Ultrapotent Anesthetics Use and Safety

- Sathya K. Chinnadurai
- DVM, MS, DACZM, DACVAA, DACAW

Properties of Ideal Restraint Drug

- High Therapeutic Index
- Compatible with other drugs
- Works in multiple species
- Short induction period
- Completely reversible
- Non-irritating
- Small volumes
- Stable solution
- Economical

Ultrapotent Anesthetics

- High potency or high concentration, compounded formulations
- UP opioids require special DEA certification
- Include opioid and non-opioid drugs
  - Alpha-2 agonists

Etorphine HCl, 10 mg/ml

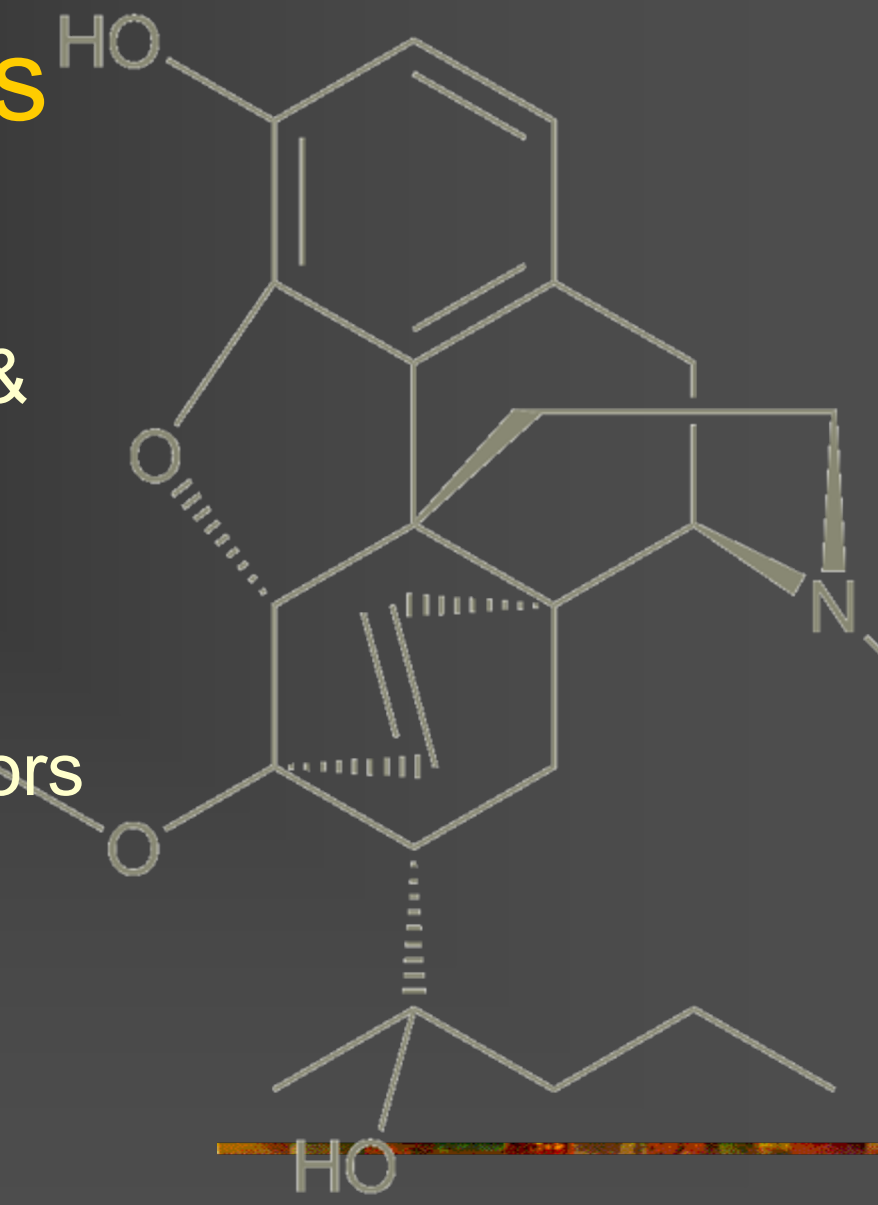
Ultrapotent Anesthetics

- Rapid, reversible anesthesia
- IM administration
- Zoo and field use
- Megavertebrates
- Hoofstock
- Some carnivores

Ultrapotent Opioids

Etorphine (M99)

