If there is one thing you remember from this lecture, it is that parasites are everywhere and that they are a normal part of life.

I could have said "if there is one thing you take away with you this evening, it is parasites", but this may have given the wrong idea about Gresham's plumbing.

It is remarkable, but true: All animals and plants are normally infected with parasites. Being parasitized is normal. It is only us WEIRD (Western, Educated, Industrialised, Rich, Democratic) people that do not have (many) parasites.

If parasites are ubiquitous, normal and natural, does this mean that we should learn to embrace our parasites? Probably not, because they often cause a lot of harm – it is their harm-causing that is their defining feature. Because animals, ourselves included, have evolved in the intimate presence of parasites, things can sometimes go awry when we don't have them. We will come back to this in due course.

Let us go back to the very beginning and ask, what is a parasite?

It is obvious really – a parasite is something that takes from and harms its hosts. We use the word parasite in everyday language. Thieves, fraudsters and other ne'er-do-wells are parasites. Parasites cause harm and loss.

Zoologically, it can actually be a bit more difficult to define a parasite because there are lots of different types of associations between animals. Given this continuum of associations, to define a parasite we need to draw a line on that continuum, and this is arbitrary.

The types of associations between organisms are mutualism, commensalism, symbiosis, as well as parasitism. In mutualism, commensalism and symbiosis, the association of another organism with a host is one that doesn't cause harm to the host. To say this more precisely, the association with a mutualist or a commensal doesn't cost the host anything more than the host gains from the association. In mutualism, commensalism and symbiosis, the host does at least as well out of the relationship as the other organism. Parasitism is different because the host loses as the parasite gains.

Here we are thinking about a host, which for our purposes is a multicellular animal. This could be a mammal like us or other vertebrates (birds, fish, reptiles, amphibians), as well as invertebrates – insects, slugs and snails etc. Parasites are things that live with these host animals and cause some harm to them. This causing harm is the defining feature of parasites.

If we want to get picky, defining exactly when harm is caused can be difficult. Imagine a great big elephant with a tiny worm in its belly – can we really say that the elephant is being harmed by one worm? Theoretically, perhaps, but not anything that we could really measure. Of course, with 10,000 worms in its belly an elephant might be obviously ill. It is also tricky to define harm, because sometimes whether a parasite infection causes harm depends on the host – a parasite might harm one individual host, but not another. Still, parasite is a useful term – something that lives with a host and usually causes harm to the host.

Parasites are everywhere. If we jump ahead for a moment and think about human worm infection, then the scale of this parasitism is enormous. Over a billion people have worms, mainly the young and poor of the developing world. Moreover, multiple parasite infections overlap, for example worms and malaria are both very prevalent in the tropics. For parasites of animals, one study measured all the parasite (mainly worms) biomass in a not very remarkable salt marsh in California. The parasite biomass was equivalent to that of c. 10 elephants – which is something you would notice on the salt marsh. The reproductive capacity of these parasites was also enormous, equivalent to 1-2 elephants per day for 200 days.

What sorts of things are parasites?

There are lots of things that live with hosts and cause harm. There are viruses – these give you coughs and sneezes. There is Ebola and HIV too. Other infections are bacteria, such as those that can give you food poisoning. These are parasites in the sense that they live with hosts and cause harm, but these are typically studied by microbiologists, not parasitologists. As a parasitologist, I am more interested in animals (not viruses, not bacteria) that are parasites.

There are two sorts of animals that are parasites: protozoa, which are single celled animals, and worms, which are multi-celled animals. I am going to spend most time of on worms, because I find them most interesting. But, before we do this it is worth mentioning the protozoan parasites. You will know some of them – malaria, and sleeping sickness are both protozoa infections, living in host blood and transmitted by insect vectors. You might also have heard of Toxoplasma (causing toxoplasmosis), where humans can become infected from cats. Toxoplasmosis in pregnant mothers is dangerous for her foetus. You may also have heard of Giardia, a protozoa
that lives in the gut, causing terrific diarrhoea. Protozoa are important and widespread parasites.

Having met these protozoa, let us now concentrate on worm parasites. These are multicellular animals that make their living in and on other animals.

You could be forgiven for thinking that worms are all the same. They are not. There are just two main types of parasitic worms – round worms and flat worms. (The garden earthworms you are familiar with are a third type of worm, the segmented worms – the annelids – but these are not parasites.)

