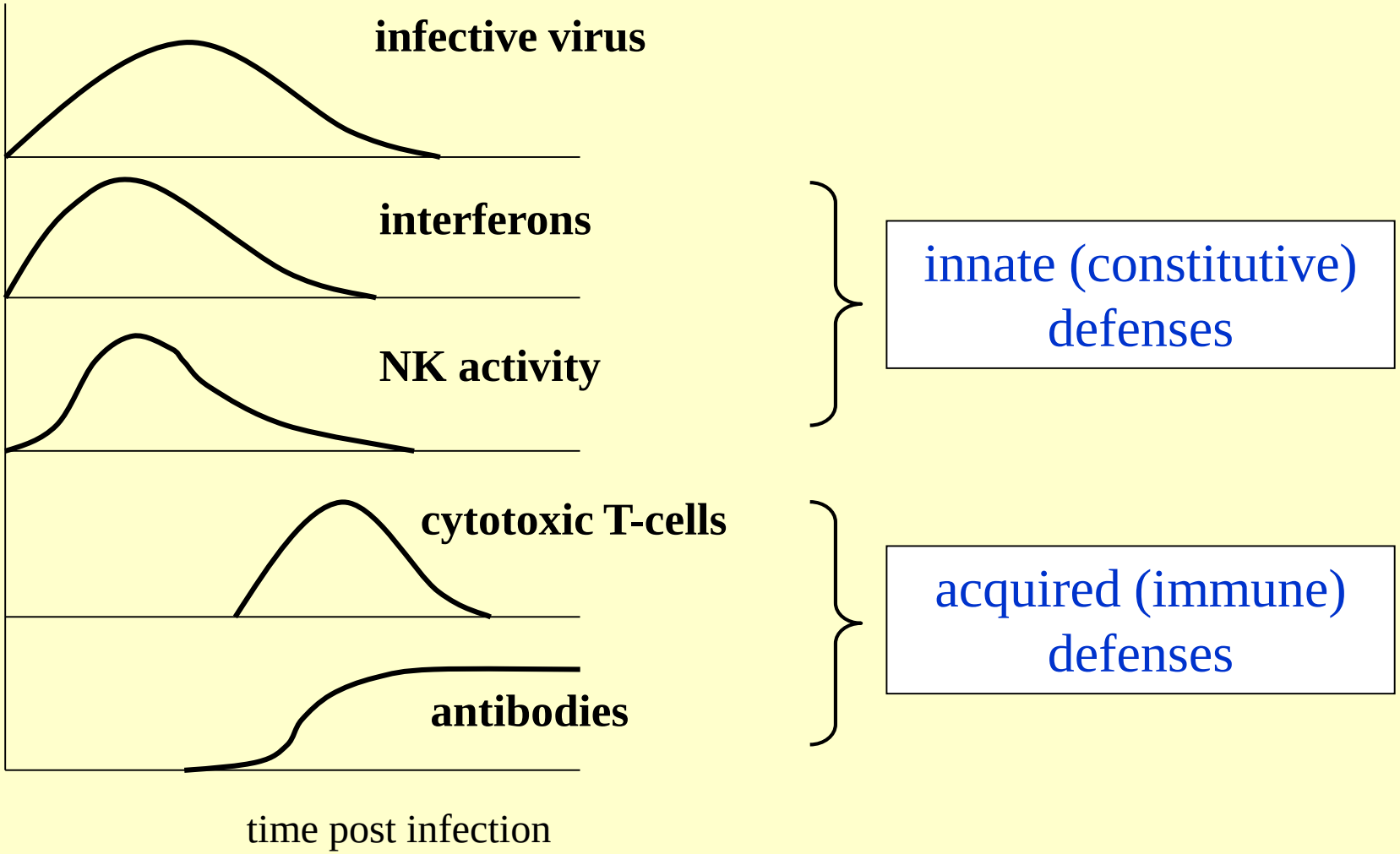
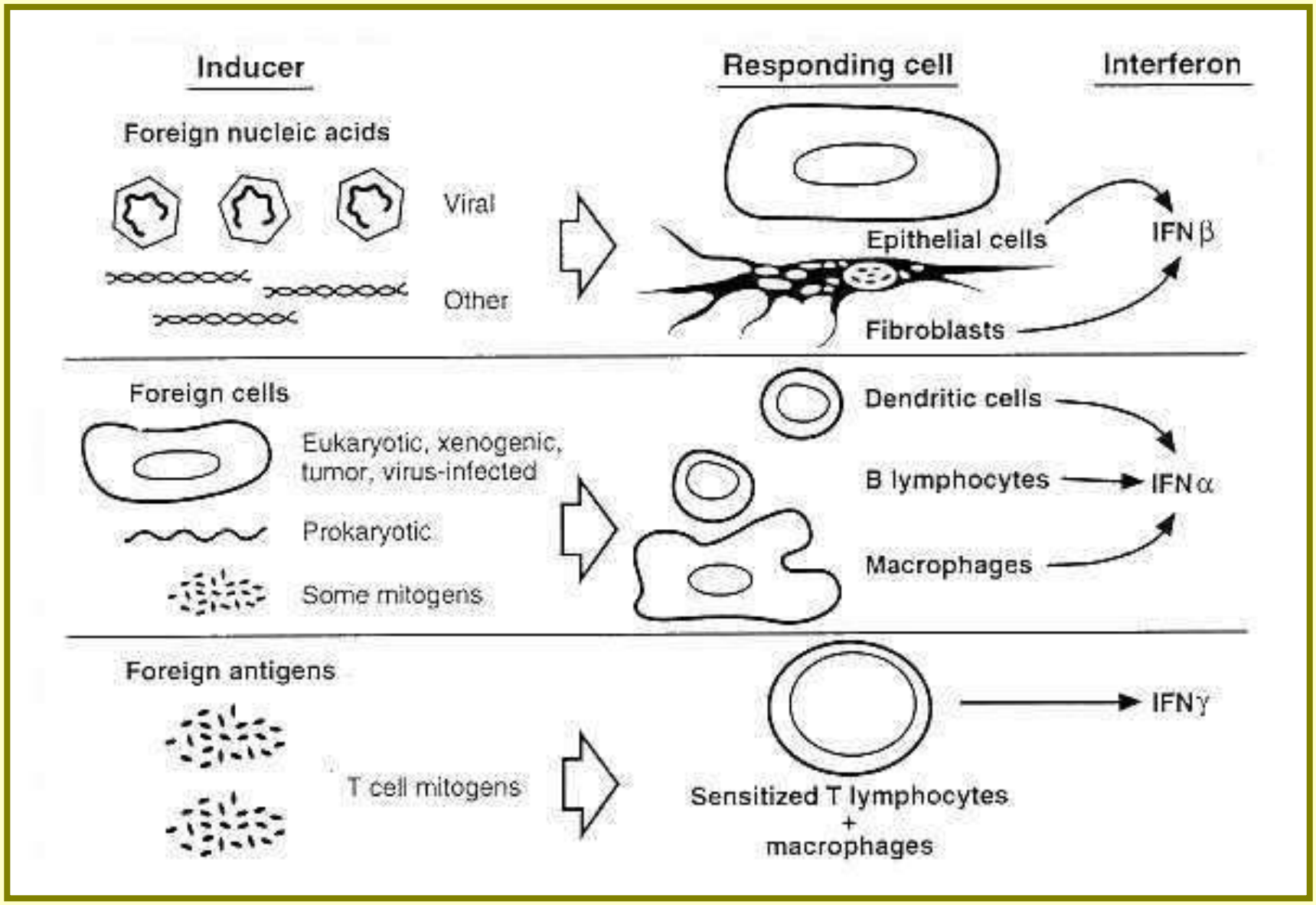
Host defenses in viral infections