- Synthesized by Bentley & Hardy 1963
- Used for elephant immobilization 1973
- ***μ***, *δ*, and *κ* opioid receptors
- 1000-4000x more potent than morphine



Ultrapotent Opioids

- Carfentanil
  - analogue of fentanyl
  - 100 times more potent than fentanyl and 10,000 times more than morphine
- Thiafentanil (A3080)
  - slightly less potent than carfentanil, with shorter duration

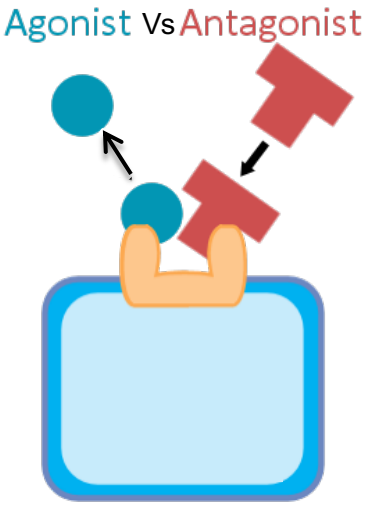
Pharmacokinetics-Opioids

- Highly lipophilic drugs
  - Rapidly distributes throughout extravascular compartments, including the brain and adipose tissue
  - Sequestration in fat can prolong activity
- Metabolized mainly by the liver and excreted via the kidney

Agonists and Antagonists

Agonists - Drugs that occupy receptors and activate them.

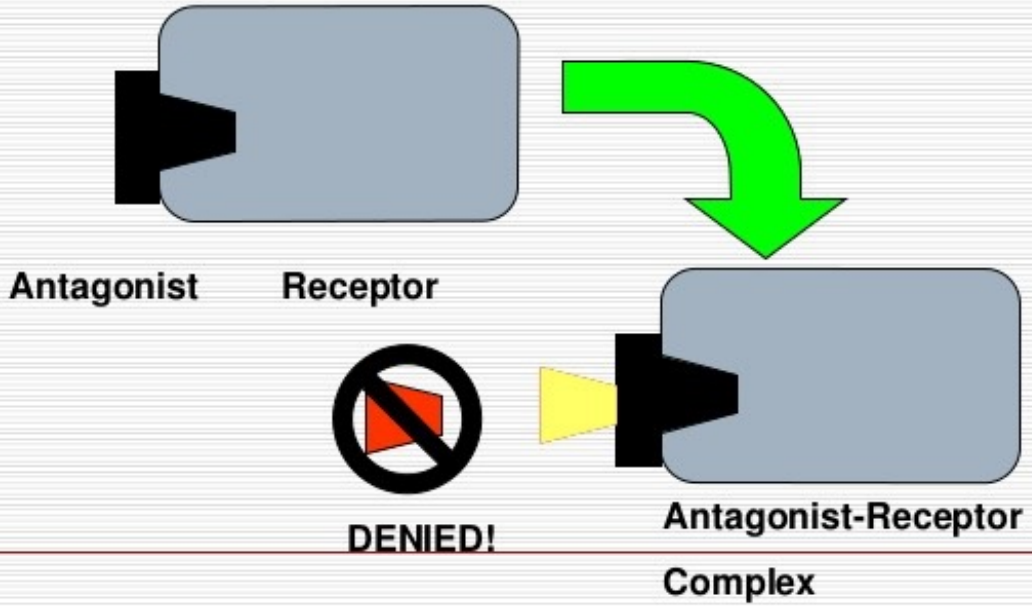
Antagonists - Drugs that occupy receptors but do not activate them
Antagonists block receptor activation by agonists.


