significant complications are rare. It is recommended to perform thoracocentesis rather than subject unstable trauma patients to radiography initially. Ultrasonography is a quick and less stressful way of confirming haemothorax and can also be used to detect pneumothorax – although the latter requires much more experience and expertise.

If radiography is performed, everything should be prepared before bringing the patient to the radiography room and minimal restraint should be used. If tolerated, oxygen supplementation is provided by mask or flow-by. The intention here is to produce an image that allows the anatomical area affected to be identified and not to produce the perfect thoracic radiograph. Even a rotated dorsoventral radiograph can provide more than enough information for the patient's initial management. A dyspnoeic animal should never be restrained in dorsal recumbency and it is typically best to minimise the amount of time spent in lateral recumbency.

Pneumothorax

Pneumothorax is essentially the accumulation of air in the pleural cavity; lung sounds will be dull dorsally although in more severe cases they may be quieter more diffusely. **Closed** pneumothorax usually results from leakage of air secondary to a lesion within the lung parenchyma, although it may also occur for example due to damage to the airways or oesophagus. **Open** pneumothorax involves loss of integrity of the thoracic wall (e.g. following penetrating trauma) while a **tension** pneumothorax occurs if a one-way valve is formed at the site of air leakage such that air taken in during inspiration leaks into the pleural space but cannot be expelled. The result is a rapid and potentially life-threatening increase in intrapleural pressure (essentially a pleural compartment syndrome) with severe respiratory and cardiovascular compromise and immediate thoracocentesis followed by continuous drainage is required. In the author's experience tension pneumothorax is rare.

Thoracocentesis (see below) is by no means required in all cases of traumatic closed pneumothorax and the air will be resorbed over days to weeks. The decision to perform thoracocentesis should be guided by whether the pneumothorax is thought to be compromising respiration in a clinically significant way.

Clinical improvement following thoracocentesis is generally associated with aspiration of 20-30 ml/kg or more of air although improvement may be noted with removal of smaller volumes in animals with other concurrent thoracic injuries, most commonly pulmonary contusions. In the author's experience thoracocentesis does not usually need to be performed more than twice for traumatic pneumothorax and chest drain placement is infrequently indicated. If a chest drain is needed, bear in mind that a wide bore drain is not needed for draining air and a small bore drain, for example one designed to be placed percutaneously using the Seldinger technique, can be successfully employed. The need for surgical intervention is rare.

As well as occurring as a result of trauma (blunt or penetrating), pneumothorax may also be *spontaneous* following rupture of pulmonary lesions (e.g. bullae, tumours, sub-pleural blebs) or iatrogenic (e.g. following thoracocentesis or fine needle lung aspiration). Pneumothorax that occurs spontaneously is often more severe than following trauma and chest drain placement and surgical intervention are more likely to be indicated.

Pulmonary Contusions

Pulmonary contusions represent areas of alveolar and interstitial haemorrhage and oedema and probably represent the most common thoracic injury in dogs and cats following trauma. Not all affected animals develop associated clinical signs and pulmonary contusions may occur with or without other thoracic injuries. Clinical signs may develop acutely or over several hours and lung auscultation will reveal louder lung sounds, either harshness or crackles; occasionally severe contusions resulting in consolidation of a lobe occur and then lung sounds may be quieter over the affected area as there is no air movement through the consolidated lobe. It can be difficult to hear crackles in animals with a low tidal volume, e.g. during panting or tachypnoea.

Radiographic changes may lag behind clinical signs by up to 24 hours. Radiographic abnormalities (patchy or diffuse alveolar or interstitial lung changes) may persist for a variable period of time despite clinical improvement. There is no specific treatment for pulmonary contusions and management typically involves oxygen supplementation, cage rest, analgesia as indicated for concurrent injuries, minimal stress and time.

Intravenous fluid therapy does not have to be withheld but caution is advised. Hypovolaemia is common in patients with pulmonary contusions at time of presentation and the aim of fluid therapy should be to restore acceptable tissue perfusion while avoiding excessive fluid administration. It may be acceptable in some cases to leave the patient mildly hypovolaemic rather than risk worsening pulmonary contusions; current evidence in humans seems to support the notion of keeping patients with parenchymal lung injury 'on the dry side' without leaving them hypoperfused or allowing them to become dehydrated.

In the author's experience clinical signs associated with pulmonary contusions resolve in most cases (generally within 2-7 days) but their presence may necessitate that investigation and management of other non-life-threatening injuries (e.g. long bone fractures) be postponed until respiratory status has improved adequately.

Diuretics are not recommended in the treatment of pulmonary contusions and are contraindicated in hypovolaemia. There is probably a rationale to administer one single low dose of furosemide (e.g. 0.5 mg/kg IV to a cat, 1 mg/kg IV to a dog) to these patients as furosemide is thought to have a number of different mechanisms of action that may potentially improve oxygenation beyond just the clearance of congestive oedema. However these patients should not be treated in the same way as a patient with pulmonary oedema from congestive heart failure and remember that furosemide is contraindicated in the presence of hypovolaemia or dehydration.

The incidence of bacterial pneumonia following pulmonary contusions is very low and the indiscriminate use of antibiotics in these cases is not recommended.

Haemothorax

Haemothorax is accumulation of blood in the pleural space. It is not uncommon to detect a small volume of pleural effusion following blunt thoracic trauma that is presumed to be secondary to haemorrhage. However, in the author's experience, clinically significant haemothorax is relatively rare; it would be associated with lung sounds that are dull ventrally. The pleural space can accommodate a considerable volume of blood without causing clinically significant respiratory compromise and haemothorax should not be drained unless it is thought to be significantly contributing to dyspnoea; the blood will be resorbed over several days. This is especially important as anaemia secondary to haemorrhage is relatively common following trauma, particularly in cats. Potential secondary complications of having blood in the pleural space for a few days are infection and a retained fibrohaemothorax causing lung restriction; in humans the former is considered rare and the latter even rarer – to the author's knowledge there is no veterinary data available on this.

If haemothorax is drained, it is sensible to remove as small a volume (e.g. 20 ml/kg) as possible that is expected to allow clinical improvement in respiratory status (i.e. so that the remainder may be resorbed). Surgical intervention for traumatic haemothorax is seldom required.

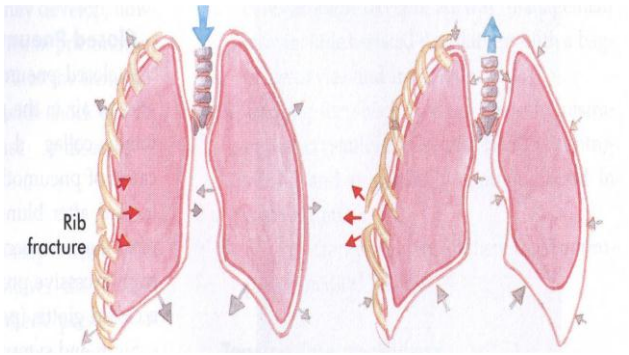
Aside from trauma, haemothorax may also occur as a result of severe coagulopathy, in particular due to anticoagulant rodenticide intoxication; other less common causes are neoplasia, pulmonary thromboembolism, lung lobe torsion and iatrogenic causes.

Rib Fractures and Flail Segment

It is very unusual for rib fractures to occur in dogs and cats without at least one other significant thoracic injury.

Rib fractures are often only diagnosed radiographically and they typically do not require specific intervention. Rib fractures are however reported to be very painful and a liberal approach to analgesia is therefore recommended in these cases. Ventilation may be compromised in painful animals especially if rib fractures are present.

A flail segment may be created if 2 or more adjacent ribs are fractured both dorsally and ventrally, i.e. so that the segment is no longer stabilised by attachment to the sternum or spine. This flail segment then moves paradoxically in relation to the rest of the chest wall during respiration, i.e. the flail segment moves in on inspiration and out on expiration.



Although large flail segments may cause hypoventilation, flail segments typically do not contribute significantly to dyspnoea and stabilisation is not usually indicated. Their significance lies more in the fact that they are typically associated with other significant thoracic injuries, especially pulmonary contusions, and that they are often very painful. These factors are more likely to be responsible for any respiratory compromise identified. Flail segments are rare in dogs and cats.

Traumatic Diaphragmatic Rupture

Although listed here as a thoracic injury, acquired diaphragmatic rupture typically occurs as a result of blunt abdominal trauma. Circumferential and right-sided diaphragmatic tears are most common in dogs and cats and the liver is reportedly the most commonly herniated organ. In addition, the stomach, small intestine and spleen are often involved in left-sided hernias and the small intestine and pancreas in right-sided hernias.

Respiratory dysfunction is a common presenting sign of traumatic diaphragmatic rupture although it may be minimal or even absent in a number of cases. The aetiology of respiratory compromise is usually multifactorial and may include:

- Loss of mechanical function of the diaphragm (most important muscle for inspiration)
- Pleural space-occupying material causing lung lobe compression and progressive atelectasis. This material predominantly constitutes abdominal organs but possibly also air (pneumothorax) and fluid (haemothorax, transudate)
- Concurrent thoracic injuries – e.g. pulmonary contusions, rib fractures
- Other factors such as pain and hypovolaemia

In some animals with diaphragmatic rupture acute respiratory decompensation may occur as a result of accumulation of a significant volume of abdominal viscera in the pleural space. In such cases, holding the animal upright to allow abdominal contents to return to the peritoneal cavity is potentially life-saving.

Diagnosis

Radiography is commonly used in animals with suspected diaphragmatic rupture and consistent findings include:

- Complete or partial loss of the diaphragmatic line
- Mediastinal shift
- Obscuring of the cardiac silhouette
- Cranial displacement of abdominal viscera and gas shadows

Orthogonal views are recommended but diagnosis may be difficult for example if displaced viscera are obscured by pleural fluid or in the absence of visceral displacement. Positive contrast gastrography or peritoneography may be required in these cases.

Timing of radiography must be carefully chosen and it is not a priority in unstable patients in which the additional stress may cause rapid decompensation.

If facilities and expertise allow, **ultrasonography** provides an alternative, reliable and less stressful means of diagnosing diaphragmatic rupture. This may be especially helpful earlier on in unstable patients or in those with significant pleural effusion obscuring radiographic detail.

Timing of surgical intervention

The timing of surgical intervention for diaphragmatic rupture has been the subject of some debate. Some authors recommend a delay of more than 24 hours following trauma to ensure adequate time for stabilisation of other concurrent conditions (e.g. hypovolaemic shock) and injuries (e.g. pulmonary contusions) thereby reducing the risks associated with general anaesthesia and major surgery. However current literature suggests that surgical intervention within 24 hours of admission in stable patients does not worsen the prognosis and therefore timing of surgical intervention should be made on an *individual case basis.*

Diaphragmatic rupture repair is more likely to be associated with a successful outcome when performed as an elective procedure with adequate staffing and time for thorough planning and preparation.

If a prolonged period of stabilisation is provided, patients must be monitored very closely for any deterioration in clinical status that may for example occur as a result of gastric entrapment and distension or strangulation of displaced intestine. More emergent surgical intervention may then be required and needle decompression of the stomach is appropriate in a severely compromised patient while being prepared for surgery.

A thoracostomy tube may be placed intraoperatively prior to closure of the diaphragmatic defect to allow residual air to be removed from the pleural cavity following repair. Bear in mind that a wide bore drain is not needed for draining air and a small bore drain, for example one designed to be placed percutaneously using the Seldinger technique, can be successfully employed. In order to avoid re-expansion pulmonary oedema (thought to be associated with cytokines and inflammation) some authors recommend only aspirating a proportion of the residual air immediately postoperatively, i.e. as much as is necessary for satisfactory ventilation to occur, with the remainder being removed over the subsequent 8 -12 hours. A thoracostomy tube will also allow monitoring for complications such as pneumothorax or haemothorax as well as repeated administration of local anaesthesia.

If a thoracostomy tube is not placed, it is important to remove residual air from the pleural cavity by other means to prevent respiratory compromise. This is ideally done through the diaphragm before the final suture is tightened but may be achieved via thoracocentesis during recovery.

Thoracocentesis

Background

'Thoracocentesis' refers to ***aspiration of air or fluid from the pleural cavity.***

The pleural cavity represents the space between the visceral pleura (covers the surface of the lungs) and the parietal pleura (lines the inside of the thorax).

In healthy animals, the pleural cavity contains only a tiny volume (few millilitres) of lubricating fluid. However a variety of disorders may result in accumulation of sometimes vast quantities of air or fluid in the pleural cavity resulting in lung compression and dyspnoea.

- In normal dogs and some normal cats, lung sounds can usually be heard diffusely on both sides of the chest (and they are typically a little louder cranioventrally); in some normal cats at rest lung sounds may be barely audible anywhere.
- Pneumothorax (accumulation of air in the pleural cavity) results in dull lung sounds dorsally
    - Pneumothorax may be uni- or bilateral
- Pleural effusion (accumulation of fluid in the pleural cavity) results in dull lung (and heart) sounds ventrally
    - Pleural effusion is generally bilateral

Indications

- **Diagnostic:**
    - To confirm the presence of fluid or air in the pleural cavity
    - To obtain fluid samples for cytological, chemical and/or microbiological analysis
- **Therapeutic** – to relieve dyspnoea due to compression of the lungs by space-occupying material in the pleural cavity

Note: thoracocentesis is frequently performed in order to achieve both these goals simultaneously.

Note: in animals with severe dyspnoea it is often appropriate to perform thoracocentesis on the basis of clinical suspicion alone without confirmation of pleural air or fluid by radiography. Animals with severe dyspnoea are often highly vulnerable to the stress of radiography and *blind thoracocentesis may be less stressful and life-saving in such cases.*
Ultrasonography may provide a minimally stressful imaging modality for animals with dyspnoea secondary to pleural fluid and/or air. Although the detection of pleural air is more challenging, identifying pleural effusion by ultrasonography is relatively straightforward even in novice hands.

Equipment list

- Clippers
- Surgical scrub materials
- Sterile gloves
- Needle:
    - Butterfly needle: typically 21-23 gauge for cats and small dogs; or
    - Over-the needle intravenous catheter and extension tubing: 14-20 gauge depending on patient size
    - Appropriate needle or catheter size depends on patient size and nature of material to be aspirated
- Sterile 3-way tap or 'centesis valve'
- Syringe: typically 20 ml for cats and small dogs, 60 ml for larger dogs
- Sample pots: sterile EDTA, serum and additive-free containers
- Kidney dish, jug or similar
- Three people (ideally)

Procedure

1. Allow the patient to stand or to sit in sternal recumbency as preferred, and restrain gently; minimal restraint often works best
    - Lateral recumbency may be acceptable for pneumothorax
2. Provide flow-by/mask oxygen supplementation (if tolerated)
3. Clip a patch of fur in the 7^{th}-9^{th} intercostal space on both sides of the chest and scrub the area on one side
    - The choice of which side to start with should be guided by auscultation, ultrasonography (or a dorsoventral radiograph if one has been taken)
    - If pneumothorax is suspected, use an area in the dorsal third of the thorax
    - If pleural fluid is suspected, use an area in the ventral third of the thorax
    - If pleural air or fluid has not yet been confirmed, use an area half-way up the thorax
4. Wearing sterile gloves attach the butterfly needle to the 3-way tap or centesis valve and attach the 3-way tap/centesis valve to the syringe. Note that the 3-way tap/centesis valve is therefore located away from the patient. In larger animals an intravenous catheter is attached to extension tubing that is then attached to the 3-way tap/centesis valve.
5. Insert the needle gently but swiftly into the pleural cavity at a right angle to the chest wall and with the bevel facing dorsally; apply gentle suction to the syringe as the needle is inserted:
    - The needle should be inserted just in front of (cranial to) the rib to avoid hitting the intercostal nerves and vessels that lie behind/caudal to each rib
    - Once in the pleural cavity the needle can be angled caudally or ventrally to lie flat against the thoracic wall thereby keeping the needle away from the lung surface
6. Continue to aspirate until negative pressure is reached or it feels like the lung is being scratched by the needle.
    - With (pocketed) pleural fluid in particular, it is often necessary to reposition the needle (and sometimes the patient) to remove as much as possible
7. Record the total volume of air or fluid removed from the pleural cavity; aseptically transfer samples of pleural fluid into the sample pots
8. Aspiration may need to be repeated on the other side of the thorax. This will depend on:
    - Whether the patient has improved adequately after aspiration on the first side
    - Individual patient considerations, e.g.
        Is residual fluid or air likely to be reabsorbed?
        Is additional fluid or air likely to form?
        Are there other thoracic abnormalities (e.g. pulmonary contusions) that would make the patient less able to cope with residual fluid or air?
        How well did the patient tolerate the procedure on the first side?

Complications

Clinically significant complications associated with thoracocentesis are rare; it is typically a simple and safe procedure that is potentially life-saving. Reported complications include pneumothorax and haemorrhage from laceration of the intercostal vessels.

Notes

Excessive manual restraint is contraindicated in all dyspnoeic animals including those in which thoracocentesis is being performed; this is especially the case for cats

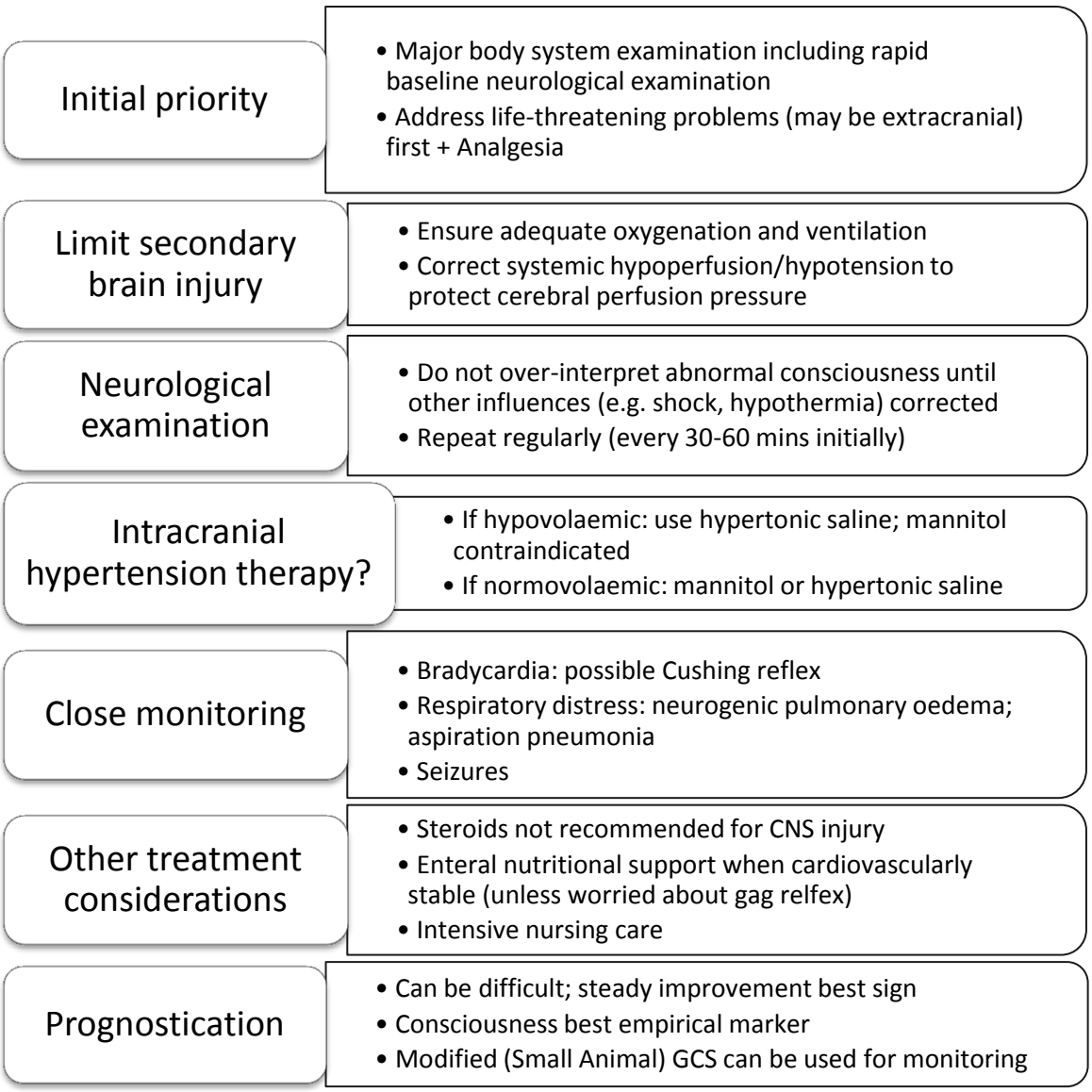
Many animals with severe dyspnoea due to pleural space disease will allow thoracocentesis to be performed with minimal manual restraint and without any chemical restraint. It is important to allow the patient to direct the procedure to some extent – work with the patient rather than try and force him/her into submission!

