FLAGELLATE INFESTATIONS AND INFECTIONS

GIARDIASIS, OR LAMBLIA; TRICHOMONIASIS; PROWAZEKIASIS, CERCOMONIASIS, CHILOMASTIXIASIS AND TETRAMITIASIS

WILLIAM EVERETT MUSGRAVE, M.D.
SAN FRANCISCO

Because of the apparently increasing interest in the United States in the flagellates, and in compliance with numerous requests, a brief summary of the problem has been prepared from my Philippine records. No attempt is made to consider the biology of the parasites, because that is well done in a number of publications on parasitology.

LAMBLIA

The synonyms of the term lamblia, or giardiasis, are flagellate diarrhea (in part), tropical diarrhea (in part), and monad diarrhea (in part). It may be defined as an infection or infestation, principally of the intestine, by *Lamblia intestinalis* (R. Blanchard, 1888), characterized by chronic diarrhea with intermittent acute exacerbations, digestive disturbances and nervous symptoms, or by the presence of the parasites without symptoms. *Lamblia intestinalis* is one of the common parasites, and lamblia one of the common diseases, of the tropics. The intestinal or usual form of the disease is noted more than 1,500 times in my hospital records, and it is much more frequently encountered in ambulatory patients. It is, and has been for years, recognized by clinicians in the tropics as a disease of importance, particularly in children; and experimental reproduction and other research work are attracting more attention to it in temperate climates.

Predisposing Causes.—Infestation with *Lamblia* is cosmopolitan. Evidences of infection, with the production of harmful symptoms, is somewhat more restricted, and appears to be influenced by a number of factors, some of which are known. Tropical climates and the summer weather of the temperate zone favor the infestation and development of infection in carriers. Children are especially susceptible, and the infection is more severe in them than in adults. In the tropics, the infection is relatively higher and more severe among foreigners than among the native races. The presence of other diseases or debility from any cause is a noticeable predisposing factor. Other intestinal infections appear to predispose to lamblia; but this probably is due to the frequent common sources of the various infecting agents, a fact which also explains the frequency of mixed infections.

Etiology.—The disease is an infection by *Lamblia intestinalis*, acting alone or in conjunction with other somewhat similar parasites. For discussion of the biology of the parasite, any of the numerous books on animal parasites may be referred to. The methods of invasion and the pathogenicity for and locations in the human host may be discussed here. It is generally considered that the parasite has no free living cycle. Its transmission, therefore, must be directly or indirectly from one host to another; and there is ample evidence that such are the methods of transmission to the human host. The direct method from infected excretions to the mouth probably is important, particularly in children. Grassi infected himself with the

cysts; and, recently, well controlled experiments have proved the practicability of this method of infection. The cysts are thrown off in great numbers in the discharges from infected persons and from animals, such as rats, rabbits and mice; but the duration of their infectivity under these conditions is not known, and therefore the indirect methods of transmission may not be accurately predicted. Stiles and Keister consider the carrying of the spores from infected discharges to food by the common house fly the most important method of transmission. These authors believe that *Lamblia* found in animals is a distinct species and that human infection is dependent on transmission directly or indirectly from a human host. Some students accept the specific identity of the human and animal *Lamblia*, and thus greatly broaden the infective opportunities.

It is generally recognized, and has been experimentally demonstrated in some cases, that water, vegetables, cereals and other foods may be contaminated with spores or encysted forms from the discharges of infected persons or animals, and that new infections occur through eating or drinking infected substances. It has been suggested that the spores may be transmitted through the air, in dust, as is known to be the case with certain other parasites. The occasional infestation of the respiratory tract appears to strengthen this view as to a possibly practical method of transmission. In the vast majority of instances, invasion is through the mouth; but the occasional finding of the cysts in bronchietatic secretion suggests possibilities of entrance through the respiratory system. The parasites are most numerous in the intestine, but have been found in the mouth, in vomited material, and in the discharges from liver abscesses which have been operated on. The pathogenicity of *Giardia* for the human host now is generally accepted, and certainly there can be no question of its disease-producing properties, at least under certain conditions. This fact is supported by numerous reports from various countries, and has been experimentally proved by inoculation, originally by Grassi on himself, and since that time by other investigators. Mice also have been infected by feeding the cysts of *Lamblia* from infected human discharges.

