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PARASITOLOGY

Textbook

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2019

МИНИСТЕРСТВО НАУКИ И ВЫСШЕГО ОБРАЗОВАНИЯ
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The textbook is compiled in accordance with the requirements of the state educational standard of higher professional education in the field of training 31.06.01 "Clinical medicine". It contains theoretical and practical material to the main sections of Parasitology, as well as drawings, diagrams and tables that allow to learn the basics of medical parasitology.
It is suitable for 1st year students and teachers of the medical faculty.

Executive editor doctor of medical sciences,
Professor S.P. Sapozhnikov

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Для студентов I курса и преподавателей медицинского факультета.

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INTRODUCTION TO PARASITOLOGY

Parasitism is the most common way of life; more than 50% of all animal species are parasites. Parasites occur in all animal species and they may have a profound effect on the health of people, domestic animals and wildlife.

Parasitology is the study of parasitism; a multidisciplinary subject covering many topics including morphology, taxonomy, biology, behavior, life-cycles, pathogenesis, epidemiology, ecology, physiology, biochemistry, genetics and molecular biology, as well as the diagnosis, immunology and treatment of infections.

Parasites live at the expense of their hosts whereas other symbionts may be mutualists (living in mutual benefit with host) or commensals (living without benefit or detriment to host). Parasites may infect the gastrointestinal tracts or circulatory systems of their hosts, they may invade different tissues and organs or they may live on the external surfaces of their hosts. Many infections may be asymptomatic whereas others may cause acute (transient) or chronic (persistent) clinical diseases ranging markedly in severity (mild to fatal).

Parasitic infections may cause mortality (fetal, neonatal, adult death), morbidity (disease manifest by enteritis, fever, anemia, etc.), production losses (reduced meat, milk, fiber production), and tissue lesions (reduced marketability of product). Despite many advances in parasite treatment and control, infections still persist due to many factors, including urbanization (crowding together); more intensive farming systems, greater translocation of animals, further land and marine development, inadequate effluent disposal, emergence of parasite drug resistance, and spread of vector insecticide resistance.

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Many types of organisms have adopted a parasitic mode of existence; that is, they require a host for their own survival. Three major groups of parasites are recognized: protozoa (belonging to the kingdom Protista), and helminths and arthropods (belonging to the kingdom Animalia, or Metazoa).

Protozoa. Over 10,000 species of single-celled protozoa have been described in the gut, blood or tissues of vertebrate and invertebrate hosts. Parasitic flagellates cause enteric diseases such as giardiasis, urogenital diseases such as trichomoniasis, systemic diseases such as sleeping sickness, and tissue diseases such as Chaga's disease and kala azar. Parasitic amoebae cause dysentery, meningoencephalitis and corneal lesions. Spore-forming sporozoa cause many serious diseases: Apicomplexa cause coccidiosis, malaria and tick fevers; Microspora parasitize fish and insects; and Ascetospora cause seasonal mortalities in oysters. Parasitic ciliates cause diarrhoea or lesions in humans and animals while commensal species cause serious fouling problems in aquaculture.

Helminths. Around 50,000 species of multicellular helminths (worms) have been described from a wide range of hosts. Roundworms (nematodes) cause much morbidity and mortality in humans and animals throughout the world. Serious infections include filiariases, hookworm and threadworm diseases. Larval and adult tapeworms (cestodes) may be found in many vertebrate hosts. Some species do not cause clinical disease whereas others may cause severe weight loss, diarrhea, abdominal pain or space-occupying lesions. Flukes (trematodes) include many important species such as sheep liver fluke and human schistosomes or blood flukes.

Arthropods. Thousands of arthropods are parasitic at some stage in their life-cycles. Many cause serious diseases and limit agricultural productivity. Parasitic insects include biting and sucking lice which may cause skin lesions or anemia, fleas which may cause allergic dermatitis, and various flies which suck blood as adults or produce larvae which feed on host tissues. Parasitic arachnids include ticks which feed on blood and may cause anemia or paralysis and mites which feed on skin and may cause mild itching, hair loss or severe mange.

1. OVERVIEW OF PARASITOLOGY

Three general environments are available for life as we know it: terrestrial, aquatic and biotic. By definition, parasites are those animals which occupy the last niche, i.e. live in or on another species, their host. Parasitism is a form of symbiosis, an intimate relationship between two different species. There is a biochemical interaction between host and parasite; i.e. they recognize each other, ultimately at the molecular level, and host tissues are stimulated to react in some way. This explains why parasitism may lead to disease, but not always. It is often a life-long relationship for the parasite, which cannot survive without its host. While it is often claimed (even by definition) that a parasite must damage its host in some way (to distinguish parasitism from commensalism and mutualism), in practice this can be impossible to establish, because we know so little about most symbiotic relationships; certainly, many human parasitic infections are asymptomatic (which is not the same as non-pathogenic).

Origins

Parasitism must have arisen very early in the history of life on Earth, when primordial micro-organisms learnt to survive inside other cells which they had invaded either passively (e.g. by phagocytosis) or actively (e.g. by penetration). When multicellular organisms with alimentary tracts appeared, they would have inevitably (accidentally or intentionally) eaten free-living micro-organisms (and, later, free-living helminths). Ingested animals that managed to survive in this new environment would have appreciated the nutrient-rich environment; energy saved in looking for food could then be diverted to proliferating and resisting the host's efforts to dislodge them. With time, these parasites became so adapted to life in the host; they "forgot" how to survive outside. However, to succeed, they still needed to produce offspring that could negotiate the outside world to find new hosts.

Not surprisingly, all parasitic animals have free-living counterparts to which they are clearly related, and the greatest diversity of parasites is still found within the alimentary tracts of "higher" animals. As host species diverged with evolution, they "carried" with them their parasites. It is virtually the rule today that parasitic protozoa and helminths found in any vertebrate species have almost iden-

tical relatives in related vertebrates, and most of them are exquisitely host-specific. For example, the two common amoebae of the human colon, *Entamoeba histolytica* and *E. coli*, have almost identical relatives within a wide range of vertebrate hosts. There is even *E. moshkovskii*, a species that has been found only in sewers, which probably evolved from parasitic species! *E. ging*ivalis occurs only in the human mouth, and has lost its cystic stage, presumably because trophozoites are so efficient at transferring between hosts. The same occurs with helminths, e.g. the roundworm of the human small intestine, *Ascaris lumbricoides*, has counterparts in pigs, dogs, cats, flying foxes, elephants, dolphins and many other mammals.

Once established in the host intestine, some parasites "learned" to invade the gut mucosa and deeper tissues, or to survive in the guts of predators that consumed their original hosts. Involvement of invertebrate "micro-predators" in such life-cycles could then have led to parasite transmission via blood or tissue ingestion. Other parasites, in their infective stages, developed the ability to invade via the skin. It is not too difficult to conceptualize how complex life-cycles, utilizing a range of different hosts, might have arisen. Many examples of "missing links" in parasite evolution can still be found today; although far more are well-and-truly extinct. It is misleading to think of extant protozoan or helminth species as "primitive", for they have been evolving as long as all other species, including Homo sapiens, and utilize sophisticated survival mechanisms that we are only beginning to understand.

Parasitism clearly has advantages over independent existence, for parasites greatly outnumber free-living animals, both in terms of individuals and species; from an evolutionary viewpoint, it is the ultimate life-style. The obvious benefit to the parasite is that its host provides, gratis, a relatively stable, nourishing home. The energy saved in seeking food, shelter and transport is then concentrated on reproducing and evading host defense mechanisms, which are provoked in virtually every case, although not always obviously.

Fields of study

Medical Parasitology is the study of those organisms which parasitize humans. According to the definition above, parasites could include the viruses, bacteria, fungi, protozoa and metazoa (multicellular organisms) which infect their host species. However, for his-

torical reasons (and because they are NOT classed as animals), the first three have been incorporated into the discipline of Microbiology. Parasitology claims those protozoa (unicellular animals), helminths (worms) and arthropods (insects and arachnids) whose existence depends on the availability of host animals, i.e. they are obligate parasites. Some rare parasites are called facultative, because they can survive and reproduce without a host, but very few that infect humans belong to this group (e.g. free-living amoebae). While we could argue about whether certain insects and mites are "temporary parasites" or "micro-predators", insects as a group belong to the discipline of Entomology, while ticks and mites are the concern of Acarology. Another crude way of distinguishing these is to label them ectoparasites (living on the host body surface), in contrast to the endoparasites (which live inside the host). The major contribution of insects in Parasitology is as vectors of several infections, although several are true parasites in their own right.

The disciplines also differ in ways other than taxonomic boundaries. In Microbiology, while morphology or staining properties (e.g. with Gram's stain) are important in the basic categorization of the organisms, species identification generally depends on culturing and identifying specific enzymatic reactions, antigenic configurations or DNA sequences; i.e. the test-tube is important. In Parasitology, morphological recognition remains foremost, so that parasites (or their vectors) are still identified on characteristic shapes and sizes; i.e. the microscope rules supreme. Sub-speciation or strain-typing is less well-developed, and may depend on molecular configurations or host-specificity. Culture has been a basic tool in Microbiology almost from its inception, and cell-culture is especially important in Virology (where viruses are not observed directly, but initially recognized by their effects on cultured cells). In Parasitology, culture was for a long time virtually impossible for most organisms, including protozoa. Nevertheless, in recent years, technical advances have allowed the in vitro cultivation of increasing numbers of parasite species, including even some helminths, although this is a procedure still in its infancy and used largely in research, rather than for routine clinical diagnosis. Advances in molecular biology are revolutionizing all the biological sciences, including Parasitology. However, the organisms still must be identified initially on their morphology, and

this is the basis of most parasite diagnoses made in clinical pathology laboratories.

Every known species (living and extinct) is assigned a unique combination of genus and species names which, by convention, are printed in italics or underlined. Infections with parasites are often indicated by the abbreviated genus name plus the suffix -osis. Some authorities use the suffix -iasis if the infection causes disease, but this distinction is often meaningless or impossible to establish. Purists argue that -osis belongs to species names derived from Greek, while those with Latin parentage deserve -iasis (it becomes tricky if you don't know the name's origins). Either can be used, depending on which sounds better (although a recent international convention aims to standardize all this), and we must be tolerant of the many exceptions, e.g. tuberculosis (mycobacteriosis), malaria (plasmodiosis), elephantiasis (lymphatic filariasis, or filariosis). If more than one parasite belongs in the genus, then the species name may be added to qualify the infection, e.g. schistosomiasis mansoni (not italicised).

Life cycles

While parasites are adapted to living in or on their hosts, they can only survive by producing offspring capable of finding new hosts. The key to understanding their dispersal through the world is through knowledge of their life-cycles or modes of transmission, involving many aspects of parasite biology, reproduction and epidemiology.

Protozoa, in their motile, feeding, growing, asexually-multiplying forms are known as trophozoites (*trophe* = nutrition; *zooite* = minute animal); these are adapted for existence in the host and, generally, are unable to survive the rigours of life outside. Under appropriate conditions, which we do not yet understand, some trophozoites of gut protozoa coat themselves in a protective shell and shut down metabolically, to become cysts. These are designed to survive in the outside world long enough to reach new hosts. In the most highly-evolved protozoa (apicomplexans), which are obligate intracellular parasites, asexual division of the trophozoite (schizogony; *schizein* = to divide, or split; *-gony* = reproduction) leads to the generation of many merozoites (*meros* = piece, segment) which then invade other host cells. Eventually, instead of undergoing further schizogony, merozoites undergo sexual reproduction (gamogony)

developing into either macrogametocytes (female) or microgametocytes (male). Fertilization results in the formation of a zygote, termed an oocyst (= egg-cyst), which is designed to survive in the outside world so that it may infect another host. The ripe (sporulated) oocyst contains infective "seeds" known as sporozoites, which arise during its maturation (*sporogony* = generation of spores).

The metazoan parasites (multi-celled worms and arthropods) generally are dioecious, i.e. adults occur as separate males and females. Tapeworms and most flukes are the exceptions (hermaphrodites). After copulation, females produce fertile eggs, each containing an embryo. This undergoes embryonation developing into a juvenile or larva which will hatch out under suitable conditions. The egg may be the infective stage, or larvae may develop in the outside world to infectivity, or larvae may develop further in one or more intermediate hosts before they are able to re-infect their definitive hosts. Because their larvae must develop outside the host, adult helminths cannot multiply directly within an individual host (in stark contrast to protozoa which can proliferate to large numbers).

Many parasites complete their developmental cycle in a single host species (monoxenous life-cycles) while others require multiple host species (heteroxenous life-cycles). When multiple hosts are involved, the definitive host is that species in which the adult (or sexual) form of the parasite occurs, whereas the intermediate host is the species which supports the development and/or multiplication of the non-sexual, or larval (for helminths), stages of the parasite. Intermediate hosts which physically carry the infective stage from one host to another are also termed vectors; they are mechanical vectors if they simply transmit the parasite (unchanged and non-multiplied), and cyclical vectors if they also function as true intermediate hosts that support essential development and/or proliferation of the parasite. Intermediary hosts may be optional in some helminth life-cycles; the parasite might not undergo essential development in them, although it may increase in size. These paratenic hosts carry parasites through food chains to the definitive host, ensuring successful transmission even when the hosts are thinly dispersed through the environment. Some parasites exhibit low specificity for their definitive and/or intermediate hosts and so can develop in a range of animal species.

A zoonosis is a human infection caused by an organism which occurs naturally in other animals, known as reservoirs of infection. Most parasite life-cycles that are known have only been worked out quite recently; i.e. within the last 100 years. Information is therefore fragmentary and many ambiguities exist. We could argue about whether the mosquito genus Anopheles or the primate species Homo sapiens is the definitive host for malaria parasites as gamogony in initiated in the human but culminates in fertilization in the mosquito.

Host specificity

Parasites can be very particular about which host species they will use; this can apply to definitive as well as intermediate hosts. A parasite that is specific for a single host species is said to be oioxenous, one that parasitizes closely-related hosts is stenoxenous, while one that parasitizes unrelated hosts is euryxenous. Host-specificity is determined by a complex of factors, some obvious and others still obscure. The first requirement is that the prospective host shares its environment with the parasite (ecological specificity); e.g. parasites of dolphins might not have much luck infecting humans who do not live near the sea (although modern food transport networks have changed this!). Secondly, host behaviour must expose it to the parasite (ethological specificity); e.g. people who eat dolphin food (fish) may acquire parasites intended for dolphins. Finally, once the parasite comes into contact with the host, it must recognize appropriate cues and feel comfortable within its new surroundings (physiological specificity); e.g. if a parasite of dolphins thinks it is in a large fish or a dolphin when it arrives in the human gut, it may then behave accordingly. Obviously, this last determinant of host-specificity is the one we understand least.

Parasites interact with host secretions and surfaces and membranes: they must recognize and respond to molecular configurations (receptors/ligands). Detection of subtle variations in metabolites allows them to follow road-maps; they need to make critical changes in behavior and development according to changes in host physiology/behavior (neural/endocrine cues); and they must be satisfied with their diet (host intestinal contents, blood and/or tissues). Clearly, all these combinations are unique for each host species, and vary even among individuals within a species, within an individual host throughout its own life cycle and even throughout a 24-hour day.

Likewise, each population of parasites is heterogeneous, so some individuals succumb very easily if in the wrong host ("losers") whereas others persist and may come close to full development ("pioneers"). This is the driving force of evolution, and parasites are the most rapidly evolving animals.

Epidemiology

This is the descriptive and analytical study of how diseases or infective organisms are distributed in human populations. A parasite is endemic to a geographical region if it is sustained by transmission amongst people living there. An infection maintained in animal populations is enzootic (which must apply to all zoonoses), although this term is going out of fashion. An infection acquired locally (usually in an endemic region) is autochthonous. Infected people who bring an organism into a non-endemic area are labelled imported cases; should the parasite then transfer to another person in that region, the secondary case becomes an introduced infection. If the parasite then establishes in this new population, it becomes newly-endemic.

The level of infection in a population is measured by prevalence and incidence. Prevalence refers to the prevailing level of a condition within a defined population, and is best applied to conditions without a clearly identifiable onset, such as most helminthic infections, chronic toxoplasmosis, Chagas' disease (or malignant, degenerative or metabolic diseases). It is measured by a single study of a population over a brief time-period (cross-sectional survey measuring point prevalence or period prevalence). Incidence refers to the number of new cases acquired per unit of population per unit of time, and is more meaningful for acute, short events (incidents), with an identifiable beginning (or end!) e.g. many viral infections, acute malaria (or deaths, or accidents). It can be measured only by monitoring a population over a sufficient period of time (longitudinal study) and determining the rate increase or decrease (difference in prevalence over time). Obviously, the incidence, prevalence and duration of a particular condition are closely and simply inter-related. An epidemic occurs when the incidence of new cases significantly exceeds the usual rate; if the disease is protracted, this will be reflected by an increase in prevalence as well.

Quantitation of infection

Infective organisms have been categorized as either micro-parasites, which are multiplicative, i.e. they multiply directly within the host (all the microbes, plus protozoa) or macro-parasites, which are cumulative, i.e. they generally cannot multiply in the host; their numbers depend on how many infective eggs or larvae are taken on board. Ectoparasites do not happily fit into this classification, for they are clearly "macro", but often can multiply to huge populations on the one host. However, their development may be considered "external", as they usually reside outside the host on the surface. The term "infestation", sometimes used for macro-parasitic infections, is going out of fashion, but can be applied to contaminated inanimate objects, e.g. a house infested with fleas, or bushland infested with ticks.

Infection with micro-parasites is an all-or-none situation; you either have measles, influenza, bubonic plague, toxoplasmosis, giardiasis, etc., or you don't. It is not often possible, or necessary, to quantify reliably the intensity of such an infection (number of organisms on board a host). Note that mean intensity differs from mean abundance: the former being the average number of parasites per infected host; the latter being the average number of parasites in all hosts, i.e. including non-infected hosts. In many instances, the severity of disease is not reliably related to the numbers of parasites detectable in blood, tissues or secretions (a notable exception is malaria, in which the percentage of infected red cells can be estimated and sometimes is important clinically). In the case of helminths and arthropods, which are generally visible macroscopically as discrete individuals, the number of organisms is meaningful, because it can be measured and does influence the likelihood or severity of disease. Therefore, in epidemiological studies of macro-parasitic infections, their intensity becomes important, in addition to incidence and prevalence. Virtually all population studies have shown that the intensity of infection does not follow a normal distribution, but exhibits an "aggregated" or "over-dispersed" pattern: a small number of hosts harbor most of the parasites, whereas most individuals carry few or no parasites. This phenomenon has been characterized mathematically ("negative binomial distribution"), but remains to be explained from first principles.

Clinical and pathological considerations

While, by definition, a parasite should evoke a host reaction, there need not be any obvious adverse effects because, in the great majority of cases, infected individuals exhibit little evidence of disease. In many cases, it can be difficult or impossible to determine whether an organism is a parasite or commensal (e.g. many intestinal protozoa, and worms). However, other parasite infections do cause serious disease, to such an extent that they become major public health problems. It is generally assumed that, the longer a parasite and its host species have co-evolved, i.e. have had time to adapt to each other, the less pathogenic the infection becomes. On the other hand, infections with parasites that are poorly adapted to humans (e.g. zoonoses) are more likely to cause serious disease. However, there are many exceptions to these "rules". Remember, clinicians generally only see those individuals who develop disease; there may be many more who remain well, even though infected. Clinicians often liken this scenario to observing an "iceberg" – they generally only see the tip-of-the-iceberg (hosts with disease) while the bulk remains hidden (hosts with subclinical infections, asymptomatic carriers).

The development of disease depends on both host factors (susceptibility/resistance) and parasite factors (pathogenicity/virulence). Hosts have been shown to be more susceptible to disease by virtue of their age (neonates and geriatrics), gender (females, mainly during pregnancy and lactation), nutritional state (malnourished), physiological state ('stressed' hosts) and immunological competency (greater in immunosuppressed or immuno-compromised hosts). From the parasite perspective, the major important determinant for the development of disease is parasite pathogenicity (or virulence), i.e. capacity to induce disease, including the inter-related factors of invasiveness (motility, enzyme secretion, presence of specific tissue receptors, induction of phagocytosis), fecundity (rate of producing offspring), means of egress from host, stimulation and/or suppression of immunity and inflammation, production of exo- and endo-toxins and resistance to host defenses. Such virulence-determinants often correlate directly with the parasite's capacity to survive and reproduce, but they also may adversely affect host survival and fecundity. This applies a pressure on host populations that selects out more resistant individuals; it has even been argued that parasites serve to improve the fitness of their host species (Red Queen Hypothesis), and were a major influence in the

evolution of sex! However, genetic changes that increase resistance to infection often handicap the host in other ways, generating a dynamic equilibrium between protection against infection and susceptibility to other diseases (balanced polymorphism). There is no doubt that infectious organisms exert a powerful and continuous evolutionary pressure on host populations (and vice versa).

Parasitic diseases

In the field of infectious diseases, it is conceptually important not to confuse etiological agents with their effects on the host. An infection occurs when an organism, i.e. the parasite, is found in its host. Some experts don't like to label this an infection, unless there is evidence of a response in host tissues; this applies particularly to commensal organisms, which normally occur on human skin or in the gastrointestinal tract, but which cause disease only when they breach the surface barriers. Infection is a host-organism interaction; it cannot exist without a host. Presence of infective organisms in the environment, e.g. in food, on fomites or in water, is not infection, but contamination (or "infestation"). For instance, we should not talk about "infected water supplies".

Moreover, an infection is not the same as a disease, which is a pathological change in the host, i.e. abnormalities induced in tissues by direct mechanic-chemical damage and/or release of toxins and/or inflammatory mediators. Illness occurs when the host suffers the effects of the disease and becomes a patient, i.e. complains of symptoms (subjective, felt by the patient) which interfere with normal life, and perhaps manifests clinical signs (objective, detectable by the doctor), always with psychosocial undertones and ramifications. This is summarized as follows:

Where you start in the above sequence depends on whether you are the parasite or the patient! The illness is what the patient complains about to the doctor (often with judicious prompting), the disease is what the clinician may detect on physical examination (and the pathologist confirms in laboratory tests or at autopsy), and the causative organism (or its products, or antibodies to it) is what the diagnostic laboratory usually seeks and identifies. In any particular patient, all of these apparent components might be totally unrelated, so that linking them together becomes a major and still unresolved difficulty, even in some very common infections. Such distinctions may seem pedantic, but their appreciation helps in understanding

stages in the evolution of an infectious disease, and is important to minimize confusion. Many people are infected; in fact, every one of us has at some time harbored at least one parasite species, and most of the world's people carry many parasites most of the time. However, relatively few are diseased, and not all of them suffer illness. Infections without illness are called subclinical or asymptomatic. Note that this does not mean being free of disease.

The interval between exposure to infection and the onset of illness is known as the incubation, latent or pre-patent period or phase. Some authorities define this period as the time from exposure to the time of becoming infective to others, but not all agree with this. Others define the latent period as the time from exposure to the first occurrence of recognizable specific manifestations, be they symptoms, signs, positive serology or other laboratory findings; if for symptoms, then it is called the incubation period. With many parasitic infections in endemic areas, these definitions may be of little use clinically, because people are repeatedly being exposed to infection.

An infection is patent when direct evidence of the organism can be detected, e.g. in the patient's faces, blood or secretions, regardless of whether symptoms have appeared. Some infections may be patent but subclinical; others may cause illness, yet not be patent. However, the individual who has patent infection is essential to transmission of the organism, because it can then be transferred directly to other hosts, to vectors, or into the environment, where it may need to develop through stages to infectivity. Obviously, the detection of patency depends on the sensitivity of the test being used to identify the organism.

Often, indirect evidence of infection is the best that can be offered by the diagnostic laboratory, in the form of circulating antibodies generated against antigens of the infecting organism. Apart from the issues of accuracy (measure of true positive and true negative reactions), specificity (measure of false positive reactions) and sensitivity (measure of false negative reactions), another difficulty common to all antibody tests is distinguishing between ongoing active infection and recently resolved or past infection. In other cases, serology may be even less adequate, for the simple reason that a test has not been developed, and the infection is known as cryptic. In some infections, specific monoclonal antibodies can be used to identify parasite antigens, and the polymerase chain reaction is becoming increasingly available to identify nucleotide sequences from infective

organisms, although the limitations of these technological advances have not been well-established.

Usually, disease results predominantly from the host's efforts to deal with the parasite, involving immunological and other less well understood responses to an organism which refuses to go away, and which utilizes effective strategies to avoid being damaged. The principles (and even details) of host responses to infecting organisms apply equally to microbial and parasitic infections and, as we learn more about the precise mechanisms, the more difficult it becomes, in the clinical context, to justify the separation of these groups of pathogens. Obviously, viruses may succumb more readily than worm larvae to protective mechanisms involving antibodies, complement, lymphocytes, phagocytes and other effector cells and molecules, but all infections initially trigger similar basic repertoires of responses. A major discriminating influence is whether the organisms are intracellular or extra-cellular, which partly determines the class of MHC molecules with which they interact. The minute parasitic protozoa that multiply in host cells have much in common with viruses, so that host responses to these infections and the resulting diseases can be so similar that, clinically, they may be indistinguishable.

Furthermore, patients have only a limited range of symptoms to complain about, so that generally it is impossible to diagnose the causative organism from the clinical features. However, a careful history, taken to evaluate the likelihood of exposure to specific parasites, often narrows the range of options (differential diagnosis), and indicates the specimens which should be sent to the laboratory for definitive diagnosis. This can be much cheaper (and much more satisfying for the clinician - and the patient) than running a battery of tests blindly, and is essential for effective treatment and suitable preventive measures.

Parasitological parameters

Parasitic infections can be studied from many angles: we can focus on the parasites, their hosts, the environments they share and the ways in which they interact. People working in this field come from numerous backgrounds, including zoology, physiology, biochemistry, immunology, molecular biology, pharmacology, ecology, economics, anthropology, sociology, engineering, agriculture, education, mathematics and, of course, human and veterinary medicine. Specif-

ic disciplines focus on specific aspects, thus parasitological knowledge may be fragmentary. In order to obtain (retain) a holistic overview, many parasitologists use a parametric approach to organize information. The following headings have proven useful:

- Etiology (study of causative agent; in this case, the parasitic organism): Colloquial and scientific (binomial) species name, broad group e.g. amoeba, nematode; forms (developmental stages) occurring in hosts (adult, larva, cyst, trophozoite, etc.); approximate size/shape and appearance.
- Life cycle (summary of biology): Hosts – definitive, intermediate, paratenic; anatomical locations and sites of multiplication; development and survival in hosts/environment.
- Epidemiology (dispersal in populations): distribution, worldwide and in endemic areas; prevalence, by age, sex, occupation; transmission into and out of hosts; ecological determinants, i.e. geography, climate, vectors, human behaviour and resources (housing, hygiene, sanitation, nutrition, occupation, animal reservoirs, medical facilities, preventive and control measures).
- Pathogenesis (dispersal within host; mechanisms of disease): Sites affected; mechanical and/or chemical damage; local and systemic host responses (acute and chronic); effectiveness of immunity; effects on transmission; host resistance/susceptibility.
- Clinical manifestations (how patient affected): logical extension of knowledge on pathogenesis; known mainly which organ system(s) involved and how manifests; symptoms and signs.
- Diagnosis (how detected): Specimens required; how and when collected, preserved, transported; how examined in lab; reliability of results (sensitivity, specificity, predictive values); safety aspects (i.e. infectivity of clinical specimens, their handling and disposal).
- Treatment (therapy): Is it necessary? Effective? Safe? Types of drugs; dosages; spectrum of activity, mode of action; contraindications, side-effects; compliance; susceptibility/resistance.
- Prevention/control (prophylaxis/intervention/management): public health concerns (individual, family, community: who is at risk?); chemoprophylaxis (necessary under what conditions?); interruption of transmission; behaviour modification; patient/community education; prospective/retrospective screening programmes, vaccination (availability, strategies); environment/food/water contamination, purification/disinfection.

2. PROTOZOAN PARASITES

The name '*protozoa'* literally means 'first animals' and early classification systems grouped the protozoa as basal members of the animal kingdom. However, they were recognized as a discrete assemblage on the basis of their unicellularlity and were assigned to the taxon Protozoa (but still invariably figured as the trunk of the animal tree of life). Members of the subkingdom Protozoa are quite disparate; indeed, the taxon has never been considered a natural assemblage of organisms but rather one of convenience. More recently, the protozoa have been classified together with several algal and fungal groups in the kingdom Protista (protozoa representing the motile protists). Irrespective of contemporary classification systems, most parasitological texts continue to use the name protozoa for historical reasons.

Protozoa are eukaryotic organisms (with a membrane-bound nucleus) which exist as structurally and functionally independent individual cells (including those species which are gregarious or form colonies). None have adopted multicellular somatic organization characteristic of metazoan organisms. Instead, protozoa have developed relatively complex subcellular features (membranes & organelles) which enable them to survive the rigors of their environments. Most protozoa are microscopic organisms, only a few grow to a size large enough to be visible to the naked eye. As unicellular eukaryotes, protozoa display all the same essential life activities as higher metazoan eukaryotes: they move about to survive, feed and breed.

Biodiversity

Four main groups of protozoa are recognized on the basis of their locomotion using specialized subcellular and cytoskeletal features (fig. 1):

- Amoebae use pseudopodia (singular: pseudopodium) to creep or crawl over solid substrates. Pseudopodia (or 'false feet') are temporary thread-like or balloon-like extensions of the cell membrane into which the protoplasm streams. Similar amoeboid motion has been observed in cells of many life-forms, especially phagocytic cells (e.g. human macrophages).
- Flagellates use elongate flagella (singular: flagellum) which undulate to propel the cell through liquid environments. Flagella are 'whip-like' extensions of the cell membrane with an inner core of microtubules arranged in a specific 2+9 configuration (2 single central microtubules surrounded by 9 peripheral doublets). This configu-

ration is conserved throughout eukaryotic biology, many organisms produce flagellated cells (e.g. human spermatozoa).

- Ciliates use numerous small cilia (singular: cilium) which undulate in waves allowing cells to swim in fluids. Cilia are 'hair-like' extensions of the cell membrane similar in construction to flagella but with interconnecting basal elements facilitating synchronous movement. Ciliated cells are found in specialized tissues and organs in many other higher life-forms (e.g. human bronchial epithelial cells).
- Sporozoa ('spore-formers') were originally recognized not on the basis of their locomotion, but because they all formed non-motile spores as transmission stages. Recent studies, however, have shown that many pre-spore stages move using tiny undulating ridges or waves in the cell membrane imparting a forward gliding motion, but the actual mechanisms involved are not yet known.

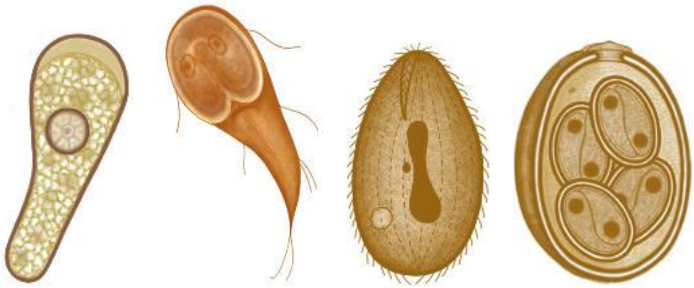

Figure 1. Four main groups of protozoa:
a – amoebae; *b* – flagellates; *c* – ciliates; *d* – sporozoa
[http://www.onlinebiologynotes.com/category/parasitology]

Protozoan biodiversity (or species richness) includes counts (or estimates) of some 32,000 extant (living) species and another 34,000 extinct (fossil) species (especially foraminifera). Of those alive today, some 21,000 species occur as free-living organisms in aquatic or terrestrial environments, whereas the remaining 11,000 species are parasitic in vertebrate and invertebrate hosts. There are approximately 6,900 flagellate species (1,800 parasitic, 5,100 free-living), 11,550 amoebae species (250 parasitic, 11,300 free-living), 7,200 ciliate species (2,500 parasitic, 4,700 free-living) and 5,600 sporozoan species (all parasitic).

Life cycles

Most protozoa have enormous reproductive potential because they have short generation times, undergo rapid sequential development and produce large numbers of progeny by asexual or sexual processes. These characteristics are responsible for many protozoan infections rapidly causing acute disease syndromes. Parasites may multiply by asexual division (fission/splitting or internal/endogenous budding) or sexual reproduction (formation of gametes and fertilization to form zygote, or unique process of conjugation where ciliates exchange micronuclei).

