PARASITES AND PEOPLE

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MACMILLAN

First published 1984
Published by
Higher and Further Education Division
MACMILLAN PUBLISHERS LTD
Houndmills, Basingstoke, Hampshire RG21 2XS and London

Associated companies in Auckland, Delhi,
Dublin, Gaborone, Hamburg, Harare, Hong Kong,
Johannesburg, Kuala Lumpur, Lagos, Manzini,
Melbourne, Mexico City, Nairobi, New York,
Singapore and Tokyo

For Susan Arnold

ISBN 978-0-333-32545-2 ISBN 978-1-349-17659-5 (eBook)
DOI 10.1007/978-1-349-17659-5

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Preface & Acknowledgements

Until relatively recently, parasitology when applied to animal hosts was seen mainly as a rather specialized branch of zoology. Today it encompasses biochemistry, genetics, immunology, molecular biology, nutritional science, pharmacology and population biology. When man is the host, parasitology's interdisciplinary character becomes even more diverse as anthropology, economics, medical science, politics and sociology make their contributions. Parasitology is of much importance for those who live in the developing countries of the world and my concern for practical aspects was first aroused by my colleagues at Cornell University, New York. Professor Michael Latham and Dr. Lani Stephenson took me to work with them in Africa and Dr. Eduvigis Carrera and Dr. Patricia Day Bidinger shared with me their studies in Panama and India. I very much hope that *Parasites and People* will interest and help those who are beginning to work for the relief of human suffering.

The production of this book owes much to the efforts of Dr. P.L. Clarke, Science Editor of The Macmillan Press Ltd., and to Ms Paula Disanto Bensadoun, Mrs. Zina Bulstrode and Miss Linda Keymer. The entire manuscript

was read and improved by Dr. Jean Martin, The Molteno Institute, University of Cambridge. Dr. Anne Keymer, also of The Molteno Institute, and Dr. G.E. Dappen, Department of Biology, Nebraska Wesleyan University, commented on several chapters. Mr. J. D. Crompton, University College, Oxford, helped me with various editorial chores. I thank them all and I accept full responsibility for the errors and mistakes that may remain.

The book could not have been written without the contributions of many scientists whose ideas, results and experiences are made freely available through libraries and learned journals. The text would have been unreadable if I had cited so many authors, but I am fully aware of my debt to them. I am also pleased to thank the copyright holders who kindly gave me permission to reproduce and use the following materials: Academic Press for Figure 2.1 redrawn from fig. 1.3 in *Medical Virology* (1970) by F. Fenner and D.O. White; American Institute of Biological Sciences for Tables 5.1, 5.2 and 5.3 which are based on tables 1 and 2 and information on page 679 in an article from *BioScience* 32 (1982) by D.W.T. Crompton and M.C. Nesheim; Blackwell Scientific Publications Ltd. for Table 7.3 based on table 2.1 in *Essential Immunology* (1971) by I.M. Roitt, and for Figure 2.3 redrawn from fig. 2.3 in *Animal Microbiology* 1 (1977) by A. Buxton and G. Fraser; Food and Agriculture Organization of the United Nations for Table 4.1 based on information on page 54 in *Human Nutrition in Tropical Africa*, 2nd edition (1979) by M.C. Latham; Harper and Row Publishers Inc. for Figure 2.2 redrawn from fig. 2.2 on page 19 in *Microbiology* (1980) edited by B.D. Davis, R. Dulbecco, H.N. Eisen and H.S. Ginsberg; Longman Group Ltd. for Table 4.2

abstracted from table 13.1 in *Human Nutrition and Dietetics*, 6th edition (1982) by S. Davidson, R. Passmore, J.F. Brock and A.S. Truswell, and for Table 4.3 abstracted from table 1.1 in *Practical Haematology*, 4th edition (1974) by J.V. Dacie and S.M. Lewis; Dr. Arno Peters of Bremen for Figure 5.1 which is based on his projection of the world; World Health Organization for Figure 4.1 redrawn with modifications from the flow diagram on page 8 in *W.H.O. Technical Report Series* No. 485 (1972), and for Figure 4.2 redrawn with modifications from fig. 1 (after Mata *et al*) in the chapter by J.E. Gordon in *Nutrition in Preventive Medicine* (1976) edited by G.H. Beaton and J.M. Bengoa.

Figures 2.5, 6.2 and 7.1 are redrawn from figs. 1.29, 1.54, 3.2, 3.6, 3.11, 3.12, 3.13, 3.14, 3.25, 3.27 and 9.9 in *Parasitic Worms* (1980) by myself and S.M. Joyner, which was published in the Wykeham series of Taylor and Francis Ltd., London. Finally, I wish to acknowledge that I have not traced the appropriate source of permission for Figure 5.3 which is based on graphs in a mimeographed article entitled 'International nutritional considerations: the point of view from the under developed world' by F.B. Monckeberg.

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Abbreviations

°C	degrees Celsius
DNA	deoxyribonucleic acid
e.g.	for example
GNP	gross national product
H_2O	water
MJ	megaJoule
MW	molecular weight
N	north
%	percentage
r.b.c.	red blood cell
RE	reticulo-endothelial (system)
RNA	ribonucleic acid
S	south
spp.	species (plural)
U.K.	United Kingdom
U.S.A.	United States of America
U.S.$	United States dollar
h	hour
min	minute
sec	second
yr	year

l	litre
dl	decilitre
ml	millilitre
kg	kilogram
g	gram
mg	milligram
m	metre
mm	millimetre
µm	micrometre
nm	nanometre

Other abbreviations are explained in the text and tables.

1

Host-Parasite Relationships

Life on earth probably began about 3500 million years ago and since then an enormous diversity of micro organisms, animals and plants has evolved and become adapted to live in one of the three major habitats of the planet. Probably all readers will accept that land and water form two of the habitats. The third equally extensive habitat is that formed by the bodies of the living organisms themselves. This book is about the living relationship between man and the organisms which live inside him, often causing chronic and even fatal disease.

For our purposes, a parasite is an organism that must spend part of its development on or in another living organism which is known as the host. During the relationship, the host provides the parasite with food, shelter and the exact conditions necessary for the parasite's growth and survival. In many cases, the parasite initiates the onset of disease. The capacity of a parasite to cause disease is known as its pathogenicity and the intensity or severity of this effect is sometimes called its virulence. A host-parasite relationship has been described as a state of conflict

between the resistance of the host to the injurious attacks of the parasite. This may be an over-simplification and rather too dramatic a view of all host-parasite relationships. It certainly seems to apply, however, in the examples involving man that will be discussed in this book.

Definitions in biology are often unsatisfactory because so many exceptions can usually be found. The following chapters ought to give a better concept of a parasite than any attempt at an all-embracing definition. There are, however, several general features of hosts and parasites and their interactions which may be summarized in advance.

1. Host species are nearly always much larger and nearly always have longer life spans than their parasite species.
2. Hosts and parasites possess different genetic material and belong to different species. (The point about species avoids the debate about whether a baby is a parasite while it grows in the mother's womb).
3. Parasites often occupy rather precise sites within their hosts.
4. Parasites frequently possess special structures which enable them to maintain their positions on or inside the host.
5. Parasites usually have much higher reproductive potential than their hosts.
6. Parasites invariably stimulate the immune responses of their hosts, but the result does not always protect the host.
7. Many mechanisms have evolved to ensure the spread of parasites between hosts.

8. Different host-parasite relationships last for different periods of time varying from a few days to several years.
9. Different host-parasite relationships show differing degrees of specificity. A relationship is said to have high specificity when a parasite is known to live in one species of host only (e.g. *Enterobius vermicularis* in man). Conversely, a relationship has low specificity when a parasite may live in several species of host (e.g. *Schistosoma japonicum* in man, cattle, dogs, goats, buffaloes, pigs and rats).

Words like specificity, pathogenicity and virulence are part of the everyday jargon of parasitologists and there are other terms which should now be introduced. A parasite is said to have a direct life cycle when only one species of host is involved in its development and an indirect life cycle when more than one is needed. When two or more hosts are employed in the life cycle, the one in which the parasite attains sexual maturity is called the final or definitive host while the other host or hosts are called intermediate hosts. Parasites which are exposed on the outer surfaces of hosts and can be seen directly with little or no dissection of host tissues are known as ectoparasites. Those which cannot be seen because they are located somewhere inside the host are known as endoparasites. This book is confined to a discussion of certain endoparasites of man including viruses, bacteria, fungi, protozoa and worms. The ectoparasites of man consist chiefly of lice, fleas, ticks and occasionally vampire bats. These ectoparasites are often important medically not only because of the irritation and discomfort that they cause but also because they spread other virulent microscopic parasites.

By convention, organisms like viruses and bacteria are said to cause infectious disease while those like protozoa and worms are said to cause parasitic disease. Similarly, virologists and bacteriologists have specialized in the study of infectious diseases while parasitologists have concentrated on the other groups. This rather arbitrary separation has not been adopted in this account of human host-parasite relationships. Nor has man been treated from the physiological or biochemical points of view as anything other than an animal, albeit a particularly recent one, that has evolved in the same manner as parasites and other living things. In some respects, however, man is different from all other animals, notably in his language, art, religion, technology and social organization. The formation and structure of human communities have led to the development of several features of host-parasite relationships that only occur when man is the host. Some of these, and the points noted above, will be illustrated in what follows.

2

Parasitic Organisms

The endoparasites that regularly infect and afflict man usually belong to one of five groups: viruses, bacteria, fungi, protozoa and worms. Each group is different from the others, but all have some features in common as regards their biology and host-parasite relationships. Most emphasis in the remaining chapters of this book will be placed on 17 parasites which are representatives of the five groups and which infect man (Table 2.1).

VIRUSES

Viruses (Table 2.2) are unable to obtain energy or synthesize protein, and their reproduction or replication cannot occur unless their genetic material has gained entry into the appropriate kind of host cell. In effect, all known viruses are obligate intracellular parasites. Probably every kind of living organism can be infected by viruses and more than a hundred are recognized as parasites of man alone.

Viruses are minute particles ranging in appearance from 20nm diameter spheres to brick-shaped structures with a largest dimension of about 300nm (Fig. 2.1),

Table 2.1 Some parasites of man

	Parasite	Disease
VIRUSES (Table 2.2)		
1	Rabies virus	Rabies
2	Influenza virus	Influenza
BACTERIA (Table 2.3)		
3	*Salmonella* spp.	Enteritis and Typhoid fever
4	*Vibrio cholerae*	Cholera
5	*Treponema pallidum*	Syphilis
6	*Mycobacterium leprae*	Leprosy
FUNGI		
7	*Trichophyton capitis*	Ringworm
PROTOZOA (Table 2.4)		
8	*Leishmania donovani*	Visceral leishmaniasis (Kala Azar)
9	*L. tropica*	Cutaneous leishmaniasis
10	*Trypanosoma cruzi*	Chagas's disease
11	*T. brucei* and relatives	Sleeping sickness
12	*Plasmodium falciparum* and relatives	Malaria
WORMS (Table 2.5)		
13	*Schistosoma mansoni* and relatives	Schistosomiasis
14	*Taenia saginata*	Taeniasis
15	*Ascaris lumbricoides*	Ascariasis
16	*Necator americanus*	Hookworm disease
17	*Onchocerca volvulus*	River Blindness

although little was known about their size and shape until the transmission electron microscope became available to biologists. In general, a virus consists of a capsid or protein coat which surrounds either DNA or RNA; viruses containing both types of nucleic acid have not been found. Sometimes the viral capsid is enclosed inside a loosely fitting envelope formed from a mixture of fat and protein. Only the viral nucleic acid enters the host cell which then responds to the instructions contained therein by making and assembling all the parts

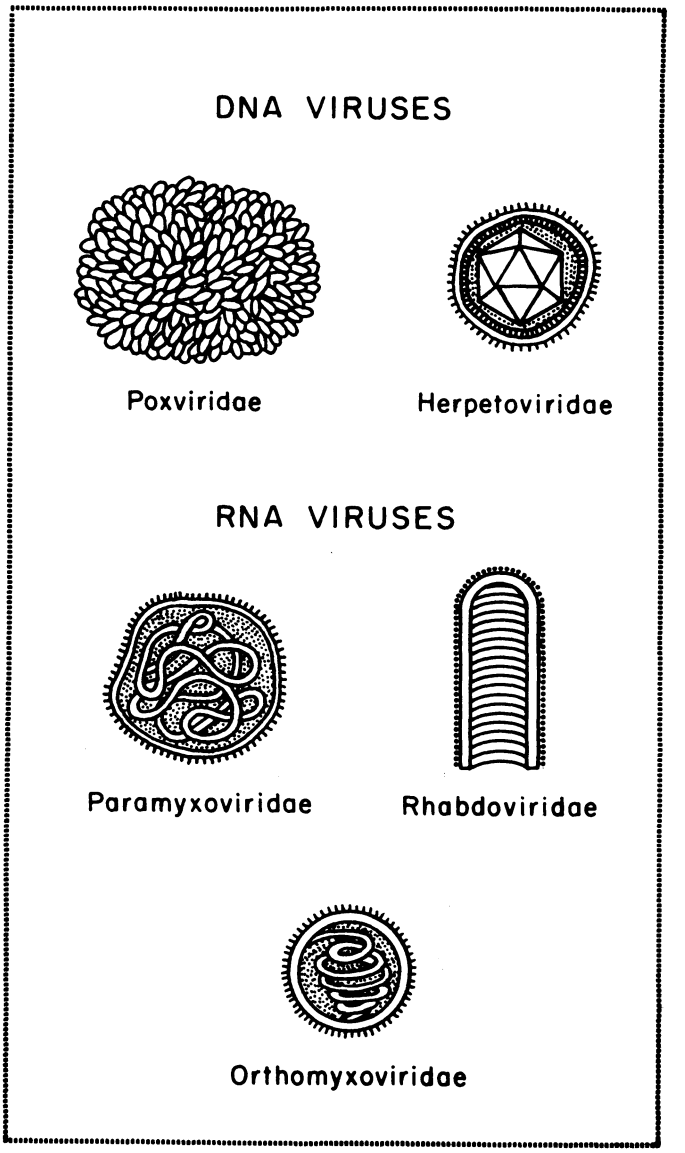

Fig. 2.1 Diagrammatic interpretations of the morphology of virus particles (Redrawn from Fenner and White, 1970).

for new virus particles. It is to be expected that disease will occur when cells are diverted from their normal function in the body to produce virus particles and when cells burst and are destroyed as the new particles are released. This is not to imply that the course of all viral infections is a rapid affair ending with the sudden death of the host cell; some viruses may persist in host cells for years as latent infections.

Most of the viruses that require animal cells as hosts are probably transmitted during a direct life cycle, but some have an indirect life cycle which involves their replication in the tissues of arthropods. Such viruses are known as arboviruses (arthropod-borne) and the insects and ticks which feed on blood are important agents of transmission.

Botanists and zoologists deal with large organisms which live for a long time and have an easily observed structure. Consequently plants and animals may be arranged or classified into related groups; ultimately a sound classification leads to a better understanding of the organisms under study. Owing to the minute size of viruses and other problems there is not yet complete agreement among virologists about how to classify the material they study. One simplified scheme has been used in Table 2.2.

BACTERIA

Bacteria abound in the free-living and parasitic habitats of the planet and many of the kinds that infect man (Table 2.3) cause serious disease. Most bacteria measure around 1-2 μm in length with some as big as 15μm (spirochaetes). Common forms of the main types of bacteria are illustrated in Fig. 2.2.

Table 2.2 Major groups of viruses infecting man (Based on Fenner and White, 1976)

Virus Group	Size (nm)[a]	Envelope	Ether sensitivity[b]	Route of entry[c]	Examples
DNA VIRUSES					
Papovaviridae	45-55	-	R	C	Papilloma virus (warts).
Herpetoviridae[d]	100-200[e]	+	S	V	Herpes simplex (cold sores); Varicella-zaster virus (chicken pox and shingles).
Poxviridae[d]	100x240x300	-	R[f]	Re	Variola (smallpox)[g].
RNA VIRUSES					
Picornaviridae	20-30	-	R	E	Poliovirus (poliomyelitis); Rhinovirus (common cold).
Togaviridae	30-90	+	S	AB	Flavivirus (yellow fever).
Arenaviridae	85-120	+	S		Lassa fever virus.
Orthomyxoviridae	80-120	+	S	Re	Influenza virus[h].
Paramyxoviridae[d]	100-300	+	S	Re	Paramyxovirus (mumps); Measles virus.
Rhabdoviridae[d]	70x180	+	S	B	Rabies virus[h].

[a] Dimensions. [b] R, resistant; S, Sensitive.
[c] AB, arboviruses transmitted by arthropods; B, bite (or scratch) of infected animal; C, direct contact or scratching; E, enteric viruses enter host through gut; Re, respiratory viruses enter host through respiratory tract; V, various.
[d] See Fig. 2.1. [e] Includes envelope. [f] Some are sensitive.
[g] In 1980, W.H.O. declared smallpox eradicated. [h] See Chapter 3.

Table 2.3 Major groups of bacteria infecting man. (Based on Davis, Dulbecco, Eisen and Ginsberg, 1980).

Bacterial group	Shape (Fig. 2.2)	Motility[a]	Examples
GRAM-POSITIVE			
Micrococcaceae	cocci	Im	[b]*Staphylococcus aureus* (Bacteremia and abscesses)
Lactobacillaceae			*Streptococcus* spp. (puerperal fever; sore throat; impetigo; rheumatic fever)
Corynebacteriaceae	rods	Im	*Corynebacterium diphtheriae* (diphtheria)
Bacillaceae	rods	Mf	*Clostridium perfringens* (gangrene) *C.tetani* (tetanus)
GRAM-NEGATIVE			
Enterobacteriaceae	rods	Mf	*Salmonella* spp.[c] (typhoid fever and food poisoning)
Neisseriaceae	cocci	Im	*Neisseria gonorrhoeae* (gonorrhoea)
Brucellaceae	cocci	Im	*Bordetella pertussis* (whooping cough)
Spirillaceae	curved rods	Mf	*Vibrio cholerae*[c] (cholera)
OTHER TYPES			
Actinomycetales	rods		*Mycobacterium leprae*[c] (leprosy)
Spirochetales	spiral	M	*Treponema pallidum*[c] (syphilis)

[a] Im, immotile; M, motile; Mf, motile with flagella.
[b] Pyogenic or pus-producing cocci.
[c] See Chapter 3.

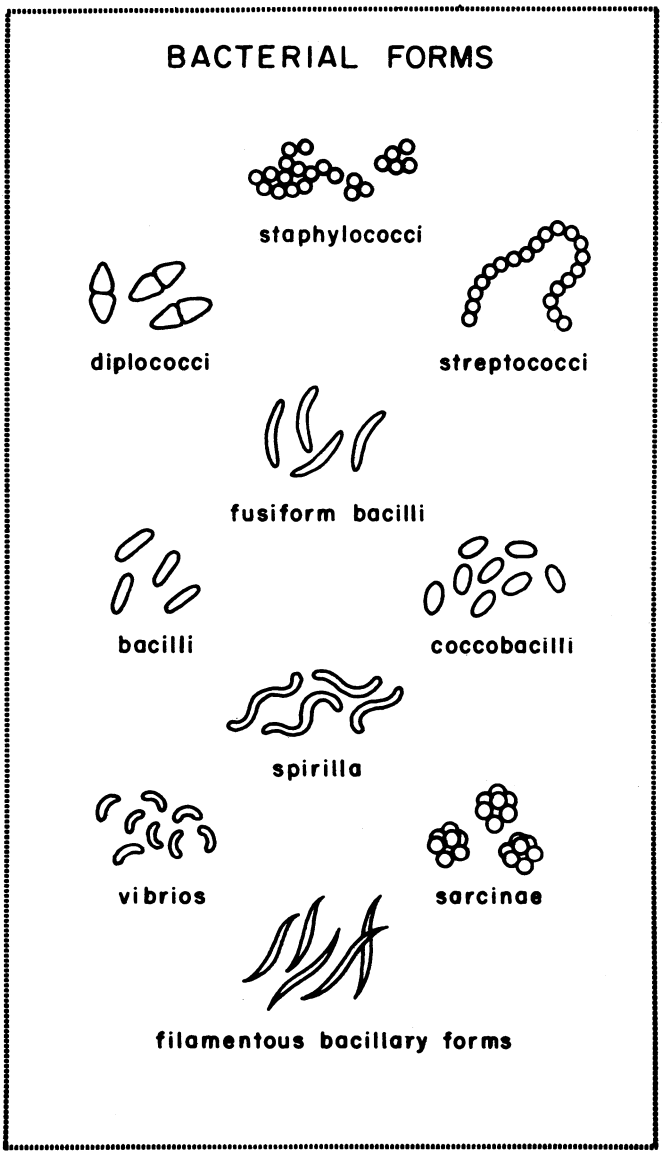

Fig. 2.2 Different forms of bacteria (Redrawn from Davis, Dulbecco, Eisen and Ginsberg, 1980).

Nearly all bacteria have a complex and rigid cell wall which either stains violet when treated with Gram's* stain or does not stain. This arbitrary division of bacteria into Gram-positive or Gram-negative groups is a most useful feature as regards their identification and reflects a basic chemical difference between the cell walls of the two types. In both cases, the main component of the bacterial cell wall is a protein-carbohydrate mixture called peptidoglycan, a strong material ideally suited to protecting the cytoplasm and genetic material of the bacteria. Some bacteria possess a slimy carbohydrate capsule which coats the cell wall and some possess flagella which extend through the cell wall from the cytoplasm and form the basis of their mobility. Many types of Gram-negative bacteria have pili which are tiny hair-like extensions of the cell wall; these may enable bacteria to make contact with each other or with host surfaces.

