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Pain in reptiles: a review for veterinary nurses

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ABSTRACT: Reptiles are very likely to have the same pain experience as mammals, as the structures involved with nociception and processing are homologous. However, there is a big difference in expressive behaviours of pain between reptiles and mammals. This makes pain assessment challenging. Difficulty in pain assessment, along with other factors, makes poor pain management a welfare issue in the veterinary and the wider reptile - keeping context. Research in reptile pain is very limited so far; this article aims to provide some basic information on assessing pain in reptiles.

Keywords: reptiles; pain; assessment; analgesia

Introduction

Pain management in animals is relatively neglected and the use of analgesics relatively low (Flecknell, 2008). Although the understanding of pain and analgesia in domestic mammals has been exponential in the last 20 years, the knowledge obtained is said to be only a fraction of what is required to make appropriate treatment recommendations (Sladky and Mans 2012). Some years ago, a study by Read (2004) showed that although 98% of reptile veterinarians in a survey said that reptiles feel pain, provision of analgesia was uncommon. The reasons for this included: failure to recognise painful patients, lack of efficacy data, concern over adverse effects, and little or no experimentally determined drug doses or pharmacokinetic information. Over 75% of the reptile veterinarians in this survey considered their recognition of pain in reptiles to be inadequate.

In older literature referring to reptile emergency and critical care, the subject of pain is rarely mentioned.

Since then, there has been an increase in pharmaceutical research for reptile analgesia. This is not without challenges, as reptilian drug metabolism differs from mammals.

Failure to consider or recognise pain

The challenges of assessing reptile pain are numerous. There are over 8,000 species (Mosley 2009), each with their own highly evolved physiological and behavioural adaptations to live successfully in the wild. Reptiles are one of the most phylogenetically diverse animal classes, with three main orders: Chelonia, Sauria and Serpentes. Therefore, pain behaviours vary significantly between orders, species, as well as between individuals.

As nurses, we may feel relatively proficient at assessing pain in two of the common pet mammal species – dogs and cats. In contrast, there are hundreds of captive reptile species.

Many reptiles do not exhibit pain behaviours when observed. They do not display overt behaviours such as vocalisation, as a dog may do. Therefore, changes in behaviour related to pain may be subtle, and overlooked (Read, 2004 and Sladky et al 2007). They may even alter their responses in the presence of human observers - as found by Fleming and Robertson (2012) in thermal tests on juvenile green iguanas. In this study, iguanas became immobile when observed, and often did not respond to the thermal stimulus, in comparison to the non – observed group.

Species that are less familiar to humans and have a shorter domestication history are evolved to be less likely to display pain behaviours to us, because they are less likely to receive help. By contrast, familiar domesticated species such as dogs and horses have coevolved with humans for a long time, and behavioural communication in these relationships have been successful, mostly to the advantage of both parties.

There is a difference between considering and recognising pain. There are numerous sociological, cultural and gender differences in why the assessor may fail to *consider* pain in their patients, and these have been discussed previously.

The ability to consider pain is often linked to level of empathy (Jackson, Meltzoff and Decety, 2005). Empathy cannot be taught, only facilitated (Davis, 1990).

However, the ability to *recognise* pain is a skill that can be taught (or learnt).

For a more detailed overview of why pain may not be recognised or considered in a veterinary context, and therefore analgesia not prescribed, see Bradbury and Morton (2017).

Generally, it is well known that in humans, the gold standard of pain assessment is verbal self – report. In animals, the gold standard of pain assessment has not been determined. It has been suggested to be the animals 'response to analgesia' (Viñuela-Fernández, 2015). 'Response' is a wide term, but for most veterinary staff in clinical practice this points towards the physiological and behavioural response of a patient. Behaviour is fundamental to both welfare assessment and pain assessment; as it is immediate (real – time rather than retrospective), and reflects the emotional state of an animal.

Assessment by 'response to analgesia', also relates to the notion - when faced with insufficient knowledge - of giving the 'benefit of the doubt'. This is because the contrary has not been proven.

Because our knowledge of pain assessment in reptiles is so limited, if we suspect but are uncertain whether the reptile is in pain, it is a welfare obligation to give the patient the benefit of the doubt, and administer analgesia (Cracknell 2007, National Research Council 2009, Sladky and Mans 2012). There are no circumstances that analgesia should be withheld in animals that are painful or suspected to be painful, because relief of pain is a welfare priority.

Although reptile pain assessment and management is still in very early days, we do have very basic (but increasing) knowledge of what painful reptiles look like and what analgesics can be used.

