6th EDITION

MEDICAL PARASITOLOGY

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DEDICATION

Marietta Voge

Marietta Voge, co-author of the first five editions of *Medical Parasitology,* died in July, 1984, on the eve of her 66th birthday. She was preparing to retire from teaching at the University of California, Los Angeles, and had begun work on the present revision of this book.

Marietta was born in Jugoslavia, and she attended school in Switzerland before coming to the United States at the end of World War II. She subsequently became a naturalized U.S. citizen, graduated from the University of California, Berkeley and received her Ph.D. from that institution in 1950. In 1951, she moved to Los Angeles, and soon joined the faculty of the newly organized medical school at UCLA. Early demonstrating her unusual abilities as a teacher, she attracted a distinguished group of graduate students and post-doctoral fellows. Married to a teacher of Slavic languages, she had one son, who now resides in Japan.

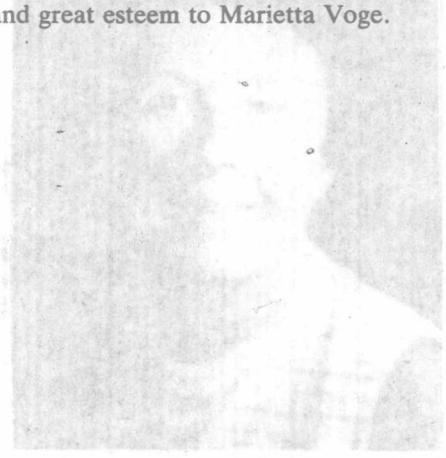
Her research interests centered on the tapeworms. An authority on the systematics of hymenolepid cestodes, she also became involved in the cultivation of cestodes *in vitro,* and in the use of scanning electron microscopy in the study

of developmental changes in cestodes and schistosomes. Marietta was also an accomplished lapidarist and gemologist, pianist, short-story writer, painter, gardener, linguist and world traveler. Her travels took her to such places as the interior of Papua New Guinea, where she lived for some months as the only white person in an isolated native village, to Kenya for a sabbatical year, on several occasions to Egypt and the near East, to Sri Lanka, to China at the invitation of the government of the People's Republic with a Schistosomiasis Delegation in 1975 and throughout South and Central America and Mexico.

It was in Marietta's 80-year-old home, a few miles from the UCLA campus, that the various aspects of her multifaceted life came together. There she had her grand piano, and against walls on which hung a Miró and a Chagall leaned in recent years an ever-changing selection of her own art, ranging from earlier fanciful sketches, mainly of birds, to more recent still lifes and nudes. On the overfilled bookcases rested specimens of her lapidary work, minerals and (perhaps in an old slidebox) beautifully cut gemstones, as well as artifacts from all over the world. Books and papers were scattered in unruly profusion, and in and out—in what often seemed a perpetual open house—moved colleagues and students from the university, fellow art students, musicians and visitors from all over the world.

With the hope that it will live up to her expectations, this book is dedicated with love and great esteem to Marietta Voge.

E.K.M.



FOREWORD

After publication of the Fifth Edition of this book, Marietta Voge and I decided that we would undertake the next edition (this one) ourselves, but that it would then be time to think about adding one or more co-authors. We also considered it desirable that one such co-author have research interests in protozoology, as both of us were primarily helminthologists. With the untimely death of Doctor Voge, that schedule has had to be revised.

Doctor David John has undertaken the revision of most of the protozoology, and of the entomology sections of this edition. His own introduction to human parasitology was through the First Edition of this book. In addition to his training in general and human parasitology and his research interests in protozoology (primary amebic meningoencephalitis), he has a background in public health. He taught at the Medical College of Virginia before assuming his present position. Like Doctor Voge, he is a devotee of the scanning electron microscope, and one of his SEMs adorns the cover, as hers do the end pages of this book. A welcome collaborator, he adds depth to our coverage.

E.K.M.

PREFACE

It seems that an approximate 5-year cycle has become established for revision of this text. No sweeping changes have been made in this edition, but we have tried to give increased emphasis to epidemiology, immunology and to the mechanisms of disease production and of drug action. A rather large number of new illustrations have been added, as well as two new color plates. The somewhat awkward tables, which in the two previous editions showed distribution of the more important parasitic diseases, have been replaced by maps which we hope will better serve the same purpose. These are intentionally grouped together, so that the clinician, knowing his patient's travel history or plans, may quickly review the possibilities of parasitic disease, either from the aspect of therapy or that of prevention.

