Craig and Faust's

CLINICAL PARASITOLOGY

FAUST
AND
RUSSELL

SEVENTH EDITION

Craig and Faust's

CLINICAL PARASITOLOGY

By

ERNEST CARROLL FAUST, A.B., M.A., PH.D., LL.D.

Emeritus Professor of Parasitology, Department of Tropical Medicine and Public Health, Tulane University School of Medicine, New Orleans, Louisiana; Consultant, U.S. Public Health Service; Member, Expert Panel on Parasitic Diseases, World Health Organization; Member, Committee on Revision, U.S. Pharmacopeia, 1951-1960; Field Coordinator, Tulane-Colombia Program in Medical Education, U.S. Operational Mission, International Cooperation Administration, 1956-1961

AND

PAUL FARR RUSSELL, M.D., M.P.H., D.SC. (HON.)

Visiting Lecturer, Tropical Public Health, Harvard School of Public Health; Consultant to Surgeon General, U.S. Army; Consultant to Agency for International Development; Member Malaria Panel and Formerly Chairman, Expert Committee on Malaria, World Health Organization; Formerly Malaria Consultant to Tennessee Valley Authority, and to the United States Public Health Service; Staff Member Emeritus, The Rockefeller Foundation.

Seventh Edition, Thoroughly Revised,

352 Illustrations and 8 Coloured Plates

LONDON

HENRY KIMPTON

134 GREAT PORTLAND STREET, W.1

1964

Seventh Edition

First Edition, 1937
Second Edition, 1940

Third Edition, 1943
Reprinted, 1943
Reprinted, 1944

Fourth Edition, 1945
Reprinted, 1946
Reprinted, 1947
Reprinted, 1948
Reprinted, 1949

Fifth Edition, 1951
Reprinted, 1951
Reprinted, 1953

Sixth Edition, 1957

Printed in the United States of America

CONTENTS

Section I

GENERAL INTRODUCTION AND ORIENTATION

Section II

PROTOZOA AND PROTOZOAN INFECTIONS

Section III

HELMINTHS AND HELMINTHIC INFECTIONS

Craig and Faust's

CLINICAL PARASITOLOGY

By

ERNEST CARROLL FAUST, A.B., M.A., PH.D., LL.D.

Emeritus Professor of Parasitology, Department of Tropical Medicine and Public Health, Tulane University School of Medicine, New Orleans, Louisiana; Consultant, U.S. Public Health Service; Member, Expert Panel on Parasitic Diseases, World Health Organization; Member, Committee on Revision, U.S. Pharmacopeia, 1951-1960; Field Coordinator, Tulane-Colombia Program in Medical Education, U.S. Operational Mission, International Cooperation Administration, 1956-1961

AND

PAUL FARR RUSSELL, M.D., M.P.H., D.SC. (HON.)

Visiting Lecturer, Tropical Public Health, Harvard School of Public Health; Consultant to Surgeon General, U.S. Army; Consultant to Agency for International Development; Member Malaria Panel and Formerly Chairman, Expert Committee on Malaria, World Health Organization; Formerly Malaria Consultant to Tennessee Valley Authority, and to the United States Public Health Service; Staff Member Emeritus, The Rockefeller Foundation.

Seventh Edition, Thoroughly Revised,

352 Illustrations and 8 Coloured Plates

LONDON

HENRY KIMPTON

134 GREAT PORTLAND STREET, W.1

1964

Seventh Edition

First Edition, 1937
Second Edition, 1940

Third Edition, 1943
Reprinted, 1943
Reprinted, 1944

Fourth Edition, 1945
Reprinted, 1946
Reprinted, 1947
Reprinted, 1948
Reprinted, 1949

Fifth Edition, 1951
Reprinted, 1951
Reprinted, 1953

Sixth Edition, 1957

Printed in the United States of America

PREFACE TO THE SEVENTH EDITION

DURING the quarter of a century since the first edition of this volume was published, there have been many notable advances in the knowledge of diseases caused by animal parasites and those transmitted by animal vectors. Although much of the wealth of information acquired has consisted in observations and experimental data supplementing earlier investigations, the perspective has been broadened in many ways, particularly in attempts to understand the metabolism of the parasites, their bionomics and natural history. These aspects of human parasitology have provided a clearer appreciation of man as host and of the potential pathogenicity of the parasites under a great variety of environmental conditions. New basic information has opened pathways on the one hand for improved methods of diagnosis and treatment and on the other hand to effective control and in some cases even to eradication.

