VIROLOGY

(A virus is a bad news wrapped in proteinP.B. Medawar)

INTRODUCTION TO VIROLOGY.

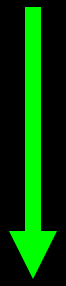
- HISTORICAL ASPECTS
- CLASSIFICATION
- REPLICATION
- TRANSMISSION
- PATHOGENISIS.

HISTORICAL ASPECTS

- Word virus used for any noxious agent or a poison in ancient times.
- Next ---> used nonspecifically for any infectious agent.
- Later the term “filterable viruses” was used for infectious agents that present in clinical specimens which can not be cultured and remain infectious after passage through bacteriological filters.

MILESTONES IN VIROLOGY

- 1796--->Jenner- small pox vaccination.
- 1884--->Vaccine for Rabies.
- 1880--->With the development of bacterial isolation and culture method.



Discovered filterable viruses.

- 1890---> Ivanowski- TMV
  Father of science of virology
- 1902---> Yellow fever virus.
- 1964---> EBV
- 1975---> HBV

Lecture -1: Classification and properties of viruses

- Prof: N. P. Sunil Chandra

General properties of viruses

Definition of a virus.

- Viruses are obligatory intracellular parasites that contain either DNA or RNA. They depend on synthetic machinery of the cell for replication

- **VIRION**:-

  Complete infectious virus particle.

- **COMPOSITION AND STRUCTURE**:-

  All composed of single spp: of Nucleic Acids, {NA} either single stranded or double stranded RNA or DNA.

- **CAPSID**:-

. Protein coat which enclose NA.

. Composed of similar repeating protein molecules [morphological units]

or

aggregates of morphological units.

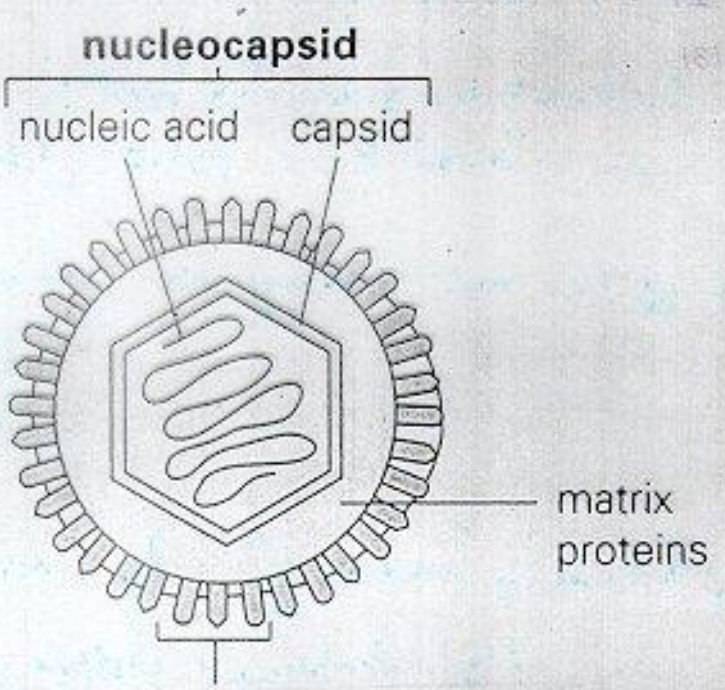
= Capsomeres.

- **NUCLEOCAPSID**:-

  Structure composed of NA surroun--ded by the capsid.
- Some viruses are naked nucleocapsids
- Others:- Enclosed in a phospholipid bilayer of cellular origin. = Envelop.

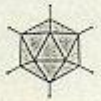
SPIKES:- Envelopes are covered with surface projections.

STRUCTURE OF ENVELOPED VIRUS



Construction of an enveloped virus.

VIRUS MORPHOLOGY, VARIETY AND SIZE

non-enveloped DNA virus	enveloped DNA viruses
 parvovirus	 herpes virus
 adenovirus	 poxvirus
non-enveloped RNA virus	**enveloped RNA viruses**
 poliovirus	 retrovirus (HIV)
 rotavirus	 paramyxovirus
scale: 1cm = 100nm	

Examples of virus morphology, variety and size.

MORPHOLOGY

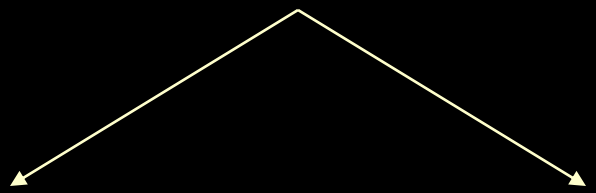
- 4 broad morphological classes based on EM observation.

1. Spherical.
2. Rod shape.
3. Complex.

} Viruses of man and animals.

4. Tad pole shape.---> Bacteriophage [viruses of bacteria]

- EM---->Permit visualization of virus symmetry.
- All spherical viruses have nucleocapsids of :-



Icosohedral symmetry

Helical symmetry

- ICOSOHEDRAN:-

  Polyhedran with 20 equilateral triangular faces , 12 vertices , and 30 edges.

- Helical viruses which infect verfibrates ;

  ---> Surrounded by envelop.

  ---> Appear to be flexible.

