Therapeutics of Pilocarpine.

By

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HABITAT.

Pilocarpine is an alkaloid of Pilocarpus, and to this primary action the crude drug owes its principal effect.

The plant from which pilocarpine is derived grows in Brazil, South America.

DESCRIPTION.

It is about ten (10) to fifteen (15) C.M. long and from four (4) to six (6) C.M. broad. Short stalk, of a dull green color, coriaceous, pellucid- punctuate, mostly smooth; when bruised, slightly aromatic. Taste somewhat bitter and pungent.

CONSTITUENTS.

From this plant several other alkaloidal products are derived such as Jaborine $C_{22}H_{32}N_4O_4$; Pilocarpudine $C_{10}H_{14}N_2O_2$; Jaborandine whose composition is not exactly known.

Pilocarpine is the hydrochlorate of an alkaloid obtained from pilocarpus with alcohol and hydrochloric acid by distillation and evaporation. The residue is dissolved in a slight excess of ammonia and chloroform, shaken with water, and then neutralized with hydrochloric acid. On evaporation crystals of hydrochlorate are formed. The properties of Pilocarpine, small white crystals having no odor but slightly bitter taste, are very soluble in water and alcohol, but almost insoluble in ether or chloroform.

The drug can be used for a sialogogue cathartic or diaphoritic.

Depending on the dose and for the end to which it is intended.

Pilocarpine increases enormously salivary secretions, and in a somewhat less degree the gastric and intestinal secretions. It also stimulates peristaltic action of the stomach and bowels, thus acting as a purgative. The secretion of the salivary glands is due to a direct excitation of the secretory nerve (Chorda tympani) ending in the gland cells. Even after pilocarpine has been injected directly into the glands, its action is set aside by the injection of Atropine. The three (3) main glands, Parotid, Submaxillary and Sublingual, become tense and tender under the influence of pilocarpine, and the secretions from these glands are rich in salts and ptyaline, and contains a small per cent of urea. The unstriped muscular fibres of the stomach and intestines are stimulated by the action of the drug upon the efferent nerve endings and muscular tissue.

Pilocarpine is absorbed into the circulation but exerts no influence upon the blood. Given in toxic doses it has a depressant action on the heart. The effect on the domestic animals is probably due to stimulation of the peripheral vogi or inhibitory cardiac ganglia, although Ringer's experiments proved that the ventricular contractions of the frog's heart were slowed by pilocarpine when freed from the inhibitory ganglia, and he attributes its action to stimulation of the heart muscle and motor ganglia situated therein.

As far as the respiration is concerned it is not directly affected by the drug, but the bronchial secretions are greatly increased, and when toxic doses are given, odema of the lungs and dyspnoea are the result.

In small therapeutic doses of pilicarpine the respiration is not noticeably increased, but in man the secretion becomes enormous. The salivary secretions in the lower animals supplant that of the skin in man. The secretions may even extend to cause an increased supply in the production of milk, and it has even been said that the hair grows more luxuriantly. In case of much sweating the temperature of the body is reduced by the evaporation of the moisture. When the alkaloid is given internally it has a tendency to contract the pupil.

Thus we see that pilocarpine possesses two (2) important actions. 1. To increase the secretions in salivary glands, stomach, intestines, sudoriporous, lachrymal and mammary glands, kidneys, bronchial and nasal mucous membranes. 2. To stimulate the involuntary muscles of the stomach intestines, heart, uterus, bladder, spleen vessels and iris. All these actions are brought about by the drug acting upon the periphery of the nerve endings in the glands and on the muscular fiber as well as on the efferent nerve terminations. It is prescribed when immediate action is desired. Therefore the hydrochlorate is generally used and given subcutaneously