The cytoplasmic contents of a bacterium are enclosed by a cell membrane lining the surface of the cell wall (Fig. 2.3). The cytoplasm does not surround a prominent nucleus like most cells of higher organisms. Instead, the DNA is loosely arranged in the cytoplasm and there is no nuclear membrane. The bacterial cytoplasm also contains ribosomes in which RNA is located and where protein and numerous enzymes are manufactured. Some bacteria use oxygen to obtain energy from their nutrients, some can survive for relatively long periods without oxygen while others are killed by the presence of oxygen.

Bacteria are capable of rapid growth, asexual reproduction and forms of reproduction that involve

* GRAM - Hans Christian Joachim Gram. Danish Physician, 1853-1938.

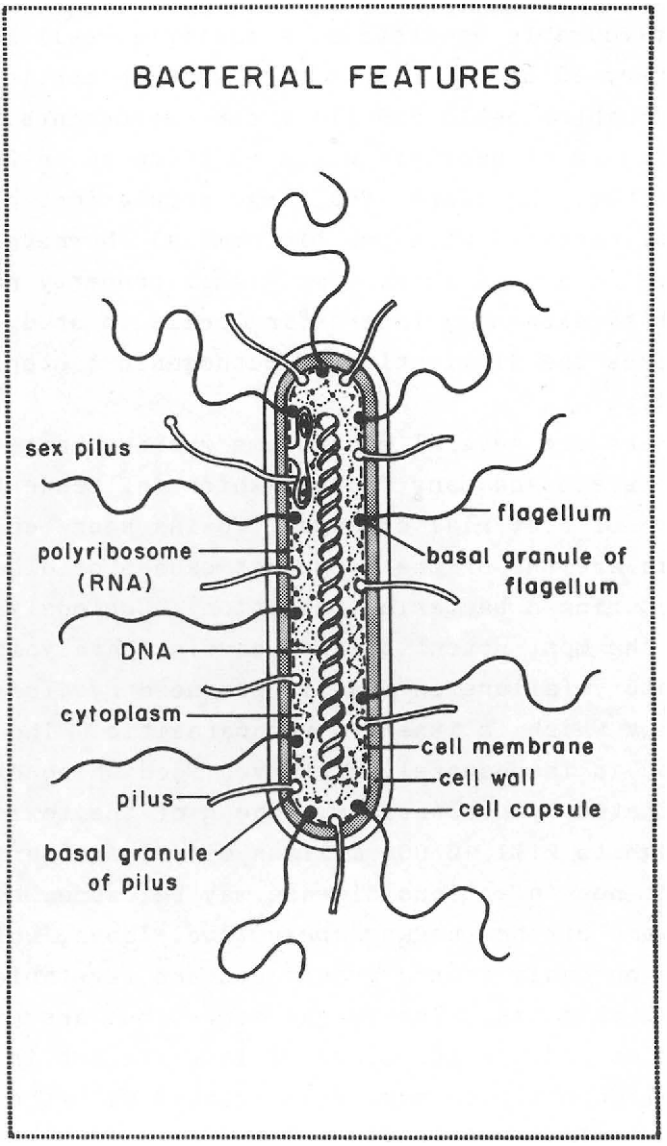

Fig. 2.3 Highly diagrammatic representation of the structures and features of bacterial cells (Redrawn from Buxton and Fraser, 1977).

the incorporation of DNA from other bacteria. The reproductive potential of a bacterium is enormous and, under favourable conditions, a bacterial cell may divide once every 20 min. If this rate were to continue for the 2 daughter cells and all their descendents, about 2 million kg of bacteria would be produced in 24h. It is possible, therefore, for large populations of new types of bacteria with new biochemical characteristics to arise in a very short time. This property not only makes them extremely interesting cells to study, but also makes the elimination of pathogenic bacteria very difficult.

There are several mechanisms whereby bacteria cause disease and many factors which influence the severity of bacterial disease. Toxins secreted by the bacteria are one of the commonest causes of disease and damage during a bacterial infection. Curiously, perhaps one of the most potent toxins, causing paralysis and respiratory failure in man, is produced by *Clostridium botulinum* which is itself never parasitic. The toxin is found in inadequately preserved food which has been contaminated by *C.botulinum*. One g of the toxin would be enough to kill 10 000 million mice. Another unpleasant non-infectious disease may be caused by secretions of the fungus *Aspergillus flavus*, which thrives on badly stored groundnuts and vegetables in tropical climates. The fungal secretions are called aflatoxins and the incidence of liver cancer in certain tropical communities may be associated with the exposure of the people to aflatoxins.

Not surprisingly there is no agreed scheme of bacterial classification, but the information given in Table 2.3 may provide an introduction to the extent and importance of parasitic bacteria as far as man is concerned.

FUNGI

Fungi are classified as plants because their cells, like plant cells, have rigid walls and because they do not move about. Fungi differ from plants, however, in that they lack chlorophyll. Like animals, fungi need sources of complex nutrients and these are obtained from the remains of dead organisms. Some fungi have become adapted to the parasitic mode of life and they cause diseases of plants and man's crops including mildew, rust and wilt. Probably as few as 100 species of fungi are parasites of animals. These include *Trichophyton* spp., which causes ringworm of the human skin (Chapter 3), and *Candida albicans* which causes an irritating disease of the vagina. A few fungal infections in man affect and damage the lungs.

Candida, like numerous other species of fungus, is a small organism whose cells differ from those of bacteria by having a more complex internal structure and a nucleus. Fungal cells are often arranged in filaments, called hyphae, and a mass of these is known as the mycelium. Reproduction in the fungi may occur by both asexual and sexual processes. Asexually, another cell may arise by budding and another organism by spore formation. Sexual reproduction depends on the production of gametes and conjugation which provide opportunities for the mixing of genetic material and mutations to occur

Although this book deals with parasites, the reader must remember that not all bacteria and fungi are undesirable pathogens which must be eradicated. Life on earth depends on the contribution of bacteria to soil composition and their role in recycling carbon, nitrogen and sulphur. Life for modern man would be less interesting without the use of bacteria and fungi for

the manufacture of cheese, yoghurt, bread, beer and wine, and certainly less pleasant in many big cities without bacterial breakdown of sewage. Many modern men owe their lives to the incalculable effects of penicillin, streptomycin and other antibiotics. Penicillin was discovered in 1928 when Alexander Fleming noticed that the growth of a culture of *Staphylococcus* (Table 2.3) had been affected by the presence of another organism which was identified as the mould or fungus *Penicillium notatum*. Eventually, techniques were devised to obtain large quantities of the bactericidal principle from the fungus and the first medical antibiotic came into use. It is interesting to note that in several parts of Europe, long before anyone was aware of antibiotics, country people used to prepare wound dressings from a paste of water and mouldy bread; in all probability the mould would be *P.notatum*. Further exciting efforts are now being made to harness the synthetic properties of micro-organisms for the benefit of mankind as industrialized countries embark into the era of genetic engineering and biotechnology.

PROTOZOA

The protozoa form a large group of unicellular animals. There are problems with this generalisation; some protozoa seem to be like plant cells and even possess chlorophyll and some species are found in colonies. In general, however, many of them display the characteristics of animals and there are representatives in all the habitats of the earth. Protozoa are microscopic in size although some species can just about be seen by eye without any aids to magnification. Most are highly motile animals and many have elaborate flagella, cilia and undulating membranes as aids to locomotion (Fig. 2.4). Some protozoa have special

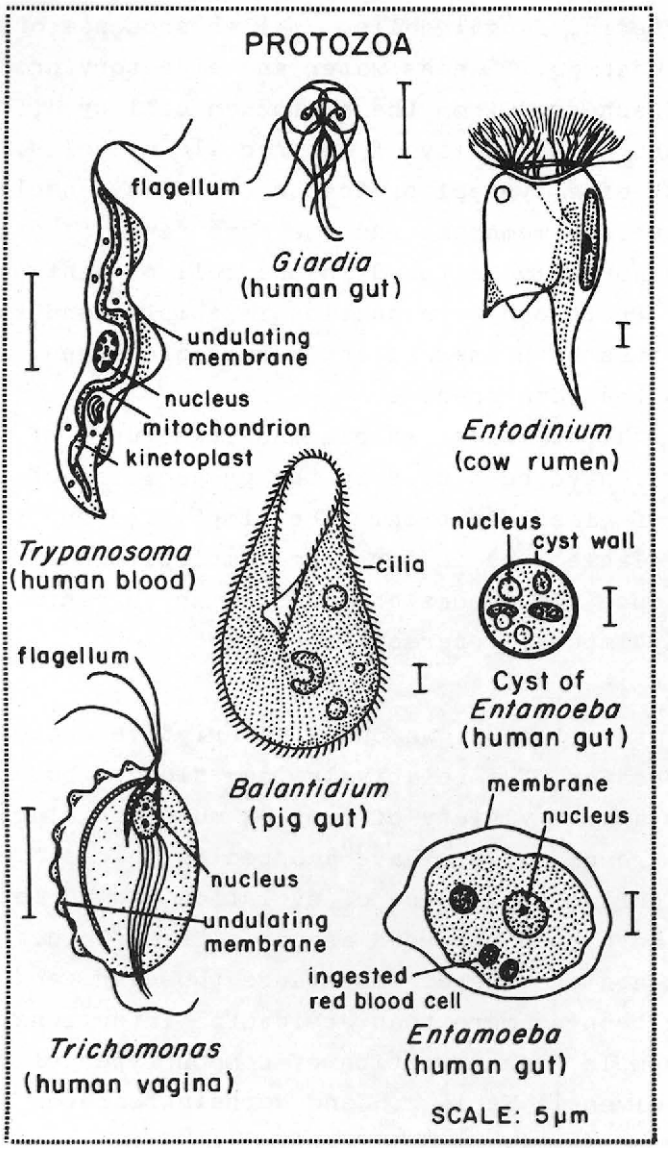

Fig. 2.4 The morphology of different types and developmental stages of protozoa.

feeding organelles and structures for attachment to surfaces. Other protozoa engulf and digest particles like bacteria, fungal cells, smaller protozoa or bits of plant debris. Excess water and excretory products may be discharged from the protozoan cell by diffusion or through the activity of contractile vacuoles. The cytoplasm of a typical protozoon contains a nucleus with a nuclear membrane and the same range of organelles as would normally be found in the cell of a higher animal. Protozoan reproduction is complex and varied and involves both asexual and sexual processes, sometimes in the same species.

The varied sizes, shapes and structures of protozoa (Fig. 2.4) have been used in the preparation of several schemes of classification. The simplified one that follows (Table 2.4) is far from complete and is intended to introduce the groups of protozoa which contain some extremely important parasites of man.

WORMS

The term 'worm', which is descriptive and denotes the possession of a relatively long slender body, is used for a wide variety of complex multicellular animals. Several groups of worm have adopted the parasitic mode of life during the course of evolution and at least 70 species have been recorded as parasites of man. Not all of these are of general importance, however, and some may have been no more than accidental infections.

A simple classification of common types of parasitic worm is given in Table 2.5 and certain features are illustrated in Fig. 2.5. Perhaps the fact that worms are easily seen either in the stools or in vomit or in tunnels beneath the surface of the skin has led to the normal feelings of revulsion that man has for them. Worms do not usually cause such acute diseases as

Table 2.4 Major groups of protozoa including parasites of man[a]

Protozoan group	Features	Examples from Man
Dinoflagellata	Mostly free living and important in plankton.	-
Flagellata	Mostly parasitic with 1 to 4 flagella and a prominent kinetoplast containing DNA; indirect life cycle.	[b]African *Trypanosoma* spp. (sleeping sickness) S.American *T. cruzi* (Chagas's disease) *Leishmania* spp. (Leishmaniasis; RE-cell disease)
	Mostly parasitic with flagella; direct life cycle	*Trichomonas vaginalis* (genital irritation)
	Many flagella; live in gut of termites where they digest wood.	-
Amoebae	Protozoa with 'naked' surface; free living and parasitic; often form cysts; direct life cycle.	*Entamoeba histolytica* (dysentry)
Sporozoa	Sexual and asexual reproduction, important intracellular parasites of wild and domesticated animals.	*Toxoplasma gondii*[c] (varied disease and symptoms in man)
	Sexual and asexual reproduction, indirect life cycle; parasitic in vertebrate blood cells; produce black pigment.	*Plasmodium* spp.[b] (malaria)
Piroplasma	Intracellular parasites causing serious disease in many animals; indirect life cycle.	-
Ciliata	Protozoa with cilia, many free-living, but many important for nutrition and health of ruminants.	-

[a]See also Fig. 2.4. [b]See Chapter 3. [c]Not all experts would place *Toxoplasma* here.

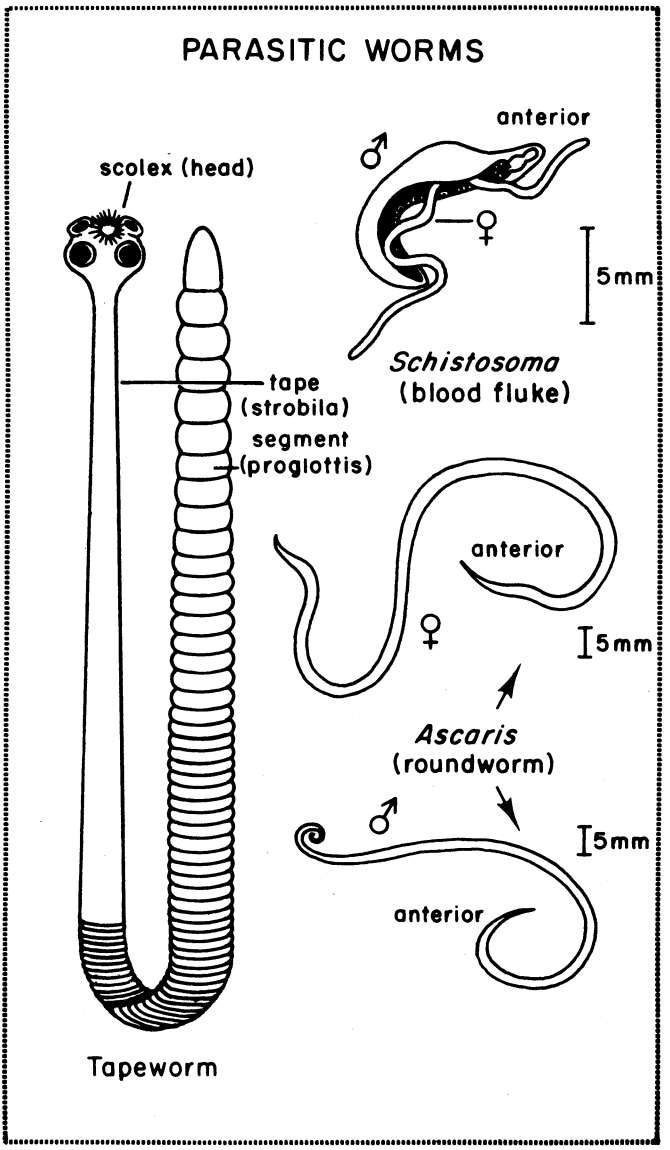

Fig. 2.5 Different forms of parasitic worm (Redrawn from Crompton and Joyner, 1980).

viruses, bacteria and protozoa although some species are undoubtedly responsible for much chronic illness in developing countries.

Some of the endoparasitic flatworms (Table 2.5) have life cycles involving several hosts. Digenean flukes develop first by an asexual process in the tissues of a snail. The stage emerging from a snail generally encysts on or in the tissues of another animal, the second intermediate host. The definitive host becomes infected when the encysted forms are unknowingly swallowed, invariably while the second host is being eaten. Adult digenean flukes are usually to be found feeding on the linings of the alimentary tract, bile duct and gall-bladder, pancreatic duct, urinogenital tract and lungs of their definitive hosts. The blood flukes of man, *Schistosoma* spp. (Table 2.5, see Chapter 3) are exceptions to this pattern. They have only one snail intermediate host and man becomes infected when the stage which might have been expected to encyst on a second intermediate host bores through his skin while it is exposed to contaminated fresh water (Fig. 3.5). Schistosomes are also atypical examples of flukes because their sexes are separate (Fig. 2.5) whereas most species are hermaphrodites.

Adult tapeworms (Table 2.5, Fig. 2.5), which are another type of flatworm, are spectacular animals varying in length from a few millimetres to several metres. Most tapeworms are easily recognized by their white colour and flattened body composed of a long chain of segments. The segments are generated in the anterior part of the tape, the reproductive organs develop in the middle and the reproductive activity occurs at the posterior end. Nearly all tapeworms are hermaphrodites and nearly all attain sexual maturity in the small

Table 2.5 Major groups of parasitic worms (helminths)

Worm group	Features	Examples from man
PLATYHELMINTHES (FLATWORMS)		
Monogenean flukes	Direct life cycle; usually hermaphrodites; usually ectoparasites of skin and gills of fish.	-
Digenean flukes	Indirect life cycle involving asexual reproduction in snail; usually hermaphrodites; usually endoparasites.	*Clonorchis sinensis* (Chinese liver fluke) *Paragonimus westermani* (Oriental lung fluke) *Schistosoma* spp. (Blood fluke)
Cestoda or tapeworms	Body in form of flattened chain of segments; usually hermaphrodites with indirect life cycle; no gut.	*Diphyllobothrium latum* (Broad tapeworm) *Taenia saginata* (Beef tapeworm)
NEMATODA (ROUNDWORMS)	Body in form of cylinder with tapering ends; sexes separate; direct and indirect life cycles; body cavity and gut; cuticle is moulted during development.	*Ascaris lumbricoides* (Roundworm) *Ancylostoma duodenale* and *Necator americanus* (Hookworms) *Dracunculus medinensis* (Guinea worm) *Onchocerca volvulus and Wuchereria bancrofti* (Filarial worms)
ACANTHOCEPHALA (SPINY-HEADED WORMS)	Retractile proboscis; body cavity; no gut; sexes separate; indirect life cycle involving arthropod intermediate host.	-

intestine of a vertebrate host. The life cycle is usually indirect and the definitive host becomes infected by swallowing immature parasites while eating the intermediate host.

Nematodes (Table 2,5, Fig. 2.5) are another group with endoparasitic representatives. They are called roundworms because they are usually circular in cross section. Most are a few millimeters in length, but *Ascaris lumbricoides* (Figs. 2.5, 3.7), a very common parasite of man, is often over 200mm long and so many people assume that all nematodes are of a similar size. Innumerable nematodes live in the soil and many species are highly destructive parasites of the roots of plants. It is possible that the cost of plant-parasitic nematodes to agriculture is far greater than the cost of animal-parasitic nematodes to man and domestic animals. Of course, no price can be attached to pain and illness; the relief of suffering must be given high priority.

Apart from their cylindrical shape, nematodes may be recognized by their possession of a cuticle which is moulted during development, the form of their body cavity and musculature, and the structure of their gut. Tapeworms, in contrast, do not possess a gut and absorb nutrients from the host environment through their body surface. Nematodes appear always to have separate sexes and the life cycle may be either direct or indirect. Some nematodes enter their hosts in food, some bore through the skin, some pass across the placenta from mother to foetus during pregnancy and some are transmitted by insects. Even those biologists who are anxious to eradicate certain species of nematode would readily agree that they have evolved into a most successful group of animals.

3

Parasites of Man

Further details about 17 parasites of man may be obtained from the summary tables and diagrams in this chapter. These parasites have been chosen because they all cause disease and because their host-parasite relationships illustrate the typical features of parasitism outlined in Chapter 1. For example, adult *Schistosoma mansoni* (Fig. 3.5) lives only in the mesenteric veins of man and not throughout the vascular system. *Taenia saginata* (Fig. 3.6) possesses a specialized attachment organ. The course of an infection of *Mycobacterium leprae,* and the type of disease that may or may not develop, depends on the form of the immune response. Infections with *Onchocerca volvulus* (Fig. 3.9) may last for years whereas infections with influenza virus usually last for a few days. *Plasmodium falciparum* (Fig. 3.4) is a parasite with a high specificity for man in contrast to rabies virus which appears to infect and replicate successfully in many mammalian hosts.

Man serves as host for many other organisms not described in this chapter; in addition to other pathogens, the skin, and the alimentary and respiratory

tracts support vast numbers of micro-organisms which are referred to as the normal microbial fauna and are acquired soon after birth. There is also a characteristic community of micro-organisms living inside the vagina. Experiments with chickens and other animals reared from hatching or birth under strictly germ-free conditions with good nutrition have repeatedly shown that an animal can grow and survive without its normal microbial flora. In the real world, however, the normal microbial flora forms an inseparable part of every man, woman and child and may help to (1) impede the establishment of pathogens, (2) provide a continuous source of stimulation to the immune and inflammatory responses of the alimentary tract and (3) synthesize certain vitamins. It is also important to stress when considering pathogenic parasites that not everyone who comes into contact with a parasite will become infected and that many of those who do may never show the signs and symptoms of disease. Also, the information in the summary sheets is of a general nature and is not likely to apply in every particular to an individual infected with a given parasite. By a simple analogy, there is no reason to expect any man from a group to weigh exactly the average weight of the men in that group.

