# ANTI-VIRALS — FOR Resp. Tract INFECTIONS

## (1) Neuraminidase Inhibi.

- Oseltamivir & Zanamivir = effective against both Type-A & Type-B influenza virus
- Don't interfere ē immune resp. to influ. vaccine

→ Prior to exposure adm = prevent infection.

→ Within 24–48hr after onset of symp = ↓ (intensity & duration of symp)

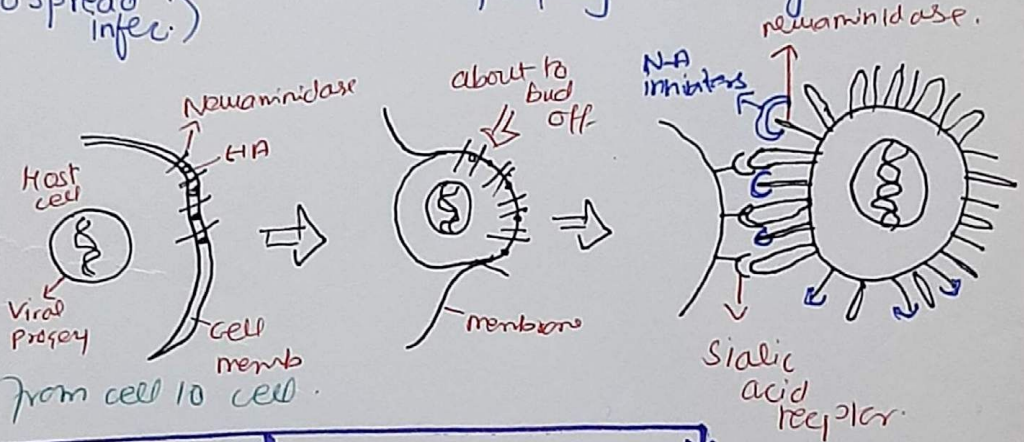
## MOA

- Influenza virus employ specific enzy. Neuraminidase — That is inserted into host cell membs for the purpose of releasing newly formed virions (sialic acid recept)

From cough or sneeze or contamin. surface → influenza virus enter RT or GIT or eye (conjuctiva) → colonize the epithelial lining of nasal pharynx or resp. mucose → Virus bind → enter the cell → genome is release → use host cell mech. to transcript and translate ⇓ viral glycoprotein Produce (HA & Neuramini

These viral component trafficked to host cell plasma memb where viral progeny assembly occurs ⇐ viral then Buds from plasma memb to release to EC-space (To spread infec.) ⇐ Before releasing they bind to Sialic acid recep. Neuraminidase break this bond and cause the viral progeny to release in spaces.

- Oselta/Zana–bind to neuramidase & thereby prevent the release of new virons And their spread from cell to cell.




### Pharmacokinec.

Oseltamivir = (prodrug) ↓ • Orally active • Prodrug. IN LIVER • BY HYDROLYSIS ⇓ Active form

Zanamivir = • NOT Active orally • Adm via INHALATION

- Elimin via urine

bird flue (H5N1)

### ADRs

- Oselta: GI discomfort (↓se when taken ē food).
- Zana = resp. irritation ↓ CAUTION IN INDI (Asthma) (COPD) ⇓ Bronchospasm may occur.

### Resistance

- Mutation in NM However mutant strain is less infective & less virulent

# (B) ADAMATANE ANTIVIRALS

- Effectiveness limited to Type-A – wide spread resistance, NOT recomm in USA – for TYP-A.

## MOA

Amantadine & Rimantadine interfere @ Junction of viral M2 protein → Blocking the uncoating of virus particles.

## KINECTICS

### Absorp.

well-abs. after oral-adm.

### Metabo.

- Amantadine: Body + CNS (cross-BBB)
- Rimand = CNS (BBB) ← as much as Amanti

### Excretion

Amant → uncharge in urin → dose adj req'in renal disease.

Riranta → metab & excrete → Parent + metab = urine.

Aman. also use in Parkinson = where it facilitate Dopamine.

## ADRs

### Amantadine

Mainly CNS-associated → insomnia, dizzi, ataxia

- serious ADR = Hallucin. & seizures.

CAUTION → Psychiatric prob; cerebral atherosclero; epilepsy

### Rimantadine

- fewer CNS

BOTH DRUGS → GI intolera

Avoid: PG, BF

**Resistance**: change in one A.A in M2 protein (mature)

- cross-resistance
- Rapid transmiss of resistant strains.

## RIBAVIRIN

- Synthetic guanosine analogue.
- broad-spectrum of effect for RNA & DNA virus.
- use: infants & young child @ severe RSV infect
- effective in chronic Hep-C when use in comb @ interferon

### Mechanism

- Inhibition of RNA & DNA replication
- Drug → 5'phosph (phosphorylate) → 3'phosp (derivative)

5'monopho. inhibit cellular enzyme inosine 5'-pho dehydro thus blocking IMP → xanthine 5-MP (conversion) ↓ guanosine triphosp (GTP) level

= ↓ xanthine & Guanin = purines

Inhibit GTP depend mRNA capping & RNA-dep RNA polymerase (that catalyze replic of RNA from RNA).

