MEDICAL PARASITOLOGY

Third Edition

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EDWARD K. MARKELL, Ph.D., M.D.
Department of Internal Medicine, Permanente Medical Group,
Kaiser Foundation Medical Center, Oakland, California;
Clinical Professor of Community and Preventive Medicine,
Stanford University School of Medicine, Palo Alto, California

MARIETTA VOGE, M.A., Ph.D.
Professor of Medical Microbiology,
Department of Medical Microbiology and Immunology,
School of Medicine, University of California, Los Angeles

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PREFACE TO THE THIRD EDITION

This edition of *Medical Parasitology* differs in a number of ways from earlier ones. The most obvious change, perhaps, is in the arrangement, which in former editions was by organ systems; in the present one it is taxonomic. The authors consider the organ system approach an excellent one for teaching purposes, but experience has convinced us that a text arranged in this manner is cumbersome for use in courses otherwise designed.

We have attempted to increase the book's usefulness to physician and student by including more clinical diagnostic material, such as x-rays and electrocardiograms, and an expanded section on pathogenesis and treatment. While this material may be of no direct interest to the laboratory technician, the section on methods has been revised with the technician primarily in mind. References have been inserted at the end of each chapter.

Several new disease entities have been described within the past few years, and the more important of these have been included.

A filmstrip has been prepared for optional use. It shows many of the organisms described, as seen in the diagnostic laboratory, and we hope it will be of special value to those whose access to slide material is limited. Mrs. Patricia E. Quinn very kindly located for us much of the material photographed.

We are especially grateful to our colleagues, Dr. Larry Ash, Dr. William Balamuth, Dr. Ralph Barr, Dr. Paul Basch, Dr.

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THE AUTHORS

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Chapter 1

INTRODUCTION

With the nearly simultaneous development of the antibiotic drugs, DDT and other insecticides, and various new antiparasitic agents, it was for a time widely believed that the infectious diseases would for all practical purposes disappear from the clinical scene. That this has not happened is obvious. Bacterial resistance appeared early; alterations in the normal bacterial flora, sometimes combined with iatrogenic modifications of host resistance, have resulted in the appearance of numbers of organisms in unfamiliar pathogenic roles. DDT and other insecticides not only have failed to eliminate the vectors of malaria, filariasis, and other parasitic diseases, but have themselves brought on problems too well known to require mention here. The development of resistance to the synthetic antimalarials has been an ominous occurrence in recent years. The increased mobility of large segments of the population exposes them to a largely undiminished threat of parasitic infection, and the speed of transportation insures that many will return to their native shores before their infections become patent. For this reason it remains necessary that all physicians have some familiarity with the parasitic diseases, no matter how "exotic."

With the ever-increasing pressure of a crowded medical curriculum, the time allocated to the study of protozoan, helminthic and arthropod parasites has been severely curtailed in many institutions. The same demands of an expanded technology have depleted the ranks of laboratory technologists with good training in the field of parasitology. The primary purpose of this book is to serve as a guide both to the clinical diagnosis and treatment and to the laboratory diagnosis of the protozoan and helminthic diseases of medical importance in this country, and to a lesser extent to the arthropods in relation to disease. We cannot limit ourselves to those organisms which are indigenous to this country or seen here with some frequency.

While intended primarily for the medical student and physician, it is hoped that this book will prove equally useful to the medical technologist and all others concerned with the laboratory identification of the animal parasites of man. The success of the cooperative diagnostic efforts of the physician and laboratory technologist depends upon a mutual appreciation of their several problems. In the chapters dealing with technical methods, the problems of the technologist are discussed; the physician will be better able to utilize his laboratory service if he understands them. The manner in which parasitic organisms are acquired, and how they produce disease in man, is perhaps of no direct importance to the technologist. Yet, a basic understanding of these matters should not only make the technologist's work more interesting, but also enable him to do it better and more efficiently.

A word of explanation should be given concerning the illustrations. They are largely original, and have been planned to emphasize points of diagnostic importance. The drawings which accompany the chapter on intestinal protozoa are all made at the same magnification, to facilitate a comparision of size ranges between different organisms, and within a single species. Structures not of importance from the standpoint of identification have been omitted from the majority of drawings, with the purpose of emphasizing those features to which especial attention should be paid. Nuclear structure is of great importance in the identification of many species of intestinal protozoa, but the variation which may be encountered is often a source of confusion. Drawings of nuclei alone, illustrative of the range of nuclear variation in the different species, have been included. These are not drawn to scale, but are all shown at the same size.

A series of transparencies has been prepared for supplemental use with this book. Its use is not mandatory, but it is hoped that they will help, particularly in situations where good laboratory reference materials are not readily available.

