Chemical Immobilization of Wild Ruminants

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Historically, pharmacological immobilization can be traced back to certain tribes from South America who used curare-coated arrows in their quest for food. Though this method was effective and curare derivatives were used for many years, an effort began in 1958 by rangers in South Africa to develop new and hopefully more efficacious methods to immobilize animals for research.[1] Since that time, great strides have been made in developing new drugs and techniques for delivery of these drugs. It is the purpose of this paper to consolidate and review the latest developments in animal immobilization.

Compounds

Many different classes of compounds including anesthetics, analgesics, sedatives and tranquilizers have been used to immobilize animals. Today, however, only a few of these compounds can be used on a regular basis due to federal regulations. One of these regulations, the FDA's Controlled Substances Act of 1970, restricts the use and distribution of some of the more potent drugs such as opioids.[2] Fortunately, there are other drugs which are just as effective and more accessible.

Opioids

This class of drugs has three advantages: (1) they are easy to administer (due to the high potency of the members used, less than 1 ml can immobilize most animals), (2) their high therapeutic index, and (3) the availability of antagonists to reverse their effects. The most two popular opioids are the highly potent thebain derivatives: etorphine,[3,4] and carfentanil.[5,6] Because of their extreme potency, opioids must be handled with care by the people administering them; accidental self-injection or con-

tact with mucous membranes can be lethal.

Etorphine was first introduced in 1963 as a viable alternative to diethylthiambutene for the immobilization of large ungulates. It quickly became one of the main immobilizing agents used in South Africa, and since then many other countries have done research on the safety and efficacy of etorphine. At moderate doses, etorphine induces sedation but the animal usually remains standing, and higher doses will cause the animal to become sternally recumbant. However, to obtain surgical anesthesia, a neuroleptic such as xylazine must be used in combination with etorphine.[7] This combination will also decrease the respiratory and renal depression attributed to etorphine alone.

When etorphine was first introduced the dose was calculated by trial and error, but now recommended doses are available for many species (Appendix I). Most are in the range of 1.0-1.75 mg/45 kg (100#), however, the exact dosage of etorphine varies depending on the species and the health and excitement of the animal.[4] It is commercially available in the United Kingdom as a 2.45% solution combined with acetylpromazine, and it is approved for use as a 1% solution by zoos in the United States.

Carfentanil is a highly potent synthetic opioid, reported to be 50-100% more potent than etorphine.[6] It is supplied as a 1% solution which must be diluted with sterile saline (1:4) for use in most species. Doses of .9-1.5 mg/45 kg have been used to immobilize mule deer[6] and moose.[5] In these studies, it was used either alone or in combination with acetylpromazine or xylazine, the latter two drugs being used to increase muscle relaxation. More research must be done to evaluate carfentanil before it is released for more extensive use. Only one company is licensed to distribute the drug in the United States.

A distinct advantage of opioids as immobilizing agents is that their action can be reversed by

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the use of opioid antagonists. These antagonists include diprenorphine, cyprenorphine, naloxone, and nalorphine. When they are used in animals not under the influence of one of the other opioids, all with the exception of naloxone will bind to opiate receptors of the body and cause a morphine-like response. However, when used after the aforementioned opioids, they reverse the opioid effects. This is thought to be a type of competitive inhibition, displacing the more potent opioids.

Dosages of each of the antagonists should be checked before any opioids are used. There is quite a wide dosage range depending on the immobilizing agent used. For example, a 10 mg dose of etorphine requires 20 mg of diprenorphine to reverse its effects;[3] however, the same dose of carfentanil requires 100 mg of diprenorphine for adequate reversal.[6]

Sedative Analgesics

Xylazine, an alpha-2 adrenoreceptor agonist, is the most commonly used drug in the sedative analgesic category. It has many of the same effects as the opioids without the CNS stimulation. Xylazine produces muscle relaxation and sedation (in most animals) and some analgesia.[8] However, animals under the influence of xylazine can still react to painful stimuli, so proper restraint must always be employed when using this drug to prevent injury to the animal and personnel.

Sedation can be obtained with doses of .5-2.0 mg/kg, whereas complete immobilization requires 3-8 mg/kg. Dosages can vary depending on age, degree of excitement, and species, e.g. Jacobsen[9] has found that black-tailed deer that were alarmed required twice the dose of deer that were calm. Fawns weighing 10-20 kg required dosages higher than either younger or older animals.

