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AMOEBIASIS AND AMOEBIC DYSENTERY: A BRIEF RESUME

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During the past few years there has been a great increase in interest in human infections with the dysentery amoeba, *Endamoeba histolytica*, and it is important that physicians, biologists, and the public in general have accurate information regarding this interesting animal parasite and its effect on man. Increased interest has led not only to the discovery of many more cases of infection than were previously supposed to exist, but it has also led to many false diagnoses of amoebic dysentery based upon inaccurate observations. There are many causes for the symptoms of dysentery, and it is only by careful identification of *Endamoeba histolytica* in the intestinal discharges that a diagnosis of amoebic dysentery can be made.

There are five species of amoebae which inhabit the large intestine of man, namely, *Endamoeba histolytica, Endamoeba coli, Endolimax nana, Iodamoeba bütschlii* (*williamsi*), and *Dientamoeba fragilis*. Of these *Endamoeba histolytica* is the only one which invades the tissues or causes any disturbance in the intestine. The other four are all commensals, that is, they live entirely upon food material in the lumen of the intestine and do not possess any toxin which can cause damage to the tissues. Because of the lack of damage produced by these non-pathogenic amoebae their presence in the intestine can be ignored except for their differentiation from *Endamoeba histolytica*. The term "amoebiasis," therefore, is by common consent limited to infection with *Endamoeba histolytica*. This term, however, refers to the presence of *Endamoeba histolytica* wherever it may occur in the body and whether or not clinical symptoms are produced by it.

One sometimes hears the term "intestinal protozoiasis" used to cover infections with any of the intestinal protozoa, including amoebae, flagellates, ciliates, and sporozoa. This is such a broad term and is so indefinite that its use should be discouraged, for it suggests that many of these protozoa may be harmful to the host whereas only a few of them have been demonstrated to cause any damage.

Description and Life History of *Endamoeba histolytica*

Endamoeba histolytica exists in two well defined forms, the trophozoite or motile form and the cyst. In the process of formation of the cyst from the motile form there is a stage called the precystic stage which is of short duration and not of great importance.

In its motile form *Endamoeba histolytica* varies from 10 to 35 micra in diameter. When it is active it changes its shape rapidly and may become greatly elongated and may have a pointed posterior end. As it moves along its front end is blunt and consists of a constantly forming pseudopodium. Small particles of fecal debris often become attached to the pointed posterior end. This amoeba moves rapidly, frequently changes its direction, and may thrust out pseudopodia from any part of the body. These may determine the new direction of motion or they may be withdrawn. The pseudopodia consist of the ectoplasm of the amoeba which is usually clear and highly refractile. In contrast to this the endoplasm is finely granular. It contains the nucleus and food material. The nucleus is about 10 micra in diameter, is always spherical, and in the fresh condition is hardly visible. When stained with iodin or haematoxylin it has a definite rim of chromatin material which may be finely beaded or crescentic in outline. The nucleus also contains a small spherical nucleolus or karyosome, usually situated in the center. The nature of the food material in the endoplasm depends upon the environment in which the amoeba is living. In cases of acute amoebic dysentery where there is blood in the stools the food material in the amoebae usually consists entirely of red blood cells, twenty or more of which may be present in a single amoeba. In amoebae which have invaded the body tissues red blood cells are not so often found. In skin lesions and in cultures where many bacteria are present they may be found in the amoebae. Sometimes small vacuoles are also present in the endoplasm and may be formed around the food material.

Little is known about the conditions which determine the development of the cysts from the motile forms. Cysts are practically never found in the body tissues. They usually develop after the amoebae move downward in the large intestine and they often develop in cultures. Their development is undoubtedly for the purpose of forming a resistant stage which can survive outside the body of the host and continue propagation in a new host. The mature cyst varies from 6 to 16 micra in diameter, is usually spherical, and contains four nuclei having the same structure as that in the motile form. The cyst also may contain vacuoles of glycogen and banana-shaped "chromatoidal bodies" which probably represent food material.

The motile forms are very fragile. They may continue to be motile for several hours after being passed in the stools if the material is kept moist and warm, but they lose their motility if the temperature is lowered to 70° F. and soon disintegrate. Drying kills them instantly. The cysts, on the other hand, are resistant to low temperature, almost to the freezing point. They can be kept in water at room temperature for about ten days and at 40° F. for six or seven weeks.

