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SOME MODERN CONCEPTIONS OF AMEBIASIS[1]

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INTRODUCTION

IN 1875 a Russian physician, F. Lösch, first observed and described the active stage of *Endamoeba histolytica* in the dysenteric stools of a patient, and at necropsy found motile amebae in material obtained from ulcers of the colon. Moreover, he succeeded in infecting one of four dogs inoculated with amebae present in the bloody-mucous exudate of the patient. Yet Lösch failed to appreciate the role which his "Amoeba coli" played in the disease with which it was associated. The studies of Koch[2] and of Kartulis[3a,b] in Egypt, of Hlava[4] in Prague, of Osler,[5] Stengel,[6] Musser[7] and Dock[8] in the United States provided uncontestable evidence that the ameba discharged in dysenteric stools was causally related to amebic colitis, while Quincke and Roos,[9] Huber[10] and Schaudinn[11] demonstrated a cystic stage of the parasite. Meanwhile Councilman and Lafleur[12] had provided a basic pathological study of amebiasis and in 1913 Walker and Sellards demonstrated experimentally in human volunteers in the Philippines that the disease was produced by feeding cysts of *Endamoeba histolytica,* while infection without disease resulted from feeding cysts of *Endamoeba coli.* By 1924

[1] Alvarenga Prize Lecture of the College of Physicians of Philadelphia, delivered on October 13, 1943.

[2] R. Koch, *Wien. Med. Wochenschr.,* 33: 1248–1252; 1548–1551, 1883.

[3a] S. Kartulis, *Arch. f. path. Anat.,* 105: 521–531, 1886; b. *Centralbl. f. Bakt. u. Parasitenkde.,* 2: 745–748, 1887.

[4] O. Hlava, *Zeitschr. d. böhm. Aerzte in Prag.,* 1887.

[5] Wm. Osler, *Johns Hopkins Hosp. Reports,* 1: 53–54, 1890.

[6] A. Stengel, *Med. News, Phila.,* 57: 500–503, 1890.

[7] J. H. Musser, *Univ. Med. Mag.,* Phila. 9 pp., 1890.

[8] G. Dock, *Med. Record,* N. Y., 40: 7–8, 1891.

[9] H. Quincke and E. Roos, *Berlin klin. Wochenschr.,* 30: 1089–1094, 1893.

[10] J. C. Huber, *Deutsch. Med. Wochenschr.,* 29 (Beih.): 267, 1903.

[11] F. Schaudinn, *Arb. aus d. kaiserl. Gesundh.-Amte,* 19: 547–576, 1903.

[12] W. T. Councilman and H. A. Lafleur, *Johns Hopkins Hosp. Reports,* 2: 395–548, 1891.

Boeck and Drbohlav[13] had perfected a technique for the *in vitro* cultivation of *E. histolytica* and by 1927 Craig[14] had demonstrated specific complement-fixing properties of *E. histolytica* antigen.

During this period of approximately fifty years the ideas that amebiasis was strictly or primarily a tropical disease and usually manifested itself as a fulminating dysentery or a liver abscess became gradually modified. Little by little, as epidemiologic studies were carried out, the discovery was made that amebiasis is practically cosmopolitan in its distribution, although as a rule its incidence is higher and its clinical expressions are more severe in the Tropics than in cooler climates. Dysentery and liver abscess were found to be only two of its more dramatic manifestations. There might be a history of an acute or subacute appendicitis or of general colonic distress without dysentery or even without diarrhea. There might be no apparent intestinal disturbance but a mild toxic state, with moderate leukocytosis and a low-grade fever. The patient might be considered symptomless by the uncritical diagnostician and yet at necropsy extensive amebic ulceration of the colon might be demonstrated. Throughout this period both by direct and indirect methods there developed increasing evidence that *Endamoeba histolytica* is always actually or potentially a pathogen and that it is capable of invading and destroying the host's tissue without the aid of pathogenic bacteria.

Hosts of Endamoeba histolytica

In addition to man the following hosts have been described as infected in nature or susceptible of experimental infection with *Endamoeba histolytica*—dogs, cats, monkeys, rats, pigs, guinea-pigs and rabbits.