  Acquire ; ⟶ Rod shape

  or

  Spherical shape

- Envelop viruses

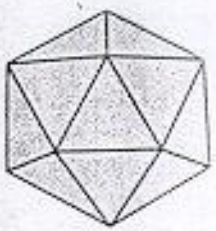
Treatment with ether

Disrupt lipid envelop

[Loss of infectivity]

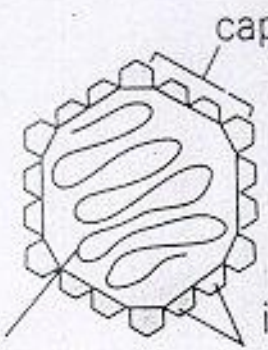
VIRUS SYMMETRY AND CONSTRUCTION

icosahedral symmetry of nucleocapsid



20 faces

construction of nucleocapsid of non-enveloped virus with icosahedral symmetry



Symmetry and construction of the viral nucleocapsid.

- Pleomorphism :-

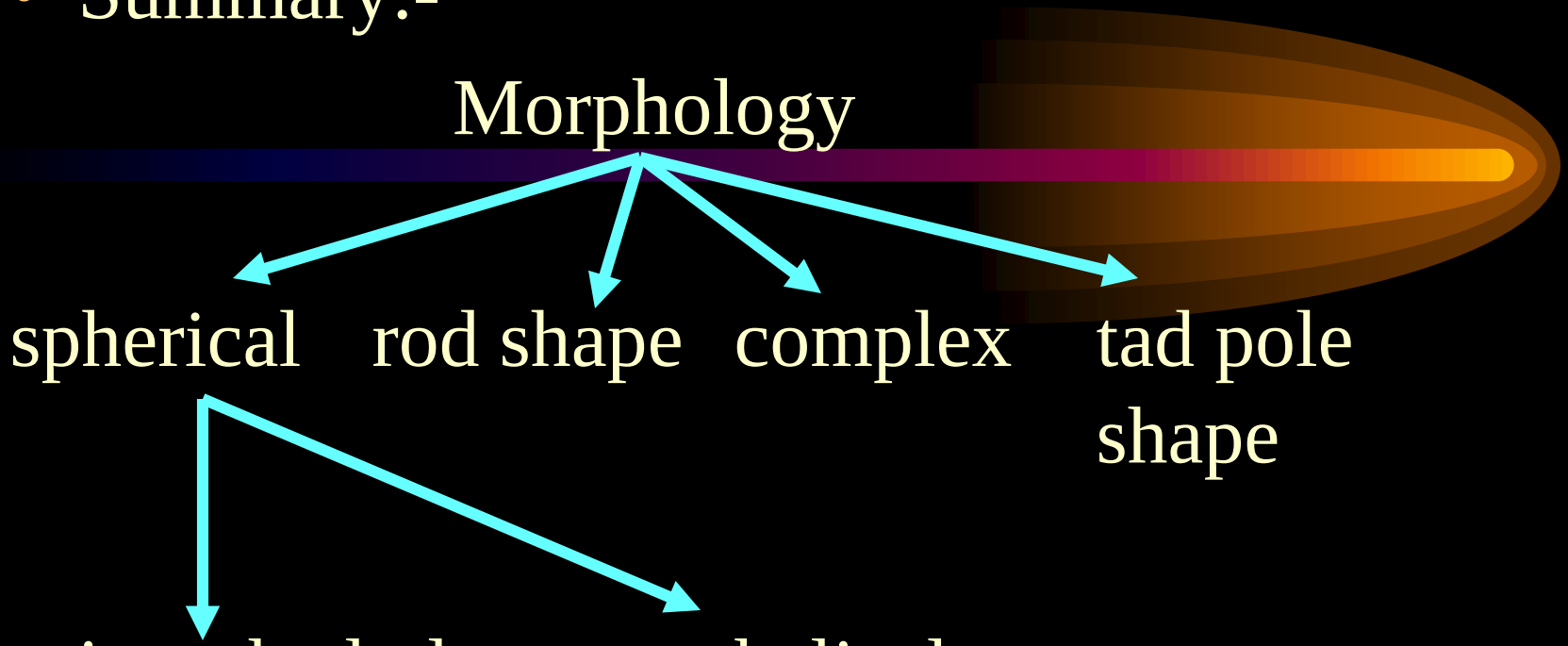
Partly due to, → Envelop

→ Nucleocapsid flexibility.

Complex viruses:-

Viruses which do not fit into → Helical or Icosohedral symmetry

- Summary:-


Morphology
spherical
rod shape
complex
tad pole shape
icosohedral symmetry
helical symmetry

CLASSIFICATION

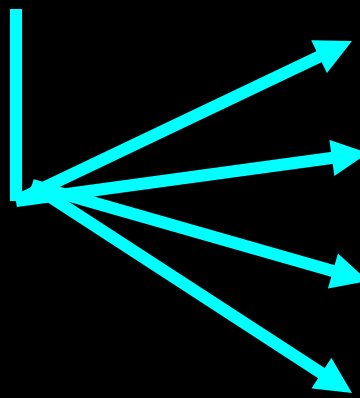
- Historically viruses classified according to;
  1. Disease symptoms.
  2. Host range.
  3. Affected organs → Dermotropic
     Neurotropic
  4. Epidemiological criteria → Arbo viruses
     Enteric
     Respiratory

- Rapid progress in virology led to the increase no: of viruses discovered

Revision of nomenclature in Taxonomic order was needed.

