IMMUNE RESPONSE TO INFECTIOUS DISEASES

Range of micro-organisms capable of causing infection & disease

- Viruses
- Bacteria
- Fungi
- Protozoa
- Helminths
- Arthropods
- Prions

Site of Infection

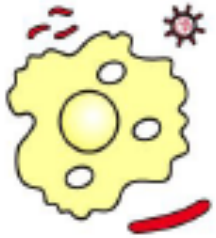
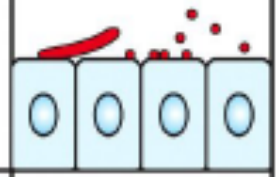
	Extracellular		Intracellular	
	Interstitial spaces, blood, lymph	Epithelial surfaces	Cytoplasmic	Vesicular
Site of infection				
Organisms	Viruses Bacteria Protozoa Fungi Worms	*Neisseria gonorrhoeae* *Mycoplasma* spp. *Streptococcus pneumoniae* *Vibrio cholerae* *Escherichia coli* *Helicobacter pylori* *Candida albicans* Worms	Viruses *Chlamydia* spp. *Rickettsia* spp. *Listeria monocytogenes* Protozoa	*Mycobacterium* spp. *Salmonella typhimurium* *Yersinia pestis* *Listeria* spp. *Legionella pneumophila* *Cryptococcus neoformans* *Histoplasma* *Leishmania* spp. *Trypanosoma* spp.
Protective immunity	Antibodies Complement Phagocytosis Neutralization	Antibodies, especially IgA Antimicrobial peptides	Cytotoxic T cells NK cells	T-cell and NK-cell dependent macrophage activation

Figure 10-4 Immunobiology, 6/e. (© Garland Science 2005)

Immune response to Infection

Comprises 2 main arms:

1. Innate immunity

2. Adaptive (acquired) immunity

Innate Immunity

①Mechanical barriers; i.e. bactericidal agent, microbiota.

②Humoral component; i.e. acute phase proteins, interferons, and Complement

③Cell component; i.e. phagocytes, natural killer cells, and eosinophils)

Innate Immune System

- Ability to recognize PAMPS through PRRs on DC and MØ.

- Lipotechoic acid (Gram +ve) and Lipopolysaccharide (Gram –ve) bacterial cell walls recognized by TLR on MØ leading to macrophage activation & cytokine production

Adaptive Immune System

- Initially slow to respond
- prevents re-infection with the same pathogen
- Specific immunity
- Memory (faster, more vigorous immunological response on re-exposure)

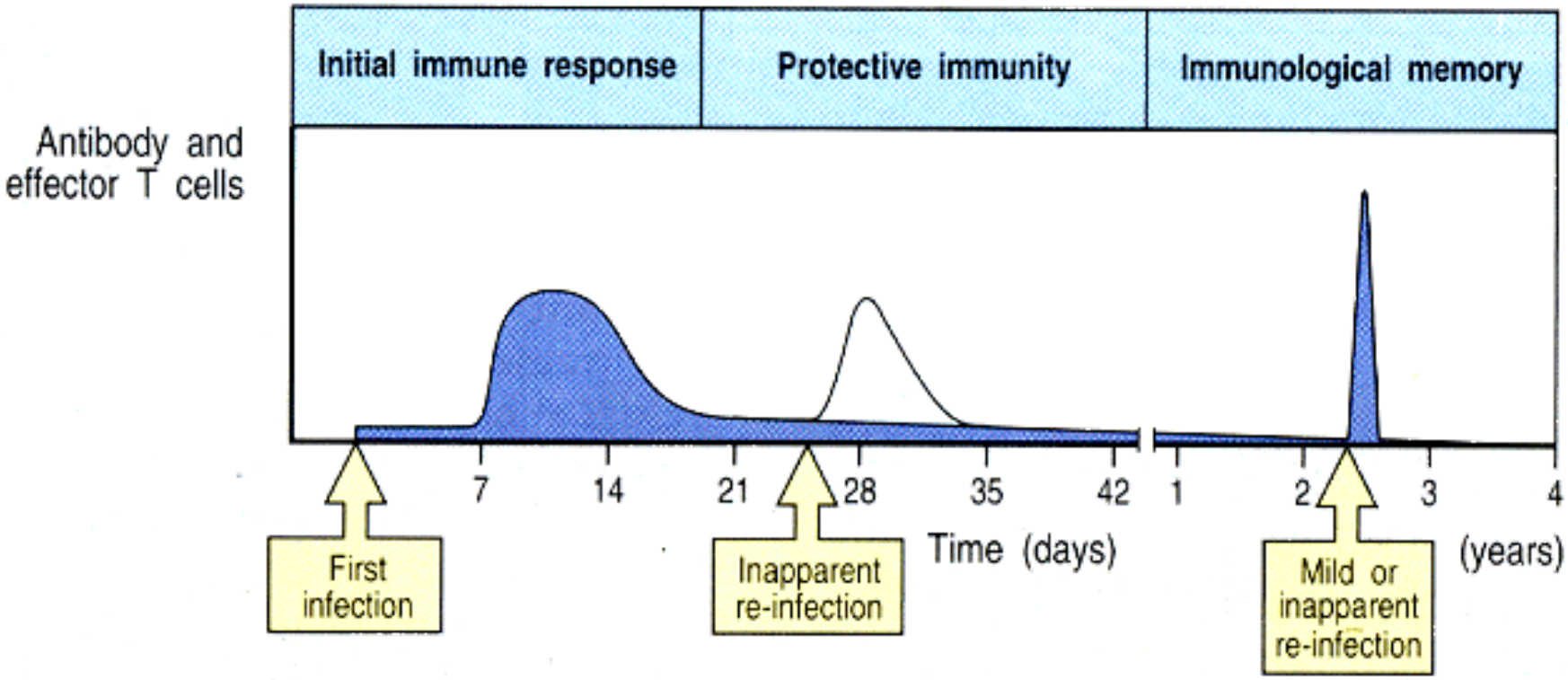
①Humoral-mediated response; Antibodies (Ab)

