John Alexander, Editor
BACKGROUND
This overview has been generously prepared by Professor Rick Atwell at the invitation of the Veterinary Practitioners Board of NSW. The format of "questions and answers" will lead some overlap in the discussion under different topics. The Board would like to thank Professor Atwell most sincerely for the immense amount of information contained in this document attached. This discursive overview is not a complete revision of the disease but is written as an educational aid for veterinarians and nurses by the leading educationalist in this field, and may also be useful assisting with client education.

Some aspects of Tick Toxicity with regard to the current state of knowledge, and based on some on-going clinical problems as seen in general veterinary practice

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Summary
The progress of confirmed and suspected tick toxicity cases is rarely straightforward. Communication between the veterinarian and the client needs to be very clear and frequently updated to ensure the clinician's thoughts are conveyed and understood by the client. Correct words and simple practical terms need to be used when describing the disease, the prognosis and the costs for the complete treatment, to ensure there is no confusion in the owner's mind. If the probable diagnosis is made without the finding of a tick, the owner needs to know that the clinician has weighed up the clinical signs, season, geography, access, and has determined that this is the most probable diagnosis and treatment needs to be initiated as soon as possible. The specific treatment is tick antiserum.

Question 1

Are clinical signs of Tick Toxicity always "classical"?

While tick toxicity (TT) produces lower motor neurone (LMN) signs with ascending weakness/paresis, some clinical signs such as altered voice (meow or bark) and coughing/vomiting of 'sea foam' can be missed as important clues of TT. Not all animals will display all signs.

Early signs may include change or loss of voice (due to laryngeal paresis), hindlimb incoordination, change in breathing rate and effort, gagging or coughing, regurgitation or vomiting and pupillary dilation. Hind limb paralysis begins as slight to pronounced incoordination and weakness. As paralysis ascends, the animal becomes unable to move hindlimbs and forelimbs, stand, sit, or lift its head. Sensation usually is preserved. Breathing abnormality is of greater prognostic importance than limb paralysis. Respiratory rate may initially increase but, as the disease progresses, becomes slower and obviously labored, especially on expiration. Regurgitation of oesophageal contents, saliva pooling, depression of the gag reflex, and attempts to clear the throat may produce a characteristic harsh, groaning respiratory sound. Temperature is normal in the early stages. Paralyzed animals with low body mass (especially cats) may become hypothermic. Conversely, animals kept

at high ambient temperatures may need to cool themselves by panting, adding to respiratory difficulty.

Question 2.

Making the diagnosis.

A practitioner will make a diagnosis based on the highest probability taking into account the expression of clinical signs/season/geography and within the limitations posed by the experiences of the veterinarians, hospital facilities and financial constraints.

If you have an animal with voice changes (usually the most commonly unasked question of owners), and it is said to be 'off' and shows LMN signs then choices are simple, based on season, access and geography.

Simple Differential Diagnosis

- **Snake** – bleeding? access? area? season? short-term early signs? Paralysis and then longer onset of LMN, pupils usually dilated, no chest issues of the tick type;
- **Tick** – access? crater? season? travel? less pupil issues? no bleeding?
- **Ciguatera and toad fish** - beach access to rotting organic matter;
- **Organo-Phosphate** – access? availability? pinpoint pupils?
- **Botulism** – dogs, dead or paralysed, water bird access;
- **Other rare causes** - If the common differentials have been ruled out then you need to look into the more rare diseases

If you can't locate a tick (and mild LMN disease persists) and you feel it is a tick toxicity, I suggest you clip all over, especially the head and neck. A clipped-off tick and crater are very diagnostic.

The use of acaricidal washes and sprays in lieu of clipping is not an effective option as they take over 24 hours to kill ticks and no product will kill an attached tick. Bathing can also be a very stressful procedure when every effort must be made to avoid stress.

If severe LMN signs are present *and* no tick or crater can be found, *and* you have good three-way communication with the owner, *and* you have excluded snake and organophosphate on their lower probability, then proceed with tick antiserum (TAS) as soon as possible. This is after confirming cost and payment arrangements and ensuring that the owner knows an engorged tick has not been found.

