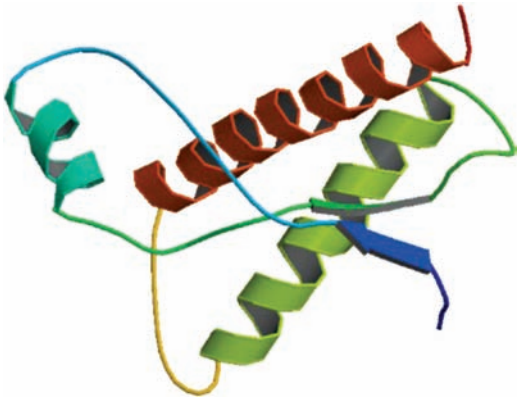
Chapter 7

Characteristics of other microorganisms and infectious agents



Prion protein, as found in bovine spongiform encephalopathy (BSE)

KEY FACTS

- Nonliving particles are capable of causing infections and include viroids and prions.
- Viroids are ss (single-stranded)RNA and prions are small proteins; only prions cause disease in humans.
- Chlamydias and rickettsias are both prokaryotic cells but differ from normal bacteria in that those species of importance are generally obligate intracellular parasites.
- Mycoplasmas are small bacteria devoid of cell walls. They are, however, capable of growing on cell-free medium.
- Mycoplasmas are resistant to cell-wall acting antibiotics such as the penicillins and cephalosporins.

Chapter 1 described the variety of microorganisms within the environment, while the major groups of bacteria, fungi, viruses and protozoa are dealt with in separate chapters. The purpose of this chapter is to briefly discuss those other clinically important microorganisms, which essentially lie outside these groupings and which might otherwise be overlooked.

Figure 7.1 gives rather a simplistic representation of the different agents under consideration showing the progression from nonliving chemicals through to complex, free living cell forms. It is not intended to suggest an evolutionary pathway.

7.1 Nonliving infectious particles

It is evident that chemicals and toxins can cause us harm but we do not tend to think of them as infectious agents. Being an infectious agent implies the ability to reproduce in the host and to be able then to transmit copies of that agent to another susceptible individual. Consequently, the term is often reserved for cellular structures which are capable of metabolism and are endowed with 'life'. However, when we considered viruses in Chapter 6 it

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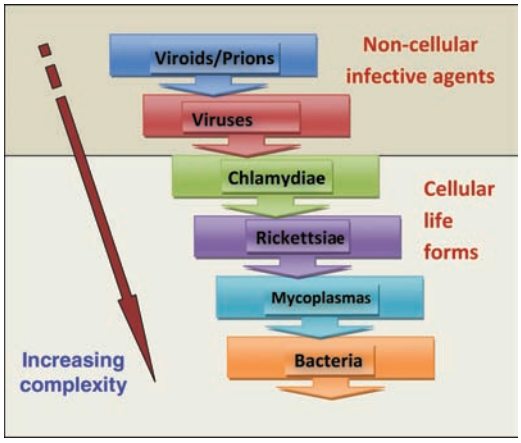

Figure 7.1 Schematic representation of the gradually increasing complexity from nonliving infectious particles through to free living microbes.

was apparent that our definition of living things isn't as straightforward as we first imagined.

However, viruses are not the simplest agents capable of causing infections and there are a number of simple chemicals which fall into this category.

7.1.1 Viroids

Viroids are small circular single-stranded RNA molecules which are not found complexed with protein. They are not infectious agents of humans and the most studied viroid has only 359 nucleotides (one tenth the size of the smallest known virus) and this causes disease in potatoes.

7.1.2 Prions

Prions are small self-replicating proteins which are devoid of nucleic acid. The smallest known prion contains only 250 amino acids. These agents are associated with a number of diseases:

- Creutzfeld–Jakob Disease (CJD) in humans.
- Scrapie in sheep.
- Bovine spongiform encephalitis (BSE) in cattle.

They are not infectious in the conventional sense. There are normal proteins in the membranes of the CNS which have the same amino acid composition as prion proteins but they have a different conformation. When prions are ingested they accumulate in the CNS membranes and by an autocatalytic process they convert normal proteins to abnormal ones. These abnormal proteins cannot be destroyed by the body and lead to the destruction of CNS tissue in the brain.

Prions are highly resistant to heat and so are not destroyed by normal cooking or sterilization procedures. This is of concern because prions present in infected animals such as sheep and cows can enter the food chain and lead to disease in humans. In addition, any pharmaceutical products derived from animal products can pose a potential risk. A serious problem is the sterilization of surgical instruments which may have been used on a patient suffering from CJD. In this case the recommended treatments usually involve immersion in either 1N NaOH or 20 000 ppm hypochlorite for at least an hour and then autoclaving at 121 °C for one hour.