Table 3.1 Rabies virus. (Rhabdoviridae: Table 2.2).

Size
Beyond resolution of light microscope; bullet-shaped particles (Fig. 2.1), 70 x 180 nm with envelope.

Life cycle
Direct and/or indirect (see below).

Definitive hosts
Man. Natural infections occur in many species of mammal and all experimental infections attempted so far have been successful.

Reproduction
Like other viruses.

Location in man
In cells of muscles, connective tissue, various glands and central nervous system.

Method of transmission to man
Virus particles enter body through skin abrasions. For man, bite of infected dog usually source of infection; virus present in dog's saliva.

Distribution
Worldwide, with U.K. still a notable exception.

Parasitological diagnosis
Prominent inclusions, called Negri bodies after their discoverer, may be observed in a preparation of nerve tissue from an infected host. Another indirect but fast and accurate immunological test for the presence of rabies virus in a host is also available. Any animal (dog, cat or whatever), even if it appears healthy, should be kept under close observation if it bites a person.

Disease
RABIES or HYDROPHOBIA. In man, virus spreads from point of entry to central nervous system causing destruction of nerve tissue and leading to coma and death. The nearer the bite to the brain, the shorter the incubation period of the disease and the sooner the death of the victim.

Notes
Rabies virus infects many species of wild mammal and the recent increase in wildlife rabies, for example in skunks in North America, has resulted in increased risk of human exposure to the virus. In parts of South America, vampire bats are important reservoirs and transmitters of rabies virus; many infected bats appear to remain healthy for a long time.

Table 3.2 Influenza virus (Orthomyxoviridae: Table 2.2).

(Three Types known as A, B and C, have been recognized by immunological tests).

Size
Beyond resolution of light microscope; roughly spherical particles (Fig. 2.1), 80 x 120 nm with envelope.

Life cycle
Direct.

Definitive hosts
Man. Natural infections occur and experimental infections have been established in various animals and animal cells in culture.

Reproduction
Like other viruses.

Location in man
Inside cells lining respiratory tract.

Method of transmission to man
Virus particles enter respiratory tract in airborne droplets.

Distribution
Worldwide.

Parasitological diagnosis
Immunological methods used to identify viral types.

Disease
INFLUENZA. Fever, sore throat, severe headache and upper respiratory tract becomes inflamed and susceptible to secondary invasion by those bacteria which can cause pneumonia.

Notes
Influenza occurs in successive epidemics which spread rapidly once they begin. During the epidemic of 1918-19 over 20 million people died, probably from secondary pneumonia. More than 80 million cases occurred during the 1957-58 epidemic. Children of school age appear to be the most susceptible to infection and elderly people suffer the highest fatality rate. New forms of the 3 types of virus are responsible for the epidemics.

Table 3.3 SALMONELLA spp. (Enterobacteriaceae: Table 2.3).

(More than 1800 types of *Salmonella* have been identified and about 1000 can infect man. By international agreement each type has been given a name, usually after the place where it was first isolated).

Size
Microscopic rods, measuring 2-4 x 0.5 μm.

Life cycle
Direct and/or indirect (see below).

Definitive hosts
Man and various species of bird and mammal including domesticated forms.

Reproduction
Like other bacteria.

Location in man
Salmonella may become dispersed throughout body and may multiply in lymphatic tissues.

Method of transmission to man
By oral route in contaminated food and drink, water, inadequately pasteurized* dairy products, shellfish from dirty water, dried coconut, meat and poultry products including eggs. Household pets are also sources of infection.

Distribution
Worldwide.

Parasitological diagnosis
Depending on form of disease, blood, urine and stool samples should be collected and microbiological cultures prepared.

Diseases
(depending on type of *Salmonella*). TYPHOID and PARATYPHOID; SEPTICAEMIA; GASTROENTERITIS or FOOD POISONING. The variety of symptoms is too complex to include here.

Notes
The life cycle may be described as indirect because some types of *Salmonella* do not always pass directly from man to man, but may be acquired from infected animals.

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*Killing bacteria in milk by heat treatment is called pasteurization after Louis Pasteur (1822-1895).

Table 3.4 VIBRIO CHOLERAE (Spirillaceae: Table 2.3).

Common name
Vibrios.

Size
Microscopic, comma-shaped, measuring 1.5-2 x 0.5-0.6 μm.

Life cycle
Direct.

Definitive host
Man.

Reproduction
Like other bacteria, but spores are not formed.

Location in man
Vibrios multiply in lumen of small intestine and become attached to surfaces of enterocytes (intestinal epithelial cells).

Method of transmission
Vibrios enter body by oral route as contaminants of food and drinking water in densely populated places where high standards of cleanliness cannot be maintained.

Distribution
Sub-continent of India and South-East Asia; *V.cholerae* carried by travellers to many countries.

Parasitological diagnosis

By isolating vibrios from faeces of infected person and growing them under specific culture conditions.

Disease
CHOLERA. Within a few days of acquiring vibrios, host experiences vomiting, abdominal pain and profuse diarrhoea. Volume of watery stools may be up to 1 litre per hour and death from dehydration is the likely fate of an untreated case. Cholera enterotoxin is responsible for the fluid loss.

Notes
In an outbreak of cholera, there may be as many as 100 infected people who do not show any ill effects for every person in a state of collapse. These seemingly healthy carriers, however, continue to spread the pathogenic vibrios in the community.

Table 3.5 TREPONEMA PALLIDUM (Spirochetales: Table 2.3).

Common name
Treponemes.

Size
Microscopic, spiral-shaped organisms (spirochaetes), measuring 5-15 μm x 0.2 μm.

Life cycle
Direct.

Definitive host
Man. Experimental infections in rabbits.

Reproduction
Usually by transverse fission.

Location in man
Treponemes multiply at site of entry and some travel via blood and lymph to bones, nervous system, brain and heart.

Method of transmission
Through small abrasions during sexual intercourse.

Distribution
Worldwide.

Parasitological diagnosis
By observations of living treponemes displaying characteristic spiral motility. Procedure requires a drop of fluid from a lesion and a good quality light microscope equipped with oil immersion lens and dark-field illumination. Fixed and stained treponemes may be observed, but diagnosis usually dependent on some form of immunological test.

Disease
SYPHILIS. After infection, onset of disease recognized by development of typical ulcer followed by fever and skin rash. Ultimately, perhaps years later, severe symptoms are seen resulting from degenerative changes in arteries and central nervous system.

Table 3.6 MYCOBACTERIUM LEPRAE (Actinomycetales: Table 2.3).

Size
Microscopic, slender rods, measuring 3-10 x 0.5 μm.

Life cycle
Direct.

Definitive host
Man. Experimental infections established in mouse and nine-banded armadillo, *Dasypus novemcintus*.

Reproduction
Mycobacterium leprae has not yet been grown in culture, but probably reproduces like other types of bacteria. Generation time extremely slow: cell of bacterium *Escherichia coli* may divide in about 20 min whereas cell of *M. leprae* takes about 12 or 13 days to divide under ideal conditions in mice.

Location in man
Bacteria inside macrophages associated with skin and nerve-endings in skin, growing best in cooler parts of body.

Method of transmission
Probably occurs through skin when infected and uninfected people meet. Bacteria may be shed into the air when infected people sneeze or cough.

Distribution
Widespread, in Africa, India and South-East Asia.

Parasitological diagnosis
By identifying bacteria in a smear from a suspected skin lesion.

Disease
LEPROSY. Two main forms, tuberculoid leprosy (TT) and lepromatous leprosy (LL), depending largely on immune response of host (Chapter 7) to activities of bacterium. Disease develops slowly and sufferers have typical skin lesions. Numbness, weakness, damage to nerves. TT less serious than LL which often results in hideous deformities of limbs. Probably no other parasitic disease has so much fear and social stigma attached to it. In the Middle Ages in European countries, lepers (sufferers of leprosy) were driven out of their homes and forced to live as beggars and to ring a bell or shake a rattle as a warning of their approach.

Table 3.7 TRICHOPHYTON spp. (Fungi; Dermatophytes).

Size
Microscopic.

Life cycle
Direct.

Definitive hosts
Man and various domesticated animals.

Reproduction
Asexually through production of spores.

Location in man
Spores settle on skin; hyphae grow inside horny layer (keratinized tissue) of skin.

Method of transmission to man
By direct contact with infected person or by indirect contact with infected skin debris.

Distribution
Worldwide, particularly in tropical and sub-tropical countries.

Parasitological diagnosis
Microscopic to confirm fungi and culture methods to identify types.

Disease
RINGWORM. Tinea capitis or tonsurans (ringworm of the scalp); Tinea corporis (ringworm of the body); Tinea cruris (ringworm of the groin); Tinea pedis (athlete's foot). Fungi generally grow in an annular pattern to form typical round lesions of ringworm infection. Ringworm of scalp occurs during childhood and is rare after puberty.

Table 3.8 LEISHMANIA DONOVANI and L. TROPICA (Flagellate protozoa; Table 2.4. Fig. 3.1).

(Morphological differences between one species of *Leishmania* and another are not obvious. Modern approaches to leishmanial taxonomy are beyond the scope of this book. Consequently, *L. donovani* and *L. tropica* are used to indicate two general groupings and nothing more).

Size

Microscopic, about 1-4 μm in diameter and about 14-20 μm in length while inside mammalian cells. With locomotory flagellum while developing in insect host.

Life cycle

Indirect (Fig. 3.1) involving female blood-sucking sandflies (Diptera: Phlebotomidae). Sandflies very small (about 3 mm) and breed in cracks in rocks and walls.

Definitive hosts

Leishmania donovani. Man, dog, cat, sheep, horse. *L.tropica*. Man, dog, gerbil, various wild rodents and forest animals.

Reproduction

Asexual, multiplication by binary fission inside mammalian cells and in midgut of insect host.

Location in man

Leishmanias occur inside macrophages and cells of RE system located in spleen, bone marrow, liver, lymph nodes and skin.

Method of transmission to man

Usually enter the body through bite made in skin when female sandfly feeds on blood. *Phlebotomus* and *Lutzomyia* most important sandflies in leishmanial life cycle.

Distribution

(Principal regions associated with the types of disease). *Leishmania donovani*: India; East Africa; China; Mediterranean countries; South America. *L. tropica*: Mediterranean region to Central and Northern India; Central Asia; West Africa; Central and South America.

Parasitological diagnosis

Identification of leishmanial organisms in biopsy specimens of spleen and bone marrow or in fluid from skin ulcers.

Disease

LEISHMANIASIS. *Leishmania donovani*. VISCERAL leishmaniasis (Dum-dum fever and Kala azar). Fatal disease if untreated. Fever accompanies invasion of RE cells, particularly in liver and spleen which both become enlarged. *L. tropica*. CUTANEOUS leishmaniasis. Leishmanias invade RE cells in skin where unsightly ulcers develop. South American leishmanias cause MUCOCUTANEOUS leishmaniasis in which target cells are often in mucous membranes of head. In time, dreadful facial disfigurement may occur in cases of mucocutaneous leishmaniasis.

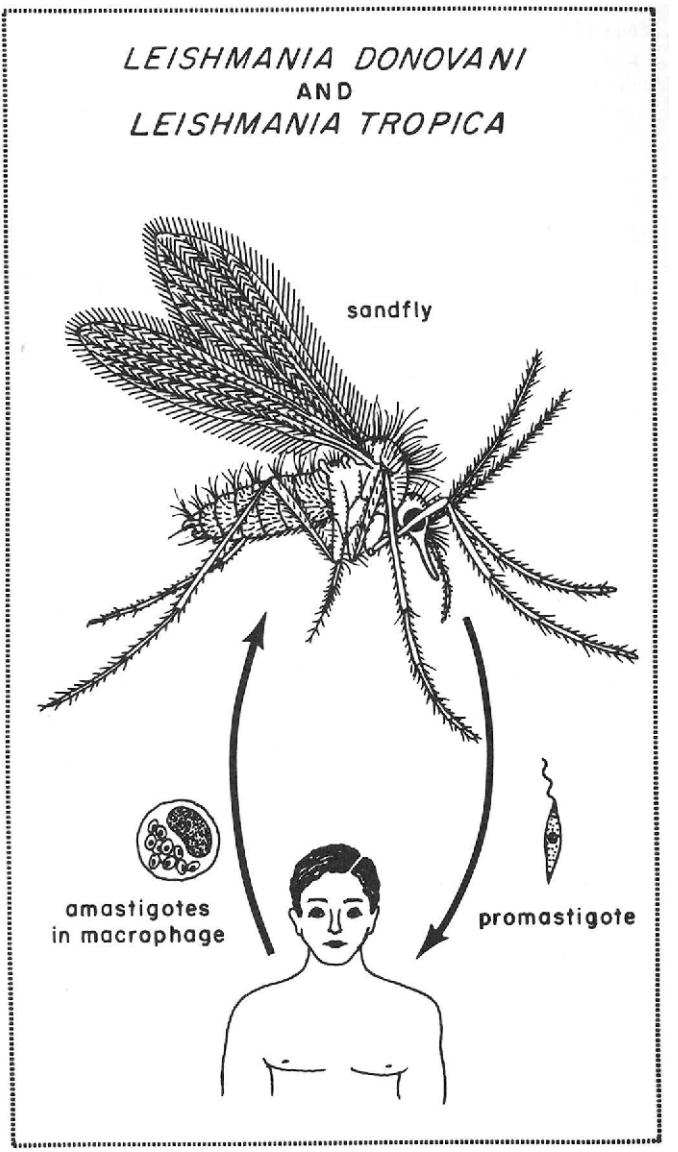


Fig. 3.1 Life cycle of *Leishmania* spp.

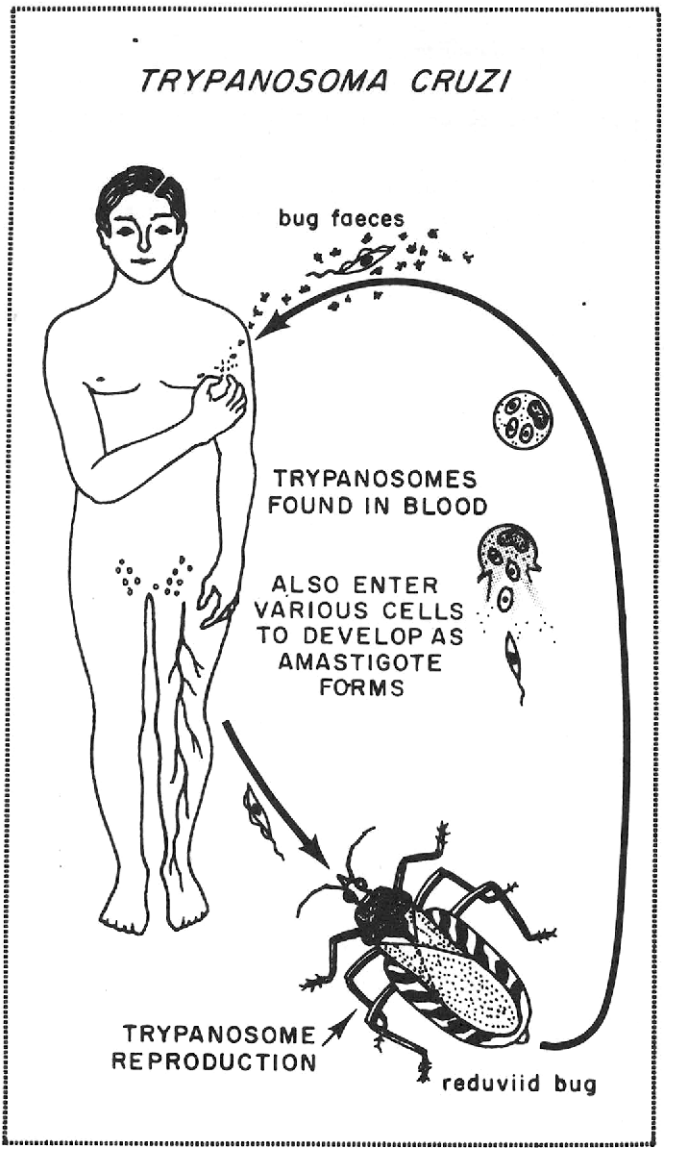


Fig. 3.2 Life cycle of *Trypanosoma cruzi*.

Table 3.9 TRYPANOSOMA CRUZI (Flagellate protozoon: Table 2.4, Fig. 3.2).

Common name
South American trypanosomes.

Size
Microscopic, about 20 μm in length with locomotory flagellum.

Life cycle
Indirect (Fig. 3.2) involving male and female, nymphal and adult stages of blood-sucking bugs (Hemiptera: Reduviidae). Bugs breed in houses.

Definitive hosts
Man (Table 5.3), armadillo, opossum, dog, cat, pig, and probably many species of wild and domesticated mammal.

Reproduction
Asexual; binary fission in midgut of insect and in certain cells of mammalian host.

Location in man
Trypanosomes occur in blood plasma and lymph. They also enter cells of RE system and heart muscles where they round up and divide.

Method of transmission to man
When feeding, blood-sucking bugs produce large amounts of urine which flushes infective trypanosomes out of gut and over bite enabling them to enter body.

Distribution
From southern parts of U.S.A., through Mexico and Central America to Argentina.

Parasitological diagnosis
Either by finding trypanosomes in a stained blood film (parasite is usually observed to have been fixed in a characteristic crescent shape) or by allowing susceptible, infection-free bugs to feed on blood from suspected case and then searching for developing trypanosomes in test host (xenodiagnosis).

Disease
CHAGAS'S DISEASE. Acute and chronic forms of the disease occur in young children and adults respectively. Fever, headache and weakness; bodily tissues, including heart muscle cells, are destroyed.

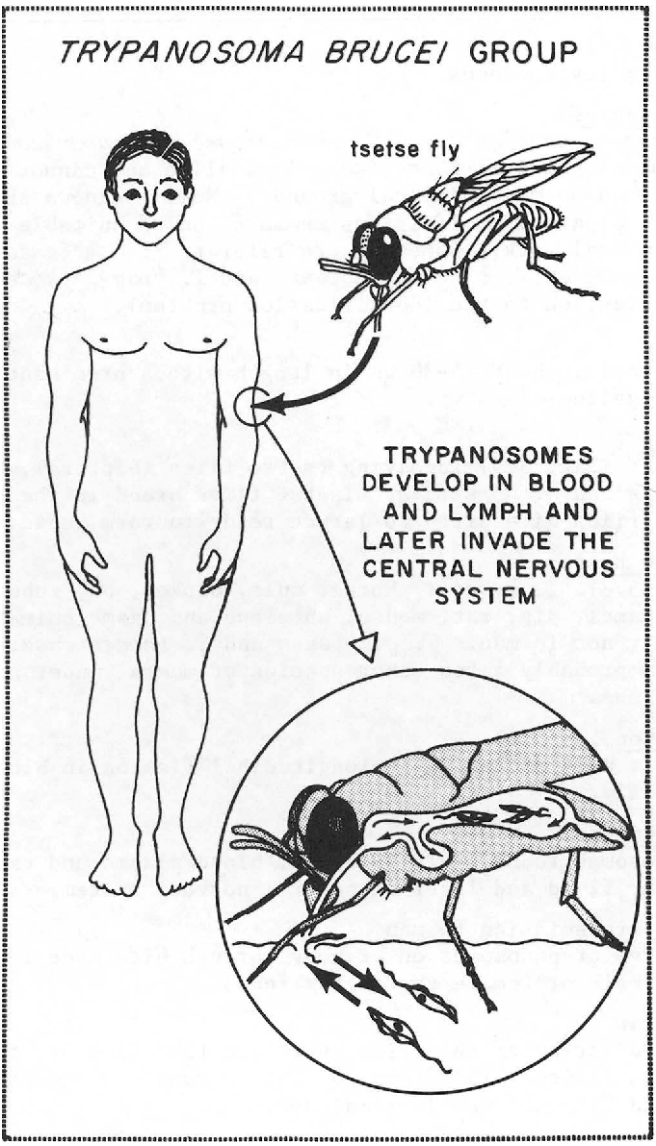


Fig. 3.3 Life cycle of *Trypanosoma brucei* group.

Table 3.10 TRYPANOSOMA BRUCEI and related species (Flagellate protozoa: Table 2.4, Fig. 3.3).

Common name

American trypanosomes.

Related species

Trypanosoma gambiense and *T. rhodesiense*. (*Trypanosoma brucei*, *T. gambiense* and *T. rhodesiense* look alike and cannot be distinguished on morphological grounds. Most is known about *T. brucei*, a parasite of various mammals and so suitable for experimental work. Some workers refer to *T. gambiense* and *T. rhodesiense* as *T. brucei gambiense* and *T. brucei rhodesiense* to draw attention to the identification problem).

Size

Microscopic, about 15-30 μm in length with a prominent, locomotory flagellum.

Life cycle

Indirect (Fig. 3.3) involving tsetse flies (Diptera), *Glossina palpalis* and *G. morsitans*. Tsetse flies breed in the bush; female flies give birth to larvae ready to form pupae.

Definitive hosts

(Table 5.3). *T. brucei*: Horse, mule, donkey, ox, zebu, sheep, goat, camel, pig, rat, mouse, antelope and "game animals". Probably not in man. *T. gambiense* and *T. rhodesiense*: Man mainly; probably a few other species of mammal under natural conditions.