Agonist Vs Antagonist

Opioid Antagonists

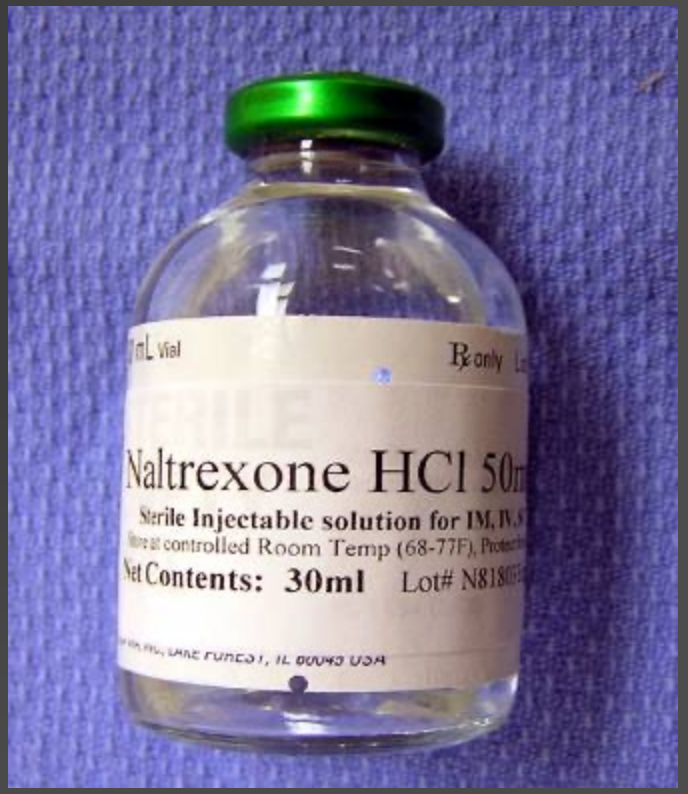
- Naloxone/Naltrexone
  - Displace opioid agonists at receptor due to greater affinity
  - CNS stimulation, minimal CV effects
  - Remember – analgesia reversed too
- Drug specific information
  - Naltrexone activity 2-9x > Naloxone, longer duration of action
  - Naloxone – duration of action is shorter than opioids so may get renarcotization

Competitive Antagonism



Opioid Reversal for Animals

- Naltrexone HCl, 50 mg/ml
- Given IM, IV or split
- High doses in humans rarely associated with liver failure



Opioid Antagonists

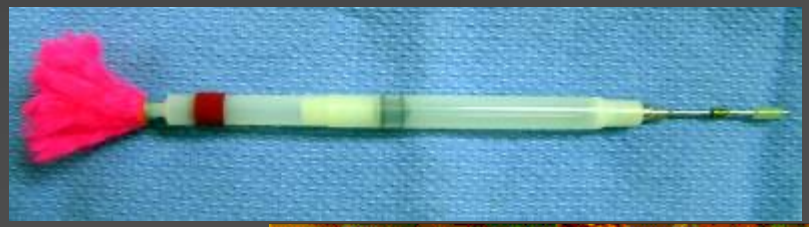
- To reverse carfentanil
  - 100mg of naltrexone for every 1 mg of carfentanil
- To reverse etorphine
  - 25mg to 1mg etorphine (some use higher)
- To reverse thiafentanil
  - 10-50mg to 1 mg thiafentanil
- Naloxone: less potent and shorter duration
  - Approved for human use

Renarcotization

- Duration of action of reversal often shorter than the opioid
- Recurrence of sedation after apparent recovery
- Risk of injury, drowning, conspecific aggression
- Using shorter acting opioids can reduce the risk
- Reducing dose of opioid needed by adding alpha-2 or ketamine

Theoretical Lethal Human Dose

- Absorbed via inhalation, injection, broken skin or through mucous membranes
- Etorphine HCl: 0.05 mg
- Carfentanil Citrate: 0.02mg
- Doses used in animals: 0.5-10.0 mg
- An animal dose could contain 10 to 200 lethal human doses

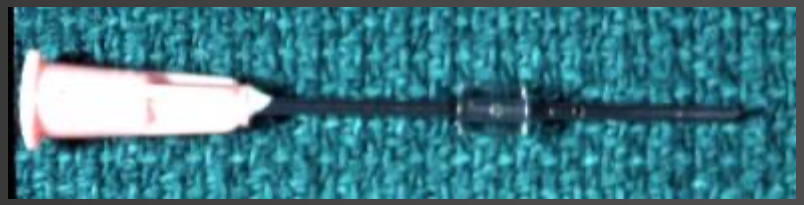


Personal Protective Equipment

- Reversal agent drawn up before narcotic
- Long-sleeves and long pants
- Gloves
- Face shield

