

as in the nerve fibre. Evidently at intervals at which the soma of the motoneurons has subnormal excitability for synaptic stimuli, it has normal and even possibly supernormal excitability for induction shocks.

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Use of Liver Extract Intramuscularly in the Course of Acute Amebiasis in Dogs.*

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Previous communications from this laboratory^{1, 2, 3} have demonstrated the amebostatic and possibly amebicidal properties of whole raw liver and of powdered liver extract administered orally to dogs which had been experimentally infected with human strains of *Endamoeba histolytica*. The present investigation deals with dogs, similarly infected and suffering from acute amebic enteritis, treated with liver extract intramuscularly. In 6 such animals a commercial product, generously furnished us by Parke, Davis and Co., was used; in a parallel series of 8 dogs we prepared our own sterile fresh liver extract. In both series 1 cc. of the extract represented 5 gm. of fresh pig's liver. Alternately 2 cc. of the extract was injected respectively into the right and left gluteus muscles. The results of the investigation, together with the clinical history of the animals and brief autopsy reports, are presented in the following protocols. In all cases the same human strain of the organism, previously passed through several dogs, was utilized. We are indebted to Col. Chas. F. Craig for certain complement fixation tests on these dogs.

Dog 211

Nov. 2, 1934 Inoculated intracecally with trophozoites (T) of *E. histolytica* obtained from dysenteric exudate of dog 210; animal healthy, about one year old.

" 5 *E. histolytica* T+ first recovered by intracecal aspiration; stool diarrheic.

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¹ Kagy, E. S., and Faust, E. C., *Proc. Soc. Exp. Biol. and Med.*, 1930, **28**, 252.

² Faust, E. C., and Kagy, E. S., *Am. J. Trop. Med.*, 1934, **14**, 235.

³ Faust, E. C., Scott, L. C., and Swartzwelder, J. C., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 540.

- " 7-10 Stools semi-dysenteric; *E. histolytica* T+++; r.b.c., (Nov. 8) 4,765,000, (Nov. 10) 4,480,000; Hb % (Tallqvist), 70.
 " 12 Infection acute; marked tenesmus; stools dysenteric; animal losing weight; r.b.c., 4,325,000; given *liver extract* (2 cc.) intramuscularly.
 " 14 *Liver extract* (2 cc.); dehydration and emaciation marked; r.b.c., 4,515,000; Hb %, 55.
 " 16 *Liver extract* (2 cc.); infection fulminating; animal eats well but passes copious dysenteric stools; r.b.c., 3,310,000; Hb %, 50.
 " 18 *Liver extract* (2 cc.); infection still fulminating; *E. histolytica* T+-.
 " 19-20 Condition becoming grave; *E. histolytica* T++++; r.b.c., (Nov. 20), 1,780,000; Hb %, 45.
 " 21 Animal sacrificed; extremely emaciated and dehydrated; organs essentially normal except large bowel, which was riddled with many deep craterous amebic lesions, containing myriads of active *E. histolytica*.
- Dog 212
 Nov. 3, 1934 Inoculated intracecally with trophozoites (T) of *E. histolytica*, obtained from dysenteric exudate of dog 210; animal about one year old, in excellent condition.
 " 6 First found positive (*E. histolytica* trophozoites in flecks of bloody mucus in stool).
 " 9 Stools dysenteric; *E. histolytica* T+++; tenesmus; animal losing weight; r.b.c., 5,905,000; Hb % (Tallqvist), 60.
 " 10 Condition the same; r.b.c., 6,125,000.
 " 12 Marked tenesmus; infection acute; *liver extract* (2 cc.) intramuscularly.
 " 13 Condition the same, r.b.c., 6,525,000.
 " 14 *Liver extract* (2 cc.); losing weight; marked tenesmus and slight anorexia.
 " 15 Animal becoming dehydrated; stool dysenteric, with many *E. histolytica* T; r.b.c., 6,930,000.
 " 16 *Liver extract* (2 cc.); condition acute.
 " 17 Animal becoming emaciated; marked tenesmus; stool bloody, diarrheic; *E. histolytica* T++++; r.b.c., 6,690,000.
 " 18 *Liver extract* (2 cc.); rapidly losing weight; stool dysenteric.
 " 19 Condition unchanged; r.b.c., 6,625,000.
 " 21 *Liver extract* (2 cc.); condition unchanged.
 " 22 r.b.c., 6,340,000; Hb %, 80.
 " 24 *Liver extract* (2 cc.); condition unchanged.
 " 25 Animal weak, inactive; condition acute; r.b.c., 6,025,000.
 " 26 *Liver extract* (2 cc.); stool dysenteric; *E. histolytica* T+++; r.b.c., 6,130,000.
 " 30 Infection continues to fulminate; r.b.c., 5,850,000.
- Dec. 3 Animal gravely ill; sacrificed; autopsy showed extreme emaciation; food undigested; all organs negative except large bowel, which was riddled with typical amebic lesions, containing myriads of active *E. histolytica*.
- Dog 213
 Nov. 5, 1934 Inoculated similarly from dog 210; animal fat and active, about one year old.
 " 8 *E. histolytica* trophozoites (T) first found in flecks of blood in stool; r.b.c., 4,935,000; Hb % (Tallqvist), 60.
 " 9 Stool semi-formed to diarrheic, with flecks of blood and mucus; *E. histolytica* T+; slight tenesmus.
 " 10 Stool semi-dysenteric; *E. histolytica* T+++; r.b.c., 4,730,000.
 " 12 *Liver extract* (2 cc.) intramuscularly; r.b.c., 4,985,000.
 " 13 Infection acute; r.b.c., 5,165,000.
 " 14 *Liver extract* (2 cc.); condition unchanged; tenesmus; animal losing weight.

