SOME EFFECTS OF TRIFLUPROMAZINE HYDROCHLORIDE IN GOATS

Thesis for the Degree of M. S.

MICHIGAN STATE UNIVERSITY

Saroj Kant Jha

1959

SOME EFFECTS OF TRIFLUPROMAZINE HYDROCHLORIDE IN GOATS

by

Saroj Kant Jha

AN ABSTRACT

Submitted to the College of Veterinary Medicine
Michigan State University of Agriculture and
Applied Science in partial fulfillment of
the requirements for the degree of

MASTER OF SCIENCE

Department of Surgery and Medicine

1959

Approved 

SAROJ KANT JHA

ABSTRACT

This study was made to determine the effects of triflupromazine hydrochloride (vetame*) on respiratory rate, pulse rate, arterial blood pressure, rectal temperature, electrocardiogram, and spontaneous motor activity of goats. A permanent loop of the left carotid artery was established for recording arterial blood pressure. A Sanborn multichannel recorder and electromanometer were used for recording blood pressure, electrocardiogram and pulse rate. A New Haven pedometer was used for recording spontaneous motor activity. Respiratory rates were determined by means of a stethoscope. Three dose levels of vetame were used intravenously--0.5, 1.0 and 2.0 milligrams per pound of body weight. Readings were made at 30 minute intervals. With 0.5 milligram and 1.0 milligram doses, three readings were taken. With 2.0 milligram doses, readings were usually taken at 30 minute intervals up to a minimum of six hours. Some of the readings, due to technical or mechanical difficulty, could not be recorded.

After administration of the drug, depression, labored breathing, cyanosis of mucous membranes of varying degree, salivation and incoordination of hind quarters were the symptoms observed. When the drug was administered at the rate of 0.5 milligrams per pound of body weight,

---

*E. R. Squibb and Sons, New Brunswick, New Jersey.

respiratory rate was lowered in 71.4 percent of the goats at 30 minutes, and in 57.1 percent at 60 and 90 minutes. When it was injected at the rate of one milligram per pound of body weight, respiratory rate was lowered in 62.5 percent at 30 minutes, and in 75 percent at 60 minutes. Statistically, the difference between the normal and the 30 and 60 minute readings was insignificant. At the rate of two milligrams per pound of body weight, respiratory rate was lowered in all goats.

At 0.5 milligrams per pound of body weight, pulse rate was increased in 85.7 percent at 30 minutes, and at one milligram it was increased in 75 percent of animals throughout. In the former case, it was statistically insignificant, but in the latter it was found significant at the five percent level. At two milligrams per pound of body weight fluctuating pulse rate was recorded.

At 0.5 milligrams, blood pressure was decreased in 57.1 percent of the animals at 30 minutes. At one milligram, lower blood pressure was recorded in 75 percent at 30 minutes, in 62.5 percent at 60 minutes, and in 85.7 percent at 90 minutes, but statistically the changes were insignificant. At two milligrams, blood pressure was lower in all goats up to 60 minutes, in 80 percent up to 120 minutes, and in 40 percent throughout the period of observation.

At one milligram, rectal temperature was lowered in

two of three goats at 30 and 60 minutes, and normal temperature was recorded in all at 90 minutes. At two milligrams, lower rectal temperature was recorded in all animals from 30 to 420 minutes. The changes were statistically insignificant.

No electrocardiogram change was found which could be attributed to this drug.

The drug showed its spontaneous motor activity depressant action in 75 percent of eight goats. This change was found to be statistically significant at the five percent level.

SOME EFFECTS OF TRIFLUPROMAZINE HYDROCHLORIDE IN GOATS

by

Saroj Kant Jha

A THESIS

Submitted to the College of Veterinary Medicine
Michigan State University of Agriculture and
Applied Science in partial fulfillment of
the requirements for the degree of

MASTER OF SCIENCE

Department of Surgery and Medicine

1959

Dedicated to

My parents--Ratikant and Aagam

and

My wife--Veena

ACKNOWLEDGMENTS

A deep sense of gratitude is expressed to Dr. Wm. V. Lumb, Associate Professor, Department of Surgery and Medicine, without whose untiring assistance, guidance and encouragement this project would never have been a success.

Thanks are due to Dr. R. F. Johnston, Associate Professor, Department of Physiology and Pharmacology, for his precious help and assistance.

Appreciation is expressed to Dr. W. O. Brinker, Professor and Head of the Department of Surgery and Medicine, and to Dr. B. V. Alfredson, Professor and Head, Department of Physiology and Pharmacology for facilities and equipment offered in carrying out this research.

Sincere thanks are due to Mr. Art Berkey, a sophomore student, for his assistance in this project.

Appreciation is expressed to those members of the teaching staff, Department of Surgery and Medicine, who have, in one way or another, helped in this project.

Thanks are also due to the fellow graduate students for their invaluable assistance.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF PICTURES

CHAPTER I

INTRODUCTION

In human medicine, tranquilizing drugs have been used for numerous indications. However, most of the use is for mental disturbances. According to Rose (37), in 1957 fifty million prescriptions were written for these drugs in the United States alone. Thus, in 1957 in the United States, five percent of patients under medication at any time were receiving tranquilizers.

These drugs have also been introduced into veterinary medicine for various indications. Their use as chemical restraint in place of physical restraint has been found very satisfactory (24). Encouraged by their successful effects, pharmaceutical concerns are now synthesizing many new ataractic compounds.

About nineteen tranquilizing drugs are available at present in human and veterinary medicine. Triflupromazine hydrochloride, a phenothiazine derivative, is a new addition to them. Drugs of this group depress the central nervous system. This depression causes clinical soothing or obvious tranquilization. Besides their sedative action, they also exert some action on other body systems. If these actions are within certain limits, the animal's life is not endangered. But, on the contrary, if the

the action is too severe, the animal may be depressed beyond recovery. With this in mind, the effect of this drug on blood pressure, electrocardiogram, body temperature, respiratory rate, pulse rate, and spontaneous motor activity has been studied.

Effects of different tranquilizers on dogs, horses, and cattle have been studied by many persons. A search of the literature reveals that almost no work has been done on the effect of tranquilizers in goats.

CHAPTER II

REVIEW OF THE LITERATURE

A. Tranquilizing Drugs

"Tranquilizers" or "ataraxics" are agents that quiet seriously disturbed psychotics, cause remission of schizophrenic and paranoic symptoms, bring peace of mind to overwrought neurotics or antagonize the manifestations of hallucinogenic agents (5).

According to Tyndel (45), "ataractic drugs constitute a new method of control of the disturbed patient, thus creating a feeling of security for both patient and staff".

According to pharmacological actions, there are two distinct classes of tranquilizers (5): Class I - Central relaxants. The most important among these are meprobamate, mephenesin, glyketal and styramate. Class II - The autonomic suppressants. The reserpine and other rauwolfia compounds and phenothiazine derivatives constitute the members of this class.

Mephenesin, which was produced by Berger (3) in 1946, was the first compound of Class I. It was put on the market as a safe muscle relaxant. Berger (4) found that meprobamate produced muscle relaxation and sedation as well. Smith and co-workers (39) reported that mepro-

bamate was not a true tranquilizer because its main action, to relax skeletal muscle, resulted in relief of tension and excitement.

Reserpine and related alkaloids are derived from the root of Rauwolfia serpentina (Ophioxylon serpentinum). This plant grows in India and other neighboring countries. For hundreds of years, it has been used in India against snake bite, insanity, corneal opacity, diarrhea, dysentery and also as an ecbolic (30, 48). The plant was named by Plumier after Leonhard Rauwolf, a German physician and botanist who made extensive study and use of it (36). In 1931, Sen and Bose first reported on the hypotensive effect of Rauwolfia serpentina (38). The first report of the use of this drug in hypertension in the United States was made in 1952 by Wilkins, Judson and Stanton (49, 48). Wilkins reported that unlike other sedatives Rauwolfia did not produce grogginess, stupor and incoordination, and his patients appeared to be relaxed, quiet and tranquil (23). The powerful acting alkaloid reserpine was isolated from Rauwolfia by Mueller, Schlittler and Bein in 1952 (32). Damm and Trautner reported that reserpine reduced blood pressure by exerting an effect on the central nervous system (11). Today practically all commercial drug houses market it under some trade name.

The majority of the tranquilizers available at present are phenothiazine derivatives. Phenothiazine was prepared by Bernthsen (46, 43) in 1885. In 1940, Taylor

and Sanderson (43) reported anthelmintic properties of phenothiazine useful in veterinary medicine. At the Rhone-Poulenc Research Laboratory at Vitry-Sur-Seine (France), various amine derivatives of phenothiazine were reported to possess antihistaminic and vagal ganglio-blocking activity (46). Winter (50) reported that di-methyl aminopropyl phenothiazine prolonged the sleep-producing effects of hexobarbital. Interest was thus stimulated in the usefulness of this and related compounds as adjuncts in anesthesiology. In 1950, a systematic search was begun at the Rhone-Poulenc Research Laboratories to discover other compounds in this same chemical series which might possess clinical usefulness (46). Thus, chlorpromazine was synthesized by Carpentier of France in December, 1951 (47). According to Lehman (26) Laborit was the first to take chlorpromazine out of the laboratory into clinics, and Delay and Deniker were the first to introduce chlorpromazine (Largactil) in psychiatry in Europe.