Protozoan developmental stages occurring within hosts generally consist of feeding trophozoites, and they may be found intracellularly (within host cells) or extracellularly (in hollow organs, body fluids or interstitial spaces between cells). While trophozoites are ideally suited to their parasitic mode of existence, they are not very resistant to external environmental conditions and do not survive long outside of their hosts. To move from host-to-host, protozoan parasites use one of four main modes of transmission: direct, faecal-oral, vector-borne and predator-prey transmission (fig. 2).

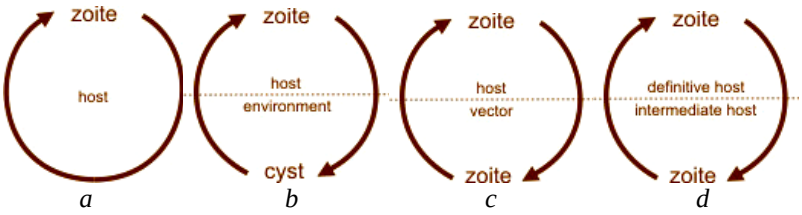

Figure 2. Four main modes of transmission:
a – direct; *b* – faecal-oral; *c* – vector-borne; *d* – predator-prey transmission
[http://www.onlinebiologynotes.com/category/parasitology]

- Direct transmission of trophozoites through intimate body contact, such as sexual transmission (e.g. *Trichomonas* spp. flagellates causing trichomoniasis in humans and bovine infertility in cattle).
- Faecal-oral transmission of environmentally-resistant cyst stages passed in faeces of one host and ingested with food/water by another (e.g. *Entamoeba histolytica*, *Giardia duodenalis* and *Balantidium coli* all form faecal cysts which are ingested by new hosts leading to amoebic dysentery, giardiasis and balantidiasis, respectively).

- Vector-borne transmission of trophozoites taken up by blood-sucking arthropods (insects or arachnids) and passed to new hosts when they next feed (e.g. *Trypanosoma brucei* flagellates transmitted by tsetse flies to humans where they cause sleeping sickness, *Plasmodium* spp. haemosporidia transmitted by mosquitoes to humans where they cause malaria).
- Predator-prey transmission of zoites encysted within the tissues of a prey animal (e.g. herbivore) being eaten by a predator (carnivore) which subsequently sheds spores into the environment to be ingested by new prey animals (e.g. tissue cysts of the sporozoan *Toxoplasma gondii* being ingested by cats, and tissue cysts of the microsporan *Thelohania* spp. being ingested by crustaceans).

2.1. *ENTAMOEBA HISTOLYTICA*
[causes amoebic dysentery in man]

Classification: Taxonomic ranks under review.
- Protista (unicellular eukaryotes).
- Sarcomastigophora (with pseudopodia and/or flagella).
- Sarcodina (amoeboid protista).
- Lobosea (locomotion by broad lobopodia).
- Amoebida (naked amoebae with simple life-cycles).

Entamoeba histolytica is a common protozoan parasite found in the large intestine of human. The parasite is responsible for amoebiasis and liver absceses. It is the third leading parasite cause of death in the developing countries.

Parasite morphology. Parasite occurs in three stages; trophozoite, precyst and cyst (fig. 3).

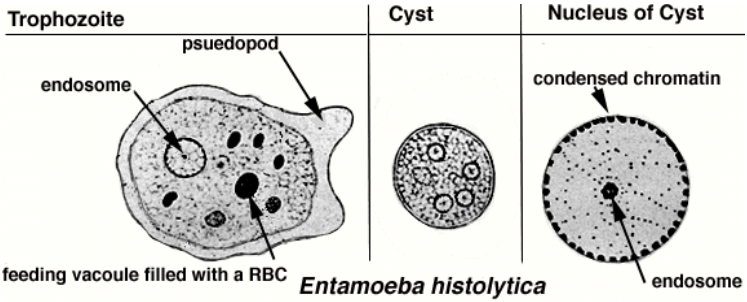

Figure 3. Three stages of *Entamoeba histolytica*
[https://smart.servier.com/category/medical-specialties/infectiology/]

Trophozoite:

- It is the growing and feeding stage of parasite.
- Sape; not fixed because of constantly changing position.
- Size: ranging from 18–40 μm; average being 20–30 μm.
- Cytoplasm: cytoplasm is divided into two portion; a clear transparent ectoplasm and a granular endoplasm. Ingested RBCs, tissue granules and food materials are also found in endoplasm.
- Nucleus: It is single, spherical shape and size ranging from 4–6 μm Nucleus contains central karyosome and fine peripheral chromatin.
- Trophozoites are actively motile with the help of pseudopodia.
- Trophozoites are anaerobic parasite, (present in large intestine).

Pre cyst:

- It is the intermediate stage between trophozoite and cyst.
- It is smaller in size, 10–20 μm.
- It is round or slightly ovoid with blunt pseudopodium projecting from periphery.
- No RBC or food materials are found on its endoplasm.

Cyst:

- It is the infective form of parasite.
- Shape: It is round or round or oval in shape.
- Size: 12–15 μm in diameter.
- It is surrounded by a highly rectractile membrane called cyst wall. The cyst wall is resistant to digestion by gastric juice in human stomach.
- Nucleus: A mature cyst is quadrinucleated.
- Cytoplasm: Cytoplasm shows chromatid bars and glycogen masses but no RBCs or food particles.
- Mature cyst passed out in stool from infected patient and remained without fouther development in soil for few days.

Life cycle:

- It is relatively simple and consists of infective cyst and invasive trophozoites stage (fig. 4).
- Life cycle completes in single host, ie human. Human get infected with *E. histolytica* cyst from contaminated food and water.
- Infection can also acquire directly by ano-genital or oro-genital sexual contact.

- The mature Cyst is resistant to low pH of stomach, so remain unaffected by the gastric juices.
- The cyst wall is then lysed by intestinal trypsin and when the cyst reaches the caecum or lower part of illium excystation occurs. The neutral or alkaline environment as well as bile components favor excystation.
- Excystation of a cyst gives 8 trophozoites. Trophozoites are actively and carried to large intestine by peristalsis of small intestine. Trophozoites then gain maturity and divide by binary fission.
- The trophozoies adhere to mucus lining of intestine by lectin and secretes proteolytic enzymes which causes tissue destruction and necrosis. Parasite, when gain access to blood, migrates and causes extra-intestinal diseases.
- When the load of trophozoites increases, some of the trophozoites stop multiplying and revert to cyst form by the process of encystation.
- These cysts are released in faeces completing the life cycle.

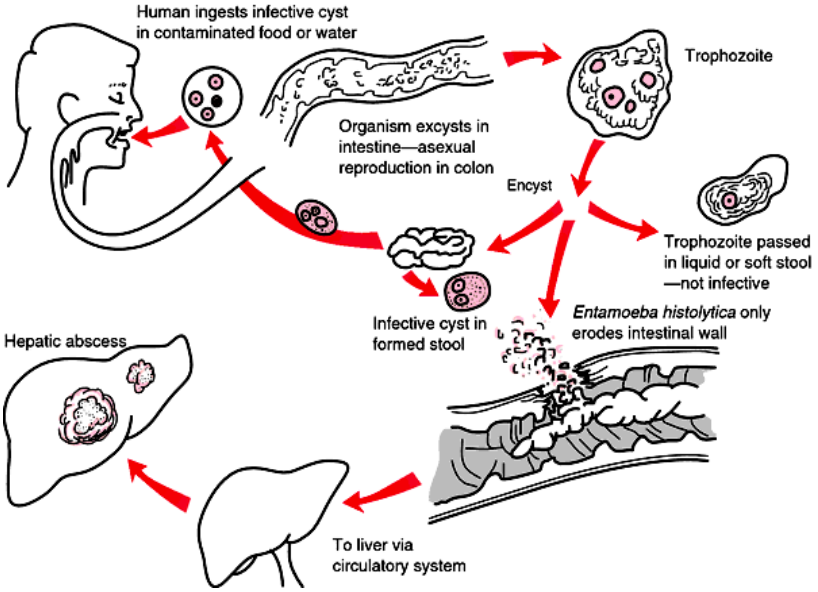

Figure 4. Life cycle of *Entamoeba histolytica*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Site of infection. Trophozoites generally infect the large intestinal mucosa but under certain conditions they may perforate the gut and invade other organs (especially liver, lungs and brain).

Pathogenesis. Many infections remain asymptomatic whereas others cause severe diarrhoea (amoebic dysentery), ulceration and perforation of the colon, and secondary lesions in other organs. Virulence factors are not yet known.

Mode of transmission. Trophozoites passing posteriad condense into spherical precysts (containing chromatoidal bars) which then mature into cysts (containing 4 nuclei). The cysts are very resistant to environmental conditions and are usually ingested with contaminated food or water.

Differential diagnosis. Infections are diagnosed by repeated stool examinations for trophozoites and cysts. Considerable expertise is required to differentiate pathogenic species from harmless commensals on the basis of nuclear and cyst morphology.

Treatment and control. Patients may be treated with luminal, hepatic and/or tissue amoebicides as warranted (metronidazole). Control may be facilitated by maintaining high standards of hygiene and ensuring proper water and sewage treatment.

2.2. *GIARDIA LAMBLIA*

[this species causes giardiasis (diarrhea) in vertebrates]

Classification:

- Protista (unicellular eukaryotes).
- Sarcomastigophora (with pseudopodia and/or flagella).
- Mastigophora (flagellates).
- Zoomastigophora (zooflagellates, without chloroplasts).
- Diplomonadida (zoites with two nuclei).

Giardia lamblia is also known as intestinilis or *G. duodenalis*. It was first observed by Antony von Leewenhoek (1681) while examining his own stool and Lambi (1859) describe the parasite and named it as *Giardia labmlia*. Giardia is the only intestinal flagellate known to cause endemic and epidemic diarrhea in human. Inhabits the small intestine of human.

Parasite morphology. *G. lamblia* exists in two morphological form- trophozoite and cyst (fig. 5).

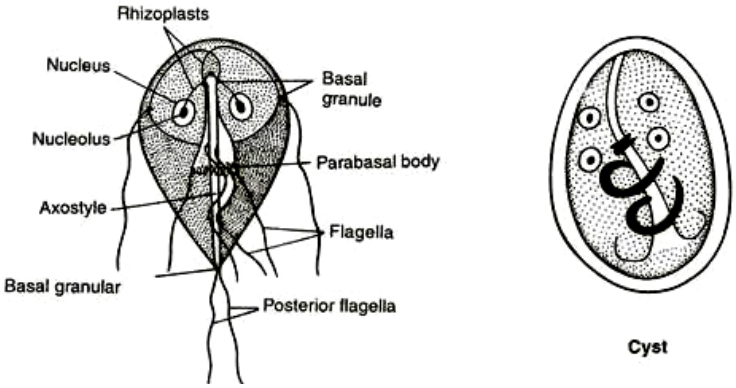

Figure 5. Morphology of *Giardia lamblia*
[https://smart.servier.com/category/medical-specialties/infectiology/]

Trophozoite:

- It is the active feeding stage of parasite which is responsible for colonization in intestine.
- The shape of trophozoite is pear shape or tennis racket shape with broad round anterior end and a tapering posterior end.
- It measures 9–21 μm in length and 5–15 μm in breadth.
- The dorsal surface is convex while ventral surface is concave with a sucking disc (adhesive disc) which acts as an organ for attachment.
- Behind the adhesive disc lies a pair of large curved and transverse median bodies, unique to
- It is bilaterally symmetrical and all organs of body are paired. They have two median bodies, two axostyle, two nuclei and four pairs of flagella.
- Each nucleus consists of large central karyosome giving a characteristic face like appearance to the parasite in stained preparation.
- Cytoplasm is uniform and finely granulated.
- Motility shown typical ‘fallling leaf type’ motility.

Cyst:

- It is an infective stage of parasite.
- A fully mature cyst is oval or ellipsoidal in shape and measures 8–12 μm in length and 7–10 μm in breadth.
- Cyst is surrounded by a thick cyst wall. Cytoplasm is granulated and is separated from the cyst wall by clear space.
- The axostyle lies more or less diagonally.
- A cyst contains 4 nuclei.
- The remaining of flagella and the margins of sucking disc may be seen inside the cytoplasm.

Life cycle:

- Life cycle of G. lamblia is simple and completes in a single host, man. No intermediate host is required (fig. 6).
- Infection is acquired orally by ingestion of cyst from contaminated hand or water or food.
- Excystation occurs in th stomach and in the duodenum in the presence of gastric acid, pancreatic enzymes (chymotrypsin and trypsin). An acidic environment with a pH 1.3–2.7 is required for excystation.
- Each cyst excysts to produce two trophozoites in the duodenum within 30 minutes of ingestion.
- These trophozoites multiplies in the intestine by bunary fission. Then they adhere to enterocytes through their ventral sucker mediated possibly through surface mannose-binding lectin present on the surface of trophozoites.
- Some of the trophozoites then pass down on the large intestine where they again encyst in the presence of neutral pH and bile salts.
- The process of encystation begins with the appearance of encystation specific secretory vesicles (ESVs) in the cytoplasm of trophozoites, followed by production of cyst wall within 15 hours.
- Within 24 hours after appearance of ESVs, the trophozoite is covered with these cysts wall proteins, resulting in formation of cyst.
- Formation of cyst begins by shortening of flagella followed by condensation of cytoplasm and finally secretion of thick hyline cyst wall.

- These encysted trophozoites then undergo another phase of nuclear division and produces quadrinucleated mature cyst.
- The cysts which are the infective form of parasite are excreted in faeces and life cycle is repeated.

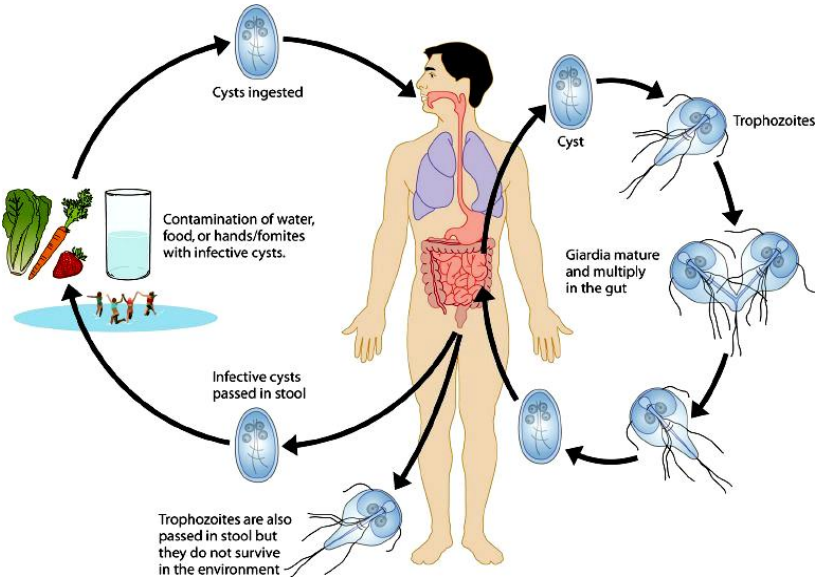

Figure 6. Life cycle of *Giardia lamblia*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Site of infection. Flagellated trophozoites are found in the small intestines of their hosts, especially the duodenum. Trophozoites have been observed swimming with a distinct corkscrew motion in luminal content as well as adhering to the gut mucosal surface with their ventral adhesive discs (when they detach, they leave distinct oval impressions in the microvillous layer).

Pathogenesis. Infections interfere with the normal absorptive functioning of the small intestines, thereby causing osmotic overload of the large intestines resulting in watery diarrhoea. Attached parasites may physically blanket the small intestinal mucosa significantly reducing the surface area for absorption. It is also thought some parasite molecular products may exert a chemical action on mucosal cells. Infections apparently damage and increase the turnover rate of

epithelial cells culminating in villous atrophy which further reduces the surface area for absorption. These factors contribute to malabsorption of fats and other nutrients resulting in watery diarrhoea and steatorrhea accompanied by dehydration, intestinal pain and flatulence. Most clinical infections are self-limiting and resolve spontaneously but some persist leading to chronic weight loss, retarded growth and 'failure-to-thrive' syndrome. Young individuals are most susceptible to clinical infections and focal outbreaks are common in child day-care centres and among intensively-reared and housed young animals. Not all infected individuals, however, develop clinical signs but may remain asymptomatic carriers.

Mode of transmission. Infections are passed between hosts by the faecal-oral transmission of encysted parasite stages. When trophozoites pass through the colon, they form nonflagellated cysts which are excreted and contaminate the environment. The cysts are said to be reproductive in that they undergo nuclear division as they mature becoming quadrinucleate. Following their ingestion by a new host, they excyst in the small intestine releasing two trophozoites. Excystation stimuli include various post-gastric digestive conditions (bile salts, enzymes, pH, microaerophilic conditions, etc). Most infections are transmitted accidentally by 'hand-to mouth' contact whereby objects contaminated with faecal material are placed in the mouth (e.g. contaminated fingers, utensils, clothing, etc). The cysts are quite resistant to external environmental conditions and can survive for some time, particularly in cool moist conditions. The cysts also contaminate water supplies and cause infections when subsequently ingested with drinking water or the consumption of food-stuffs diluted or washed with contaminated water. Infections have also been associated with recreational water use, including swimming pools, lakes and water-theme parks. Conventional water treatment procedures (filtration and chlorination) are not wholly effective against Giardia cysts as they are quite small and hardy.

Differential diagnosis. Faecal cysts may be detected by routine coprological examinations (stained smears, or sedimentation/flotation concentration techniques) but test sensitivity is poor due to intermittent cyst excretion. Endoscopic techniques (gastroscopy through to duodenum) have been used in chronic cases to

detect trophozoites in intestinal biopsy material. More recently, sensitive and specific immunological techniques have been developed to detect parasite antigens in faecal preparations (coproantigen tests). Similar monoclonal antibody immunoreagents are also used in many countries to detect cysts in water samples using immuno-magnetic separation techniques.

Treatment and control. Flagel (metronidazole) is the drug of choice for giardiasis despite mild side-effects (such as nausea). However, there are growing problems with metronidazole-resistant parasite strains. Other nitroimidazole derivatives (tinidazole), nitrofurans (furazolidone), acridine drugs (quinacrine) and microtubule inhibitor anthelmintics (albendazole) have been reported effective. Control depends largely on good sanitation, proper effluent disposal and effective water treatment (well-maintained sand filtration or microfiltration, optimum chlorination or ozonation).

2.3. TRICHOMONAS VAGINALIS

[this species causes trichomoniasis in human]

Trichomonas vaginalis, a flagellate, is the most common pathogenic protozoan of humans in industrialized and developing countries. The infection is transmitted sexually.

Parasite morphology. Trichomonas vaginalis only exists in trophozoite stage. Cystic stage is absent (fig. 7). Trophozoite inhabit the vagina in female, the prostate and seminal vesicles in male and urethra in both sexes. The trophozoites of Trichomonas, measuring 14–17 μm × 5–15 μm have a single nucleus, four anterior flagella and a single lateral flagellum attached to pellicle to form an undulating membrane. They are actively motile, pear-shaped. The inner margin of

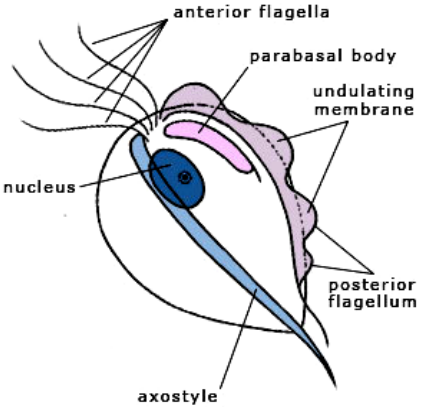

Figure 7. Morphology of *Trichomonas vaginalis* [https://smart.servier.com/category/medical-specialties/infectiology/]

this membrane is supported by a filament. There is also a central skeletal rod or axostyle. The cytoplasm contains a large number of hydrogenosomes and sometimes viral particles.

The parasite may also invade the urethra and associated glands of male and are frequently detected in the urine. T. vaginalis was first of all discovered by Donne in 1836 in the vaginal discharge. Powell (1936) and Wenrich (1947) described it in detail.

The parasite is cosmopolitan in distribution.

Life cycle. T. vaginalis is a monogenetic parasite (fig. 8). The natural hosts are human beings, where the parasite lives as a colourless pyriform flagellate measuring usually 15 to 18 μm in length and 5 to 15 μm in breadth. They exist only in trophozoite phase and there is no cystic phase. A single elongated nucleus lies at the round anterior end.

Mode of transmission. The mode of transmission is direct. Man is the only source of infection. Infection from infected female to healthy one passes on through sexual intercourse in which male play and intermediary role. Since, the parasite is also found in the urethra of males, transmission may occur from infected male to healthy female and vice versa. The parasite does not survive more than 24 hours outside the body of the host.

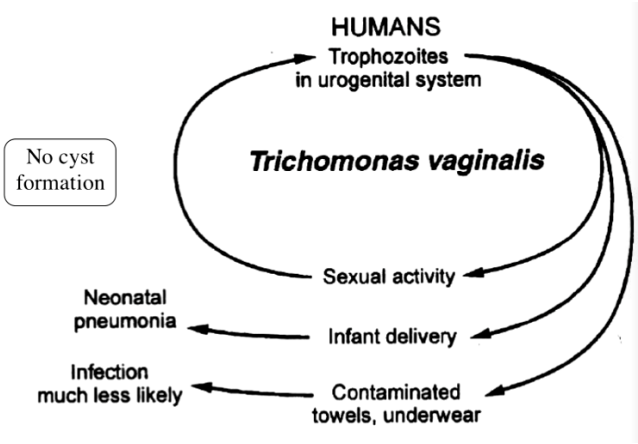

Figure 8. Life cycle of *Trichomonas vaginalis*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Pathogenesis. The parasite produces symptoms which are collectively called as trichomonad vaginitis. The disease is characterised by burning sensation, itching and creamy white frothy discharge from vagina. The vaginal walls become tender and prone to bacterial infection. Urethral infection in male causes dysuria, frequency of urination and dirty-white discharge containing leukocytes, epithelial cells and trichomonads. Secondary bacterial infections may occur.

Treatment and control. Drugs having arsenic and iodine compounds are useful. Antibiotics like Aureomycin and Terramycin are also being used. Local cleansing and drying of the vaginal mucosa also help to control the parasite population. Carbasone is used in case of infection in males. Metronidazole has replaced the old treatment.

Prophylaxis:

1. Attention to personal feminine hygiene.
2. Detection and treatment of infected male and female partners.

2.4. TRYPANOSOMA SPP.

Classification:

- Protista (unicellular eukaryotes).
- Sarcomastigophora (with pseudopodia and/or flagella).
- Mastigophora (flagellates).
- Zoomastigophora (zooflagellates, without chloroplasts).
- Kinetoplastida (presence of extranuclear DNA, kinetoplast).

Family Trypanosomatidae

All species are characterized by the possession of a kinetoplast, a unique structure formed by massed DNA (circles or lattice) within the single large mitochondrion closely associated with the flagellar basal body. Four main developmental stages are formed: trypomastigotes (with a posterior kinetoplast and an emergent flagellum forming a long undulating membrane); epimastigotes (with an anterior kinetoplast and an emergent flagellum forming a short undulating membrane); promastigotes (with an anterior kinetoplast and a short emergent flagellum, but no undulating membrane); and amastigotes (with a kinetoplast but no emergent flagellum or undulating membrane). Many trypanosome species are parasitic only in insects whereas others are transmitted by insect vectors to a wide range of verte-

brate hosts. Three main groups infect the blood and/or tissues of humans and animals causing severe clinical diseases (table 1):

- Salivarian trypanosomes which undergo anterior station (foregut) development in the insect vector and are transmitted via saliva to the blood of vertebrate hosts (e.g. tsetse flies transmit *T. brucei* which causes sleeping sickness in humans and nagana in cattle).
- Stercorarian trypanosomes which undergo posterior station (hindgut) development in vectors and are transmitted via faecal contamination of bite site to infect blood and tissues of vertebrate hosts (e.g. reduviid bugs transmit *T. cruzi* which causes Chagas' disease in humans).

Table 1

Characteristics of Trypanosoma spp.

Trypanosoma species	Mastigote length, μm	Vertebrate hosts	Disease	Insect vector	Distribution
T. b. gambiense	16-30	man, domestic animals	sleeping sickness	tsetse fly	West Africa
T. b. rhodesiense	*18-30*	man, some ruminants	sleeping sickness	tsetse fly	East Africa
T. b. brucei	18-42	ruminants, monogastrics	nagana	tsetse fly	tropical Africa
T. cruzi	15-24	man, domestic / wild animals	Chagas' disease	bugs	America

TRYPANOSOMA BRUCEI [this species causes sleeping sickness in humans]

Parasite morphology. The parasite forms trypomastigotes in vertebrate hosts and epimastigotes in the insect vector (fig. 9). The trypomastigotes (with posterior kinetoplast and long undulating membrane) are pleomorphic in size ranging from 16–42 μm in length by 1–3 μm in width. They occur as elongate slender dividing forms (with long free flagellum) or stumpy non-dividing infective (metacyclic) forms (with no free flagellum). The epimastigotes (with anterior kinetoplast and short undulating mem-brane) are also variable in size ranging from 10–35 μm in length by 1–3 μm in width (fig. 10).

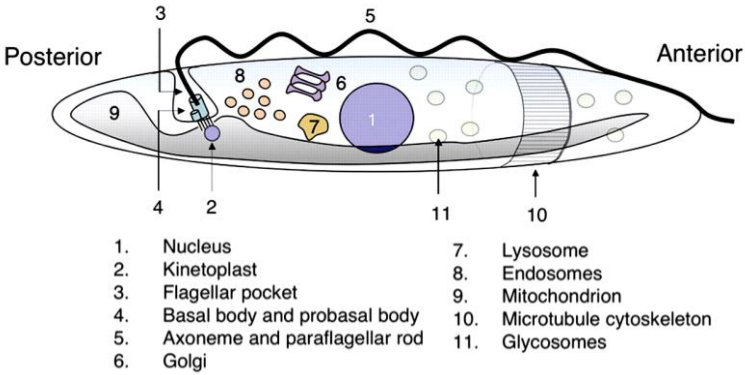

Figure 9. Morphology of *Trypanosoma brucei*
[https://smart.servier.com/category/medical-specialties/infectiology/]

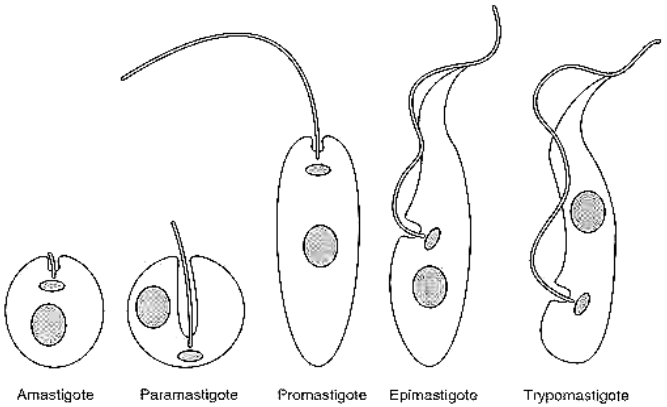

Figure 10. Morphological stages of *Trypanosoma brucei*
[http://www.onlinebiologynotes.com/category/parasitology]

Host range. Salivarian trypanosomes are confined to tropical Africa, corresponding in distribution with their tsetse fly vectors. Three closely-related subspecies are found: *Trypanosoma brucei brucei (T. b. brucei)* which is primarily parasitic in native antelopes and other wild ruminants (asymptomatic carriers, trypanotolerant) but infects introduced domestic animals; *T. b. rhodesiense* which causes acute disease in humans in East Africa; and *T. b. gambiense* which produces a much more chronic disease in humans in West Africa.

Site of infection. Trypomastigotes are found extracellularly in the blood and lymph of infected individuals (including lymph nodes and spleen) but may invade the central nervous system and other tissues.

Pathogenesis. The disease is known as Old World (African) trypanosomiasis. Although there are many regional common names given depending on the parasite subspecies and hosts involved, the disease is often called sleeping sickness in humans, and nagana in animals. Parasites injected into the host by the insect vector first cause an inflammatory reaction characterized by a localized tender reddish swelling (known as a chancre). Trypanosomes then multiply in the plasma and interstitial fluid causing acute to subacute febrile illness. A classic sign of *T. b. gambiense* infection is the enlargement of the cervical lymph glands at the back of the neck (known as Winterbottom's sign). *T. b. rhodesiense* infections in humans usually cause acute systemic disease with haemolymphatic involvement, swollen lymph nodes, fever and rapid weight loss. *T. b. gambiense* usually causes chronic disease with neurological involvement, meningoencephalitis, lethargy and coma (hence 'sleeping' sickness). Parasite development occurs in cyclic waves moderated by host immune responses. Trypanosomes have a glycoprotein coat on the outer surface of the cell membrane which is highly antigenic and leads to the production of host antibodies which act, together with complement, to lyse parasites. Trypanosomes, however, repeatedly change the molecular arrangement of the coat so some individuals avoid immune destruction and divide to produce a new wave of infection. This antigenic variation is under genetic control and while synthesis of successive variant surface glycoproteins does not occur in a fixed sequence, it is not entirely random. The repeated cycles of host antibody production and parasite destruction leads to cyclic fevers, macroglobulinemia, microvascular damage, coagulopathy, and perivascular inflammation. When parasites penetrate the blood-brain barrier (within weeks for *T. b. rhodesiense* or up to years for T. *b. gambiense)*, they cause encephalitis, coma and death. The clinical course of *T. b. brucei* infections depends on the susceptibility of the host species. Horses and dogs are particularly susceptible and may succumb within 2–3 weeks Cattle and pigs are more refractory to disease and may survive for several months. Clinical signs include anaemia, fever, oedema and progressive paralysis. Native animal

species (antelope and other wild ruminants) are trypanotolerant and may act as asymptomatic carriers.

Mode of transmission. All salivarian trypanosomes are transmitted by tsetse fly vectors (*Glossina spp.*). Metacyclic trypomastigotes ingested during feeding transform into procyclic trypomastigotes in the midgut. These stages migrate through gut membranes and invade the salivary glands where they transform into epimastigotes which undergo anterior station development to produce infective metacyclic trypomastigotes which are injected during feeding (fig. 11).

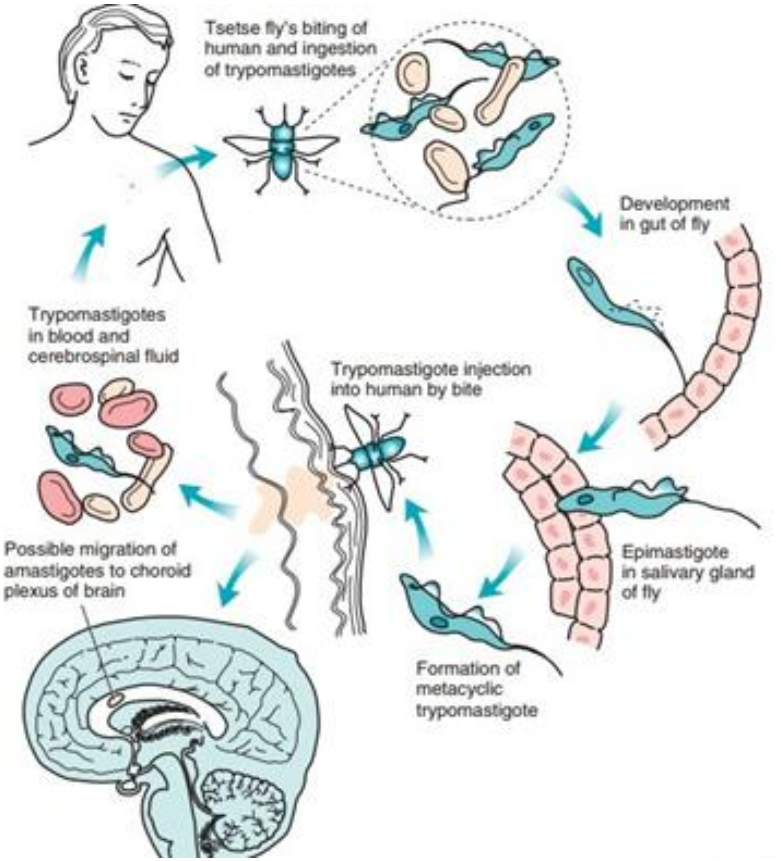

Figure 11. Life cycle of *Trypanosoma brucei brucei*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Infections were conventionally diagnosed by the direct detection of parasites in blood, bone marrow or cerebrospinal fluid by microscopic examination before or after centrifugation. In vitro cultivation has proven difficult and in vivo inoculation into laboratory animals yields variable results. More recently, a variety of immunoserological tests have been developed to detect host antibodies using fluorescent, agglutination or enzyme markers. Card-agglutination and dot-spot tests are available for field use. Molecular characterization techniques utilizing polymerase chain reaction (PCR) amplification of parasite DNA have yielded good results in species/strain differentiation with certain genes (e.g. SRA gene, serum-resistant-associated).