For many years, the main disadvantage of using xylazine was the lack of a good reversal agent and therefore long periods of unnecessary immobilization. Recently, research has been done on an alpha-2 adrenoreceptor blocker called yohimbine. It has been used extensively and with good success in white-tailed deer,[7,10-13] mule deer,[13,14] moose,[5] and bighorned sheep.[13,14] The average arousal time after intravenous injection of yohimbine is 4 min. If 4-aminopyridine is used along with yohimbine, arousal occurs in an average of 2.5 min.[13] This is due to the complementary effects of these two drugs, an acetylcholine releaser and an alpha-2 blocker respectively.

Tolazoline, a vasoactive amine used in human cardiotherapy, has also been successfully used as a xylazine reversal agent by some zoos and researchers. Studies done on dogs[15] and cattle[16] have found it to be a suitable substitute for yohimbine, and in some cases was the preferred drug due to its more complete and longer lasting reversal.[17] More research must be done to substantiate these claims.

Tranquilizers

The most commonly used tranquilizers are the phenothiazine derivatives. These drugs cause sedation and muscle relaxation, but are not potent enough to be used alone. In a study by Pusateri,[18] promazine was used as an oral immobilizing agent in pronghorn antelope. Doses of 2-17 mg/kg had no effect on these animals no matter what the age or condition. It has also been the author's experience that twice the recommended equine dose of promazine HC1 (5 mg/kg) added to grain would not sufficiently tranquilize a tame, 6 year old, female white-tailed deer for capture. However, acetylpromazine is very useful when used in conjunction with opioids or phencyclidine derivatives to decrease their side effects. When used in combination with other agents, acetylpromazine dosages range from .05-.5 mg/kg.

Another group of tranquilizers frequently used are the benzodiazepine derivatives. Diazepam (Valium) has been used as an oral immobilizing agent. It, unlike the promazines, has enough sedative action to make tame pronghorn antelope manageable.[18] It was most effective in the adult animal at a dose of 7-23 mg/kg. Fawns were not affected significantly by these doses.

Neuromuscular Blocking Agents

These agents have been used for many years to immobilize wild ruminants. The most popular drug in this class is succinylcholine. However, in recent years, its use has diminished mainly because of its low therapeutic index and the lack of a safe and effective reversal agent. An overdose of succinylcholine will cause diaphragmatic paralysis, which is lethal if resuscitation equipment is not available. Therefore, its use is not recommended. Dosages of .02-.05 mg/kg have been used in the past with only moderate death losses.[1]

Phencyclidine Derivatives

The phencyclidine derivatives, which include phencyclidine and ketamine, are classified as dissociative anesthetics. This means they dissociate the central nervous system causing immobilization.[8] These drugs also cause catatonia and increased salivation while having minimal effect on reflexes such as swallowing and blinking.

Phencyclidine (PCP) was first used by Harthoorn in the late 50's.[1] It was found to be an effective anesthetic agent for small ruminants, but was taken off the market in the 70's because of human abuse. Ketamine, on the other hand, is still getting limited use in small ruminants such as black-tailed deer. It is usually used in combination with xylazine to decrease the catatonia. In one study, this combination was used on white-tailed deer at a dosage of 1-2 mg/kg xylazine and 6-8 mg/kg ketamine. This is equivalent to a 1:1 combination of small animal Rompun (20 mg/ml) and Ketaset (100 mg/ml) used at a rate of 1 ml/5-10 kg.

Another combination is ketamine and acetyl-promazine. This was used by the author at 3 times the recommended dose in an attempt to anesthetize a 2 month old male white-tailed deer. At this dose, the fawn became only slightly ataxic. No more was given because of the threat of hyperthermia and hypoxia from high environmental temperature and excitement.

Delivery Methods

Over the years, many methods have been developed to deliver the drugs to animals. At this time, there are three systems that are frequently used: the pole syringe, projectile syringe, and baits.[3]

Pole Syringe

The pole syringe is not used that often unless facilities are adequate to keep the animals closely confined, which may increase the likelihood of injury to the animal and personnel.[1] The lack of confinement precludes its use on free ranging animals. The pole syringe is, however, a good system to use in vaccination and antibiotic administration in captive animals.

Projectile Syringes

The most frequently used system for the delivery of immobilizing agents is the projectile syringe or dart. The two main components of this system are the projectile and the projector.

There are many types of syringes in use today. They all work on the same principle: the use of some material in a closed chamber to exert a force to push the plunger.