According to Johnston (23), in 1954 Lehman and Henrahan reported that chlorpromazine relieved nausea and vomiting. In the same year, Kline reported that reserpine relieved nausea and hypertension. These persons further reported that chlorpromazine and reserpine also reduced greatly the anxiety, tension and hostility of patients without severely affecting mental and physical well being.

As reported by Lehman, Delay and Deniker proposed

a generic name "neuroplegic" drugs for these compounds (26). Fabing (17) suggested a second generic name "ataractics" or "ataraxics" for these drugs. The latter names have been derived from the Greek word "ataraktos", meaning without confusion, cool and steady. "Ataraxia", the Greek noun, means freedom from confusion and peace of mind. In English, it is ataraxy, meaning freedom from disturbance of mind or passion. This name and its synonym "tranquilizer" have gained wide-spread general usage by both doctors and laymen.

The following tranquilizers are already available on the market:

a. Chlorpromazine (largactil, thorazine, megaphen)
b. Promazine (sparine)
c. Promethazine (phenergan) - mostly used as an antihistaminic drug
d. Mepazine (paxital, pacatal)
e. Procloperazine (compazine)
f. Perphenazine (trilafon)
g. Mephenesin
h. Meprobamate (miltown, equanil)
i. Glyketal
j. Styramate
k. Hydroxyzine (atarax)
l. Benactyzine (suovitil)
m. Azacyclonol (frenquel)
n. Ethylcrotonyl urea (nostyn)
o. Phenaglycodol (acalo ultran)

p. Capsodiamin (suvren)

q. Diparcol

r. Reserpine and other Rauwolfia alkaloids

s. Ethyl isobutrazine

Trifluprомazine hydrochloride (vesprin, vetame) is an addition to the above list.

Chlorpromazine, which is a phenothiazine derivative, has been extensively studied. Because it is pharmacologically very similar to trifluprомazine hydrochloride, its pharmacological actions are reviewed.

In 1953, chlorpromazine hydrochloride was shown to be effective in suppressing nausea and vomiting caused by a wide variety of clinical conditions (19). Moyer (31) in 1954 showed it to be an effective antiemetic agent. Boyd et al. (7), in 1954, reported that chlorpromazine hydrochloride effectively inhibited and, in many instances, completely suppressed apomorphine induced vomiting in dogs. In 1955, Benaron and others (2) concluded that chlorpromazine could be expected to produce excellent results in the large majority of pregnant women with vomiting or hyperemesis. They further reported that it did not have any harmful effect on either the mother or the child. Estrada (16) in 1956 reported that chlorpromazine was invaluable in persistant emesis in dogs.

Das et al. (12) in 1954 reported dramatic changes

in the behavior of monkeys due to chlorpromazine. Aggressive rhesus monkeys (Macaca mullatta) became peaceful and no restraint was required outside the cage. Estrada (16) in 1956 reported that due to chlorpromazine unfriendly dogs acquired a more friendly attitude and "shy" dogs became less "shy".

In 1956, Martin and Beck (28) reported that chlorpromazine was administered at the rate of one milligram per kilogram of body weight to a belligerant mare. She then allowed her foal to suckle which prior to this time she had refused to do.

In 1956, Duff et al. (15) reported that when chlorpromazine was administered intravenously, increase of blood volume flowing through skin of hands and feet of healthy persons was observed. They further observed that the heart rate was slightly increased. Spur and others (40) observed that chlorpromazine in doses of two milligrams and five milligrams per kilogram of body weight produced an initial hypotension in anesthetized dogs. This was followed by return of mean arterial blood pressure to near control levels. During the next sixty to sixty-five minutes, there was a secondary decline in the blood pressure to hypotensive levels.

Dobkin and others (14) reported that pulse rate showed a moderate rise following chlorpromazine administration.

In 1956, Martin and Beck (28) reported that repeated doses of chlorpromazine hydrochloride, over a three day period at the rate of two milligrams per kilogram of body weight, produced a fall in circulating erythrocytes and in hemoglobin concentration of horses. Hoerlein and Marsh (22), in 1957, reported that chlorpromazine hydrochloride, when injected into calves, lowered blood counts and hematocrit values for twenty-four hours.

In 1954, Stevenson and Albert (41) observed that intramuscular injection of chlorpromazine in human hypertensives decreased both systolic and diastolic pressure during standing, but had no significant change in recumbent blood pressure. Pea et al. (34), in 1954, observed that acute hypotension developed in human patients after chlorpromazine administration. In 1954, Moyer et al. (31) also reported about its hypotensive action. Azima and Durost (1), in 1957, reported that chlorpromazine had moderate hypotensive effect. Blood pressure fell in all cases; systolic on an average dropped by 25 mm. of mercury, whereas diastolic fell 15 mm. of mercury in twenty-four hours. Renzetti and Padget (35) observed that the arterial blood pressure decreased to a variable degree after administration of chlorpromazine in man.

Feldman et al. (18) reported that rapid intravenous injection of chlorpromazine caused a drop in

blood pressure and intramuscular injection of the drug caused a moderate drop in blood pressure in a mongrel cat. Martin and Beck (28) reported that two to four milligrams per kilogram of chlorpromazine intramuscularly produced a slight tachycardia and hypotension in horses.

Moyer and others (31) reported that none of the human control subjects showed changes in electrocardiogram (ECG) after chlorpromazine administration. However, they further observed that changes in ECG might occur in seriously ill patients. Boyd et al. (7) reported that large doses of chlorpromazine hydrochloride produced a respiratory phasic sinus arrythmia. Dobkin and others (14) observed that after chlorpromazine administration the ECG showed frequent sinus arrythmia.

Stowe (42) mentioned that chlorpromazine had a depressant action on the central nervous system of man and domesticated animals.

Dobkin and others (14) reported that chlorpromazine depressed gastric secretion in man. Haverlock et al. (20) reported that chlorpromazine reduced the volume of gastric secretion, but did not significantly change the free acidity.

Duff et al. (15) reported that after administration of chlorpromazine to humans oral temperature regularly fell a little. Martin and Beck (28) reported that two to four milligrams per kilogram of chlorpromazine in

horses produced a slight fall in rectal temperature. Hoerlein and Marsh (22) reported that there was a slight (0.6 to 1.0° F.) fall of temperature from one-and-one-half to twenty-four hours after chlorpromazine administration in calves. Owen and Neal (33) reported that chlorpromazine caused slight hypothermia in horses (0.5 to 1.0° F.).

Martin and Beck (28) reported that of ten trials in which spontaneous motor activity was measured, in six there was a decrease in activity during the twenty-four hour period following chlorpromazine administration, and in four trials, the activity increased. Davis (13) reported that chlorpromazine in rhesus monkeys produced a marked reduction in all activities when administered in quantities significantly smaller than those required to produce "taming".

Brodey and Christensen (9) concluded that chlorpromazine appeared to have a potentiating effect on pentobarbital anesthesia in dogs.

Estrada (16) in 1956, reported good effects using chlorpromazine as a preanesthetic sedative in conjunction with pentobarbital anesthesia in dogs. Azima and Durost (1) observed that chlorpromazine potentiated the effect of barbiturates in man. In 1957, Owen and Neal (33) reported that chlorpromazine potentiated chloral hydrate anesthesia in horses.

Dobkin and others (14) stated that after

administration of chlorpromazine to humans respiratory rate varied; usually it was slightly increased, while, in some cases, respiration became irregular. Martin and Beck (28) reported that chlorpromazine at the rate of two to four milligrams per kilogram of body weight in horses produced a slower, more regular and deeper breathing pattern. Hoerlein and Marsh (22) reported that respiratory rate increased from 36 per minute to 50 per minute half an hour after injection of chlorpromazine hydrochloride. It decreased to 34 per minute one-and-one-half hours after injection, 32 per minute after five hours, and 32 per minute after twenty-four hours. Feldman and Kidron (18) reported that high doses of chlorpromazine in humans caused short apnea followed by transient hyperpnea. Renzetti and Padget (35) observed that chlorpromazine had a respiratory depressant action.

Friend et al. (19) reported that dryness of mouth, occasional mild sedation, and rarely a mild transient attack of faintness, palpitation and flushing of the face were the only side effects observed in man. Azima and Durost (1) observed drowsiness while Hodges and Lazerte (21) reported a persistant jaundice and fatal agranulocytosis. Bernstein and Klotz (6) described nasal stuffiness, dermatitis, photosensitivity, pruritis, influenza-like syndrome, agranulocytosis, jaundice and laryngeal edema as side

effects. Martin and Beck (28) in 1954, reported that intramuscular injections caused local reaction in horses. They also reported a decrease in circulating erythrocytes and hemoglobin concentration after three to five days of treatment.

Kurtz (25) stated that chlorpromazine was used in humans for the following indications :

Manic psychosis

Senile agitation

Schizophrenia

Anxiety reactions

Chronic anxiety or chronic neurotic tension

Sedation of acute alcoholism

Potentiation of barbiturates and narcotics

Nausea and vomiting of pregnancy

Vomiting and anorexia caused by radiation therapy

Lehman (26) reported that chlorpromazine was used in human beings for manic states, acute psychotic breakdown, anxiety and panic states, delirium, porphyria, chronic schizophrenia and epilepsy.

