

1

Animal associations

1.1 Introduction

In this introductory chapter we will introduce the concept of parasitism as a lifestyle and explain why it is such a difficult term to define. We shall also introduce some of the terms that are commonly used by parasitologists. Like all branches of science, parasitology has a number of associated specialist terms such as 'intermediate host', 'definitive host' and 'zoonosis' that need to be understood before it is possible to make sense of the literature. We will explain why the study of parasites is so important and why parasites are likely to remain a problem for many decades to come. We will end by introducing the study of taxonomy because this will help inform the chapters on specific groups of organisms as well as the chapters on diagnosis, treatment, and control. Taxonomy is nowadays something of a Cinderella subject among biologists but it cannot be ignored because scientists must agree on the names things are to be called if they are to communicate with one another.

1.2 Animal associations

All animals are in constant interaction with other organisms. These interactions can be divided into two basic types: *intra-specific interactions* and *inter-specific interactions*.

Intra-specific interactions are those that occur between organisms of the same species. They range between relatively loose associations such as those between members of a flock of sheep, to highly complex interactions such as those seen in colonial invertebrates (e.g. Bryozoans and some of the Cnidaria (jellyfish and sea anemones)). For example, the adult (medusa) stage of certain jellyfish may appear to be a single organism but it is actually composed of colonies of genetically identical but polymorphic individuals. These colonies divide labour between themselves in a similar manner to that of organ systems within a non-colonial organism, for example, some colonies are specialised for reproduction while others are specialised for feeding.

Inter-specific interactions are those that take place between different species of organism (Figure 1.1). As with intra-specific interactions, the degree of association can vary between being extremely loose to highly complex. Odum (1959) classified these interactions on the basis of their effect on population growth using the codes '+' = positive effect, '-' = negative effect, and '0' = no effect. This leads to six possible combinations (00, 0-, 0+, etc.) and these too can be broken down into further subdivisions (Toft *et al.*, 1993). Some authors also include a consideration of the direction and extent of any physiological and biochemical interactions between the two



Figure 1.1 Different species will occasionally co-operate for mutual benefit

organisms. A wide range of terms have been suggested in an attempt to compartmentalise these interactions (e.g. phoresis, mutualism, predation) but these are merely convenient tags and they cannot be defined absolutely. This is because the variety of organism interactions is extremely broad and even within a single interaction there are a host of variables such as the relative health of the two organisms that determine the consequences of the interaction for them both. It is therefore not surprising that there is a multiplicity of definitions in the scientific literature and it is not unusual for two authors to arrive at two different terms for the same type of interaction between species. In this section, we will discuss symbiosis, commensalism, phoresis, mutualism and finally parasitism, with some examples of each.

1.2.1 Symbiosis

The term symbiosis is usually translated as ‘living together’ and is derived from the Greek *syn* meaning ‘with’ and *biosis* meaning ‘life’. It was originally used in 1879 by Heinrich Anton de Barry to define a relationship of ‘any two organisms living in close association, commonly one living in or on the body of the other’. According to this original definition, symbiosis covers an extremely wide range of relationships. Some authors state that both organisms in a symbiotic relationship benefit from the association (i.e. it is [++]) although this is clearly a much more restrictive definition and it is more appropriately referred to as mutualism. However, some authors state that symbiosis and mutualism are synonymous – this only adds to the confusion. For the purposes of this book we will keep to de Barry’s original definition.

Symbionts Strictly speaking, a ‘symbiont’ is any organism involved in a symbiotic relationship. However, the vast majority of scientists tend to restrict the term to an organism that lives within

1.2 ANIMAL ASSOCIATIONS

3

or upon another organism and provides it with some form of benefit – usually nutritional. The association is therefore referred to as a host: symbiont relationship and the majority of symbionts are microorganisms such as bacteria, algae or protozoa. Where the symbiont occurs within the body of its host, it is referred to as an endosymbiont, while those attached to the outside are referred to as ectosymbionts. Two types of endosymbiont are recognised: primary endosymbionts (or ‘p-endosymbionts’) and secondary endosymbionts. Primary endosymbionts form obligate relationships with their host and are the product of many millions of years of co-evolution. They are usually contained within specialised cells and are transferred vertically from mother to offspring. As a consequence, they undergo co-speciation with their host and form very close host-specific relationships. By contrast, secondary endosymbionts are thought to be the product of more recent host: symbiont associations and, in the case of insects, the symbionts are contained within the haemolymph (blood) rather than specialised cells or organs. Secondary endosymbionts tend to be transmitted horizontally and therefore do not show the same close host: symbiont relationship. It is not known how endosymbionts begin their association with their hosts but some authors suggest that they arise from pathogens that attenuated over time. The suggestion that a parasite–host relationship tends to start off acrimoniously and then mellow with time was once widespread in the literature, but while this may sometimes occur, it is not a foregone conclusion.

The importance of symbionts to blood-feeding organisms Although blood contains proteins, sugars and lipids as well as a variety of micronutrients and minerals, it lacks the complete range of substances most organisms require to sustain life and to reproduce. Consequently, many of the animals which derive most or all of their nutrition from feeding on blood (haematophagy) have evolved symbiotic relationships with a variety of bacteria that provide the missing substances, such as the B group of vitamins. The need for supplementary nutrients is particularly acute in blood-sucking lice (sub-order Anoplura) because they have lost the ability to lyse (break up) red blood cells and therefore many nutrients will remain locked within these cells. In many cases, the bacteria are held within special cells called mycetocytes that are grouped together to form an organ called a mycetome. Although these terms appear to indicate the involvement of fungi, they originate from a time when scientists did not distinguish between the presence of yeasts and bacteria within cells. Many scientists continue to use the term ‘mycetocyte’ regardless of the nature of the symbiont but others use the term ‘bacteriocyte’ where it is known that the cells harbour only bacteria. In blood-feeding leeches belonging to the order Rhynchobdellida (there is a popular misconception that all leeches feed on blood; many of them are actually predatory), mycetomes are found surrounding or connected to the oesophagus. Mycetomes are not found in all blood-feeding leeches and in the medicinal leech, *Hirudo medicinalis*, the symbiotic bacteria are found within the lumen of the gut (Graf *et al.*, 2006). The bacteria present in *Hirudo medicinalis* have been identified as *Aeromonas veronii* (earlier work on leeches often refers to it as *Aeromonas hydrophila*), a species of bacteria that has been associated with a number of other blood-feeding organisms. *Aeromonas veronii* has also been reported as causing wound infections in humans and inducing septicaemia and gastroenteritis. (Graf, 1999). Leeches are extremely useful in modern medicine, particularly to aid wound drainage following plastic surgery, but one of the risks associated with their application is that the patient acquires an *Aeromonas* infection. These infections are often trivial but they can become serious and lead to the formation of an abscess or cellulitis (e.g. Snower *et al.*, 1989). This is a difficult problem to solve because the symbiotic bacteria are essential for the leeches.

Box 1.1 The role of symbionts in the life of tsetse flies and their transmission of trypanosome parasites

Tsetse flies, like most other blood-feeding organisms, harbour bacterial symbionts that facilitate the breakdown of the blood meal and provide essential nutrients to the fly. In the case of tsetse flies, these are principally B group vitamins, vitamin H (Biotin), folic acid and pantothenic acid and in the absence of the symbionts, the adult female fly is unable to reproduce. Tsetse flies have at least three different symbionts that are found within certain gut epithelial cells and these are passed on from the female fly to her larvae as they develop in her uterus. Of these symbionts, *Sodalis glossinidius* is thought to be the most important in influencing the establishment of trypanosomes in the tsetse fly. Tsetse flies have an effective immune system that protects them from invading micro-organisms. This includes the production of lectins that attach to and kill the invading organisms and toxic reactive oxygen species such as superoxide and hydrogen radicals (Macleod *et al.*, 2007). However, *Sodalis glossinidius* releases N-acetylglucosamine which interferes with the activity of the lectins and scavenges reactive oxygen species, thereby allowing the trypanosomes to establish. It is possible that there are differences between strains of *Sodalis glossinidius* in the production of N-acetylglucosamine and this may be (to a greater or lesser extent) the reason why there are differences in the susceptibility of tsetse flies to infection with trypanosomes.

In nymphs and adult males of the human body louse, (*Pediculus humanus*; sub-order Anoplura) intracellular symbionts are found within a mycetome that is sometimes referred to as the 'stomach disc'. This mycetome is located on the ventral side of the mid-gut but unlike the leeches mentioned above, there is no actual connection between the mycetome and the lumen of the gut (Sasaki-Fukatsu *et al.*, 2006; Perotti *et al.*, 2008). In adult female lice, the bacteria re-locate to the oviducts and the developing eggs. This is in keeping with the observation that primary endosymbionts are transmitted within the eggs (i.e. transovarially) to the offspring. The bacteria associated with *Pediculus humanus* have been identified as belonging to the gamma (γ) proteobacteria and have been given the name *Riesia pediculicola*. Interestingly, molecular phylogenetic analysis is unable to distinguish between the symbiotic bacteria isolated from human head lice (*Pediculus humanus capitis*) and human body lice (*Pediculus humanus humanus*). This adds support to phylogenetic analysis of the lice themselves (Light *et al.*, 2008) that indicates that although head lice and body lice occupy different ecological niches and body lice tend to lay their eggs on clothing while head lice attach their eggs to hair shafts, they are two morphotypes of the same species rather than two separate species. One suggestion is that the body lice evolved from head lice relatively recently in human evolution following the common practice of wearing clothing. The association between *Riesia* and *Pediculus* is estimated to be between 12.95 and 25 million years old, which makes it one of the youngest host: primary endosymbiont relationships so far recorded (Allen *et al.*, 2009). In common with other primary endosymbionts, *Riesia* has undergone a reduction in genome complexity and lost genes: this is because it has come to rely on its host for the provision of many nutrients, protection from the environment and protection from predators. In addition, because its transmission is via the eggs of its host, each louse symbiont population is in

reproductive isolation and unable to undergo recombination with other strains of *Riesia* in other lice. This has led to the suggestion that *Riesia* will lack the capacity to develop rapid resistance mechanisms to antibiotics, and because the *Riesia* is essential for the lice, killing the symbiont would result in host mortality (Perotti *et al.*, 2008).