The chief value of pilocarpine in veterinary medicine consists in its use as a purgative, to stimulate secretions and contractions of muscular fibers in combination with physostigmine. It is used in nearly all colics and in obstruction from twist and intussusception with physostigmine It can be used as a substitute for eserine for application to the eye (in 1 to 2 per cent) and is less painful. It is the most efficient

antidote to atropine, but should be administered in about four (4) times that of atropine. It has been recommended in dropsy of cardiac origin, not uncommon in dogs, but is dangerous since it tends to produce pulmonary odema and a weak heart in the subject. Pilocarpine has been highly recommended by German veterinarians in cerebral and spinal meningitis to assist absorption of effusions. It stimulates in its elimination, and is of service, sometimes in chronic eczema psoriases, prurigo, and chronic urticaria. It has been recommended in chronic rheumatism as an elimitive and in acute inflammation of the brain, and in laminitis without rational bases. Small doses have been used to stimulate a failing milk secretion, and prevent excessive sweating in general debility. The drug is contra-indicated when there is impairment of the respiratory functions, a weak or fatty heart and in unconsciousness, when excessive secretion may obstruct the air passages. If given for obstruction in alimentary canal and does not remove it, the danger is increased by forming a larger obstruction, intended. It is generally used in connection with the Sulphate of Eserine as a purgative, in this case it is a synergist.
It can be used as a myotic by stimulating the third nerve endings, but is of minor importance in this respect compared with some other drugs.
Its primary action is upon the salivary glands, causing an abnormal increase in the flow of saliva, also secretions are increased in all parts of the body. Probably in no case other than impaction will pilocarpine, if given with eserine, show its true worth. While eserine will cause the contraction of the muscular fibres of the intestines, pilocarpine will

cause the secretion of liquids which are of paramount importance in the active principle of all purgatives. The synergist action of pilocarpin as a purgative, causing the secretions from the intestines, acts upon the mucous membranes of the bowels, lubricating a passage for the compact mass to pass along, which would otherwise remain obstinate, regardless of the contractions of the muscular fibers of the intestines, caused by the eserine.

CASE NO. 1.

A horse was examined and the following conditions noted.

Temperature 98.6

Pulse 42 per minute.

Respiration 11 " "

One grain of pilocarpine was dissolved in sterile water and injected into the of the neck. In ten (10) minutes peristalsis was noticeably increased, and in fifteen (15) minutes the movements of the intestines could be plainly heard fifteen (15) feet distant, and was kept up for a period of a quarter of an hour, when they gradually subsided. The next sympton was noticed on the mouth. The animal at periods acting as if trying to masticate something. This was kept up for a period of about 10 minutes and then the saliva was seen dropping from its closed lips. This dripping condition continued for about 10 minutes when on opening the animal's mouth, a large amount (1/2 pint) made its escape. Inflatiss was passed several times. In thirty five (35) minutes after giving the dose hypodermically the pulse, respiration, and temperature

was taken again. Respiration showed no increase innumber whatever, while the temperature rose .3- three tenths of a degree and the pulse increased four beats per minute.

CASE No. 2.

A second inoculation was made on a dissecting subject April 16-1907. A grain and a half being given hypodermically into the tissue of the neck. The pulse, respiration and temperature were as follows: /

Temperature 102.2

Pulse 45. per minute..

Respiration 8. " "

After giving the dose, no noticeable symptom was noticed for ten (10) minutes. Then a slight peristaltic movement was noticed which gradually increased for ten (10)minutes and then gradually subsided. Animal soon began champing and saliva began to flow from its half closed mouth. On holding the animals mouth shut for a few minutes and then suddenly opening it, there escaped a half pint or more of accumulated saliva. Deglutition was constantly being performed by the animal. This abnormal flow of saliva was kept up for thirty-five (35) minutes. During the time the symptoms manifested themselves, the animal defecated once. The faeces being rather soft. The pulse increased from forty-five beats to fifty-four (54) per minute. The temperature rose from 102.2 degrees to 103.4 degrees a rise of 1.2 degrees in one hour. No increase in the respiration being noticed. During the action of the drug the animal showed a slight degree of

CASE NO. 3.

