Masaryk University
Faculty of Medicine

Antivirals in Dentistry

Antivirals for Infection Control and Prevention in Dentistry

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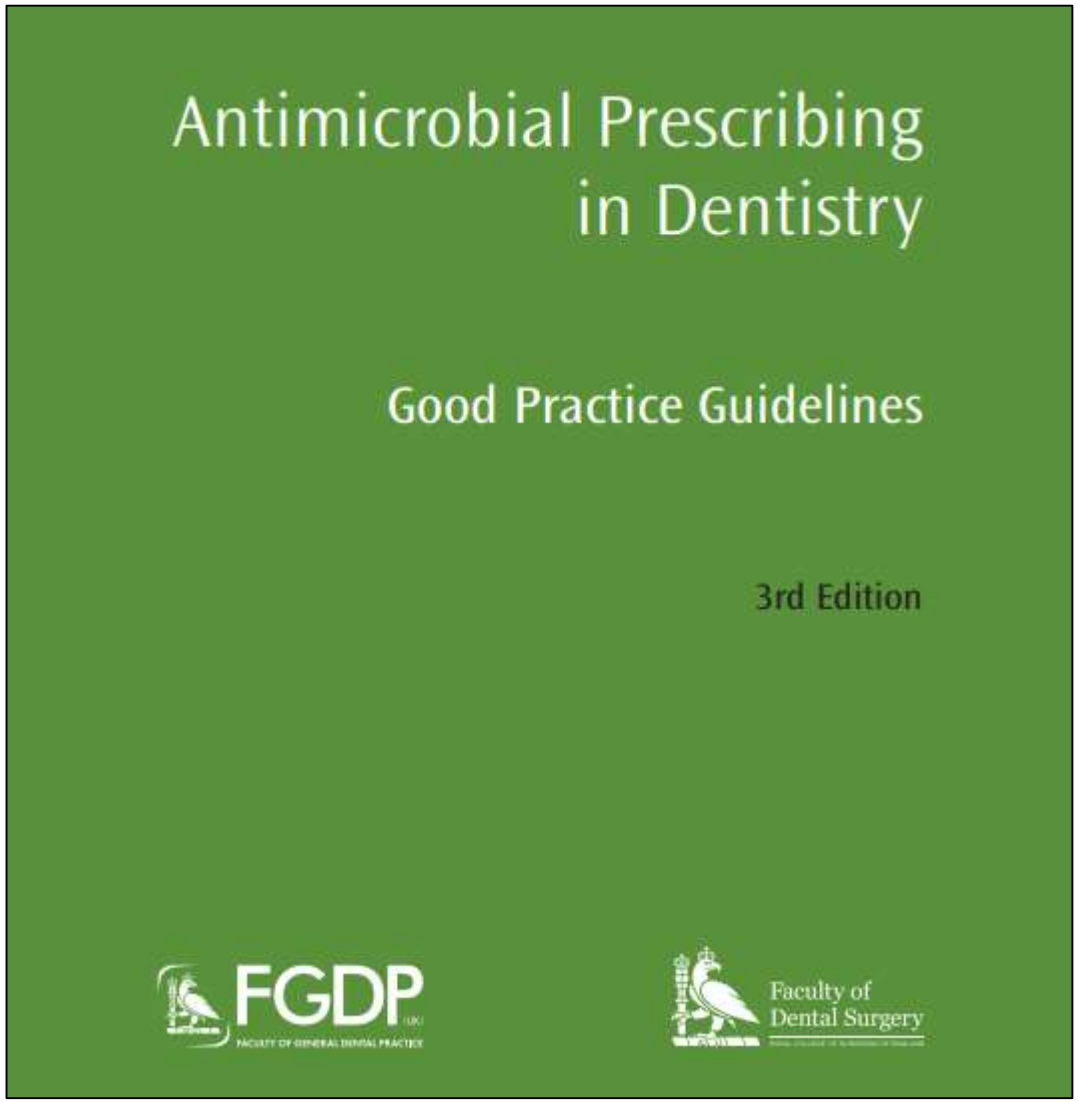
Learning Objectives

- Understand the role of antiviral drugs in dental infections
- Identify Common Oral Viral Infections
- Identify antiviral classes commonly used in dentistry
- Explain the Mechanism of Action of Antiviral Agents
- Distinguish Between Different Types of Antivirals

Before we start…



Palmer, N. (Ed). Antimicrobial Prescribing in Dentistry: Good Practice Guidelines. 3rd Edition. London, UK: Faculty of General Dental Practice (UK) and Faculty of Dental Surgery; 2020.

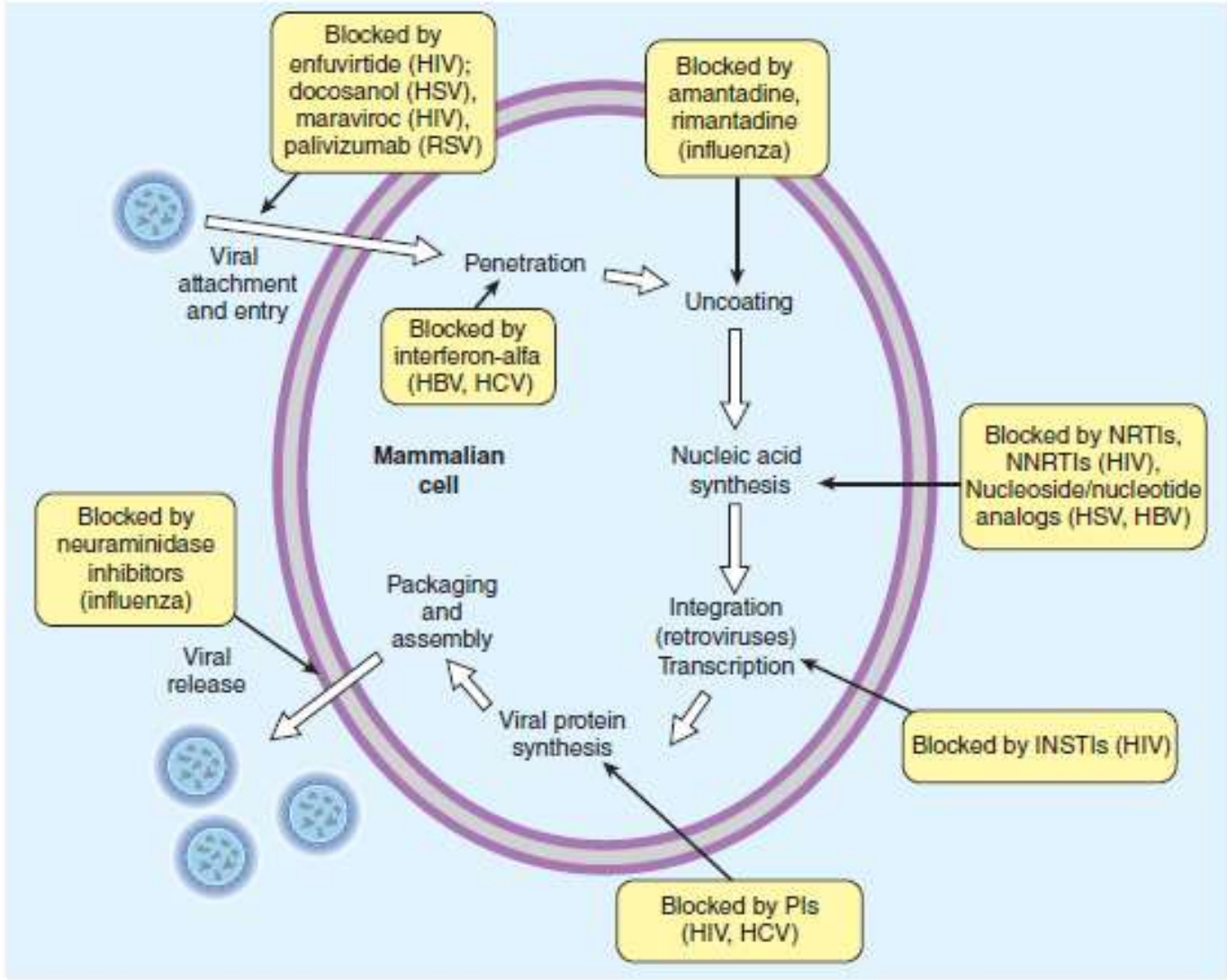
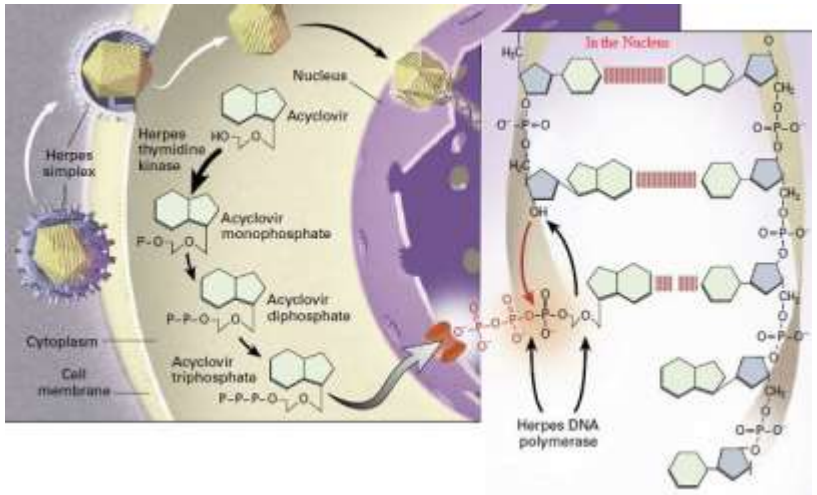


FIGURE 49–1 The major sites of antiviral drug action. *Note:* Interferon alfas are speculated to have multiple sites of action. (Modified and reproduced, with permission, from Trevor AJ, Katzung BG, Masters SB: *Pharmacology: Examination & Board Review*, 9th ed. McGraw-Hill, 2010. Copyright © The McGraw-Hill Companies, Inc.)

