Antiviral Drugs chemotherapy

The No. of antiviral drugs is very small because

- The viruses are obligate intracellular parasite
  - So
  - Its difficulty to induce selective toxicity against viruses
- Drugs are relatively ineffective because
  - Many cycles of the viral replication accure during incubation period when the health of the patient in well
- Some of viruses are latent in the cells e.g.
  - Herpes virus
- The emergency of drugs resistant by the viral mutant

We need antiviral drugs for

- Against viruses to which vaccine are not available
- To reduce of morbidity and economic loss due to viral infection
- To treat increased No. of immune suppression patient

Antiviral drugs may be target of the following stage in viral replication

- Attachment of the virus to host cell and uncoating of the viral genome
- Reverse transcription of the certain viral genome
- Translation of viral protein
- Assembly maturation and release of progeny virus particles

Mechanism of action

Inhibition of early Events

Drugs include

- ①Amantidin)synthetic amine(
  - Inhibit influenza A viral uncoating
  - So use as
    - Prophylactically
    - therapeutically
- ②Rimantidin
  - Is derivative of amantidin
  - Have action against A and B influenza virus with fewer side effect

Inhibition viral nucleic acid synthesis

- A suger nitrogen base (Nucleoside analogs) (N-a(
  - Mainly used against herpes and HIV
  - mode of action
    - Inhibition of enzyme of metabolic pathway of Purina and pyramidin
    - Inhibition of polymerases which is important for nucleic acid replication
    - Some of analogie5 may be incorporated into nucleic acid
      - So
      - Block further synthesis of NA
    - Inhibit cellular enzyme as well as viral encoded enzyme
- Nucleotide analog
  - ❶Nitrogen
  - ❷Sugar
    - Mode of action
    - -attach to phosphate group.
    - -they have ability to persist in cell.
  - ❸Phosphate group