As in previous editions, a fairly extensive list of references follows each chapter. Growing with each edition, the reference list would have become unmanageable had we not arbitrarily chosen to eliminate most of those prior to 1979. Even so, their number has increased. We hope that they will prove helpful to the clinician faced with a difficult diagnostic or therapeutic problem, or to those with special interests which cannot be fully pursued in a text such as this.

It is an unfortunate fact that a number of parasitic diseases have acquired new prominence because of their association with the acquired immunodeficiency syndrome (AIDS). Medical students and physicians, as well as other medical professionals such as nurse practitioners, medical technologists and public health personnel, must have a basic understanding of the diagnosis, prevention and treatment of these and other human parasitic infections. The aim of this book has been, and continues to be, to provide such fundamentals.

We are indebted to the many people who have helped with this and previous editions. Our special thanks to Drs. Lawrence Ash, Ralph Barr, Paul Basch, Jack Frenkel and Jerrold Turner.

Our wives, Nancy Markell and Rebecca John, have helped with typing, proofreading and preparing the index, but more importantly they have been a constant source of encouragement and steadfast support, for which we are deeply grateful.

The staff of the W. B. Saunders Company, and especially Mr. Baxter Venable, Mr. Robert Butler, Ms. Susan Colaiezzi-Short and Ms. Margaret Shaw, have been as always most considerate and helpful.

THE AUTHORS

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INTRODUCTION

With the nearly simultaneous development of the antibiotic drugs, the synthetic pesticides 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. Refugees from many war-torn areas have brought with them infections seldom encountered by physicians in North America and Europe. For these reasons it remains necessary that all physicians have some familiarity with the parasitic diseases, no matter how "exotic."

Modifications of the environment, as typified by construction of the Aswan Dam and the Transamazon Highway in Brazil, have brought about major increases in parasitic disease. Flooding of vast areas with the creation of Lake Nasser has resulted in new habitats for the snail hosts of schistosomiasis and a tremendous upsurge in incidence of that disease, brought in by infected construction workers. Building the Transamazon Highway necessitated the importation into the area of large numbers of susceptible laborers, causing them to be exposed to enzootic diseases of the area, notably leishmaniasis. It behooves us to consider the impact of such projects upon the ecology before rather than after the damage is done.

A very significant development of the past few years has been the appearance of the acquired immunodeficiency syndrome (AIDS), primarily affecting male homosexuals but with evidence of increasing spread into the heterosexual community as well. This highly lethal condition results in greatly increased prevalence and severity of a number of parasitic, viral and bacterial diseases.

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, and to a lesser extent to the arthropods in relation to disease.

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 humans. 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 the laboratory service if he or she 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 or her 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 that accompany the chapter on intestinal protozoa are all made at the same magnification, to facilitate a comparison of size ranges between different organisms and within a single species. Structures not important from the standpoint of identification have been omitted from the majority of drawings, with the purpose of emphasizing those features to which special 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.

With reference to therapy for parasitic infections, it must always be borne in mind that most drugs intended to disembarrass the host of his parasites do so on the basis of differential toxicity. That is to say that the antiparasitic agent is, one hopes, 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 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 etiologic agents,

the worldwide literature of tropical medicine and publishes periodic summaries of work in certain fields as well as occasional comprehensive clinical reviews.

TEXTS AND MONOGRAPHS

Adams, A. R. D., and Maegraith, B. G. 1980. *Clinical Tropical Diseases*. 7th Ed. 621 pp. Blackwell Scientific Publications, Oxford.

Ash, L. R., and Orihel, T. C. 1984. *Atlas of Human Parasitology*. 2nd Ed. 212 pp. Am. Soc. Clin. Pathol., Chicago.

Beaver, P. C., Jung, R. C., and Cupp, E. W. 1984. *Clinical Parasitology*. 9th Ed. 825 pp. Lea & Febiger, Philadelphia.

Binford, C. H., and Connor, D. H. (Eds.) 1976. *Color Atlas of Tropical and Extraordinary Diseases*. Vols. I and II. Armed Forces Institute of Pathology, Washington, D.C.

Brown, H. W., and Neva, F. A. 1983. *Basic Clinical Parasitology*. 339 pp. Appleton-Century-Crofts, Norwalk, Connecticut.

Brown, W. J., and Voge, M. 1982. *Neuropathology of Parasitic Infections*. 240 pp. Oxford University Press, Oxford.

Bruce-Chwatt, L. J. 1980. *Essential Malariology*. 354 pp. William Heinemann, London.

Campbell, W. C. 1983. *Trichinella and Trichinosis*. 581 pp. Plenum Press, New York.