Guanosine analogues

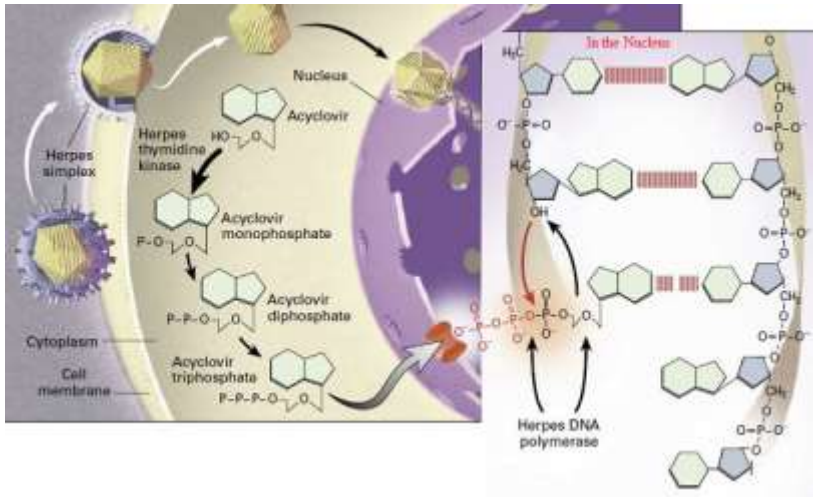
- **aciclovir** – active against **HSV**,**VZV, CMV** (not latent forms of VZV and HSV)
  - **PO administration** – poor absorption – low bioavailability
    - **Indications**: mild mucocutaneous lesions and genital lesions or for herpes prophylaxis in immunocompromised individuals
  - **IV administration**
    - **Indications**: severe herpes infections - HSV encephalitis
  - Accumulates only in infected cells - viral kinase necessary for initial phosphorylation
  - **Mechanism of action**:
    - competition with deoxyGTP for the viral DNA polymerase
    - chain termination following incorporation into the viral DNA
  - Low bioavailability but well distributed to tissues
  - Cleared primarily by glomerular filtration and tubular secretion
  - Resistance possible – alteration of viral kinase



M.O.A: These drugs act as **guanosine analogues** that get phosphorylated and **interrupt viral DNA synthesis**

Guanosine analogues

- **valaciclovir (PD)**
  - **Prodrug** of acyclovir
  - ↑ Oral bioavailability
- **famciclovir**
  - **Pro-drug** of **penciclovir**
  - **Indication**: Herpes Zoster (HSV)
- **valganciclovir**
  - **Pro-drug** of **ganciclovir**
    - activity against CMV is up to 100 times greater than that of acyclovir
    - ganciclovir is administered intravenously
    - intravitreal injections of ganciclovir is possible **CMV retinitis**
    - valganciclovir is administered orally
  - **Indication**: HSV and **mainly CMV**
    - Prophylaxis and treatment of CMV infection (retinitis)



M.O.A: These drugs act as **guanosine analogues** that get phosphorylated and **interrupt viral DNA synthesis**

Very specific to **aciclovir** and **ganciclovir**

Nephrotoxicity

Hypotension

CNS symptoms

Delirium, seizures usually at toxic levels of **aciclovir** after IV administration. **ganciclovir** too

Adverse Effects

aciclovir – generally **very safe** – does not affect cells that are not infected by virus due to the necessity of thymidine kinase for the activation

Pancytopenia

GIT disturbances

Nausea, vomiting

Bone marrow suppression (especially **ganciclovir**)

↓ TTP

With **aciclovir** and **valaciclovir**

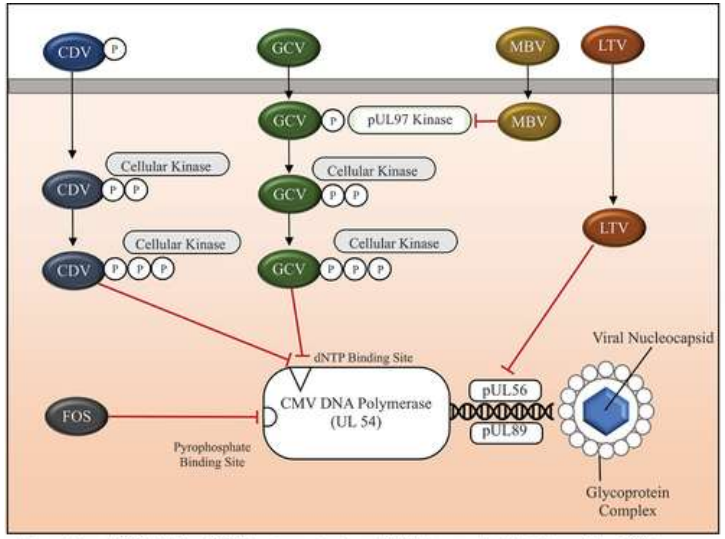
Most characteristic side effect

Other drugs used to treat virus from Herpesviridae family

- **DNA replication inhibitors**
  - Target the **DNA polymerase** → inhibits viral DNA replication and mRNA formation → therefore there is ↓ mRNA → ↓ proteins → ↓ less viral assembly → ↓ new viruses

  - **cidofovir**
    - Double phosphorylation and **direct inhibition of DNA polymerase**
    - Indication: **acyclovir**-resistant **HSV** infections and as an alternative of **ganciclovir** in **CMV**

  - **foscarnet**
    - Only drug for Herpesviridae family that does not require phosphorylation – acts as an analogue
    - **Mechanism of action:**
      - Competitive inhibition of:
        - DNA polymerase (resistance common due to mutated forms of this enzyme)
        - RNA polymerase
        - HIV reverse transcriptase
    - Indication: **acyclovir**-resistant **HSV** infections and as an alternative of **ganciclovir** in **CMV**

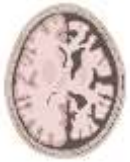


Abbreviations: CDV; cidofovir, CMV; cytomegalovirus, dNTP; deoxynucleotide triphosphates, FOS; foscarnet, GCV; ganciclovir, LTV; letermovir, MBV; maribavir

Characteristic of **cidofovir** and **foscarnet**. **cidofovir** is usually combined with **probenecid** and IV saline to decrease toxicity

Nephrotoxicity

Adverse Effects



CNS symptoms

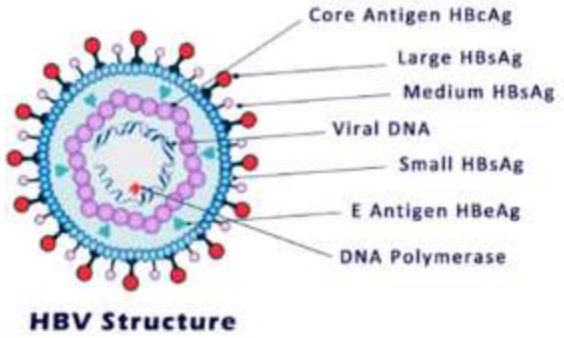
Electrolyte imbalances

Seizures and hallucinations can occur because of **foscarnet** use and because of the electrolyte imbalance

Nephrotoxicity due to **foscarnet** can be severe and manifest with electrolyte disturbances usually affecting the balance of **calcium, phosphate, and magnesium**

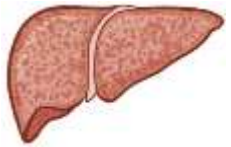
Most characteristic side effect

Hepatitis B



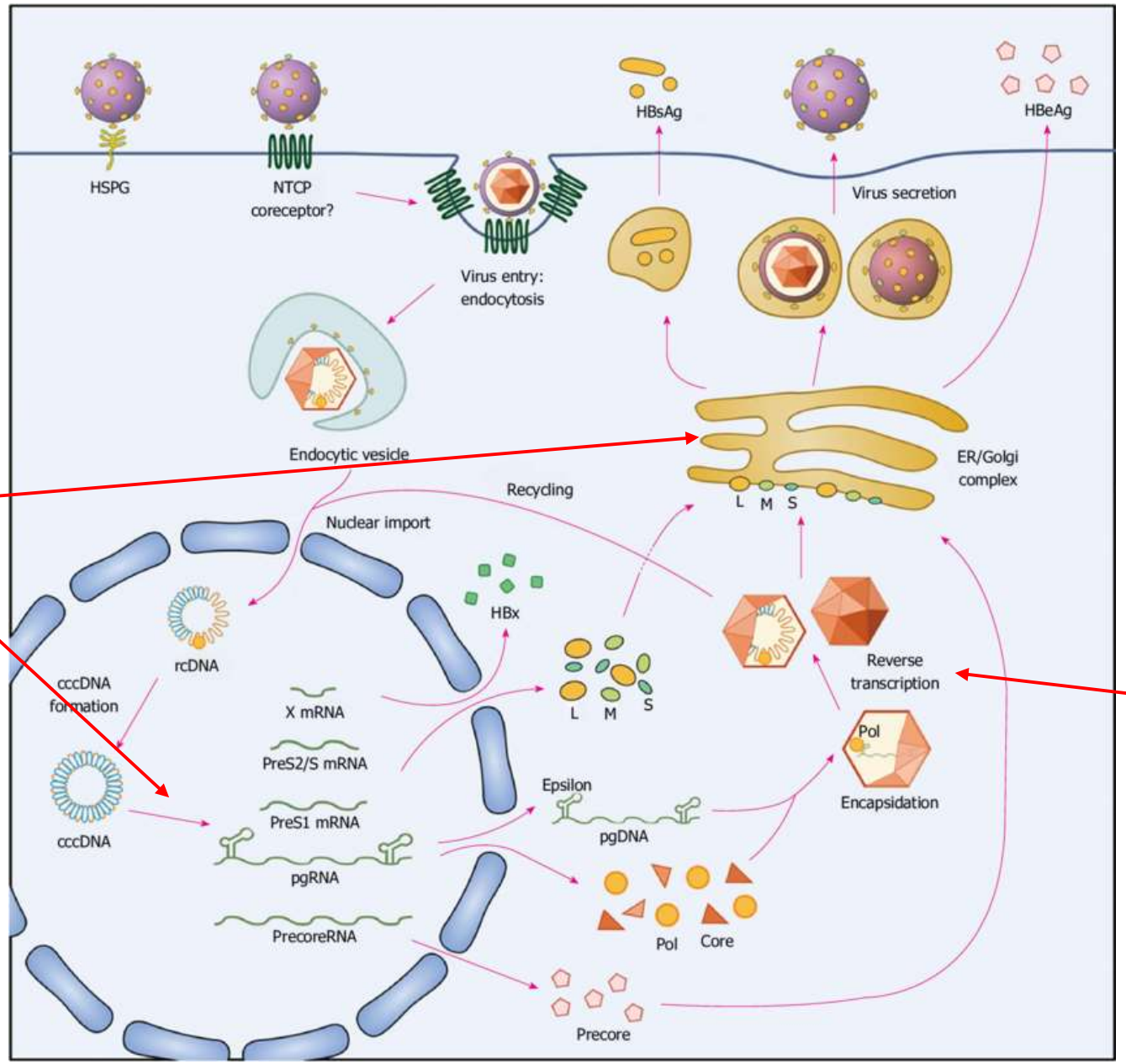
HBV Structure

- HBV→ Hepnadnaviridae family → partially double DNA stranded virus
- Causes acute or chronic liver disease → Periportal area
  - Only pathogenic species in Hepnadnaviridae family in humans
  - 6 weeks to 6 months of incubation period
  - Transmission: perinatal (at childbirth), IV and sexual
- 2 types:
  - Acute hepatitis → less than 6 months → penetration of lymphocytes → CD8+ T-lymphocyte activation → apoptosis → Liver damage and inflammation
    - May cause acute liver failure
    - Up to 10% evolve to chronic