Nucleoside analogs include

❶Acyclovire

①Name as

Acycloquanosin or zovirax

②active against

HSV-1
HSV-2

varicellā zoster

little effect

DNA viruses

host cell

❸Mode of action

Acyclovir HSV thymidine kinase

↓

Acyclovire monophaphat

↓ Cellular kinase

Acyclovir triphosphat (ACV-TP(

↓

Incorporated in to growing herpes DNA chain

↓

Inhibition the action of the viral DNA polymerase

Explanation

Infected of cells with HSV or HIV

↓

Viral thymidin kinase is formed by the viruses inside the cell

↓ Which acton

The cyclovire converted it to ACV-TP

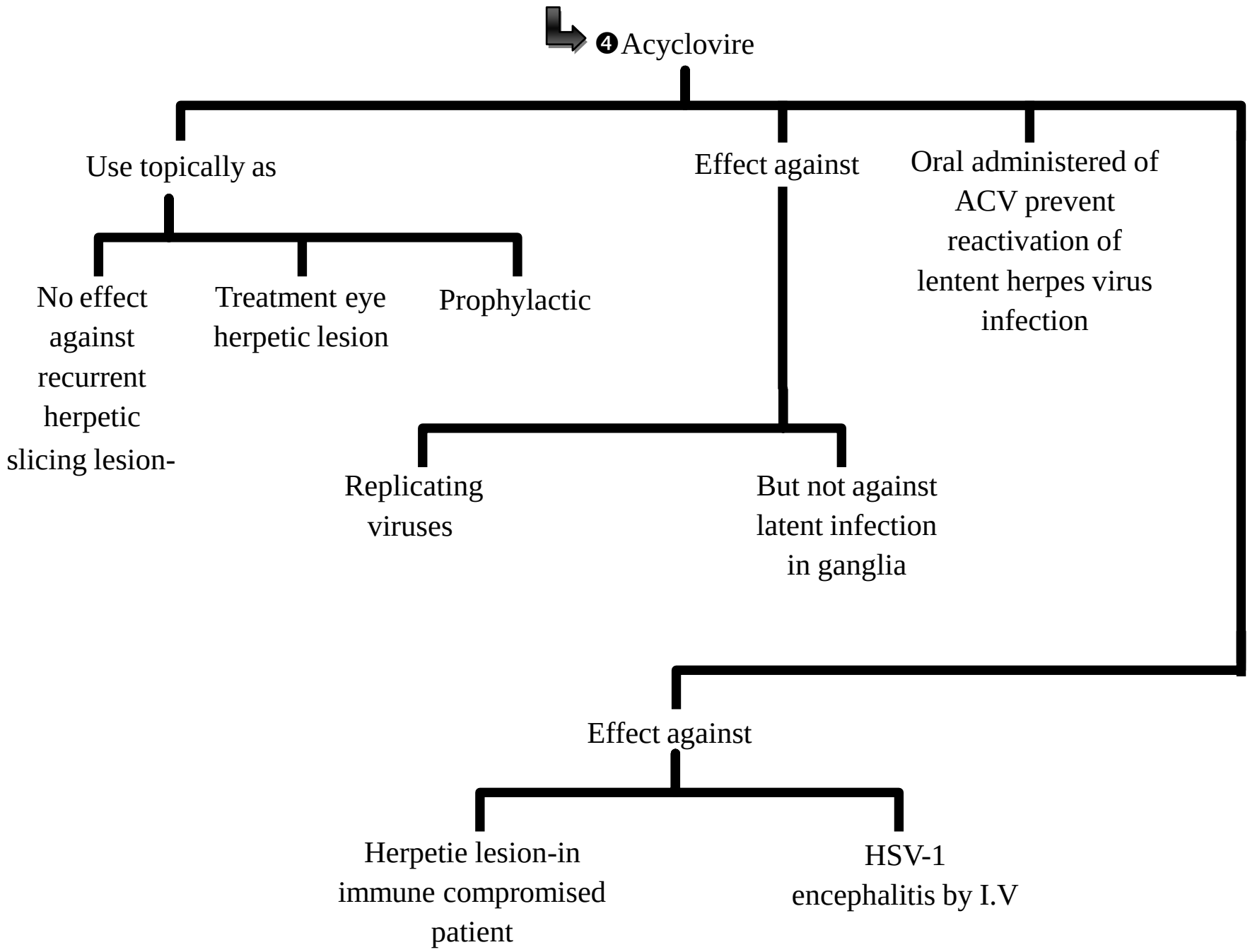
↓ Then the action of cellucar kinase

ACV-TP

❹Acyclovire usage

↓

Page 4

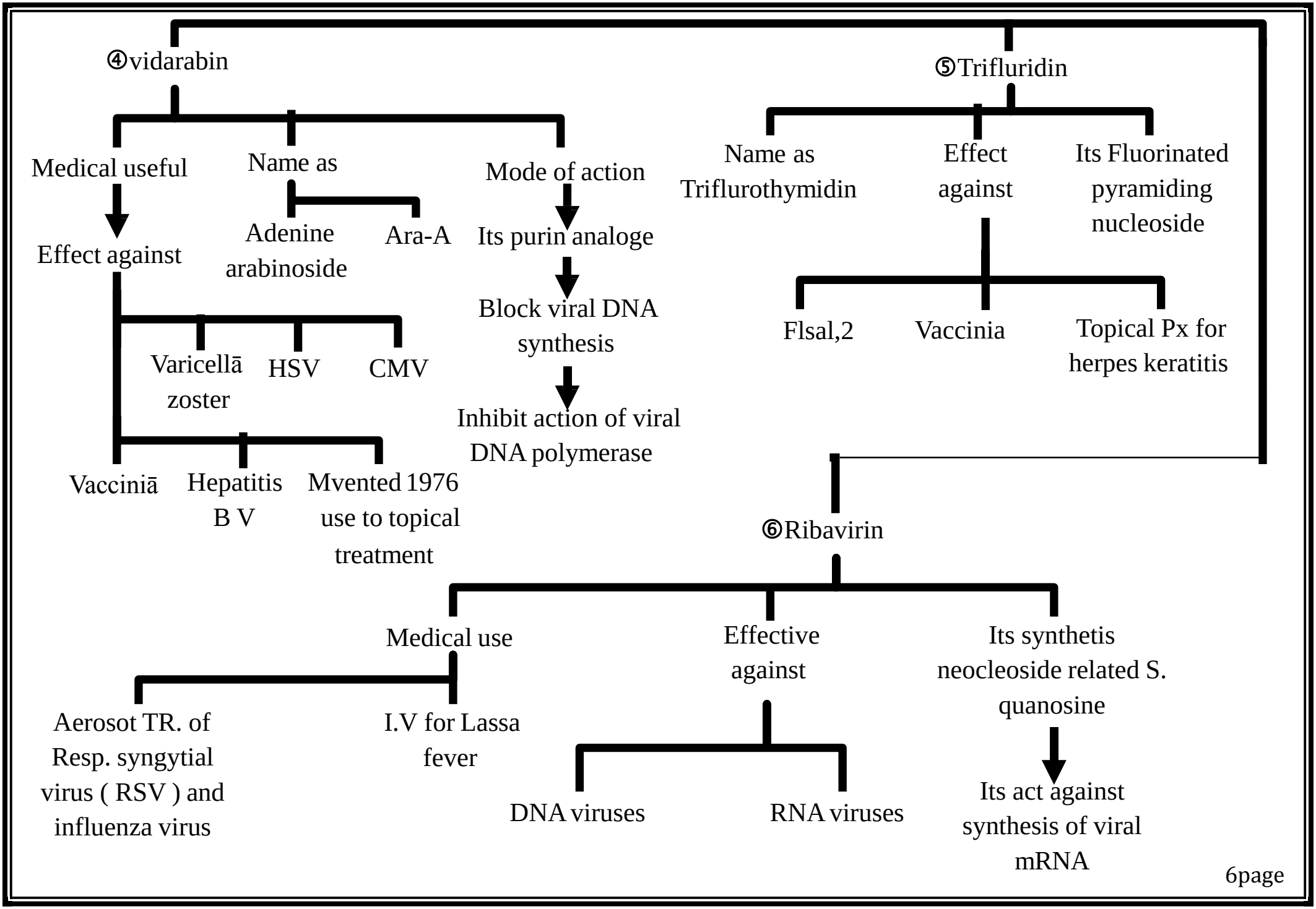

❹Acyclovire
Use topically as
Effect against
Oral administered of ACV prevent reactivation of lentent herpes virus infection
No effect against recurrent herpetic slicing lesion-
Treatment eye herpetic lesion
Prophylactic
Replicating viruses
But not against latent infection in ganglia
Effect against
Herpetie lesion-in immune compromised patient
HSV-1 encephalitis by I.V

