Essentials of Medical Parasitology
SECOND EDITION
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Apurba S Sastry MD DNB MNAMS PDCR
Hospital Infection Control Officer
Officer in-charge HICC
Antimicrobial Stewardship Lead
Associate Professor
Department of Microbiology
Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India

Sandhya Bhat MD DNB MNAMS PDCR
Professor
Department of Microbiology
Pondicherry Institute of Medical Sciences (PIMS)
(A Unit of Madras Medical Mission)
Puducherry, India

Co-Editor
Debadutta Mishra MD, Fellow (Parasitology)
Ex Senior Resident
Department of Microbiology
JIPMER, Puducherry, India

Forewords
Lynne S Garcia MS CLS FAAM
Author of the famous book ‘Textbook of Diagnostic Parasitology’
Sujatha Sistla MD
Professor and Head, Department of Microbiology, JIPMER, Puducherry, India

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It is a proud moment to announce the release of the second edition of *Essentials of Medical Parasitology*. The first edition was widely appreciated among faculty and students. The second edition has also been designed in a similar fashion taking all your feedback and suggestions into consideration. The newer concepts and recent advances incorporated are as follows:

**Chapter 1 (General Introduction to Parasitology):** Updates on newer antiparasitic drugs with their mechanism of action have been added in this chapter.

**Chapter 2 (Introduction to protozoa):** Taxonomic classification of protozoa has been updated. Changes in nomenclature of parasites have been included.

**Chapter 3 (Amoeba):** Updates such as *Entamoeba bangladeshi*, latest diagnostic methods for *E. histolytica*, update on pathogenesis of *E. histolytica*, and recent advances in laboratory diagnosis and treatment of free-living amoebae have been incorporated. Newer free-living amoebae such as *Sappinia pedata, Vahlkampfia, Hartmannella* and *Paravahlkampfia* have been included. Many controversies have been resolved such as possible role of immature cyst of *E. histolytica* in transmission of infection and possible association of *E. bangladeshi* and *E. moshkovskii* with intestinal amoebiasis.

**Chapter 4 (Intestinal and genital flagellates):** In giardiasis, recent updates in genotyping, pathogenesis, epidemiology, laboratory diagnosis, treatment and drug resistance have been included. Many interesting changes have been incorporated such as existence of pseudocyst in *Trichomonas vaginalis*, InPouch TV diagnostic system for culturing *T. vaginalis*, virulence factors of *T. vaginalis*, existence of cyst in *Dientamoeba fragilis*, updates in laboratory diagnosis and treatment in *T. vaginalis* and *D. fragilis*.

**Chapter 5 (Hemoflagellates):** Leishmaniasis underwent a major update. Epidemiology has been thoroughly updated. Clinical Features and laboratory diagnosis of visceral leishmaniasis have been revised. Treatment regimens of all types of leishmaniasis have been updated according to WHO guideline. Note on leishmaniasis elimination program and vaccination strategies has been incorporated. Trypanosomiasis has been updated with recent advances in laboratory diagnosis, epidemiology and clinical manifestations.

**Chapter 6 (Malaria parasite and Babesia):** Updates have been made in topics such as *Plasmodium knowlesi*, epidemiology of malaria, malaria elimination in India, advances in laboratory diagnosis such as quantification of malaria parasites, RDT under NVBDCP, molecular methods, automated systems, advances in treatment of vivax and falciparum malaria according to NVBDCP guideline, antimalarial drug resistance and its mechanism, and geographical distribution, prophylaxis against malaria including malaria vaccine strategies and trials (WHO, 2018) with a special note on RTS, S/AS01 vaccine. Babesiosis has been revised with incorporation of updates in laboratory diagnosis and treatment.

**Chapter 7 (Opportunistic Coccidian parasites):** *Toxoplasma gondii* has been thoroughly updated in pathogenesis including *Toxoplasma* encephalitis, life cycle, laboratory diagnosis with a special emphasis on diagnosis of congenital toxoplasmosis and update on IgG avidity test. *Cryptosporidium* has been revised with interesting facts such as *C. hominis* as human pathogen rather than *C. parvum*, recent advances in pathogenesis and laboratory diagnosis. The recent change of nomenclature of *Isospora* to *Cystoisospora* has been incorporated. *Sarcocystis* also underwent a major change. The controversy about non-existence of *Sarcocystis “lindemanni”* has been clarified and accordingly the life cycle has been revised.

**Chapter 8 (Miscellaneous protozoa):** Microsporidia has been updated with recent advances in laboratory diagnosis, inclusion of new species such as *Tubulinosema*. The proposal of change in nomenclature of *Balantidium* to *Neobalantidium* has been mentioned. *Blastocystis* species needs a special mention, as recently it has been increasingly reported to be associated with human disease. This topic is thoroughly revised in all aspects from life cycle to its pathogenic potential and laboratory diagnosis and treatment.
Chapter 9 (Introduction to helminths): Typographical errors are rectified; differences between cestodes, trematodes and nematodes have been updated.

Chapter 10 (Cestodes): *Diphyllobothrium latum* has been updated in its epidemiology, pathogenesis and laboratory diagnosis. Epidemiology of *Spirometra* has been revised. Taeniasis has been thoroughly updated in its laboratory diagnosis with incorporation of revised DelBrutto's diagnostic criteria and epidemiology. Update has been made in echinococcosis in the areas of genotyping, advances in laboratory diagnosis with special mention on USG and other imaging methods, and treatment modalities.

Chapter 11 (Trematodes or Flukes): General outline of life cycle of all trematodes has been described which will help students to understand and memorize the life cycles easily. Recent advances in laboratory diagnosis and recent updates in geographical distribution of all trematodes have been incorporated. Less common liver flukes such as *Dicrocoelium* and *Eurytrema* and less common intestinal flukes such as *Nanophyetus salmincola* have been incorporated.