Once TAS infusion is completed and, depending on how ill the animal is, clip if necessary in an attempt to locate tick (or crater), to confirm the diagnosis and to remove it or kill it *in situ*. Most dogs given TAS improve within 6 to 12 hours

Question 3

If I am not sure of my diagnosis will antisera do any harm?

Tick antiserum has no deleterious effects provided it is given under sterile conditions, and is given slowly to avoid any TAS reaction (seen in approximately 3% of dogs). Anaphylaxis is a rare occurrence and could theoretically occur with any animal. It is an unpredictable and individual event, both in severity, frequency and in outcome. If TT is the most probable cause of a LMN presentation at the time then there is no error in recommending treatment with antiserum.

Question 4

How to locate ticks and what to do when you find one.

It is best to locate ticks by finger walking, using both hands to walk eight fingers through the coat in a systematic coverage

of the animal. If you feel a lump, then part the coat and use your finger and thumbs to verify the 'invisible' tick. Take care with long-haired dogs and tan to brown coloured coats that disguise ticks so easily. With short-haired dogs you can use the palms of your hands to feel for lumps, going with the hair flow. Once felt you can sometimes see the raised hair-coat where before it was not obvious. Flicking the tick gently with your first finger is also a good way to verify viability, looking for leg movement etc.

Clipping has no outcome on survival but makes it easier to find the tick especially on the neck, ears and face. If TAS is in circulation any tick secretion is neutralized, so initially, in a high probability diagnosis, the tick location is less of a priority than TAS use.

Concentrate searching on shoulder, neck, ears, face and head. Over 80% of ticks are located forward of the forelegs (both in experimental 'pour-on' tick loading and in natural cases; AVJ 2001). Rarely a tick will be located in the ear canal, mouth, anus etc. Between the toes can also be a less common site.

Most dogs have only one tick (e.g. 500 cases averaged 1.1 ticks). Dogs and cats are not the natural hosts and most ticks fall off dogs when observed in containment pens with 'pour-on' tick loading. So the case you see may have had many ticks on it but only one has found it suitable to stay.

Ticks can fall onto hosts from higher branches and attach from lower vegetation e.g. at the end of grass/seed heads and can brush onto lower face, forelegs, depending on the size of the host and the head carriage at the time. Ticks can be blown with the wind and have been seen falling from considerable heights in native northern Qld vegetation. In crude ex-vivo experiments (using broom handles and regular inversion) ticks will continually move upwards (they have a gravity sensor) until they reach a cross branch or the end of the structure. If they follow a cross branch they then proceed to the end of that as well, thus helping to explain the location and the variable height of tick sources.

If a feeding tick detaches for example an unsuitable or dead host, it can reattach to another host or to another site. In experimental loadings this will usually be more caudal e.g. to axilla or to groin.

Ticks have no head, eyes, ears, face, nose etc. but have many sophisticated sensing systems (movement, CO_2, gravity) and are armed with many physiologically-active chemicals that preserve the feeding site (anti-clot, anti-platelet, analgesic, anti-inflammatory). Their feeding apparatuses are physically consistent with the fingernail material (keratin types most likely vary) and do not cause local tissue issues if left in the skin i.e. in the old crater. There is no need to remove 'the head', as is still propagated widely. In self-experiments (n=2), such material has slowly 'fallen out' from the crater leaving very normal skin.

However some people are extremely allergic to tick secretions and in these people great care must be taken as some outcomes are lethal. Even though it doesn't sound plausible, simple movement of the tick can be the instigator of a human allergic response. In such people, de-waxing the tick gently (see below) or cutting the body of the tick in half with scissors is the simplest solution, thus leaving the tick to degenerate. This information is based on repeated such therapy of a known allergic child.

When a client has located the tick(s) themselves prior to attending the vet hospital, if it is a very short trip it is best to leave tick in

place as most modern owners are reluctant to pluck a tick well, and it is better for you to see the tick *in situ.* (Merial 2008 data suggests that tick pluck at clinic or at house had no affect on outcome but distances to clinics and times involved were not recorded).