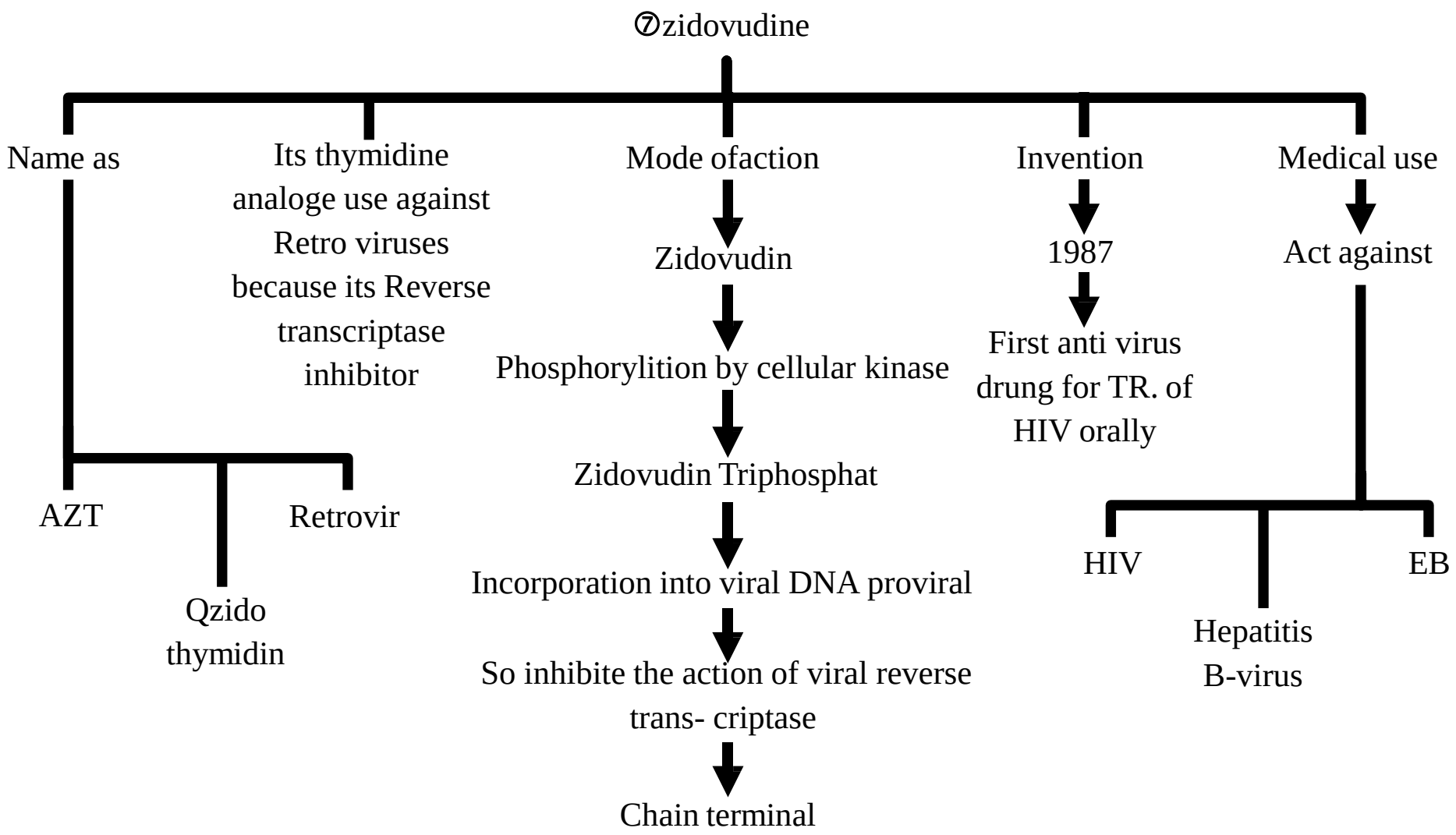
②Ganciclovire

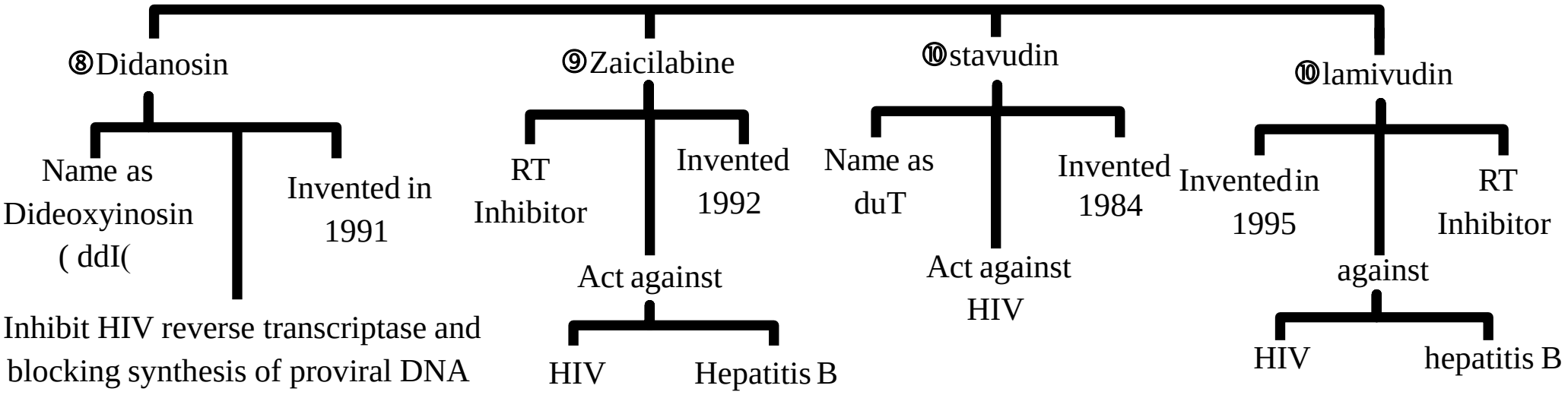
- Mode of action
  - Inhibition of viral DNA polymerase by the same mechanism of Acyclovir
  - But CMV not have thymidin kinase
  - So directly acting upon by cellular kinase
  - Inhibition viral DNA polymerase
- Act against cytomegal virus
- Name as
  - Methyl quinine derivatives