With reference to therapy for parasitic infections, it must always be borne in mind that any drug intended to disembarrass the host of his parasites does so on the basis of differential toxicity. That is to say that the antiparasitic agent is, hopefully, more toxic to parasite than to host. However, in some cases the margin is slim, and individual variation in host resistance may render it even slimmer. Frequently, toxic side effects are to be expected as the price of therapeutic effectiveness. It is to be hoped that, before treatment, the clinician will always ask himself whether the parasite is causing, or has a reasonable potential of causing, more trouble than may be anticipated from the treatment to be used. Treatment of certain parasitic diseases is changing almost as rapidly as that of the bacterial infections, and it is essential for the physician to keep abreast of the advances in this field. Review articles on this subject are seen occasionally in the medical journals, in such publications as the *Annual Review of Medicine, The Medical Letter on Drugs and Therapeutics,* and in the *Tropical Diseases Bulletin.* Under the title of "Current Concepts in Therapy," treatment of the parasitoses is considered from time to time in the *New England Journal of Medicine.*

A listing of some of the more important texts and monographs, written in English, is given at the end of this chapter. Some of the English language journals devoted to parasitology and tropical medicine are also listed. The *Tropical Diseases Bulletin* has already been mentioned. This monthly abstracting journal, published in England, is invaluable. It lists, under headings of the various etiological agents, the world-wide literature of tropical medicine, and publishes periodic summaries of work in certain fields as well as occasional comprehensive clinical reviews.

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Wilmot, A. J. 1962. *Clinical Amoebiasis.* 166 pp. Blackwell Scientific Publications, Oxford, England.

SOME JOURNALS WHOLLY OR IN PART DEVOTED TO MEDICAL PARASITOLOGY AND TROPICAL MEDICINE

American Journal of Tropical Medicine and Hygiene
Annals of Tropical Medicine and Parasitology
Current Therapy
Journal of Parasitology
Journal of Tropical Medicine and Hygiene
Journal of Tropical Pediatrics
Parasitology
The Medical Letter
Transactions of the Royal Society of Tropical Medicine and Hygiene
Tropical Diseases Bulletin

Chapter 2

PARASITES, PARASITISM AND HOST RELATIONS

In view of the tremendous numbers and diversity of living things, and the varied circumstances of their existence, it is not surprising that they should obtain their nourishment in many different ways. These various methods have basic similarities, so that frequently it is difficult to draw a firm line between one method of nutrition and another. Many terms have been devised to describe the relationships which exist between different kinds of plants and animals, at the fundamental food-seeking or food-supplying level. These terms are not always used by everyone to denote the same thing, with the result that they may lead to confusion rather than clarity. We need not concern ourselves here with many terms which have been created to designate slight differences in relationship, and shall adopt somewhat rigid definitions of those which we do consider. However, it must be emphasized that any one organism may at different times exhibit different nutritional habits, or at the same time obtain its nutriment in more than one way. *If a definition is helpful in the understanding of a biological process, it is worthwhile, but it should never be allowed to channel or limit one's ideas.*

In a consideration of the major nutritional relationships between different species, we will limit ourselves to those involving different kinds of animals, with the understanding that much, but not all, of what is said may be extended to cover animal-plant interrelationships as well. Fundamentally, there are two different ways in which an animal may obtain food at the expense of other animals. It may attack another living animal, consuming part or all of its body for nourishment, and in the process frequently but not necessarily killing it. This process is known as *predation;* the attacker is the predator and the victim the prey. Or an animal may derive its nutrition from already dead animals, either devouring those dead of natural causes or taking the leavings of a predator. Animals which subsist in this manner are known as *scavengers.* Some animals are pure predators, others pure scavengers, but many predators are not averse to an occasional bit of scavenging. Some animals always seek their food by their own efforts, or in association with others of their own species. This is the most conspicuous and perhaps the most common way in which animals go about obtaining food; it is this large group to which we commonly refer when we speak of scavengers and predators.

Other animals, still in essence predators or scavengers, have become so modified that they are unable to obtain food except in close association, either continuous or at intervals, with members of another species. This association of two species, perhaps primarily for food-getting on the part of one or both members of the group, is known as *symbiosis.** Symbiosis means literally "living together" and may also involve protection or other advantages to one or both partners. Different forms of symbiosis may be distinguished, on the basis of whether or not the association is detrimental to one of the two partners. *Commensalism,* from the Latin for "eating at the same table," denotes an association which is beneficial to one partner and at least not disadvantageous to the other. A specialized type of commensalism, known as *mutualism,* is seen where such associations are beneficial to both organisms. *Parasitism,* on the contrary, is a symbiotic relationship in which one animal, the host, is to some degree injured through the activities of the other animal, the parasite. Parasitism, like other forms of symbiosis, necessarily involves an intimate relationship between the two species, and it is this close and prolonged contact which differentiates parasitism from the predatory activities of many non-parasites.