Chapter 12 (Intestinal nematodes): Flowcharts depicting life cycles of all intestinal nematodes have been included which will help for better understanding and memorizing. Latest update in laboratory diagnosis has been incorporated. Newer nematodes infecting man such as *A. ceylanicum* has been included. A detailed note on soil-transmitted helminths and WHO’s deworming strategy for prevention and global elimination has been discussed.

Chapter 13 (Nematodes of lower animals that rarely infect man): All the parasites under this chapter have been thoroughly revised in their laboratory diagnosis, epidemiology and life cycle. *Thelazia* species needs a special mention, as it has been discussed in detail.

Chapter 14 (Somatic nematodes): Recent advances in laboratory diagnosis, treatment and epidemiological distribution of lymphatic filariasis, onchocerciasis and loiasis have been incorporated. A special note on filariasis elimination program and its strategies have been discussed. The current status of global dracunculiasis elimination has been discussed. Trichinellosis has been revised in its laboratory diagnosis and pathogenesis.

Chapter 15 (Laboratory diagnosis of parasitic diseases): This chapter definitely needs a special mention. It is thoroughly updated with latest advancement in methods of stool examination, blood examination methods, serological, molecular, imaging and other techniques for the diagnosis of parasitic diseases.

Chapter 16 (Medical entomology): Vectors and their role in disease transmission have been updated.

Appendices: All the appendices have been thoroughly updated. A new annexure comprising morphology of stool parasites according to their relative size has been incorporated.

Inclusion of more tables, flowcharts, real images and schematic diagrams was made for better understanding.

Clinical case-based essay questions have been incorporated at the end of each chapter.

Most features of the first edition have been maintained: Such as concept of more content-less pages, concise, bulleted format and to-the-point text, simple and lucid language, and separate boxes for summary of laboratory diagnosis and treatment for quick review.

As you know, human errors are inevitable; and no book is immune from it. We would request all the readers to provide any errata found and also valuable suggestions and updates via e-mail.

We are confident and hoping that you all will fall in love with the book.

Apurba S Sastry
drapurbasastry@gmail.com

Sandhya Bhat
sandhyabhatk@gmail.com
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1. General Introduction: Parasitology  3
Medical Parasitology deals with the study of animal parasites, which infect and produce diseases in human beings.

**TAXONOMY OF PARASITES**

According to the binomial nomenclature as suggested by Linnaeus, each parasite has two names—a genus and a species name.

These names are either derived from: names of their discoverers, Greek or Latin words of the geographical area where they are found, habitat of the parasite, or hosts in which parasites are found and its size and shape.

All parasites are classified under the following taxonomic units—the kingdom, subkingdom, phylum, subphylum, superclass, class, subclass, order, suborder, superfamily, family, genus and species.

The generic name of the parasite always begins with an initial capital letter and species name with an initial small letter, e.g. *Entamoeba histolytica*.

**PARASITE**

Parasite is a living organism, which lives in or upon another organism (host) and derives nutrients directly from it, without giving any benefit to the host.

Protozoa and helminths (animal parasites) are studied in Medical Parasitology.

**Parasites may be classified as:**

- **Ectoparasite**: They inhabit the surface of the body of the host without penetrating into the tissues. They are important vectors transmitting the pathogenic microbes. The infection by these parasites is called as infestation, e.g. *Sarcoptes scabiei* causing scabies

- **Endoparasite**: They live within the body of the host (e.g. *Leishmania*). Invasion by the endoparasite is called as infection.

The endoparasites are of following types:

- **Obligate parasite**: They cannot exist without a parasitic life in the host (e.g. *Plasmodium* species)
- **Facultative parasite**: They can live a parasitic life or free-living life, when the opportunity arises (e.g. *Acanthamoeba*).
- **Accidental parasite**: They infect an unusual host (e.g. *Echinococcus granulosus* infect humans accidentally)
- **Aberrant parasite or wandering parasite**: They infect a host where they cannot live or develop further (e.g. *Toxocara* in humans).

**HOST**

Host is defined as an organism, which harbors the parasite and provides nourishment and shelter.

**Hosts may be of the following types:**

- **Definitive host**: The host in which the adult parasites replicate sexually (e.g. *Anopheles* species), is called as definitive host. The definitive hosts may be human or nonhuman living things

- **Intermediate host**: The host in which the parasite undergoes asexual multiplication is called as intermediate host. (e.g. in malaria parasite life cycle, humans are the intermediate hosts)

- **Laboratory diagnosis of parasitic diseases**

- **Treatment of parasitic diseases**
SECTION 1  Introduction

Hosts can also be:
- **Reservoir host**: It is a host, which harbors the parasites and serves as an important source of infection to other susceptible hosts. (e.g. dog is the reservoir host for echinococcosis)
- **Paratenic host**: It is the host, in which the parasite lives but it cannot develop further and not essential for its life cycle (e.g. fresh water prawn and crab for Angiostrongylus cantonensis, big suitable fish for plerocercoid larva of Diphyllobothrium latum and freshwater fishes for Gnathostoma spinigerum). It functions as a transport or carrier host
- **Amplifier host**: It is the host, in which the parasite lives and multiplies exponentially.

**HOST-PARASITE RELATIONSHIP**
The relationship between the parasite and the host, may be divided into the following types:

- **Symbiosis**: It is the close association between the host and the parasite. Both are interdependent upon each other that one cannot live without the help of the other. None of them suffer any harm from each other
- **Commensalism**: It is an association in which the parasite only derives the benefit without causing any injury to the host. A commensal is capable of living an independent life
- **Parasitism**: It is an association in which the parasite derives benefit from the host and always causes some injury to the host. The host gets no benefit in return.