More and more as diseases are viewed from a global point of view and as their effects on humankind are better appraised, it is realized that control and prevention in population groups are much more effective measures against disease than treatment of individual patients. This does not mean that the physician-patient relationship is minimized or eliminated, but that clinical experience is coördinated with public health practice to provide a more rapid and satisfactory solution to the problem. Perhaps the best single example of the effective application of this principle to an infectious disease is the eradication of malaria from large areas of several countries during the past decade, with the expectation of widespread eradication during the next decade. This task has been accomplished primarily through intelligent application of anti-anopheline toxicants such as DDT, supplemented by administration of one or more of the newer anti-malarial drugs.

But there should be no complacency. Parasites still dominate man in many areas. For example, in 1962 Normal Stoll, who has been studying hookworm infections throughout the world for forty years, stated that, "As it was when I first saw it, so it is now, one of the most evil of infections. Not with dramatic pathology as are filariasis, or schistosomiasis, but with damage silent and insidious. Now that malaria is being pushed back, hookworm remains *the great infection* of mankind. In my view it outranks all other worm infections of man combined, with the possible exception of ascariasis, in its production, frequently unrealized, of human misery, debility and inefficiency in the tropics."

So, too, schistosomiasis presents a serious problem as it continues to widen its spread, increase its incidence, and bedevil man's attempts to irrigate dry land in several tropical and subtropical areas.

Human diseases such as toxoplasmosis, visceral larva migrans, and arthropod-borne virus infections, are becoming more important.

Many of these infectious organisms are fundamentally parasites of lower animals, hence the need for increased emphasis on zoönoses in relationship to human exposure and susceptibility.

Parasites have been studied for many years but the authors stress the continuing need to support research. For example, insect resistance to toxicants and parasite resistance to chemotherapy, especially among the *Plasmodia*, have become increasingly troublesome and much more investigation is required to solve these problems.

As knowledge concerning the parasites of man accumulated it was necessary to add new information to successive editions of CLINICAL PARASITOLOGY. However, the volume could not be enlarged indefinitely without altering its original purpose, namely, to provide a textbook rather than an encyclopedia for students of parasitology, clinicians and public health workers. The present edition provides a complete revision or reëvaluation of the subject matter. Wherever necessary new material has been added, recent information has been incorporated into text and tables and new illustrations have been provided.

We are grateful for the many helpful comments and suggestions which have been generously provided by our colleagues; we express our thanks to Miss Helen Day, secretary to the senior author, for her patient and efficient clerical help; and we express our sincere appreciation to Lea & Febiger, our publishers, for continued coöperation during the preparation and publication of this volume.

NEW ORLEANS, LA. ERNEST CARROLL FAUST
WESTOVER, NORTH EDGECOMB, MAINE PAUL F. RUSSELL

CONTENTS

Section I

GENERAL INTRODUCTION AND ORIENTATION

Section II

PROTOZOA AND PROTOZOAN INFECTIONS

Section III

HELMINTHS AND HELMINTHIC INFECTIONS

CLINICAL PARASITOLOGY

SECTION I

General Introduction and Orientation

CHAPTER 1

THE PARASITE AND ITS ENVIRONMENT

ALL ANIMAL and plant forms originated and developed as free-living organisms which were obliged to compete with others for their existence. Only those which developed satisfactory adjustments and adaptations were able to survive. Among this group were many species in different phyla of the Animal and Plant Kingdoms which came to depend on their associates for shelter and food. In some instances the remarkable adaptations to a parasitic life suggest that this interrelationship has existed for a long time, probably measured in tens of thousands of years. Other groups of parasites appear to have more recently acquired a parasitic mode of life, and a few of these have not yet become irreversibly committed to parasitism. Still others are only now developing the earliest adaptations to a parasitic mode of life.