Differentiating between normal and abnormal behaviour

As with any patient consultation, a thorough history taking of the husbandry should be taken in order to get a fuller picture of the patient's problem. Recognising abnormal behaviour needs to be species and context specific:

- The species should be identified, and species - specific behaviours should be known
- Determine whether the patient is arboreal, aquatic, terrestrial, fossorial
- Determine whether it is diurnal, nocturnal, or crepuscular
- Determine whether it is a prey/ predator species
- Determine the stage of ecdysis; the hibernation status; socialization level; reproductive status; preferred optimum body temperature and humidity; the temperature and humidity it is kept at; the home environment (opportunity to express normal behaviour) cage furniture; UV lighting; dietary information.
- Determine whether these conditions are correct.

An owner assessment is a necessary part of every patient examination. As most of us know, some owners are very good at knowing their animal's normal behaviour. However, many owners may not be, and are frequently biased towards their own understanding and beliefs about their pet's care and condition (Mosely 2009). In addition, they may assume that an abnormal behaviour is normal (or vice versa). Once confident that the abnormal behaviour is indeed abnormal, and not due to husbandry or external causes (such as stress), a thorough examination or diagnostic work up is required, and pain may be a factor to consider.

The neurological structures associated with pain perception and processing in reptiles is homologous to that of mammals (Bennett 1998, Sladky and Mans 2012). Reptiles similarly possess mu, kappa and delta opioid receptors in the CNS (Perry and Nevarez 2018). However, it is clear that across the reptile species, there are differences in opioid receptor affinity, leading to the variability of drug efficacy results we see in research to date (Thompson, Knotek, Corriveau and Inoue, 2016). Furthermore, the scarcity of reptile pain research makes decisions regarding analgesia difficult. As with all animals, multi - modal analgesia is gold standard. The following information gives a basic review of opioids, NSAIDs and local anaesthesia in reptiles.

Opioids

Chelonia

Most pain research in chelonia has been on red – eared slider turtles. Sladky, Kinney and Johnson (2009) found that in this species, opioid dependent thermal antinociception appeared to attributable mainly to mu - opioid receptor activation with a relatively minor contribution of delta opioid receptor activation. Studies show that morphine or hydromorphone is superior to butorphanol or buprenorphine in thermal tests (Sladky et al 2007, Kinney, Johnson and Sladky 2011, Mans, Lahner, Baker, Johnson and Sladky, 2012).

The Kinney study concludes that morphine administration leads to a quicker return to pre – surgical behaviour following unilateral gonadectomy in comparison to saline or butorphanol. However, there were effects of morphine and anaesthesia on turtle behaviour. This is one of the first studies to suggest a dosing interval of

This tortoise was hospitalised following a cystotomy at a previous veterinary practice and clinically deteriorating. He had a CT that showed intracoelomic gas and effusion, sediment in the bladder, and a surgical site secondary infection (already reported by bloods/swabs of the surgical site) visualised on the images.

The tortoise was severely dehydrated on bloodwork and clinical exam, evident from the dull corneas and crusting around the eyes, mouth and nares, and showing signs of pain and illness with closed eyes and very little movement. He was started on IM morphine injections. He was placed on a thick bed in case there was pain or discomfort associated with the surgical site.

Bearded dragon with follicular stasis. Notice the swollen/gravid abdomen, the half - closed eyes and the dark colour changes. There is likely to be a degree of abdominal discomfort with this condition.

In this photo you can see the colour changes to the ventral aspect of her chin, and the inability to support her weight.

This baby tortoise was attacked by a dog and following flushing and cleaning of the area under sedation, was dressed and bandaged. She was on fluids, antibiotics and morphine IM every 24 h. It was very difficult to tempt this patient to eat or move about, even when tempting to handfeed with tiny pieces of her favourite food. Inappetance can be a non-specific pain behaviour. In this photo she was not attempting to carry her own weight with her legs. Note the dull eyes and demeanour. She was eventually euthanased, due to no clinical improvement.

Tortoise with a right hind fracture. This patient was started on morphine IM Q24 h, meloxicam once hydrated, and had a sling support to reduce movement of the fractured leg. Note the half - closed eyes, dull demeanour and withdrawn posture.

Iguana with MBD: Iguana showing neurological signs and musculoskeletal malformation as a result of metabolic bone disease. Note the twisted appearance to the hindlimb digits and tail. This patient was unable to mobilise properly and was very sick when admitted.

24-48 hours in this species, and perhaps chelonia in general.

Wambugu, Towett, Kiama, Abelson and Kanui (2010) found that morphine (at 7.5, 10 and 20 mg/kg) and pethidine (at 20 and 50 mg/kg) significantly decreased the time Speke's hinged tortoises spent with its limb retracted post irritant (formalin) injection. Hydromorphone (but not buprenorphine) worked in antinociceptive tests in red - eared slider turtles (Mans et al 2012).