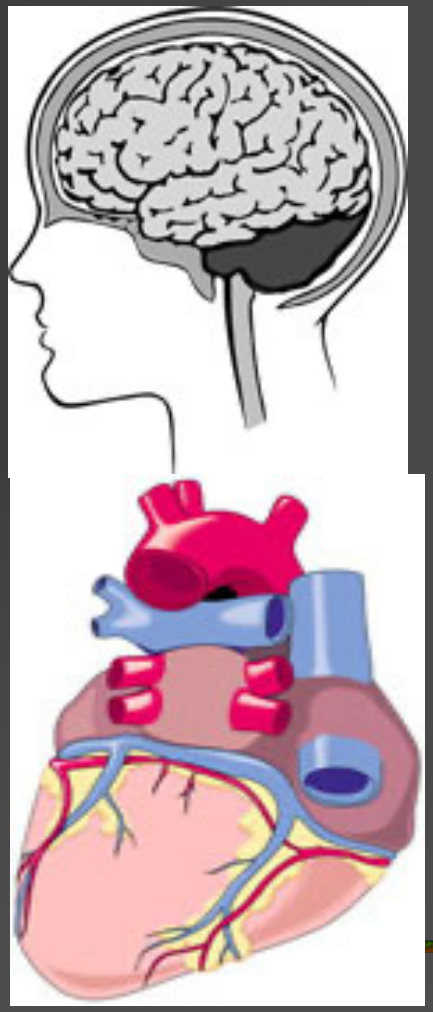
Potential Points of Exposure

- Drawing up drug
- Making dart
- Darting accident
- Retrieving dart
- Contact with dart wound



CNS and CV effects in Humans

- Sedation
- Lethargy
- Seizures
- Coma
- Respiratory depression and arrest
- Hypotension
- Bradycardia



Opioid Side Effects in Animals

- Wide safety margin and dose range
- Excitement, aimless wandering
- Myopathy (secondary)
- Respiratory depression
- Hypertension, bradycardia
- Regurgitation
- Muscle rigidity
- Renarcotization

Not Just Ultrapotent Opioids

Occupational Medicine 2010;**60**:494–495
Advance Access publication on 23 June 2010 doi:10.1093/occmed/kqq088

CASE REPORT

Accidental poisoning with detomidine and butorphanol

N. Hannah

Department of Medicine, Raigmore Hospital, Inverness, UK

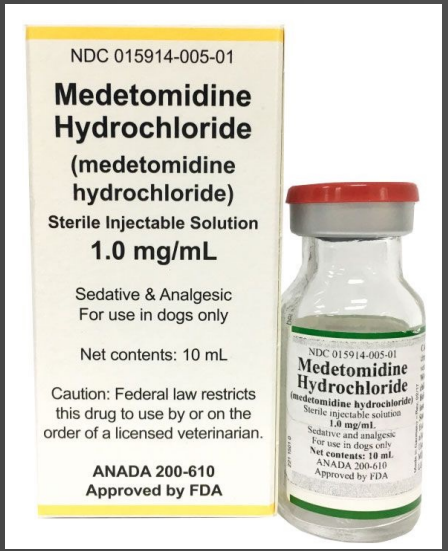
Correspondence to: N. Hannah, FY2, Department of Medicine, Raigmore Hospital, Old Perth Road, Inverness IV2 3UJ, UK. Tel: +44 (0)1463 704 000 ext. 6514; fax: +44 (0)1463 704596; e-mail: neilhannah@nhs.net

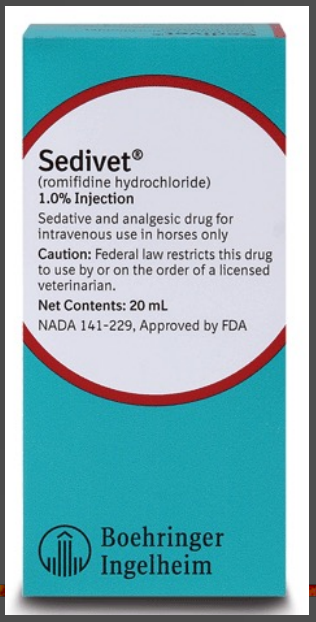
Abstract This is a case report concerning a veterinarian who spilled detomidine and butorphanol on dermatitic hands while sedating a horse. This resulted in acute poisoning from which the patient spontaneously recovered with supportive management. Veterinarians often suffer from occupational dermatitis and handle strong sedatives with no gloves while working around unpredictable animals. Thus, this group is at risk of accidental self-poisoning from this method.

Key words Butorphanol; detomidine; drugs; farmers; poisoning; veterinarian; workers.