One type of syringe uses compressed gas, mainly air or CO_2.[1] These darts are inexpensive to fill with gas, pressures can be varied, and the syringe can be reused many times. However, some method must be devised to stop leakage of the immobilizing agent from the needle. A plastic or silicone collar fitted over the opening in the needle is usually

used. The collar is pushed back on impact and the immobilizing agent is delivered.

Another type of syringe uses an acid-carbonate system.[19] This syringe uses a pelleted or powdered carbonate separated from the liquid acid by a diaphragm or plug. On impact, the diagram is broken and the chemicals mix. To accomplish this, various lead weights are used (Figure 1). These syringes have the disadvantage of delayed drug release, since it takes time for the chemical reaction to occur. They also have a tendency to bounce out before injection is complete. These problems can be remedied by the use of barbed needles.

The last major type of syringe (projectile) is the percussion cap syringe, which is probably the most widely used. Caps or powder charges are used to inject the agent. They have some type of internal triggering mechanism to set off the charges, which vary in size depending on the syringe volume.

The main disadvantage of this type of syringe is the tissue damage, which includes large hematomas, and internal damage, caused by the excess force of the injection. Some advancements are being made to decrease this damage.

A recently developed syringe is a modification of the projectile syringe called the radio telemetry dart. This dart is a combination of a spring loaded syringe and a radio transmitter. This helps in locating animals darted in heavy cover. The dart is only available in New Zealand at this writing.[7]

There are also other less frequently used projectiles. These are grooved darts which hold pastes and powdered agents. They have the disadvantage of inaccuracy in the dosage and are therefore not used frequently.[1]

To deliver the projectiles on target, a good projector is needed. The three types used most frequently are the powder gun, CO_2 gun, and blow-gun.

The most accurate and most widely used of these is the powder gun. Most models use different size charges to vary the range, but only two companies make models with a fine adjustment for ranges from 6-100 m.[1] The ability to vary the range is very important. The longer the range, the harder the impact and the more damage there is to the animal. To prevent this, shorter ranges should be used whenever possible.

Another commonly used propellent is CO_2. Many rifles and pistols are available and most use an easily obtained CO_2 cartridge. These guns have some advantages at shorter ranges, but since they use an expandable gas, variations in the temperature and canister pressure will affect the velocity of the projectile. This is partially counteracted by the use of larger canisters and experience.
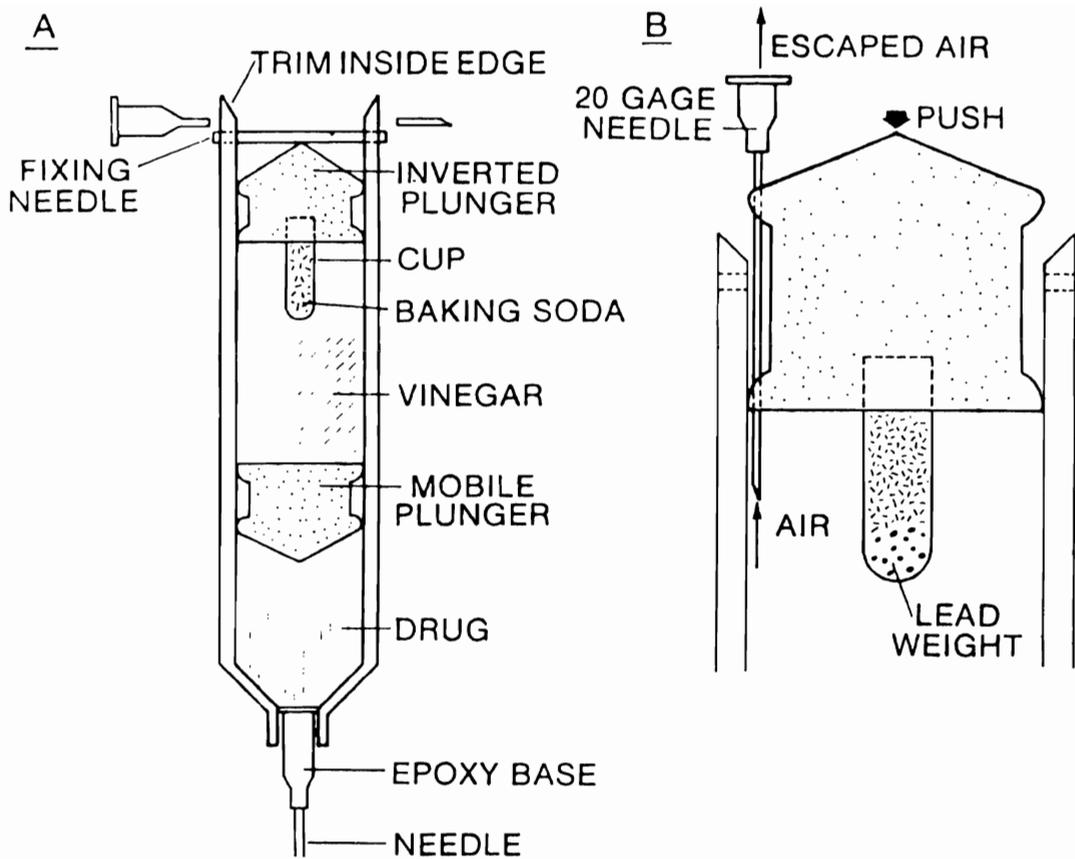
FIGURE 1.[19]