Darling,[15] Ware,[16] Fischer,[17] Bausche and Motais,[18] Faust[19, 20] and Boyd[21] have described spontaneous amebiasis in dogs either in isolated instances or in epidemics among small groups of dogs. Lösch,[22] Hlava,[4] Harris,[23] Dale and Dobell,[24] Andrews,[29] Faust,[19, 20, 25, 26, 27, 28] Swartzwelder[30] and Tobie[31] have demonstrated the infectibility of dogs with trophozoites or cysts of human strains of *E. histolytica*. On the basis of previously published data and extensive personal observations Faust[26] concluded that dogs usually obtain their infection from man but do not constitute a normal source of exposure for human beings. The lesions in the dog may be few and superficial or extensive and deep-seated. The symptoms may be acute or chronic or spontaneous recovery may result after a short period of colonization by the amebae in the bowel wall. Occasionally liver abscess may develop following invasion of the intestine.

Many workers have infected kittens with human strains of *E. histolytica*. Among the more important investigators have been Marchoux,[32] Craig,[33] Wenyon,[34] Baetjer and Sellards,[35] Dale and Dobell,[24] Kessel,[36] Rees,[37] Meleney and Frye[38] and Deschiens.[39] Kittens develop a fulminating, frequently fatal amebic dysentery and are therefore excellent for acute experiments. There appear to be no records of their infection in nature.

Many species of Old and New World monkeys are naturally infected with strains of *Endamoeba histolytica* indistinguishable from those occurring in man. The incidence of natural infection in these animals is usually high, while experimentally induced infection with simian or human strains is easily accomplished. Although amebic invasion of the monkey's large bowel has been demonstrated[40] the parasite usually lives in relative equilibrium with its simian host so that acute symptoms seldom develop.

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[13] W. C. Boeck and J. Drbohlav, *Am. Jour. Hygiene*, 5: 371–407, 1925.

[14] C. F. Craig, *Am. Jour. Trop. Med.*, 7: 225–240, 1927.

[15] S. T. Darling, *Proc. Canal Zone Med. Assn.*, 6: 60–62, 1915.

[16] F. Ware, *Jour. Comp. Path. and Therap.*, 19: 126–130, 1916.

[17] W. Fischer, *China Med. Jour.*, 32: 13–20, 1918.

[18] J. Bausche and F. Motais, *Bull. Soc. Path. Exot.*, 13: 161–165, 1920.

[19] E. C. Faust, *Proc. Soc. Exp. Biol. and Med.*, 27: 908–911, 1930.

[20] E. C. Faust, *Porto Rico Jour. Pub. Health and Trop. Med.*, 6: 391–400, 1931.

[21] J. S. K. Boyd, *Jour. R. Army Med. Corps*, 56: 1–13, 1931.

[22] F. Lösch, *Arch. of path. Anat.*, 65: 196–211, 1875.

[23] H. F. Harris, "On the Alterations Produced in the Large Intestine of Dogs by the *Amoeba coli*, by Heat and by Various Chemic Substances. Phila. 143 pp., 1901.

[24] H. H. Dale and C. Dobell, *Jour. Pharmacol. and Exp. Therap.*, 10: 399–459, 1917.

[25] E. C. Faust, *Am. Jour. Trop. Med.*, 11: 231–237, 1931.

[26] E. C. Faust, *Proc. Soc. Exp. Biol. and Med.*, 29: 659–661, 1932.

[27] E. C. Faust, *Jour. Pediat.*, 2: 53–58, 1933.

[28a] E. C. Faust and E. S. Kagy, *Am. Jour. Trop. Med.*, 14: 221–233, 1934; b. 14: 235–255, 1934.

[29] J. Andrews, *Am. Jour. Trop. Med.*, 12: 401–404, 1932.

[30] J. C. Swartzwelder, *U. S. Pub. Health Reports*, 52: 1447–1451, 1937.

[31] J. E. Tobie, *Proc. Soc. Exp. Biol. and Med.*, 45: 691–693, 1940.

[32] E. Marchoux, *Compt. Rend. Soc. biol. Paris*, 51: 870–871, 1899.