1.2.2 Commensalism

The term ‘commensalism’ is derived from the Latin *commensalis* and means ‘at the same table together’. Most definitions indicate that one species benefits from the association and the other is unharmed (0+). The concept of ‘harm’ within any definition leads to complications because it may be difficult to measure and depends upon the circumstances. Similarly, a ‘benefit’ may not be immediately apparent and it is possible that some of the associations that are commonly cited as commensal involve a degree of benefit to both parties (++) albeit they may not benefit to the same extent. A commensal association may be ‘facultative’, in which both species are able to live independently of one another, or ‘obligatory’, in which one of the associates must live in association with its partner. For example, in many of the warmer parts of the world, the cattle egret (*Bulbulcus ibis*) is often observed riding on the back of cattle and big game from which it swoops down periodically to capture lizards and insects that are disturbed as its ride moves through the undergrowth. The egret is perfectly capable of living apart from cattle but it benefits from its mobile ‘vantage point-cum-beater’. The egrets are not thought to remove many ectoparasites from the cattle and they get their Arabic name *Abu Qerdan* ‘father of ticks’ from the large number of ticks associated with their nesting colonies. The cattle, therefore, appear to gain little from the relationship although it is likely that the egret acts as an early warning system of the approach of predators. African Cape Buffalo (*Synceros caffer*) have a good sense of smell but notoriously poor eyesight and are therefore vulnerable to predators approaching from downwind. The red-billed oxpecker (*Buphagus erythrorhynchus*) is sometimes said to have a similar commensal relationship with cattle but this is almost certainly not the case. Unlike cattle egrets, the red-billed oxpecker has an obligatory relationship with cattle and big game, and far from removing ticks, it feeds primarily on scabs and wound tissue pecked from their host. This can delay wound healing and thereby make the affected animal vulnerable to infections and infestations with blowfly larvae (Weeks, 2000).

The amoeba, *Entamoeba coli* (not to be confused with the gastrointestinal bacterium *Escherichia coli* which is also abbreviated to *E. coli*) is a common commensal that lives within the human large intestine. Unlike its highly pathogenic cousin, *Entamoeba histolytica*, *Entamoeba coli* does not invade the gut mucosa or consume red blood cells and it feeds on bacteria and gut contents. *Entamoeba coli* is of little interest *per se*, but due to its morphological similarity to *Entamoeba histolytica*, it is important to be able to distinguish between the two species in faecal samples.

1.2.3 Phoresis

This association is usually described as one in which one species provides shelter, support or transport for another organism of a different species. This interaction may be temporary or

permanent. For example, apart from the first instar, the larvae and pupae of the blackfly *Simulium neavei* attach themselves to the outer surface of freshwater crabs. The larvae feed by filtering out phytoplankton and detritus from the water and the crabs act as a suitable firm yet mobile substrate on which to attach. An appreciation of this association is important because adult *Simulium neavei* are important vectors of the *Onchocerca volvulus* – the nematode that causes the disease ‘river blindness’ (see Chapter 3).

1.2.4 Mutualism

Mutualistic (from Latin, *mutuus* meaning ‘reciprocal’) relationships are those in which both species benefit from the association in terms of their growth and survival (++)). Some authors further restrict the definition to one in which neither of the partners in the association is capable of living on their own, while others are less prescriptive. The association between *Wolbachia* bacteria and the filarial nematode, *Onchocerca volvulus*, is clearly mutualistic. The bacteria are confined to the cells of the reproductive tissues and hypodermis of the female worms. The *Wolbachia* provide metabolites which are demonstrably essential to the worms. If the bacteria are removed, for example, by exposure to the antibiotic tetracycline, the worms are unable to establish themselves in their host and grow and, in the case of adult worms, the female is rendered infertile (Taylor and Hoerauf, 1999). The bacteria are therefore a potential target for the chemotherapy of filarial nematode infections.

Whether or not the relationship between the Cnidarian *Hydra viridis* and its algal partner *Chlorella* should be considered mutualistic depends upon the strictness of one’s definition. *Hydra viridis* are capable of growing and reproducing in the absence of their algal partner but there is some debate in the literature whether the strains/species of *Chlorella* associated with *Hydra viridis* can survive independently. The algae live within vacuoles in the endodermal cells of the *Hydra* and thereby impart the *Hydra*’s characteristic green coloration. Whether this provides camouflage that is any way beneficial is not known. When the *Hydra* reproduces by budding, its algal partner is passed on to the offspring; the algae are not essential to the budding process but *Hydra viridis* seldom undergoes sexual reproduction if the algae are absent. Experiments in which the algae are removed from the *Hydra* by exposure to high light intensities (Habetha *et al.*, 2003) indicate that the nature of the relationship varies depending upon the environmental conditions. Like other *Hydra* species, *Hydra viridis* obtains its food by capturing prey on tentacles that are armed with nematocysts, while the alga carries out photosynthesis and releases the sugars maltose and glucose-6-phosphate that can potentially be used by *Hydra viridis*. If there is suitable illumination and plenty of prey for the *Hydra*, the growth of *Hydra viridis* with and without algae is similar. This indicates that the sugars released by the algae have little importance for the *Hydra*. If, however, there is illumination but no food for the *Hydra*, then those *Hydra* lacking algae die after a few weeks, while those containing algae reduce in size but are able to survive for at least three months and will feed again if presented with food. Therefore, if *Hydra viridis* is starved, then the symbiotic algae play an important role in its survival. By contrast, if *Hydra viridis* are kept in the dark but with plenty of prey available, those lacking algae grow much better than those containing them. Furthermore, the algal population declines by about 60% although they are not lost entirely and the *Hydra viridis* remain pale green. This indicates that under these conditions, the algae must be receiving nutrients from the *Hydra* to such an extent that the nature of the relationship has changed from mutualism to one akin to parasitism.

1.2.5 Parasitism

Parasitism is a surprisingly difficult term to define and there are numerous explanations in the literature. For the purposes of this book, the following definition has been used: 'Parasitism is a close relationship in which one organism, the parasite, is dependent on another organism, the host, feeding at its expense during the whole or part of its life (– +).' It is frequently a highly specific relationship that always involves a degree of metabolic dependence of the parasite upon its host and often, though not always, results in measurable harm to the host. The association is usually prolonged and although it may ultimately result in the death of the host, this is not usually the case. It is therefore distinct from predation in which a predator usually kills and consumes its prey within a short period of time. However, owing to the complexities of animal relationships, there are always 'grey areas' in which any definition starts to become unstuck. This is particularly apparent in the case of blood-feeding. Mosquitoes and tsetse flies would not be considered parasites because they only feed for a few seconds or minutes before departing; in contrast, hookworms and crab lice would be considered parasitic, because they are permanently associated with their host. Blood-feeding leeches, however, are free-living organisms that remain attached to their host for several hours while taking a blood meal; some authors consider them to be parasites while others define their feeding as a type of predation.

Box 1.2 From welcome guest to villain: the derivation of the term 'parasite'

The word 'parasite' is derived from the Greek '*para*' meaning 'beside' and '*sitos*' meaning 'food'. In Ancient Greece, the term 'parasite' had religious connotations and nothing to do with infectious organisms. According to a stone tablet in the temple of Heracles (Hercules) in Cynosarges, the priest was required to make monthly sacrifices in the presence of 'parasites' who were to be drawn from men of mixed descent. Refusal to act as a parasite would result in being charged with committing an offence. (Cynosarges was an area near to the city walls of Athens. In addition to the temple, there was also a gymnasium and it was where the Cynic philosophers gave classes.) Subsequently, the word was debased and came to mean someone who shared one's food in return for providing amusement and flattery. The '*parasitus ridiculus*' was a popular character in Greek and early Roman comedies and they even had joke books to help them should they run out of witticisms. The greed of the parasite was a constant source of fun for dramatists and he was often given crude nicknames such as 'little brush – because he swept the table clean'. Double entendres were as popular over 2000 years ago as they are today and the Latin for little brush '*peniculus*' is also a diminutive for penis (Maltby, 1999).

Some organisms are obligate parasites and at a particular stage in their life cycle they have to live as parasites of their host while others are facultative parasites and can develop as parasites or free-living organisms depending upon the circumstances they find themselves in. For example, the larvae of the warble fly *Hypoderma bovis* have to develop as parasites of cattle and are therefore obligate parasites. By contrast, the larvae of the blowfly *Lucilia sericata* are facultative parasites because they are able to develop as parasites should the eggs be laid upon a live sheep or as free-living detritivores if the eggs are laid on a dead sheep.