7.2 Viruses

Viruses have been dealt with in Chapter 6 and so no further information will be provided. The following characteristics are presented simply for completeness:

- Viruses are not cells.
- They are static structures – they have no metabolic ability of their own.
- They lack ribosomes and rely on host biosynthetic machinery for protein synthesis.
- Their genome is *either* DNA or RNA.

7.3 Chlamydiae

Chlamydiae are primitive small prokaryotic cells, which, when stained with the Gram staining procedure, appear Gram-negative. This is because their cell wall lacks the peptidoglycan present in most other bacteria. Their genome size is only about a quarter the size of that found in *E. coli*. They are obligate intracellular parasites which, unlike viruses, do possess some independent enzymes but lack an ATP generating system.

Unlike most bacteria, chlamydiae occur in two different morphological forms:

- A small elementary body (approximately 0.3 μm in diameter), which is the infectious form.
- A larger initial (reticulate) body (0.8 to 1.2 μm in diameter), which develops from the elementary body once inside the host cell. The initial body replicates by binary fission.

These agents are important pathogens for humans and cause a range of different disease states.

7.3.1 Trachoma

7.3.1.1 Eye infections

Chlamydia trachomatis is the most common *infective* cause of blindness in the world (the most common noninfective cause is cataract). It is primarily a problem in developing countries where lack of water and poor hygiene has led to approximately 500 million people being affected, of which 6 million are totally blind. The chlamydiae cause repeated infections of the eyelids and conjunctiva, which ultimately causes the eyelids to inflame and turn inwards. The eyelashes then continually abrade the surface of the eye resulting in scarring, further infection of the cornea and subsequent blindness. Despite their devastating consequences these infections are easily treated with antibiotics such as tetracycline, but such products are not readily available in many parts of the world where these infections are commonplace.

In developed countries the same organism can cause a milder form of conjunctivitis.

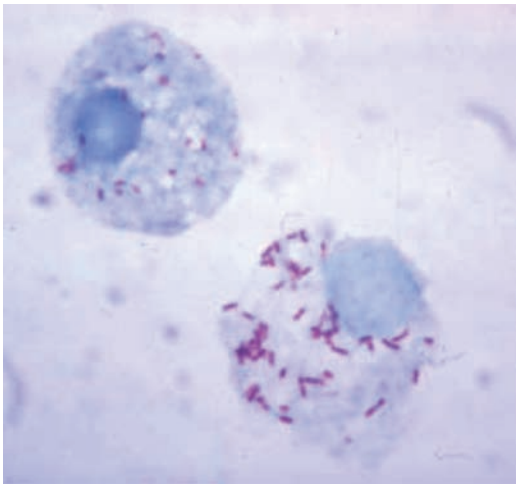

Figure 7.2 Gimenez stain of tick haemolymph cells infected with *Rickettsia rickettsii*. *Source:* Centers for Disease Control and Prevention (CDC); http://commons.wikimedia.org/wiki/File:Rickettsia_rickettsii.jpg.

7.3.1.2 Genital tract infections

Different serogroups of the species *C. trachomatis* which causes trachoma are responsible for sexually transmitted infections of the urethra, cervix, fallopian tubes or uterus. These infections are quite widespread and it is estimated that in the US approximately 3 million people are affected each year.

7.3.1.3 Respiratory tract infections

C. psittaci can give rise to a form of pneumonia (psittacosis) usually acquired as a result of contact with infected birds. *C. pneumoniae* can cause a range of upper and lower RTIs such as sore throat, otitis media, bronchitis, pharyngitis, laryngitis and pneumonia.

7.4 Rickettsiae

These are small (0.7 to 2 μm), Gram-negative bacteria, which are pleomorphic – varying in shape from cocci to filaments depending on the environment (see red-stained cells in Figure 7.2). Most (but not all) are obligate intracellular parasites, which have a requirement for coenzyme A, NAD and ATP. Intracellular multiplication is by binary fission but is very slow and the generation time can be in the order of 8 hours. These agents are infectious pathogens and all except *Coxiella burnetii* are transmitted to humans via an arthropod vector (fleas, ticks and lice).

Louse-borne infection

- Rickettsiae multiply in the cells of the gut wall of a louse and get into its faeces.
- Humans are infected by rubbing faeces or crushed louse into skin abrasions.
- Infection might also occur by inhalation of dried faeces.
- The louse does not bite!

