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**Experiments on the administration of tartar emetic by various routes.****By H. JOCELYN SMYLY.**

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Tartar Emetic is used intravenously in the treatment of Trypanosomiasis, Kalaazar and Schistosomiasis. It has been found by us in the treatment of Kalaazar that the average dose tolerated by human beings is 2 mg. per kilo of body weight given three times a week by intravenous injection of 2 percent aqueous solution. Intravenous injection is difficult in the case of infants, and the following experiments were made to ascertain if a more convenient route would serve in such cases. It cannot be given by mouth on account of its emetic action; subcutaneous injection leads to painful necrosis and possibly ulceration; there remains the possibility of intraperitoneal, of intramuscular and of rectal administration.

Experiments on intramuscular injection were made in four rabbits and one man; intraperitoneal injection in five rabbits; and rectal injection in three patients with Kalaazar.

**Intramuscular Injection.** Four rabbits were injected with daily doses, ranging in number from one to forty, of 4 mg. per kilo body weight given in various dilutions, some in one place, others at different places at each injection. The rabbits were autopsied and the tissues examined microscopically. Haemorrhage in the muscle followed by necrosis occurred after every injection.

A patient, male, age 22, weight 48 kilos, suffering from Kalaazar, was given 11 intramuscular injections of chemically pure tartar emetic during 46 days, in doses varying from 2 mg. in 4 cc. to 40 mg. in 10 cc. The larger doses gave rise to severe pain and inflammatory swellings.

**Conclusion.** This method invariably caused pain, swelling and necrosis, and is impracticable for continued treatment.

**Intraperitoneal Injections.** Five rabbits were given daily intraperitoneal injections of tartar emetic, of varying doses and for

different periods, dissolved in 10 cc. of normal saline per kilo of body weight, as follow:

1. 4 mg. per kilo b. w. for 6 doses: sacrificed.
2. 6 mg. per kilo b. w. for 40 doses: sacrificed.
3. 10 mg. per kilo b. w. for 5 doses: died.
4. 10 mg. per kilo b. w. for 6 doses: died.
5. 20 mg. per kilo b. w. for 2 doses: died.

No. 3 had peritonitis, from which *B. coli* was recovered by culture. Nos. 4 and 5 died of antimony poisoning.

Nos. 1 and 5 showed no peritoneal inflammation. Nos. 2 and 4 showed mild peritonitis, the great omentum being matted in a mass on the greater curvature of the stomach. In No. 2 there were adhesions between the colon and caecum.

Conclusion. This method causes too much irritation to be safely used in children, but may serve in laboratory animals.

Rectal Injection. Three cases were treated daily by this method. After the bowel had been washed out with a plain water enema, 100 cc. of normal saline containing the prescribed dose was injected and was almost always successfully retained. Antimony was detected in the urine in each case but not estimated quantitatively.

Case 1. Male, age 14, weight 18 kilo. Duration of disease three weeks. Symptoms and signs of Kalaazar, but organism not recovered. Doseage 40 mg. to 300 mg. Total 5.78 gm. in 51 days. Result: cured.

Case 2. Male, age 15, weight 31.6 kilos. Duration of disease 1½ years. *Leishmania donovani* obtained by liver puncture and blood culture. Doseage 60 mg. to 1.0 gm. Total 18.44 gm. in 50 days. Disease became worse under treatment. Developed cancrum oris, and was discharged against advice.

Case 3. Male, age 11, weight 22.5 kilos. Duration of disease 1½ years. *L. donovani* obtained by liver puncture and culture. Doseage 0.060 to 0.800 gm. Total 9.6 gm. in 37 days. Disease became worse under treatment. On starting intravenous treatment, showed immediate improvement, which continued for 2 months, following which began to get worse, and antimony treatment was stopped after 4½ months intravenous medication.

Result: The absorption of antimony from the colon in amount insufficient to effect cure apparently produced an antimony-resistant *Leishmania*.

Conclusion: The method fails to cure well-marked cases of Kalaazar and may render them very intractable to further treatment.

The results of this work indicate that intravenous injection is the only practicable route for the administration of tartar emetic in the treatment of human cases of Kalaazar.

## 99 (2622)

### The effect of ephedrine on experimental shock and hemorrhage.

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In our previous report,<sup>1,2</sup> it was shown that ephedrine, an alkaloid isolated from Ma Huang, possesses sympathomimetic actions. Its outstanding feature is its circulatory stimulation by acting on both the cardiac accelerator ganglia and endings. The rise in blood pressure and pulse rate lasts for more than 15 minutes, and sometimes indefinitely.

The purpose of the present paper is to report the influence of ephedrine in hemorrhage and in shock induced by different methods. All the results were obtained from dogs. Histamine in the dosage of 2-3 mg. per kg., or Witte's peptone in dosage of 50 mg. per kg., caused a fall in blood pressure as low as 30-40 mm. hg., but a subsequent intravenous injection of ephedrine always brought it back to the initial level, and maintained it there for more than 3 hours, when the animal was killed. In surgical and traumatic shock, produced by pinching of the liver, exposure and manipulation of intestines, insertion of ice bags into the abdominal cavity, and opening of windows in the operating room, the external temperature being 25° C., the blood pressure in one experiment fell from 150 to 53 mm. hg. within eight minutes, but

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<sup>1</sup> Chen, K. K., and Schmidt, Carl F., *Proc. Soc. Exp. Biol. and Med.*, 1924, **xxi**, 351.

<sup>2</sup> Chen, K. K., and Schmidt, Carl F., *J. Pharm. and Exp. Ther.*, 1924.