Ticks can be killed with any de-waxing agent e.g. methylated spirits, kerosene, turpentine, nail polish remover etc., causing acute dehydration and death (ticks are very susceptible to dehydration and to both very moist and dry conditions). There is no valid proof that ticks get irritated and secret more toxin with such a chemical death. Tick squeezing does not cause toxin secretion. Bursting the tick is another acceptable method to kill the tick in animals, as mouthparts do not cause an issue and the tick remnants will slowly be dislodged.

Tick hooks seem to be the most effective and their use, clockwise or anti-clockwise, has no difference on outcome (in older medical texts the tick had to be twisted one way only!). Based on the microanatomy of the tick it is far better to remove by twisting rather than by direct pulling. Twist and pull will disengage the barbs whereas direct pulling will often remove a plug of tissue and cause variable pain in different breeds or individuals. For example greyhounds perhaps because of thinner skin appear to feel more pain.

Question 5

Why is it so hard to detect some ticks?

Even when professional tick searchers (e.g. many tick trials) know exactly (e.g. by photographs) where a tick was loaded it can be incredibly hard to find some ticks. They can be flat, against the skin, under similar coloured hair and not yet engorged. For example a third day attached tick that is still up-regulating genes to feed and reproduce and has not started active feeding but has secreted some saliva (and therefore toxin), may be extremely difficult to locate. So if experienced tick loaders (e.g. 10 ticks/dog) and searchers (up to 32 dogs on days 1, 2, 3 and 4) find some ticks hard to locate, when they have a dog surface area map of where each tick is loaded, then it is understandable that one tick on a small number of in-practice animals maybe impossible to find. This is especially so when people are not experienced with a large tick caseload.

Question 6

The interplay of the tick and the use of Tick Antiserum (TAS)

Remember to give TAS asap, but this is not to say that the source of the toxin should not be removed whenever feasible. As TAS has a short clinically-effective half-life, believed to be a large antibody and removed by the normal processes of the host, an unidentified tick could in theory secrete beyond the half-life in a particular individual. It is not documented, but the half life of TAS is believed to be only days (not weeks) so a second dose of TAS may be considered in a non-responding proven TT case after 3 to 5 days of hospitalization (e.g. if the tick has not been located or there is a second identified tick; this does not refer to another tick which loaded after the animal had been discharged from the first tick intoxication). However this event is extremely rare as most ticks cause clinical signs 3 to 5 days after attachment. Slowly recovering animals are suffering the effects of bound toxin and are therefore not responsive to more TAS (*AVJ 2001*) either systemically or at the tick site.

Other *Ixodes sp* ticks take three days to progressively up-regulate their genes for saliva, gut enzymes, absorption and reproductive activity. In control conditions with 1 or 10 ticks per dog it is not until the tick is 4mm wide (measured laterally across the back of the tick) which usually happens

on the fourth day, or greater than 72 hours of attachment, correlating well with the original observations of clinical disease taking 3 to 5 days to occur.

Of course, with any biological interplay, there can be marked variability. Although these are often quoted they are in the minority. For example a dry climatic season and hot dry weather will reduce tick viability and very much slow down feeding behaviour and therefore the onset of clinical signs. Toxin is only secreted as saliva is produced prior to each blood feed, so the feeding frequency and not tick size or number determines the amount of toxin placed in the tick feeding site. In very viable seasons the toxin secretion rate will be higher and animals will be intoxicated more quickly, possibly shunting more toxin more rapidly into the peri-vascular or non-TAS effective zone, so progressing the clinical scores occurs more quickly than otherwise. So an NMJ (neuromuscular) score of 2 presented in the last hour may proceed to a score 3 more quickly than usual, upsetting any previous prognosis. The rate of toxin absorption cannot be determined, so it is unwise to presume that a clinical score will stay as it was particularly in the first six hours after presentation. Based on the wide variety of signs, chest complications, lack of an objective method to determine toxin or finite protective antibody levels, a guarded prognosis should always be given. Mortality up to 10% has been recorded in an up-to-date hospital, but individually it is either 0 or 100%. The 506 dog study by Merial in 2008 recorded a 6% mortality based on case data from 42 clinics from Cairns to Lakes Entrance.