Treatment and control. Historically, arsenical drugs have been used despite major toxicity problems. Melarsoprol and trypursamide are used to treat chronic infections (involving CNS signs). Other drugs have proven more effective against systemic infections (suramin, pentamidine) and neurological infections (berenil, eflornithine, difluoromethylornithine). Prevention involves avoiding being bitten by tsetse flies, but this can be difficult as they are persistent daytime feeders and can bite through thin clothing. Control measures based on vector eradication (using insecticidal sprays, fly traps, or clearing vegetation) and managing wild game reservoirs of infection (by fencing, culling or creating wildlife corridors) have only proven partially effective. Some recent success has been recorded in breeding trypanotolerant domestic livestock (e.g. Ndama cattle).

TRYPANOSOMA CRUZI [this species causes sleeping sickness in humans]

Chagas disease (American trypanosomiasis) is caused by *Trypanosoma cruzi*. This flagellate naturally occurs in many mammals in Central and South America. It is transmitted by highly coloured bugs of the genera Triatoma, Rhodnius and Panstrongylus, also known as kissing bugs. These arthropods live in burrows or nests of animals and in dark, sheltered areas of human homes. They particularly prefer to inhabit cracks in the walls of mud or adobe houses in Latin America. Chagasiasis is disease of mainly poor people.

Life cycles. Most of the vectors of *T. cruzi* are known to defecate while sucking blood. It is believed that the arthropod is attracted to the carbon dioxide in the host's exhaled breath and that is why it

mainly bites on the face, arms and shoulders. As it sucks blood, it defecates and rubs some of the faeces on the wound causing infection. The host may be prompted to rub the wound and contaminate it with the bug's faeces. Other methods of acquiring infection include blood transfusion, through the mammary glands, organ transplantation and by accidental ingestion of the infected reduviid bugs. Animals become infected by eating the bugs or licking their bites. Cats can become infected through eating infected rodents.

On entering the body tissues, the parasites or trypomastigotes invade cells in the body, particularly muscle and nerve cells, while some are taken up by the macrophages. these intracellular parasites lose their flagella, transform into amastigotes, and start diving for 4 to 5 days to produce large numbers of trypomastigotes. the parasitised host cells rupture, liberating trypomastigotes into the blood stream and body tissues. Once more, some of the trypomastigotes are ingested by macrophages while others invade new cells and another multiplication process begins. however, trypomastigotes that are free in the blood system do not divide. Infection in the triatomine vector begins when it sucks blood that is infected with trypomastigotes. On reaching the vector's midgut, the trypomastigotes transform into epimastigotes, which divide to produce more parasites. After division, the parasites proceed to the hindgut where they change into metacyclic trypomastigotes that are infective to a host (fig. 12).

Pathogenesis. The early phase of the infection is characterized by the inflammatory tissue reaction and acute lymphadenitis. The infection is acute during its early stages with characteristic swollen face especially around the eyes. There may be severe headache, inflammation of the tear gland and swelling of the lymph glands of the neck. These symptoms would seem to suggest that the eye might be the usual site of infection, the insect biting the lids of the eyes, causing the host to rub the infected bug faeces onto the eyes. Other symptoms include enlargement of the spleen and liver, fever and anaemia. The prognosis, especially in children, is usually bad and fatalities are common. If the patient survives the acute phase, the infection goes into a chronic stage with mild symptoms that last for months or years. The mildness of the symptoms, however, masks the extent of the seriousness of organ damage that may be taking place. Organs that are usually affected by *T. cruzi* include the heart, kidney, central nervous system,

thyroid, adrenal glands, oesophagus and colon. The most affected organ is usually the heart and most of the deaths are due to heart failure. A person may drop dead suddenly only to discover that he has probably been suffering from chronic chagas disease. Damage to the sympathetic nervous system of the alimentary canal can lead to enlarged oesophagus and inability to swallow. Examination of the patient during the chronic phase of the infection reveals enlarged spleen, and liver, general oedema and anaemia. The patient may be fidgety and nervous.

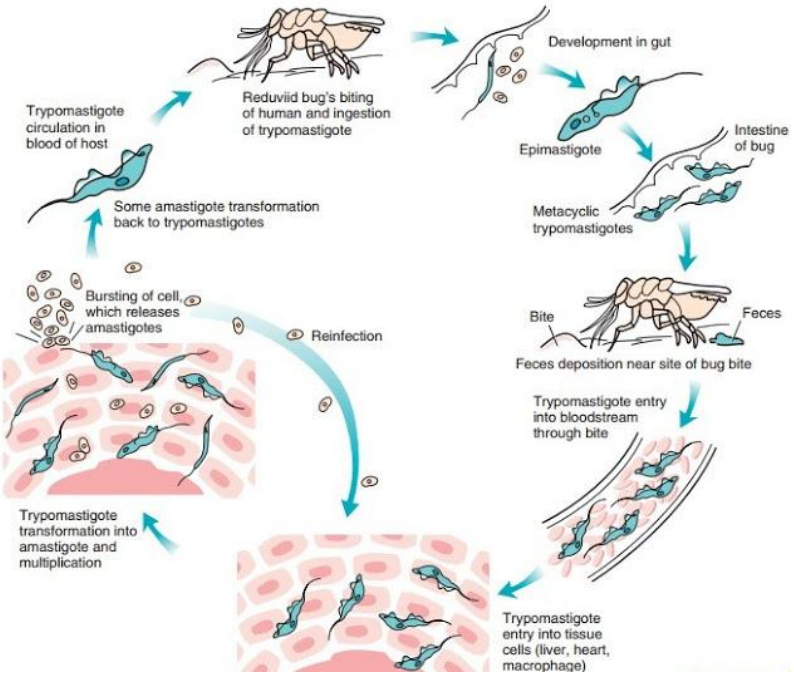

Figure 12. Life cycle of *Trypanosoma cruzy*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. The parasites can be detected in blood smears taken from an early infection. However, it is difficult to find parasites in the circulation in chronic infections. A technique known as zenodiagnosis is usually used to detect parasites in old chronic cases. Zenodiagnosis involves allowing unfed parasite-free bugs to

imbibe blood from suspected individuals and if the parasites are present, they are detected in the faeces of insects about 4 weeks later.

Treatment and control. There is no effective treatment for Chagas disease. However, two compounds, nifurtimox and benznidazole, whose efficacy and safely are still in doubt, have recently been introduced. Both drugs require a long administration of two to three months and are therefore not suitable for a widespread use.

2.5. LEISHMANIA SPP.

Classification:

- Protista (unicellular eukaryotes).
- Sarcomastigophora (with pseudopodia and/or flagella).
- Mastigophora (flagellates).
- Zoomastigophora (zooflagellates, without chloroplasts).
- Kinetoplastida (presence of extranuclear DNA, kinetoplast.

LEISHMANIA SPP. [these species cause cutaneous, or visceral leishmaniasis in humans]

Parasite morphology. Two developmental stages are formed: amastigotes and promastigotes. The amastigotes are small spherical non-flagellated cells ranging from 2–4 μm in diameter. The nucleus and kinetoplast are surrounded by small ring of vacuolated cytoplasm and the cells are among the smallest nucleated cells known. Promastigotes are thin elongate cells with an anterior kinetoplast and an emergent free flagellum. They are generally lance-like in shape and range in size from 5–14 μm in length by 1.5–3.5 μm in width. Different para-

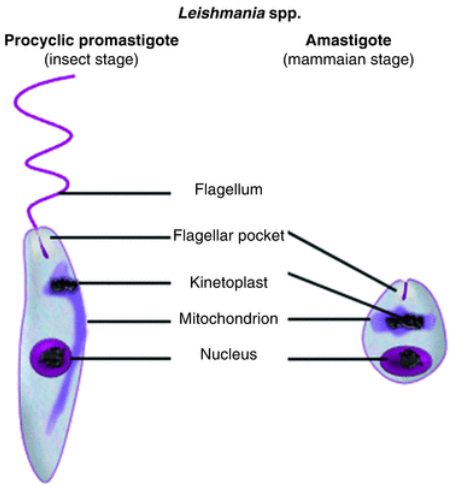

Figure 13. Morphology of *Leishmania spp*. [https://smart.servier.com/category/medical-specialties/infectiology/]

site species are generally not differentiated by morphological differences, but rather on the basis of geographical, biological and clinical features (fig. 13).

Host range. *All Leishmania* spp. infect mammals and are most commonly found in humans, dogs and rodents (table 2). Infections are confined to tropical areas, different parasite species being found in the Old World (Middle-East and Africa) and the New World (Central and South America).

Table 2

Characteristics of Leishmania spp.

Leishmania species	Vertebrate hosts	Disease	Insect vector	Distribution
Cutaneous leishmaniasis				
L. tropica minor	humans, dogs	dry cutaneous	*Phlebotomus*	Mediterranean
L. tropica major	humans, dogs, rodents	wet cutaneous, oriental sore	*Phlebotomus*	Mediterranean
L. mexicana mexicana	humans, rodents	chicleros ulcer, cutaneous	*Lutzomyia*	Central America, Mexico
Visceral leishmaniasis				
L. donovani donovani	humans, dogs, foxes	kala azar, dum-dum fever, Old World visceral	*Phlebotomus*	Mediterranean, South America

Site of infection. Amastigotes invade macrophage cells of the reticuloendothelial and lymphoid systems of the skin, nasopharynx or viscera depending on the parasite species. The parasites survive within phagosomes but resist digestion by lysosomal enzymes. They multiply and grow, ultimately rupturing the host cell and releasing stages to infect new macrophages, including those which circulate in the blood (monocytes).

Mode of transmission. All species are transmitted by small blood-sucking sandflies, notably Phlebotomus spp. in the Old World and Lutzomyia spp. in the New World. Only the females feed on blood. Amastigotes ingested during feeding transform in the midgut or hindgut into promastigotes which multiply by binary fission. The parasites migrate forward to the foregut and proboscis where some become swept away by saliva into the bite site when the fly feeds (fig. 14).

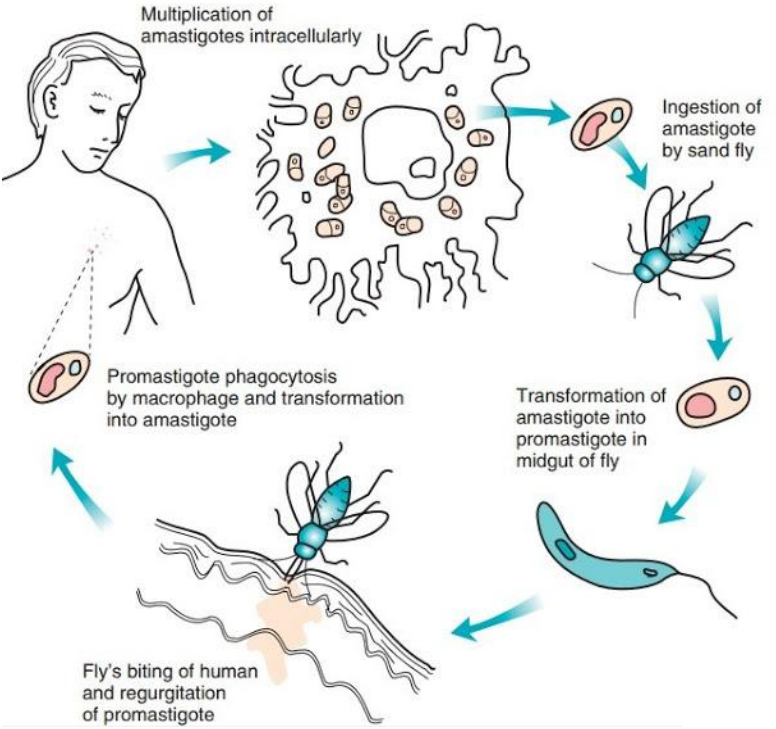

Figure 14. Life cycle of *Leishmania spp.*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Pathogenesis. The parasites cause three distinct types of clinical disease, cutaneous, mucocutaneous and visceral leishmaniasis. Old World cutaneous leishmaniasis is caused by L. tropica and L. aethiopica while New World cutaneous leishmaniasis is caused by L. mexicana and L. braziliensis. Infections generally involve only one or a few lesions at the bite site; they do not spread to other sites. Active lesions appear as open sores/ulcers with pronounced inflammation. Most lesions heal spontaneously, leaving the host with solid protective immunity to re-infection. However, under certain conditions (esp. immuno-compromised hosts), some L. aethiopica infections may spread giving rise to disseminated cutaneous leishmaniasis (not unlike leprosy in appearance). Infections by L. braziliensis are also often confined to single skin lesions, but sometimes they spread

to the mucocutaneous junction in the pharynx and may cause severe destructive nasopharyngeal lesions. Visceral leishmaniasis is caused by L. donovani whereby infected macrophages congregate in the viscera, notably the liver and spleen, producing hepatosplenomegaly, oedema and anaemia. It is a slow but progressive illness, with bouts of irregularly recurring fever, and is invariably fatal, unless treated.

Differential diagnosis. Amastigotes may be detected microscopically in biopsy tissues, smears or secretions before or after culture. Parasites are best visualized using Giemsa's or Leishman's stains, and suitable culture media include conventional nutrient agar-blood mixtures. Serological tests have been developed but there are difficulties in distinguishing between recent and chronic infections and between infections by different parasite species, although a delayed-type hypersensitivity (DTH) skin test has shown good promise as a marker of cured symptomatic or asymptomatic visceral infection. Modern molecular characterization techniques have used the polymerase chain reaction (PCR) to amplify parasite DNA from host tissues.

Treatment and control. Some cutaneous infections require no treatment as lesions may heal within several months. Systemic therapy with pentavalent antimonials (sodium stibogluconate or meglumine antimonate) is the treatment of choice for disfiguring and visceral infections. The development of antimonial drug resistance, however, is a growing problem in many endemic areas, including South America, India and the Middle-East. Pentamidine or amphotericin B can be used if antimonials are ineffective, and miltefosine and aminosidine (paromomycin) have shown promise as treatment options, especially when combined with immunotherapy using the tumour-necrosis factor-alpha (TNF) inhibitor pentoxifylline. Preventive measures include protection from sandfly bites but this can be difficult as they are so small that they can penetrate most mosquito nets. Reducing the size of reservoir host populations (especially dogs) has proven beneficial in many endemic urban areas. Many cutaneous infections, however, are acquired in forests away from human habitation, as the reservoir hosts are wild animals (esp. rodents). The prevention of sandfly bites in forest areas is almost impossible but may be minimized by the use of protective clothing, insect repellants and insecticidal sprays in houses.

2.6. BALANTIDIUM COLI

Classification:

- Protista (unicellular eukaryotes).
- Ciliophora (with cilia, nuclear dualism, pellicular alveoli, reproductive conjugation).
- Kinetofragminophorea (‘lower holotrichs’, little distinction between oral and body ciliature).
- Rhabdophora (noncurved tubular cytopharyngeal apparatus = rhabdos).
- Litostomatea (‘simple mouths’, special somatic kineties).
- Trichostomatia (endosymbionts).
- Vestibulifera (distict oral depression = vestibulum).

Family Balantidiidae

These ciliates are monoxenous (one-host) endocommensals in vertebrates, some species of which can become histophagous parasites. The trophozoites have a uniform covering of somatic ciliary rows and a cytostome at the base of an anterior vestibulum.

BALANTIDIUM COLI [this species causes balantidiasis in humans]

Parasite morphology. Two developmental stages are formed: trophozoites and cysts. Trophozoites are variable in size ranging from 30–120 μm in length. They are oblong-spherical in shape and are covered by longitudinal kineties (rows of cilia). At the anterior end there is a depression (vestibulum) leading to the cytostome (mouth). Internally, they contain a single large kidney-shaped macronucleus and single small micronucleus. The cysts appear as membrane-bound ovoid bodies ranging from 40–60 μm in diameter (fig. 15).

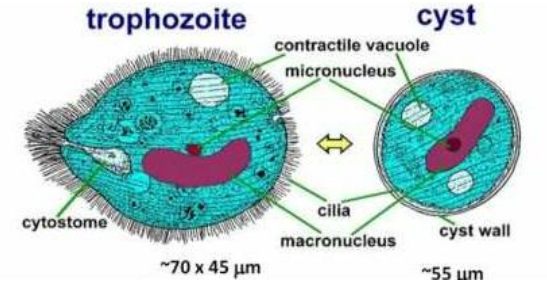

Figure 15. Morphology of *Balantidium coli*
[https://smart.servier.com/category/medical-specialties/infectiology/]

Host range. Several Balantidium spp. have been recorded throughout the world in various species of crustacea, insects, fish, amphibia and mammals (including humans). Infections by B. coli are particularly prevalent in pigs, monkeys and humans, especially in the tropics, with zoonotic transmission frequently implicated by epidemiological studies.

Site of infection. Ciliates are found in the large intestines of their hosts. They are actively swimming organisms and they reproduce asexually (by transverse fission) and sexually (by conjugation).

Pathogenesis. Infections are usually not associated with any changes in the colonic mucosa. Healthy individuals often exhibit spontaneous recovery or become symptomless carriers. However, under certain conditions, the organisms produce proteolytic enzymes which digest away the epithelium producing flask-shaped ulcers. This stimulates inflammatory changes with lymphocytic infiltration and haemorrhage and secondary bacterial invasion may follow. Infections may cause a dysentery-like syndrome, involving diarrhoea, tenesmus, nausea, vomiting, anorexia, headache, insomnia and weakness. Colonic ulceration involves mucosal sloughing, necrosis, fluid loss, haemorrhage, occasional abscess formation and sometimes perforation of the bowel.

Mode of transmission. Infections are passed horizontally between hosts by faecal-oral transmission. Cysts passed in the faeces of infected hosts contaminate the environment. When ingested with contaminated food or water, the cysts excyst releasing trophozoites in the digestive tract.

Differential diagnosis. Infections are diagnosed by coprological examination and the detection of characteristic cysts in faecal material or trophozoites in colonic biopsy material.

Treatment and control. Clinical infections may be treated with metronidazole, di-iodohydroxyquin, tetracycline or carbarsone. Prevention and control depends on strict hygiene to prevent the contamination of food and water supplies, particularly by pig faeces. Effluent from intensive piggeries should not be used to fertilize vegetable gardens or edible crops. In developing countries, pigs should not be left to roam free in rural villages, but are best confined to pens and stys where proper waste disposal can be practiced.

2.7. PLASMODIUM SPP.

Classification:

- Protista (unicellular eukaryotes).
- Apicomplexa (cells with cluster of organelles known as apical complex).
- Haematozoea (vector-borne parasites infecting blood cells of vertebrates).
- Haemosporidia (blood-dwelling spore-formers, insect vectors).

Family Plasmodidae

These parasites are transmitted to vertebrate hosts by insect (notably mosquito) vectors. In vertebrates, they form amorphous developmental stages (plasmodia) in blood cells (mostly erythrocytes). All stages have a reduced apical complex (lacking a conoid). Hundreds of species have been described in mammals, birds and reptiles; most causing no apparent harm but those infecting humans causing one of the worst fever scourges of mankind, malaria. Parasites undergo exoerythrocytic schizogony in hepatocytes of vertebrates then repeated cycles of intraerythrocytic schizogony with some stages subsequently undergoing gametogony. Many species produce haemozoin pigment granules as a byproduct of haemoglobin metabolism. Gametes ingested by insect vectors undergo fertilization in the gut forming motile zygotes (ookinetes) which form oocysts on the outer gut wall. The oocysts produce thousands of sporozoites which infect the salivary glands and are injected into vertebrate hosts during feeding.

PLASMODIUM SPP. [these species cause malaria in humans].

Parasite morphology: Malarial parasites form four developmental stages in humans (hepatic schizonts and then intraerythrocytic trophozoites, schizonts and gamonts) and three developmental stages in mosquitoes (ookinetes, oocysts and sporozoites). Liver schizonts appear as clusters of small basophilic bodies (merozoite nuclei) located within host hepatocytes, measuring 40–80 μm in diameter when mature. Intraerythrocytic stages consist of small rounded trophozoites (ring forms) measuring 1–2 μm in diameter, amorphous multinucleate schizonts measuring up to 7–8 μm in length, and micro- (♂) and macro- (♀) gametocytes ranging in length from 7–14 μm. The morphological characteristics (size, shape and appearance) of the blood stages are characteristic for each *Plasmodium spp*.

Microgametocytes have a larger more diffuse nucleus (ready for gamete production) while macrogametocytes have darker-staining cytoplasm (plentiful ribosomes for protein synthesis). In the mosquito, long slender microgametes (15–25 μm in length) produced by exflagellation fertilize the rounded macrogametes to form motile ookinetes (15–20 × 2–5 μm) which migrate through the gut wall to form ovoid oocysts (up to 50 μm in diameter) on the exterior surface. The oocysts produce thousands of thin elongate sporozoites (~15 μm long) which infect the salivary glands.

Host range. Humans are hosts for four main species, although they can occasionally be infected by other species from nonhuman primates (table 3). Most species are confined to tropical and subtropical areas depending on the distribution of their insect vectors. On a global basis, ~40% of infections are due to *P. falciparum*, ~10% are due to *P. malariae*, ~50% *to P. vivax* and <1% to *P. ovale*.

Table 3

Characteristics of Plasmodium spp.

Plasmodium spp.	Vertebrate hosts	Periodicity	Vectors	Pathogenicity
P. falciparum	humans	48 hours + irregular	*Anopheles*	moderate
P. ovale	humans	48 hours	*Anopheles*	moderate
P. vivax	humans	48 hours	*Anopheles*	low
P. malariae	humans, monkeys	72 hours	*Anopheles*	low

Pathogenesis. The disease malaria is characterized by its long persistence in infected individuals in endemic areas, with characteristic recrudescences or relapses, sometimes after years of subclinical infection. However, infections in highly susceptible individuals, such as children, pregnant women and travellers, can produce acute severe and even fatal disease. Clinical expression is characterized by cyclic paroxysms of fever/chills (produced by host inflammatory responses), haemolysis and erythrophagocytosis (resulting in anaemia), and organ hypoperfusion due to ischaemia (arising through cytoadherence of infected cells to vascular endothelia, disseminated intravascular coagulation, erythrocyte rosetting, and haemozoin pigment accumulation). Vague prodromal signs may first develop prior to parasitaemia, including headache, anorexia and mild fever. Thereafter,

characteristic febrile paroxysms and haemolytic anaemia develop and become progressively worse. Depending on the parasite species involved, severe complications may arise, including splenic rupture, cerebral signs, haemolytic anaemia, cardiac, pulmonary and renal failure. Paroxysms coincide with intraerythrocytic parasite developmental cycles (tertian = 2 day cycle, quartan = 3 day cycle) and may be accompanied by dizziness, nausea, vomiting, delirium, hepato/splenomegaly, leucopenia and thrombocytopenia. Infected cells are removed from the circulation by erythrophagocytosis during passage through the spleen. Some uninfected cells may also be removed if damaged or coated with debris or parasite antigens, thus exacerbating anaemic conditions. As the parasites grow within erythrocytes, they ingest and digest haemoglobin leaving behind characteristic dark pigment deposits, termed haemozoin (metabolic byproducts containing the indigestible iron-containing part of the haemoglobin molecule). Haemozoin may accumulate in organs and tissues resulting in impaired function. Infected erythrocytes (especially by *P. falciparum*) develop sticky protrusions by which they adhere to vascular endothelial cells, or clump together, resulting in restricted blood flow, ischaemia and end-organ anoxia (table 4).

Table 4

Pathogenesis of Plasmodium spp.

Characteristic	*P. falciparum*	*P. malariae*	*P. ovale*	*P. vivax*
Type of malaria:	malignant tertian	benign quartan	benign quartan	benign quartan
Erythrocytic cycle:	48 hours	72 hours	48 hours	48 hours
Exoerythrocytic cycle:	9 days	14-15 days	9 days	8 days
Gametocytes:	crescent	ovoid	ovoid	ovoid
Distribution:	worldwide in tropics, subtropics & temperate regions	scattered in tropics and subtropics	*Anopheles*	moderate

Site of infection. Sporozoites injected by mosquitos first undergo massive amplification by asexual exoerythrocytic schizogony in liver cells. Some sporozoites of P. vivax and P. ovale may also exhibit arrested development in the liver forming hypnozoites (dormozoites) which are quiescent stages responsible for malaria relapses.

Merozoites released from the liver then invade erythrocytes and transform into trophozoites which undergo schizogonous division (fig. 16). This cycle of asexual multiplication in the red blood cells occurs with regular periodicity. Ultimately, intraerythrocytic gametocytes are formed which do not divide further in the human host. When ingested by mosquitoes during feeding, the gametocytes mature and undergo fertilization in the gut forming motile ookinetes which migrate through the gut wall to form oocysts. The oocyst then produces hundreds of sporozoites which migrate into the salivary glands (once infected, mosquitos remain infected for life).

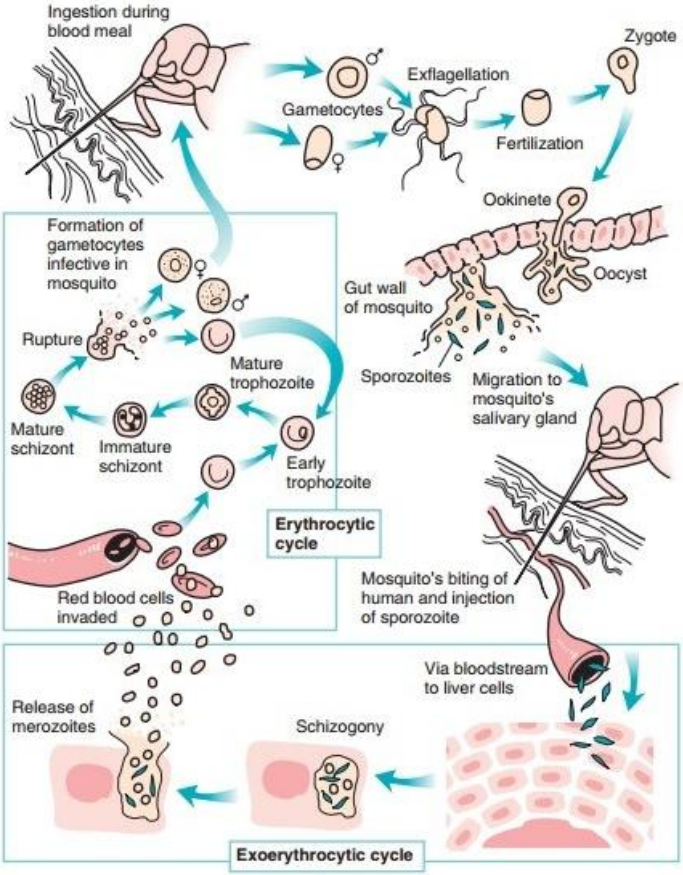

Figure 16. Life cycle of *Plasmodium spp.*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Mode of transmission. Infections are vector-borne, being transmitted by female mosquitos, mainly Anopheles spp. Although 390 mosquito species are found worldwide, only a few are considered to be important vectors. Only the female mosquitoes feed on blood as they require high protein diets in order to reproduce and lay rafts of eggs. The mosquito is not simply a vector; it acts as the definitive host in which sexual reproduction of the parasite occurs. Gametocytes ingested during feeding undergo fertilization forming an ookinete then an oocyst which produces numerous sporozoites eventually infecting the salivary glands. Sporozoites are injected into new hosts when the mosquito next feeds as saliva has anticoagulant properties and prevents blood from clotting in the mouthparts. Once a mosquito is infected, it is infected for life and continues to transmit infections (fig. 17).

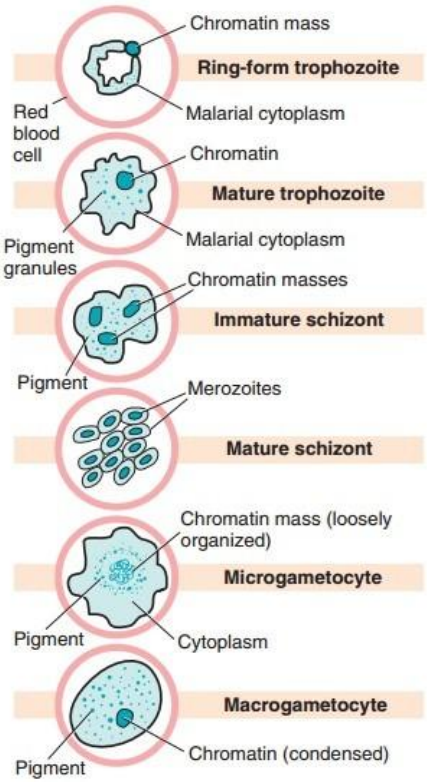

Figure 17. Life cycle stages of malaria
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Diagnosis is conventionally made by a combination of clinical symptomatology and the detection of parasites in thick or thin peripheral blood smears stained with one of the Romanowsky's stains, usually Giemsa's, Leishman's or Field's stains. Fluorochrome stains have also been used to detect parasites in blood samples, but the morphological features of the stages detected are often obscure. It is important that infections by individual parasite species be differentiated as it impacts on treatment and prognosis. All infections should be considered to be immediately life-threatening, and a complete clinical history should be taken (symptoms/signs), including history of travel, transfusions, recreational drug use, and previous medications (especially anti-malarials). Immunoserological tests have also been developed and several fluorescence, haemagglutination and enzyme immunoassays are being used, particularly for mass screening. Molecular biological techniques using polymerase chain reaction (PCR) amplification of gene fragments have also been developed and have shown great potential for the detection of drug resistance in Plasmodium.

Treatment and control. A variety of drugs have been developed for therapeutic (treatment) and prophylactic (preventive) use. While most enjoyed years of efficacy, there are now widespread problems with drug resistance amongst the parasites. Early explorers noticed that Peruvian Indians used brews from 'fever bark' (Cinchona) trees to stave off fevers. The active drug quinine was isolated from the bark around 1820 and this become the mainstay for malaria treatment throughout the world, essentially based on Cinchona tree plantations in tropical colonies. Supply shortages due to the World Wars prompted research on synthetic drugs. Pamaquine, mepacrine and chloroquine were developed in the 1930s, proguanil in the 1940s, and pyrimethamine in the 1950s. Chloroquine, in particular, was found to be highly effective, cheap to produce and had low toxicity. However, resistance to chloroquine emerged in the 1960s and soon spread around the world. Sulphonamides were developed in the 1960s, mefloquine and a series of related drugs in the 1970s, and artemisinin was discovered in a Chinese herbal remedy in the 1980s. A holistic and strategic approach to the treatment of infected individuals is required based on whether suppressive, radical or preventive treatment is required, and the level of drug resistance present. Anti-

malarial drugs of choice are primaquine, chloroquine (despite the emergence of chloroquine-resistant strains), sulfadoxine, pyrimethamine, mefloquine, quinine and tetracycline. Preventive measures based on vector control programmes had many early successes (including those using DDT), but the rapid emergence of insecticide resistance (and the recognition of the toxicity of DDT and its prohibition) have led to the resurgence of malaria in many countries. At present, the best protection is the avoidance of mosquito bites, using screens, bed nets, insect repellants, and residual insecticide sprays.

2.8. TOXOPLASMA GONDII

Classification:

- Protista (unicellular eukaryotes).
- Apicomplexa (cells with cluster of organelles known as apical complex).
- Coccidea (gamonts small and intracellular, form small resistant spores called oocysts).
- Eimeriida (gametes develop independently without syzygy; known as coccidian parasites).

Family Toxoplasmatidae:

This family belongs to the tissue cyst-forming coccidia: heteroxenous (two-host) parasites cycling between predator and prey hosts (transmission to predator via carnivorism of tissue cysts, and to prey via faecal-oral transmission of spores). Parasites undergo sexual reproduction termed gamogony (♂ microgametes fertilize ♀ macrogametes) in the gut of the predator (= definitive host) resulting in the formation of small spores (oocysts). The oocysts undergo endogenous sporogony (forming sporocysts and sporozoites) and are shed in host faeces. When ingested by prey (= intermediate hosts), the parasites multiply by asexual merogony (schizogony) and then form cysts within host tissues (especially striated muscles and brain). The cysts may remain dormant in the tissues for months or years until eaten by a predator.