A low dose of a pure opioid (e.g. 0.1 mg/kg methadone) may be administered prior to the procedure both as an anxiolytic and to provide some analgesia. However this delay is not appropriate in patients with very severe dyspnoea or considered to be in imminent danger of death.

Conservative sedation (e.g. 0.3 mg/kg butorphanol ± 0.01 mg/kg acepromazine) may be required to allow thoracocentesis to be performed in one smooth and successful procedure and judicious chemical restraint is safer than excessive manual restraint in all cases. Drugs with potentially significant respiratory or cardiovascular depressive effects at clinical doses must be avoided.

It is generally necessary to remove approximately 10-20 ml/kg or more of air or fluid from the pleural cavity to make a significant difference to an animal's breathing. In animals with multiple causes of respiratory compromise (e.g. concurrent traumatic pneumothorax and pulmonary contusions), it should be noted that removal of smaller volumes of air or fluid may result in clinical improvement as even some increased expansion may be of benefit to already compromised lungs.

Traumatic Brain Injury (Closed head injury)



Central nervous system

Mentation

Normal mentation (awareness, consciousness) is alert with normal response to environmental stimuli. Types of abnormal mentation are:

Depressed/obtunded:	Decreased functional activity; mentally dulled; drowsy; less responsive to environmental stimuli

Stuporous:	Unresponsive to normal environmental stimuli but responsive to painful stimuli
Comatose:	Unresponsive to environmental or painful stimuli
Hyperaesthetic:	Increased sensitivity to a normal level of stimulation
Confused/disorientated (delirious):	Responding to environmental stimuli in an inappropriate manner

Abnormal mentation may be due to one or both of:

- Primary CNS disorder: concurrent cranial ± peripheral nerve abnormalities more likely
- Primary abnormalities in other systems, e.g. hypoperfusion, hypothermia, hypoglycaemia: concurrent cranial ± peripheral nerve abnormalities less likely

When assessing mentation, consider whether the patient's consciousness may be affected by any other concurrent abnormalities. Abnormal mentation that is not explained by abnormalities in other systems gives a high index of suspicion for a primary central nervous system disorder.

> Remember it may not be possible to reliably interpret mentation until other concurrent abnormalities that can affect consciousness have been adequately addressed (e.g. fluid therapy for hypovolaemia, warming for hypothermia).

Gait

Gait abnormalities are most often related to central or peripheral neurological disorders.
Multiple limb involvement usually means more serious disease.
Recumbency may be due to a primary CNS disorder but also e.g. cardiovascular compromise; respiratory embarrassment; severe pain. Most animals with primary central neurological recumbency do not have cardiovascular instability.

NOTE: in a recumbent patient in which there is sufficient concern it is essential to assess the integrity of the spinal cord by checking for deep pain sensation in the limbs +/- tail as indicated – and to recheck if you do not feel that the patient is in a condition to respond consciously when you first test this!

Rational approach

As always, the priority in the management of traumatic brain injury (TBI) is to address potentially life-threatening problems first and it must be remembered that these may not be intracranial, i.e. some animals with TBI will have more pressing extracranial injuries. In reality however, all these abnormalities will be addressed to some degree by any interventions provided as they do not exist in isolation.

The underlying injuries that result from head trauma can be separated into two categories: primary injury and secondary injury. Primary injury (e.g. concussion, contusion – parenchymal haemorrhage and oedema, laceration; extra-axial haemorrhage may not be as rare as previously thought) occurs as an immediate result of the traumatic event and nothing can therefore be done about this.

The prime aim in the management of traumatic brain injury (TBI) is to limit secondary brain injury that may occur as a result of various mechanisms including:

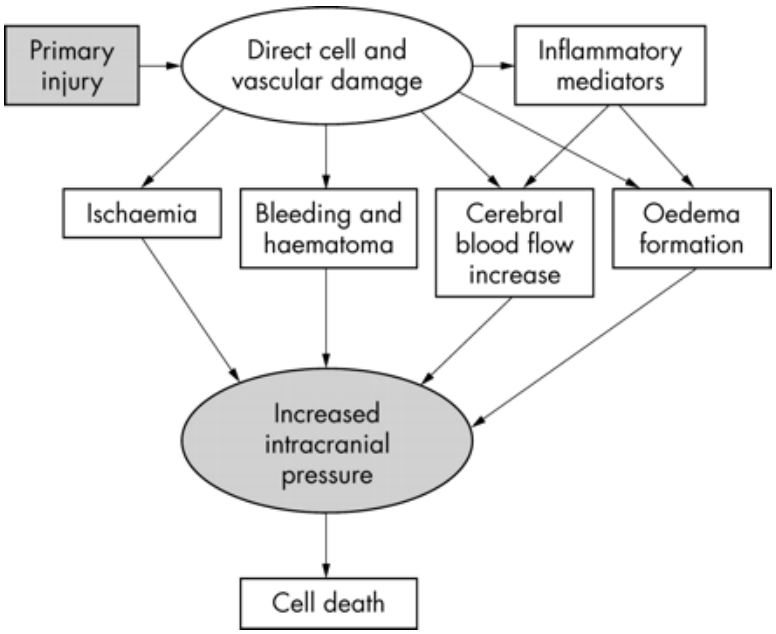
- Hypoxia
- Ischaemia due to hypoperfusion
- Raised intracranial pressure (ICP)
- Active haemorrhage
- Compromise to blood brain barrier

Secondary injury is largely mediated through:

- Increased activity of excitatory neurotransmitters
- Generation of reactive oxygen species (ROS)
- Production of pro-inflammatory cytokines
- All can contribute to neuronal cell damage and possibly cell death

Oxidative damage:

- ROS preferentially damaging to cell membranes containing high levels of polyunsaturated fats and cholesterol
- Brain tissue lipid-rich so particularly sensitive
- Thought to play a major role



Earlier discussions of TBI tended to focus on the detrimental effects of raised ICP via impairment of cerebral blood flow and the potential for brainstem compression and herniation. However secondary brain injury is significantly perpetuated by hypoxia and systemic hypoperfusion; it is also affected by hypo/hypercapnia, hyperthermia, and hypo/hyperglycaemia. **The priority is therefore to ensure that the brain receives an adequate supply of well-oxygenated (but not excessively oxygenated!) arterial blood in a patient with adequate ventilation.** Treatment for possible raised ICP is just one part of this therapy.

Ensuring adequate oxygenation and ventilation

Cerebral hypoxia must be avoided as much as possible and this is partly dependent on there being sufficient oxygen in the systemic arterial circulation. Ideally this is monitored using arterial blood gas analysis to measure arterial partial pressure of oxygen (P_aO_2). In humans, based on some clinical data and some animal experimental data, there is a suggestion that the aim of oxygen supplementation should be to find a balance between too little and too much. Too little, i.e. hypoxia, is clearly likely to be harmful but there is also increasing evidence that, as has been suggested/shown for other organs such as the lungs, too much oxygen, i.e. hyperoxia, may also be harmful by promoting oxidative injury. As described above, oxidative injury is one of the main mechanisms of secondary injury in TBI.

A suggested 'sweet spot' is a P_aO_2 of 200-300 mmHg remembering that a normal patient on room air (F_iO_2 0.21) has a P_aO_2 of approximately 100 mmHg and a normal patient on 100% oxygen (F_iO_2 1.0) has a P_aO_2 of approximately 500 mmHg. As a guideline, non-invasive means of oxygen supplementation may achieve 30-60% (i.e. F_iO_2 0.3-0.6) which in a normal animal should equate to P_aO_2 of 150-300 mmHg. In other words a patient receiving non-invasive oxygen supplementation will hopefully be close to the 'sweet spot' unless there are problems with their oxygenation. However if a patient is intubated and receiving invasive oxygen supplementation, a level of 100% is not likely to be appropriate having the potential to be harmful and should be titrated down quickly to achieve the 'sweet spot'.

Arterial blood gas analysis is unavailable in many clinics and pulse oximetry must therefore be used. Remember that this measures the saturation of haemoglobin with oxygen (S_pO_2) and once a patient reaches 100% saturation, it is not possible to know how much additional oxygen is being taken on board (dissolving in the plasma, contributing to oxygen partial pressure). A patient with an S_pO_2 of 100% may have a P_aO_2 of for example 120 mmHg or 600 mmHg! In other words for our TBI patient, once we have achieved an S_pO_2 of (close to) 100%, it will be difficult to tell whether we are 'overdoing it' in terms of supplementation in the absence of arterial blood gas analysis. One suggested approach is to provide whatever level of oxygen supplementation that is needed to achieve an S_pO_2 of (close to) 100% and then increase the level of supplementation slightly but no more than that. This is somewhat empirical lacking evidence base in humans and even more so in veterinary patients but it is intended to try and find that balance between too little and too much oxygen supplementation.

If pulse oximetry is not available then essentially the take home message is that all patients with significant TBI should receive empirical oxygen supplementation for a timeframe that is decided based on the individual patient.

As well as considering the patient's oxygenation status, their carbon dioxide status is something else that ideally should be considered and is predominantly dependent on ventilation. In the past hyperventilation was recommended as a treatment for raised intracranial pressure because it lowers arterial CO_2 levels which causes cerebral vasoconstriction; it can therefore potentially reduce intracranial pressure. However it is now believed that this cerebral vasoconstriction is harmful, considerably more so than the raised ICP it was attempting to address, because it reduces cerebral perfusion. Hyperventilation may worsen morbidity and mortality and it is therefore no longer recommended. Hypercarbia is also to be avoided and the recommended target is a P_aCO_2 or end-tidal CO_2 within the normal range (approximately 35-45 mmHg). This will require either access to arterial blood gas analysis or a capnograph/capnometry. Moreover unless the patient is intubated our ability to influence ventilation is relatively limited. Nevertheless any processes that may interfere with adequate ventilation (e.g. pneumothorax; pain) must be addressed appropriately.

Ensuring adequate cerebral perfusion

Cerebral blood flow, and hence oxygen and nutrient delivery to the brain and carbon dioxide removal from the brain, is driven by the pressure gradient between mean arterial pressure (MAP) and intracranial pressure (ICP):

CPP = MAP – ICP
(CPP = cerebral perfusion pressure)

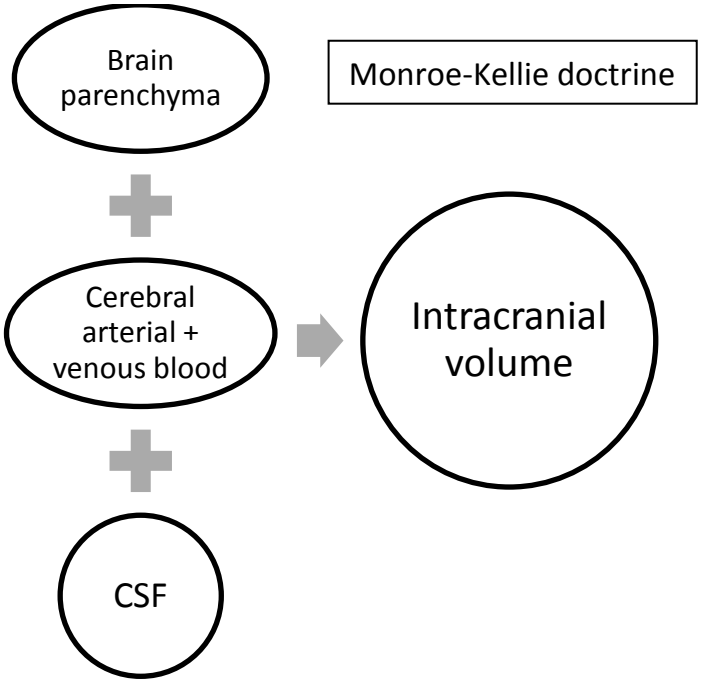
Normal homeostatic mechanisms protecting cerebral blood flow may be lost in TBI and cerebral blood flow (CBF) becomes largely dependent on systemic blood pressure. The normal brain is capable of maintaining a constant CBF over a systemic MAP range of 50–150mmHg. TBI may compromise this cerebral pressure autoregulation and CBF becomes even more dependent on CPP. Even small decreases in CPP can lead to changes in CBF and result in ischemic injury to the brain parenchyma. **Maintenance of an adequate CPP is a cornerstone of modern brain injury therapy.**

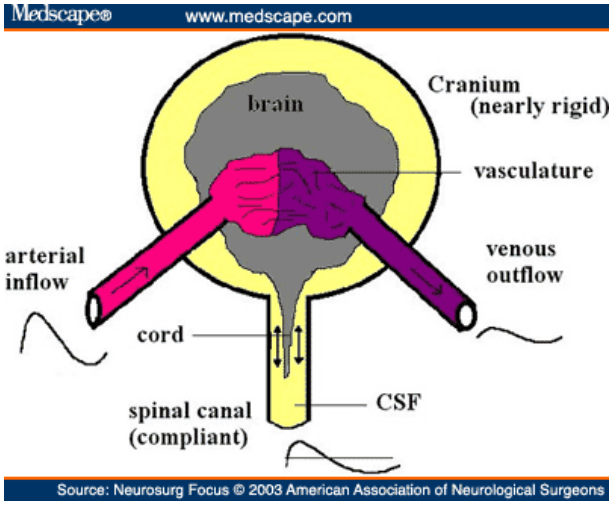
Mean arterial pressure (MAP):

The head trauma patient may well present with systemic hypotension (i.e. decreased MAP) especially if there has been multisystem trauma with significant blood loss. Traumatic brain injury may also result in a systemic inflammatory state with subsequent systemic vasodilation that may cause or contribute to hypotension. Mean arterial pressure can be measured non-invasively using an oscillometric device and a reasonable target MAP is 80 mmHg. If only Doppler sphygmomanometry is available, then a systolic blood pressure of 100 mmHg is considered equivalent.

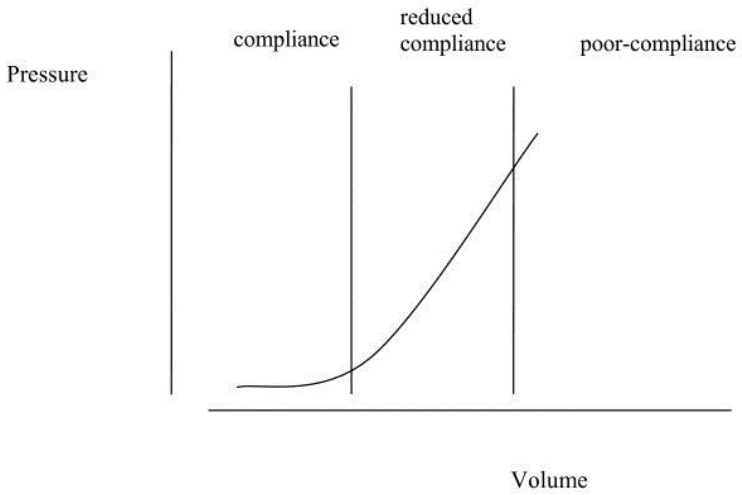
Regardless of whether blood pressure monitoring is or is not available, it is essential to ensure that hypoperfusion identified on the basis of physical examination is corrected. Blood pressure monitoring is not a substitute for regular assessment of physical perfusion parameters.

Raised intracranial pressure:

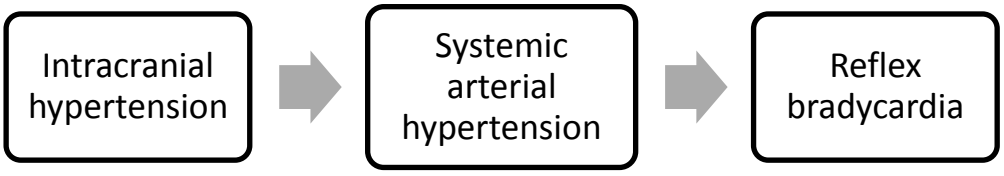




The Monroe-Kellie doctrine states that intracranial volume is equal to the volume of the brain parenchyma plus the volume of the cerebral arterial and venous blood plus the volume of the cerebrospinal fluid (CSF). Intracranial pressure is the pressure exerted between the incompressible rigid skull and these 3 intracranial compartments. There is normally a balanced dynamic equilibrium such that if the volume of one component increases, the volume of one or more of the other components must decrease (Monroe-Kellie hypothesis) or ICP increases – this is known as *intracranial compliance* and it occurs by fluid shifts in the brain vasculature and CSF pathways. However intracranial compliance has limitations and its efficacy decreases as ICP increases. If ICP increases beyond the limits of compensation, cerebral perfusion is compromised and ischaemia occurs; eventually global brain ischaemia and subsequent brain death results. This is a possibility in closed head injury where the skull is intact.



Direct measurement of ICP is not practical in general in veterinary medicine at this time and is restricted to research and perhaps a few referral centres. Measurement of optic nerve sheath diameter using ultrasonography is being explored in human medicine; the retrobulbar optic nerve sheath is continuous with the subarachnoid space so its diameter may reflect intracranial pressure. To the author's knowledge this is not something that has yet been reported in veterinary patients. Therefore *the presence of elevated ICP is inferred*. The cerebral ischaemic response (Cushing reflex) is the most specific marker available – intracranial hypertension causes systemic hypertension and a consequent reflex bradycardia.



These findings should prompt aggressive treatment for raised intracranial pressure as the Cushing reflex occurs late and signals possible/probable life-threatening intracranial hypertension. Other less specific findings that may suggest intracranial hypertension include otherwise unexplained deterioration of mental status, dilated non-responsive pupils, loss of physiological nystagmus and decerebrate posturing.

Neurological examination

Hypoperfusion can have a significant effect on neurological status as can hypothermia and hypoxaemia. These abnormalities must therefore be addressed before drawing conclusions about the patient's level of consciousness.