Ciba Foundation. 1974. *Parasites in the Immunized Host: Mechanisms of Survival*. Ciba Foundation Symposium 25 (new series). 280 pp. Associated Scientific Publishers, Amsterdam.

Ciba Foundation. 1974. *Trypanosomiasis and Leishmaniasis with Special Reference to Chagas' Disease*. Ciba Foundation Symposium 20. 353 pp. Associated Scientific Publishers, Amsterdam.

Cohen, S., and Warren, K. S. (Eds.) 1982. *Immunology of Parasitic Infections*. 2nd Ed. 848 pp. Blackwell Scientific Publications, Oxford.

Erlandsen, S. L., and Meyer, E. A. (Eds.) 1984. *Giardia and Giardiasis*. 407 pp. Plenum Press, New York.

Flisser, A. K. W., Laclette, J. P., Larralde, C., Ridaura, C., and Beltran, P. (Eds.) 1982. *Cysticercosis: Present State of Knowledge and Perspectives*. 700 pp. Academic Press, New York.

Frazier, C. A. 1969. *Insect Allergy: Allergic Reactions to Bites of Insects and Other Arthropods*. 493 pp. Warren H. Green, Inc., St. Louis, Missouri.

Garcia, L. S., and Ash, L. R. 1979. *Diagnostic Parasitology. Clinical Laboratory Manual*. 2nd Ed. 174 pp. C. V. Mosby Company, St. Louis, Missouri.

Garnham, P. C. C. 1966. *Malaria Parasites and Other Haemosporidia*. 1114 pp. Blackwell Scientific Publications, Oxford.

Isliker, H., and Schürch, B. 1981. *The Impact of Malnutrition on Immune Defense in Parasitic Infestation*. 199 pp. Hans Huber Publishers, Berne, Switzerland.

James, M. T., and Harwood, R. F. 1979. *Entomology and Human and Animal Health*. 7th Ed. 548 pp. Macmillan, New York.

Katz, M., Despommier, D. D., and Gwadz, R. W. 1982. *Parasitic Diseases*. 264 pp. Springer-Verlag, New York.

Kean, B. H., Mott, K. E., and Russel, A. J. (Eds.) 1976. *Tropical Medicine and Parasitology. Classic Investigations*. Vols. I and II. Cornell University Press, Ithaca, New York.

Kim, C. W., Ruitenberg, E. J., and Teppema, J. S. (Eds.) 1981. *Trichinellosis*. 433 pp. Reedbooks, Ltd., Chertsey, Surrey, England.

Kreier, J. P. (Ed.) 1980. *Malaria*. Vols. I, II, III. Academic Press, New York.

Malek, E. A., and Cheng, T. C. 1974. *Medical and Economic Malacology*. 398 pp. Academic Press, New York.

Manson-Bahr, P. E. C. and Apted, F. I. C. 1982. *Manson's Tropical Diseases*. 18th Ed. Williams & Wilkins, Baltimore.

Martinez-Palomo, A. 1983. *The Biology of Entamoeba histolytica*. 161 pp. John Wiley & Sons, Inc., New York.

Molyneux, D. J., and Ashford, R. W. 1983. *The Biology of Trypanosoma and Leishmania Parasites of Man and Domestic Animals*. 274 pp. Taylor and Francis, London.

Mostofi, F. K. 1967. *Bilharziasis*. 357 pp. Springer-Verlag, New York.

Muller, R. 1975. *Worms and Disease. A Manual of Medical Helminthology*. 161 pp. William Heinemann, London.

Mulligan, C. H. W. (Ed.) 1970. *The African Trypanosomiases*. 950 pp. George Allen and Unwin Ltd., London.

Peters, W., and Gilles, H. M. 1981. *A Color Atlas of Tropical Medicine and Parasitology*. 2nd Ed. 400 pp. Year Book Color Atlas Series, Year Book Medical Publishers, Inc., Chicago.

Reeder, M. M., and Palmer, P. E. S. 1981. *Radiology of Tropical Diseases with Epidemiological, Pathological and Clinical Correlation*. 1030 pp. Williams & Wilkins, Baltimore.

Ristic, M., and Kreier, J. P. (Eds.) 1981. *Babesiosis*. 589 pp. Academic Press, New York.

Strickland, G. T. (Ed.) 1984. *Hunter's Tropical Medicine*. 6th Ed. 1057 pp. W. B. Saunders Co., Philadelphia.

Symposium on the Kidney and Parasitism. 1979. Kidney International, *16*:1–74.

Warren, K. S., and Mahmoud, A. A. F. 1984. *Tropical and Geographical Medicine*. 1175 pp. McGraw-Hill Book Co., New York.

