Medical parasitology

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SECOND EDITION

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Preface

This text, under a change in coauthorship, is the outgrowth of a manual developed by the senior author for the teaching of medical parasitology to medical students, technologists, and practicing physicians. It is not intended to replace more detailed texts but rather to serve as a guide for the student and to be supplemented with adequate lecture and laboratory instruction.

Study questions and references have been updated and enlarged generally. Significant corrections, changes, and additions have been made throughout, particularly in diagnosis and treatment. The use of photographs has been increased, and color plates depicting the malaria parasites have been added. The general format of dividing the material into the three major categories of medical protozoology, medical helminthology, and medical arthropodology has been maintained. As is common for all texts wherein information on treatment is presented, it must be kept in mind that new drugs and regimens almost certainly have been released since the revision has gone to press and therefore current literature should also be consulted. The appendixes have been greatly enhanced with numerous laboratory procedures and techniques that should prove useful to the laboratory technologist. The role of arthropods in world health and economy has been emphasized. A table depicting the important vector-born diseases, their etiologic agents, and the present and future prospects for methods of control has been added.

Grateful appreciation is expressed to The Medical Letter, Inc., 56 Harrison Street, New Rochelle, New York, for permission to use their extensive information on drugs for parasitic infections and infestations; to Mr. Charles M. Bailey, Department of Biomedical Communications, University of Miami, School of Medicine, for his assistance in photography; and to Miss Irene V. Wester for her patience and skill in typing the various drafts of the manuscript.

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Contents

CHAPTER 1

Introduction to medical parasitology

Medical parasitology is that branch of the medical sciences dealing with the members of the animal kingdom living in and on the body of humans and with aspects of this host-parasite relationship having medical significance. This science includes the study of vectors, reservoirs, definitive and intermediate hosts, and all factors of an ecologic and epidemiologic nature associated with disease transmission and prevention.

The parasites of medical importance may be divided into the following three major groups for convenience of study:

Protozoa—one-celled organisms
Helminths—worms
Arthropods—insects and their allies

As with most disciplines, parasitology also uses many terms unique unto itself. It is not advisable to learn all these terms at one sitting since their use in context, in most instances, will convey their meaning with greater clarity and impact. It is desirable, nevertheless, to become familiar with basic terms for purposes of early orientation. The *parasite* is the animal agent that parasitizes man, the *host*. Other parasitized animals that may serve as a source of infection for humans are called *reservoir hosts*. Some parasites are *obligatory* guests unable to survive outside a host, whereas others are *facultative* and capable of an independent existence outside the host. Those causing harm to the host are *pathogens*, whereas the harmless (nonpathogenic) species are known as *commensals*. The arthropods, living on the body surface no matter how brief a period of time, are called *ectoparasites*, whereas the protozoa and helminths living within the body are called *endoparasites*. The former cause *infestations* and the latter, *infections*. Confusion in terminology may exist in some instances wherein arthropods actually become endoparasitic. Fly larvae, for example, may live in the gastrointestinal tract in the same environment with the protozoa and helminths. In the opinion of some authors, such parasites cause an infection and are truly endoparasites.

Although parasites, in general, are more common in the tropics and subtropics than elsewhere in the world, they are by no means confined to these areas. Two chief reasons accounting for their prevalence in tropical climes are (1) the increased density of population as opposed to that in the temperate and frigid regions, and (2) poor sanitation and public health practice. The ability of suitable vectors, when involved in transmission, to propagate more readily and sometimes exclusively in such areas is also involved. In countries where malnutrition is widespread, the debilitated condition of large populations further enhances the indifference to sanitation. Thus, in an environment with very few factors detrimental to the survival and dissemination of parasites, the low level of sanitation ensures the widespread prevalence of the parasitic diseases.

