after moulting or after a prolonged fast the venom was ten times more active than after a plentiful meal or before the moult. It is estimated that 1 gm. of the cobra venom will kill 165 adults. It is to toxalbumins or, more accurately, protoalbumoses and heteroalbumoses that the properties of venoms are essentially due. *Colubridæ* venoms pass slowly through vegetable membranes and with great difficulty through animal parchments. The viperine venoms are not dialyzable and when heated to 72 C. become almost inert. The venoms of *Colubridæ* destroy the coagulability of the blood, asphyxia supervenes and the death struggle is brief. The venoms of *Viperidæ*, on the other hand, produce violent local changes. Injected into the peritoneum of an animal, there is an enormous afflux of sanguinolent serosity; the capillary vessels of the serous membranes immediately become distended, allowing the blood to filter through their walls, and the animal succumbs in a few hours. The hemolytic action of the venoms of *Viperidæ*, especially the rattlesnake, is very weak. A wide range of differences is exhibited by the various venoms as regards the hemolytic power in the presence of normal heated serum. If cobra venom be added in increasing doses, hemolysis augments up to a certain point, beyond which the destruction of corpuscles shows progressive diminution. The leucocytosis is much more intense and rapid with cobra than with rattlesnake poisoning.

If the therapeutic measures which we possess could be applied promptly in each case of poisoning by the bite of a venomous snake, the mortality would be much lower than the present, from 25 to 40 per cent. The venoms are partially neutralized by ammonia and by potassium permanganate, but the best chemical antidote is 2 per cent. solution of the hypochlorite of lime, which will immediately and surely destroy the venom by contact. When possible to apply the ligature proximal to the wound, we have a means which controls the intake of venom, but endangers the viability of the member so constricted. Calmette states that Halford's method, injection of ammonia near the wound, is worthless, and that Mueller's, free stimulation with strychnin and generous feeding, is no better. In this case, the Mueller treatment was instituted at the suggestion of Dr. Charles Wardell Stiles, of the Hygienic Laboratory. Animal experiments certainly confirm all that Calmette has claimed for his serum, antivenine.

The dose of antivenomous serum is 10 c.c. of the liquid or 1 c.c. of the dried preparation, dissolved in 10 c.c. of warm sterile water and injected under the skin where absorption is rapid, regardless of the location of the bite. In desperate cases, injection may be made into a vein or the subcutaneous dose may be trebled. The time that elapses between the infliction of the wound and the use of the serum bears a definite relation to the efficiency of the serum; as little time as possible should be lost in employing this valuable agent.

The case herein reported may be used by the Mueller school as an argument in favor of that particular treatment, and likewise it may be a source of comfort to the Calmette followers to know that the patient recovered after the use of the serum; A Mueller¹ states:

Cases may occur in which the quantity of strychnin required to subdue the symptoms and to be injected in a few hours may amount to a poisonous dose, but to urge this as a reason against the use of it is—to say the least of it—puerile, since the two poisons neutralize each other, the strychnin not causing

muscular spasms until it has completely disposed of the snake poison.

To inject in urgent cases one-sixth, in mild cases one-twelfth, of a grain every half hour until the effects of the snake poison are entirely removed, is perfectly safe practice which none who follow it will have cause to regret.

Calmette² says:

"Neurotoxin being the essentially active substance in venoms, and that to which the dangerous properties of poisonous snakes as regards man and domestic animals are especially due, it is the effect of this that it is most necessary to prevent. Consequently, the first quality that an antivenomous serum ought to exhibit in order to be capable of being used in the therapeutics of poisoning is the possession of an antineurotoxic power as high as possible. This antineurotoxic power is easily obtained by employing cobra venom for the fundamental immunization of the horses destined for the production of the serum. Antineurotoxic serum thus prepared shows itself perfectly capable of preventing all effects of intoxication from cobra bites, which are much the most frequent in India. In the same way it shows itself sufficiently efficacious with regard to colubrine and viperine venoms, the neurotoxic activity of which may cause death. But as it does not possess any preventative action upon the local effects or hemorrhagin, to which the noxiousness of certain viperine venoms—such as those of *Lachesis*—are almost exclusively due.