[33] C. F. Craig, *Am. Med.*, Phila., 9: 854–861; 897–903; 936–942, 1905.

[34] C. M. Wenyon, *Jour. London School Trop. Med.*, 2: 27–, 1912.

[35] W. A. Baetjer and A. T. Sellards, *Johns Hopkins Hosp. Reports*, 25: 234–241, 1914.

[36] J. F. Kessel, *Am. Jour. Hyg.*, 8: 311–355, 1928.

[37] C. W. Rees, *Arch. Path.*, 7: 1–26, 1929.

[38a] H. E. Meleney and W. W. Frye, *Am. Jour. Hyg.*, 17: 637–656, 1933; b. 25: 313–327, 1937.

[39] R. E. A. Deschiens, *Compt. Rend. Soc. biol. Paris*, 127: 939–941, 1938.

Pigs, guinea-pigs, rabbits and rats are probably incidental hosts of *Endamoeba histolytica* and in nature apparently play no important role as reservoirs of the infection.

SOURCES AND METHODS OF EXPOSURE TO INFECTION

On the basis of information concerning amebic infection in hosts other than man it must be concluded that man is primarily, in fact, almost exclusively responsible for his own infection. Although it has been demonstrated experimentally[22, 30] that infection in dogs can be accomplished by feeding the trophozoites in a bloody-mucous menstruum, it is hardly conceivable that this stage serves as a source of human infection. On the other hand, there is a wealth of records of infection in susceptible experimental animals, which, with the critical experiments of Walker and Sellards[41] on human volunteers, demonstrates that cysts constitute a ready source of infection, and that the method of their entry into the body is by the oral route.

In what way or ways do cysts of *Endamoeba histolytica,* discharged from the bowels of infected individuals, reach the human mouth? The most common hypotheses predicate water, food, flies and contact contamination. While each of these hypotheses fits well into the epidemiology of amebiasis, there is a paucity of direct proof for any one of them.

The *water hypothesis* is supported by circumstantial evidence, and hence indirect proof, in the case of the hyperendemicity of amebic dysentery in Manila and the Panama Canal Zone in the early days of American occupation, together with a marked diminution in the incidence and the intensity of the disease soon after the installation of sanitary water and sewerage systems in these localities. Moreover, the report of specialists in the 1933 Chicago hotel outbreak of amebic dysentery (Bundesen *et al.*)[41] concluded that drinking water contaminated by cross-connections with sewage pipes was responsible for the epidemic. One member of the investigating committee, the late Dr. F. W. O'Connor, lived in the hotel for one month, drank water from the faucet in his room and acquired amebic dysentery with amebic liver abscess. Although these are very important epidemiologic data, the fact remains that in none of these instances were cysts of *Endamoeba histolytica* reported to have been actually isolated from the contaminated water. Again, it is also plausible, but not confirmed, that shallow wells in rural areas may serve as a source of infection for the amebiasis which is widely disseminated throughout the Southeastern United States.

The *food hypothesis* is accepted by many epidemiologists as the most satisfactory explanation for the extensive distribution of amebiasis. In Oriental countries where truck crops and small fruits are fertilized with human nightsoil, it is conceivable that infection may be acquired from eating raw lettuce, celery, radishes and strawberries, provided fermentation of the nightsoil or desiccation of the cysts does not kill the cysts. A more likely contamination of food is that due to food handlers. Milam and Meleney[42] found a correlation between *E. histolytica*-infected mothers in rural Tennessee and familial amebiasis. Schoenleber[43] found that anti-amebic treatment of *E. histolytica*-positive food handlers on the island of Aruba, off the coast of Venezuela, reduced both the incidence rate of amebiasis and the amebic colitis rate 92 per cent. in three years. Surveys on food handlers in Chicago,[44] in San Francisco[45] and in Philadelphia,[46] have demonstrated a higher incidence of amebiasis in this group than in the population at large, but Sapiro and Johnson[47] found no evidence in navy personnel that food handlers constituted any particular hazard in the dissemination of the infection.