In addition to poor sanitation and public

health practice, the prevalence of many parasitic diseases is aided and abetted by the customs, taboos, and habits of the people. This fact is especially pertinent for those disease agents transmitted in food and drink and by hand-to-mouth contamination. Thus, amebiasis, which is particularly prevalent wherever night soil (human feces) is used as fertilizer or where sewage contaminates drinking water, occurs not only in the tropics but also within the Arctic Circle. In areas where the schistosomes prevail, the habits of the natives, who use the same irrigation ditches or freshwater streams for the washing of clothes, bathing, and, all too frequently, urination and defecation, serve to keep infected the appropriate snail inhabitants that constitute a perennial source of reinfection for man. Trichinosis would no longer be a health menace in the United States (where it is not uncommon) if uncooked garbage was not fed to hogs, or if inadequately cooked pork products were no longer consumed.

Parasites that are well adjusted to their hosts live more or less in a state of "armed truce," benefiting from their association with a minimum of damage to their keepers. Tissue repair may keep pace with tissue damage, and in an otherwise healthy well-nourished person, no symptoms may be discernible. Some parasites may live as commensals at times, whereas under different circumstances they may become pathogenic, causing severe damage, even death, to the parasitized individual. Variations from host to host occur for a given parasite. Some parasites are harmless at all times, but their similarity in morphology to the pathogens makes their recognition imperative so that errors in diagnosis are avoided.

The adaptation of parasites to their hosts sometimes results in complicated pathways, both within and outside the human body. The route or course of a parasite followed from any one stage of development throughout its life history back to that same stage is known as its life cycle. The life cycle of a parasite consists of two essential parts, each important in its own right. Through an understanding of the route followed by a parasite within the human body from the time and site of entry until it makes its exit from the host we are led to an understanding of the symptomatology and pathology of the disease. Frequently the method of diagnosis and route of medication to be employed may be suggested. Knowing the whereabouts of the parasite outside the body is essential to an understanding of the epidemiology of disease and its prevention.

In medical parasitology, probably more than in the other medical sciences, the diagnosis of a disease will almost always depend on the laboratory findings. The incubation period, the time from infection to the first clinical manifestations of disease, is of concern to the physician; the prepatent period, the time when parasites can be first observed, is of importance to the laboratory diagnostician. Clinical signs and symptoms will, at best, be only suggestive of the cause of infection. Thus the laboratory diagnosis of the parasitic diseases of humans becomes, in reality, the chief and frequently the only method of diagnosis available. It has been said that the famous French police, the Sûreté Nationale, have as their motto *Cherchez la femme*—"Search for the woman"—and you will solve the crime. We may well paraphrase that by saying: "Search for the parasite" and you will diagnose the case. Parasites can and do occur in nearly every part of the human body and techniques specific to their particular location must be employed for their recovery. Less often, when recovery is impossible, other procedures must be resorted to in order to make a diagnosis.

The ultimate goal of the physician is to make the patient well. This task usually involves either complete eradication of the parasite or a reduction in its number. Unfortunately, most antiparasitic drugs, effective against the parasite, are also toxic to the host. Therefore the physician must carefully weigh

the disease entity against the treatment. Since the protozoa multiply within the host much as bacteria do, their complete eradication is usually necessary and treatment to this end must be employed. The worms, in contrast, usually do not increase their numbers per se, and symptoms and signs can frequently be controlled by a reduction in number so that unnecessary drug therapy is avoided. For example, one should distinguish between hookworm disease requiring medical treatment and hookworm infection that can be managed by diet rich in protein. During World War II many a G.I. was hospitalized and treated because hookworm eggs were found in his stool. He suffered unduly from the toxic drugs used in an attempt to rid him of every last worm, when, in fact, his military environment with its good diet and the wearing of shoes would have adequately resolved the problem.

REVIEW QUESTIONS

1. What are the three major branches of medical parasitology?
2. Give a broad definition of a parasite.
3. Why is the laboratory diagnosis of most parasitic diseases of humans so important?
4. What two factors determine the geographic distribution of parasites?
5. What is the significance of the life cycle of a parasite from a medical point of view?
6. What is the rationale behind the treatment of protozoa? Of helminths?