So cases can deteriorate inexplicably and unpredictably and ticks can be hard to locate. Some 4 to 10% of dogs will die, most with lung disease (aspiration or pulmonary oedema) irrespective of the most up-to-date proven therapy, which is simply TAS and antibiotic therapy.

It is possible as a profession that we downgrade the fact that the tick produces a potentially lethal toxin, and we do not equate it as we would with another toxicity (e.g. Lead or Arsenic) where we more correctly presume and accept mortality. We cannot save every case; severe signs indicate a profound toxin load.

Question 7

Does the disease vary in different areas so clinicians see different presentations?

There is now good proof that TT varies with geographic areas i.e. different signs predominate; and between seasons (tick viability factors). They do vary within a season and data from one practice shows that the more severe cases are seen when the prevalence is the highest.

Simply put, when the ticks are most active and viable, access to the animal is the highest, local weather suits blood feeding (i.e. not too cold or hot) and the host is most susceptible, the most severe cases should present.

Your clinic may be different and it may draw cases from different environmentally tick-suitable areas i.e. each practice may have particular 'worst case' factors. Different areas may find that a combination of these factors may dominate and so different 'worse case weeks' appear at different times. For example access may be that people are walking dogs into bushy areas due to ideal local environmental factors, so access becomes the driving force for intoxication. Ticks may have been blown into yards that back onto a reserve and ticks have been seen to 'fall' from higher branches[1].

1. This is based on feedback from CE seminars and the March issue of Aust Vet Practitioner (2011) covers many of these unusual observations.

Ticks will be most toxic when they are young, in ideal weather conditions and are able to attach to a host they like and then feed well.

Over 90%[2] of ticks will leave dogs and cats if they are loaded on the dorsum of the animal. In TAS producing dogs, ticks more readily attach in such situations as the dogs have been selected for tick-holding capacity. If all is in favour they will stay, attach and intoxicate the animal, once past the gene up-regulation stage.

Single-organ TT can occur, for example CHF, pulmonary oedema, undiagnosed aspiration pneumonia, or just a local affect e.g. pupil-blink dysfunction of one eye. Oesophageal disease occurs in the majority of dogs but does not usually present as a mega-oesophagus case, that is, it is silently dilated. However it has been recorded as a single-organ TT in three dogs. Most dogs go home with an enlarged oesophagus (on X-rays) but do not develop disease. A stable sea-like foam presented (regurgitated/'vomited') in the cage or about the face is a strong indicator that this animal has oesophageal dysfunction. Usually the paws are also coated in slimy hair-matting material. Such a case has a high probability of a paralysed and enlarged oesophagus with retained saliva and foam production. Suction should be instigated and the animal positioned head right shoulder-high (if left lateral) or placed in a dorso-ventral propped position, all in an attempt to avoid laryngeal aspiration.

True vomiting with bile (i.e. from the small intestine) is usually associated with a more severe case and associated prognosis. It is sometimes hard to separate vomiting from regurgitation but using the sea-foam and yellow bile is a helpful approach. The cause of vomiting is unresolved in TT but could be associated with a direct effect of the toxin on gut motility and influencing the control of bacterial passage through the intestinal wall. (Retching can be simply attempting the clear material in the pharynx and larynx and should be recorded as such and not presumed to be vomiting or regurgitation until material is seen in the cage or on the dog. The URT will need to be cleared in such cases.)

Question 8

What are some unusual factors and associated clinical signs?

Tick toxicity (paralysis, poisoning) is a multi-organ disease but usually presents as a 'seen to be' ascending LMN disease occurring 3 to 5 days after tick attachment. There can be a wide variety of timings e.g. 8 days due to the particular feeding behaviour, type of host, cold weather etc. An altered voice is the first symptom that we can detect but the (subjective) gag reflex may not be as reliable as we think to gauge neuro-muscular/upper respiratory tract function. This was probably incorrectly extrapolated from human URT assessment procedures; (see Australian Veterinary Practitioner, Google 'gag reflex'). The tail function is usually the last to be lost but there is no published explanation for this late occurrence when the hind limbs are affected so early.

So summarizing-

- voice changes,
- hind leg weakness ranging to four-leg paralysis (NMJ scores 1 to 4), superimposed on
- chest complications of pulmonary oedema (about 5%) and pneumonia (at 9% but data are not strong).