Interferon induction



Interferon α/β inducer molecules of viruses

- double stranded RNA *(RNA viruses are stronger inductors than DNA viruses)*

  RNA replication complex,

  mRNA secondary duplex structure

- certain viral proteins

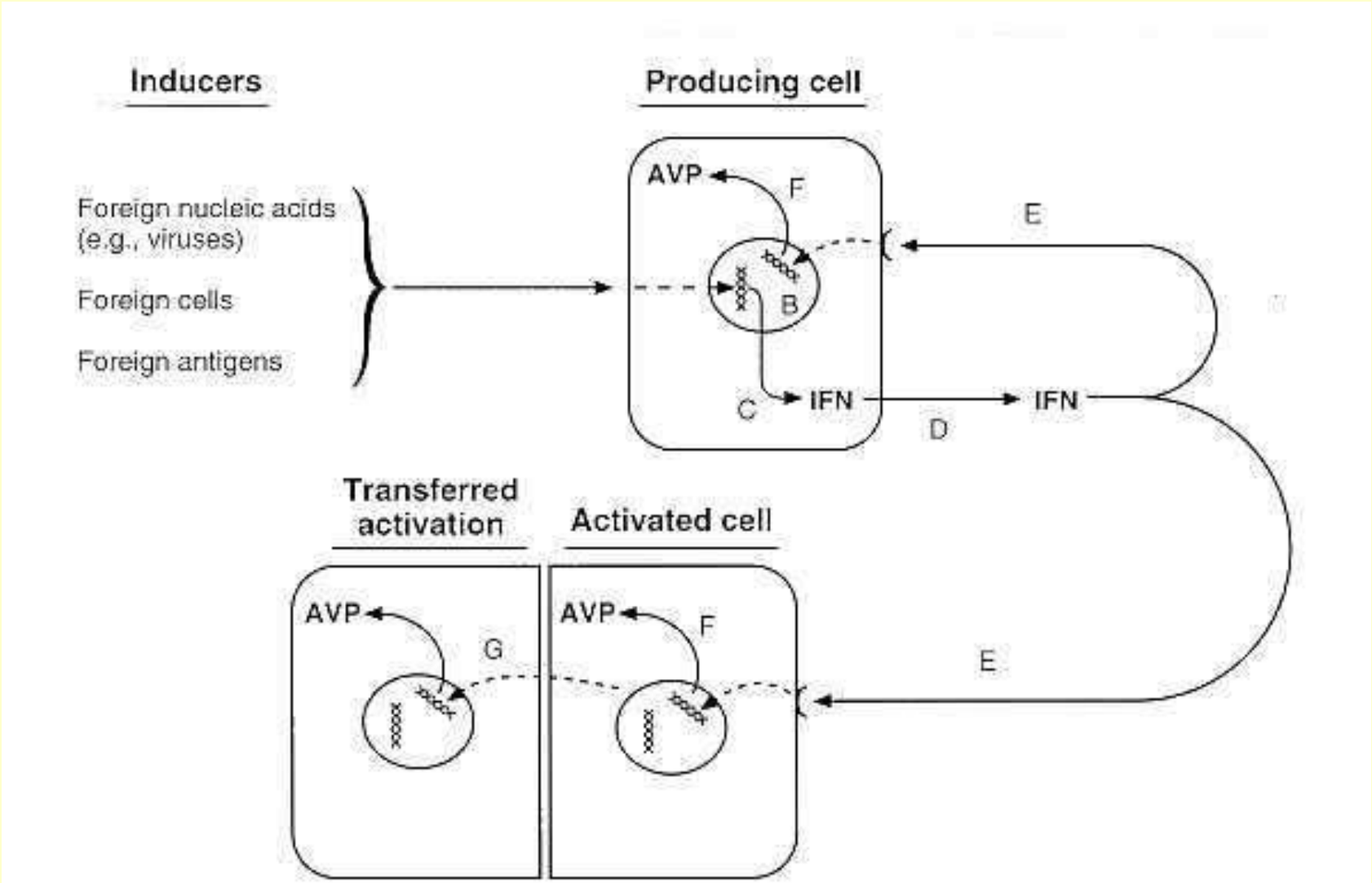
  e.g. *envelope glycoproteins of paramyxoviruses*