Reproduction

Asexual; multiplication by longitudinal fission in blood and in tsetse fly.

Location in man

Trypanosomes found early in lymph, blood plasma and extracellular fluid and later in central nervous system.

Method of transmission to man

Infective trypanosomes enter body through bite made in skin when either male or female tsetse fly feeds.

Distribution

Widely distributed in Africa where tse-tse flies are found (between latitude 15° N and 25° S); *Trypanosoma rhodesiense* in East and *T. gambiense* in remainder.

Parasitological diagnosis

By finding trypanosomes in blood, lymph or cerebrospinal fluid.

Disease

TRYPANOSOMIASIS or SLEEPING SICKNESS. (*Trypanosoma brucei* causes nagana in cattle). Headache, weakness and fever followed by characteristic "sleepiness" as nervous system affected. Anaemia occurs.

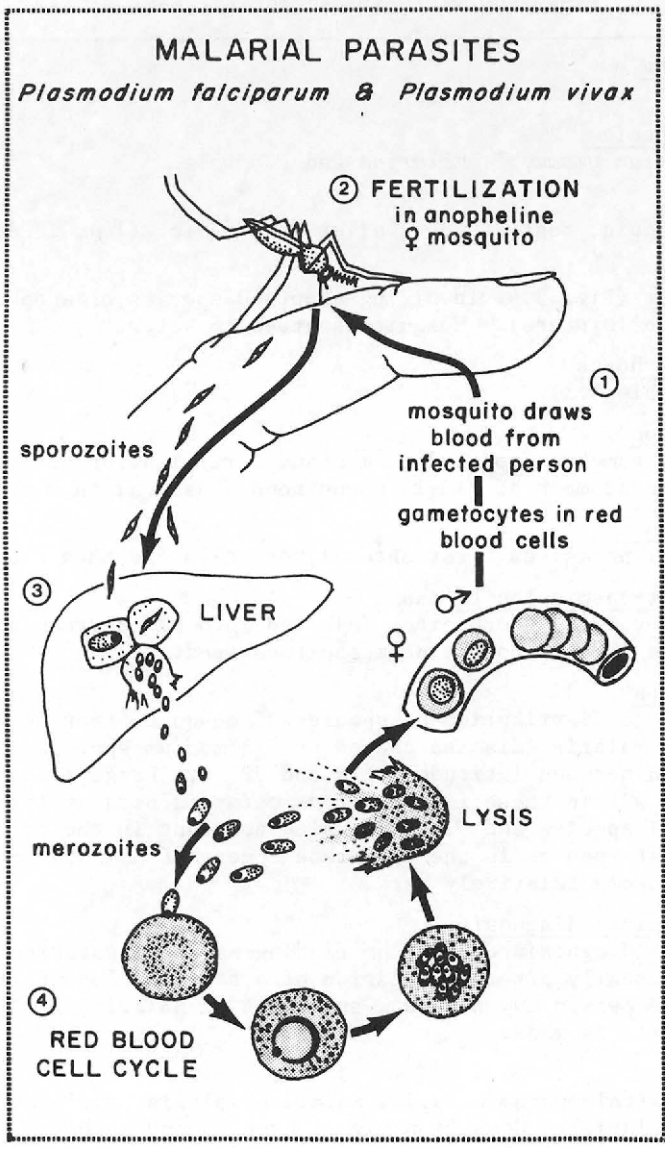


Fig. 3.4 Life cycle of *Plasmodium falciparum* and *P. vivax*. The development of *P. falciparum* involves only one cycle of multiplication in the liver.

Table 3.11 PLASMODIUM FALCIPARUM and related species (Sporozoan protozoa; Table 2.4, Fig. 3.4).

Common name
Malarial parasites.

Related species
Plasmodium vivax, P. malariae and *P. ovale.*

Size
Microscopic, most stages smaller than r.b.c. (7 μm in diameter).

Life cycle
Indirect (Fig. 3.4) involving about 60 species of anopheline mosquito (Diptera). Mosquitoes breed in water.

Definitive hosts
Man (Table 5.3).

Reproduction
Sexual; gametes produced in man and fertilization occurring in blood in stomach of female mosquitoes. Asexual in man.

Location in man
Malarial parasites first enter liver cells and then r.b.cs.

Method of transmission to man
Fully developed sporozoites injected into bloodstream when infected FEMALE anopheline mosquitoes feed.

Distribution
Depends on distribution of species of mosquito that serve as hosts. Malaria (disease caused by *Plasmodium* spp.) has been recorded between latitude 64° N and 32° S. Large areas free of disease within these limits. *Plasmodium falciparum* is commonest tropical species and *P. vivax,* also abundant in the tropics, is commonest species in the temperate zones. *Plasmodium malariae* and *P. ovale* relatively rare.

Parasitological diagnosis
Definite diagnosis depends on finding malarial parasites in blood, usually after examination of a stained blood film. Infected person may not show any signs of malaria at time when blood film is made.

Disease
MALARIA (falciparum malaria, malariae malaria, ovale malaria and vivax malaria). Condition highly complex and involves bouts of high fever, headache, nausea, destruction of r.b.cs. and anaemia. Spleen enlargement. Death often occurs in untreated cases of falciparum malaria.

Notes
About 3000 species of mosquito are known and many neither suck blood nor transmit disease. The benign species pollinate flowers and serve as food for birds and other predators.

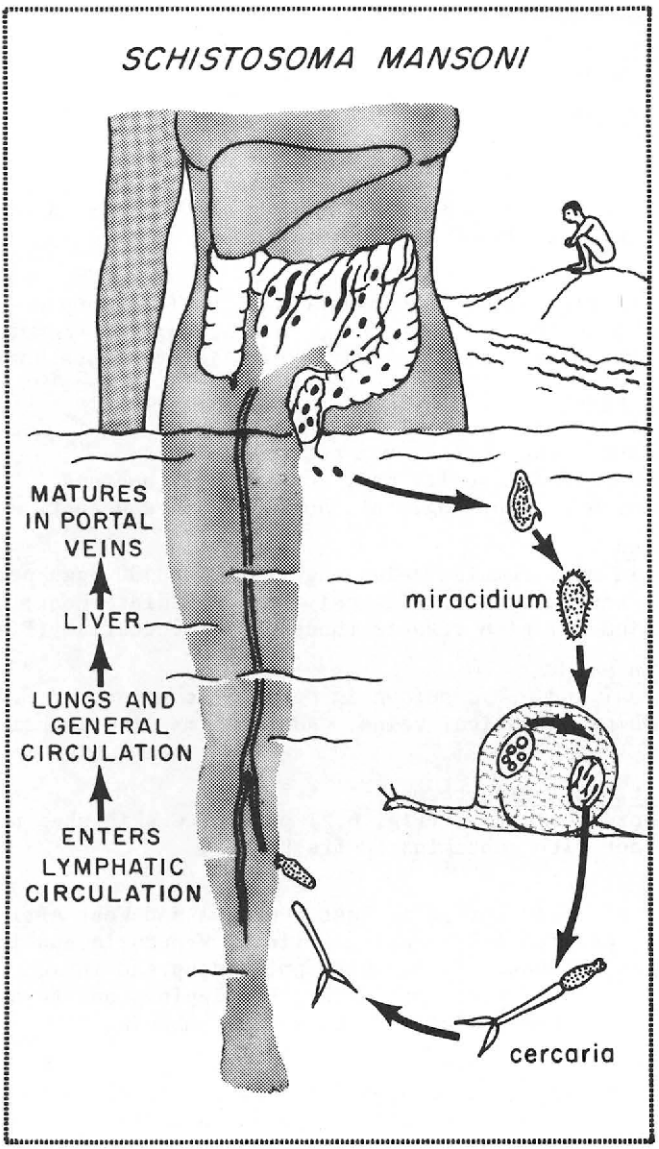


Fig. 3.5 Life cycle of *Schistosoma mansoni*.

Table 3.12 SCHISTOSOMA MANSONI and related species (Digenean flukes: Table 2.5, Fig. 3.5).

Common name

Blood flukes.

Related species

Schistosoma haematobium and *S. japonicum*.

Size

Adult males of the 3 species measure 6-20 x 0.5-1.1 mm and adult females measure 10-30 x 0.16-0.3 mm.

Life cycle

Indirect (Fig. 3.5). Freshwater snails, for example *Biomphalaria* spp. *(S. mansoni)*, *Bulinus* spp. *(S. haematobium)* and *Oncomelania* spp. *(S. japonicum)*, form intermediate hosts.

Definitive hosts

(Table 5.3).

S. mansoni: man, baboon and rodents.

S. haematobium: usually man, occasionally baboons.

S. japonicum: man, dog, rat, buffalo, pig and goat.

Reproduction

Sexual in man; females releasing from 300-3500 eggs per worm per day for several years. Asexual in intermediate host; one miracidium may give rise to thousands of cercariae (Fig. 6.2).

Location in man

S. mansoni and *S. japonicum* in mesenteric veins and *S. haematobium* in vesical veins. Adult worms live in pairs (Fig. 2.5).

Method of transmission to man

Water-borne cercariae (Fig. 6.2) penetrate skin when people are in contact with contaminated freshwater.

Distribution

S. mansoni: Widespread in East, Central and West Africa, in S. America, particularly Brazil, Surinam, Venezuela and in some Caribbean Islands. *S. haematobium*: Widespread in many countries of Africa. *S. japonicum*: China, Philippines and to a lesser extent in Vietnam, Thailand, Laos and Cambodia.

Parasitological diagnosis

By finding large spined eggs (Fig. 6.2; eggs characteristic for each species) in either stool or urine samples.

Disease

SCHISTOSOMIASIS. A chronic, debilitating condition in which much tissue damage is caused after spined eggs have become trapped in organs like the liver and in bladder wall.

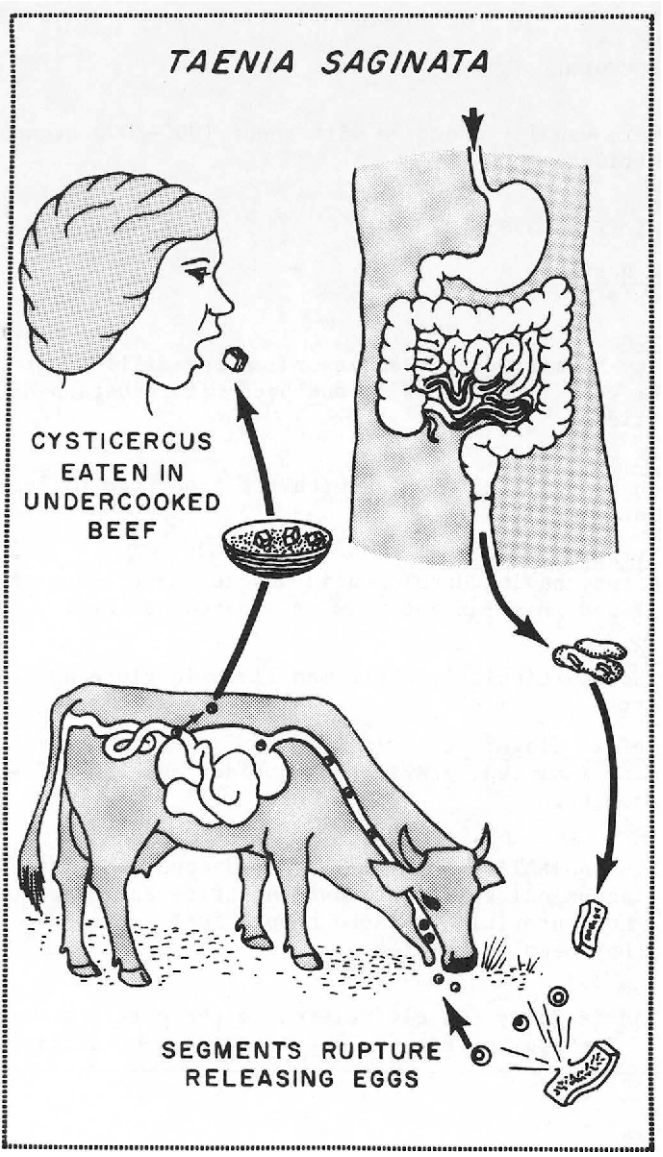


Fig. 3.6 Life cycle of *Taenia saginata*.

Table 3.13 TAENIA SAGINATA (Cestoda; tapeworms: Table 2.5, Fig. 3.6).

Common name
Beef tapeworm.

Size
Adult worm usually about 5m with about 1000-2000 segments (proglottides).

Life cycle
Indirect (Fig. 3.6).

Definitive hosts
Man (Table 5.3).

Reproduction
Sexual by hermaphroditic adults releasing millions of eggs per worm per year. Eggs usually enclosed within detached proglottides.

Location in man
Attached by scolex to mucosa with the tape free in lumen of small intestine.

Method of transmission to man
Cysticercus, having developed in muscle and tissues of cattle, is swallowed when man eats raw or undercooked beef.

Distribution
Worldwide, particularly where man lives in close association with cattle.

Parasitological diagnosis
By finding isolated, gravid proglottides and eggs (Fig. 6.2) in stool samples.

Disease
TAENIASIS SAGINATA. A relatively mild condition involving nausea, abdominal pain, depressed appetite and headache. Perhaps not surprisingly, some people feel worse once their problem has been identified.

Notes
Taenia saginata is closely related to the pork tapeworm *T. solium*. The eggs of the two species cannot be distinguished.

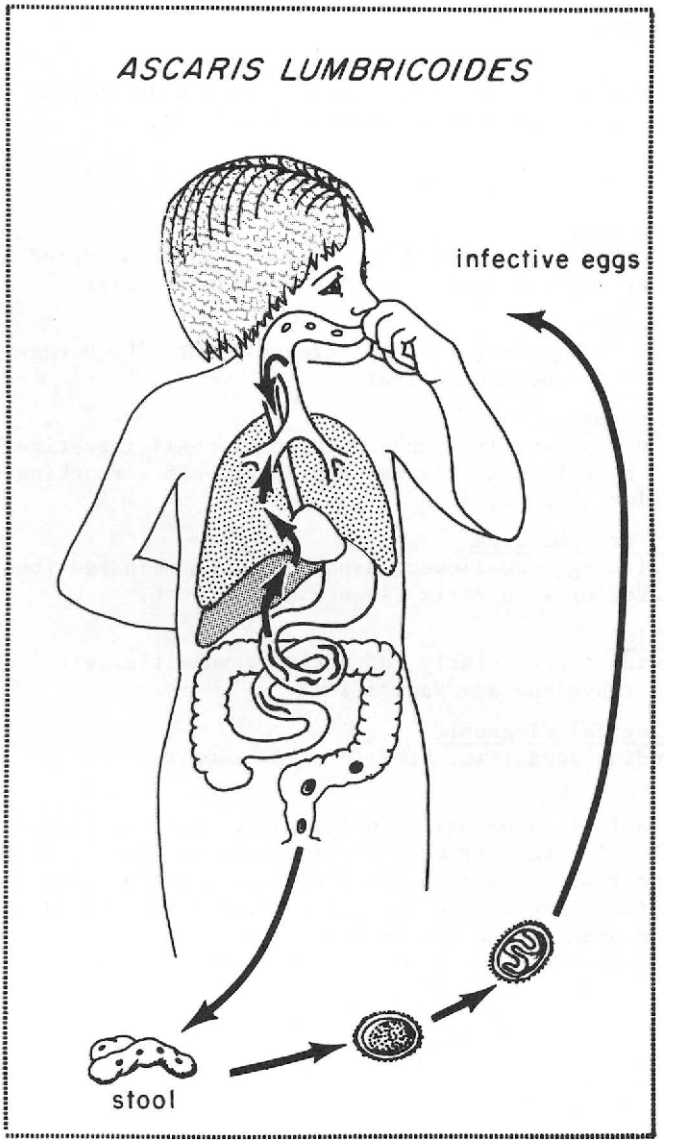


Fig. 3.7 Life cycle of *Ascaris lumbricoides*.

Table 3.14 ASCARIS LUMBRICOIDES (Nematoda: Table 2.5, Fig. 3.7).

Common name
Roundworm.

Size
Adult female 200-400 x 3-6 mm and adult male 150-300 x 2-4 mm. Posterior end of male is curved (Fig. 2.5).

Life cycle
Direct (Fig. 3.7).

Definitive host
Man (Table 5.3) provided *A. lumbricoides* is accepted as a separate species from *A. suum* which infects pigs.

Reproduction
Sexual; females reported to release about 200000 eggs per worm per day, for perhaps a year.

Location in man
Adult worms usually found in lumen of small intestine. Larval stages move through tissues and lungs before reaching small intestine (Fig. 3.7).

Method of transmission
Infective eggs swallowed, usually in contaminated food or drinking water or when dirty fingers enter mouth.

Distribution
Worldwide, particularly in settled communities with poor facilities for hygiene and sanitation.

Parasitological diagnosis
By finding eggs (Fig. 6.2) in stool samples.

Disease
ASCARIASIS. Abdominal pain and nausea with disturbed functioning of alimentary tract. Consequences serious, particularly for undernourished young children with relatively heavy infections. Intestinal obstruction may occur. Respiratory problems sometimes develop when larvae are in the lungs.

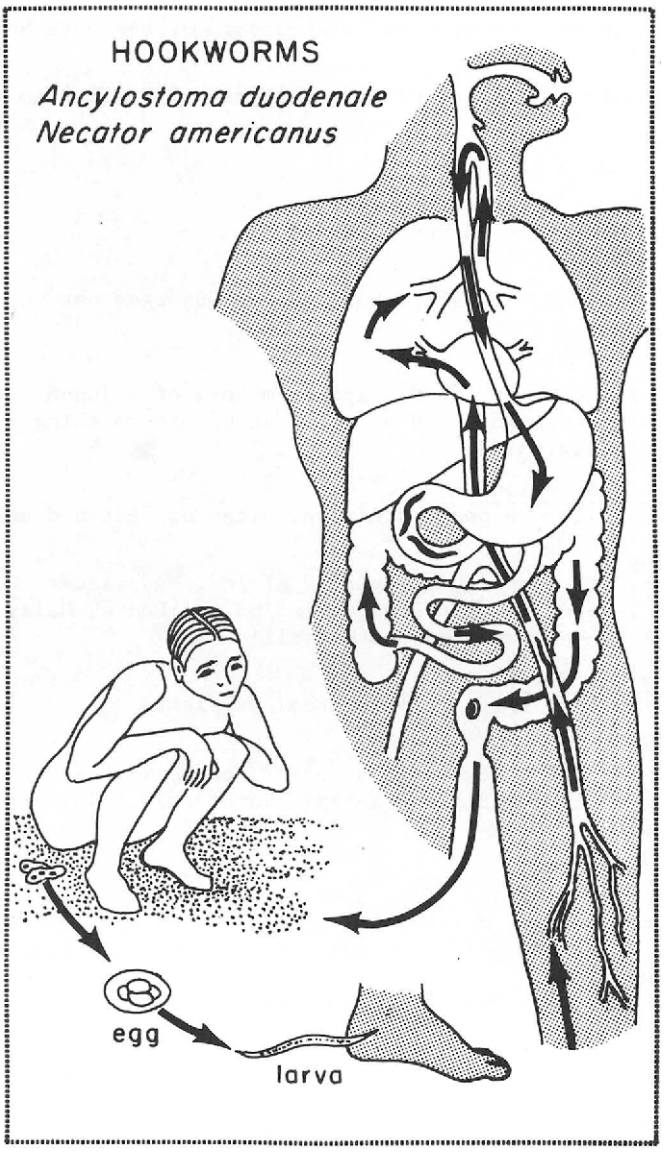


Fig. 3.8 Life cycle of hookworms.

Table 3.15 NECATOR AMERICANUS (Nematoda: Table 2.5, Fig. 3.8).

Common name
Hookworm (name also applies to *Ancylostoma*, see note below).

Size
Adult female 9-11 x 0.4 mm and adult male 5-9 x 0.3 mm.

Life cycle
Direct (Fig. 3.8).

Definitive hosts
Almost exclusively in man (Table 5.3).

Reproduction
Sexual; females releasing about 6000-20000 eggs per worm per day, for perhaps years.

Location in man
Adult worms usually found gripping mucosa of jejunum. Larval stages move through tissues and lungs before reaching small intestine (Fig. 3.8).

Method of transmission
Third-stage larvae penetrate skin, often of feet and ankles.

Distribution
Widespread in tropics, especially Africa, Madagascar, Colombia, Brazil, Venezuela, West Indies, India, Sri Lanka, Malaysia, China, Indonesia and the South Pacific.

Parasitological diagnosis
By finding eggs (Fig. 6.2) in stool samples.

Disease
HOOKWORM DISEASE. *Necator* and other hookworms are blood suckers and chronic iron deficient anaemia may result. Intestinal damage also occurs.

Notes
Ancylostoma duodenale (Fig. 3.8) is another important but less common hookworm of man than *N. americanus*. It is not usually possible to distinguish the eggs of *Necator* from those of *Ancylostoma*.