Alpha-2 Agonists

- Xylazine
- Detomidine
- Romifidine
- Dexmedetomidine
- Medetomidine
  - + High Concentration



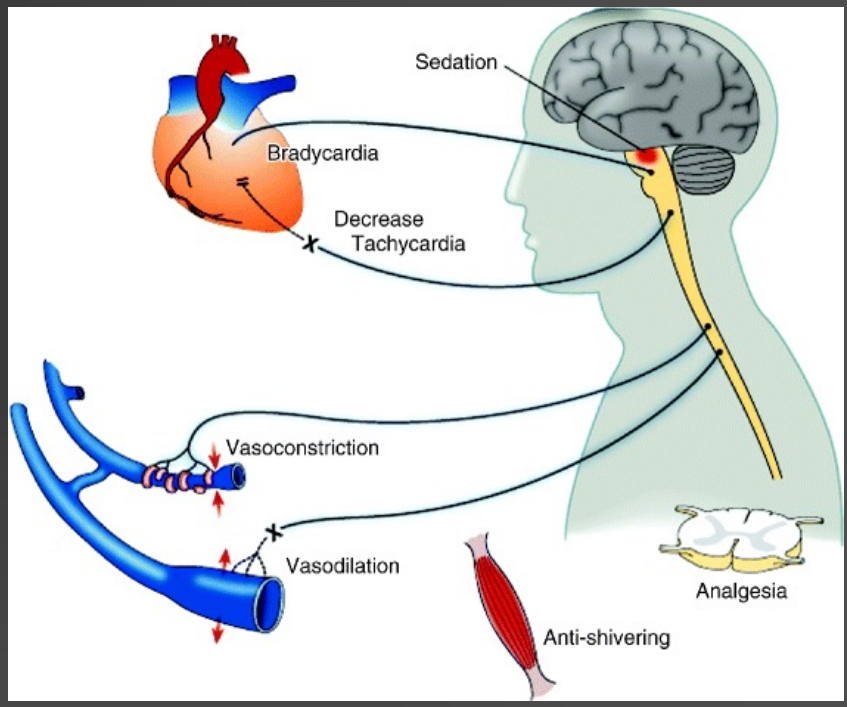


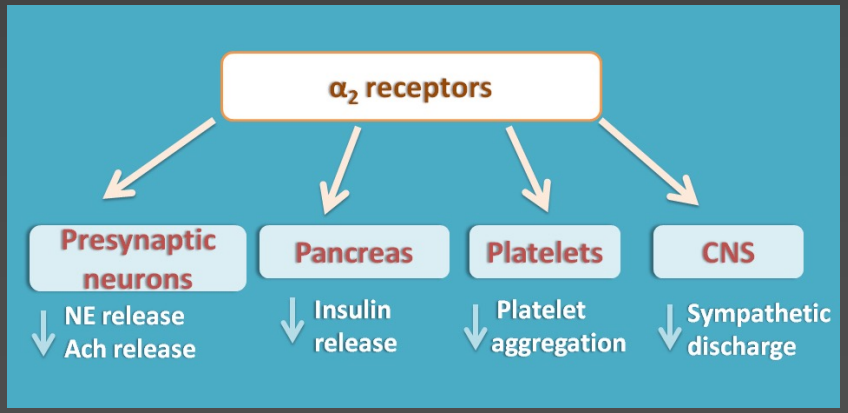
Alpha-2 Agonists

- Potent, reliable sedation
- Used in many veterinary species
  - Exotics
  - Wildlife
- Reversible

Alpha-2 Receptor Location

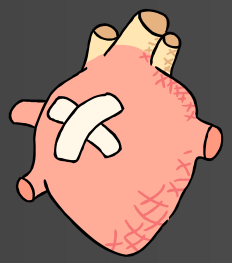
- Brain (locus ceruleus)
- Spinal cord (dorsal horn)
- Peripheral vasculature
- Other tissues