TOXOPLASMA GONDII [this species causes toxoplasmosis in numerous vertebrate species]

Parasite morphology. Four developmental stages are formed; schizonts, tissue cysts, gamonts and oocysts. Schizonts appear as small basophilic intracellular bodies which divide rapidly to form

small collections of tachyzoites (measuring 4–5 × 1–2 μm). Tissue cysts (measuring 10–100 μm in diameter) are surrounded by a thin primary cyst wall (<0.5 μm thick) and contain hundreds of basophilic bradyzoites (measuring 3–4 by 1–2 μm). Gamonts exhibit sexual differentiation, with microgamonts (♂) apparent as multinucleate basophilic stages ultimately shedding small biflagellated microgametes; and macrogamonts (♀) evident as uninucleate eosinophilic cells with a single ovoid nucleus. Oocysts are small ovoid stages (10–13 × 9–11 μm) and contain two round sporocysts, each containing four elongate sporozoites (isosporid-like 1:2:4 configuration).

Host range. Infections have been detected worldwide in a diverse range of vertebrate hosts; carnivores, herbivores, insectivores, rodents, pigs, primates (including humans) and occasionally birds. Sexual development and oocyst formation only occurs, however, in feline hosts. Only one parasite species is considered valid due to the lack of intermediate host specificity. Various strains, however, are recognized on the basis of their variable infectivity, growth, virulence and gene expression. Recent genetic studies indicate that T. gondii propagates primarily by clonal, asexual or uniparental clonal reproduction, and various strains have been allocated to three clonal lineages (Types I, II and III) on the basis of analyses of multiple independent single-copy loci as well as microsatellite markers. Type I strains are most often associated with disease in immunocompetent adults and in congenital infections, type II strains with immunocompromised individuals, and type III strains with patients with ocular toxoplasmosis. The prevalence of infections varies according to host populations and geographic location but seroprevalence estimates range from 5–75% in many countries.

Site of infection. In cats, parasites undergo asexual and sexual multiplication in intestinal epithelial cells culminating in the formation of oocysts 3–5 days after infection. In all other vertebrate hosts, parasites undergo asexual multiplication in a wide range of extraintestinal locations (cells of the lymphatic and circulatory systems, nervous tissue, skeletal musculature, etc.). During the acute phase of infection, the parasites divide rapidly forming small groups of 8–32 tachyzoites which lyse the host cells. As infections become chronic, the parasites divide more slowly forming large accumulations of bradyzoites particularly within the brain, heart and skeletal

muscle (fig. 18). These tissue cysts are surrounded by a thin cyst wall and they persist for months or even years after infection. Cyst formation coincides with the development of host immunity (not sterile immunity but rather a state of premunition).

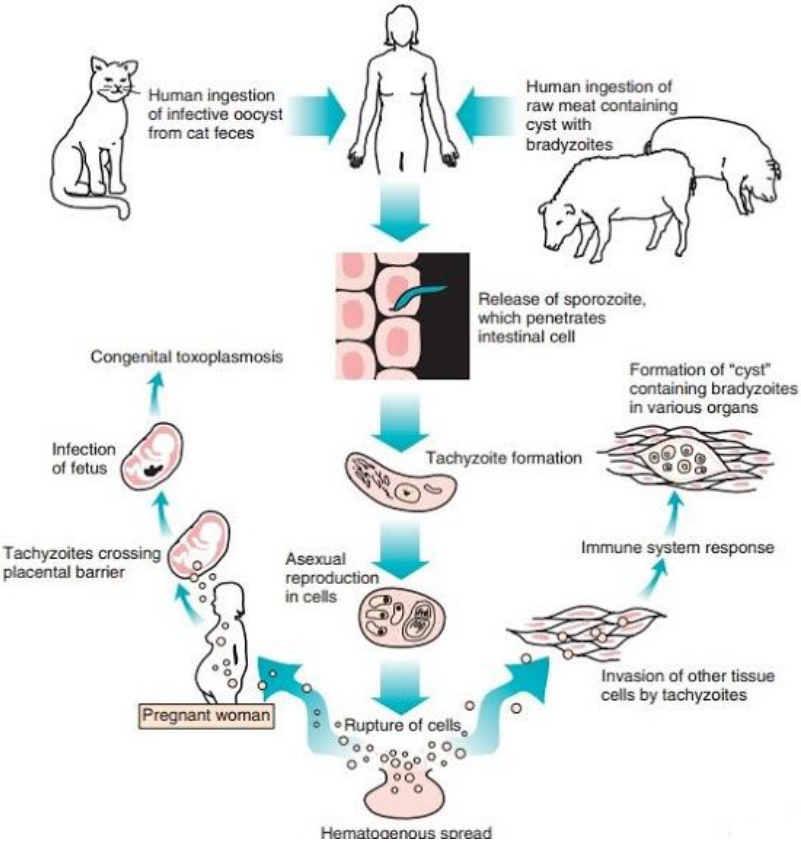

Figure 18. Life cycle of *Toxoplasma gondii*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Pathogenesis. Many host species exhibit an age-related resistance to disease therefore most infections in adults and weaned individuals are asymptomatic. In susceptible hosts, symptomatic infections may be acute, subacute or chronic. Acute infections by proliferating tachyzoites cause flu-like symptoms, including lymphadenitis,

fever, headache, muscle pain and anaemia. Symptoms generally subside with the development of immunity, but may sometimes persist producing subacute disease, characterized by extensive lesions in the lung, liver, heart, brain or eyes. Postnatal infections often involve lymphadenitis, myocarditis, central nervous system involvement and retinochoroiditis. Chronic infections by encysted bradyzoites usually cause few clinical signs, although degenerating cysts have been associated with hypersensitive inflammatory reactions, resulting in, for example, encephalitis, myocarditis and/or chorioretinitis. The tissue cysts lay quiescent (dormant) in the tissues for some time, occupying little space and apparently causing few functional deficits, although there is contradictory evidence that infections may be associated with some learning disabilities, slower reflexes and altered behaviour in intermediate hosts. Latent cyst infections may be reactivated in immunocompromised patients (i.e. those undergoing immunosuppressive therapy or with acquired immunodeficiencies) resulting in cell lysis, expanding focal lesions, rapid dissemination, encephalopathy and meningoencephalitis. Infections may also be transmitted transplacentally. If the mother/dam contracts infection during pregnancy, parasites may cross the placenta and infect the foetus causing spontaneous abortion, stillbirth or congenital abnormalities, such as hydrocephalus, brain calcification, chorioretinitis and mental retardation. Nonetheless, if the mother/dam is infected prior to pregnancy, her immunity is transferred to her foetus which is consequently protected. Infections in cats by enteric sexual developmental stages are generally subclinical, transient and leave the cat with a solid protective immunity against subsequent oocyst production.

Mode of transmission. Infections are transmitted horizontally between hosts by the ingestion of oocysts excreted by cats, and vertically between mother and offspring by transplacental or even transmammary transmission of proliferative tachyzoites. Infections may also be transferred between intermediate hosts through the food chain via carnivorism, the ingestion of fresh or undercooked meat containing viable cysts. Bradyzoites released during digestive processes are resistant to enzymatic digestion and revert back to tachyzoite stages which infect the host, multiply, spread and lead to new cyst formation. Infections are more prevalent in human populations which have traditional cultural practices involving the con-

sumption of raw or partially cooked meat (e.g. steak tartare, partly cured smallgoods). Oocysts excreted by cats take 1-5 days to sporulate before they become infective and they are resistant to external environmental conditions and may remain viable in contaminated soil and water for some time.

Differential diagnosis. Parasites may be detected in autopsy or biopsy material by histology, immunolabelling or in vivo culture following inoculation into laboratory rodents. Zoites in smears stain well with Giemsa and other Romanowsky stains while cysts in sections have silver-positive walls and the bradyzoites are strongly PAS (periodic acid-Schiff) positive. Monoclonal and polyclonal antibody labels have also been used to detect parasites in tissue sections, and molecular studies using polymerase chain reaction (PCR) amplification techniques have detected parasite DNA in host tissues. Most infections, however, are diagnosed serologically and a range of immunoassays (fluorescence, agglutination and enzyme-based) are commercially available. Recent/acute infection is indicated by a 4-16 fold increase in specific antibody titre over a two-week period, or by the detection of specific IgM antibody titres.

Treatment and control. Chemotherapy is successful when pyrimethamine and sulphonamides are given together as they act synergistically. The toxic side-effects of bone marrow depression can be relieved by the administration of folinic acid. Clindamycin and spiramycin have also been reported to be effective. The risk of transmission can be reduced by maintaining high standards of hygiene (particularly where cats are involved), by thoroughly cooking or deep-freezing meat prior to consumption and washing potentially contaminated foodstuffs. Molecular vaccines are currently being developed for high risk patient groups, and a live vaccine using a low-virulent non-persistent strain has been marketed to protect sheep against toxoplasmosis.

3. HELMINTH PARASITES

The word ‘helminth’ is a general term meaning ‘worm’, but there are many different types of worms. Prefixes are therefore used to designate types: platy-helminths for flat-worms and nemat-helminths for round-worms. All helminths are multicellular eukaryotic invertebrates with tube-like or flattened bodies exhibiting bilateral symmetry. They are triploblastic (with endo-, meso- and ecto-dermal tissues) but the flatworms are acoelomate (do not have body cavities) while the roundworms are pseudocoelomate (with body cavities not enclosed by mesoderm). In contrast, segmented annelids (such as earthworms) are coelomate (with body cavities enclosed by mesoderm).

Many helminths are free-living organisms in aquatic and terrestrial environments whereas others occur as parasites in most animals and some plants. Parasitic helminths are an almost universal feature of vertebrate animals; most species have worms in them somewhere.

Biodiversity

Three major assemblages of parasitic helminths are recognized: the Nemathelminthes (nematodes) and the Platyhelminthes (flatworms), the latter being subdivided into the Cestoda (tapeworms) and the Trematoda (flukes):

- Trematodes (flukes) have small flat leaf-like bodies with oral and ventral suckers and a blind sac-like gut. They do not have a body cavity (acoelomate) and are dorsoventrally flattened with bilateral symmetry. They exhibit elaborate gliding or creeping motion over substrates using compact 3-D arrays of muscles. Most species are hermaphroditic (individuals with male and female reproductive systems) although some blood flukes form separate male and female adults.
- Nematodes (roundworms) have long thin unsegmented tube-like bodies with anterior mouths and longitudinal digestive tracts. They have a fluid-filled internal body cavity (pseudocoelum) which acts as a hydrostatic skeleton providing rigidity (so-called ‘tubes under pressure’). Worms use longitudinal muscles to produce a sideways thrashing motion. Adult worms form separate sexes with well-developed reproductive systems.

- Cestodes (tapeworms) have long flat ribbon-like bodies with a single anterior holdfast organ (scolex) and numerous segments. They do not have a gut and all nutrients are taken up through the tegument. They do not have a body cavity (acoelomate) and are flattened to facilitate perfusion to all tissues. Segments exhibit slow body flexion produced by longitudinal and transverse muscles. All tapeworms are hermaphroditic and each segment contains both male and female organs.

Unlike other pathogens (viruses, bacteria, protozoa and fungi), helminths do not proliferate within their hosts. Worms grow, moult, mature and then produce offspring which are voided from the host to infect new hosts. Worm burdens in individual hosts (and often the severity of infection) are therefore dependent on intake (number of infective stages taken up). Worms develop slowly compared to other infectious pathogens so any resultant diseases are slow in onset and chronic in nature. Although most helminth infections are well tolerated by their hosts and are often asymptomatic, subclinical infections have been associated with significant loss of condition in infected hosts. Other helminths cause serious clinical diseases characterized by high morbidity and mortality. Clinical signs of infection vary considerably depending on the site and duration of infection. Larval and adult nematodes lodge, migrate or encyst within tissues resulting in obstruction, inflammation, oedema, anaemia, lesions and granuloma formation. Infections by adult cestodes are generally benign as they are not invasive, but the larval stages penetrate and encyst within tissues leading to inflammation, space-occupying lesions and organ malfunction. Adult flukes usually cause obstruction, inflammation and fibrosis in tubular organs, but the eggs of blood flukes can lodge in tissues causing extensive granulomatous reactions and hypertension.

Life cycles. Helminths form three main life cycle stages: eggs, larvae and adults. Adult worms infect definitive hosts (those in which sexual development occurs) whereas larval stages may be free-living or parasitize invertebrate vectors, intermediate or paratenic hosts. Nematodes produce eggs that embryonate in utero or outside the host. The emergent larvae undergo 4 metamorphoses (moults) before they mature as adult male or female worms. Cestode eggs released from gravid segments embryonate to produce 6-hooked embryos (hexacanth oncospheres) which are ingested by intermediate hosts. The oncos-

pheres penetrate host tissues and become metacestodes (encysted larvae). When eaten by definitive hosts, they excyst and form adult tapeworms. Trematodes have more complex life-cycles where 'larval' stages undergo asexual amplification in snail intermediate hosts. Eggs hatch to release free-swimming miracidia which actively infect snails and multiply in sac-like sporocysts to produce numerous rediae. These stages mature to cercariae which are released from the snails and either actively infect new definitive hosts or form encysted metacercariae on aquatic vegetation which is eaten by definitive hosts.

Helminth eggs have tough resistant walls to protect the embryo while it develops. Mature eggs hatch to release larvae either within a host or into the external environment. The four main modes of transmission by which the larvae infect new hosts are faecal-oral, transdermal, vector-borne and predator-prey transmission (fig. 19):

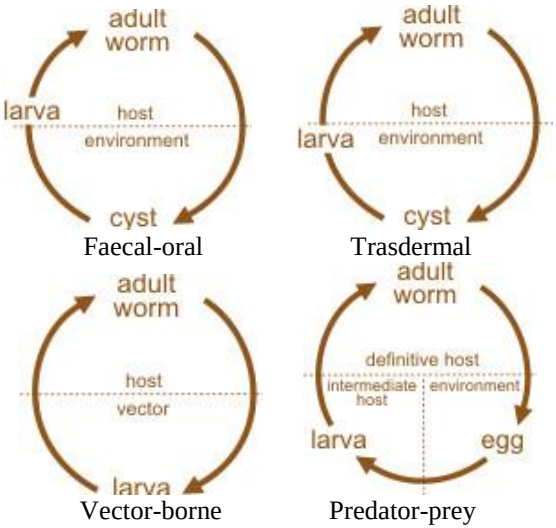

Figure 19. Modes of Helminths transmission
[http://www.onlinebiologynotes.com/category/parasitology]

Faecal-oral transmission of eggs or larvae passed in the faeces of one host and ingested with food/water by another (e.g. ingestion of Trichuris eggs leads directly to gut infections in humans, while the ingestion of Ascaris eggs and Strongyloides larvae leads to a pulmonary migration phase before gut infection in humans).

Transdermal transmission of infective larvae in the soil (geohelminths) actively penetrating the skin and migrating through the tissues to the gut where adults develop and produce eggs that are voided in host faeces (e.g. larval hookworms penetrating the skin, undergoing pulmonary migration and infecting the gut where they feed on blood causing iron-deficient anaemia in humans).

Vector-borne transmission of larval stages taken up by blood-sucking arthropods or undergoing amplification in aquatic molluscs (e.g. Onchocerca microfilariae ingested by blackflies and injected into new human hosts, Schistosoma eggs release miracidia to infect snails where they multiply and form cercariae which are released to infect new hosts).

Predator-prey transmission of encysted larvae within prey animals (vertebrate or invertebrate) being eaten by predators where adult worms develop and produce eggs (e.g. Dracunculus larvae in copepods ingested by humans leading to guinea worm infection, Taenia cysticerci in beef and pork being eaten by humans, Echinococcus hydatid cysts in offal being eaten by dogs).

3.1. *FASCIOLA HEPATICA*

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Platythelminthes (flatworms).
- Cercomeridea (with oral sucker and bifurcate intestine).
- Trematoda (trematodes, with posterior sucker).
- Digenea (digenetic life-cycle, larval miracidia, snail vectors).
- Echinostomatida (miracidia with one pair protonephridia, simple-tailed cercariae).

Family Fasciolida

These worms (known as liver flukes) have soft flat leaf-like bodies with two ventral suckers and a blind gut (mouth but no anus). Adults possess both male and female reproductive organs (hermaphroditic) and they have digenetic life-cycles involving at least two hosts and several developmental stages. Miracidia are released from eggs into water where they infect snails (obligate intermediate hosts) and undergo massive asexual proliferation through sporocyst and redia stages eventually releasing cercariae into the water. Vertebrate

(definitive) hosts become infected by the ingestion of encysted stages (metacercariae) on aquatic vegetation. Infections may cause chronic debilitating diseases in domestic animals and humans.

FASCIOLA HEPATICA [this species causes hepatic fibrosis in ruminants and humans]

Parasite morphology. These flatworms form seven different developmental stages: eggs, miracidia, sporocysts, rediae, cercariae, metacercariae, and adult flukes. The eggs are operculate ('hatch' at one end), brown and ovoid (130–150 μm in length by 65–90 μm in width). Miracidia are pyriform motile larval stages (150–200 μm long) covered with cilia. Sporocysts are pleomorphic sac-like bodies (0.3–1.5 mm in diameter) containing germinal cells which give rise to small rediae (embryos). Mature cercariae (~0.5 mm long) are free-swimming gymnocephalous stages with simple elongate club-shaped tails, which are subsequently shed when they encyst on vegetation to form membrane-bound metacercariae (~0.2 mm in diameter). Mature flukes are leaf-shaped (2.0–3.5 cm long by 1.0–1.5 cm wide) with a conical apex demarcated by wider 'shoulders'. They are dorsoventrally flattened, the tegument is covered with scaly spines, and they have two suckers (distome arrangement with the oral sucker and acetabulum close together). They have a bifurcate blind gut and each worm is hermaphroditic, possessing both male and female reproductive organs (fig. 20).

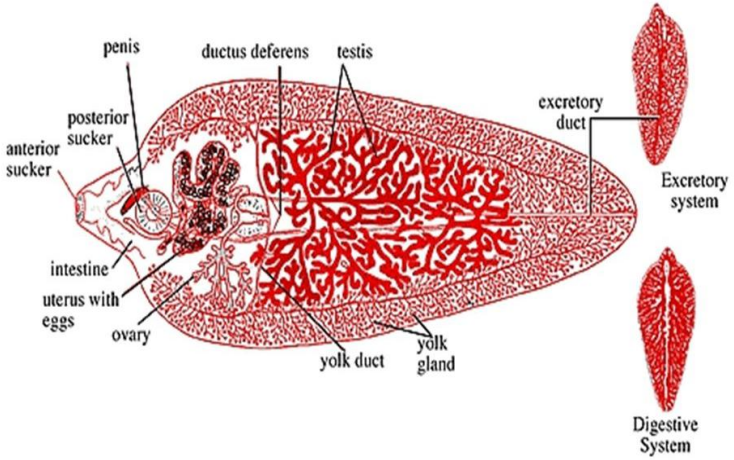

Figure 20. Morphology *of Fasciola hepatica* (liver fluke) [https://smart.servier.com/category/medical-specialties/infectiology/]

Host range. Liver fluke infections are distributed throughout many sheep and cattle producing areas around the world, particularly temperate regions with high rainfall or irrigated pastures where snail vectors are abundant. F. hepatica has been reported in sheep, cattle, goats, pigs, macropods, rats, rabbits and many other animals, and occasionally in humans (mainly from western Europe, northern Africa and South America). It has been estimated that some 250 million sheep and 350 million cattle are at risk of fascioliasis.

Site of infection. Immature flukes undergo transient migration through the liver parenchyma and then settle as mature flukes in the bile ducts of their definitive hosts. In some (uncommon) hosts, aberrant flukes may be found encapsulated in lungs, skin or other organs. In snail intermediate hosts, several asexual multiplicative stages are formed; sporocysts first developing in tissues near the site of penetration (foot, antenna, gill), rediae then migrating to glandular tissue (hepatopancreas and gonads) and culminating in the release of tailed cercariae.

Pathogenesis. Infections have been associated with two types of liver disease in domestic animals: acute or subacute necrotic disease due to juvenile flukes; and chronic fibrotic disease due to adult flukes. Penetration of the liver capsule by immature flukes generally does not cause much damage, but their subsequent migration through the liver parenchyma may cause significant necrosis (liver rot). Mass migration of juveniles may produce extensive traumatic tissue damage, coagulative necrosis, haemorrhage, urticaria, eosinophilia, leukocytosis, pallor, anaemia, and can be fatal. Acute infections in sheep can also be complicated by secondary bacterial infection causing clostridial necrotic hepatitis (‘black disease’). Chronic infections by the long-lived adults feeding on the lining of the bile ducts may result in progressive loss of condition, biliary epithelial hyperplasia, duct fibrosis, biliary obstruction and cholangitis, jaundice, and eventually a fibrotic hardened liver. Sheep may become anaemic and emaciated, developing submandibular oedema (bottle-jaw) and ascites. In cattle, the bile ducts often become calcified producing a ‘clay-pipe’ or ‘pipe-stem’ liver. Chronic fascioliasis causes significant economic losses to many animal industries through mortality, reduced meat, milk and fibre production, condemned livers, secondary infections and expensive treatments (fig. 21).

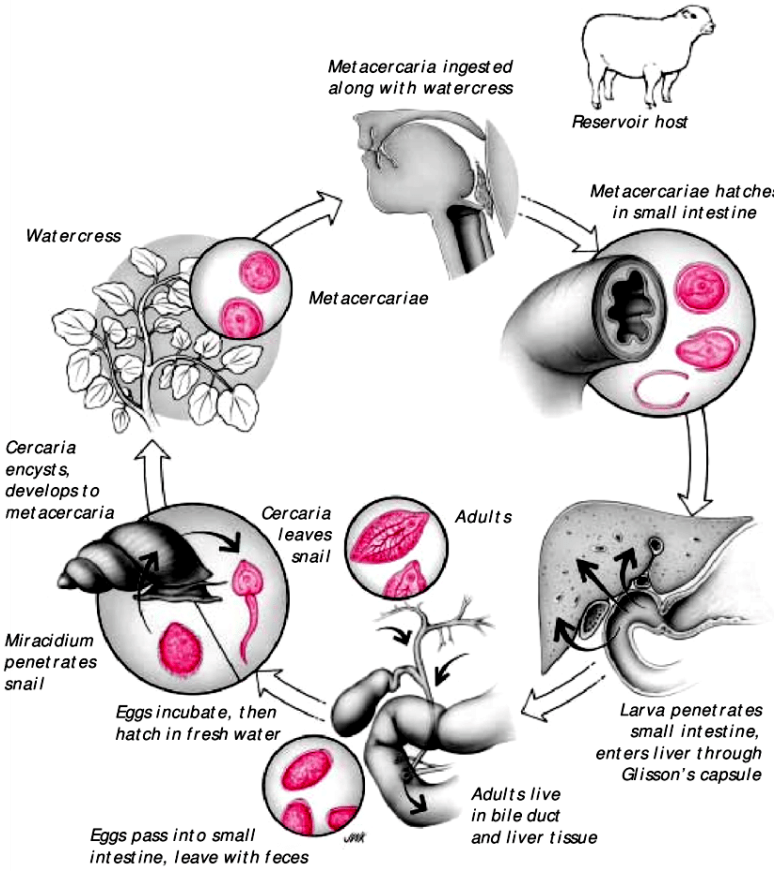

Figure 21. Life cycle of *Fasciola hepatica*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Mode of transmission. Digenean trematodes have indirect life-cycles, involving mammalian definitive hosts and molluscan intermediate hosts. Transmission between the two hosts occurs within water, via the formation of motile and encysted larval stages. Adult flukes produce numerous eggs (up to 300 per day) which are shed in host faeces. The eggs embryonate in water in a few days to form miracidia, which hatch out in 9–10 days in warm weather (longer when colder). Miracidia actively seek snail hosts by chemotaxis, and must penetrate snail tissues within a few hours or die after 24 hours. F. hepatica exhi-

bits high intermediate host-specificity and will only develop in freshwater amphibious lymnaeid snails. These snails are pulmonate (with lungs), small (0.5–2.5 cm long) and delicate; their shells being thin, fragile, lacking an operculum and the apertures located on the right-hand side (dextral). They live in freshwater and/or wet soils and survive dry periods by burrowing and aestivating. Various *Lymnaea spp*. are suitable intermediate hosts; the most common being L. (Galba) *truncatula* in most continents, Once the miracidia penetrate a snail, they form mother sporocysts that lack digestive organs but feed by absorption. Sporocysts produce multiple daughter rediae by asexual reproduction (an important amplification mechanism for all trematodes). Rediae have mouths and guts and feed on snail tissues, eventually maturing to single-tailed cercariae which bore their way out of the snail. Cercariae begin emerging 5–7 weeks after infection and several hundred (sometimes thousands) of cercariae may be produced. Parasites can also survive for months in aestivating snails buried in the soil during dry periods. Emergent cercariae swim to suitable substrates and form encysted metacercariae by shedding their tails and producing thick cyst walls. Metacercariae are quiescent infective stages which can survive on aquatic vegetation or in water for several weeks. Mammals become infected when they ingest metacercariae with food or water (many human infections have been linked to the consumption of watercress). Metacercariae excyst in the small intestines releasing juvenile worms which penetrate the gut wall and migrate around the body cavity for several days. They move to the liver and burrow through the capsule into the parenchyma where they wander for 5–6 weeks before settling in the bile ducts. Worms become sexually mature and begin producing eggs 8–13 weeks after infection. Adult flukes can live for up to 10 years but most infections in domestic animals exhibit marked seasonal variation.

Differential diagnosis. Infections are conventionally diagnosed by coprological examination for fluke eggs in faecal samples, usually following their concentration by sedimentation/flotation techniques. Blood biochemical tests can also be used to show elevated plasma levels of hepatic enzymes, notably glutamate dehydrogenase (GLDH) during acute stages and gamma glutamyl transpeptidase (GGT) during chronic stages. Immunoserological tests

have also been developed to detect host antibodies against parasite excretory/secretory antigens in attempts to facilitate early diagnosis. Molecular studies are currently being used to examine parasite strain variation and host reactions to identify virulence factors and protective responses.

Treatment and control. Subacute and chronic infections may be treated with triclabendazole or bithionol, which show excellent trematocidal activity with few side-effects. Preventive measures are based on breaking the cycle of transmission by reducing faecal contamination of water bodies, reducing snail populations using molluscicides (usually copper sulphate) or draining swampy fields, restricting access of livestock to aquatic vegetation, and avoiding watercress. Snail control is often difficult, particularly in high rainfall areas where even temporary pools may harbour large snail populations (they aestivate in the ground during dry conditions). Feral or wild animals (such as rabbits) may also continue to act as reservoirs of infection for domestic livestock.

3.2. PARAGONIMUS WESTERMANI

[this species causes hepatic paragonimiasis in humans]

Paragonimus Westermani – Lung Fluke. Human lung fluke, Paragonimus westermani, infects 22 million people in Africa, Asia and South and Central America. Southeast Asia in particular is affected because raw seafood is very popular there. Humans get infected with the disease, paragonimiasis, by eating raw crabs or fish that are carrying the parasite. Even properly cooked sushi can cause infection, if the cook or waiter is careless when preparing the food. In Asia about 80% of freshwater crabs are infected with the lung fluke.

Parasite morphology. Adult lung flukes are 4–6 mm wide, 3–5 mm thick and 7–12 mm long. They are red-brown looking almost like a coffee bean. They hold on to tissue with two suckers. The oral sucker is in the front and just before the center of its lower body is the ventral sucker (fig. 22).

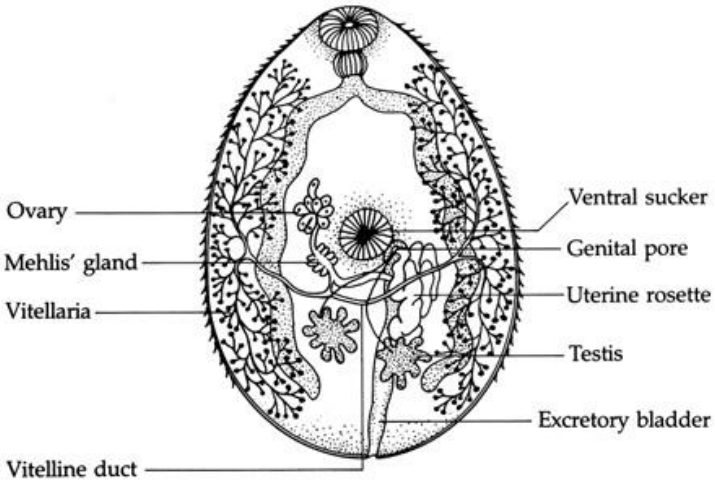

Figure 22. Morphology of *Paragonimus Westermani* (lung fluke) [https://smart.servier.com/category/medical-specialties/infectiology/]

Life cycle of a lung fluke begins, when the female lays eggs that are carried out from the human lungs in the sputum by the motion of microvilli. Then the eggs are taken through the gastrointestinal tract and out of the body. If the feces get in contact with water, then after two weeks larvae called miracidia hatch and start to grow. A miracidium finds a snail and penetrates its skin. In 3–5 months miracidium develops further and produces another larval form called cercaria. The cercaria crawls out of the snail to find fresh water crayfish (a lobster-like creature) or crabs. It finds its way to the muscles of the crab and starts forming a cyst. Within two months it transforms into metacercaria which is the resting form of cercaria. If a human eats this infected crab raw, the metacercaria cyst gets into the stomach. Once inside the beginning of the small intestine, duodenum, the metacercaria excysts and penetrates the intestinal wall. It continues through abdominal wall and diaphragm into the lungs where it forms a capsule and develops into an adult. Male and female lung worms reproduce and the cycle starts again. Sometimes lung fluke larvae accidentally travel to the brain or other organs and reproduce there. But because the secretion of the eggs from the brain is blocked the life cycle will

not happen. If the worm goes to the spinal cord instead of the lungs, the host might become paralyzed. If it infects the heart, the host could die.

Symptoms. The fluke provokes the development of a fibrous tissue capsule with bloody purulent material containing eggs. There is inflammatory infiltrate around the capsule. The symptoms include a dry cough, followed by production of blood stained rusty brown sputum. Pulmonary pain and pleurisy may develop. Worms may migrate to the brain where they lay eggs and cause a granulomatous abscess resulting in symptoms similar to epilepsy.

Differential diagnosis. Diagnosis is based on history and symptoms. Eggs are found in rust colored sputum, often being examined for tuberculosis.

Treatment and control. Praziquantel taken orally is quite effective. Adequate cooking of crustaceans is a preventive measure. Improved sanitary conditions have lowered the infection rate in endemic areas. To interruption of the life cycle of the parasite can eliminate its spread, which measures include chemotherapy, use of molluscacides etc. Specific measure to change the eating habits of the people by health ed-ucation is considered to be the most important measure to control the dis-ease.

3.3. CLONORCHIS SINENSIS

[this species causes clonorchiasis in humans]

The Chinese liver fluke, the trematode *Clonorchis sinensis* was found from the biliary passage of a Chinese in Calcutta, India in 1874 firstly. The worm is the causal agent of clonorchiasis. “Chinese liver fluke” is widely distributed in China (mainland, Hong Kong and Taiwan), Japan, Korea, and Vietnam.

Parasite morphology. Adult worm. It is flat with pointed anterior and rounded posterior end, measuring about long 10~25 mm, wide 3~5 mm. It is relatively a small fluke. The tegument lacks spines. Oral sucker is larger than ventral sucker. Ventral sucker is located one-fifth of the way from the anterior end. The presence of two large, deeply lobulated and branched testes with 7 branches situated in the posterior third of the body, one behind the other, and

anterior uterus. Mature egg The eggs are flask-shaped, operculated and relatively smaller in size, and measure 29 × 17 mkm. They are yellow-brown, containing a well-developed miracidium, and possessing a small knob at the posterior end giving an appearance of aelectric bulb (fig. 23).

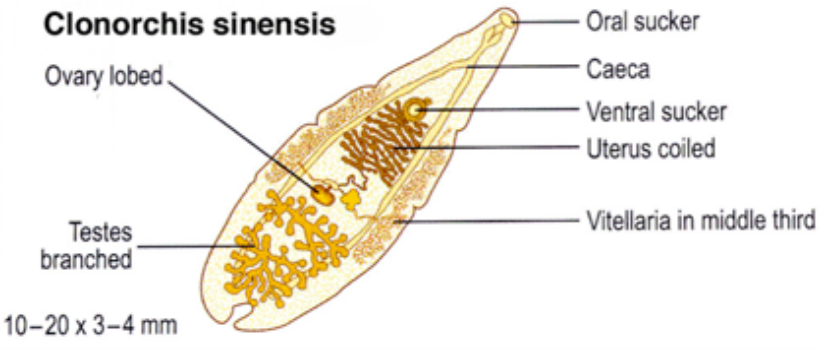

Figure 23. Morphology of *Clonorchis sinensis*
[https://smart.servier.com/category/medical-specialties/infectiology/]

Life cycle. *C. sinensis* requires one definitive host and two different intermediate host for completion of its life cycle. In definitive host: adult worm matures in the bile ducts of definitive host, which include human or mammalian animals. After eating raw or under-cooked fish or crustaceans with metacercaria, definitive host will be infected. The young flukes excystin the duodenum. The route of migration to the liver is not clear; but it seems probable that juveniles migrate up the common bile duct to the liver. After about one month of infection, adult worms are developing. Mammalian, i.e. cats, dogs and rates etc. are important reservoir hosts. In the first intermediate host: Eggs are hatched into miracidia after being eaten by a suitable snail, then develop into a sporocyst; sporocyst trans-forms into redia; redia produce cercariae with long tail. In the second intermediate host: When contacting fish or crustaceans in freshwater, the cercaria will bores through the skin, coming to muscle and encysting (fig. 24).

