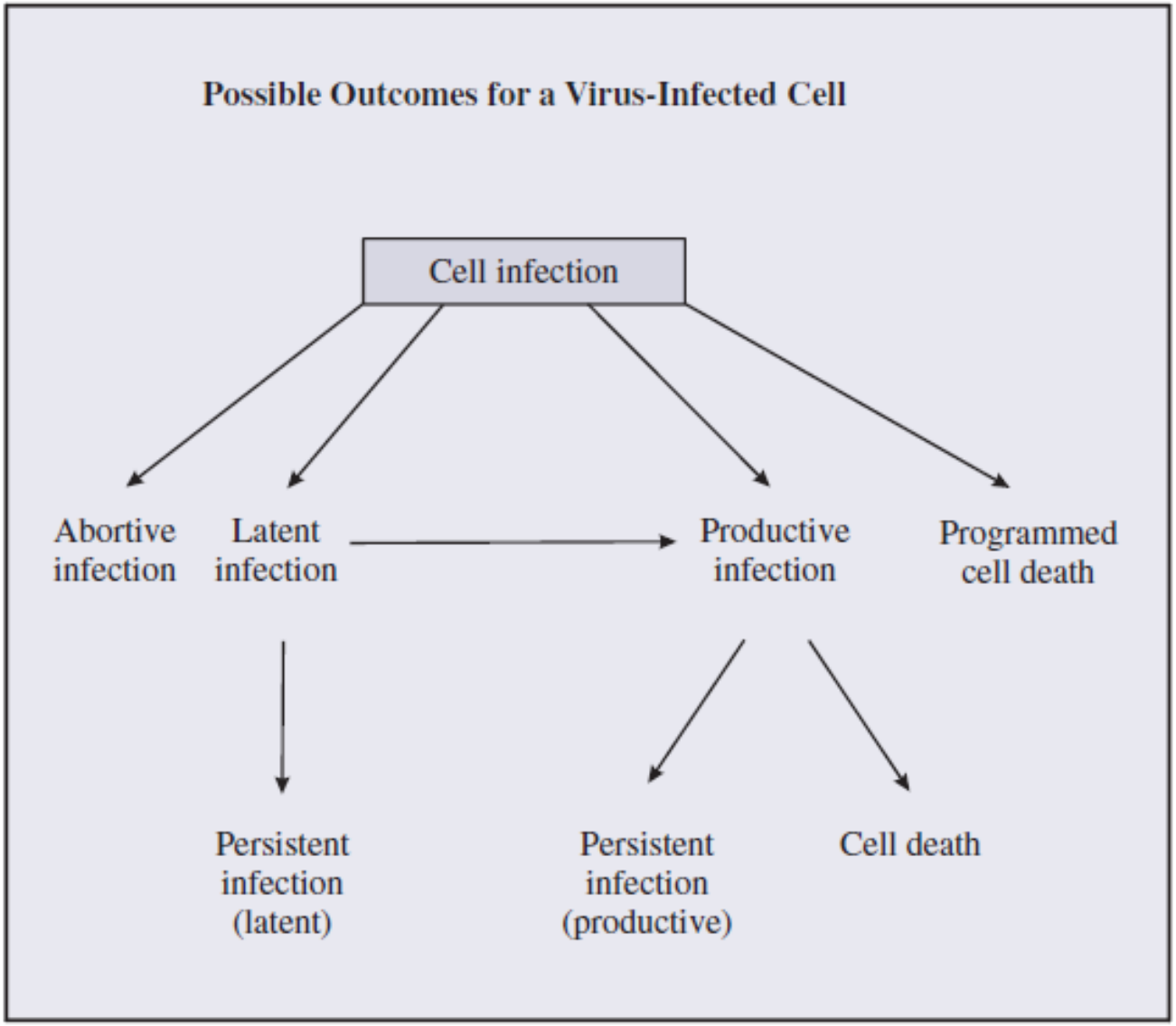
Outcomes of the virus infection for the host



In the previous few chapters we have looked at aspects of the virus replication cycle that culminate in the exit of infective progeny virions from an infected cell. When this is the outcome the infection is said to be **productive**. Virions may be released when the host cell lyses, or the cell may survive releasing virions for a period, which may be short, as in the case of HIV infection, or it may be long, as in the case of hepatitis B virus infection.

Some virus infections, however, are not productive, for a variety of reasons.