**Disease**: The disease is the clinical manifestation of the infection, which shows the active presence, and replication of the parasite causing damage to the host. It may be mild, severe and fulminant and in some cases may even cause death of the host.

**Carrier**: The person who is infected with the parasite without any clinical or subclinical disease is referred to as a carrier. He can transmit the parasites to others.

**TRANSMISSION OF PARASITES**

It depends upon:
- Source or reservoir of infection
- Mode of transmission.

**Sources of Infection**
- **Man**: Man is the source or reservoir for a majority of parasitic infections (e.g. amoebiasis, enterobiasis, etc.) The infection transmitted from one infected man to another man is called as anthroponoses
- **Animal**: The infection which is transmitted from infected animals to humans is called as zooneses. The infection can be transmitted to humans either directly or indirectly via vectors. (e.g. echinococcosis from dogs and toxoplasmosis from cats)
- **Vectors**: Vector is an agent, usually an arthropod that transmits the infection from one infected human being to another. Vector can be biological or mechanical. An infected blood sucking insect can transmit the parasite directly into the blood during its blood meal.

**Contaminated soil and water**: Soil polluted with human excreta containing eggs of the parasites can act as an important source of infection, e.g. hookworm, Ascaris species, Strongyloides species and Trichuris species.

Water contaminated with human excreta containing cysts of E. histolytica or Giardia lamblia, can act as source of infection

- **Raw or under cooked meat**: Raw beef containing the larvae of Cysticercus bovis and pork containing Cysticercus cellulosa are some of the examples where undercooked meat acts as source of infection
- **Other sources of infection**: Fish, crab or aquatic plants, etc.

**Modes of Transmission**
The infective stages of various parasites may be transmitted from one host to another in the following ways:
- **Oral or feco-oral route**: It is the most common mode of transmission of the parasites. Infection is transmitted orally by ingestion of food, water or vegetables contaminated with feces containing the infective stages of the parasite. (e.g. cysts of E. histolytica, and ova of Ascaris lumbricoides)
- **Penetration of the skin and mucous membranes**: Infection is transmitted by the penetration of the larval forms of the parasite through unbroken skin (e.g. filiform larva of Strongyloides stercoralis and hookworm can penetrate through the skin of an individual walking bare-footed over fecally contaminated soil), or by introduction of the parasites through blood-sucking insect vectors. (e.g. Plasmodium species, Leishmania species and Wuchereria bancrofti)
- **Sexual contact**: Trichomonas vaginalis is the most frequent parasite to be transmitted by sexual contact. However, Entamoeba, Giardia and Enterobius are also transmitted rarely by sexual contact among homosexuals
- **Bite of vectors**: Many parasitic diseases are transmitted by insect bite (Table 16.2 in Chapter 16) such as—
CHAPTER 1 General Introduction: Parasitology

malaria (female *Anopheles* mosquito), filariasis (*Culex*), leishmaniasis (sandfly), Chagas’ disease (reduviid bug) and African sleeping sickness (tsetse fly)

- **Vertical transmission:** Mother to fetus transmission is important for few parasitic infections like *Toxoplasma gondii*, *Plasmodium* species and *Trypanosoma cruzi*

- **Blood transfusion:** Certain parasites like *Plasmodium* species, *Babesia* species, *Toxoplasma* species, *Leishmania* species and *Trypanosoma* species can be transmitted through transfusion of blood or blood products

- **Autoinfection:** Few intestinal parasites may be transmitted to the same person by contaminated hand (external autoinfection) or by reverse peristalsis (internal autoinfection). It is observed in *Cryptosporidium parvum*, *Taenia solium*, *Enterobius vermicularis*, *Strongyloides stercoralis* and *Hymenolepis nana*.

**LIFE CYCLE OF THE PARASITES**

The life cycle of the parasite may be direct (simple) or indirect (complex).

- **Direct/simple life cycle:** When a parasite requires only one host to complete its development, it is referred as direct/simple life cycle (Table 1.1)

- **Indirect/complex life cycle:** When a parasite requires two hosts (one definitive host and another intermediate host) to complete its development, it is referred as indirect/complex life cycle (Table 1.2). Some of the helminths require three hosts (one definitive host and two intermediate hosts) (Table 1.3).

**PATHOGENESIS OF PARASITIC DISEASES**

The parasites can cause damage to humans in various ways.

- **Mechanical trauma:**
  - **Eggs:** Trematode eggs being large in size, can be deposited inside the intestinal mucosa (*Schistosoma mansoni*), bladder (*Schistosoma haematobium*), lungs (*Paragonimus*), liver (*Fasciola hepatica*) and can cause mechanical irritation

- **Larvae:** Migration of several helminthic larvae (hookworms, *Strongyloides* or *Ascaris*) in the lungs produce traumatic damage of the pulmonary capillaries leading to pneumonitis