2. Data is owned by a company purchased by Pfizer Animal Health

(Note, single-organ only disease as above, and elsewhere – see C and T, CVE, December 2012).

Dysrhythmia is unusual whereas urethral obstruction, mainly in males, is not uncommon and can persist, reinforcing the fact that this disease is one of intra-cellular excess-calcium dysfunction. While weakness is seen as the basic clinical presentation, it is spasm (intra-cellular Ca^{2+} dysfunction) of various tissue systems that actually causes the signs (e.g. Ach secreting neuromuscular unit, urethra, feline airways, canine diastolic cardiac dysfunction etc.).

We must also not forget that dogs go home with oesophageal dilation, a long QT interval, inducible weakness, secondary fatigue muscle damage if worked too soon (unproved hypothesis), and a potential for undiagnosed focal pneumonia that was not detected, or too small or too deep an area to auscultate crackles. These dogs often return with a cough, single, not loud or paroxysmal as with chronic bronchitis.

Cats can develop signs consistent with distal obstructive airway disease, (DOAD or 'asthma'), for example an expiratory wheeze, prior to four-leg paralysis. Usually they have an unusual gait and weakness e.g. they walk a few steps, stop, and sit with pelvis well under the chest. These animals will not be precision-jumping up or down as they are far weaker than they appear. It would not be surprising to have such cases diagnosed as asthma (with the obstructive auscultation etc.) to return the next day with TT. Again the history of loss of voice and loss of active jumping and climbing are critical to support the subtle observations of systemic weakness with DOAD as an established TT sign.

Neuromuscular weakness can be very easily induced in recovered animals. They stop walking, sit or lie in an unusual posture and hyperventilate. With rest they recover but with enthusiastic working dogs, with weather and exercise demands, it is possible to induce more severe muscle fatigue issues. This may explain why such owners state that good working dogs do not gain their original capacity. Second stage fatigue occurs with persistent exercise and induces structural disease whereas first stage fatigue is recoverable with rest.

Question 9

What drugs do I use with confidence and appropriate data support?

The only two drugs that effect outcome (i.e. survival) are TAS and antibiotics in severe cases (n=506, Merial 2008). There are drugs that are associated with altered morbidity but individual drug trials would be necessary to prove these effects, especially when morbidity is so hard to assess, apart from times to recovery.

From a general view there are indicated drugs e.g diuretics if you have confirmed pulmonary oedema that needs treating; anti-anxiety for severe distress, as we perceive it to be; atropine for profuse salivation (but care with eye/tear and gut function, and pseudo-ptyalism and upper respiratory tract (URT) and upper gastrointestinal tract (UGIT) issues).

The best therapy plan in general practice is to confirm TT – tick or crater, high probability of TT with LNM signs, examine and score the case [VAS (Visual Analogue Scale) overall and respiratory, NMJ score] and check for highly reliable, poor prognostic signs (e.g. crackles and inspiratory dyspnoea at presentation; wheeze and expiratory dyspnoea 24 hr later; facial signs of anxiety and helplessness). High VAS (>75%) and NMJ 4 also offer poor prognoses. Check that the case is not hypo- or hyperthermic

and proceed with TAS asap. Warm the TAS and give over 20 minutes if you wish to avoid any TAS reactions.

Give antibiotics if highly scored and/or if there are URT/UGIT complications - megaoesophagus (gaging regularly) or if dog is brachycephalic (aspiration potential, obstructed breathing).

Other drugs and procedures (including O_2, ventilation, suction etc.) are then used as needed and not continued or repeated unless indicated at each non-stress-inducing assessment. For example, anti-anxiety and oxygen therapy may be regularly used but care must be taken with continuing use of others e.g. diuretics, atropine etc. (In two separate studies well over 50 different products were being used on tick cases – these were mainly non-acaricidal medications.)

Question 10
How do I effectively kill ticks?

There is no 100% effective preventive for all cases in all areas. The very best protection (unpublished data) is offered by using two products at once (of different basic mechanisms) but expense could be a negative factor.

Most acaricidal products will take more than 24 hours to kill ticks, and no product will kill attached ticks.