The principal argument against the pathogenic properties is the frequent presence of the organisms in persons without symptoms of disease. This argument formerly was applied to many bacterial and parasitic diseases, from cholera to amebiasis. Such an argument needs no reply, in the light of our present knowledge of infections and immunity.

Pathology.—The nature of the lesions and the methods by which they are produced are difficult to determine because (1) death rarely results from the pure *Lamblia* infection; (2) mixed infections are the rule, and (3) lesions found at necropsy may be due to or influenced by the associated parasites and bacteria. Such evidence as is available indicates that the parasites produce a catarrah condition of the mucosa of the small intestine, and that either primarily or as secondary invaders they aggravate lesions of the intestine caused by other agents. It is not unlikely that the unknown cysts or egglike bodies sometimes encountered in sections through amebic and other intestinal lesions may be *Lamblia*. In their flagellate stage, the parasites probably are limited to the small intestine in distribution, except in diarrhea, when active forms frequently are seen in feces. Encysted forms are never constantly present in the formed stools when the small intestine is infested. That the cysts may reach

1. Although probably not zoologically correct, the word lamblia is used for historical and sentimental reasons.
more distant organs is shown by their presence in the contents of liver abscesses.

Symptoms.—Lambia may be transiently present in the stools of persons showing no symptoms of disease. If permanent parasitism may be established without symptoms, it must be exceptional, depending on the nature and duration of similar cases of infection with other pathogenic organisms. We have encountered no instance of prolonged parasitism without symptoms. The characteristic and usual symptoms of intestinal infection are a chronic diarrhea, with exacerbations and intermissions, during which there may be constipation, very much as is seen in amebic colitis. There is nothing distinctive about the diarrhea except its persistence and the difficulty in obtaining a permanent cure, particularly in children. The stools are of the usual type; and in severe cases there may be some tenesmus and blood, but this is exceptional. Microscopically, there is mucus, usually blood cells and either motile or encysted Lambia. The parasites usually are quite numerous when the diarrhea is severe, and during intermissions only a few or no cysts may be found after prolonged search. In a child under my care for a pure infection of Lambia for more than two years, and who was finally sent to the United States because of the persistence of the disease and the consequent anemia and lack of development, there were frequent periods of six or seven weeks when there would be no diarrhea, and only a few cysts could be found in the stools. Such intermissions invariably were followed with exacerbations of acute diarrhea, usually with some blood, and the specimens would contain myriads of the motile Lambia organisms. More or less indigestion is usual in the well-established cases, and occasional nausea and vomiting is not rare. The nervous symptoms complained of are irritability, insomnia and occasional headache. Infections elsewhere than the intestine, such as in the lungs, stomach and liver abscess, are so rare and so frequently associated with other diseases that they are only mentioned.

Diagnosis.—This is based on the persistent presence of Lambia in the diarrheal stools for which there is no other logical cause. In the mixed infections with other flagellates, so often seen, Lambia may be considered the most important causative agent. Diagnosis should not be made on a single examination, for obvious reasons.

Prognosis, Prophylaxis and Treatment.—The infection usually is a chronic one, particularly in children, and very resistant to treatment. Among foreign children in the tropics, where it shows its greatest intensity and persistence, it may be necessary to advise a change to a temperate climate in order to secure recovery. Public health measures consist in the proper disposal of feces, and the destruction of flies, rats, mice and other animals known to harbor the parasites. Important personal measures consist in using safe drinking water, avoiding uncooked food, and maintaining scrupulous cleanliness about the discharges, particularly where there are children. There is no known specific remedy. Various drugs, such as tartar emetic, ipecac, emetine, quinin, methylene blue, arsphenamin, arsenic and thymol, have been used intravenously, internally or by enema. Enemas are useful when there is diarrhea, and for this purpose a 1:2,000 solution of thymol has given me the greatest satisfaction. It is, of course, impossible to reach the breeding ground of the parasites in the small intestine by local methods. Of all internal remedies, thymol in 0.25 to 0.5 gm. doses given in capsule with lactose has given me the best results. General measures to conserve the patient’s strength and control the diarrhea are indicated.