  penton (capsid) of adenoviruses

Viral interference

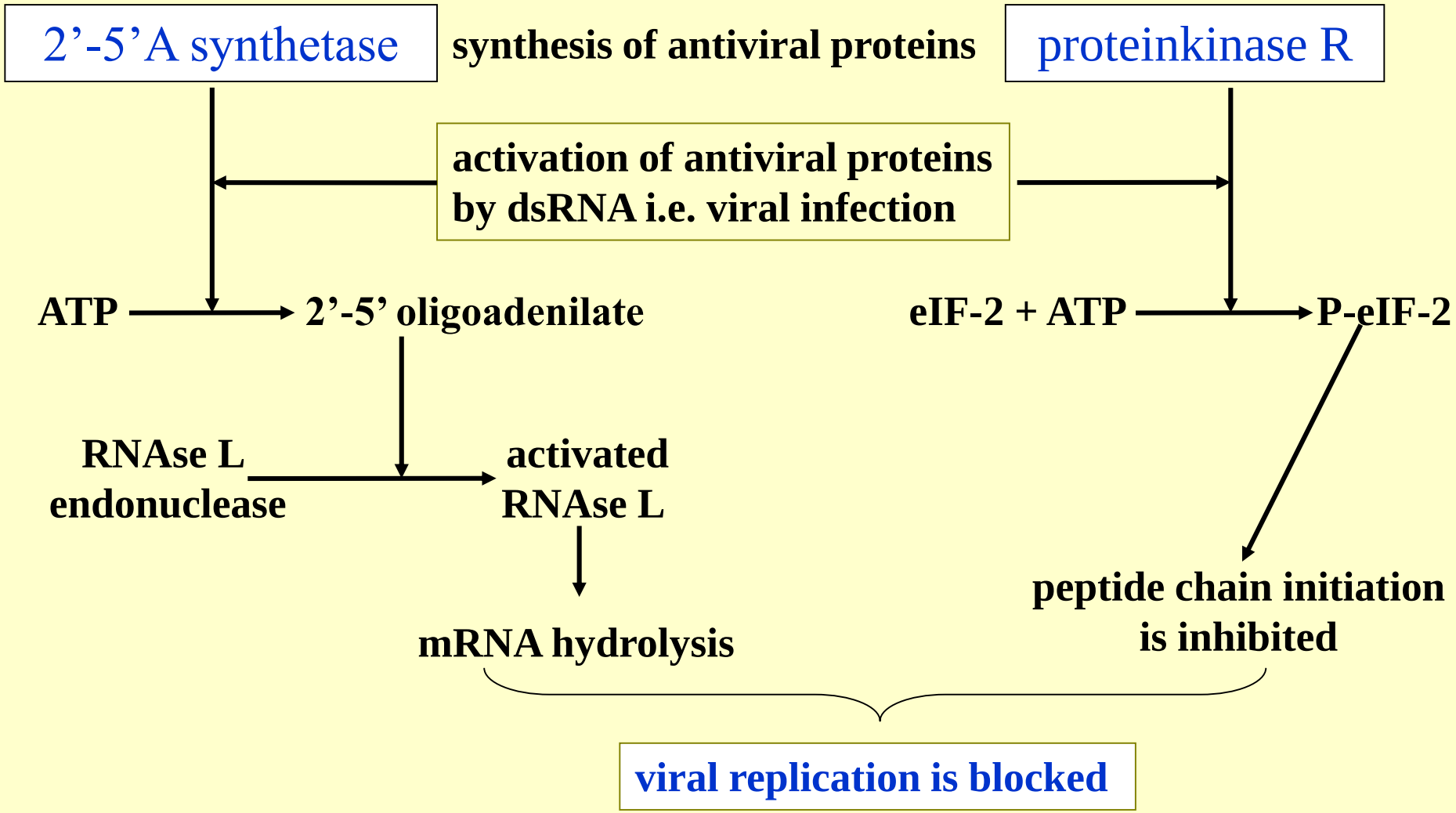
- Infection by an interferon inductor virus renders the tissue resistant to other virus infections
- *only until the initial infection lasts*
  (thereafter the tissue becomes susceptible to other viral infections)
- medical importance:
  e.g. oral (live) poliovirus vaccine can be ineffective in other viral infections

Effect of interferon α/β on target cells



Activated cells gain resistance before infection – spreading infection is inhibited