Troughton et al. (44) reported the use of chlorpromazine in dogs for; hysteria, prior to local anesthesia, to control chronic vomiting in pyometra, for heat stroke, and in shock due to trauma. Estrada (16) used this with mineral oil and parenteral purgative in removing hair balls from a cat. In 1957, Clifford (10) reported preanesthetic use of

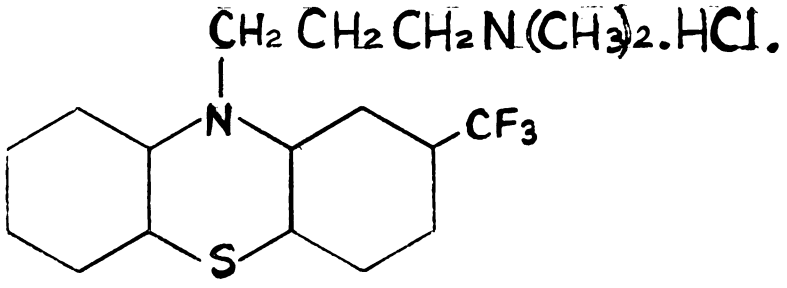
chlorpromazine with pentobarbital anesthesia in cats.

Troughton et al. (44) recommended the use of chlorpromazine in horses for shoeing, clipping, colic, preanesthetizing, tetanus, painful conditions and prior to travel. Martin et al. (28) reported the use of chlorpromazine for quieting horses. Lundvall and Campbell (27) reported sufficient relaxation of penis in stallions following chlorpromazine administration.

Troughton et al. (44) used chlorpromazine for preanesthetic medication in cattle. Lundvall and Campbell (27) reported relaxation of the penis in bulls following chlorpromazine administration. Ward (8) used tranquilizer for handling nervous dairy animals at milking time. There was no noticeable effect on either milk production or butter fat content. When a large dose of tranquilizer was used, the cow became "dopey" and would not eat much. This resulted in low milk production until the effects of the tranquilizer wore off.

B. Triflupromazine Hydrochloride

Triflupromazine hydrochloride (46) (vesprin, vetame) is 10-(3-dimethylaminopropyl)-2-(trifluoromethyl) phenothiazine hydrochloride. Its empirical formula is $C_{18}H_{19}F_3N_2S.HCL$. Its structural formula is



It is a white powder with a melting point of 172 to 174° C., and is soluble in water to about 1 gram in 10 cc. It is soluble in ethanol and acetone, but is insoluble in ether. The pH of a two percent aqueous solution is 4.1. At pH 6.4, the compound precipitates from aqueous solutions.

Median lethal intravenous dose for dogs was 16.7±4.2 milligrams per kilogram. Ataxia was the first sign of disability. Struggling during injection, followed occasionally by convulsions was observed in dogs receiving 45 milligrams per kilogram intravenously. They also showed extreme depression of motor activity. Death was immediately preceded by violent convulsions and seemed to result from asphyxiation.

Trifluprom azine was administered to dogs in the dose of 10 to 80 milligrams per kilogram of body weight each day, five days a week for 15 to 16 weeks. There was no change in erythrocyte and leucocyte counts and in hemoglobin values. No significant changes were observed in the electrocardiogram or the blood pressure

reading.

In dogs, no tremors or extensor rigidity were seen the first day after intramuscular administration of 30, 45, and 60 milligrams per kilogram of body weight as a 20 percent aqueous solution. Two dogs which were given 100 milligrams per kilogram of body weight in 20 percent aqueous solution exhibited some signs of local irritation. The immediate effect of the drug on blood pressure was depressant. As a persistent effect, pulse rate fell with trifluprom azine in unanesthetized dogs. There was insignificant change of pulse rate in anesthetized dogs.

In humans, vesprin has been of great value in the alleviation of restlessness, anxiety, insomnia, anorexia and other emotional side effects commonly accompanying the withdrawal of alcohol. Because of its "tranquilizing effect", vesprin often either eliminated or lessened the need for the administration of barbiturates or other sleep inducing drugs during alcohol withdrawal.

Vesprin has been found to produce a unique type of "sedation" characterized by sleep, cooperation, easy arousability and mental clarity without depressing vital functions. It has been used with great success pre and postoperatively. It has been noted to be particularly beneficial in apprehensive children in whom a tranquilizing effect was desirable.

It has been indicated in the prevention and control of nausea and vomiting associated with a

variety of clinical disorders. It has been found useful in the prevention and treatment of nausea and vomiting associated with certain drugs, radiation therapy, nitrogen mustard therapy and intravenous cholangiography. It has been useful in early nausea and vomiting of pregnancy up to and including the 12th week. It was also found useful for the management of pernicious vomiting of pregnancy.

Excellent results have been reported with vesprin as an adjunct to narcotics and general anesthetics during the first and second stages of labor. No apparent effects on the newborn have been encountered following its use in obstetrics.

Vesprin has been used as an effective agent in the treatment of several mental disorders. The drug was found useful in the management of psychomotor agitation associated with various acute and chronic psychoses including schizophrenia, mania, depression, delirium, senile psychoses and psychoses due to organic brain disease and mental deficiency. It might be used in mental disorders associated with epilepsy. It has shown a unique ability to control psychomotor agitation without producing marked sedation or drowsiness.

Drowsiness or somnolence, if it occurred, was seldom sufficiently intense to require discontinuation of this drug therapy and generally subsided after the first few weeks of treatment. Allergic phenomena and

photosensitivity have been encountered comparatively infrequently. Symptoms of weakness and dizziness, anxiety and restlessness have been reported to occur occasionally. These symptoms could be relieved readily by moderation of dosage. Orthostatic hypotension and simple tachycardia both transitory in nature occasionally were encountered following parenteral use of the drug.

In both animal experiments and in clinical studies, vesprin has exhibited pharmacological activities similar to those of chlorpromazine. It has been observed that trifluprom azine caused less persistent depression of the blood pressure in unanesthetized animals than did chlorpromazine. It was observed that trifluprom azine as an antiemetic agent was at least five times as potent as chlorpromazine. In terms of dosage required, it was found two to five times more potent than chlorpromazine in controlling psychotic manifestations.

C. Carotid Loop

In 1950, McClymont (29) described the establishment of carotid loops in cattle. He made an incision about 18 cm. long along a line immediately dorsal to the upper limit of the jugular vein, which was raised by digital pressure. By blunt dissection, the carotid artery was reached and was separated from the structures of the carotid sheath. Any smaller vessels were ligated and cut close to the main vessel. A

second incision was made parallel to the first and 7 cm. dorsal to it. The consequent strip of skin was freed from the subcutaneous tissues. Traction was applied to the middle of the length of the freed artery. The skin was then wrapped around the artery to form a sheath, open along the medial side. The two free edges of the sheath were then sutured together. There was considerable elastic pressure of the artery on the sutures. Bandaging of the loop relieved this pressure to some extent. The two free edges of the skin, left after formation of the sheath from the strip of skin, were then sutured together. Care was taken to obtain good approximation at the junction of the loop with the adjoining skin surface. A considerable edematous swelling usually formed cranial to the incision, but disappeared after a few days.

CHAPTER III

MATERIALS AND METHODS

All the goats used in this experiment were mature females of mixed breed and age. Their body weights varied from forty to one hundred and ten pounds. Some of them were pregnant. They were housed in a separate boxstall and all were maintained on the same feed and management routine. Food supplied consisted of alfalfa hay and ground dairy feed*. No additional dietary supplements were added to the feed. Water was available at all times. All animals were examined for internal parasites and many of them were found to be suffering from coccidia and strongyle infestation. They were treated for strongyles with phenothite** at the rate of one to two ounces, depending on body weight. For coccidia, they were given teniatol*** at the rate of one ounce per animal.

Each goat was fasted for about twenty-four hours before the operation to establish the carotid loop for this experiment. About four hours before the operation,

---

*Okemos Elevator Co., Okemos, Michigan.

**Fort Dodge Lab., Fort Dodge, Iowa.

***Pitman-Moore Co., Division of Allied Laboratories, Inc., Indianapolis, Indiana.

one ounce of turcapsol* was administered through a stomach tube to retard fermentation.

Ten minutes before the operation, the goat was given vetame** at the rate of one milligram per pound of body weight intravenously either in the cephalic or the saphenous vein. The left side of the neck was then clipped liberally and the goat secured to the operating table in right lateral recumbency. Atropine sulphate (1/75 grain) was mixed with 10 cc. of surital***. This mixture was injected intravenously for effective anesthesia and prevention of excessive salivation. After the goat was anesthetized, the site of operation was thoroughly scrubbed with liquid germicidal detergent***.

The operator's hands were thoroughly scrubbed with liquid detergent. Sterile gloves and a sterile surgical pack were used during the operation. The area of operation was covered with a sterile shroud. An incision approximately four inches long was made. The loop was established according to the method of McClymont (29) with the following exceptions:

a. the subcutaneous tissue was not removed from the strip of skin.

---

*Pitman-Moore Co., Division of Allied Laboratories, Inc., Indianapolis, Indiana.

**E. R. Squibb and Sons, New Brunswick, New Jersey.

***Parke, Davis and Co., Detroit, Michigan.

b. the first skin incision was made at the junction of the middle and lower third of the jugular furrow.

c. the second incision was made ventral to the first incision.

d. normal saline solution was used on the exposed artery to prevent drying.

A wooden stand with sling was developed for this experiment. The goat was weighed and placed on the sling with its legs through the holes of the sling. The two forelimbs were tied together, and the two hind limbs were tied together using separate ropes. The head was secured to the stand (Figure 3).

For recording arterial blood pressure and electrocardiogram, a Sanborn multichannel recorder* and a Sanborn electromanometer* were used. These were calibrated before each use. The needle electrodes of the ECG were inserted through the skin and secured with adhesive tape. Using four channels, three ECG leads and the carotid blood pressure were recorded simultaneously.