**Table 1.2: Indirect/complex life cycle—parasites requiring one definitive host and one intermediate host**

<table>
<thead>
<tr>
<th>Parases</th>
<th>Definitive host</th>
<th>Intermediate host</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Leishmania</em> species*</td>
<td>Man</td>
<td>Sandfly</td>
</tr>
<tr>
<td><em>Trypanosoma cruzi</em></td>
<td>Man</td>
<td>Reduviid bugs</td>
</tr>
<tr>
<td><em>Trypanosoma brucei</em></td>
<td>Man</td>
<td>Tsetse fly</td>
</tr>
<tr>
<td><em>Taenia solium</em> (intestinal taeniasis)</td>
<td>Man</td>
<td>Pig</td>
</tr>
<tr>
<td><em>Taenia saginata</em></td>
<td>Man</td>
<td>Cattle</td>
</tr>
<tr>
<td><em>Hymenolepis diminuta</em></td>
<td>Man</td>
<td>Rat flea</td>
</tr>
<tr>
<td><em>Schistosoma</em> species</td>
<td>Man</td>
<td>Snail</td>
</tr>
<tr>
<td><em>Trichinella spiralis</em></td>
<td>Man</td>
<td>Pig</td>
</tr>
<tr>
<td>Filarial worms</td>
<td>Man</td>
<td>Mosquito (<em>Culex, Aedes, Anopheles</em>) and flies (blackflies and deerflies)</td>
</tr>
<tr>
<td><em>Dracunculus medinensis</em></td>
<td>Man</td>
<td>Cyclops</td>
</tr>
</tbody>
</table>

*Man acts as intermediate host*

<table>
<thead>
<tr>
<th>Parases</th>
<th>Definitive host</th>
<th>Intermediate host</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Plasmodium</em> species</td>
<td>Female <em>Anopheles</em> mosquito</td>
<td>Man</td>
</tr>
<tr>
<td><em>Babesia</em> species</td>
<td>Tick</td>
<td>Man</td>
</tr>
<tr>
<td><em>Sarcocystis lindemanni</em></td>
<td>Cat and dog</td>
<td>Man</td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em></td>
<td>Cat</td>
<td>Man</td>
</tr>
<tr>
<td><em>Echinococcus granulosus</em></td>
<td>Dog</td>
<td>Man</td>
</tr>
<tr>
<td><em>Taenia solium</em> (Cysticercosis)</td>
<td>Man</td>
<td>Man</td>
</tr>
</tbody>
</table>

*Note: In *Leishmania* and *Trypanosoma*, the definitive and intermediate host terminologies are not applicable as there is no sexual cycle. The better terminologies used are vertebrate host (man) and the invertebrate host (insect vectors)*

**Table 1.3: Indirect/complex life cycle—parasites requiring one definitive host and two intermediate hosts**

<table>
<thead>
<tr>
<th>Parases</th>
<th>Definitive host</th>
<th>First intermediate host</th>
<th>Second intermediate host</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Diphyllobothrium</em> species</td>
<td>Man</td>
<td>Cyclops</td>
<td>Fish</td>
</tr>
<tr>
<td><em>Fasciola hepatica</em></td>
<td>Man</td>
<td>Snail</td>
<td>Aquatic plant</td>
</tr>
<tr>
<td><em>Fasciolopsis buski</em></td>
<td>Man</td>
<td>Snail</td>
<td>Aquatic plant</td>
</tr>
<tr>
<td><em>Paragonimus</em> species</td>
<td>Man</td>
<td>Snail</td>
<td>Crab and fish</td>
</tr>
<tr>
<td><em>Clonorchis</em> species</td>
<td>Man</td>
<td>Snail</td>
<td>Fish</td>
</tr>
<tr>
<td><em>Opisthorchis</em> species</td>
<td>Man</td>
<td>Snail</td>
<td>Fish</td>
</tr>
<tr>
<td><em>Gnathostoma spinigerum</em></td>
<td>Cat, dog and man</td>
<td>Cyclops</td>
<td>Fish</td>
</tr>
</tbody>
</table>
SECTION 1  Introduction

- **Adult worms**: Adult worms of hookworm, *Strongyloides, Ascaris* or *Taenia* get adhere to the intestinal wall and cause mechanical trauma.

- **Space-occupying lesions**: Certain parasites produce characteristic cystic lesion that may compress the surrounding tissues or organs, e.g., hydatid cysts and neurocysticercosis.

- **Inflammatory reactions**: Most of the parasites induce cellular proliferation and infiltration at the site of their multiplication, e.g., *E. histolytica* provokes inflammation of the large intestine leading to the formation of amoebic granuloma. Adult worm of *W. bancrofti* causes mechanical blockage and chronic inflammation of the lymphatics and lymph vessels. Trematode eggs can induce inflammatory changes (granuloma formation) surrounding the area of egg deposition.

- **Enzyme production and lytic necrosis**: Obligate intracellular parasites of man (*Plasmodium*, *Leishmania* and *Trypanosoma*), produce several enzymes, which cause digestion and necrosis of host cells. *E. histolytica* produces various enzymes like cysteine proteinases, hydrolytic enzymes and amoebic pore forming protein that lead to destruction of the target tissue.

- **Toxins**: Some of the parasites produce toxins, which may be responsible for pathogenesis of the disease, e.g., *E. histolytica*. However, in contrast to bacterial toxin, parasitic toxins have minimal role in pathogenesis.

- **Allergic manifestations**: Many metabolic and excretory products of the parasites get absorbed in the circulation and produce a variety of allergic manifestations in the sensitized hosts. Examples include schistosomes causing cercarial dermatitis, rupture of hydatid cyst producing anaphylactic reactions and occult filariasis (tropical pulmonary eosinophilia).

- **Neoplasia**: Some of the parasitic infections can contribute to the development of neoplasia (e.g., *S. haematobium* causes bladder carcinoma, *Clonorchis* and *Opisthorchis* cause cholangiocarcinoma).

- **Secondary bacterial infections**: Seen in some helminthic diseases (schistosomiasis and strongyloidiasis).

**IMMUNOLOGY OF PARASITIC DISEASES**

The immune response against the parasitic infections depends on two factors:

1. **Host factors**: Immune status, age, underlying disease, nutritional status, genetic constitution and various defense mechanisms of the host.