The *fly hypothesis* has not been given as great emphasis as the two views previously considered. In city populations essentially free of the dangers of filth flies this hypothesis obviously is not tenable, but in rural areas and throughout the Tropics and the Orient there is circumstantial evidence that flies may play the essential role in the rapid dissemination of the disease. Craig[48] attributed an epidemic of amebic dysentery in an Army post at El Paso, Texas, to flies. The writer made a similar observation in a foreign hill station in China during the summer of 1921. Moreover, amebiasis is particularly prevalent in fly-infested regions from Morocco to Peking. Thomson and Thomson,[49] Wenyon and O'Connor,[50] Roubaud,[51] Root[52] and Pipkin[53] have demonstrated viable cysts of *E.*

[40] C. M. Johnson, *Am. Jour. Trop. Med.,* 21: 49–58, 1941.

[41] E. L. Walker and A. T. Sellards, *Philip. Jour. Sci. (B),* 8: 253–331, 1913. H. N. Bundesen, J. I. Connolly, I. D. Rawlings, A. E. Gorman, G. W. McCoy and H. V. Hardy, *Nat. Inst. Health Bull.* No. 166, pp. 187, Washington, D. C., 1936.

[42] D. F. Milam and H. E. Meleney, *Am. Jour. Hyg.,* 14: 325–336, 1931.

[43] A. W. Schoenleber, *Jour. Trop. Med. and Hyg.,* 44: 41–43, 1941.

[44] M. Hood, *Am. Jour. Trop. Med.,* 23: 327–332, 1943.

[45] H. G. Johnstone and M. K. Iverson, *Am. Jour. Trop. Med.,* 15: 197–209, 1935.

[46] D. H. Wenrich, R. M. Stabler and J. H. Arnett, *Am. Jour. Trop. Med.,* 15: 331–345, 1935.

[47] J. J. Sapiro and C. M. Johnson, *Am. Jour. Trop. Med.,* 19: 255–265, 1939.

[48] C. F. Craig, *Mil. Surgeon,* 40: 286–302, 1917.

[49] D. Thomson and J. D. Thomson, *Jour. R. Army Med. Corps,* 27: 1–31, 1916.

[50] C. M. Wenyon and F. W. O'Connor, "Human Intestinal Protozoa in the Near East." London. 218 pp., 1917.

[51] E. Roubaud, *Bull. Soc. Path. Exot.,* 11: 116–171, 1918.

[52] F. M. Root, *Am. Jour. Hyg.,* 1: 131–153, 1921.

histolytica in both the gut and dejecta of flies after experimental feedings, while Frye and Meleney[54] found that flies caught in four of twelve dwellings which housed human cyst passers contained viable cysts of *E. histolytica.*

The *direct contact hypothesis* is probably applicable to a wide range of unsanitary situations in warm moist climates but in cooler climates may also apply, particularly to institutional groups, as children's asylums, mental hospitals and prisons. Outbreaks of amebic dysentery in prisons are much more frequent than the medical literature indicates. Mental hospitals have been found to be particularly afflicted with amebiasis from Panama[55] to Sweden,[56] and the infection has been found in children's homes from New Orleans to Saskatoon.[57] In New Orleans several children's homes and one infant asylum have been studied by the Department of Tropical Medicine of Tulane University since 1929. In all these institutions the incidence was found to be high, beginning with children slightly over one year of age and increasing rapidly to the period of adolescence (Faust).[27] Epidemiologic studies carried out at the infant asylum[57a] have demonstrated that identifiable cysts of *Endamoeba histolytica* were recoverable from the bottom of the laundry chute, from underpanties washed in tepid water, from play objects, floors and from the bottom of the children's wading pool. Although the place was apparently clean and the water supply was uncontaminated, a careful study of the habits of the children showed that direct contact contamination was prevalent. In certain mental hospitals and prisons the opportunities for gross transfer of amebic cysts from one individual to another are much greater than in the average children's home.

An examination of the evidence concerning the methods of exposure to amebiasis leaves much to be demonstrated. Without being hypercritical the student of scientific medicine will reserve judgment until more direct proof has been presented as to how in each situation amebiasis is actually perpetuated.