Readings were taken with three dose levels of vetame, one-half, one and two milligrams per pound of body weight. With the animal in the stand, a 20 gauge needle was inserted into the lumen of the carotid loop

---

*Sanborn Company, Waltham, Massachusetts.

and connected to the manometer tube. The normal reading was then recorded. After the reading, the needle was stoppered. This stopper was removed, the needle was flushed and cleaned of clot with heparinized water prior to each subsequent reading.

Readings were taken on four goats, 9, 13, 18 and 20, to determine the effect of the sling without vetame. Two of them, 9 and 18, were placed in the sling before each reading and then were taken out. Three readings, at half an hour intervals, were taken.

Goats 13 and 20 were kept on the sling continuously, and three readings were recorded at intervals of 30 minutes (Table XII).

A pedometer* was used to note the effect of vetame on spontaneous motor activity of the goat. A thin layer of cotton was applied to the front leg and the pedometer, covered with a second layer of cotton, was secured by adhesive tape. The normal reading was taken after twenty-four hours and the pedometer was reset to the zero line. It was again fixed to the leg as mentioned above and vetame was injected intravenously at the rate of one milligram per pound of body weight. Twelve hours later, vetame was again injected intravenously at the rate of one milligram per pound of body weight. At the end of the twenty-four hour

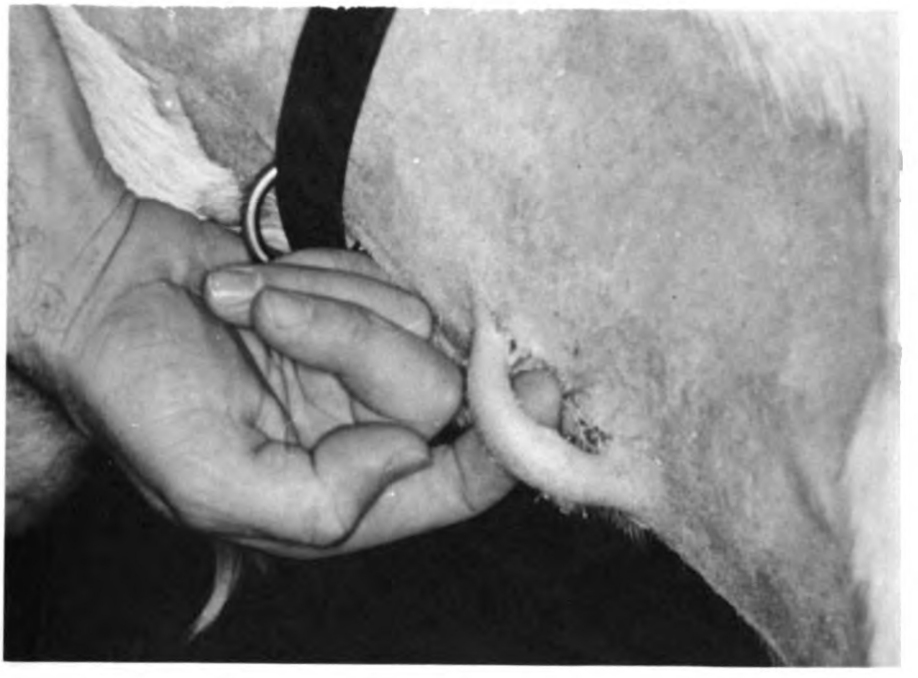
---

*New Haven Clock and Watch Co., New Haven, Connecticut.

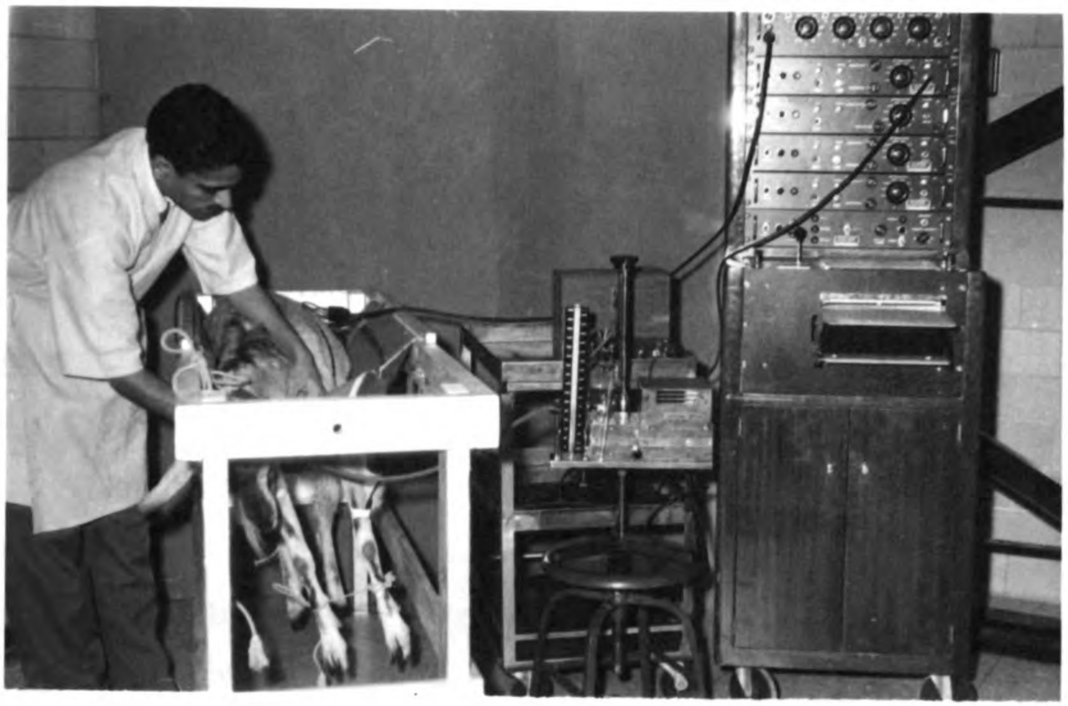
period, the pedometer was removed from the goat and this reading was used for comparison with the normal. In each of two goats, 2 and 20A, only one milligram of vetame was injected.

T-tests were run on the results obtained from measuring respiratory rate, pulse rate, blood pressure, rectal temperature and spontaneous motor activity.

1. Method of connecting manometer and ECG leads to goats.



2. Close-up of carotid loop in goat 9.



3. Complete apparatus showing from left to right goat stand, electromanometer, and Sanborn multichannel recorder.

4. New Haven pedometer for recording spontaneous motor activity.

CHAPTER IV

RESULTS

General symptoms observed after vetame administration:

A. At 0.5 milligram per pound of body weight.

About five minutes after intravenous administration of vetame, the goats became depressed. There was labored breathing, the mucous membranes became slightly cyanotic and there was slight dribbling of saliva.

B. At one milligram per pound of body weight.

About five minutes after intravenous administration of the drug, the animals became depressed, kept eyes half closed, and there was labored stertorous breathing and slight cyanosis of the mucous membranes. Some frothy salivary secretion was observed on the animal's lips.

C. At two milligrams per pound of body weight.

There was an excessive frothy, thick salivary secretion. The mucous membranes were more cyanotic. In the case of goat 14, there was violent movement of the whole body and extreme difficulty in breathing following which it died. Frequent urination and passage of flatus were seen. In almost all goats, incoordination of hind quarters was also observed.

In many of these animals, there was trembling of the whole body. Goat 9 passed coffee-colored urine about four hours after drug administration.

Effects of the drug on respiratory rate:

A. At 0.5 milligrams per pound of body weight (Table I).

Seven goats, varying in body weight from forty to one hundred and ten pounds were used. The average weight was 91.9 pounds. Definite respiratory depression was observed in five goats and stimulation in one. In goats 9, 13, 20 and 24, respiratory depression was observed up to 90 minutes after drug administration. In goat 20A, slight respiratory depression was observed 30 minutes after drug administration, and respiratory rate was normal after 60 minutes. In goat 10, the respiratory rate was stimulated up to 90 minutes after drug administration. In goat 18, respiratory rate was observed to be slightly higher than normal 60 minutes after drug administration and slightly lower after 90 minutes. The mean respiratory rate for the group was lower than the mean normal respiratory rate throughout. Statistically the difference was insignificant at the five percent level.

B. At one milligram per pound of body weight (Table II).

There were eight goats in this series, varying

from forty to one hundred and ten pounds in body weight, with mean body weight of 94.1 pounds. In five goats, 9, 10, 13, 14 and 18, the respiratory rate remained below normal throughout. In two goats, 20 and 20A, the respiratory rate remained higher than the normal. In one goat, number 24, it was slightly higher than normal 30 minutes after drug administration, but became slightly lower 60 minutes later. It was again normal 90 minutes after drug administration. The mean normal respiratory rate. Statistically the difference was insignificant at the five percent level.

C. At two milligrams per pound of body weight (Tables III, IV, V, VI and VII).

There were five animals in this group, varying from forty to one hundred and ten pounds in body weight with mean weight of 92 pounds. In all these animals, respiratory rate was lower than normal, even 420 minutes after drug administration. In goat number 14, the respiratory rate dropped to 7 just prior to death.