Yamaguchi, T. (Ed.) 1981. *A Colour Atlas of Clinical Parasitology*. 296 pp. Lea & Febiger, Philadelphia.

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
Experimental Parasitology
Journal of Parasitology
Journal of Tropical Medicine and Hygiene
Journal of Tropical Pediatrics
Parasite Immunology
Parasitology
Parasitology Today
The Medical Letter
Transactions of the Royal Society of Tropical Medicine and Hygiene
Travel Medicine International
Tropical and Geographic Medicine
Tropical Diseases Bulletin
Tropical Doctor

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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 that 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 that have been created to designate slight differences in relationship, and shall adopt somewhat rigid definitions of those that 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 biologic 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 shall 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, 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 that 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 that is beneficial to one partner and at least not disadvantageous to the other. A specialized type of commensalism, known as *mutualism*, is seen when 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 that 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 that cannot survive in any other manner is called an *obligate parasite*. A *facultative parasite* is an organism that may exist in a free-living state or as a commensal and that 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 *endoparasites*, while those that 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. Those blood-sucking arthropods, which lead an independent existence except for occasional nutritional forays, may be referred to 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 parasitic at all times or whether at times it can 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 we 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 that make possible existence in an environment otherwise

*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.

unsuitable. Such pre-adaptive changes might be in the nature of increased resistance to the enzymatic activities of the host. Further physiologic 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 morphologic adaptations to their way of life. As might be expected, these modifications are more striking in those groups that are wholly parasitic than in those that contain both free-living and parasitic species. Organs not necessary to a parasitic existence are frequently lost. The only group of protozoans that contains nothing but parasitic forms is the phylum Apicomplexa. Members of this phylum have no locomotor organelles, although these structures are present in one form or another in all other phyla 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.

On a more basic level, the parasitic mode of existence may result in profound biochemical changes. An excellent discussion of this subject is given by Meshnick and Cerami (1984). One of the most significant adaptations involves the loss of certain metabolic pathways common to free-living organisms, a process aptly referred to as "streamlining." The parasite, no longer able to synthesize certain necessary cellular components, obtains them instead from its host. Profound differences between metabolic pathways in parasite and host characterize the Kinetoplastida (*Leishmania* and *Trypanosoma* species in man), *Entamoeba histolytica, Giardia lamblia* and *Trichomonas vaginalis*, as well as most if not all of the helminth parasites. These metabolic differences between parasite and host may afford opportunity for strategic chemotherapeutic efforts, as will be seen later.

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. It does this 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 that it bears.

Once within the host's body, the parasite is subject to those defense mechanisms mobilized in the immune response. Continuance of a parasitic relationship depends upon how successfully the immune response of the host is overcome. Many different defense mechanisms have been evolved, and these will be discussed in consideration of the individual parasites. Immune evasion may involve such

factors as location of the parasite in relatively protected sites, changes in the parasite surface antigenic structure brought about in a variety of ways, and active modification of the host immune response by products of parasite metabolism (David, 1984).

Increased reproductive capacity has already been mentioned as characterizing two parasitic groups in contrast with 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 egg 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 that 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 egg 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 that 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 truly parasitic at times 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 or within the gastrointestinal tract, or they may even be ectoparasitic. Invasion and destruction of host tissue may be distinguished from injury that 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, toxic symptoms are seen, but their precise etiology is unknown. *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 that 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 *Plasmodium vivax*, which are related to the presence or absence of the Duffy blood group. There is also considerable evidence that suggests 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. A high protein diet has been found to be unfavorable for the development of many intestinal protozoa, while a diet low in protein has been shown 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 that 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 re-infection, 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. As yet no useful vaccines have been developed for protozoal or helminthic infections. 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 re-infection, they do seem to stimulate resistance during the time that the parasites are still in the body. This resistance to hyperinfection is known as premunition. Premunition may be of great importance in endemic areas in limiting the extent of infection with plasmodia, hookworms and other parasites.

In recent years, exciting new areas of research have dealt with the role of eosinophils in killing young schistosomes and microfilariae, the ability of older schistosomes to induce immunosuppression in the host, the discovery of host-like antigens on the surface of some parasites, and the phenomenon of antigenic variation in trypanosomes.

There is also increasing evidence of the importance of the "secretions and excretions" of protozoa and helminths as antigenic substances stimulating host resistance. In *Trypanosoma lewisi* infections in rats, the metabolic products of the parasites are more effective in producing immunity than are the dead trypanosomes themselves. Various immunologic tests have been devised based on the ability of