Following initial stabilisation perform a more in-depth neurological assessment
Repeat regularly (e.g. every 30-60 mins initially) to detect either deterioration or efficacy of any therapy instituted

Mentation[1] (Consciousness)	Normal Depressed/obtunded Stuporous Comatose Hyperaesthetic Confused/disorientated	Abnormalities typically relate to: ➢ Diffuse lesion or widespread multifocal lesions of both cerebral hemispheres ➢ Or, focal lesion affecting (ascending reticular activating system (ARAS) of) brainstem Coma typically indicates: ➢ Severe bilateral or global cerebral injury ➢ Or, severe brainstem damage ➢ Guarded prognosis
Pupils	Symmetry, size, PLRs (direct + consensual) ➢ Normal size pupil with slow PLR (least severe) ➢ Miotic pupil with intact PLR ➢ Pinpoint pupil with no PLR ➢ Mydriatic pupil with no PLR (most severe)	Normal PLRs = adequate function of rostral brainstem, optic chiasm, optic nerves, retinae Miotic pupils = diffuse forebrain injury Progression to mydriasis may indicate brain herniation ➢ Herniation places pressure on oculomotor n. (III) which interrupts parasympathetic input resulting in dilated pupils Herniation may also compress brainstem Fixed, unresponsive and midrange pupils seen with cerebellar herniation Brain herniation associated with severe disability and death if not treated rapidly and aggressively
Other cranial nerves	Especially:	Menace responses Blink and gag reflexes Jaw tone
Oculocephalic reflex	Moving head side-to-side or up/down should elicit physiological nystagmus[2]	Abnormality following TBI typically due to brainstem lesion

Respiratory pattern	TBI may cause irregular respiratory patterns	Hyperventilation Cheyne-Stokes respiration: progressively deeper and sometimes faster breathing followed by gradual decrease that results in apnoea Ataxic respiration (irregular rate, rhythm and excursion) Apnoea
Motor function[3]	Hemiparesis/plegia: Tetraparesis/plegia:	Unilateral brainstem damage (also some spinal cord lesions) More diffuse brainstem damage (also cervical spinal cord lesion)
Posture[4]	Decerebrate rigidity: Decerebellate rigidity:	Extreme extensor rigidity of all 4 limbs with no periods of relaxation; lateral recumbency and possible opisthotonos; marked changes in mentation (usually stuporous or comatose); very grave prognosis. Extensor rigidity of thoracic limbs with flexion of pelvic limbs due to sublumbar muscle contraction flexing hips; or extensor rigidity of all 4 limbs if ventral cerebellum affected. May occur episodically. Mentation usually normal. Better prognosis than decerebrate rigidity.

[1] Mentation:

- Depressed/obtunded = Decreased functional activity; mentally dulled
- Stuporous = Unresponsive to normal environmental stimuli but responsive to painful stimuli
- Comatose = Unresponsive to environmental or painful stimuli
- Hyperaesthesia = Increased sensitivity to normal level of stimulation
- Confused/disorientated (delirious) = Responding to environmental stimuli in an inappropriate manner

[2] In a normal animal as the head is moved, the pupils will initially remain looking in the original direction (i.e. forwards) but will then 'catch up' with the rest of the head. At the end of each movement, the head should be stabilised and cessation of nystagmus noted.)

[3] Animals that are not comatose should maintain voluntary motor activity unless trauma has occurred to the brainstem, the spinal cord, or a peripheral nerve.)

[4] Schiff-Sherrington posture:

- Must be distinguished from decerebrate and decerebellate rigidity
- May occur as a result of an acute severe lesion of the spinal cord between T2 and L3
- Pelvic limb flaccid paralysis accompanied by extensor rigidity or at least increased tone of thoracic limbs when the animal is in lateral recumbency
    - Thoracic limbs otherwise neurologically normal
- Spinal cord lesion interrupts ascending inhibitory impulses originating in lumbar grey matter and terminating on cells responsible for extension of thoracic limbs

Schiff-Sherrington posture does not indicate that the spinal cord injury is irreversible.

Findings consistent with brainstem injury:

- Mentation: comatose
- Bilateral fixed (mid-position) dilated unresponsive pupils
- Absence of gag reflex

- Irregular respiratory patterns or apnoea
- Abnormal oculocephalic reflex

Diagnostic imaging

Diagnostic imaging of the head is not routinely indicated but would be indicated in a patient that:

- Fails to respond to aggressive extracranial and intracranial stabilisation
- Deteriorates acutely after initially responding to therapy
- Shows progressive neurological signs

Although plain skull radiographs may reveal fractures, it can be difficult to obtain radiographs of interpretable quality and plain radiographs do not provide clinically useful information with respect to brain injury. Referral to a specialist centre for advanced imaging (computed tomography (CT) or magnetic resonance imaging (MRI)) should therefore be considered if affordable and once the patient has been stabilised.

CT is the standard of care in human TBI, being widely available and less expensive than MRI. CT offers rapid scan times that are faster than MRI as well as better visualisation of fractures and per-acute haemorrhage. Abnormalities associated with increased ICP include:

- Subdural or intracerebral haematomas
- Subarachnoid haemorrhage
- Cerebral infarcts
- Diffuse brain injury
- Generalised cerebral oedema often with shift of midline structures and ventricular compression

However it is possible that MRI may provide key prognostic information by detecting subtle parenchymal damage not evident on CT.

Modified Glasgow Coma Scale (The Small Animal Coma Scale)

The MGCS is a quantitative way of grading and monitoring brain injury by scoring three categories from 1-6; the categories are motor activity; brainstem reflexes; and, level of consciousness. We'll come back to the MGCS when we discuss prognostication.

Treatment

As mentioned, the priority in the management of TBI is to **ensure the brain receives an adequate supply of well-oxygenated blood**. This involves:

Oxygen supplementation

See notes above. If adequate oxygenation cannot be achieved non-invasively the patient should be anaesthetised, intubated and ventilated; however there are practical and financial considerations to providing this management.

Optimising cerebral perfusion

Intravenous fluid therapy:

Early fluid resuscitation is essential to correct systemic hypoperfusion and ensure adequate cerebral blood flow. A replacement isotonic crystalloid is the typical first choice but a synthetic colloid may be needed if there is an inadequate response. Although commonly referred to as isotonic, Hartmann's (buffered lactated Ringer's solution, compound sodium lactate) is in fact mildly hypotonic with a slightly

lower sodium concentration than that of the extracellular fluid. In theory the tendency towards plasma hypoosmolarity that may follow its administration may have consequences in terms of promoting some cerebral oedema (as water moves down a concentration gradient from the capillaries into the brain parenchyma). Whether or not this occurs in any clinically significant way remains to be investigated but it may be more rational to use normal saline (0.9% sodium chloride), which is isotonic, rather than Hartmann's in resuscitating TBI patients. Hypertonic saline is an appropriate choice in some cases (see below). It is preferable to avoid hypervolaemia as this may increase intracranial pressure, especially when there is a damaged blood-brain barrier, but it is crucial to only be conservative once hypovolaemia has been corrected.

Intracranial hypertension therapy (see below)

Minimise increases in cerebral metabolic rate:

Steps must be taken to minimise increases in cerebral metabolic rate that may worsen TBI further. Anti-seizure therapy should be used immediately if indicated and any patient that is distressed (flailing, constant vocalisation) sedated; this sedation can be achieved using opioids but also with anticonvulsant medications even if the patient is not seizuring as anticonvulsant agents often have sedative properties.
Treat hyperthermia that may occur secondary to direct trauma to the thermoregulatory centre in the hypothalamus and/or seizure activity (also due to pain or excitement). Hyperthermia is undesirable as it increases cellular metabolism and vasodilation leading to increased ICP.

Intracranial hypertension therapy

Treatment for raised ICP includes measures to promote venous drainage from the brain, e.g. keep the head elevated 15-30° above horizontal; minimise jugular compression (e.g. avoid jugular venepuncture, do not restrain around neck area). However the most effective therapy involves medical therapy for cerebral oedema.

"The mainstay of intracranial-pressure reduction is…the rudimentary approach of shrinking the brain by exposing it to the dehydrating effects of serum hyperosmolarity."

The brain parenchyma contains a large proportion of water (more so than for other organs) making brain volume very responsive to changes in water content. The intact blood-brain barrier is highly impermeable to both sodium and mannitol; these substances therefore induce an osmotic gradient between blood and brain tissue. The beneficial effect of hyperosmolar therapy requires that the blood–brain barrier be intact. In regions of brain-tissue damage, as in traumatic contusion, the barrier is disrupted and allows equilibration of molecules between blood and the interstitial fluid of the brain. Thus, hyperosmolar agents exert their effect largely by removing water from the remaining normal brain tissue. It follows that hyperosmolarity reduces intracranial pressure in proportion to the volume of undamaged brain tissue.

When should medical therapy be implemented?

It is not always entirely clear when this point is reached however the Cushing reflex would definitely be considered an indication. Medical therapy is also considered rational in a patient with progressive neurological signs secondary to TBI and there may be an argument for its use in any patient with moderate-to-severe head injury that is refractory to aggressive extracranial stabilisation.

Hypertonic saline or mannitol?

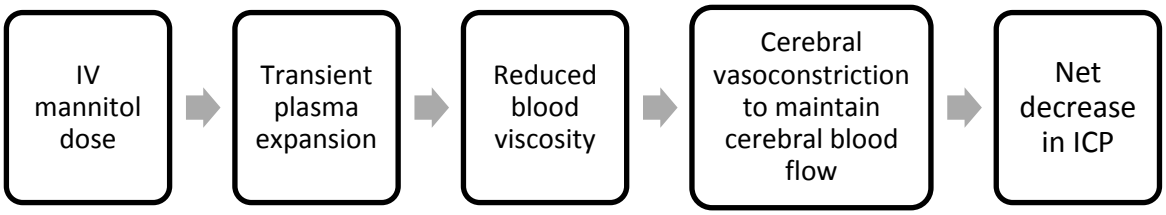
At the present time, the evidence base that exists does not support one of these fluids being more effective than the other for the reduction of intracranial hypertension. In a normovolaemic patient, either can be chosen.

Mannitol (dehydrating osmotic agent) is contraindicated in hypovolaemic patients; hypertonic saline

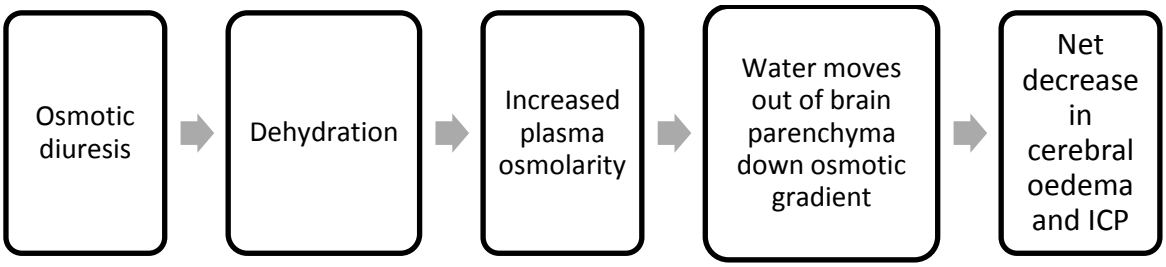
(volume-expanding solution) on the other hand is a rational choice in hypovolaemia as it may serve to both restore intravascular volume (albeit transiently) and reduce intracranial pressure at the same time.

Mannitol:

Mannitol is the most longstanding medical therapy for cerebral oedema. It is a white crystalline organic compound that is dissolved to form a hyperosmolar sugar alcohol solution. There is some debate about how mannitol achieves a reduction in intracranial pressure. One main effect may be via a rheological mechanism as follows: intravenous administration of mannitol causes transient plasma expansion which reduces blood viscosity; this leads to cerebral vasoconstriction to maintain cerebral blood flow and the net result is a decrease in ICP. This effect occurs immediately and may persist for up to 75 minutes.



Because mannitol solution is hyperosmolar, it is also likely to cause an osmotic diuresis; the resulting dehydration increases plasma osmolarity that then reduces cerebral oedema as water moves out of the brain down a concentration gradient. The onset of this osmotic effect is likely to be after 15-30 minutes and it may peak after 1 hour and persist for 6-8 hours.



Mannitol may also have an effect as a reactive oxygen species scavenger which may limit secondary oxidative injury.

Mannitol is given at 0.5-1.5 g/kg IV over 10-20 min and can be repeated every 2-8 hours (max 3 doses in 24 hours) but discontinue therapy if there is no positive response to a single dose.

Contraindications for mannitol use include hypovolaemia/dehydration, congestive heart failure, pulmonary oedema and anuric renal failure. High doses of mannitol can cause acute renal failure by as yet unknown mechanisms. Older resources quote active intracranial haemorrhage as a contraindication; however there is no evidence base for this as such and there is no way of knowing whether our patients are experiencing active haemorrhage so this author's recommendation is to disregard this as a concern. Given the osmotic diuretic effect, mannitol administration should be followed with an isotonic crystalloid to prevent dehydration or hypovolaemia. The solution can crystallise when stored at room temperature so make sure to dissolve all crystals before use and the use of an in-line filter (i.e. same as is used for blood transfusion) is also recommended.

Hypertonic saline:

Hypertonic saline (e.g. 7.2-7.5% sodium chloride (~ 2400 mOsm/l; normal plasma osmolality ~ 290 mOsm/l) is osmotically active. The infused sodium raises the plasma osmolarity creating a concentration gradient for water to leave the brain tissue thereby reducing brain water and ICP. It also dehydrates endothelial cells thereby increasing blood vessel diameter, improving CBF and reducing ICP. Hypertonic saline may also modulate any inflammatory response. It is especially indicated in hypovolaemic TBI patients as it will both restore intravascular volume and reduce cerebral oedema.

Recommended doses (over 5 mins): Dogs: 4-7 ml/kg IV; cats: 2-4 ml/kg IV

Other treatment considerations

Analgesia:

Once a rapid baseline neurological examination has been performed, analgesia should be administered. A pure opioid is the agent of choice as these agents are rapidly acting; methadone is preferable to morphine as the latter may induce emesis which could worsen raised ICP. If available, fentanyl can be an excellent choice in these patients. Remember that NSAIDs are contraindicated in hypovolaemic patients which many trauma patients are likely to be. Analgesia may also contribute to sedation which can be helpful as mentioned previously.

For quite some time it had been said that ketamine is contraindicated in the presence of raised ICP as it may worsen this. However there is increasing evidence to suggest that by increasing systemic arterial pressure via vasoconstriction ketamine may increase cerebral perfusion pressure; this effect of ketamine may in fact be more beneficial for the brain than any adverse effect it may have by directly increasing ICP. Regardless, a current perspective is that in the presence of raised ICP ketamine is no better but also no worse than any other agent that may be being considered in its place; moreover it lacks hypotension as an adverse effect which may make it an attractive choice over other sedatives.
Steroids:

The use of methylprednisolone succinate for central nervous system injury was a longstanding practice in both human and veterinary medicine. However it was not one based on clinical evidence. More recent clinical trials in humans have not shown positive effects on outcome and some have suggested possible increases in morbidity and/or mortality. Considering the potential adverse effects (e.g. gastrointestinal ulceration, increased risk of infection/immunosuppression, hyperglycaemia, increased catabolism) of these agents, current recommendations are that methylprednisolone should not be used for traumatic brain injury. “Given the lack of evidence for any beneficial effect of corticosteroids after TBI, and strong evidence in the human literature showing a detrimental effect on neurological outcome, corticosteroids should not be administered in TBI”. [In patients with brain tumours, glucocorticoids may lower intracranial pressure by reducing vasogenic oedema surrounding the brain tumor; oedema results from the flow of fluid into the extracellular space of the brain parenchyma through an incompetent blood–brain barrier (BBB).]

The author will occasionally use corticosteroids at an anti-inflammatory dose (e.g. dexamethasone 0.1 mg/kg) for animals with significant soft tissue swelling due to head trauma but this is a different indication and dosing regimen to the previous use of steroids for CNS injury.

Nutritional support:

TBI may result in a hypermetabolic and catabolic state. Nutritional support is very important once the patient is stable and improving but should not be started in animals that remain cardiovascularly unstable (feeding may worsen cardiovascular status further) or severely neurologically compromised (due to risks of aspiration if gag reflex is still absent). Ideally avoid syringe feeding as this provides inadequate calorific

intake, poses the potential risk of aspiration and is unlikely to be patient friendly in the presence of head injuries. A naso-oesophageal or naso-gastric tube is an option although may not be ideal with facial injuries; some animals do not tolerate these tubes well and may also sneeze which could worsen raised ICP. An oesophagostomy tube is preferred once the patient is stable for anaesthesia. Parenteral nutrition may be employed in the interim if available.

Decompressive surgical therapy

There is still no consensus in people as to if and when surgery should be pursued and the effect of surgical intervention on clinical outcome remains unclear. With the increasing availability of advanced imaging surgical therapy may come to play a greater role in veterinary medicine. Possible indications include:

- Open or depressed skull fractures
- On-going haemorrhage
- Foreign body or haematoma removal
- Declining neurologic status despite aggressive medical therapy

Comment on hyperglycaemia following TBI

Hyperglycaemia is seen relatively commonly following TBI and is thought to be due to a response that includes the sympathetic nervous system and the adrenal medulla (i.e. catecholamines!). It is associated with increased mortality or worsened neurological outcomes in humans and experimental animals but does it actually worsen injury, is it just a marker of injury severity, or both? Hyperglycaemia following TBI in dogs and cats does appear to at the very least be a marker of the severity of injury but at this time there is no evidence to suggest that it has a detrimental effect on outcome. Therefore specific therapy is not indicated but it is important to avoid iatrogenic hyperglycaemia – e.g. don't use corticosteroids!

Monitoring

Animals with traumatic brain injury must be monitored very closely including regular reassessment of neurological status, possibly with repeat MGCS assessments. In particular look out for the following three developments.

Bradycardia: the onset of previously undetected bradycardia may signal an increase in ICP and should prompt immediate treatment.

Respiratory distress: brain injury can give rise to **neurogenic (non-cardiogenic) pulmonary oedema** that usually develops within minutes to a few hours of the event. Thoracic radiographs typically show a caudodorsal distribution of lung field changes consistent with pulmonary oedema (interstitial to alveolar pattern). The mainstay of treatment is oxygen supplementation, strict rest, minimal stress, usual supportive measures for dyspnoeic patients, and time – and addressing the primary cause if that is appropriate/on-going. Clinical improvement is typically noted within 24 - 48 hours. The mechanisms behind neurogenic pulmonary oedema are still to be fully unravelled. We know what types of events cause it (e.g. traumatic brain injury, neck injury, seizures, upper respiratory obstruction), and some of the likely mechanisms have been identified. These mechanisms result in oedema that is probably due to a combination of increased capillary permeability, and hydrostatic pressure changes (as with cardiogenic oedema). There is probably a rationale to administer one single low dose of furosemide (e.g. 0.5 mg/kg IV to a cat, 1 mg/kg IV to a dog) to these patients as furosemide is thought to have a number of different mechanisms of action that may potentially improve oxygenation beyond just the clearance of congestive oedema. However these patients should not be treated in the same way as a patient with pulmonary oedema from congestive heart failure and remember that furosemide is contraindicated in the presence of hypovolaemia or dehydration.