As mentioned above, some organisms, such as the human body louse *Pediculus humanus*, are parasitic at all stages of their life cycle, while others are only parasitic at one or more stages. For example, the blood fluke *Schistosoma haematobium* is a parasite of humans during its adult stage and of snails during two of its larval stages but it also has two non-feeding free-living stages. The act of being a parasite is therefore 'stage-specific'. Some estimates suggest that as many as 50% of all known species are parasites at some point in their life cycle. However, this estimate is subject to the caveat that there is some debate about what constitutes a species, especially among the prokaryotes. The number of species is also reflected in the interests of biologists in different groups of animals. For example, insects have been studied intensively for over 200 years and this is probably at least partly the reason why they are said to account for 72% of all known species. In one order alone, the 'species-rich' order Hymenoptera (bees, wasps), approximately 100,000 species are classed as parasitoids. By contrast, mites and nematodes have proved much less popular and the diversity of their parasitic species is probably vastly underestimated. Nevertheless, parasitism is a remarkably common lifestyle and parasites (and their hosts) have been described from all the major groups of living organisms including the Archaea, Bacteria, Fungi, Plantae, Protozoa, invertebrates and vertebrates. There is some debate as to whether viruses should be considered to be parasitic organisms. At one level, this would appear to be self-evident since viruses are incapable of maintaining themselves or reproducing except when within their host cell. However, being composed of complex organic molecules and having the capacity to evolve is not necessarily synonymous with being a living entity, especially when those attributes are dependent upon existing within a host cell. The arguments against viruses being alive are discussed in detail by Moreira and López-García (2009). In this book, we will mainly consider parasitic helminths (flatworms and nematodes), arthropods and protozoa. The relationships between parasites in these groups and their hosts have been extensively studied and some of them have a major impact on our health and that of our domestic animals.

1.2.6 Intra-specific parasites

Although most parasitic relationships involve two different species of animals, it is not unknown for intra-specific parasitism to take place. This is most often associated with adaptations to sexual reproduction in which the male attaches to the female and becomes dependent upon her for the provision of nutrients. For example, in certain deep-sea angler fish belonging to the suborder Ceratioidea, the larval fish develop in the upper 30 metres of sea water and then gradually descend to deeper regions as they metamorphose into adults. The adolescent males have a very different morphology to the females: they are much smaller, they have larger eyes and in some species they develop a large nasal organ that is presumably involved in their search for females. Furthermore, the males cease feeding and rely upon reserves laid down in their liver during the larval period to fuel their swimming. Upon finding a suitable female, the male grasps onto her using special tooth-like bones that develop at the tips of his jaws (his actual teeth degenerate during metamorphosis). Once he has attached, the male grows (although he remains much smaller than his consort) and his testes mature. His skin and blood vessels fuse with hers at the site of attachment and he remains attached for the rest of his life and draws all his nourishment from her. Some authors suggest that the male must find a virgin female but although most females carry only a single male, there are records of females with three or more males attached to them. This is presumably an adaptation to life in the deep-sea regions in which the opportunity to locate suitable mates is limited. It does,

however, beg the question of how sexual selection takes place because it is unusual in nature for a female to mate with just one male for life, especially if that male is the first one to turn up. This type of relationship is not found in all ceratioid anglerfish; in some species the males are facultative parasites rather than obligate ones as described in the above scenario, while in other species the males are free-living, capable of capturing their own food, and form only temporary attachments to females. Molecular evidence suggests that the development of the parasitic males is a variable phenomenon among anglerfish and has evolved and subsequently become lost on several occasions (Shedlock *et al.*, 2003; Pietsch, 2005).

1.2.7 Parasitoids

The term parasitoid is restricted to certain parasitic insects whose hosts are almost exclusively other insects – although a few species attack certain crustacea, spiders, millipedes, centipedes and earthworms. Some parasites cause mortality and may even depend on the death of their host to effect transmission to the next stage of their life cycle, but host death is not inevitable. By contrast, parasitoids slowly consume their host's tissues over a period of time so that the host remains alive until the parasitoid has completed its development. At this point the host dies either through the loss of vital tissues or through the parasitoid physically eating its way out of its host. Parasitoids are all parasitic during their larval stage and the adult insect is free-living and feeds on nectar, pollen or is predatory, depending upon the species. Parasitoids can develop as endoparasites within their host or as ectoparasites attached to the outside but with their mouthparts buried deep within the host's body. The larva has only the one host in or on which it develops and those that are endoparasites tend to exhibit the most host specificity. This lifestyle is therefore distinct from those insects such as warble flies (e.g. *Hypoderma bovis*) and bot flies (e.g. *Gasterophilus intestinalis*) which exhibit a more 'traditional' parasitic way of life that does not inevitably result in the death of the host. Many of the order Hymenoptera (bees, ants, wasps) are parasitoids and it is also a common lifestyle among the Diptera (true flies) but it is absent or very rare among the other orders. By contrast, most of the insect orders are hosts to parasitoids. Hyperparasitism is also common in which a parasitoid parasitises another species of parasitoid. Parasitoids are effective for the control of agricultural pests, particularly within closed environments such as greenhouses. However, they have had limited success as control agents for parasites, their vectors, or intermediate hosts.

The parasitoid lifecycle typically begins with the adult female locating a suitable host and either injecting one or more eggs into the host or attaching them to the outer surface. Sometimes she also injects a toxin that temporarily or permanently disables her victim. The host is chosen on the basis of its stage of development which may be anywhere from the egg to the adult stage.

Box 1.3 Parasitoid: virus interactions

A number of endoparasitic wasps belonging to the families Icheumonidae and Braconidae have a fascinating relationship with certain polydnviruses. The viruses replicate within the calyx cells of the wasps' ovaries and are secreted into the oviducts. When a wasp injects her eggs into a suitable host, usually a caterpillar, the virus is transmitted as well. The viruses are unable to

replicate within the caterpillar but they can invade several cell types within which they integrate into the genome and cause the expression of substances that facilitate the establishment of the parasitoid. For example, one of the main immune responses that insects express in response to an invader is encapsulation (see Chapter 6). Encapsulation first depends upon the invader being recognised, and then a co-ordinated response occurs, during the course of which the invader is surrounded by amoeboid-like cells present in the haemolymph and then killed through the production of toxic chemicals and/or lack of oxygen, or the invader is physically isolated and therefore unable to damage the host. Wasp eggs that are implanted into suitable hosts without the virus are quickly encapsulated and killed. It is thought that the virus may cause the caterpillar to express protein tyrosine phosphatases and thereby interfere with the encapsulation process. Protein tyrosine phosphatases dephosphorylate the tyrosine residues of a number of regulatory proteins and are therefore closely involved in the regulation of signal transduction. Altering the levels of regulatory proteins makes it impossible for the host to develop an effective immune response and the parasitoid egg is able to develop unmolested. The viruses also have other effects on the parasitoid's host including preventing its further development once it reaches the stage at which the parasitoid is to emerge. The polydnaviruses therefore have a mutualist-like relationship with the parasitoid within which they replicate. They are vertically transmitted as an endogenous 'provirus' that is integrated into the wasp genome but has a pathogenic relationship with the parasitoid's host, within which it is unable to replicate (Webb *et al.*, 2006). Not all wasp parasitoids have relationships with viruses but they are still capable of causing similar disruption to the host immune response and host development through the injection of toxins. This has led some authors to suggest that the polydnaviruses found in the Ichneumonidae and Braconidae may have evolved from wasp genes. Many workers, however, think that the two wasp families, probably independently, evolved relationships with existing viruses (Dupas *et al.*, 2008; Espagne *et al.*, 2004).

1.2.8 The concept of harm

The term 'harm' is often used when describing interactions between organisms but is particularly pertinent to the description of parasitism. Unfortunately, harm is a difficult term to define and is not always easy to measure. For example, parasites are usually much smaller than their host and a single parasite may have such a minor impact that it cannot be measured in terms of its effect on the physiology and well-being of the host. By contrast, a large number of the same parasite could lead to serious illness or even death. Similarly, a low parasite burden may have little impact upon a healthy, well-nourished adult host but the same number of parasites infecting an unhealthy, starving young host may prove fatal. A common analogy is that a single glass of water will not harm you and may even do you good, but the rapid consumption of a thousand glasses of water would kill you. Does that mean that water is beneficial or poisonous? Clearly, it can be both and, likewise, harm is dependent upon the context in which it is being considered. It is therefore not a good idea to make the ability to record measurable harm a prerequisite for the classification of the relationship between two organisms. Indeed, it is now recognised that, in certain instances, low levels of parasitic infection may actually be beneficial to the well-being of the host (Weinstock *et al.*, 2004). Nevertheless, many parasites have the capacity to cause morbidity, that is, a diseased

state, and some may cause mortality (death). The possible beneficial consequences of low parasite burdens will be discussed in more detail in Chapter 8.

The morbidity that parasite infections induce is often reflected in a reduction in the host's fitness as measured in terms of its growth or reproductive output. This is often attributed to the direct pathogenic effect of the parasite, such as through the loss of blood and the destruction of tissues or competition for resources (e.g. gut parasites feeding on nutrients in the intestine). However, in reality, the situation is far more complicated than this. Although a functional immune system is crucial to an organism being able to protect itself against pathogens, they are energetically costly and these costs often have to be traded off against other physiological processes. Ilmonen *et al.* (2000) demonstrated this by injecting one group of breeding female pied flycatchers (*Ficedula hypoleuca*) with a diphtheria-tetanus vaccine and a control group with a saline solution. The vaccine was not pathogenic and did not induce an infection but it did cause the activation of the birds' immune system. They found that the birds injected with the vaccine exhibited a lower feeding effort, invested less in self-maintenance and had a lower reproductive output, as determined by fledgling quality and number. The authors therefore concluded that the energetic consequences of activating the immune system can be sufficient to reduce the host's breeding success.