- International Committee on Taxonomy of viruses. [ICTV]

- Viruses should be given ;



Species

Genus

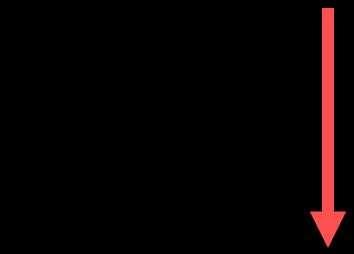
Sub family

Family names

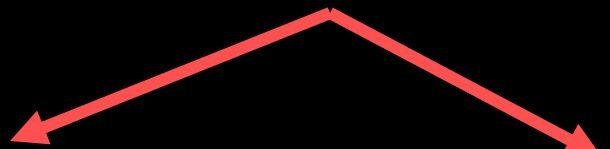
[latinized]

- Family -----Viridae eg; Herpes viridae.
- Sub family ---- Virinae Gamma herpes virinae.
- Genera ----- Virus
- Species ----- Virus

- Current classification is based on ;
    1. Architecture of the virus particle.
    2. Nature of the genetic material.



Two broad groups



Ribo viruses
[RNA viruses]

Deoxyribo viruses
[DNA viruses]

- Further classification is based on ;
    1. Strandedness of NA.
    2. Symmetry of the nucleocapsid
    3. Enveloped or not.
    4. No: of capsomeres etc.

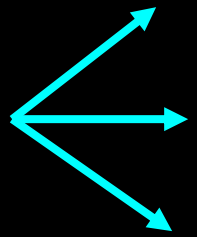
- Further distinctions are based on ;
    1. Biological properties.
    2. Antigenic relationships.

- Families are grouped into Genetic classes
  1. Double stranded DNA genome.
  2. Single stranded DNA genome.
  3. Double stranded RNA genome.
  4. Positive single stranded RNA genome.
  5. Negative ,, ,, ,, ,,
  6. Positive ,, ,, ,, ,,
     - Where replication cycle involves a DNA intermediate.
  7. Double stranded DNA genome.
     -Where replication cycle involves a RNA intermediate.