They are quickly killed, however, by a temperature of 115° F. and by drying. They can survive for at least forty-eight hours in the intestines of cockroaches and flies. They possess sufficient resistance to facilitate transmission from one host to another. They enter the new host by the mouth, are resistant to the acid of the stomach, and pass into the small intestine. Here the four-nucleated amoeba within the cyst becomes active and emerges through an opening in the cyst wall. Each nucleus divides into two, and finally eight small motile amoebae are formed. These take up their residence in the upper end of the large intestine, multiply and invade the tissues if possible. It is evident, therefore, that amoebiasis is transmitted from person to

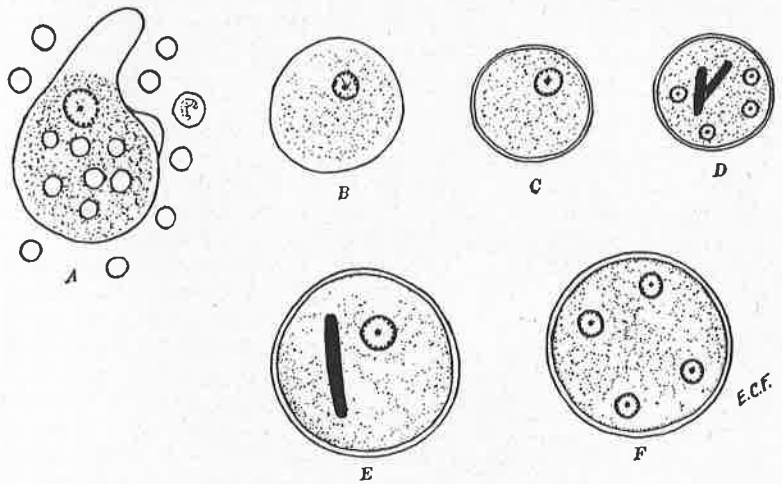

Fig. 1. Drawings illustrating life cycle of *Endamoeba histolytica*. *A*, motile form containing seven red blood cells. Other red blood cells and a white blood cell are shown outside the amoeba. *B*, precystic stage; *C*, small one-nucleate cyst; *D*, small four-nucleate cyst containing chromatoidal bodies; *E*, large one-nucleate cyst containing chromatoidal body; *F*, large four-nucleate cyst. Magnified X 1100. (After E. C. Faust, from Craig, C. F., *Amebiasis and Amebic Dysentery*. Charles C. Thomas, Springfield, Illinois. 1934.)

person only in the cyst form. In cases of acute amoebic dysentery the cysts ordinarily do not have time to develop before the amoebae are evacuated from the intestine, so that the chief sources of infection are chonic cases and carriers who pass cysts in the stools rather than acute cases who pass only the motile forms.

There are both large and small races of *Endamoeba histolytica*. The cysts of the large races average about 13 micra in diameter, those of the small races about 8 micra. Some persons pass only large or small cysts, while in others both large and small cysts are found, and in still others intermediate sizes are also found. In acute cases of

amoebic dysentery the amoebae are nearly always large, while the small forms alone are usually found in persons having no symptoms. It is generally believed, therefore, that the small races are less pathogenic than the large races, but it is possible that the small size is due to an unfavorable environment and that under favorable conditions the larger forms may develop and show greater pathogenic activity.

History

Although dysentery has been a common disease of man since ancient times it was not until 1875 in St. Petersburg, Russia, that Loesch first discovered an amoeba in the discharges of a dysenteric patient. Kartulis in Egypt soon found that this was the apparent cause of the so-called "tropical dysentery" common in that country, and Robert Koch, discoverer of the tubercle bacillus and the cholera bacillus, while working in Egypt first found amoebae in the tissues of the large intestine. Councilman and Lafleur in Baltimore first described the pathology of amoebic infection in 1891, and Shiga, a Japanese investigator, discovered in 1898 that the common epidemic type of dysentery was caused by a bacillus. In 1904 Schaudinn first clearly differentiated the motile form of *Endamoeba histolytica* from the non-pathogenic *Endamoeba coli* and, in 1908 Huber differentiated the cysts of these two organisms. From that time until after the Great War various investigators discovered the other intestinal amoebae, thus placing diagnosis on a firm basis. The Great War stimulated the examination of large numbers of people for amoebiasis and since that time extensive surveys have been made in various parts of the world. These have shown that amoebic infection is common and has world-wide distribution. In 1924 Boeck and Drbohlay developed a practical method for cultivating *Endamoeba histolytica* in artificial media.