(A) Diagram of a completely assembled blow-gun syringe (Without the tail piece).
(B) Diagram showing the proper procedure for positioning the inverted plunger into the syringe tube.

The last major type of projector and the least expensive to use is the blow-gun. Light weight aluminum models are available commercially, however, inexpensive homemade versions can be constructed out of common PVC water pipe of various diameters and lengths.[20,21] They have a range of up to 30 m which restricts their use to closely confined animals in zoos and wild animal parks. Because of the limited range and problems with the darts, they are used infrequently.

One last delivery system that is used infrequently is the crossbow. It is cumbersome and inaccurate at distances greater than 40 m. It also needs specially constructed darts with extra flighting. Therefore, it is only used on thick skinned animals at close range and is not recommended for use on most ruminants. For example, it is used occasionally on elephants.

Baits

The final method used to deliver immobilizing agents is the bait. Baits have been used periodically in the past to immobilize animals. The advantage of this method is that the animals do not have to be stressed in any way before they are immobilized. The baits can be placed at an existing feeding station before the animals appear. Then they can be observed from a distance until the drug takes effect. The only real problems with the use of baits are dosage and efficacy.[18]

Most ruminants are herd type animals. If more than one animal is to be captured, enough agent must be provided to accomplish this. However, not all animals in the herd eat the same amount of bait. So some of the animals are overdosed and others are underdosed. But this problem is minor compared to that of efficacy. The only drug to show any promise as a bait is diazepam. Attempts to use other drugs such as succinylcholine or promazine were not successful.

Physiological Effects of Capture

There are many physiological and metabolic changes that occur as a result of immobilization.[22-25] Not all of these changes are caused by the immobilizing agent. In fact, most changes are due to the capture of the animal. The most common of these is capture myopathy.

Capture myopathy is a multifaceted condition associated with capture.[22] It has been studied extensively in the past few years, but the exact etiology has not been discovered. Capture myopathy seems to be related to a metabolic acidosis caused by extreme exertion over a short period of time. This can be seen histologically as necrosis of the large mus-

cle masses of the legs and other areas. This leads to the collapse of the animal and eventual death from acidosis, predation or other factors.

T.R. Spraker has described four separate syndromes related to capture myopathy.[7] These are the peracute and acute death syndromes, ataxic myoglobinuric syndrome and the ruptured muscle syndrome. The first two are mainly the result of the metabolic acidosis and concurrent hyperkalemia. The ataxic myoglobinuric syndrome is similar to azoturia in horses and death is due to kidney and muscle lesions. The last syndrome, ruptured muscle syndrome, is the result of muscular necrosis leading to rupture of the gastrocnemius muscles, which eventually leads to the animal's death from predation or starvation.

Some attempts have been made to try to decrease the incidence of capture myopathy including tranquilizing animals with a bait before darting. Although no one method has worked, the less stress put on the animal prior to, during, and after immobilization, the less damage there is going to be.

There are some biochemical changes caused by immobilization that are not as harmful to the animal as capture myopathy. Recently, researchers found that the so called hematologic normals for the white-tailed deer[24] and some antelope[25] were actually stress hemograms. They found that initial blood samples had increased glucose, total protein (TP), and packed cell volume (PCV). Wesson et al. found the PCV and TP of white-tailed deer immobilized with phencyclidine and promazine to be decreased after 30 minutes and became stable at these levels.[24] Jacobson[25] and Wesson et al.[24] found glucose levels to be increased after a short delay. The increase in the glucose was thought to be due to the release of epinephrine. The increase in the PCV and TP were caused by contraction of the spleen and peripheral blood pooling and protein catabolism respectively, which are also due to the release of epinephrine. Other researchers also found the calcium, phosphorus,[23] and potassium[25] to be decreased after immobilization. These changes also were due to the stress of handling and not from the drugs themselves.

