Acute, chronic and latent infections

This chapter deals with the principles of acute, chronic and latent infections, and may give examples of viruses to demonstrate these principles. It is beyond the scope of this chapter to give details about how each individual viral infection is unique.

Acute primary infection

In an acute viral infection (Fig. 1), the virus replicates without the immune system having any recall for that virus' antigens. The body, therefore, relies on innate immune response initially, and the virus replicates at the point of origin, and, depending on the virus, may spread to local lymph nodes and then to further organs via the blood, for example Varicella. Some viruses, such as human papillomavirus, only replicate locally, although a systemic antibody response may be seen.

Soon after infection, as viral levels are increasing, the immune system responds, triggering a cellular as well as humoral immune response. IgM usually appears first, and then disappears after the acute infection; IgG appears after IgM, and may continue for long periods, sometimes for life. Depending on the site, other immunoglobulins, such as IgA on mucosal surfaces, may be significant in controlling infection and preventing re-infection.

Symptoms usually coincide with the period of viral replication, and usually subside after the virus is cleared. The arrow indicates the possibility of post-infectious symptoms – often due to immune responses, e.g. certain rashes, or Guillain-Barré syndrome. Varicella is shown in Fig. 6 of Chapter 49, as an example.

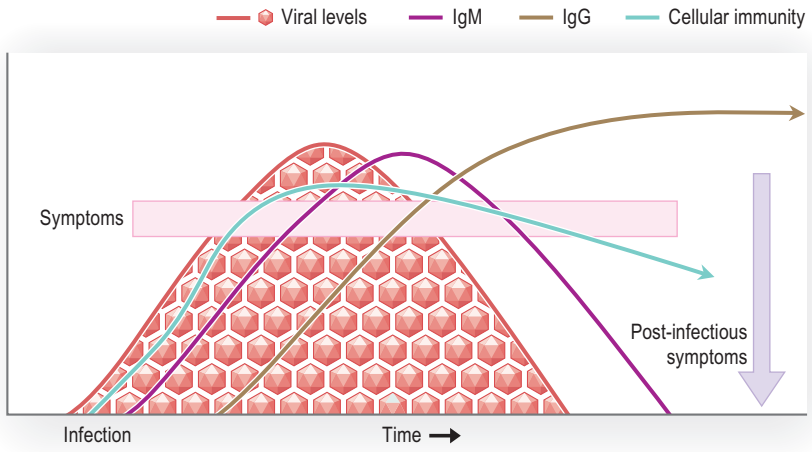

Fig. 1 **Acute infection – primary infection.**

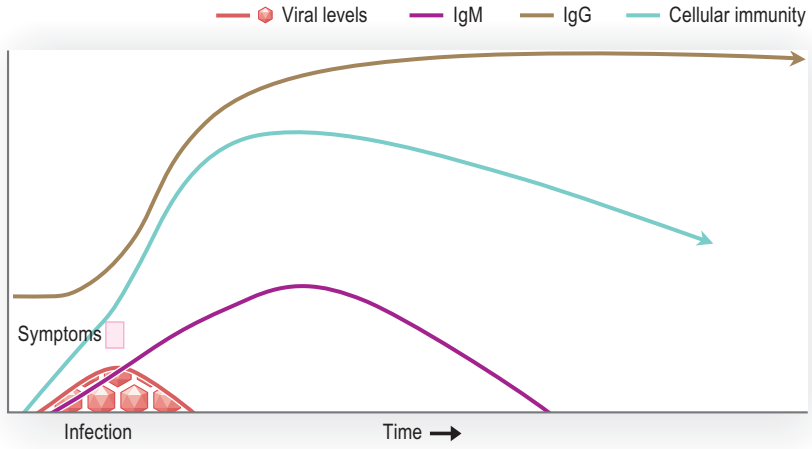

Fig. 2 **Acute infection – secondary infection.**

Acute secondary infection

When a re-infection (Fig. 2), occurs with the same virus, the immune system is able to rapidly respond, as immune memory occurs. Viral replication is suppressed more quickly than with a primary infection, and levels do not usually become significant. Symptoms are often absent and, if they occur, they are usually much milder than with a primary infection.

It should be noted that with some acute infections, such as influenza, one strain may not provide optimal immunity against another strain, and re-infections may present in the way primary infections do. The extent to which the immune response to one virus is protective against a related virus and the extent to which immune memory is able to prevent symptoms with a re-infection both depend on the virus in question.

In some cases, re-infection with a related strain leads to worsening of symptoms, or different symptomatology, such as with Dengue virus infection, where immunity to one strain enables the replication of other strains via uptake into monocytes; the virus therefore replicates by antibody-mediated enhancement of infection. It is in cases such as these that Dengue haemorrhagic fever and Dengue shock syndrome occur.

Chronic infection, reactivation and disease progression

In some cases, clearance of the infecting virus is not possible. Viruses have a variety of methods to escape from the immune system, and some enable the virus to remain in the host indefinitely. Some chronic infections can eventually be cleared, although some are rarely cleared and some cannot be cleared.