1.3 Parasite hosts

'Parasite host' is the term used to define the organism on or in which the parasite attaches and from which it derives its nutrition. The host is usually not related taxonomically to the parasite although this is not always the case (see intra-specific parasites). Most parasites are highly host-specific and only infect one host species or a group of closely related species. This is due to the complex adaptations the parasite is required to evolve in order to identify, invade and survive within their host. For example, the nematode *Ascaris suum* is primarily a parasite of pigs while *Ascaris lumbricoides* is primarily a parasite of humans. A few parasite species, however, are able to exploit a wide range of hosts. For example, the protozoan parasite *Toxoplasma gondii* is capable of infecting, growing and asexually reproducing in virtually all warm-blooded vertebrates although sexual reproduction only takes place within the small intestine of cats.

1.3.1 Protozoa and helminths as hosts

Parasites can be infected by viruses although there is limited published information on how these affect their biology. Viruses have been identified in many parasitic protozoa, such as *Entamoeba histolytica* (Mattern *et al.*, 1974) and *Giardia lamblia* (Wang and Wang, 1986), and it would be surprising if they were not common in helminth parasites. Parasites are also infected by prokaryotic (e.g. bacteria) and eukaryotic (e.g. fungi, and protozoa) parasites. Those parasites that infect other parasites are known as hyperparasites. For example, the microsporidian *Nosema helminthorum* is parasitic on the tapeworm *Moniezia expansa* that lives within the small intestine of sheep and goats (Canning and Gunn, 1984). The infective cysts of *Nosema helminthorum* must therefore first be consumed by a sheep and then come into contact with and penetrate the tegument (tapeworms lack a gut of their own) of the tapeworm. Within the tapeworm, *Nosema helminthorum* reproduces and causes numerous raised opaque bleb-like patches but is not thought to be especially

pathogenic. Related microsporidia affect a range of other platyhelminth parasites (Canning, 1975) but there are remarkably few reports of them infecting parasitic nematodes (e.g. Kudo and Hetherington, 1922). The discovery of microsporidia infecting the free-living nematode *Caenorhabditis elegans* (Hodgkin and Partridge, 2008; Troemel *et al.*, 2008) has opened up the potential of developing a laboratory model for studying both nematode immunity and the biology of microsporidia. This is because *Caenorhabditis elegans* is a commonly used model organism whose full genome has been sequenced. Microsporidia cause a number of pathogenic infections in humans and domestic animals and a simple laboratory model would prove extremely useful, for example, in the development of drug treatments.

1.3.2 Classes of hosts for parasites

Hosts can be divided into classes, depending upon the role they play in the parasite's life cycle. The 'definitive' (or final) host is the one in, or on, which the parasite reaches maturity and undergoes sexual reproduction, while the 'intermediate' host is the one in which the parasite undergoes its developmental stage(s). There may be just one or several intermediate hosts and the parasite may or may not undergo asexual reproduction during this time but it cannot develop into an adult or reproduce sexually. In this way, a parasite can exploit its hosts to maximum effect by combining the reproductive power of asexual reproduction in the larval stage with the advantages of sexual reproduction during the adult stage.

Parasites are able to concentrate more of their energies on reproduction than free-living animals would, since they do not have to worry about food, shelter and fluctuations in environmental conditions. This is important because the chances of any offspring locating and establishing themselves within a suitable host are very low. The completion of the parasite's life cycle is sometimes dependent upon the death of the intermediate host, leading to consumption of the larval form by the definitive host. In this situation, the parasite is often very pathogenic in its intermediate host but has relatively minor effects on the definitive host. The intermediate host is not always killed or consumed by the definitive host. For example, after undergoing asexual reproduction in the snail intermediate host, the cercariae of the liver fluke *Fasciola hepatica* physically and chemically bore their way out and swim off to transform into metacercaria attached to aquatic vegetation. The snail survives the damage to its tissues and the lifecycle is completed when the metacercariae are consumed by the sheep definitive host.

A paratenic host is one that a parasite invades and is able to survive within but where it is unable to undergo further development. Paratenic hosts are not usually essential for a parasite to complete its life cycle although they may provide a useful bridge between the infective stage/intermediate host and definitive host. For example, the definitive hosts of the nematode *Capillaria hepatica* are primarily rodents, though a range of other mammals, including humans, can be infected. Human infections are rare, but potentially fatal. The adult worms reside in the liver and the eggs they produce remain there until the definitive host dies or is consumed by a predator. Although the definitive host is infected by ingesting the eggs, these do not embryonate while in the liver and therefore consuming egg-infested liver does not lead to an infection. Instead, the eggs pass through the gut then pass out with the faeces and ultimately embryonate to the infective stage in the soil. Alternatively, if the definitive host dies naturally, the liver decomposes and the eggs reach the soil where they embryonate. Infective embryonated eggs of *Capillaria hepatica* have been described from earthworms, which would ingest them while feeding on soil and detritus, and as many

rodents will consume earthworms, it is thought that the worms act as a paratenic host facilitating the transfer of the infection to the definitive host.

1.4 The co-evolution of parasites and their hosts

Evolution can be defined as a change in gene frequency between generations, but in order for this to occur, three criteria need to be met. First, there must be genetic variation within the population. If the population is genetically homogeneous, then variation can only occur sporadically through random mutation. The second criterion is that the variation must be heritable: if the variation cannot be passed on to offspring, then it will be lost regardless of the benefits it imparts. The third and final criterion is that the variation must influence the probability of leaving reproductively viable offspring. If the variation imparts benefits, then the organism possessing it would be expected to leave more offspring; however, unless these are reproductively viable, the variation would be quickly lost from the gene pool. Parasites live in close association with their hosts and the two organisms will co-evolve. The nature of the host: parasite relationship may therefore change with time. For example, provided the above three criteria are met, the host can be expected to evolve resistance/susceptibility factors depending upon the pressure exerted by the parasite. Although ever greater resistance to infection may appear to be 'ideal', this is unlikely to arise if the energetic cost impacts on the ability to leave viable offspring. At the same time, the parasite can be expected to evolve virulence/avirulence factors.

Box 1.4 Parasites in the fossil record

Most parasites lack the sort of hard structural features that would ensure their preservation in the fossil record. It is therefore impossible to be sure whether parasitism has always been such a common 'lifestyle'. Conway Morris (1981) suggested that a survey of the commensals, symbionts and parasites of those organisms that have remained apparently unchanged for millions of years (the so-called 'living fossils') might reveal unusual organisms and provide insights into animal associations but an in-depth study still needs to be done. For example, horseshoe crabs (Phylum Chelicerata, Subclass Merostomata) have existed almost unchanged for hundreds of millions of years. There is little published information on their parasites although flatworms of the family Bdellouridae are found only in association with horseshoe crabs (Lauer and Fried, 1977).

Copepod ectoparasites that are morphologically similar to those in existence today have been identified attached to fossil teleost fish dating to the Lower Cretaceous (Cressey and Boxshall, 1989). Evidence of nematode parasites is largely restricted to those infecting insects that became trapped in amber (Poinar, 1984). Helminth eggs can be identified in coprolites (fossilised faeces) but while there have been extensive studies on animal and human faeces found in archaeological sites (Sianto *et al.*, 2009), there is less data on coprolites dating back millions of years. As with any faecal analysis, one has to remember that the presence of an organism within faeces may not be a consequence of parasitism but result from passage through the gut following accidental consumption (e.g. eggs of a parasite of another animal) or invasion of faeces after it was deposited (e.g. eggs of a detritivore). Where animals were preserved in special circumstances, such

as being rapidly mummified under desiccating conditions or frozen in tundra, it is possible to identify soft-bodied parasites with greater accuracy. For example, nematodes and botfly larvae can be identified from woolly mammoths that died thousands of years ago on the Siberian tundra (e.g. Grunin, 1973; Kosintsev *et al.*, 2010).

Sometimes the presence of parasites is inferred from the pathology they cause (e.g. Lukševics *et al.*, 2009). For example, the pearls found in mussels and oysters often form as a consequence of infection by trematode parasites. Pearls thought have been caused by trematode parasites have been identified in fossil mussels dating back to the Triassic era (250–200 million years ago) (Newton, 1908; Brown, 1940). Dinosaurs almost certainly had their full complement of parasites although their evidence is sadly lacking from the fossil record. However, marks found on the bones of the dinosaur *Tyrannosaurus rex* are thought to resemble the pathology caused by the protozoan parasite of birds *Trichomonas gallinae* (Wolff *et al.*, 2009). Poinar and Poinar (2008) have even suggested that parasites were a major factor in the ultimate extinction of the dinosaurs.