Intracellular changes mediated by interferon α/β receptor



Immune modulatory effects of interferons

- activation of NK cells
- upregulation of MHC I expression on the cell surface

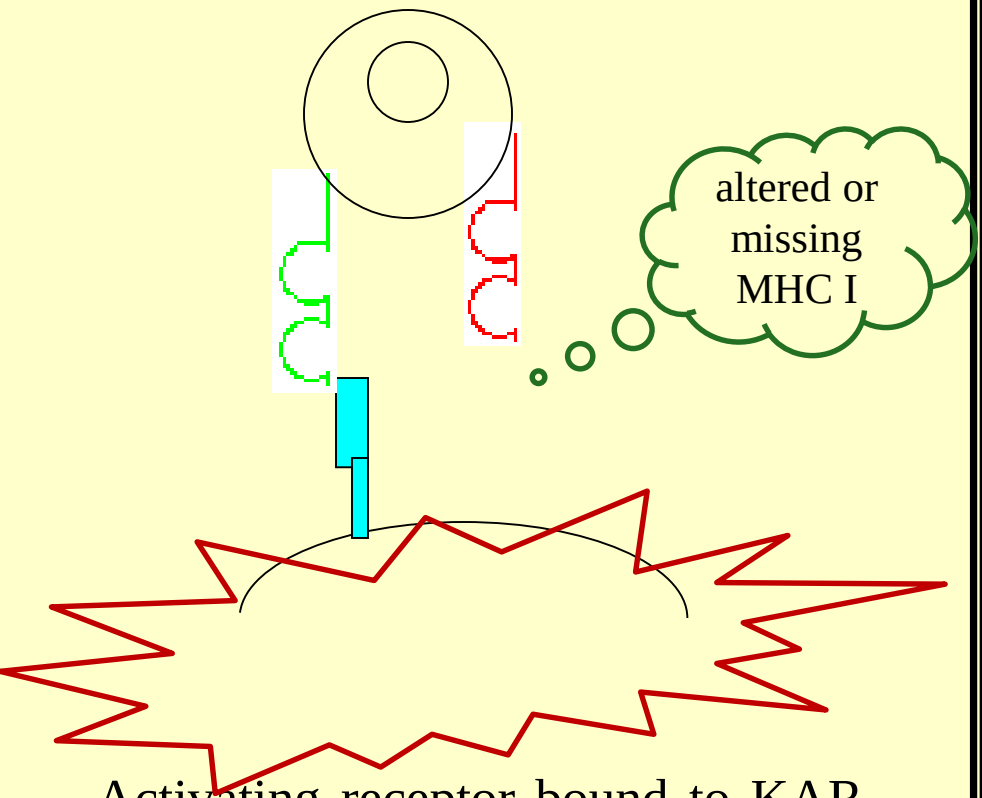
→ α/β and γ interferons

- Th1 induction
- activation of macrophagess
- upregulation of MHC II expression on certain cells

→ only γ interferon (immune interferon)

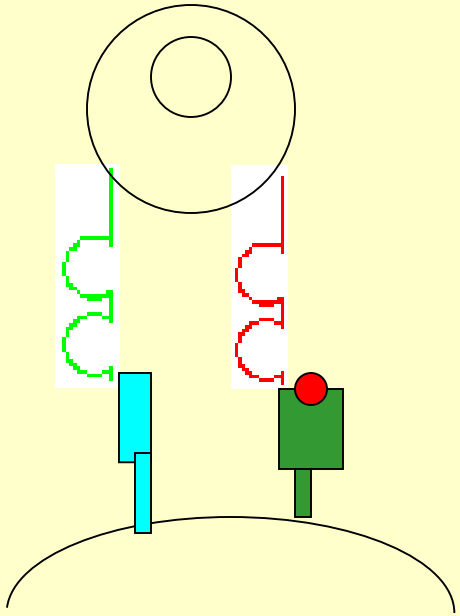
NK cells

A



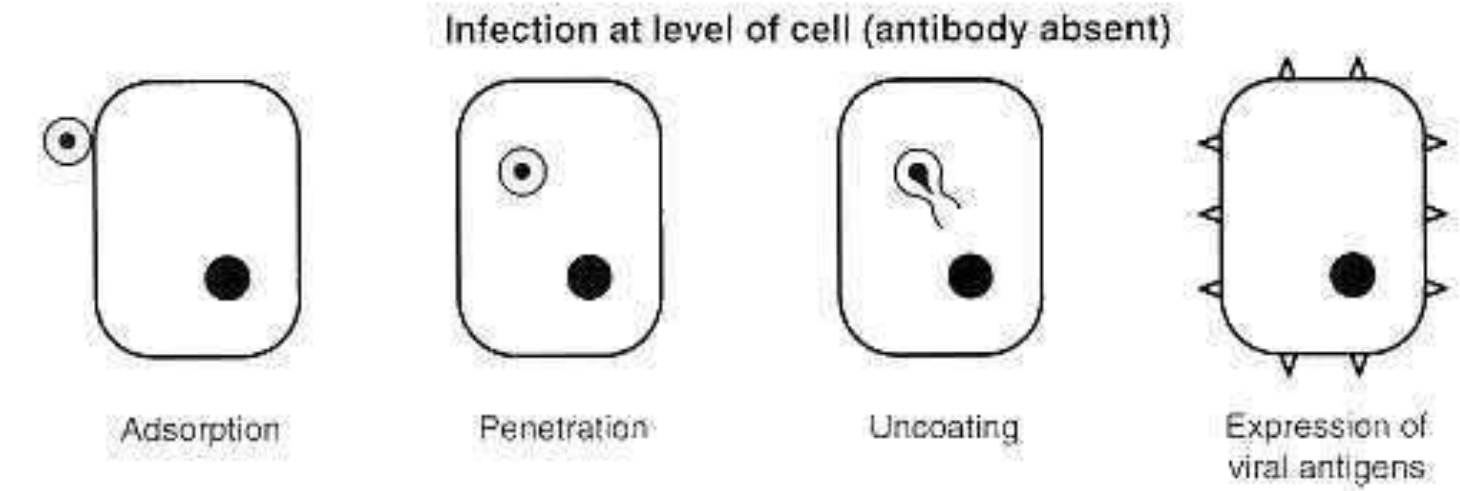
Activating receptor bound to KAR. Without enough MHC, KIR can't bind. NK cell only receives activating stimulus, which results in target cell death.