Distribution and Epidemiology

It is now generally recognized that in temperate zones having reasonably good sanitation from five to ten per cent of the population harbor *Endamoeba histolytica.* In poorly sanitated areas of the temperate zone, such as Korea and China, the incidence varies from about 25 to 50 per cent. Our own state-wide survey of the rural areas of Tennessee showed an average incidence of 23 per cent, with a wide variation in different parts of the state. For instance, four adjoining counties on the eastern part of the Highland Rim each had an incidence of between 40 and 50 per cent, while the average for West Tennessee was only about 14 per cent. Faust found an incidence of about 45 per cent in southwestern Virginia and an incidence of between 7 and 27 per cent in certain groups of people in New Orleans. The high rates of infection just quoted do not mean that such a large proportion of the people are suffering from symptoms produced by the dysentery amoeba. Most infected persons may be classed as "carriers," and never have and perhaps never will suffer from amoebic dysentery. But these people are potential sources of infection for

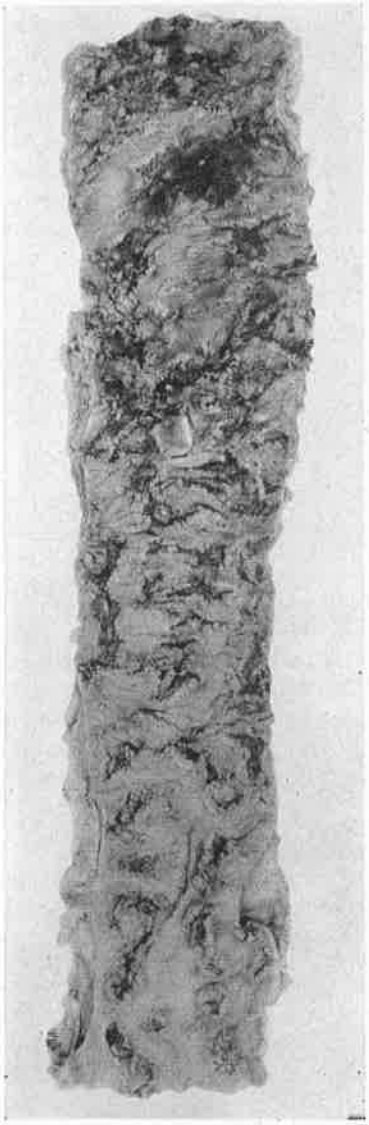

Fig. 2. Acute amoebic dysentery. Large intestine showing characteristic ulcers. (From Army Medical Museum collection and Craig's Amebiasis and Amebic Dysentery.)

others who, when they become infected, may develop severe symptoms. All infected persons are therefore of concern to the community.

The factors mainly responsible for a high incidence of infection are: lack of proper disposal of feces, personal uncleanliness, impure water supplies, and an abundance of flies. Minor differences in the habits of people may make a great difference in the incidence in adjacent areas. For instance, in our Tennessee studies the main difference in the sanitary habits of the people on the Highland Rim and in West Tennessee seemed to be only that on the Highland Rim many of the people deposit their excreta out of doors about the farm houses whereas in West Tennessee the chicken house or some small shed is more often used. Custom, therefore, as well as intelligence makes a great difference in the transmission of this as well as of many other disease organisms.

It is difficult to determine in any one situation what is the chief source of infection or method of transmission. Soiled hands of mothers who prepare food and handle children must be a common source of spread in families, and many instances of the infection of entire families in the absence of infection in neighboring families have been reported. Public food handlers have also been blamed for spreading the infection and are undoubtedly dangerous if they are very uncleanly in their habits, but they are probably not as important a source of amoebic infection as they are of typhiod fever, because amoebae are much less numerous in the stools than bacteria, they do not multiply outside the host, and even the cyst forms are quickly killed by drying on the skin of the

hands. Flies undoubtedly play a part in transmission where they are very numerous and have access to feces, food, and the faces of children, but usually they must play a relatively minor role. One epidemic, however, in an army camp has been ascribed to flies as the chief transmitting agent. Milk is probably a very rare source of infection, if indeed it is ever involved.