PATHOGENESIS

The stage of *Endamoeba histolytica* most likely to produce infection in man is the freshly ripened four-nucleate cyst, which is present in formed stools of infected individuals within a few hours after the stools have been passed. If these cysts gain entry to the mouth and are swallowed, they pass unmodified through the stomach into the small bowel. On arrival in a neutral or slightly alkaline medium of the latter the four-nucleate organism within the cyst wall becomes activated while the wall itself becomes weakened. This characteristically results in the ameba affecting an escape through a little rent in the wall. Thereupon a small amount of cytoplasm becomes associated with each of the four nuclei (or at times a supernumerary division of the nuclei may occur), with the result that four- or eight-minute metacystic trophozoites are formed. These trophozoites now pass down the remaining portion of the ileum, through the ileo-cecal valve and into the large bowel.

Stasis of material *en transit* through the intestine normally first occurs at the level of the cecum. If the metacystic trophozoites come in contact with the cuticula of the intestinal epithelium at this level for only a short time (probably measurable in minutes), they are enabled to establish a little "foothold," which constitutes their *entree* to tissue invasion. At times they may be swept past the cecum into the colon or rectum, where they may become attached, or perchance they may be passed out the anus in feces without having had an opportunity to make tissue contact.

The exact method by which the trophozoites establish themselves in the mucosa of the large bowel has been studied experimentally in dogs,[28] kittens[37, 58] and monkeys,[59] and is parallel in human amebiasis.[60] By lysis a very small cavity is produced in the superficial portion of a principal or gland cell. This may occur with equal likelihood at the tip of an interglandular prominence, part way down the crypt or at the base of the crypt. By continued lytic action, aided at times by mechanical activity of the pseudopodia, the ameba continues its invasion into the cell, utilizing the digested cell substance as food. Following growth, it multiplies by binary fission and thus a small colony becomes established. If these various factors are optimal, the colony may be formed within twenty-four hours or less after initial contact with the surface of the mucosa.

Once entry into the intestinal epithelium has been effected and the colony has started, the direction of tissue penetration and destruction is towards and through the muscularis mucosae. If lodgment was originally secured part way down a crypt, destruction of the superficial portion of the cells continues to the base. If the colony first became established at the base of the crypt, erosion of cells in this area occurs. In neither case do the amebae immediately

[53] A. C. Pipkin, *Proc. Soc. Exp. Biol. and Med.*, 49: 46–48, 1942.
[54] W. W. Frye and H. E. Meleney, *Jour. Parasitol.*, 18: 118, 1931.
[55] S. T. Darling, *Proc. Canal Zone Med. Assn.*, 4: (1), 41–47, 1911.
[56] R. M. Svensson, *Parasitol.*, 20: 237, 1928.
[57] M. J. Miller, *Jour. Parasitol.*, 25: 355–357, 1939.
[57a] G. L. Ivanhoe, *Am. Jour. Trop. Med.*, 23: 401–419, 1943.
[58] K. Hiyeda, *Am. Jour. Hyg.*, 12: 401–423, 1930.
[59] R. Hegner, C. M. Johnson and R. M. Stabler, *Am. Jour. Hyg.*, 15: 394–443, 1932.
[60] W. M. James, *Ann. Trop. Med. and Parasitol.*, 22: 201–225, 1928.

come in contact with intestinal blood capillaries and thus rather extensive destruction may occur in a limited area without hemorrhage. If, on the other hand, the original site of colonization was at the tip of an interglandular prominence, the amebae come in contact with blood capillaries as soon as they penetrate into the tunica propria below the epithelium, so that early hemorrhage results. In the average case the lesion progresses unhindered as a more or less capillary column until it reaches the muscularis mucosae where somewhat more resistant tissue is encountered. This causes a temporary pyramiding of the amebae, but soon some of them break through into the submucosa. There is now a tendency for the amebae to progress radially in this less resistant tissue, frequently gaining entrance into lymphatic capillaries and at times invading mesenteric venules. The usual result is the enlargement of the lesion basally in the submucosa, so that in section it is similar to a bottle with a narrow neck and expanded base. This is the typical uncomplicated amebic lesion.