First Intermediate host: fresh-water snails eg. *Parafossarulus striatulus, Alocinma longicornis, Bithynia fuchsian*us. Second intermediate host: fresh-water fish i.e. Ctenopharyngodon iddellus.

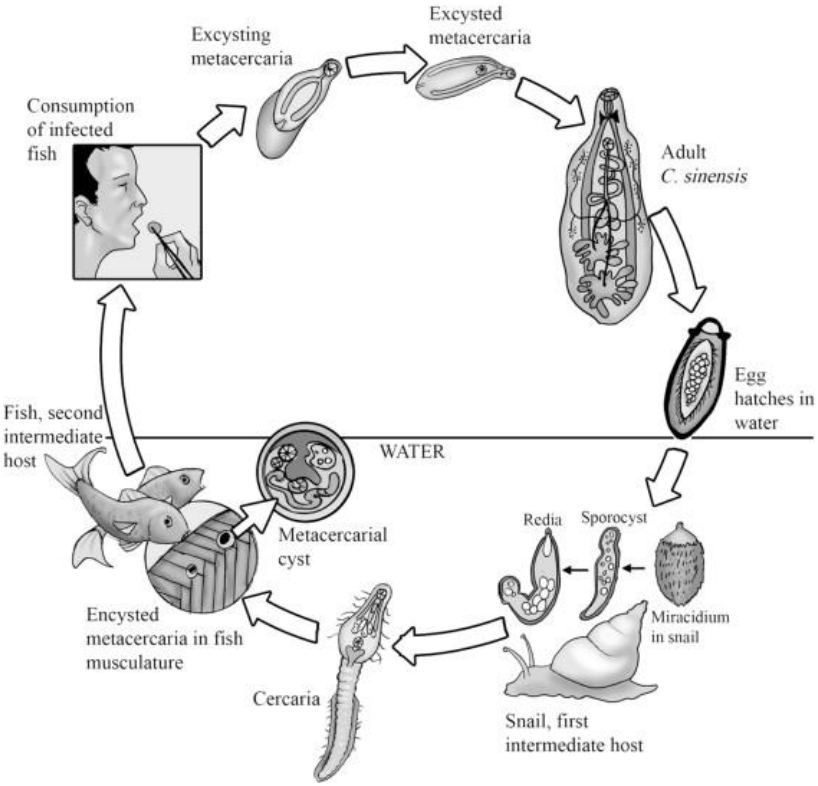

Figure 24. Life cycle of *Clonorchis sinensis*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Symptoms. The worm causes irritation of the bile ducts that become dilated and deviated. The liver may become enlarged (hepatomegaly), necrotic and tender and liver function may be impaired. Modest infections result in indigestion, epigastric discomfort, weakness and loss of weight. Heavier infections produce anemia, hepatomegaly, slight jaundice, edema, ascites and diarrhea.

Differential diagnosis. Diagnosis is based on symptoms and presence of endemic infection in the area. Definitive diagnosis is dependent on finding the characteristic eggs in the feces or biliary drainage.

Treatment and control. Praziquantel has proven to be of value. Fish should be cooked well before consumption. Sewage must be treated before disposal.

3.4. SCHISTOSOMA SPP.

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Platythelminthes (flatworms).
- Cercomeridea (with oral sucker and bifurcate intestine).
- Trematoda (trematodes, with posterior sucker).
- Digenea (digenetic life-cycle, larval miracidia, snail vectors).
- Strigeatida (miracidia with 2 pairs protonephridia, fork-tailed cercariae).

Family Schistosomatidae

Unlike all other trematodes, schistosomes are not hermaphroditic but dioecious, forming separate sexes. Adult worms have elongate tubular bodies, each male having a unique gynecophoral canal (schisto-soma = split body) in which a female worm resides. They live inside visceral blood vessels and are commonly known as blood flukes. They have digenetic life-cycles involving aquatic snails as obligate intermediate hosts. Eggs deposited in the circulation penetrate the gut or bladder to be excreted with faeces or urine. In water, the eggs release miracidia which infect snails and undergo asexual proliferation through sporocyst stages eventually releasing cercariae back into the water. Vertebrate hosts become infected by direct penetration of the skin. Infections may cause chronic debilitating diseases in humans and some domestic animals.

***SCHISTOSOMA* SPP**. [these species cause schistosomiasis/bilharzia in humans and ruminants]

Parasite morphology. Blood flukes form five different developmental stages: eggs, miracidia, sporocysts, cercariae and adult

worms. Eggs are round to oval in shape, operculate (hinged at one end) and contain a developing embryonic larva (miracidium). Differences in egg morphology can be used to distinguish between Schistosoma species: S. mansoni producing oval eggs (115–175 × × 45–7 μm) with a sharp lateral spine, *S. japonicum* forming round eggs (70–100 × 50–70 μm) with a rudimentary lateral spine; and S. haematobium producing oval eggs (110–170 × 40–70 μm) with a sharp terminal spine. Miracidia are elliptical free-swimming larval stages (~200 μm long) covered with cilia. Sporocysts appear as pleomorphic sac-like bodies which contain developing cercariae. Mature cercariae are elongate free-swimming larval stages (400–600 μm long) consisting of a tapering head (with prominent penetration glands) and a forked tail (furcocercous). Adult flukes are elongate tubular worms (10–20 mm long), with rudimentary oral and ventral suckers. Males are shorter and stouter than females, and they have a longitudinal cleft (gynecophoral canal or schist) in which the longer slender female lies folded (fig. 25).

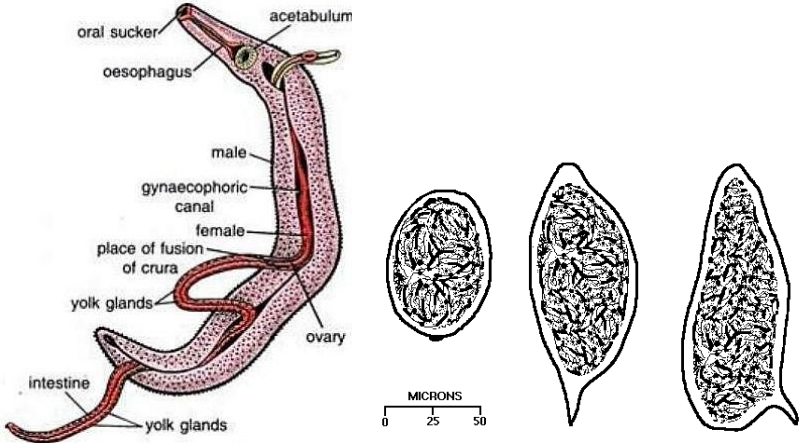

Figure 25. Adult worms (male and female) and eggs of *Schistosoma spp.* [https://smart.servier.com/category/medical-specialties/infectiology/]

Host range. Schistosomes are important human and animal parasites throughout Africa, Asia and South America, predominantly in rural areas supporting agriculture and inland fisheries. Parasite

distribution is linked to that of their snail intermediate hosts, which differ in their habitat preferences for slow-flowing or still waters. Many human activities also influence parasite distribution, especially the construction of irrigation channels and dams, and flood irrigation of crops. It has been estimated that over 200 million people may be infected worldwide. Infections have been recorded throughout human history, first being mentioned in ancient Egyptian papyri dated from 2000-1000 BC. Haematuria (bloody urine) became the scourge of Napoleon's army in northern Africa at the turn of the 18th century, and the disease later became known as bilharzia in honour of the discoverer of the causative agent. Schistosoma spp. vary in their specificity for intermediate hosts, some only developing in humans (and possibly primates) while others may infect domestic and wild animals, acting as reservoirs for human infection (table 5).

Table 5

Characteristics of *Schistosoma spp.*

Parasite species	Definitive host	Site of infection	Egg excretion	Snail vector	Geographic location
S. haematobium	humans, primates	veins of urogenital system	urine	*Bulinus*	Africa
S. mansoni	humans, rodents	intestinal mesenteric veins	faeces	*Biomphalaria*	Africa, America
S. japonicum	humans, carnivores	intestinal mesenteric veins	faeces	*Oncomelania*	SE Asia

Site of infection. Paired adult worms live inside blood vessels in specific sites within the human body. S. mansoni lives principally in the portal veins draining the large intestine, *S. japonicum* in the mesenteric veins of the small intestines, and *S. haematobium* infects veins of the urinary bladder plexus. Fluke eggs penetrate into the lumen of the intestines or bladder to be voided with host faeces or urine. Many eggs, however, may be swept away in the

host circulation and become trapped in various host tissues and organs.

Pathogenesis. Schistosomiasis (or bilharziasis) is unusual amongst helminth diseases for two reasons: much of the pathogenesis is due to the eggs (rather than larvae or adults); and most of the pathology is caused by host immune responses (delayed-type hypersensitivity and granulomatous reactions). The course of infection is often divided into three phases: migratory, acute and chronic. The migratory phase occurs when cercariae penetrate and migrate through the skin. This is often asymptomatic, but in sensitized patients, it may cause transient dermatitis (‘swimmers itch’), and occasionally pulmonary lesions and pneumonitis. The acute phase (sometimes called Katayama fever) is coincident with first egg release and is characterized by allergic responses (serum sickness due to overwhelming immune complex formation), resulting in pyrexia, fatigue, aches, lymphadenopathy, gastrointestinal discomfort and eosinophilia. The chronic phase occurs in response to the cumulative deposition of fluke eggs in tissues and the host reactions that develop against them. Not all the eggs laid by female worms successfully penetrate the gut or bladder walls, many are swept away in the circulation and become trapped in organs where they elicit strong granulomatous responses. Eggs become surrounded by inflammatory cells forming characteristic pseudotubercles, which may coalesce to form larger granulomatous reactions (polyps). The encapsulated eggs die and eventually calcify. The resultant effects on host organs and tissues are manifold, and include intestinal polyposis, abdominal pain, diarrhoea, glumerulonephritis, pulmonary arteritis, cardiovascular problems including heart failure, and periportal (Symmer’s clay pipe-stem) fibrosis. Portal hypertension often leads to hepatomegaly, splenomegaly, ascites, and sometimes gross enlargement of oesophageal and gastric veins (varices) which may burst. Cerebral granulomas have been associated with focal epileptic convulsions, while spinal cord granulomas may cause transverse myelitis. Infections by S. haematobium often cause haematuria (blood in urine) and progressive disruption of the bladder wall may lead to carcinoma.

Mode of transmission. Schistosomes have indirect digenetic life-cycles, involving sexual reproduction in vertebrate definitive hosts and asexual reproduction in snail intermediate hosts. Parasites are transmitted between hosts by motile aquatic stages which actively seek hosts. Female worms produce numerous eggs (200–3,000 per day) which seek to exit the host by penetrating the gut or bladder wall and being passed with host faeces or urine. When deposited in water, the embryonated eggs hatch releasing free-swimming miracidia which only live for several hours. In that time, they actively seek suitable intermediate hosts (amphibious snails) using chemotaxis and phototaxis (despite absence of eyespots). All Schistosoma spp. demonstrate quite narrow host specificity for particular snails: S. mansoni infects Biomphalaria spp. (large flat spiral snails ~14 mm in diameter with ~3 whorls and apical aperture), S. japonicum infects Oncomelania spp. (small elongate snails ~8 mm long with 4–5 whorls and dextral (right-sided) aperture), and S. haematobium infects Bulinus spp. (medium ovoid snails ~12 mm long with 2–3 whorls and sinistral (left-sided) aperture). The miracidia invade the soft tissues of the snail and form a mother sporocyst near the site of penetration. Daughter sporocysts are produced 2–6 weeks after infection and they migrate to other organs in the snail. Schistosomes do not produce redia stages; instead the sporocysts produce cercariae which are released into the water in their thousands beginning 4 weeks after infection. The fork-tailed cercariae are rapid swimmers and they periodically swim to surface of the water and then sink to bottom for up to three days. They are attracted to skin secretions and when they come into contact with a prospective definitive host, they attach and actively penetrate the skin within minutes, losing their tails in the process. Inside the host, the schistosomula (little schistosomes) are carried in blood and/or lymph to the portal vessels in liver, where they develop for 3 weeks. Young worms then pair and migrate to their predilection sites in the veins of the gut or bladder. Egg production begins from 4–8 weeks after infection, and adult worms normally live for 2–5 years, although some may survive much longer (fig. 26).

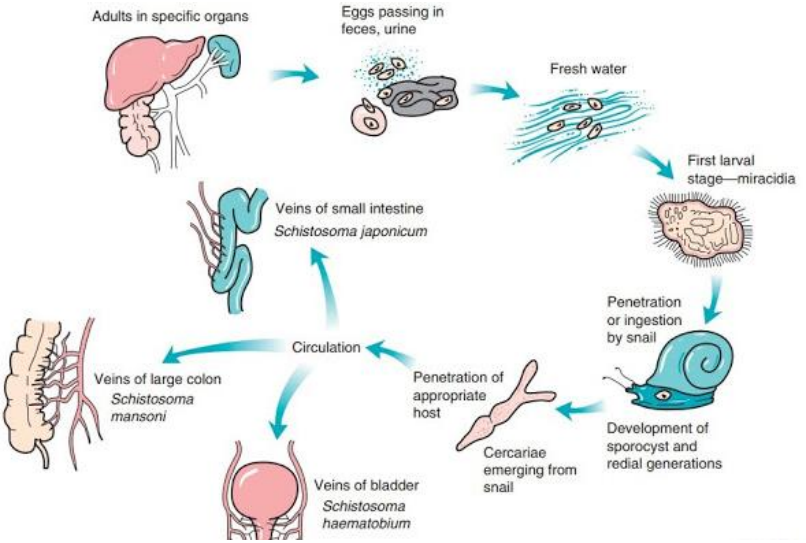

Figure 26. Life cycle of *Schistosoma spp.*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Infections are conventionally diagnosed by the detection of fluke eggs in faecal or urine samples, often after concentration by sedimentation/flotation or filtration techniques. The eggs are sufficiently characteristic to facilitate specific diagnosis. On occasion, microscopy of rectal biopsies has been used to diagnose S. haematobium infections. Immunoserological tests have been developed to detect host antibodies against infection but they have experienced cross-reactivity problems and cannot discriminate between previous and active infection. More recently, molecular techniques have been used to detect parasite antigens or DNA in host samples; some tests showing good correlations with parasite burdens.

Treatment and control. The drug of choice for the treatment of all Schistosoma spp. is praziquantel, a single oral dose being very effective, with low toxicity and good tolerance, even in severe clinical cases. Nitridazole and metrifonate are effective against S. haematobium, and oxamniquine against S. mansoni, but they have mild side-effects. While timely treatment is effective, cured individuals rapidly become re-infected in endemic areas. Various

control programmes have therefore been developed based on mass chemotherapy in conjunction with preventive measures, including improved sanitation, snail vector control, modifying habitats and farming practices, and public education campaigns. Water contamination can be reduced by preventing the ingress of parasite eggs as well as curtailing the asexual amplification cycle in snail hosts. The provision and use of latrines contains sources of infection, and modern biocomposting toilets appear to be effective in killing parasite eggs when used properly. Snail populations may be reduced by the strategic use of molluscicides (niclosamide or copper sulphate), draining marshes and swamps, and clearing channels of vegetation. Irrigation practices can be modified to avoid long-standing still waters, and different or improved crops can be used which are less dependent on lengthy immersion in water. In endemic areas, farmers (and visitors) need to be aware of the dangers of immersion in potentially contaminated waters.

3.5. TAENIA SAGINATA. TAENIA SOLIUM

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Platythelminthes (flatworms).
- Cestoda (tapeworms).
- Eucestoda (segmented, hermaphroditic).
- Cyclophyllidea (terrestrial cycles, scolex with suckers).

Family Taeniidae

Tape-worms have flat ribbon-like bodies, with an anterior scolex (hold-fast organ with suckers and sometimes hooks) and a posterior tape (strobila) made up of segments (proglottids). Adult worms lack a gut (they absorb nutrients) and they are hermaphroditic (segments containing both male and female reproductive organs). They have indirect life-cycles involving encystment of larvae (metacestodes) in the tissues of intermediate hosts and their transmission to definitive hosts by carnivorism. Various species are parasitic in mammals, birds, reptiles and amphibians. Adult stages are rarely pathogenic, but the encysted larval stages may cause space-occupying lesions (cysticerci) in domestic animals and humans.

TAENIA SAGINATA [beef tape worm, species causes taeniasis in humans]

TAENIA SOLIUM [pork tape worm, species causes taeniasis and cysticercosis in humans]

Parasite morphology. These tape-worms form three developmental stages: eggs, larvae and adults (fig. 27). The morphological characteristics of the adults are distinctive; all adults having an anterior scolex (holdfast organ), with four muscular suckers, surmounting a long (up to 10 m) strobila (tape) made up of numerous (as many as 2,000) proglottids (segments). The scolex of T. solium is spheroidal, around 1 mm in diameter and is armed with two circles of 22–32 hooks, while that of T. saginata is cuboidal, around 2 mm in section and un-armed. Adult worms are hermaphroditic with segments containing both male and female reproductive organs. Anterior segments are usually immature and broader than long, middle segments with fully developed genitalia are square, and posterior segments are gravid (filled with eggs) and longer than broad. The eggs of both species are similar in morphology; being spherical, 40–48 μm in diameter, surrounded by a thick striated wall, and containing a hexacanth (six-hooked) embryo (oncosphere). The larval stages (metacestodes) of *T. saginata* and *T. solium* form distinctive pearly-white cysts (cysticerci) which appear as small (8–10 mm in diameter) fluid-filled bladders (hence the common name of bladder-worms), each containing a single invaginated protoscolex (infective stage).

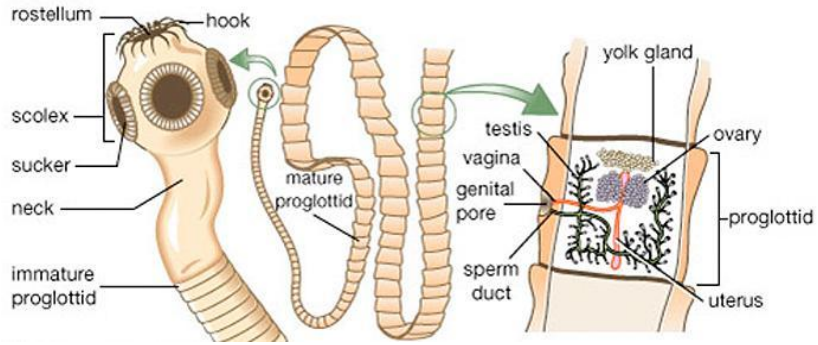

Figure 27. Morphology of *Taenia solium*
[https://smart.servier.com/category/medical-specialties/infectiology/]

Host range. Numerous Taenia spp. are found in carnivores and herbivores throughout the world. Many species appear to have two scientific names because the larval stages in herbivores were often named (as Cysticercus, Strobilocercus or Coenurus spp.) before it was realized they were developmental stages of adult Taenia tapeworms in carnivores. *T. solium* infections are endemic in humans and pigs in many areas where pork products are common, including regions throughout South and Central America, Eastern Europe, South Africa, China and Indonesia. *T. saginata* infections are cosmopolitan and occur in humans and cattle in most pastoral (beef and dairy) areas throughout the world (fig. 28).

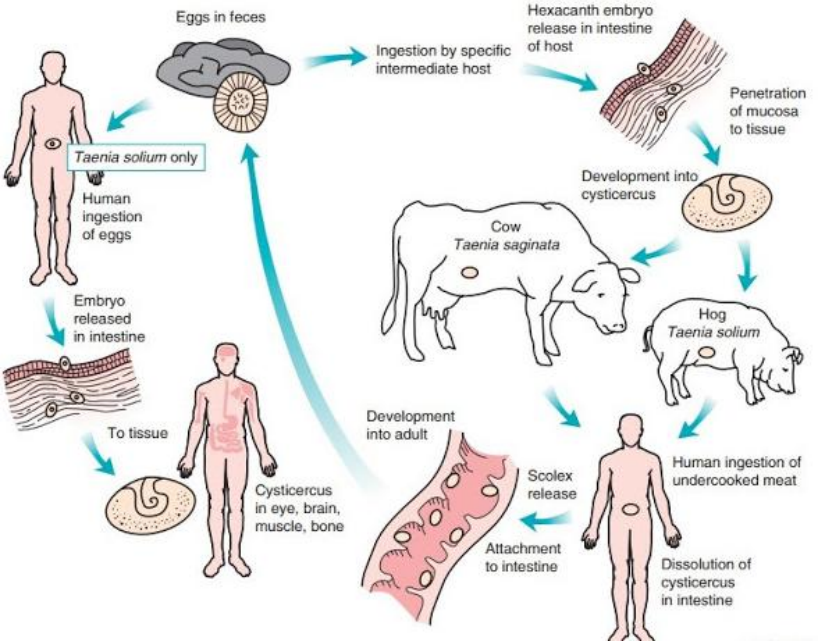

Figure 28. Life cycle of *Taenia spp.*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Site of infection. Adult tape-worms lay in the lumen of the small intestines of their definitive hosts, attached to the mucosa only by their scoleces. Larval stages (metacestodes) may develop in a range of tissues and organs in their intermediate hosts, particularly in muscles, visceral organs and sometimes the brain.

Pathogenesis. Infections in humans by the large adult tapeworms generally only involve 1–2 worms, and often do not involve any distinct symptoms, although there may be vague abdominal pains, with mild intermittent diarrhoea or constipation, and generalized allergic manifestations, including urticaria, anal pruritis, and eosinophilia. Infections by the encysted larval stages (cysticerci) do not appear to cause any severe clinical disease in their normal hosts (cattle and pigs) even when present in relatively high numbers. The cysts often occur in skeletal muscle, connective tissues of the skin and the liver, and while they may occupy space, they generally do not cause organ enlargement, tissue displacement or untoward pressure on surrounding areas. Degenerating cysticerci tend to calcify and are palpable in the tissues. Heavy infections by live and calcified cysts impart a measly appearance to the flesh and may lead to the condemnation of the carcase. Unfortunately, humans may also be infected with *T. solium* cysticerci through the process of self-infection when eggs are accidentally ingested (and possibly by retrofection when eggs carried upwards by reverse peristalsis hatch in the gut). Cysticerci may develop in virtually every organ and tissue of the human body, although they show an affinity for subcutaneous connective tissue, eye, brain, muscles, heart, liver, lungs and coelom. Humans are quite susceptible to pressure necrosis, particularly when cysticerci develop in the brain (neurocysticercosis with cerebral signs, headaches, seizures, and coma) or eyes (ocular signs, pain, and loss of vision). Degenerating cysticerci may elicit severe acute, and even fatal, inflammatory responses before their eventual calcification.

Mode of transmission. These tape-worms have indirect life-cycles: involving predator-prey transmission where carnivores acquire infections by ingesting larval stages in meat. Adult worms produce thousands of eggs which are excreted with host faeces. The eggs are very resistant to desiccation and sewage treatment and can live for weeks on pastures. They are ingested by intermediate hosts with contaminated feed, drinking water, or are physically transferred to the mouth. The eggs hatch releasing the oncospheres which use their hooks to penetrate the gut wall into the circulation where they carried mainly to the skeletal muscles and connective tissues. Over 3 months, they metamorphose into thin-walled cysticerci; each con-

taining a single tiny protoscolex invaginated into the lumen. These encysted larval stages are transmitted to their definitive hosts by carnivorism, when infected meat or offal is consumed. After ingestion, the outer bladder is digested away releasing the protoscolex which evaginates, attachs to the small intestinal mucosa and grows into an adult in about 10 weeks. Adult worms may live for as long as 25 years and they will produce billions of eggs in that time.

Differential diagnosis. Intestinal infections in humans are diagnosed by the detection of gravid segments or eggs in faecal samples. The eggs of T. saginata and T. solium are identical, but the gravid segments of T. saginata are more active than those of T. solium, and they have more lateral branches of the uterus (15–32 compared to 7–13). Infections by cysticerci can only be seen and felt when in superficial locations. Modern medical imaging techniques (magnetic resonance imaging (MRI) and computerized axial tomography (CAT) scans) may detect cysticerci in soft tissues, while X-rays generally only detect calcified cysticerci. Immunoserological tests have been developed to detect host antibodies against purified antigens and appear to be sensitive and specific.

Treatment and control. Anthelmintic treatment is effective in killing adult tape-worms but does not kill eggs. Single doses of praziquantel or niclosamide can cure infections in definitive hosts, while daily doses of praziquantel given for 1–2 weeks are effective against larval cysticercosis in intermediate hosts. Mebendazole and albendazole also appear to be effective against adult and larval stages. The prevention of infections involves breaking the transmission cycle; through stringent meat inspection for ‘measly’ meat, condemnation of infected carcases for human consumption, proper cooking or freezing of meat (pickling meat often does not kill larvae), sanitary disposal of faeces, prohibiting the use of sewage for fertilizing pastures, washing salad vegetables and strict personal hygiene.

3.6. DIPHYLLOBOTHRIUM LATUM

[fish tape worm, species causes diphyllobothriasis in humans]

Diphyllobothrium latum, the fish tapeworm, is the biggest tapeworm in humans. It causes a parasitic infection called diphyllobothriasis which is acquired by eating raw fish infected with the parasite.

Diphyllobothriasis is found in Chile, Peru, Uganda and in the Northern Hemisphere (northern Asia, Europe and America) in areas of rivers and lakes. Diphyllobothrium latum is the most common and mostly found in Scandinavia, the Baltics and western Russia (fig. 29).

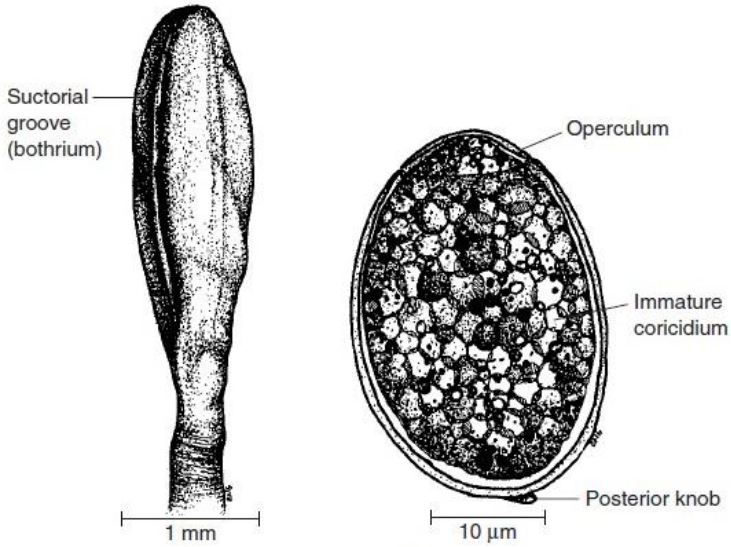

Figure 29. Scolex and egg of *Diphyllobothrium latum*
[https://smart.servier.com/category/medical-specialties/infectiology/]

The **life cycle** of *Diphyllobothrium latum* starts, when immature eggs are passed in the feces of an infected human. The eggs mature in water within three weeks and form oncospheres. Larvae called coracidia hatch and get eaten by freshwater crustaceans such as copepod. After ingestion coracidia develop into procercoid larvae. If the copepod is eaten by a small fish (second intermediate host), the procercoid larvae penetrate the gut and migrate to muscle tissue where they develop into plerocercoid larvae (sparganum), the infective stage for humans. Usually a third intermediate host is needed because humans do not usually eat raw fish this small. If a trout, walleyed pike or perch eats the smaller fish, the plerocercoid larvae once again penetrate the gut and migrate to fish flesh. If a human eats the infected fish raw or undercooked the plerocercoid larvae develop into adults in the small intestine.

The adults attach to the intestinal mucosa with two shallow, bilateral grooves (bothria) of their scolex. The scolex is 3 mm long and 1 mm wide. The long, flat body consists of segments, proglottids, that are produced by the neck. Full grown proglottids are about 10 mm wide and 3 mm long. As proglottids mature, they release eggs and eventually break off from the body. A *Diphyllobothrium latum* proglottid is characterized by a rosette-shaped uterus at its center. The eggs are ellipsoidal or oval measuring 55–75 µm by 40–50 µm. They are passed in the feces unembryonated (immature). From the start of the infection it takes about six weeks for the eggs to appear in the feces. One adult tapeworm can shed up to a million eggs per day. It can grow over 10 meters long and live up to 20 years (fig. 30).

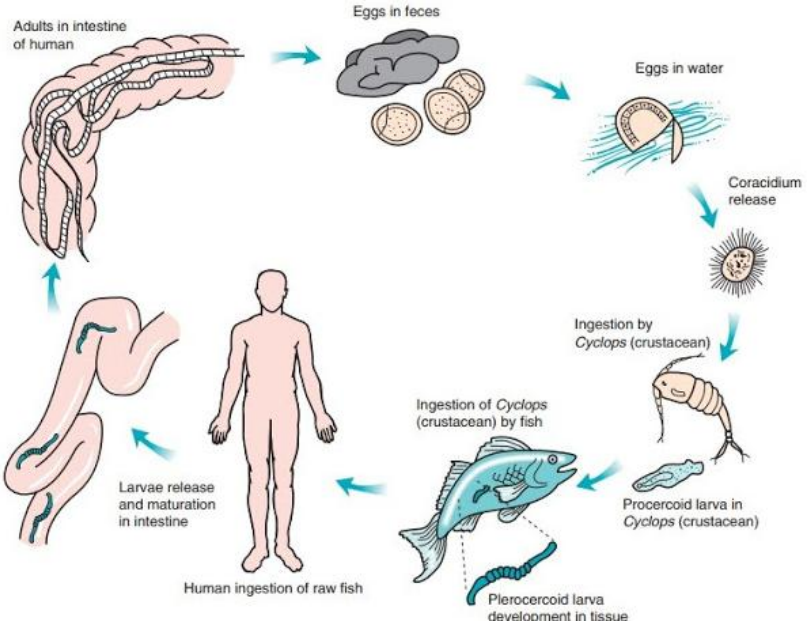

Figure 30. Life cycle of *Diphyllobothrium latum*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

People who eat raw fish are at risk of getting infected with the larvae that are sometimes present in the fish flesh. Some fishermen eat their catches raw using salt to kill parasites. Salting the fish is usually not enough to kill larval Diphyllobothrium latum. Some

housewives taste fish as they are preparing it and might ingest the tiny larva. Women get infected more often than men because they usually prepare meals for the family. Raw fish is included in many regional cuisines, for example, carpaccio di persico (Italy), ceviche (Latin America), marinated herring (Scandinavia), sashimi and sushi (Japan) and tartare maison in (France).

Pathogenesis. Diphyllobothriasis is usually asymptomatic. In some cases, it causes severe vitamin B12 deficiency because *D. latum* can absorb most of the B12 intake. In some cases, it can lead to neurological symptoms. Diphyllobothriasis symptoms include: constipation, diarrhea, fatigue, obstruction of the bowel, pernicious anemia (caused by vitamin B12 deficiency) which can lead to subacute combined degeneration of spinal cord, stomach pain, vomiting, weight loss. Migrating proglottids can cause inflammation of the bile duct or the gall bladder.

Diphyllobothriasis is **diagnosed** by examining a stool sample to find eggs or sometimes proglottids. Identification is restricted to genus level which actually does not matter when treating the disease since all Diphyllobothrium species respond to the same drugs. When doing research the specific worm species can be identified by performing PCR on purified eggs.

Prevention. Cook fish properly. If you eat sashimi or sushi, freeze it first at -10 °C (or below) for two days to kill the tapeworm larvae. Do not defecate in water (rivers, lakes etc.). If the fish tapeworm larvae cannot get in touch with the intermediate hosts, they cannot infect humans.

3.7. ECHINOCOCCUS GRANULOSUS

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Platythelminthes (flatworms).
- Cestoda (tapeworms).
- Eucestoda (segmented, hermaphroditic).
- Cyclophyllidea (terrestrial cycles, scolex with suckers).