The flat worms – the Platyhelminthes – come in a few varieties. Some flatworms are free-living, such as planaria, which with a good eye you can find in ponds. There are three types of parasitic flatworms: the monogeneans, digeneans and tapeworms (also called the cestodes). The monogenean flatworms usually live on their hosts - they are ectoparasites. Some typical ones live on fish gills. Again, with a sharp eye (and perhaps a hand lens) you can see these on fish gills. A favourite is Diplozoon paradoxum – a great name, and biologically fascinating species. When you see it on a fish the worm appears X-shaped, which is because two hermaphrodite individuals come together and grow into one another. They permanently plumb their reproductive systems into one another – so they are always having sex. These worms live on the gills of their hosts, feeding off the host blood – this is the harm they cause to their hosts.

The second types of parasitic flatworms are the digenean flatworms. These are internal parasites – endoparasites. Evolutionarily they were originally parasites of snails, secondarily adding other animals to their lifecycle, so that now digenean parasites are characterised by always having a snail as one host, and then a second host – sometimes humans, sometimes, fish, birds etc. The human disease Bilharzia – caused by the parasite Schistosoma – is a digenean flatworm.

The final types of flatworms are cestode tapeworms. These mainly live in the gut of their hosts and, as their common name suggests, they are long tape-like worms. They are remarkably well adapted to being parasites. In their evolutionary history they have lost their gut and instead absorb all their food (which is the host's food in the host's gut) directly through their surface. At the front end (called a scolex) they have suckers and hooks so that they can attach themselves to the host gut. The rest of their body has a ribbon-like appearance, each bit being called a proglottid, though these aren't proper segments.

More importantly worm wise – important because I am interested in them – are nematodes. Nematode are roundworms. They are the most abundant and speciose group of multicellular animals on the planet, but probably the least seen.

Nathan Cobb, an American nematologist, in 1914 said of them “In short, if all the matter in the universe except the nematodes were swept away, our world would still be dimly recognizable ... we should find its mountains, hills, vales, rivers, lakes, and oceans represented by a film of nematodes. The location of towns would be decipherable, since for ... human beings there would be corresponding massing of certain nematodes. Trees would still stand in ghostly rows representing our streets and highways. The location of various plants and animals would still be decipherable.”

He makes the point very well. If you wanted just one type of animal to best represent animal life on the planet today, it would be nematodes.

Many nematode roundworms are parasites. These are mainly parasites of the host gut, but also of some body cavities, and the lymphatic system.

Let us meet some nematode worms.

This is Ascaris lumbricoides. I will start with this because it is a big worm – a female is about 30 cm long. Its normal home is its host gut. They are very common parasites of people – over a billion people (particularly the young and poor of the developing world) have these worms in their guts. These female worms are essentially egg-making factories. Most of the body of these worms is made up of ovaries and uteri, so that they can lay 200,000 eggs a day (over 100 a minute). Each egg contains a larval worm surrounded by a thick, resistant egg shell so that the eggs can survive for long periods in the environment, waiting ready to infect a new hosts.

Are there any worms we all know?

We probably all share a guilty (worm) secret. When you were younger and in bed one night you may have had an incredibly itchy anus – and one would have scratched that itch. This itch was probably because of pinworms, Enterobius vermicularis. That night the female worms migrated to your anus to lay eggs. This itched and when you scratched, her eggs got under your finger nails and then in your mouth. The guiltier secret is that when you had that itchy anus, other members of your family probably did too – but of course we don't talk about it.

Worms of Kings and Pharaohs

Whipworms, technically, Trichuris infect people, including Kings and Pharaohs. The worm's common name comes from its shape, which looks like a whip. The bottom end of these worms is the whip handle, the head-end the tip of the whip. These worms live far down in the host gut, towards the rectum, and use their thin, head-end
to burrow into the gut tissue, with the back end sticking out. The shape of the whipworms' eggs is very distinctive, and these have been found in the mummified intestinal remains of Egyptian Pharaohs, as well as in Richard III's remains.[13]

Let us grant these nematode worm parasites a thoughtful mind, and let us enquire what they may be thinking.

Nematodes are pretty simple animals.[14] They have a nervous system consisting of a few hundred nerve cells. Nematode brains are a collection of probably a hundred or so nerve cells. But, for the next little while let us grant that this is a brain, and that these worms have consciousness, insight and thought, and so let us try and see what it might be like to be a parasitic worm.