B



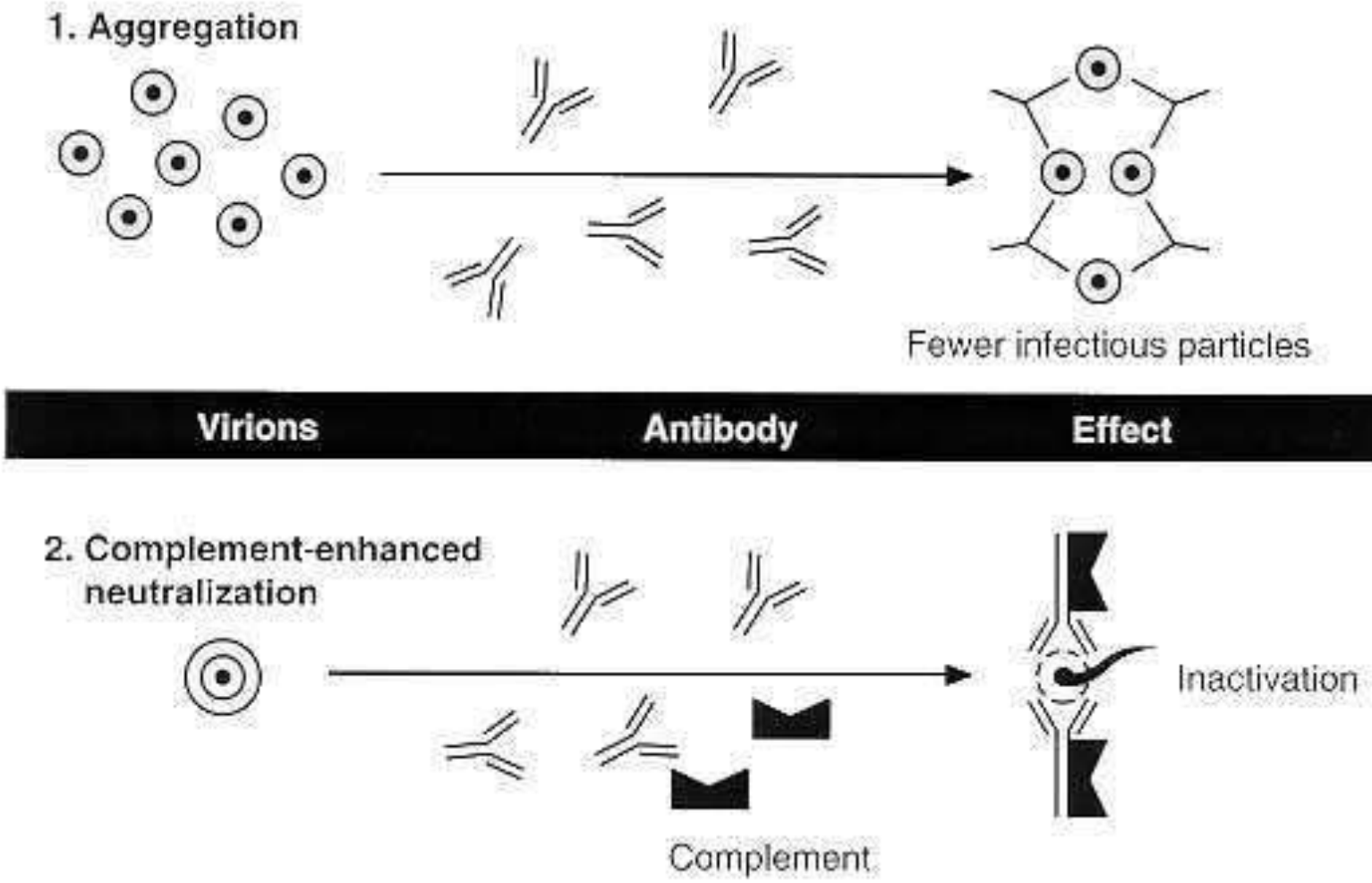
Activating receptor bound to KAR. When MHC is present in adequate amounts, NK cell receives BOTH activating and inhibiting stimuli. Thus, target cell death is averted.