Aspiration pneumonia is another possible cause of respiratory distress in a neurologically compromised patient following TBI.

Seizure activity: seizure activity will increase cerebral metabolic rate, increasing cerebral oxygen demand and therefore the risk of hypoxic injury. It may also worsen cerebral oedema thereby exacerbating raised intracranial pressure (ICP) and can cause hyperthermia. Anti-seizure medication must therefore be administered at the first sign of seizure activity. Seizures are rare following head trauma in dogs and cats, both acutely and also in the long-term; although the role of prophylactic anticonvulsant therapy remains unclear, it is generally not recommended to be used in either the short- or long-term.

Nursing care

Patients with traumatic brain injury may be recumbent for prolonged periods and the value of adequate nursing in such cases should not be underestimated.

The most important measures are as follows:

- TLC, gentle handling (independent of interventions)
- Minimise stress: be calm and quiet around the patient, provide a dimly lit quiet environment, use gentle restraint and minimise/group interventions
- Use well-padded bedding to prevent pressure sores and ensure bedding is dry, clean and comfortable
- Turn every 2-4 hours if recumbent to prevent atelectasis (lung collapse)
- Lubricate eyes every 4-6 hours to prevent corneal drying and ulceration
- Appropriate bladder management: express or catheterise if necessary and prevent urinary soiling; catheterisation increases the incidence of urinary tract infection – the risk is greater with in-dwelling catheters versus intermittent catheterisation, and the risk increases the longer an in-dwelling catheter is left in situ.
- Tempt to eat if appropriate
- Perform regular physiotherapy in patients that are likely to be recumbent for prolonged periods

Prognosis

Clearly the desired end-point is for a live patient with a good quality of life. It is important not to make too hasty judgements as dogs and cats can compensate for considerable loss of cerebral tissue. Prognostication can be very difficult. In human medicine clinically-derived prognostic calculators such as the IMPACT Prognostic calculator (International Mission for Prognosis and Analysis of Clinical Trials in TBI; www.tbi-impact.org) or the CRASH Prognosis model (www.crash.lshtm.ac.uk) can help to at least guide prognostication if not being completely definitive. In human and veterinary patients signs of slow but steady improvement are likely to be the most practical guide. Level of consciousness is the most reliable empirical measure of impaired cerebral function and it provides information about the functional capabilities of the cerebral cortex and the ascending reticular activating system (RAS) in the brainstem. The paper mentioned previously suggests:

MGCS score	Suggested prognosis
3-8	Grave
9-14	Guarded
15-18	Good

Platt SR, Radaelli ST, McDonnell JJ. The Prognostic Value of the Modified Glasgow Coma Scale in Head Trauma in Dogs. J Vet Int Med 2001. 15(6):581-584.

However there is limited data available correlating survival with MGCS score so this system may be better used to objectively assess progression rather than as a prognostic indicator. This is especially the case in patients that have polysystemic injuries – such injuries clearly also affect prognosis but this patient cohort was excluded from the above study.

Very recently in 2014 the MGCS has been modified further and made available for free as an app for iOS and Android. The app allows users to use the MGCS to assess their patient's neurological status and prognosticate – bear in mind the caveats – but it also allows this data to be submitted to a server database. Furthermore two weeks later the user is asked to submit further information for the same patient in terms of progression and outcome. In this way it is hoped that real clinical data can be collected, contribute to an evidence base and allow refinement of the MGCS especially with regard to prognostication.

FOR A FREE AUDIO PODCAST EPISODE ON TRAUMATIC BRAIN INJURY, SEE:
http://www.veteccsmalltalk.com/episode/22

Feline Sacrocaudal/Tail Pull Injury

The sacrocaudal region of the vertebral column contains the peripheral nerve roots of the cauda equina rather than the spinal cord. Injury to the sacral and caudal (coccygeal) nerve roots most commonly occurs as a result of sacrocaudal fractures or luxations/subluxations secondary to motor vehicle accidents and bite wounds. Distraction and possible avulsion of the nerve roots may also occur as a result of a tail pull injury where traction is applied to the tail as it is trapped (e.g. beneath a tyre) and the cat tries to escape. Complete or partial, reversible or irreversible neurological dysfunction may occur depending on the extent of the injury to the nerve roots.

The sacral spinal cord segments (S1 to S3) and nerve roots contribute to the pelvic and pudendal nerves.

Pelvic nerve:

- Transmits sensory information from and parasympathetic motor innervation to the detrusor muscle of the bladder
- Transmits sensory information from and parasympathetic motor innervation to smooth muscle of the descending colon

Pudendal nerve:

- Transmits sensory information from the external urethral sphincter, anal sphincter and perineal area
- Provides motor innervation to the external urethral sphincter and the striated muscle of the anal sphincter

Neurons from the S1 segment also contribute to the sciatic nerve. The caudal spinal cord segments provide sensory and motor innervation to the tail via the caudal (coccygeal) nerves.

Neurological examination

Tail

Reduced or absent tail sensation, motor function or tone
Tail sensation test may have more prognostic value if performed at the tail base

Perineum

Perineal urinary and/or faecal soiling
Sacral nerve injury causes reduced or absent perineal reflex and anal sphincter tone (dilated anal sphincter) with possible constipation and faecal incontinence.

- Perineal reflex: stimulation of either side of the anus with a pair of forceps results in reflex contraction of the anal sphincter and flexion of the tail

Perineal sensation (e.g. by stimulating the perineum by closing forceps on the perineal skin area and assessing any conscious response from the cat) may also be reduced or absent.

Bladder

Flaccid distended bladder that is usually easy to express manually due to reduced urethral sphincter tone; urinary incontinence may occur (loss of the detrusor reflex may result in overflow of a full bladder with dribbling of urine)

Pelvic limbs

Pelvic limb weakness, lameness or ataxia – may be due to sciatic nerve involvement and/or pelvic or pelvic limb fractures
Pelvic limb postural reactions (paw placement, hopping) may also be reduced and pelvic limb segmental reflexes (withdrawal, patellar) may be abnormal.

Prognosis

At this time there are no prognostic indicators that allow clinicians to definitively distinguish between animals that will recover and those that will not.

The prognosis for cats in which only the tail is affected is very good including with respect to possible return of tail function. Thereafter the prognosis is generally associated with the severity of neurological injury to the peripheral nerve.

The most severely affected animals (dilated anus with no anal tone; absent tail sensation and motor function) may not recover. Recovery, in particular with respect to tail sensation and motor function, can take weeks to months to occur. However, a prolonged absence (longer than 2 weeks) of perineal deep pain perception, particularly when this is associated with a flaccid, areflexic anal sphincter, is suggestive of a severe lesion to the nerves exiting from the sacral segments (pudendal and pelvic nerves) and is a poor prognostic indicator. As a guideline, most cats that do not recover urinary control after 4 weeks are likely to remain incontinent.

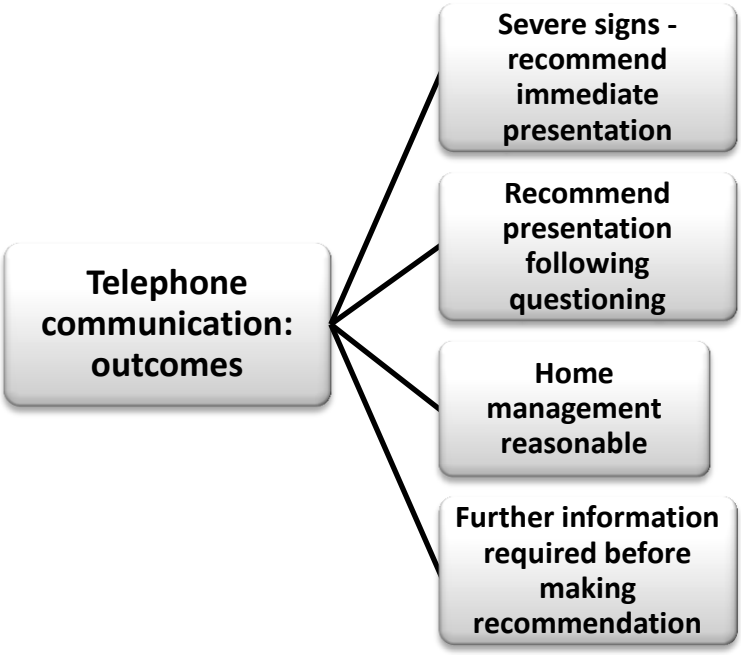
A discussion of appropriate management for animals with prolonged recovery is beyond the scope of these notes.

GENERAL APPROACH TO (NEUROMUSCULAR) INTOXICATION

General Approach to the Poisoned Patient

Suspected or witnessed poisoning is a common reason for presentation of small animals to emergency clinics, with dogs being much more commonly affected than cats. These notes present a general approach to the poisoned patient before going on to describe some of the more commonly implicated poisons in greater detail.

Telephone communication



Initial telephone communication is perhaps no more important than in the intoxicated patient. The important questions to ask are summarised below.

Was exposure witnessed or is it suspected? If suspected, based on what evidence?
What poison/poisons are involved? Can the owner provide more specific details – quantity, concentration etc.?
Where appropriate, does the owner have access to the container?

- The owner should be asked to bring this with them if the animal is presented to the practice

What is the animal's signalment and estimated body weight?
How long ago did exposure occur?
By what route did exposure occur?
Is the animal showing clinical signs? If so, what are they, when did they start and what is their progression?
Is the owner sure that this is the only animal to be affected?
Does the animal have any pre-existing medical conditions?
Is the animal currently taking any medications?

Nurses are frequently the first members of staff with which owners ringing about suspected or witnessed poisoning will communicate. It is therefore imperative that all nurses are well rehearsed in the questions that are important to ask and advice should be sought from the veterinary surgeon if there is any concern.

On the basis of the information obtained a recommendation should be made as to whether the animal needs to be presented to the practice or may be managed conservatively at home. In some cases, the animal will be exhibiting marked clinical signs and questioning should be kept to a minimum with immediate transport to the practice being the only appropriate recommendation. In other cases, it is necessary to obtain further information before a recommendation can be made.

Further information

The purpose of seeking additional information about the poison in question is to ascertain if possible the severity of exposure that has or may have occurred:

Has potentially toxic exposure occurred? Has lethal exposure occurred? What are the expected clinical signs? Would the animal be expected to have developed clinical signs by now? If signs are present, are they reported to be early or late signs of intoxication? Is their progression typical?

A number of sources of information are available with respect to veterinary toxicology that includes:

- The Veterinary Poisons Information Service (VPIS) in the United Kingdom
- Toxcall in the United Kingdom
- The ASPCA Animal Poison Control Center in North America
- Pet Poison Helpline in North America
- Books on veterinary toxicology
- The internet: only reliable up-to-date sources should be used (e.g. www.vin.com, www.ivis.org, www.merckvetmanual.com). The internet is also useful for determining ingredients and concentrations in cases where for example only a proprietary product name is available

Some information that may be useful when calculating exposure dosages is:

- 1 standard teaspoon = ~ 5 ml; 1 standard tablespoon = ~ 15 ml
- 1 fluid ounce (oz) = 29.6 ml; 1 ml = 0.034 oz
- 1 lb = 0.454 kg; 1 kg = 2.2 lb
- 1% solution = 10 mg/ml = 1 g/100 ml
- 1 part per million (ppm) = 1 mg/kg for solid substances, 1 mg/l for liquid substances
- *w/w:* an abbreviation for 'by weight'; used to describe the concentration of a substance in a mixture or solution. In strict terms, 8% w/w means that the mass of the substance in question is 8% of the total mass of the solution or mixture. The metric symbol g/g has the same meaning as w/w.

Home management

If the decision is made for the animal to be monitored at home, the owner must be thoroughly briefed both on what signs to observe the animal for and the typical timeframe for their onset and progression. In general, if there is any doubt as to the animal's condition, veterinary examination should be recommended. Owners should be advised on appropriate measures to implement during transportation. For example keeping unconscious animals warm or keeping seizuring animals cool and protected from injury.

Inducing emesis at home:

In some cases in which poison ingestion has occurred within a suitable period of time, it may be appropriate for the owner to induce emesis at home, for example if financial concerns or practical constraints preclude presentation to the practice. In addition, if a considerable delay is anticipated prior to presentation, and the owner has ready access to an appropriate emetic, inducing emesis prior to departure from home may be advisable to minimise further absorption of the poison in transit. The owner must be questioned carefully to ensure that contraindications to inducing emesis do not exist.

CONTRAINDICATIONS TO INDUCING EMESIS include:

Significantly altered mentation: increases the risk of aspiration of vomitus; in particular in depressed animals in whom there may be dysfunction of the gag reflex
Respiratory distress and pre-existing conditions (e.g. laryngeal paralysis) may predispose the animal to aspiration.
Animals that are **already vomiting** clearly do not require emesis to be induced.
Emesis should not be induced following ingestion of a **caustic or corrosive agent** (e.g. acids or alkalis) as it will potentially expose the oropharyngeal and oesophageal mucosa to further injury. Consumption of milk or water should be encouraged (if not contraindicated) to dilute the poison.

Agents for inducing emesis at home [C – cats; D – dogs]

Agent	Dose	Comments
Soda crystals (washing soda)	D, C: 1 crystal	Used most often Place on tongue at back of mouth Emesis usually within 10 minutes Can be repeated NB. Not caustic soda (sodium hydroxide)
Syrup of ipecacuanha (7%)	D: 1-2 ml/kg per os C: 3.3 ml/kg per os	Emesis usually within 30 minutes Can be repeated once Bitter taste therefore poor compliance Available in UK?
Hydrogen peroxide (3%)	D, C: 1-3 ml/kg per os	Emesis usually within 10 minutes Can be repeated once Care to avoid aspiration

It is very important to **make sure that soda crystals (washing soda) are used for emesis, as owners have inadvertently administered caustic soda (sodium hydroxide) instead**. This is very harmful following ingestion causing severe injury to the oropharyngeal and oesophageal mucosa with potentially fatal consequences. It may be increasingly difficult to access washing soda in the form of crystals and powdered equivalents will likely make dosing more challenging.

Table salt is an unreliable emetic and may induce or exacerbate hypernatraemia with potentially severe consequences. Its use as an emetic is not recommended, especially in the home environment where owners may accidentally give excessive quantities. Ad lib access to water is imperative if table salt is used.

General clinical approach

- Perform major body system examination and institute immediate life-saving measures as necessary
- Perform emergency database
- Obtain thorough history at first reasonable opportunity
- Minimise further systemic absorption of poison
- Administer antidote if available
- Promote elimination of any poison already absorbed
- Perform further clinical evaluation as appropriate
- Provide symptomatic, supportive and nursing care as appropriate
- Ensure close monitoring and regular repeat clinical evaluation as appropriate

OR:

R Resuscitation/Stabilisation. Risk Assessment.
S Symptomatic/Supportive care, monitoring, nursing care
I Investigations

D Decontamination
E Enhanced elimination
A Antidotes
D Discharge!

History

In patients presenting with severe clinical signs (e.g. seizures, severe muscle tremors) history-taking should not be prioritised over initial stabilisation, especially as specific antidotes are not available for the majority of poisons to which dogs and cats are exposed. Ultimately treatment is directed at the patient and not the poison.

All the information already described should be obtained at the appropriate time. In some emergency patients, clinical signs and progression are compatible with possible intoxication without an immediately suggestive history. In such cases, the owner must be carefully and thoroughly questioned to establish whether a potential source of poison exists that the owner has not considered.

Historical findings associated with possible poison exposure are:

- Sudden and rapid onset of an illness (especially gastrointestinal, neurological, cardiac dysrhythmias, liver or kidney failure) in a previously healthy animal especially after a period of being unsupervised
- Sudden onset of progressive tremors, muscle twitching or seizures in a previous healthy animal
- Possible exposure to poisons including change of diet, access to new areas or environment
- Access to veterinary or human medications

Initial stabilisation – major body system examination

As for all emergency patients, a major body system (cardiovascular, respiratory, central neurological) examination should be performed and immediate measures taken to correct potentially life-threatening problems. Rectal temperature is also usually measured early as part of the primary survey where abnormalities, hyperthermia in particular, are suspected.

Cardiovascular assessment:
Cardiovascular assessment should focus on assessing systemic perfusion (using heart rate, peripheral pulse rate and quality, mucous membrane colour, capillary refill time) and on the detection of possible dysrhythmias. Numerous toxins (e.g. methylxanthines, illicit drugs) can cause severe life-threatening dysrhythmias (ventricular or supraventricular) that might require immediate recognition and appropriate treatment.

Respiratory assessment:
Respiratory assessment should evaluate respiratory rate, effort and thoracic auscultation. Patients may aspirate during vomiting or seizure activity resulting in aspiration pneumonia. Severe twitching and seizure activity can also cause non-cardiogenic pulmonary oedema. Oxygen supplementation via flow-by or via a mask should always be administered to patients with respiratory distress.

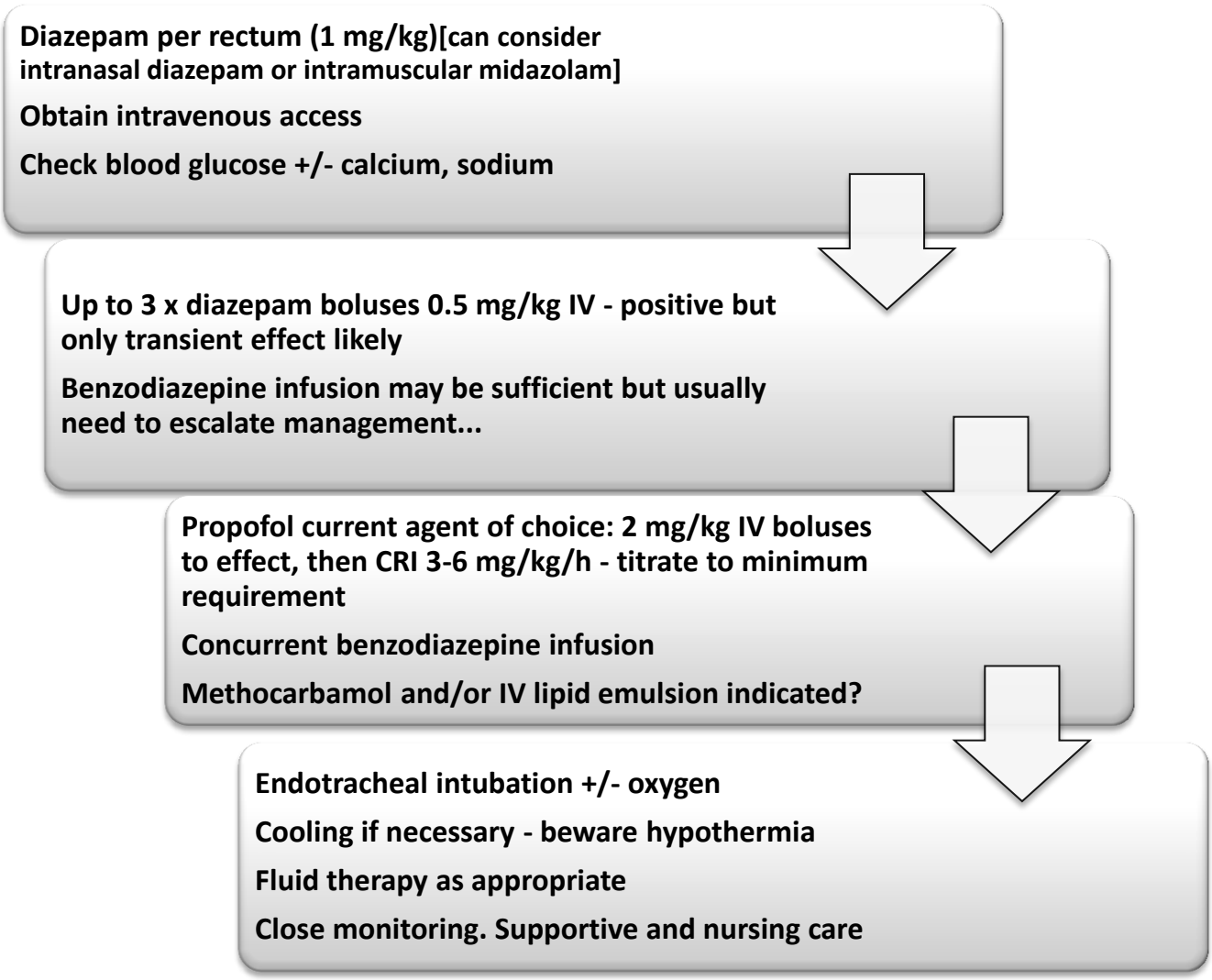
Neurological assessment:
The patient's mentation will influence the decontamination procedure chosen. Patients should also be assessed for muscle tremors, twitching or seizures. Seizure activity and severe muscle tremors should be addressed rapidly.