At times in man, the monkey and the dog the lesion may be confined to the mucosa, in which case tissue destruction may be very superficial and spontaneous evacuation of the colony may occur with healing by growth of simple columnar epithelium.[31] Or repair may keep up with tissue destruction and only shallow microscopic depressions or craters will result.[61] In kittens much more intensive destruction usually occurs.

These uncomplicated amebic lesions are essentially different from those produced by *Shigella dysenteriae*. In primary amebiasis the sites of entry into the bowel wall are typically pinpoint and separated from one another, with a raised annulus surrounding each opening. There is little, if any, hyperemia or inflammation and microscopically there is no infiltration of neutrophiles. In bacillary colitis the surface of the bowel is hyperemic and inflamed and the lesions are confluent, while microscopically there is extensive invasion of neutrophiles. The amebic lesion is typically columnar in the mucosa but is continued into a bulbar base in the submucosa. The lesion of *Shigella* colitis rarely extends below the superficial half of the mucosa.

Once the characteristic bottle type of amebic lesion has been developed it may by extension reach the muscular coats of the bowel and even perforate through the serosa. Amebae which have secured entry into mesenteric venules in the submucosa and muscularis may be carried to the liver, where they may set up multiple small colonies (amebic hepatitis) or one or more large cavernous abscesses. Again, extensive colonization in the submucosa may result in undermining tunnels, with the junction of adjacent colonies and complete loss of arteriolar blood supply for the overlying tissues. Amebae extruded from primary lesions in the upper levels of the large bowel may by regurgitation be carried back to the posterior segment of the ileum or become lodged on the ileo-cecal valve where secondary lesions may develop. Or, perhaps more often, the organisms will pass down the bowel, come in contact with the mucosa at lower levels and there initiate secondary colonies.

In the average host parasitized by *Endamoeba histolytica* the majority of primary lesions occurs in the cecal area, including the cecum, appendix, the distal segment of the ileum and the ascending colon. The other focus of high frequency is the rectal area, including the sigmoid colon and the rectum. Even after numerous secondary lesions have been developed the cecal area still contains a preponderance of the total number of lesions.[61] Except in fulminating acute amebiasis or infections of long-standing the middle segment of the large bowel is only incidentally involved.

Although it has been demonstrated that bacteria are not necessary for successful entry of *Endamoeba histolytica* into the bowel wall,[62, 63] the older amebic ulcers are frequently complicated by bacterial invasion. Moreover, amebic colitis may be superimposed on a pre-existing *Shigella* colitis or *vice versa*.

It will next be useful to inquire into the chances of infection and of tissue invasion by *Endamoeba histolytica*. Infection is contingent on a number of factors which vary considerably under different conditions. First of all is the question of exposure. Qualitatively there must be viable organisms which have an opportunity of gaining entrance to the mouth and of being swallowed. On reaching the small bowel cysts must be capable of excysting. If the medium is too acid or the intestinal juices are too weak or are diluted too much by food in the process of digestion it is altogether likely that excystation will not occur and thus the cysts will pass through the large bowel and be evacuated without providing an opportunity for an infection to become established. Even though excystation occurs, if the number of metacytic trophozoites is scant the chances of their coming in contact with the cuticular surface of the epithelium of the large bowel are very remote, particularly if they are in the midst of a considerable menstruum of partly digested food or feces. Moreover, hypertonicity of the bowel is likely to carry the organisms through the bowel too rapidly for them to make temporary contact with the mucosal surface. Probably human beings in mildly endemic areas are often exposed to a few viable cysts which actually excyst in the ileum

[61] E. C. Faust, *Am. Jour. Trop. Med.*, 21: 35–48, 1941.

[62] E. C. Faust and J. C. Swartzwelder, *Proc. Soc. Exp. Biol. and Med.*, 32: 954–958, 1935.

[63] W. W. Frye and H. E. Meleney, *Am. Jour. Hyg.*, 18: 543–554, 1933.

but never have an opportunity to colonize in the bowel. On the other hand, in areas of hyperendemicity repeated exposure to large numbers of viable cysts provides the appropriate setting for development of heavy infections in a large group of the population.