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PART ONE

Medical protozoology

CHAPTER 2

Introduction to the protozoa

The protozoa are single-celled animals comparable in function to multicellular animals and not to isolated cells from such organisms. Beneath the cell membrane lies the ectoplasm, which is more gelatinous in contrast to the relatively fluid inner endoplasm. Both are colloidal states of the cytoplasm, however, and are reversible. The nucleus or nuclei may be vesicular or compact, depending on the species. Vesicular nuclei contain nucleoplasm and one or more densely staining bodies called endosomes or karyosomes. Chromatin material may or may not be present adjacent to the inner wall of the nuclear membrane. Compact nuclei have solid chromatin material. Organelles may be present in protozoa in the form of cilia, flagella, pseudopodia, undulating membranes, kinetoplasts, etc., and function in various ways.

Protozoa vary in size, shape, and morphologic details and on these bases are divided into classes, orders, families, genera, and species.

The classes of medical importance are as follows:

Sarcodina—amebas
Mastigophora—flagellates
Ciliata—ciliates
Sporozoa—sporozoa

Parasites are also categorized according to the areas of the body invaded. Thus those found in the intestinal tract are known as intestinal protozoa; those found in the mouth, vagina, and urethra are known as atrial or, more specifically, oral and urogenital; those found in the blood and body tissues are blood and tissue protozoa.

GEOGRAPHIC DISTRIBUTION

Protozoa, in general, have a cosmopolitan distribution and may be found wherever humans make their homes. This range extends from the arctic wastelands to the torrid tropics. The majority of the species are found, and the greatest intensity of infection occurs, in the tropics and subtropics. Where vectors are involved, distribution may be quite restricted, as in the case of tsetses in the transmission of African sleeping sickness.

HOST-PARASITE RELATIONSHIP

The pathogenic protozoa are somewhat like bacteria in that they multiply within the host and, unless stopped by the defense mechanisms of the patient or by artificial means such as chemotherapy, they may eventually destroy the host. The onset of infection may be acute and fulminating, with sudden death, or never more than subclinical. A chronic state may follow clinical manifestations and may sometimes persist throughout the life of the host, being interrupted with exacerbations of the disease. The chronic state represents a kind of "armed truce" between host and parasite, each waiting for the opportunity to take advantage of a favorable situation. When the balance of power tips one way or the other, one becomes the victor, the other the vanquished, unless equilibrium is again reached. Thus, the protozoa vary in their pathogenicity from host to host and within a given

host from time to time. The majority of the intestinal protozoa live a benign existence, although some may, at times, produce a very severe disease and death. The blood and tissue parasites are pathogenic to a varying degree. Dissemination of the protozoa throughout the body is not uncommon, with foci of infections being established in various organs and tissues of the host. Some show no tissue specificity at all, whereas others tend to settle in certain organs or cells to the exclusion of others. Thus, symptomatology and pathology, in some instances, may be highly suggestive of the etiologic agent. The invasion of the posterior cervical lymph nodes by the African trypanosomes, for example, has given rise to "Winterbottom's sign," a sign of diagnostic value in African sleeping sickness.

Tissue response of the host varies among the protozoa. For example, little or no cellular reaction occurs with extraintestinal amebiasis, whereas hyperplasia of the reticuloendothelial system is seen in the leishmaniases. In contrast with the helminths, there is no eosinophilic response, though the number of circulating leukocytes may be changed; a leukopenia, for instance, is typical in kala-azar, whereas in extraintestinal amebiasis a leukocytosis may occur.

The nature of the immune response is varied and, in many instances, poorly understood. There appears to be a stronger natural immunity in blacks as compared with whites. This is exemplified in benign tertian malaria in which paroxysms, when present, are usually much milder. Immunity, in many instances, also seems to increase with age, the greater pathogenicity occurring in infants and children. Since protozoa multiply within the host and may remain present for as long as the life-span of the host, it is difficult to distinguish premunition (immunity resulting from the presence of parasites) from a sustained, acquired immunity resulting from an old infection. Some healthy individuals appear to be completely refractory to infection, as evidenced, for example, by the inability to establish *Entamoeba histolytica* by the oral feeding of viable cysts. In most, however, patency can be demonstrated even though the host response may vary from a subclinical infection to a fulminating case terminating in death. The state of health of the host has a marked effect on the immune response. Such factors as malnutrition, alcoholism, and debilitating diseases contribute to a breakdown in the immune mechanisms and greatly enhance the chances for successful establishment of infection. *Balantidium coli*, a parasite to which healthy individuals are highly immune, is almost nonexistent in the United States, where the general level of nutrition is high, among those exposed to this parasite, whereas in many of the undeveloped countries of the world balantidiasis is common.