  - Chronic hepatitis → more than 6 months → insufficient T-cell response, or, if large amounts of HBs antigen bind to neutralizing antibodies → risk of hepatocellular carcinoma

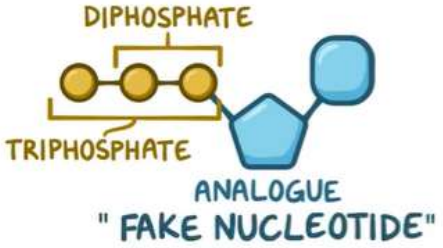
Jaundice



IFN-alfa

Use of Reverse Transcriptase Inhibitors

Reverse Transcriptase Inhibitors in HBV



- Target the Reverse Transcriptase→ inhibits viral DNA production→ new virions will not be produced
  - HBV: DNA polymerase is the target
  - HCV: RNA-dependent RNA polymerase is the target

  - **Nucleoside reverse transcriptase inhibitors**

    - **lamivudine**
      - **Mechanism of Action: reverse transcriptase inhibitor** - competing with deoxy**cytidine** triphosphate for incorporation into the viral DNA, resulting in chain termination
      - Chronic therapy associated with **resistance (mutation in DNA polymerase enzyme)**
      - Lamivudine has an **excellent safety profile**
      - Adverse effects: Headache, nausea, diarrhoea, dizziness, myalgia, and malaise
      - 80% oral bioavailability: 150 mg bid or 300 mg

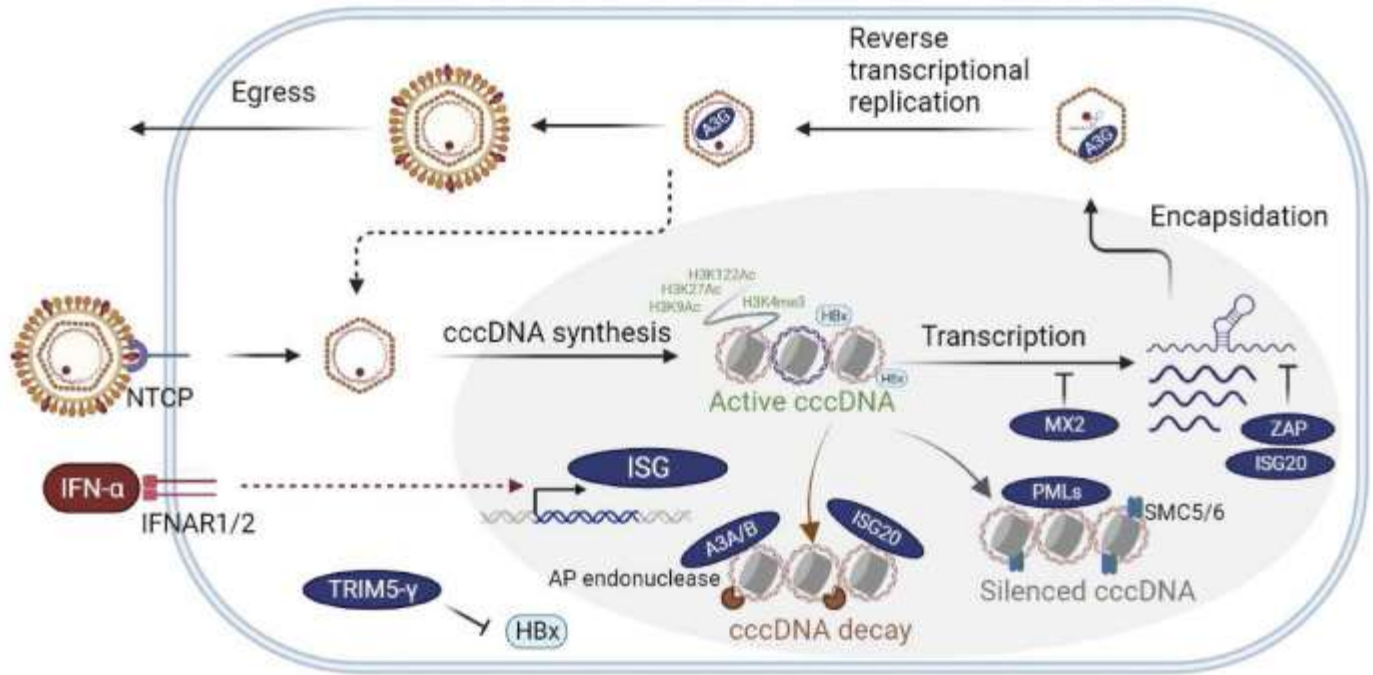
    - **entecavir**
      - **Mechanism of Action: reverse transcriptase inhibitor** - cyclopentyl **guanosine** nucleoside analogue
      - **Resistance** is harder to come by when compared to **lamivudine**
      - **entecavir** is **well tolerated**
      - Adverse effects: headache, fatigue, dizziness, nausea, and upper abdominal pain
      - 100% oral bioavailability

Reverse Transcriptase Inhibitors in HBV

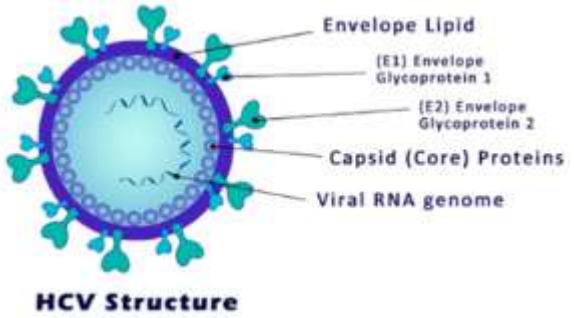
- Target the Reverse Transcriptase→ inhibits viral DNA production→ new virions will not be produced
  - **Nucleotide Reverse transcriptase inhibitors (-fovir)**
    - **adefovir**
      - **Given as a pro-drug (poor oral absorption)**
      - Mechanism of action: phosphorylated by cellular kinases to the active diphosphate metabolite and then competitively inhibits HBV DNA polymerase
      - Adefovir is **well tolerated**
      - **Adverse effects:** headache, diarrhoea, asthenia, abdominal pain
        - **Lactic acidosis** and **hepatic steatosis** (characteristic of NRTIs)
        - **Fanconi syndrome** is also characteristic of NRTIs (Phosphaturia, Glycosuria, Aminoaciduria)
    - **tenofovir**
      - **Given as a pro-drug (poor oral absorption)**
      - Nucleotide analogue of adenosine
      - Maintains activity against lamivudine- and entecavir-resistant hepatitis virus isolates
      - Lower rate of emergence of resistance in patients with chronic HBV infection
      - **Adverse effects:** nausea, abdominal pain, diarrhoea, dizziness, and fatigue
        - **Lactic acidosis** and **hepatic steatosis** (characteristic of NRTIs)
        - **Fanconi syndrome** is also characteristic of NRTIs (Phosphaturia, Glycosuria, Aminoaciduria)

Interferons in HBV

- **interferon alpha (Type I)**
  - **Mechanism of action**:
    - induces **enzyme (APOBEC3G) expression** → binding to viral DNA polymerase → degradation of nucleic acid → stop to the viral replication
    - Increase **MHC expression** → Natural killer (NK) T cell activation
  - **Intramuscular** or **subcutaneous** injection
  - Common form: Interferon + Polyethylene glycol = **Pegylated Interferon** – improvement of pharmacokinetic properties
  - Main indications chronic HBV and chronic HCV
  - INFa2A and INFa2B being used
  - **Adverse effects**:
    - **Flu-like symptoms** - fever, malaise, nausea, and vomiting
    - **Bone marrow suppression** – pancytopenia
    - **Neurotoxicity** - sleepiness, depression, and behavioural disturbance
    - **Liver dysfunction** - elevated liver enzymes

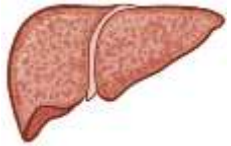

Egress
Reverse
transcriptional
replication
Encapsidation
A3G
H3K122Ac
H3K27Ac
H3K9Ac
H3K4me3
HBx
cccDNA synthesis
Transcription
Active cccDNA
NTCP
MX2
ZAP
ISG20
IFN-α
IFNAR1/2
ISG
PMLs
SMC5/6
A3A/B
ISG20
AP endonuclease
TRIM5-γ
HBx
cccDNA decay
Silenced cccDNA