Effect of the drug on pulse rate:

A. At 0.5 milligram per pound of body weight (Table I).

Elevation of pulse rate was observed in six of seven goats 30 minutes after drug administration. In goat 9, a lowered pulse rate was observed at

30 minutes. In three goats, 20, 20A and 24, there was a rise in pulse rate at 60 minutes, in two, 13 and 18, pulse rate was lower than normal at 60 minutes. In the remaining two, 9 and 10, pulse rate was normal at 60 minutes. In three, 18, 20 and 20A, there was a higher pulse rate at 90 minutes, in two, 10 and 13, the pulse rate was lower than normal. The mean pulse rate was higher than the mean normal pulse rate 30 and 60 minutes after drug administration, and was lower at 90 minutes. Statistically the change was insignificant at the five percent level.

B. At one milligram per pound of body weight (Table II).

Of eight goats, there was increased pulse rate in six, 9, 10, 13, 14, 20 and 24, 30 minutes after drug administration. In one goat, 18, there was no change 30 minutes after drug administration, whereas in goat 20A, there was depression in pulse rate at 30 minutes. In six of the goats there was increased pulse rate 60 minutes after drug administration; there was no change in number 10, and in number 18 the pulse rate was lower. In six goats, 9, 14, 18, 20, 20A and 22, there was increased pulse rate after 90 minutes, whereas in one goat, 13, there was lower pulse rate after 90 minutes. The mean pulse rate was observed to be higher than the normal throughout. Statistically the changes were significant at

the five percent level.

C. At two milligrams per pound of body weight (Tables III, IV, V, VI, VII).

Five animals were used and pulse rate was recorded in all of them. The mean pulse rate after drug administration was very slightly lower in one, but was higher in the remaining four. The pulse rate fluctuated widely in all animals during the postadministration period.

Effects on rectal temperature:

A. At one milligram per pound of body weight (Table II).

Readings were taken in three goats. There was slight lowering of temperature in two goats 9 and 20, 30 minutes after drug administration, whereas in the other, there was no change. There was slight lowering of temperature at 60 minutes in goats 9 and 13. Normal temperature was recorded 90 minutes after drug administration in all three. The mean temperature readings were lower than the mean normal temperature throughout. Statistically changes were insignificant at the five percent level.

B. At two milligrams per pound of body weight (Tables III, IV, and V).

Rectal temperature was recorded in three goats. In two, 10 and 20A, temperatures lower than normal were recorded even 420 minutes after drug administration.

In the third goat, 13, lower body temperature was recorded up to 360 minutes after drug administration, at which time recordings ceased. The mean temperature in all three remained lower than the mean normal temperature throughout.

Effect on arterial blood pressure:

A. At 0.5 milligram per pound of body weight (Table I).

There were seven animals in this series. In four, there was decreased blood pressure, whereas in three there was an increase in blood pressure 30 minutes after drug administration. After 60 minutes, there was a decrease in three, and an increase in four. At 90 minutes, there was low blood pressure in two of them, and high in four. Due to technical difficulties a 90 minute reading was not made in goat 9. The mean arterial blood pressure was always lower than the normal mean blood pressure. Statistically the changes were insignificant at the five percent level.

B. At one milligram per pound of body weight (Table II).

There were eight animals in this group. Six showed lower blood pressure after 30 minutes, and in two, there was slight rise in blood pressure after 30 minutes. Five animals showed lower blood pressure after 60 minutes, and three showed a rise

in blood pressure. Six of them showed lower blood pressure after 90 minutes, and one showed a rise in blood pressure at 90 minutes. Technical difficulties prevented making a 90 minute reading in goat 10. The mean blood pressures at 30, 60 and 90 minutes were lower than the mean normal blood pressure. Statistically changes were insignificant at the five percent level.

C. At two milligrams per pound of body weight (Tables III, IV, V, VI, and VIII).

Of five goats, there was lower blood pressure in four. In one animal, 13, blood pressure was lower up to 120 minutes after drug administration, at which time it rose above normal and remained until recordings ceased at 360 minutes.

Effect on spontaneous motor activity: (Table XI)

Eight goats used in this experiment varied from forty to one hundred and twenty pounds with an average weight of 91.8 pounds. Six of them showed decrease in activity after drug administration, whereas two showed increase in activity. Normal mean distance traveled was 1.57 miles and mean decrease after drug administration was 0.64 miles or 40.7 percent. Statistically changes were significant at the five percent level.

Effect on electrocardiogram:

A. At 0.5 milligram per pound of body weight (Table VIII).

Of the seven animals in this series, none demonstrated similar electrocardiograms. In goat 9, inverted T waves were found in lead I at 30 minutes. In animal 10, there was increase in QRS potential in lead I at 60 minutes. In goat 13, all waves decreased in potential in leads I and II. There was complete absence of the P wave in the normal and all subsequent readings in animal 18. Goat 20 showed slight decrease in QRS potential at 60 minutes in lead I. There was increase in QRS and T potentials in lead I at 30 minutes, but decrease in these at 60 minutes in goat 20A. Decrease in QRS potentials in leads II and III at 30 minutes and decrease in potential of the T wave in lead III at 90 minutes was recorded in animal 24.

B. At one milligram per pound of body weight (Table IX).

Six of eight goats in this group showed some electrocardiogram change, whereas the remaining two did not. In goat 9, both QRS and T potentials were decreased at 30 minutes in lead I. They were decreased and the T wave was inverted in lead I at 60 minutes. The QRS potential decreased in leads I and II at 90 minutes. In animal 10, slight increase in the T wave was noted in lead II at 30

minutes. QRS potentials in lead I and II were increased in goat 13 at 30 and 60 minutes. In leads II and III in goat 14, atrial fibrillation type of electrocardiogram was exhibited both in pre and post drug administration periods. It also showed decreased QRS potential at 30 minutes in all the three leads. P and T waves were inverted and QRS potential was found increased in lead I at 60 minutes in goat 18. Animal 20 showed increased QRS potential and inverted T waves in lead I at 30 minutes.

C. At two milligrams per pound of body weight (Table XI).

In goat 9, QRS potentials were partially inverted in lead I at 60 minutes. In goat 10, QRS potentials were increased at 30 minutes in lead I. There was increase in T wave potentials in lead II at 60 minutes. In goat 13, QRS potential was increased in lead I and III and T waves were inverted in lead III at 30 minutes. QRS potentials were decreased in lead I, whereas they were increased in lead III at 60 minutes. QRS potential increased in lead I and lead III at 90 minutes. QRS potentials were also increased in lead I from 150 to 300 minutes. T wave potentials increased at 210 and 240 minutes in lead I. The T wave was increased in lead II at 150 minutes and decreased at 180 in lead III. QRS

potential was increased from 30 to 90 minutes and again from 210 to 300 minutes in lead III. Inverted T waves were observed at 30, 210 and 240 minutes in lead III. At 180 minutes, T wave potential was decreased. In goat 14, increased potential and inverted T waves were recorded at 30 and 60 minutes in lead I. Increased T wave potentials were found in lead II at 30 and 60 minutes. P wave was absent from lead II at 30 minutes. QRS potentials were increased in lead II at 60 minutes, and some QRS waves were also inverted. In goat 20A, QRS potentials were found increased at 60, 150 and 180 minutes in lead I and lead II. T wave potentials increased at 180 minutes in lead I. An inverted P wave was observed at 180 minutes in lead III. QRS potentials increased at 300 minutes in lead III.

Effect of sling:

A. On goats continuously on sling.

There was no change in rectal temperature in either of them. In goat 13, respiratory rate was slightly lowered at 30 minutes, but was normal at 60 minutes. In goat 20, respiratory rate was lower at 30 minutes, but increased at 60 minutes. In both of these goats, pulse rate increased at 60 minutes. Rise in both systolic and diastolic pressure was recorded in both goats at 60 minutes.

B. On goats not continuously on sling.

There was little change in pulse rate,

respiratory rate, and rectal temperature. In goat 9, there was a slight rise in systolic blood pressure, but a fall in diastolic at 30 and 60 minutes. In animal 18, there was a slight fall in systolic blood pressure at 30 and 60 minutes. There was a drop in diastolic at 30 minutes, but very slight rise at 60 minutes.

CHAPTER V

DISCUSSION

This investigation was undertaken to determine the effects of triflupromazine hydrochloride on the arterial blood pressure, pulse rate, respiratory rate, electrocardiogram, rectal temperature, and spontaneous motor activity in goats.

In the beginning, efforts were made to measure direct blood pressure in the brachial or the femoral artery. Difficulties were experienced in cannulating the vessel owing to the development of perivascular hematomata. It was decided, therefore, to form permanent carotid loops. Originally, subcutaneous tissue was removed from the strip of skin forming the loop. However, two of three loops thus established became necrotic. In subsequent goats, therefore, the freed carotid artery was placed subcutaneously. Due to development of hematomata during cannulation of the artery recourse was taken again to loop formation. This time, no subcutaneous tissue was removed from the strip of skin, and results were quite satisfactory. Three goats died after loop formation, all three bleeding from the loop before death. At necropsy, hemorrhage was given as the cause of death.

In one case, a piece of wire with blood stained tip was found near the loop. This wire might have caused perforation of the artery. A horned goat was found to butt the other goats and this might have caused damage to the loops resulting in hemorrhage in the other two goats.

Extreme difficulties were experienced in the beginning of the experiment for want of a suitable stand. Jumping and struggling of goats during the experiment led to unsuccessful readings. In the end, a stand and a sling were prepared which served the purpose very well.

The first effect noticed after drug administration was depression. This was followed by labored breathing. Cyanosis of the mucous membranes developed in varying degrees depending upon the amount of drug administered. The amount of salivation also was directly dependent upon the amount of vetame injected. Incoordination of hind quarters was a constant symptom in all animals.