DEFINITION OF TERMS COMMONLY EMPLOYED IN PARASITOLOGY

Parasitology is the area of biology concerned with the phenomena of dependence of one living organism on another. The *parasite* lives at the expense of its *host*, usually a larger organism, which provides physical protection and nourishment. If the parasite derives benefit without reciprocating but without injury to the host, the relationship is referred to as *commensalism;* if the relationship is beneficial to both associates, it is *mutualism*. Close association of the two is *symbiosis*. *Predators*, which temporarily attack and destroy animals or plants in order to obtain food, usually feed on smaller or weaker organisms which are their *prey*.

Many animals which are related to parasitic species are free-living. Among the parasitic forms there are some which depend on plants as their hosts, and are frequently of great economic importance. Others live on or within invertebrate animals, while still others parasitize vertebrate hosts. *Clinical parasitology* is concerned primarily with the animal parasites of man and their medical significance, as well as their importance in human communities.

HOST-PARASITE INTERRELATIONSHIPS

In a majority of instances only one host is required for a parasite to carry on its life cycle. There may be relatively "fast" host specificity for a particular species of parasite, as, for example, the intestinal flagellate of man, *Giardia lamblia*, and the human body louse, *Pediculus humanus*. Certain anopheline mosquitoes have a preference for human blood when it is available (*i.e.*, they are anthropophilic). Other parasites are less discriminating and man constitutes only one of several satisfactory hosts. The Chinese liver fluke (*Clonorchis sinensis*), the Oriental blood fluke (*Schistosoma japonicum*) and the trichina worm (*Trichinella spiralis*) are representative of this group. In many instances man is only incidentally involved as a host, while domestic or wild animals serve as *reservoirs* of the parasite.

Multiple host-species susceptibility to a parasite introduces the concept of *zoönosis* (literally disease of animals, but today employed for those diseases of animals which are transmissible to man): if the parasitosis is common to man and reservoir hosts, it is referred to as a *euzoönosis;* if man is an infrequent, hence incidental, host, it is a *parazoönosis*. Garnham (1959) stated that the zoönotic process is dynamic, and that the best zoönotic species are the least differentiated ones. Modern civilization tends to disrupt the natural course of many euzoönoses, so that man becomes involved in their cycles, at times with disastrous consequences.

Organisms which cannot exist without a host are *obligate parasites*. Others under favorable circumstances may live either a parasitic or free-living existence; they are *facultative parasites*, as for example, under appropriate circumstances, *Strongyloides stercoralis*. In addition, some free-living animals or those which parasitize other hosts, are at times recovered in a living or dead state from human excreta; they are referred to as *spurious parasites* of man.

In microbiology the relationship of the parasite to its host is designated as an *infection*. This is likewise the appropriate designation for all animal species which are *endoparasites*, whereas those which are *ectoparasites* (*i.e.*, are attached to the skin, or temporarily invade the superficial tissues of the host's body) produce an *infestation*. This distinction is employed irrespective of the size of the invader, but infestation of the host is most frequently applied to species of arthropods and leeches. In the more limited sense *parasitosis* is the state of infection or infestation with an animal parasite.

Some animal parasites of man are normally harmless commensals. Notable among these are several intestinal amebæ and flagellates. On the other hand, a great majority of the animal parasites are harmful, causing local and systemic damage of one type or another. These species are *pathogens*.

When an individual harboring a parasite is reinfected with the same species of parasite, this is *superinfection*. In case the infected person is his own direct source of the reëxposure, it is *autoinfection*, which may be external, *viz.*, perianal or anus-to-mouth *via* fingers, or internal in the mode of reinfection.