Trichomoniasis

Trichomoniasis may be defined as an infestation or infection of the intestine, less frequently of the stomach, mouth, air passages, vagina, bladder and other organs, by species of the genus Trichomonas, characterized by no definite symptoms or by those due to local irritation.

Species of Trichomonas are among the most cosmopolitan and widespread parasites infesting man. Opinions regarding their influence in the causation of disease vary from the belief that they are entirely harmless, to the other extreme, in which they are charged with responsibility for severe dysentery and other pathologic conditions. The weight of evidence appears to attach slight importance to them when in small numbers in otherwise healthy persons, and to consider that their etiologic importance increases when in large numbers, or in persons already debilitated from other causes, or when, as usually is the case, they are associated with other parasites.

Etiology.—Infestations and infections with symptoms are reported from many countries. However, both infestation and the prevalence of disease symptoms are more frequent in the tropics. Children are more susceptible than adults, and the debilitated more so than the healthy. Foreigners are more likely to show symptoms of infection than are natives of the tropics. The biology of the various species of Trichomonas is not considered here. They are usually classed as strict parasites of man and other animals, with an encysted stage during which they are transferred directly or indirectly from one host to another. They usually enter directly into the digestive tract, but may be found in the respiratory passages, the vaginal and urinary canals and elsewhere. For convenience, the disease may be discussed as intestinal, respiratory and genito-urinary.

Intestinal Trichomoniasis.—This is the usual type and the one of most importance. As determined by stool examination, the percentage varies between 10 and 75, or more, of the inhabitants in different tropical localities. The number of persons harboring the parasites who show diarrhea or other symptoms which may reasonably be charged to the infection varies from 10 to 50 per cent. of all classes, and is much higher among those heavily infected. Trichomonas intestinalis is the species usually present, but various other closely allied flagellates frequently are associated with it. The pathogenicity of Trichomonas in diarrheal conditions is pretty generally accepted by experienced clinicians in the tropics, though not by all. Some even credit it with being the cause of dysentery among children. Mello-Leitao considers primary trichomoniasis, either alone or with Lambia infections, the most common form of dysentery among children in Rio de Janeiro; and Escomel reports 152 cases of dysentery from the same cause in Peru. Derrieu and Raynaud report it from Algeria; Brumpt, in a patient from Tonkin, and many other observers from various places recognize the disease-producing properties of these flagellates. Lynch believes that Trichomonas found in the intestine, mouth, lungs and vagina is the same organism, and that it excites existing inflammatory conditions. He was successful in infecting rabbits both from cultures of the parasites and from infected secretions.
Symptoms.—The symptoms of intestinal infection are diarrhea, usually not severe, worse in the morning and accompanied by flatulence and more or less indigestion. There may be moderate secondary anemia, and usually there are nervous symptoms, such as irritability, insomnia and headache. Not infrequently, Trichomonas occurs in the stomach as well as the intestine, and usually is associated with pronounced symptoms. One of the most interesting reports in this connection is that of Frank Smithies' two cases. In both of these, constipation was present instead of diarrhea. Other prominent symptoms were nausea, flatulence, abdominal distention, colicky pains, headache, neuralgia and exhaustion. Smithies suggests that the cleavage products of protein contained in large numbers of these parasites may be a not inconsiderable influence as (1) a gastro-intestinal irritant; (2) an altering metabolic change in digestive glands, or (3) a source of so-called intoxication symptoms, clinically.

Treatment.—The treatment is the same as that already given for lambliasis. The parasites are difficult to remove both by microscopic examination and by clinical symptoms to exhibit a periodicity in numbers, as is true of most pathogenic parasites. Vigorous special treatment is not indicated in the absence of symptoms.

