PROCEEDINGS.

VOL. 28. MAY, 1931. No. 8.

Peiping Section.

Peiping Union Medical College, March 26, 1931.

5530

Some Observations on the Pharmacological Action of Gelsemicine, an Alkaloid from Gelsemium Sempervirens, L.

HSIANG-CH'UAN HOU.

From the Department of Pharmacology, Peiping Union Medical College.

Gelsemicine is a new alkaloid isolated by Chou[1] from the rhizome and roots of the American *Gelsemium sempervirens, L.* This alkaloid is the most toxic yet isolated. Using gelsemicine hydrochloride the minimum lethal dose for male rabbits given intravenously was found to be 0.05 mg. per kilo; for dogs 0.6 mg. per kilo; subcutaneously for albino rats 0.0001 mg. per gram, and subcutaneously for frogs 0.03 mg. per gram.

The toxic symptoms observed for the mammals were similar. There was a preliminary quietening of the animal with some slowing of the respiration. Tremors followed by incoordination of movement, and loss of power developed in 5 to 15 minutes. At the same time the respiration became either slow and deep or rapid and shallow, the result being a decrease in minute volume. In 15 to 30 minutes after the injection there were developed intermittent tetanic convulsions alternating with great prostration. Respiration now became slow and shallow. The animal usually gasped for breath, grunting and crying at times. Defecation and urination usually occurred. In the dog there were marked salivation, retching, and

[1] Chou, ***Chinese J. Physiol.*, 1931, in press**

sweating of the paws. Respiration rapidly became weaker until it finally stopped. Heart beats remained strong for 15 to 30 seconds after the cessation of respiration. Consciousness was apparently retained until a few minutes before death.

With a sublethal dose the animal remained quiet after the last convulsion and the respiration gradually returned to normal. There was complete recovery one to 2 hours after the injection.

Smaller doses produced only some quietening of the animal and some lessening of pain sensation. There was a very slight degree of narcosis.

Dogs under luminal or ether anesthesia were much more susceptible to gelsemicine hydrochloride. One-tenth of the ordinary minimal lethal dose caused death from respiratory failure in a few minutes.

Action Upon Respiration. Dogs under luminal anesthesia showed an increase in amplitude as well as in rate of respiration when a dose smaller than one-tenth of the toxic dose was given. With a larger dose there was depression preceded by a transient stimulation. Lethal doses produced no stimulation but a progressive depression until paralysis finally set in. Atropinization did not modify this action of gelsemicine. Normal rabbits exhibited the same findings. There was no antagonism but rather a synergism between a small stimulative dose of gelsemicine and a depressive dose of morphine.

Action Upon Circulation. Circulation was not affected until some time after a marked depression of the respiration. When asphyxia set in there was a slowing of the heart rate and a lowering of blood pressure. Peripheral organs such as leg, intestine and nose showed no change until there was a marked weakening of the respiration. The leg volume then decreased, the intestinal volume increased. The spleen showed an increase in volume with a dose which stimulated the respiration and a marked decrease with a dose which depressed respiration.

That there was no direct action upon the mammalian heart was shown by observation upon a dog with a heart oncometer. As long as the respiration was kept up there was no essential change of the tracing even with 20 times the minimal lethal dose for anesthetized animals.

Perfusion of the frog heart showed that gelsemicine HCl in a concentration of 1:1,000,000 produced a stimulation of the heart rate and amplitude. With a concentration of 1:500,000 there was no change or only a slight stimulation followed by moderate depression. When the concentration was 1:50,000 there was a progressive

slowing of the heart beat with a decrease in amplitude until finally the ventricular beats became irregular or even stopped.

Action on the Isolated Intestine and Uterus. Freshly isolated intestine and uterus from rabbits and dogs were used. The tissue was suspended in Locke's solution kept at 38°C. Gelsemicine HCl in a concentration of 1:1,000,000 in Locke's produced an increase in the amplitude as well as in the rate of contractions of the isolated intestine of rabbit or dog. Higher concentration resulted in an increase in tone followed by a diminution both in amplitude and rate. When the concentration of the gelsemicine HCl was increased to 1:100,000 the decrease in rate and amplitude was very marked and the tone was also decreased. In this stage the action of barium chloride was completely antagonized. Atropinization did not alter the action of gelsemicine.

Isolated rabbit or dog uterus reacted toward gelsemicine somewhat differently from the intestine in that there was a marked preliminary increase in tone with all the concentrations given above. There was a greater increase with the higher concentration, followed by a gradual decrease of tone until it was lower than normal. The normal rhythmical movements decreased in both rate and amplitude. The curve obtained simulated that with barium chloride although the action of the latter was partially antagonized. Ergotoxinization and atropinization did not alter the action of gelsemicine.

Action on the Pupil. Two rabbits were tried. After application of a drop of 0.2% solution of gelsemicine hydrochloride a gradual mydriasis developed in about 20 minutes. The mydriasis was not complete but the light reaction was eventually lost. Both animals died in about one hour after the administration of the drug, apparently due to rapid absorption from the conjunctiva.

5531

Acid-base Paths in Human Subjects.

S. H. LIU AND A. B. HASTINGS.

From the Departments of Medicine of the Peiping Union Medical College, and the University of Chicago.

Using the micro-acid-base technique[1] a study has been made of

[1] Shock, N. W., and Hastings, A. B., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 780.