Tramadol is a synthetic opioid analogue that acts as a mu - opioid agonist and serotonin norepinephrine reuptake inhibitor, and is controversial as an effective analgesic in mammals. However there has been a promising study using this drug in nociceptive tests in red - eared slider turtles (Baker, Sladky and Johnson 2011) and yellow - bellied sliders (Giorgi et al 2015b). Tapentadol is a similar drug, as a centrally acting mu - opioid receptor agonist and norepinephrine reuptake inhibitor, and has shown success in a pharmacokinetic, pharmacodynamic and thermal nociceptive study in yellow - bellied sliders at 5 mg/kg IM (Giorgi et al 2015a). Both of these drugs require further research (Perry and Nevarez 2018).

Therefore so far, morphine, hydromorphone and pethidine, with tramadol and perhaps tapentadol show the most promise in chelonia. Research so far suggests that opioids should be given as a pre - med at least 24–48 h prior to surgical intervention in chelonia.

Sauria

There appears to be less research in the lizard species compared to chelonia, but again the pure mu - opioid agonists seem to be recommended. Morphine (but not butorphanol) induced analgesia in bearded dragons using thermal nociceptive tests (Sladky et al 2008), and another study showed no effect of butorphanol in

Iguana with MBD: X-ray of the above iguana. Note the reduced bone density in the extremities. There is potentially a degree of bone pain with metabolic bone disease, and muscle ache and strain as muscle is built up to compensate the inadequate bone growth. The treatment plan included injectable tramadol.

This bearded dragon was suffering from severe oral stomatitis, which had meant he had been unable to eat for some time. Note the poor body condition. The patient has closed eyes and a darkened ventral chin, that could indicate pain and/or general illness. The patient had a swab taken and the gums were cleaned. He was given fluids, and started on antibiotic injections, and IM tramadol injections to be given at home. There is a risk of refeeding syndrome when gavage feeding dehydrated patients such as this, so the decision was to rehydrate before considering feeding.

Bearded dragon exhibiting a postural pain behaviour. Note also the dark discolouration to the ventral neck and head. This patient had an intestinal disorder and parasite burden and was possibly suffering from visceral pain or discomfort.

green iguanas (Fleming and Robertson 2012). Kanui, Hole and Miaron (1990) designed three tests to measure nociception in crocodiles in thermal tests ('lift foot', 'lift toes', 'not using foot', 'try to escape') and subsequently found morphine to reduce these behaviours in these tests (Kanui and Hole 1992).

Often, certain drugs are recommended in literature, such as buprenorphine, but few actual studies have been done to prove analgesic efficacy, or results have been inconclusive (Mosley, 2015).

In other cases, pharmacokinetic studies have been done, such as transdermal fentanyl on skinks (Gamble, 2008) but no efficacy or behavioural research.

We can conclude that morphine, and perhaps other pure mu - agonists such as hydromorphone and fentanyl, and additionally tramadol, show the most prospect for lizards.

Serpentes

There is an extraordinary lack of research regarding pain management and analgesia in snakes, and what we have so far appears difficult to draw conclusions from.

Sladky et al (2008) looked at morphine and butorphanol doses in bearded dragons and corn snakes and the effect on thermal withdrawal latencies. It was found that corn snakes given the higher end of the dose ranges of butorphanol appeared to work in thermal stimulus tests (had longer latencies to withdrawal) but there was no effect of morphine (the opposite was true for bearded dragons; see previous section). However, later, it was concluded the dose used was not recommended (Perry and Nevarez 2018): maybe the snakes were heavily sedated instead of analgesed.

A study by Williams, James, Bertelsen and Wang (2016) looked at irritant injections (capsaicin) into ball pythons treated with either saline, butorphanol or morphine. In normal untreated snakes, capsaicin causes an increase in heart rate, assumed to be a physiological indicator of pain. However, they found that neither morphine or butorphanol at the doses used had any effect on the heart rate after the capsaicin injection. However, butorphanol caused more of a sedative effect and a low heart that was evident *prior* to the capsaicin (post butorphanol injection).

This little leopard gecko had several husbandry related issues, having reproductive disease being a persistent egg layer, osteopenia, severe metabolic bone disease (MBD), suspect hepatic lipidosis, and dysecdysis (difficulty shedding) in all four limbs, with necrosis occurring at the distal ends. She walked on the dorsal aspects of her carpi. Note the abnormal weight bearing on the hind limbs, and inflamed digits. There is likely to be a degree of pain or discomfort associated with all of her conditions, therefore her treatment plan included oral tramadol to take at home.

