Poliovirus is transmitted between humans by an oral-faecal route. Ingestion of contaminated material delivers virus to the gut where initial replication occurs. Similarly, the oral poliovirus vaccine replicates in the gut but due to attenuation does not cause disease or disseminate to the blood. The poliovirus receptor CD155 is expressed on many cell types that include gut epithelial cells (and M cells) and cells of monocyte lineage (these include macrophages and dendritic cells). It is unclear whether replication in gut epithelial cells occurs first or if virus is transported directly across the epithelium by M cells. Once in the lamina propria the virus targets mucosal lymphoid tissue such as the Peyer’s patches and infects macrophages and dendritic cells. This facilitates virus spread to other lymphoid tissues by trafficking of infected cells. In lymphoid tissue wild-type poliovirus but not vaccine strains access the blood and disseminate to other organs including the CNS.
Ingestion of material contaminated with poliovirus or administration of oral poliovirus vaccine delivers the virus to the gut where initial replication takes place. Gut epithelial cells express the poliovirus receptor CD155 and may be an initial site of replication. Alternatively, uptake of virus by M cells can occur which directly transports virus across the gut epithelium. Once in the lamina propria virus can infect cells of the monocyte lineage such as macrophages and dendritic cells that also express CD155 receptors. These cells are abundant in mucosal lymphoid tissues such as the Peyer’s patches. Virus can also disseminate to other lymphoid tissues such as tonsils and lymph nodes via trafficking of infected cells. A cell-mediated immune response to virus occurs in the gut as well as a humoral immune response that generates mucosal neutralising antibodies (important in enterovirus infection) and establishes long-term immunity.
Wild-type poliovirus initially replicates in the gut and then disseminates to the bloodstream via secondary lymphoid tissues. Once in the bloodstream the virus gains access to the central nervous system. It is unclear how this occurs but potentially involves three mechanisms. (1) Trafficking of infected monocytes across the blood-brain barrier during the natural turnover of perivascular macrophages and microglial cells (transmigration). (2) Direct infection of brain capillary endothelial cells may occur since these cells express the poliovirus receptor CD155 (endothelial cell infection). (3) Entry into the central nervous system via axonal migration of virus into the spinal cord in peripheral motor neurons (axonal migration). Neurons express the poliovirus receptor CD155 and once poliovirus is present in the brain and spinal cord damage to motor neurons due to virus replication can cause paralysis.
An antibody response is mounted against wild-type poliovirus and the vaccine strain following infection of the gut. Virus or viral antigens are trapped by follicular dendritic cells in the B cell zone of mucosal secondary lymphoid tissues such as the Peyer’s patches for presentation to B cells. B cells that recognise viral antigens are then activated by CD4+ follicular helper T cells and differentiate into plasma cells that secrete virus-specific secretory IgM and IgA. Memory B cells are also generated that mediate long-term immunity. CD4+ T cells are activated by interaction with antigen presenting cells such as macrophages and dendritic cells that have engulfed viral antigens. Secretory antibodies are actively transported across the gut epithelium to the lumen where they can opsonise virus and reduce infectivity.
Plasma B cells present in the gut lamina propria secrete dimeric IgA and pentameric IgM. The epithelial cells of the gut (and also the respiratory tract) express the polymeric immunoglobulin receptor (PIgR) that binds to the J chain of dimeric IgA and pentameric IgM. The antibody-receptor complex is then actively transported through the epithelial cell from the basolateral membrane to the apical membrane. The receptor-bound antibodies are then released into the gut lumen by enzymatic cleavage of the receptor leaving a small protein attached to the antibody (called the secretory component). In the lumen, the antibodies can opsonise viruses by binding to antigens expressed on the virus surface thereby reducing infectivity and promoting clearance.
An additional mechanism of immune control that is mediated by mucosal antibodies produced in the gut (and the respiratory tract) is the potential for these antibodies to bind antigens on viruses that have been released or transported across the epithelium. IgA and IgM secreted by B cells in the lamina propria can initially bind to viruses before binding to the polymeric immunoglobulin receptor. In this way the antibody-antigen complex can be excreted across the epithelium and returned to the gut lumen to reduce viral spread.