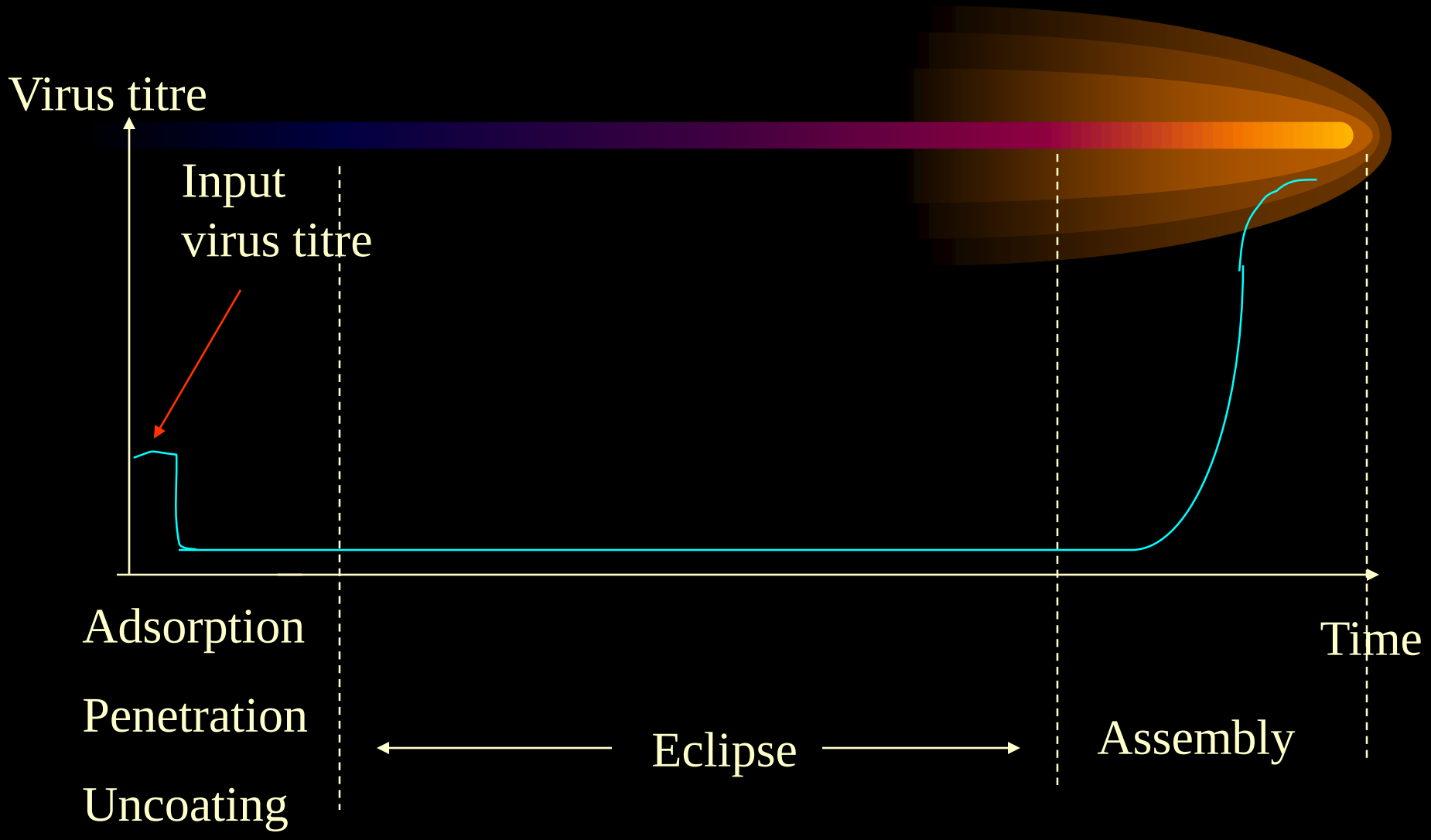
REPLICATION

VIRUSES AND THE HOST CELL.

Life cycle is divided into 3 phases;



- Adsorption and Penetration
- Eclipse
- Assembly and Release


Virus titre
Input
virus titre
Adsorption
Penetration
Uncoating
Eclipse
Assembly
Time

- ADSORPTION:-
- Viruses adsorb to ---> specific cell surface molcules. [receptors]

  ie; Influenza ---sialic acid recidues.

  HIV --- CD4 on Th cells.

  EBV --- C3d [CR2]
- Following adsorption → Penetration occurs via either,

  Pinocytosis

  Fusion [Enveloped viruses],

  Direct, or,

  Disruption of cell membrane integrity.

- ECLIPSE.

. No virus particle can be seen in the host cell by , EM or infectivity measurements.

. At this stage ,

input virus ----> “ uncoated ” [disassembled]

. Virus NA is replicating.

. New viral protein are synthesized.

[Eclipse contd]

- Mechanisms are complex.
- Important points are ,

1. Replication of viral NA ,

Highly specific

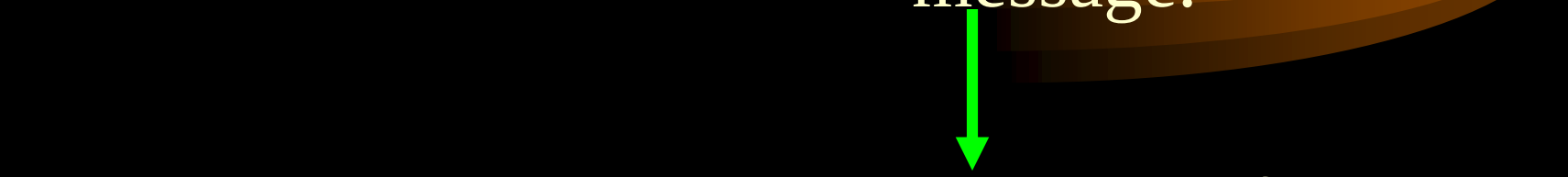
Controlled process

Viruses have own polimerase

or

Proteins that modify host polilimerase.

2. Viral genome----> must be a message or , transcribed to a message.



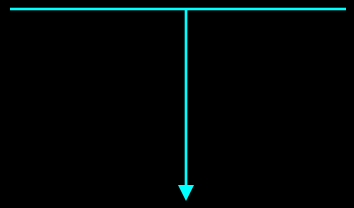
Translation of the RNA to give virus specified proteins.

- + ve strand RNA - same sense as m RNA
  i.e. Polio
- - ve strand RNA- a complement of message
  i.e. Measles

- ASSEMBLY AND RELEASE

At the end of the eclipse phase,

Progeny genomes + Newly synthesized virus proteins



Assemble to form new virus particles.

{poorly understood}

Assembly and release contd;

- Protein subunit ---> icosohedral structure

- Progressive addition of protein subunits around the NA molecule

helical structure

Assembly and release contd;

- Release:- → cell lysis
  → enveloped viruses
  → bud out from the plasma membrane and acquire envelop in the process

Viruses and disease

- 1. Necrosis : cell death → Polio, HSV, VZV
- 2. Proliferative changes - Initial short lived hyperplasia ----> Necrosis.

  Occur in “Pock” lesions with extensive inflammatory reaction.

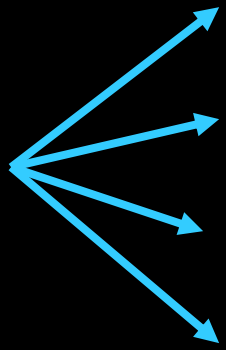
- 3. Proliferative changes ---> leads to neoplastic transformation.
  [tumor viruses]
- 4. Inclusion bodies ;
  - Characteristic feature of many viruses.
  - May occur in nucleus or cytoplasm.

- Secondary infection

  Damage to epithelium---->Secondary bacterial infection

Viruses in the multicellular host

- 1. Requirements of any virus :-
    1. Portal of entry.
    2. Tissue in which to multiply.
    3. Portal of exit.
    4. Means of transmission.