Alpha-2 Agonist: Cardiovascular Effects

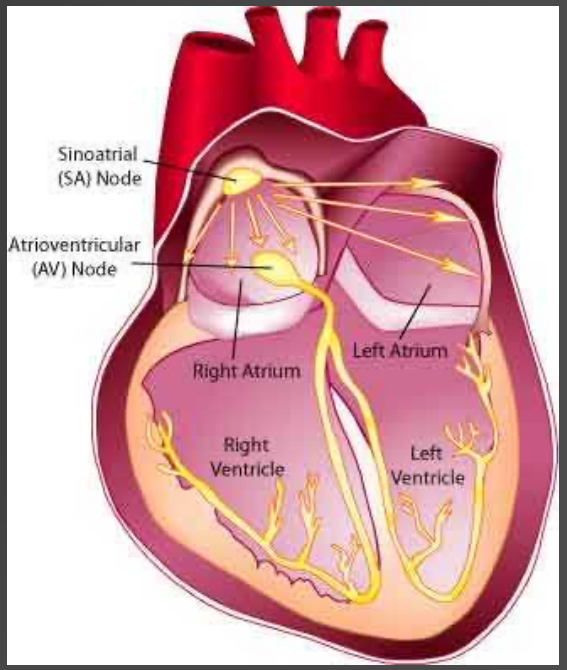
- Biphasic CV response

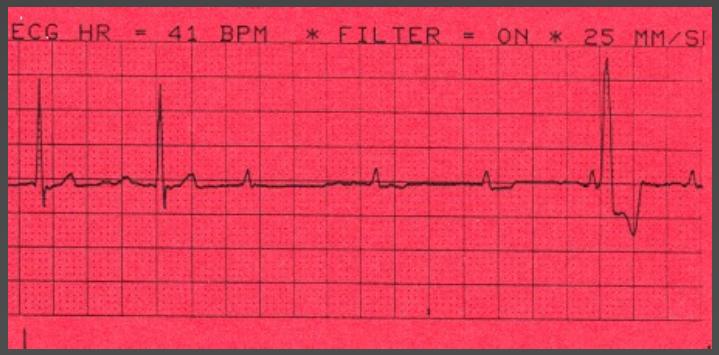


- 1st phase
  - Binding of α-2 receptor in vasculature
    - vasoconstriction
    - increased systemic vascular resistance (SVR)
- Increased blood pressure
- **Reflex bradycardia**

Alpha-2 Agonist: CV Effects

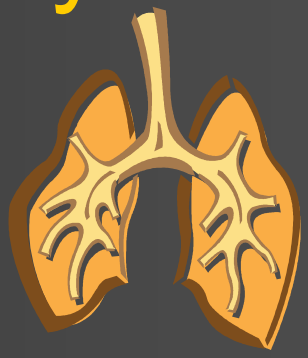
- Slowed electrical conduction though heart
  - negative dromotropy
  - bradycardia
  - heart block
    - 1st, 2nd, 3rd degree
  - ventricular arrhythmias





Xylazine premedication- dog

Alpha-2 Agonist: Respiratory Effects



- Mild to moderate respiratory depression
  - Effects respiratory centers in medulla
  - Depress response to hypercapnia
  - Effects greater with other CNS depressants
- Can cause hypoxemia in some species
  - Activation of pulmonary intravascular macrophages
  - Pulmonary edema

Alpha-2 Antagonists

- Compete for alpha-2 receptor
  - bind, but do not activate the receptor
- Reverse both the sedation and analgesia
- Reversal agents
  - Choose agent with similar alpha-2:alpha-1 specificity
  - Dose based on dose of agonist not mg/kg dosage

Alpha-2 Antagonists

- Reversal Agents
  - yohimbine (for xylazine)
  - atipamezole (for (dex)medetomidine)
  - tolazoline least specific reversal (preferred in ruminants)

- Preferable to choose reversal with similar specificity as agonist
  - Can use any to reverse any agonist
    - More difficult to estimate dose

Potential risks at post-mortem

DOI: 10.7589/2017-06-132

Journal of Wildlife Diseases, 54(2), 2018, pp. 362–365

Tissue Residue Levels after Immobilization of Rocky Mountain Elk (*Cervus elaphus nelsoni*) using a Combination of Nalbuphine, Medetomidine, and Azaperone Antagonized with Naltrexone, Atipamezole, and Tolazoline

Lisa L. Wolfe,[1,5] Pauline Nol,[2] Matthew P. McCollum,[2] Travis Mays,[3] Morgan E. Wehtje,[2] William R. Lance,[4] Mark C. Fisher,[1] and Michael W. Miller[1] [1]Colorado Division of Parks and Wildlife, 4330 Laporte Avenue, Fort Collins, Colorado 80521, USA; [2]US Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Wildlife Livestock Disease Investigations Team, 4101 Laporte Avenue, Fort Collins, Colorado 80521, USA; [3]Texas A&M Veterinary Medical Diagnostic Laboratory, Texas A&M University System, 483 Agronomy Rd., College Station, Texas 77841, USA; [4]Wildlife Pharmaceuticals, Inc., 1230 Ash Street, Windsor, Colorado 80550, USA; [5]Corresponding author (email: lisa.wolfe@state.co.us)