Hepatitis C

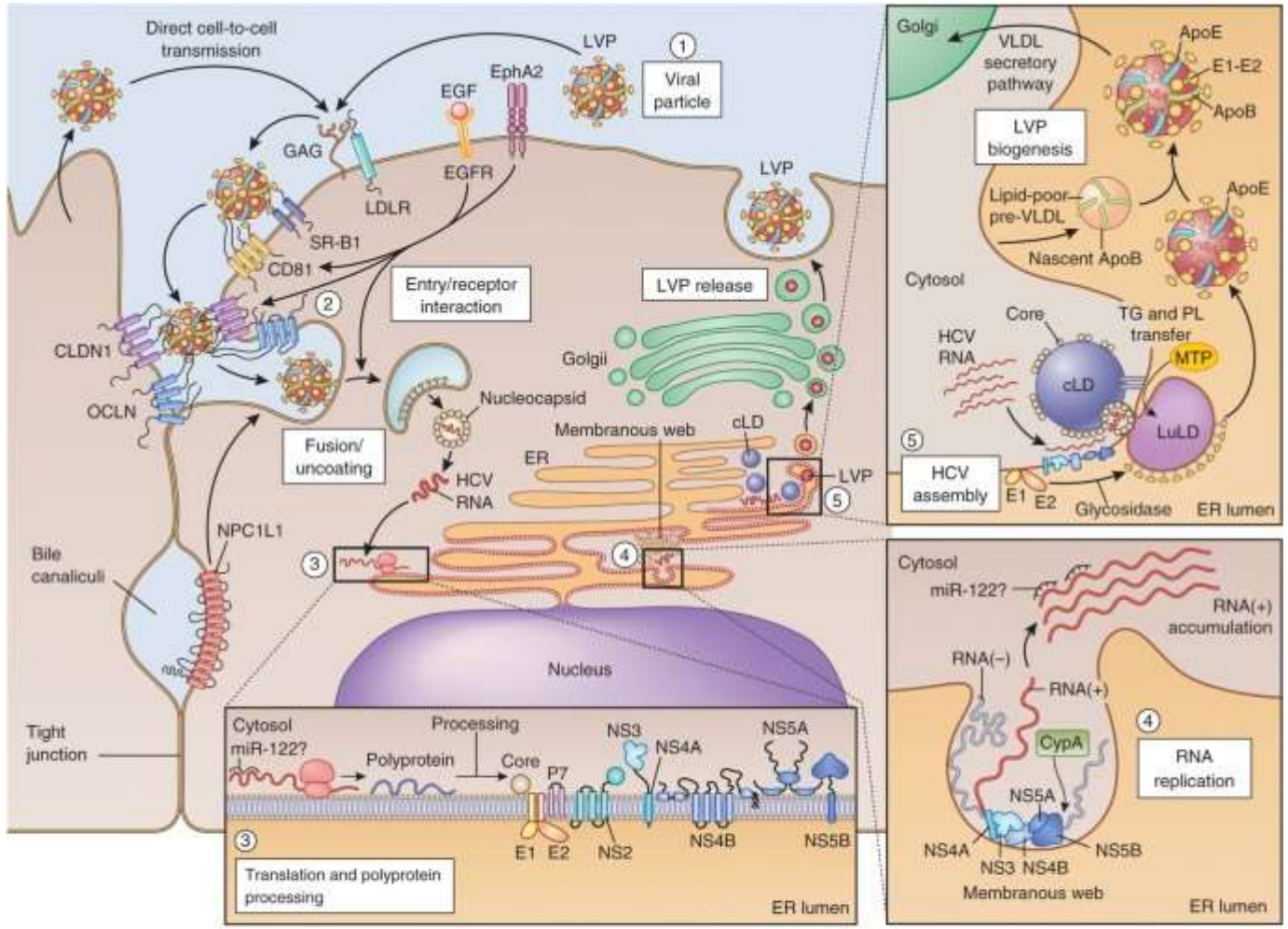


HCV Structure

- **HCV**→ Flaviviridae family → Single strand RNA (+)
- Causes:
  - **Acute** liver disease → mild symptoms → fatigue, nausea, decreased appetite, and joint and muscle pain
  - **Chronic** liver disease → no symptoms → Cirrhosis after 10/15 years → risk of hepatocellular carcinoma or Liver failure (more common)
  - **Fulminant** hepatitis → Liver Failure



- Infects hepatocytes and B Lymphocytes
- Symptoms: cryoglobulinemia, autoimmune haemolytic anaemia; glomerulonephritis, leukocytoclastic vasculitis, which is an; diabetes; hypothyroidism; and skin conditions
- Transmission: blood and sexual contact

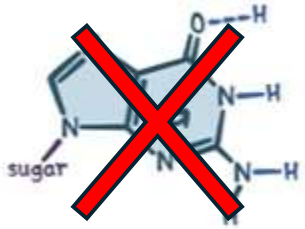


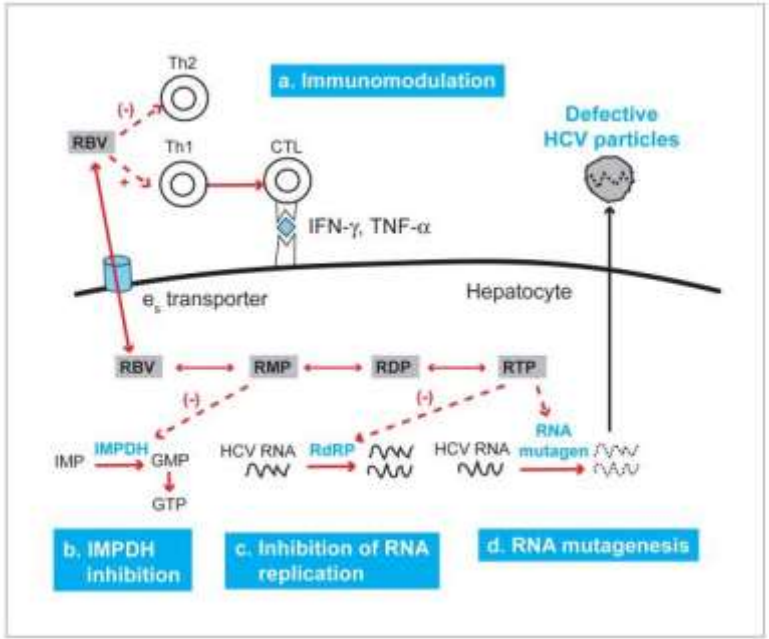
Points of intervention in the HCV life cycle

① The viral particle (neutralizing antibodies, virocidal peptides)
② Entry and receptor interaction (antibodies and small molecules targeting receptors, kinase inhibitors)
③ Translation and polyprotein processing (NS3-NS4A protease inhibitors)
④ HCV RNA replication (NS5B polymerase and NS5A inhibitors, miR-122 antagonists, cyclophilin inhibitors, statins, PI4KIIIα inhibitors)
⑤ Assembly and virion morphogenesis (NS5A inhibitors, DGAT1 inhibitors, glycosidase inhibitors, MTP inhibitors)

HCV therapy

- **Inosine-5′-phosphate dehydrogenase inhibitor**
  - **ribavirin**
    - Dephosphorylated to a monophosphate in the nucleus
    - Cell without nucleus like erythrocytes have accumulation of ribavirin
    - **Typical Adverse Effects**: Headache, Nausea, fatigue and abdominal pain
    - **Specific Adverse Effects**: rash, itching, insomnia, cough, haemolytic anaemia
    - Not safe in pregnancy - teratogenic
    - Combined with **interferons** → Chronic HCV (In the past)



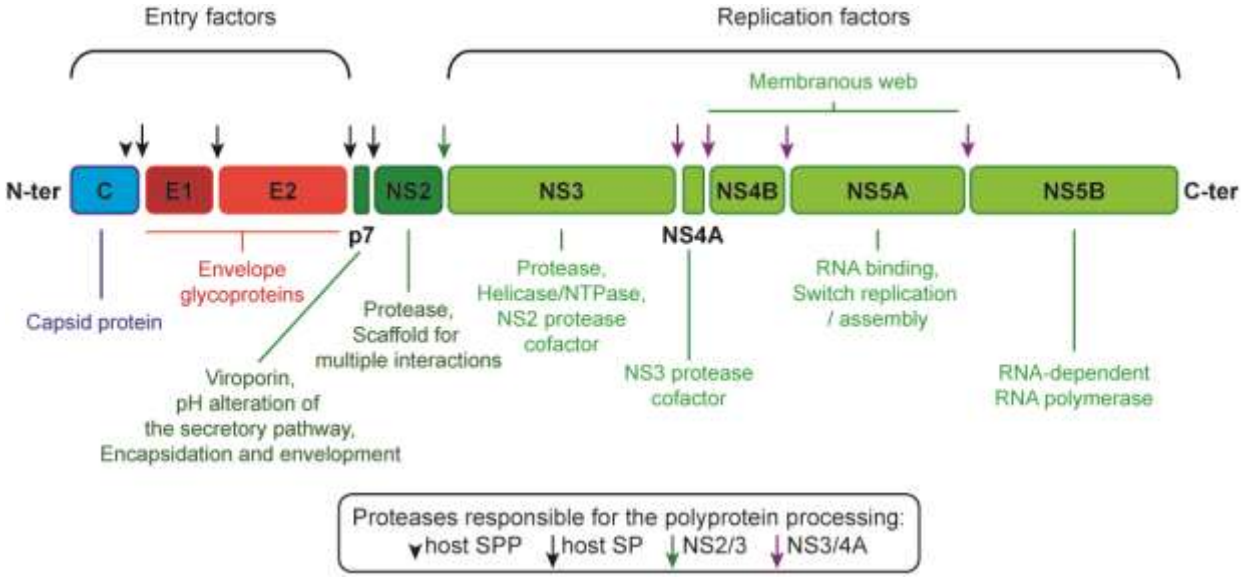


M.O.A: ribavirin causes **inhibition of inosine-5′-phosphate dehydrogenase**, reducing the synthesis of guanine nucleotides, which in turn **reduces the synthesis of viral RNA**

HCV therapy

- **HCV NS3/4A protease inhibitors (-previr):** Sime**previr**, Parita**previr**, Glecapr**evir**
  - Enzyme involved in post-translational processing and replication of HCV. No structural proteins and functional being formed.
  - Highly bound to plasmatic proteins
  - Metabolised via CYP3A (risk of DDIs)

- **Newer DAAs**
  - **PO administration**
  - Interferon-free combinations—with or without **ribavirin**
  - ↑ efficacy and tolerability
  - ↑ dosing schedules
  - ↓ genotype specificity
  - ↓ potential drug-drug interactions
  - Expensive
  - **NS5A inhibitors** and **NS5B polymerase inhibitors**