Defends against viruses when outside cells, bacteria, toxins, fungi, parasites.

② Cell-mediated response; T lymphocytes

Defends against pathogens (all viruses, some bacteria, fungi and protozoa) that have entered into our own cells. Thus much more destructive as destroys both pathogen and host cell.

Immunological Memory

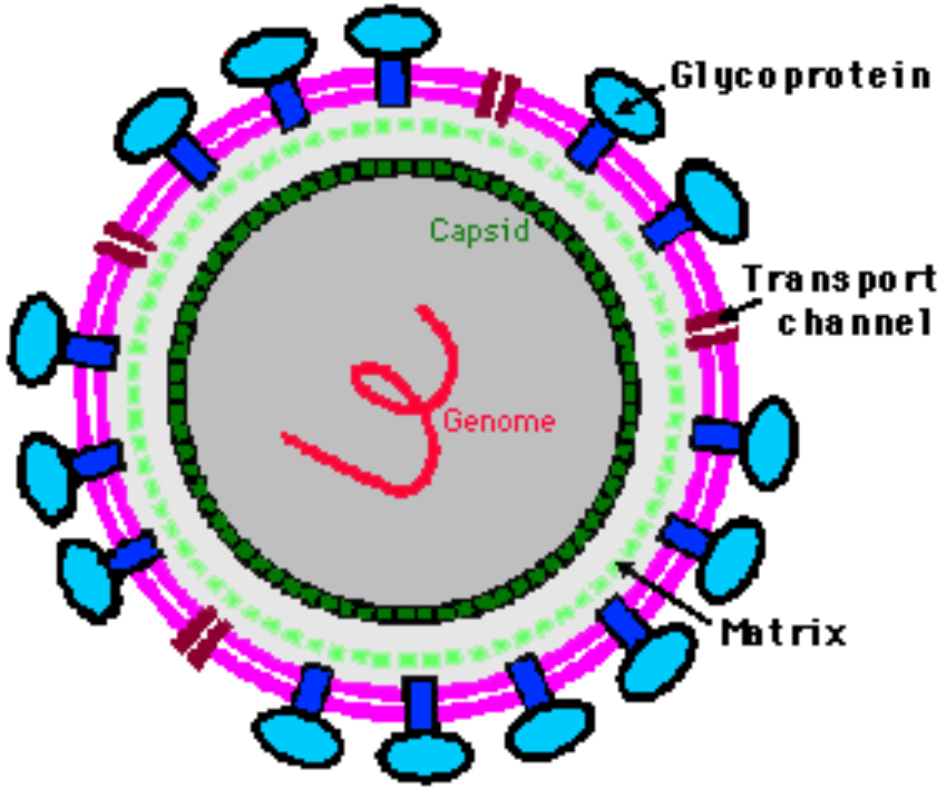


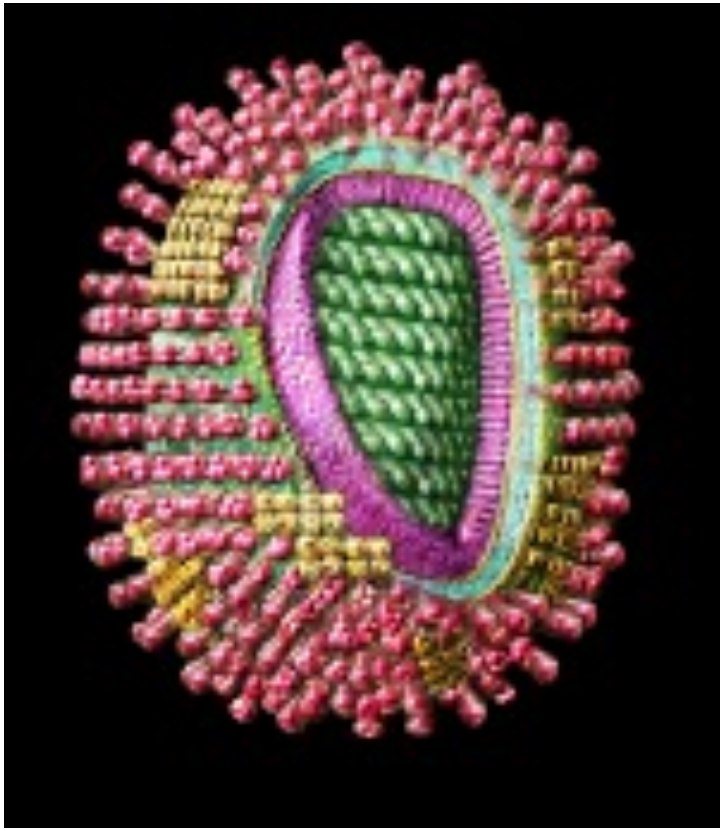
Immunity to virus infections

Flu Attack! How A Virus Invades Your Body

https://www.youtube.com/watch?v=Rpj0emEGShQ

Basic viral structure

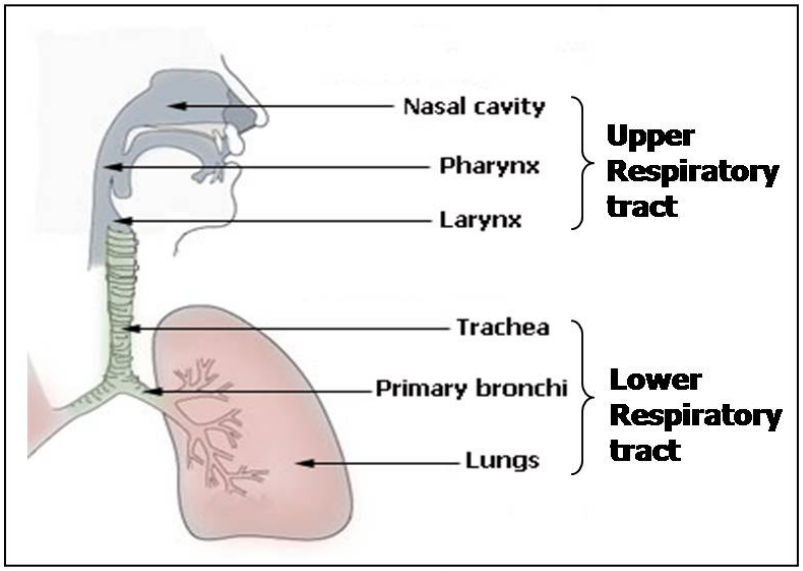




Capsid: Protects genome
Matrix proteins: Maintain virus structure
Glycoproteins: assist in entering the cell without damage
(human viruses are enveloped)
SYMMETRICAL SHAPE

Respiratory system – virus entry point

Respiratory system is a closed system designed to prevent host invasion derived from inhaled air



Most common respiratory viruses:
- Adenovirus
- Influenza virus
- Respiratory syncytial virus
- Rhinovirus

Symptoms: cough, runny nose (rhinorrhoea), airway mucus production (bronchitis), fever, scratchy throat (pharngytis), congestion up to 14 days.

Susceptibility
Immunocompromised
Infants (immature immune system)
HIV infected
Underlying pulmonary disease ie Cystic fibrosis, chronic lung disease, asthma