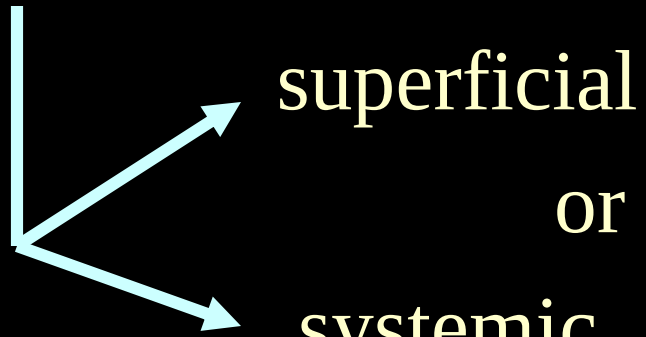


1. Portal of entry :-

- Mucosal surfaces → Respiratory
  - GIT
  - Urogenital
  - Conjunctiva
- Skin {need damage to cornified layer}
- Blood ← Abrasion
  - Direct introduction
  - Vectors

2. Target tissue for amplification

- Infection may be :-



Superficial infections

- Virus replication at portal of entry.
- Short incubation period.
- Acute infection of short duration.

Eg: Common cold

{ Rhino virus,
Influenza,
Rota virus }

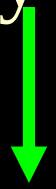
Systemic infections

- Long incubation period.
- Replication at multiple sites
- Outcome dependant on host immune response.

