Verbos; the doing words

The commonest forms of greeting are short questions; opening gambits like ‘How are you?’ These are often followed by equally short questions, one of the commonest of which is ‘and what do you do?’ Our contemporary culture defines us according to what we do. Our identity and for some, their meaning in life, is based on occupation: doctor, pathologist, teacher, researcher. And what do you do?

Doing words

This question can be usefully applied to microorganisms. What can each one of them do? The words used to speak of their actions are the classic doing words; verbs to the grammarian and linguist. Along with substantives (nouns, naming words) verbs lie at the heart of the most basic of sentences. They are so critical to the language we use that some sentences have a single verb as their only word. But before looking at the red-blooded action verbs, there are some basic verbs that hardly get noticed because they are there in everyday us; camouflaged by the mundane functions they serve. These verbs are used to refer to a state of being or having and usually only have a subject. Sounds a little complicated, but that’s because these action words fly under the radar. They include to be, to exist, to survive, to grow, to divide, and to die. The bacteria responsible for tuberculosis;
Mycobacterium tuberculosis
, therefore survives in phlegm.

It grows in laboratory culture, it divides in order to replicate and it dies when exposed to antimicrobial therapy. Viruses do not survive for long outside a suitable cellular host, in which they replicate and after treatment with antiviral therapy they die.

Intransigent intransitives

Verbs with a subject (the microorganism) but no object are sometimes called “intransitive”, to distinguish them from the vigorous actions packed into transitive verbs that have both subject (microorganism) and object (e.g. victim). Examples of these red-blooded action words are to colonise, to invade, to infect, to transmit, to inoculate, to cause, to harm and to kill. So *Plasmodium falciparum*, the protozoan that causes malaria invades red blood cells and an Anopheles mosquito transmits the infective stage of the parasite, it harms many infected people every year and kills some of them.

Speaking in code

There is something sinister about a microorganism that lurks in the shadows of human consciousness, hidden from view by virtue of its small size, waiting for an opportunity to pounce.

Perhaps this is why some of the early words for outbreaks of infectious disease were based on words that indicated a sudden strike. ‘Plague’ is one such word that carries a great burden of fear and loathing. The machinery that drives what these microorganisms do or are capable of doing is their genetic code. Bacteria, fungi, helminths (worms) and protozoa are all smart enough to have both main types of nucleic acid; DNA and RNA. Its organisation differs between and to a lesser extent among these different categories of microscopic life. But the essential idea common to all of them is that their full potential is wrapped up in a series of genetic letters, words, phrases and sentences in their DNA which gets converted first into RNA and then into proteins. Viruses are arguably even smarter and more efficient, it a little lazy. They have only one type of nucleic acid; either DNA or RNA, and rely on a range of mechanisms to fill the gaps left by lacking either RNA or DNA. These efficiency savings are made at the expense of the host cell they infect in order to continue living the life to which they have become accustomed.

The soul of the microbe

The reason this is all so important to the actions of microorganisms is that without DNA, RNA and proteins action there is no life. No verb ‘to be’. Nor ‘to survive’, let alone grow, divide or any of those vicious transitive verbs concerned with invasion, infection, harm and death. Note that this molecular machinery determines the action of the microorganism in question. DNA holds the plan and must be copied from generation to generation with a high degree of accuracy to guarantee continued survival and operation of the downstream molecular machinery. Changes obviously arise, either due to accidental reading errors, or the loss and gain of DNA from another source as these living things go about their daily business. Sometimes damage occurs to the DNA and it either reduces the microbe’s fitness for sustained survival, or it may alter its ability to adapt to changes in the external environment. DNA (and for the RNA virus, the RNA) contains the will or intent of the beast. It is about as close as we can get to the soul of the microorganism. By itself, DNA is still not enough to result in action, even in independent biological existence. There is still a need for conversion of the code locked away in strands of DNA into bite-sized chunks of readable message. This is done by the production of messenger RNA, which acts as a molecular go-between. Its message is read in the ribosome by ribosomal RNA, which converts genetic code into peptides and ultimately proteins. The generation of mRNA is the highest point upstream in the entire process that can be used as molecular evidence for life. Anything less (e.g. the presence of microbial DNA) is not proof of action, even at the intransitive level.