Family Taeniidae

Cyclophyllidean tape-worms have flat ribbon-like bodies, with an anterior scolex (hold-fast organ with suckers and sometimes hooks) and a posterior tape (strobila) made up of segments (prog-

lottids). Adult worms lack a gut (they absorb nutrients) and they are hermaphroditic (segments containing both male and female reproductive organs). They have indirect life-cycles involving encystment of larvae (metacestodes) in the tissues of intermediate hosts and their transmission to definitive hosts by carnivorism. Various species are parasitic in mammals, birds, reptiles and amphibians. Adult stages are rarely pathogenic, but the encysted larval stages may cause serious space-occupying lesions, including hydatid cysts in humans.

ECHINOCOCCUS GRANULOSUS [this species causes hydatid disease in mammals, humans]

Parasite morphology. Tape-worms form three different developmental stages: eggs; larvae; and adults. Adult *E. granulosus* worms are small (2–6 mm long) and have a scolex with only three attached segments. The scolex has four lateral suckers and the rostellum is non-retractable and armed with a double crown of 28–50 recurved hooks. The anterior segment is immature, the middle segment is mature with functional testes and ovaries, and the posterior segment is gravid with the uterus filled with eggs. The eggs are typical for most taeniid species and are small and round (30–43 μm in diameter), thick-shelled and contain a hexacanth (6-hooked) embryo (oncosphere). The encysted larval (metacestode) stage is known as a bladder-worm or hydatid, and it produces multiple infective stages (protoscoleces, apparent as invaginated scolices already containing suckers and hooks) either directly from the germinal layer of the cyst wall, or by forming brood sacs (hydatid sand) by endogenous (internal) or exogenous (external) budding of the germinal layer. *E. granulosus* forms fluid-filled unilocular cysts with endogenous budding of brood capsules, *E. vogeli* forms fluid-filled polycystic cysts with exogenous budding, and *E. multilocularis* forms fluid-free multilocular or alveolar cysts with exogenous budding (fig. 31).

Host range. E. *granulosus* occurs in most sheep and cattle producing areas around the world, being most prevalent in South America, East Africa, Southeast Asia and China. Canids (dogs, dingoes, wolves, and coyotes) act as definitive hosts for adult worms, while omnivorous/herbivorous mammals (humans, domestic animals and wildlife) serve as intermediate hosts for encysted larval stages (table 6).

Table 6

Characteristics of Echinococcus spp.

Parasite species	Definitive host	Intermediate host	Metacestode	Cyst morphology
Echinococcus granulosus	candid	omnivore	unilocular hydatid cyst	fluid-filled sphere with germinal membrane proliferating endogenously to form brood capsules
Echinococcus vogeli	bush dog	paca/rat	polycystic hydatid cyst	fluid-filled with germinal membrane budding exogenously to form new cysts and endogenously to form septae
Echinococcus multilocularis	dog/cat	rodent	multilocular (alveolar) hydatid cyst	no free fluid, germinal membrane budding exogenously to form multiple cysts

Site of infection. The small adult tape-worms attach to the mucosa of the small intestines in dogs, sometimes in their thousands. The larval stages (hydatids) most commonly infect visceral tissues and organs, especially the liver, in their mammalian intermediate hosts, although cysts may be found in many other locations, including the brain and long bones.

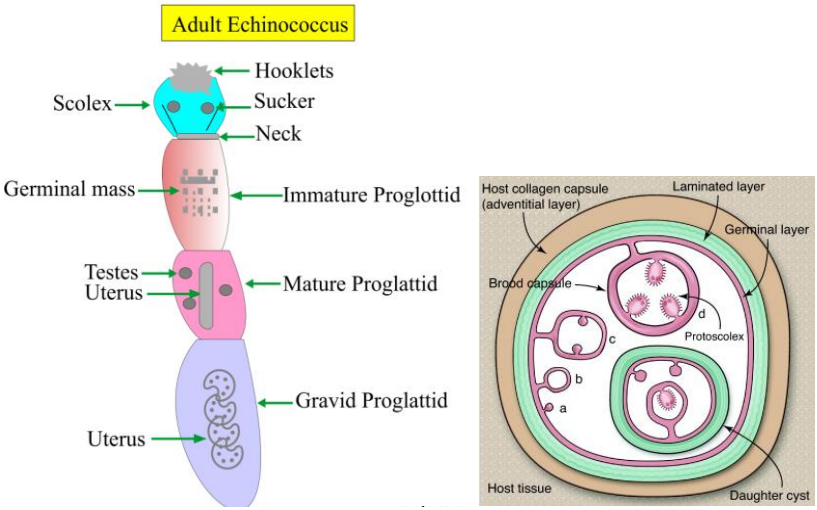

Figure 31. Adult worm and hydatid cyst of *Echinococcus granulosus* [https://smart.servier.com/category/medical-specialties/infectiology/]

Pathogenesis. The adult stages are considered benign and do not cause disease in dogs, as the worms do not invade or feed on host tissues. Encysted larval stages generally do not cause clinical disease in domestic livestock as they are often confined to visceral tissues. However, significant pathological changes occur in humans when the slowly-growing cysts put pressure on surrounding tissues and produce chronic space-occupying lesions. Cysts may grow around 1 mm per month and can become extremely large, up to 30 cm in diameter with litres of fluid containing thousands of protoscoleces. Organ enlargement may be accompanied by a variety of clinical signs depending on the size and location of the cysts. Compression of liver may result in jaundice, portal hypertension and abdominal distention. Cysts in the lung may cause haemoptysis (coughing up blood), dyspnoea (difficulty breathing) and chest pain. Cysts in the brain or spinal cord can provoke acute inflammatory responses and numerous neurological sequalae, including epilepsy and blindness. Cyst rupture has been associated with acute clinical signs (such as peritonitis and pneumothorax), and the sudden release of hydatid fluid may cause severe allergic reactions (such as asthma and anaphylactic shock). Protoscoleces released from ruptured cysts can regress and form new hydatid cysts throughout the body.

Mode of transmission. Tape-worms have an indirect life cycle involving predator-prey transmission between definitive (canid) and intermediate (mammalian) hosts. Mature tape-worms release numerous thick-shelled eggs which are excreted with dog faeces. The eggs are very resistant to external environmental conditions and can survive for months on pasture. Herbivores and omnivores become infected by ingesting eggs; either on herbage, in water, or by hand-to-mouth transfer. Following ingestion, the eggs hatch releasing the oncosphere which uses its three pairs of hooks to penetrate the gut, enter the circulation and settle in various organs and tissues (frequently in the liver after being filtered out by portal capillaries). They form hydatid cysts over many months and eventually produce multiple infective protoscoleces. When mature cysts in offal or carcases are eaten by canids, the cyst wall is digested away freeing the protoscoleces, which evaginate and attach to the small intestinal mucosa. They mature to adult worms in about 8 weeks and may live for 5-20 months. Various strains of E. granulosus have been recognized based

on differences in parasite morphology, development, biochemistry, genetics and host specificity. Strains are often adapted to particular intermediate host species and do not develop well in other species. Infections are well adapted to pastoral cycles involving farm dogs and domestic livestock (notably sheep and cattle), as well as sylvatic cycles involving wild carnivores (wolves, coyotes, dingoes) and free-ranging herbivores (such as deer, moose and wallabies). Infections in human populations occur more frequently in rural areas, particularly where local traditions are conducive to transmission; e.g. feeding dogs offal, eating dog intestines, not burying the dead, and even using dog faeces to tan hides.

Differential diagnosis. Infections in dogs may be diagnosed by the detection of eggs, and occasionally worms, in faecal samples. Immuno-coprological tests have also been developed to detect parasite antigens in faecal samples. Infections in intermediate hosts are generally diagnosed well after the larvae have encysted. Clinical symptoms of a slow-growing tumour accompanied by eosinophilia are suggestive. Cysts may be visualized by various medical imaging techniques (computerized axial tomography (CAT) scans, X-rays, ultrasound). Several immunoserological tests have been developed to detect host antibodies against crude and purified parasite antigens, and an intradermal (Casoni) test using hydatid fluid has been used in surveys.

Treatment and control. Despite some promising indications, the treatment of hydatid disease with conventional anthelmintic drugs has not proven wholly effective, being complicated by the large size and inaccessible location of cysts and their thick, possibly impenetrable, walls. Variable results have been obtained using praziquantel and mebendazole, while albendazole and niclosamide have been less effective. The only remaining treatment option is for the surgical removal of cysts, provided they are in favourable sites. Surgeons must take care not to rupture cysts as protoscoleces may spread to new sites to form more cysts. Scolicide chemicals, such as cetrimide, may also be used during surgery to sterilize excision sites. In contrast, infections by adult worms in dogs can be successfully treated with praziquantel, and it is advisable to confine dogs and/or use purgatives to facilitate the collection and disposal of infected faeces. Preventing dogs from becoming infected involves eliminating

offal and other potentially infected material from their diets, curbing their hunting behaviour, properly disposing of carcases in the field, and culling wild and feral dogs. Several countries have developed highly successful hydatid eradication campaigns based around dog management and treatment. Recently, a recombinant vaccine has been developed to prevent hydatid formation in domestic herbivores, and is undergoing further evaluation. While control may be possible in situations involving pastoral cycles, there will be many problems accessing wildlife involved in sylvatic cycles.

3.8. ASCARIS LUMBRICOIDES

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Nemathelminthes (nematodes).
- Secernentea (Phasmidea) (with chemoreceptors known as phasmids).
- Ascaridida (intestinal roundworms).
- Ascaridoidea (large worms, three prominent lips).

Family Ascarididae

The ascaridoids are "round-worms" of the small intestine of many animals, including humans. They are characterized by their large size, three prominent anterior lips and the absence of a bursa. Round-worms have simple direct life-cycles involving faecal-oral transmission of infective eggs. Female worms produce numerous eggs which are excreted with host faces and must undergo embryonation before becoming infective. Larvae hatch from ingested eggs and undergo pulmonary migration before developing into adult worms in the small intestines. Adult worms generally eat the food of their hosts, but heavy infections cause tangles of worms which can obstruct the gut. Clinical infections are typically found in young individuals, although older individuals may serve as sources of infection.

ASCARIS LUMBRICOIDES [this species may cause gut obstruction in humans]

Parasite morphology. The parasite forms several different developmental stages: eggs, larvae, and adults (male and female).

Fertilized eggs appear as round-oval tan-coloured stages (45–75 μm long by 35–50 μm wide) surrounded by a thick albuminous mamillated (lumpy) outer coat. Before insemination or in early stages of oviposition, female worms may also excrete unfertilized eggs which are more elongate (85–95 × 45 μm) and decorticated (not mamillated). Fertilized eggs are excreted unembryonated, but then develop first-stage then second-stage infective larvae. When hatched in the host, these small larvae (1.2–1.8 mm long) invade host tissues and undertake pulmonary migration. Large adult worms develop in the gut, female worms measuring 20–50 cm long by 3–6 mm wide, while males are smaller, measuring 15–30 cm long by 2–4 mm wide with two simple spicules 2.0–3.5 mm long. Adults have a striated cuticle and three small, but conspicuous, lips around the apical mouth (fig. 32).

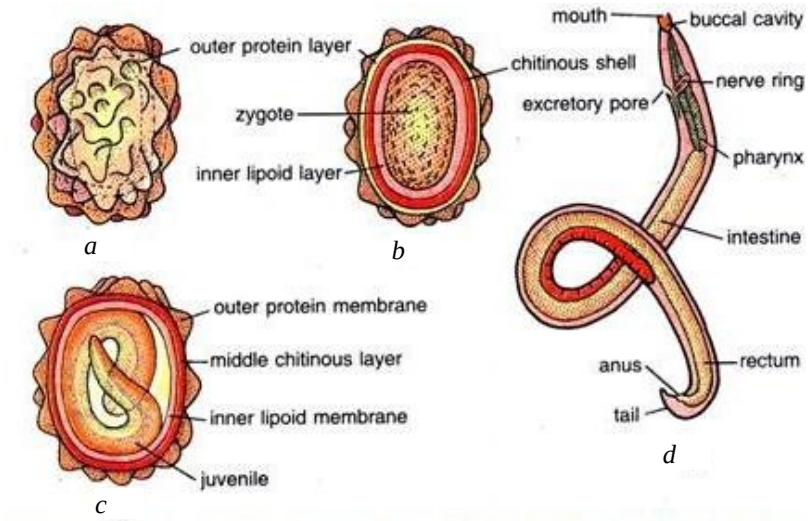

Figure 32. Morphology of *Ascaris lumbricoides*:
a – entire mammilated egg; *b* – mammilated egg in section;
c – embryonated egg; *d* – adult worm
[http://www.onlinebiologynotes.com/category/parasitology]

Host range. A. lumbricoides is common in many human populations around the world, particularly in tropical and subtropical

countries with high rainfall, as well as in temperate regions with warm summers. Infections are particularly prevalent in countries where nightsoil (human faeces) is used to fertilize vegetable crops. It is estimated that almost one quarter of world population (1 billion people) may be infected. Infections are over-dispersed in local populations, where large numbers of parasites occur in a small number of individuals. Children are most susceptible to clinical infection; although a range of predisposition factors have been reported, involving various combinations of environmental, social, behavioural and genetic factors. A similar species, A. suum, occurs in pigs, especially in developing countries with free-ranging village or feral pigs. Modern husbandry practices in developed countries have resulted in a significant decline in the incidence of infections in pigs. There is considerable biological and epidemiological evidence to suggest zoonotic transmission of A. suum to humans, although recent molecular studies have shown limited gene flow between human and pig ascarid populations. While the whole life cycle of A. suum may not be completed in non-porcine hosts, their larvae can undergo extensive migration in a number of hosts (humans, cattle, sheep, etc) leading to allergic manifestations.

Site of infection. Adult worms live in the lumen of the small intestine, where the females lay numerous eggs which are shed in host faeces. Prior to the development of adult worms, the infective larvae undertake a curious circuitous migration through the lungs, ending up in the gut from where they started. This pulmonary migration phenomenon is considered an evolutionary relict behaviour preserved from ancestral forms. The larvae migrate through the gut wall into blood/lymph and are carried to the lungs where they penetrate into air spaces and move up the respiratory tree to the epiglottis where they are swallowed.

Pathogenesis: Infections by small numbers of worms may remain asymptomatic, although some individuals may develop allergic reactions (urticaria, eosinophilia). Larger numbers of worms, however, can cause significant health problems for the host. Following infection, pulmonary migration by larvae may cause petechial haemorrhages, oedema, inflammation, and pulmonary congestion (pneumonitis, or Loeffler's pneumonia) with cough, chest pain and

difficulty breathing. Migrating larvae lost or trapped in other tissues often die causing focal inflammation and vague symptoms difficult to diagnose. Adult worms developing in the gut feed on luminal content, they steal liquid nourishment from the host contributing to protein energy malnutrition and impaired carbohydrate absorption. Moderate-heavy infections may cause a variety of digestive disorders, poor growth and development in small children, abdominal pains, restlessness, insomnia and allergic responses (rashes, asthma). Heavy infections may also cause life-threatening gut obstructions where tangles of worms form a bolus mechanically blocking the gut. To the great consternation of their hosts, worms may also occasionally wander upstream (obstructing biliary or pancreatic ducts, sometimes even being regurgitated) or downstream (infecting the appendix, or being passed in faeces).

Mode of transmission. Infections are passed between hosts by the faecal-oral transmission of eggs containing infective larvae. Freshly-excreted eggs require 9–40 days for embryonation before they become infective. Embryonation occurs faster in warm moist soil (especially clay) and water (~10 days at 30 °C). The eggs are very resistant to external environmental conditions and can survive high temperatures (up to 45 °C) and dry conditions (down to 6% humidity). Experimental studies have shown that eggs may remain viable in soil for several years. They are also dispersed in the environment by wind, water, earthworms and insects (cockroaches). Eggs in soil/water may be transferred to the mouth by contaminated hands or ingested with foods (uncooked vegetables, washed salads and fruits) or soil (pica = dirt-eating, especially by young children). Once ingested, the eggs hatch releasing infective larvae which invade the gut and migrate via the blood/lymph to the lungs over 8-10 days. They break into the airspaces (alveoli) of the lungs and move up the bronchi and trachea to the pharynx where they are swallowed. They moult in the small intestines and mature to adult worms. Females begin egg production 60–65 days after infection and produce huge numbers of eggs (up to 200,000 per day). The adult worms may live for 6 months to 2 years, so the entire parasite life cycle can range from 2 months up to 5–10 years (fig. 33).

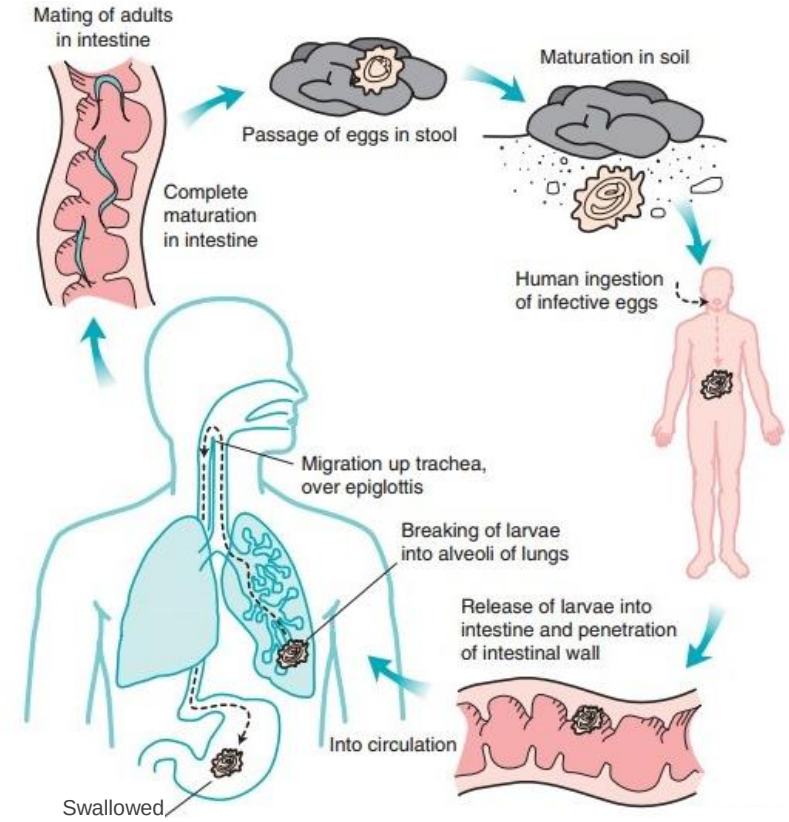

Figure 33. Life cycle of *Ascaris lumbricoides*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Established infections are diagnosed by the microscopic detection of eggs in faecal material, often using sedimentation and/or flotation concentration techniques. Imaging techniques have been used to examine gut obstructions and masses of worms appear as filling defects in X-rays. Differential diagnosis of infections during the larval migration stage is difficult due to non-specific nature of any clinical signs. Larvae have sometimes been detected in sputum samples but are difficult to identify by untrained personnel.

Treatment and control. Various anthelmintic drugs have proven effective for the treatment of infections. Mebendazole appears to

be the drug of choice, although it sometimes may cause some worms to wander. Suitable alternatives include pyrantel and levamisole, while albendazole has also been used. Once diagnosed, infections can be successfully treated, but the individual often returns to the heavily contaminated environment and quickly becomes re-infected. Environmental decontamination is difficult because the eggs are very resistant to chemicals; they can embryonate in dilute formalin, potassium dichromate, acid solutions and many commercial disinfectants. Because infections accumulate in their hosts (worms do not multiply in hosts), control measures involve avoiding behaviours conducive to the uptake of eggs; such as improving personal hygiene, maintaining sanitary conditions, and proper disposal of excreta. Fresh faecal material should not be used to fertilize edible crops, but it can be processed by microbial biocomposting before use (high temperature processing destroys egg viability).

3.9. ANCYLOSTOMA / NECATOR

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Nemathelminthes (nematodes).
- Secernentea (Phasmidea) (with chemoreceptors known as phasmids).
- Strongylida (strongyles, bursate nematodes).
- Ancylostomatoidea (hookworms, with cutting plates/teeth).

Family Ancylostomatidae

These worms are characterized by their bent mouths, the anterior ends being bent dorsally, hence the common name of “hook-worms". They have a well-developed buccal capsule with cutting plates or teeth, and are voracious blood-feeders in the small intestines of mammals, including humans, dogs, cats, sheep and cattle. Male worms have a well-developed bursa (copulatory clasping organ) at their posterior ends. Hook-worms have direct life-cycles, involving a geo-helminth phase. Eggs voided with faeces hatch releasing free-living rhabditiform larvae which subsequently develop into infective filariform larvae that are ingested or actively penetrate the skin of their hosts (causing cutaneous larval migrans). Juvenile worms migrate through the lungs (causing pneumonitis) before developing into adults in the small intestines (causing iron-deficiency anaemia and growth retardation).

ANCYLOSTOMA DUODENALE [this species causes Old World hookworm disease in humans]

NECATOR AMERICANUS [this species causes New World hookworm disease in humans]

Parasite morphology. Hook-worm developmental stages include eggs, four larval stages and adult worms. Eggs appear as oval thin-shelled bodies, measuring 55–77 μm in length by 35–42 μm in width. Freshly-excreted eggs contain a developing embryo in the early stages of cleavage (2–8 cells). The first two larval stages are rhabditiform (free-living) and characterized by a long narrow buccal chamber and flask-shaped muscular oesophagus. Third stage larvae measure up to 0.6mm in length and are filariform, non-feeding infective stages characterized by a closed mouth, elongate oesophagus with posterior bulb (strongyliform) and pointed non-notched tail. Fourth-stage larvae migrate and live in host tissues. Adult hookworms have a creamy-white tough cuticle, a prominent anterior hook and a large oval buccal capsule with specialized structures to aid in feeding, *Ancylostoma* spp. having 2 pairs of fused ventral teeth, and *Necator* having two ventral cutting plates. *Ancylostoma* females measure 10–13 × 0.6 mm, while males measure 8–11 × 0.4 mm. The adults of *Necator* are slightly smaller. All male worms have a pronounced posterior copulatory bursa, consisting of two broad lateral lobes and a smaller dorsal lobe, all supported by fleshy rays (fig. 34).

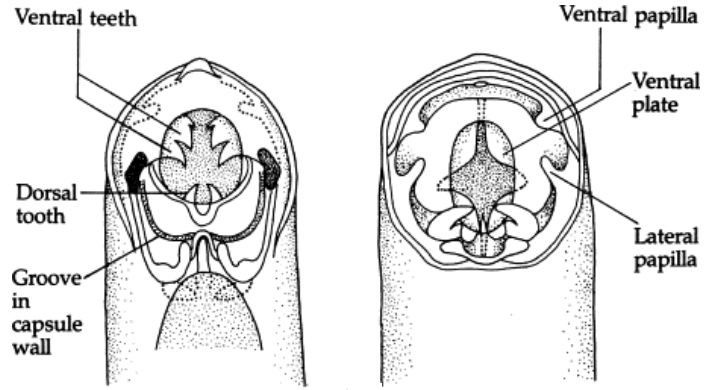

Figure 34. Hookworm buccal capsules:
a – ancylostoma; *b* – necator
[http://www.onlinebiologynotes.com/category/parasitology]

Host range. Hook-worm's infections have been reported in numerous mammalian species throughout the world, mainly in tropical and subtropical regions because the larvae cannot develop below 22 °C (table 7). They are most common in rural areas with high annual rainfall and shaded sandy or loam soils ideal for larval development (not clay or gravel). *Ancylostoma* can survive at lower temperatures than *Necator* and were a common finding in miners and tunnel builders in Europe. It is estimated that around 800 million people are infected with hook-worms worldwide, with 1.6 million suffering from anaemia and 55,000 deaths annually. *A. duodenale* is the Old World human hookworm and is entrenched on most continents. *N. americanus* is the New World human hookworm, although it probably came to such areas with the slave trade.

Table 7

Characteristics of Ancylostoma and Necator

Parasite species	Hosts	Oral structures	Geographic distribution
Necator americanus	humans	2 cutting plates	Africa, India, Asia, China, central America
Ancylostoma duodenale	humans	2 pairs teeth	Europe, Africa, India, China, Asia, patchy distribution in North and South America

Site of infection. Adult hook-worms use their bent mouths to attach to the small intestinal mucosa. Infective larvae invade dermal tissues, particularly in sites which have come into close contact with the ground (feet, hands and buttocks). Migrating larvae move through the lungs (pulmonary migration) and some may undergo arrested development deeper in the gut tissues or in muscles (hypobiotic larvae of *A. duodenale*).

Pathogenesis. Many people may be infected with hook-worms but remain asymptomatic. In general, disease development depends on the parasite species involved, the intensity of infection, and the nutritional condition of the individual. Sequential parasite development causes three phases of disease; a cutaneous phase where invading larvae may cause dermatitis, a pulmonary phase where migrating larvae may cause pneumonitis, and an intestinal phase where adult worms may cause anaemia. Infective larvae penetrate the skin and invade blood vessels in the dermis, moderate to heavy

infections giving rise to an allergic dermatitis with papular, and sometimes vesicular, focal rash and pruritis (condition known as ground itch). Larvae from animal hook-worms can also penetrate human skin but do not complete their development. Instead, they aimlessly tunnel through the skin for several days or weeks leaving red itchy wounds that may become secondarily infected. The resultant condition is known as cutaneous larval migrans (or creeping eruption) and is characterized by local dermatitis, pruritis (itching) and inflammation (oedema, erythema). The next phase of disease occurs when larvae undergo pulmonary migration, having been carried to the lungs where they break out into airspaces (alveoli) causing focal haemorrhages and allergic pneumonia (severity dependent on numbers). Once worms reach the small intestines, they attach to the mucosa by ingesting a tissue plug into their mouths and commence feeding on blood. They have voracious appetites and individual adult *Necator* worms may consume 0.03 ml blood per day, while those of *Ancylostoma* may take up to 0.26 ml blood per day. Blood loss from the host may result in a profound iron-deficiency anaemia and hypoproteinaemia. The worms appear to be wasteful feeders as not all blood ingested is digested, some is apparently used for respiration and passes through the worm but degrades in the intestines resulting in black tarry faeces (melena). Blood loss is further exacerbated by intestinal lacerations as worms move to new feeding sites from time to time, secreting proteolytic enzymes and anticoagulants, and leaving microscopic ulcers. Infections involving <100 *Necator* are frequently mild whereas >100 worms produce more damage and >1,000 may be fatal. Fewer *Ancylostoma* cause greater disease because they suck more blood, 100 worms may cause severe disease. Patients with heavy infections have severe protein deficiency, dry skin and hair, oedema, and potbelly in children with delayed puberty, mental dullness, heart failure and death. Disease is intensified by malnourishment and immunological impairment.

Mode of transmission. Hook-worms have direct life-cycles involving a geo-helminth stage where infective larvae in the soil actively penetrate the skin or oral mucosa of their hosts. Female worms produce numerous eggs (up to 9,000 eggs per day for *Necator* and

30,000 eggs per day for *Ancylostoma*) which are excreted with host faeces. The eggs embryonate rapidly in warm moist conditions and hatch within 1–2 days, releasing free-living rhabditiform larvae which feed on bacteria and organic debris. The larvae moult once after ~3 days and then transform 2–5 days later into non-feeding ensheathed filariform larvae which are the infective stages. They remain viable for several weeks in light sandy soils under warm moist conditions. The larvae also exhibit short vertical migration, moving to the surface in moist conditions and host-seeking by rhythmically waving back and forth, but retreating back into the soil in dry conditions. *Necator* larvae must penetrate the skin to infect humans (transdermal or percutaneous transmission), but *Ancylostoma* can penetrate the skin or oral mucosa, be passed in mother's milk (transmammary transmission) and even cross the placenta to infect the foetus (transplacental transmission). Some evidence suggests that *A. duodenale* larvae may survive in paratenic hosts and lead to human infection through the ingestion of undercooked meat, including rabbit, lamb, beef and pork. Ingested larvae may undertake pulmonary migration, but most undergo a histotrophic stage by penetrating mucosal glands before returning to the lumen and maturing into adults. Larvae which penetrate the skin actively secrete collagenase to break down basement membranes and dermal ground substances. The larvae enter the circulation and migrate over 2–7 days to the lungs where they break into respiratory alveoli and move up the trachea to be swallowed. Once they reach the small intestines, they moult, attach to mucosa and become sexually differentiated, moult again and grow into adult worms. The prepatent period (from infection to egg excretion) ranges from 4–7 weeks, although *A. duodenale* may undergo arrested larval developmental for up to 38 weeks. Hypobiotic larvae remain dormant in gut or muscles and recommence their development later coinciding with the seasonal return of environmental conditions more favourable to transmission. Infections may persist for years, as *Ancylostoma* adults have been found to live for up 5 years, and *Necator* adults for up to 15 years (fig. 35).

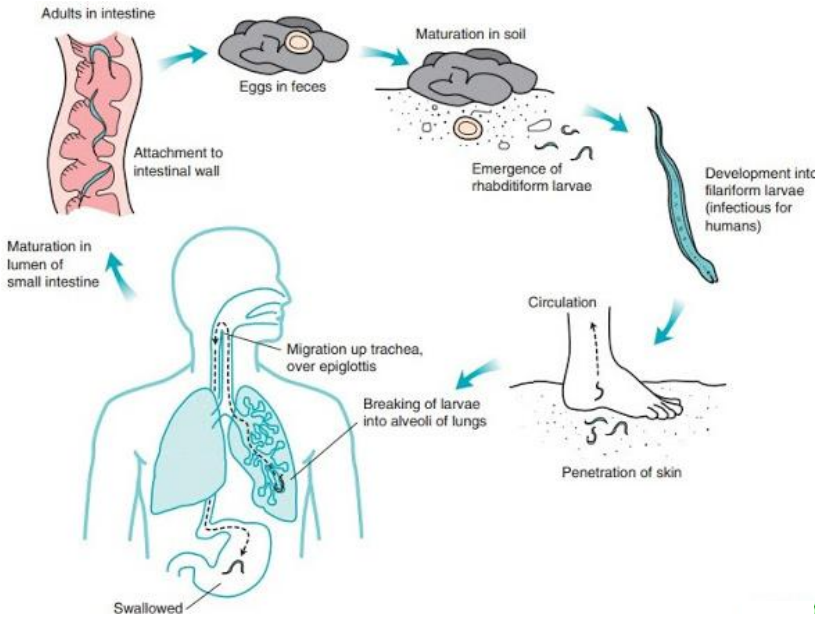

Figure 35. Life cycle of hookworms
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. The diagnosis of hookworm disease on the basis of clinical symptomatology (notably chronic anaemia and debility) is highly suggestive, but requires confirmation by the detection of parasite eggs in faecal samples by microscopy, preferably after concentration. Because the eggs of hookworms (Ancylostoma and Necator) and thread-worms (Strongyloides) are virtually identical, faeces should be kept for larval cultures (on moistened filter paper in a closed tube for a few days) to differentiate infections (hookworm larvae have a larger buccal cavity and smaller genital primordium), since treatment options are quite different. Several immunoserological tests have been developed to detect host antibodies against hookworm antigens, but they generally do not discriminate between patent or previous infections. Radiographic findings include intestinal hypermotility, proximal jejunal dilatation and coarsening of the mucosal folds.

Treatment and control. Various anthelmintic drugs have been used to cure infections, and are best used in conjunction with dietary

supplementation, especially iron replacement. The most effective drugs are mebendazole, albendazole and pyrantel pamoate. Levamisole is less effective and treatment has adverse side-effects. Older drugs, such as bephenium and tetrachlorethylene, are still used in many areas throughout the world because they are cheap. Salicylanilides have also proven effective against animal Ancylostoma infections. While chemotherapy works, mass treatment programmes are only partly effective as most cured individuals return to heavily contaminated areas and rapidly become re-infected. Infection appears to stimulate little protective immunity. Control programmes must include prophylaxis to prevent infections as well as environmental management to reduce soil contamination. People should be encouraged to wear solid shoes in endemic regions and to thoroughly wash salad vegetables. Building and education campaigns should be introduced to improve sanitary conditions, as promiscuous defaecation, associated with poverty and ignorance, keeps soil contamination high. Nightsoil (faecal waste) should not be used to fertilize gardens or vegetable crops. Dog faeces should not be left on lawns or parks (especially well-watered ones) where people congregate. Several countries have successfully controlled infections, mainly through regular periodic mass treatment, the provision of latrines and institutionalized public education.

3.9. TRICHURIS TRICHIURA

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Nemathelminthes (nematodes).
- Adenophorea (Aphasmidea) (without chemoreceptors known as phasmids).
- Trichocephalida (Enoplida) (thread-head).
- Trichuroidea (whipworms, anterior end long and narrow, stichosome pharynx).