Humoral immunity I

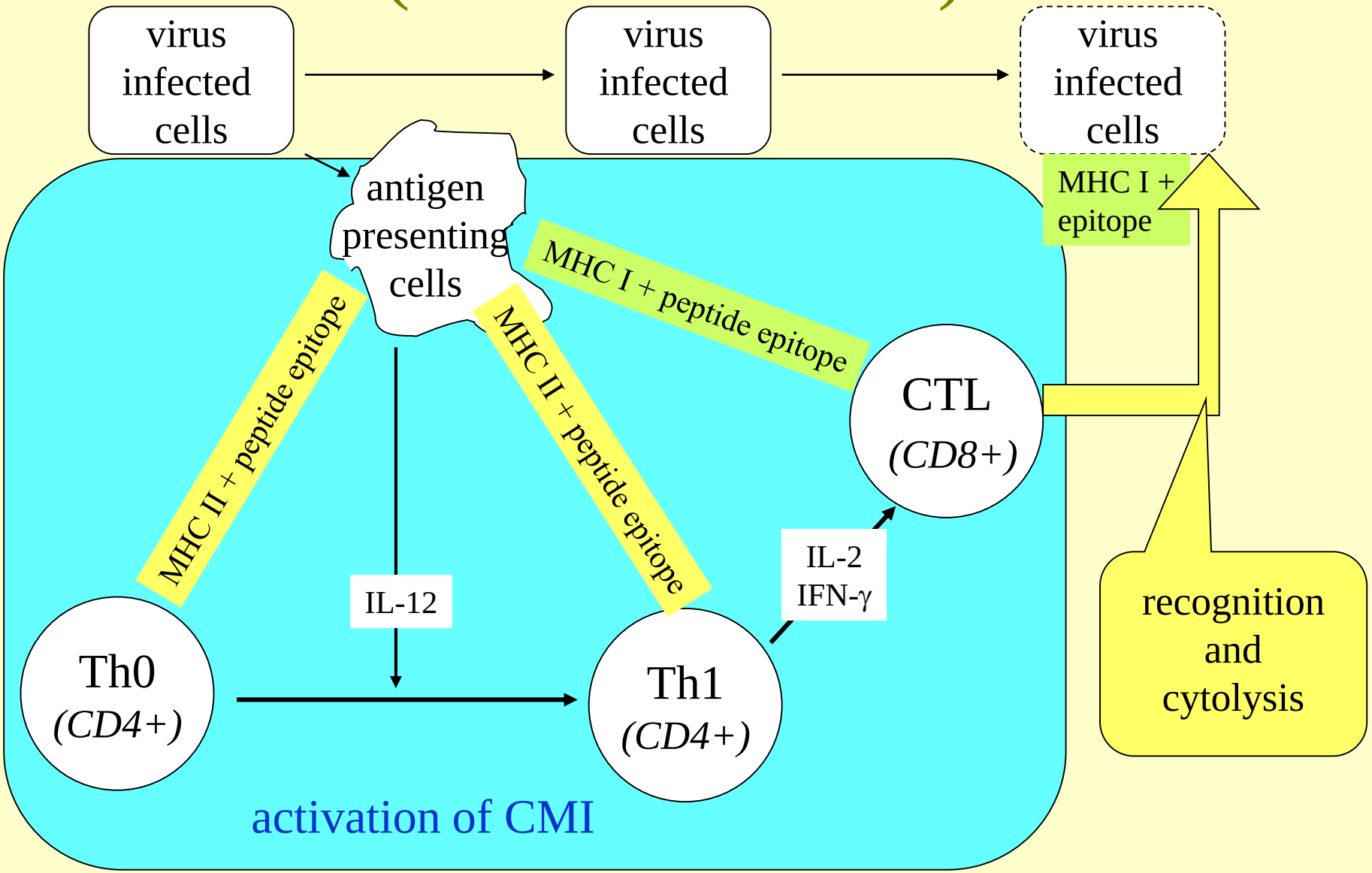


or ADCC

Humoral immunity II



Cell mediated immunity - CMI (MHC restriction)



Viral escape from immune surveillance

- Immunosuppression
- Escape from antibodies
- Escape from cell mediated immunity

Immunosuppression by viruses

- Destroying lymphocytes *(HIV, measles virus)*
- vIL-10 of EBV
- Inhibiting the antigen presenting function of dendritic cells and macrophages *(HIV, measles)*
- Inhibiting the replication & differentiation of progenitor cells in bone marrow (hCMV)

Escape from antibodies

- High mutation rate of RNA viruses (HIV, HCV)

  - *immune selection of escape variants*

- Antigen drift of influenza viruses

- Antigen shift of influenza A virus

  - *genome segmented for the viral proteins*

  recombination of genomic segments

Escape from cell mediated immunity

- Hiding from immune responses

  - *renal tubules (hCMV), salivary gland (EBV)*

  - *non replicating host cell, no viral expression*

    (HSV, VZV in sensory neurons
- MHC I downregulation on the target cell surface *(adenoviruses, hCMV, HIV, HTLV)*
- Inhibiting MHC II expression *(HIV, measles virus, hCMV)*