1.4.1 Evolutionary relationships between host and parasite

It is often stated that the longer a parasite and its host have been living in association, the less pathology is caused. This is based on the reasoning that if the parasite kills its host, then it will effectively ‘commit suicide’ because it will have destroyed its food supply. Consequently, over time, it is to be expected that the parasite will become less harmful to its host – that is, it becomes less virulent. However, this assumption has been questioned because a pathogen’s virulence is often a reflection of its reproductive success. For example, let us consider two hypothetical strains of the same nematode species, A and B, that lives in the gut of sheep. Strain A is highly virulent and causes the death of the sheep while strain B is relatively benign and seldom causes any mortality. At first glance, one might expect that strain B would leave more offspring because its host lives for longer. However, if virulence was linked to the nematode’s reproductive output and the eggs were released at a time when they were likely to infect new hosts, then it would be strain A that would bequeath more of its genes to subsequent generations. Consequently, the proportion of strain A in the nematode population would be expected to increase with time and there would be constant selection for ever increasing virulence. The sheep and the parasites may eventually be driven to extinction by these changes but no animal alive, including humans, gives any indication of being able to plan wisely for the future.

The hypothetical scenario described above naturally begs the question of, if this is true, why does life still exist today? This is because, on this basis, parasites and other pathogens should have killed everything off many millions of years ago. The answer is that the scenario is too simplistic and all host: parasite or pathogen relationships involve a complex array of competing factors. Consequently, the evolutionary end-point of any relationship is very case-dependent. Sometimes the parasite becomes more virulent, and sometimes its virulence attenuates to an intermediate level but one cannot assume that the natural end-point is a mutually beneficial form of mutualism. Indeed, the relationship between a parasite and its host is often likened to a ‘co-evolutionary arms race’ in which the parasites attempt to acquire more resources from the host in order to produce their offspring while the host evolves mechanisms for reducing its losses and eliminating the

parasite. This has given rise to the ecological theory known as the Red Queen's Race. The name is derived from the Red Queen in Lewis Carroll's *Alice Through the Looking Glass* who says, 'Now, here, you see, it takes all the running you can do, to keep in the same place' (Ladle, 1992).

Parasites and other pathogens are generally smaller than their hosts and reproduce faster. Consequently, they might be expected to win any arms race because of their ability to select for adaptations that overcome any new measure the host is able to generate that limits the parasite's acquisition of host metabolites. However, hosts that are comparatively long-lived usually have sophisticated immune systems that are able to identify and kill or neutralise new parasite variants. The host is therefore not a constant environment for the parasite. Parasite virulence is also affected by the mode of transmission. Horizontally transmitted parasites, especially those with a wide host range, can 'afford' to be highly virulent because there are lots of potential hosts and if one or more of them dies, it has no direct consequences. However, when the parasite is vertically transmitted (e.g. via the eggs of its host or across the placenta), there is a direct link between the effect of the parasite on its host and its own reproductive success. For example, if the parasite is so virulent that it kills the female host before it can reproduce, then the virulent parasite's genes will not be transmitted. Similarly, if it kills the host's eggs while they are *in utero* or reduces the number of host eggs that are produced or survive to become adults and reproduce themselves, then the parasite is compromising its own reproduction. It is therefore to be expected that, as a general rule (there will always be exceptions), vertically transmitted parasites should be less pathogenic than those that are transmitted horizontally. There is some support for this hypothesis. For example, Tompkins *et al.*, (1996) found that two ectoparasites of swifts – a louse and fly – that are vertically transmitted, had no effect on nestling growth or fledgling success even when the numbers of these parasites was artificially increased or the birds were stressed. Similarly, in feral pigeons, Clayton and Tompkins (1995) observed that a vertically transmitted louse had little impact on the birds' health but horizontally transmitted ectoparasitic mites caused so much distress that the birds' reproductive success was reduced to zero.

1.4.2 Parasites and the evolution of sexual reproduction

Sex has fascinated biologists (among others) for generations. In particular, from a logical point of view, sexual reproduction does not make sense because of what is referred to as the two-fold cost of sex. First, the males, which usually constitute in the region of 50% of the population, serve only to inseminate the females and do not reproduce themselves. Furthermore, a great deal of time and effort is often employed in searching for a mate and mating can itself be an energetically expensive and potentially dangerous process. By contrast, in an asexually reproducing organism, 100% of the population is able to reproduce. Consequently an asexually reproducing population is theoretically able to grow faster and respond to any changes in the environment (e.g. increased food supply) faster than one that reproduces sexually. The other 'cost' of sexual reproduction is that the gametes are haploid and the process of recombination at meiosis means that an individual is only able to pass on 50% of its genes to each of its offspring. Consequently, useful genes and gene combinations could be lost in the process of generating new genetic variants. Despite these problems, and several others, the vast majority of organisms undertake sexual reproduction and therefore it must have some major advantage(s).

There are several theories why so many organisms reproduce sexually and these are admirably evaluated by Sherratt and Wilkinson, (2009). One of the most popular theories is that of Hamilton

et al. (1990) who suggested that sexual reproduction has arisen as a mechanism by which organisms can limit the problems of parasitic infections. As we have seen, parasites can potentially reproduce faster than their hosts and therefore they will evolve to overcome the most common combination of host resistance alleles. As a consequence, hosts with rarer resistance alleles will then be at a competitive advantage and ultimately one of these will become the most common resistance allele combination in the host population. And so the arms race will continue with the parasites adapting to the most common resistance allele combination and the host generating new allele combinations. The process of recombination ensures that (provided the initial gene pool is sufficiently diverse) there will be a constant supply of novel resistance alleles. Furthermore, a resistance allele combination to which parasites have adapted need not be lost from the population because it may prove useful again in the future. By contrast, in an asexually reproducing organism, the offspring will have the same resistance allele combinations as their parents and once parasites have overcome these, then the whole population is vulnerable to disease.

If sexual reproduction has arisen as means of reducing the depredations of parasites, then one would expect it to be common where parasites are abundant and challenge is frequent. By contrast, asexual reproduction would be expected to be favoured where parasites were absent or the level of challenge reduced. Although there are several instances of exactly this in the literature, they remain remarkably few. The best-known example is that of the snail *Potamopyrgus antipodarum* that originated in New Zealand and has since spread to many parts of the world. It exists as sexually reproducing populations, asexually-reproducing populations, and mixed sexually- and asexually-reproducing populations. Positive correlations have been described between the extent of parasitism by parasitic flatworms and the frequency of sexual reproduction in the snails. Sexual reproduction is rare where flatworm parasite challenge is low and, conversely, it is common where the parasite challenge is high (Lively, 1987; Lively and Dybdahl, 2000). Another commonly cited example is that of minnow populations living in Mexico (Lively *et al.*, 1990). These minnows exist as both asexually-reproducing and sexually-reproducing populations, but those reproducing sexually tend to have lower parasite burdens (except where inbreeding has resulted in reduced genetic diversity). However, it is becoming increasingly accepted that although parasitic infections may be a major factor in the evolution and maintenance of sexual reproduction, there are probably many other factors also involved.

Most multicellular parasites reproduce sexually themselves, although some combine it with asexually-reproducing larval stages (e.g. schistosomes), and even some parasitic protozoa (e.g. trypanosomes) exhibit something akin to sexual reproduction. This would suggest that even endoparasites living in protected environments such as the gut or bloodstream of another animal remain vulnerable to infections. It certainly shows a need to adapt within the host to factors such as the immune response and (in mammalian hosts) drug treatments.

1.5 Parasitism as a 'lifestyle': advantages and limitations

Provided one can get away with it, stealing is easier than having to make something oneself or to earn enough money to purchase it. It should therefore come as no surprise that many organisms have adopted a parasitic lifestyle to some extent. If one takes the view that the main purpose of any organism's existence is to ensure that as many of its genes as possible are transferred into the next generation, then all organisms should maximise their reproductive output. However, producing

1.5 PARASITISM AS A 'LIFESTYLE': ADVANTAGES AND LIMITATIONS

17

offspring is energetically costly and these costs have to be traded off against other activities such as finding food and then digesting and absorbing it, finding a mate, protecting oneself against predators and the environment. By living upon or within a host, a parasite can reduce many of these costs and thereby devote more of their time and energy to reproduction. Most parasites stay in association with their host for the duration of a life cycle stage and therefore, having located and infected their host, the need for sensory apparatus and locomotion are reduced because the parasite has access to a guaranteed food source. This guarantee also means that the parasite does not have to extract as much energy as possible from each 'unit of resource'. Instead, it can afford to be wasteful and many parasites have reduced metabolic pathways. Furthermore, there is no need to lay down metabolic reserves beyond those required for the next life cycle stage. Parasites rarely need well-developed food gathering apparatus and in some cases, such as the tapeworms, they have dispensed with a mouth and gut altogether, relying on nutrients being absorbed across the body wall.

1.5.1 Main advantages of a parasitic lifestyle

Because parasites live within or upon their host, they have a reduced need to maintain body surfaces and behaviours that protect them from desiccation, heat, cold, because this is done by the host. Similarly, the parasite is to a large extent protected from predators and pathogens, which would have to overcome the host's immune system before locating the parasite. Even ectoparasites are protected to some extent because hosts are not always able to distinguish between a predator that is attempting to take a bite out of them from one that is intent on removing a flea or louse.

A parasite will be transported wherever the host goes and therefore the limits of its dispersal depend upon the dispersal powers of its host, coupled with whatever other special needs the parasite has to complete its life cycle (e.g. the presence of a suitable vector or environmental conditions). Consequently, a parasite does not have to devote energy to dispersal.

If the benefits are so enormous, this therefore begs the questions why there are not more highly specialised parasites and why parasitism tends to be extremely common among some groups of organisms but rare among others. For example, there are comparatively few parasitic higher plants, Lepidoptera or vertebrates.