Respiratory Trichomoniasis.—This type has been reported by a number of observers who consider the parasites pathogenic in the air passages, especially following some injury. Dolly reports a case of gangrene of the lung in which large numbers of Trichomonas were the apparent cause. They have been discovered in bronchiectatic sputum, and reported in cases of chronic bronchitis. Steam inhalations of creosote and terebene caused the disappearance of the flagellates, and was followed by recovery in two cases of bronchiectasis in my practice. There is no method of determining the pathogenic rôle of the parasites in these cases, but, as in the gastro-intestinal type, their disappearance usually is simultaneous with improvement in the patients.

Genito-Urinary Trichomoniasis.—Trichomonas vaginalis is frequently found in the vaginal canal in women residing in the tropics. The same or a similar species is found in the female bladder and, rarely, in the male bladder. Those from the bladder usually are found in the urine, indicating more or less cystitis; but the part played by the flagellates in its production has not been sufficiently studied.

TETRAMITIASIS; CHILOMASTIXIASIS; CERCOMONIASIS; PROWAZEKIASIS

Flagellate protozoa belonging to these genera and species, and perhaps others not yet classified, are found inhabiting chiefly the intestine and occasionally other parts of the human body. Their distribution is widespread as parasites of man, several lower animals and invertebrates. Their association with diarrhea and other disease symptoms in man is cosmopolitan, but, as in the case of Giardia and Trichomonas, the highest incidence of infestation and the most frequent association with symptoms are found in the tropics. The methods of invasion are similar to those already described for Lamblia, which is by direct or indirect transmission of the cysts or spores from the discharges of one host to the digestive canal of another. This may take place directly by faulty personal hygiene, or indirectly by infected food and water or by flies, or perhaps even wind may carry the spores. The most interesting and important point in connection with these infections is the question of pathogenicity of the parasites, and here there is the widest difference of opinion. Some authorities consider the parasites harmless; but the weight of evidence among men working in warm climates assigns pathologic importance to them, at least under conditions of mass invasion of the parasites or decreased resistance on the part of hosts. Marques da Cunha and Torres consider Chilomastix the cause of chronic diarrhea in children in Brazil, and Gobel reports similar conditions in Tunis.

The symptoms and treatment of intestinal infections, which are the only ones of medical importance, are similar to those already described for Lamblia.

If the common parasites discussed briefly in this paper do not have pathogenic significance, they certainly "are an awful lot in bad company."

393 Market Street.

VITAMINS IN ICE CREAM*

ARTHUR H. SMITH, Ph.D.
NEW HAVEN, CONN.

The study of the vitamins in ice cream has two points of value. In the first place, it adds an important item of a statistical nature to the evidence which is still accumulating concerning the accessory food factors; for the already large consumption of ice cream in the United States is on the increase, and popularity of the frozen sweet is bound to spread to other countries. Secondly, through the experiments here reported, one may estimate the effect of pasteurization and of freezing and storage on the vitamins in such a mixture as ice cream.

The plan of the experiment was to test the ice cream for the various accessory food factors before freezing, and to repeat the tests on the same mixture after freezing. White rats were used in the tests for vitamins A and B, the technic of Ferry* being followed. For the antiscorbutic vitamin, the procedure of Sherman, Lamer and Campbell,† with the following diet, was employed: soy bean meal (autoclaved), 83 per cent.; filter paper pulp, 3 per cent.; cod liver oil, 5 per cent.; dried yeast, 3 per cent.; calcium lactate, 3 per cent.; sodium chloride, 3 per cent.

When the frozen ice cream was used as the source of the accessory food substance, it was first melted on the water-bath, care being taken that the temperature of the mixture did not rise above that of the room. Plain vanilla ice cream containing 10 per cent. butter fat was employed throughout the experiments.

VITAMIN A

Two kinds of protein were used in the diets for vitamin A study. One, casein-Merck, which had been heated in air at 105 C. for twenty-four hours and then extracted with hot alcohol and ether, contained traces of the fat soluble factor, with the result that the animals grew from four to eight weeks at a subnormal rate and usually developed ophthalmia while still making this slow gain. On the other protein, casein-Harris, which was prepared from a good grade of commercial casein by dissolving in caustic alkali, and filtering sparkling clear, reprecipitating and wash-

* From the Sheffield Laboratory of Physiological Chemistry, Yale University.