- An infection may become **latent** with the virus genome persisting, perhaps for the lifetime of the cell, and perhaps in the daughter cells if the cell divides.
- An infection may be **abortive**, in which case neither a latent infection nor a productive infection is established. One cause of an abortive infection is a virus with a mutated genome; the virus is said to be defective. It is unable to undergo a complete replication cycle, unless the cell is also infected with a virus that can provide the missing function(s). A virus that is able to provide functions for a defective virus is known as a helper virus.

Some virus infections persist in their hosts for long periods, sometimes for life. In some cases persistent infections are productive, e.g. HIV; in other cases persistence may take the form of periods of latency alternating with periods of productive infection, e.g. many herpesviruses. Long-term infection with some viruses may lead to the development of cancer in the infected host.

Over time the organisms that are hosts to viruses have evolved anti-viral defences, but the viruses have not sat idly by. The relationship between a virus and its host usually involves an arms race and viruses have developed various countermeasures against host defences.

Non-productive infection

Under some circumstances a virus infects a cell, but the replication cycle is not completed. If the virus genome persists in the cell the infection is said to be latent; otherwise, it is an abortive infection.

Latent infections

When a latent infection is initiated the virus genome is maintained in the infected cell either as a sequence of DNA integrated into the cell genome, or as multiple copies of covalently closed circular DNA (Figure 9.7).

In eukaryotic cells the virus DNA is associated with host cell histones, which play roles in the maintenance of latency.

In the case of retroviruses, the integration of a copy of the virus genome into the cell genome is an early stage in the virus replication cycle. When the infection is latent events do not progress beyond this stage, but if the intracellular environment changes to become favourable for replication of the virus then the latent infection may progress to a productive infection.

The phenomenon of latent phage infection of a bacterium is known as **lysogeny** and the phage is said to be **temperate**. The phage genome (the prophage) can persist in the cell in ways similar to the persistence of latent animal virus infections (Figure 9.7).

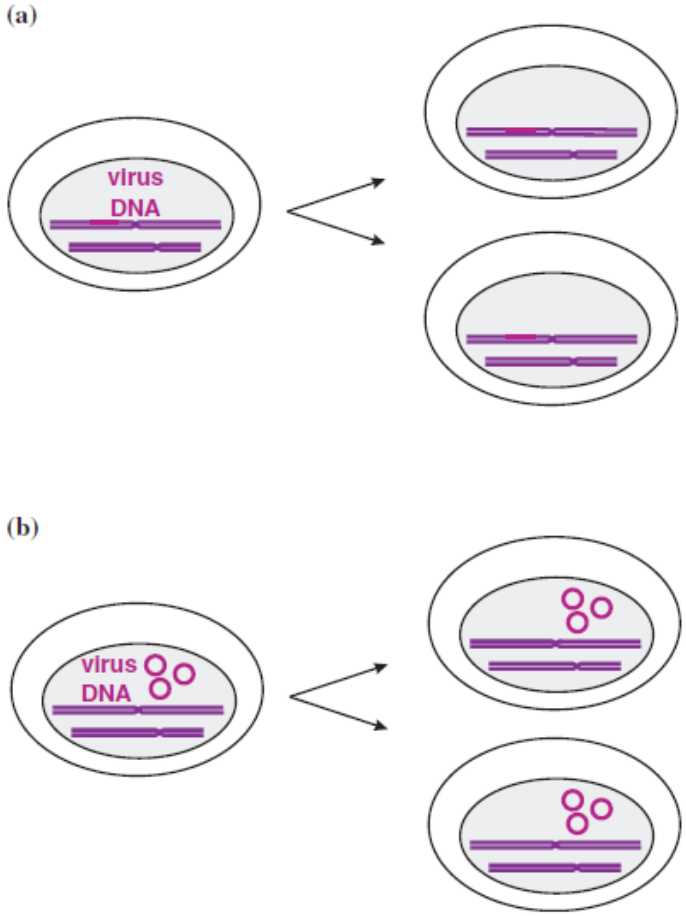


Figure 9.7 *Maintenance of virus genomes in cells with latent infections.* (a) Virus DNA integrated into a cell chromosome. After infection of the cell the virus genome is integrated into the genome of the host cell, e.g. retroviruses. (b) Virus DNA present as multiple copies of circular molecules. After infection of the cell the virus genome is circularized and replicated, e.g. herpesviruses. If a latently infected cell divides the virus genome is normally replicated along with the cell genome so that each daughter cell contains a copy/copies of the virus genome.

In many cases the prophage is integrated into the bacterial genome, but some prophages persist as non-integrated circular DNA.

Many latent infections may be activated to become productive infections, a process known as induction. This may occur if the following happen.