Parasitism as a way of life may be the only possibility for a given organism, or it may be but one alternative. An organism which cannot survive in any other manner is called an *obligate parasite.* A *facultative parasite* is an organism which may exist in a free-living state, or as a commensal, and if opportunity presents itself may become parasitic. It is implicit in this term that the organism does not of necessity have to be a parasite at any stage of its existence. Some animals are obligatory parasites at one or more stages of their life cycles, but free-living at others. The term "temporary parasite" is sometimes applied to such animals. Parasites living within the host may be distinguished as *endo-*

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*The definitions given here for symbiosis, commensalism and mutualism differ from those used by many authors. However, they conform to the recommendations of the Committee on Terminology of the American Society of Parasitologists.

parasites, while those which are found upon the surface of the body are called *ectoparasites.*

Small organisms, such as mosquitoes, which must periodically seek out other and larger forms on which to nourish themselves, have occasionally been called "intermittent parasites." This unhappy use of the term "parasite" comes from the assumption that a predator must be larger and stronger than its prey, whereas a parasite is small and weak. This generalization is certainly true of most predators and parasites, or at least of the most obvious ones. However, the essence of the parasitic relationship, which separates it from predation, is the protracted and intimate association between parasite and host. The association between the mosquito and its victim is neither prolonged nor intimate. Cameron (1956) refers to those blood-sucking arthropods which lead an independent existence except for occasional nutritional forays as micropredators.

Many organisms customarily considered to be parasites are actually commensals. *Entamoeba coli* lives within the lumen of the intestine, subsists there upon the bacterial flora of the gut, and does its host no appreciable harm. This is a symbiotic relationship in which no advantage or disadvantage accrues to the host, whereas the ameba is supplied with food and protected from harm. Other cases are less definite. There is considerable controversy over the question of whether *Entamoeba histolytica* is at all times parasitic or if it can at times have a purely commensal relationship with its host.

Adaptations to Parasitism

The parasitic relationship probably evolved very early in the history of living organisms. We know little about how such relationships arose, but may hypothesize that we can see in the facultative parasite one possible initial step along the road to obligate parasitism. The possibility of the adaptation of a parasitic mode of existence may depend upon what is known as "pre-adaptation," or evolutionary changes which make possible existence in an environment otherwise unsuitable. Such pre-adaptive changes might be in the nature of increased resistance to the enzymatic activities of the host. Further physiological adaptations to parasitism might involve the loss of enzymes or enzyme systems which are then supplied by the host. Such losses may be expected to make a parasitic or at least symbiotic relationship obligatory.

Certain groups of parasites exhibit profound morphological adaptations to their way of life. As might be expected, these modifications are more striking in those groups which are wholly parasitic than in those containing both free-living and parasitic species. Organs not necessary to a parasitic existence are frequently lost. The only class of Protozoa which contains nothing but parasitic forms is the Sporozoa. Members of this class have no locomotor organelles, although these structures are present in one form or another in all other classes of Protozoa, even in their parasitic representatives. Most of the free-living turbellarian flatworms are provided with a ciliated epidermis in the adult stage. Cilia are not found on the parasitic members of this group, or on the related, but strictly parasitic, trematodes and cestodes. A digestive tract, of moderate complexity in the turbellarians, is generally reduced in the trematodes and is absent in the cestodes. The reproductive system is very highly developed in the two latter groups; this seems a reflection of the difficulties inherent in transfer of these organisms to new hosts. Specialized attachment organs in the form of suckers and hooks have been developed in the parasitic flatworms. Body size may be greatly affected by the parasitic state. Although we think of parasites as small organisms, many of them are much larger than their free-living relatives. The majority of free-living turbellarians are under half a centimeter in length, and while some land planarians may reach a half meter, none approaches the length of 10 meters or more seen in some tapeworms. Most free-living nematodes barely attain naked-eye visibility as adults, but *Ascaris* can reach 35 cm. and *Dracunculus* as much as a meter in length.

Specialized mechanisms for effecting entrance into the body or tissues are seen in some parasites. *Entamoeba histolytica* elaborates a proteolytic enzyme which aids its penetration of the intestinal mucosa. No such enzyme has been found in the commensal *E. coli.* The cercarial stage in the life cycle of the blood fluke is able to penetrate through the skin of man to produce infection. This it does with the aid of penetration glands which produce an enzyme capable of digesting the skin. The embryo of *Hymenolepis nana,* before developing into a cysticercoid larva, penetrates an intestinal villus with the help of the six hooklets which it bears.