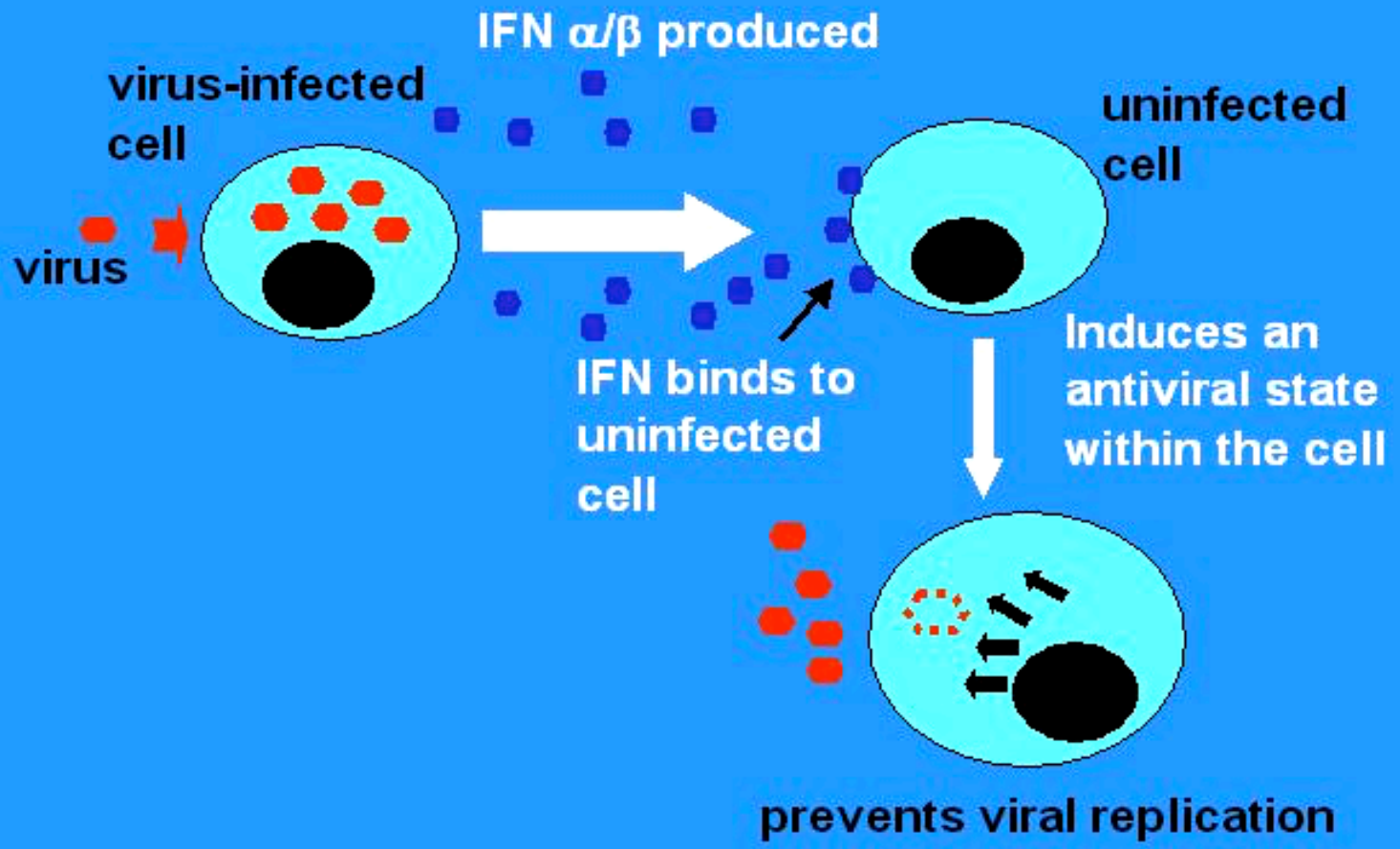
1-Interferon (IFN)

- Viral infection directly stimulate the production of IFN
- THUS Induce a state of antiviral resistance in uninfected cells.

① Type I IFNs; IFN α and β
produced by cells infected by viruses

② Type II IFNs; IFN γ
produced by antigen activated T cells (T_H1) and NK cells and therefore stimulate Tc, MØ, NK, and enhance the expreesion of MHC I and MHC II