Guttwilig, Abbott, Johnson and Sladky (2012) found that neither butorphanol, morphine, fentanyl or tramadol worked in corn snakes at the doses used during thermal tests, but fentanyl patches and tramadol were successful in ball pythons. Fentanyl has had success in pharmacokinetic studies also in ball pythons (Darrow, Myers, KuKanich and Sladky 2016). However there has still been query over its antinociceptive effects (Kharbush et al., 2017).

This information we have really highlights the need to further knowledge in pain processing and pain management in snake species. Snakes more often present with thermal burns than other reptile species, although will very obviously react and withdraw from a skin incision if inadequately analgesed or anaesthetised during surgery. One theory is that they may process thermal noxious stimulation differently to other noxious stimulation compared to other reptiles. The evolution of limblessness may have altered spinal cord receptor and function (Sladky et al 2008). It is known that snakes possess many cutaneous mechanoreceptors that detect vibrations from prey or shifting substrate, but because they have very few thermoreceptors, will

This leopard gecko presented with tail tip necrosis due to dysecdysis (difficulty shedding). Note the sore forelimb digits. The necrosed tail was removed via manual autotomy, which is removing it along the natural fracture plane that geckos would normally do themselves in the wild if caught by a predator ('dropping their tail'). This method has better outcomes than surgical amputation. The procedure was done under sevofluorane anaesthesia, with an injection of hydromorphone given IM beforehand.

Shell wound tortoise: This tortoise presented with a wound to her leg and shell that had infected large areas of the ventral shell scutes. Note the dull half- closed eyes and lethargic demeanour.

Shell wound tortoise: The same tortoise viewed ventrally. A CT showed severe osteopenia with suspected pathological fractures and possible sequestra, and a small amount of gas present in the coelom (body cavity), and coelomic effusion. Coincidentally the CT also showed multiple follicles in the coelom. The owner opted for treatment over euthanasia and this tortoise received hydromorphone in hospital and went home on oral tramadol.

allow themselves to be burned by heating elements in a cage (Mader, 2006).

This calls into question whether research should be using thermal stimulus tests to measure nociception in snakes. Although thermal tests are reproducible and have provided a framework for much of the pain research so far in other reptile species, maybe this is an inappropriate study design for snakes.

Tortoise (bite wounds): Pictures of a tortoise that presented being chewed by rats due to being ill and weakened by a long period (years) of suboptimal husbandry (kept in the garden).

With kind permission from Stacey Vickery

Tortoise (bite wounds)

It is difficult to draw conclusions for analgesia protocols in snakes so far, but generally we can only extrapolate from what we know works with, at best, the other reptile orders, which includes the pure mu - agonists, with fentanyl having the most success to date in snakes.

Similarly to mammals, there has been a move away from use of butorphanol and buprenorphine in reptiles. Butorphanol is a partial kappa opioid receptor agonist and partial mu - opioid receptor antagonist and agonist. It may or may not produce antinociceptive effects at high doses but the evidence suggests so far that it is either ineffective or only a very mild analgesic in reptiles, similarly to mammals, and is no longer recommended.

Buprenorphine is a weak partial mu, kappa, delta opioid receptor agonist and

Tortoise (bite wounds): After cleaning the wounds, the patient was sent home on IM tramadol injections, antibiotics, wound cleaning, and advised to keep indoors on padded and clean bedding to reduce further discomfort, before moving to an appropriate indoor set up once healed.

With kind permission from Stacey Vickery

antagonist. Similarly, the studies carried out so far show buprenorphine to be ineffective to date.

In conclusion, there is a general acceptance of the pure mu agonists for effective opioid pain relief in reptiles, however the ideal dosing regimen is largely unknown (Posner and Chinnadurai, 2013).

Non – steroidal anti inflammatories (NSAIDs)

Many of the doses for studying NSAIDs in reptiles are extrapolated from mammal data (Mosley 2015) and there is not enough data in reptiles to be confident of their efficacy (Perry and Nevarez 2018). So far it is advised to use a non - selective COX inhibitor over selective inhibitors (Royal, Lascelles, Lewbart, Correa and Jones 2012, Sadler et al 2016).

Chelonia

Meloxicam has shown variability between the few species studies with regards to bioavailability and plasma levels (Balko and Chinnadurai 2017). The only studies done so far have been pharmacokinetic, with doses of 0.2 mg/kg studied in a few species (Di Salvo, Giorgi, Catanzaro, Deli, della Rocca 2016 and Uney, Altan, Aboubakr, Cetin, Dik, 2016). Lai et al (2015) found 0.1mg/kg meloxicam was insufficient in a pharmacokinetic study in loggerhead sea

Comfortable posture in a bearded dragon, 24 hours post salpingohysterectomy (due to follicular stasis). It has been noted in other sources (Eatwell, 2010) that bearded dragons showing abdominal discomfort due to a surgical site will lift the abdomen off the ground to avoid contact with the floor. This patient was deemed very comfortable by the vet on examination, and you can observe that she is not showing any lifting posture. She received hydromorphone on admission the day before, and her premedication included hydromorphone, dexmedetomidine and ketamine.