Body temperature:
In appropriate cases, rectal temperature should be measured as early as possible during initial examination as muscle fasciculations and seizure activity can cause hyperthermia. If hyperthermia is present it is important to initiate active cooling. Hypothermia may also occur following bathing or sedation. Close monitoring of rectal temperature for either development and appropriate intervention is therefore required.

Initial stabilisation – treatment of seizures and muscle tremors

A variety of poisons include neurotoxicity amongst their mechanisms of action. Examples include: metaldehyde, pyrethroids; theobromine (chocolate), caffeine, organophosphates, tremorgenic mycotoxins, strychnine. Seizures and/or muscle tremors are common signs of poisoning requiring symptomatic treatment.

Summary of approach to stabilisation of intoxicated patient presenting with seizures and/or severe muscle tremors:



In patients intoxicated with tremorgenic poisons (e.g. metaldehyde, permethrin), it can be difficult to differentiate severe muscle tremors from seizure activity. However if the poison in question is known to be one associated with severe tremors or sufficient clinical suspicion exists, the use of **methocarbamol** (Robaxan©) may be indicated and may avoid the need for anaesthesia. This is a centrally-acting muscle relaxant related to guaiphenesin whose precise mechanism of action remains unclear. The manufacturer's recommended dose in dogs and cats is 44-220 mg/kg IV with a typical upper limit of 330 mg/kg in a 24 hour period; the use of low rate methocarbamol infusion has also been described. However to the author's knowledge an injectable preparation of this agent is not currently available in the United Kingdom. The oral preparation (tablets) can be crushed, dissolved in water and given via orogastric or nasogastric intubation in patients that are unable to swallow; alternatively it can be administered per rectum using a feeding tube or Foley catheter for example. In the absence of methocarbamol, the management of patients with tremors is the same as for those with seizures.

The aim of treatment is to achieve adequate control of tremors; complete abolition of tremors is neither likely nor necessary and may require excessive drug administration.

Treatment often starts with the administration of **diazepam per rectum** at 1 mg/kg; this can facilitate intravenous catheter placement in seizuring/tremoring patients but may be omitted if a catheter can be rapidly placed without it.

- Proprietary rectal diazepam tubes may be used
- Injectable diazepam may be diluted with water or saline to increase the volume to be administered and then infused per rectum
    - Using injectable diazepam allows more accurate dosing but involves a greater time delay in preparation
    - Depending on the size of the animal, the use of a well-lubricated long intravenous catheter (with stylet removed), urinary catheter or nasooesophageal feeding tube will allow the diazepam to be administered more proximally in the rectum. This should minimise spillage from the anus and maximise drug absorption.
- The rectal mucosa has an extensive blood supply and drug absorption should occur readily so long as the solution is in contact with the mucosa and not mixed into faecal material.
- Intranasal diazepam administration has also been described although the author has no experience with this technique.
- Intramuscular midazolam has been used to treat children in status epilepticus and may have a role in the initial management of veterinary patients with seizures/severe tremors but this remains to be clarified.

Once an intravenous catheter is successfully placed, **additional diazepam can be administered intravenously** (0.5 mg/kg IV); in animals with severe poisoning it is common to see a marked but very transient positive effect. The diazepam bolus is typically repeated no more than twice more before additional treatment is instituted. In some cases it is sufficient to start the patient on a benzodiazepine infusion alone. In others patients, more intensive treatment is required although a benzodiazepine infusion may still be used to provide some skeletal muscle relaxation and reduce the required doses of other agents that may have more cardiorespiratory depressant effects:

- Midazolam is used most commonly: 0.1-0.5 mg/kg/hour (or 0.1-0.5 mg/kg IV as intermittent boluses)
- Diazepam: 0.1-1 mg/kg/hour

At the present time, **propofol** is usually the first agent of choice when management needs to be escalated. It is given as 2 mg/kg aliquots slowly intravenously until visible motor activity is alleviated. Propofol is then continued as a constant rate infusion initially at 3-6 mg/kg/hour but very much titrated to effect so that the patient is on the lowest rate necessary to prevent motor activity. Endotracheal intubation is performed and vital parameters monitored and recorded regularly.

Endotracheal intubation should be performed in all anaesthetised patients to protect the airway and prevent aspiration. Oxygen supplementation is not mandatory unless specific indications exist.

Propofol infusion:

The use of a syringe driver is preferred to allow accurate administration of a propofol infusion. However a solution of propofol in normal saline can be made and administered via a fluid administration set using an infusion pump. These patients are recumbent and immobile, and although not ideal, it may therefore be possible to manage them adequately without the use of a syringe driver or an infusion pump if one is not available.

There seems to be some debate about the use of **phenobarbital** in patients with suspected neuromuscular intoxication. If seizures are present, the seizure focus may persist for a short while but should resolve as the toxin is cleared from body so only short-term anticonvulsive therapy is needed. On-going benzodiazepine therapy during propofol anaesthesia may suffice: anti-convulsive; cause better muscle relaxation and less respiratory depression than phenobarbital. Ultimately phenobarbital use may

be matter of individual clinician preference and/or individual patient circumstances; perhaps especially indicated where propofol infusion cannot be administered.

Alternatives to propofol infusion:

If financial or practical constraints preclude the use of a propofol infusion, **pentobarbital** (short-acting barbiturate) boluses may be a viable alternative. However, to the author's knowledge, a sterile formulation of this agent for injectable use is no longer readily available (in the UK?) and the risks associated with using non-sterile preparations available for euthanasia must clearly be borne in mind and discussed with the owner.

- The recommended dose is 5-20 mg/kg slowly IV to effect (e.g. 3 mg/kg aliquots every 90 seconds)
- As barbiturates are cumulative, it is essential to monitor the patient closely for possible progressive and severe respiratory depression

Sterile pentobarbital preparations used to be used widely for the management of some neurological intoxication patients before propofol became available. Although the use of non-sterile formulations (used for euthanasia) is clearly not ideal, the risk-benefit assessment falls firmly on the side of benefit if euthanasia is the only other alternative due to financial constraints! Patients have been treated successfully using these non-sterile formulations with no apparent clinically significant complications related to lack of sterility.

Increasing anecdotal experience with the use of **medetomidine/dexmedetomidine** in this patient population but must be judicious (e.g. start with microdose medetomidine (e.g. 0.5-2 µg/kg IV as needed or 0.5-2 µg/kg/hour infusion)).

The use of **alfaxalone** may be considered but at least in the United Kingdom would be considerably more expensive than propofol. At this time there is much less experience with its use for neurotoxicity than for propofol but this may increase in time and it is certainly a viable alternative if, for example, propofol is in short supply. Dosing guidelines in dogs and cats are broadly similar and as follows:

- 2-3 mg/kg IV bolus, followed by
- 6 mg/kg/hour infusion titrated to effect

Thiopentone (barbiturate) and **inhalant anaesthetic agents** may also be considered.

As mentioned above, patients on a propofol infusion are usually also treated with on-going benzodiazepine (midazolam, diazepam) therapy. These agents cause muscle relaxation and act in a propofol-sparing capacity.

Discontinuing propofol infusion: there is no set-time frame as such for how long the patient needs to be kept on a propofol infusion; this is something that needs to be worked out on an individual patient basis. Generally an attempt is made to wean the patient off the propofol every 6-12 hours by reducing the infusion for example by 25% every 30 minutes (i.e. so weaning is done over 2 hours); if the patient is on a benzodiazepine infusion as well, this is typically continued unaltered until the patient is off propofol and then also weaned off gradually.

Intravenous fluid therapy may be required to correct hypovolaemia and/or dehydration. Fluid therapy is also indicated in the management of poisons that are nephrotoxic (e.g. non-steroidal anti-inflammatory agents) and those that are largely dependent on renal excretion. Oxygen supplementation is indicated in patients with respiratory compromise, for example from aspiration following vomiting, and in the contexts of certain poisons such as carbon monoxide.

Emergency database

An emergency database for the intoxicated patient may consist of one or more of the following if possible:

- Manual packed cell volume (PCV) and serum total solids (TS)
- Blood glucose, electrolyte, urea and creatinine concentrations
- Venous (or arterial) lactate
- Peripheral blood smear examination
- Electrocardiogram (ECG)
- Non-invasive blood pressure (NIBP)

It is recommended to perform an emergency database in all intoxicated patients although the timing of this should be governed by the facilities available and the emergency database must not be prioritised at the expense of emergency treatment. The exception to this is blood glucose concentration. Checking for hyper- or hyponatraemia and hypocalcaemia is also recommended if possible although these abnormalities are much less frequently implicated than hypoglycaemia as a cause of neurological signs in small animals.

Blood glucose concentration should be checked as soon as possible in all animals that present either seizuring or with marked neurological abnormalities. Clinical signs of hypoglycaemia usually relate to brain dysfunction due to neuroglycopaenia (i.e. reduced cerebral glucose availability) and to sympathetic nervous system stimulation. Depending on the severity of the hypoglycaemia, clinical signs range from mild (e.g. lethargy, weakness) to moderate (e.g. depression, ataxia, muscle tremors) to very severe (e.g. collapse, seizures, coma). Hypoglycaemia (probably only moderate-to-severe) can also cause sinus bradycardia/bradydysrhythmia.

The blood glucose levels at which signs develop can vary between individuals, but in general:

- Clinical signs usually do not occur until blood glucose is < 3 mmol/l
- Secondary neurological signs are unusual while blood glucose > 1.5-2 mmol/l

The appropriate treatment for hypoglycaemia depends on the blood glucose concentration, the clinical signs, and in some cases the cause and suspected chronicity.

Topical mucosal therapy:

- Either a proprietary topical 'fast acting' glucose solution (e.g. Glucogel®, BBI Healthcare) or sugary water or honey for example can be applied to the gums or other mucosal surfaces.
- This route of treatment is unlikely to resolve the hypoglycaemia but may alleviate clinical signs sufficiently while other routes of intervention are instigated.
- Dosing is usually empirical.

Enteral therapy:

- Enteral therapy may be adequate in less severe cases and is the most physiological route of supplementation
- Patients are fed small amounts of palatable food regularly (e.g. every 1-2 hours) and in some cases sugar solutions, honey or similar are included.
- Contraindications for enteral therapy include inability or refusal of the patient to eat voluntarily, absent gag reflex, obtundation or vomiting.

Parenteral therapy:

- More severe cases of hypoglycaemia require more aggressive intervention in the form of parenteral therapy; this is usually intravenous but intraosseous administration may be required in some cases.

- Glucose is administered until clinical signs are controlled but a starting dose of 0.25-0.5 g/kg is usually recommended – this is equivalent to 0.5-1.0 ml/kg of a 50% glucose (dextrose) solution.
- 50% glucose solution should be diluted (e.g. with an equal volume of crystalloid solution) prior to administration as it can cause venous irritation and inflammation (phlebitis).
- Clinical signs usually resolve quickly with treatment
    - Occasionally animals that are showing signs of brain dysfunction, including seizures, continue to do so despite establishing normoglycaemia – signs may or may not eventually abate. This phenomenon may be due to continued neuroglycopaenia despite normoglycaemia or due to residual injury suffered during the hypoglycaemic period.

Following bolus administration of glucose (which can be repeated), a glucose infusion is usually required to prevent recurrence of clinical signs. Some glucose solutions for infusion are available commercially (e.g. 0.9% sodium chloride + 5% glucose) but they can also be readily constituted.

Glucose solutions for long-term infusion are usually of 2.5% or 5% concentration. Occasionally it is necessary to administer a 10% glucose solution. The tonicity/osmolarity of this solution may pose a risk of phlebitis when administered via a peripheral vein and if possible it is recommended to infuse through a central vein (larger blood flow and more rapid dilution reduce the risk of localised adverse effects on the vessel).

Treatment of hypoglycaemia should be guided by clinical signs and if available, regular monitoring of blood glucose concentration.

Additional tests that may be indicated at the appropriate time in certain poisoned patients include acid-base analysis, urinalysis (e.g. oxalate crystals in ethylene glycol poisoning) and calcium measurement (e.g. hypocalcaemia may occur in ethylene glycol poisoning). Abdominal radiographs taken at the appropriate time may reveal ingestion of items containing heavy metals or certain enteric-coated or sustained-release drug formulations. Routine haematology and biochemistry profiles may become indicated as case management progresses and may also identify pre-existing conditions that may have implications with respect to management of individual patients.

Coagulation testing may also be indicated in some cases. It should always be performed in coagulopathic animals with suspected anticoagulant rodenticide or xylitol poisoning. Since factor VII has the shortest half-life, the extrinsic coagulation pathway is affected first, so prothrombin time (PT) is prolonged before and more severely than activated partial thromboplastin time (aPTT)in rodenticide poisoning. If the animal is experiencing haemorrhagic diathesis both PT and aPTT will be prolonged. If facilities to perform PT/aPTT are not available in-house, and a significant delay is anticipated in obtaining the results, activated clotting time (ACT) can serve as a useful screening test in animals with clinical evidence of haemorrhage. A tube containing dichotomous earth (e.g. Fuller's earth) and facilities to warm the tube (to 37^0C) is all that is required for this test.

Lactate:

Extreme muscle activity (e.g. seizures, trembling/tremors) may cause hyperlactataemia due to relative oxygen deficiency (energy requirements greater than aerobic metabolism can provide) and increased glycolysis. This abnormality usually resolves quickly once stabilisation has been achieved. Unless physical perfusion parameters are also suggestive of hypoperfusion, this raised lactate should not prompt aggressive fluid therapy for presumed hypovolaemia.

Gastrointestinal decontamination (GID)

Toxin exposure is usually via ingestion and gastrointestinal decontamination (GID) is frequently indicated. This consists of emptying of the stomach followed by administration of an adsorbent to minimise

absorption of any poison remaining in the gastrointestinal tract. Cathartics used to be used in the past but seem to have fallen out of favour to some extent more recently. It should be noted that as is often the case with veterinary, and sometimes, human medicine there is little in the way of evidence base for many of the decisions made in the treatment of some poisonings and opinions vary between the relative merits of one approach versus another, whether gastric emptying or just activated charcoal should be used, for which poisons activated charcoal should be used and so on.

Gastric emptying:

In the absence of contraindications, induction of emesis is the most expeditious means to empty the stomach; feeding a small meal first may increase the effectiveness of this approach. Older resources used to say that gastric emptying should only be performed if the patient presents within 2 hours of poison ingestion. However clinical experience suggests that sometimes significant decontamination can be achieved even up to 6 hours post-ingestion so a less limited approach is recommended nowadays. Drugs used to induce emesis are summarised below.

Drugs used to induce emesis [C – cats, CNS – central nervous system, D – dogs]

Drug	Dose	Comments
Apomorphine	D: 0.02-0.1 mg/kg SC, IM, ocular (IV)	Drug of choice, emesis usually in 5-15 minutes Centrally-acting Protracted vomited occurs sometimes Sedation, respiratory depression, ataxia possible but relatively rare Naloxone reverses CNS and respiratory-depressive effects but not dopaminergic emetic effects Experimental pharmacokinetic study suggests 'topping up' initial dose may not induce emesis but could exacerbate sedation; however clinical experience suggests it does induce emesis Ocular route: apply to conjunctival sac; lavage thoroughly with saline following emesis to minimise drug absorption; highly dependent on compliance but can be quite successful; both tablets dissolved in water and injectable preparations have been used by this route
Apomorphine	C: 0.01-0.02 mg/kg SC, IM (IV)	Use lowest possible dose Not recommended by some due to possible significant sedation Naloxone reverses CNS and respiratory-depressive effects but not dopaminergic emetic effects
Medetomidine	C: 20 µg/kg IM, IV	Alpha$_2$-adrenergic agonist Use atipamezole to reverse effects once emesis has occurred Use very cautiously due to potential cardiorespiratory depression; sedated cats that have not vomited are often reported!
Xylazine	C: 0.4-0.5 mg/kg IM, SC	Alpha$_2$-adrenergic agonist Effects reversed by yohimbine – availability? Atipamezole may also reverse effects Use very cautiously due to potential cardiorespiratory depression Clinical use may be limited by restricted availability in small animal-only practices

See Appendix 2 for a blog post on inducing emesis in cats from July 2014.

As mentioned previously, **contraindications to inducing emesis** include:

- Significantly altered mentation due to increased risk of aspiration of vomitus; in particular in depressed animals in whom there may be dysfunction of the gag reflex
- Respiratory distress and pre-existing conditions (e.g. laryngeal paralysis) that may predispose the animal to aspiration
- Animals that are already vomiting
- Ingestion of a caustic or corrosive agent (e.g. acids or alkalis) – emesis will potentially expose the oropharyngeal and oesophageal mucosa to further injury. Consumption of milk or water should be encouraged if not contraindicated to dilute the poison.

Administering anti-nausea/anti-emetic medication following successful gastric emptying:

Although inducing emesis is a quick and effective means of gastric emptying, vomiting is clearly an unpleasant experience and some patients may vomit for a protracted period; this can be witnessed by repeated episodes of vomiting with only small amounts of frothy/bilious material produced and a nauseous sorry-looking patient! As such, once the patient has vomited sufficiently that gastric decontamination has occurred, anti-nausea/anti-emetic medication may be administered. Furthermore this may allow activated charcoal administration to commence sooner as well. Apomorphine acts as a dopamine agonist stimulating the chemoreceptor trigger zone to cause vomiting; metoclopramide is a dopamine antagonist and may therefore be the most sensible anti-emetic drug after apomorphine use and is now licensed in dogs and cats (Vomend®, Eurovet). Maropitant (Cerenia™, Pfizer Animal Health) is a neurokinin-1 receptor antagonist that is also licensed in dogs and cats and is an alternative option here; however it is typically more expensive than metoclopramide and a single dose lasts for 24 hours which is unnecessary in these patients.