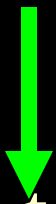
Eg: Measles
Varicella
Rubella

- INFECTION AND REPLICATION DURING SYSTEMIC VIRUS INFECTION

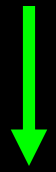
Primary multiplication



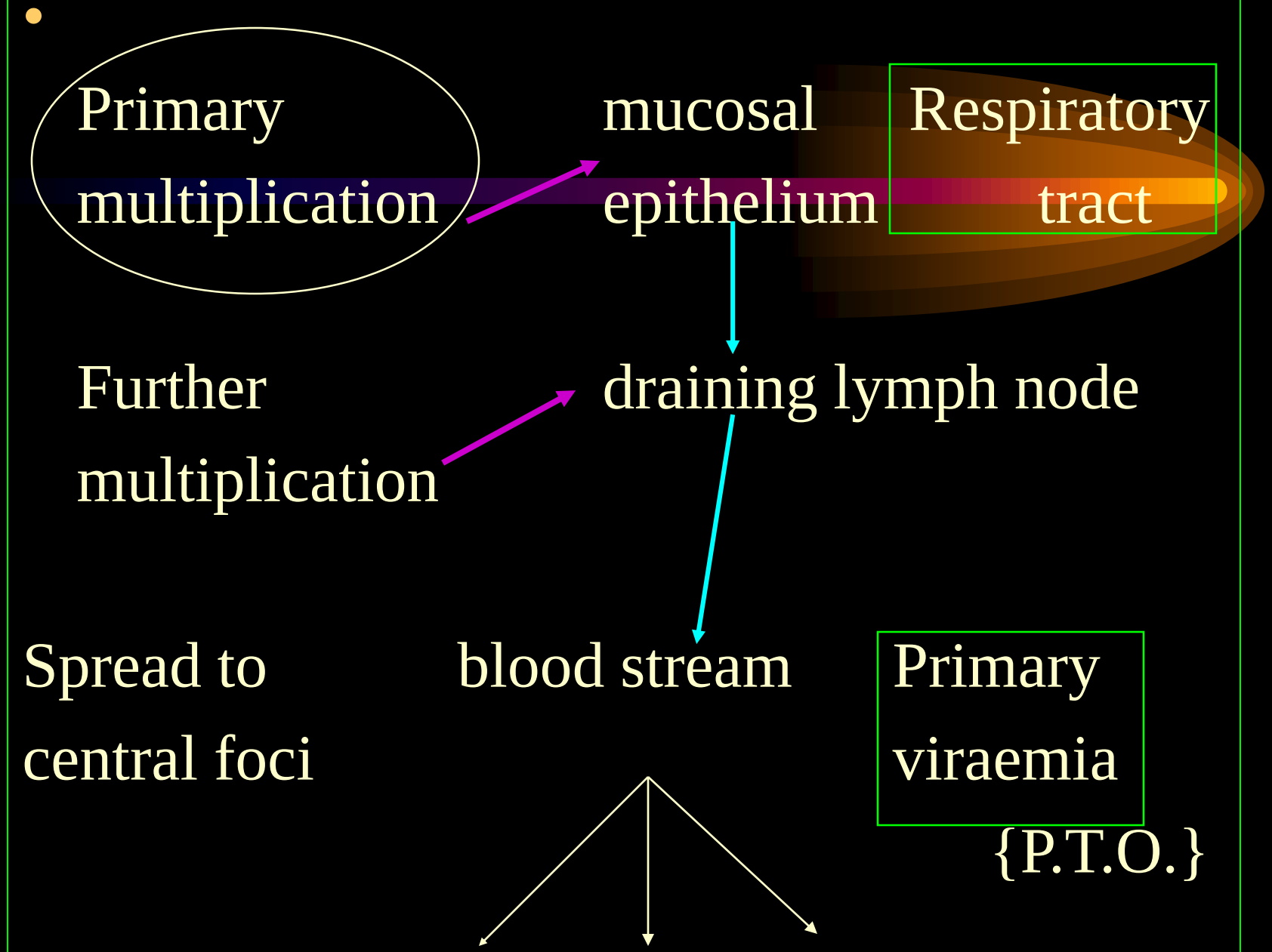
Amplification



Spread to target organs

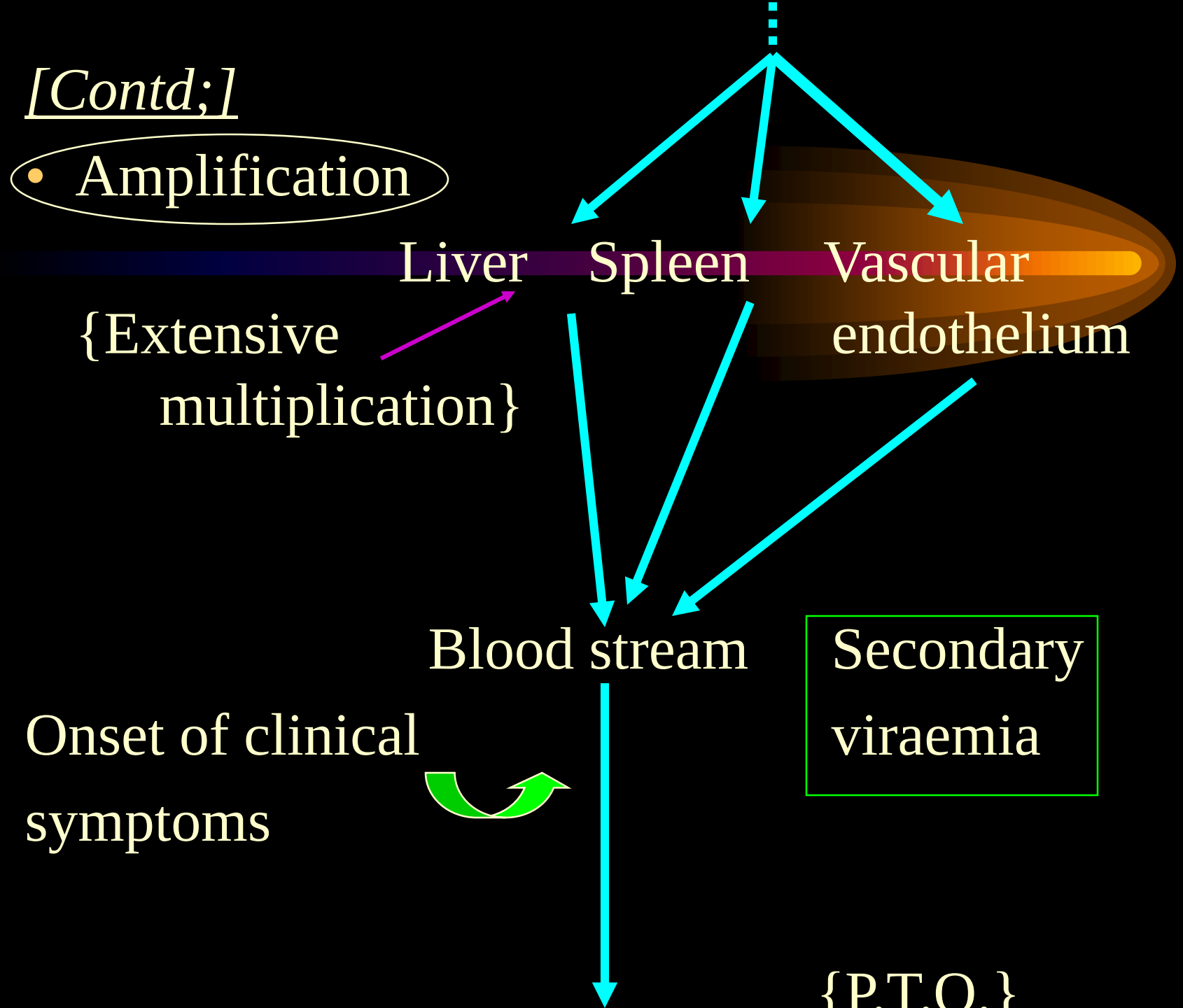


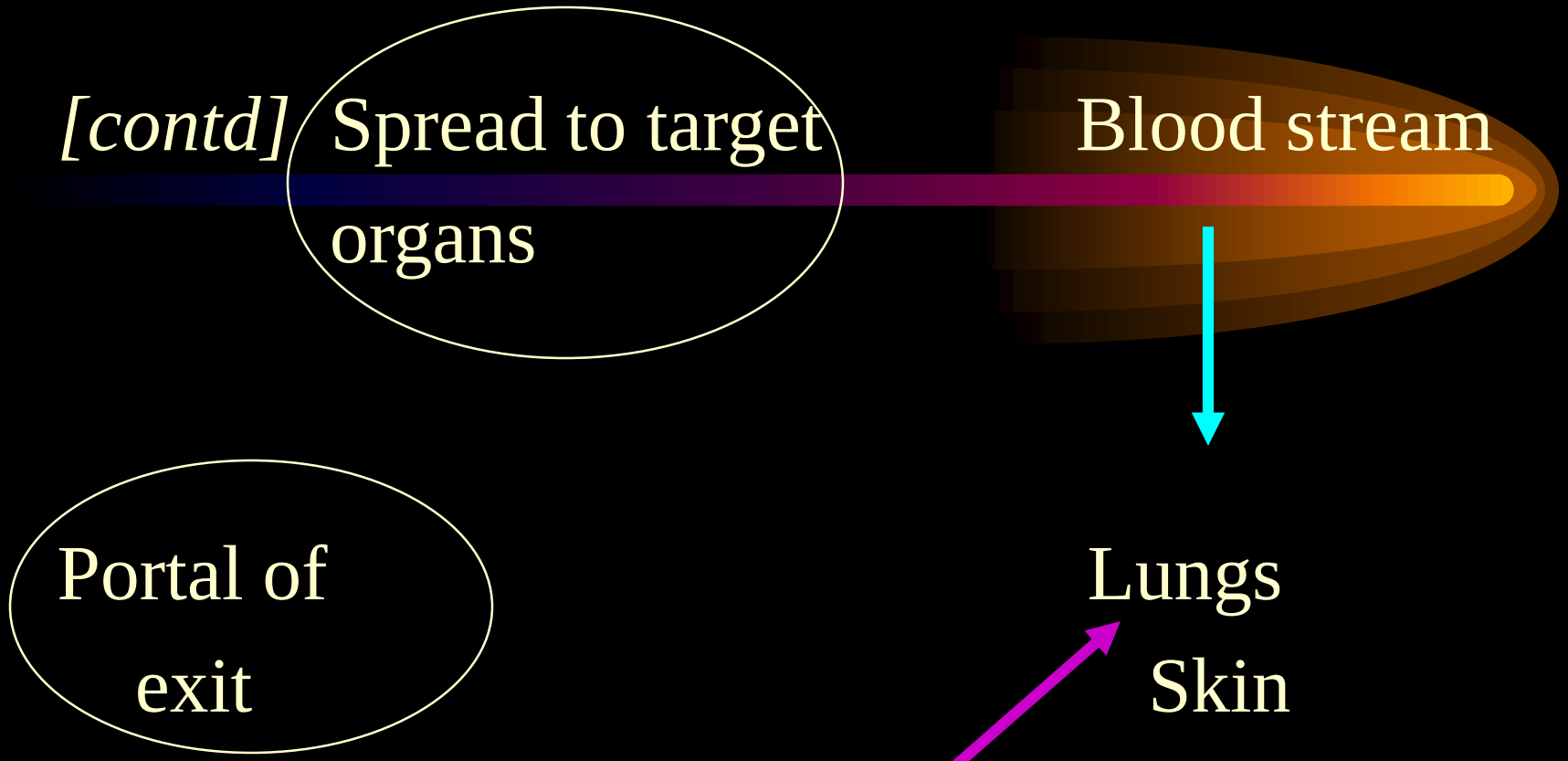
Exit portal


Primary multiplication
mucosal epithelium
Respiratory tract
Further multiplication
draining lymph node
Spread to central foci
blood stream
Primary viraemia
{P.T.O.}

[Contd;]

- Amplification




[contd]
Spread to target organs
Blood stream
Portal of exit
Lungs
Skin
multiply at target sites

3.Exit portal

- Examples:-

Respiratory tract - Measles
- Rubella
- Flu
- Varicella

Oropharyngial epithelium
- Herpes simplex
- EBV

4. Transmission mechanisms

- Examples:-

Respiratory aerosols - Rubella
- Influenza
- Rhino virus
- Measles
- VZV

Oral contact / Salivary transfer - HSV