The virulence of the particular strain of ameba also undoubtedly has considerable influence on initial colonization and continued tissue invasion. There is specific evidence based on experiments with human strains of *Endamoeba histolytica* in cats and dogs[38a, 62, 64] that different strains vary in their pathogenicity, but specific evidence is lacking in support of the view, predicated by Brumpt[65] and other European workers, that certain human strains of *E. histolytica* are nonpathogenic. An additional fact concerning this organism is significant, namely, that its virulence can be considerably enhanced by rapid passage through susceptible hosts.[38b, 62] This last property of the ameba may explain the rapidity with which an epidemic of amebic dysentery develops once heavy initial infection has been provided.

The factors thus far considered concerning opportunities for infection have been extrinsic in character and have not dealt with host susceptibility. Certain animals are undoubtedly completely resistant to infection with *Endamoeba histolytica*. In others, as the rat, there is suggestive evidence that colonization may possibly take place without the necessity of tissue invasion. On the other hand, in man, the monkey, the dog and the cat the evidence preponderates in favor of the view that infection can not be maintained for any length of time without tissue invasion. The kitten is a delicate test animal in amebiasis because it is highly susceptible to infection, the lesions develop rapidly and the infection is frequently fatal in a relatively short time. Monkeys are also readily infected with both human and simian strains of *Endamoeba histolytica,* but dysentery seldom results and typically only cysts are discharged in a semi-formed stool. In many respects the dog constitutes a particularly good laboratory animal for the study of amebiasis. If young dogs are properly conditioned for infection, at least 90 per cent. tissue invasion may be secured.[28, 31] In dogs the period of incubation can be shortened and the intensity of the infection can be increased by rapid passage of the organism from dog to dog.[62]

Thus, in the dog acute dysentery can be produced, comparable to that in the cat or to fulminating amebic dystentery in man. On the other hand, by appropriate technics the infection in the dog can frequently be transformed into a chronic state or at times terminated, even without the administration of specific anti-amebic drugs. Amebiasis in man varies both qualitatively and quantitatively. At times it resembles infection in the kitten; more frequently it simulates the infection in the dog; in the majority of cases, however, it is less severe and is comparable to simian infection.

Probably the most important single intrinsic factor which determines whether amebiasis in the susceptible animal is acute, chronic or relatively asymptomatic is the degree of host resistance based on the nutritional level. In general, carbohydrates provide an opportunity for *Endamoeba histolytica* to multiply, and animal proteins reduce this capacity,[66a, 66b, 67] but the problem is not so easily solved. In conditioning dogs for experimental infection with human strains of *E. histolytica* the writer found[19] that salmon and unfortified white bread provided a suitable low resistance diet for inducing and maintaining amebic infection, but that salmon alone was equally effective. Since these animals developed an anemia, it was important to discover if the cause was lack of the antianemic factor. Ventriculin exascerbated the condition, but fresh raw liver controlled it. Whole raw liver or freshly expressed juice of raw liver produced best results, providing amebostatic and at times amebicidal action.[28b] Moreover, fresh liver was much more effective than desiccated liver, while commercial liver extract or freshly extracted liver juice passed through a Seitz filter, when introduced parenterally, was ineffectual in controlling acute amebiasis, although both preparations stimulated erythropoiesis (Faust and Swartzwelder).[68] The most interesting finding in this series of experiments developed when finely ground-up fresh liver or fresh liver juice was employed as a high retention enema in dogs suffering from acute amebic colitis. The disease was as effectively controlled as when the fresh liver was fed to the animals.[28b]

Vitamins conceivably have a very important role in the control of amebiasis, but in so far as the writer knows this problem has not been subjected to critical experimental or clinical study.

An additional point in the evaluation of amebiasis in man concerns racial or group tolerance to the infection. There is no clear evidence indicating that race or sex is in itself important, but there are good epidemiologic data indicating that long exposure of a particular population group to strains of *Endamoeba histolytica* tends to establish a host-parasite equilib-

64 W. W. Frye and H. E. Meleney, *Am. Jour. Hyg.*, 27: 580–589, 1938.

65 E. Brumpt, *Trans. R. Soc. Trop. Med. and Hyg.*, 22: 101–114, 1928.

66a. R. Hegner and L. Eskridge, *Am. Jour. Hyg.*, 21: 121–134, 1935; b. *Jour. Parasitol.*, 23: 105–106, 1937.