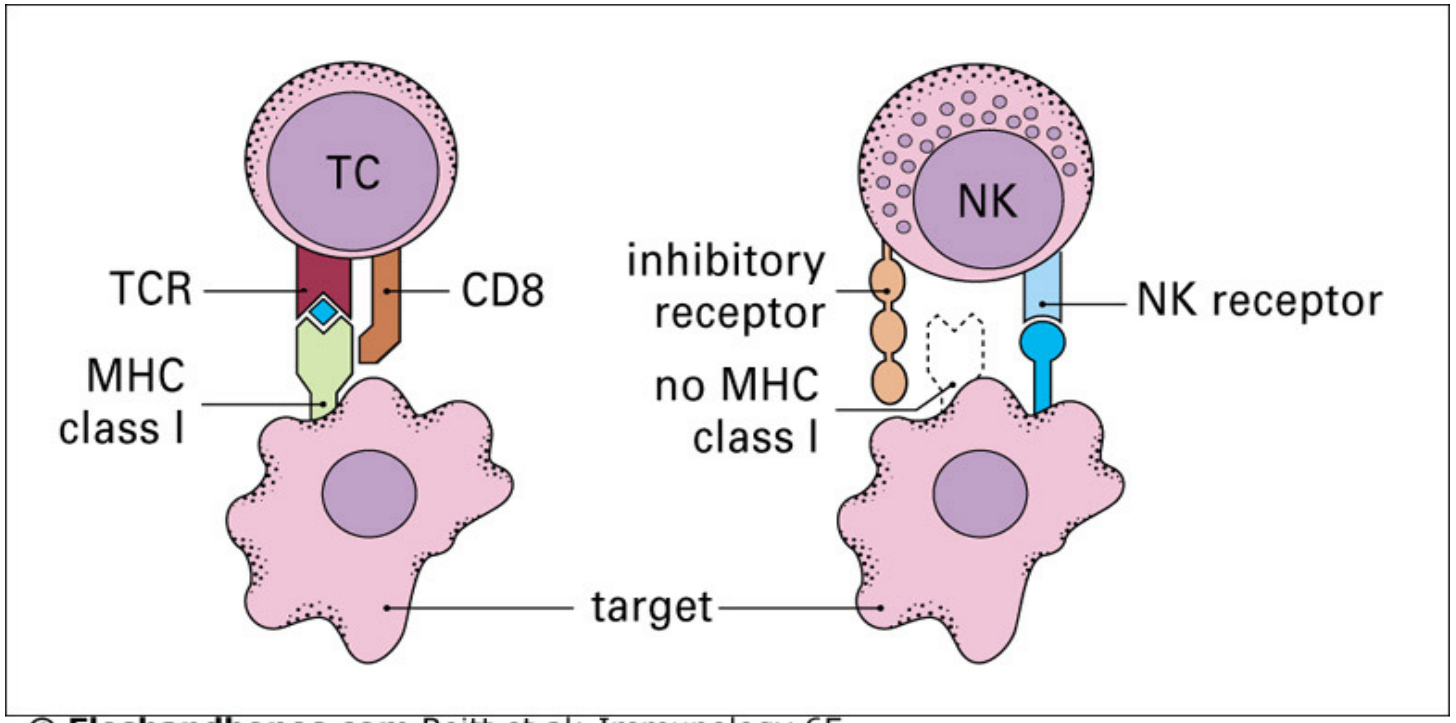
Antiviral action of interferon



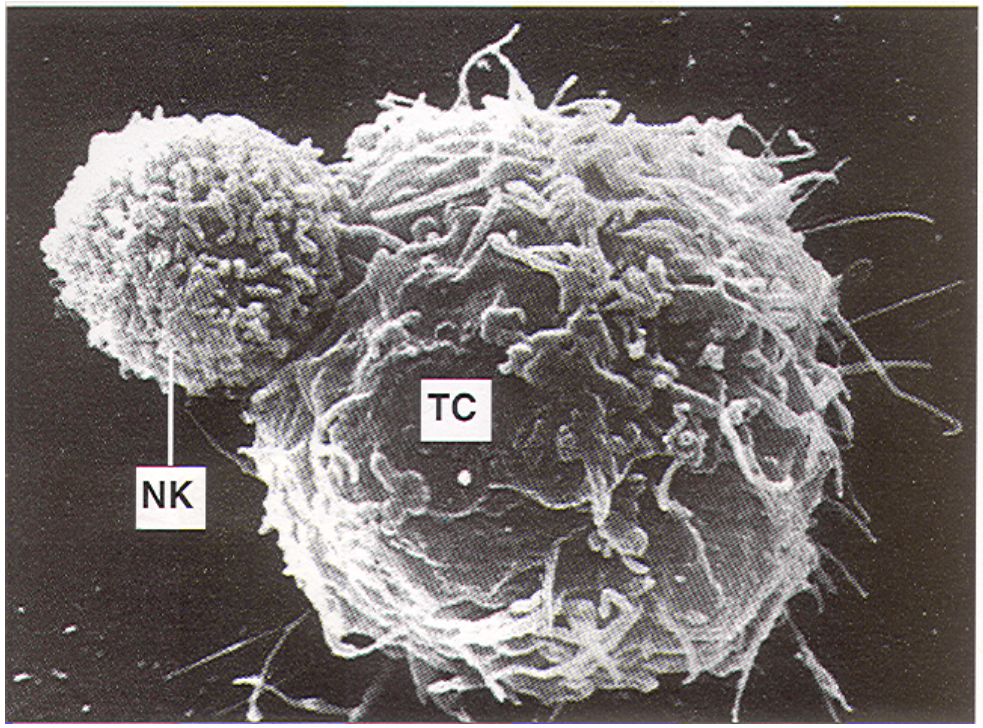
2- Natural Killer (NK) cells

- ✧ Recognise cells which do not express MHC-I
- ✧ No antigen specificity
- ✧ Have cytotoxicity function i.e. can lyse target cells

Recognition of target cells by Tc cells and NK cells



NK cell mediated killing



Increased by exposure to IFN α and β and also to IFN γ, TNF α or IL12 from phagocytes.

