Virus Infection

Virus infection of higher organism is cumulative result of al process of replication and gene expression and its range in complexity and duration from a very brief, superficial interaction between the virus and its host to infection that may encompass the entire life of the host

Immune response to virus infection in animals

The most significant response to virus infection in vertebrate is the activation of both cellular and humoral arms of immune system.

The major impact of the humoral immune response is the clearance of virus from the body that is serum neutralization stop the spread of virus to uninfected cells.

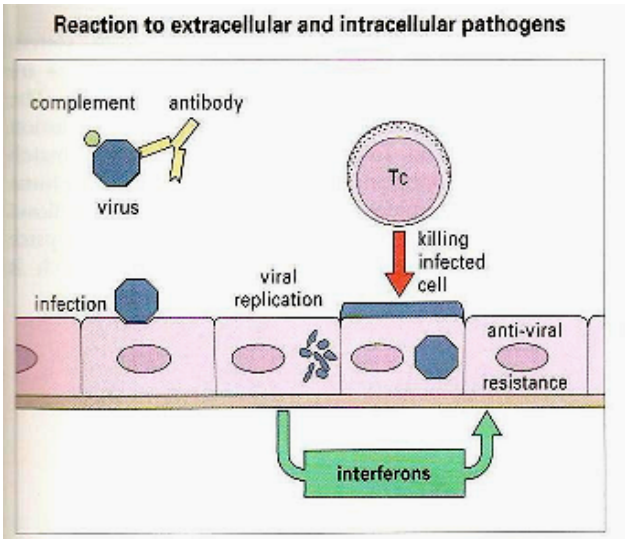


Fig. 1.18 Different immunological systems are effective against different types of infection, here illustrated as a virus infection. Antibodies and complement can block the extracellular phase of the life cycle, and promote phagocytosis of the virus. IFNs produced by infected cells can signal to uninfected cells, and induce a state of antiviral resistance in them. Viruses can only multiply within living cells; Tc cells are effective at recognizing and destroying the infected cells before significant replication has occurred.

Virus infection induces at least three classes of immunoglobulin IgG, IgM, IgA.

IgM is large, multivalent molecule that most effective at cross-linking large targets (e.g. bacterial cell wall or flagella) but is probably less important in compacting virus infection.

In contrast, the production of IgA is very important for initial protection from virus infection. Secretory IgA is produced at mucosal surface and results in mucosal immunity an important factor in preventing infection from occurring.

IgG is probably the most important class of Abs for direct neutralization of virus particles in serum and other body fluids.

Direct virus neutralization by antibody result from number of mechanisms

1- Conformational changes in virus capsid by antibody binding or blocking the function of virus target molecule (receptor binding).
2- Binding of Abs to virus lead to pathogenesis of Abs coated target molecules by mononuclear cells or polymorphonuclear leukocytes (PMN). This process is mediated by the presence of Fc receptor on the surface of these cells.

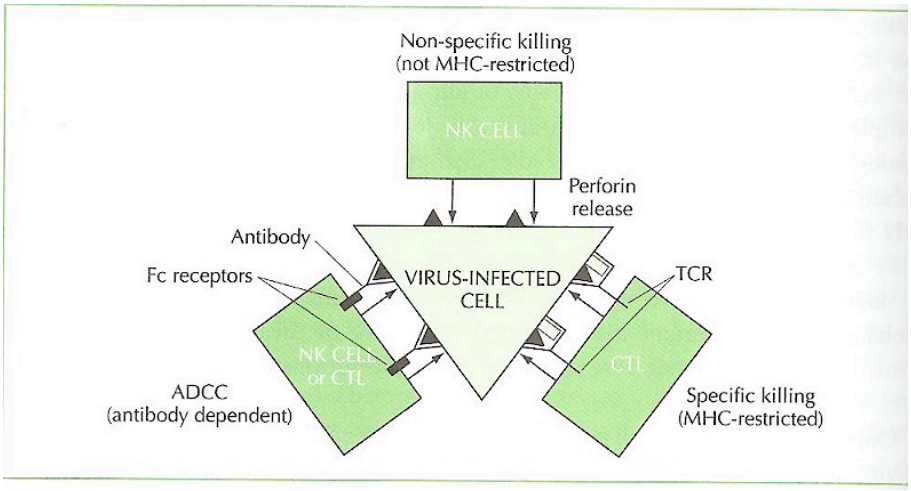
   In some case opsonization of virus by binding with non-neutralizing Abs can enhanced virus uptake and this occur with rabies virus and human immunodeficiency virus (HIV)?
3- Antibody binding lead to activation of complement cascade which assists in neutralizing of virus particle through morphological alternation.

