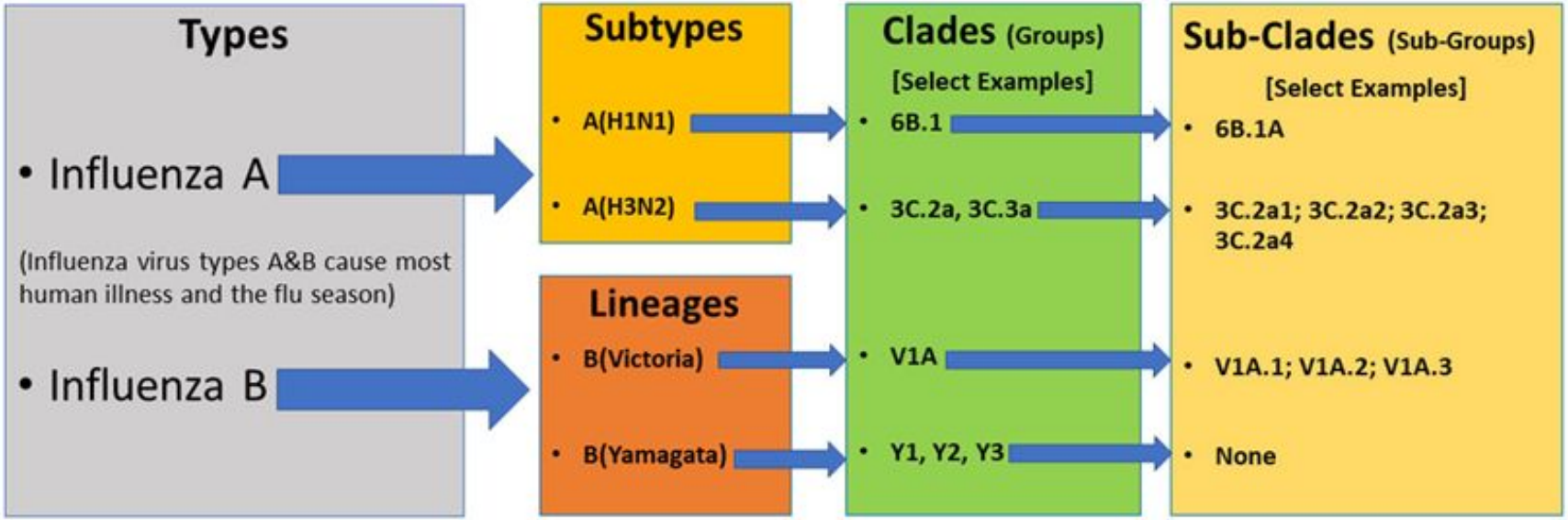
ANTI-INFLUENZA AGENTS

Presentation prepared by
Donetskova Victoria
Student of 6.3.11b group

Influenza virus strains classification

- by core proteins (A, B, or C)
- by species of origin (avian, swine)
- geographic site of isolation



Anti-influenza drugs approved for use

- neuraminidase inhibitors (oral oseltamivir, inhaled zanamivir, IV peramivir)

have activity against both influenza A and influenza B, and there is currently a low level of resistance

- adamantanes (amantadine, rimantadine)

have activity against influenza A viruses only, and in recent past seasons there was a high level of resistance (>99%) among both influenza H3N2 and influenza A H1N1

The neuraminidase inhibitors

- These agents competitively and reversibly interact with the active enzyme site to inhibit viral neuraminidase activity

Early administration is crucial because replication of influenza virus peaks at 24–72 hours after the onset of illness

Oseltamivir

- Orally administered prodrug that is activated by hepatic esterases and widely distributed throughout the body
- Potential adverse effects include nausea, vomiting, and headache. Rash is rare
- Taking oseltamivir with food does not interfere with absorption and may decrease nausea and vomiting

Zanamivir

- Is administered directly to the respiratory tract via inhalation

Of the active compound, 10–20% reaches the lungs; the remainder is deposited in the oropharynx

- Potential adverse effects include cough, bronchospasm (occasionally severe), reversible decrease in pulmonary function, and transient nasal and throat discomfort

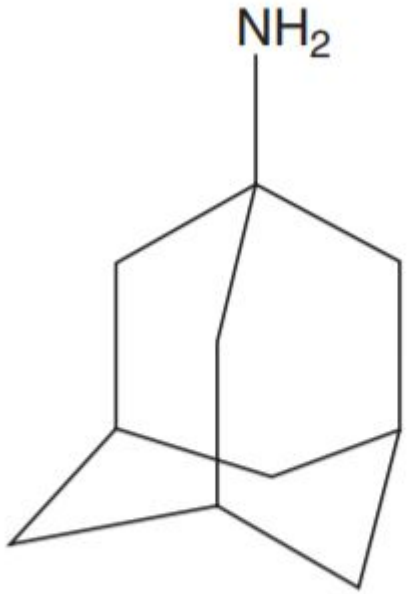
Zanamivir administration is not recommended for patients with underlying airway disease

Peramivir

- A cyclopentane analog
- Has activity against both influenza A and B viruses
- Is approved as a single 600-mg IV dose for the treatment of acute uncomplicated influenza in adults
- The main potential side effect is diarrhea, although serious skin or hypersensitivity reactions (e.g., Stevens-Johnson syndrome, erythema multiforme) have been rarely reported

Amantadine and rimantadine

- 1-aminoadamantane hydrochloride amantadine and its α-methyl derivative
- tricyclic amines of the adamantane family
- Mechanisms of Action - 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
- The most common adverse effects are gastrointestinal (nausea, anorexia) and central nervous system (nervousness, difficulty in concentrating, insomnia, light-headedness)



AMANTADINE

PHARMACOLOGICAL CHARACTERISTICS OF ANTIVIRALS FOR INFLUENZA

	AMANTADINE	RIMANTADINE	ZANAMIVIR	OSELTAMIVIR	PERAMIVIR
Spectrum[f]	A	A	A, B	A, B	A, B
Route/formulations	Oral (tablet/ capsule/syrup)	Oral (tablet/syrup)	Inhaled (powder) Intravenous[a]	Oral (capsule/syrup) Intravenous[a]	Intravenous
Oral bioavailability	>90%	>90%	<5%[b]	80%[c]	Not applicable
Effect of meals on AUC	Negligible	Negligible	Not applicable	Negligible	Not applicable
Elimination $t_{1/2}$, h	12–18	24–36	2.5–5	6–10[c]	20
Protein binding, %	67%	40%	<10%	3%[c]	<30%
Metabolism, %	<10%	~75%	Negligible	Negligible	Negligible
Renal excretion[e]	>90%	~25%	100%	95%[c]	90%
Dose adjustments	$Cl_{cr} \leq 50$ Age ≥ 65 years	$Cl_{cr} \leq 10$ Age ≥ 65 years	None[d]	$Cl_{cr} \leq 30$	$Cl_{cr} \leq 50$