Water may act as a source of infection under a number of different conditions. In India wells are known to be heavily contaminated with human excreta and must be largely responsible for the tremendous number of infections in native villages. Where polluted streams are used for drinking water in the tropics or where such water is accidentally consumed as it was during the stock yards fire in Chicago in 1934, there is ample opportunity for infection. The introduction of a pure water supply in the Panama Canal Zone was coincident with a dramatic drop in the number of cases of amoebic dysentery. Polluted wells and springs in the United States when used by families over a long period of time may contribute to the incidence of infection. The Chicago epidemic of amoebic dysentery in 1933 called attention to a subtile danger which lies in the pollution of water which has previously been made potable by chlorination. The improvements in plumbing, air conditioning, and other cooling systems which have been installed from time to time in hotels and other public buildings which were built a generation or more ago may not be an unmixed blessing. Opportunities for back syphonage, for cross connections between sewer pipes and water pipes and for leaking of sewer pipes within buildings have been shown to be sources of contamination of drinking water. The Chicago epidemic is a striking illustration of this. Although engineers have called attention to this danger for a number of years, public health officials and city governments have not yet seen the importance of spending sufficient sums of money for the inspection of such buildings to prevent water contamination. One of the important factors involved is the fact that it requires about one hundred times as strong a chlorine solution to kill cysts of *Endamoeba histolytica* as it does to kill the typhoid bacillus, so that in the Chicago epidemic although the residual chlorine in the drinking water was sufficient to prevent an epidemic of diarrhea or typhoid fever it left cysts of the amoeba in an infectious state. It has been found that sand filteration will remove the cysts of amoebae from the water, but even this will not prevent later pollution from defective plumbing.

Another important aspect of the epidemiology of amoebiasis is the variability in the clinical manifestations of the infection. Most people who become infected with *Endamoeba histolytica* never show any clinical symptoms of the infection. Some suffer from mild gastrointestinal disturbances that may be diagnosed as diseases of the stomach, gall-bladder, or appendix or even as neurasthenia. Not more than ten per cent of infected persons, and in some regions even less than that, develop active amoebic dysentery. There are two reasons for this. One is that different individuals seem to differ greatly in the susceptibility of the intestine to the invasion of the amoeba. The

general condition of the body, the diet, climatic conditions, the consumption of alcohol, and possibly other factors seem to be responsible for this variation. The other important factor is an apparent difference in the ability of various strains of *Endamoeba histolytica* to cause ulceration in the intestine. Studies which we have made in Tennessee showed that strains of amoebae obtained from the hill country where there was a high incidence of infection but little amoebic dysentery produced on the average much milder lesions in kittens than strains obtained from an epidemic of acute amoebic dysentery in the bottomland of West Tennessee. All of these strains were of the large variety, so that size was not a factor in their pathogenic activity. Strains of amoebae which we secured from Chicago produced the most severe ulceration in kittens of any strains which we have studied, and this coincides with the fact that many of the cases of amoebic dysentery in the Chicago epidemic were of unusual severity.

Pathology

Endamoeba histolytica attacks the tissues of the body both by its mechanical penetration and by a toxin which causes a dissolution of the tissues. As the amoeba works its way through the mucous membrane, the cells and intercellular structures disintegrate and finally ulcerate. The amoebae advance to the deeper tissues by direct penetration and by passing into the lymph vessels and blood vessels. They spread out in all directions in advance of the destructive process so that the deeper tissues are often more widely destroyed than the mucous membranes, thus producing the so-called "bottle neck" ulcers. Bacteria follow the amoebae into the exposed tissues and increase the destruction. The smallest lesions may be almost invisible while large ones may extend for several inches and communicate with each other by tunnels under the surface. The ulcerative process may penetrate to the outer surface of the intestine and lead to perforation and peritonitis, or it may heal and leave scars which cause thickening or obstruction of the intestine. The nature of the amoeba toxin is such that the body does not respond as it does to most bacterial infections by the accumulation of white blood cells of the polymorphonuclear variety. A few mononuclear cells accumulate but are of little value in the defense of the body against the infection.