These escape methods include:

- integration of the viral genome into the host's genome (e.g. HIV)
- suppression of MHC-I and MHC-II molecules, preventing the immune system from killing infected cells (e.g. herpesviruses)
- up-regulation or down-regulation of cytokines or cytokine response (e.g. HIV), thereby altering immune responses
- inhibition of viral replication to induce latency (herpesviruses)
- infection of immune-privileged areas, where the immune system cannot eliminate the virus (e.g. human papillomavirus)
- infection of lymphocytes
- mutation that changes the viral antigens so that previous immune responses are not effective against the mutant (e.g. HIV)
- blocking apoptosis pathways (e.g. human papillomaviruses).

In cases where viral infection becomes chronic (Fig. 3) viral levels may vary and the degree to which symptoms are experienced may vary. Hepatitis B virus, for instance, may have occasional flare-ups of infection in addition to progressive liver damage, while HIV exhibits a slow disease progression. Some individuals are unable to clear viruses that most people can clear, for instance rare cases of chronic poliovirus excretion or rubella virus in congenitally infected infants.

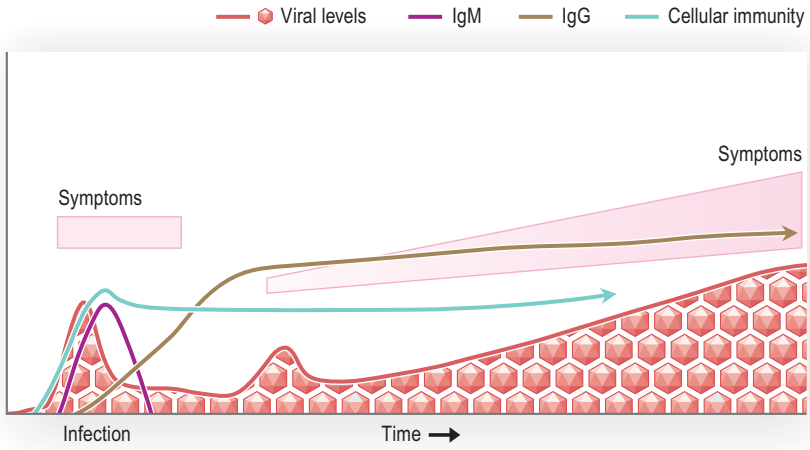

Fig. 3 **Primary infection followed by chronic infection, with periods of reactivation, and disease progression.**

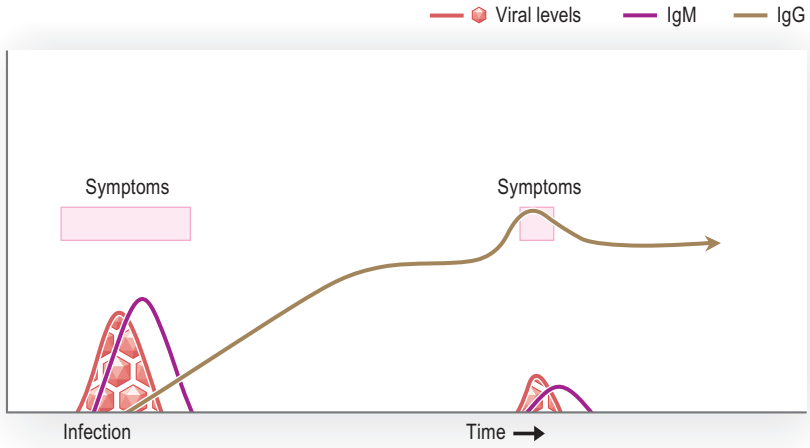

Fig. 4 **Primary infection followed by latent infection, with a period of reactivation.**

Latent infection and reactivation

Chronic infection (Fig. 4) is characterised by some degree of replication during the phases where the virus is not active. Examples of this would be rubella virus in cases of congenital infection, where replication levels are high, and HIV, where levels of virus increase over time.

Latent infection is characterised by absence of replication during inactive periods. Varicella virus, for instance, exhibits true latency, and can reactivate as shingles (Fig. 5). Other viruses that undergo periods of true latency include hepatitis B virus and JC virus. Viruses that can undergo true latency may also replicate at low levels, as in the case of chronic hepatitis B infections.

The progression of disease is similar to that described under chronic viral infections – periods of active replication can occur, with return of symptoms. When such reactivation occurs, IgM levels may again be detectable.

An example of a latent viral infection that causes disease when it reactivates in an immunocompromised host is JC virus, causing progressive multifocal leukoencephalopathy (PML), and also varicella, which causes shingles when it reactivates.

An example of a chronic viral infection that causes disease when it reactivates is chronic hepatitis B infection.

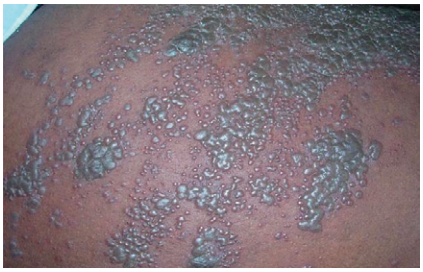

Fig. 5 **Varicella zoster virus reactivates as shingles.** (Photo courtesy of Prof. HF Jordaan, University of Stellenbosch.)