2. **Parasitic factors**: Size, route of entry, frequency of infection, parasitic load and various immune evasion mechanisms of the parasites.

Broadly, the host immunity against the parasitic diseases may be of two types:

1. **Protective immune response**
   - i. Innate immunity
   - ii. Adaptive/acquired immunity.

2. **Unwanted or harmful immune response** (hypersensitive reactions).

**Protective Immune Response**

Both innate and acquired immunity play an important role in protecting the hosts against parasites. Some of the parasitic infections can be eliminated completely by the host immune responses (complete immunity) while few are difficult to eliminate. In some infections, the immune defense of the host is sufficient to resist further infection but insufficient to destroy the parasite. Immunity lasts till the original infection remains active and prevents further infection. This is called as *infection immunity* or *premunition* or *concomitant immunity* or *incomplete immunity*. This is observed in malaria, schistosomiasis, trichinosis, toxoplasmosis and Chagas’ disease.

**(i) Innate Immunity**

Innate immunity is the resistance which an individual possesses by birth, due to genetic and constitutional makeup.

**Factors influencing innate immunity**

- **Age of the host**: Both the extremes of age are more vulnerable to parasitic infections. Certain diseases are common in children like giardiasis and enterobiasis while certain infections occur more commonly in adults like hookworm infection. Congenital infection occurs commonly with *Toxoplasma gondii*; whereas newborns are protected from falciparum malaria because of high concentration of fetal hemoglobin.

- **Sex**: Certain diseases are more common in males like amoebiasis, whereas females are more vulnerable to develop anemia due to hookworm infection.

- **Nutritional status**: Both humoral and cellular mediated immunity are lowered and neutrophil activity is reduced in malnutrition.

- **Genetic constitution of the individuals**: People with hemoglobin S (sickle cell disease), fetal hemoglobin and thalassemia hemoglobin are resistant to falciparum malaria, whereas Duffy blood group negative red blood cells (RBCs) are resistant to vivax malaria.

**Components of innate immunity**

- **Anatomic barriers (skin and mucosa)**: Skin is an important barrier for the parasites that enter by cutaneous routes like schistosomes, hookworm and *Strongyloides*
CHAPTER 1  General Introduction: Parasitology

- **Physiologic barriers:** It includes temperature, pH, and various soluble molecules like lysozyme, interferon, and complement. Gastric acidity acts as a physiologic barrier to *Giardia* and *Dracunculus*.

- **Phagocytosis:** Phagocytes like macrophages and microphages (neutrophils, basophils and eosinophils) act as first line of defense against the parasites.

- **Complements:** They play an important role for killing the extracellular parasites by forming membrane attack complexes; which leads to the formation of holes in the parasite membrane.

- **Natural killer cells:** Natural killer (NK) cells are another important mediator of innate immunity. They play a central role in killing few of the helminthic parasites.

(ii) Acquired/Adaptive Immunity

This is the resistance acquired by an individual during life following exposure to an agent. It is mediated by antibody produced by B lymphocytes (humoral immune response) or by T cells (cell mediated immune response).

**Cell mediated immune response**

- When a parasite enters, the parasitic antigens are processed by the antigen presenting cells, (e.g. macrophages) which present the antigenic peptides to T helper (T\_h) cells. The antigen presenting cells also secrete interleukin-1 (IL-1) that activates the resting T\_h cells. Activated T helper cells differentiate into T\_h\_1 and T\_h\_2 cells.

  - T\_h\_1 secrete interleukin-2 (IL-2) and interferon gamma. Interleukin-2 activates the cytotoxic T cells (T\_c) and NKs, which are cytotoxic to the target parasitic cells. They produce perforin and granzyme that form pores and lyse the target cells.

  - IFN-\gamma activates the resting macrophages which in turn become more phagocytic and release free radicals like reactive oxygen intermediate (ROI) and nitric oxide (NO) that kill the intracellular parasites.

- T\_h\_2 release IL-4, IL-5, IL-6 and IL-10 which are involved in activation of B cells to produce antibodies [immunoglobulin E (IgE) by IL-4]. IL-5 also acts as chemoattractant for the eosinophils. Eosinophilia is common finding in various helminthic infections.

**Humoral immune response**

T\_h\_2 response activates the B cells to produce antibodies which in turn have various roles against the parasitic infections. They are:

- **Neutralization** of parasitic toxins (mediated by IgA and IgG)

- **Preventing** attachment to the gastrointestinal tract (GIT) mucosa (mediated by secretory IgA)

- **Agglutinating** the parasitic antigens thus preventing invasion (mediated by IgM)

- **Complement activation** (by IgM and IgG): Complements bind to the Fc portion of the antibody coated to the parasitic cells. Activation of the complements leads to membrane damage and cell lysis.

- **Antibody dependent cell-mediated cytotoxicity** (ADCC) is important for killing of the helminths. NK cells bind to the Fc portion of the IgG antibody coated to the helminths. Activation of NKs leads to release of perforin and granzyme that in turn cause membrane damage and cell lysis.

- **Mast cell degranulation:** IgE antibodies coated on mast cells when get bound to parasitic antigens, the mast cells become activated and release a number of mediators like serotonin and histamine.

**The Unwanted or Harmful Immune Responses**

Sometimes immune responses may be exaggerated or inappropriate in the sensitized individuals on re-exposure to the same antigen. Such type of immunopathologic reactions are called as hypersensitivity reactions that may be harmful to the hosts causing tissue damage. These are of four types (Table 1.4).

**Parasitic Factors that Evade the Host Immune Response**

Sometimes, the hosts find it difficult to contain the parasitic infections mainly because of the following reasons:

- Large size of the parasites

- Complicated life cycles

- Antigenic complexity.