67 D. R. Lincicome, *Am. Jour. Hyg.*, 36: 321–337, 1942.

68 E. C. Faust and J. C. Swartzwelder, *Proc. Soc. Exp. Biol. and Med.*, 33: 514–518, 1936.

rium for the homologous strains of the parasite. In such groups of human beings, even with constant exposure due to primitive sanitary conditions and a correspondingly high rate of infection with a heavy "load" of parasites, clinical manifestations are uncommon.[20, 38a, 69] Nevertheless, individuals from outside the hyperendemic areas who are exposed to the same strains of *Endamoeba histolytica* not uncommonly develop a fulminating amebic colitis. It appears, therefore, that long-time constant exposure to amebiasis tends to produce considerable tolerance to the amebae, with consequent reduction in invasion and in destruction of tissue.

(To be concluded)

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

ANTON JULIUS CARLSON

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Time magazine, in its February 10, 1941, issue, placed the picture of Anton Julius Carlson on its cover and in the story called him "a Scientist's scientist." By popular vote of its 25,000 scientist members and by action of its council, the American Association for the Advancement of Science seems to have proven *Time's* assertion; for they have elected Dr. Carlson president of the association for 1944. Yet perhaps the designation is too narrow; Carlson is really the common man's scientist.

Few scientists of any period have been known so widely to the laity or have carried so variegated a load of civic, humanitarian and similar extra-curricular responsibilities. From the time of the last war, Carlson has progressively emerged from the confines of the laboratory to give freely of his time and effort and enthusiasm to serve the broad interests of science and education and to promote the intelligent application of these to human affairs. His skill as writer and speaker, his joy in a rough-and-tumble argument and his high scientific standing have placed him in great demand as lecturer, editor, adviser, legal expert, organizer, executive and plain fighter on "our" side—witness the joy of faculties all over the country when he, as president of the American Association of University Professors, was battling for them in "the den of deans."

Carlson's early boyhood was spent on the Swedish countryside. According to his own reminiscences, most of his time was devoted to herding goats. Surely the earthiness of the farmer was worn deeply into him: for to-day, after half a century in urban American life, there is little veneer over his directness of manner or simplicity of manners; just as he still says when excited, "It gives me the yim yams." Then followed a period as carpenter's apprentice in Chicago, which led to a denominational education at Augustana College and his placement as a minister in Montana. This phase also left its imprint, for Carlson's effectiveness as a teacher and protagonist is due as much to the evangelical zeal and revivalist's skill with which he presents his case as it is to the hard-headedness and logic of what he says.

Next came his long and passionate affair with science. It was love at first sight (of the writings of Jacques Loeb) and a stormy wooing and wedding. His first researches, one proving the neurogenic origin of the heart beat in Limulus and one showing a parallelism between the speed of action of a nerve and of the muscle it controls, were classics and soon brought him fame and his long-held position at the University of Chicago. Here, from 1904 to his retirement three years ago, he was first a member and then chairman of the department of physiology, teacher of a generation of scientists, a power on the campus and in national societies and an indefatigable worker. Here he, and his loyal colleague, Arno B. Luckhardt, performed studies on the stomach and hunger, on the whole digestive system, on the endocrines, on diet, on the lung, on all parts of the body.

Here he began his lecture schedule at seven in the morning and taught his daily way through classroom and laboratory until the mental scalps of his students were piled deep. He pulled no punches in his comments on their performance, and he was feared. But the kind heart below the rough tongue was also evident, and he was loved and followed.

World War I took Dr. Carlson (ending as Lieutenant-Colonel) to Europe and finally into Hoover's food rehabilitation group. The contact with starvation and other health problems, as well as the many intense experiences, launched Carlson into his next phase. He then threw himself into the national activities already mentioned. His recent commitments include, for example, the following: President of the Research Council on the Problems of Alcohol; the