Increased reproductive capacity has been already mentioned as characterizing two parasitic groups in contrast to their free-living relatives. Most metazoan parasites exhibit such an increase, which in some cases involves larval stages as well as adults. The chances of a particular ovum successfully infecting a new host are usually very small, and if more than one host species is involved, the chance of successful completion of the cycle becomes still smaller. If a parasite is successful in infecting an intermediate host, it is obviously advantageous if the larval stage which develops there can multiply to produce many additional organisms, capable of infecting the definitive or a second intermediate host. Such a modification is seen in the trematodes and many of the cestodes, where a single ovum develops in the intermediate host into a larva which in turn produces many larvae of a more advanced kind.

Effects of Parasites upon the Host

A parasite, by definition, is an organism which to some degree injures its host. However, we have already found that many organisms which are loosely termed parasites are in reality commensals. (Some may be at times truly parasitic and at other times commensal in their relationship to the host) In many instances it cannot be said with certainty whether or not an organism injures the host. Even if we can be fairly sure that some injury is produced, we may not be able to detect it. Thus a distinction is made between hookworm disease and hookworm infection, on the basis of the presence or absence of clinical symptoms. Overt symptoms of infection with this parasite may depend upon the number of worms present, upon the nutritional status of the host or both.

Injury to the host may be brought about in a wide variety of ways. Some of these mechanisms are common to all parasites, even if this term is used in its broad sense to include bacteria, viruses and fungi. The most widespread type of injury is that brought about by interference with the vital processes of the host, through the action of secretions, excretions or other products of the parasite. Such interference is probably largely or exclusively on the level of the host enzyme systems. Parasites producing such effects may be in the tissues or organs of the host, in the blood stream, within the gastrointestinal tract, or may even be ectoparasitic. Invasion and destruction of host tissue may be distinguished from injury which does not involve gross physical damage, although both types of injury reflect biochemical changes brought about in the host tissue by the parasites. When the giant intestinal fluke, *Fasciolopsis buski,* is present in large numbers, absorption from the intestinal tract of its secretions and excretions may lead to severe toxicity. *Entamoeba histolytica* erodes the intestinal wall, destroying the tissues locally by means of a proteolytic enzyme. Malarial parasites invade and multiply in red blood cells, which are destroyed in the process. The helminth parasites, by virtue of their size, may damage the host in other ways impossible for the smaller parasites. In addition to its toxic effects, *Fasciolopsis buski* may produce severe local damage to the intestinal wall by means of its powerful suckers. *Ascaris* may perforate the bowel wall, cause intestinal obstruction if present in large numbers, and invade the appendix, bile duct or other organs. Some parasites exert their effects by depriving the host of essential substances. Thus hookworms suck blood, and by so doing may deprive the host of more iron than is replaced by his diet, and so bring about an anemia. The broad fish tapeworm, *Diphyllobothrium latum,* selectively removes vitamin B_{12} from the alimentary tract, producing a megaloblastic anemia in some infected persons.

Effects of the Host on the Parasite

The effects of the parasite on the host are more obvious than those which operate in the reverse direction, but the latter are nonetheless important. The genetic constitution of the host may profoundly influence the host-parasite relationship. It is now well known that there are racial variations in resistance to certain strains of *Plasmodium vivax*. There is also considerable evidence which suggests that possession of the sickle cell trait, an inherited characteristic, is also associated with increased resistance to infection with the malarial parasite, *P. falciparum*.

The diet or nutritional status of the host may be of major importance in determining the outcome of a parasitic infection (Frye, 1955). A high protein diet has been found to be unfavorable for the development of many intestinal protozoa, while a diet low in protein was shown by Elsdon-Dew (1953) to favor the appearance of symptoms of amebiasis and the complications of this disease. It has been shown that a carbohydrate-rich diet favors the development of certain tapeworms, and the presence of carbohydrate in the diet is known to be essential for some of these worms. The general nutritional status of the host may be of considerable importance both in determining whether or not a particular infection will be accompanied by symptoms and in influencing their severity if present. Major nutritional disturbances may influence resistance through their effects upon the immune mechanisms of the host.

While the fundamental immune processes are generally considered to be the same in infection with the animal parasites as in bacterial, viral and mycotic infections, the details are much better known for bacteria and viruses than for the larger forms. Every species of animal is naturally resistant to infection with many organisms which parasitize different species. As we have seen in the case of certain strains of malaria, resistance may also be a racial phenomenon. In some cases it has been possible to adapt parasites to hosts which they normally infect poorly, or not at all. This does not necessarily involve changes in the host's natural resistance, but rather changes in the parasite. Acquired immunity can be demonstrated in many parasitic diseases. This is generally found to be at a lower level than that produced by bacteria and viruses. Absolute immunity to reinfection, such as is generally seen following infection with smallpox, measles, whooping cough and a number of other viral and bacterial diseases, occurs but rarely following protozoal infections and probably never with helminth infections of man. Primary infection with *Leishmania* seems to confer a degree of immunity to reinfection. While many protozoal and helminthic infections confer no long-lasting immunity to reinfection, they do seem to stimulate resistance during the time that