Cloacal prolapse: This tortoise (hiding in its shell) presented with cloacal prolapse which it had for two days, due to a massive parasite burden found by faecal sample.

Cloacal prolapse: The patient received hydromorphone and fluids on admission. It was impossible to replace the prolapse due to the extent of the problem, and the owners opted for euthanasia.

Young tortoise presenting with shell wounds after being attacked by a dog. Note the closed eyes and almost collapsed state. He was administered hydromorphone on admission.

This iguana is 24 h post replacing a cloacal prolapse that was likely due to a reproductive cause. She had hydromorphone on admission and her premedication included hydromorphone, dexmedetomidine and ketamine. It is very difficult to assess post - operative pain in reptiles, but she appeared to be in minimal discomfort. She was posturing the affected area comfortably and was fairly alert and moving around the vivarium reasonably well.

turtles. Ketoprofen has been studied at 2 mg/kg in the sea turtle (Hannon, 2015).

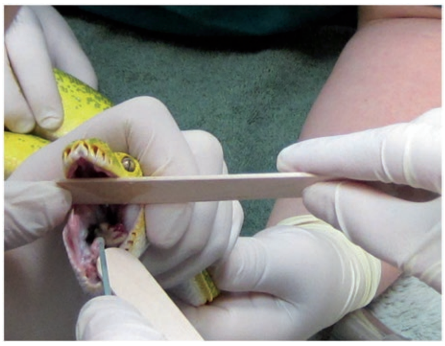
Sauria

Studies on meloxicam showed good bioavailability after oral administration of a 0.2 mg/kg dose in green iguanas (Divers et al., 2010). Ketoprofen has been studied at 2 mg/kg IV in green iguanas and shown a long half-life of 31 h; but if given IM, the half-life is only 8.3 h and bioavailability only 78% (Tuttle et al 2006).

Serpentes

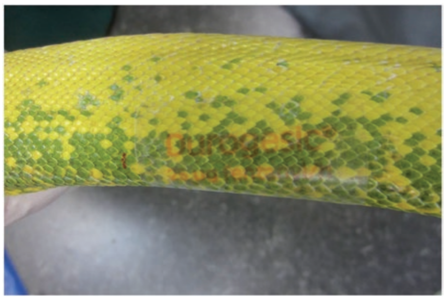
Again, snakes appear to have very little or no research regarding NSAIDs. One study by Olesen, Bertelsen, Perry and Wang (2008) showed no effect of meloxicam at 0.3 mg/kg in ball pythons.

The data available currently are not sufficient to determine an ideal NSAID dosing protocol in reptiles.



Green tree python: Patient with severe stomatitis. This patient was administered a fentanyl patch.

With kind permission from Tariq Abou – Zahr



Green tree python: the fentanyl patch (just visible!) on the afore- mentioned python.

With kind permission from Tariq Abou – Zahr

Albino Burmese python presenting with thermal burns. The patient was on morphine IM Q24 h. The burns were dressed and bandaged.

With kind permission from Stacey Vickery and Tariq Abou – Zahr

Local anaesthetics

Despite the scarcity of research on local anaesthesia in reptiles, and the lack of information regarding toxic doses, local anaesthetics are quite commonly used with no side effects commonly reported (Perry and Nevarez 2018).

Chelonia

Intrathecal local anaesthesia is indicated in surgery of the hindlimbs, cloaca, genitalia and urinary bladder. Successful

Young Tokay gecko with a dislocated stifle. The dislocation was resolved and leg splinted under sedation. The patient started on IM tramadol injections.

With kind permission from Sara Jones

Bearded dragon 1: Patient presenting with a week - long history of anorexia and lethargy. He also had mites. He was semi – collapsed and dehydrated. Due to cost limitations, bloods and faecal samples were taken only.

Bearded dragon 2: The patient improved slowly with fluids and supportive care. He was started on IM tramadol just in case there was any pain present (that would be especially difficult to ascertain due to the collapsed state). He was starting to move around his vivarium. Small amounts of gavage feeding commenced on day three.

Bearded dragon 3: The patient deteriorated again after four days (note the closed eyes, weak posture and blackened chin). This possibly may have been the illness showing through now that the shock and dehydration had been corrected. The blood results came back showing heterophilia; indicating a possibility for coelomitis among other differentials; the owners opted for no further diagnostics and euthanasia.