Adaptive Immunity

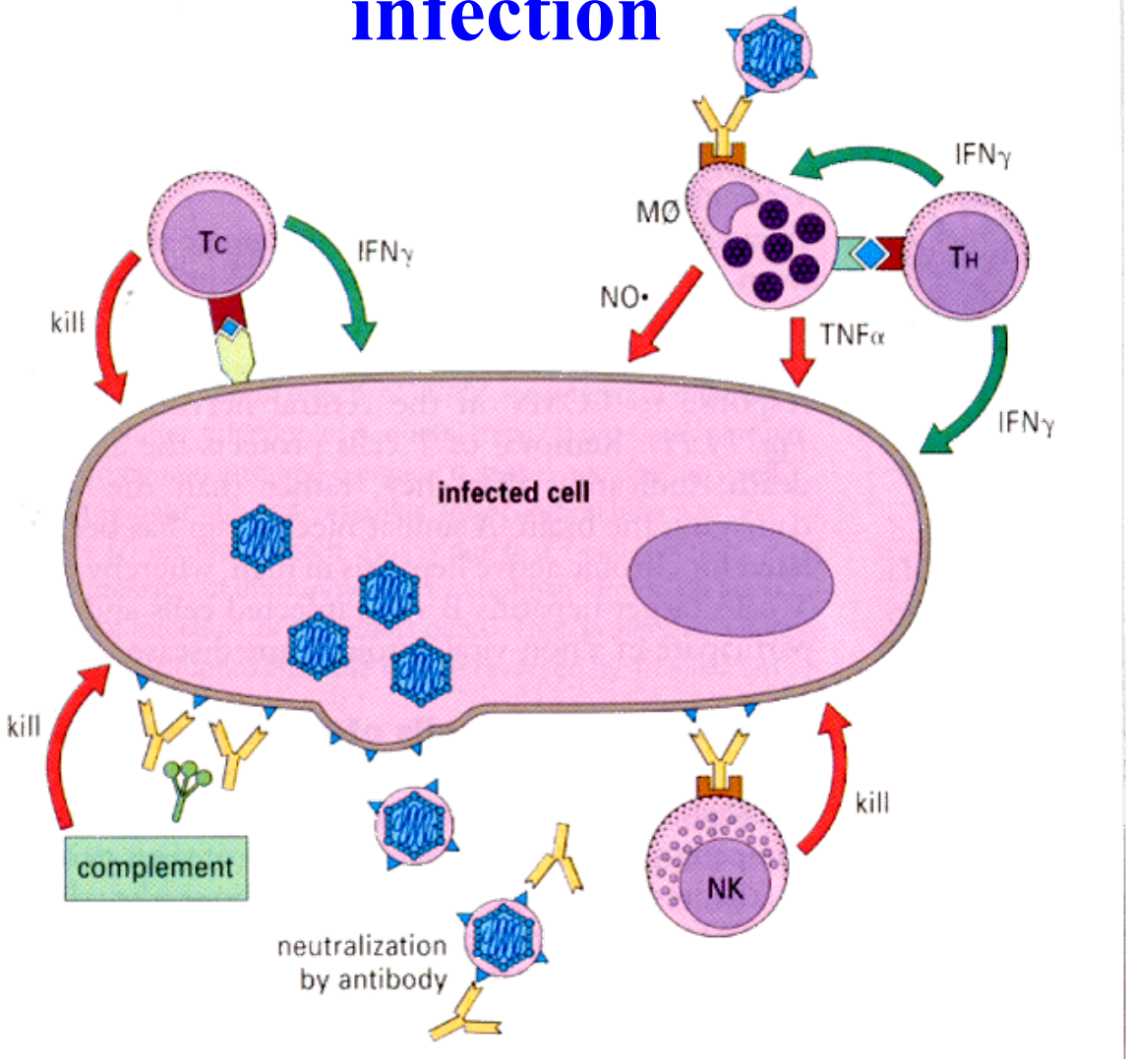
Combination of both

Humoral-mediated (Ab) AND Cell-mediated response

ANTIBODY RESPONSE

- Antibodies provide a major barrier to prevent virus spread between cells and different tissues.
- Recognise antigens on virus particles and on the surface of virus-infected cells.
- Three important types against viruses: IgG, IgA, IgM

Antibody function against viral infection



Antiviral Effects of Antibody

Target	Agent	Mechanism
Free virus	Ab alone	Blocks binding to cell Blocks cell entry Blocks uncoating of virus
	Ab + complement	Damage to envelope Blocks virus receptor
Virus-infected cells	Ab + complement	Lysis of infected cells Opsonisation for phagocytosis
	Ab bound to infected cells	Ab dependent cytotoxicity by NK. Neutrophil or macrophages

Cellular immunity mediated by T lymphocytes

① CD8+ T_C cytotoxic T lymphocytes (CTL)

- MHC class I restricted
- Recognise virally infected cells
- Lysis (destruction) of these cells

② CD4+ T helper (T_H1) lymphocytes

- MHC class II restricted
- Antigen present by professional APCs
- Provide help for immune system
- (e.g. cytokines, interferons)

How virus evade the immune response?