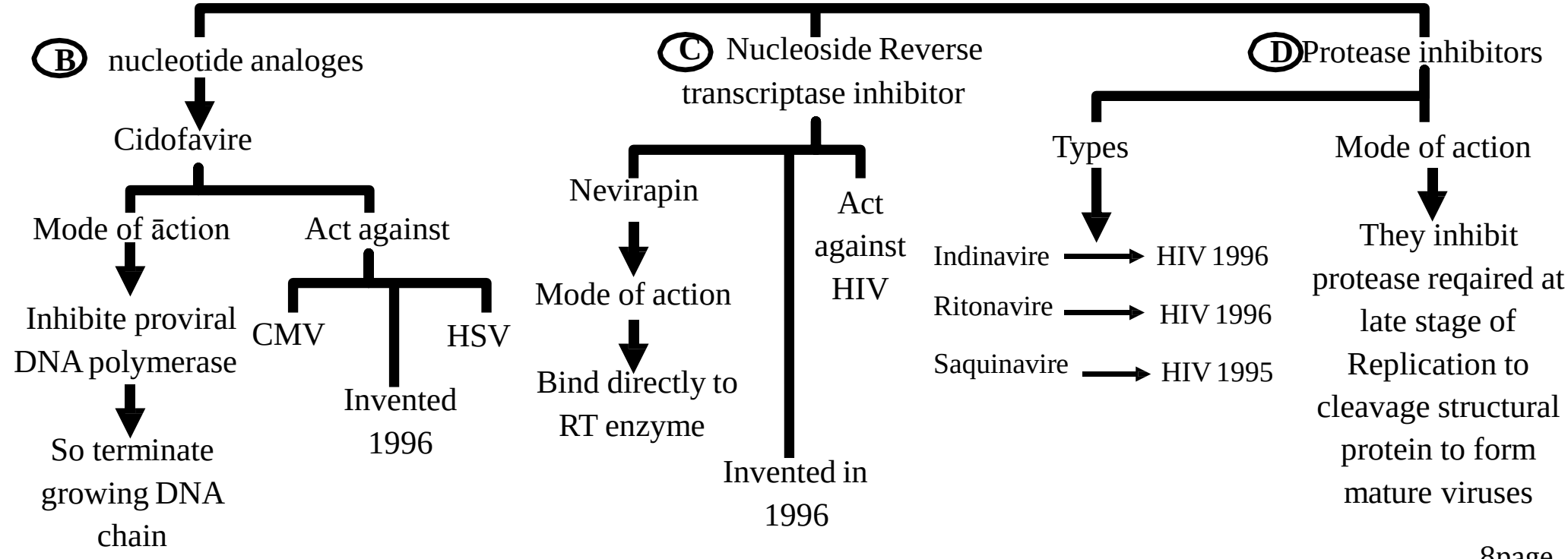
③ Idoxuridine

- Usage or clinical useful
  - Not use systemic because it affect also against cellular DNA
    - So too toxic when use systemically
  - Topical TR. of keratoconjunctivitis due to HSV
- Name
  -)IDU, IUDR(
- Mode oF actron
  - Its halogenated pyrimidine
  - So
  - Incorporated into viral and cellular DNA after phosphorglation by cellular kinase
  - Mis matching bairing of quinine


④vidarabin
Medical useful
Name as
Mode of action
Effect against
Adenine arabinoside
Ara-A
Its purin analoge
Block viral DNA synthesis
Inhibit action of viral DNA polymerase
Varicellā zoster
HSV
CMV
Vacciniā
Hepatitis B V
Mvented 1976 use to topical treatment
⑤Trifluridin
Name as Triflurothymidin
Effect against
Its Fluorinated pyramiding nucleoside
Flsal,2
Vaccinia
Topical Px for herpes keratitis
⑥Ribavirin
Medical use
Effective against
Its synthetis neocleoside related S. quanosine
Aerosot TR. of Resp. syngytial virus (RSV) and influenza virus
I.V for Lassa fever
DNA viruses
RNA viruses
Its act against synthesis of viral mRNA


⑦zidovudine
Name as
Its thymidine analoge use against Retro viruses because its Reverse transcriptase inhibitor
Mode ofaction
Invention
Medical use
AZT
Qzido thymidin
Retrovir
Zidovudin
Phosphorylition by cellular kinase
Zidovudin Triphosphat
Incorporation into viral DNA proviral
So inhibite the action of viral reverse trans- criptase
Chain terminal
1987
First anti virus drung for TR. of HIV orally
Act against
HIV
Hepatitis B-virus
EB