- A eukaryotic host cell moves into another phase of the cell cycle.
- The host cell is irradiated with ultra-violet light. This might trigger, for example, a latent phage infection to replicate and lyse the host cell, or a latent herpes simplex virus infection to replicate and cause a cold sore.
- A host organism becomes immunocompromised. This is another trigger that can reactivate a latent herpes simplex virus infection.
- The host cell becomes infected with a second virus that provides a function that the first virus lacks. Terms used for the first and second viruses in this relationship are satellite virus and helper virus, respectively.

Abortive infections

An abortive infection is one where the infection is nonproductive and the virus genome does not persist in the cell as a latent infection. An infection might be abortive for reasons concerning the cell, the environmental conditions and/or the virus.

Some virions may contain mutated genomes that may be able to initiate the replication cycle, but may not have the full set of functional genes necessary to complete it. Such virions are said to be **defective**, and if they infect cells without the means of complementing the mutated or missing genes the result is an abortive infection.

There are a number of types of defective virus. One type is known as a **defective interfering particle (DIP)**. DIPs often arise in the laboratory after animal viruses have been passaged several times in cell culture.

Most DIPs contain less nucleic acid than the standard virus from which they were derived. By themselves DIPs are either non-infectious or they can initiate only abortive infections. The standard virus can act as helper virus to a DIP, so in cells that are coinfected with a DIP and the standard virus the DIP is able to replicate its genome and produce progeny DIPs.

Productive infections

Spread of infections within multicellular hosts

Progeny virions from the first-infected cell of a multicellular host may infect cells nearby, for example common cold viruses and rotaviruses might infect other epithelial cells lining the respiratory tract and the intestinal tract, respectively. Most adjacent animal cells are separated from each other only by their plasma membranes, providing opportunities for direct cell-tocell spread for some viruses.

Plant viruses are able to spread from cell to cell by passing through plasmodesmata, and each plant virus encodes between one and four specialized proteins that enable them to do this. These proteins are known as movement proteins (MPs) and they act in a variety of ways. Some MPs form complexes either with virus RNA or with virus RNA plus coat protein molecules; other MPs form tubular structures through which fully encapsidated virus RNA is transported (Table 9.2). MPs are multifunctional proteins with other roles in the virus replication cycles.

In some circumstances progeny virions from infected cells may be transported to distant sites in the host, where susceptible cells may become infected. In the animal body the blood and the nerves may act as transport vehicles, while in plants transport may occur via the phloem.

Table 9.2 Involvement of plant virus movement proteins (MPs) in the spread of infection via plasmodesmata

Mode of transport through plasmodesmata	Virus examples
Virus RNA–MP complexes transported	Tobacco mosaic virus Cowpea chlorotic mottle virus
Virus RNA–coat protein–MP complexes transported	Cucumber mosaic virus
Virions transported through tubules composed of MP	Cowpea mosaic virus

Disease

Many virus infections result in no disease in the host, while at the other end of the scale a virus infection may result in fatal disease, such as rabies or AIDS.

Disease may be manifest as symptoms and/or signs. In medical terminology symptoms are subjective features, such as abdominal pain and fatigue, whereas signs are objective features, such as blood in the faeces and skin rashes. Symptoms can be recognized only by the infected individual, whereas signs can be recognized by others.

Infection with some viruses, such as dependoviruses, some herpesviruses and some reoviruses, apparently never causes disease, while infection with other viruses, such as human parvovirus B19, poliovirus and hepatitis B virus, may or may not result in disease. Infections that do not result in disease are said to be **subclinical** or **asymptomatic**.

Not all viruses are pathogens (disease-causing agents) and some are pathogenic only under certain circumstances. For pathogenic viruses factors that can affect the outcome of infection include the following.

- *The virulence of the virus strain.* The virulence of a virus (or any micro-organism) is a measure of the severity of disease it is capable of causing. Influenza A type H5N1 can be said to be more virulent in humans than types H1N1 and H3N2 as type H5N1 causes more severe disease than the other two types.
- *The dose of virus.* A larger dose of virus may result in a shorter incubation period (the time between infection and the first appearance of signs and/or symptoms).

Host factors that can affect the outcome of infection include the effectiveness of immune systems, and these in turn vary with age and nutritional status of the host. It should be noted that a strong immune response by the host does not guarantee the elimination of the virus. HIV continues to replicate in the presence of high levels of HIV-specific antibody and T cells. In some cases signs and/or symptoms may result from the host's immune response against the virus. The measles rash and herpes simplex lesions are clinical manifestations of attempts by the human body to destroy virus-infected cells.