1.5.2 Main limitations of a parasitic life style

Any would-be parasite must first overcome the putative host's immune defences and adapt to its internal physiological environment. This is not easy and as a consequence, most parasites are highly host-specific. However, host-specificity places the parasite in a difficult situation because its existence then becomes dependent upon that of its host. Should the host become extinct, then its parasites will follow suit unless they are able to infect other organisms. Furthermore, for the individual parasite, finding hosts is seldom easy. Although many parasites produce huge numbers of offspring, the chances of any one of them managing to locate a suitable host and reproduce successfully are extremely small. The advantages and disadvantages of the parasite lifestyle are summarised in Table 1.1.

Table 1.1 Summary of advantages and disadvantages associated with the parasite lifestyle

Advantages	Disadvantages
Once host located, no need for further searching	Extreme host specificity can increase vulnerability to extinction
Food permanently available	
Limited requirement for complicated food capturing mechanisms	Must locate at optimal site on/in host to ensure food/survival
Reduced need for food processing	
Protection from environmental extremes	Must adapt to host's internal physiological environment (internal parasites only)
Protection from predators and diseases	Must overcome host's immune defences
Reduced need for dispersal because host (+ vector) carries the parasite.	Spread limited by host's geographic range
Can devote larger proportion of energy intake to reproductive output than a free-living organism	Transmission can be extremely risky and most offspring die before establishing in a new host

1.6 The economic cost of parasitic diseases

Parasitic diseases afflict large numbers of us humans: in 2004, the WHO estimated that on a global scale, infectious and parasitic diseases were responsible for 16.7% of male and 15.6% of female deaths. Malaria was the parasitic disease causing most deaths (1.5%) although it may come as a surprise that many more people die in traffic accidents (2.2%) and from diarrhoeal diseases (3.7%). In 2009, it was estimated that there were approximately 225 million clinical cases of malaria and these resulted in about 781,000 deaths. Most of these cases occurred in children younger than 5 years old living in Africa (<http://www.rollbackmalaria.org>). Some 50% of global deaths from malaria and 47% of all cases occur in just five countries: Nigeria, Democratic Republic of Congo, Uganda, Ethiopia, and Tanzania. Although these figures indicate the seriousness of malaria, they also demonstrate that malaria control programmes are working. In 2000, there were estimated to be 233 million clinical cases that resulted in approximately 985,000 deaths (WHO, 2011). Consequently, despite the rise in the human population in malaria-endemic regions, in the past decade there has been a reduction in the number of people developing clinical malaria and proportionately fewer people are dying from the disease.

1.6.1 Economic consequences of parasitic diseases of humans

Inevitably, parasitic diseases cause financial losses to both an individual, their family, and to the wider society as a consequence of both morbidity ('illness') and mortality ('death'). These costs can be divided into the direct costs associated with the diagnosis and treatment of the disease and indirect costs that result from a person's inability to work or reduced efficiency/productivity. Although the direct costs are relatively easy to measure, it is the indirect costs that usually have the most serious consequences for both an individual (personal mortality excepted) and society. This is because most parasites cause chronic disease that can persist for months or even years. For example, a study in Africa in 1987 found that the cost of a person suffering from a typical uncomplicated episode of malaria was US\$9.87, of which the direct costs amounted to only 18.6% of the

1.6 THE ECONOMIC COST OF PARASITIC DISEASES

19

total and the remaining 81.4% were owing to the indirect costs (Shepard *et al.*, 1991). Although US\$9.87 might sound like a small sum of money, at the time it was equivalent to 12 days of productive work which was being lost. Indeed, the enormous cost of parasitic diseases in developing countries is seldom appreciated. For example, in Southern India, lymphatic filariasis is estimated to cost in the region of US\$811 million per year and cause productivity losses as high as 27% in the weaving sector (Ramaiah *et al.*, 2000). Parasitic diseases that cause disfigurement, such as lymphatic filariasis, can result in social exclusion that further traps the sufferer in poverty. Perera *et al.* (2007) relate how patients suffering from lymphatic filariasis in Sri Lanka can become so isolated that they will not venture out to seek freely available treatment at government clinics, let alone to look for paid employment.

1.6.2 Economic consequences of parasitic diseases of domestic animals

Similarly, for domestic animals, there are the direct costs of diagnosis and treatment along with mortalities, but the losses that result from lost productivity (e.g. milk yield, live weight gain) or work capacity (e.g. draught oxen, camels, donkeys) are much greater. For example, in 1997, losses in the dairy and beef industry in Australia owing to abortion outbreaks induced by neosporosis (*Neospora caninum*) were in the region of Aus\$25 million per year (Ellis, 1997). This figure, like most cost estimates of the effects of neosporosis, does not take into account sporadic abortions or the losses owing to reduced productivity (Reichel, 2000). There are no figures for the economic cost of *Neospora caninum* infection in dogs but many dog owners will spend large sums of money on the welfare of their pets and pedigree dogs can sell for hundreds or even thousands of pounds. Consequently, control of the disease in dogs is of concern to owners as well as a means of preventing its transmission to cattle. In developing countries, the economic costs of parasitic diseases of livestock can have consequences for the expansion of agriculture and also the ability of human populations to feed and clothe themselves. For example, in Africa, trypanosome parasites cause the wasting disease known as Nagana in cattle and other domestic livestock. The condition is debilitating and potentially fatal and it has been estimated to result in annual losses of over US\$ 1.3 billion (Shaw, 2004). Similarly, East Coast fever in cattle (caused by *Theileria parva*) is currently mainly restricted to East, Central, and Southern Africa where it causes annual losses of hundreds of millions of pounds and prevents large areas of land from being used for farming. East Coast fever is mainly controlled through the use of acaricides to kill the tick vectors but because the tick populations are becoming increasingly resistant to these chemicals, there is a fear that the ticks will spread and consequently so will the disease.

1.6.3 Estimating the costs of morbidity due to disease

It is currently common practice to measure the consequences of disease and other causes of morbidity in terms of disability-adjusted life years (DALYs). These are calculated by summing an estimate of the disease's or condition's potential for reducing lifespan and an estimate of the amount of time a person suffering from the disease/cause is disabled (www.who.int/evidence/bod). One DALY is the equivalent of the person losing a year of healthy life:

$$\text{DALY} = \text{number of years of life lost through premature mortality} \\ + \text{years of life lived with disability}$$

In some studies, the DALY model is refined to place greater value on the life of a young person than of an older person. This is done on the basis that a young person has (potentially) a longer productive life in front of them than an older person. DALYs enable the researcher to compare a wide variety of mortality factors. For example, a person committing suicide or dying in a traffic accident would suffer premature death but there would be little or no disability (assuming they died instantly) while a person with malaria may suffer prolonged ill health and ultimately die prematurely years later. The results of comparative studies can help prioritise funding and policy decisions and determine the effectiveness of health initiatives. For example, in 2006 it was estimated that mass drug administration to prevent the transmission of geo-helminths (e.g. *Ascaris* and *Trichuris*) would cost between US\$2 and US\$9 per DALY averted. By comparison, the frequent blood transfusions that are required to treat certain forms of thalassaemia can cost over US\$10,000 per DALY averted and are therefore only available to the most affluent families or those where the treatment is provided by the government (Laxaminarayan *et al.*, 2006).

Although DALYs can yield useful information, their application to parasitic diseases has been criticised (e.g. Hotez, 2007; Payne *et al.*, 2009). In particular, the estimation of the years of life with disability includes a weighting factor that is meant to account for the severity of the disease. This is difficult to estimate for many parasitic diseases. For example, DALY calculations for the global effect of schistosomiasis vary from 3 million to 70 million and for hookworm infection from 1.5 million to 22.1 million. If the upper figures are used, then schistosomiasis and hookworm infections would rank alongside malaria (DALY = 46.5 million) as the most important of all parasitic diseases but if the lower figures are used, then their importance is considerably reduced (Hotez *et al.*, 2010). The estimate is further complicated by the fact that people are often co-infected with a variety of parasite species and parasite–pathogen interactions (e.g. *Leishmania*–HIV) can have major implications for disease progression and outcome.

1.6.4 Economic consequences of parasitic diseases of wildlife

Whether it is appropriate to use economic costing when considering wildlife is a controversial topic: how much is a blackbird worth? Nevertheless, parasitic diseases can have profound effects on wildlife populations and these must be borne in mind in wildlife management and conservation. For example, 20–80% of white-tailed deer fawns in the Southern USA used to die each year as a consequence of infection (mostly in the umbilical region) with the larvae of the New World Screw-worm (*Cochliomyia hominivorax*) (Fuller, 1962). The fly also caused enormous economic losses to the cattle industry and therefore a control programme was instigated. This was so successful that *Cochliomyia hominivorax* was eradicated from the USA in 1964 and therefore (and unintentionally) a previously major cause of deer mortality was reduced to zero. Before the control programme commenced, *Cochliomyia hominivorax* was often spread to new locations through the transport of infected cattle. This movement of parasites can have devastating effects for local wildlife if they are susceptible. For example, on the Galapagos Islands, the populations of several of the species of Darwin's finches have been devastated following the arrival of *Philornis downsi* – a fly which has ectoparasitic larvae. The fly probably came to the islands in the 1960s among imported fruit and vegetables. The adult flies are free-living but their blood-feeding larvae are ectoparasitic on nestling birds and have caused high mortalities (Fessl *et al.*, 2010). Wildlife tourism is big business and a major source of income in both developing and developed countries and therefore parasitic diseases that afflict wildlife can have serious economic consequences.