If the amoebae make their way into the blood vessels, they may be carried to the liver where single or multiple abscesses may develop. Such abscesses may be very large and may burst into the peritoneal cavity or through the diaphragm into the pleural cavity or the lung. Secondary abscesses have been found in the brain and in some other organs. If an amoebic abscess or amoebic ulceration of the intestine is drained by surgical procedure, infection of the skin may occur, producing an extensive gangrenous ulcer.

Clinical Manifestations

It has been stated above that most persons infected with *Endamoeba histolytica* do not suffer from clinical symptoms. Whether in these cases the amoebae are living as commensals in the lumen of the intestine without attacking the tissues or whether the ulcers are so small that they do not give rise to symptoms is difficult to determine. Many autopsies have been performed in which amoebic ulcers have been found in the colon in persons who had never suffered from clinical symptoms. On the other hand, it is known that in monkeys,

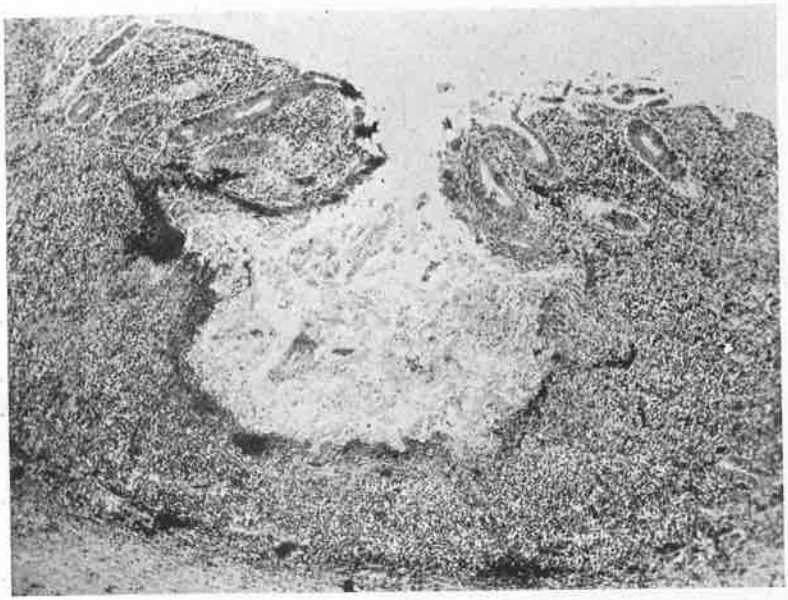

Fig. 3. Typical bottle-neck ulcer of amoebic dysentery. Magnified X 75. (From Army Medical Museum collection and Craig's Amebiasis and Amebic Dysentery.)

which harbor amoebae indistinguishable from *Endamoeba histolytica,* no lesions can usually be found. Furthermore, the fact that *Endamoeba histolytica* can be cultivated in artificial media indicates that it can multiply without invading the tissues.

The incubation period from the time of infection to the time symptoms are produced may vary from a week to several months or perhaps years. An attack of amoebic dysentery may begin suddenly with high fever, prostration, severe abdominal pain, and a diarrhea which soon becomes bloody. More often the first symptoms are vague. There may be no fever and the first evidence of dysentery may be a small amount of blood or mucus which gradually increases in severity. Rarely, as in the Chicago epidemic, cases progress rapidly to perforation or gangrene of the intestine and die within a week or two. More

often, however, the first attack subsides and the patient may be partially or completely well for weeks or months, after which a second attack occurs, usually of less severity. The typical picture is that of a recurring dysentery of a mild nature with gradual loss of weight and strength, and in the intervals between attacks abdominal pain varying in severity and frequency and often associated with constipation.