When this drug was injected intravenously at the rate of 0.5 milligram per pound of body weight, respiratory rate was lowered in 71.4 percent of goats at 30 minutes, 57.1 percent at 60 and 90 minutes. When it was injected at a dose of one milligram per pound of body weight, the respiratory rate was lowered in 62.5 percent of the animals at 30 minutes,

in 75 percent at 60 minutes, and in 50 percent at 90 minutes, but results were statistically insignificant at the five percent level. At the rate of two milligrams per pound of body weight, respiratory rate was lowered in all goats.

When action of the drug on the individual animal was considered, it was observed that in goats 9 and 13 the respiratory rate was lowered at all the three dose levels. In goat 10, respiration rate was increased at 0.5 milligram dose, but it was decreased at one and two milligrams doses. In goat 14, respiratory rate was lowered at both one and two milligrams dose levels. This goat died 60 minutes after administration of 2.0 milligrams per pound, perhaps due to respiration failure. In goat 18, respiratory rate increased at 0.5 milligram, but was depressed at one milligram. In goat 20A, respiratory rate increased at 0.5 and two milligrams per pound of body weight. In goat 24, the respiratory rate was decreased at 0.5 milligrams per pound of body weight. Taking these facts into consideration, it was observed in this experiment that the drug caused some respiratory depression in a majority of the goats, though not in all goats.

With a 0.5 milligram dose, pulse rate was increased in 85.7 percent of the animals at 30 minutes, in 42.8 percent at 60 and 90 minutes.

At the five percent level results were statistically insignificant. At the one milligram dose level, pulse rate increased in 75 percent of the animals throughout. These results were statistically significant at the five percent level. When two milligrams per pound of body weight was used a fluctuating pulse rate was recorded. Thus, at 0.5 milligram and one milligram dose levels, this drug increased pulse rate in the majority of goats of this experiment.

At 0.5 milligrams, blood pressure was decreased in 57.1 percent of the cases at 30 minutes, in 42.7 percent at 60 minutes, and in 28.5 percent at 90 minutes. At one milligram, lower blood pressure was recorded in 75 percent at 30 minutes, in 62.5 percent at 60 minutes, and in 85.7 percent at 90 minutes. At the five percent level results were statistically insignificant. At two milligrams, blood pressure was lower in all goats up to 60 minutes, in 80 percent up to 120 minutes, and in 40 percent throughout. Thus, the drug caused hypotensive effect at all doses in the majority of cases. This hypotensive effect lasted longer with higher doses of the drug.

With one milligram, temperature was lowered in two out of three goats at 30 and 60 minutes. Normal temperature was recorded at 90 minutes in all three animals. At two milligrams, lower rectal temperature was recorded in all the three animals from 30 to 420

minutes. Thus, the drug showed some hypothermic effect in goats. These changes were statistically insignificant at the five percent level.

Spontaneous motor activity was recorded and in 86.6 percent of the animals the activity was lowered. In two goats, it was administered in a single dose rate of one milligram per pound of body weight. Lowered spontaneous motor activity was recorded in one of these two goats. In all of eight goats, lowered spontaneous activity was recorded in 75 percent, and the changes were statistically significant at the five percent level.

For testing the effect of the drug on spontaneous motor activity it was administered to goat 20A at one milligram per pound of body weight. This goat showed symptoms of stimulation and behaved in a peculiar fashion. She was found hanging from the hay rack with her head down, and it is thought she would have suffocated if not set free. Due to this stimulation, a second dose was not administered to her. After this incident, owing to its small body weight, only one milligram of vetame per pound of body weight was used in goat 2.

No consistent changes from normal were found in the electrocardiograms after drug administration, however some showed erratic variations.

No definite effect of the sling was noted.

Goats 1, 9, 10, 13, 14 and 20 were pregnant. 1, 9, 13 and 20 subsequently produced kids. No bad effect of the drug was evident in the dams or kids. Goat 10 was found to be pregnant on x-ray examination one month after the drug administration. Thus, in this case also there was no effect of the drug on pregnancy. Goat 14 died during the experiment due perhaps to respiratory failure.

Three goats died after the experimental work was completed. On post mortem, death was attributed to hemorrhage. There had been bleeding, but it did not appear so profuse that it could cause the death of the goat. Due to use of the drug at three dose levels, there may have been a blood dyscrasia. This blood dyscrasia followed by hemorrhage might have hastened death. Therefore, it is suggested that during subsequent work with this drug in goats, blood examinations should be done.

Based on this use of the drug in goats, it could be surmised that the safe intravenous tranquilizing dose in this animal is one milligram per pound of body weight.

SUMMARY AND CONCLUSIONS

1. Vetame was administered intravenously to goats at three dose levels--0.5 milligram, 1.0 milligram and 2.0 milligrams per pound of body weight, and the following observations were made:
   a. General symptoms
   b. Effect on respiratory rate
   c. Effect on pulse rate
   d. Effect on arterial blood pressure
   e. Effect on electrocardiogram
   f. Effect on rectal temperature

   To determine the effect of the drug on spontaneous motor activity during a 24 hour period, 2 doses of vetame were administered to six goats with a 12 hour interval between the first and second doses. A single dose of one milligram per pound of body weight was used in two goats.
2. Depression, labored breathing, cyanosis of mucous membranes of varying degree, salivation and incoordination of hind quarters were the symptoms observed after intravenous administration of vetame to goats.
3. The drug caused respiratory depression in the majority of goats, though not in all of them. Statistically the depression was insignificant.

4. An increased pulse rate was observed in the majority of cases at 0.5 and 1.0 milligram dose levels. Statistically the difference was insignificant at 0.5, but significant at 1.0 milligrams.
5. The drug caused hypotension at all dose levels in the majority of goats, but it was statistically insignificant. The hypotensive effect lasted longer with higher doses of vetame.
6. Some hypothermic effect was seen, which was statistically insignificant.
7. Depression of spontaneous motor activity was noted in six of eight animals tested with a pedometer. It was statistically significant at the five percent level.
8. No changes were observed in electrocardiograms that could be definitely attributed to this drug.

TABLE I

EFFECTS OF VETAME

(0.5 milligram per pound of body weight)

Goat Number	Body Weight in Pounds	Respiration per Minute			
		Normal	Minutes Postinjection		
			30	60	90
9	100	25	15	14	—*
10	100	25	30	28	28
13	110	32	27	26	26
18	100	22	22	24	20
20	100	50	38	36	36
20A	40	20	15	20	20
24	93	45	32	22	30
Mean	91.9	31.3	25.5	24.3	26.6

*Due to technical difficulty no recording was made.

TABLE I

(Continued)

EFFECTS OF VETAME

(0.5 milligram per pound of body weight)

Goat Number	Pulse per Minute			
	Normal	Minutes Postinjection		
		30	60	90
9	110	90	90	—*
10	90	110	90	80
13	110	120	100	100
18	110	120	100	120
20	150	160	160	160
20A	100	110	120	150
24	100	120	110	100
Mean	110	118.5	112.8	101.6

*Due to technical difficulty no recording was made.

TABLE I

(Continued)

EFFECTS OF VETAME

(0.5 milligram per pound of body weight)

Goat Number	Blood Pressure (mm. of Hg)			
	Normal	Minutes Postinjection		
		30	60	90
9	143*/120**	114/95	120/108	—***
10	125/95	110/88	140/105	140/115
13	122/98	140/117	146/108	130/102
18	132/99	95/88	122/102	106/85
20	100/78	107/85	105/86	105/85
20A	122/88	112/85	100/84	103/90
24	125/100	140/125	138/120	135/119
Mean	124.1/96.8	116.8/97.5	123.0/101.8	119.8/99.3

*Systolic

**Diastolic

***Due to technical difficulty no recording was made.

TABLE II

EFFECTS OF VETAME

(1.0 milligram per pound of body weight)

Goat Number	Body Weight in Pounds	Respiration per Minute			
		Normal	Minutes Postinjection		
			30	60	90
9	100	28	16	14	—*
10	100	38	32	15	—
13	110	45	26	32	30
14	110	26	14	20	20
18	100	35	15	23	25
20	100	15	35	35	33
20A	40	14	19	21	20
24	93	15	16	14	15
Mean	94.1	22.7	21.6	21.7	23.8

*Due to technical difficulty no recording could be made.

TABLE II

(Continued)

EFFECTS OF VETAME

(1.0 milligram per pound of body weight)

Goat Number	Pulse per Minute			
	Normal	Minutes Postinjection		
		30	60	90
9	90	130	160	130
10	90	120	90	___*
13	100	140	110	90
14	80	90	90	100
18	100	100	80	120
20	100	160	110	120
20A	120	90	150	160
24	80	110	150	140
Mean	95	117.5	117.5	122.3

*Due to technical difficulty no recordings could be made.

