The oral poliovirus vaccine (OPV) is an attenuated strain of poliovirus that is capable of a low level of replication in the gut. Due to attenuating mutations in the virus genome the vaccine strain does not cause disease or disseminate to the bloodstream and central nervous system. Virus replication in the gut triggers an adaptive immune response including antiviral T cell responses and humoral responses that generate mucosal neutralising antibodies. Very rarely due to underlying immune dysfunction the vaccine strain can revert to virulence due to back mutations introduced during unchecked rounds of replication. These mutations can restore the ability of the virus to disseminate to the central nervous system and cause poliomyelitis.
In agammaglobulinaemic recipients of the oral poliovirus vaccine, there is an impairment of the humoral immune response to viral replication in the gut. The vaccine strain of poliovirus is an attenuated live replicating virus and since mucosal antibodies play an important role in the control of enterovirus infections, the virus can be permitted to undergo many rounds of replication which ultimately may lead to reversion of the vaccine strain to a virulent phenotype. Genetic mutations can accumulate in the viral genome that reverse the attenuating mutations originally introduced into the vaccine strain. This is particularly common to RNA viruses such as poliovirus where the mutation rate is high due to a lack of proof-reading by the RNA polymerase. Reversion of the vaccine strain to wild-type virus restores the ability to disseminate to the central nervous system.
Infants with agammaglobulinaemia receive partial protection from infection with enteric organisms if they are breastfed due to the presence of maternal immunoglobulins directed towards common gut pathogens. However, the infant’s own mucosal immune response plays a more important role in immunity to gut infections, particularly the humoral immune response that generates mucosal antibodies. Mucosal antibodies play a major role in control of enterovirus infections and patients with agammaglobulinaemia have increased susceptibility. Mucosal antibody responses are also important role in the respiratory tract and impairment may lead to increased respiratory tract infections.
Due to impaired humoral immune responses in the infant gut and only partial protection offered by maternal antibodies in breastmilk, the oral poliovirus vaccine strain can undergo multiple rounds of replication which can introduce genetic mutations into the virus genome that reverts the vaccine strain to wild-type poliovirus. This may take many months to develop but once a revertant is generated it restores the ability of the virus to disseminate to the bloodstream and central nervous system causing poliomyelitis. Paralysis occurs due to destruction of motor neurons in the spinal cord and brain mediated by viral infection of these cells.
The presence of antiviral neutralising antibodies in breastmilk may provide partial protection from uncontrolled replication and spread of infant administered oral poliovirus vaccine strains in agammaglobulinaemia. However, uncontrolled replication of the virus due to impaired infant humoral immune responses can facilitate reversion of the virus to a virulent phenotype. Multiple rounds of viral replication can introduce genetic mutations into the vaccine strain viral genome that reverse attenuation. Virus revertants may be partially controlled by maternal antibodies, however after weaning, the reverted virus can enter the blood and disseminate to the central nervous system causing poliomyelitis. Shedding of poliovirus revertants from the infant gastrointestinal tract also poses a health risk to contacts.