Flea-borne infection

- Flea infected when it takes a blood meal from an infected animal.
- Rickettsiae pass into faeces.
- Humans are invaded by fleas and are infected through faeces in same way that they are infected by the louse.

Mite- and tick-borne infection

- An insect picks up a microorganism when it bites an infected host.
- It passes the microorganism onto humans when they are bitten subsequently.

7.4.1 Rickettsial diseases

Rickettsial disease is characterized by multiplication of the cells in the vascular endothelium (the inner lining of the blood vessels). They cause symptoms on the skin, CNS and liver and tend to persist in the body for extended periods of time. As with most arthropod infections there is no person

Table 7.1 The different rickettsial diseases and their characteristics.

Microorganism	Disease	Arthropod vector	Vertebrate reservoir	Severity of disease
R. rickettsii	Rocky Mountain spotted fever	Tick	Dogs, rodents	+
R. akari	Rickettsial pox	Mite	Mice	−
R. conorii	Mediterranean spotted fever	Tick	Dogs	+
R. prowazekii	Epidemic typhus	Louse	Human	++
R. typhi	Endemic typhus	Flea	Rodents	−
R. tsutsugamushi	Scrub typhus	Mite	Rodents	++
Coxiella burnetii	Q fever	None	Sheep, goats, cattle	+
Rochalimaea quintana	Trench fever	Louse	Human	+

to person spread of disease. A few important examples are given below and are summarized in Table 7.1.

7.4.1.1 Rocky Mountain spotted fever

- This chiefly occurs in rural populations whose work brings them into contact with wildlife and tick-infested stock.
- It may also be spread through ticks of domestic animals.
- A severe rash covers the entire body (Figure 7.3).
- This can develop into gangrenous necrotic lesions.
- Multiple organs may be affected.
- There can be up to 30% mortality.

Figure 7.3 Child's hand showing typical rash of Rocky Mountain spotted fever. *Source:* PHIL ID #1962; Centers for Disease Control and Prevention.

7.4.1.2 Typhus (epidemic, murine and scrub)

- One of the classic epidemic diseases of history.
- Characterized by sudden onset, high fever, malaise, severe headache, generalized rash.
- It has 40% mortality.

7.4.1.3 Q fever

- Named after Q for query (coined in 1930s).
- Caused by *Coxiella burnettii*.
- Spread by deer ticks but can arise from sources other than insect bites, such as inhalation, ingestion and cuts.
- Acute febrile illness.
- Sudden onset, headache, pulmonary involvement.
- Complications – chronic endocarditis.

7.5 Mycoplasmas

These are the smallest prokaryotic cells capable of an independent existence and are therefore able to grow on standard microbiological media. However, they are quite fastidious in their nutritional requirements and do need complex growth media. The cells lack peptidoglycan in their walls; hence they have little rigidity and are variable in shape and size. Instead of the normal cell wall structure mycoplasmas have a triple layered membrane comprising proteins and lipids. Some species have cholesterol in their membranes, which is unusual as this is normally absent from bacteria and fungi and is only found in human membranes.

Table 7.2 Characteristics of different groups of infectious agents.

Characteristic	Bacteria	Mycoplasmas	Chlamydiae	Ricketssiae	Viruses	Prions	Viroids
Can lead independent existence	Yes	Yes	No	No	No	No	No
Independent protein synthesis	Yes	Yes	Yes	Yes	No	No	No
Ability to generate metabolic energy	Yes	Yes	No	No	No	No	No
Rigid envelope	Yes	No	Variable	Yes	Variable	No	No
Mode of reproduction	Binary fission	Binary fission	Binary fission	Binary fission	Variable and complex	None	None
Nucleic acid content	DNA and RNA	DNA and RNA	DNA and RNA	DNA and RNA	DNA OR RNA	None	RNA
Susceptibility to 'true' antibiotics[a]	Yes	Yes	Yes	Yes	No	No	No

[a]See Chapter 9.

There are three main genera of pharmaceutical interest, namely *Mycoplasma; Ureaplasma* and *Acholeplasma.* While a number of these are important pathogens of birds and animals *M. pneumoniae* is the most important human pathogen. It causes atypical pneumonia as well as genital-tract infections (nonspecific urethritis) and other joint and inflammatory conditions.

Because mycoplasmas do not contain any peptidoglycan in their cell walls the infections cannot be treated with antibiotics which act on this structure (principally, but not exclusively, the β-lactam antibiotics). However, mycoplasmas are susceptible to other antibiotics such as tetracyclines or erythromycin.

Table 7.2 summarizes the main features of the various infectious agents described in this chapter.

Acknowledgement

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