SOURCES OF EXPOSURE TO INFECTION OR INFESTATION

Exposure may occur from one or more of the following sources: (1) contaminated soil or water; (2) food containing the immature infective stage of the parasite; (3) a blood-sucking insect; (4) a domestic or wild animal harboring the parasite; (5) another person, his clothing or immediate environment which he has contaminated, or (6) one's self. Each of these sources will be briefly illustrated.

Soil polluted with human excreta is commonly responsible for exposure to infection with *Ascaris lumbricoides, Trichuris trichiura,* human hookworms, and *Strongyloides stercoralis.* Water may contain viable cysts of parasitic amebæ, intestinal flagellates, *Tænia solium* eggs and the infective cercarial stage of the human blood flukes. Freshwater fishes constitute the source for fish tapeworm (*Diphyllobothrium latum*), as well as several types of intestinal and liver flukes; crabs and crayfishes, for the Oriental lung fluke; hog flesh, for *Trichinella spiralis* and *Tænia solium;* beef, for *Tænia saginata:* buffalo nuts (*Trapa* spp.), for the giant intestinal fluke (*Fasciolopsis buski*), and watercress (*Nasturtium officinale*), for the sheep liver fluke (*Fasciola hepatica*). Blood-sucking arthropods transmit malarial parasites, leishmanias, trypanosomes, filarial worms, viruses, rickettsias, bacteria and spirochetes. Dogs are the direct source for human infection with the hydatid cyst of *Echinococcus granulosus,* as well as cutaneous larva migrans due to *Toxocara canis,* while herbivorous animals commonly constitute the source for human infection with *Trichostrongylus* spp. Other human beings are directly responsible for all or a considerable amount of infection with the pathogenic ameba (*Entamœba histolytica*), the pinworm (*Enterobius vermicularis*) and the dwarf tapeworm (*Hymenolepis nana*). Autoinfection accounts for some of these parasitoses and for some reinfections with *Strongyloides stercoralis.*

PORTAL OF ENTRY INTO THE BODY

In the case of internal parasites, the most common portal of invasion is through the mouth. This is the entrance for the intestinal protozoa (for most species in the encysted stage); the common roundworms *Ascaris lumbricoides, Trichuris trichiura,* and *Enterobius vermicularis,* and the dwarf tapeworm *Hymenolepis nana* (all in the fully embryonated egg stage); *Trichostrongylus* spp. as a free-living infective larva; and for *Trichinella spiralis, Tænia solium, T. saginata, Diphyllobothrium latum,* intestinal flukes, liver flukes and the lung fluke, from eating food containing the mature larval stages of these worms.

A few important roundworms, *viz.,* species of hookworms and *Strongyloides,* actively enter the body from the soil *via* the skin route, as do the blood flukes (*Schistosoma* spp.) from fresh water. A large number of parasites which have a required developmental stage in blood-sucking arthropods are introduced percutaneously when the arthropod punctures the skin to feed. Among these parasites are the agents of malaria, the leishmanias, trypanosomes, filarial worms, many viruses and rickettsias, and a few species of bacteria and spirochetes.

Other methods of transmission include: (1) inhalation of the eggs of *Enterobius vermicularis* and at times *Ascaris lumbricoides* from the air into the posterior pharynx; (2) transplacental (*i.e.*, congenital) infection with *Toxoplasma gondii*, and occasionally of malaria parasites and perhaps blood flukes, and (3) by sexual intercourse in the case of *Trichomonas vaginalis*.

THE BIOLOGICAL INCUBATION PERIOD

Exposure vs. Infection.—Exposure to infection is the act or process of *inoculation*, whereas *infection* connotes a "take," whereby the infective agent becomes established in the host. Often the term "infection" is employed carelessly when inoculation is intended. For example, a person may be exposed by ingesting cysts of *Entamœba histolytica* without colonization of the ameba, so that no infection is produced.