There are a number of mechanisms by which the parasites evade the host immune responses (Table 1.5).

**LABORATORY DIAGNOSIS OF PARASITIC DISEASES**

It plays an important role in establishing the specific diagnosis of various parasitic infections. Following techniques are used in diagnosis of parasitic infections (discussed in detail in Chapter 15):

- Parasitic diagnosis—either microscopically or macroscopically

- Culture methods

- Immunodiagnostic methods (antigen and antibody detection)

- Intradermal skin tests

- Molecular methods

- Xenodiagnostic techniques

- Animal inoculation

- Imaging techniques.
### Table 1.4: Hypersensitivity reactions seen in parasitic diseases

<table>
<thead>
<tr>
<th>Hypersensitive reactions</th>
<th>Parasitic diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type I hypersensitivity reactions</strong>&lt;br&gt;These are allergic or anaphylactic reactions, occurring within minutes of exposure to parasitic antigens due to IgE mediated degranulation of mast cells</td>
<td>• Cercarial dermatitis (Swimmer’s Itch) in schistosomiasis&lt;br&gt;• Loeffler’s syndrome in ascariasis&lt;br&gt;• Ground itch (Hookworm infection)&lt;br&gt;• Anaphylaxis due to leakage of hydatid fluid (<em>Echinococcus granulosus</em>)&lt;br&gt;• Casoni’s test (hydatid disease)&lt;br&gt;• Tropical pulmonary eosinophilia (occult filariasis)</td>
</tr>
<tr>
<td><strong>Type II hypersensitivity reactions</strong>&lt;br&gt;These are mediated by IgG or rarely IgM antibodies produced against the antigens on surfaces of the parasitic cells causing antibody mediated destruction of the cells by i) the complement activation or ii) by the NK cell activation (ADCC - antibody dependent cell mediated cytotoxicity)</td>
<td>• Anemia in malaria&lt;br&gt;• Black water fever in malaria following quinine therapy&lt;br&gt;• Myocarditis in Chagas’ disease&lt;br&gt;• Killing of the helminths by NK cells</td>
</tr>
<tr>
<td><strong>Type III hypersensitivity reactions</strong>&lt;br&gt;Immune complexes are formed by the combination of parasitic antigens with the circulating antibodies (IgG) which get deposited in various tissues</td>
<td>• Nephrotic syndrome in <em>Plasmodium</em> <em>malariae</em>&lt;br&gt;• Katayama fever in schistosomiasis&lt;br&gt;• African trypanosomiasis&lt;br&gt;• Onchocerciasis</td>
</tr>
<tr>
<td><strong>Type IV hypersensitivity reactions</strong>&lt;br&gt;This is T-cell mediated delayed type of hypersensitivity reaction. Previously sensitized T helper cells secrete a variety of cytokines, on subsequent exposure to the parasitic antigens. Usually, the pathogen is cleared rapidly with little tissue damage. However, in some cases, it may be destructive to the host resulting in granulomatous reaction</td>
<td>• Elephantiasis (in filariasis)&lt;br&gt;• Granulomatous disease in schistosomiasis and other helminthic infections&lt;br&gt;• Leishmaniasis</td>
</tr>
</tbody>
</table>

**Abbreviations:** IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M; NKs, natural killer cells.

### Table 1.5: Immune evasion mechanisms of the parasites

<table>
<thead>
<tr>
<th>Immune evasion mechanisms</th>
<th>Parasites involved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>By intracellular location</strong>&lt;br&gt;Plasmodium species, Babesia species, Trypanosoma species, Toxoplasma species, Leishmania species and Microsporidia</td>
<td></td>
</tr>
<tr>
<td>Enters an immunologically protected site soon after infection</td>
<td><em>Plasmodium</em> species entering into hepatocytes</td>
</tr>
<tr>
<td>Leave the site where the immune response is already established</td>
<td><em>Ascaris</em> undergoes intestinal phase and migratory lung phase during its life cycle</td>
</tr>
<tr>
<td>Survives in macrophages by preventing phagolysosome fusion</td>
<td>Leishmania, Trypanosoma and Toxoplasma</td>
</tr>
<tr>
<td><strong>Antigenic shedding (capping):</strong> Surface membrane antigens of the parasites bound to the antibodies undergo redistribution so that the parasite is covered by a folded membrane that later extrude as a cap containing most of the antibodies that were originally bound to the membrane</td>
<td>Entamoeba histolytica, Trypanosoma brucei and <em>Ancylostoma caninum</em></td>
</tr>
<tr>
<td><strong>Antigenic variation:</strong> By change of antigenic composition, the parasites can be protected from the antibodies which are formed against the original antigens</td>
<td><em>P. falciparum</em> (pf-EMP protein), <em>Giardia</em> and Trypanosoma brucei</td>
</tr>
<tr>
<td><strong>Antigenic mimicry:</strong> The adult flukes of <em>Schistosoma</em> get coated with the host red cell antigens and histocompatibility antigens, so that they are not recognized as foreign and live free from host attack</td>
<td><em>Schistosoma</em> species</td>
</tr>
<tr>
<td>Inhibit antibody binding</td>
<td><em>Schistosoma mansoni</em></td>
</tr>
<tr>
<td>Lymphocyte suppression</td>
<td><em>Schistosoma mansoni</em></td>
</tr>
<tr>
<td>Polyclonal stimulation of lymphocytes</td>
<td><em>P. falciparum</em>, Trypanosoma brucei, Babesia, Trichinella and <em>E. histolytica</em></td>
</tr>
<tr>
<td>Suppression of immune system</td>
<td>Trypanosoma, <em>Plasmodium</em> and <em>Leishmania</em></td>
</tr>
</tbody>
</table>
CHAPTER 1  General Introduction: Parasitology

TREATMENT OF PARASITIC DISEASES

Treatment of parasitic disease is primarily based on chemotherapy and in some cases by surgery.