Family Trichuridae

Trichurid worms are known as "whip-worms" because they have a broad short posterior end and a very long narrow whip-like anterior end (with a stichosome pharynx) which is embedded in the mucosa of the lower intestines of humans and domestic animals. Heavy infections may cause dysentery, anaemia, malnutrition, and occasional-

ly rectal prolapse. They have simple direct life-cycles involving the faecal-oral transmission of eggs containing infective larvae. Eggs excreted with host faeces contaminate soil, food and water supplies and have a characteristic barrel-shape with mucoid polar plugs at each end.

TRICHURIS TRICHIURA [these species cause trichuriasis in humans]

Parasite morphology. Whipworms form three different developmental stages; eggs, larvae and adults. The eggs are ellipsoidal to barrel-shaped, measuring 50–70 μm in length by 25–35 μm in width and have two distinct mucoid polar plugs. They are typically unembryonated in faecal samples and develop infective larvae in the external environment. Adult worms have elongate whip-like bodies (3–7 cm long), with a long thin anterior end that suddenly becomes thick at the posterior end. The mouth is a simple opening without lips and the oesophagus is thin, tubular and surrounded by glandular stichocytes (whole structure referred to as stichosome pharynx). Adult female worms measure up to 7 cm in length and the uterus contains many lemon-shaped eggs. Adult male worms are smaller measuring up to 5cm in length and they have a tightly coiled posterior end and a single spicule with a spiny, eversible sheath (fig. 36).

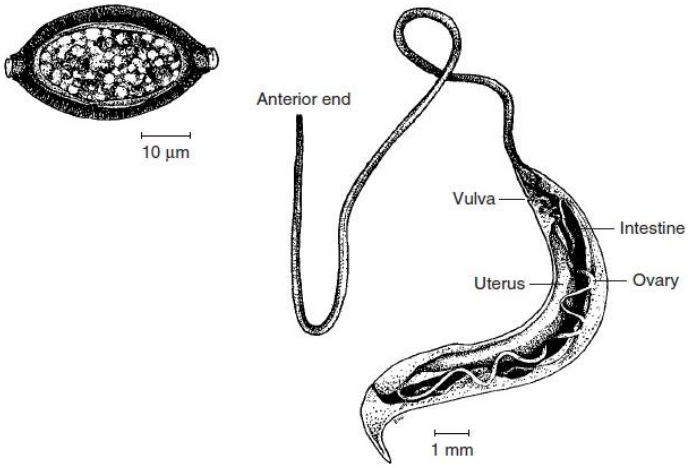

Figure 36. Female *Trichuris trichiura* and eggs [http://www.wormbook. /genomes Trichiuruis]

Host range. The species *T. trichiura* is found in human populations throughout the world, mainly in tropical and subtropical regions. It is estimated that around 10% of the world population (800 million people) may be infected. Parasites are very prevalent in regions where human excrement (nightsoil) is used to fertilize vegetable gardens. Infections are typically over-dispersed, where a few individuals harbour most of the worms.

Site of infection. Juvenile worms develop in glands of the caecal and colonic mucosa where they moult and grow. Adult worms have their anterior ends embedded in the mucosa with their posterior ends dangling into the lumen.

Pathogenesis. Small worm burdens rarely cause disease, while heavier infections may produce a variety of conditions, ranging from local enteric disturbances to systemic conditions and occasionally death. The anterior ends of the adult worms are embedded in the mucosa where they feed on fluids, digested tissues and possibly blood. They may cause significant trauma to the mucosa with chronic haemorrhage leading to dysentery and anaemia. Pathogenesis has been related to host inflammatory responses, involving markedly reduced cell-mediated responses and elevated IgE responses, characteristic of local tissue anaphylactic responses. Persistent infections have been associated with malnutrition, growth retardation, and reduced cognitive function in children. Chronic infections may also cause finger (and occasionally toe) clubbing evident as odd thickening of the ends of the digits. Heavy infections may produce tenesmus (urgency) causing the host to strain and possibly suffer rectal prolapse.

Mode of transmission. Whipworms have a direct developmental cycle whereby embryonated eggs are directly infective to the definitive host. Infections are transmitted by the faecal-oral route, involving the ingestion of eggs with contaminated food, water or soil. Fertilized female worms produce numerous eggs (3,000–10,000 per day) which are excreted with host faecal material. The eggs embryonate in around 10 days and develop infective larvae in about three weeks in moist shady soil (or up to 4 months in cold conditions). Eggs are dispersed in the environment by anthropogenic activities as well as by wind, water and insects (houseflies can act as mechanical vectors). When ingested, infective larvae emerge from the eggs and invade the mucosa of the lower intestines where they tunnel, grow and moult to form adults. Patent infections may develop in 8–12

weeks and can persist for 1–4 years. Infections may also accumulate in hosts as they are constantly re-infected from their heavily-contaminated environments (fig. 37).

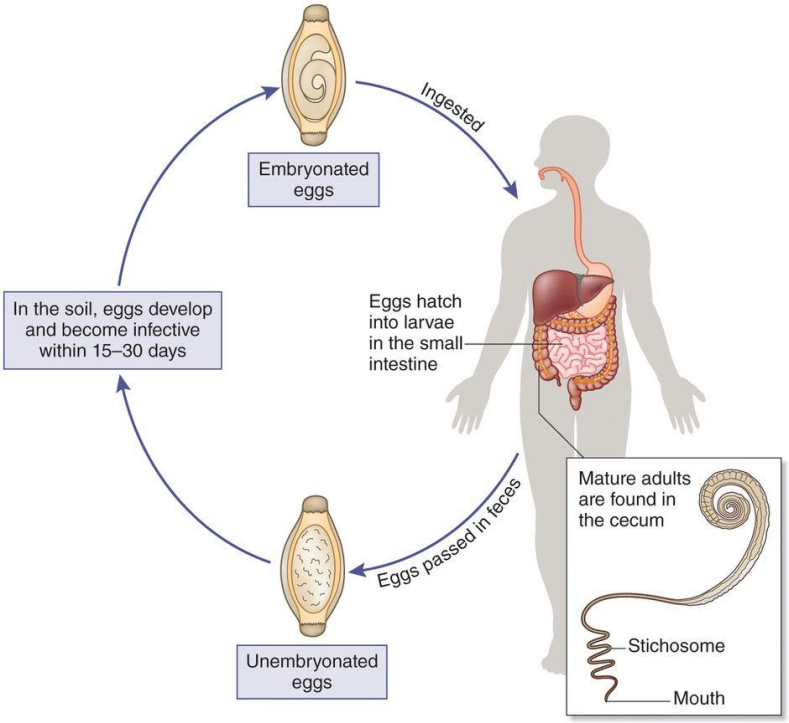

Figure 37. Life cycle of *Trichuris trichiura*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Infections are routinely diagnosed by coprological examination of faecal samples, usually following concentration, and the microscopic detection of the characteristic eggs. In individuals with rectal prolapse, worms can be seen macroscopically attached to the mucosa. Colon endoscopy has also been used to reveal the presence of worms.

Treatment and control. Whipworms are resistant to many anthelmintic treatments due to their relative inaccessibility. Mebendazole and albendazole have proven effective, and pyrantel/oxantel pamoate and flubendazole have some activity. Thiabendazole is also

effective but has unpleasant side-effects. Prevention of infections is best achieved by thorough washing of vegetables, salads and fruits with clean water prior to consumption. Control measures include education programmes to improve personal hygiene and sanitary conditions, prohibiting the use of excrement as fertilizer (or ensuring it is processed by suitable microbial biocomposting prior to use) and regular deworming campaigns.

3.11. ENTEROBIUS VERMICULARIS

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Nemathelminthes (nematodes).
- Secernentea (Phasmidea) (with chemoreceptors known as phasmids).
- Oxyurida (pinworms; pointed tails).
- Oxyuroidea (eggs attached around anus of host).

Family Oxyuridae

Oxyurid worms are commonly called "pin-worms" because of their characteristic tapering shape and pointed tails. They have simple direct life-cycles involving faecal-oral transmission of eggs containing infective larvae. The eggs, however, are oviposited around the anus (perineum) where they are subsequently dislodged and ingested by their hosts. Pinworms are common in many animal species, and infections in humans may cause intense pruritis (itching), irritability, insomnia and sometimes diarrhoea.

ENTEROBIUS VERMICULARIS [this species causes perianal pruritis (enterobiasis) in humans]

Parasite morphology. These worms form three developmental stages: eggs, larvae and adults. The eggs are elongate-oval in shape, measure 50–60 μm in length by 20–30 μm in width, and are characteristically asymmetric about the long axis being distinctly flattened on one side. Infective larvae develop rapidly within the eggs. Adult worms appear as elongate whitish tubes with pointed tails. They have three lips surrounding the anterior mouth, a large oesophageal bulb, and a conspicuous anterior cuticular inflation (swollen head). Male worms are 1–4 × 0.2–0.4 mm in size, have a single spicule 100–140 μm long, and their posterior ends are strongly curved ventrally. Female worms are 8–13 × 0.3–0.6 mm in size and have pronounced slender pointed tails.

Host range. The species *E. vermicularis* is the most common worm found in humans worldwide, particularly in temperate regions. They are commonly found as group infections in children, in families and in institutions (where contact between individuals is high and hygiene may be low). They are estimated to infect some 400 million people, but few countries consider them to be of public health significance due to their low pathogenicity. Infections are more irritating than debilitating, causing embarrassment, low morbidity and rarely mortality. However, individual families often spend considerable time and money trying to rid themselves of infections. Numerous pin-worm species have been described from a range of mammals, birds, reptiles, amphibians, insects and millipedes, but they appear to be highly host-specific. Curiously, dogs and cats do not become infected with pin-worms so companion animals should never be considered as sources of human infection.

Site of infection. Adult worms tend to congregate in the ileocaecal region of the gut where they attach to the mucosa, but they may wander throughout the intestines from the stomach to the rectum. Fertilized female worms migrate out through the anus and deposit eggs of the perianal skin.

Pathogenesis. While many infections remain asymptomatic, worm burdens may increase with time resulting in damage to the intestines by adult worms and/or damage to the perineum resulting from egg deposition. Adult worms attach to the mucosa and feed on intestinal content, bacteria and possibly epithelial cells, causing minute ulcerations which may lead to mild catarrhal inflammation with diarrhoea, eosinophilia and bacterial infection. More commonly, however, infections are characterized by intense perianal itching (pruritis ani) caused by host sensations and reactions to female worms depositing sticky eggs on the skin. Patients vigorously scratch themselves attempting to relieve the itching, but in doing so, often cause skin damage, bleeding, bacterial infection and intensified itching. Heavy infections in children may cause restlessness, irritability, anorexia, insomnia, nightmares, bed-wetting, nausea and vomiting. Occasionally, wandering worms have been associated with appendicitis, vaginitis, and rarely, extra-intestinal granulomas in ectopic sites.

Mode of transmission. Pinworms have direct life-cycles involving the oral ingestion of eggs containing infective larvae (fig. 38). The eggs, however, are not excreted with faecal material, but are

attached to the perianal skin. Such transmission is therefore not strictly faecal-oral, but rather contaminative, involving the transfer of eggs to the mouth via host behaviours or inanimate objects. Gravid females migrate out through the anus onto the perineum, particularly during the night, and leave trails of eggs (up to 10,000) as they crawl about. After oviposition, the females die whereas the males die soon after copulation. Larvae develop within the eggs within six hours and become infective. The eggs are dislodged by host scratching and contaminate hands, bedding, clothing, toys, and furniture. They are very light and easily disseminated with house dust by the slightest of air currents. They remain viable in cool moist conditions for up to one week. Following ingestion, the eggs hatch in the small intestine and the larvae migrate to the large intestine and mature over 2–6 weeks. Alternatively, eggs trapped in perianal folds may hatch and the larvae may enter the intestines directly via the anus (process called retro-infection). Occasionally, larvae may enter the vulva and infect the vagina of women. The parasite may complete its whole life cycle in 2–13 weeks, and infections may become progressively heavier due to continual parasite uptake (through auto-infection, re-infection and retro-infection).

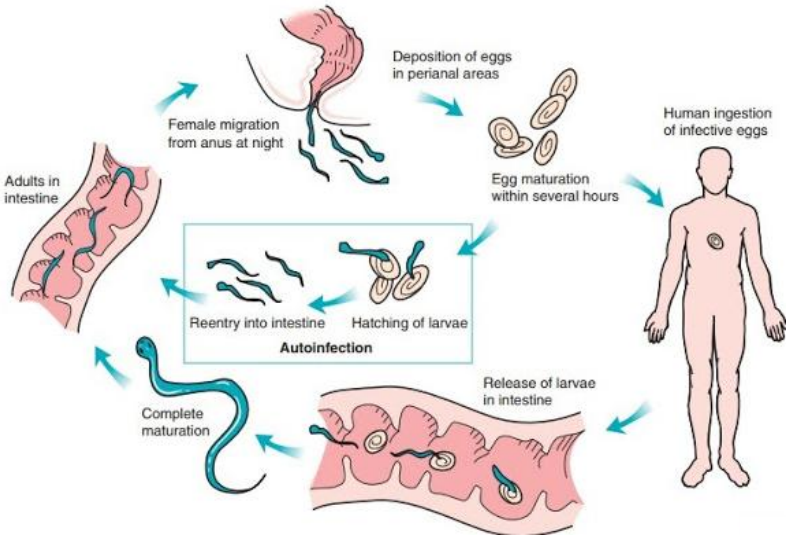

Figure 38. Life cycle of *Enterobius vermicularis*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Worm eggs are rarely found in faeces so conventional coprological examination techniques are not used. Instead, infections are best diagnosed by the macroscopic detection of adult worms or the microscopic detection of eggs on the perineum. Motile worms may be seen on perianal skin glistening under bright light when close visual examinations are conducted during the night or early in the morning. Adult worms may sometimes be observed on the surface of fresh stool samples. Alternatively, sticky-tape may be quickly applied to the perianal skin first thing in the morning and then stuck onto a glass slide for microscopic examination of adherent eggs (aptly-named perianal sticky-tape test). Parents of infected children should be trained to collect appropriate samples to respect patient rights and privacy (especially involving minors) and alleviate any shame or embarrassment.

Treatment and control. Anthelmintic treatment for pin-worm infections is readily available from most pharmacies. The drug of choice is mebendazole, although albendazole, levamisole and pyrantel pamoate are also effective. Piperazine has been used for many years but requires a longer course of treatment. Treatment should be repeated after about 10 days to kill any newly-acquired worms. It is advisable to institute whole group treatment where appropriate, so that other group, cohort or family members do not continue to act as sources of infection. To avoid constant re-infection, it is imperative that strict personal hygienic precautions are introduced, particularly frequent hand-washing. Household decontamination is difficult as infective eggs can survive for many days in cool moist house dust and for a few days on toys or furniture. Nonetheless, clothes, bed linen and towels should be laundered in hot water, dusty areas should be well vacuumed and potentially contaminated surfaces should be cleaned. While the eggs are very resistant to many disinfectants, they are susceptible to desiccation in dry conditions.

3.12. DRACUNCULUS MEDINENSIS

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Nemathelminthes (nematodes).
- Secernentea (Phasmidea) (with chemoreceptors known as phasmids).

- Camallanida (copepod intermediate hosts).
- Dracunculoidea (weakly-developed buccal cavity, large guinea worms).

Family Dracunculidae

These worms include some of the largest known nematodes, several species measuring up to 80 cm long. They have heteroxenous (two-host) life-cycles involving vertebrate definitive hosts (in which tissue-dwelling worms develop) ingesting aquatic copepodid intermediate hosts (in which infective larvae develop). Female worms do not lay eggs but birth live larvae (ovoviviparous). Infections in humans cause painful blisters through which larvae are released. Infections have been described throughout human history; the iconic 'staff-with-serpent' adopted as the official symbol of medicine may depict the traditional means of worm removal by winding it onto a stick.

DRACUNCULUS MEDINENSIS [this species causes dracunculiasis in humans]

Parasite morphology. Guinea-worms develop through four larval stages prior to the formation of large adult worms; eggs are not produced. First-stage larvae appear as thin white tubular stages measuring up to 400 μm in length and having a rhabditiform pharynx. The third-stage larvae are longer, measuring up to 600 μm in length, and they have a filariform pharynx. Adult worms exhibit marked sexual dimorphism; males measuring from 2-4 cm in length with unequal spicules, while creamy-white females grow up to 80cm in length by 2 mm in width and contain thousands of embryos. In young females, the vulva is located around the midbody but it becomes atrophied and non-functional in adults, as does the intestine due to the high internal pressure generated by the gravid uterus. Although the worms are very long and thin, they are not true filarial worms and are grouped separately.

Host range. Infections of humans by *D. medinensis* have been recorded many times in history, being described as 'little snakes' by Greek and Roman scholars, 'fiery serpents' in Biblical texts (Numbers 21:4-8), and colloquially named Medina-worms, guinea-worms or dragon-worms. Infections occur throughout semi-desert areas of sub-Saharan Africa, India, the Middle-East and Brazil, mainly in rural areas where water is drawn from wells or shallow ponds during

the rainy season. It has been estimated that the prevalence of infections has decreased markedly (from 15 million in 1980 to 4 million in 1986 and 60,000 in 1997) due mainly to systematic preventive campaigns fostered by the World Health Organization. *D. medinensis* infections have occasionally been reported in dogs, cats, cattle, horses and other mammals.

Site of infection. Ingested infective larvae penetrate the gut and invade subcutaneous connective tissues, migrating mainly to the axillary and inguinal regions. Maturing female worms migrate from deep connective tissues to peripheral subsurface locations, particularly in the extremities of limbs (legs and arms) although they can occur elsewhere.

Pathogenesis. Despite their eventual enormous size, infections by guinea-worms usually do not produce any clinical signs until the mature female worms migrate to the skin and provoke the formation of a papule then a blister. Migration may sometimes produce vague allergic reactions, including nausea, dizziness, diarrhoea, rash and local oedema. Infections generally produce two types of lesions: subcutaneous or deep abscesses around dead worms (involving many inflammatory cell types) that tend to calcify; or cutaneous papules which rapidly become blisters through which females release live larvae. Skin lesions may involve local erythema, urticaria, inflammation, ulceration and intense burning pain (fiery serpent of biblical times). Patients seek to relieve symptoms by immersing the affected region in cool water. Lesions are initiated by the deposition of larvae in the tissues and the induction of hypersensitivity reactions which ultimately produce blisters through which larvae, and parts of the adult worm, emerge (a unique means for tissue-dwelling parasites to seek egress from their hosts). In uncomplicated cases, lesions may only last for several weeks until the worm is completely expelled. However, many cases involve secondary bacterial infection of the worm track with persistence of the lesion, chronic ulceration and possible sequelae, involving disseminated infections, phlegma of limbs, contractures of tendons, fibrous ankylosis or arthritis in the joints, or even tetanus.

Mode of transmission. The parasites have a unique indirect life-cycle, involving copepods (Cyclops, water fleas) as intermediate hosts. Adult female worms cause skin blisters which eventually rup-

ture, thus releasing any larvae deposited in the tissues and also exposing the anterior portion of the adult worm. The exposed portion may rupture, or the gravid uterus may prolapse from the worm. Muscular contractions of the body wall force thousands of larvae out in periodic spurts (half a million per day); the contractions often being instigated by contact with water. Females usually die within 2–6 weeks of penetrating the skin. Liberated larvae are infective for less than a week and they actively move about in water attracting copepodid crustaceans which ingest them. Copepods breed best in standing waters such as ponds and open wells, so infections are common in remote rural areas reliant on such water supplies. The larvae penetrate into the haemocoel of the copepods, especially dorsal to the gut, and develop into infective third-stage larvae over 12–15 days (at 25 °C). Humans become infected by swallowing infected copepods with drinking water. The infective larvae penetrate the intestinal wall and migrate for about 3 months through connective tissues where male and female worms develop and mate. The males die after mating, while the fertilized females migrate to subcutaneous sites and grow to essentially become non-feeding bags full of larvae. Gravid females begin to emerge from the skin around 10–14 months after infection (fig. 39).

Figure 39. Life cycle of *Dracunculus medinensis*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Differential diagnosis. Infections become obvious once a blister forms and part of the female worm emerges. Milky clouds of larvae can also be seen under low magnification when the lesion is placed in water. Immunoserological tests have been developed to detect host antibodies formed against parasite antigens during the pre-patent period of infection.

Treatment and control. The traditional means of curing infections involves the slow extraction of worms by winding them onto a stick a few centimetres a day for several weeks. Excessive force should not be used to avoid breaking the worm and complicating lesions and reactions. Surgical removal may be successful when worms are restricted to superficial sites, but can be difficult when worms are threaded through tendons or deep fascia. Preventive measures involve breaking the cycle of transmission by reducing contamination of water supplies and eliminating copepod hosts. Public education programmes have been developed to discourage infected persons from entering ponds or wells to collect drinking water or to bath. Local water supplies can be treated with temephos (Abate, cyanamid) which kills copepods for several weeks. Drinking water can also be purified by boiling or filtering through fine-meshed cloth (<0.15 mm). The World Health Organization has accredited the global decline in the prevalence of infections to the adoption of many of these simple preventive measures.

3.13. WUCHERERIA BANCROFTI

[this species causes Lymphatic filariasis – Elephantiasis in humans]

Lymphatic filariasis is a parasitic disease caused by thread-like worms called *Wuchereria bancrofti*. The parasite is carried from person to person by mosquitoes. 120 million people are infected in subtropical and tropical Asia (mostly in India), Africa, the Pacific and the Americas (mostly in Brazil, Haiti, Guyana and the Dominican Republic). Lymphatic filariasis is the leading cause of permanent disability worldwide. Out of the 120 million more than 30% are severely incapacitated by the disease. Over one billion people in over 80 countries are at risk of getting infected.

The **life cycle** of *Wuchereria bancrofti* starts, when a male and a female mate inside lymphatic vessels of an infected human. The fe-

male releases thousands of microfilariae (prelarval eggs) into the bloodstream. When the host is awake, the microfilariae tend to stay in deep blood vessels. During the sleep they travel near the surface in peripheral blood vessels. This behaviour enables them to get ingested by the night biting mosquito. When ingested by the mosquito, the microfilariae migrate through the wall of the proventriculus and cardiac portion of the midgut eventually reaching the thoracic muscles. Within 1–2 weeks they mature into first-stage larvae and eventually into infective third-stage larvae which migrate through the hemocoel to the mosquito's prosbocis. When the mosquito bites another person, the larvae are injected into the human skin. They migrate to the lymph vessels and mature into adults within six months. Adult females can live up to seven years (fig. 40).

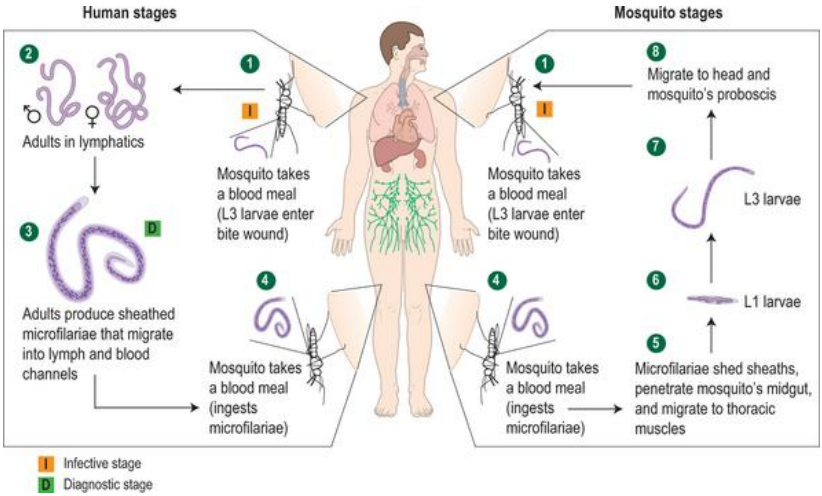

Figure 40. Life cycle of *Wuchereria bancrofti*
[https://www.tuyenlab.net/2016/09/parasitology-atlas-of-diagnostic]

Morphology. Adult female *Wuchereria bancrofti* is about 80–100 mm long and 0.24–0.30 mm in diameter, whereas a male is about 40 mm long and 0.1 mm in diameter. A microfilaria is about 240–300 μm (micrometers) long and 7.5–10 μm thick. It is sheathed and has nocturnal periodicity, except the South Pacific microfilaria which does not have marked periodicity. It has a gently curved body,

and a tail that is tapered to a point. The nuclear column (the cells that constitute its body) is loosely packed. The cells can be seen individually under a microscope and do not extend to the tip of the tail. A mosquito is the intermediate host and carrier. The most common vectors/carriers are: *Anopheles* species in Africa; *Culex* species in the Americas; *Mansonia* and *Aedes* species in the Pacific and in Asia.

Pahogenesis. Repeated mosquito bites during several months are usually needed to develop lymphatic filariasis. In some cases, lymphedema (swollen tissue caused by obstruction of the lymph fluid) may develop within six months and elephantiasis within a year. Citizens of tropical and subtropical areas have the biggest risk whereas tourists have a very low risk. *Wuchereria bancrofti* infection is usually asymptomatic. Some people can develop lymphedema, swelling, which is prevalent in the legs, but sometimes also in the arms, genitalia and breasts. The swelling and decreased flow of the lymph fluid will expose the body to skin and lymph system infections. Over time the disease causes thickening and hardening of the skin, a condition called elephantiasis which can be fatal. Filarial infection might also cause pulmonary tropical eosinophilia syndrome, which is mostly found in patients living in Asia. Pulmonary tropical eosinophilia syndrome can cause: cough, shortness of breath, and wheezing. In addition to eosinophilia there might be high levels of IgE (Immunoglobulin E) and antifilarial antibodies.

Diagnosis for lymphatic filariasis is traditionally done from a blood sample by microscopic examination. The sample has to be taken during the night to ensure the microfilariae are present in the bloodstream. The blood can also be studied to check for the presence of antibodies (antifilarial IgG4) that the human body develops to fight against antigens excreted by adult female *Wuchereria bancrofti* worms. A new method of a highly sensitive "card test" has been developed to detect antigens without laboratory equipment using finger-prick blood droplets taken anytime of the day. Molecular diagnosis by polymerase chain reaction (PCR) is possible, too.

Treatment and control. For infected patients is usually done using a drug called diethylcarbamazine (DEC). The medicine kills the microfilariae in the bloodstream and sometimes adult worms in the lymph vessels. It has some side effects which include: dizziness, fever, headache, nausea and muscle and joint pain. DEC should only be

used, if *Wuchereria bancrofti* has been identified. This is because most people with lymphedema are not infected with parasites. DEC can worsen In some cases, lymphedema can be prevented from getting worse by exercising the swollen leg or arm to improve the lymph flow. The swollen skin is vulnerable to bacterial infections because immune defences cannot work properly due to the impaired flow of fluids. That is why the skin must be kept clean.

To **prevent** new infections, avoid infective mosquitoes between dusk and dawn (the time when they mostly feed). A mosquito net can be applied all around your bed. Mosquito repellent applied on your skin or the use of long trousers and sleeves might keep the mosquitoes away. Mass treatments are given to whole communities in some endemic countries. Programs to eliminate lymphatic filariasis in more than forty countries are decreasing the risk of infection.

3.14. TRICHNELLA SPIRALIS

[this species causes Trichinellosis in humans]

Trichnella spiralis is a nematode parasite of humans that is cosmopolitan in its geographical distribution. It is nearly unique among helminthic parasites in that all stages of development occur within a single host; over 100 species of mammals have been reported to be susceptible to infection. The infective encysted larvae may remain viable in the host's musculature for many years; they may also survive long periods in decaying and putrefying muscle. *Trichnella spiralis* causes trichinellosis, a zoonotic infection in human. Humans are infected when parasite-infected meat (port in most in-stances) is ingested.

Tidemann in Germany and Peacock and Owen in London first discovered the encysted larval stage of *Trichinella spiralis* in the muscles of an infected man.

Morphology. The adult worms are very small and slender with slightly tapered anterior ends, white and just visible to the naked eye. The male measures 1.4~1.6 mm in length and 0.04~0.05 mm in diameter. The female size is 3~4 × 0.06 mm. Its pharynx is one third or half of worm body long, and posterior part of pharynx consists of a column of cells called of stichocytes. The reproductive system of both sex worm is single tract, and the single uterus is fille d with developing

eggs in its posterior portion, whereas the anterior portion contains fully developed, hatched juveniles or larva. The cyst is found in skeletal muscle commonly, its size is about 0.25~0.5 × 0.21~0.42 mm. Usually, there is more than one larvae in a cyst (fig. 41).

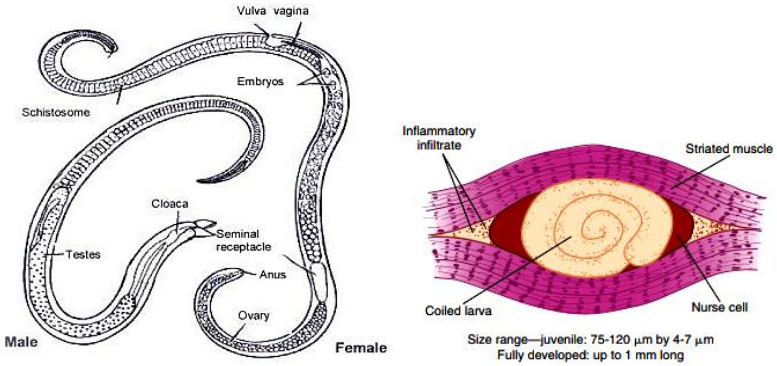

Figure 41. Morphology of *Trichinella spiralis*
[http://www.wormbook. Trichinella/genomesTrichinella]

Life cycle. All stages of development occur within a single host such humans, pigs, dogs, rats and cats etc. Adult worms reside in small intestine, and larvae reside in skeletal muscle. However, two different hosts are required to complete the life cycle. Primary host: Pig is the primary host. Natural host: rodents, carnivores and various other species of omnivorous animals are the other natural hosts. Man is an accidental host and is the dead end for the parasite. When man consumes raw or rare flesh infected with cysts of Trichnella, the cysts are digested out of the muscle in the stomach; the larvae are resistant to gastric juice. After passage to the small intestine, the larvae penetrate the villi of the small intestine, molt, and develop into mature adult within 48 hours. After fertilization, the gravid female burrow deep into the mucosa, discharging larvae beginning 5 to 46 days after infection and continuing for 2 to 4 weeks or occasionally longer. Widely disseminated via lymphatics and the bloodstream, larvae enter most organs, but persist only in individual skeletal muscle fibers. Increasing almost ten-fold in size over succeeding weeks, larvae gradually become surrounded by a cyst wall of muscle. Although the capsules calcify within six months to two years, the larvae within remain viable for months to years, rarely for decades (fig. 42).

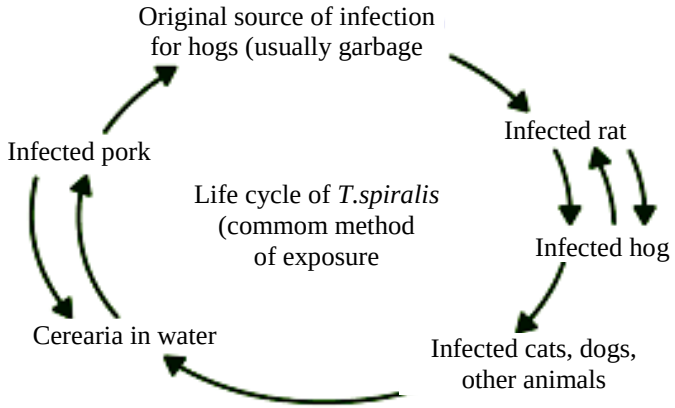

Figure 42. Life cycle of *Trichnella spiralis*
[http://www.wormbook. Trichinella/genomesTrichinella]

Pathogenesis. Adult worm and both migratory and encysted larvae are pathogenic. Adult female worms present in the intestine cause gastrointestinal disturbances; migrating larvae cause various allergic manifestation such as fever, oedema of the face, eosinophilia, and encysted larvae in the skeletal muscles cause muscular pain. The process of pathological change can be divided three phases. The phase occurs within the first week after ingestion of infected meat, during the intestinal phase; this phase is associated with the development of larvae develop into adult. For invading of larvae and adult worms, the wall of intestine is damaged. Microscopic ulceration, mucosal hyperemia, localized edema, punctate hemorrhages, and intestinal inflammation may main pathological changes. Gastrointestinal signs and symptoms includ fever, disgusting, vomiting, abdominal discomfort, diarrhea etc. Migratory phase (7-9 days after exposure) is associated with penetration of the newborn larvae into muscle cells, initiating a strong inflammatory response. Later, the fibers enlarge, and edema, nuclear proliferation, and intestinal inflammation ensue, and fibrosis. Early symptoms of this stage are swelling of the eyelids and facial edema. Following this, muscle swelling, tenderness, pain on movement, and fever usually develop. Encystation of the larvae andtissue repair. The formation of cyst result in the stimulation of larvae and tissue reparation. With encystation, the in-

flammation disappears gradually, the clinical manifestation become light, but the muscular pain can still last for months.