TABLE II

(Continued)

EFFECTS OF VETAME

(1.0 milligram per pound of body weight)

Goat Number	Blood Pressure (mm. of Hg)			
	Normal	Minutes Postinjection		
		30	60	90
9	130*/105**	105/93	120/100	105/85
10	133/100	135/105	143/108	—***
13	105/83	75/63	110/88	115/90
14	120/100	115/102	105/92	97/84
18	130/97	110/94	135/98	118/99
20	122/95	88/77	118/97	110/92
20A	122/100	142/133	120/100	110/95
24	125/98	98/82	102/90	103/90
Mean	123.4/93.6	108.5/93.6	119.1/96.6	108.3/90.7

*Systolic

**Diastolic

***Due to technical difficulty no recording could be made.

TABLE II

(Continued)

EFFECTS OF VETAME

(1.0 milligram per pound of body weight)

Goat Number	Rectal Temperature (Fahrenheit)			
	Normal	Minutes Postinjection		
		30	60	90
9	103.8	103.4	103.6	103.8
10	——— *	———	———	———
13	103.4	103.4	103.2	103.4
14	———	———	———	———
18	———	———	———	———
20	103.6	103.4	103.6	103.6
20A	———	———	———	———
24	———	———	———	———
Mean	103.6	103.4	103.6	103.5

*Due to technical difficulty no recording could be made.

TABLE III

EFFECTS OF VETAME IN GOAT 9

(2.0 milligrams per pound of body weight)

Time in Minutes	Respiration per Minute	Pulse per Minute	Blood Pressure (mm. of Hg)
Preinjection normal	22	140	135*/115**
30	22	140	116/102
60	17	130	117/103
90	18	120	120/107
120	17	120	126/115
150	14	140	135/121
180	14	150	120/105
210	13	150	131/115
240	15	130	136/118
270	***		
300	13	130	120/100
330	14	150	115/ 95
360	15	160	122/ 97
390	15	150	112/ 94
420	16	140	112/ 92
Mean of 13	15.6	139.2	121.7/104.9

*Systolic

**Diastolic

***Due to technical difficulty no recording could be made

TABLE IV

EFFECTS OF VETAME IN GOAT 10

(2.0 milligrams per pound of body weight)

Time in Minutes	Respiration per Minute	Pulse per Minute	Blood Pressure (mm. of Hg)	Temperature (Fahrenheit)
Preinjection Normal	38	90	145*/95**	103.0
30	30	132	95/78	102.8
60	23	110	98/88	102.2
90	—***	—	———	———
120	—	—	———	———
150	17	110	88/69	102.0
180	—	—	———	———
210	15	130	104/80	102.2
240	22	130	108/84	102.4
270	19	110	112/80	102.4
300	30	120	110/82	102.5
330	18	100	112/75	102.8
360	16	100	108/80	102.7
390	21	120	100/85	102.8
420	20	110	100/78	102.8
450	25	110	90/72	103.0
Mean of 12	21.3	115.1	102/79.2	102.5

*Systolic

**Diastolic

***Due to technical difficulty no recording could be made.

TABLE V

EFFECTS OF VETAME IN GOAT 13

(2.0 milligrams per pound of body weight)

Time in Minutes	Respiration per Minute	Pulse per Minute	Blood Pressure (mm. of Hg)	Temperature (Fahrenheit)
Preinjection-Normal	30	100	125*/ 92**	103.6
30	24	140	112/ 92	102.2
60	—***	100	118/ 97	——
90	27	110	115/ 98	102
120	—	—	——	——
150	29	100	165/135	102
180	29	90	145/117	102.4
210	23	90	140/115	102.7
240	24	100	130/ 95	102.8
270	20	100	145/112	——
300	23	100	155/119	102.8
330	—	—	——	——
360	25	110	165/140	103.4
Mean of 12	25	104.0	139/112	102.5

*Systolic

**Diastolic

***Due to technical difficulty no recordings could be made.

TABLE VI

EFFECTS OF VETAME IN GOAT 14*

(2.0 milligrams per pound of body weight)

Time in Minutes	Respiration per Minute	Pulse per Minute	Blood Pressure (mm. of Hg)
Preinjection Normal	18	100	125**/112***
30	10	120	78/60
60	7	110	100/88
Mean	8.5	115	89/74

*The goat died at 65 minutes after drug administration.

**Systolic

***Diastolic

TABLE VII

EFFECTS OF VETAME IN GOAT 20A

(2.0 milligrams per pound of body weight)

Time in Minutes	Respiration per Minute	Pulse per Minute	Blood Pressure (mm. of Hg)	Temperature (Fahrenheit)
Preinjection Normal	30	120	115*/70**	103.6
30	16	120	70/45	102.6
60	16	120	95/82	101.8
90	—***	—	———	———
120	20	120	100/75	101.6
150	18	130	90/74	101.6
180	20	110	70/48	100.4
210	—	—	———	———
240	16	140	90/70	100.6
270	22	150	90/65	102.4
300	19	160	102/68	102.6
330	15	140	80/50	101.4
360	13	140	85/70	101.5
390	16	140	90/70	102.8
420	16	110	70/55	102.8
450	—	—	———	———
480	16	140	82/56	103.0
Mean of 13	17.1	132.3	85.7/63.7	101.9

*Systolic

**Diastolic

***Due to technical difficulty no recordings could be made.

TABLE VIII

EFFECTS OF VETAME ON ELECTROCARDIOGRAM

(0.5 milligram per pound of body weight)

Goat Number	Preinjection	At 30 Minutes	At 60 Minutes	At 90 Minutes
9	Normal	Inverted T wave in lead I	———	———
10	Normal	———*	QRS potential increased in lead I	———
13	Normal	———	All waves decreased in potential in leads I & II	———
18	Complete absence of P wave	Complete absence of P wave	Complete absence of P wave	Complete absence of P wave
20	Normal	———	Slight decrease in QRS potential in lead I	———
20A	Normal	———	All waves increased in potential in lead I but decreased in leads II & III	———
24	Normal	Decrease in QRS potential of leads II & III	———	Decrease in T wave in lead III

*No deviation from normal.

TABLE IX

EFFECTS OF VETAME ON ELECTROCARDIOGRAM

(1.0 milligram per pound of body weight)

Goat Number	Preinjection	At 30 Minutes	At 60 Minutes	At 90 Minutes
9	Normal	QRS potential in lead I decreased. T wave in lead II decreased	T wave decreased and inverted in lead I	QRS potential decreased in leads I & II
10	Normal	T wave slightly increased in lead II	——— *	———
13	Normal	QRS potential increased in leads I & II	QRS potential increased in leads I & II	———
14	Atrial fibrilation in leads II & III	QRS potential decreased in all leads. Atrial fibrilation in leads II & III	Atrial fibrilation in leads II & III	Atrial fibrilation in leads II & III
18	Normal	QRS potential increased and T wave inverted in lead I	———	———

*No deviation from normal.

TABLE X

EFFECTS OF VETAME ON ELECTROCARDIOGRAM

(2.0 milligrams per pound of body weight)

Goat Number	Lead I	Lead II	Lead III
9	QRS partially reversed 60 minutes after drug.	Normal	Normal
10	QRS potential increased 30, 90, 150, 180, 210, 270 and 300 minutes after drug. TP internal decreased 30 and 60 minutes after drug. T internal decreased 60 and 210 minutes after drug.	QRS potential increased, TP internal decreased 30 minutes after drug and T wave increased 60 and 150 minutes after drug.	QRS potential increased 30, 60, 90, 210, 270 and 300 minutes after drug. TP internal decreased 30 minutes after drug. T inverted 30 and 210 minutes after drug. T decreased 180 minutes after drug.
14	QRS potential increased and T inverted 30 and 60 minutes after drug.	Absence of P wave. T wave increased 30 minutes after drug. QRS potential increased and T wave increased 60 minutes after drug.	QRS potential increased 30 and 60 minutes after Some reverse 60 minutes after drug.
20A	QRS potential increased 60, 150, 180 minutes after drug. TP internal very slight 150, 330 minutes after drug. T wave increased 180 minutes after drug.	QRS potential increased 60 and 180 minutes after drug. TP internal decreased 150 minutes after drug.	QRS potential increased 300 minutes after drug. TP internal decreased 150, 300 minutes after drug. Inverted P 180 minutes after drug.

TABLE XI

EFFECT OF VETAME ON SPONTANEOUS MOTOR ACTIVITY

Goat Number	Weight in Pounds	Intravenous Dose Milligrams per Pound Body Weight	Reading* in Miles for 24 Hours Before Drug (A)	Reading* in Miles for 24 Hours After Drug (B)	Difference Between Readings (A and B) in Miles
1	100	2	3.00	1.00	-2.00
2	60	1	0.12	0.82	+0.70
3	100	2	0.80	1.25	+0.45
5	120	2	1.50	0.88	-0.62
9	110	2	1.70	1.25	-0.45
10	100	2	2.25	0.70	-1.55
20A	40	1	2.00	1.31	-0.69
23	105	2	1.20	0.25	-0.95

*As recorded with a Pedometer, New Haven Clock and Watch Company, New Haven, Connecticut.

TABLE XII

EFFECTS OF SLING

A. Goat not continuously on sling.

Goat Number	Respiration per Minute			Pulse per Minute		
	Start	At 30 Minute	At 60 Minute	Start	At 30 Minute	At 60 Minute
9	17	15	15	80	80	80
18	26	26	26	105	108	106

Goat Number	Blood Pressure (mm. of Hg)			Temperature (Fahrenheit)		
	Start	At 30 Minute	At 60 Minute	Start	At 30 Minute	At 60 Minute
9	140*/127**	141/115	145/115	104.0	103.8	103.9
18	138/106	130/100	135/107	103.8	103.6	103.8

*Systolic

**Diastolic

TABLE XII

(Continued)

EFFECTS OF SLING

B. Goat continuously on sling.

Goat Number	Respiration per Minute			Pulse per Minute		
	Start	At 30 Minute	At 60 Minute	Start	At 30 Minute	At 60 Minute
13	37	33	37	100	100	110
20	24	22	29	70	70	85

Goat Number	Blood Pressure (mm. of Hg)			Temperature (Fahrenheit)		
	Start	At 30 Minute	At 60 Minute	Start	At 30 Minute	At 60 Minute
13	$\frac{127^{*}}{103^{**}}$	$\frac{131}{104}$	$\frac{131}{109}$	103.8	103.8	103.8
20	$\frac{130}{95}$	$\frac{130}{97}$	$\frac{132}{110}$	104.0	104.0	104.2

*Systolic

**Diastolic

BIBLIOGRAPHY

1. Azima, H. and Durost, H.: Comparison of the Effects of Promazine and Chlorpromazine in Mental Syndromes. Canad. M.A.J. 77,(1957): 671-675.