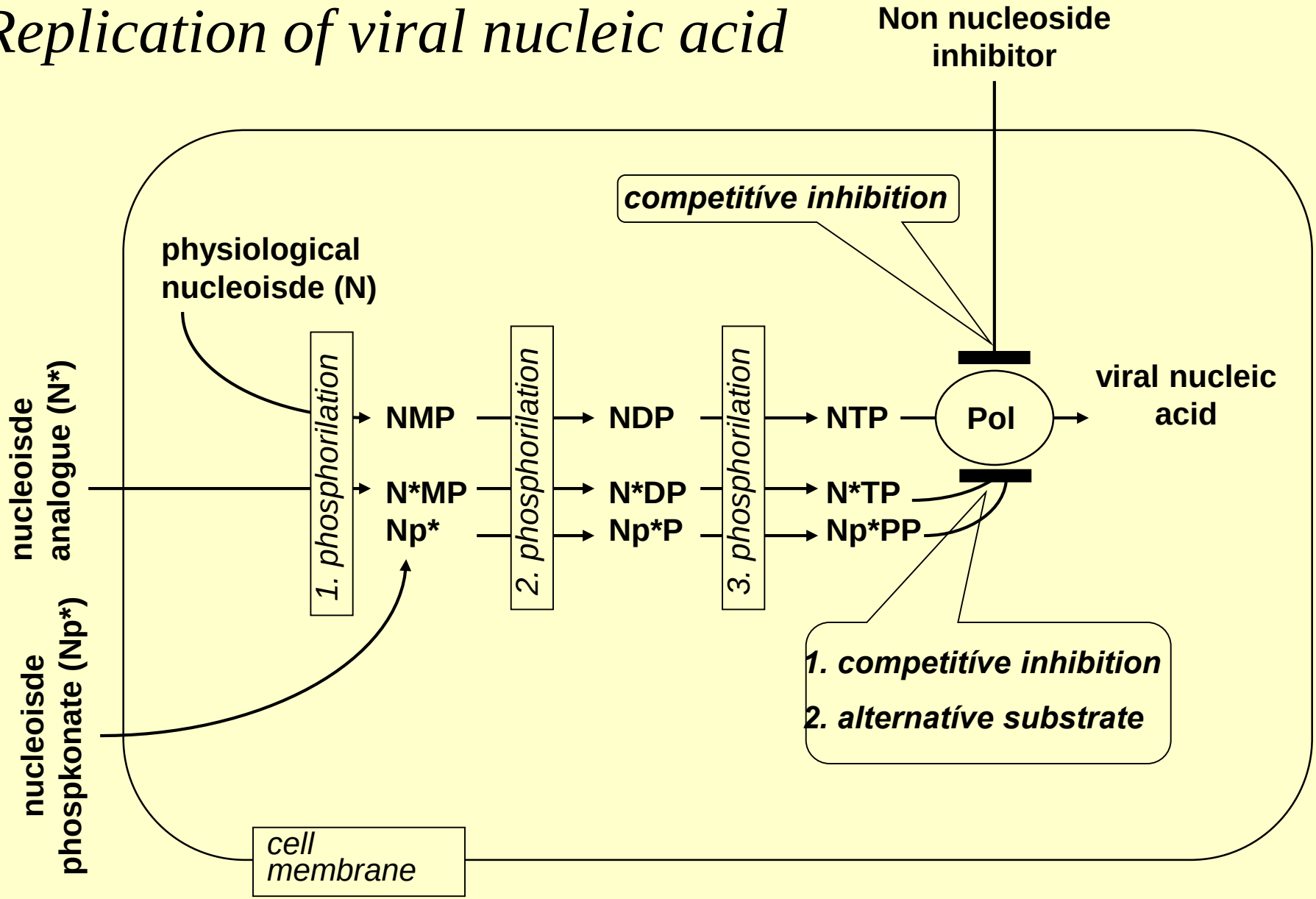
ANTI-VIRAL CHEMOTHERAPY

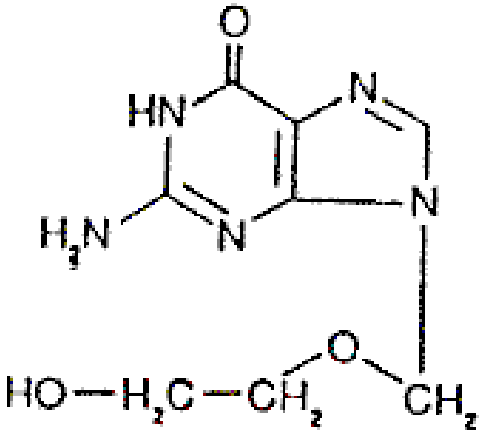
- Antiviral drugs are available to treat **only a few viral diseases**.

Stages in virus replication which are possible targets for chemotherapeutic agents

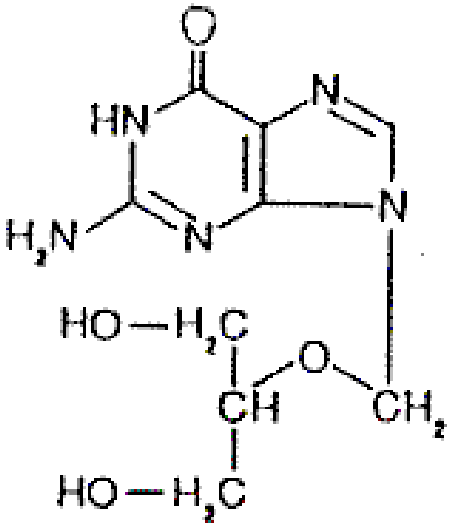
- Attachment to host cell
- Uncoating - (Amantadine)
- Synthesis of viral mRNA - (Interferon)
- Translation of mRNA - (Interferon)
- Replication of viral RNA or DNA - (Nucleoside anologues)
- Maturation of new virus proteins (Protease inhibitors)
- Budding, release (neuraminidase inhibitors)