Gastric and colorectal lavage:

In patients in which induction of emesis is contraindicated or unsuccessful, gastric lavage may be appropriate for gastric emptying. However it is contraindicated following ingestion of caustic or corrosive substances and where the risks of general anaesthesia are considered unacceptable. In some cases (e.g. metaldehyde poisoning), following gastric lavage, the author will perform additional lavage via a stomach tube inserted as proximally as possible per rectum. Colorectal lavage is continued until clear fluid is returned and activated charcoal suspension is then instilled. The anus may be plugged with a swab for example for a short period of time to minimise leakage of the activated charcoal.

Activated charcoal:

Activated charcoal acts as an adsorbent binding to toxins and allowing their passage through the gastrointestinal tract while preventing or minimising further systemic absorption. It is typically administered once gastric emptying has been performed and should be given as soon as possible. If an emetic has been employed for gastric emptying enough time must be allowed for the emetic effects to subside before activated charcoal is administered; administering an anti-emetic to facilitate this is an option. In some cases activated charcoal is administered initially via stomach tube at the end of gastric lavage.

Different substances are bound to different degrees by activated charcoal, and potentially not at all in some cases. However, detailed information on this is relatively limited. Unless contraindicated, the use of activated charcoal in almost all cases of oral poisoning is probably reasonable and may also help following topical poisoning (see below). Activated charcoal should not be used following ingestion of caustic or corrosive substances, in patients that are vomiting or seizuring, or where there is any possibility of gastrointestinal perforation/obstruction/ileus. It should also potentially be avoided if oral medications or

antidotes are needed and if gastrointestinal endoscopy or surgery is likely in the near future. Vomiting and constipation following administration of multiple doses are the main complications reported. Hypernatraemia due to osmotic effects with movement of water from the circulation into the gastrointestinal tract is a potential adverse effect that is suspected to be rarely clinically significant but more information is needed and it is more likely when using products that also contain sorbitol. It can be avoided by close attention to fluid balance as indicated.

The recommended dose in dogs and cats is 1-5 g/kg to be repeated as necessary (typically every 4 to 6 hours) until black faeces are detected; in theory the ratio of activated charcoal to toxin should be 10:1, but in reality the amount of toxin in the gastrointestinal tract is rarely/never known. Doses up to 8 g/kg have been used. However given the concern mentioned above regarding possible hypernatraemia, a rational approach is probably to use low doses accurately measured and at well-spaced out intervals, and to not administer this product to patients that are either already dehydrated or have been exposed to a poison that may itself induce hypernatraemia. Activated charcoal is often successfully administered in food to dogs. However compliance is likely to be much poorer in cats and a risk/stress-benefit assessment should be made on an individual case basis. Various proprietary preparations are available with accompanying dosing guidelines, including powdered formulations (e.g. BCK Granules®, Fort Dodge) that can be added to food or made into a slurry and administered by mouth, and suspensions (e.g. Charcodote®, Pliva Pharma Ltd).

Topical poisoning

Washing the patient is recommended to minimise irritation of and absorption via the skin; this should also minimise absorption through ingestion following grooming. Washing is usually done using mild soap or detergent followed by copious rinsing with water and then drying the animal as thoroughly as possible. Powdered toxins may be vacuumed off before washing. All individuals involved in handling the animal should take care to wear gloves and preferably an apron so as to avoid self-contamination. In some cases it may be appropriate for the owner to wash the animal at home. However in compromised or non-compliant animals, veterinary care is recommended.

Clipping the coat of long-haired patients may help to maximise decontamination. Chemical restraint may be preferable during washing to allow protection of the eyes and in some cases general anaesthesia with endotracheal intubation is safest to minimise the risk of aspiration. Vital parameters including rectal temperature should be monitored closely throughout.

Oily substances may be more successfully removed using commercial hand-cleaning degreaser formulations (e.g. Swarfega Hand Cleaner® products) but it is important to ensure that such preparations are thoroughly washed off the animal subsequently.

Sticky substances (e.g. glues, paints) can be removed from the coat by applying butter or margarine (the contaminant dissolves in the high fat medium) and then washing off with soapy water. Otherwise allow the contaminant to dry in situ and then clip the fur off.

The use of activated charcoal is generally recommended following topical poisoning. This is to minimise gastrointestinal absorption that may occur following ingestion from grooming. In addition, some poisons undergo enterohepatic circulation following absorption from the skin and thereby become available in the gastrointestinal tract.

In cases in which the skin has come into contact with an acidic or caustic substance, the affected area should be very thoroughly lavaged (‘the solution to pollution is dilution’) using normal saline or indeed warm water; use of other agents may result in neutralisation with the associated chemical reaction causing skin burns. The same is true in cases of ocular contamination and in both cases the animal should be appropriately analgised and chemically restrained to allow comprehensive lavage to be

performed. Damaged skin is highly susceptible to mechanical injury and gentle lavage is therefore mandatory.

Diuresis

Diuresis is most indicated in the treatment of poisoning by agents for which renal excretion of either the primary intoxicant or its metabolites is a significant feature (e.g. NSAIDs, salicylates, phenobarbital). Standard intravenous isotonic crystalloid therapy is employed to promote renal excretion with or without additional diuretic administration. Isotonic crystalloid therapy is administered at a rate of 1-4 mL/kg/hour above calculated fluid requirements and the patient must be monitored closely to ensure that adequate urine production occurs. In cases of aggressive diuresis, close monitoring of hydration status and electrolyte concentrations is indicated.

Antidotes

In a significant proportion of canine and feline patients a diagnosis of poisoning is made presumptively with the poison in question remaining unknown. Furthermore, specific antidotes or antagonists do not exist for the majority of potentially poisonous substances to which dogs and cats may be exposed. That said, the majority of clinical cases reported are due to a relatively small number of poisons for which in some cases specific treatments are available. Intravenous lipid emulsion is an antidotal therapy that is gaining increasing impetus (see below).

Examples of poisons and their antidotes include:

Poison	**Antidote**
Benzodiazepines	Flumazenil
Cardiac glycosides (including *Bufo* toad toxicosis)	Digoxin immune Fab (Digibind)
Cyanide	Hydroxycobalamin (Cyanokit) – vitamin B12 precursor
Ethylene glycol (antifreeze)	Fomepizole (4-MP) or ethanol
Iron	Deferoxamine – iron chelator
Lead	Succimer (2-3-dimercaptosuccinic acid)
Muscarinic mushrooms	Atropine
Opioids/opiates	Naloxone (Narcan)
Organophosphates	Atropine for muscarinic signs; 2-PAM (Paralidoxime) for nicotinic signs
Paracetamol (acetaminophen)	N-acetylcysteine
Serotonin syndrome caused by serotonergic substances	Cyproheptadine may help
Vitamin K antagonist anticoagulant rodenticides	Vitamin K_1
Zinc (and other heavy metals, e.g. copper, mercury, lead)	D-penicillamine

Toxicological testing?

In a significant number of dogs but also cats poisoning is unwitnessed and patients are treated based on suspicion or presumption. As such being able to perform toxicology and poison testing on some form of body fluid/tissue to confirm the diagnosis on the face of it seems very attractive. However there are some considerations to bear in mind:

1. Availability of testing: this has traditionally been very limited; in some cases it has been possible to make use of human diagnostic laboratories but infrequently. In the United Kingdom for example a new service is available (Carmichael Torrance Veterinary Diagnostic Laboratory, http://ctdslab.co.uk/toxicology-and-poison-testing/) which employs gas chromatography mass spectrometry and offers a variety of options e.g. wide-ranging small animal toxicology panel;

screening for groups of agents (e.g. vitamin K antagonist rodenticides, drugs of abuse); single agent screening. This laboratory also offers 'sudden death investigation' in the form of post-mortem +/- toxicology screening. Clearly it may be that whatever poison is involved in a particular case, ante- or post-morten, is not one the laboratory can test for.

2. Practicalities of testing: are the samples that are required ones that can be realistically/safely obtained and can they be reasonably transported to the laboratory, e.g. is freezing required, is immediate transportation required, etc.?
3. Time delay in obtaining results: this is a major drawback in the context of managing actual on-going clinical patients as by the time results are obtained most poisoned patients will either be improved/normal or potentially will have been euthanised/died. For example results from the laboratory mentioned above can be expected 'within five days'.
4. Will the results actually matter? Confirming poisoning may clearly be considered important for a variety of reasons e.g. to confirm a clinical suspicion, to afford pet owners additional information, to prevent repeat exposures, to facilitate investigations etc. However it is important to bear in mind that in many cases poisoned patients are managed symptomatically according to their clinical syndromes and progression and antidotes are not available for a significant number of potential poisons. As such even if results could be obtained within a clinically helpful timeframe they may not in fact alter clinical management – but they of course might and would at least help confirm the suspicion!

Intravenous Lipid Emulsion (ILE)

The use of intravenous lipid emulsion (ILE) for intoxication was originally investigated experimentally in the 1970s and 1980s. Subsequently there have been a growing number of case reports of its use in clinical patients first in human medicine and more recently in veterinary medicine, mostly relating to the treatment of haemodynamically or neurologically-significant poisonings. Early reports in humans focused on treatment of local anaesthetic systemic toxicity (LAST) – for which it has now become a fixed part of the treatment approach – but the use of ILE in people has now been reported for a wide variety of drugs and other toxic substances. Further clinical studies are needed to determine the safety, effectiveness and risk:benefit ratio of this therapy but a growing number of experimental studies and case reports suggest that ILE may become a valuable addition to the veterinary clinician's emergency drug arsenal.

Intravenous lipid emulsion

A variety of lipid emulsion preparations have been used clinically for several decades for example in parenteral nutrition or as a vehicle for delivery of lipid-soluble drugs (e.g. propofol). ILEs are oil-in-water emulsions consisting of triglyceride-containing oils, a phospholipid emulsifier (10% or 20%), and glycerin. Although others are available, the most commonly used preparation for treating toxicosis at the moment is Intralipid 20% which is a soybean-oil-based emulsion of long-chain triglycerides.

The fat droplets in ILEs are similar to endogenous chylomicrons and are cleared by skeletal muscle, splanchnic viscera, myocardium, and subcutaneous tissues. Glycerol and free fatty acids are the breakdown products of the triglyceride, phospholipid, and choline components of ILE and are used by body tissues as energy sources.

Mechanisms of action

The precise mechanism of action through which ILE increases the rate of recovery and augments conventional resuscitation efforts in various cases of lipophilic drug toxicosis is currently unknown. It may be that this treatment has several potential mechanisms of action and one or more may be involved to a

greater or lesser degree depending on the specific toxin in question. Current theories regarding ILE's main mechanisms of action are thought to relate to a 'lipid sink' sequestration effect and/or a metabolic effect that improves cardiac performance; however other mechanisms of action are also likely.

'Lipid sink' effect:

At this time it is thought that the 'lipid sink' effect is likely to be the predominant mechanism. This theory suggests that administered lipid remains in the circulation where it physically binds to circulating toxin thereby trapping it in the plasma and reducing the free concentration of the toxin, i.e. the toxic compound is sequestered into a lipid compartment within the bloodstream. As the ILE circulates throughout the body, fat droplets containing the toxin are cleared by skeletal muscle, splanchnic viscera, myocardium, and subcutaneous tissues, which help dilute and clear the offending toxin from the body. Trapping the toxin in the circulation means that there is less available for binding to tissue and organ receptors with subsequent toxic effects. Moreover in some cases it may be that the 'lipid sink' effect is strong enough to actually pull lipophilic toxins away from their sites of action into the circulation, especially from the heart and brain. In other words the lipophilic toxins move down their concentration gradient away from the tissues and into the circulation where they are then trapped in the lipid sink.

The degree of lipid solubility of a substance, referred to as its lipid partition coefficient, may affect the clearance rate of the offending toxin following ILE administration. Given the 'lipid sink' mechanism of action, it makes sense that lipid emulsions may be most effective in the treatment of intoxication with substances that have high lipid solubility.

The time frame (acute versus chronic) that ILE may prove beneficial in treatment may depend on the individual toxin's half-life. If the toxin's detrimental side effects are the result of a metabolite formed from the toxin, then ILE therapy may or may not be beneficial unless it is given in the acute setting to decrease metabolite formation.

'Redistribution':

Another suggested mechanism of ILE as an antidote, instead of or in addition to sequestering toxin in the bloodstream, is that it may augment distribution of the toxin to fat soluble tissues rather than biologically active sites, i.e. so the toxin is not trapped in the circulation but it is instead taken up by tissues in which it is not biologically active.

Improved cardiac performance:

The beneficial effects of ILE therapy may be linked to improvements in cardiac function through either the direct benefit (e.g. utilisation of free fatty acids as an energy source by the myocardium, an increase in intracellular calcium) of lipids on the myocardium or the reversal of cardiovascular dysfunction caused by the specific toxicant.

Veterinary indications

ILE has been used as an antidote in human medicine for actually quite some time – maybe 15 years or so – but it is definitely true to say that it took some time to gain wider recognition. One of the issues that is often discussed when it comes to medical practice is the so-called 'knowledge translation gap'. What this means is that people start reporting a potentially new and even game-changing therapy but it can take quite some time, often years, before this therapy becomes part of the practice of clinicians on a widespread basis. And this relates to issues of delays in publication, access to publications and so on; on the plus side with the increasing use of social media and free open access education there are definitely moves towards cutting the delay in knowledge translation.

In humans ILE was first used for treating local anaesthetic systemic toxicity and that is the most established of its uses. And in fact there are societies and bodies such as the American Society of

Regional Anaesthesia that have produced guidelines for the use of ILE in LAST. And then ILE started to be used for other intoxications – mostly drug-related but not exclusively. What is interesting is that somewhat unusually nowadays intravenous lipid emulsion as an antidote has not undergone the sorts of phased clinical trials that maybe we would have expected it to. If we look at the published literature in human medicine it is surprising to see how little there is relatively speaking. Although this is speeding up a little at the moment in 2014 there are no prospective randomised controlled trials looking at the use of ILE as an antidote and there certainly aren't any metanalyses or systematic reviews. We are basically talking about a number of case reports and last year (2014) a case series of 48 cases from the Lipid Registry was reported.

So what about the veterinary literature? If you research the veterinary literature you will find around 14 case reports or series with the first published in 2009; there is also a large retrospective case series of baclofen poisoning in dogs and cats in which the use of ILE is mentioned for some of the cases. And then there are three clinical practice review-type articles.

Now again as with the human literature all of the veterinary studies are single case reports or very small series and the vast majority are retrospective in nature. There are no powered prospective randomised controlled trials. There are certainly issues that we have to be aware of in terms of generalising case report data to all our patients. Also there is this concept of publication bias where people are less inclined to report, and especially journals are less inclined to publish, cases in which a positive effect is not seen, i.e. negative cases. In the human literature on ILE, reports of successful outcome significantly outweigh those of treatment failure. And perhaps all one can really say is that there is a view that ILE is associated with improvement in some cases without establishing this as a causal relationship.

Many reports discussing the use of ILE as an antidote still refer to it as an 'experimental' therapy. And the reason for this is that there has been no "proper" phased clinical introduction and evaluation. Having said that in veterinary medicine ILE is so not alone in that regard and we don't persist in referring to the myriad other drugs that we use without a proper clinical basis as experimental!

LAST is relatively rare in veterinary patients but ILE should be used in the treatment of cases in which it occurs. In veterinary medicine, ILE is generally considered in the treatment of toxins with a high morbidity or known potential for mortality, especially if traditional therapies are proving to have limited efficacy or are cost prohibitive – the latter can often prompt requests for euthanasia. ILE can have adverse effects (see below); however it is relatively safe and it is typically used when the risk-benefit assessment falls on the side of potential benefit being greater than potential risk. Response to treatment can vary from no apparent efficacy through to complete resolution of clinical signs and the lipid solubility of the toxin in question is thought to be a major factor in determining efficacy. Anecdotal reports of successful use of ILE in the management of veterinary patients are becoming more commonplace, but until controlled clinical studies are published caution should be taken to avoid viewing ILE as a "silver bullet" with guaranteed results and to remember that essentially it is still an experimental therapy.

Toxins for which ILE is currently recommended to be considered include:

- Baclofen
- Macrocyclic lactones (e.g. ivermectin, moxidectin, milbemycin; out of interest, moxidectin is reported to be 100 times more lipophilic than ivermectin)
- Metaldehyde
- Pyrethrins
- Beta-blockers (especially the more lipophilic ones such as propanolol)Calcium channel blockers
- Cyclobenzaprine (a human muscle relaxant)
- Local anaesthetics
- Psychotropics (selective serotonin reuptake inhibitors (SSRIs), selective serotonin and norepinephrine reuptake inhibitors (SSNRIs), cyclic antidepressants)
- Ibuprofen? (single case report in 2014)*
- Tramadol?

There are also anecdotal reports of its use for e.g. tremorgenic mycotoxins, strychnine. It is notable that a lot of the drugs/toxins for which ILE has been used are ones that cause neuromuscular signs or haemodynamic compromise as part of their toxidrome. It is likely that in time this list will grow as more evidence is acquired. As always, prior initial stabilisation of the patient if possible is essential, especially with respect to cardiovascular status, and ILE should be considered supplementary to, rather than a substitute for, traditional therapies.

(* There is thus far a single case report published of a dog that had ingested a very large amount of ibuprofen that had resulted in severe neurological and some haemodynamic compromise as can occur with NSAIDs in very high overdoses. The dog reportedly started to improve three hours after ILE administration and went on to make a full recovery. Furthermore plasma ibuprofen levels were measured before and after ILE administration; a high toxic level was detected prior to ILE that had reduced to zero after ILE administration; there is no mention in the paper about any interference ILE-induced lipaemia could have on this analysis. Potentially at this time it may not be a case of using ILE in every case of NSAID intoxication as standard therapies usually result in a successful outcome, but reserving ILE for the more extreme cases?)

Dosing guidelines

At this time ILE is used off-label in veterinary patients and much information has been extrapolated from use in human medicine. Optimal treatment protocols will likely vary between toxins and possibly species; however, currently this information is not available. Several different ILE infusion protocols have been published all using 20% lipid solutions; there have been no safety studies evaluating the use of ILE in the clinically poisoned veterinary patient, and careful monitoring and risk assessment is important.

Protocol using Intralipid 20%:

- Administer 1.5 ml/kg as a slow IV bolus over 2-3 minutes; follow with CRI 0.25 ml/kg/min for 30-60 minutes
- Monitor serum every 2 hours
- If patient remains symptomatic:
    - Can repeat bolus and infusion dose as above when serum becomes clear (non-lipaemic)
        - If no improvement after 3 doses (bolus + infusion), discontinue ILE treatment
    - Do not repeat ILE if serum is very orange or yellow
- Monitor patient until clinical signs resolved and serum no longer lipaemic in case signs return once the lipid has been metabolised

As commercially available ILE preparations are isotonic, they can be safely administered through a peripheral intravenous catheter.
Although relatively large volumes of ILE are given in a short space of time, it is worth noting that the total amount of lipid infused per 24 hours in toxicological applications is still lower than the maximal amount recommended for parenteral nutrition administration.

Usage guidelines

Unopened ILE is generally stored at room temperature and an unopened container will have a shelf life of up to 2 years. Specific indications for storage vary depending on the manufacturer, type of emulsion, and packaging. When using these products, strict aseptic techniques are imperative to prevent risk of bacterial contamination of the ILE, resulting in potential bacteraemia, but also destabilisation of the emulsion. Preparations should not be used after their shelf-life has expired.