Viral efficiency

This all applies to a greater or lesser extent to bacterial, fungi and parasites, which have both DNA and RNA. Viruses are that little bit more complicated on account of their smaller size, the smaller size of their genetic code and the specific type of interaction with their host cell. DNA viruses are generally on the bigger size as viruses go, and dine out on the host cell’s account, making use of their RNA to get the job of growth and replication done. RNA viruses, on the other hand, have to go into reverse gear and make a mirror image of their RNA template before they can crank the molecular machinery into action. Though this sounds a roundabout way of doing their stuff, it is so efficient that the RNA viruses are generally the most efficient at cellular infection, replication and subsequent transmission. The most successful are so efficient that they are responsible for the single largest infectious disease event to have affected the planet’s human population; the influenza pandemic of 1918-1919. Viruses add another twist to our consideration of action words in the language of infection. Their need to pursue a life as compulsory prisoners of the cells of more complex living things means that they are obligate invaders. They known their transitive verbs, demonstrating cellular, invasion, infection, subversion, harm and death, and appear to have a smaller repertoire of verbs of state. Yes, they replicate prodigiously, but being, existence and survival are of lesser concern to these lean and mean molecular machines.

Action by numbers

The verbs are so important to language that they are able to pack a lot more meaning by quite simple variations such as the number of subjects performing the action, the relative time it happens, whether the microorganism was caught up in the action and if there was an element of doubt or ambiguity. The number of bacteria (e.g. *Staphylococcus aureus*) that infect a surgical wound is likely to be a lot more than one solitary cell, but by convention we usually speak of monobacterial infection in the singular, and polymicrobial infections (e.g. enteric Gram negative bacilli such as *E.coli* and anaerobic bacteria such as *Bacteroides fragilis*) in terms of 'they infect' - plural. However, bacteria invade, harm or kill, while a single bacterium usually lacks the punch to do so. If it did, it invades, harms or kills, but usually just survives or dies. The one person normally left out of the language of infection is the first person (singular and plural i.e. 'I' and 'we'), because we generally don't leave microorganisms to speak for themselves.

A sense of occasion

That brings us onto the interesting question of relative time, revealed in language of infection through a variation in the action word called tense. The tense of a verb has nothing to do with pressure or tension. It is the way the action word changes to show that we're talking about actions in the past, present or future. So this would look like the influenza virus caused millions of deaths during the 1918-1919 pandemic, it still causes annual epidemics today, and will infect many more people in future. There are further subtleties to the tense options open to us, particularly in the past with past historic, pluperfect and imperfect. Ross River virus was discovered in Northern Queensland in 1959, where it had probably been the cause of infection for some time. Other arbovirus infections were also a problem in the area and continue to cause periodic outbreaks to this day.

Turning the tables

A variation on the action words of infection is the passive voice, which we use to put the emphasis on the object of the action. This form is now under threat because the men of science prefer direct language, seeking the passive as a bit round about. Still, it has its use to show cause and effect relationships: the influenza pandemic of 2009 was caused by the H1N1/09 variant of the influenza virus. The passive turns the focus of the verb around, which is necessary if you need to indicate that a patient is the victim of an external biological agent. It is equally useful when you want to claim success for the antibiotic you prescribed: the *S. aureus* septicaemia was cured by a course of intravenous flucloxacillin [prescribed by me, of course].

Terms & conditions

Action words can be very logical, revealing the use of a series of deductive steps that link one series of events to their predicted consequences. The tenses used for this are known as the conditional. We use this form of the verb to show our workings: if you need to confirm the *S. aureus* bacteraemia, you could collect a set of cultures. The workings of microorganisms are also subject to conditional actions: if *S. aureus* spreads via the blood stream, it could cause endocarditis. This can have a further sense of relative time added to provide a much richer and more specific sense of when these conditional events could occur: if *S. aureus* had spread via the bloodstream, it could have caused endocarditis (past conditional), or (future conditional) if *S. aureus* is going to spread via the bloodstream, it will have caused endocarditis by the time we get all the laboratory results back. Beyond conditional lies the murky world of the subjunctive, a subject many have managed to avoid encountering through secondary school and even university.

The subjunctive is used to give a sense of doubt, ambiguity or uncertainty that goes beyond the logical links of the conditional. Staying on the familiar ground of invasive staphylococcal infection, we encounter a subjunctive construction such as *S.aureus* might have been the cause of fatal septicaemia, but without any laboratory evidence it is unclear whether it were a virulent strain or not.

Simple sentence constructor

The simplest of sentences need an action word as an absolute minimum. The shortest sentences are commands; single doing words in the imperative: Survive! Grow! Divide! Replicate! As these commands are only issued directly to the subject and it would be very unusual to address microorganisms directly, the shortest meaningful sentence in the language of infection is a combination of an action word with a naming word: *S.aureus* grows; *M.tubercul osis* survives; influenza virus replicates. These are all intransitive verbs. To get into the more exciting actions of the intransitive verbs we need to add in at least another naming word as an object; Anopheles mosquitoes transmit *Plasmodium* species, *S.aureus* causes endocarditis. Short sentences these may be, but they can start to convey the processes we have come to know as infection. The following chapters will add some of the extra components of language that give breadth and depth to the living world under the microscope lens.

TJJI as at 1730hr, 3rd April, 2010.