Where is my home, and what does it feel like being here?

My home is a person's gut. It is nice and warm in here – a steady 37°C. There is a lot of space too – this goes on for several metres, but I prefer to stay put in just one small area.[15]

Even in one part of this tube, there are different places. There is a large centre space, usually full of mashed up food, and teaming with bacteria. Away from the centre then there's tissue with a fuzzy surface (villi of the gut), and I can crawl through these projections. If you poke around below this surface then there's this warm salty blood.

What do I do here all day?

The same as most other animals, eat so that I can reproduce – which evolutionary is the only point of life. I eat this mush in the centre. It's all partly digested host food and I swim around in it, so I can just shovel it into my mouth. I need a lot of food because I reproduce a lot – in fact as a female most of my body is ovaries. I just lay these eggs and they disappear down this deep dark tunnel.

Other worms I see around live a bit differently. Other worms keep themselves away from this central space, and stay over there on that fuzzy mucosa. They seem to feed just occasionally on the host blood.[16] It is very nutritious, so a few small blood meals does them fine.

Other worms go in below the surface – you never see them out here in the centre. As soon as they arrive, they burrow below the fuzzy mucosa, and spend their lives continually mining away.[17]

We all lay eggs in the same way, and they all disappear down the tunnel.

Who are my neighbours, and how do we get on?

Quite often it is lonely here – you can be a worm all by yourself. This is bad news because we all need to have sex with other worms to be able to reproduce. If you are by yourself then you are really stuck. But occasionally it gets really crowded in here, and then there are worms everywhere.[18]

When it is like this we have to spread out a bit to make room for everyone, and then there is some fights over food.[19]

Of course there is a lot else here beyond worms. There are these single celled animals – *Giardia* we see now and again.[20] There are huge amounts of bacteria too.[21] A lot of this we can use as food, but some of these can be harmful to us, so we have to be careful.

Overall, some of our neighbours are nice to have, others are not so good.[22]

What is not so good?

Even though here is a nice steady place to live and there is plenty to eat (as long as there are not too many other worms), this host immune system can be just terrible. The blood drinkers have it worse – there are cells and toxins in the blood made by the host that tries to kill us. Even out here, a long way from the mucosa, the immune response can get to me. Cells of the immune system, and various molecules and toxins, are released from the mucosa, and drift over and come and attack us. It is there all the time. When it gets really bad then the whole area becomes really inflamed, everything is disturbed, and then it is a very unpleasant place to live.[23]

What do we do to cope with this immune response?

We do a lot – we cannot afford not to. We find the best thing is to stop the immune response in the first place. We have learnt how to spit out our own molecules that trick the host immune response into turning itself down and away from us, to give us all some respite.[24]

We have been around a very long time, so the host immune system has evolved with us always being around. Having worms and other infections is normal for the host immune system. We are so common and we have been around for so long, that we and our immunomodulation of the host immune response has helped to evolutionarily mould the host immune system itself.
What this now means is that if hosts do not have worms then they are missing the immune system down-regulation, so that their immune systems can be over active, and then allergies can develop.[25]

Getting on, getting in, and getting out

What we are all trying to do is to get our children into other hosts – and the better the host they get into the better for them. We want them to have the best start in life. The eggs we produce eventually leave our hosts and end-up in the outside. My eggs have a big thick shell so that they can last outside for months. Our strategy is to contaminate the outside world with these eggs, and then to rely on a host accidently eating the eggs.

When this happens, the egg passes right through the stomach – and the thick egg shell protects the inside of the egg from the stomach acid, but also tells the larva inside the egg to get ready to get out of the egg. Once past the stomach, my eggs hatch and larval worms come out, these migrate, eventually growing into adult worms, and so the cycle continues.

Of course this means that I have two lives – one inside my host and one outside of the host. I have to turn on and off different genes when I am in these different places. Inside the host it is always 37°C, not very much oxygen, and there is the host immune response. Outside of the host, there is plenty of oxygen, the temperature changes a lot, but there is no immune response. I have to lead two sorts of life in my one life.[26]

Parasite transmission is intimately linked to normal biological and ecological processes. The production of waste – defecation urination – often liberates macro-parasite infective stages into the environment, which then contaminates the environment. This can lead to direct oral contamination, for example when a herbivore grazes on pasture.[27]Parasite transmission can be by direct host-host contact, for example by ecto-parasite arthropods. Predation upon prey is also a common means of parasite transmission. Any bit of wildlife biology you see (or see on the BBC) is actually also a study in parasite transmission.