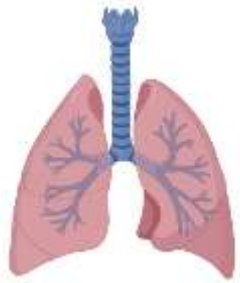
HCV therapy

- **NS5A inhibitors (-asvir):** Ledip**asvir**, Velpat**asvir,** Daclat**asvir**
  - NS5A protein → viral replication and the assembly of HCV → mechanism of action of the HCV NS5A inhibitors → unclear
  - Drugs inhibits the NS5A which prevents RNA replication and viral assembly of HCV
  - Highly bound to plasmatic proteins
  - Metabolised by CYP3A (risk of DDIs)
  - Inhibitors of PgP (**daclatasvir** and **ledipasvir**) → (risk of interactions with PgP inducers → **rifampin** or **St. John's wort**)
  - **Side Effects**: headache and fatigue. In general **well tolerated**
  - Used in combinations:
    - **ledipasvir** + **sofosbuvir** (most common combination)
    - **daclatasvir** + **sofosbuvir**
    - velpatasvir + sofosbuvir
    - elbasvir + grazoprevir
    - ombitasvir + dasabuvir + paritaprevir + **ritonavir** (**pharmacologic "booster"** to increase plasma concentrations of paritaprevir via its effect on CYP3A)

HCV therapy

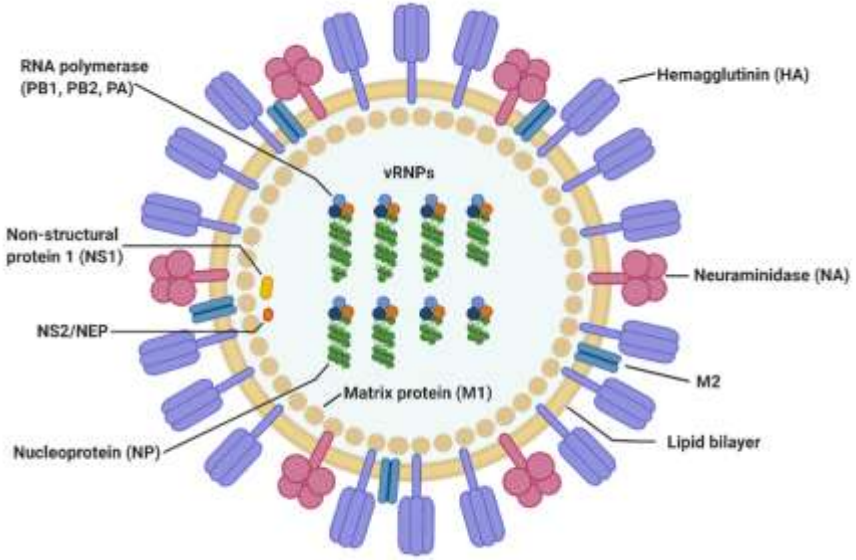
- **NS5B inhibitors (-uvir)**
  - NS5B protein → NS5B acts as an RNA dependent RNA polymerase so it is used to make more RNA. → The drugs will prevent the formation of more HCV RNA
  - Two classes of polymerase inhibitors and these act at distinct stages of RNA synthesis:
    - **Nucleoside/nucleotide analogues → sofosbuvir**
      - Target the **catalytic site of NS5B** and are activated within the hepatocyte through phosphorylation to nucleoside triphosphate, which competes with nucleotides, resulting in chain termination.
      - **Prodrug** → converted by cellular kinase to its pharmacologically active uridine analog 5'-triphosphate form
      - PgP substrate (risk of DDIs)
      - Side effects: fatigue, headache, and asthenia
    - **Non-nucleoside analogues → dasabuvir**
      - Act as **allosteric inhibitors of NS5B**
      - As combination: Ombitasvir + Dasabuvir + Paritaprevir + Ritonavir
      - CYP3A substrate (risk of DDIs)
      - Side effects: nausea, pruritus and insomnia

Influenza virus



- **Influenza** → Single strand RNA (-)
- Classification according the surface protein
  - Influenza A and B: **Hemagglutinin** and **neuraminidase** → binds through sialic acid residues
  - Influenza C: hemagglutinin esterase fusion → binds to host cell

Pneumonia

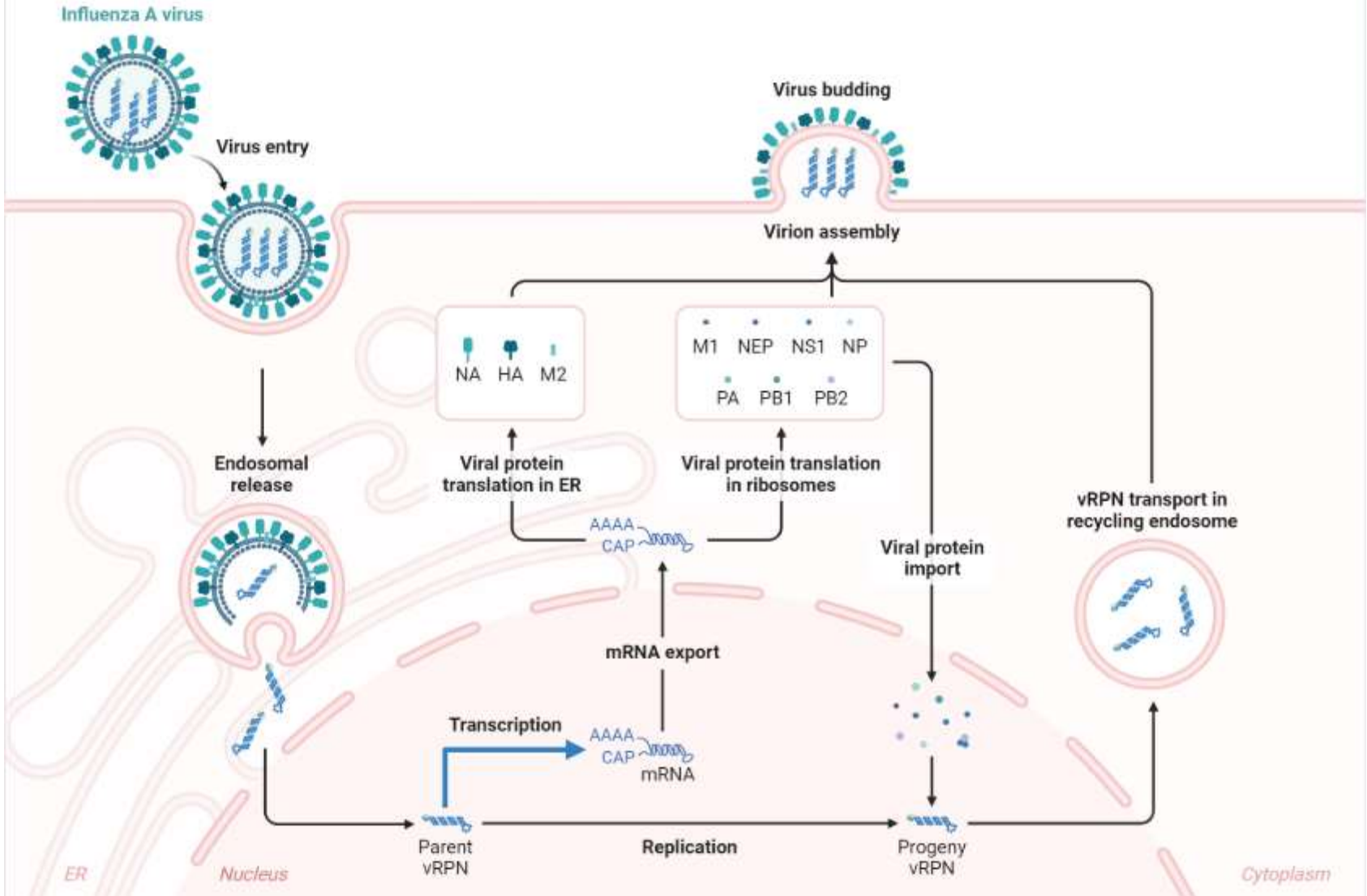


Adamantanes inhibitors (**amantadine**)

Neuraminidase inhibitors (oral **oseltamivir**, inhaled **zanamivir**)

BioRender Disease Mechanisms – Infectious Diseases

Influenza Virus Life Cycle



Influenza virus

These drugs do not work in **Influenza C since it lacks neuraminidase**!

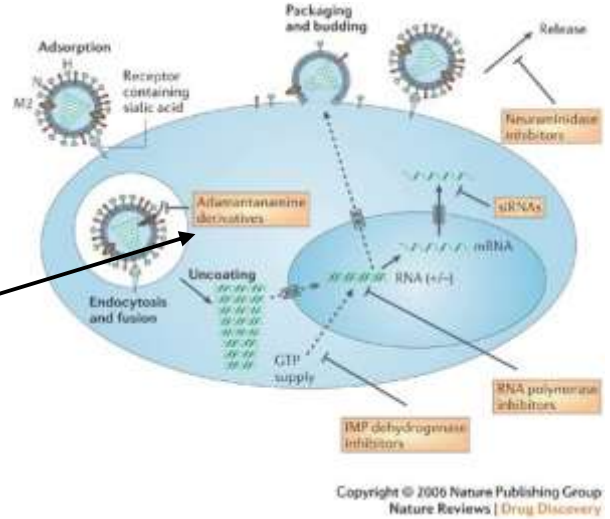
- **Neuraminidase inhibitors**
  - **Mechanism of action:** inhibit viral neuraminidase activity at low nanomolar concentrations → ↓ release of influenza virions
  - Reduction of symptoms in 2 days
    - **oseltamivir** → **PO administration**
      - **Prodrug**
    - **zanamivir** → Inhalation **administration**
  - Can be used prophylactically
    - Young children
    - Elderly individuals
    - Pregnant women
    - Immunosuppressed individuals

Represent high-risk groups!