Liver abscess may occur as a complication of an attack of dysentery or may be the first clinical evidence of amoebic infection. In the latter case the ulceration in the intestine must have been too small to

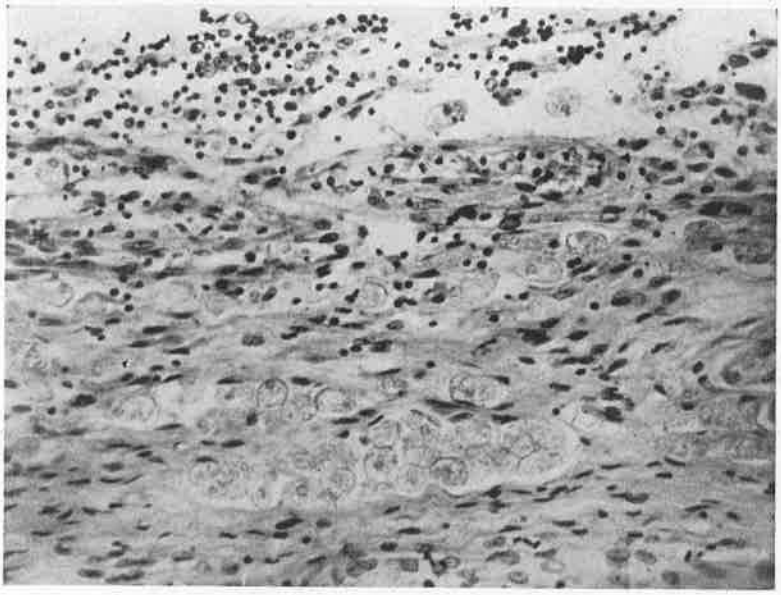

Fig. 4. Section of large intestine showing invasion of muscular coat by *Endamoeba histolytica*. Magnified X 300. (From Army Medical Museum collection and Craig's Amebiasis and Amebic Dysentery.)

give rise to clinical symptoms. When a liver abscess develops there is usually a rise in fever to 101°-103° F., with pain in the liver region. The patient is usually prostrated and the blood usually shows an increase of polymorphonuclear leucocytes. If the abscess is not diagnosed, even more severe symptoms will be caused by its rupture. A purulent infection of the pleura may develop or the patient may cough up the characteristic brownish red material from rupture of the liver abscess into a bronchus.

Treatment

There are three main groups of drugs which are useful in the treatment of amoebiasis. These are the ipecac group, the iodin group,

and the arsenic group. The active principle of ipecac is emetine, which is usually administered hypodermically. It is very effective in relieving the acute symptoms of amoebic dysentery and is indispensable in the treatment of amoebic abscess of the liver, but it often fails to produce a complete cure. It is dangerous because it is toxic to the heart muscle, and its use should be limited to a short period, not over a week. In most cases one of the other drugs is preferable.

The iodin group of drugs includes chiniofon (yatren, anayodin) and vioform. These are given by mouth and chiniofon can also be given by rectum when the ulceration involves the lower part of the large intestine. Both drugs are practically non-toxic in the usual dosage.

The arsenic group includes carbarsone, treparsol, and acetarsone (stovarsol). Of these carbarsone is the best, being most effective against the amoeba and practically non-toxic. It can be given by rectum as well as by mouth. The other two arsenic drugs often cause symptoms of arsenic poisoning if given in large enough doses or for a long enough period to be effective.

At best the treatment of amoebiasis is difficult. The patient should be under the care of a physician familiar with the best method of treatment. Several courses of treatment are usually necessary to assure a cure. Early cases respond better than recurrent cases, for in the latter there are usually scars and pockets in which the amoebae are protected from the drug. Although the amoebae always disappear from the stools during treatment they may reappear some time later. A patient should not be considered cured until repeated stool examinations have been negative for a period of a year or more.

Diagnosis

The diagnosis of amoebic infection rests almost entirely upon finding characteristic motile forms or cysts of *Endamoeba histolytica* in the stools or motile forms in lesions elsewhere in the body. Obviously it is necessary to be able to differentiate *Endamoeba histolytica* from the other intestinal amoebae and from body cells which are often found in dysenteric stools. It is impossible to lay too much emphasis upon this point. It requires several months of training for a technician to become reliable in the identification of these forms. If actively motile amoebae showing typical rapid motion and containing red blood cells can be found in the stools the diagnosis is not difficult, but it is probable that many cases which are not amoebic are so diagnosed through lack of proper observation. Cases of bacillary dysentery, ulcerative colitis, and even cancer of the intestine are sometimes diagnosed as amoebic dysentery in these days of enthusiasm over the amoeba. On the other hand, amoebae are sometimes not numerous in the stools, especially in chronic cases, and repeated examinations of fresh specimens may be necessary before the amoebae are found. In the absence of active dysentery the motile forms are usually not present in the stools and the cysts must be