Antiparasitic Drugs

Various chemotherapeutic agents are used for the treatment and prophylaxis of parasitic infections (Table 1.6).

Surgical Management

For management of parasitic diseases like echinococcosis (or hydatid disease) and neurocysticercosis surgery is indicated. Semi-conservative surgery is followed wherever possible; for example, PAIR (percutaneous aspiration, injection and reaspiration) is done for treatment of hydatid disease.

Table 1.6: Common antiparasitic drugs, their mechanism of action and clinical indications

<table>
<thead>
<tr>
<th>Drugs for amoebiasis</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole, tinidazole</td>
<td>Bioactivated to form reduced cytotoxic products which damage DNA</td>
<td>DOC for the amoebic colitis, amoebic liver abscess, and other extraintestinal amoebiasis</td>
</tr>
<tr>
<td>and ornidazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dehydroemetine</td>
<td>Inhibits protein synthesis</td>
<td>Parenterally used for severe hepatic amoebias</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Probably by concentrating in parasite food vacuoles</td>
<td>Used for extraintestinal amoebias</td>
</tr>
<tr>
<td>Paromomycin (Aminoglycoside)</td>
<td>Inhibits protein synthesis by binding to 16S ribosomal RNA</td>
<td>Effective luminal agent</td>
</tr>
<tr>
<td>Diloxanide furoate</td>
<td>Unknown; it is thought to interfere with protein synthesis</td>
<td>Effective luminal agent</td>
</tr>
<tr>
<td>(Acetanilide compound)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iodoquinol (8-hydroxyquinoline compound)</td>
<td>Unknown</td>
<td>Luminal agent</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Complex and multifaceted</td>
<td>DOC for Naegleria fowleri</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs for flagellates</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal/Genital Flagellates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giardiasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole and tinidazole</td>
<td>Bioactivated to form reduced cytotoxic products which damage DNA</td>
<td>DOC for giardiasis</td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>Interference with the PFOR enzyme dependent electron transfer reaction which is essential for anaerobic energy metabolism</td>
<td></td>
</tr>
<tr>
<td>Furazolidone</td>
<td>Cross linking of DNA</td>
<td>Given to children</td>
</tr>
<tr>
<td>Paromomycin</td>
<td>Protein synthesis inhibitor in nonresistant cells by binding to 16S ribosomal RNA</td>
<td>Can be given in pregnancy</td>
</tr>
</tbody>
</table>

| Trichomoniasis              |                                                                                      |                                                                        |
| Metronidazole or tinidazole | Bioactivated to form reduced cytotoxic products having nitro groups which damage DNA | DOC for trichomoniasis, given to both the partners                     |

<table>
<thead>
<tr>
<th>Drugs for hemoflagellates</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chagas’ disease (American trypanosomiasis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifurtimox</td>
<td>Forms nitro-anion radical metabolite, which reacts with the nucleic acids of the parasite, causing a significant breakage in the DNA</td>
<td>Chagas’ disease</td>
</tr>
<tr>
<td>Benznidazole</td>
<td>Production of free radicals, to which Trypanosoma cruzi is particularly sensitive</td>
<td>Effective in the treatment of reactivated T. cruzi infections caused by immunosuppression (AIDS patients or patients of organ transplants)</td>
</tr>
</tbody>
</table>

| Sleeping sickness (African trypanosomiasis) |                                                |                                                                        |
| Pentamididine                | Accumulates to micromolar concentrations within the parasite to kill it by inhibiting enzymes and interacting with DNA | DOC for East African sleeping sickness                                 |
| Suramin                      | Trypanocidal activity; inhibits enzymes involved with the oxidation of reduced NADH | DOC for West African sleeping sickness                                 |

Contd...
### SECTION 1  Introduction

#### Drugs for malaria

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium stibogluconate</td>
<td>Inhibition of the parasite's glycolytic and fatty acid oxidative activity resulting in decreased reducing equivalents for antioxidant defense and decreased synthesis of ATP</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Meglumine antimoniate</td>
<td>Bind to ergosterol and disrupts cell membranes</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>Discussed earlier under giardiasis</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Miltefosine</td>
<td>Can trigger programmed cell death (apoptosis)</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Probably, concentrating in parasite food vacuoles, preventing the polymerization of the hemoglobin into the toxic product hemozoin</td>
<td>DOC for uncomplicated benign malaria</td>
</tr>
<tr>
<td>Artemisinin derivative (Artemisinin or arteether)</td>
<td>Generate highly active free radicals that damage parasite membrane</td>
<td>DOC for complicated or falciparum malaria</td>
</tr>
<tr>
<td>Quinine</td>
<td>Probably similar to chloroquine; still not clear</td>
<td>DOC for complicated or falciparum malaria</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Same as chloroquine</td>
<td>DOC for complicated or falciparum malaria</td>
</tr>
<tr>
<td>Primamaquine</td>
<td>Generating reactive oxygen species</td>
<td>DOC for relapse of vivax and ovale malaria</td>
</tr>
<tr>
<td>Sulfadoxine-pyrimethamine</td>
<td>Inhibits the production of enzymes involved in the synthesis of folic acid within the parasites</td>
<td>DOC for complicated or falciparum malaria</td>
</tr>
<tr>
<td>Lumefantrine</td>
<td>Accumulation of heme and free radicals</td>
<td>Complicated or falciparum malaria</td>
</tr>
</tbody>
</table>