- " 15 r.b.c., 5,340,000.
 " 16 *Liver extract* (2 cc.); tenesmus and marked anorexia.
 " 17 r.b.c., 4,750,000.
 " 18 Condition fulminating; colon and rectum very hemorrhagic.
 " 19 *Liver extract* (2 cc.); r.b.c. 4,405,000; marked loss of weight.
 " 20 Animal refuses food; weak and inactive; r.b.c., 4,310,000.
 " 21 *Liver extract* (2 cc.); condition unchanged; complement fixation +++++.
 " 23 *Liver extract* (2 cc.); lower bowel profusely hemorrhagic; *E. histolytica* T++++.
 " 25 Animal rapidly growing worse, with blood freely flowing from rectum; r.b.c., 4,115,000; Hb %, 50.
 " 26 *Liver extract* (2 cc.); animal in grave condition.
 " 27 Animal *in extremis*, sacrificed; autopsy showed some emaciation; organs essentially negative, except large bowel, which showed numerous deep amebic ulcers in cecum, lower colon and rectum, but especially in appendix, which was almost perforated.
- Dog 220
 Nov. 24, 1934 Inoculated intracecally with *E. histolytica* trophozoites (T) from dog 213; dog active, healthy, about one year old.
 " 28 First positive by intracecal examination; *E. histolytica* T+ in bloody mucus.
 " 30 Bloody mucus in stool with trophozoites ++.
 Dec. 2 Marked tenesmus; animal eating well but losing weight.
 " 4 Condition becoming acute.
 " 5-8 No change in animal's condition.
 " 10 Animal becoming emaciated and dehydrated; tenesmus; *E. histolytica* T+++ in stool consisting mostly of dysenteric discharges.
 " 11-16 No change in animal's condition.
 " 18 *E. histolytica* T++ in bloody exudate; r.b.c., 4,265,000; Hb % (Tallqvist), 80.
 " 20 *E. histolytica* T+++; *liver extract* (2 cc.) intramuscularly; r.b.c., 4,115,000.
 " 23 r.b.c., 4,595,000; Hb %, 70.
 " 24 Infection acute; *liver extract* (2 cc.); r.b.c., 4,050,000; Hb %, 70.
 " 26 *Liver extract* (2 cc.).
 " 28 r.b.c., 4,445,000; Hb %, 60.
 " 29 *Liver extract* (2 cc.); r.b.c., 4,685,000; Hb %, 70.
 " 31 *Liver extract* (2 cc.); animal losing weight; tenesmus and anorexia; dysenteric stools numerous; r.b.c., 4,620,000; Hb %, 70.
- Jan. 2, 1935 Condition of animal acute but not fulminating; *liver extract* (2 cc.).
 " 3 Condition fulminating; r.b.c., 4,520,000; Hb %, 70.
 " 5 No change in condition.
 " 7 Animal sacrificed; complement fixation ++; at autopsy no essential pathology of organs except in large bowel in which appendix, mid-colon and rectum contained many relatively shallow amebic lesions, filled with active trophozoites.
- Dog 222
 Nov. 27, 1934 Inoculated intracecally with trophozoites (T) of *E. histolytica* obtained from dog 217; animal healthy, about 1 year old.
 " 30 First positive by intracecal tube; *E. histolytica* T+ in flecks of bloody mucus.
 Dec. 1-4 Infection becoming acute; animal fed 100 gm. chopped raw liver to control infection.
 " 5 Animal refuses regular food; given 200 gm. raw liver.
 " 7-9 Animal noticeably improved on raw liver by mouth.
 " 10-11 Animal given tinned salmon to exacerbate infection.
 " 12-19 Animal on regular diet; infection again acute; r.b.c., 6,645,000; Hb %, 80.