The parasite zoo is a ubiquitous and abundant part of the natural world and of the animals we see all the time. These parasites have profound effects on animal biology, but are fascinating organisms in their own right.

I hope you have enjoyed your brief tour around The Parasite Zoo.

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[3]The World Health Organisation measures, and so compares, infectious disease using DALYs (Disability Adjusted Life Years) and YLDs (Years Lost to Disability). These are compound measures of the number of people infected with the parasite and how much harm that parasite causes to individuals. That harm can be making people feeling ill, or that harm can be death. These DALYs and YLD allow comparisons between the harm caused by acute, infections that frequently kill people, and chronic individuals that make people ill, but for long periods of time. For example, in 2012 WHO estimated that malaria caused the loss of 4 million YLD, and HIV/AIDS 4.5, whereas worms parasites caused 5 million (See: WHO Health Statistics and Information Systems, Estimates for 2000-2012, Disease Burden : who.int/healthinfo/global_burden_disease/estimates/en/index2.html).


[5]In human and other animals the malaria parasite, Plasmodium, lives in host red blood cells where they grow. During their life-cycle, they burst out of the red blood cells every few days (with the cycle length depending on the species of Plasmodium), and this causes the fevers associated with malaria. In sleeping sickness the parasite, Trypanasoma, lives free in the host blood system. The parasite multiples in the blood until it is held back by the host immune response, until a new antigenic type escapes the host immune response and multiples rapidly.

[6]These are also (in)famous for their regenerative ability, including in some species the ability to re-grow a decapitated head. (See: https://www.newscientist.com/article/mg21929275.100-flatworm-given-power-to-regrow-its-head/)

[7]Schistosom豪宅 and female adults live in host blood vessels. Males and females get together and live permanently in copulo (the female being held by the male). The females’ eggs, which usually have spines, are released into the blood. The aim of these eggs is to get out of the host, which they do (depending on the species). by tearing through into the bowel or into the bladder. This causes a lot of damage. Equally, a lot of these eggs get lodged in the host liver, just because the liver is heavily vascularised. Consequently, much of the disease of schistosomiasis is liver disease. Outside of the host the eggs hatch to release a larva which infects a snail. This interaction is highly species-specific - only certain species of snail can be infected. Within the snail
there are several rounds of asexual reproduction, ending up with motile larval stages (cercariae) being released by the snails. These cercariae are looking to infect new hosts, which they do by penetrating the host skin. This life-cycle tells you that transmission is by having exposed skin in water where there are Schistosoma-infected snails. Typically this means that it can be greatest in children and in those adults whose occupations cause them to be exposed to water.

[8] Each proglottid is an independent hermaphroditic unit – it has male and female reproductive structures. They can self fertilise, though cross-fertilisation is preferred. Within each proglottid eggs begin to develop and grow until the proglottid is full of eggs. The string of proglottids along the length of a tapeworm are in successive stages of development. When a proglottid is mature, it then falls off the end of the worm and is passed out of the host in its faces, so that the eggs are outside, ready to continue the life-cycle.


[11] This life-cycle is simple and direct. Eggs are passed from the host in faeces, and the resistant eggs persist in the environment. When these are accidently eaten by a new host in its gut the eggs hatch releasing the larva. Then something, apparently very odd, happens. The larval worm, now in the gut, burrows out of the gut into the blood stream, which is how it travels to the lungs. In the lungs the worm penetrates from the blood side to the air side (through the alveoli), and then it is coughed up in mucus and this is swallowed, so that the worm is, again, in the gut. During this migration, the worms are moulting to more advanced larval stages, so that by the time it gets back to the gut it is an adult. This within-host migration is common among different types of nematodes, likely pointing to how these worms evolved from free-living nematode ancestors into parasites. This period of maturation is very important in the growth and development of reproductive capacity of the worms.

[12] The human pinworm is called Enterobius vermicularis. In the 1980s a helminthologist at the Musée National D'Histoire Naturelle had a son who had pinworms. Being a committed helminthologist Dr Hugot carefully examined his son's worms and discovered a second species of human pinworm named Enterobius gregorii after the son with the worms. (See: Hugot 1983 Annales de Parasitologie Humaine et Comparee 58:403-404.)