⑧Didanosin
Name as Dideoxyinosin (ddI(
Invented in 1991
Inhibit HIV reverse transcriptase and blocking synthesis of proviral DNA
⑨Zaicilabine
RT Inhibitor
Invented 1992
Act against
HIV
Hepatitis B
⑩stavudin
Name as duT
Invented 1984
Act against HIV
⑩lamivudin
Invented in 1995
RT Inhibitor
against
HIV
hepatitis B


B nucleotide analoges
Cidofavire
Mode of āction
Inhibite proviral DNA polymerase
So terminate growing DNA chain
Act against
CMV
HSV
Invented 1996
C Nucleoside Reverse transcriptase inhibitor
Nevirapin
Mode of action
Bind directly to RT enzyme
Act against HIV
Invented in 1996
D Protease inhibitors
Types
Indinavire → HIV 1996
Ritonavire → HIV 1996
Saquinavire → HIV 1995
Mode of action
They inhibit protease reqaired at late stage of Replication to cleavage structural protein to form mature viruses

Other types of antiviral agent

- foscarnet
  - Name as phosphonophormic acid
    - Its organic anglog of inorganic pyrophosphate
  - Act against
    - Viral DNA polymerase
    - RT
  - action against
    - HSV
    - CMV
    - EBV
    - HBV
    - Retro v.
- Methi sazone
  - It inhibite protein synthesis of pox viruses by blocking translation of late mRNA

Interferon (IFN(

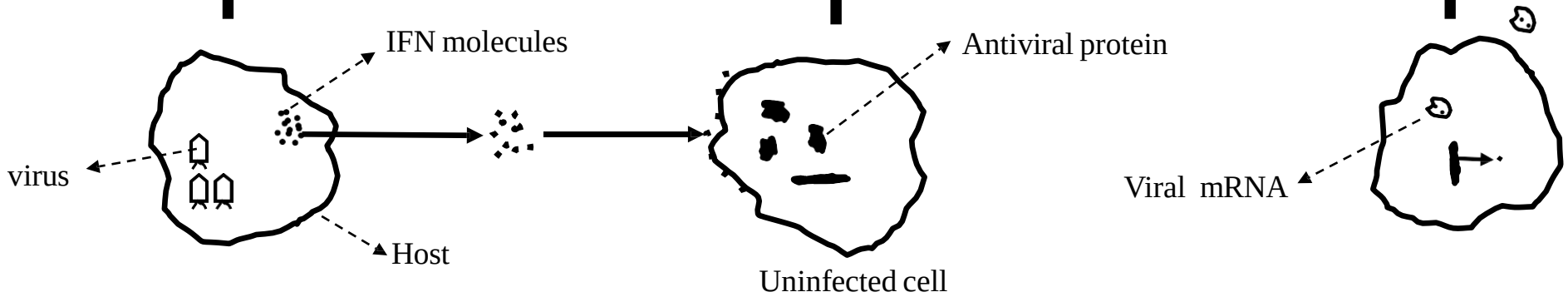
- They are host coded protein produced by all vertebrate species
- Inducer of interferon synthesis
  - RNA viruses stronger than DNA viruses
  - DS RNA
  - Bacterial endotoxin and mitogen
- Classes of IFN
  - IFN Alpha
    Produce by <u>leukocyte</u> induced by viruses DS (RNA(
  - IFN-Beta
    Produced by <u>fibroblast</u> induced by viruses DS (DNA(
  - IFN-gamā
    Produced by lymphocyte
    Induced by mitogen

Characters of IFN

Its host species specific

Not viral species specific in human or any other species

Play primary important role in defence of the host against viral infections



❶Viral infection induce production of interferon from the host cell

❷interferon bind to uninfected cells and stimulate these cell to produce of anzyme or protein (antiviral protein(

❸these antiviral protein blocking translation of mRNA to viral protein

These antiviral protein are

Page 11

These antiviral protein are

- Protein kinase
)ds RNA dependent) phosphory lation of inactivation of celluar inhibition factor
  ↓
  Inhibition of protein synthesis
- Oligonucleo tide synthetase
)Z-A synthetase(
  ↓
  activation of cellular endonuclease
  ↓
  Deg redation of viral mRNA
- Cellular endo kinase

Some of viruses counteract interferons by

- Production of specific viral protein
  ↓
  Block activation of protein kinase
  e.g
  - adeno
  - Herpes
- Neutralize of 1FN-gamā receptor
- Activation cellular inhibitor of protein kinase
  e.g.
  - Influenza n.
  - Polio v.