Zanamivir carries risk of **bronchospasm** in patients with Asthma and COPD

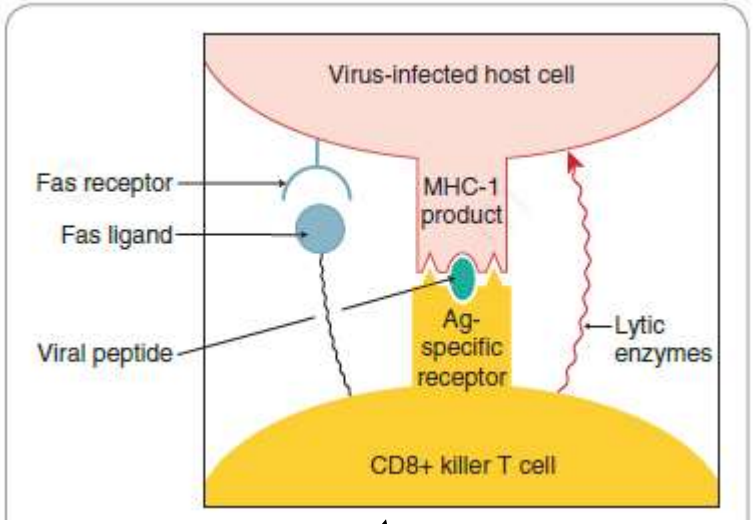
- **Side effects:** GIT disturbances → nausea, vomiting, dyspepsia, and diarrhoea (less common with **zanamivir**)

Influenza virus



- **Adamantanamine derivatives**
  - **amantadine** and **rimantadine**
    - **Block the M2 proton ion channel of the virus particle and inhibit uncoating of the viral RNA within infected host cells**, thus preventing its replication
    - Only active against **Influenza A**
    - **amantadine** is excreted unchanged in the urine, whereas **rimantadine** undergoes extensive metabolism by hydroxylation, conjugation, and glucuronidation before urinary excretion
    - High prevalence of resistance
    - **Adverse effects**:
      - gastrointestinal (nausea, anorexia)
      - central nervous system (nervousness, difficulty in concentrating, insomnia, light-headedness)
      - increase QT interval (**amantadine**)

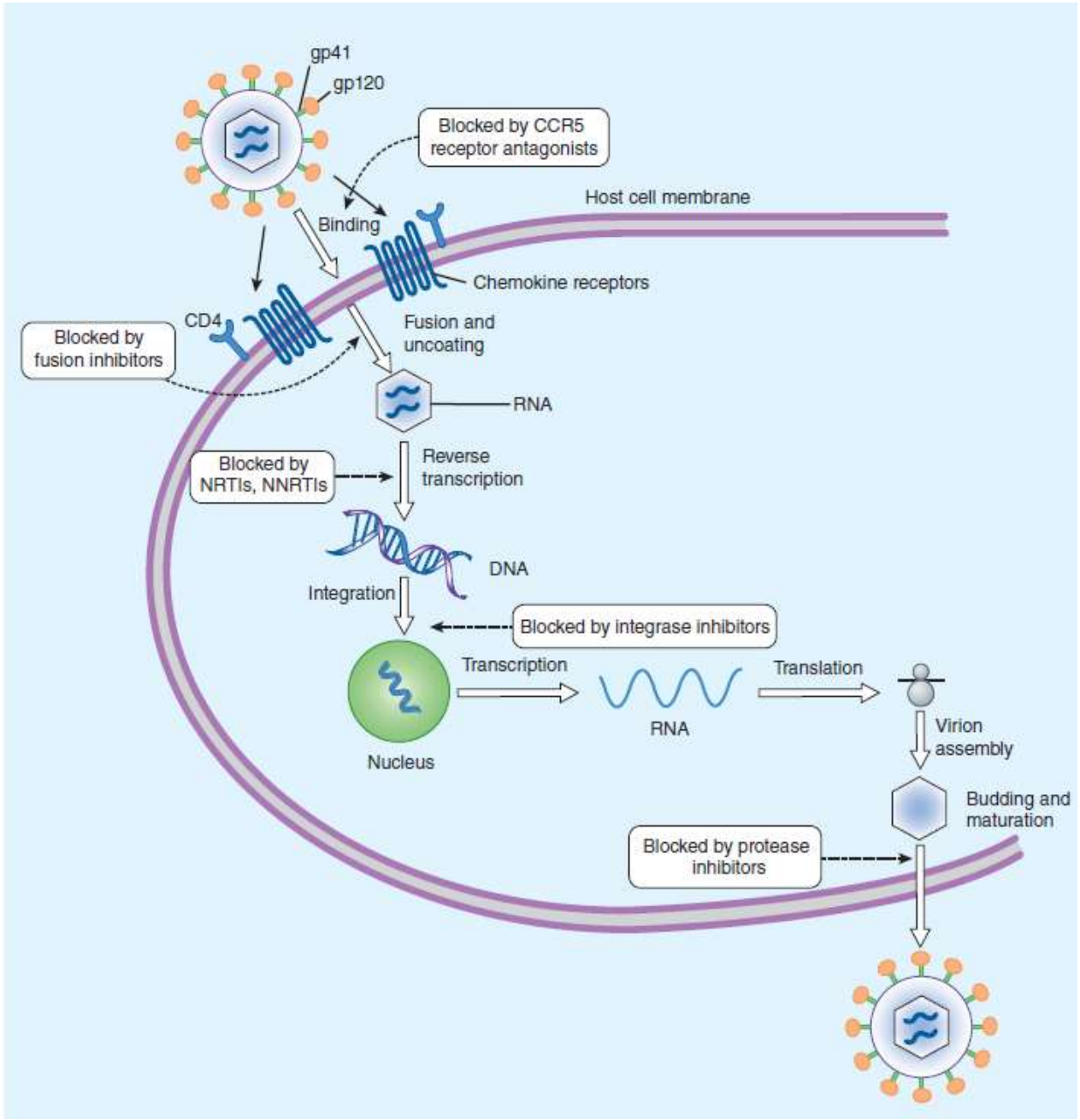
HIV virus



- **HIV**→ Single strand RNA (retrovirus)
  - HIV-1 → responsible for human AIDS → significant immunosuppression
  - HIV-2
- Affects mainly CD4+ lymphocytes and CD8+ Cytotoxic T-Cell
  - Lysis of the host lymphocytic cells is the defining characteristic of the infection
- Infection is initially contained by the action CD8+ Cytotoxic T-Cell
  - Direct interaction with infected cells → apoptosis
  - Production of cytokines

  This capability is lost over time!
- Replication is error prone → Easier to evade the action of the lymphocytes
- Intracellular HIV remains latent for a long time
  - Up to 12 weeks there is a sharp decline in CD4+ that drop to half pf their quantity in a period of 12 weeks
  - The production of CD4+ and CD8+ is eventually exhausted
  - 7 years after the initial infection → constitutional symptoms and opportunistic diseases appear
  - Death after 4 to 5 years

  Drug regimens allows patient to have a near similar life-expectancy to HIV-free people


gp41
gp120
Blocked by CCR5 receptor antagonists
Host cell membrane
Binding
Chemokine receptors
CD4
Blocked by fusion inhibitors
Fusion and uncoating
RNA
Blocked by NRTIs, NNRTIs
Reverse transcription
DNA
Integration
Blocked by integrase inhibitors
Transcription
Translation
RNA
Nucleus
Virion assembly
Budding and maturation
Blocked by protease inhibitors