Diagnosis of Trichinosis depends on a combination of clinical manifestations with a history of ingesting meat that may contain larvae; immunodiagnosis; muscle biopsy.

Prevention, treatment and control. Deep freezing at -15 °C for 20 days or -30 °C for 6 days and thorough cooking at 70 °C for above kills the larvae in the pork. Smoking, curing or drying of meet are not dependable methods for killing the larvae. Regular inspection of meat, avoidance of eating raw or undercooked pork and meat of other wild animals; and avoidance of feeding raw garbage to pigs will prevent transmission of infection to man. Treatment of the immature worms in the small intestine is usually successful and will abort or markedly inhibit systemic disease, so treatment of the intestinal phase in all cases up to six weeks after infection is advisable. Albendazole is the effective drug for trichinellosis. Mebendazole is also recommended, it is believing to kill both adult worms and larvae.

4. ARTHROPOD PARASITES

Arthropods form a huge assemblage of small coelomate animals with "jointed limbs" (hence the name arthro-pods). They exhibit segmentation of their bodies (metamerism) which is often masked in adults because their 10–25 body segments are combined into 2–3 functional groups (called tagmata). They exhibit varying degrees of cephalization whereby neural elements, sensory receptors and feeding structures are concentrated in the head region. Arthropods possess a rigid cuticular exoskeleton consisting mainly of tanned proteins and chitin. The exoskeleton is usually hard, insoluble, virtually indigestible and impregnated with calcium salts or covered with wax. The exoskeleton provides physical and physiological protection and serves as a place for muscle attachment. Skeletal plates are joined by flexible articular membranes and the joints are hinges or pivots made from chondyles and sockets.

Biodiversity

The main arthropod assemblages include crustaceans (crabs, lobsters, crayfish, shrimp), arachnids (spiders, scorpions, ticks, mites) and insects (beetles, bugs, earwigs, ants, bees, termites, butterflies, moths, crickets, roaches, fleas, flies, mosquitoes, lice). Most parasitic arthropods belong to 2 main classes: the 6-legged insects, and the 8-legged arachnids.

- Insects have 3 distinct body parts, commonly called the head, thorax and abdomen. The head has 2 antennae and the thorax has 6 legs arranged in 3 bilateral pairs. Many insect species also have 2 pairs of wings attached to the thorax. Parasitic insect species include fleas, flies and lice which actively feed on host tissues and fluids at some stage in their life-cycles.
- Arachnids have 2 body parts known as the prosoma (or cephalothorax) and opisthosoma (or abdomen). The cephalothorax has 8 legs arranged in 4 bilateral pairs and arachnids do not have wings or antennae. Important parasitic assemblages include the ticks and mites which bite into tissues and feed off host fluid.

Collectively, arthropods account for a substantial share of global biodiversity, both in terms of species richness and relative abundance. There are over 1,000,000 species of insects and over 50,000 species of arachnids. They are very successful and adaptable organisms and are capable of forming large populations due to their rapid

and fertile reproduction rates. Many species are also able to withstand adverse environmental conditions by undergoing periods of developmental arrest (diapause). The protection afforded by their exoskeletons allows them to colonize many habitats and they overcome the problem of growing larger in a non-expandable exoskeleton by undergoing periodic moulting (or ecdysis) which is mediated by hormones. Developmental stages between moults are referred to as instars. Moulting is a complex process and its timing is mediated by many environmental and physiological cues. It involves detachment of the hypodermis from the procuticle, partial resorption of the old cuticle, production of a new epicuticle, dehiscence (splitting) of the old cuticle, emergence of the animal, stretching and expansion of the new cuticle by air and/or water intake, and then sclerotization of the new cuticle.

Life cycles. Adult arthropods are generally small in size; most are visible but some remain microscopic. Arthropod sexes are separate and fertilization is internal. A wide range of mating behaviours, insemination and egg production strategies are involved. In most species, the egg develops into a larva: i.e. a life cycle stage that is structurally distinct from the adult and must undergo metamorphosis (structural reorganization) before becoming an adult. This metamorphosis may be complete (involving major changes during a pupation stage) or incomplete (involving gradual changes in nymph stages). For example, the grub-like larval stages of flies and fleas form cocoon-like pupae where they undergo complete metamorphosis and emerge as radically-different adult insects. In contrast, the larval instars (or nymphs) of lice, ticks and mites undergo incomplete metamorphosis through a series of moults gradually becoming more adult-like in appearance.

Arthropods are involved in nearly every kind of parasitic relationship, either as parasites themselves or as hosts/vectors for other micro-organisms (including viruses, bacteria, protozoa and helminths). They are generally ectoparasitic on, or in, the skin of vertebrate hosts. Many species are haematophagous (suck blood) while others are histophagous (tissue-feeders) and bite or burrow in dermal tissues causing trauma, inflammation and hypersensitivity reactions. Infestations are transmitted from host-to-host either by direct contact or by free-living larvae or adults actively seeking hosts.

- Direct transmission of infective stages occurs when hosts come into close contact with each other or share quarters, bedding or clothing. Larvae, nymphs or adults may cross from one host to another, while eggs or pupae may contaminate shared environments. Insects (fleas and lice) and arachnids (mites) rely on close contact between hosts.
- Many adult insects actively seek hosts in order to feed or lay eggs. Winged insects (mosquitoes, flies) fly to new hosts to feed while fleas jump onto passing hosts. Some adult flies (botflies) do not feed on their hosts but deposit eggs from which larvae emerge and feed on host tissues and exudates.
- Tick larvae actively seek hosts by climbing vegetation and questing for passing hosts. Some species complete their life cycle on the same host (one-host ticks) while others detach after feeding and drop to the ground to moult before seeking new hosts as nymphs or adults (two-host or three-host ticks).

Taxonomic overview

Insects exhibit extraordinary biodiversity, both in terms of species richness (numbers of species) and relative abundance (population sizes). Most parasitic species belong to three main groups: the jumping fleas (*Siphonaptera*); the winged flies (*Diptera*); and the wingless lice (*Phthiraptera*).

- Fleas are bilaterally-flattened wingless insects with enlarged hindlimbs specially adapted for jumping (up to 100 times their body length). Jumping feats are accomplished using elastic resilin pads which expand explosively when uncocked from the compressed state. Fleas undergo complete metamorphosis whereby grub-like larvae form pupae from which adult fleas emerge. The larvae are not parasitic but feed on debris associated mainly with bedding, den or nest material, whereas the adult stages are parasitic and feed on host blood. There are some 2,500 flea species, most parasitic on mammals (especially rodents) and some on birds. They vary in the time spent on their hosts ranging from transient feeders (rodent fleas) to permanent attachment (sticktight fleas and burrowing chigoes).
- Flies and mosquitoes are winged insects with two pairs of wings attached to the thorax and a well-developed head with sensory and feeding organs. They undergo complete metamorphosis involving a pupation stage. Different species vary in their feeding habits,

both as adults (parasitic or free-living) and larvae (parasitic or free-living). There are over 120,000 species belonging to 140 families. Two main suborders are recognized on the basis of structural differences, Nematocera (adult stages parasitic, larval stages often free-swimming) and Brachycera (adult stages parasitic or free-living, larvae stages often predaceous).

- Lice are small wingless insects, dorsoventrally flattened, with reduced or no eyes and enlarged tarsal claws for clinging. All lice undergo gradual metamorphosis and there are no free-living stages. Eggs are cemented to hair/feathers whereas nymphs and adults cling to hair/feathers. Two orders of lice are recognized on the basis of their mouthparts: the Mallophaga (chewing/biting lice) with some 3,000 species infesting birds and mammals; and the Anoplura (sucking lice) with 500 species found on mammals.
- Ticks are epidermal parasites of terrestrial vertebrates that may cause anaemia, dermatosis, paralysis, otoacariasis and other infections (transmit viral, bacterial, rickettsial, spirochaete, protozoal and helminth pathogens). They feed mainly on blood and their mouthparts are armed with small backward-facing teeth to aid in attachment. All ticks undergo gradual/incomplete metamorphosis whereby larval and nymphal instars resemble adults. The integument is relatively thick and respiration occurs via spiracles (usually only one pair) and trachea. Two major families of ticks are recognized on the basis of many morphological features: the Ixodidae (hard ticks with a tough cuticle and a large anterodorsal scutum) with some 650 species that infest mammals, birds and reptiles; and the Argasidae (soft ticks with a leathery integument and no scutum) with 160 species that infest mainly birds and some mammals.
- Mites are microscopic arachnids which undergo gradual or incomplete metamorphosis. Adults and nymphs have 4 pairs of legs whereas larvae have 3 pairs. Over 30,000 species of mites have been described, many are free-living species, some are plant parasites while others are parasitic on terrestrial and aquatic hosts. Most parasitic species feed on skin debris or suck lymph, some burrow into the skin, some live in hair follicles, and some in the ear canals. Their mouthparts are variable in form but the hypostome is never armed with teeth. The integument is usually thin and three orders are recognized on the basis of their respiratory systems: the Mesostigmata

with respiratory spiracles (stigmata) near the third coxae; the Prostigmata (Trombidiformes) with spiracles between the chelicerae or on the dorsal hysterosoma; and the Astigmata (Sarcoptiformes) without tracheal systems as they respire through the tegument.

4.1. IXODES

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Arthropoda (arthropods, segmented body, exoskeleton, jointed appendages).
- Chelicerata (2 body parts, 8 legs, first mouthparts chelicerae, no antennae, wingless).
- Arachnida (abdomen without appendages).
- Acari (ticks and mites, ectoparasites).

Family Ixodidae

Ticks are obligate blood-sucking ectoparasites with two body parts and eight legs. Ixodid (hard) ticks have a characteristic hard cuticle, a terminal capitulum which can be seen in dorsal view and a large shield-shaped plate (scutum). Ticks undergo incomplete metamorphosis whereby eggs hatch larvae which moult to nymphs and then adults. Male and female ticks exhibit marked size and/or colour differences, with males generally being smaller and plainer. Eggs are laid on the ground and emergent larvae (seed ticks) quest for hosts upon which to feed. All ticks have specific life-cycles involving one, two or three hosts depending on whether moulting occurs on or off the host. Some 650 species of hard ticks infest mammals, birds and reptiles. Three species are of particular medical and/or veterinary importance in Australia: the scrub or paralysis tick Ixodes holocyclus, the cattle tick Rhipicephalus (Boophilus) microplus and the brown dog tick Rhipicephalus sanguineus.

IXODES HOLOCYCLUS [this species causes tick paralysis in humans and companion animals]

Parasite morphology. Ticks form four developmental stages; eggs, larvae, nymphs and adults. Eggs appear as small brown ovoid bodies (<0.5 mm long) clustered together in large masses. The small emergent larvae (<1 mm long) have six legs, whereas the larger nymphs (<2 mm long) and adults (2–3 mm long) have eight legs.

Engorging females swell markedly in size and become dark blood-filled sacs (measuring up to 1–2 cm in diameter). Ticks have two body parts: a small inconspicuous anterior gnathosoma (containing sensory palps, feeding chelicerae and a barbed hypostome); and a large posterior sac-like idiosoma (to which the legs are attached anteroventral). They have a hard chitinous covering (scutum) covering the whole dorsal surface of adult male ticks but only the anterior idiosoma of larvae, nymphs and adult female ticks. Ixodids are prostriata ticks where the anal groove is located in front of the anus. Adult I. holocyclus ticks are inornate without notches (festoons) or pigmented 'eyes' on the scutum (fig. 43).

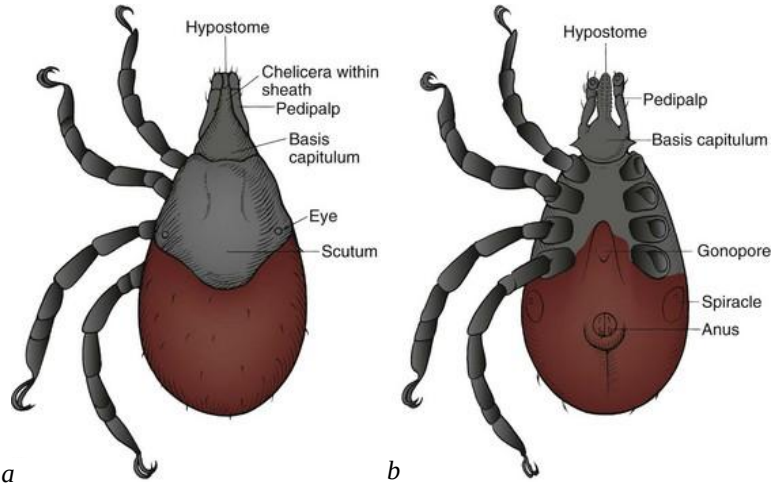

Figure 43. Morphological features of ticks (family *Ixodidae*):
a – dorsal aspect; *b* – ventral surface
[https://www.researchgate.net/figure/Anatomy-of-a-hard-tick-Ixodidae]

Host range. The genus Ixodes contains over 200 species of 3-host ticks which are ectoparasitic on small mammals. Ticks are often named after a particular host (e.g. dog tick) but they are generally not host-specific, but rather host-preferential, attempting to feed on many passing animal species. The paralysis tick, *I. holocyclus*, is found along the east coast on a range of native animal species, especially bandicoots which appear to be resistant or immune to any toxic effects. The ticks, however, can infest a range of domestic animals

(dogs, cats, lambs, foals) and humans, all being more susceptible to toxic sequalae. In America, I. pacificus and I. dammini from rodents, deer and other wildlife act as vectors for Lyme disease (caused by the spirochaete *Borrelia burgdorfi*).

Site of infection. Larval, nymphal and adult ticks are obligate but transient ectoparasites that attach to the skin of their hosts. Most species have preferred (predilection) sites of attachment on different hosts, often involving cryptic areas among skin folds which are difficult for hosts to groom. Ticks on humans often move to the head behind the ears, or attach to the skin under tight-fitting clothing (such as elasticized waist-bands). Infestations on animals generally involve the head, neck, back and groin (fig. 44).

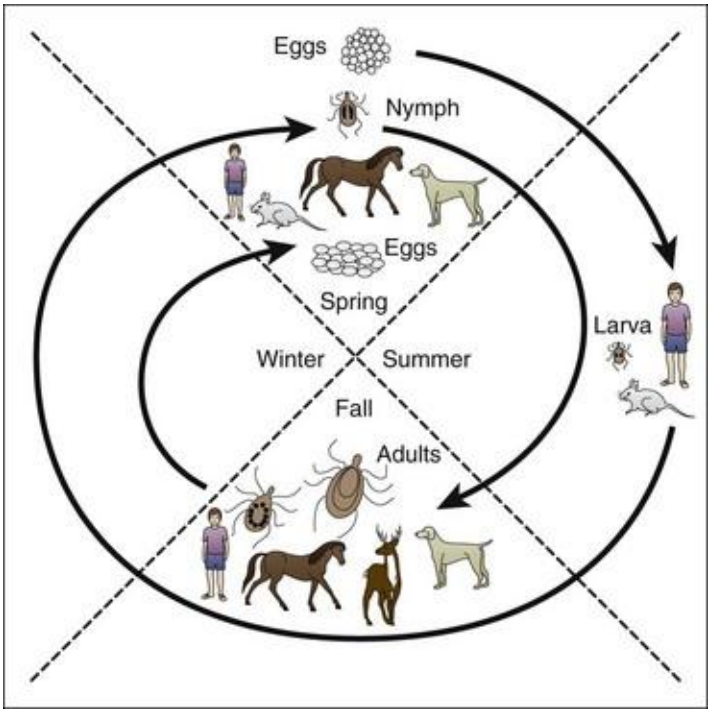

Figure 44. Life cycle of Ticks Family *Ixodidae*
[https://www.researchgate.net/figure/
Anatomy-of-a-hard-tick-Ixodidae]Pathogenesis]

Pathogenesis. Mouthparts of feeding ticks are embedded in the host forming a tubular food channel through which saliva is injected and blood is ingested. Ticks are relatively long-lived, feeding periodically and taking large blood meals. Tick bites cause irritation, inflammation, hypersensitivity, and even anaemia when present in large numbers. Local reactions to bites vary considerably, although small granulomatous reactions consisting of mixed inflammatory cells with fibrosis are common. Infestation of humans and domestic animals by toxin-producing species, such as *I. holocyclus*, can result in ascending motor paralysis due to neurotoxic anticoagulants released by engorging females. Clinical signs may appear within 3 days of attachment, first paralysing the legs, then the arms and finally the thorax and throat. Death can result from respiratory failure unless the tick is removed. Tick bites often become infected, especially when ticks are forcibly removed leaving their mouthparts embedded in the skin. Many tick species also transmit viral, bacterial, rickettsial, and protozoan diseases of medical and veterinary importance.

Mode of transmission. Ticks actively seek hosts, not by pursuing them but by sedentary questing; i.e., climbing vegetation and waiting for hosts to brush past. Ticks are prone to desiccation so they quest more actively when hydrated, and return to humid ground level when dehydrated. Once contact is made with a host, the ticks migrate to suitable or preferred sites of attachment. For three-host tick species, larvae, nymphs and adults all feed on different hosts. Blood feeding takes from 3-10 days after which they drop from the host and moult to the next developmental stage or lay eggs. Time spent off the host may be as long as one year for each developmental stage so the entire life cycle may take up to three or more years. Each female tick can lay several thousand eggs leading to heavy contamination of the environment by larval stages (‘seed’ or ‘pepper’ ticks).

Differential diagnosis. Infestations are detected by visual detection of feeding stages attached to the skin, especially large engorging females. Evidence of recent infestation may be seen at predilection sites as small inflamed nodules. Differential diagnosis is performed by removing ticks and examining them microscopically for species-specific morphotypic characters.

Treatment and control. Individual ticks attached to hosts can be physically removed, preferably by sliding fine forceps under their mouth parts and then exerting gentle backwards pressure until the tick lets go. Excessive force should not be used to avoid squeezing tick contents into the wound as well as to avoid tearing the mouthparts out leaving them behind. Tick removal may be aided by wiping the attached tick with oil or dabbing it with chloroform. A variety of treatment and control strategies have been developed for tick infestations of domestic animals but their efficacy is diminished in many instances by the persistence of ticks on wildlife reservoirs, especially in areas where wildlife and domestic stock constantly intermingle. Many native animal species are genetically resistant to heavy tick infestations. This is being exploited in cross-breeding programs e.g. Bos indicus cattle are tick-resistant whereas Bos taurus cattle are susceptible. More recently, several experimental vaccination programmes have been developed whereby tick gut antigens are used to stimulate protective antibody responses against feeding ticks. Various acaricides have proven effective for treatment when used as dips, sprays pour-ons or slow-release ear-tags. Domestic animals have been treated successfully with topical organophosphates (dichlorvos, cythoate, diazinon, malathion, fenthion, propetamphos, phormet) and pyrethroids (permethrin, deltamethrin), as well as with parenteral macrocyclic lactones or closantel. Companion animals may be treated with topical acaricides, such as fipronil, imidacloprid, selamectin, amitraz and the organophosphates. However, there are growing concerns about the development of resistance to acaricides in some tick populations. Many states and countries have adopted legislature which restricts stock movement into and from endemic areas and facilitates appropriate quarantine. Various management strategies (such as pasture rotation or spelling, cultivation or burning pastures) have also been used to minimize the transmission of infestations and reduce tick burdens on pastures.

4.2. PEDICULUS

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Arthropoda (arthropods, segmented body, exoskeleton, jointed appendages).
- Uniramia (with antennae, first mouthparts mandibles).
- Insecta (insects, 3 body parts, 6 legs, many with wings).
- Anoplura (sucking lice, wingless, ectoparasites, incomplete metamorphosis).

Family Peliculidae

Lice are small wingless dorsoventrally flattened insects with three body parts, head, thorax and abdomen. The head has two antennae and the thorax has six legs arranged in three bilateral pairs. All lice undergo gradual metamorphosis and there are no free-living stages. Eggs are cemented to host hairs whereas nymphs and adults cling to hairs using enlarged tarsal claws. Over 500 species of sucking lice parasitize mammals. The sucking mouthparts are retracted in the narrow head when not feeding. The mouthparts are introduced directly into host blood vessel (solenophage mode of feeding).

PEDICULUS CAPITUS, Human lice [this species causes head lice infestation in humans]

Parasite morphology. Head lice form three developmental stages: eggs, nymphs and adults. Eggs (commonly called nits) appear as white ellipsoidal operculate bodies (0.8 × 0.3 mm) which are glued to hair shafts. Nymphs are similar in appearance to adults, but are smaller measuring 1–2 mm in length. Adult lice have elongate dorsoventrally flattened bodies (2–4 mm long) which appear opaque although darker internal organs can be seen mainly in the abdomen. Head lice are known colloquially as cooties, greybacks, or mechanized dandruff (fig. 45).

Host range. P. capitus is highly host-specific for humans and will not infest other animals. Some authorities regard head lice as a unique species (*P. capitus*) while others consider it to be a subspecies (*P. humanus capitus*) closely related to body lice (P. humanus corporis). Only body lice colonies can be bred in the laboratory after their adaptation to feeding on rabbits. Body lice are 2–4 mm in size and spends most of the time in host clothing. Their life

cycle is completed in 2–4 weeks. Eggs attached to fibres in clothes hatch in 7 days and there are 3 nymphal moults taking 8–9 days. Pubic lice (or 'crabs') are also found on humans. These lice belong to a separate species (*Phthirus pubis*) which have grasping tarsi reminiscent of crab pincers. Infections are not confined to the pubic region, but may also involve the armpits, beard, moustache, eyebrows and eyelashes. The lice remain in position for some time with mouthparts inserted in skin and the bites cause intense pruritus. The life cycle is completed in less than 1 month and infestations are transmitted mainly venereally, but can be passive especially in crowded situations.

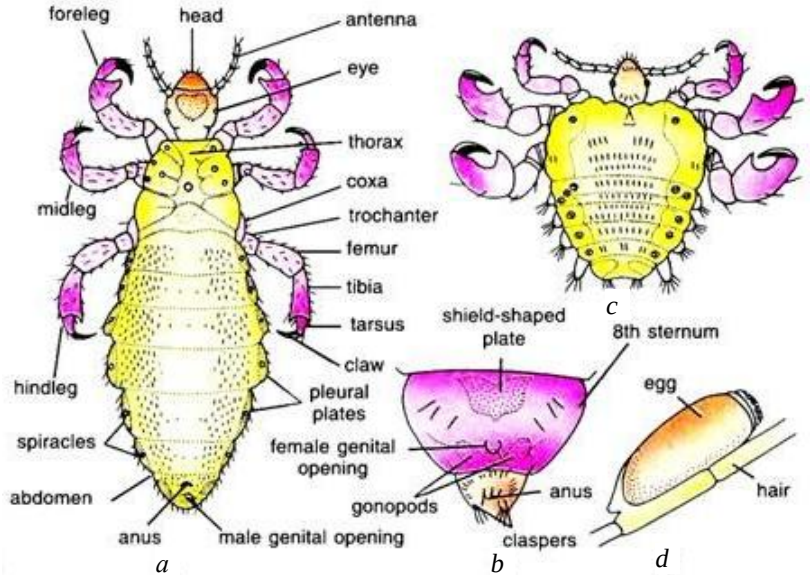

Figure 45. Morphology of human lice:
a – Human head louse; *b* – posterior end of the female head-louse;
c – Human pubic louse; *d* – egg or nit
[https://extension.entm.purdue.edu/publichealth/insects/louse]

Site of infection. All developmental stages of head lice can be found attached to, or grasping, hairs on the head, especially at the back of the neck and behind the ears. They are highly site-specific

and head lice transplanted to other body regions attempt to migrate back to the head.

Pathogenesis. Nymphs and adults of both sexes feed by piercing the skin and sucking blood about every 2–3 hours. Light infestations may only cause moderate itching of the scalp exacerbated by sensitization to louse saliva. Heavy infestations, however, may cause considerable discomfort as the bites produce red papules, fever, aches and intense pruritus which induces scratching leading to dermatitis and secondary infections. Heavy louse infestation is known as pediculosis and is often associated with crowded conditions and poor sanitation.

Mode of transmission. Once hatched, head lice undergo gradual metamorphosis whereby nymphs moult several times before forming adults. No free-living stages are formed and lice do not survive long off their hosts. Infestations are therefore transmitted between hosts by direct physical contact, although some transmission via contaminated clothing or bedding cannot be entirely dismissed. The complete life cycle takes 2-3 weeks, and louse populations often exhibit pronounced seasonal fluctuations, apparently linked to crowding during winter housing, particularly in temperate regions. Female head lice lay around 90 eggs which are cemented singly onto hair shafts.

Differential diagnosis. Infestations are diagnosed by finding live lice or empty eggs shells in the hair either by direct visual examination or using a fine-toothed nit comb (using hair conditioner to untangle hairs and trap lice).

Treatment and control. Many insecticides (e.g. malathion, carbamyl and pyrethrins) can be used to control lice and they are available in many hair care products (shampoos or lotions). Repeat washing are required within 10 days as most insecticides have limited activity against eggs. Over recent years, mounting problems with insecticide resistance have been encountered, and researchers are currently exploring herbal remedies. During infestations, daily grooming with nit combs is recommended to remove eggs and lice. Some countries still enforce home quarantine of infested school-children to curtail outbreaks. Inter-personnel hygiene must be improved and clothing and bedding should be well laundered.

4.3. SARCOPTES

Classification:

- Metazoa (Animalia) (multicellular eukaryotes, animals).
- Arthropoda (arthropods, segmented body, exoskeleton, jointed appendages).
- Chelicerata (2 body parts, 8 legs, first mouthparts chelicerae, no antennae, wingless).
- Arachnida (abdomen without appendages).
- Acari (ticks and mites, ectoparasites).
- Astigmata (Sarcoptiformes) (without tracheal system, respire through tegument).

Family Sarcoptidae

Mites are small wingless arachnids with two body parts, eight legs and no antennae. Astigmatid mites are weakly sclerotized, lack stigmata and tracheae and respiration occurs directly through the tegument. They include many species of medical and veterinary significance and cause skin conditions known as mange, scab and scabies. Sarcoptid mites burrow in the skin of their hosts and lack claws but have suckers at the ends of their legs. They undergo incomplete metamorphosis whereby eggs hatch larvae which transform to nymphs and then adults. All feeding stages are parasitic and infestations are transmitted directly between hosts by contact.

SARCOPTES SCABEI [this species causes scabies in humans]

Parasite morphology. Mites form four developmental stages: eggs, larvae, nymphs and adults. The eggs are oval and large compared to the size of the adult mites (about half their length). Emergent larvae have three pairs of legs but undergo metamorphosis to form nymphs then adults which have four pairs (pairs 3 and 4 do not project beyond the body margin). These developmental stages are variable in size but successively become larger. Adult female mites are the largest (0.3–0.6 mm long) while adult males are smaller (up to 3 mm long). They have circular bodies which are flattened ventrally and covered with fine transverse striations. They have two body parts, the anterior gnathosoma bearing specialized feeding structures including palps and chelicerae, and the posterior idiosoma bearing the legs and elongate sensory setae (fig. 46).

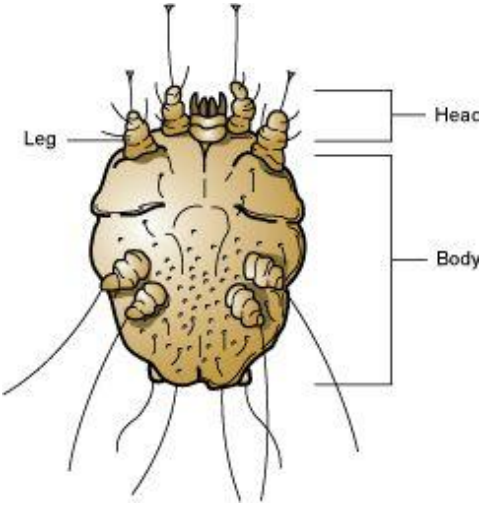

Figure 46. Morphology of *Sarcoptes*
[https://extension.entm.purdue.edu/publichealth/insects]

Host range. Sarcoptes scabiei (scabies/sarcoptic mange mites) are minute skin parasites of homiotherms throughout the world. Different subspecies are found on different mammals and are responsible for causing mange in animals and scabies in humans. Although the cross-transmission potential of many subspecies has not been established, zoonotic transmission is thought to occur although such infestations do not appear to become permanently established on humans.

Site of infection. Sarcoptid mites are ectoparasitic and live on the skin of their hosts where the females burrow to lay their eggs. Infestations can occur anywhere on the body, but are more common in areas where the skin is thin and wrinkled, such as between the fingers, toes and genitals of humans, and the ears, muzzle and face of animals.

Pathogenesis. Infestation by mites is known as acariasis and can produce severe dermatitis. Nymphs and males do not burrow, but females form long tortuous tunnels in the horny layer of skin, depositing eggs and faeces, causing intense itching and rashes. Burrows may be 2–3 cm in length and may be excavated at up to 5 mm per day. Mites reproduce on their hosts so infestations can become progressively worse without further exposure. Common signs are papular eruptions with erythema, pruritis and alopecia. The scabies itch takes 6–8 weeks

to appear after the patient becomes sensitized, and is characteristically noctural and aggravated by warmth. As infestations progress, the skin becomes thickened and crusted with exudates. Septic pustules due to secondary infections are common in severe infestations, particularly when hosts scratch causing traumatic damage. A rash is sometimes evident around the waist, buttocks, wrists or ankles due to cell-mediated immune reactions. In immunocompromised patients, extensive thickening and crusting of the skin may occur.

Mode of transmission. Mites spend most of their lives in intimate contact with their hosts, so transmission between hosts is mainly by direct physical contact. Female mites lay 1–3 eggs per day and they mature within 4 days. Emergent larvae moult 2–3 days later to form nymphs which then moult several times over several days before forming adults. Larvae and nymphs move out of the burrows and find food and shelter in hair follicles. Adults feed and mate on the surface, the males die and the fertilized females start burrowing. The entire life cycle is usually completed within 3 weeks but can take as little as 12 days under the right conditions. Epidemics of scabies occur in human populations in 20–30 year cycles or in times or famine or war. However, mites are common in poor communities with inadequate washing facilities (fig. 47).

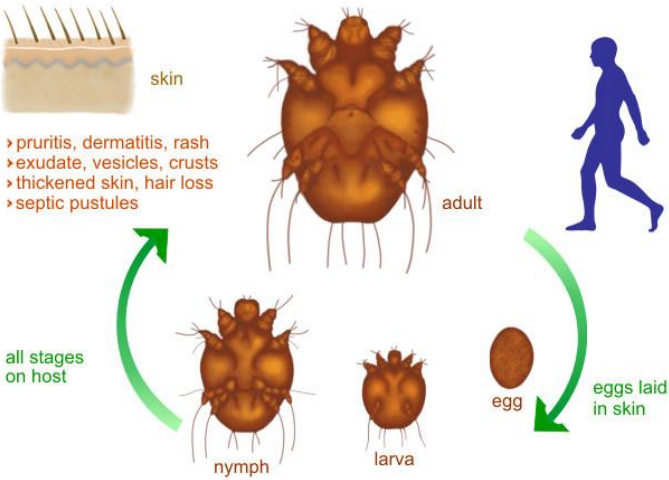

Figure 47. Life cycle of *Sarcoptes scabiei*
[https://extension.entm.purdue.edu/publichealth/insects]

Differential diagnosis. Confirmation of suspect infestations is generally done by microscopic examination of skin scrapings or by wiping black ink over affected areas to reveal burrows.

Treatment and control. Scabies responds to whole body treatment from the neck down with acaricides, such as malathion, gamma benzene hexachloride, benzyl benzoate or crotamiton for infants. Many formulations contain surfactants which serve to soften crusts and remove skin scales. Hair can also be clipped from affected areas and the skin cleaned with anti-seborrhoeic shampoos prior to acaricide treatment. Lime-sulphur dips have also been used at 10 day intervals for treating dogs and cats. Treatments should be repeated weekly for several weeks to ensure newly emergent mites are killed. Infested animals should be isolated or treatments extended to animals in close proximity. Corticosteroids can also be used in severely distressed animals to reduce pruritis and prevent further excoriation.

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