Once opened and/or mixed with other fluids, ILE should be refrigerated between uses and used within 24 hours. If prolonged therapy (> 24 hours) is required, a new bag or vial must be used.

There is also some evidence – experimental at the time of writing (Nov 2014) – that ILE can be administered intraosseously to good clinical effect.

Adverse effects

Hypertriglyceridaemia and lipaemia are unavoidable, but typically transient and inconsequential, developments with the use of ILE. ILE has a high safety margin; adverse effects are uncommon but may be caused by contamination of the lipid product or direct reaction to the emulsion. There are very few reports thus far in clinical patients. The choice between potential or theoretical adverse side effects of ILE versus consequences of an unsuccessful resuscitation is clear. Obviously, ILE should be considered on a case-by-case basis including a careful assessment of risk versus benefit. Nevertheless caution should be exercised in estimates of safety based on low overall numbers. Serious adverse events with any drug therapy may be rare and require many thousands of administrations to identify an effect which holds clinical significance.

Contamination:

As ILE preparations are rich in nutrients contamination is a concern although this is less when they are used in isolation as opposed to in total parental nutrition formulations. Contamination may occur due to poor handling and aseptic technique and may result in local or systemic infection.

Direct reaction:

Direct reactions to ILE are reportedly rare but may be acute (anaphylactoid hypersensitivity reaction) or delayed/sub-acute ('fat overload syndrome'); the latter is usually the result of the administration of excessive volumes or high administration rates overwhelming the endogenous lipid clearance mechanisms. In people, FOS can result in fat embolism, hyperlipidaemia, hepatomegaly, icterus, splenomegaly, thrombocytopenia, increased clotting times and haemolysis; no information is currently available from veterinary patients apart from one report of presumed ILE-induced haemolysis in a dog that recovered fully with appropriate management.

Other potential adverse effects:

Other potential adverse effects, including pancreatitis, are possible but it should be stressed that in general adverse effects to ILE therapy are considered rare; with respect to pancreatitis a possible increase in serum amylase may occur following ILE administration but this finding should not be equated with pancreatitis and the diagnosis should be made by other better means. Currently there are no published reports of this but the potential for ILE to 'trap' drugs (e.g. anticonvulsants) being used therapeutically must be borne in mind and may be suspected if clinical deterioration is associated with ILE administration. ILE-induced lipaemia may interfere with laboratory tests and ILE causes false elevations in blood glucose concentrations with certain glucose analysers. Although the impact of ILE use on laboratory analysis is often listed as a 'complication' the author would not necessarily label it in this way; it is an undesirable consequence of the use of ILE that can potentially have clinically significant consequences in the management of some patients, but perhaps not a 'complication' per se. There is some discrepant evidence but ultracentrifugation of blood samples may allow laboratory tests to be performed after ILE use. In human medicine there are a very small number of case reports in which the use of ILE and the development of acute respiratory distress syndrome (ARDS) has been temporarily associated but of course this does not mean that ILE use caused the ARDS, i.e. association is not the same as causation. Concern has recently been raised that increasing blood carriage capacity for toxin in the absorptive phase of intoxication with early administration of ILE might increase absorption from the gastrointestinal tract paradoxically increasing intoxication; again this remains speculative at this time. In 2014 two cases of asystole that developed very soon after ILE administration were reported but again it was impossible to attribute causation rather than temporal association to these scenarios, i.e. did ILE administration cause the asystole or was it coincidence in patients that were clearly very sick. In both

cases spontaneous circulation returned within a few minutes of asystole with CPR (although both patients died subsequently in hospital).

A 20% lipid emulsion is preferred over the 10% lipid emulsion due to the higher proportion of free phospholipid available in the 10% formulation. Free phospholipids are thought to increase the potential for adverse effects due to their interference with lipoprotein lipase activity, which decreases ILE clearance. Large volumes of lipid emulsion are required for effective treatment. Propofol is therefore not recommended for use as an ILE formulation due to the high amounts of anesthetic that would be delivered with its lipid emulsion vehicle

Interested individuals can explore the use of lipid emulsion therapy further here: http://www.lipidrescue.org/

Neuromuscular toxins

Metaldehyde (Slug bait)

Metaldehyde is a cyclic tetramer of acetaldehyde that is commonly used as a pesticide against slugs and snails (molluscicide). Commercial pellet preparations usually contain 1.5-8% metaldehyde w/w in a cereal base. The pellets are often blue or green in colour and the cereals and other additives make slug/snail baits palatable to dogs. Cats as usual are more discerning and metaldehyde poisoning has only been reported in a few cases; the information provided in these notes is essentially applicable to both species. Liquid preparations containing higher concentrations of metaldehyde are also available as are granular and powdered preparations. Metaldehyde baits sometimes contain additional herbicides and pesticides, most commonly carbamate insecticides. Metaldehyde may also be found in fuel packs for camping stoves.

Toxic dose

A fatal oral dosage of metaldehyde in dogs of 60 mg/kg body weight has been reported although some authors quote much higher values. Clinical signs may be expected to occur at a range of typically much lower dosages. A lethal dose of 207 mg/kg has been reported in cats. As always, check with poisons information resources for the most recent information.

Toxicokinetics

Metaldehyde may be absorbed intact from the gastrointestinal tract but its subsequent distribution, metabolism and excretion remain to be fully clarified. Acid hydrolysis occurs in the stomach producing acetaldehyde which is then absorbed rapidly and converted to carbon dioxide (probably eliminated via the lungs) or excreted in urine. The half-life of metaldehyde in people is estimated at approximately 27 hours but is unknown in dogs.

Mechanism of toxicity

The precise mechanism of toxicity of metaldehyde remains to be elucidated but it is known to readily cross the blood-brain barrier and impairment of GABA activity is currently thought to be most implicated. As GABA is an inhibitory neurotransmitter a decrease in its activity may be responsible for the increased neurological activity seen in metaldehyde poisoning. A decrease in the concentration of other neurotransmitters in the central nervous system, such as serotonin (5-HT) and noradrenaline, may also be involved.

Clinical signs

Clinical signs due to metaldehyde poisoning often occur quickly (e.g. within 30-60 minutes of ingestion) but may take up to several hours to appear. The typical presentation involves central nervous system and muscular signs including twitching, tremors, muscle spasms and hyperaesthesia, with opisthotonos and seizures (including status epilepticus) being seen in severe cases. Hyperthermia is frequently identified in metaldehyde poisoning and presumed to occur due to the marked neuromuscular activity (hence it is sometimes referred to as the 'shake and bake syndrome'). Hyperthermia may contribute significantly to the pathophysiology and clinical presentation.

Case management

As above under 'Initial stabilisation – treatment of seizures and muscle tremors'.

It is important to check blood glucose concentration in any animal presenting with central neurological signs. In metaldehyde poisoning, normo-, hyper- or hypoglycaemia (typically only mild) may be seen.
Likewise excluding sodium and calcium abnormalities in particular may be appropriate according to the patient's history.
Hyperlactataemia may be present and is most likely to be due to extreme muscle activity (relative oxygen deficiency) rather than hypoperfusion (absolute oxygen deficiency).
A minimum emergency database should be performed at the appropriate time.

Treatment of metaldehyde poisoning should always be instituted as early as possible and should be aggressive. A conservative approach in a dog with severe neurological signs may result in preventable irreversible brain injury and potentially respiratory failure. **Induction of emesis is only appropriate in asymptomatic animals and *dogs showing neuromuscular signs should be fully anaesthetised and subjected to thorough gastric and colorectal lavage* including activated charcoal deposition**.

External stimulation should be kept to a minimum (e.g. cotton wool balls/swabs in the ears, dim lighting, minimise noise and passage of personnel). Fluid therapy and appropriate nursing measures should be instituted throughout.

Metaldehyde is lipid soluble and it is probable that intravenous lipid emulsion (e.g. Intralipid®) therapy has a role to play in treating these patients. Limited anecdotal experience support this suggestion although at the time of writing, to the author's knowledge, there is no published information in either experimental or clinical settings in human or veterinary medicine. The prognosis for metaldehyde poisoning with standard treatment is good and survival rates are high. As there is currently no published evidence that ILE therapy is effective in metaldehyde poisoning, it can be argued that its use at this time is probably best reserved for cases where either euthanasia on financial grounds seems increasingly likely, i.e. due to on-going costs associated with standard treatment, or where clinical signs are really very severe. ILE therapy is generally considered to be safe with little risk but there are potential adverse effects and as such a risk-benefit assessment is always indicated for what is still considered an 'experimental' treatment. The author has a special interest in ILE therapy and takes a more liberal view to its use in metaldehyde poisoning.

Clinical signs may persist for 24 hours or more; usually less than 48 hours. The prognosis for full recovery is good and survival rates are very high for animals that receive prompt and aggressive management and survive the initial 24-hour period following intoxication. Dogs recovering from severe metaldehyde intoxication may very occasionally have temporary blindness and liver failure is a serious but very infrequently reported delayed (2-3 days) development.

Pyrethrins/Pyrethroids

Sources

Pyrethrins are naturally occurring insecticidal esters of chrysanthemic acid and pyrethric acid extracted from the *Chrysanthemum cinerariaefolium* plant; pyrethroids (e.g. permethrin) are synthetic pyrethrins. Many topical and household insecticidal preparations containing these compounds are marketed for the control of flea and lice infestations amongst others in dogs and cats. These preparations are widely available from a variety of outlets.

Synthetic pyrethroid insecticides are now most commonly used in small animal patients as topical spot-on formulations and the accidental or misguided inappropriate use of canine products on cats is the most commonly encountered cause of poisoning. In addition cats may directly contact or lick the product once applied to a dog in the household including from the dog's bedding.

Toxic dose

The toxic dose for permethrin in cats is unknown. Dermal application of 100 mg/kg permethrin may prove life-threatening if untreated. As always, check with poisons information resources for the most recent information.

Mechanism of toxicity

Pyrethrins and pyrethroids alter the kinetics of neuronal sodium channels causing repeated nerve firing. In addition some of these compounds may also inhibit gamma aminobutyric acid (GABA) receptors resulting in hyperexcitability of nervous tissue. Hepatic glucuronidation is one pathway involved in the metabolism of some of these compounds and glucuronyl transferase deficiency and therefore more inefficient glucuronide conjugation may be part of the explanation for the apparent sensitivity of cats to pyrethroids, i.e. as they have slower excretion of and therefore more prolonged exposure to accumulating metabolites.

Oral exposure

Oral exposure should be treated by gastrointestinal decontamination if appropriate, including activated charcoal if patient compliance allows. Pyrethrins and pyrethroids are highly fat soluble and low fat foods should therefore be fed in the short-term to reduce further absorption.

Clinical signs

Clinical signs usually develop within a few hours of exposure but can be more delayed. Minor and usually self-limiting signs include hyperaesthesia, hypersalivation, ataxia, mydriasis, paw flicking and ear twitching. These signs may be accompanied by other non-specific signs such as lethargy or transient vomiting and diarrhoea. Severe neurotoxicity resulting from excessive exposure may result in marked depression, ataxia, potentially violent muscle tremors, seizures and death. Protracted gastrointestinal signs may also occur.

Treatment

No specific antidote and management is as above under 'Initial stabilisation – treatment of seizures and muscle tremors'
Topical decontamination (mild detergent + lukewarm water)
Methocarbamol

It is important to check blood glucose concentration in any animal presenting with central neurological signs. Likewise excluding sodium and calcium abnormalities in particular may be appropriate according to the patient's history.
Hyperlactataemia may be present and is most likely to be due to extreme muscle activity (relative oxygen deficiency) rather than hypoperfusion (absolute oxygen deficiency).

A minimum emergency database should be performed at the appropriate time.
Active cooling may be needed initially but bear in mind that temperature will fall with control of signs, washing and sedation/general anaesthesia – it does not usually take much to make a cat hypothermic!

External stimulation should be kept to a minimum (e.g. cotton wool balls/swabs in the ears, dim lighting, minimise noise and passage of personnel). Fluid therapy and appropriate nursing measures should be instituted throughout.

Pyrethrins and pyrethroids are highly fat soluble and there is increasing evidence, both published and anecdotal, that intravenous lipid emulsion (e.g. Intralipid®) therapy has a beneficial role to play in treating these patients. The prognosis for this type of poisoning with standard treatment is reasonable and some would argue that the use of ILE at this time may therefore be best reserved for cases where either euthanasia on financial grounds seems increasingly likely, i.e. due to on-going costs associated with standard treatment, or where clinical signs are (very) severe. ILE therapy is generally considered to be safe with little risk but there are potential adverse effects and as such a risk-benefit assessment is always indicated for what is still considered an 'experimental' treatment. The author has a special interest in ILE therapy and takes a more liberal view to its use in pyrethrin/pyrethroid toxicity but would not recommend its use for example in mild cases expected to be self-limiting with little need of any kind of medical therapy.

Prognosis

The prognosis for full recovery is reasonable despite severe poisoning in animals receiving early and appropriately aggressive intervention; neurotoxicity is fully reversible. In severe cases clinical signs may take 72 hours or more to resolve.

Avermectins and Milbemycins (Macrocyclic lactones)

The macrocyclic lactones (macrolides) include 2 groups, avermectins and milbemycins:

- Avermectins include ivermectin and selamectin
- Milbemycins include moxidectin and milbemycin

These structurally similar compounds are derived from natural compounds produced by soil-dwelling fungi from the genus *Streptomyces.*

Sources

Macrocyclic lactones (MLs) are parasiticides able to kill a wide range of arthropods and nematodes. They are used in many species and found in a wide variety of parasiticide products including some oral and topical preparations used in companion animals. Dogs and cats may also be exposed to large animal products either accidentally or by intentional administration. Many formulations intended for large animals are concentrated so it is easy for accidental overdoses to occur. Many cases of ivermectin poisoning in dogs occur from the ingestion of equine products (usually spilled or dropped) or ingestion of manure from treated horses.

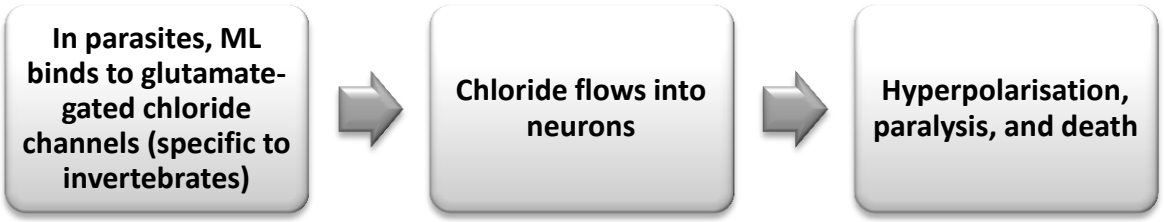
Toxic dose, Toxicokinetics, Mechanism of toxicity

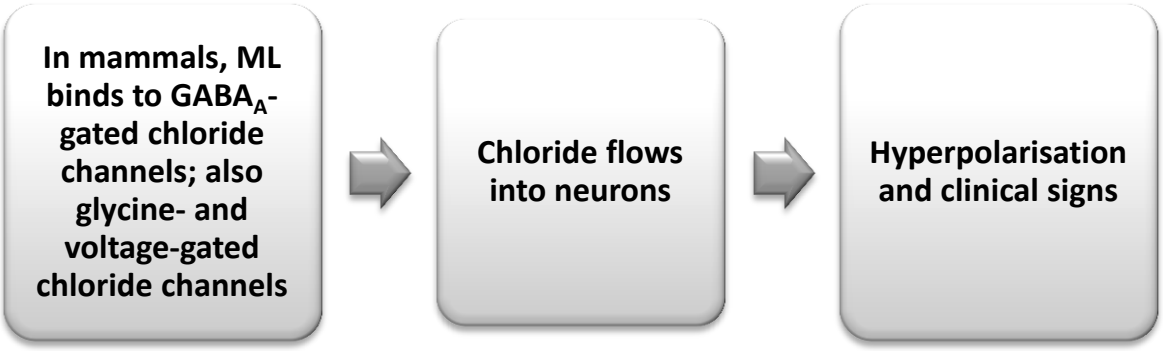
Reported toxic doses in dogs and cats following ORAL exposure:

Macrocyclic lactone	Acute toxic dose (mg/kg) following oral exposure		
	Normal dogs	**ML-sensitive dogs**	**Cats**
Moxidectin	1.9-2.8	1.0	1.0
Selamectin	None found	5.0	None found
Ivermectin	0.2-2.5	0.1-0.4	None found

One main mechanism by which the MLs exert their effect is by binding ligand-gated chloride channels. Binding of glutamate-gated chloride channels, which are specific to invertebrates, causes influx of chloride ions into the parasite neurons leading to hyperpolarization, paralysis, and death.

In mammals, MLs bind to gamma-aminobutyric acid type A–gated chloride channels ($GABA_A$ receptors). GABA is the primary inhibitory neurotransmitter in the brain, and postsynaptic binding of GABA to its receptors serves to modulate firing of excitatory neurons, such as glutamatergic neurons. MLs are believed to bind $GABA_A$ receptors at sites different than those where GABA, benzodiazepines or barbiturates bind. Because $GABA_A$ receptors are only present in the CNS, binding of MLs is prevented by the blood-brain barrier (BBB). However, in overdoses, enough ML permeates the BBB that binding to $GABA_A$ receptors, as well as to glycine- and voltage-gated chloride channels, occurs. Subsequent chloride influx causes hyperpolarisation and decreased firing of the excitatory neurons that express these chloride receptors and channels, leading to clinical signs.





In general, the MLs have relatively fast oral absorption. They also are all highly fat soluble, have a large volume of distribution, and accumulate in fat tissue resulting in a long elimination half-life. Specific information about metabolism and amounts of drug or metabolites eliminated in bile and urine in the dog or cat is lacking at this time. Enterohepatic circulation probably occurs for at least some MLs. Bear in

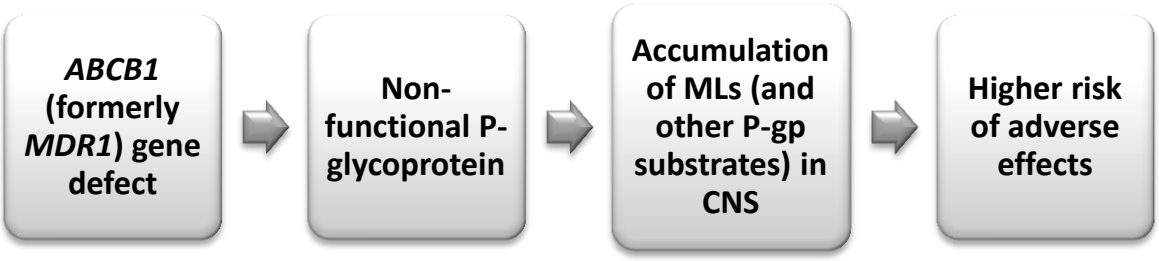
mind that differences in product formulation can alter pharmacokinetic parameters significantly even for the same agent.