① Inhibition of humoral immune response

- Virus undergoes mutation, selection and therefore change the structure of viral proteins Heamagglutinin (HA) and neuraminidase (NA)
- Antigenic variation (Antigenic drift, antigenic shift)

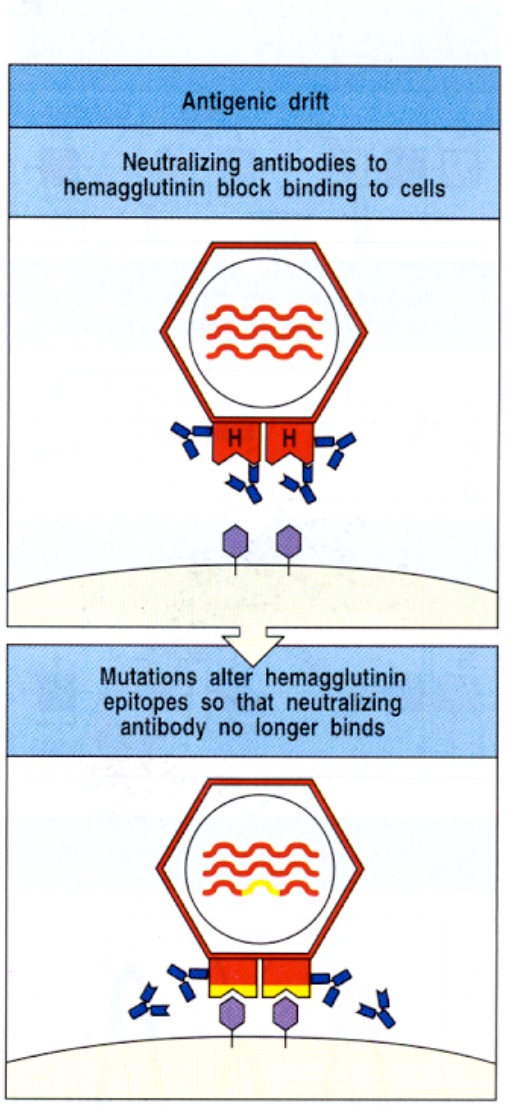
② Inhibition of apoptosis

③ Inhibition of Tc and NK cells

④ Interference with Antibody and IFN

Avoiding the immune response

Antigenic drift in influenza virus avoids neutralising antibodies.



Antigenic Drift:

Slow change in epitopes (principally HA) by mutation: results in epidemics seen each winter

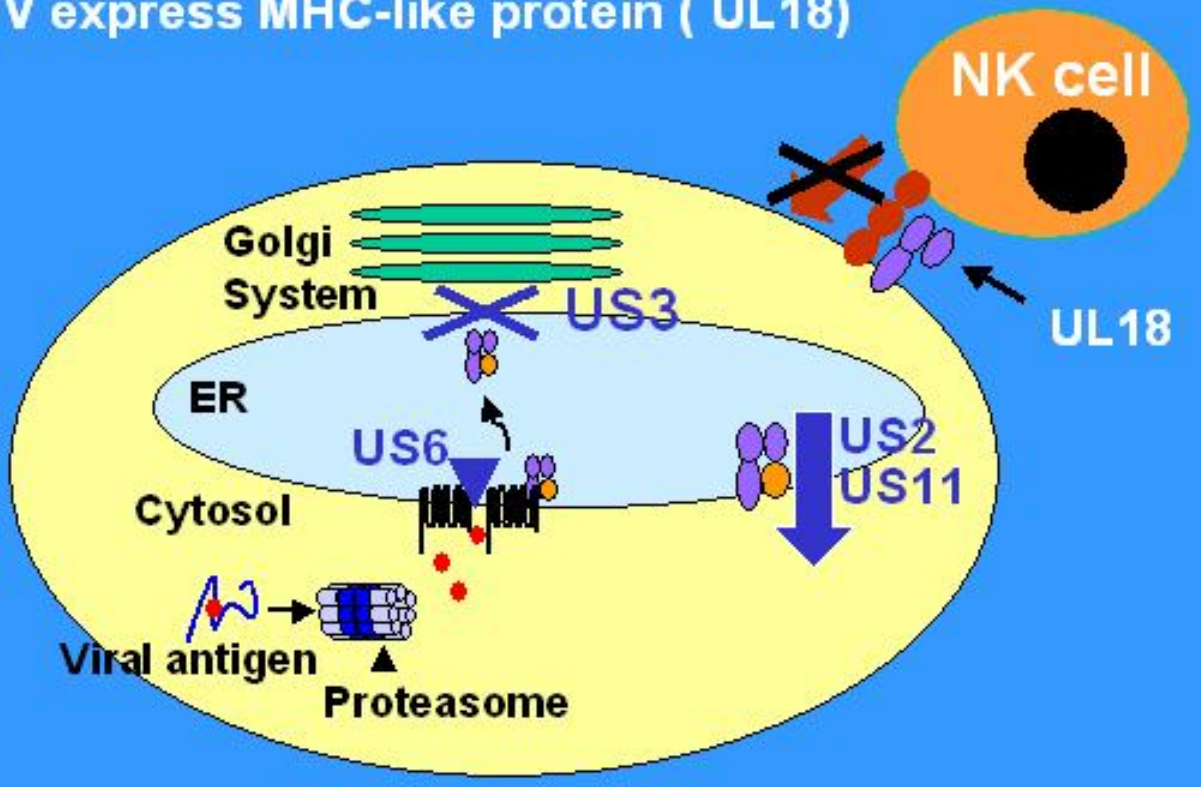
Antigenic Shift:

Major change due to reassortment when two or more viruses infect the same cell. Mixing of segmented genomes. Results in brand new virus and thus pandemics

Prevention of Natural Killer (NK) recognition of herpesvirus infected cell

HCMV infection causes down regulation of MHC class I
Cells become targets for NK cells

HCMV express MHC-like protein (UL18)



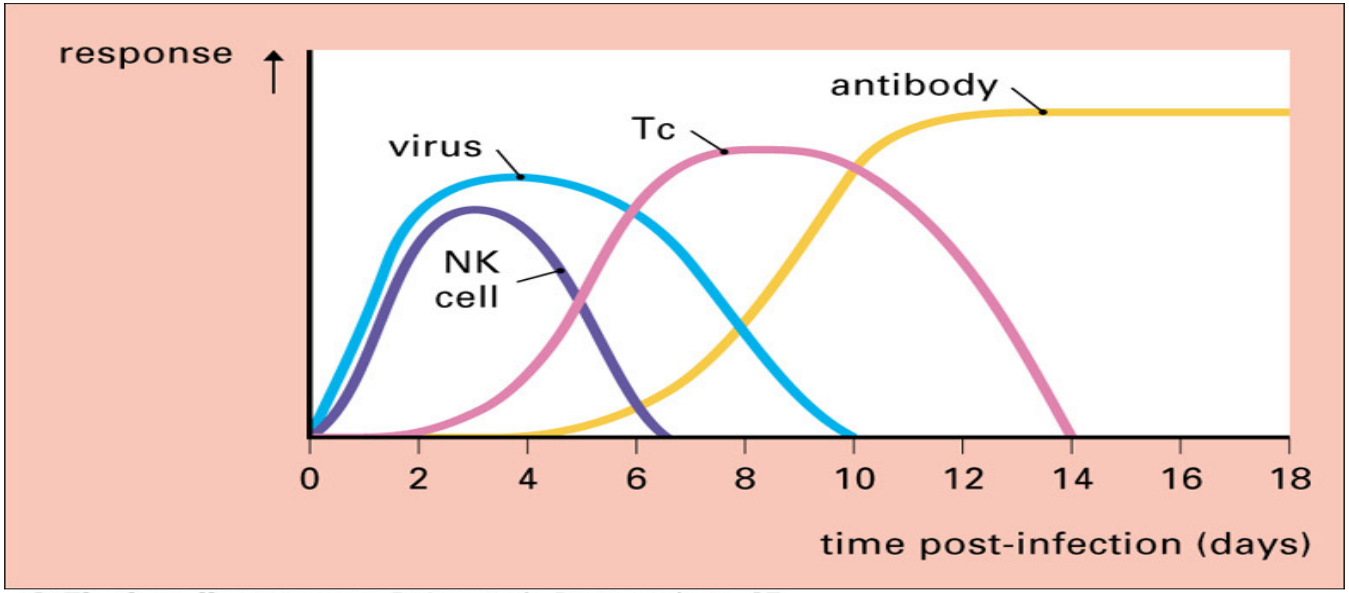
What actually happens to the virus

NK, Interferon's and later CD8 cytotoxic cells stop replication.

Proteins such as complement, antibody and surfactant, bind viral particles. These are removed by Phagocytes such as neutrophils and macrophages.

Host response to acute virus infection

e.g. influenza virus



NK cells (and interferon) are detected first
Cytotoxic T cells are then activated
Antibody (neutralising) then appears

Major Components of Viral Immunity

	Innate response	Adaptive response
Soluble factors	Interferons α, β and γ	Antibodies
Cells	NK cells Phagocytes	T lymphocytes CD8 cytotoxicity CD4 cytokines

Summary

- Understanding the immune response to infection can inform vaccine development.

- Important immune effector mechanisms directed against virus infection

1. innate immunity (e.g. interferon, NK cells)

2. adaptive immunity (e.g. antibodies, T cells)