Replication of viral nucleic acid

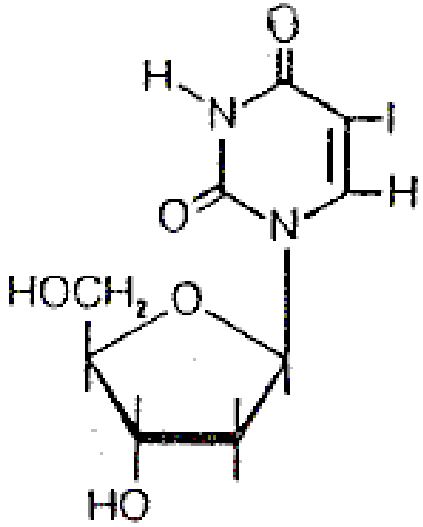




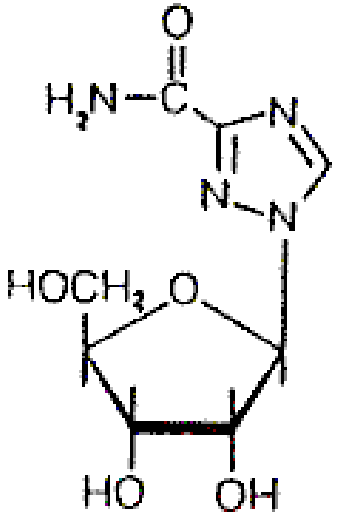
ACYCLOVIR
(acycloguanosine)



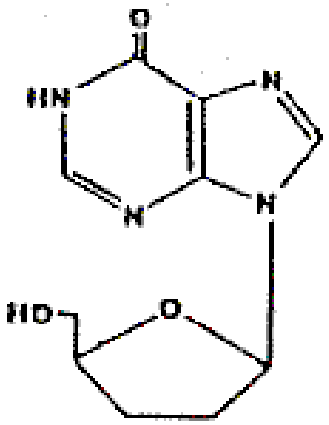
GANCYCLOVIR



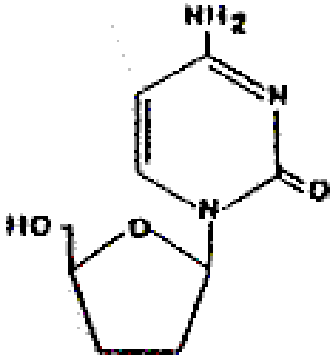
IDOXURIDINE



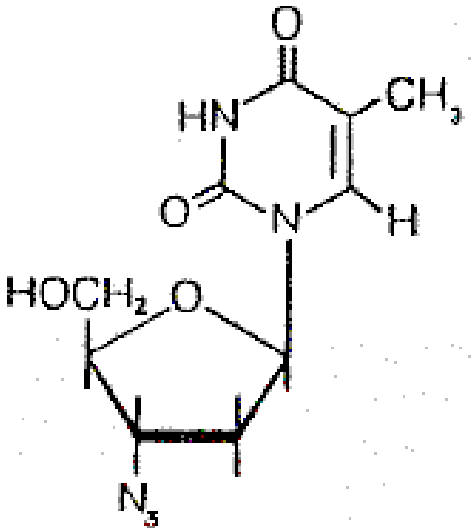
RIBAVIRIN



DIDEOXYINOSINE



DIDEOXYCYTIDINE



ZIDOVUDINE
(azidothymidine)

Immunoglobulin Therapy

"Normal" Immune globulin

This is a pooled product, prepared from the serum of normal blood donors. It contains low titres of antibody to a wide range of human viruses. It is mainly used as prophylaxis against:

- **hepatitis A** virus infection,
- **parvovirus** infection, and
- **enterovirus** infections (in neonates).

Immunoglobulin Therapy

Hyper-immune globulin

Immunoglobulin may be prepared from the serum of selected individuals who have high titres of antibody to particular viruses. Examples include:

- **Zoster** immune globulin
  Prevention of Varicella in immunocompromised children and neonates.
- Human **Rabies** immunoglobulin
  Post-exposure prophylaxis in an individual who has been bitten by a rabid animal.
- **Hepatitis B** Immune globulin
  Non-immune individual who has been exposed to HBV.
- **RSV** Immune globulin
  Treatment of respiratory syncitial virus infections in the very young.

- Vaccines are available for:
- Hepatitis B virus — *recombinant protein*
- Hepatitis A virus — *inactivated virus*
- Influenza — *inactivated virus*
- Measles
- Mumps
- Polio
- Rubella
- Rabies — *inactivated virus*
- Yellow Fever
- Varicella Zoster

Attributes - live vaccines

(*Measles, Mumps, Polio, Rubella, Zoster, Yellow fever)*

- **Good immune response**
  - Both Cell Mediated Immunity and antibody responses.
  - Immunity is long lived
  - Single dose
- **Safety**
  - Danger of reversion to virulence, or
  - Severe disease in immunocomprised
- **Stability**
  - Organisms in the vaccine must remain viable in order to infect and replicate in the host
  - Vaccine preparations are therefore very sensitive to adverse storage conditions
  - Maintenance of the cold chain is very important.

- **Attributes – Non live vaccines**

- **Immune response**
  - **poor; only antibody - no cell immediated immune response.**
  - **response is short-lived and multiple doses are needed.**
  - **may be enhanced by the incorporation of adjuvants into the vaccine preparation (see below)**
- **1. Safety**
  - **Inactivated, therefore cannot replicate in the host and cause disease.**
  - **Local reactions at the site of injection may occur.**
- **2. Stability**
  - **Efficacy of the vaccine does not rely on the viability of the organisms.**
  - **These vaccines tend to be able to withstand more adverse storage conditions.**


illennium 1999/40
enner's vaccination / P Brookes
20