sought for. In making surveys it has been found that only one-third to one-half of the persons actually harboring *Endamoeba histolyica* can be detected on one examination of the feces and it requires three preparations after a saline purge or six preparations of formed feces to detect practically all of the infected persons. This is because the amoebae seem to multiply and encyst irregularly.

A complement fixation test on the blood similar to the Wassermann reaction for syphilis has been devised by Craig which is positive in most persons harboring *Endamoeba histolytica* and is of some value in the diagnosis of difficult cases and in determining a cure.

Prevention

From what has been said it is obvious that the prevention of amoebiasis depends mainly upon good hygiene and sanitation involving the proper disposal of feces, careful washing of hands by all persons handling food, protection against flies, prevention of fly breeding, and furnishing and protection of pure water supplies. These measures involve the activity of public health officials, physicians, and educators. It is the function of public health officials to supervise water and sewage systems in cities and to encourage the installation of sanitary measures in rural communities. They can also to a certain extent supervise public food handlers, but it is not considered feasible at the present time to examine such persons routinely for *Endamoeba histolytica.* Physicians can do much toward prevention by accurate diagnosis, by prompt and adequate treatment, and by instructing the families in which they practice concerning hygienic measures in the home which will prevent the acquisition and spread of intestinal infections. Educators have an important function to perform in teaching students the causes and modes of prevention of individual diseases and the general measures of personal hygiene. They can reinforce the efforts of public health officials in a much more practical way than is done in many schools at the present time.

Summary and Conclusion

The purpose of this paper has been to give a general summary of what is known concerning amoebiasis, which is the most important protozoan infection of the intestine of man. The life history of the dysentery amoeba has been outlined, the prevalence, distribution and modes of transmission have been considered, the disease produced by the parasite has been described, and its treatment and prevention have been briefly discussed. We possess enough knowledge to control amoebiasis and to prevent its spread. What is needed is a concerted effort on the part of the medical profession, public health agencies, educators, and the public toward better sanitation and personal habits which will prevent this and other organisms which produce intestinal infections from gaining access to the human body.

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SOME THINGS OF SCIENTIFIC INTEREST IN WEST TENNESSEE[1]

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The original paper was largely a somewhat detailed outline of some of the scientific possibilities in West Tennessee. Attention was called to some recent work in archaeology and some suggestions were made as to future possibilities. The importance of the clays, this section's greatest mineral resource, was emphasized. This territory has a great and varied field for botanists and is also a rich field for the zoologists. It holds great possibilities for inland fresh-water biology. It is a region of great interest to geologists and paleontologists, containing one of the world's greatest fossil deposits of its kind. Reelfoot Lake and its environs constitute the greatest center of scientific interest, but they do not contain all there is in this end of the State.

[1]This is an abstract of a five-page illustrated paper read before the Tennessee Academy of Science at the Reelfoot Lake Biological Station, April 26, 1935.

ANNOUNCEMENT OF ANNUAL MEETING OF THE TENNESSEE ACADEMY OF SCIENCE

The regular annual meeting of the Tennessee Academy of Science will be held in Room 202, Industrial Arts Building, George Peabody College for Teachers, Nashville, Tennessee, on November 29-30. All members are urged to attend and present papers.

Authors should send to Dr. A. E. Parkins, George Peabody College, Nashville, Tennessee, at once the title of their paper, the time required for presentation, preferred position on the program, and whether lantern, 16mm., or regular motion picture machine will be needed for presentation. In the case of demonstrations, please indicate microscopes or other accessories needed.

It is planned to have a Botanical Section again as usual. Members desiring to present papers in this section should send titles and other information about their papers to Dr. Jesse M. Shaver, George Peabody College for Teachers, Nashville, Tennessee.

It is also desired that each author send a brief abstract of his paper in order that proper publicity may be secured.