LIFE CYCLES

Among the protozoa, life cycles are quite simple, with few exceptions. The intestinal and atrial protozoa multiply asexually by binary fission in the active feeding, growing, trophozoite stage. Encystation, when present, occurs by the extrusion of undigested food particles, loss of organelles such as flagella and cilia, and the secretion of a cyst wall, which protects the organism against adverse environmental influences. Various factors, such as a change in pH, O_2 tension; degree of dehydration, and inherent determinants, have been suggested as the cause of this phenomenon. Nuclear division may or may not take place in the cyst stage. Transmission to humans of the intestinal parasites occurs chiefly through the ingestion of contaminated food and drink; of the atrial forms, transmission occurs by droplet contamination and sexual intercourse. When present in the life cycle, cysts are the transmissible stage, being able to withstand adverse environmental changes outside the host as well as gastric acidity within the host.

The hemoflagellates are members of the same family and bear a close relationship

to one another. Of the four morphologic forms or stages that may be present, all species have at least one stage in an arthropod and another stage in human beings and reservoir vertebrate hosts, asexual reproduction by longitudinal division occurring in both. In one species, all four morphologic forms are present in the life cycle. The arthropod serves as the vector or carrier to human beings and other animals. Geographic distribution is thus determined by the ecology of the arthropod hosts.

The sporozoa are unique among the parasitic protozoa in that both asexual and sexual reproduction occurs. The definitive or final host harbors the sexual stages, and the asexual forms are found in the intermediate host. Various stages of growth are appropriately designated. Man may serve as both hosts, as in the case of some coccidia, or only the intermediate host, as in malaria.

REVIEW QUESTIONS

1. What is a vesicular nucleus? A compact nucleus? An organelle? Give examples of each.
2. What are the classes of protozoa of medical importance?
3. Discuss the nature of the host-parasite relationship of the protozoa in human beings.
4. How are most intestinal protozoa transmitted? Atrial protozoa? Hemoflagellates?
5. What is a definitive host? An intermediate host? Give an example of each.

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CHAPTER 3

The amebas (Sarcodina)

The following amebas are parasitic in humans:

Atrial (oral)
- *Entamoeba gingivalis*

Intestinal
- *Entamoeba histolytica*
- *Entamoeba coli*
- *Entamoeba polecki*
- *Endolimax nana*
- *Iodamoeba bütschlii*
- *Dientamoeba fragilis*

The amebas have often been described as naked bits of protoplasm. By means of protoplasmic extensions called pseudopodia the trophozoites are able to move on a substrate and engulf food. The nature of this movement, as in the case of *Entamoeba histolytica* is, at times, of diagnostic significance. Reproduction occurs by binary fission. When pathogenicity is associated with the organism, it is only the trophozoite stage that is involved. They are all cosmopolitan in distribution.

The trophozoite is a delicate, fragile organism readily destroyed by the gastric juice of the stomach and, among the intestinal forms, not transmissible to humans. When seen in the feces, it occurs most commonly in soft, mushy, poorly formed or watery stools. Flushing of the cecum by catharsis may result in the passage of these stages, when only cysts are seen in formed stool.

In a fresh saline mount, trophozoites are usually difficult to identify. Nuclei are not readily discernible without stains, and though motility characteristics and pseudopod formation are described in the literature as being of diagnostic value, many times there is an overlapping of characteristics among the species, making identification difficult (Table 1).

During the process of encystation the amebas pass through a period when many identifying characteristics of the trophozoite stage are lost and the diagnostic features of the cyst have not as yet made an appearance. These precyst forms are best identified after staining with iron-hematoxylin, trichrome, or other stains when nuclear detail may be studied.