Box 1.5 How malaria has influenced the course of history

Malaria has influenced the course of history for thousands of years and remains relevant today. The symptoms of chronic and repeated infections of malaria are quite distinct and the disease can be identified with almost complete certainty from historical descriptions from Ancient civilisations of Egypt, Sumeria, China and India. For example, a Chinese medical text, the *Nei Cheng*, written in approximately 2700 BC refers to epidemics of the ‘Mother of Fevers’ that is undoubtedly malaria. The authors describe the cyclical fevers and enlarged spleen that are features of malaria. Similarly, the symptoms of malaria can be identified from the writings of Hippocrates in Ancient Greece (~500 BC). Some authors have suggested that the decline of the Ancient Greek and Roman civilisations was associated with effects of malaria epidemics (Poser and Bruyn, 1999). More recently, in 1943, an outbreak of malaria among Allied troops during the Second World War seriously compromised their attempts to invade Sicily. American troops suffered similar problems with malaria during the Viet Nam War in the 1960s. Although malaria caused only about 0.2% of fatalities among the American troops, the debilitating effects reduced the combat strength of some units by up to 50%. The Viet Cong were aware of the problems that malaria caused the American troops and intentionally sabotaged local mosquito and malaria control programmes. They were successful in undermining malaria control over large areas, but as a consequence the combat strength of their own troops was also severely compromised (Drisdelle, 2010).

Today malaria is often thought of as a tropical disease but it used to be a common problem in many of the temperate regions of the world. Malaria was a major cause of mortality in parts of Italy and Greece as late as the 1920s (Snowdon, 2006). Malaria existed in the UK until the early years of the twentieth century, particularly in the fenland regions, and was known as ‘the ague’ (Reiter, 2000). The potentially fatal consequences of the ague are alluded to in works by Geoffrey Chaucer (c.1343–1400) and William Shakespeare (1564–1616) so the disease was obviously common enough for their audiences to be familiar with it. Samuel Pepys (1633–1703) describes suffering from the ague in his diaries and Oliver Cromwell (1599–1658) died as a consequence of an attack of the ‘tertian ague’ in September 1658.

1.7 Why parasitic diseases remain a problem

Whenever a seemingly simple but intractable problem arises, a commonly heard refrain is ‘If we can put a man on the moon, why can’t we . . .?’ As we have seen, parasitic diseases cause suffering to us and to our domestic animals and the economic costs are enormous. Furthermore, many parasitic diseases could be controlled by simple measures such as providing safe drinking water and appropriate waste disposal facilities. So, one might ask, why do parasitic diseases continue to afflict so many people and impact so heavily on agriculture?

As with so many apparently simple questions, the reason parasitic diseases are such a problem does not have a single simple answer and is also tied up with the most exasperating factor of all – human behaviour (Table 1.2). To begin with, human parasitic diseases are predominantly (although not entirely) a problem of poor people who live in insanitary conditions and do not have a healthy diet. The diseases are therefore most prevalent in developing countries and neither

Table 1.2 Summary of factors contributing to the problems of parasitic diseases

Poverty
Lack of sanitation
Complacency
Poor nutrition
Lack of health infrastructure
Lack of government interest
Corruption
Urbanisation
Social conflict/wars
Movement of non-immune people to regions where they become infected from the resident population.
Movement of infected people to regions where they infect non-immune resident population
Man-made environmental damage
Natural disasters
Lack of effective drugs/parasite resistance
Increasing resistance of vectors/intermediate hosts

the government nor individual people have money to spare. For example, according to the World Health Organisation (WHO, 2009), in 2006 the total healthcare expenditure in Zimbabwe as a percentage of the GDP (gross domestic product) was higher than it was the UK (9.3% vs 8.2%). However, in terms of total expenditure per capita, Zimbabwe was able to devote only US\$38 per person per year to healthcare while the UK spent US\$2815. It goes without saying that US\$38 does not buy a lot of medicines.

Humans are extremely adaptable creatures and will survive under remarkably harsh environmental and political regimes. This adaptability can degenerate into acceptance and complacency on the parts of both individuals and governments. Because parasitic diseases are so prevalent in developing countries, there is a tendency not to prioritise them: periodic fevers and diarrhoea become an accepted part of everyday life. Furthermore, parasitic diseases tend to cause chronic disease and although the patient may ultimately die, the condition does not capture the attention of the local or world media. For example, the Ebola virus is well known in the developed world because of its appalling pathology and images of patients being treated by nurses and doctors dressed in spacesuit-like protective clothing. However, although the Ebola virus causes about 70% mortality, the numbers of people who have actually died of the infection are relatively few. The fact that Ebola virus has been touted as a possible biological warfare agent has also helped to engender interest in the disease and funds to study and control it. By comparison, Human African Trypanosomiasis (often referred to as 'sleeping sickness') causes 100% mortality if untreated and kills many more people than Ebola but is seldom mentioned in the media. The reason is simple, Human African Trypanosomiasis kills slowly by comparison and those who suffer are among the poorest in Africa and live in some of the most war-torn and disorganised regions of the continent.

In addition to being poor, the countries in which parasitic diseases are most problematic are often unstable and suffer high levels of corruption. Consequently, those in control often devote much of their revenue to the trappings of power and military spending: many developing

1.7 WHY PARASITIC DISEASES REMAIN A PROBLEM

23

countries spend only 2–3% of their GDP on healthcare. This means that even less of not very much money is available for the treatment and control of parasitic diseases. The instability of the regimes and conflicts which can last for decades make it difficult to provide health services and co-ordinate control strategies. They also lead to the destruction of basic infrastructure and the decline in agricultural and commercial activity – and this contributes to poverty and malnutrition. At its worst, conflicts lead to large numbers of refugees who are frequently housed in squalid campsites which lack proper sanitation. These displaced people are often in poor health and malnourished, they take their parasites with them wherever they go and they are highly vulnerable to the local strains of parasites wherever they are relocated to. For example, the civil wars in the Central Asian states such as Tajikistan, which occurred after the break-up of the Soviet Union in the early 1990s, displaced people to neighbouring countries including Afghanistan. The most common type of malaria in Tajikistan at that time was caused by *Plasmodium vivax*, whereas in Afghanistan, the more virulent *Plasmodium falciparum* was found and drug-resistant strains were circulating. Some of the refugees who returned home in the late 1990s were infected with drug-resistant *Plasmodium falciparum* and since there was a suitable mosquito vector, this form of malaria was transmitted among people who had never left Tajikistan (Pitt *et al.*, 1998). Natural disasters, such as cyclones and earthquakes, can lead to similar destruction of infrastructure and refugee problems. Widespread flooding can also provide suitable breeding conditions for mosquitoes and thereby increase the spread of mosquito-borne diseases such as malaria. For example, the widespread flooding in Mozambique which occurred in 2000, led to an increase in malaria and water-borne diseases.

Damage to the environment caused by humans can also encourage the spread of disease by making conditions more suitable for vectors and intermediate hosts and/or the survival of parasite eggs and cysts. For example, clearance of the rainforests in the Amazon produces open sunlit pools that are ideal breeding grounds for the mosquito vector of malaria *Anopheles darlingi* (Harris *et al.*, 2006). Also, as people move into these clearings to live or work, they come into contact with infectious agents which are not adapted to living in humans but can still cause disease (i.e. zoonoses). Climate change is also thought to be affecting the transmission and range of a number of parasitic diseases (Patz, 2001, 2004; Patz *et al.*, 2002; Haines and Patz, 2004).

The way we live and organise our societies also contributes to the spread of parasitic diseases. Throughout the world there is an increase in urbanisation which means that more people are living in close proximity together and where sanitation remains poor, this can facilitate the spread of contaminative diseases and those vector-borne diseases in which the vector can survive in an urban environment (e.g. certain mosquito species). The increased use of cars and motorised transport has resulted in large numbers of used tyres entering the ecosystem. Used tyres retain water after it has rained and make excellent breeding grounds for some mosquitoes. There is a huge international market in used tyres that are loaded onto ships and moved between countries. In the process, mosquitoes are also moved around the world and notorious vectors of disease such as *Aedes albopictus* are now established in countries (e.g. Spain) where they were formerly absent (Roiz *et al.*, 2007). People are also much more mobile than they used to be and cheap air travel means that millions of people are now rapidly travelling between countries for leisure and business but also, and in large numbers, as economic migrants and political refugees. Consequently, they become exposed to diseases to which they have no previous experience, and hence immunity, and are therefore vulnerable to infection. Similarly, those who are already infected (but may not be aware of the fact) carry their diseases with them and could potentially transmit their infections to

a non-immune population on arrival (Myers, 1999, 2000a, 2000b, 2000c). For domestic animals it is possible to instigate legislation that governs their movement and a 'passport scheme' that ensures that they have received appropriate vaccinations and/or drugs and/or undergo a period of quarantine upon arrival in their country of destination. However, this cannot be done so easily for humans. Some countries insist that all persons entering their borders have documentation proving they have received certain vaccinations (e.g. yellow fever) but there are few anti-parasite vaccines and even where effective prophylactic medicines are available to treat parasites (e.g. antimalarials), it is notoriously difficult to persuade people to take them as prescribed.