Bearded dragon (eyelid biopsy): This patient had a small biopsy of a mass on his lower eyelid. The patient was administered tramadol as a premedication and IV alfaxan for the anaesthetic.

Bearded dragon (eyelid biopsy). Recovering from the surgery. It is very difficult to assess post – operative pain in reptiles due to the long recoveries from anaesthesia (in comparison to birds or mammals). He was also in fairly poor body condition, which can prolong anaesthetic recovery.

Asian grass lizard presenting with a sore eye. After examination and treatment, the patient went home on oral tramadol. With kind permission from Sara Jones

intrathecal analgesia/anaesthesia has been described in phallectomies of hybrid Galapagos tortoises (Rivera et al 2011). Mans, Steagull, Lahner, Johnson and Sladky (2011) found 60% of turtles had a complete motor block in the cloacal sphincter, tail and hindlimbs after one intrathecal injection of lidocaine, bupivacaine and morphine, and 90% had a complete motor block after a repeat injection 15 minutes later, if the first injection was unsuccessful. The clinical technique is described by Mans (2014). A study on endoscopically sexing hatchling Chinese box turtles found lidocaine on its own to be insufficient (Hernandez-Divers, Stahl and Farrell 2009) - it is recommended that general anaesthesia is used as well (Perry and Nevarez 2018).

Sauria

Wellehan, Gunkel, Kledzik, Robertson and Heard (2006) describe using a nerve locater and mandibular nerve blocks in some species of crocodilians having a dental examination. Probing the blocked side of the jaw with a needle resulted in no movement at all, whereas probing the unblocked side inconsistently resulted in movement of the animal.

Serpentes

The author found no research about use of local anaesthesia in snakes.

The studies to date show that local anaesthesia has been mainly successful and shows potential. So far, there is no evidence of adverse effects with the doses used, but toxic doses are still unknown and more research is needed.

Signs of pain in reptiles

Despite it being early days in research, there are some known general physiological and behavioural signs of pain. These are very basic and not species or context specific, but can provide groundwork for future studies. They are listed below.

Physiological

- High heart rate, respiratory rate or abnormal respiration
- Darkening of the skin or colour changes (in some species, e.g. bearded dragon, chameleons)
- Constipation
- Muscle contractions
- Dysecdysis (difficulty shedding)
- Unusual gait/locomotion/lameness

Dull or closing eyes
Mouth gaping
Anorexia

Behavioural
Increased lethargy, or increased restlessness
Avoidance and withdrawal, or exaggerated flight response
Aggression
Self - mutilation of affected area
Reaction on palpation of affected area (not always)
Immobility or reluctance to move
Stinting (snakes)
Change in temperament
Insomnia
Hunched/abnormal posture or resting position
Hiding in cage or in shell
Aerophagia
Decreased coiling (snakes)
Decreased interactive behaviours
S - shape posture in snakes with abdominal pain
Aversive and sudden movements
Flinching
Holding the head elevated and/or extended
Reluctance to lie down
Unwilling to perform normal movements
Limb guarding
Vocalisation
Head down and dragging plastron along the ground (chelonia)
Weight loss and cachexia
Flattening themselves out
Innapetance, anorexia or pica
Going limp when handled.

Stoskopf (1994), Read (2004), Hawkins (2006), Schumacher (2007), Eatwell (2010), Girling (2013), Posner and Chinnadurai (2014), Cital (2015), Mosley (2015), Ayers (2016), Nevarez (2016), Perry and Nevarez (2018).

Common painful conditions

Often pain is a main contributing factor in the clinical signs and symptoms, which can be often non – specific, such as 'lethargy' and 'anorexia'. Listed below are commonly encountered conditions in reptiles that are painful.

- surgical intervention
- trauma
- fractures or shell wounds
- osteoarthritis
- metabolic bone disease
- renal disease
- gout
- neoplasia
- stomatitis
- coleomitis (equivalent to peritonitis in mammals)
- osteomyelitis
- thermal burns
- abscesses
- GI disease, such as impactions, vomiting
- reproductive conditions, such as dystocia and follicular stasis

Schumacher (2007), Wenger (2007), Posner and Chinnadurai (2014).

Signs of stress in reptiles

Pain in many species of animal is difficult to differentiate from stress. Many patients are likely to behave completely differently in hospital than they do at home. Some stress behaviours are detailed below. It is evident that many of these behaviours may overlap with the pain behaviours described earlier.