Summary

Since 1958, major improvements have been made in immobilizing agents and delivery systems. They have gone from the use of curare-tipped arrows to the present use of potent opioids in sophisticated syringes delivered by highly accurate rifles. However, there is still a long way to go. New immobilizing agents will need to have fewer side effects, faster immobilizing action, and an easily

Dosages of Immobilizing
Agents in Common Species

Species	Etorphine	Diprenorphine	Xylazine	W/Narcotics	Yohimbine
Roan Antelope	3-4 mg	2x Etorphine	3 mg/kg	1.5-2 mg/kg[a]	—
Sable Antelope	3-6	2x Etorphine	3	.15[a]	—
Eland	5-10	2x Etorphine	3	.2-8[a]	—
Wildebeeste	3-5	2x Etorphine	1.5-3	—	—
Blesbok	2-3	2x Etorphine	—	—	—
Gazelle	2-3	2x Etorphine	2-4	.27[b]	—
Impala	2-5	2x Etorphine	3	.2-1.6[b]	—
Blackbuck	2-3	2x Etorphine	3	—	—
Bison	4-10	2x Etorphine	.6-1.0	.2-.3[a]	—
Gaur	5-7	2x Etorphine	—	—	—
Yak	3-8	2x Etorphine	.4-1.0	—	—
Fallow Deer	2-4	2x Etorphine	5-8	.38 mg/kg[a]	—
Wapiti	3-6	2x Etorphine	2	30 mg[a]	.6 mg/kg
White-tailed	3-6	2x Etorphine	3-5	.35-.6 mg/kg[a]	.1-.6
Mule Deer	2-4	2x Etorphine	4.4	40-100 mg[a]	.09-.4
Caribou	2-5	2x Etorphine	2	—	—
Moose	4-8	2x Etorphine	.7-1.5	.15-.53 mg/kg[b]	.15[c]
Aoudad	2-4	2x Etorphine	.62-1.5	—	—
Bighorn	2-4	2x Etorphine	.8-1.0	20-50 mg[a]	.1-.3 mg/kg
Pronghorn	1.5-5 mg	2x Etorphine	1-1.2 mg/kg	—	—

[a] with ½ dose of Etorphine
[b] with .18-.25 mg/kg Fentanyl
[c] with .3 mg/kg 4-aminopyradine

Species	Promazines	Succinyl Choline	Ketamine	Phencyclidine
Roan Antelope	.4 mg/kg[a]	14 mg	—	—
Sable Antelope	.4 mg/kg[d]	—	—	—
Eland	.1 mg/kg[b]	27 mg	—	—
Wildebeeste	—	—	—	—
Blesbok	—	—	—	—
Gazelle	—	—	—	—
Impala	—	—	900-1200 mg	90 mg
Blackbuck	—	.6-3 mg	—	—
Bison	—	55-60 mg	—	50 mg
Gaur	—	—	—	—
Yak	—	—	—	—
Fallow Deer	—	2-5 mg	—	—
Wapiti	10-20 mg Ace[a]	12-25 mg	—	—
White-tailed	—	6-8 mg	—	—
Mule Deer	—	8.5-16 mg	—	1.54 mg/kg[a]
Caribou	—	.055-.14 mg/kg	—	—
Moose	—	12-18 mg	—	—
Aoudad	—	25 mg	5-7 mg/kg	1.5-2.6 mg/kg
Bighorn	5-10 mg Ace[a]	—	—	—
Pronghorn	.08-.11 mg/kg	2 mg	—	—

[d] with Xylazine.

administrable form. These drugs should also have a fast and effective antagonist, eg. yohimbine's reversal of xylazine or diprenorphine's reversal of etorphine and carfentanil.

The delivery systems also need some improvement. The injury caused by the impact of the darts must be decreased. This could significantly decrease losses especially after release. The most significant improvement in this area is the radio telemetry syringe. Their use should significantly decrease the loss of animals in thick cover and make it possible to immobilize animals in areas that were bypassed before. With these improvements alone, the incidence of death in immobilized animals and possibly even the incidence of capture myopathy will be decreased.

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