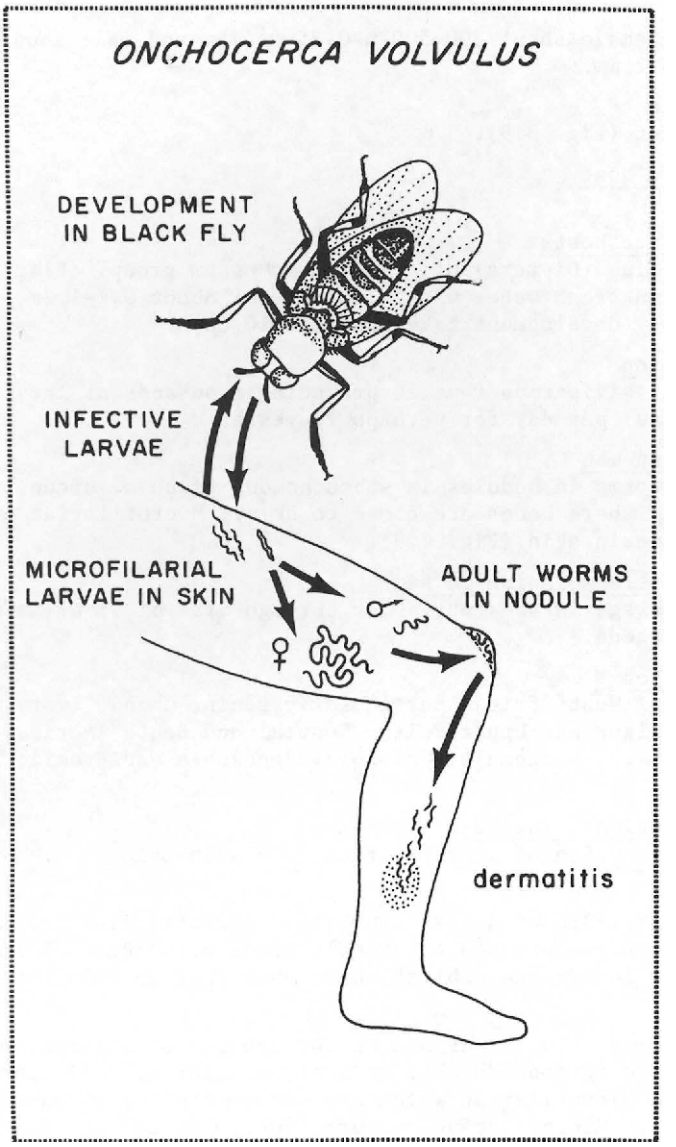


Fig. 3.9 Life cycle of *Onchocerca volvulus*.

Table 3.16 ONCHOCERCA VOLVULUS (Nematoda: Table 2.5, Fig. 3.9).

Size
Adult female about 300-500 x 0.25-0.4 mm and male about 20-40 x 0.15-0.2 mm.

Life cycle
Indirect (Fig. 3.9).

Definitive host
Man.

Intermediate hosts
Blackflies (Diptera) of *Simulium damnosum* group. Blackflies breed in fresh water with flow rate of about 0.7-1.2m per sec. Blackfly development takes about 8-10 days.

Reproduction
Sexual; viviparous females producing thousands of larvae (microfilariae) per day for perhaps 20 years.

Location in man
Adult worms in nodules in subcutaneous tissues, often in regions of body where bones are close to skin. Microfilariae unsheathed and live in skin (Fig. 3.9).

Method of transmission to man
Third-stage larvae enter body through bite of *Simulium damnosum* as it feeds.

Distribution
Tropical West Africa, particularly Benin, Ghana, Ivory Coast, Mali, Niger and Upper Volta, Central and South America, including Mexico, Guatemala, Colombia, Venezuela and Brazil, and the Yemen.

Parasitological diagnosis
Identification of microfilariae in a skin snip.

Disease
ONCHOCERCIASIS or RIVER BLINDNESS. Microfilariae are main pathogenic agents and frequently cause blindness. Form of the disease in savanna habitat worse than that in rain-forest.

Notes
Onchocerca volvulus is one of the species of filarial nematode which are of considerable medical importance. All species produce microfilariae which are transmitted by blood-feeding insects. Microfilariae measure 150-350 μm and are found in either blood or skin.

4

Man as Host

At present the earth supports about 4200 million people. Man *(Homo sapiens)* is a recent species; his earliest relatives probably existed about 15 million years ago, but it is only within the last few million years that *Homo* came into being. Modern man has evolved rapidly and the world's population is growing quickly, particularly in the developing countries. The growth in population must be associated with man's capacity to change his environment to suit his needs. In the developed countries, such changes have generally brought relief from the effects of parasitic disease, but in the developing countries, the relief has still to materialize (Chapter 5).

Modern man's striking differences from all other animals have contributed to the development of social and community life which in turn have led to successful health care on the one hand and the spread of some parasites and improved opportunities for their transmission on the other. In other respects, modern man forms part of the third, or living habitat on the earth (Chapter 1) and within the world's population of people, or within an individual person, are a series of micro-

habitats or environments with their own characteristic faunas. For example, certain parasites live in the blood, or the alimentary tract or in the nervous system. Each parasite described in Chapter 3 has a particular habitat or series of habitats during its relationship with man. Some knowledge of the composition of the normal or healthy human body is useful when attempting to understand disease because disease is damage to the structure or functioning of a part of the body. Every living body, however, is endowed with control and regulatory mechanisms which act to keep the body in a constant state. This does not mean stagnation; the processes which maintain bodily constancy are known as homeostatic mechanisms. For example, blood sugar concentrations are kept within a certain range, body weight is maintained within a given range once adulthood has been attained, and body temperature is closely regulated. The activities of some parasites in some people impinge on the complex networks of homeostatic control and when the body's reserves are depleted disease sets in.

The summarized information about the human body presented in this chapter is concerned with average values and measurements obtained from the statistical treatment of results from surveys of all kinds of people. It is not likely that any person will be exactly the same as the man, woman or child who may emerge below.

THE HUMAN LIFE CYCLE

Nine months after conception, a baby is born and embarks on the series of stages that are illustrated diagrammatically in Fig. 4.1. On average, about 105 male babies are born for every 100 females, but women

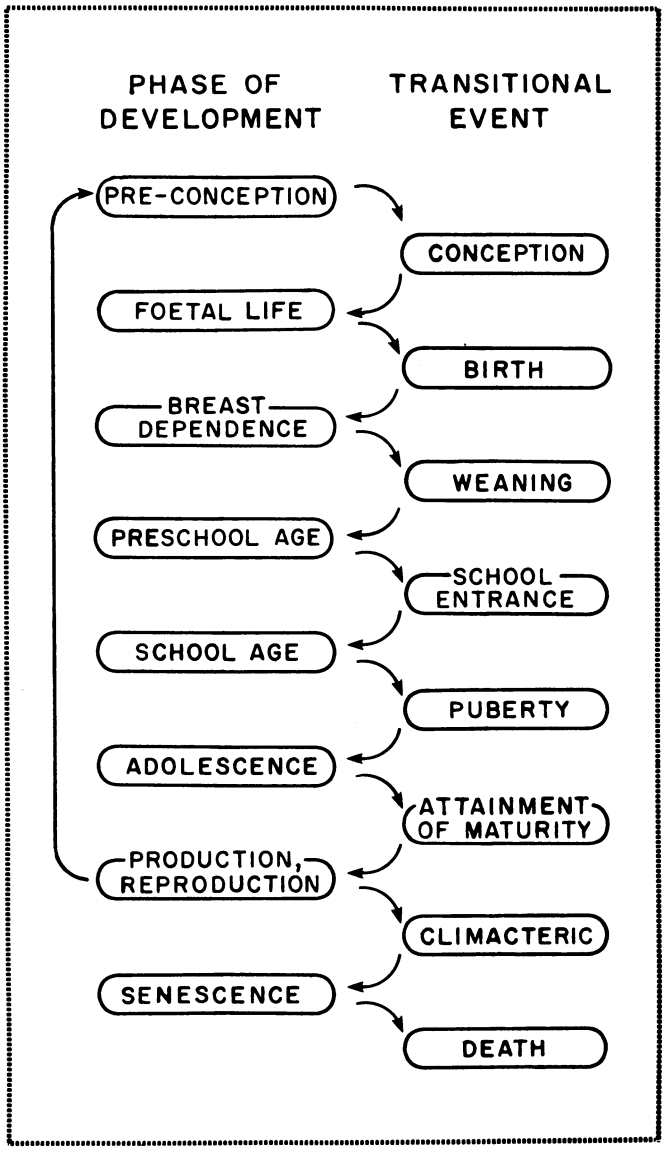


Fig. 4.1 Events during the human life cycle (Redrawn from W.H.O. Technical Report Series 485, 1972).

usually live longer than men. At every stage in this series, the human being is susceptible to some type of parasitic infection. The pre-school period in a child's life, between weaning and school entrance (Fig. 4.1), seems to be a time when parasitic disease is very serious in developing countries and when growth and development (Fig. 4.2) are sensitive to the effects of disease and undernutrition.

ADULT BODY COMPOSITION (Table 4.1)

An average man between the ages of 20 and 39, weighs about 65-70kg and is about 1.6-1.7m tall. On most days, he spends about 8h in bed and 8h at work. The rest of his time is spent in walking, eating and a range of light activities. An average woman weighs about 55-60kg and is about 1.5-1.6m tall. Her time is generally spent similarly to a man's although women in developing countries tend to do much heavier work than their counterparts in the developed nations. The body is made up of about 5×10^{13} cells which may, like red blood cells, live in relative isolation or may adhere to similar cells to form organs like muscles. Cells undergo continual repair and replacement, although at different rates of turnover; for example nerve cells are long lived and not easily repaired, while the cells lining the small intestine live on average for about 24-36h and are quickly replaced.

NUTRITION

The growth, development and healthy working of the body, the maintenance of its composition and the energy for all forms of physical, chemical and electrical activity depend on the quality and quantity of the food that is eaten. Carbohydrate, fat and protein are the chief components of our food, but vitamins, minerals

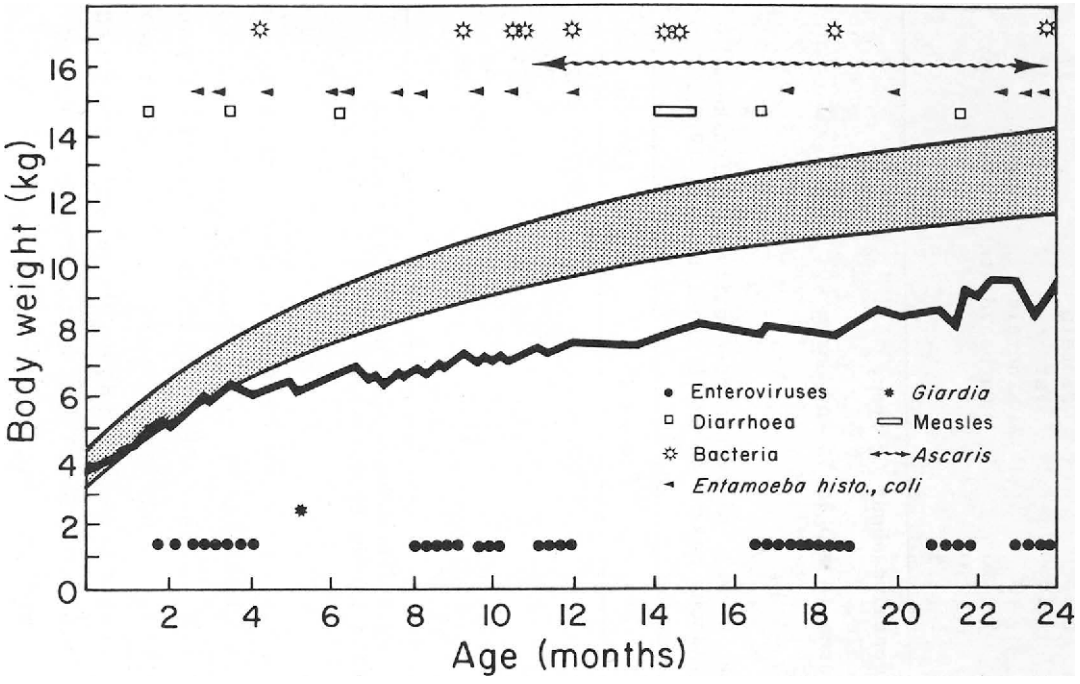


Fig. 4.2 Observations on the establishment of infections in a young child from a rural community in Central America (Redrawn from Gordon, 1976 and based on Mata *et al*, 1967). The broad stippled band represents the range of normal or standard growth as measured by body weight. The solid line shows the body weight of the child.

Table 4.1 Body composition. (After Latham, 1979)

Element	%	Compound	% body weight
Oxygen	65	Water	63
Carbon	18	Protein	17
Hydrogen	10	Fat	12
Nitrogen	3	Minerals	7[a]
Calcium	1.5	Carbohydrate	1
Phosphorus	1.0		
Others	1.5		

[a]The adult body contains about 4g iron;
2.5g in haemoglobin,
0.5g in the tissues in myoglobin and enzymes,
1.0g in storage.

Table 4.2 An example of recommended daily food intakes. (After Davidson, Passmore, Brock and Truswell, 1975).

Age (yr)		Energy (MJ)	Protein (g)[a]
Infant	<1	3.3	20
Child	5	7.5	30
Boy	15	12.0	54
Girl	15	9.6	48
Man	35	13.0	56
Woman[b]	35	9.2	46

[a]Type of protein may affect amount that needs to be eaten.
[b]Intakes for a woman should be increased during pregnancy and breast feeding.

and trace elements are also essential for a healthy life. There is still no internationally agreed list of recommended daily intakes of different nutrients because different proteins in different parts of the world have different nutritional value. However, a well balanced diet ought to contain about 58% carbohydrate, 30% fat and 12% protein and an example of daily intakes for energy (best supplied as complex carbohydrate and fat) and protein is given in Table 4.2. An ideal diet is not digested completely; some of the carbohydrate needs to be in the form of indigestible fibre.

Clean water is a crucial ingredient of every diet and an essential element of food production. About 7500 litres of water are reckoned to be needed to produce each kg of food eaten in the U.S.A.

SKIN

The skin is the largest organ of the body and may form as much as 16% of the body weight. Its area is $1.8m^2$ in an adult man and $1.6m^2$ in an adult woman. The structure of the skin is shown in Fig. 4.3. On average the epidermis and dermis together vary in thickness from 1-2mm, and the outer horny layer, which consists of hardened dead cells, also varies in thickness according to the part of the body. For example, the horny layer on the soles of the feet and the palms of the hands tends to be thicker than elsewhere. A sulphur-containing protein called keratin provides the characteristic structural component of the skin.

The skin has many functions including protection from mechanical, chemical and physical injury. It is a barrier that many infectious agents must cross if they are to become established in the human host and it forms the principal environment of several parasites of major importance to man (Chapter 3). The breasts or mammary glands, hair, nails and teeth are all skin derivatives.

BLOOD

Our average man, weighing about 70kg, contains about 5 litres of blood which is a mixture of fluid and cells. The blood, heart and blood vessels transport gases, nutrients, hormones, antibodies (Chapter 7), waste products, ions, water and certain parasites to all parts of the body. The fluid part of the blood or plasma consists of about 90% water in which are dissolved

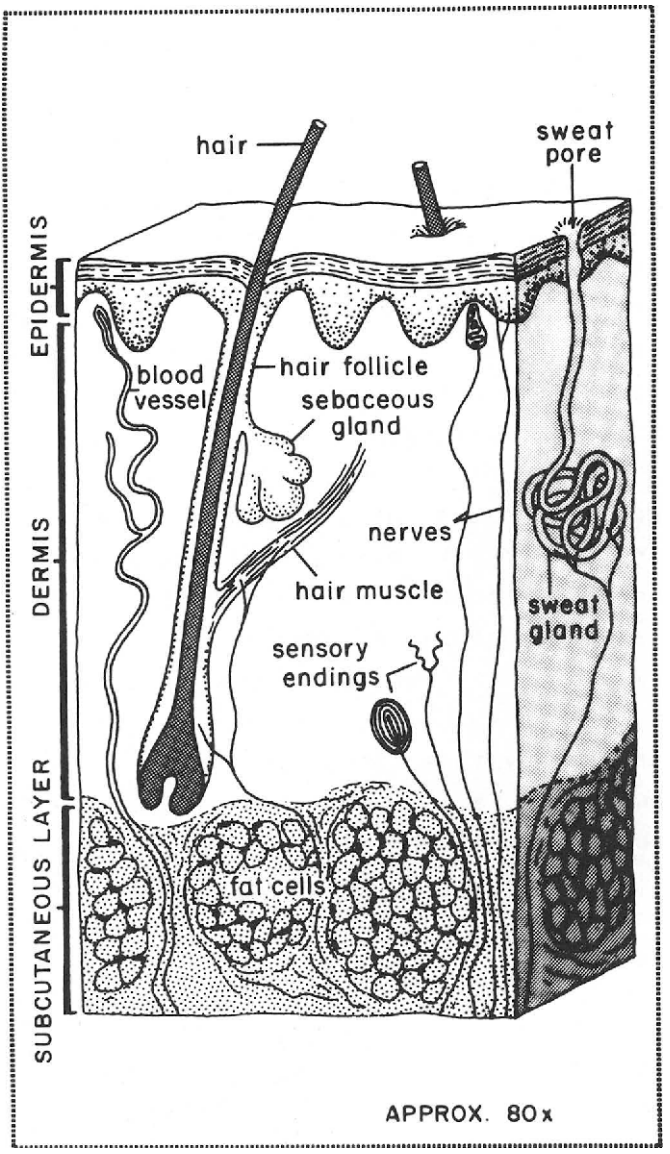


Fig. 4.3 Diagrammatic representation of the structure of human skin.

salts, amino acids and sugars. The blood has a clotting property achieved in part through the action of a protein called fibrinogen. When the fibrinogen and cells have been removed from a sample of blood, the remaining fluid is called serum.

The r.b.cs. contain haemoglobin which functions in oxygen transport. A litre of blood contains about 197ml of oxygen in combination with haemoglobin and 3ml of oxygen dissolved in the plasma. The blood is pumped round the body by the heart and oxygen reaches the tissues at a rate of about 1000ml/min in a healthy person. Further information about blood and blood cells is given in Table 4.3.

The blood cells originate from stem cells in the bone marrow. Some cells like lymphocytes (Table 4.3) are long lived, perhaps for years, whereas r.b.cs. are in circulation for about 120 days before being removed by the spleen, an organ located in the left side of the body cavity near the stomach. The spleen has several functions. It serves as a site of blood storage, containing many white cells including lymphocytes and phagocytic cells, and it acts as a blood filter by removing old, damaged and diseased r.b.cs. from the circulation. As many as 2 million may be taken out of circulation every second by the spleen.

ALIMENTARY TRACT

The alimentary tract in man consists of the mouth, pharynx, oesophagus, stomach, small intestine, large intestine and anal region (Fig. 4.4). On being swallowed, food passes quickly to the stomach where it is exposed to the action of pepsin and hydrochloric acid, secreted by the cells lining the stomach. Up to 2 litres of dilute hydrochloric acid solution are pro-

Table 4.3 Features of human blood. (After Dacie and Lewis, 1974).

	Man	Woman	Infant[a]	Child (1yr)	Child (11yr)
Mean blood volume (ml)	60–80 per kg body weight				
Mean plasma volume (ml)	40–50 per kg body weight				
Mean red cell count (x $10^6/mm^3$)	4.5–6.5	3.9–5.6	4.0–5.6	3.6–5.0	4.2–5.2
Mean haemoglobin (g/dl)[b]	13.5–18.0	11.5–16.5	13.6–19.6	11.0–13.0	11.5–14.8
Mean white cell count (per mm^3)[c]	4000 - 11000		10000–25000	6000–18000	4500–13000
Mean platelet count (per mm^3)	150000 - 400000				

[a] Values for infants usually determined from cord blood at birth.
[b] Haemoglobin concentrations affected by pregnancy, altitude, disease and nutrition.
[c] Polymorphonuclear cells, including lymphocytes, macrophages and eosinophils, are different types of white cell mobilized in body during parasitic infections. Polymorphs and macrophages engulf foreign particles like bacteria by a process known as phagocytosis.