2. Benaron, H. B. W., Dorr, E. M., Roddick, W. J., Johnson, R. P., Gossack, L., and Rucker, B. E.: The Use of Chlorpromazine in the Obstetric Patient--A Preliminary Report on the Treatment of Nausea and Vomiting of Pregnancy. Am. J. Obst. and Gynec. 69,(1955): 776-779.

3. Berger, F. M.: The Mode of Action of Mephenesin. Brit. J. Pharm. 2,(1946): 241-250.

4. Berger, F. M.: The Pharmacological Properties of 2-Methyl-2-N-Propyl 1-1, 3-Propanediol Dicarbomate (Miltown), A New Interneuronal Blocking Agent. J. Pharm. and Exper. Ther. 112,(1954): 413-423.

5. Berger, F. M.: The Chemistry and Mode of Action of Tranquilizing Drugs. Ann. N.Y. Acad. Sci. 67,(1957): 685-700.

6. Bernstein, C. and Klotz, S. D.: Allergenicity of Tranquilizing Drugs. J.A.M.A. 163,(1957): 930-933.

7. Boyd, E. M., Boyd, C. E., and Cassell, W. A.: The Antiemetic Action of Chlorpromazine Hydorchloride. Canad. M.A.J. 70,(1954): 276-280.

8. _____: Breeder's Gazette, September 1958, as reported in The Jen-Sal Journal, March 1958, 9.

9. Brodey, R. S. and Christensen, A. T.: Chlorpromazine Hydrochloride as a Preanesthetic Agent for Pentobarbital Sodium Anesthesia in the Dog. J.A.V.M.A. 129,(1956): 410-412.

10. Clifford, D. H.: Effect of Preanesthetic Medication with Chlorpromazine, Meperidine, and Promazine on Pentobarbital Anesthesia in the Cat. J.A.V.M.A. 131,(1957): 415-419.

11. Damm, G. and Trautner, H.: Treatment of Arterial Hypertension with Rauwolfia Alkaloid--Reserpine (Serpasil). Dtsch. Med. Wschr. 79, (1954): 39.

12. Das, N. N., Dasgupta, S. E., and Werner, G.: Changes of Behaviour and Electroencephalogram in Rhesus Monkeys Caused by Chlorpromazine. Arch. Intern. De. Pharma. Dyn. Et De Therapie. 99,(1954): 451-457.

13. Davis, G. D.: Effects of Central Excitant and Depressant Drugs on Locomotor Activity in the Monkey. Am. J. Phys. 188,(1957): 619-623.

14. Dobkin, A. B., Lamoureux, L., Letienne, R., and Gilbert, R. G. B.: Some Studies with Largactil. Canad. M.A.J. 70,(1954): 626-628.

15. Duff, R. S., McIntyre, J. W. R., and Butler, N. G. P.: Cardiovascular Actions of Chlorpromazine with Particular Reference to Peripheral Vascular Disease. Brit. M.J. 1,(1956): 264-266.

16. Estrada, E.: Clinical Use of Chlorpromazine in Veterinary Medicine. J.A.V.M.A. 128,(1956): 292-294.

17. Fabing, H. D.: Designation of "Tranquilizing Agents" in Neuro Pharmacology. J.A.M.A. 158, (1955): 1461.

18. Feldman, S. and Kidron, D. P.: Experimental Studies with Chlorpromazine Arch. Intern. De. Pharma. Dyn. Et De Therapie. III,(1957): 70-85.

19. Friend, D. G. and Cummins, J. F.: New Antiemetic Drug. J.A.M.A. 153, (1953): 480-81.

20. Haverlock, B. J., Stevenson, T. D., Sjoerdsma, and Terry, L. L.: The Effects of Reserpine and Chlorpromazine on Gastric Secretion. Am. J.M.Sc. 230,(1955): 601-604.

21. Hodges, H. H. and Lazerte, G. D.: Effects of Chlorpromazine. J.A.M.A. 158,(1955): 114-116.

22. Hoerlein, A. B. and Marsh, C. D.: Action of Chlorpromazine Hydrochloride in Calves. J.A.V.M.A. 131,(1957): 227-230.

23. Johnston, R. F.: Toxicological Studies of Certain Tranquilizing Drugs. Doctor's Thesis, University of Minnesota, 1958.

24. Knowles, J. O.: Clinical Experience with Tranquilizing Agents. J.A.V.M.A. 130,(1957): 10-11.

25. Kurtz, P. L.: The Current Status of the Tranquilizing Drugs. Canad. M.A.J. 78,(1958): 209-215.

26. Lehman, H. E.: Colloque International on Chlorpromazine and the Neuroleptic Drugs. Canad. M.A.J. 73,(1955): 989-990.

27. Lundwall, R. L. and Campbell, R. L.: Chlorpromazine Hydrochloride for the Examination of the Penis in Bulls. J.A.V.M.A. 131,(1957): 86-87.

28. Martin, J. E. and Beck, J. D.: Some Effects of Chlorpromazine in Horses. Am. J. Vet. Res. 17,(1956): 678-86.

29. McClymont, G. L.: A Note on the Establishment of Carotid Loops in Cattle. The Aust. Vet. J. 26,(1950): 138-139.

30. Moore, R. B., Pierce, W. J., and Dennison, A. D.: The Story of Reserpine. J. Ind. S.M.A. 47, (1954): 853-861.

31. Moyer, J. H.: Laboratory and Clinical Observations on Chlorpromazine--Hemodynamics and Toxological Studies. Am. J. Med. Sci. 227,(1954): 283-90.

32. Mueller, J. M., Schlittler, E., and Bein, H. J.: Reserpine, Der Sedative Wirkstoff Aus Rauwolfia Serpentina Benth. Experientia. 8,(1952): 338.

33. Owen, L. N. and Neal, P. A.: Sedation with Chlorpromazine in the Horse. The Vet. Rec. 69,(1957): 413-417.

34. Pea, E. L., Shea, J., and Fazekas, J. F.: Hypotensive Action of Chlorpromazine. J.A.M.A., (1954): 1249-50.

35. Renzetti, Jr., A. D. and Padget, W. R.: The Acute Respiratory Effects of Chlorpromazine in Man. J. Lab. Clin. Med. 50,(1957): 400-409.

36. Rieppel, F. W.: Leonhard Rauwolf. Ein Beitrag Zu Seiner Biographie. Dtsch. Med. Wschr. 80, (1955): 653-655.

37. Rose, T. F.: The Use and Abuse of the Tranquilizers. Canad. M.A.J. 78,(1958): 144-148.

38. Sen, G. and Bose, K. C.: Hypotensive Effect of Rauwolfia Serpentina. Ind. Med. Wo. 2,(1931): 194.

39. Smith, R. T., Hermann, I. F., Kron, K. M., and Peak, W. P.: Meprobamate (Miltown) in Rheumatic Diseases. J.A.M.A. 163,(1957): 535-538.

40. Spur, G. B., Steven, M. H., and Farrand, E. A.: Cardiovascular Effects of Chlorpromazine in the Dog. Am. V. J. of Phys. 186,(1956): 525-528.

41. Stevenson, T. D. and Albert, S.: Blood Pressure in Patients with Hypertension Following Intramuscular Chlorpromazine. Proc. Soc. Exp. Bio. and Med. 86,(1954): 726-728.

42. Stowe, C. W.: Pharmacological Sedation and Restraint of Large Animals. M.S.U. Vet. 16, (1956): 173-176.

43. Taylor, E. L. and Sanderson, K. M.: Phenothiazine--A Remarkably Efficient Anthelmintic. Vet. Rec. 52,(1940): 635-647.

44. Troughton, S. E., Gould, G. N., and Anderson, J. A.: A Report on the Use of Chlorpromazine Hydrochloride. Vet. Rec. 67,(1955): 903-906.

45. Tyndel, M.: Ataractic Drugs in the Psychiatric Hospital. Canad. M.A.J. 76,(1957): 582-583.

46. _____: Vesprin (Squibb Triflupromazine Hydrochloride)--Revised Summary of Information for Clinical Investigators. December 12, 1958.

47. Weiss, W. A., McGee, J. P., Pa, D., Branford, J. O., and Hands, E. C.: Value of Chlorpromazine in Preoperative Medication. J.A.M.A. 161,(1956): 812-815.

48. Wilkins, R. W., Judson, W. E., and Stanton, J. R.: Proc. New England Cardiovasc. Soc., 1951-52: 34.

49. Wilkins, R. W. and Judson, W. E.: Use of Rauwolfia Serpentina in Hypertensive Patients. New England J.M. 248,(1953): 48.

50. Winter, C. A.: The Potentiating Effect of Antihistaminic Drugs Upon the Sedative Action of Barbiturates. J. Pharm. Exp. Therap. 94,(1948): 7.