Development of the Infection.—Once the successful parasite has entered the body of the host, characteristically it is carried or actively migrates to a location where it matures and produces progeny. This may be a relatively simple procedure or it may be lengthy and complicated. For example, for *Entamœba histolytica* it consists of excystation of the protoplast in the lumen of the ileum and division into as many small metacystic trophozoites as there were nuclei in the encysted stage, then passive carriage in the fecal stream through the ileocecal sphincter into the large intestine, lodgement in a glandular crypt, growth to normal size and multiplication by asexual binary division. Similarly, for fully embryonated eggs of *Trichuris trichiura* and *Enterobius vermicularis* it consists of hatching in the duodenum, migration of the larva down to the cecal level, attachment to the mucosa and development to the adult stage, followed by the production of eggs of the new generation.

In the case of *Ascaris lumbricoides* the ingested egg hatches in the duodenum. The emerging larva enters the mucosa and migrates *via* bloodvessels to the lungs, then breaks out into the air sacs and passes up the respiratory tree to the epiglottis, crawls over into the digestive tract and is carried to the small intestine where it develops into the adult form. Hookworms and *Strongyloides stercoralis*, which actively invade the skin, are carried in the bloodstream to the lungs, after which their course of migration parallels that of *Ascaris*.

Organisms which are introduced in the encysted larval stage in food characteristically become freed of their cyst wall or capsule in the duodenum. Intestinal helminths soon become attached to the mucosa, usually in the upper or middle levels of the small intestine where they mature; inhabitants of the bile ducts enter *via* the ampulla of Vater (*i.e.*, *Clonorchis sinensis*), or utilize a more indirect route (*i.e.*, *Fasciola hepatica*), and the lung fluke *Paragonimus westermani* takes a devious route through tissues and body cavities before arriving at its destination near a bronchiole.

The blood flukes (*Schistosoma* spp.), after actively invading the skin, burrow to the cutaneous lymphatics and blood vessels. Once they have entered the blood stream they are carried to the lungs, squeeze through the pulmonary capillaries and on reaching the left heart are rapidly transported through the arterial circulation into portal blood. Here they grow,

then migrate actively to the smaller mesenteric venules (*S. japonicum* or *S. mansoni*) or *via* the mesenteric and rectal venules into the vesical venules (*S. hæmatobium*).

Malarial parasites, when introduced into the human skin by an anopheline mosquito, are rapidly carried in the blood stream, which they leave in about 30 minutes. Those which secure lodgement in the liver undergo asexual multiplication in parenchyma cells before they get into visceral blood and initiate infection in the red blood cells. Trypanosomes may rapidly multiply in circulating blood (*Trypanosoma gambiense*) or may develop as intracellular parasites in macrophages near the site of inoculation or in the viscera (*Trypanosoma cruzi*). Species of *Leishmania* invariably colonize intracellularly in the reticuloendothelial system.

The filarial worms, once introduced as filariform larvæ into the skin by the infected insect, enter lymphatic vessels, in which the immature worms migrate for several weeks or months, finally developing to maturity in various sites, depending on the species of filaria, *viz.*, lymphatic system (*Wuchereria bancrofti, Brugia malayi*), subcutaneous tissues (*Loa loa, Acanthocheilonema streptocercum, Onchocerca volvulus*), or body cavities (*A. perstans* and *Mansonella ozzardi*).

End of the Biological Incubation Period.—Biological incubation is terminated as soon as the parasites or their products can be demonstrated in the feces or other excreta, in the circulating blood (*parasitemia*), by aspiration, biopsy or other diagnostic procedure. The biological incubation period varies from one or more days to weeks or months, depending on the particular species of parasite and its ability to develop in the particular host. *Biological incubation* is related to the development of the parasite. *Clinical incubation* refers to the interval between exposure and the earliest evidence of symptoms produced as a result of the infection (or infestation).