- Interaction with transparent boundaries (ITB)
- Hyper/hypo activity
- Anorexia
- Hyper alertness
- Rapid body movements
- Flattened body posture
- Head – hiding
- Inflation of the body
- Hissing
- Co – occupant aggression
- Human – directed aggression
- Clutching
- Death – feigning (snakes)
- Loop – pushing (snakes)
- Freezing
- Jaw grating
- Hesitant mobility
- Wincing
- Prolonged retraction of the head, limbs or tail
- Open mouth breathing
- Panting
- Cloacal evacuations
- Projection of penis or hemi – pene
- Voluntary regurgitation of food
- Tail autotomy
- Pseudo - vocalisation
- Venom spitting
- Squirting blood from eye
- Pigmentation change
- Atypical location

For full details of these stress behaviours and contrastingly, the 'quiescent' behaviours, see Warwick, Arena, Lindley, Jessop and Steedman (2013).

For some of the commonly used analgesic drugs and doses, see Table 1 at the end of the article.

Why is it important?

Veterinary staff have legal, welfare and moral obligations to treat pain (Bradbury and Morton 2017). Pain is described as the 'fourth vital sign' and should be an integral part of every patient assessment. It is well known that the main welfare issues with pet reptile keeping is inappropriate husbandry. Pain can be a common but under recognised factor in husbandry - related disease (for example, reproductive conditions, and bone pain or pathological fractures as a result of metabolic bone disease).

Outside of veterinary science and companion animal keeping, furthering knowledge and awareness of reptile pain is vital to improve assessment of reptiles that are involved in or farmed for the exotic pet trade. Personnel employed at check points (at airports, for instance) often have little or no knowledge or experience in animal welfare, or how to detect pain or stress in reptile exports.

Pain awareness and research may also help to change policy or improve welfare at killing in the vast number of reptile farms in the USA, Asia and Africa for the purpose of skins or food.

Determining methods of pain evaluation in reptile species is an urgent requirement for research. The challenge is that these methods must be species and context specific. However, our knowledge of reptile pain behaviours is slowly increasing. Hopefully this information will provide a basic overview of very basic pain assessment and management for the veterinary nurse in practice.

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Table 1

Drug	Dose	Route	Frequency (hours)	Type of reptile used in research	Reference book	Notes
Morphine	1–20 mg/kg	IM, SC, IT, ICe	Q24–48 h	Red-eared slider turtles, Fresh water crocodiles, Anolis lizards, Bearded dragons, Green iguana, Eastern painted turtles, Yellow spotted Amazon river turtle, Other undocumented turtle species	Meredith Exotics Formulary, 2015; Mosley, 2015; Cital, 2015; Balko and Chinnadurai, 2017; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	Wide dose range. See formulary for species specific doses. Chance of respiratory depression. 40 mg/kg has been studied (Sladky et al., 2008).
Hydromorphone	0.5–1 mg/kg	SC, IM	Q24 h	Red-eared sliders	Mosley, 2015; Balko and Chinnadurai, 2017; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	
Fentanyl	2.5 µg/h patch 12.5 µg/ h patch	TD	One patch for 24–72 h	Prehensile tailed skinks, Ball pythons	Mosley, 2015; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	PK study only. Anecdotal evidence in snakes.
Meperidine/ Pethidine	1–50 mg/ kg	IM, SC, ICe	Q4 – 24 h	Nile crocodiles, Red-eared sliders, Speke's hinged back tortoises, Lizards	Meredith Exotics Formulary, 2015; Cital, 2015; Mosley, 2015; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	No noticeable effect in snakes even at 200 mg/kg. Wide dose range. See formulary for species specific doses.
Methadone	3–5 mg/kg	IM, SC			Carpenter, 2018; Perry and Nevarez, 2018	Author cannot locate specific studies for methadone.
Buprenorphine	0.075–1 mg/kg	IM, SC	Q24 – 48 h		Meredith Exotics Formulary, 2015; Cital, 2015; Mosley, 2015; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	No evidence of analgesic efficacy.
Butorphanol	0.4–20 mg/ kg	IM, SC, IV	Q24 h	Red-eared sliders, Ball pythons, Bearded dragons, Green Iguanas, Corn snakes	Meredith Exotics Formulary, 2015; Cital, 2015; Mosley, 2015; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	Very questionable analgesic efficacy.
Tramadol	5–11 mg/kg	IM, PO, SC	Q24 – 72 h	Red-eared slider turtles, Yellow-bellied sliders, Loggerhead turtles, Bearded dragons	Meredith Exotics Formulary, 2015; Cital, 2015; Mosley, 2015; Carpenter Exotics Formulary, 2018; Perry and Nevarez, 2018	Doses of 25 mg/kg have been studied (see dose table in Cital, 2015).
Tapentadol	5–10 mg/kg	IM		Red-eared sliders, Yellow-bellied sliders	Balko and Chinnadurai, 2017; Perry and Nevarez, 2018; Carpenter Exotics Formulary, 2018	
Meloxicam	0.1–0.5 mg/kg	PO, SC, IM, IV	Q24 – 48 h	Most species	Meredith Exotics Formulary, 2015; Carpenter Exotics Formulary, 2018; Cital, 2015; Mosley, 2015; Perry and Nevarez, 2018	Insufficient evidence for efficacy so far. Do not give to dehydrated, hypovolaemic, hypotensive patients or those with GI disease or clotting disorders.
Carprofen	1–4 mg/ kg loading dose, then half the loading dose for maintenance	SC, IM, PO, IV	Q24 for initial dose then Q24 – 72 h to maintain.	Most species	Meredith Exotics Formulary, 2015; Carpenter Exotics Formulary, 2018; Cital, 2015; Mosley, 2015	Do not give to dehydrated, hypovolaemic, hypotensive patients or those with GI disease or clotting disorders. Insufficient evidence for efficacy.
Flunixin	0.1–2 mg/kg	IM	Q12 – 24 or 48 h	Most species	Carpenter Exotics Formulary, 2018; Mosley, 2015; Cital, 2015	Insufficient evidence for efficacy.
Ketoprofen	2 mg/ kg	IM, SC, IV, PO	Q24–48 h	Green iguanas, Bearded dragons, most species	Meredith Exotics Formulary, 2015; Carpenter Exotics Formulary, 2018; Mosley, 2015	Insufficient evidence for efficacy. In green iguanas, IM, IV Q24 h at this dose may be too frequent.