HIV treatment

HAART
therapy

Use of combination of drugs

Suppress replication

Restore immunocompetence of the host

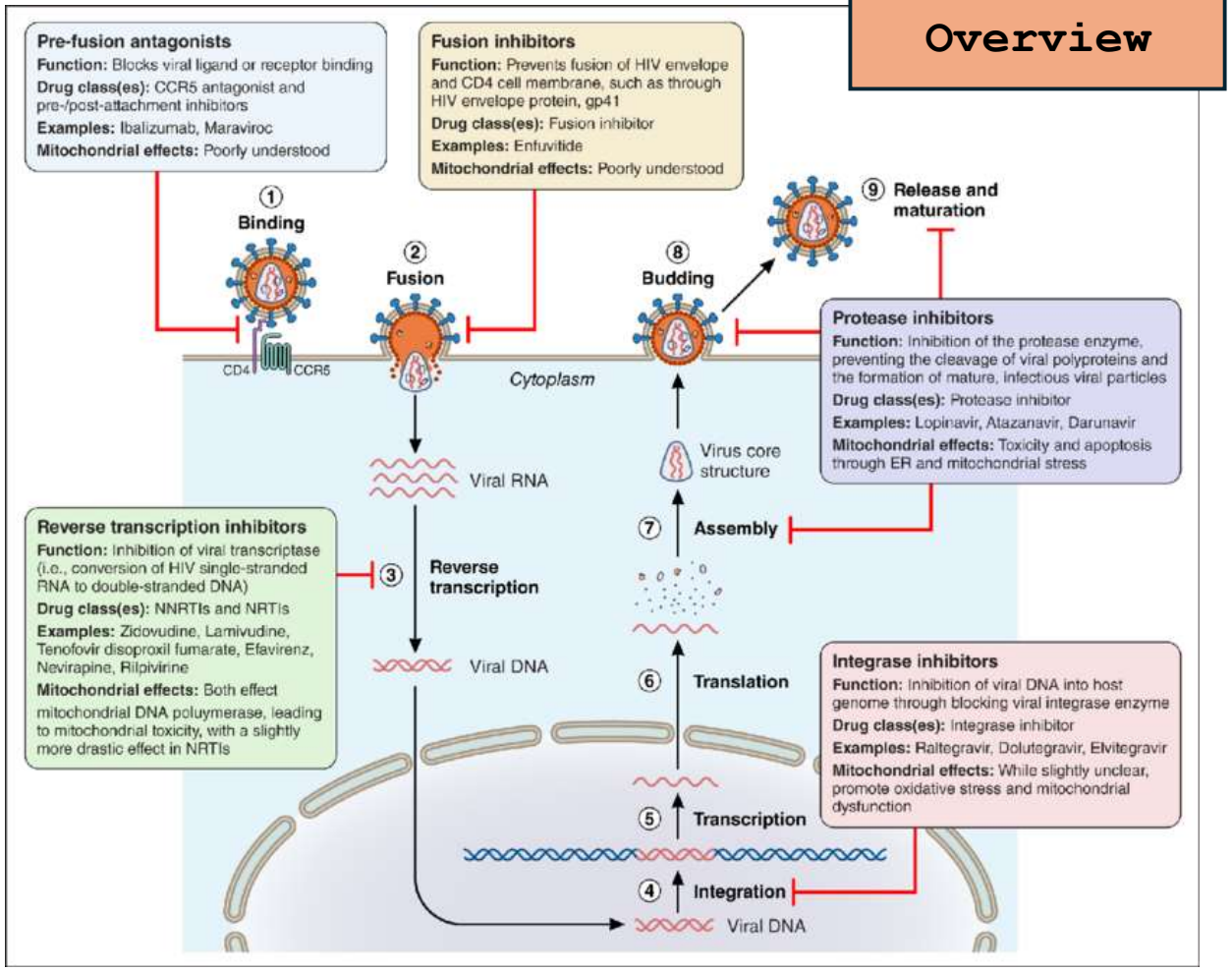
2 NRTIs + NNRTIs

2 NRTIs + Integrase Inhibitor

2 NRTIs + Protease Inhibitor

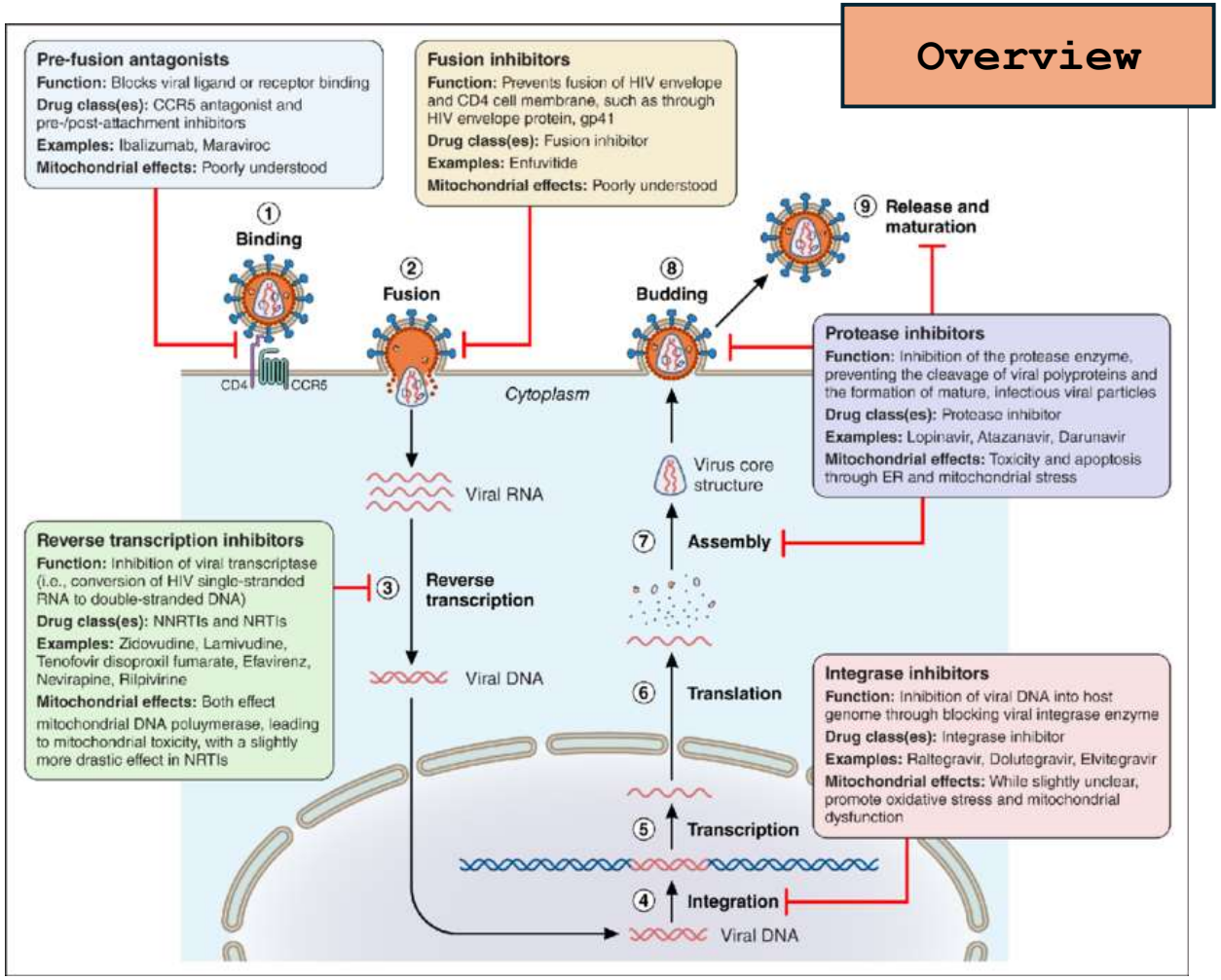
- **Entry/Fusion Inhibitors**
- **Inhibitors of integrase**
- **Protease Inhibitors**
- **Reverse transcriptase inhibitors**
  - NRTIs
  - NNRTIs

Overview



HIV treatment

- **Entry/Fusion Inhibitors**
  - Not part of HAART put rather adjuvant therapy
- **enfuvirtide**
  - Binds **GP41** (HIV envelope) – Prevents fusion
- **maraviroc**
  - Binds **CCR5** receptor on the host cell – Prevents binding
  - Homozygous mutation of CCR5 – immunity
  - Heterozygous mutation of CCR5 – diminished efficacy



HIV treatment

- **Reverse Transcriptase Inhibitors**
  - NRTIs - Nucleoside reverse transcriptase inhibitor
  - NNRTIs - Non-Nucleoside reverse transcriptase inhibitor
  - Foundation of HAART
  - Block conversion of viral RNA to double stranded DNA

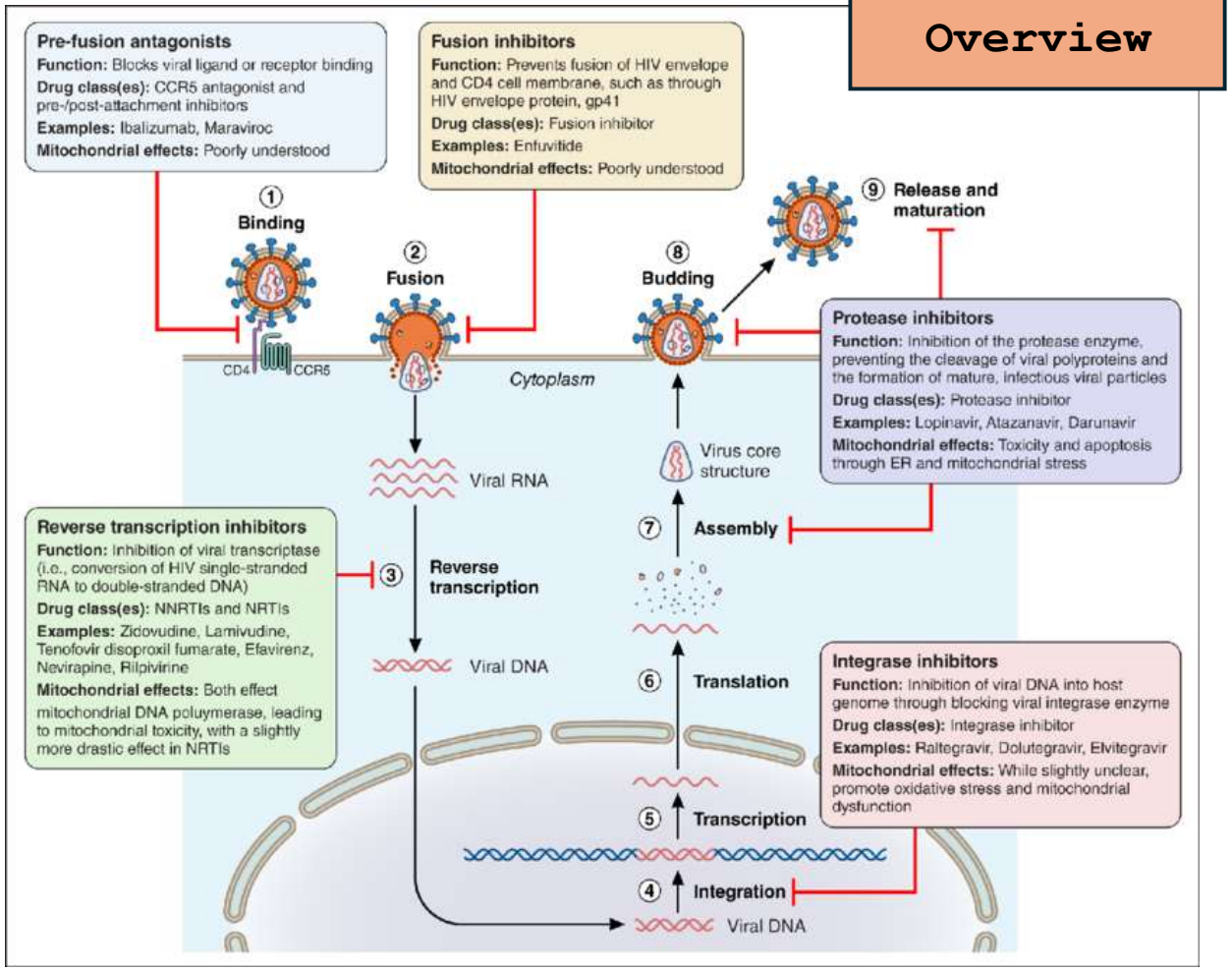
NRTIs

zidovudine
emtricitabine
tenofovir

NNRTIs

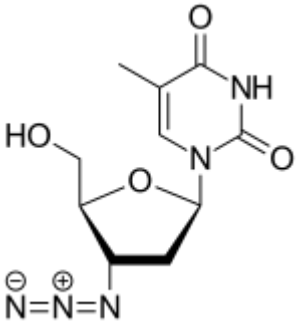
nevirapine
efavirenz
etravirine
delavirdine

Overview



HIV treatment

- **NRTIs - Nucleoside reverse transcriptase inhibitors**
  - **Phosphorylation** is necessary
  - Lacks a 3-OH
    - Essential for activity – DNA nucleotide possess a 3-OH-group
    - Prevents the formation of bond



  - **Side effects** associated with **mitochondrial toxicity**
    - **Peripheral neuropathy**
    - **Hepatic steatosis**
    - **Lactic Acidosis**
    - Pancreatitis (specific to didanosine)
    - **Lipoatrophy** (specific to **zidovudine** **and** stavudine)

  - **Other side effects:**
    - Peripheral **Neuropathy**
    - **Bone Marrow suppression** (**zidovudine**)

Typical of medication that interfere with DNA

    - **Anaemia** (specific to **zidovudine**)
    - Hypersensitivity reactions → accompanied by nausea, vomiting, diarrhoea → (specific to abacavir) → Screening for HLA-B*5701
    - **Nephrotoxicity** → (specific to **tenofovir**)

NRTIs

zidovudine
abacavir
emtricitabine
stavudine
tenofovir (NT)
didanosine

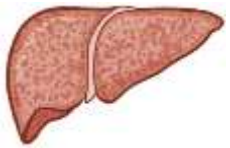
zidovudine is safe in pregnancy!