On May 20-1907 a case was brought to the clinic, and diagnosed as impaction. The animal seemed to be suffering with intense pain. It was turned over to one of the senior students for treatment. After a careful examination, it was decided to give a hypodermic injection of eserine. At the first injection of 1 1/2 grains and waiting one hour he received no satisfactory action. A second injection with increased dose gave no results. A grain and a half of pilocarpine was administered along with 1 1/2 grains of eserine. In 10 minutes an increased peristaltic movement was noticed, with slight uneasiness. In fifteen (15) minutes after the use of pilocarpine faeces was passed to the amount of about twenty (20) pounds. This is one of the many cases where eserine would not give the action required without its synergist, pilocarpine.

CASE NO. 4.

On May 21st the dose was increased to two grains. This was given hypodermically into the tissues of the neck. The pulse before injecting was 30 per minute, the temperature 99.6. Respiration 10. After injecting no symptoms were noticed for nine minutes, then a slight increase in the peristaltics was noticed. In ten (10) minutes the saliva began to flow from the closed mouth, being slight at first but gradually increased until there was a constant flow. The animal soon showed signs of uneasiness, throwing its head from side to side and looking at its abdomen; but this uneasiness soon passed away. Flatus was passed several times. The peristaltic movement gradually increased until the peristaltic move-

ment could be plainly heard 20 feet away. The saliva continued to flow, and I believe that over a quart escaped besides what was swallowed.

CASE NO. 5.

I dissolved two grains into a half pint of water and used externally on the eye but secured no positive results.

CASE NO. 6.

1 1/2 grains of pilocarpine were given subcutaneously to a dog weighing about 30 pounds. The symptoms were manifested in a short time. In four minutes after injecting salivation began. This action continued throughout a period of sixty eight minutes. In four and a half minutes the animal showed acute pain and the act of vomition was noticed. The drug acted as an emetic, and the animal discharged a yellowish mucous mass on five different times. The eyes became enlarged and pupil dilated. In nine (9) minutes after injecting, the drug had acted upon the urinary organs. Micturition began, which was normal at first, and later became slightly colored, and kept dribbling for some time. The animal seemed to have no control over the action. Vomition was followsd by deep heavy breathing and number of respirations was way below the normal. All the muscles of the abdomen seemed to be brought into play. Animal's head was hanging, was unstable, and seemed to have great difficulty in keeping its equilibrium, and rapidly becoming weaker. After seventeen minutes had elapsed the animal seemed to have gained a little strength and became very restless, and the salivation had increased enormously. Large quantities escaped from its mouth and a great puddle was formed. In twenty-one

minutes the difficult respiration had somewhat subsided and animal laid down. After a short time the difficult breathing returned and was kept up for nearly a quarter of an hour. Vomition had stopped. In twenty-one minutes the pilocarpine showed its power as a purgative. The faeces that was passed somewhat resembled the discharge caused by vomition, only of a rather more consistency. As the time elapsed, the animal tried to vomit again but after several fruitless efforts gave up the attempt. In three quarters of an hour there was considerable twitching of the abdominal muscles, and the animal emitting low barks seemed to be in a semi-conscious condition. Passed faeces again. More watery than the other time. On the third passage of faeces they had become more dark in color. The animal again resumed the cumbent position and remained this way for some time. Seemed to be rapidly recovering from the effects of the drug. Six hours later the dog was killed and a post mortem held. The perito - neum was highly congested. Ingesta very watery. The inner coat of the intestines was of a deep yellowish color, mucous very slimy. The outer coat was very red and highly congested. This was about all the principal lesions.

CASE NOS.7 & 8.

On two other occasions two grains of pilocarpine were used on subjects They gave the characteristic symptoms already enumerated before.

After giving an animal a toxic dose the following symptoms will be noticed; symptoms appear in from five to ten minutes after the subcutaneous injection. Salivation alone occurs after small doses, but with toxic quantities there are present salivation, accompanied by more or less sweating, intestinal colic, purging and perhaps vomiting, a slow weak pulse and dyspnoea. Muscular tremors are observed sometimes in man, and convulsions in frogs, but spasmodic movements are uncommon in the domestic animals. The administration of an amount of five grains or more in the horse is accompanied with danger. Atropin is the physiological antagonist to pilocarpin in relation to the heart, secretions, pupils, and, in large doses, probably to the intestines. Atropine should be given along with alcoholic stimulants, or ammonia in pilocarpine poisoning.