" 20	<i>Liver extract</i> (2 cc.) intramuscularly; condition still acute; r.b.c., 6,700,000; Hb %, 75.
" 22	<i>Liver extract</i> (2 cc.)
" 23	Many dysenteric stools a day; r.b.c., 6,745,000; Hb %, 75.
" 24	<i>Liver extract</i> (2 cc.)
" 26	<i>Liver extract</i> (2 cc.); animal losing weight; marked tenesmus; many dysenteric stools daily.
" 28	Condition unchanged; r.b.c., 6,350,000.
" 29	<i>Liver extract</i> (2 cc.); animal weak and inactive.
" 31	<i>Liver extract</i> (2 cc.); infection fulminating.
Jan. 2, 1935	<i>Liver extract</i> (2 cc.); r.b.c., 6,320,000; Hb %, 80; animal acutely ill.
" 3	r.b.c., 6,225,000; Hb %, 80.
" 5	r.b.c., 6,310,000; Hb %, 70.
" 7-9	Animal critically ill.
" 11	Animal sacrificed; complement fixation +++++; extremely emaciated; no pathology except in large bowel, which showed amebic invasion of entire length; lesions only moderately deep; myriads of active amebæ.
Dog 223	
Nov. 28, 1934	Inoculated intracecally with trophozoites of <i>E. histolytica</i> (T) from dog 217; animal healthy, about one year old.
Dec. 1	First positive by intracecal aspiration; <i>E. histolytica</i> T++ in flecks of blood and mucus.
" 3	Infection becoming acute.
" 4-5	Stool dysenteric; marked tenesmus; dog refusing regular food; becoming dehydrated and inactive.
" 6-11	Animal acutely ill with amebic dysentery.
" 12	Placed on diet of raw liver (100 gm. daily) by mouth to control infection.
" 17	Animal returned to regular diet after marked improvement in condition.
" 18	Infection exacerbating; marked tenesmus; some loss in weight; r.b.c., 4,700,000; Hb %, 65.
" 19	Condition subacute; r.b.c., 4,625,000; Hb %, 60.
" 20	Condition more acute; stools more dysenteric; <i>liver extract</i> (2 cc.) intramuscularly.
" 21	Condition unchanged; r.b.c., 4,730,000; Hb %, 60.
" 22	Dysentery still severe; <i>liver extract</i> (2 cc.).
" 24	Animal eating well but losing weight; stools dysenteric with many active amebæ; r.b.c., 4,600,000; Hb %, 50; <i>liver extract</i> (2 cc.).
" 26	Many dysenteric stools daily; dog losing weight and becoming inactive again; r.b.c., 4,715,000; Hb %, 60; <i>liver extract</i> (2 cc.).
" 28	Condition unchanged; r.b.c., 4,465,000; Hb %, 60.
" 29	Dysenteric condition fulminating; r.b.c., 4,235,000; Hb %, 60; <i>liver extract</i> (2 cc.).
" 31	Condition acute; marked tenesmus; r.b.c., 4,110,000; Hb %, 60; <i>liver extract</i> (2 cc.).
Jan. 2, 1935	Loss in weight appreciable; animal weak and inactive; r.b.c., 4,310,000.
" 5	No change in condition; r.b.c., 4,180,000; Hb %, 60.
" 11	Animal sacrificed; complement fixation +++++; some emaciation and dehydration; autopsy showed no essential lesions except in large bowel, which contained many moderately deep amebic lesions with numerous active <i>E. histolytica</i> .

Similarly a series of 8 dogs (224, 226, 227, 228, 229, 231, 233, 235) was inoculated with the same strain of *E. histolytica* by the intracecal method. All became positive; when the infection became

acute they were treated intramuscularly from time to time (at 2 to 3 day intervals) with 3 cc. freshly prepared sterile raw liver extract (expressed from chopped liver, passed through a Seitz filter and preserved aseptically, all at room temperature). While these animals showed some individual variations in their resistance to the amebic infection and while the quantity and quality of the erythrocytes was maintained at a significantly high level by the liver extract, there was no apparent control of the infection.

In all members of these 2 series, with the exception of dog 211, to which probably an inadequate amount of liver extract was administered, there was a remarkably high erythrocyte count and fair hemoglobin percentage in spite of the constant loss of blood due to profuse hemorrhage from the large bowel. In practically every animal the erythrocyte count increased after liver extract therapeutics. It may be argued that dehydration of these animals provides an adequate explanation for the high erythrocyte count, yet in other dogs similarly infected by us but without liver therapy this has not proved to be the case (*i. e.*, the erythrocyte count was rapidly decreased). Furthermore, the exudate from the bowel was bloody and not watery as in uncontrolled diarrhea. In spite of the blood picture we have consistent evidence that liver extract introduced intramuscularly failed to control the amebic infection, except perhaps in so far as general body resistance was possibly maintained somewhat longer by the product. These results stand in marked contrast to those obtained by us in oral administration of raw liver, which definitely controlled the infection (as, for example, in dogs 222 and 223, in which liver by mouth prevented the infection from "getting out of hand"). We may conclude, therefore, that the fraction of raw liver which is efficacious as an amebostatic agent, is either different from that which prevents erythropoiesis, or that its amebostatic action is inhibited when it is introduced intramuscularly.