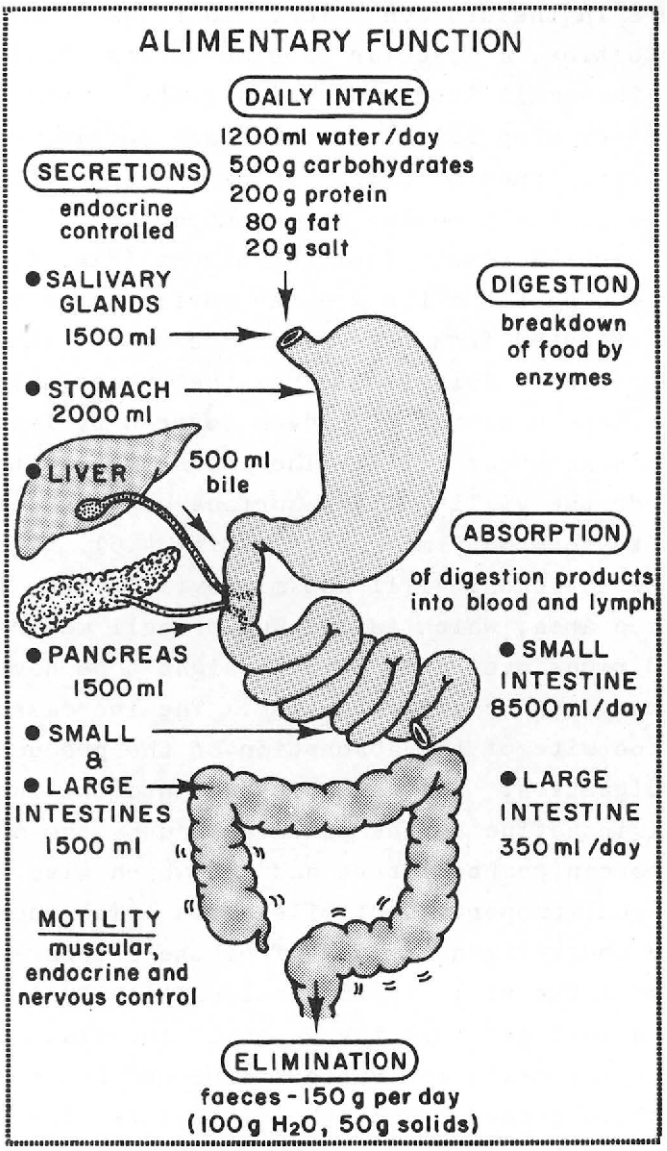


Fig. 4.4 Aspects of digestion and absorption in man.

duced daily by the stomach. The food, or chyme as it is called after reaching the stomach, may be retained for some hours in the stomach before its release into the small intestine, a muscular tube measuring about 6m in length. The small intestine has digestive, absorptive and secretory properties and these are carried out by the different types of cells lining the intestine; collectively, these cells, their supporting villi and some contractile tissue form the mucosa (Fig. 4.5).

The mucosa has a far greater surface area than might be expected from the appearance of the tubular small intestine. This is because the intestinal lining is folded into a series of ridges covered by leaf-like projections known as villi. The intestinal epithelial cells cover the villi and the surface of each cell is extended to form many microvilli (Fig. 4.5). The effect of all these ridges, villi and microvilli is to increase the surface area, which is made up of cell membranes, about 600 times over that of a straight tube having the dimensions of the small intestine. The increased surface area is the site of the absorption of the products of enzymic digestion. Enzymes secreted into the lumen of the small intestine by the pancreas and by the mucosa, digest protein, carbohydrate and fat which also requires the detergent properties of bile salts. The mucosal cells are short-lived and move from the crypts along the sides of the villi to the villous tips from which they are discharged into the lumen of the small intestine. Here the spent cells and various expended proteins from the digestive secretions of the small intestine are digested and absorbed. In this way, the body recycles some of its own material.

The large intestine is about 1.5m long and consists of the caecum, appendix, colon and rectum. Its main

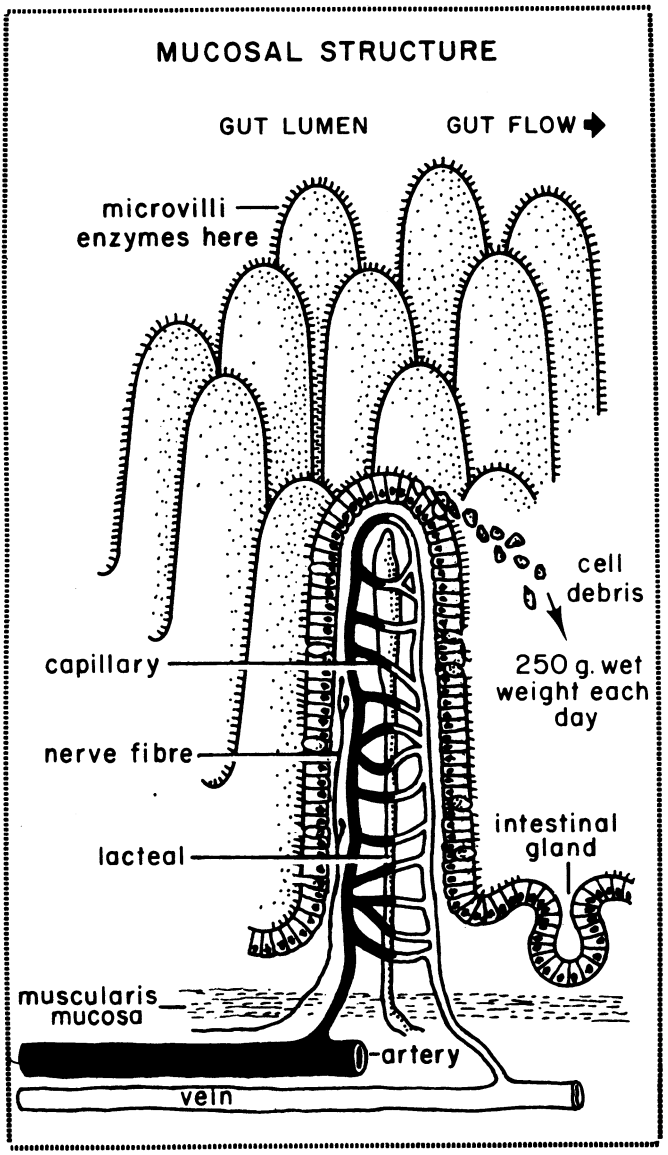


Fig. 4.5 Features of the mucosa from the human small intestine.

function is to extract water from the chyme and prepare the faeces for defaecation which varies in frequency in a healthy man from 3 times a day to 3 times a week. The large intestine also provides the habitat for a great many micro-organisms. The surface area of the lining of the alimentary tract is much greater than that of the skin and it forms another barrier to infectious agents from the environment.

OTHER SYSTEMS OF THE BODY

The skin, blood and alimentary tract have been singled out as examples of the types of micro-habitat in which parasites live in the human body. Other important micro-habitats are provided by the respiratory and the urino-genital tracts, and the nervous, lymphatic and RE systems. Parasites frequently move from one micro-habitat to another during the course of an infection. For example, *Schistosoma mansoni* (Fig. 3.5) moves from the skin, through the lymphatic and blood systems to the lungs, heart and liver before the worms become established in the mesenteric veins. Parasites occupying the respiratory and urino-genital habitats share with those from the skin and alimentary tract direct access to the host from the environment. This observation, however, does not mean that parasites of the alimentary tract always enter the body through the mouth or anus; the infective larvae of hookworms, *Necator americanus* and *Ancylostoma duodenale*, invariably penetrate the skin en route for the small intestine (Fig. 3.8).

5

The Environment of Human Parasitic Disease

An independent commission of statesmen met in the late 1970s to consider the risks, problems and resources of the peoples of the earth. Their views and recommendations were published as a report entitled "North-South: a programme for survival". The countries of the world conveniently, if somewhat arbitrarily, separate into those of the North, which happen to be the developed and industrialized nations, and those of the South, which are mainly the developing countries (Fig. 5.1). This division into North and South provides a useful basis for considering the distribution of infectious diseases in the world, the populations that are affected and the natural, social and economic conditions that make up the environment of human parasitic disease (Fig. 5.2).

The distribution pattern of infectious or parasitic disease has changed. Parasitic disease has generally declined in the North, with the exception of occasional outbreaks of influenza and the growth of sexually transmitted infections, while heart disease and cancer, which usually originate from within the body rather than through the activities of parasites, are now the major public health problems in U.S.A., Sweden, U.K. and other

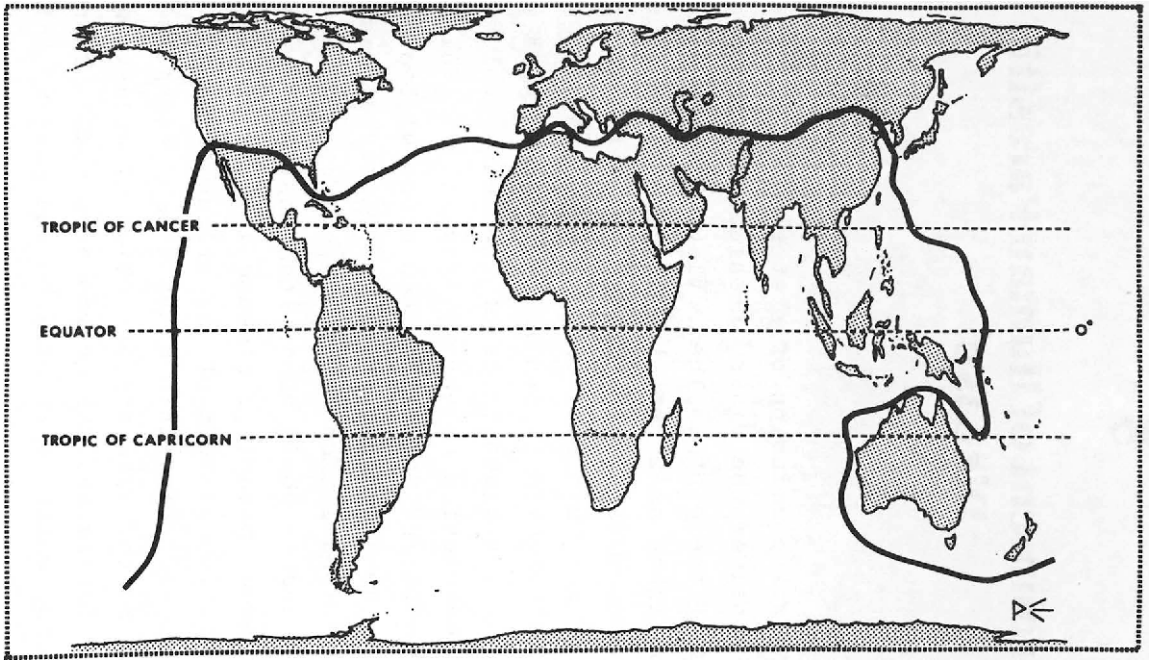


Fig. 5.1 Division of the world into countries of the North (developed and industrialized) and South (developing) (Peters projection).

countries of the North. The peoples of the South, however, continue to be exposed to the ravages of parasitic disease.

This division in the distribution of disease did not always exist. Malaria, Leprosy, Tuberculosis, Cholera and Black Death are a few of the parasitic diseases which have decimated the population of Europe during the last few hundred years. Many more people have died over the centuries from parasitic disease than in wars. Over this period, European countries were peopled by essentially self-supporting peasant farmers living in small rural communities. Parasitic disease in Europe and in the rest of the North seems to have been brought under control mainly through economic development, the advent of urban communities with piped water and sanitation, scientific development and an overall improvement in education. This transformation in the North during the last century or so has also been accompanied by vastly improved nutrition and changing attitudes towards family size and towards the role of women in the community. Much of this social revolution, or some other change, has still to happen in the South and until it does we may expect the South to remain the stronghold of parasitic disease.

Some information about the environment of human parasitic disease is given in Tables 5.1 and 5.2. Many of the countries of the South (Table 5.1; Fig. 5.1) are tropical or subtropical and the climate favours the rapid division of bacteria, the breeding of mosquitoes and flies, and the development of infectious agents like hookworm larvae. The erratic rainfall may lead to floods or droughts and so to crop failures; crops may also be lost to viral and fungal diseases or to insects and nematodes. A reduced harvest may lead to food shortages

Table 5.1 Aspects of the environment of malnutrition and parasitic disease[a] (After Crompton and Nesheim, 1982).

	North Non-tropical Developed	South Tropical Developing	All countries
Population (millions)	2443	1744	4187
% urban population	45	28	38
% rural population	55	72	62
Population density (persons per km^2)	35	32	34
% annual population increase	1.5	2.5	1.9
Mean Gross Domestic Product per capita (U.S. $)	3901 (106-11307)[b]	484 (69-6155)	2011
Deaths per 100 live births	20	120	
Life expectancy (years)	71	52	
Number people per doctor	680	3490	
Protein per capita per day (g)	94(74-113)	56(33-106)	
% of dietary energy requirement per capita per day	121(99-136)	98(72-129)	
Literacy (% population)	97	43	

[a]Data abstracted from (1) Nutrition in Preventive Medicine, W.H.O., Geneva, 1976; (2) Philips Illustrated Atlas, 1980; (3) North:South, report of the Brandt Commission 1980; (4) Report of the U.S. Presidential Commission on World Hunger, 1980.

[b]Numbers in parentheses show the range about a mean value.

Data above the broken line apply to countries that were classified according to tropical or non-tropical location. Tropical countries are defined as those situated either entirely or partially between the tropics of Cancer and Capricorn.

Table 5.2 Estimates of the occurrence of major forms of malnutrition in the world. (After Crompton and Nesheim, 1982).

ENERGY[1]	Millions of individuals with food intake below critical minimum limit, 1972-74
Africa	83
Far East	297
Latin America	46
Near East	20
	446
VITAMIN A	
Worldwide[1,2]	50 000 to 100 000 children are estimated to become blind each year with keratomalacia - many millions more with serum low vitamin A levels
NUTRITIONAL ANAEMIAS	
Developing world[1,3]	20-25% of children, 20-40% of adult females, 10% of males
Industrialized countries[4]	40% of children to 1 year, 10-15% of adult females, 10-30% of pregnant women
ENDEMIC GOITER[1,5]	
Worldwide	200 000 000

[1]FAO 1977. The figures given exclude centrally planned economies of Asia.
[2]Areas where deficiency is a major public health problem include Western Pacific, Far East, Semi Arid Zones of Africa and parts of Latin America.
[3]Primarily considered to be from iron deficiency.
[4]From Layrisse, M., M. Roche and S.J. Baker, 1976.
[5]Particularly in high mountain areas of Latin America, in the Alps in Europe, the Himalayas in Asia and in certain plateau areas of Europe, Asia, North America and Australia.

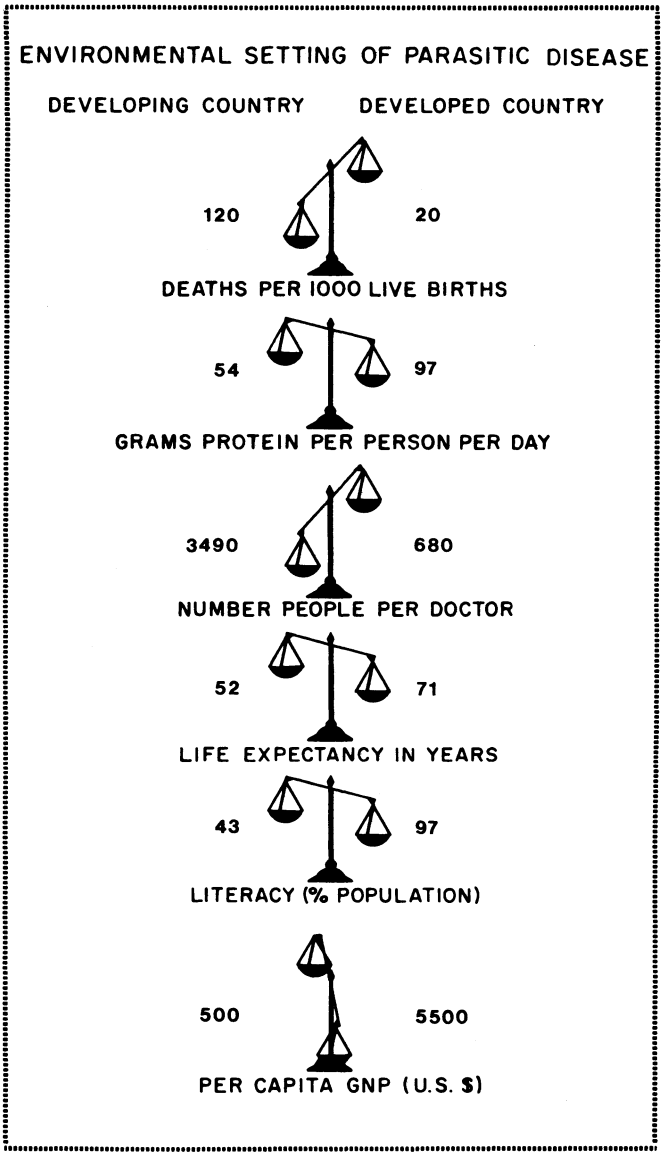


Fig. 5.2 Aspects of the environmental setting in which parasitic disease in man thrives (developing countries) or declines (developed countries).

for those who grow their own food, although other complex and interacting social factors often contribute to malnutrition. It is clear from the data in Table 5.2 that the people who bear the brunt of the world's nutritional problems live in the South; famine and pestilence have been linked since man has recorded his history (Fig. 5.3).

The largely rural populations of the South are usually poor and the economies of their countries are weak (Table 5.1). Health care, however, is relatively expensive and doctors, nurses, dispensaries, clinics and hospitals are not available to many of the people of the South. Consequently, the life cycles and transmission mechanisms of many parasites continue unchecked in ideal climatic conditions. The continuing increase in the population of the South makes more hosts available to the parasites and puts greater strains on the limited resources of the countries.

Unfortunately, the economies of the countries of the South are further strained by their having to cope with the costs of most of the world's natural disasters. Floods in India in 1978 affected 68 million people, damaged or destroyed about 4 million houses and drowned about 200 000 cattle. The estimated cost of this disaster was U.S. $1332 million.

Estimates of the prevalence of 3 protozoan and 9 helminth parasites of man are given in Table 5.3. Not all of these people will develop disease and many of those who do will survive and carry on regardless of the opportunity for medical attention or not. Other infections like measles, infant gastroenteritis and cholera are even more serious and regularly cause death and great suffering. It is reckoned that about 20 million people have died from cholera in India since 1900; despite the enormous estimate of the prevalence of *Ascaris* infect-

Table 5.3 Estimates of the prevalence of certain parasitic infections in man[a] (mainly from the South - Fig. 5.1). (After Crompton and Nesheim, 1982).

	Parasitic infection	Number of cases
P.	African trypanosomiasis (*Trypanosoma brucei* group)*	10 000 new cases per year; 35 million at risk
P.	American trypanosomiasis (*T. cruzi*)*	10 million; 35 million at risk
P.	Malaria (*Plasmodium* spp.)*+	160 million affected; 1163 million at risk
N.	Ascariasis (*Ascaris lumbricoides*)	800-1269 million
N.	Hookworm disease (*Ancylostoma duodenale* and *Necator americanus*)	726-932 million
N.	Filariasis (*Wuchereria bancrofti* and related species)*+	250-383 million
N.	Onchocerciasis (*Onchocerca volvulus*)*+	20-40 million
C.	Taeniasis (*Taenia saginata*)	38-77 million
D.	Schistosomiasis (*Schistosoma haematobium*, *S. japonicum* and *S. mansoni*)+	200-271 million

*Transmission involves insects. +Associated with fresh water.

[a]Data abstracted from W.H.O. 1977 statistics kindly supplied by Dr. Z. Pawlowski, Parasitic Diseases Section, and Peters (1978).

P Protozoa; N Nematoda; C Cestoda; D Digenea.

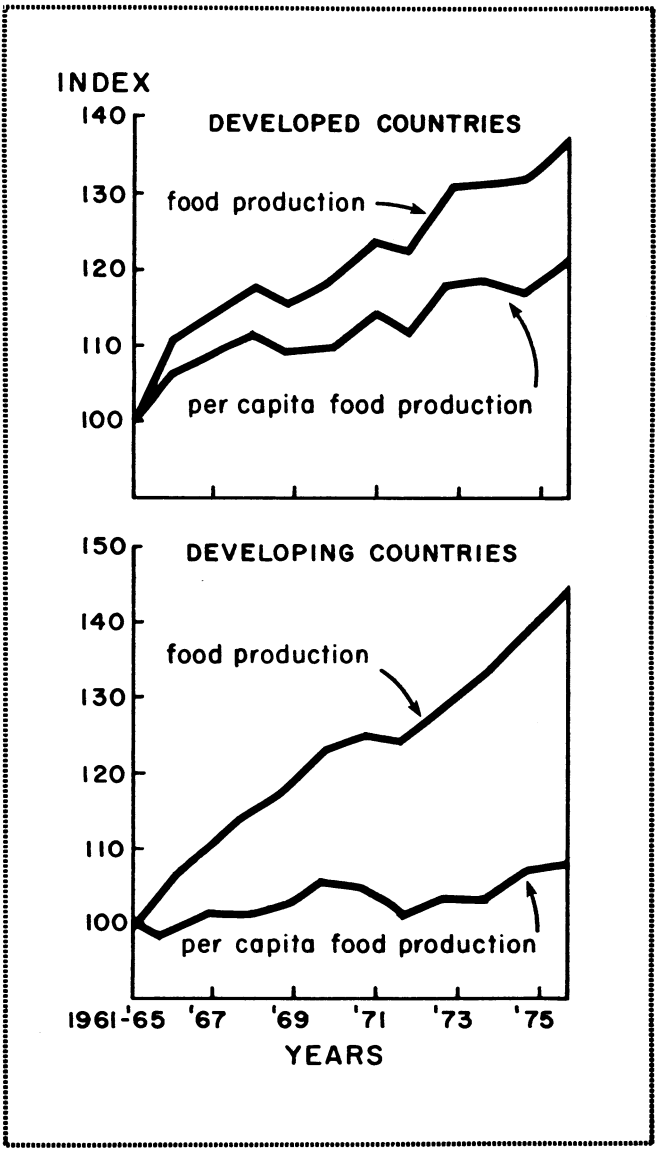


Fig. 5.3 A comparison of the food production, total and per capita, between the developed and the developing countries (After Monckeberg).

ions in man (Table 5.3), it is rare for the death of a host to occur.

