CHAPTER 3

CARDIOVASCULAR EFFECTS OF

THE TRANQUILIZERS

These agents are now more commonly classified as psychotropic or neuroleptic agents. This indicates a primary mode of action on certain functions of the central nervous system. Many of these agents have a profound effect on the cardiovascular system in addition to, or perhaps because of, their CNS activity. The CNS activity seems to be linked to the blockade of dopamine within the basal ganglia complex. The stereochemical model of chlorpromazine (one of the phenothiazine derivates) is similar to the structures of epinephrine, norepinephrine and dopamine but two-dimensional models of these compounds do not usually make the similarities apparent. Many of these compounds are apparently dopamine antagonists which act on dopamine excitatory receptors. The drugs are widely used for chemical restraint and preanesthetic agents when working with animals. The cardiovascular effects are summarized in Tables 3.1-3.9.

The phenothiazine tranquilizers are reported to decrease preload, contractility and afterload and to increase heart rate. They have been reported to produce arrhythmias along with their paradoxical antiarrhythmic properties. They have been shown to; decrease the rate of rise of phase 0 of the myocardial action potential, decrease the duration and amplitude of phase 2, and prolong phase 3. Repolarization abnormalities induced by these agents seem to be dose related.

The Butyrophenones are a group of agents which were developed from efforts to increase the analgesic potency of a series of 4-phenylpiperidines related to meperidine. They are related to the antihistamines and spasmolytics. In veterinary practice they are most frequently used in combination with
narcotic analgesics which seems to potentiate the sedative action of both agents.

The Benzodiazepines induce taming effects in animals probably by affecting neurotransmitter systems, including acetylcholine, catecholamines, serotonin, GABA and glycine. A widespread distribution of benzodiazepine receptors in the grey matter of the CNS has been demonstrated in all species studied, as opposed to a lack of receptors in white matter.1 These agents are frequently used for their calming or taming effects as preanesthetics, and also for their antiarrhythmic effects.

The Rauwolfia derivatives are known to result in depletion of catecholamine stores and, therefore, act by reducing the normal physiological response to stress. Reserpine is the major Rauwolfia derivative used, but its use has most recently been limited to studies which are designed to investigate the role of catecholamines in the cardiovascular response to a wide variety of perturbations. The recent literature using reserpine in this manner in rats, mice, rabbits, guinea pigs and hamsters is overwhelming.

One tranquilizer cannot be classified with the others included in this chapter but is extremely important as a method of chemical restraint in veterinary medicine, particularly in horses. Xylazine provides excellent sedation and calming and is widely used for that purpose in horses and cattle. It also may potentiate second degree heart block in horses. It has severe hypotensive and bradycardic effects which have a duration of approximately 1 hour with normal doses. The effects are dose-dependent, and ruminents require only 1/10 of the dose used in horses. If the animal is ill lower doses may be required.4 The drug is reported to cause decreases in preload, afterload and heart rate with no change in contractility.2 These effects seem to be attributable to either direct or indirect effects on the autonomic nervous system. Initially, following an intravenous injection, there is a transitory hypertension, via vasoconstriction of the splanchnic and peripheral vasculature. These effects have been enhanced by beta-adrenergic-blockers and blocked by alpha-adrenergic-blockers in a variety of species so tested. Bradycardia and second degree A-V block are commonly seen, probably as a result of an increase in vagal tone resulting from the hypertension. Atropine has been shown to block this reaction.80 As an analgesic, xylazine provides relief in horses for 30-60 minutes in doses of 0.2-0.4 mg/kg, IV or 0.4-0.8 mg/kg, IM.4 A brief summary of reported cardiovascular effects of xylazine is given in Table 3.9. Xylazine is sold under the trade name of Rompun® in the U.S.A.