In contrast to fleas, ticks spend so little time in the hair coat, where the products are, as they walk on top of the coat and then select an area. It is conceivable that minimal coat and product is in contact with a fast loading tick. Trials are normally conducted using 32 animals, 8/group, 3 treatments and 1 control with between 10 and 50 ticks per dog depending on what animals are used. TAS-producing dogs are selected to retain ticks well, whereas on non-TAS dogs there is a degree of tick loss due to host/tick factors. In theory it is not the number of ticks placed on an animal but the time; genes need to be up-regulated and systems activated prior to saliva/toxin secretion. Most drugs on the market have been tested in very similar facilities with most in the last ten years being done in one TAS production unit or in a pound-dog using facility. In the pound dog studies all animals are homed after the trials are completed. There is no reason to doubt the percentage claims from these data but the final trial is always the real world with its multitude of variables that may increase or reduce effectiveness. Added to this is the knowledge that tick DNA does vary over distance but there is no proof that this variation is associated with variations in toxin, disease or therapy or acaricidal effectiveness.

Tick searching is essential and finger-walking is probably the best technique to encourage with owners. There are no official publications of off-label use of products in non-indicated species. The use of off-label places the veterinarian and, unintentionally the company producing the product, in an awkward situation; the company is contacted for poor performance or worse, when it was the veterinary practice who suggested the off-label use.

Question 11
Have I got the right diagnosis in a doubtful case?

Continued reappraisal of any doubtful diagnosis, along with owner contact and ensured understanding by them of the difficulty of some cases to express their disease, is considered to be normal practice in human medicine and maybe it should

be considered more often for veterinary medicine, where our task is harder regarding patient and history.

Out-of-season tick cases are a problem as they present with lowered probability for TT. However again it is a LMN case, and when you look to the main causes (see above; and maybe others in your area you need to add to your differential diagnosis list) you progress as before – access, geography, season, travel to where, associations (beach, water fowl) etc. and again a probability, based on your experience of such LMN cases, is generated for each disease and you choose the most probable diagnosis and communicate it, knowing that the owners understand the doubtful presentation and why it is not obvious (limited disease expression, rare cause, out of season, wrong place, wrong time etc.)

Question 12

What therapy is best to use?

This depends on the signs the animal is displaying. Rarely do diastolic heart failure, pulmonary oedema, and arrhythmia need to be treated. Any dehydration will need to be corrected, and oxygen supply and ventilation may be required, again depending on severity and type of presentation. Associated with these needs will be the extent of hypoxaemia (oxygen supply, pneumonia, pulmonary oedema), air flow issues (URT & LRT obstruction) and hypercapnia due to the extent of paralysis, increased secondary respiratory muscle use and primary (reversible) fatigue.

Heavy sedation, or a low level of 'anaesthesia', using various drugs, pentobarbitone to propofol depending on preference and costs, will aid status by reducing oxygen demand due to relaxation and sedation (less stress, less 'need to breathe', less fatigue). Fatigue of primary and secondary respiratory muscles is the usual cause of the sudden respiratory failure (arrest) in non-ventilated TT cases.

Acid-base imbalance and secondary cardiac arrest can also occur, being independent of any long QT interval issues, where dogs are unexpectedly 'found' dead at home, following a normal recovery.

Answer summary.

The only two drugs proven to be of benefit regarding survival are antibiotics, in severe cases that probably have aspirated, and TAS, which must be used as soon as possible to ensure maximum effect. Once the toxin has become extra-vascular the large TAS protective antibodies cannot follow to the site of binding, and their size also ensures their removal.

TAS reactions can be avoided by giving TAS over 20 minutes but its immediate use is more important than prolonged logistic delays (to avoid any TAS reaction-usually attributed to a Bezold-Jarisch reflex). Anaphylaxis is an uncommon event as a TAS reaction is the more common cause of unexpected clinical signs with TAS use, especially if at a later stage of TAS administration. Anaphylaxis usually occurs very early with initial foreign allergen exposure (but is rate, route and quantity dependent).