Role of P-Glycoprotein:

Permeability glycoprotein (P-gp) is a transmembrane efflux protein that influences the pharmacokinetics of many of its substrates, including MLs, by actively transporting absorbed substrates back across a variety of cell membranes in the body. It essentially has a protective function because it limits entry of substrates into internal compartments. P-gp is a component of the BBB and is important in limiting the entry of MLs and other xenobiotics into the CNS.

Dogs of certain breeds and mixtures of those breeds have a defect in the *ABCB1* gene (formerly *MDR1* gene) that codes for P-gp and this defect results in production of non-functional P-gp. A lack of functional P-gp leads to accumulation of the MLs in the central nervous system (CNS) and a higher risk of adverse effects when exposed. Lack of functional P-gp may also affect ML pharmacokinetics in other ways that are as yet poorly studied.

The *ABCB1* gene mutation is typically seen in herding type breeds, primarily collies as well as Shetland sheepdogs and Australian shepherds; in addition, it has been detected in longhaired whippets, old English sheepdogs, silken windhounds, white Swiss shepherds, German shepherds, and some mixes of these breeds. Dogs can be easily tested for the gene defect.



Clinical signs

Signs of intoxication with MLs generally are related to the central nervous system secondary to enhanced neuronal inhibition and onset is typically within a few (e.g. eight) hours; can take as little as 2 hours or as long as 12 hours. Neurological depression, ataxia, mydriasis, blindness, tremors, and hypersalivation all may be seen and, as signs progress, an animal may become comatose. Confusion, agitation, hyperaesthesia and hyperthermia are possible and seizures may also occur. The blindness is typically temporary and has been associated with retinal oedema and electroretinogram abnormalities in the case of ivermectin.

The signs seen are similar in both dogs and cats for all the MLs. Depending on the dose and the breed involved and due to the long half-life of these agents, toxicosis may persist for days to weeks.

Treatment

There are no specific antidotes for ML toxicosis. Appropriate decontamination and good supportive care are the cornerstones of treatment. Some patients need to be hospitalised for several days or longer, so it is important that animal owners are advised up front regarding this possibility. However, with commitment to treatment, it is possible for even severely affected animals to make a complete recovery.

Gastrointestinal decontamination:

Gastric emptying is indicated if oral exposure was within an appropriate timeframe (e.g. 2 hours). Inducing emesis may be considered if the animal is asymptomatic, otherwise consider gastric lavage. Although the efficacy of activated charcoal in treating overdoses of MLs has not been established an initial dose is likely to be of benefit if given within the first 4 hours of ingestion given what is known regarding the absorption rate of MLs. Since there is evidence that MLs are enterohepatically circulated, it is reasonable to consider repeated doses of activated charcoal in small animal patients regardless of the route of exposure.

Symptomatic and supportive care:

Fluid therapy, good nursing care of the recumbent animal, and thermoregulation are essential for these patients. If respiratory depression develops, patients may require oxygen supplementation, intubation, and positive pressure ventilation. Nutritional support may also be needed. If bradycardia develops, a low dose of atropine or glycopyrrolate may be given.

Treatment of tremors or seizures resulting from ML toxicosis is a controversial topic, with the uncertainty of which drugs to use being the main question and the debate centring on both the binding of different agents to the GABA receptor, where on this receptor each agent binds, and how binding of one agent versus another may affect ML-induced toxicity. A number of resources suggest that benzodiazepines and perhaps barbiturates should not be used in the treatment of ML toxicosis due to the potential to worsen clinical signs. But this recommendation is based on limited theoretical information without a supportive clinical evidence base. [While benzodiazepines such as diazepam can potentiate GABAergic effects so can barbiturates and propofol which both bind $GABA_A$ receptors albeit at different sites than benzodiazepines and MLs. The present state of knowledge is that there are several different binding sites on $GABA_A$ receptors each of which binds different types of xenobiotics. The different binding sites interact allosterically with binding of a compound to one site influencing the likelihood of different compounds binding to other sites — all of which then influence opening of the channel in the receptor and subsequent chloride influx. Assessment of allosteric relationships in the $GABA_A$ receptor can be very challenging and the relationships between MLs and drugs that bind $GABA_A$ receptors have not been well investigated. Until these allosteric relationships are better established…] it is the author's opinion that diazepam, barbiturates, or propfolol may be cautiously used to attempt to control tremors or seizures.

Intravenous lipid emulsion:

Intravenous lipid emulsion therapy has been suggested to be a treatment that may shorten the duration of clinical signs of ML toxicosis and there are a small number of individual case reports that may support this notion. All of the MLs are lipophilic so lipid therapy is potentially beneficial in treating toxicity from any of the avermectins or milbemycins. Moxidectin is likely the best candidate for this therapy due to its very high lipid solubility. The effectiveness and safety of this treatment in reducing the duration of clinical signs or improving outcome with acute toxicosis in clinical patients has not been proven in human or veterinary patients but clinically significant adverse effects are currently considered to be very uncommon with ILE therapy and the risk-benefit assessment seems to fall on the side of potentially significant benefit with comparatively little risk. As mentioned above, some cases of macrolide poisoning can persist for lengthy periods of time and any therapy that may potentially minimise the chances of severe intoxication seems worthy of consideration. As such ILE therapy is recommended in patients with severe signs (e.g. severe stupor/coma, seizures) of ML intoxication.

Assuming ILE is effective in the treatment of ML toxicosis it theoretically may be less effective in dogs with a lack of functional P-gp, e.g. these dogs may have higher CNS levels of the ML and/or impaired elimination of the ML from the CNS due to non-functional P-gp.

Prognosis

The prognosis may be guarded to good depending on the exposure dose and agent involved. Severely affected dogs may require long-term care, which may be a financial burden for some owners. Depending on the dose and half-life of agent involved, recovery can take days to weeks. After recovery, long-term sequelae are not expected. Sedation and blindness seem to the longest lasting signs, but even blindness is not expected to be permanent as most dogs seem to recover visual ability.

Chocolate

A 3-year old Shih Tzu has eaten some dark chocolate 2 hours before presentation. On presentation he appears restless and excitable and on cardiovascular examination he has tachycardia above 200 bpm with peripheral pulse deficits; he vomited during the initial examination. What should you do?

A. Administer aggressive isotonic crystalloid fluid therapy as he must be in hypovolaemic shock
B. Perform an ECG as chocolate toxicity can cause dysrhythmias which must be characterised before treatment can be considered
C. Induce emesis

The correct answer is B. The dog's tachycardia with pulse deficits is most likely related to a theobromine-induced dysrhythmia and aggressive fluid therapy is not indicated in such cases. Induction of emesis is not necessary as the dog is already vomiting and may also not be advisable as he is restless and excitable which may increase the risk of aspiration.

Theobromine is a methylxanthine-derived alkaloid occurring naturally in cacao beans and found in chocolate, cocoa powder and other products produced from these beans. In addition chocolate contains a lesser amount of caffeine, also a methylxanthine.

The concentration of theobromine varies in different sources: plain (dark) chocolate and cooking chocolate generally containing significantly more than milk chocolate. The theobromine content of white chocolate is considerably lower. Cocoa beans, cocoa powder and cocoa shell mulches contain the highest concentrations of theobromine. The literature contains reports of death in dogs following consumption of chocolate, cocoa powder, cacao bean shells and cocoa bean mulch.

It is also important to remember that the theobromine concentration can vary even within types, e.g. the milk chocolate in one product could contain more or less theobromine than the milk chocolate in another product. Furthermore chocolate products may contain other toxic components such as raisins, peanuts, coffee beans or xylitol.

Toxic dose, Toxicokinetics

Fatal doses of theobromine in dogs are reported to be in the range of 90-300 mg/kg and in cats 80-200 mg/kg. It may be difficult to actually establish theobromine exposure and calculations are usually done on the basis of weight of chocolate product rather than theobromine itself. One recommendation is to perform gastrointestinal decontamination if the patient has ingested:

- More than 9 grams of milk chocolate/kg
- More than 1.25 grams of dark chocolate/kg

The following online interactive chart may prove very helpful in decision-making with these cases; the source of the information is quoted as the ASPCA but note that the author has not meticulously validated its accuracy using other references (!):

http://ngm.nationalgeographic.com/2007/10/pets/chocolate-chart-interactive

Absorption of theobromine from the gastrointestinal tract is relatively slower in dogs compared to people with complete absorption potentially taking up to 10 hours. Metabolism is primarily hepatic and enterohepatic circulation occurs. Excretion is considerably slower than in people. As always, check with poisons information resources for the most recent information.

Mechanism of toxicity

Methylxanthines inhibit cyclic nucleotide phosphodiesterases and also act as adenosine receptor antagonists. As with other methylxanthines, theobromine (and caffeine) causes central nervous system stimulation with consequent cardiac and respiratory effects. It directly stimulates the myocardium and skeletal muscle causing increased contractility (by inhibiting cellular calcium reuptake) and competitively inhibits cerebral benzodiazepine receptors. Theobromine also causes smooth muscle relaxation, especially of the bronchi, and renal diuresis.

Clinical signs

Clinical signs usually develop within 24 hours of ingestion and typically much sooner – within 4 hours. Signs may persist for 48-72 hours in some cases. Commonly reported clinical signs include vomiting, abdominal discomfort, restlessness, excitability and hyperactivity, ataxia, tachycardia, and tachypnoea or panting. In more severe cases muscle rigidity, muscle tremors, hyperthermia, seizures and dysrhythmias have been reported. Urinary incontinence, polyuria and polydipsia may also occur. Severe seizures and/or cardiovascular compromise are typically reported in fatal cases.

An **emergency database** including electrocardiogram is recommended.

Treatment

Routine GID is indicated in appropriate cases. As theobromine is absorbed slowly in dogs induction of emesis may be appropriate even after a significant delay; however it is best avoided in animals that are very hyperactive/showing neurological compromise. Theobromine undergoes enterohepatic circulation so repeated use of charcoal may enhance elimination. There is no specific antidote for theobromine poisoning and therapy is otherwise symptomatic and supportive. This may include intravenous fluid therapy, anti-emetic administration, sedation if excitability is excessive, and routine treatment of seizures.

Anti-dysrhythmic therapy may also be indicated in some cases. Severe or prolonged sinus tachycardia may be treated with an injectable beta-blocker if available. Lidocaine should be used if clinically significant ventricular tachycardia develops and may also be tried if a supraventricular dysrhythmia is present and more traditional agents for SVT such as an injectable calcium channel blocker are not available.

Prognosis

Prognosis is generally good with appropriate treatment but may be worse for animals showing marked cardiovascular or neurological signs at presentation.

(Appendix 2) Inducing Emesis in Cats

This is a blog post written by the author in July 2014.

Cats do not tend to ingest poisons as often as dogs do, this we know, and therefore the scenario in which one may be considering inducing emesis in a cat is encountered less often. That said, the Veterinary Poisons Information Service (VPIS), based in the UK, gets more or less one telephone enquiry a day about a cat that has ingested a toxin (personal communication, 2014) so it is not totally unheard of! I am going to skip some of the other talking points about gastrointestinal decontamination, especially in cats, here and just consider the circumstance in which it has been decided to induce emesis in a cat. What are the options?

Before proceeding I would like to state two points in particular outright:

1. We need to set everything that follows in the context of evidence-based medicine principles and critique. It is clear that we are really scratching around here for evidence and such things as a number of prospective randomised controlled trials followed by systematic review/meta-analysis are extremely unlikely to ever be forthcoming.
2. By referencing experimental studies I do so to convey the available information without condoning them. This is not the place to have that debate but one point that must be borne in mind, and relates to point 1. above, is that the translatability of experimental studies on small populations of cats to decision-making for individual clinical patients needs to be kept in the forefront of our minds. Admittedly cats that have poisoned themselves and in whom emesis is being considered are typically healthy but nevertheless the point is salient.

Alpha$_2$-adrenergics

For many years it has been said that xylazine is the agent of choice for inducing emesis in cats. I have never personally used it but I have met people who have and they seem anecdotally to support the notion that it is effective There are some experimental reports looking at xylazine-induced emesis (e.g. Lucot, Crampton, 1986). Colby et al (1981) found a dose of xylazine of 0.66 mg/kg injected intramuscularly in normal cats caused vomiting in 20/21 cases; other doses have been reported too (e.g. 0.4-0.5 mg/kg). I also found the Moye, Pailet, Smith (1973) paper listed below but I cannot access it to see just how 'clinical' it really is. There are a number of papers you can find that study the anti-emetic effects of various agents or methods of neuroinhibition on cats that have been or are scheduled to be treated with xylazine to induce emesis. For example see Chiu-Ming Ho et al, 2001; Kolahian, Jarolmasjed, 2010; Kolahian, Jarolmasjed, 2012; there are quite a few others!

But it is not just xylazine. Other alpha$_2$-adrenergic agonists are reported to cause vomiting in cats. You can find papers where the potential for medetomidine and dexmedetomidine to cause emesis in cats is discussed/studied. For example see Santos et al (2011) in which dexmedetomidine was used at 40 µg/kg intramuscularly; there are other papers including reference to using medetomidine at 20 µg/kg.

Clearly the main clinical use of alpha$_2$-adrenergic agonists is as sedative agents with emesis typically occurring if it does as an unwanted side-effect. A sedate cat that vomits is at increased risk of aspiration, and moreover these agents can also cause potentially profound dose-dependent cardiorespiratory compromise. I am sure it must be quite distressing to be vomiting and nauseous when also in a state of sedation! So their use is far from ideal but anecdotally relatively reliable at inducing emesis and reversal agents do exist. Atipamezole is used for (dex)medetomidine. Yohimbine has traditionally been recommended for xylazine but availability is likely to be very limited nowadays; it is suggested that atipamezole may also reverse xylazine's effects but I am not sure whether there is any substantive evidence.

Xylazine is I think still used in larger species but with the increase in small animal-only practices worldwide the availability of xylazine is something we need to consider. I know some practices that stock it solely for inducing emesis in cats; I believe an open vial must be discarded after 28 days and in most cases this will mean discarding the vial after use in only one cat. Otherwise (dex)medetomidine is the option and widely available.

Apomorphine

But the question that always comes up is what about apomorphine – can we use it in cats? Is there evidence that it works for inducing emesis? What are the potential risks? What is the risk-benefit analysis and moreover how does it compare to using the agents mentioned above?

For as long as I can remember resources that I have come across have said that apomorphine should not be used in cats. Often they do not explain why or offer substantive references; however some reasons that I have occasionally read are that apomorphine is associated with more significant side-effects in cats, especially cardiovascular depression or sedation, or that it is ineffective. I spent some time seeing what I could find in the literature.

In Batchelor at al. (2013) it says “certain important differences exist between dogs, cats…For example, D2 dopamine receptors in the AP [area postrema, chemoreceptive area] are much less important in cats than in dogs, explaining the comparative resistance to apomorphine-induced vomiting in cats. In contrast, α2 adrenergic receptors are important in the areas of the cat brainstem controlling vomiting, explaining why the α2 agonist xylazine is an effective emetic agent in cats”. Unfortunately I cannot access the reference they cite in this paper to substantiate the idea that cats are comparatively resistant to apomorphine-induced vomiting.

In Graf et al (1979) it says in the abstract “among xylazine, ipecacuanha solution, apomorphine and copper sulphate, xylazine was the most reliable emetic (1 mg/kg body weight s/c). Apomorphine was unsuitable for cats in a dose of 10-20 mg because it produced excitement and seldom vomiting”. This is obviously a considerably higher dose than we would use clinically; a typical clinical dose range in dogs is 40-100 µg/kg but you will not find a dose range for cats listed in any/many resources. You can also come across papers where emesis is reported to have been induced in cats using apomorphine as part of experimental research; for example see Ognean (2000) or Boyd (1953) – in the latter it says in the abstract “an account of experiments which indicated that, in amounts corresponding to the usual human therapeutic doses, none of the antihistaminics tested-three diphenhydramine derivatives and prornethazine hydrochloride, methapyrilene hydrochloride, and methapyrilene-8-chlorotheophyllinate-prevented apomorphine-induced emesis in dogs and cats”. Unfortunately I cannot access these papers to review them especially with respect to what doses were used.

Apomorphine administered intravenously at a dose range which included at the very bottom end doses used clinically but also very high doses (10-750 µg/kg) reportedly produced a dose-dependent fall in mean systemic arterial blood pressure in cats; this was accompanied by marked bradycardia at the higher doses (500-750 µg/kg)(Ramirez, Enero, 1980). Similar findings were also reported in a later study (De Meyer, Buylaert, Bogaert, 1982) and there are others. However we must note that apomorphine administered intravenously at actually lower doses (1.25-20 µg/kg) than we would use clinically reportedly caused a dose-dependent decrease in blood pressure in dogs as well (Bogaert, Buylaert, Willems, 1978). Of course the relevance of such experimental studies in anaesthetised animals to conscious clinical patients is questionable; while both cohorts may typically be healthy, anaesthesia and anaesthetic drugs are clearly confounders to any reliable comparison before we even get into details about the animals being comparable etc.

At (much) higher doses that we would use clinically apomorphine has been reported to cause motor activity, including limb flicking for example, in experimental cats that may be due to a central dopamino-mimetic action of the drug. For example in one study doses of between 100-2000 µg/kg were used and

“apomorphine elicited limb flicking, dose-dependent hypermotility and increase in olfactory behavior, the last two reactions with stereotypy characteristics. The animals appeared as if being scared, hyperreacting to sudden stimuli and showing total indifference to the surrounding environment”(Motles, Martinez, Concha et al, 1989). Clearly the bottom end of this dose range is 5-10 times the starting doses we may use clinically. There are other similar papers reportedly showing similar things, i.e. motor activity and behavioural changes, but again at high doses sometimes given by routes we would not use clinically.

Naloxone is said to be able to reverse adverse effects of apomorphine without impairing its emetic effect. Again I am not aware of and have not had chance to investigate what evidence if any there is for this assertion but I am pretty sure it is based on the theory behind the mechanisms by which apomorphine induces emesis versus causes other side-effects (dopamine versus opiate effects etc.).

I should also mention at this point that I have again never personally tried this but soda crystals may be considered in cats. You will also find some people suggesting that hydrogen peroxide can be used; I personally do not like this idea in cats or dogs for that matter and again have never done it. I am not going to say any more about these substances here as this is already a long blog!

So what’s the bottom line?

Well, it is a good question. Clearly we would love for all this to be evaluated ‘properly’ and according to robust evidence-based medicine principles in clinical patients…but we must not hold our breaths! I have in the past used apomorphine in 3 cats at a dose of 20 µg/kg and emesis occurred in 2 of these cats. According to some of the material above, this makes little sense as this dose is half the dose I usually start with in dogs and cats are meant to be more resistant to apomorphine! The reason I chose this ‘lower than in dogs’ dose was due to the concerns that I had come across in resources about using apomorphine in cats. I have seen some cases in which medetomidine was used as 10-20 µg/kg and emesis occurred; but I have also seen cats become very sedated with nausea but no emesis. I must re-emphasise that we are talking about very small numbers of cats here.

Based on this present round of research I think I will be tempted to give the next cat in which I want to induce emesis apomorphine at an initial dose of 40 µg/kg and then decision make from there based on what occurs. Above there are some references to cats maybe being more resistant to the emetic effects of apomorphine than dogs but thus far I am struggling to find evidence of increased susceptibility to adverse effects, especially in the dose range that we would likely use clinically. While I continue to mull this over I would love to hear your experiences/thoughts/suggestions…

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