In countries in which *Viperidæ* are very common we must therefore not confine ourselves to vaccinating animals that produce serum solely against the neurotoxin of cobra venom, for instance; we must prepare these animals, after having immunized them to cobra venom by injecting them with progressively increasing doses of the various venoms derived from snakes that are most frequently met with in the district.

Nothing, moreover, is easier than to train animals vaccinated against cobra venom to tolerate strong doses of the venoms of *Lachesis*, *Vipera russellii*, *Crotalus*, *Hoplocephalus* or *Pseudochis*. In a few months we succeed in obtaining serums very active against these different venoms.

Utilizing the horse as producer of antitoxin, I have prepared by this method polyvalent serums capable of preventing the local action of viperine venoms, and of suppressing *in vitro* their coagulant and proteolytic effects on the blood."

Calmette's serum can be purchased in New York and Chicago and should be employed in every case possible. When the serum is not immediately available, the strychnin treatment is the best substitute.

Clinical Notes

NECROSIS OF THE LIVER AFTER CHLOROFORM ANESTHESIA *

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It is not so much for its statistical value as again to call the attention of the profession to the dangers of chloroform as an anesthetic that this case is reported.

Patient.—Male, aged 19, weight 152 pounds, student, reared on a farm, good habits.

History.—Previous history is negative, except that the patient was subject to attacks of "indigestion" from childhood. He had an attack in February, 1908, which was diagnosed as appendicitis. At that time there was decided tenderness in the right iliac region over the site of the appendix, some elevation of temperature, and rigidity of the right rectus muscle. After an interval of about two weeks, the patient apparently recovered from this attack and returned to school. On April 16 of the same year he was awakened early in the morning by severe pain in the abdomen, followed shortly

2. Venoms, Venomous Animals and Antivenomous Serum Therapeutics, 1908, p. 250.

* Read before the Rochester Pathological Society, Feb. 18, 1909.

1. Australasian Med. Gaz., Sydney, 1888-9, viii, 41, 209-210.

by vomiting and diarrhea. There was nothing in the diet of the previous day adequately to explain this illness. The vomiting and diarrhea continued until about 7 a. m., shortly after which he was seen by his family physician, Dr. F. A. Wicker, of Livonia, N. Y. At this time there was no elevation of temperature and the pulse rate was 84. Severe pain and marked tenderness to slight pressure were present throughout the abdomen, but most marked over the appendix. By the next morning, April 17, the symptoms and signs of the disease had apparently abated somewhat and the patient seemed to have improved except for a slight elevation of temperature and pulse rate.

Operation.—The patient remained in this condition for the next three days, when he was operated on by Dr. Becker. An opening was made through the right rectus muscle and an abscess, thoroughly walled off, was found in the region of the appendix, containing about eight ounces of foul-smelling pus. The appendix was removed, the pus carefully wiped out and drainage inserted. The anesthetic used was chloroform and the amount employed did not exceed one-half ounce. It was administered by a thoroughly competent anesthetist, and the course of the anesthetic and the operation were uneventful, not occupying more than half an hour.

Postoperative History.—The patient recovered from the anesthetic promptly and was conscious within fifteen minutes. He apparently did well until the third day after the operation, his temperature at no time going above 100 F. and the pulse rate varying between 80 and 90. There was free drainage from the wound, no distention of the abdomen and no vomiting. There was an absence of pain. On the morning of the third day, however, his pulse dropped to 66, his temperature then being 99.2 F. About noon he was noticed by members of his family to act in an irrational manner, and apparently he did not recognize his mother. This was the first indication of mental disturbance. About two hours later acute mania developed, and it required the combined efforts of several persons to restrain him. One-eighth grain of morphin was administered hypodermatically at intervals of about two hours until the following afternoon. This served partly to control the mania. From that time he remained passive, lying on his back, pulse increasing in rapidity and becoming weaker and the temperature gradually rising. He passed urine involuntarily at intervals of about three minutes. After lying in this condition for several hours tonic convulsions developed which were most marked in the arm muscles. This was followed by coma and Cheyne-Stokes respiration. These symptoms became more and more profound until his death, which occurred five days after the operation and about forty hours after the first indication of any mental disturbance. At the time of the operation there was a slight yellow tinge to the sclera. This jaundice became general and at the time of death was rather noticeable.