Any other therapy apart from TAS and antibiotics (for pneumonia) must be tailored to need. There are no other proven drugs that affect outcome (n = 506 cases; Merial 2008 data). Morbidity is hard to assess apart from delayed recovery and progressively rising clinical scores. However, as with any other disease other therapy can be justified on clinic-pathological terms.

Significant pulmonary oedema (crackles, usually first 24 hours) needs diuresis, but not

to excess, and verified before any subsequent use. Arrhythmias that are affecting the animal understandably need routine anti-arrhythmic therapy (again not excessive and justified before each use). Hypoxemia and hypercapnia (less important of the two) need the best therapy you can offer (e.g. lower level GA and O_2 tube to carina up to full artificial ventilatory support).

Sedation would seem very justified as would minimal physical, psychological or fear-inducing disturbances (in all their forms). Recall that every disturbance means increased oxygen need in an animal that has pulmonary (transit) and alveolar (absorptive) ventilation issues. The more the need to breathe, the more work has to be done, the more oxygen is needed, the faster the remaining motor units have to be recycled, the closer the animal is to fatigue – and so the cycle continues.

You have only to see a patient "simply" just stop breathing to realize how much we underestimate their status and progressively their alveolar absorption and diffusion issues (oedema, infection and perhaps some collapse). However there are no data to conclusively guide us as to best practice for the more severe cases, apart from the first principles of critical care medicine and more general disease (e.g. urethral or ophthalmic issues). Fortunately most cases are routine as reflected in the 2008 data (Merial) and the initial study of another 500 plus animals (AVJ 2001) in a similar clinical setting.

In conclusion we must recall these animals are intoxicated by a poison of yet unclarified toxic profile (the toxin is a mixture of many chemicals) and the outcome is naturally dependent on the final level of bound toxin. This outcome is then a reflection of the toxin supply rate, the host's immune status (both natural perhaps, and artificial by TAS), the susceptibility of the host and the extent of disease expression. Owners must be aware that some deaths are expected (0-10% in 506 cases in 42 practices) and, once intoxicated, there is no way to directly reverse the basic K^+ - Ca^{2+} dysfunction. Using only 'as-indicated' therapy, avoiding whatever increases O_2 needs, providing routine hospital care and correcting primarily critical medical defects (e.g. maximizing remaining lung function) must be the basic approach to therapy. The chief aim is to keep the animal alive using indicated and justifiable therapy, allowing time for the toxin to unbind. It is believed this takes approximately two days but in individual cases set clinical signs can be prolonged e.g. heavier dogs not being able to stand, persistent urethral issues, pupil defects etc.

Animals go home with persistent sub-clinical disease and if they are again intoxicated their disease status will be more severe, as the new toxin is added to the prolonged sub-clinical toxicity of the first tick.

Troublesome individual cases can often be better resolved by discussion with an independent veterinarian who see lots of general or critical cases, or individuals who study the disease in depth. This applies particularity to the doubtful or uncertain tick toxicity (TT) case, the use of Tick Antitoxin Serum (TAS) and the need to then explain any perceived changes, which may be seen as errors by the client.

The most probable diagnosis, based on who you are, with what you have, at a set time and place and based on the first principles of clinical examination is the correct diagnosis. This may alter as either the disease expression changes or the clinical signs become more obvious, or the owner's history alters – the list is endless but any new data then resets the diagnostic process which will then lead

to a more correct diagnosis for that period of investigation and at that time. It may be the same or another – but both the previous and this current diagnosis are correct for their time, place, signs of disease, available history etc. In human medicine such a process is totally routine and accepted by both the doctors and their patients. It is only us as veterinarians who expect ourselves to be so accurate. We have trained our clients to be the same i.e. that we expect to provide the correct diagnosis, quickly, first up, often on only extremely limited data and therefore on a limited capacity to be diagnostically correct!

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Other recent support data can be found in the Merck Manual (2010), Australian Veterinary Practitioner March 2011, C&T CVE Dec 2012, and a paper soon to be published in the Australian Veterinary Practitioner 2013 (on the analyses of 506 cases of tick toxicity (TT) from 42 practices from Cairns to Lake Entrance).

There is a series of articles on diagnosis and all its complexity in the Australian Veterinary Practitioner - go to AVA web site and search under Heath and/or Atwell

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