### Kinetics

- Oral + inhala
- inhal = RSV infec. not for influenza.
- Absorp ↑ se @ a fatty meal
- Drug & meta = elimi via urine

CNS: poor penetration

### ADRs

- dose-dep: Transient anemia
- ↑ bilirubin
- Aerosol is safer However in infants = resp. function can deteriorate

PG

# HEPATITIS

- Each (A, B, C, D & E) have pathogenesis involving → replication & destruc. of Hepatocytes
- Of these Hep-B (DNA virus) & Hep-C (an RNA virus)
  - Chronic hepatitis, cirrhosis & hepatocellular carcinoma.
  - ONLY for these 2 are the therapy is currently Avail.

* - Hep-A (caused by oral ingestion) — NOT a chronic disease.

## Treatment OPTIONS

### Chronic, Hep-B

#### Injectables

- Peginterferon α-2a
  - S/C
  - Once a week
  - Better efficacy
  - Improve tolerability
- Peginterα-2b
  - IM/or S/C
  - Twice a week

#### Orals

- Lamivudine
- Telbivudine
- adefovir
- Tenofovir
- entecavir

### Chronic Hep-C

* - Preferred treatment:
" combin. of pgα-2a (or) pgα-2b plus ribavirin
[more effective than comb. of standard interferon + ribavirin]

* - For Genotype-1 HCV an NS3/4A protease inhibi (boceprevir or telaprevir) added to Pg-inter. & riban

## (1) INTERFERONS (IFNs)

- Family of naturally occuring, inducible glycoproteins = interfere the ability of virus to infect the cell.
- Synthesized by recomb. DNA Technology
- 3 sub-types exists (α, β & γ) of IS-INF-α-glycoproteins

* — INF-α-2b has been appro. — Hep-B, C, condylomata acuminata (anogenital warts caused by Human papillomavirus HPV) and cancers (Hairy cell leukemia — bone marrow produce too many B-cell — These abnormal B-cells looks hairy under microscope) & Kaposi sarcoma (cancerous tissue in lining of blood and lymph vessels)

★ - **Pegylated formulations**: The bis-monomethoxy PEG has been covalently attached to either INFα-2a or INF-α-2b

⇓

Use size of molecule

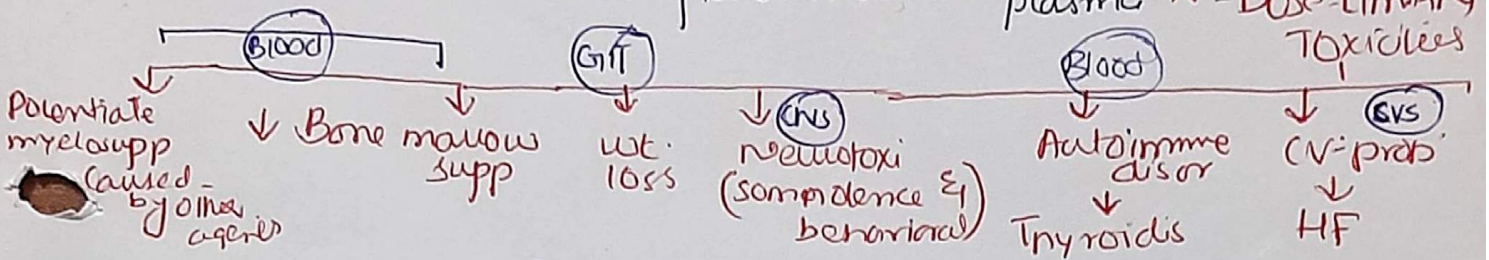
- Delay absorption from injection site → lengthens the duration
- Use clearance.

# INF

## Mechanism
- induce host cellenzy that inhibit viral RNA Translation
- ultimately leading to degradation of viral mRNA & tRNA

## Kinetics
- NOT active orally
- may be adm: IM, S/C, IV
- little amount in plasma. However its presence NOT related to effect
- cellular uptake + metab = little in plasma
- negible renal elim.

## ADR
- Flue-like symp (fever, chills, myalgias, arthralgia & GIT dis)
- Fatigue & mental depression (symp ↓ ē continued adm.)
- ★ - Dose-Limiting Toxicities




# LAMIVUDINE

## MOA
→ Cytosine Analog
- inhib. of both HBV & HIV reverse transcriptase.
- Phosphory → triphosphate (active form)
- competitively inhibit RNA-dep-DNA polymer

(also know as reverse transcriptase) it transcribes single-stand RNA into DNA → forming RNA-DNA hybrid, RNA strand is degraded by RNase-H activity and then form double strand DNA after transcribing) then DNA polymerase synthesize second DNA strand complementary. ← to first cDNA → double stranded DNA. → integrated into host Genome.

## Kinetics
- like many Nucleotide analogs
- Plasma $t_{1/2}$ < Intracellular $t_{1/2}$
- Orally absor.
- wide dis.
- excreti in urine

## ADR
- well tolerated
- rare: headache & dizziness
- ↓ Dose in renal insuf
- resis develop ē long Term Therapy