Cysts are formed by shrinkage of the trophozoites as they assume the characteristic shape for that species. Inclusion bodies, such as undigested food particles, are extruded from the cytoplasm, and a protective cyst wall is secreted by the organism. Unorganized chromatoidal material in some young cysts may, as the cyst matures, become organized into bars of diagnostic significance. The number and morphology of nuclei formed as a result of nuclear division, in some instances, will aid also in the identification of cysts.

With the exception of *Entamoeba gingivalis*, which occurs in the mouth, the amebas are intestinal in habitat. Except for this ameba and *Dientamoeba fragilis*, which are known only in the trophozoite forms, all have trophozoite and cyst stages in their life cycles.

Excystation takes place in the ileocecal region of the intestine. The young trophozoites multiply rapidly and become established in the cecum. Eventually encystation

TABLE 1. Differential characteristics of trophozoites and cysts

	Entamoeba histolytica	*Entamoeba coli*	*Endolimax nana*	*Iodamoeba bütschlii*	*Dientamoeba fragilis*
Trophozoites					
Size	Small race, average 8μ Large race, average 15μ Dysentery, average 25μ	Average 20μ (12μ to 30μ)	Average 8μ (6μ to 12μ)	Average 10μ (6μ to 20μ)	Same as *I. bütschlii*
Motility	Actively progressive and directional sluglike forms (galloping ameba)	Sluggish, rarely progressive, nondirectional; rare, sluglike forms	Similar to *E. coli*	Similar to *E. coli*	Similar to *E. coli*
Pseudopodia	Fingerlike, explosive, clear and glasslike. In old specimens, similar to those of *E. coli*	Short blunt, broad, slow, less glasslike	Similar to *E. coli*	Similar to *E. coli*	Thin, veillike, leaflike with edges or sharp corners
Red blood cells	May be present	Never present	Never present	Never present	Never present
Cytoplasm	Clean appearance	Dirty appearance; bacteria, vacuoles, crystals, etc., present	Similar to *E. coli*	Similar to *E. coli*	Similar to *E. coli*, cytoplasm thin
Nucleus (unstained)	Usually invisible in saline solution	Visible in saline, grayish to black ring	Similar to *E. histolytica*	Similar to *E. histolytica*	Similar to *E. histolytica*
Nucleus (stained)	Delicate nuclear membrane, discrete, delicate chromatin granules on periphery; karyosome delicate, usually central	Thick, coarse nuclear membrane; thick, coarse coalescing chromatin granules on periphery; karyosome coarse, thick, usually eccentric	Nuclear membrane intermedial between *E. histolytica* and *E. coli*; no chromatin granules on periphery; karyosome large, central, or eccentric on periphery	Similar to *Endolimax nana*; karyosome surrounded by achromatic granules	Similar to *Endolimax nana*; karyosome divided into 4 to 6 distinct granules
Cysts					
Size	Small race, average 8μ Large race, average 12μ	Average 8μ	Average 8μ	Average 10μ	No
Shape	Spherical, sometimes oval	Similar to *E. histolytica*	Oval, sometimes spherical	Typically varied; round, oval, elliptical, rhomboidal, etc.	Cyst
Glycogen	Diffuse mass in center of young cysts; not heavy	Dense, large, well-defined mass in center of young binucleated cysts	None visible	Well-defined glycogen mass persistent throughout life of cyst	Stage
Volutin granules	None	None	None	Black granules in clusters usually present	Present
Nuclei	1 to 4 present; not visible in saline; same as trophozoites when stained but smaller	1 to 8 present; often visible in saline; same as trophozoite when stained but smaller	1 to 4 present; usually not visible in saline; same as trophozoite when stained but smaller	1 present; not visible in saline usually; same as trophozoite when stained but small and karyosome is eccentric, near nuclear membrane	
Chromatoid	Unorganized in young cysts; later formed into bars with rounded ends in older cysts; present in over 50% of cysts	Unorganized in young cysts; later formed into splinterlike sticks with ragged edges in old cysts; present in less than 10% of cysts	None diagnostic	None diagnostic	