[13] And Ascaris eggs have also been found in these ancient remains, pointing both to the long history of human infection with worms, and the ubiquity of worm infection among humans.

[14] For one, intensively studied free-living nematode, Caenorhabditis elegans, it has about 1,000 somatic cells (i.e. excluding the cells of its reproductive organs). Of these approximate 1,000 cells, about a third are cells of its nervous system. C. elegans has a genome with about 20,000 genes, more than that of a fly (Drosophila, which has legs and wings, but only some 17,000 genes). Humans have about 25,000 genes.

[15] Different species have favoured niches. Some in the small intestine, some the large intestine, others the stomach.

[16] These are the hookworms, in humans two species Ancylostoma duodenale and Necator americanus. In their lifecycle, hosts are infected by free-living infective larvae, that penetrate the host's skin, then migrate to the lungs, where they are coughed up and swallowed, ending up in the gut. Adults in the gut lay eggs that pass out of the host in faeces. Outside of the host, larvae hatch from the eggs and then moult into infective larvae.

[17] One example of these are Strongyloides. There are species that infect humans (S. stercoralis and S. fuelleborni), as well many other species that can infect other mammals, birds, reptiles and amphibians.

[18] Nematodes and other macroparasites have an over-dispersed distribution in a host population. This means that most of the parasites are in a minority of the hosts. This can be the 20 / 80 % rule – 80% of the worms are in 20% of the hosts. This means that many hosts have none or only one or two worms, whereas a very few hosts are very wormy. These over-dispersed distributions are caused by any heterogeneities in the host-parasite system. This can be parasites being clumped in the environment (so that a few unlucky hosts get infected with most of the parasites), or hosts being differently able to resist hosts immunologically.

[19] In parasite infections there are usually density-dependent effects, as there are for free-living animals. These are most easily thought of as competition for limiting resources – if there's a certain amount of food available, if there are more individuals after that food, then everyone gets less: this is a density-dependent effect. For parasitic worms, density-dependent effects typically reduce the fecundity of worms. Competition for limiting resources does happen for parasitic worms, but density-dependent effects can also be caused by the host immune response against the worms, such that when there are more worms, then the immune response is greater and causes more harm to each individual parasite.

[20] Giardia is a protozoan (single celled animal) parasite of the gut causing diarrhoea.

[21] The vast quantity of bacteria in our intestines is called the gut microbiota. The mass of the gut microbiota is greater than the mass of our brains.
Parasites affect each other, in much the same way as free-living animals and plants interact within an ecosystem. These effects can be positive (the presence of one species of worm facilitates the success of infection by a second worm species) or negative (one worms species suppresses or interferes with the infection of a second worm species). In this way we can think of worms in guts as a multi-species, interactive ecosystem.

Hosts make immune responses against nematodes. With a bacterial infection we typically make an inflammatory immune response (called a T helper type 1, or Th1, response). But when we respond to nematodes we make a different flavour of immune response, a Th2 response, which is related to allergic type immune responses.

Nematodes (as well as other parasites) immunomodulate or immunosuppress their hosts, to favour their own survival. This can be seen experimentally as hosts infected with worms making less strong immune responses against other antigens or infections, compared with hosts that do not have worm infections. Here, the worm-induced immunosuppression is having an effect on other, 'bystander' antigens.

There are actually two inter-related explanations for why allergies have increased in recent years in the developed west. One is the Hygiene Hypothesis which suggests that by living cleaner lives (particularly less exposure to bacteria), our immune systems make less T helper type 1 (Th1) inflammatory responses with the consequence that we are prone to Th2-type allergic responses. The second, interrelated explanation is that in history people had worms in their guts and these worms were always causing some down regulation of the immune system. In the absence of worms this suppression is removed so that there is a preponderance towards greater Th2-type allergic responses.

It's intriguing that nematodes have independently evolved parasitism approximately seven times, but other types of animals (such as segmented annelid worms) have never evolved to be parasites. One thing common to all nematodes is that they are moulting animals, and have four larval stages preceding the adult stage. Nematodes remodel their surface cuticle at each moult, and have the ability to reset their physiology at these moults. We can speculate that this moulting, which generates discrete life-cycle stages, may have been useful in evolving parasitic life-cycles where very different environments (e.g. parasitic, within a host and free-living outside of a host) are encountered.

For digenean trematodes (for example *Schistosoma*) then this is indirect contamination via intermediate snail hosts.