Urine: After the operation two examinations of the urine were made. The first specimen was of acid reaction, specific gravity 1025; sugar and albumin absent. The second specimen contained trace of albumin, but in other respects was the same as the first.

Autopsy.—Permission to do a partial postmortem was obtained and was performed on the following day by Dr. Williams—about twenty-four hours after death. In deference to the wishes of the family, only the abdomen was examined. No attempt at embalming had been made. The body was that of a young male, fairly well nourished, slight, general jaundice. In the right iliac region there was the incision of the recent operation, about 6 cm. long, closed by sutures and containing a drainage tube. The edges of the wound were clean and presented to the eye nothing abnormal. The abdomen was opened in the median line, the omentum was free and apparently normal. A completely walled-off sac about the size of a lemon, made up of old adhesions, was found in the right iliac region. This sac was empty, clean and practically odorless. The peritoneum, both parietal and visceral, to the naked eye, was apparently normal. The kidneys and adrenals, pancreas and spleen, were carefully examined and presented no evidence of important pathologic change. The gall bladder and bile ducts showed very little evidence of inflammatory trouble—in fact,

the liver was the only organ in the body that exhibited signs of disease, but even the changes in this organ to the naked eye were not particularly striking. It was smaller than normal and weighed approximately 1,350 grams. Its surface was smooth. The capsule was slightly wrinkled and of normal thickness. Inflammatory adhesions were absent. The liver substance was pinkish-gray, and was softer than normal. On cutting, this softening was particularly noticeable and the friability was increased. The cut sections were yellowish-gray. There was but little bleeding. Some portions were distinctly mottled. There was very little discernible change in blood vessels or bile ducts. The lobules were made out with difficulty or not at all. Sections were made of the kidney, spleen, pancreas and liver. The liver alone presented evidence of marked change.

Microscopic Appearance: This was in striking contrast to the macroscopic appearance. The lobules were smaller than normal and were indistinctly defined. The liver cells were practically all necrotic. Occasionally, a lobule would be found in which the change was less evident at the periphery than in the central part. A fat stain was not used. The kidney section showed slight cloudy swelling, otherwise was negative.

Bacterial Examination: Stab cultures in plain agar were made from the various organs examined, including the peritoneum and abscess cavity. With the exception of the latter, all were negative. In the abscess cavity was found a mixed culture of bacilli and cocci—their identity, however, was not established.

Urine: About 50 c.c. of turbid, dark brown urine was aspirated from the urinary bladder and examined. Tests for sugar and bile were negative. Albumin was present in small amount. There was a distinct odor of acetone and a marked reaction was obtained with dilute ferric chlorid solution, suggesting the presence of diacetic acid. Microscopic examination showed a few blood cells and a few hyalin casts.

The history of the case, together with the postmortem findings, led us to attribute the death to necrosis of the liver, which we believe, in the absence of other explanation, to be due to the toxic action of the chloroform used as the anesthetic. It seems proved that chloroform can cause death in either of two ways: first, after the manner more commonly understood, by its depressing and paralyzing action on the respiratory center; and second, by its destructive action on the liver. In the former case, the amount of the drug used and the concentration of the dose bear a relationship to its toxic action and the time of death, which is immediate. In the latter instance, its toxicity is due to its action as a protoplasmic poison on the liver cells and the death, which is delayed for several hours, or even days, results, as has been reasonably explained by Wells,¹ from the perverted metabolism of that organ. Neither the extent of the destruction nor the degree of the toxicity seem to bear any relation to the amount of the anesthetic used or to the method of administration. Rather the chloroform seems to act as a fulminating agent for the marked, perverted katabolism of the liver cells, in which the liver not only fails to detoxicate the poisonous products of metabolism that are brought to it by the blood stream, but it undergoes a process of self-destruction or autolysis, and it is the combined poisons of these two perversions of function which directly induce death.

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1. Arch. Inter. Med., vol 1, p. 589.

Surgery of Peritonitis.—The wise surgeon never forgets that the diaphragmatic zone is the danger area of the peritoneum and should not be interfered with in general septic peritonitis unless it is itself the seat of primary infection, as in perforation of gastric ulcer of the lesser curvature.—G. A. Bingham, *Saskatchewan Medical Journal*, January.