HIV treatment

- **NNRTIs – Non-nucleoside reverse transcriptase inhibitors**
  - Allosteric inhibition of RNA- and DNA-dependent DNA polymerase activity → creates a hydrophobic pocket
  - Do not require phosphorylation to be active
  - 1st generation: delavirdine, **efavirenz**, **nevirapine**
  - 2nd generation NNRTIs: etravirine, rilpivirine → higher potency and less side effects
  - Substrates for CYP3A4 and can act as **inducers** (nevirapine), **inhibitors** (delavirdine), or **mixed inducers and inhibitors** (**efavirenz, etravirine**)
  - **Side effects**: Hepatotoxicity (↑ LFT) and skin rash (Stevens-Johnson syndrome)
  - Specific **side effects**:
    - **efavirenz** – vivid dreams + psychiatric symptoms (depression, psychosis) – pronounced CNS toxicity
    - **efavirenz** and **delavirdine** – teratogenic (CI in pregnancy)

NNRTIs

nevirapine
efavirenz
etravirine
delavirdine



HIV treatment

Integrase inhibitors
rs
raltegravir
dolutegravir
elvitegravir

- **Integrase inhibitors (-gravir)**
  - **Viral enzyme essential for integration** of reverse-transcribed HIV DNA into the chromosomes of host cells
  - Dolutegravir
    - Dolutegravir is primarily metabolized via UGT1A1 with some contribution from CYP3A
    - ↑ Levels - with **efavirenz**, **etravirine**, **nevirapine**, **rifampin**, or **rifapentine** **(inhbitors)**
    - ↓ Levels – with **oxcarbazepine, phenytoin, phenobarbital, carbamazepine, and St. John's wort** **(inducers)**
    - inhibits the renal OCT2 - ↑ plasma concentrations of drugs eliminated via OCT2 such as **dofetilide** and **metformin**
  - Elvitegravir
    - requires boosting - such as **cobicistat** (a pharmacokinetic enhancer that inhibits CYP3A4 as well as certain intestinal transport proteins) or **ritonavir**
    - ↓ levels – with **efavirenz or nevirapine, rifampin, rifabutin, carbamazepine, phenytoin, or St. John's wort**
    - ↑ Levels – with **azole antifungal drugs**
  - **Side effects:** **Rhabdomyolysis** and myoglobin in the urine (**↑ Creatinine kinase**)

HIV treatment

- **Protease Inhibitors (-navir)**
  - HIV protease is responsible for cleaving these precursor molecules to produce the final structural proteins of the mature virion core
  - Do not need intracellular activation
  - Substrates of CYP3A4

  - **Side effects**:
    - GIT disturbances
    - Lipodystrophy (hyperglycemia, hyperlipidemia, lipoatrophy, fat deposition)

} Avoided with **atazanavir**

  - **Specific side effects**:
    - Nephropathy (specific to **indinavir**)
    - Thrombocytopenia (specific to **indinavir**)

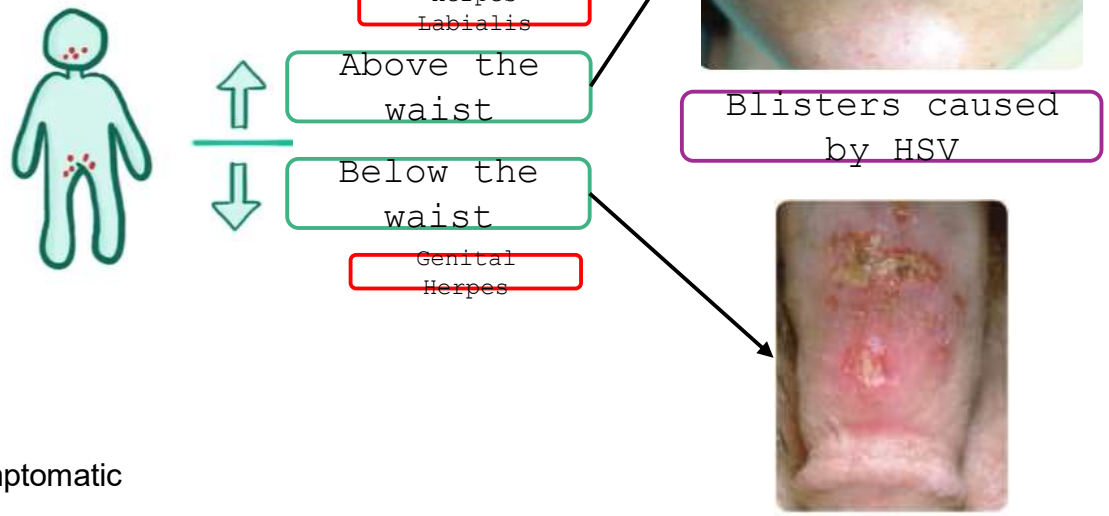
  - **ritonavir** causes **CYP450 inhibition** (pharmacokinetic enhancer rather than an antiretroviral agent)

PIs

atazanavir
indinavir
ritonavir

Common Viral infections seen in Dentistry

- Herpes simplex virus
  - HSV-1 (oral) and HSV-2 (genital) → Herpesviridae family → double DNA stranded virus
  - Usually asymptomatic → Contributes to greater transmission from person to person
    - Children more affected → gums, tongue, lips
  - Lesions on the skin and mucous membranes (blisters or ulcers)
  - Active infection → most contagious
    - Genital Secretions
    - Saliva
  - Virions remain dorment in the neurons cell body
    - Life-time infection
    - Latent-phase
    - Face: Virus in Trigeminal Ganglia
    - Genitalia: Virus in Sacral Ganglia
    - Reactivation possible → infection of epithelial cells → usually asymptomatic



Guanosine analogues

Primary herpetic gingivostomatitis

- Treatment of Herpes simplex virus
  - **Mild Cases → recurrent infection (or secondary)**

    acyclovir cream 5% to lesions every four hours (five times daily) at first **signs of infection** → Not routinely recommended

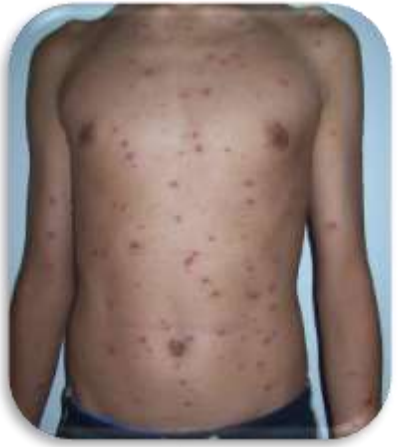
    Use of supportive measures focused on the symptoms:
    - Rest
    - Plenty of fluids
    - Soft diet
    - Antipyretic analgesics
    - Antimicrobial mouthwash to reduce secondary infection. Chlorhexidine or hydrogen peroxide are suitable agents. The use of benzydamine mouthwash may provide some pain relief

  - **Severe Cases → raised temperature, swollen lymph nodes, malaise, dehydration or if patients are immunocompromised**
    - **acyclovir** 200 mg P.O (5x day for 5 days) → Assess for possible prolongation of treatment (Adults)
      - 100 mg P.O (5x day for 5 days) → children up to 2 years old
      - 200 mg P.O (5X day for 5 days) → children between 2 and 17 years old

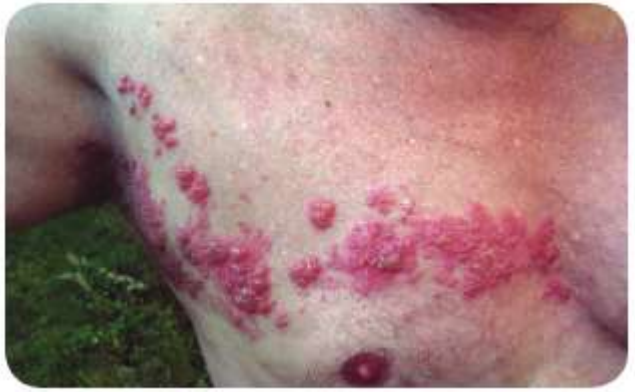
Immunocompromised may require iv administration

Common Viral infections seen in Dentistry

- **Varicella Zoster**
  - Herpesviridae family → double DNA stranded virus
  - Transmission through contact with lesions or air-droplets
    - Spreads through the lymph node and targets the skin
  - 2 forms of disease are caused
    - **Varicella** (Chickenpox) = **Primary Infection**
      - Symptoms after 2 weeks: Fever, Headache and weakness
      - Skin lesions like macules, papules, vesicles, and scabs
      - Scabs eventually fall of (after 5 days)
      - Painful sores tend appear inside the mouth
    - **Herpes Zoster** (or Shingles) = **Secondary Infection**
      - Pain and itching sensation (4 weeks to disappear)
      - Post–herpetic neuralgia possible
  - Virus remain dormant in the trigeminal ganglia and dorsal root ganglia
    - Neurons in the skin → VZV travels retrogradely to the nerve ganglia → remains dormant
    - **Reactivation** occurs with immunosuppression as Shingles



Varicella

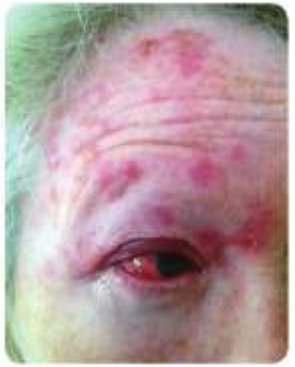


Shingles lesions

Common Viral infections seen in Dentistry

- Treatment of Varicella Zoster
  - ↓ incidence of postherpetic neuralgia and viral shedding = ↓ risk of corneal infection
  - **acyclovir** ↓ the duration of pain

  - **Recommended:**
    - **acyclovir 800mg P.O (5x day for 7 days at 4-hourly intervals)**
    - **valaciclovir**
    - **famciclovir**



Herpes Zoster ophtalmicus

  - **Clinical Advice:**
    - Elective/routine dental treatment if vesicles are open should not be performed
    - Treatment should be started up to 72 hours after the onset of the rash
    - Analgesics can be avoided (**aspirin** cannot be used → Reye's syndrome)
    - Antipruritic agents may provide relief:
      - Zinc oxide
      - Creams with camphor and menthol
      - Hydrocortisone cream
      - Calamine lotion

The End

Thank you for your attention!