

contain a large portion of the cholesterol absorbed following a labeled cholesterol meal (4), the overall data may be evaluated to show that at least 90% of the cholesterol absorbed as such during the experimental period studied was recovered in the lymph samples collected from rats No. 1, No. 2, No. 4, and No. 5. In view of the probable presence of anastomotic lymph channels draining lymph into the systemic circulation via routes which would not be shunted by a cannula in the thoracic duct, the data strongly suggest that all food cholesterol may be transported normally via the lymphatics to the systemic circulation.

Only a small fraction of the amount of cholesterol orally administered is absorbed in the intact animal and it has been demonstrated as well that cholesterol absorption occurs slowly over a period of many hours, even

days(4,7). Thus, the low percentage of the administered tritium-cholesterol dose which was recovered in the lymph samples, bloods, and livers of the experimental animals was to be expected.

It is noteworthy that the highest specific activity of cholesterol recovered from the lymph, 5.98×10^{-2} $\mu\text{C}/\text{mg}$ in the case of rat No. 4, is only approximately one-tenth the specific activity of the cholesterol fed. This large dilution must arise primarily from cholesterol of endogenous origin.

Summary. Exogenous cholesterol after its intestinal absorption was found to be conveyed into the systemic circulation by the lymph of the thoracic duct. Little or no transport occurred via the portal venous system.

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Effect of Primaquine on Experimental *Trypanosoma cruzi* Infection.* (19168)

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Since 8 - (isopropylaminoamylamino) - 6 methoxyquinoline, pentaquine or SN 13276, has some activity against *Trypanosoma cruzi* infections in mice(1,2), it seemed desirable to test the chemically related and less toxic 8-(4-amino-1-methylbutylamino)-6 methoxyquinoline, primaquine or SN 13272, against this same trypanosome. This drug has been recently tested against vivax malaria(3). Preliminary successful results in the early

stages of *T. cruzi* infection in mice are presented in this paper.

Materials and methods. A highly virulent strain of *T. cruzi* (Tulahuén strain), isolated in 1945 from a human case in the northern part of Chile, was used. Following observations on the genetic constitution of mice in relation to their susceptibility to *T. cruzi* (4), the trypanosomes have been transferred regularly every 10 days for the past year into male mice (about 8 weeks old, weighing 18-21 g) of the genetically pure C3H strain (Jackson Memorial Laboratories). After a standardized intraperitoneal injection of about 200,000 trypanosomes in 0.4 ml citrated mouse blood, trypanosomes appear in the blood in 6 to 8 hours, remain scarce for several days, suddenly increase in number at 4 to 6

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1. Goble, F. C., *J. Parasitol.*, 1949, v35, 375.

2. Jarpa, A., Christen, R., Agosin, M., Pizzi, T., and Cortes, G., *Bol. Inf. Parasit. Chilenas*, 1950, v5, 19.

3. Edgcomb, J. H., Arnold, J., Yount, E. H., Jr., Alving, A. S., Eichelberger, L., Jeffery, G. M., Eyles, D. E., and Young, M. D., *J. Nat. Mal. Soc.*, 1950, v9, 285.

days when "slender forms" are numerous, steadily increase thereafter, reach over 1000 per mm³ on the 9th day and kill the mice in 10 to 11 days. They invade the tissues as early as 12 hours and show a predilection for connective tissue.

Trypanosomes were counted daily by a reliable method used by the author and co-workers (4-6) which involves the use of a specially marked hemoglobin pipette. The drug was dissolved in distilled water at the rate of 1 mg/ml water and was given daily *per os* at the rate of 0.25 mg.

Results. Three groups of mice were treated. To the first group (10 animals), 10 daily doses were begun on the second day; to the 2nd group (10 animals), 8 daily doses were begun on the 4th day, and to the third group (2 animals which received about 380,000 trypanosomes initially), 10 daily doses were begun on the 6th day. Each group was accompanied by a similar untreated control group of the same number. Counts of trypanosomes were made daily. Results reported here cover a period of 35 days from groups 2 and 3 and for 55 days from group 1. Whereas controls died within the expected 10 or 11 days, all treated animals in the 1st group became negative in 24 hours, and the majority remained negative. Occasional trypanosomes were usually seen in one or 2 mice for 17 days and in 7 and 6 mice, respectively, on the 11th and 12th day when the controls were dead or dying. After 17 days, occasional trypanosomes were seen in 4 to 8 mice. Treated mice in the second group also lived and showed a marked decrease in trypanosomes after 24 hr (from an average of 34/mm³ to 7/mm³). Thereafter, occasional trypanosomes were usually seen in 2 to 4 of the mice (average = 0.2/mm³). The two treated mice in the third group behaved as did the mice in group

2 in spite of the fact that they contained 1568 and 1960 trypanosomes/mm³ blood, respectively, at the time of the first treatment. Four mice in group 1 died between the 37th and 54th day, and some in groups 2 and 3 were killed on the 35th day. All had only a few parasites in their blood or tissues, but some showed a mild myocarditis.

Discussion. So far, no curative drug has been found against *T. cruzi* infections. Some few substances, *i.e.*, Bayer 7602 (Ac)(7), phenanthridine compounds (8,9) and certain aminoquinolines, particularly pentaquine (1-2) act in a suppressive manner in that they prevent the death of animals during the acute stage and decrease the number of parasites in the blood. Failure to cure the infection seems to be due to an ineffective action on the tissue stages of the parasite or to a failure to reach an effective concentration in the tissues in which the parasites are located. The results in the present paper are more critical than some previously published results because they use parasitemia in the mice instead of mortality rate of the mice (10) as a criterion and deal with a highly virulent strain of trypanosomes in a genetically pure strain of mice. They indicate that, as compared to other drugs, primaquine is more effective suppressively on early stages.

Conclusions. Primaquine showed a strong suppressive action during the early stages of experimental *T. cruzi* infection in mice. Most treated animals survived infection with a virulent strain and all showed a disappearance or marked decrease in the number of parasites present in the blood. The activity of the drug seems to be stronger than other drugs so far known to be effective against *T. cruzi* infections.

4. Pizzi, T., Agosin, M., Christen, R., Hoecker, G., and Neghme, A., *Bol. Inf. Parasit. Chilenas*, 1949, v4, 48.

5. Jarpa, A., Christen, R., Agosin, M., and Pizzi, T., *Bol. Inf. Parasit. Chilenas*, 1949, v4, 49.

6. Jarpa, A., Christen, R., Agosin, M., Pizzi, T., and Cortes, G., *Bol. Inf. Parasit. Chilenas*, 1950, v5, 5.

7. Fulton, J. D., *Ann. Trop. Med. and Parasitol.*, 1943, v37, 146.

8. Browning, C. H., Calver, K. M., Leckie, M. W., and Walls, L. P., *Nature*, London, 1946, v157, 263.

9. Goodwin, L. G., Goss, M. D., Lock, J. A. and Walls, L. P., *Brit. J. Pharmacol. and Chemotherap.*, 1950, v5, 277.

10. Goble, F. C., *J. Parasitol.*, 1951, v37, 408.