birds became infected, though the spleen and liver injected birds died from shock too soon for the malarial infection to have developed.

Summary. We have reported here the failure to infect a great horned owl (*Bubo virginianus virginianus*) with the sporozoites of a strain of *Plasmodium cathemerium* of known infectivity and virulence.

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Effect of Ascorbic Acid on Guinea Pig Colon.

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Prompted by clinical reports[1-3] that the administration of ascorbic acid occasionally gives rise to intestinal colic and to an increase in intestinal motility, we have observed the effect of this drug on the isolated guinea pig colon.

Experimental. The colon was removed, and kept in Locke's solution as modified by Sollmann and Rademaekers[4] except that the $NaHCO_3$ was 0.1% to 0.2%, depending upon the pH desired (*vide infra*).

The sections were about 2 cm long and were ligated at each end, with the two knots in line in relation to the circumference of the strip. Recordings were made after the so-called Magnus method in a bath of 50 cc, with the temperature constant at 38° C. Before filling the bath the stock Locke's solution was brought to 38° C, and bubbled with a gas mixture consisting of 95% O_2 and 5% CO_2 to the desired pH as determined with the glass electrode pH meter. The bath was then filled and thereafter bubbled at a constant rate with the gas mixture through a capillary tube. The electrodes were placed in the bath and pH readings were made at frequent intervals. This technic ensured thorough oxygenation, mixing, and a constant pH which could be read at any given moment. Washings from the bath were analyzed for potassium content. These showed no increase in potassium, demonstrating the absence of leakage from the calomel electrode.

1 Anderson, S., personal communication.

2 Schade, H. A., *Klin. Wchnschr.*, 1935, **14**, 60.

3 Widenbauer, F., *Klin. Wchnschr.*, 1936, **15**, 1158.

4 Sollmann, T., and Rademaekers, A., *Arch. Internat. de Pharmacodyn. et de Therap.*, 1926, **31**, 39.

Ascorbic acid* was titrated with NaOH to a pH of about 7.4 (phenol red) and the solution adjusted so that the volume of the test dose was always 0.5 cc. After a normal tracing had been obtained for about 15 minutes, the freshly prepared solution was slowly added to the bath. Between different tests on the same strip the bath was usually renewed once or twice. The preparation remained uninjured with the concentrations of ascorbic acid (up to 10 mg%) used, and on return to normal was again responsive to the drug.

Twenty-three experiments were performed on 11 guinea pigs. In 7 of these the Locke's solution contained 0.2% $NaHCO_3$ and the pH of the bath among individual experiments varied from 7.78 to 7.83. In the other 16 the bicarbonate content was from 0.10% to 0.12% and the pH of the bath was from 7.37 to 7.53. With care individual experiments could be run for 2 hours or more with the pH constant to 0.03 of a pH, the readings being taken every 3 to 5 minutes. In no case did the addition of the sodium salt of ascorbic acid change the pH of the bath. Although the guinea pig ileum has been said to be particularly sensitive to pH changes,[5] this is apparently not true of the colon since we have often noticed that a change of as much as 0.1 pH had no effect on the normal contractions.

Results and Comments. The results of these experiments, a typical

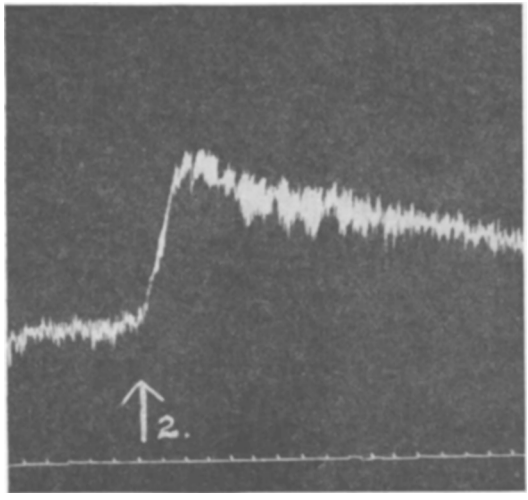

FIG. 1.

Showing the effect of ascorbic acid, 10 mg% (↑2), on the isolated guinea pig colon. Time 1 minute.

* "Cebione"—purchased from Merck & Co.

5 Code, C. F., *J. Physiol.*, 1937, **89**, 257.

tracing from which is given in Fig. 1, show that:

1. The tone of the excised guinea pig colon was greatly increased by the addition of the sodium salt of ascorbic acid to the constantly oxygenated Locke's bath.

2. This effect was obtained with reagent quality chemicals and Pyrex redistilled water with or without the addition of a trace of copper. Such addition of copper (.1-4.0 micro-mols per liter of copper ion, as chloride) was suggested by Peugnet[6] for obtaining positive results with ascorbic acid on the isolated frog heart.

3. The effect has been obtained uniformly at pH values ranging from 7.37 to 7.83. Observations at other pH figures were not made.

4. The increase in tone began in from 1 to 2 minutes and reached its maximum in from 2 to 5 minutes. Thereafter the tone gradually decreased until it reached normal.

5. The test concentration used in most cases was 10 mg% ascorbic acid. The threshold concentration (6 strips from 4 guinea pigs) was from 1 to 5 mg%. These latter figures approach those reported for human blood plasma.[7, 8]

Similar studies, but with less consistent and less striking results were made on the isolated jejunum of the guinea pig and rabbit. Kreitmair[9] obtained no effect on the rabbit intestine (small) with a concentration of ascorbic acid of 1-100,000; on a similar preparation Supniewski and Hano[10] obtained positive results with a concentration of 1-10,000 and on the intestines of the anesthetized cat following the intravenous injection of 100 mg (per kg?) of the chemical. Nishimura[11] briefly reported somewhat equivocal results on the isolated rabbit intestine.

Summary. Ascorbic acid, in the concentrations studied (up to 10 mg%), markedly increased the tone of the isolated guinea pig colon. This experimental observation is in keeping with the clinical impression that ascorbic acid administration may occasionally produce colicky pains of intestinal origin.

6 Peugnet, H. S., *Science,* 1939, **90**, (2329) 162.

7 Stephens, D. J., and Hawley, E. E., *J. Biol. Chem.*, 1936, **115**, 653.

8 Abt, A. F., Farmer, C. J., and Epstein, I. M., *J. Ped.*, 1936, **8**, 1.

9 Kreitmair, H., *Arch. f. exp. Path. u. Pharm.*, 1934, **176**, 326.

10 Supniewski, J. V., and Hano, J., *Arch. f. exp. Path. u. Pharm.*, 1935, **178**, 508.

11 Nishimura T., *Mitt. u. d. Med. Akad. zu Kioto,* 1937, **21**, 423.