- EBV
- CMV

Faeco oral - Polio

- Hepatitis A
- Rota virus

Skin dust inhalation - Small pox

Sexual - HSV

- CMV
- HBV
- HIV
- Genital papilloma

Animal bites - Rabies

Insect vectors - Jap. Encephalitis

- Dengue virus

Blood contact - HBV

{Iatrogenic, - HIV

abrasions} - CMV

Congenital - rubella, CMV, HBV, HSV, VZV

Perinatal - HSV, CMV, HBV, HIV

PATHOGENESIS

- Pathogenesis of viral infection

depend upon interactions of,

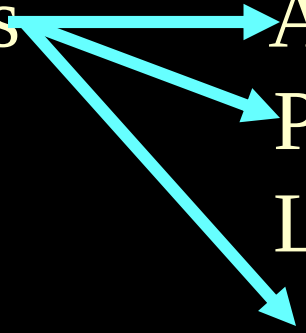
Viral factors

Host factors

- 1. Entry of virus to susceptible cells.
- 2. Viral multiplication and spread.
- 3. Effect of virus on cell functions.
- 4. Host immune response.
- 5. Virus clearance or
  Establishment- Persistent infection
- 6. Virus shedding.

- Some viruses survive within the host.
  - Persistent and latent infections.

- Viral infections



Acute

Persistent or Chronic

Latent

- Acute - Cleared following acute phase.
  Eg: Flu , Polio.