Another of the major reasons why parasites remain a problem is the lack of suitable drugs and vaccines to treat them. The development of drugs for use in human medicine takes many years and is extremely expensive. Consequently, the drug companies need to be sure that they can obtain a good rate of return for their investments. Unfortunately, the people who suffer most severely from parasitic diseases are usually poor and cannot afford expensive drugs. Similarly, the development of anti-parasite vaccines has been hampered by a combination of cost and the difficulty of generating protective immunity against parasitic infections. These issues are dealt with in detail in Chapter 10.

The control of parasites by targeting their vectors/intermediate hosts is also becoming more problematic. For a number of years this approach proved highly effective and in the 1950s it was even believed it might be possible to eradicate malaria by killing the anopheline mosquito vectors. However, some vectors are exhibiting increasing resistance against a wide range of insecticides and new chemicals are not being developed to replace those in current use. Furthermore, there are mounting concerns for the environmental damage that can result from inappropriate use of insecticides and fears over the risks they pose to human health.

1.8 Taxonomy

Correct diagnosis is essential for treatment and control of any disease and that means there needs to be consensus on the names and terms used in the identification process. Therefore, before we begin to consider specific parasites, it is necessary to have an understanding of how the taxonomic system works and its relevance to parasitology. Those who study the identification of organisms are called taxonomists and they arrange organisms into a hierarchy of categories to demonstrate their relationship to one another (Table 1.3). Not all taxonomists agree on the appropriate division for a grouping (taxon). For example, some workers consider there to be two suborders of Diptera: the Nematocera and the Brachycera and that the term Cyclorrhapha should be considered a division of the Brachycera rather than a suborder.

There is some debate about how many kingdoms exist although most modern textbooks refer to six: Archaea, Bacteria, Protista, Fungi, Plantae, Animalia. Parasitic species are common in all the kingdoms but we will be concentrating on the kingdoms Protista and Animalia. Viruses are not usually considered to be living entities and therefore do not have a kingdom of their own. However, Didier Raoult and his co-workers argue that the giant viruses called 'nucleocytoplasmic large DNA viruses' (NCLDV) should be considered as an additional distinct domain of living organisms (Boyer *et al.*, 2010). NCLDVs are so large that they can be mistaken for bacteria and their genomes are typically twice the size of other viruses. The suggestion that a specific group of viruses might be 'living organisms' has generated a great deal of controversy (Zakaib, 2011). According to Williams *et al.* (2011), the large size of the NCLDVs is a consequence of capturing

1.8 TAXONOMY

25

Table 1.3 The taxonomic hierarchy with specific reference to the sheep nasal bot fly *Oestrus ovis*

Taxonomic division	Taxon name	Common name
Kingdom	Animalia	Animals
Subkingdom	Bilateria	
Branch	Protostomia	
Infrakingdom	Ecdysozoa	Moulting invertebrates
Phylum	Arthropoda	Arthropods
Subphylum	Hexapoda	Insects and related species
Class	Insecta	Insects
Infraclass	Pterygota	Winged insects
Division	Neoptera	
Subdivision	Endopterygota	
Superorder	Panorpita	
Order	Diptera	True flies
Suborder	Cyclorrhapha	Higher flies
Superfamily	Oestroidea	Bot flies
Family	Oestridae	
Subfamily	Oestrinae	
Genus	<i>Oestrus</i>	Sheep nasal bot fly
Subgenus		
Species	<i>ovis</i> , Linnaeus, 1758	
Subspecies		

Note that only the genus name and lower taxonomic descriptors are in italics.

host DNA through horizontal gene transfer and there is insufficient evidence to consider NCLDVs as a separate domain.

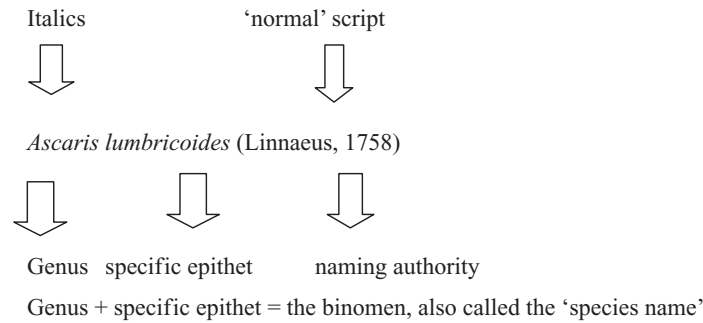
The kingdoms are subdivided into units or taxa (singular taxon) such as class, family, genus. There are no rules about how many species constitute a genus, how many orders constitute a class, or whether families are divided into subfamilies. However, it is essential that the taxon forms a natural grouping. Consequently, research, especially using molecular techniques, causes taxonomists to regularly re-arrange the hierarchy of individual species and groups of organisms. A class, family or any other category within one group of organisms is therefore not evolutionarily comparable with those in another group.

The International Commission on Zoological Nomenclature (ICZN) provides rules on legal aspects of nomenclature (e.g. precedence). However, it is not unusual for workers to continue using old names that have been superseded or to fail to agree on an accepted single name. For example, the blowflies known as *Lucilia cuprina* and *Lucilia sericata* within the UK and Europe are often called *Phaenicia cuprina* and *Phaenicia sericata* by workers in USA.

1.8.1 The binomen system

All organisms (apart from viruses) have a two-part name, or binomen – hence the term binomial nomenclature. The two parts consist of the generic (or genus) name and the trivial name (also called the specific epithet or specific name).

The trivial name may be followed by the naming authority, i.e. the name of the person who first described the organism, along with the date the description was published – this is placed in brackets.



Surprisingly, there is no universally accepted definition of what is meant by the term ‘species’. Indeed, there are currently over 20 different definitions. Furthermore, over the course of thousands of years there is never a single point at which one species becomes two: it is like attempting to identify the day one ceases being a child and becomes an adult. To further complicate matters, some species have distinct forms that are called sub-species, and these are distinguished through the use of trinomens. For example, the human body louse *Pediculus humanus humanus* and the head louse *Pediculus humanus capitis* are usually distinguished as separate sub-species. However, for many years there has been a debate about whether the reported differences in their morphology and behaviour are consistent enough to justify them being considered closely related sub-species or separate species in their own right. Current molecular evidence suggests that they are morphotypes of a single species (Light *et al.*, 2008). Similarly, there are two physiological variants of the mosquito *Culex pipiens*: *Culex pipiens pipiens* which bites only birds and *Culex pipiens molestus* which bites only humans. The two variants of *Culex pipiens* cannot be differentiated morphologically. They can be crossed in the laboratory, but, in the UK, the populations remain genetically isolated in the wild. Distinguishing between the variants is important because this mosquito is capable of acting as a vector for the potentially fatal West Nile Virus and therefore its biting behaviour has a major impact on whether the disease spreads from birds to humans.

The difficulty of differentiating between species and sub-species can give rise to ‘taxonomic inflation’ in those groups that are particularly well studied. For example, ant taxonomists tend not to recognise sub-species so everything is separated at the species level. By contrast, butterfly taxonomists are enthusiastic users of trinomens. Not surprisingly, this often results in ecological surveys revealing a greater species diversity of ants than butterflies.

Some scientists have suggested that taxonomic inflation is being driven by the increasing use of the phylogenetic concept of species rather than the older biological species concept. The traditional biological species concept operates on the premise that two organisms should be considered different species if either they are incapable of mating or, if they do mate, then their progeny are infertile. Allowances have to be made for the likelihood of gene flow between populations. For example, the fact that tigers and lions can hybridise does not mean that they are the same species, as this would never happen in the wild. By contrast, the phylogenetic species concept is based on the fact that separate populations of organisms often have distinct inheritable differences (for example, a colour pattern or the size of a body part). What constitutes an inheritable difference

sufficient to qualify a population as a 'species' would depend upon the views of the taxonomist. The increasing use of DNA analysis by taxonomists has undoubtedly contributed to the popularity of the phylogenetic species concept, because it often identifies differences in gene sequences between populations. Some workers have suggested that the adoption of a phylogenetic species concept can result in up to 48% more species than the biological approach for the same group of organisms (Marris, 2007). It also causes complications by suggesting some unlikely taxonomic relationships. For example, a particular clinical presentation of an 'atypical' pneumonia is common among AIDS patients. It is associated with infection with an organism of *Pneumocystis* spp. which was originally classified as a protozoan parasite and called *Pneumocystis carinii*. DNA analysis yielded evidence that this organism is much more closely related to fungi than protozoa. Reclassification also brought about a change in species name to *Pneumocystis jirovecii* (Stringer *et al.*, 2002).

Questions

1. With the aid of named examples, distinguish between the terms intra-specific and inter-specific animal associations.
2. Distinguish between the terms facultative and obligatory parasitism.
3. Should the red-billed oxpecker (*Buphagus erythrorhynchus*) be considered to be in a commensal relationship with cattle? Explain your answer.
4. What is the difference between morbidity and mortality?
5. Briefly explain why haematophagous organisms usually have a symbiotic relationship with microorganisms.
6. What advantage does *Hydra viridis* gain from its association with *Chlorella* when maintained in (a) constant darkness with food; and (b) constant light with food? Explain your answers.
7. What is a paratenic host and what purpose does it serve in parasite transmission?
8. Briefly explain why harm is a difficult term to define in relation to parasitism.
9. State two advantages and two disadvantages of the parasitic lifestyle.
10. Give four reasons why parasites remain a problem in developing countries.