THE METABOLISM OF ANIMAL PARASITES

Metabolism is the sum of the physical and chemical processes whereby an organism obtains substances from its immediate environment for growth, multiplication and energy. In order to grow and multiply the organism must convert available nutrient materials into its own protoplasm. This is *anabolism*. But it must also utilize foodstuffs for energy, particularly for respiration. This is *catabolism*.

Physiologists and biochemists think of metabolism of animal forms primarily in terms of respiration, *i.e.*, reserves or other sources from which oxygen is obtained and energy produced, usually measured in CO_2 output. For many of the parasitic protozoa and helminths only a small amount of free O_2 is available for metabolism so that they have developed methods of survival under anaërobic conditions. Baerstein (1963) reported that malaria parasites elaborate cytochrome oxidase, trichomonads are essentially anaërobic, while trypanosomes have both sensitive and insensitive oxidases. Anaërobiasis is typical of several of the intestinal parasites, which frequently elaborate high concentrations of glycogen, at times amounting to as much as 30 per cent on a dry-weight basis. Representative parasitic

species will be used as examples to illustrate certain metabolic pathways which have been elucidated.

The pathogenic ameba, *Entamœba histolytica*, lives only at low oxygen tension. *In vitro* this may be obtained by culturing the organism with certain bacteria (or with *Trypanosoma cruzi*) which utilize free O_2, by planting the amebæ on a thioglycollate medium, or by removing free O_2 and sealing the tube. In an atmosphere of 95% N_2 + 5% CO_2 these amebæ oxidize glucose or other hexoses to pyruvate, and this has been demonstrated to be coupled with reduction of the thiol group of cysteine to H_2S. This interdependence probably occurs during the oxidative step in the multi-enzyme system which catalyzes the conversion of hexose-di-phosphate to pyruvate. Thus, both a carbohydrate and a sulfur-containing amino acid are involved (Kun, Bradin and Dechary, 1955). It is assumed, although not demonstrated, that *E. histolytica* utilizes this same mechanism in the crypts of the large intestine and possibly also after it becomes a tissue parasite.

The trypanosomes are likewise glucose metabolizers but the intensity with which they consume this carbohydrate varies remarkably. In all species studied, both cultured and bloodstream forms, as well as cultured forms of the leishmanias, there is no evidence that the degradation of sugar proceeds to the endpoint of the glycolytic chain, namely, CO_2 and water. Moreover, "the respiration of different species of Trypanosomatidæ is apparently dependent on different enzyme systems," some being inhibited by cyanide, some moderately sensitive and some stimulated (von Brand, 1951). There is evidence that species of this group also have a "well-developed synthetic protein metabolism," as demonstrated by the synthesis of phospholipid, nucleic acid and phosphoprotein from inorganic phosphate (Moraczewski and Kelsey, 1948).

With respect to the malaria parasites, there is thus far no information concerning the type of metabolism which occurs in host tissues preceding the entry of the plasmodia into red blood cells. The erythrocytic stages not only utilize the supply of nutrient material within the red blood cells (*i.e.*, globin, etc.) and O_2 carried by these cells, but probably also obtain nourishment from the blood plasma. In addition, the plasmodium has "enzyme systems and metabolic pathways of its own . . . as evidenced by the production in the parasitized (red) cell of lactate dehydrogenase, flavine-adenine dinucleotide, glycerol oxidase, and other oxidative enzymes. It is further demonstrated by the marked increase in respiration of the parasitized cell over the normal cell" (McKee, 1951).

Considering the great variety of form, size and relationship of parasitic helminths to host tissues, one need not be surprised at the different results obtained by investigators in studying the metabolism of these forms. Bueding (1951) stated that dependence on free O_2 metabolism varies remarkably among the different species and that each of these must be investigated separately. For some species short periods of anaërobiosis are detrimental or even fatal, whereas others survive under very low O_2 tension; or utilization of free O_2, when available, may be only an outmoded function carried over from an earlier free-living existence.

The hookworms, which are firmly attached to the villi of the small in-