Lidocaine*	1–5 mg/ kg <5 mg/kg	Local infusion/ nerve block/ topical Local infiltration, intrathecal			Meredith Exotics Formulary, 2015; Carpenter Exotics Formulary, 2018; Cital, 2015; Mosley, 2015 ; Perry and Nevarez, 2018	Do not exceed 5mg/kg. Infiltrate to effect. For e.g., use 0.01ml of 2% lidocaine for IO placement in green iguanas in conjunction with chemical restraint. Dilute to 0.5 or 1% to increase volume. Toxic dose is unknown.
Bupivicaine*	1–5 mg/kg	Local infusion	Q4 – 12 h	Most species	Meredith Exotics Formulary, 2015; Carpenter Exotics Formulary, 2018; Cital, 2015; Mosley, 2015; Perry and Nevarez, 2018	Maximum dose 4mg/kg. Recommend <2mg/kg. Dilute to 0.25% to increase volume. Toxic dose unknown.
Mepivicaine	1–5 mg/ kg	Local infusion			Mosley, 2015; Perry and Nevarez, 2018	Toxic dose unknown, recommend <5 mg/ kg. Dilute to 1% to increase volume.

Other adjunctive anaesthetic agents/chemical restraint or anxiolytics such as ketamine, midazolam and medetomidine etc have not been described here but doses can be easily found from the above sources.

Studies in chelonia suggest to give a mu - opioid analgesia at least 24–48 h before surgical intervention.

*Eatwell (2010) suggests for local anaesthesia, 10 mg/kg lidocaine and 4 mg/kg bupivacaine, reducing both of these by 50% and using both drugs together.

Multiple Choice Questions

1. Antinociception in red-eared slider turtles is attributed mainly to which opioid receptor?

(a) Mu
(b) Delta
(c) Kappa
(d) Gamma

2. What percentage of reptile veterinarians in the survey considered their recognition of pain in reptiles to be inadequate?

(a) 10%
(b) 25%
(c) 50%
(d) 75%

3. Which of the following is not routinely considered a sign of pain in reptiles?

(a) High heart rate
(b) Darkening of the skin or colour changes
(c) Abnormal respiration
(d) Decreased respiratory rate

4. Which local anaesthetic technique is indicated for hindlimb or bladder surgery in chelonia?

(a) Epidural
(b) Intrathecal
(c) Femoral/ Sciatic block
(d) Bier Block

5. Decreased coiling may be a sign of pain in Serpentes.

(a) True
(b) False

6. How long before surgery is it recommended that opioids are given in Chelonia?

(a) At least 2 hours
(b) At least 6 hours
(c) At least 12 hours
(d) At least 24 hours

7. Many reptiles do not exhibit pain behaviours when observed.

(a) True
(b) False

8. The neurological structure of reptiles associated with pain perception and processing differs from that of mammals.

(a) True
(b) False

For the answers to the MCQs, please go to: http://www.bvna.org.uk/publications/veterinary-nursing-journal