- Persistent - Hep. B, HIV
  Infectious virus continuously present for many years or life time.

- Latent - Infectious virus disappears after acute phase. Reappears sometimes years later.

- Neurons :-

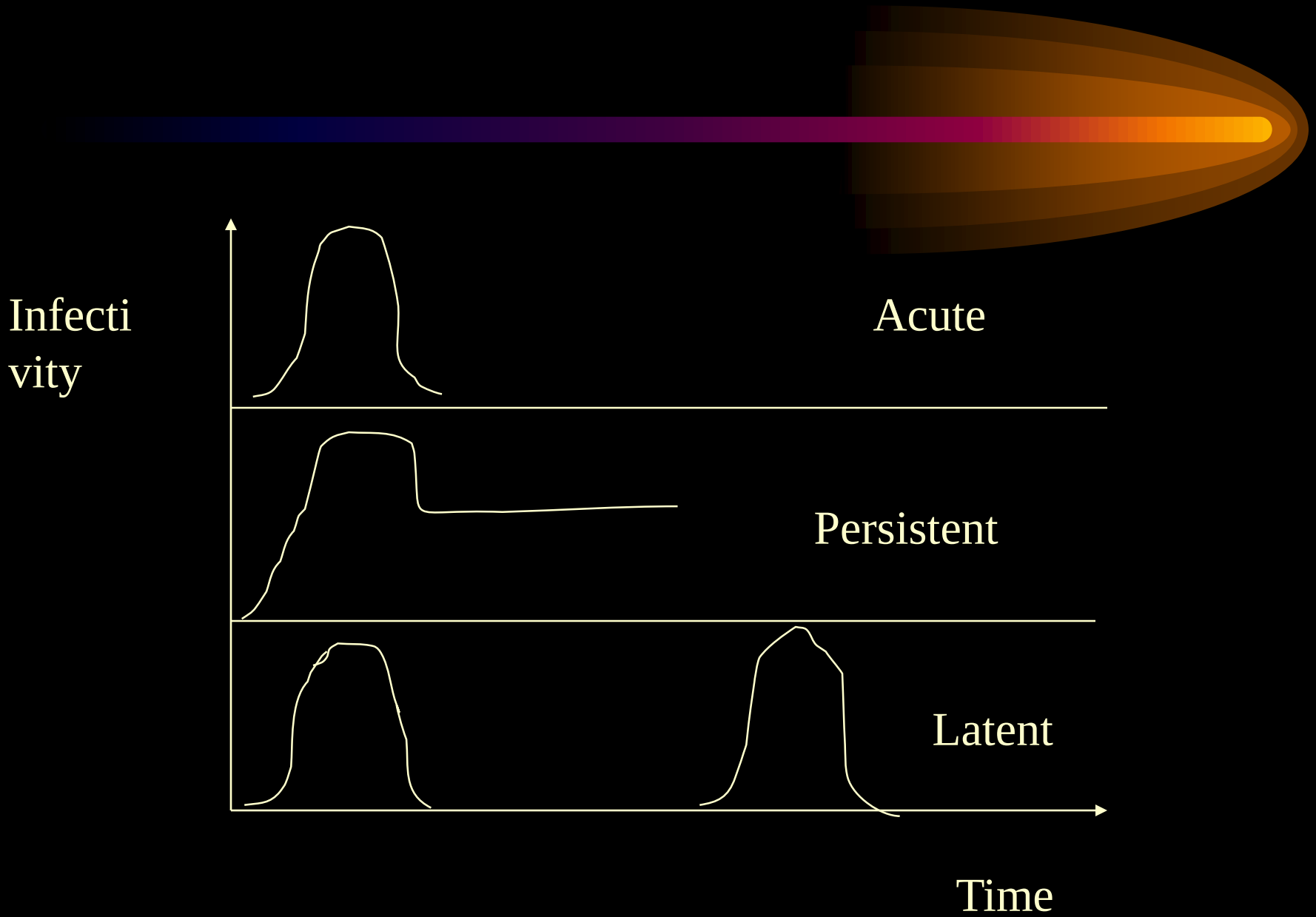
  HSV Cold sores { reactivation }

  VZV → Shingles { reactivation }

- B cells:-

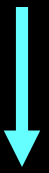
  EBV

- Retro virus:- Virus integrate into host cell chromosome as Provirus if not transcribed. = Latent.


Infecti
vity
Acute
Persistent
Latent
Time

- In an individual infected with HIV is persistently infectious - Because virus can be isolated continuously from circulation.
- Virus is replicated in some cells.

{Productive infection}



These cells are immune targets

- In other cells - Provirus is quiescent

There latently infected cells are not immune targets.

May be activated in a later stage.

Mechanisms for virus survival:-

- Failure to eliminate a virus means virus can evade immune response.
- Many viruses show mechanisms of immune evasion.

Eg:

1. Adeno virus → Interfere with transmission of class 1 molecule to the cell surface.
2. HIV, EBV, Measles → Suppression of immune response.

- 3. HIV ⟶ Cause rapid antigenic variation in the host.
- Immune evasion - can not account for persistence.

  i.e. Adeno viruses

  Pox viruses