Despite all the above mechanism, cell mediated immunity is probably more important than humoral immunity in the control of virus infection and this demonstrated by the following observation:

A- Congenital defect in cell mediated immunity result in virus infection rather than bacterial infection.
B- The function detection in AIDS patient is reduction in the ratio of T helper cell and commonly ADIS patient suffer from opportunistic viral infection like HSV, CMV, EBV.

Cell mediated immunity is effective through 3 main systems:

1- Non specific cell Killing (mediated by NK cells)
2- Specific cell killing (mediated by cytotoxic T lymphocyte CTLs)
3- Antibody-dependant cell mediated cytotoxicity (ADCC)

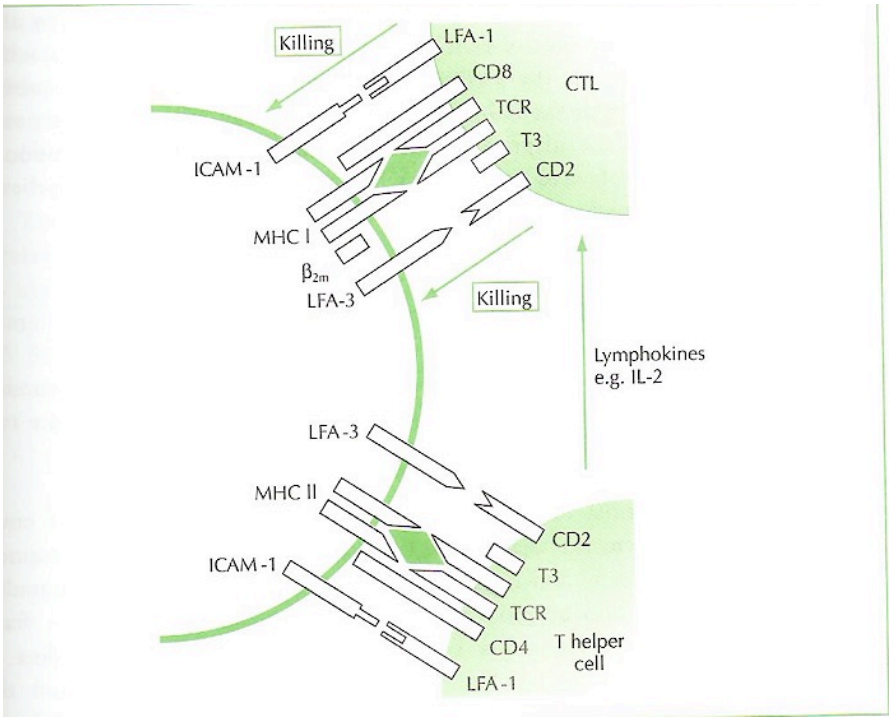


*Natural killer cells mediate cell lysis independently of conventional immunological specificity. They are not MHC restricted and are active without the requirement for sensitizing antibodies. They are therefore the first line of defense against viral infection. NK cells are the most active in the early stages of infection and their activity is stimulated by interferon -α/β.

NK cells are exist in active form but their action is inhibited by MHC class I antigens allowing recognition of self and preventing total distraction of the body. It is known that some virus disturb normal cellular MHC-I expression and this is one possible mechanism of NK recognition of infected cells.

*Cytotoxic T-lymphocytes (CTLs) are usually of CD8 (suppressor) phenotype. CTL are the major cell mediated immune response to virus infection and are MHC restricted; that is, clones of cells recognize a specific antigen only when presented by MHC-I antigen on the target cell to T-cell receptor/CD3 complex on the surface of the CTL.CT activity requires help (i.e., cytokine production) from T-helper cells.

The kinetics of the CTL response (peaking at about 7 days after infection) is somewhat slower than the NK response (e.g., 3-7 days cf. 0.5-3 days) therefore, these are complementary system.



*Antibody-dependant cell mediated cytotoxicity. These mechanisms depend on the recognition of antigen on the surface of the target cell by antibody on the surface of the effecter cell. The antibody involved is usually IgG, which is bound to Fc receptors on the surface of the T-cell. ADCC therefore requires pre-existing antibody response and enhance does not occur early during primary virus infection.