#### Drugs for babesiosis

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin plus quinine</td>
<td>Clindamycin: inhibits protein synthesis</td>
<td>DOC for severe babesiosis</td>
</tr>
<tr>
<td>Atovaquone plus azithromycin</td>
<td>Atovaquone: inhibits mitochondrial transport in protozoa by targeting the cytochrome bc, complex</td>
<td>DOC for mild babesiosis</td>
</tr>
</tbody>
</table>

#### Drugs for toxoplasmosis

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotrimoxazole (Trimethoprim-sulfamethoxazole)</td>
<td>Inhibiting folate synthesis from PABA (para-aminobenzoic acid), thus inhibiting purine metabolism</td>
<td>DOC for prophylaxis in HIV-infected people</td>
</tr>
<tr>
<td>Spiramycin</td>
<td>Inhibition of protein synthesis in the cell during translocation</td>
<td>DOC in pregnancy</td>
</tr>
</tbody>
</table>

#### Drugs for Cryptosporidium

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitazoxanide</td>
<td>Interferes with the PFOR enzyme-dependent electron-transfer reaction, which is essential to anaerobic metabolism in protozoan and bacterial species</td>
<td>DOC for Cryptosporidium infection</td>
</tr>
</tbody>
</table>

#### Drugs for Cystoisospora and Cyclospora

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cotrimoxazole (Trimethoprim-sulfamethoxazole)</td>
<td>Inhibiting folate synthesis from PABA (Paraaminobenzoic acid), thus inhibiting purine metabolism</td>
<td>DOC for Cystoisospora and Cyclospora infection</td>
</tr>
</tbody>
</table>

#### Drugs for cestodes

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praziquantel</td>
<td>Increases the permeability of the membranes of parasite cells toward calcium ions which induces contraction of the parasites, resulting in paralysis in the contracted state</td>
<td>DOC for all cestode infections</td>
</tr>
<tr>
<td>Niclosamide</td>
<td>Niclosamide uncouples oxidative phosphorylation</td>
<td>Alternative drug for cestode infections</td>
</tr>
<tr>
<td>Albendazole</td>
<td>Causes loss of the cytoplasmic microtubules leading to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depleting their glycogen stores</td>
<td>Given for cysticercosis and hydatid disease</td>
</tr>
</tbody>
</table>

#### Drugs for trematodes

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of action</th>
<th>Clinical indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Praziquantel</td>
<td>Discussed earlier under cestodes</td>
<td>DOC for most of the trematode infections</td>
</tr>
<tr>
<td>Triclabendazole</td>
<td>Binds to beta-tubulin and prevent the polymerization of the microtubules</td>
<td>DOC for Fasciola hepatica and F. gigantica</td>
</tr>
</tbody>
</table>
Drugs for nematodes | Mechanism of action | Clinical indication
---|---|---
**Intestinal nematodes**
Mebendazole or albendazole | Discussed earlier under cestodes | DOC for most of the intestinal nematodes
Pyrantel pamoate | Acts as a depolarizing neuromuscular blocking agent, thereby causing sudden contraction, followed by spastic paralysis of the helminths | Alternative drug for intestinal nematodes
Ivermectin | Kills by interfering with nervous system and muscle function, in particular by enhancing inhibitory neurotransmission resulting in flaccid paralysis | DOC for strongyloidiasis. Alternative drug for *Trichuris* infections

**Filarial nematodes**
Diethylcarbamazine (DEC) | An inhibitor of arachidonic acid metabolism in microfilaria. This makes the microfilaria more susceptible to phagocytosis | DOC for lymphatic filariasis, *Loa loa* and *Mansonella* infections
Albendazole | Discussed earlier under cestodes | Alternative drug for lymphatic filariasis, *Loa loa* and *Mansonella* infections
Ivermectin | Discussed earlier under intestinal nematodes | Used for lymphatic filariasis in Africa
Doxycycline | Targets the intracellular *Wolbachia* present inside the microfilaria | Alternative drug for lymphatic filariasis

Abbreviations: DNA, deoxyribonucleic acid; DOC, drug of choice; RNA, ribonucleic acid; PFOR, pyruvate ferredoxin oxidoreductase enzyme; ATP, adenosine triphosphate; NADH, nicotinamide adenine dinucleotide.

**EXPECTED QUESTIONS**

I. Write short notes on:
   a. Paratenic host.
   b. Reservoir host.
   c. Indirect/complex life cycle.
   d. Immune evasion mechanisms of the parasites.
   e. Antiparasitic drugs.

II. Differentiate between:
   a. Definitive host and intermediate host.
   b. Direct and indirect life cycle.

III. Multiple choice questions (MCQs):
   1. A host harboring adult or sexual stage of a parasite is called:
      a. Definitive host
      b. Intermediate host
      c. Reservoir host
      d. None of the above
   2. Parasite which may be transmitted by sexual contact is:
      a. *Trypanosoma cruzi*
      b. *Trichomonas vaginalis*
      c. *Trypanosoma brucei*
      d. *Ascaris*

3. *Cholangiocarcinoma* is associated with chronic infection of:
   a. *Paragonimus westermani*
   b. *Fasciola hepatica*
   c. *Clonorchis sinensis*
   d. *Schistosoma haematobium*

4. Which of the following parasite is transmitted by dog:
   a. *Toxoplasma gondii*
   b. *Hymenolepis nana*
   c. *Echinococcus granulosus*
   d. *Diphyllobothrium latum*

5. Blood-sucking vector may transmit:
   a. *Ascaris lumbricoides*
   b. *Ancylostoma duodenale*
   c. *Strongyloides stercoralis*
   d. *Plasmodium*

Answers
1. a  2. b  3. c  4. c  5. d