Kempner and Schepilewsky on brain emulsions and was unable to confirm their results.

Summary. We have failed to protect mice against small amounts of botulinum toxin by the injection of tyrosine and have not been able to confirm the work of Kempner and Schepilewsky. We feel that the suggestive results of 2 of our experiments on the effect of excess quantities of tyrosine on the formation of botulinum toxin are not significant in the light of the other experiments described here. We have also found that neither tyrosine nor phenylalanine had a deleterious effect on formed toxin when mixtures of the amino-acids and the toxic material were incubated together.

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Experimental Production of Gastric and Duodenal Ulcers in Dogs in Cinchophen Poisoning.

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Churchill and Van Wagoner[1] attempted to produce acute yellow atrophy of the liver by feeding cinchophen to dogs. Functional and histological damage was produced with large doses, but this did not simulate acute yellow atrophy. Numerous acute gastric and duodenal ulcers were observed at autopsy. Smaller doses of cinchophen gave definite functional damage of the liver, but histological damage was irregularly produced.

A total of 25 dogs were given cinchophen in varying doses from 22 mg. per kilo to 27 times that amount. In this series acute and chronic gastric ulcers were found in over 80% of the dogs used. These ulcers were typical grossly and microscopically. These results were published and the following possibilities of the mechanism of the production of these ulcers were listed[2]: 1. Cinchophen may have a direct toxic action on the gastric mucosa, combined with digestion by the gastric secretions. 2. The drug may combine with the mucin of the stomach and thus remove the normal protection of the gastric mucosa. 3. It may act on the autonomic nervous system and induce erosions by its neurogenic effect. 4. Cinchophen may

[1] Churchill and Van Wagoner, PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 581.

[2] Churchill and Van Wagoner, *Arch. Path.*, 1932, **14**, 860.

influence the secretion of gastric juice, either directly or through the endocrine system. 5. The drug may have a general toxic action which affects the stomach directly or by causing metabolic disturbances as a result of its effect on the liver or pancreas. 6. The nutritional disturbances resulting from the anorexia that follows the ingestion of cinchophen may be a factor in the production of ulcers.

Further experimentation is in progress to limit these possibilities by attempting to prove or eliminate certain factors.

Well nourished, apparently healthy dogs were used. Three dogs were operated: A loop of jejunum was brought to the surface and anchored. The continuity of the intestine was not disturbed. These dogs were allowed to recover from the operation, and, upon recovery, cinchophen suspended in olive oil was injected hypodermatically through the intestinal wall. The daily dose of cinchophen was calculated so that each dog received 220 mg. of cinchophen per kilo. (The human dosage can be figured as 22 mg. per kilo per day.) The dogs were fed a meat, cereal mixture by mouth. When the stools became persistently bloody the dog was sacrificed.

Dog No. 1-A, weighing 16 kg., received a daily dosage of 3.52 gm. of cinchophen, a total of 22 doses, showed persistent bloody stools and was sacrificed. Autopsy showed a large chronic gastric ulcer 4x2.5 cm. bordering on the pyloric ring and extending proximally into the lesser curvature of the stomach. No ulcers were found at the point of injection.

Dog No. 2-A weighed 4.05 kg. was operated on January 14, 1933, and started on cinchophen January 24, 1933. Daily doses of 220 mg. of cinchophen were given for 10 days. The dog died on February 2, 1933. Autopsy revealed a massive hemorrhage into the stomach. A large pre-pyloric ulcer 1.5x2 cm. on the posterior wall near the lesser curvature had perforated and the opening was sealed by omentum. There was no blood or pus in the abdominal cavity. The site of injection was 2½ feet from the pyloric ring.

Dog No. 3-A weighed 5.15 kg. at operation. After recovery the animal weighed 7.8 kg. Twenty doses of 15.7 gm. each were given daily. At this time persistent tarry stools appeared and the dog was sacrificed. Autopsy revealed an emaciated, very weak dog, weighing 4.93 kg. An ulcer was found at the superior portion of the pyloric ring. There was no further ulceration in the gastro-intestinal tract. At the site of injection there was a large intramuscular abscess. The regional lymph nodes were enlarged. The spleen showed numerous elevated, hard, pale, grey-white nodules, 0.5 cm. or less in diameter. The gum of the lower right side of the mouth showed a large ulcer-

ation with exposure of the bone. The site of injection was 4 feet from the pyloric ring.

Microscopic sections showed typical chronic gastric ulcers. The large intramuscular abscess contained a large amount of fat and many large, clear cells with vesicular nuclei. The lymph nodes and nodules in the spleen contained a definite hyperplasia of the reticulo-endothelial cells.

Summary. These experiments have allowed us to inject the drug into the gastro-intestinal tract without passing through the stomach, and should rule out any local toxic effect of cinchophen in the stomach. No ulcers developed in the mucosa of the intestine.

Conclusion. Gastric ulcers that are produced in dogs by the injection of cinchophen are not due to a local toxic action on the gastric mucosa.

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Source of Fat Found in the Thoracic Duct Lymph in Fasting.

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Thoracic duct lymph of fasting dogs contains 0.3 to 1.3% total fatty acids.[1] Further observations showed that with the continuous collection of the lymph under anesthesia, there is usually a spontaneous decline in the lipid content, amounting to 50% or even more in 4 hours. Injection of pilocarpine or secretin is followed by an increase of the lipid content of the lymph up to or considerably above the initial level, the maximum effect appearing about 4 hours after the injection. In enterectomized animals, the initial lipid content is low and does not rise following pilocarpine; nor does pilocarpine cause a rise of lipids in the lymph of dogs with common bile duct fistula.

Method. 26 dogs were fasted 3 to 8 days. Cannulation of the thoracic duct was done under nembutal anesthesia. For the preparation of the enterectomized animals, the bowel was removed from the recto-sigmoid junction to the midportion of the duodenum, the free end of the duodenum being brought to the outside through a

[1] Rony, H. R., Mortimer, B., and Ivy, A. C., *J. Biol. Chem.*, 1932, **46**, 737.