The problems for families in the South have been summarized recently by David Rowe in a publication of the World Health Organization:

"If you happen to be born and grow up in rural Africa you are likely to harbour four or more different disease-producing organisms simultaneously. And yet, as a parent, you must be fit enough to work, or your family will starve. In your village every child at times suffers the paroxysms of malaria fever and you and your wife will mourn the death of one or two children from this disease. The snails in the village pond carry schistosomiasis, and you do not consider it unusual when your children pass blood in their urine.

You take for granted the disfigured faces and fingerless hands of the beggars in the village street suffering from leprosy. If you live near a river where blackflies breed, one in ten of your friends and neighbours will be blind in the prime of life. You know that waves of killing diseases such as measles and meningitis and perhaps sleeping sickness are liable to strike your village. But, lacking effective remedies, you tend to philosophize in the face of sickness. You make the effort to walk the ten miles to the nearest dispensary when you or your child is ill, but there may be no remedies, and it may be too late ....."

Certain qualifications must be made about the data in Tables 5.1, 5.2 and 5.3. Most of the figures are estimates based on information that is not always easy to obtain. For example, not all communities are able to keep equally accurate registers of births and deaths, not all have the capacity to carry out equally reliable censuses and not all allow easy access, and for per-

fectly proper reasons, to their national records and statistics. Also the data in the tables tend to be averages or totals which do not apply to any particular country. Nor should the reader imagine that every African family is suffering all day and every day in the manner described by the writer from the W.H.O. The purpose of the quotation is to draw our attention to the environment in which human parasitic disease is to be found.

There is, however, general agreement that the people of the South are those who experience the problems of parasitic disease. The North with its currently stronger economy may yet manage to find the means for bringing some relief to the South; investment leading to gradual and acceptable change in the living conditions in the South could provide the foundation for giving people their right to healthy development.

6

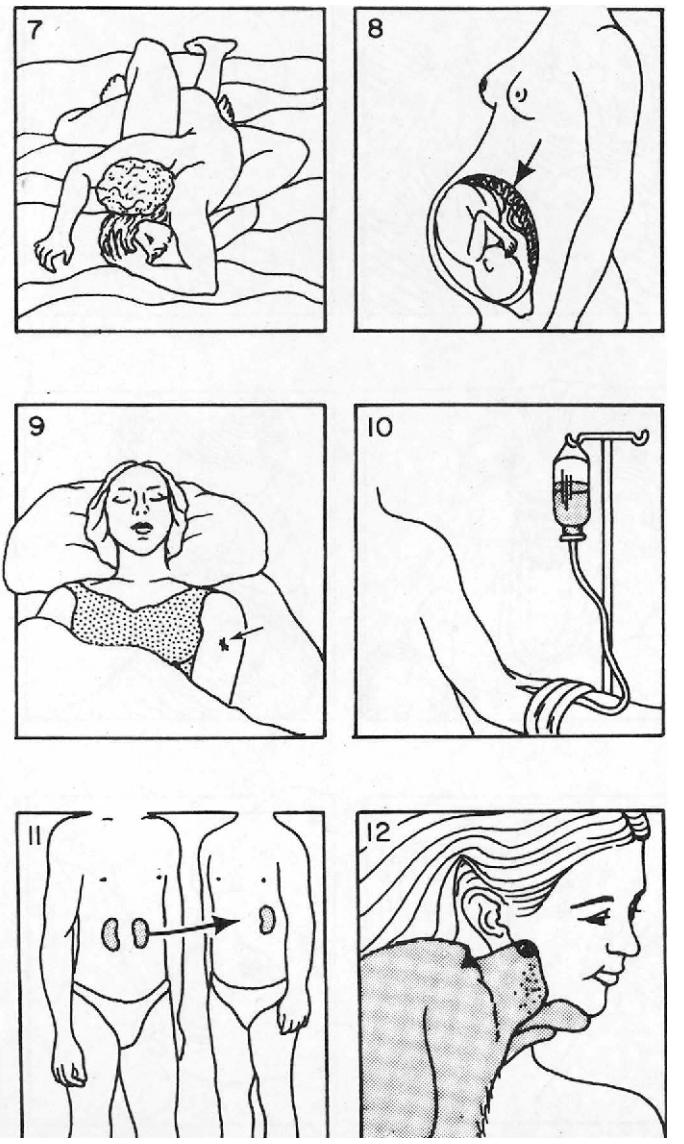
Transmission and Infection

Understanding how parasites are transmitted or how they spread from man to man is an essential part of any programme for the control of parasitic disease. Transmission is a term used to cover the events occurring from the departure of an organism from one host until contact is made with the next host. Infection is the means whereby a parasite becomes established and physiologically committed to dependence on the next host. The role of the host in transmission and in the infection process is often as important as that of the parasite. In practice, it is usually difficult to separate transmission from infection since the one leads into the other.

TRANSMISSION

Various actual and potential routes for the transmission of parasites between man are illustrated in Fig. 6.1. The principal routes covering most parasites involve: (1) the contamination of drinking water and food by microscopic parasites or stages passed in stools; (2) the contamination of the air with virus particles and bacteria when infected people cough or sneeze; (3) the

Fig. 6.1 Actual and potential routes for the transmission of infectious agents. (1) Orally through drinking. (2) Orally through normal eating. (3) Orally during ritual or ceremonial feasts; now believed to occur rarely. (4) Orally during breast feeding. (5) Orally and nasally after inhalaction of infectious agents. (6) Orally through kissing.



(7) During sexual intercourse. (8) Diaplacentally, from mother to foetus.
(9) Through the bite of an insect vector.
(10) As a result of a blood transfusion.
(11) Perhaps during organ transplantation.
(12) Through contact with pets.

transport of parasites by vectors which are usually insects and ticks; (4) direct contact in which infective agents pass from person to person as in sexual intercourse, kissing or other contacts.

INFECTION

After a host and an infective agent have come into contact, the parasite usually responds to host stimuli and establishment of the parasite occurs. For example, protozoan cysts, the larvae in the eggs of worms (Fig. 6.2) or the encysted stages of worms are activated on being swallowed by exposure to the higher temperature (37°C), the hydrogen ion concentration, the action of bile salts and the digestive enzymes in the alimentary tract. In other cases, the infective agents are already active when contact is made with the host. The cercariae of *Schistosoma* spp. (Fig. 6.2) have been studied as they penetrate mouse skin. First, a cercaria explores the skin surface for entry sites (Fig. 4.3); wrinkle crevices and hair projections appear to be the most favoured places for entry. Next, the cercaria secretes some adhesive material and becomes anchored perpendicularly to the surface of the skin. After much muscular effort the cercaria forces its way into the horny layer (Fig. 4.3) and the forked tail is shed. The surviving body of the cercaria, which is called a schistosomulum, now rests before releasing enzymes that digest the epidermis and enable it to penetrate further into the skin and the deeper tissues of the host. The entire penetration process takes up to 15 min in mice; the time may be different in man. The larvae of hookworms (Fig. 3.8) are also active penetrators of human skin, but they appear to manage without the need for any special secretions.

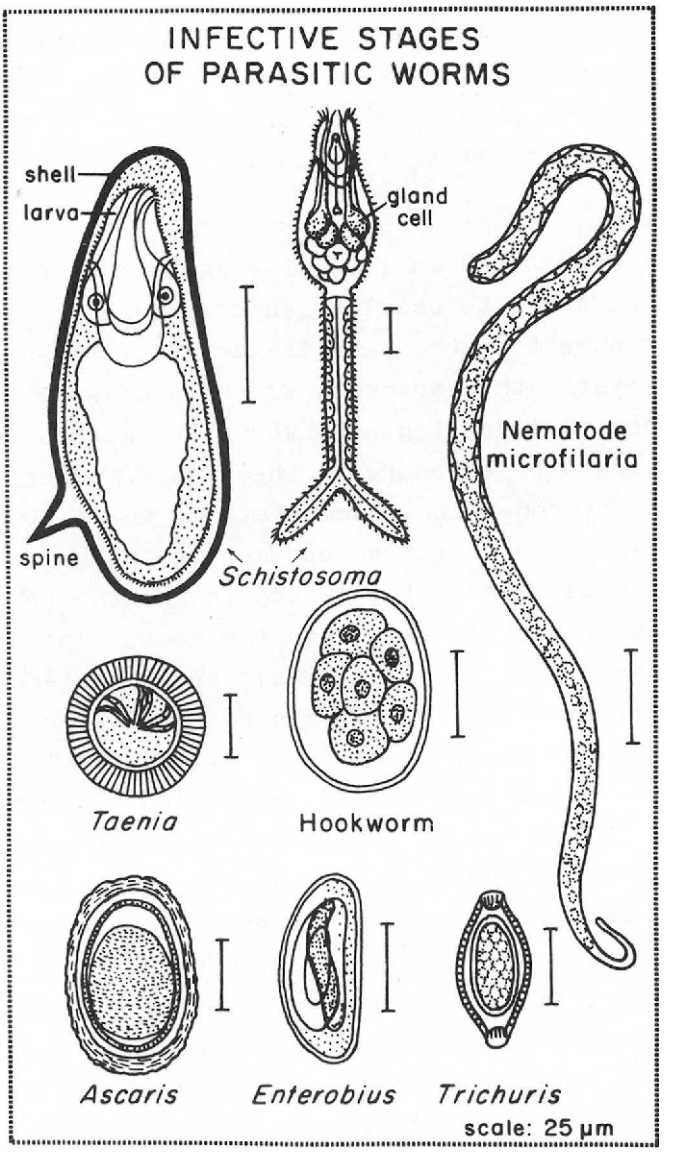


Fig. 6.2 Infective stages of parasitic worms including various eggs, a cercaria *(Schistosoma)* and a microfilarial larva *(Nematoda)* (Redrawn from Crompton and Joyner, 1980). See Figs. 3.5, 3.6, 3.7, 3.8 and 3.9.

The establishment of other parasitic infections in man involves the bites of insects (Fig. 6.1.9) ticks, dogs and vampire bats. In the case of malarial parasites, the sporozoites injected by the female mosquitoes must enter liver cells and the subsequent generations of merozoites (Fig. 3.4) may enter liver cells and r.b.cs. respectively. Viruses and certain bacteria are also obligatory intracellular parasites. Entry into cells is not a haphazard process. Phagocytic cells, whose function is to engulf foreign particles in the body, (Chapter 7), are sometimes hosts themselves for intracellular parasites which actually turn the phagocytic act to their own advantage. Normally, an engulfed particle is digested by enzymes inside a phagocytic cell, but leishmanial parasites (Fig. 3.1) are not digested. It is not clear how a parasite is able to survive inside a cell which has the capacity to destroy it. Nor is it entirely clear as to how the merozoites of *Plasmodium* (Fig. 3.4) enter r.b.cs. rather than the other cell types in the blood (Table 4.3). Molecules on the surface of the merozoite appear to interlock with molecules on the r.b.c. surface. After this intimate chemical recognition, a secretion from the merozoite (Fig. 3.4) causes the cell membrane to become less resilient and the parasite is able to push its way, encased in the host-cell membrane, into the centre of the cell. When entry is complete, the malarial parasite is seen to be enclosed in a membrane-bounded vacuole inside the cell whose outer membrane has healed.

FACTORS AFFECTING TRANSMISSION AND INFECTION

The following are some of the factors that affect the spread of parasites and the successful establishment of infections.

1. The number of infective stages available.
2. The survival properties of infective stages either in the environment of the host or in the tissues of vectors and intermediate hosts. The infective larvae of *Ascaris* may survive exposure to many chemicals and remain viable for several years provided the egg shells (Fig. 6.2) are undamaged.
3. The climatic conditions prevailing in the host's environment.
4. The behaviour of infective stages. Hookworm larvae (Fig. 3.8) stop feeding and climb on to and up objects which will improve their chances of contact with host skin.
5. The numbers, biology and behaviour of vectors and intermediate hosts.
6. The numbers of infective stages in a dose or inoculum. This factor may be of more significance for the establishment of viruses and prokaryotic parasites. About 10^8 *Vibrio cholerae* (Table 3.4) must be swallowed and about 10^3 *Salmonella typhi* (Table 3.3) before a person develops disease.
7. The conditions prevailing in the host. The minimum infective dose of *Vibrio* is halved if alkaline conditions exist when the bacteria enter the alimentary tract.
8. The immunological state and experience of the host.
9. The nutrition of the host.
10. The behaviour of the host.

These factors apply to all host-parasite relationships. When man is the host, human behaviour and culture becomes a most intriguing factor, although in practice no single factor should be considered alone since all are interrelated.

HUMAN BEHAVIOUR AND CULTURE

During his evolution, man has developed in a way which has enhanced his chances of acquiring some infections and ensured that he will avoid others. The following aspects are involved: (a) religious and tribal customs, (b) nutritional and cooking practices, (c) relationships with animals, (d) community structure and (e) health education.

Religious laws may serve to protect a community from infection. Moslems are forbidden to eat pork and in theory should never be exposed to infection with *Taenia solium* which is a close relative of *T. saginata* (Fig. 3.6). The roles of the sexes in a community, however, may tend to endanger one sex or protect another. In a long study of water contact and usage by Egyptian villagers from a region where there was a high prevalence of *Schistosoma haematobium* (Table 3.12), the observers found that men and boys were largely responsible for contamination of the water with parasite eggs while the women, with their accompanying young children, were more exposed to infection as they fetched water, cleaned vegetables and utensils or did the family washing.

Nutritional and cooking practices are important factors in the establishment and effects of human disease. The pleasure of eating rare or undercooked beef could expose the eaters to *T. saginata*, unless regional standards of animal husbandry and meat inspection are adequate. Undercooked or pickled fish may also be potentially hazardous. Sometimes, children may contract an acute infectious disease which, with the best of intentions, the mother will treat with a diet that may make the situation worse.

Man's relationships with animals, particularly domesticated animals and pets, have often been deleterious to his health. Man has lived with his domesticated animals for about 9000 years in order to obtain food, leather and materials for clothes, transport and power, company and recreation. In some tribes and communities, a man's wealth and social status depend on the size of his flocks and herds. Under certain circumstances, man may serve as an intermediate host for the tapeworm *Echinococcus granulosus* which subsequently matures in the small intestine of dogs. Normally, *E. granulosus* develops to form large cysts in and amongst the viscera of ruminant animals like cattle and sheep. The cysts will develop in the viscera of man should he swallow the infective eggs which contaminate his environment when dogs defaecate; the condition is called hydatid disease. In Kenya, the Masai and Turkana are two nomadic tribes who herd cattle and keep dogs to help them. *Echinococcus* cysts are rarely a problem for the Masai but frequently a problem for the Turkana and the explanation seems to lie in their attitude to their dogs. The Masai keep the dogs away from their homes; the Turkana encourage theirs to live with them and even assign dogs to the duties of cleaning up when babies defaecate and vomit. Thus, a close association builds up between Turkana children and dogs; the eggs of *E. granulosus* are swallowed and hydatid disease occurs. Public health authorities in developed countries have become concerned about the potential health risks that may result for man from the massive quantities of urine and faeces which our dogs deposit in our settlements. As much as 20 000 tons of faeces and 600 000 gallons of urine are left annually by dogs in the streets and parks of New York City.

The structure of a human community often affects the spread of disease. The closer together that people live, the greater their chances of acquiring parasites, particularly if the parasites leave one host and enter another through the respiratory tract. People living in close contact in crowded cities may not be more vulnerable to infection than those in old-established and spacious rural settlements provided that the sanitation systems are effective. People forced together in refugee camps or temporary housing after an earthquake or other calamity are often at risk; such conditions are usually ideal for the spread of viruses and bacteria. Every form of parasite transmission would be reduced and the consequences of established infections decreased if modern health education were to become widely available.

EPIDEMIOLOGY

Epidemiology is the study of the factors determining the frequency and distribution of diseases in communities. At one time epidemiologists were concerned mainly with massive and acute outbreaks of infections and parasitic disease, but nowadays, the frequency and distribution of mental illness, malnutrition, cancer and all aspects of public health are investigated. Epidemiology aims to discover how to prevent a disease or at least reduce the number of cases in a given area. For parasitic diseases, epidemiologists attempt to determine the prevalence and the incidence rate of a disease and whether the relation between an infectious agent and a given disease is causal or associational. Prevalence is defined as the number of cases of an infection or a disease at a certain time in a designated area. Incidence rate, the number of new cases reported in an area in a given

time, is often a more useful statistic in studies of transmission. In developing countries, however, it is not easy to obtain adequate epidemiological information about such complicated diseases as schistosomiasis (Table 3.12) where people, their contact with freshwater, their hygiene habits, their health education and the ecology of snails and reservoir hosts are involved, and transport, language barriers and communications prove difficult for the investigators.

An undisputed example of a casual relationship is seen between malaria and *Plasmodium falciparum* (Fig. 3.4). Malaria does not develop in people who do not harbour *P. falciparum* and malaria is cured when drugs are prescribed which kill the parasites. It is much harder, however, to decide whether the malnutrition which often accompanies *Ascaris* infection in young children, is caused by the *Ascaris* (Fig. 3.7) or associated with it; malnourished children may be more susceptible to *Ascaris* infection than well nourished ones. There is every possibility that the relationship between *Ascaris* and malnutrition is neither directly causal nor strictly associational and much work may be needed in many parts of the world before this particular relationship is explained.

7

Immune Responses

How do people manage to live for a normal life span if they are constantly exposed to the agents of infectious disease? How do people recover from disease? How is it that those who have recovered from certain diseases need not fear another attack? How does vaccination give long-lasting protection from a given infectious disease? What is the major problem that must be overcome before organ transplant surgery can be successful? The answer to each of these questions is to be found in our understanding of the human immune system.

Immunity is usually considered to be the ability of an organism to resist the invasion of its body by another organism and traditionally the word has been associated with resistance to parasitic or infectious disease. More fundamentally, immunity depends on the ability of an organism to distinguish between 'self' and 'not-self' which explains why immune responses not only protect against disease but also impede skin grafting and organ transplants unless special conditions prevail. In fact, the responses of the immune system to infections are often anything but protective and

much of the severity of a parasitic disease may be attributed to immune hypersensitivity (see below) rather than protection.

NATURAL AND ACQUIRED IMMUNITY

The immune responses of healthy people and of other higher animals may be classified according to whether they are natural or acquired. The natural, non-specific or innate responses are those with which a person is endowed at birth; these responses occur without previous contact with the foreign material. The acquired, specific or adaptive responses result from a state of resistance built up after contact with foreign material. Acquired responses develop relatively slowly, but may persist for many years. A brief summary of the main features of human immune responses is given in Table 7.1 and some immunological terms are defined in Table 7.2.

Several other non-specific factors contribute to a person's capacity to resist infection in addition to those listed in Table 7.1. For example, the skin (Fig. 4.3) and the mucous membranes lining the respiratory, alimentary and urinogenital tracts act as mechanical barriers to invading organisms. The wearing of clothes and shoes must have greatly reinforced the naturally protective effects of the skin. The normal flora of different parts of the body (Chapter 4) contributes to local conditions which deter the establishment and development of pathogenic micro-organisms. Non-specific responses are also influenced and sometimes determined by the genetic constitution of the host. People with the trait for sickle cell anaemia are unlikely to die from malaria caused by *Plasmodium falciparum* (Fig. 3.4). Sickling depends on a gene which directs the substitution of the amino acid valine

Table 7.1 Human immune responses.

NON-SPECIFIC RESPONSES (NATURAL OR INNATE IMMUNITY)

GUT SECRETIONS: hydrochloric acid produced by the stomach wall is bactericidal and digestive enzymes can degrade many foreign organisms.

INFLAMMATION: a process in which different types of white blood cells, after chemical attraction to foreign body or bodies in the tissues, are stimulated to neutralize them by phagocytosis.

INTERFERONS: glyco-proteins (MW 20000-40000) secreted by cells, particularly in response to virus invasion and before antibody is produced by the host. Interferons inhibit virus replication, but are not specific for the viruses that induced their formation.

LYSOZYME: an enzyme found in tears, saliva, nasal mucus and other secretions. Lysozyme breaks down the cell walls of Gram-positive bacteria.

PHAGOCYTOSIS: many white blood cells, especially polymorphonuclear leukocytes and macrophages, engulf and digest bacteria and small particles. One type of antibody (opsonin: Table 7.3) enhances phagocytosis by adherence to the target particle.

SEBUM: the secretion of sebaceous glands in the skin (Fig. 4.3). Sebum contains unsaturated fatty acids which are bactericidal. Wax in the ear and smegma on the penis are modified forms of sebum.

SPECIFIC RESPONSES (ACQUIRED OR ADAPTIVE IMMUNITY)

These responses are largely dependent on the properties and activities of LYMPHOCYTES and their derivatives.

HUMORAL IMMUNITY: depends on the synthesis and release of free antibody (Table 7.3) into the blood and body fluid by plasma cells which have been stimulated by the presence of antigen. An antibody may react with its antigen by precipitation, agglutination or lysis. Some antigen - antibody reactions require the participation of the complement system (Table 7.2) which contributes to the lysis of foreign cells.

CELL-MEDIATED IMMUNITY (C.M.I.): depends on the production of lymphocytes which have become sensitized to antigen. Contact of sensitized lymphocytes with antigen leads to a variety of reactions including the release of chemicals that may kill foreign cells or attract other host cells to deal with them.

for glutamic acid at one point in the haemoglobin molecule. People who are unlucky enough to have this gene expressed in the homozygous form will probably die from sickle cell anaemia and will not benefit from protection against falciparum malaria, but those who are heterozygotes will remain protected.

The results of much research on acquired or specific immune responses have been summarized in a few lines in Tables 7.1 and 7.2. During development *in utero*, cells from the foetal liver become established in the bone marrow. These cells become multi-potential stem cells and their progeny eventually give rise to all the white blood cells including the lymphocytes and macrophages. Late in foetal development and soon after birth (Fig. 7.1), some lymphocytes are processed most probably in the bone marrow while others are undoubtedly processed in the thymus gland to produce two populations of lymphocytes: B-cells (bone-marrow processed) and T-cells (thymus processed) which are largely responsible for humoral and cell-mediated responses respectively. Other organs of the body including the lymph nodes, liver, spleen, tonsils and the wall of the alimentary tract form important centres for the development and support of lymphocytes. The evidence for bone-marrow processing in man is largely circumstantial, but that for thymus processing is very convincing. Children born with thymus deficiencies invariably show a reduced capacity to make normal cell-mediated responses. Rats from whom the thymus is removed surgically at birth never develop a functional population of T-cells.

Specific immunity may be better understood by considering a hypothetical example of a humoral response. When an antigen (Table 7.2) enters the body for the

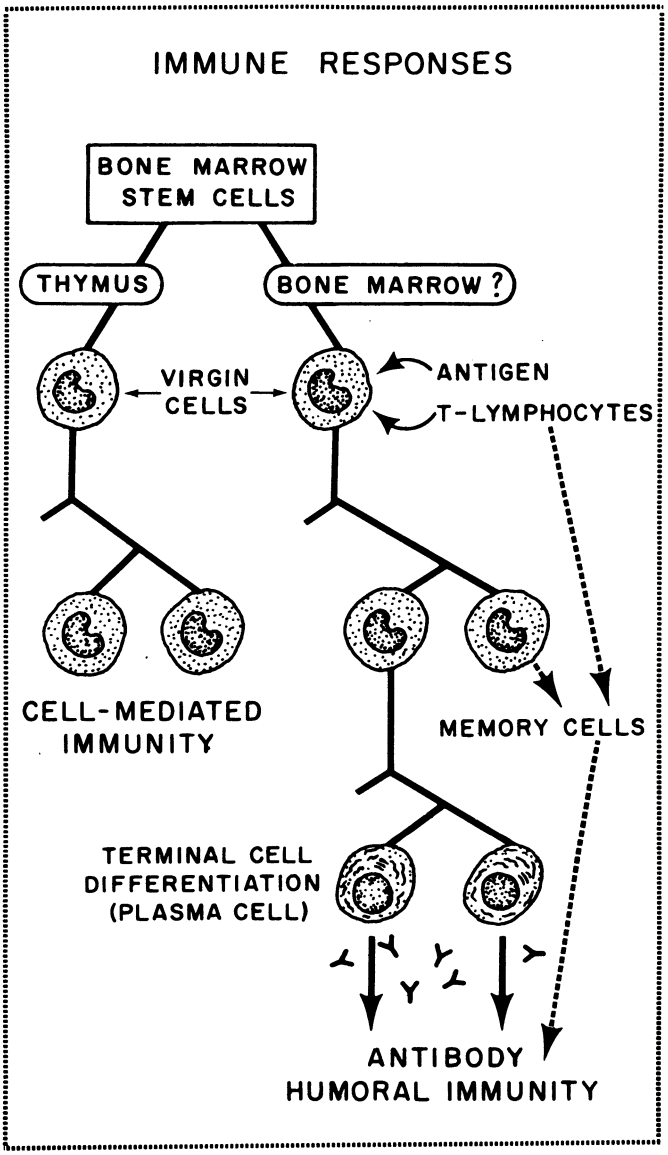


Fig. 7.1 The development of acquired immunity (Redrawn from Crompton and Joyner, 1980).

Table 7.2 Immunological terms.

Agglutination	When cells or organisms carry antigen at their surfaces, the cells will become bound together or agglutinated in the presence of the relevant antibody.
Antibody	A large protein molecule (Table 7.3) which is formed in response to antigenic stimulation and reacts specifically with that antigen or one closely related to it. Immunoglobulins also contain from about 3-15% carbohydrate depending on the class to which they belong.
Antigen	A substance which, generally, when introduced into another animal, will elicit the formation of an antibody or a hypersensitivity response. Most antigens are large protein molecules with a molecular weight of at least 10000.
Complement system	A group of proteins that are normally present in the blood. After certain antibodies have reacted with antigen on the surface of a foreign cell or micro-organism the complement proteins become activated and the cell wall is damaged irreparably. Complement proteins may be activated by other mechanisms and may be involved in other reactions besides lysis.
Lysis	The breakdown of cells or micro-organisms; in immune reactions this usually occurs when complement proteins have become activated during the combination of an antibody (lysin) with its antigen.
Passive immunity	Temporary protection from infection or disease obtained on receipt of antibody formed actively by the immune system of another individual. For example, protective antibody (IgG; Table 7.3) produced in the mother crosses the placenta and enters the developing child *in utero*. The passive transfer of antibody via mother's milk to the suckling offspring occurs in all the mammalian species examined.
Precipitation	When multivalent antigens and specific bivalent antibodies are mixed in solution, they combine rapidly to form molecular lattices which precipitate.
Vaccination	The injection or ingestion of antigen (vaccine) with the intention of producing immunity in the recipient. The vaccine may be a suspension of dead, attenuated or living organisms or toxins.

first time, a particular type of T-cell, now known as a helper cell, assists a virgin B-cell or cells to recognize the antigen. The B-cell is then activated to form two clones. Some cells form a clone of memory cells while others transform to produce a clone of plasma cells containing large amounts of rough endoplasmic reticulum; plasma cells synthesize the antibody or immunoglobin (Table 7.3). Antibody molecules respond in a highly specific manner because the sequence of amino acids making up their structure can be varied so that they fit exactly to the shape of the antigen molecule's combining site or sites. All this intricate and flexible molecular architecture is under genetic control. This type of primary response usually takes about 10 or more days to produce enough antibody to neutralize or inactivate the antigen. A secondary immune response occurs more rapidly because of the presence of the memory cells. Sometimes the memory lasts for a life time and the rapid development of a secondary response ensures that an infection never lasts long enough for disease to develop. Similar events and timing occur with cell-mediated responses. For example, the rejection of a primary skin graft by a recipient usually takes about 12-14 days, but a second graft from the same donor will be rejected within a week. These mechanisms are illustrated diagrammatically in Fig. 7.1. The reader must realize that this description of specific immune responses has been greatly simplified and immunology text books should be consulted for details. The important points to grasp are (1) that the healthy body possesses extremely sensitive mechanisms for distinguishing between self and not-self, (2) that a wide variety of reactions may occur once foreign antigen has been recognized and (3) that the nature and effectiveness of specific immune responses

Table 7.3 Physical and biological properties of human immunoglobulins (Ig; antibodies) (After Roitt, 1971).

Class designation	IgG	IgA	IgM	IgD	IgE
Molecular weight	150000	160000 (and polymers)	900000	185000	200000
Concentration in serum (mg/ml)	8-16	1.4-4	0.5-2	0-0.4	17-450 ng/ml
% of total immunoglobulin	80	13	6	1	+
No. of antibody combining sites (valency)	2	2	5 to 10	unknown	2
Placental transfer	+	-	-	-	-
Complement fixation (Table 7.2)	+	-	+	?	-
Functional notes	Prominent in secondary response; neutralizes bacterial toxins; enhances phagocytosis (opsonization); present in lymph.	Present in saliva, tears, secretions of gut and respiratory tract and in colostrum.	Secreted early during immune response: usually confined to blood.	Little is known; found on surface of antibody secreting cells.	Prominent in allergic reactions: found bound to the cells that release vasoactive amines.

may be influenced by the age, state of health and nutrition of the person concerned. It is also worth noting that both a host and its highly specific parasites ultimately depend for their survival as species on effective host resistance; the extinction of a host implies the disappearence of the parasites' environment.

ALLERGY AND HYPERSENSITIVITY

It is not always true that host responses to foreign material are protective and therefore beneficial in nature. People who suffer from hay-fever, asthma or nettle rash experience the consequences of over-active responses by their immune systems. Hypersensitivity is the effect in which further exposure of a person to an antigen leads not only to a secondary boosting of the immune response but also to some form of damage. During an attack of nettle rash, the discomfort and irritation for the sufferer far outweighs any advantageous effects of the response. Allergic or hypersensitive responses may occur very soon after exposure to antigen or may be delayed, not appearing until after about 24h. Some hypersensitivity reactions are brought about through the action of circulating antibodies while others, particularly of the delayed type, depend on interactions between sensitized T-cells and other types of white blood cell. Nearly all forms of infectious or parasitic disease may be made more serious and complex by allergic responses. The more antigens a foreign organism releases, the greater the chance must be of the host producing some antibodies that do not have any protective function. Antigens which are known to elicit a protective response are referred to as immunogens while those which elicit any other type of response are called allergens. Information about human

immune and allergic responses to a selection of parasitic infections is given in Table 7.4.

EVASION OF THE IMMUNE RESPONSE BY PARASITES

Since the human immune response functions to detect and destroy genetically foreign material, persistence of a parasite in the tissues of man for more than a week or two indicates that the parasite may circumvent immune surveillance. Latent infections of Herpes virus may persist for a life time with recurrent attacks, the blood fluke *Schistosoma mansoni* (Fig. 3.5) and filarial worm *Onchocerca volvulus* (Fig. 3.9) may also live in their hosts for years. How do such parasites exist? A blood fluke would appear to be much more foreign than the kidney that is carefully transplanted from one man to another by a surgeon. Yet the kidney survives and functions only through the concurrent use of immunosuppressive procedures.

Several explanations may be offered for the survival of parasites in immunocompetent man. First, some parasites may complete their development or reproduction more rapidly than the time needed for immune responses to react. Secondly, other parasites, for example viruses and certain protozoa like *Leishmania* and *Plasmodium* (Figs. 3.1, 3.4), live inside cells where they may not be exposed to antibodies or sensitized lymphocytes. Thirdly, the antigenicity of parasites may vary either rapidly as with *Trypanosoma brucei* (Fig. 3.3) or slowly as appears to occur with influenza virus (Table 2.2). Consequently, the immunocompetent host, which may already have had experience of the parasite during an earlier infection, finds itself confronted with what is in effect a new or primary infection because the antigens have changed. Fourthly, some parasites soon after arrival in the host may become coated with host materials with the

Table 7.4 Acquired immune responses to selected parasitic infections.

Much research has demonstrated the presence of acquired immune and allergic (hypersensitivity) responses of laboratory animals to parasitic infections. Understanding of such responses in man is developing slowly because direct experimentation is ethically impossible.

Influenza virus (Table 3.2): three basic types have been isolated (A, B and C). Protective humoral antibody (IgA) is produced and directed against viral glycoproteins, but these antigens may gradually change with time (antigenic shift) and new outbreaks of the disease occur until the immune response becomes effective.

Vibrio cholerae (Table 3.4): high degree of immunity develops to vibrios of the same strain; antibodies responsible for agglutination and neutralization of the vibrios and their toxin may be detected in serum.

Treponema pallidum (Table 3.5): humoral immunity to reinfection develops provided that the parasites are not eradicated from the host during the early part of the relationship. Treatment later in the course of the disease does not result in loss of immunity.

Mycobacterium leprae (Table 3.6): there is a spectrum of responses from the complete absence of resistance to effective protection. Hypersensitive reactions (C.M.I.) may be most destructive of host tissues during TT. Immune deficiency occurs during LL and antibodies seem to have little protective effect perhaps because the parasites are intracellular.

Leishmania tropica (Fig. 3.1, Table 3.8): C.M.I. occurs in man to cutaneous leishmaniasis and permanent protection often results after the skin lesions have healed.

Plasmodium falciparum (Fig. 3.4, Table 3.11): protective humoral antibody (IgG) is produced aiding phagocytosis of merozoites during their brief period outside r.b.cs. and engulfment of cell and parasite debris following lysis. Spleen involvement. Antigen-Antibody complexes in circulation may damage kidneys.

Schistosoma mansoni (Fig. 3.5, Table 3.12): in animal hosts, 'concomitant' immunity occurs. The antigens released by adults of a primary infection elicit a protective response and subsequent invaders are destroyed while the first worms survive. W.H.O. Expert Committee wrote in 1980, "... possible to maintain that there is no direct evidence proving that man acquires resistance to schistosomiasis."

Ascaris lumbricoides (Fig. 3.7, Table 3.14): responses are poorly understood in man, but circulating antibody is produced and acute hypersensitivity may develop. In pigs, larval antigens of living *A. suum* will induce protection from subsequent infection.

result that host immune cells do not recognize them as not-self. Finally, the host immune system may be suppressed during the presence of an infection and may be greatly overworked through responding to antigens which are allergens rather than immunogens and this problem together with other aspects of disease may weaken the host and extend a parasite's survival time.

VACCINATION

Vaccination (Table 7.2) has proved successful against diphtheria, whooping cough, measles, tetanus, poliomyelitis and smallpox, and in theory offers protection for man from malaria, schistosomiasis, hookworm disease and other parasitic infections. This progress, however, has been against diseases caused by prokaryotic parasites. What are the problems of developing vaccines for use against eukaryotic parasites? In general, eukaryotes are complex and long lived with the result that the host is bombarded by very many allergens as well as immunogens. Ideally, a vaccine should consist principally of immunogens; there is no point in priming a host to damage itself. Eukaryotes in contrast to prokaryotes have so far proved difficult to cultivate *in vitro*. This procedure enables a parasite's metabolism to be investigated and provides some of the basic information that is needed for the development of safe control methods (Chapter 8).

8

Control

THEORETICAL APPROACH TO CONTROL

Planned approaches to the control of parasitic diseases depend upon the basic reproduction rate of the disease. In qualitative terms, this rate is the number of cases resulting from a seed case in a fully susceptible population. For a disease with given characteristics in a given community, the basic reproduction rate determines whether the disease will become more or less prevalent; equilibrium will be achieved only at or above a certain critical rate. Estimations of this critical value depend on the accurate collection over time of medical data by epidemiologists (Chapter 6). The more complex the life cycle of the infectious agent, the more difficult will be the calculations.

Quantitative information about the reproduction rate of malaria (Table 3.11) is given by the following equation:

$$Z_o = \frac{ma^2bp^n}{-r \ln p}$$

where

Z_o = basic reproduction rate of malaria

m = density of vector mosquitoes

a = daily number of mosquito bites on man

b = proportion of mosquitoes with infective sporozoites in their salivary glands

p = probability of mosquito survival during one day

n = number of days required for the development of infective sporozoites

r = proportion of infected persons who revert to the uninfected state during one day

Obtaining values for several of these parameters requires detailed knowledge of mosquito population dynamics, which are regulated by ecological factors such as seasonal and climatic conditions, breeding sites and predators. Also information is required about man-mosquito interactions and the degree of natural and acquired immunity in the human community needing help. In theory, when the best possible data is available, intervention can be planned to lower Z_o below the critical value. This approach can be used in attempts to control any parasitic disease (Table 2.1) and a simple list of control measures is given in Table 8.1. Ideally, reliance on a single control measure may be unwise and an integrated approach using several methods is desirable.

The whole subject of control is exciting and frustrating, but also rewarding when progress is made. Parasites with complicated life cycles involving intermediate hosts and vectors are more vulnerable to control measures because they may be attacked while distant in time and space from man. However, obtaining reliable epidemiological data for such parasites in order to estimate Z_o is time-consuming and expensive. Parasites with direct life cycles may lend themselves to relatively straight forward epidemiological research, but their

constant closeness to man means care must be taken to avoid harming him during the application of control measures. The primary purpose of the experimental scientist in the context of control is to enable the clinician, entomologist, limnologist and engineer to shift the balance of the host-parasite relationship in favour of the host. His secondary purpose has more to do with convincing governments of the need to establish and fund control programmes; that challenge may be met if favourable cost: benefit ratios to the national economy can be demonstrated for particular treatments or control measures. For example, the provision of free anti-malarial prophylactic drugs for workers may reduce absenteeism, raise morale and lead to increased productivity.

PROBLEMS

Examples from Table 8.1 show how some attempts to control parasites lead to disappointment and even create greater problems than were caused by the undisturbed disease. The clearance of vegetation in regions where trypanosomiasis prevails (Table 3.10) destroys the habitat of the tsetse fly and disrupts the development and transmission of the trypanosomes. Wholesale removal of vegetation exposes the land to climatic elements and soil erosion occurs so that people can no longer grow enough food. Their livestock must then graze more closely together and still more erosion ensues. Loss of vegetation deprives people of fuel for cooking and timber for building; increased pressure is exerted on surviving woodland. The present health problem from onchocerciasis (Table 3.16) may have developed in part because when man cleared the forests he drove away other mammals and unknowingly substituted himself as a major source of food for blackflies.

Table 8.1 Examples of methods for the control of parasitic infection and disease.

PHYSICAL METHODS
1 Deforestation and bush-clearance (land erosion*)
2 Land drainage
3 New housing
4 Sanitation
5 Enclosed (piped) water supplies
6 Protective barriers (mosquito nets; footwear)
CHEMICAL METHODS
1 Insecticides (resistance*)
2 Molluscicides
3 Chemotherapy (resistance* and side effects*)
(a) Protective (prophylactic) use
(b) Curative (therapeutic) use
BIOLOGICAL METHODS
1 Use of pathogens or predators as control agents (ecological disturbance*)
2 Immunomanipulation (vaccination)

*Related problems.

Unforeseen problems have also arisen in the application of chemical methods to the control of parasitic disease (Table 8.1). Some 30 years ago, there was great optimism over the use of insecticides to devastate mosquito populations and so eradicate malaria. By 1958, 35 species of mosquito were known to have become resistant to commonly used insecticides and by 1971, 110 resistant species were listed. Not all of these transmit malarial parasites, but even those that do not may spread arboviruses or filarial worms. In any event, the accumulation of insecticides in the environment may have serious effects on man and other organisms.

Some parasites have developed resistance to some of the drugs that have been used for either prophylaxis or treatment (Table 8.1). This is another reason why malaria is still a major public health problem.

Resistance is the ability of a strain of a parasite to survive and multiply despite being subjected to an active drug given in usual or higher than usual doses. In the early 1960s, reports of resistance by *Plasmodium falciparum* to chloroquine came from Brazil and Colombia, and since then further reports have come from the Philippines, Malaysia, Indonesia and countries in South-East Asia. Chloroquine resistance was a serious blow to malaria control, not only because of immediate regional problems, but also because of its effects on the enthusiasm and confidence of those working to defeat malaria.

The employment of biological control agents (Table 8.1) has not always been successful. Biological control involves the reduction of a target organism's population density through the planned activity of a highly specific parasite or predator. The strategy depends on extensive knowledge of the population dynamics of the target organism; there may be much transmission and many new cases of disease before this baseline is attained. Sometimes the use of the control agent is successful at first, but then problems arise. Fresh-water fish of the genus *Gambusia* eat mosquito larvae and so were an obvious choice for introduction into South-East Asia where for a time they vigorously devoured the developing mosquitoes. However, as the insect food of the *Gambusia* declined, they turned to eating fish eggs and the protein supply for human consumption declined.

PROGRESS AND PROSPECTS

The control of parasitic disease where it actually occurs often seems to be making slow progress. Insecticide and drug resistance have obviously impeded efforts, but political discontinuities in developing countries

have also delayed or disrupted control schemes and health care. Sometimes, the programmes appear to be either too expensive for some countries or not of sufficiently high priority to claim support from their limited resources. At the same time, seemingly worthwhile projects to irrigate land or develop hydroelectric power, both of which ought to have produced more national wealth, served to spread diseases like schistosomiasis and malaria and so made control measures more urgent. The costs of health care are difficult to evaluate, but the information in Table 5.1 and knowledge of the current prevalence of parasitic disease (Table 5.3) suggests that parasitic disease declines when national and individual wealth increase. Wealth generates the market for effective drugs; a recent survey showed that in the German Federal Republic about U.S. $53 were spent on pharmaceutical products per person per year while in India the equivalent figure was about U.S. $0.70. This comparison is not offered as a criticism of the Indian position where more than a third of the country's health budget is spent fighting malaria; it simply illustrates the unequal distribution of the world's wealth. Nor is any hidden criticism implied of pharmaceutical companies whose turnover in 1977 equalled about U.S. $75 000 million and was largely directed towards the health needs of the richer half of the world's population.

Can something not be done to give every person his right to healthy development and freedom from hunger? In May 1980, the Director General of the World Health Organization stated "There is little joy in life nor any kind of justice for a child condemned to disease or early death because of the accident of birth in a developing country". This dismal view may be over-

stated. The success of the smallpox vaccination programme and the eradication of that awful disease has given renewed hope for the development and successful distribution of other vaccines. Smallpox eradication cost about U.S. $300 million and, while this appears to be a vast sum of money, it is only a tiny fraction of the U.S. $260 billion that were spent by the U.S.A. alone in putting a man on the moon. These figures emphasize again that permanent and world-wide relief from parasitic disease is ultimately going to depend on the decisions of politicians and the strength of national economies. For the present, all who have any opportunities however small to work for the control of parasitic disease should be encouraged to seize them.

Suggestions for Further Reading and Reference

(* reference textbook:
+ includes useful practical information).

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